



UNIVERSITAT DE
BARCELONA

Síntesis de inhibidores de Atg4B y desarrollo de nuevos métodos de bioconjugación basados en derivados del ácido escuárico

Ana Bilbao Girona

ADVERTIMENT. La consulta d'aquesta tesi queda condicionada a l'acceptació de les següents condicions d'ús: La difusió d'aquesta tesi per mitjà del servei TDX (www.tdx.cat) i a través del Dipòsit Digital de la UB (diposit.ub.edu) ha estat autoritzada pels titulars dels drets de propietat intel·lectual únicament per a usos privats emmarcats en activitats d'investigació i docència. No s'autoritza la seva reproducció amb finalitats de lucre ni la seva difusió i posada a disposició des d'un lloc aliè al servei TDX ni al Dipòsit Digital de la UB. No s'autoritza la presentació del seu contingut en una finestra o marc aliè a TDX o al Dipòsit Digital de la UB (framing). Aquesta reserva de drets afecta tant al resum de presentació de la tesi com als seus continguts. En la utilització o cita de parts de la tesi és obligat indicar el nom de la persona autora.

ADVERTENCIA. La consulta de esta tesis queda condicionada a la aceptación de las siguientes condiciones de uso: La difusión de esta tesis por medio del servicio TDR (www.tdx.cat) y a través del Repositorio Digital de la UB (diposit.ub.edu) ha sido autorizada por los titulares de los derechos de propiedad intelectual únicamente para usos privados enmarcados en actividades de investigación y docencia. No se autoriza su reproducción con finalidades de lucro ni su difusión y puesta a disposición desde un sitio ajeno al servicio TDR o al Repositorio Digital de la UB. No se autoriza la presentación de su contenido en una ventana o marco ajeno a TDR o al Repositorio Digital de la UB (framing). Esta reserva de derechos afecta tanto al resumen de presentación de la tesis como a sus contenidos. En la utilización o cita de partes de la tesis es obligado indicar el nombre de la persona autora.



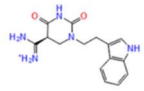
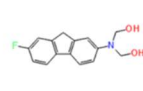


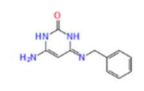
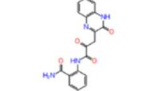


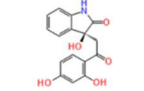
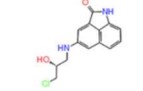


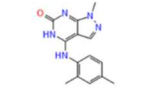
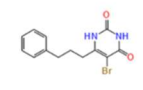


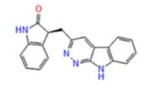
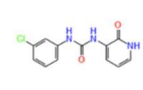


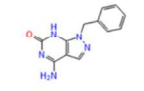
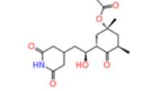


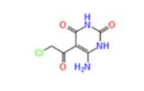
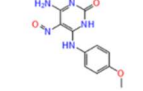


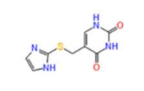
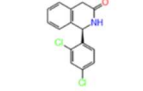
WARNING. On having consulted this thesis you're accepting the following use conditions: Spreading this thesis by the TDX (www.tdx.cat) service and by the UB Digital Repository (diposit.ub.edu) has been authorized by the titular of the intellectual property rights only for private uses placed in investigation and teaching activities. Reproduction with lucrative aims is not authorized nor its spreading and availability from a site foreign to the TDX service or to the UB Digital Repository. Introducing its content in a window or frame foreign to the TDX service or to the UB Digital Repository is not authorized (framing). Those rights affect to the presentation summary of the thesis as well as to its contents. In the using or citation of parts of the thesis it's obliged to indicate the name of the author.

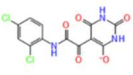
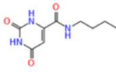
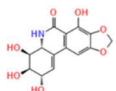
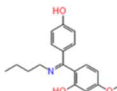
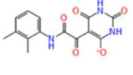
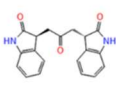
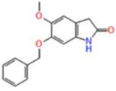
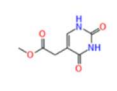
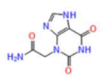
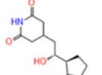
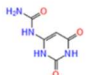
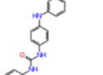
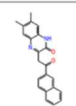
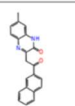
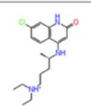
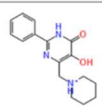
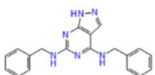
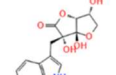
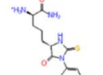
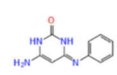
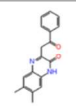
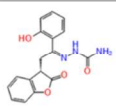
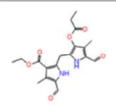
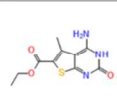
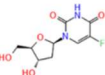
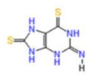
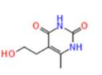
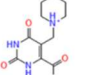
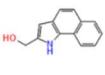
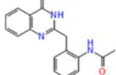
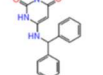
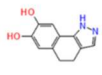
ANEXOS

Docking

Se solicitaron 250 compuestos seleccionados al NCI Developmental Therapeutics Program (<http://dtp.nci.nih.gov/RequestCompounds/>), se disolvieron en DMSO y fueron evaluados como inhibidores de Atg4B.

Tabla S1. Compuestos pertenecientes a la base de datos NCI Open Database seleccionados por HTVS frente al sitio activo de Atg4B (2ZZP_full) empleando el programa de acoplamiento Glide. Los compuestos se muestran como estereoisómeros/ tautómeros/protómeros durante el acoplamiento molecular.

 NSC: 349155 docking score: -11.651	 NSC: 62494 docking score: -11.556	 NSC: 656991 docking score: -11.17	 NSC: 141058 docking score: -11.099
 NSC: 624948 docking score: -11.073	 NSC: 10768 docking score: -10.994	 NSC: 212407 docking score: -10.789	 NSC: 646380 docking score: -10.579
 NSC: 55982 docking score: -10.558	 NSC: 91408 docking score: -10.521	 NSC: 621178 docking score: -10.499	 NSC: 611216 docking score: -10.496
 NSC: 724949 docking score: -10.389	 NSC: 725687 docking score: -10.353	 NSC: 19142 docking score: -10.306	 NSC: 211381 docking score: -10.244
 NSC: 157286 docking score: -10.244	 NSC: 316458 docking score: -10.178	 NSC: 186031 docking score: -10.096	 NSC: 329254 docking score: -10.084
 NSC: 646375 docking score: -10.077	 NSC: 664724 docking score: -9.971	 NSC: 622937 docking score: -9.942	 NSC: 32743 docking score: -9.904
 NSC: 45723 docking score: -9.901	 NSC: 336378 docking score: -9.88	 NSC: 79222 docking score: -9.867	 NSC: 62495 docking score: -9.864
 NSC: 640350 docking score: -9.853	 NSC: 126353 docking score: -9.847	 NSC: 617798 docking score: -9.831	 NSC: 310191 docking score: -9.791

 NSC: 646366 docking score: -9.782	 NSC: 39265 docking score: -9.76	 NSC: 266535 docking score: -9.726	 NSC: 602695 docking score: -9.683
 NSC: 640349 docking score: -9.675	 NSC: 186258 docking score: -9.647	 NSC: 149898 docking score: -9.625	 NSC: 173352 docking score: -9.623
 NSC: 637876 docking score: -9.612	 NSC: 123301 docking score: -9.597	 NSC: 118950 docking score: -9.568	 NSC: 164414 docking score: -9.553
 NSC: 373050 docking score: -9.526	 NSC: 373058 docking score: -9.522	 NSC: 406291 docking score: -9.499	 NSC: 101685 docking score: -9.494
 NSC: 19148 docking score: -9.491	 NSC: 617744 docking score: -9.49	 NSC: 610936 docking score: -9.417	 NSC: 211608 docking score: -9.409
 NSC: 373049 docking score: -9.404	 NSC: 648585 docking score: -9.397	 NSC: 38094 docking score: -9.365	 NSC: 723574 docking score: -9.363
 NSC: 27640 docking score: -9.335	 NSC: 29189 docking score: -9.31	 NSC: 111285 docking score: -9.307	 NSC: 52389 docking score: -9.302
 NSC: 607743 docking score: -9.302	 NSC: 401299 docking score: -9.3	 NSC: 212412 docking score: -9.249	 NSC: 251209 docking score: -9.248

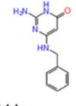
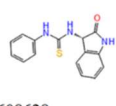
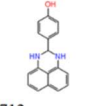
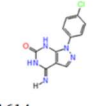
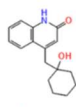
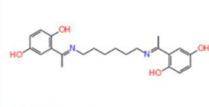
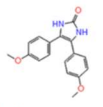
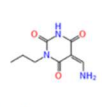
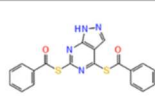
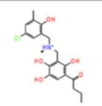
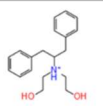
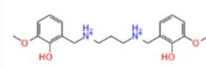
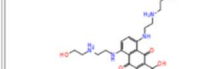
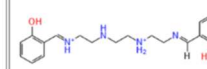
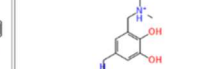
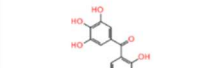
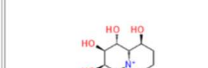
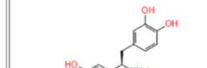
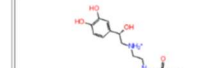
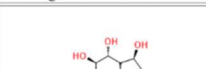
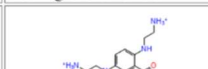

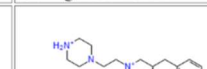
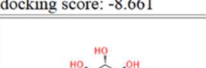
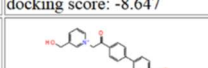


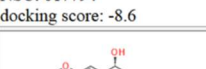
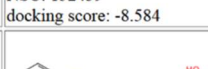
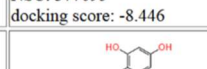
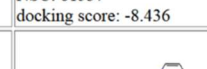
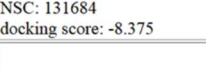
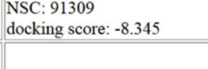
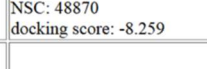
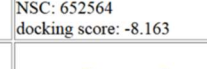
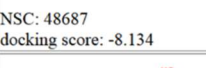
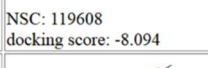
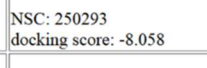
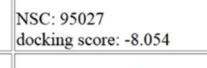
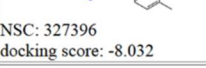

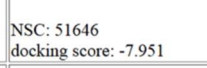
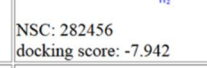
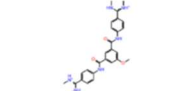
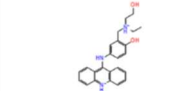
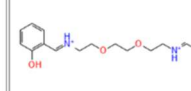
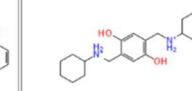
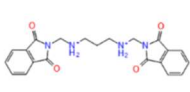
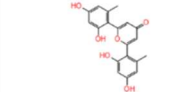
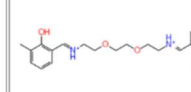
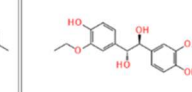
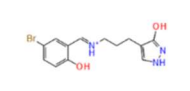
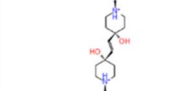
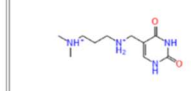
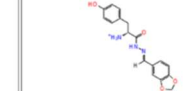
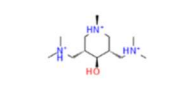
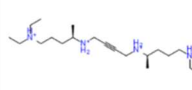
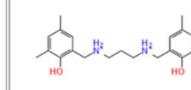
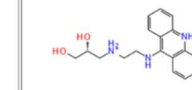
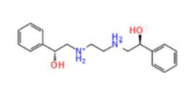
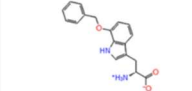
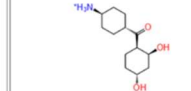
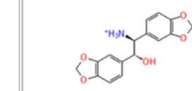
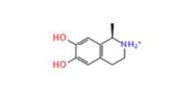
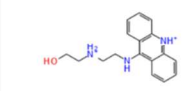
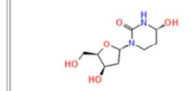
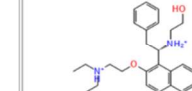
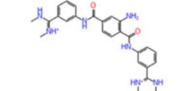
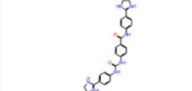
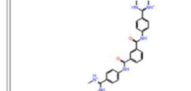
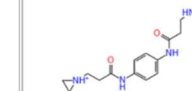
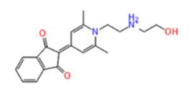
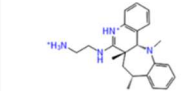
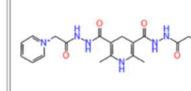
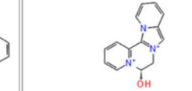
 NSC: 52444 docking score: -9.233	 NSC: 608628 docking score: -9.23	 NSC: 83713 docking score: -9.229	 NSC: 11614 docking score: -9.228
 NSC: 612216 docking score: -9.221	 NSC: 352709 docking score: -9.219	 NSC: 26692 docking score: -9.204	 NSC: 149051 docking score: -9.204
 NSC: 722944 docking score: -9.189	 NSC: 88860 docking score: -9.108	 NSC: 33565 docking score: -9.093	

Tabla S2. Compuestos pertenecientes a la base de datos NCI Open Database seleccionados por HTVS frente al segundo sitio alternativo de Atg4B (2CY7_full) empleando el programa de acoplamiento Glide. Los compuestos se muestran como estereoisómeros/ tautómeros/ protómeros durante el acoplamiento molecular.

 NSC: 86286 docking score: -10.467	 NSC: 279836 docking score: -9.857	 NSC: 43949 docking score: -9.406	 NSC: 39225 docking score: -8.981
 NSC: 680919 docking score: -8.926	 NSC: 669720 docking score: -8.731	 NSC: 118071 docking score: -8.725	 NSC: 293888 docking score: -8.707
 NSC: 625381 docking score: -8.661	 NSC: 645017 docking score: -8.647	 NSC: 299187 docking score: -8.64	 NSC: 41527 docking score: -8.601
 NSC: 617794 docking score: -8.6	 NSC: 152439 docking score: -8.584	 NSC: 377095 docking score: -8.446	 NSC: 81537 docking score: -8.436
 NSC: 131684 docking score: -8.375	 NSC: 91309 docking score: -8.345	 NSC: 48870 docking score: -8.259	 NSC: 652564 docking score: -8.163
 NSC: 48687 docking score: -8.134	 NSC: 119608 docking score: -8.094	 NSC: 250293 docking score: -8.058	 NSC: 95027 docking score: -8.054
 NSC: 327396 docking score: -8.032	 NSC: 109327 docking score: -7.986	 NSC: 51646 docking score: -7.951	 NSC: 282456 docking score: -7.942
 NSC: 94498 docking score: -7.901	 NSC: 109325 docking score: -7.884	 NSC: 117829 docking score: -7.882	 NSC: 605767 docking score: -7.879

 NSC: 66785 docking score: -7.834	 NSC: 12270 docking score: -7.829	 NSC: 51654 docking score: -7.819	 NSC: 48443 docking score: -7.805
 NSC: 143347 docking score: -7.782	 NSC: 115535 docking score: -7.77	 NSC: 51661 docking score: -7.759	 NSC: 16737 docking score: -7.731
 NSC: 328107 docking score: -7.73	 NSC: 282125 docking score: -7.728	 NSC: 153540 docking score: -7.716	 NSC: 337734 docking score: -7.685
 NSC: 130898 docking score: -7.675	 NSC: 261042 docking score: -7.664	 NSC: 11966 docking score: -7.648	 NSC: 28570 docking score: -7.637
 NSC: 70393 docking score: -7.607	 NSC: 92542 docking score: -7.579	 NSC: 667758 docking score: -7.573	 NSC: 132830 docking score: -7.538
 NSC: 123403 docking score: -7.528	 NSC: 13004 docking score: -7.509	 NSC: 613315 docking score: -7.5	 NSC: 401397 docking score: -7.445
 NSC: 80965 docking score: -7.438	 NSC: 63688 docking score: -7.437	 NSC: 55143 docking score: -7.416	 NSC: 162039 docking score: -7.355
 NSC: 364435 docking score: -7.335	 NSC: 664569 docking score: -7.323	 NSC: 658245 docking score: -7.315	 NSC: 281913 docking score: -7.303


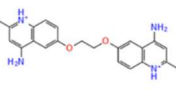

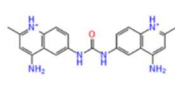
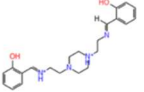
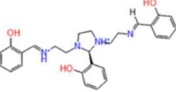
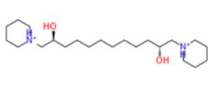
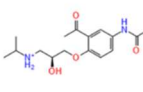
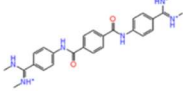

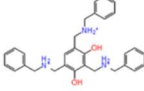
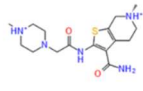
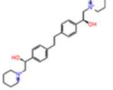
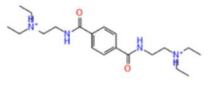
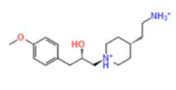


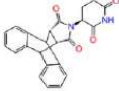
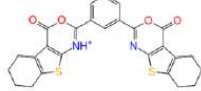
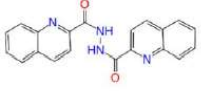
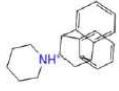
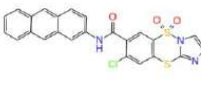
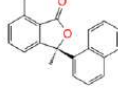


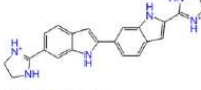
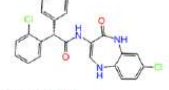
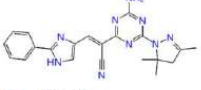
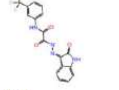
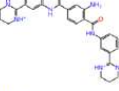
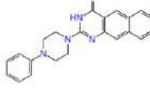
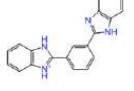
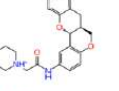
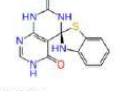

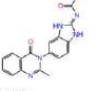
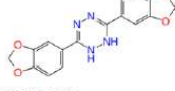
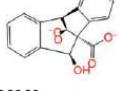
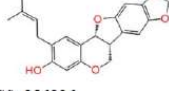
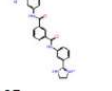
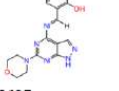
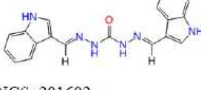
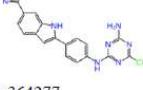
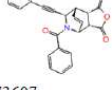
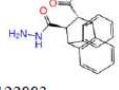
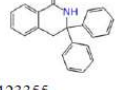
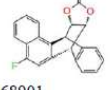
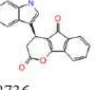
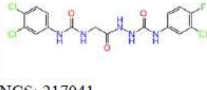
 NSC: 34318 docking score: -7.288	 NSC: 22907 docking score: -7.286	 NSC: 625255 docking score: -7.255	 NSC: 12155 docking score: -7.254
 NSC: 725602 docking score: -7.251	 NSC: 84389 docking score: -7.245	 NSC: 401011 docking score: -7.237	 NSC: 326057 docking score: -7.228
 NSC: 53312 docking score: -7.188	 NSC: 601826 docking score: -7.136	 NSC: 48454 docking score: -7.135	 NSC: 708458 docking score: -7.135
 NSC: 74105 docking score: -7.131	 NSC: 13718 docking score: -7.124	 NSC: 52643 docking score: -7.116	 NSC: 343971 docking score: -7.111
 NSC: 339180 docking score: -7.105			

Tabla S3. Compuestos pertenecientes a la base de datos NCI Open Database seleccionados por HTVS frente al sitio activo de Atg4B (2ZZP_full) empleando el programa de acoplamiento Autodock Vina. Los compuestos se muestran como estereoisómeros/ tautómeros/protómeros durante el acoplamiento molecular.

 NCS: 241470 vina score: -10.2	 NCS: 354315 vina score: -10.0	 NCS: 400842 vina score: -9.6	 NCS: 151802 vina score: -9.5
 NCS: 717956 vina score: -9.5	 NCS: 407632 vina score: -9.4	 NCS: 31075 vina score: -9.3	 NCS: 31166 vina score: -9.2
 NCS: 330687 vina score: -9.2	 NCS: 636783 vina score: -9.2	 NCS: 704320 vina score: -9.2	 NCS: 320866 vina score: -9.1
 NCS: 80117 vina score: -9.1	 NCS: 131354 vina score: -9.0	 NCS: 133357 vina score: -9.0	 NCS: 681604 vina score: -9.0
 NCS: 728031 vina score: -9.0	 NCS: 142537 vina score: -8.9	 NCS: 602693 vina score: -8.9	 NCS: 171131 vina score: -8.8
 NCS: 25353 vina score: -8.8	 NCS: 356826 vina score: -8.8	 NCS: 51187 vina score: -8.8	 NCS: 725687 vina score: -8.8
 NCS: 201602 vina score: -8.7	 NCS: 364277 vina score: -8.7	 NCS: 73607 vina score: -8.7	 NCS: 122883 vina score: -8.6
 NCS: 123355 vina score: -8.6	 NCS: 168901 vina score: -8.6	 NCS: 208736 vina score: -8.6	 NCS: 217041 vina score: -8.6

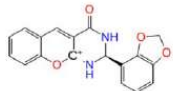

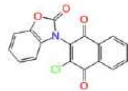

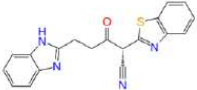
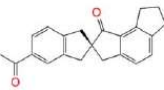
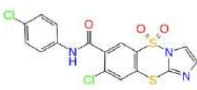
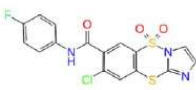
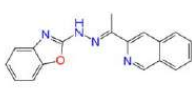

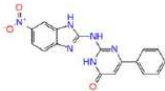

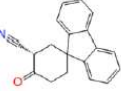
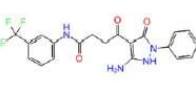
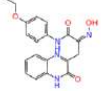
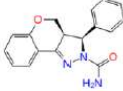
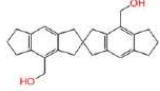
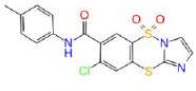

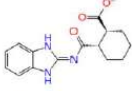
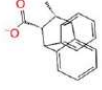
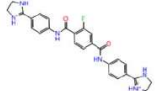




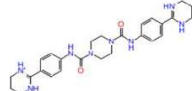

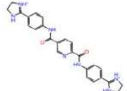

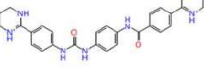
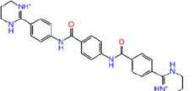
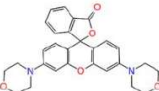
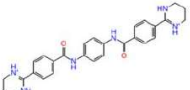

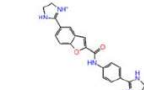

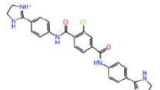

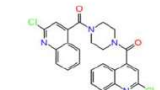

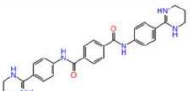

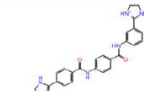
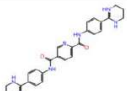


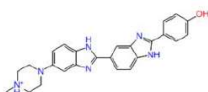

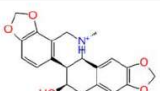



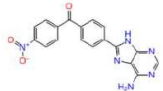
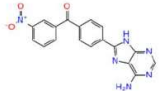
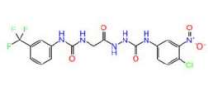
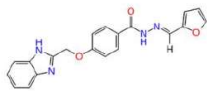
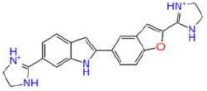
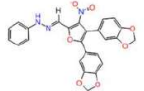
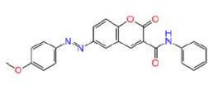
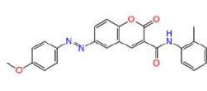
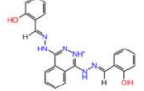
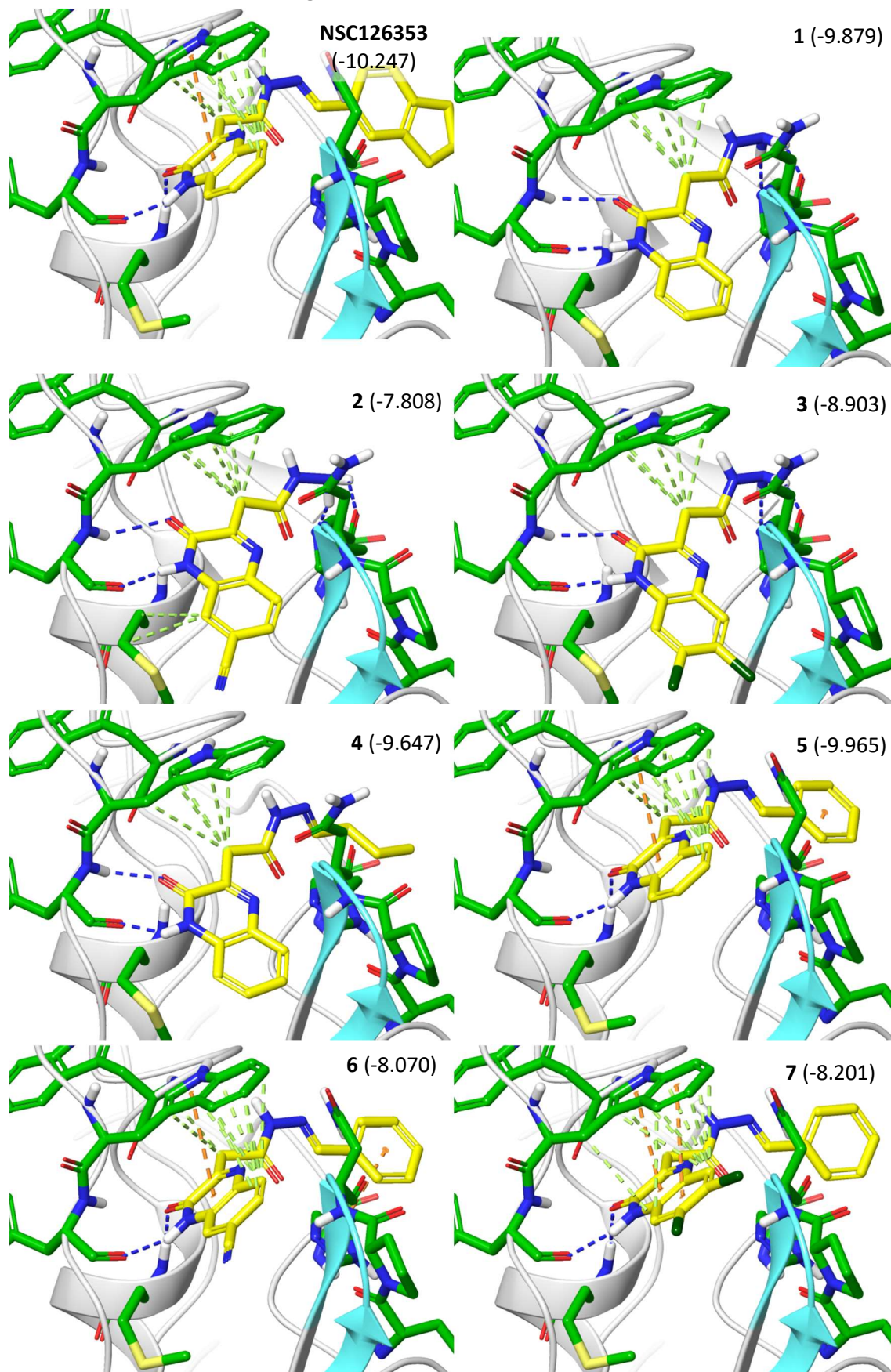
 NCS: 263638 vina score: -8.6	 NCS: 296330 vina score: -8.6	 NCS: 322341 vina score: -8.6	 NCS: 357891 vina score: -8.6
 NCS: 618679 vina score: -8.6	 NCS: 677009 vina score: -8.6	 NCS: 681167 vina score: -8.6	 NCS: 681168 vina score: -8.6
 NCS: 693638 vina score: -8.6	 NCS: 141099 vina score: -8.5	 NCS: 157308 vina score: -8.5	 NCS: 264074 vina score: -8.5
 NCS: 60502 vina score: -8.5	 NCS: 631817 vina score: -8.5	 NCS: 646377 vina score: -8.5	 NCS: 652810 vina score: -8.5
 NCS: 670438 vina score: -8.5	 NCS: 681166 vina score: -8.5	 NCS: 734133 vina score: -8.5	 NCS: 95666 vina score: -8.5
 NCS: 22090 vina score: -8.5			

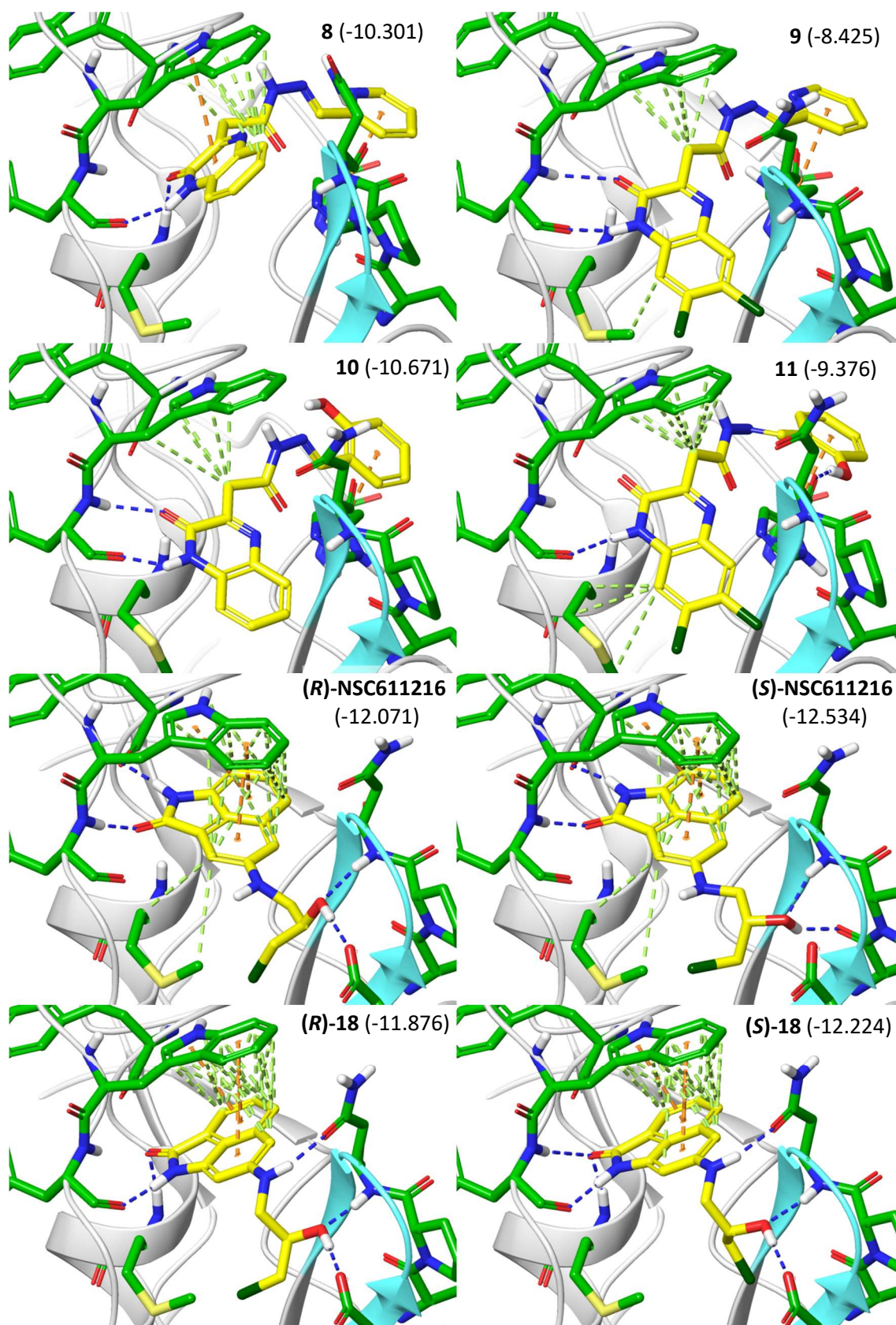
Tabla S4. Compuestos pertenecientes a la base de datos NCI Open Database seleccionados por HTVS frente al segundo sitio alternativo de Atg4B (2CY7_full) empleando el programa de acoplamiento Autodock Vina. Los compuestos se muestran como estereoisómeros/ tautómeros/protómeros durante el acoplamiento molecular.

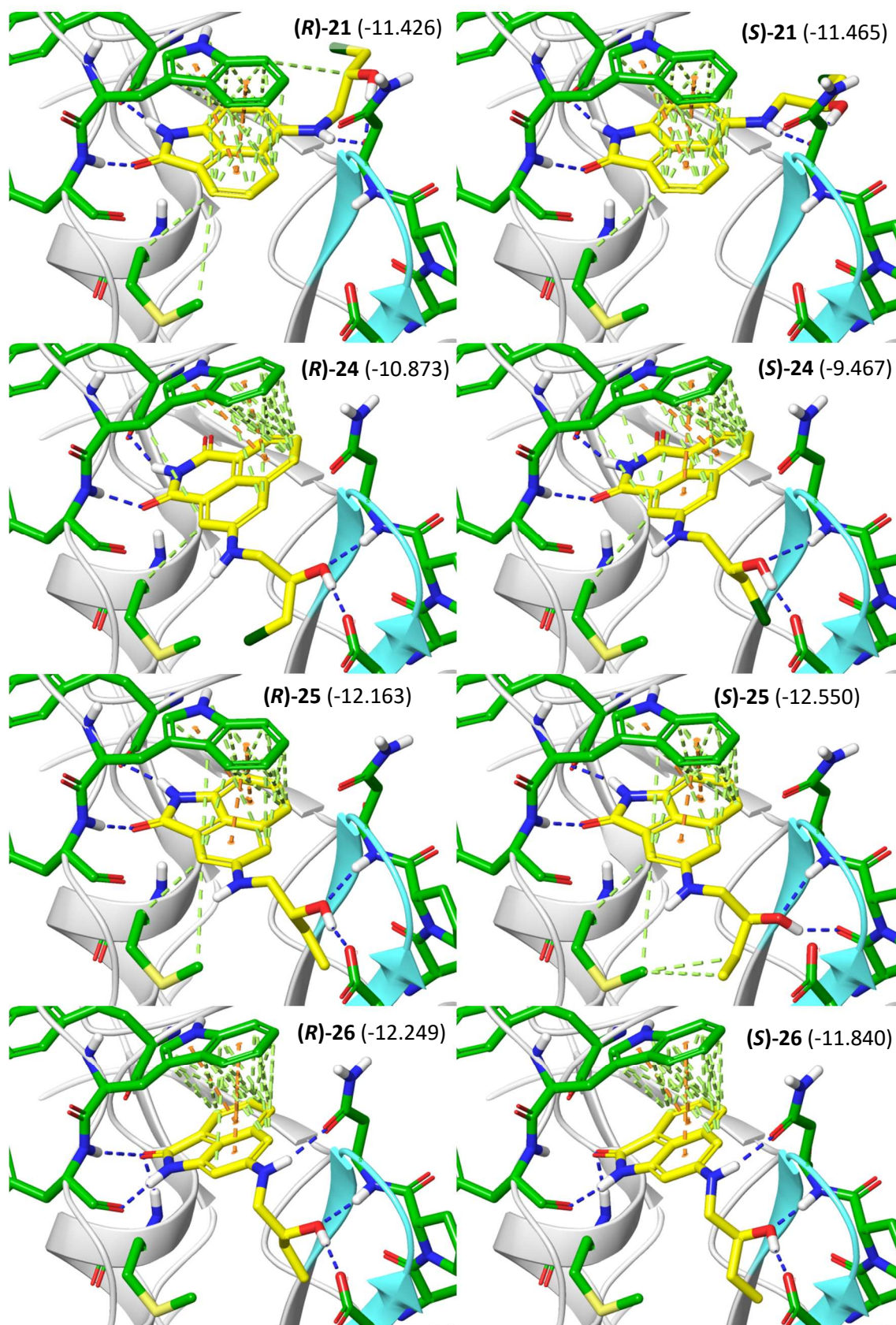
 NCS: 71204 vina score: -9.7	 NCS: 57148 vina score: -9.6	 NCS: 35843 vina score: -9.5	 NCS: 50469 vina score: -9.5
 NCS: 58480 vina score: -9.5	 NCS: 83458 vina score: -9.5	 NCS: 58479 vina score: -9.4	 NCS: 63696 vina score: -9.4
 NCS: 65372 vina score: -9.4	 NCS: 75329 vina score: -9.4	 NCS: 67734 vina score: -9.3	 NCS: 378143 vina score: -9.3
 NCS: 73849 vina score: -9.2	 NCS: 66761 vina score: -9.1	 NCS: 290111 vina score: -9.1	 NCS: 374818 vina score: -9.1
 NCS: 241572 vina score: -9.0	 NCS: 63271 vina score: -8.9	 NCS: 87042 vina score: -8.9	 NCS: 658260 vina score: -8.9
 NCS: 57153 vina score: -8.8	 NCS: 63688 vina score: -8.8	 NCS: 67737 vina score: -8.8	 NCS: 80362 vina score: -8.8
 NCS: 35847 vina score: -8.7	 NCS: 65375 vina score: -8.7	 NCS: 322921 vina score: -8.7	 NCS: 371869 vina score: -8.7
 NCS: 406034 vina score: -8.7	 NCS: 57149 vina score: -8.6	 NCS: 66757 vina score: -8.6	 NCS: 110318 vina score: -8.6

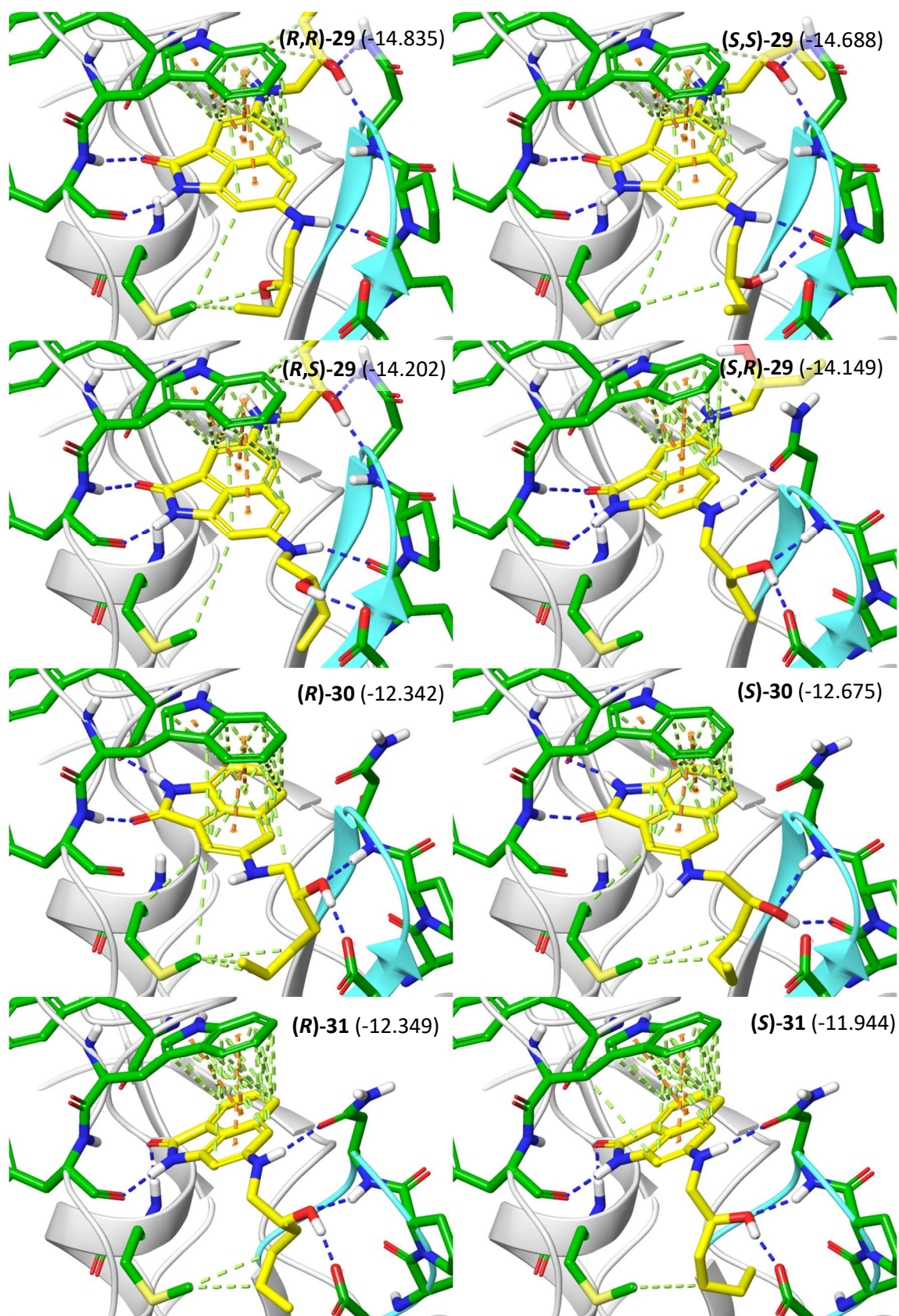
 <p>NCS: 210294 vina score: -8.6</p>	 <p>NCS: 210305 vina score: -8.6</p>	 <p>NCS: 217031 vina score: -8.6</p>	 <p>NCS: 348965 vina score: -8.6</p>
 <p>NCS: 369716 vina score: -8.6</p>	 <p>NCS: 647257 vina score: -8.6</p>	 <p>NCS: 662450 vina score: -8.6</p>	 <p>NCS: 662451 vina score: -8.6</p>
 <p>NCS: 103647 vina score: -8.5</p>			

Resultados Induced Fit Docking









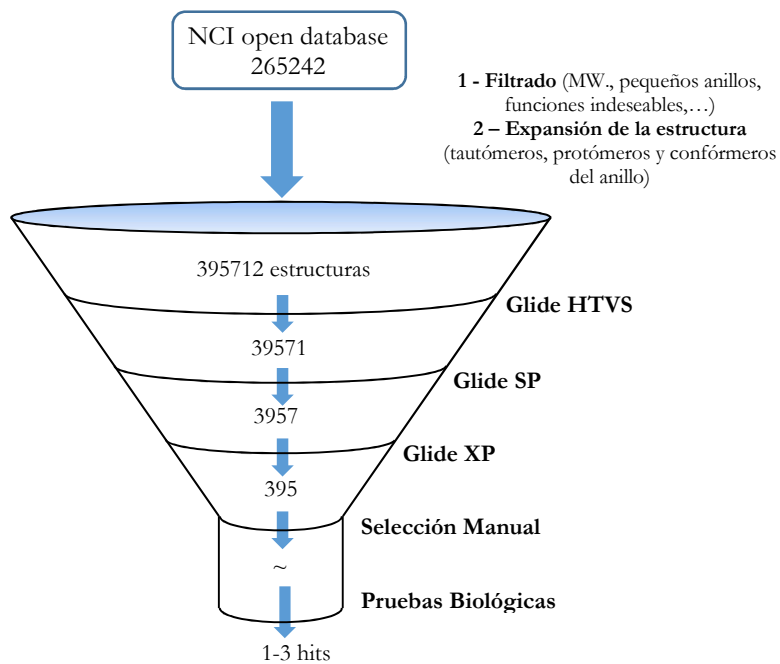


Figura S1. Embudo de selección en la identificación de los ligandos para cada una de las estructuras de Atg4B empleando el método de acoplamiento Glide.

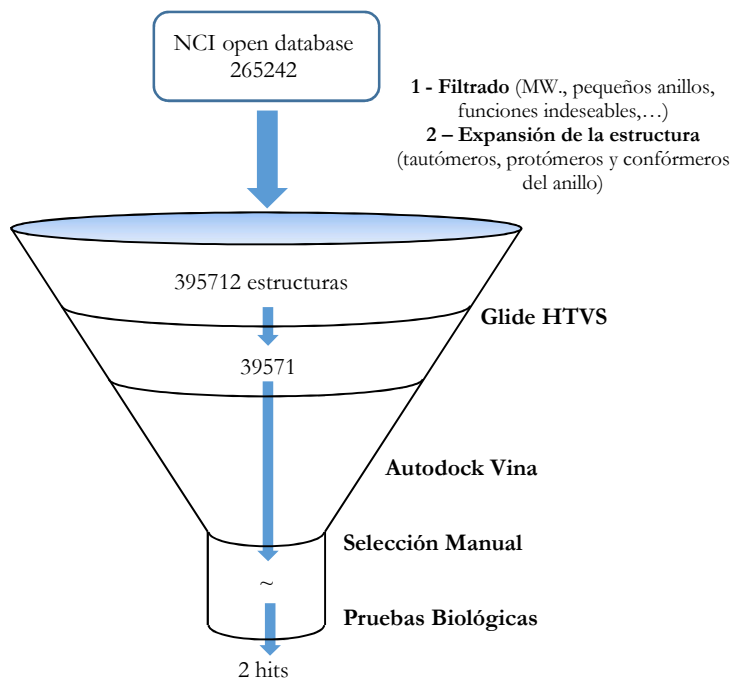
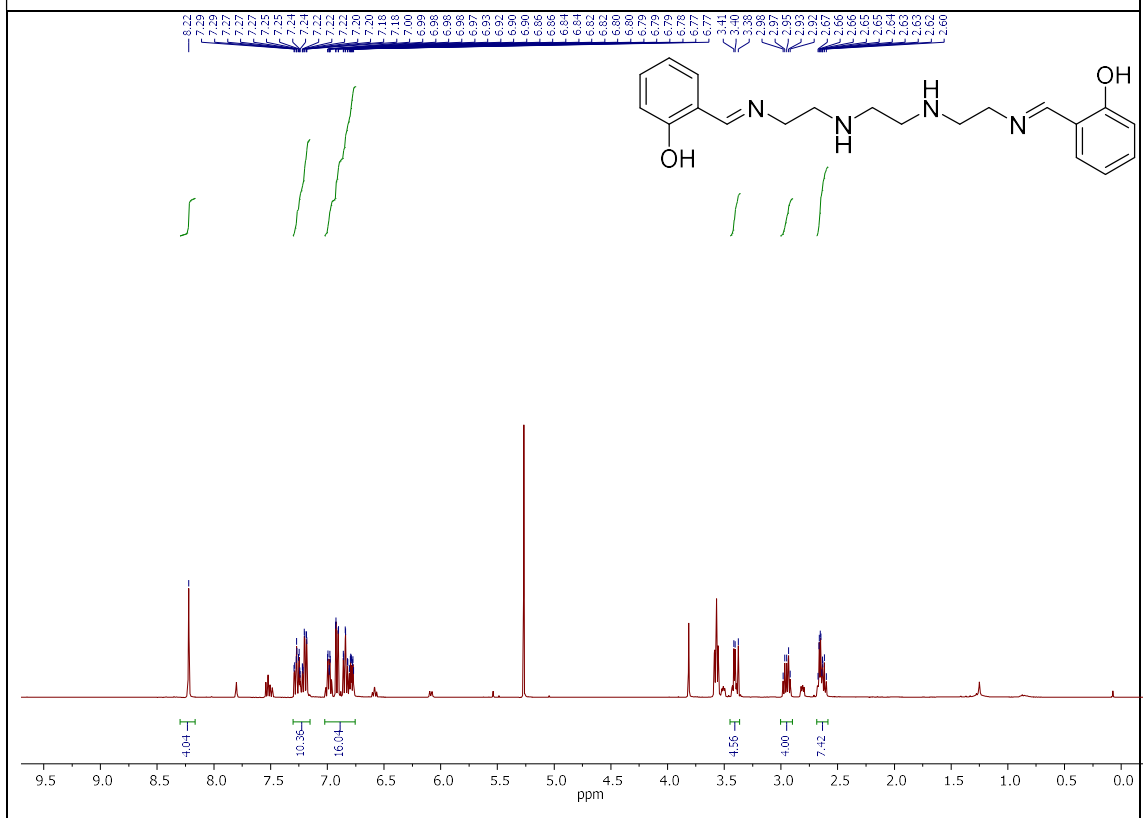


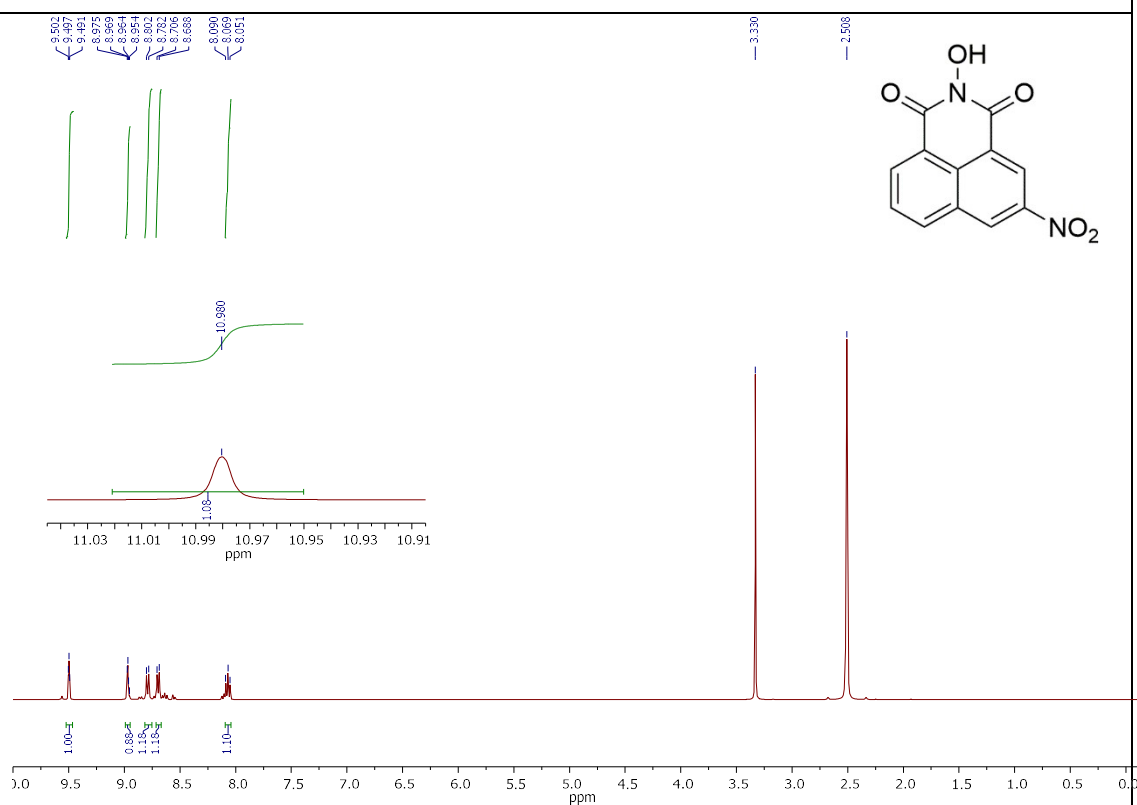
Figura S2. Embudo de selección en la identificación de los ligandos para cada una de las estructuras de Atg4B empleando el método de acoplamiento Autodock Vina.

Espectros de RMN Capítulo 1

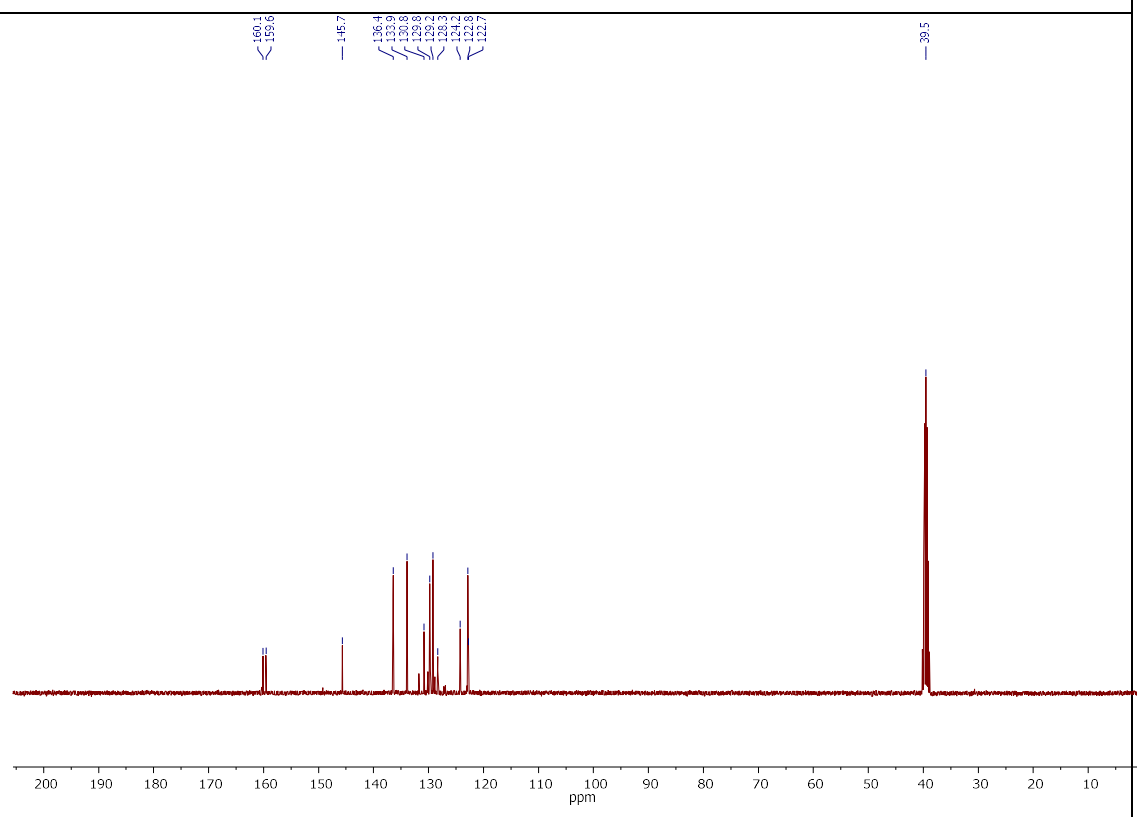
NSC43949, ^1H RMN (400 MHz, CDCl_3)



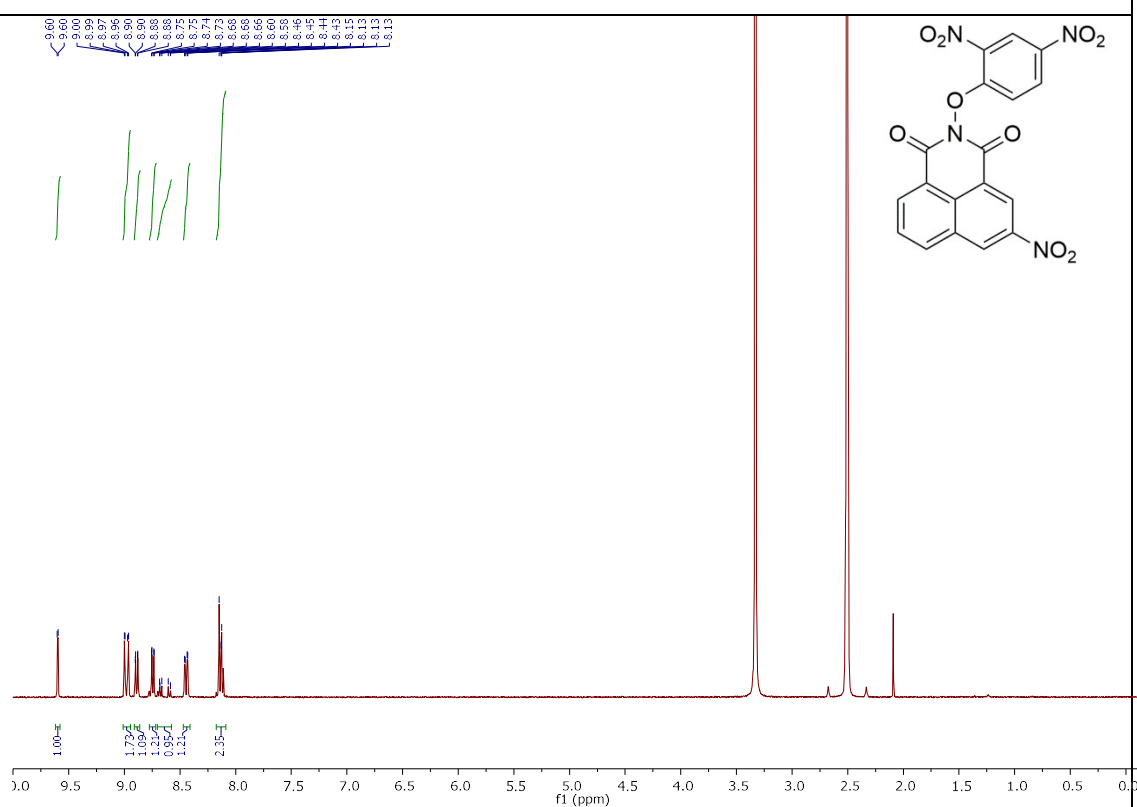
¹H RMN (400 MHz, DMSO-*d*₆)



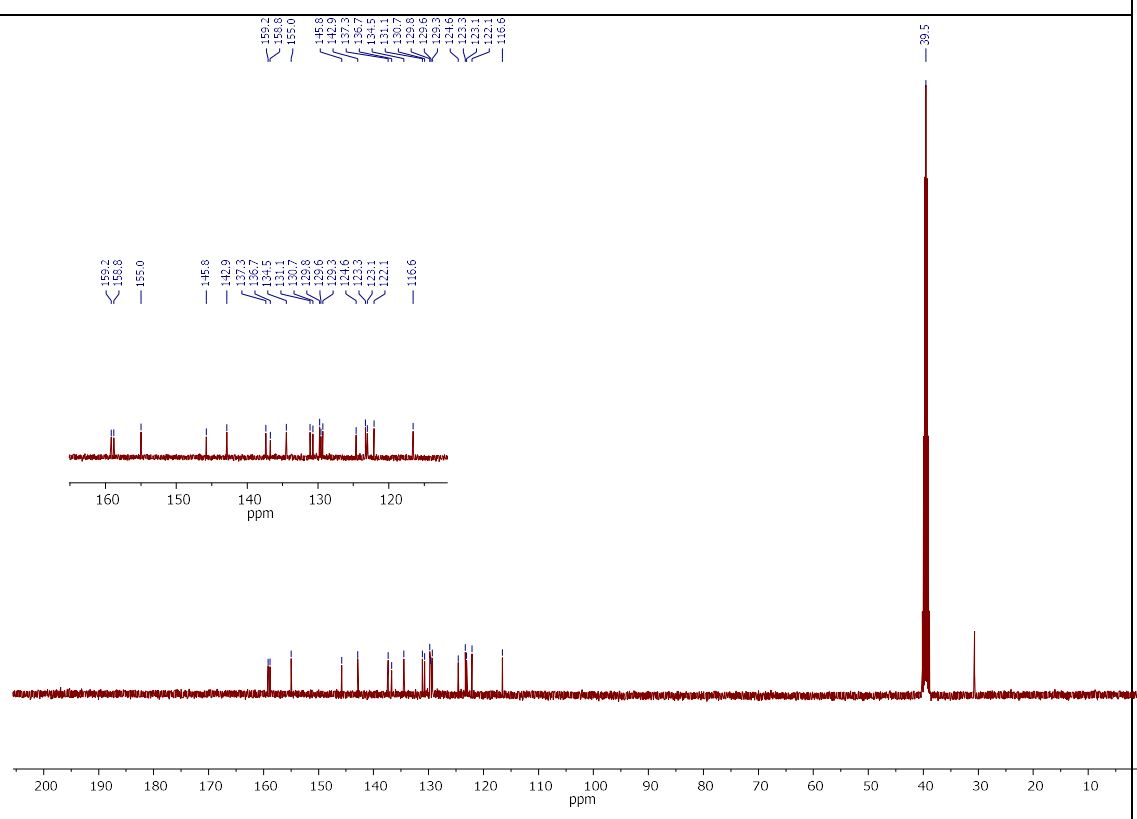
¹³C RMN (101 MHz, DMSO-*d*₆)



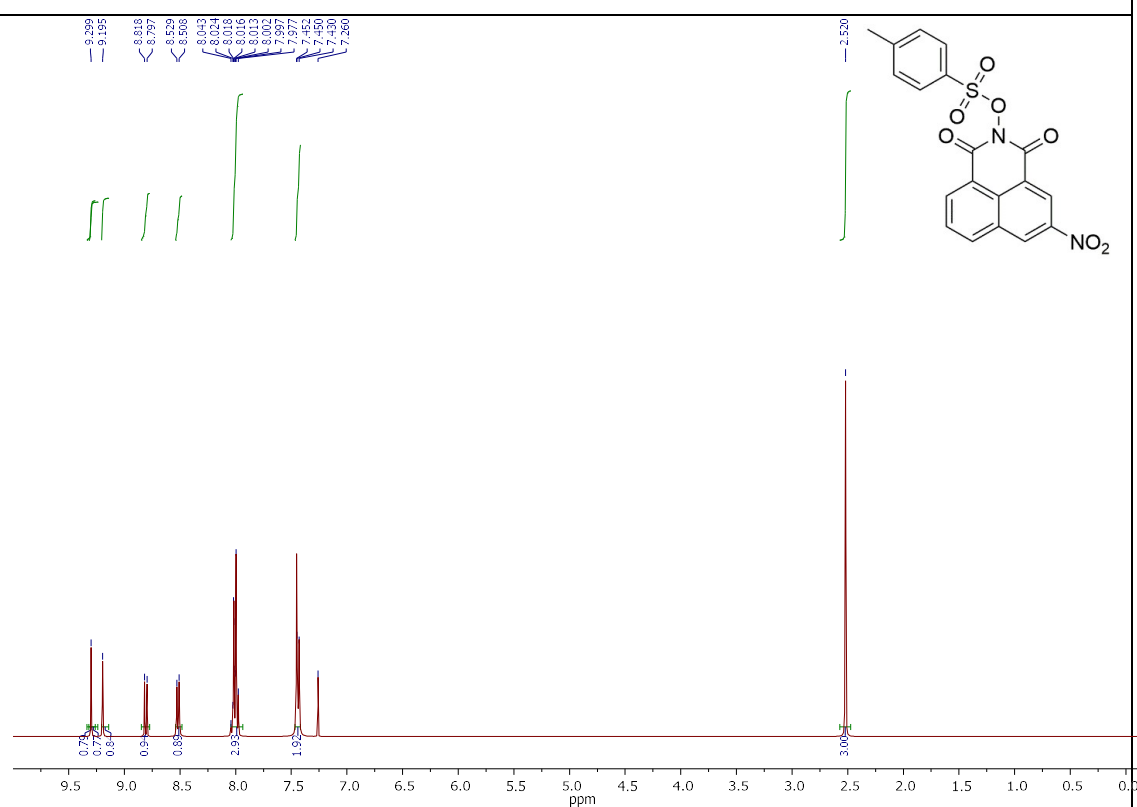
12, ¹H RMN (400 MHz, DMSO-d₆)



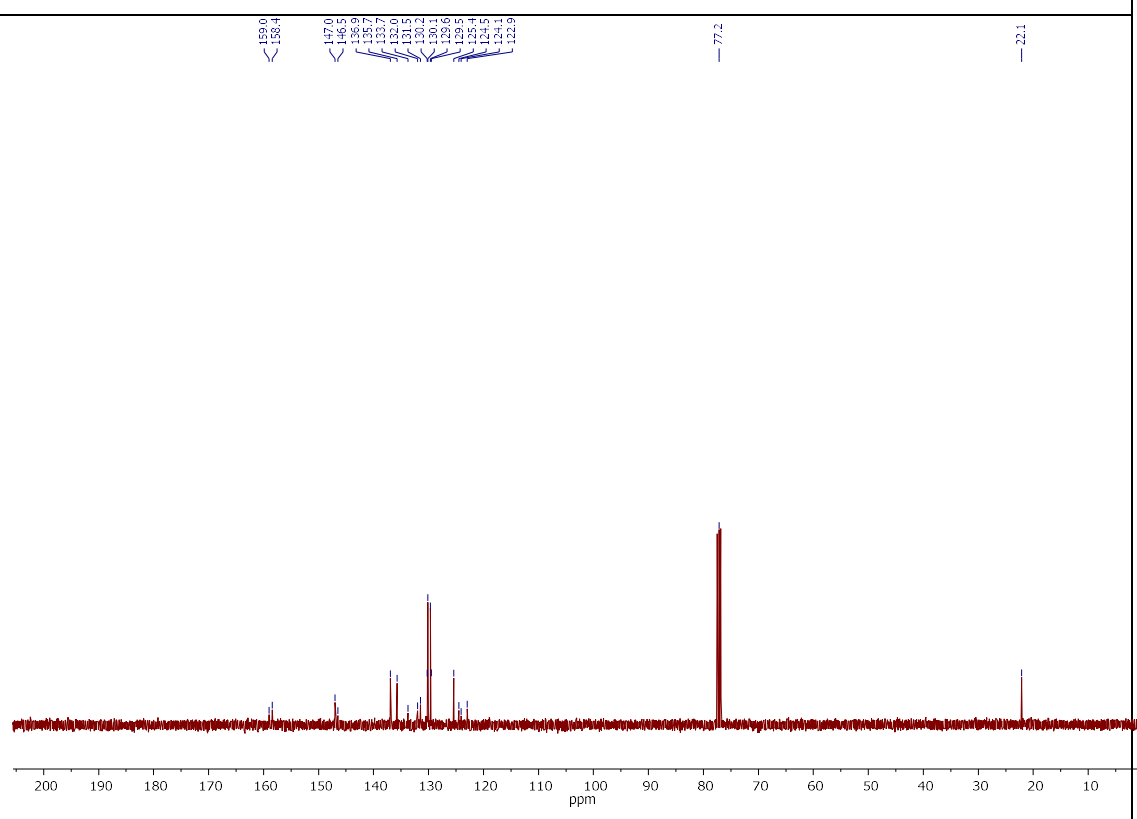
12, ¹³C RMN (101 MHz, DMSO-d₆)



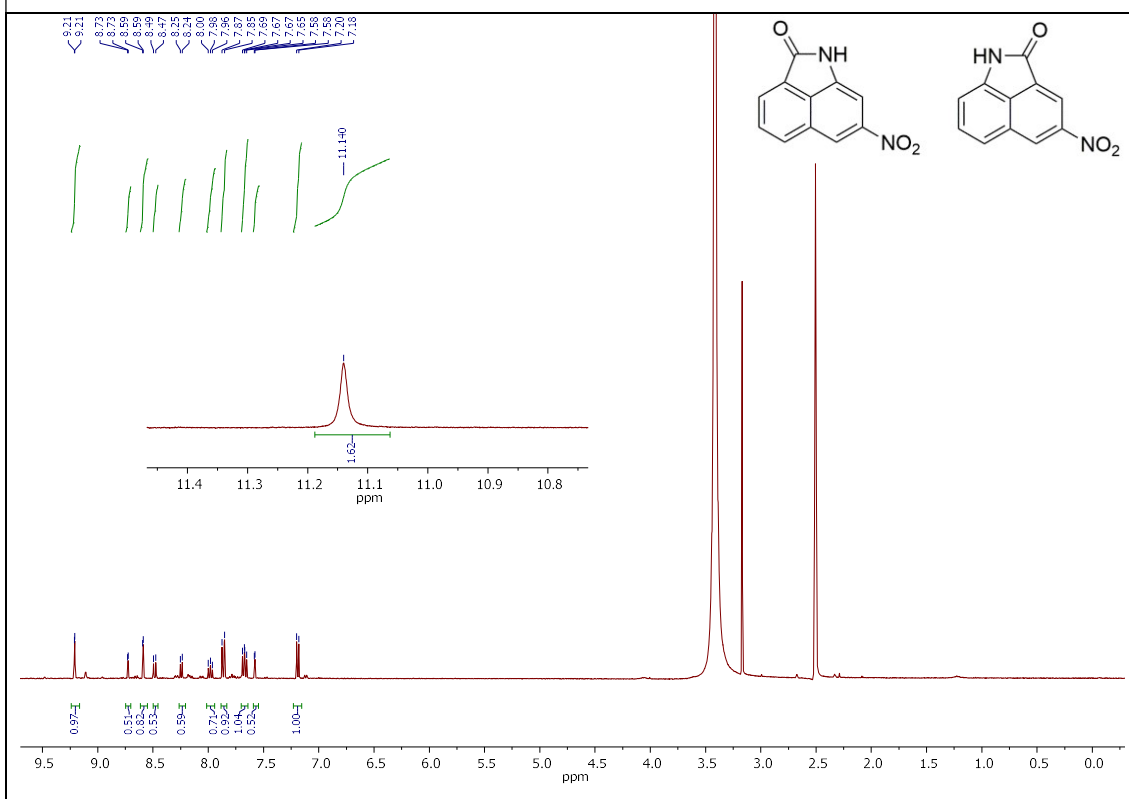
13, ¹H RMN (400 MHz, CDCl₃)



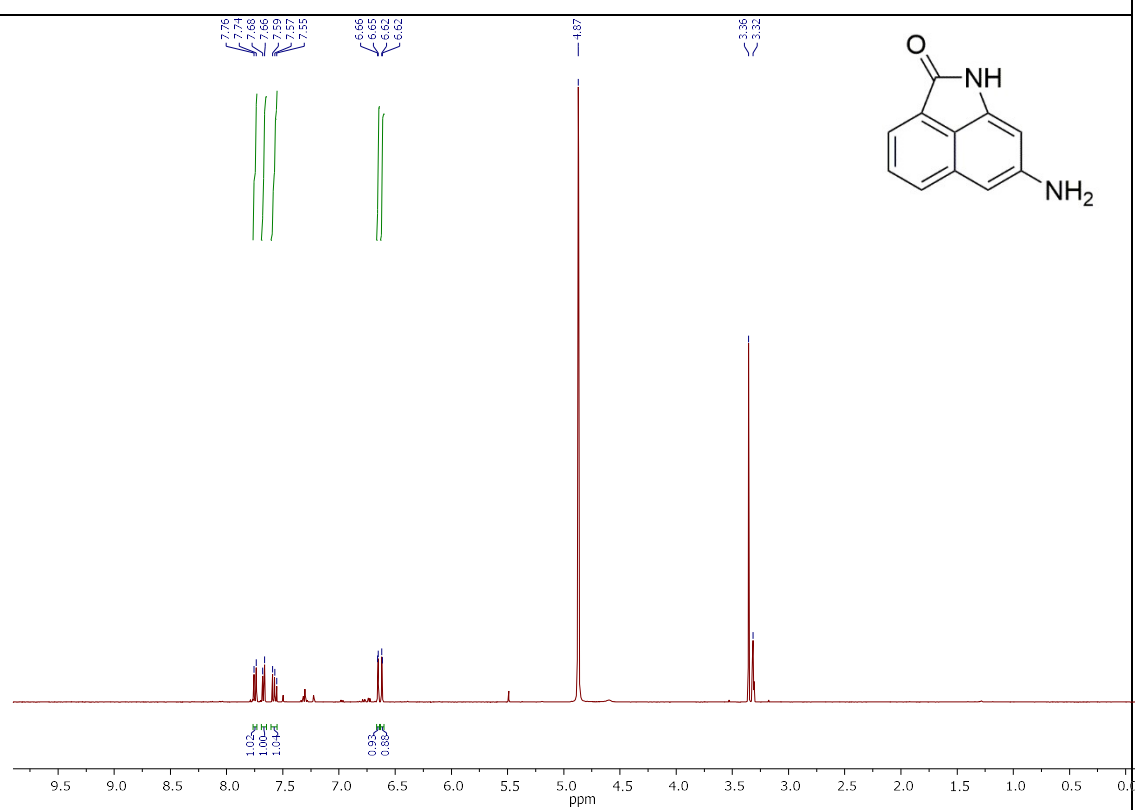
13, ¹³C RMN (101 MHz, CDCl₃)



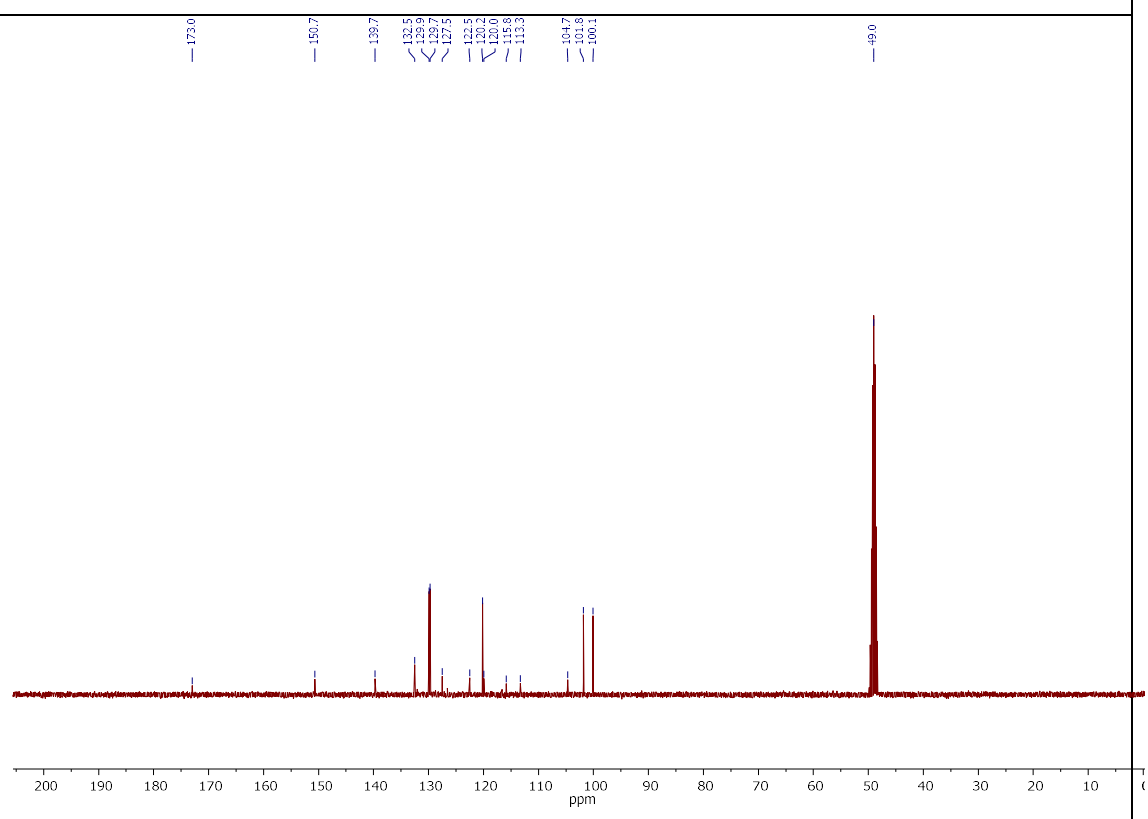
14 y 15, ¹H NMR (400 MHz, DMSO-d₆)



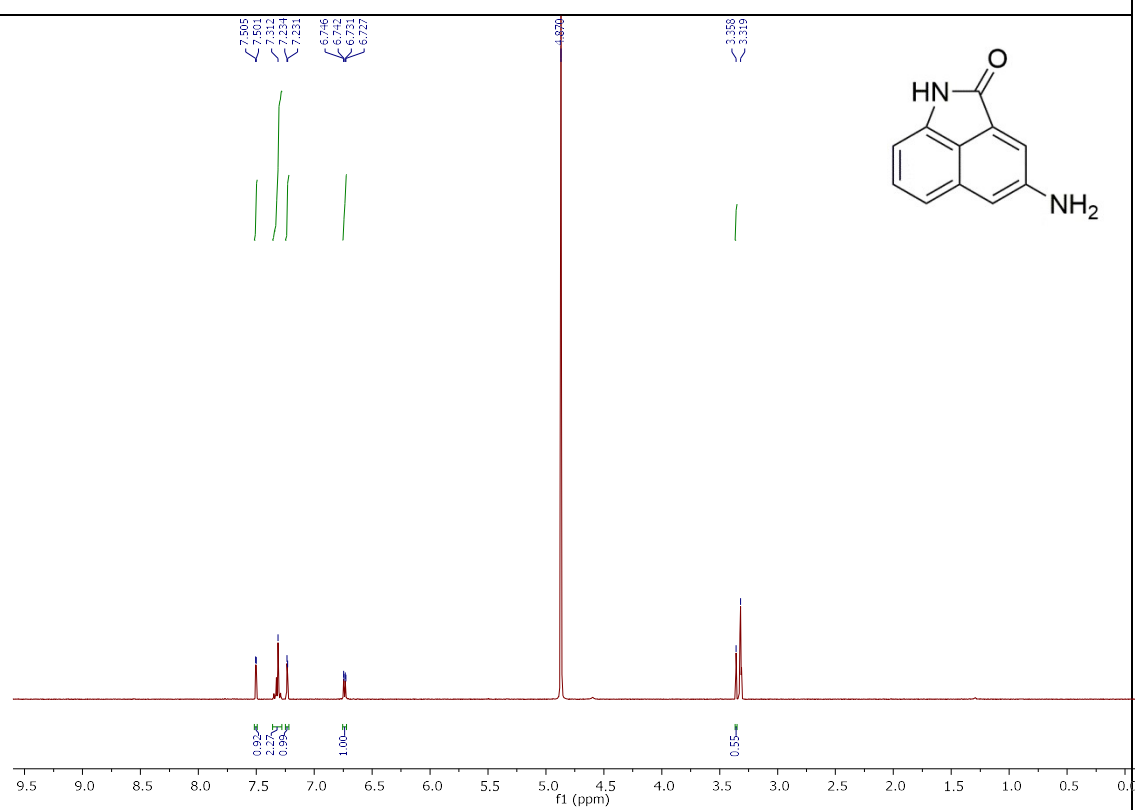
16, ¹H RMN (400 MHz, CD₃OD)



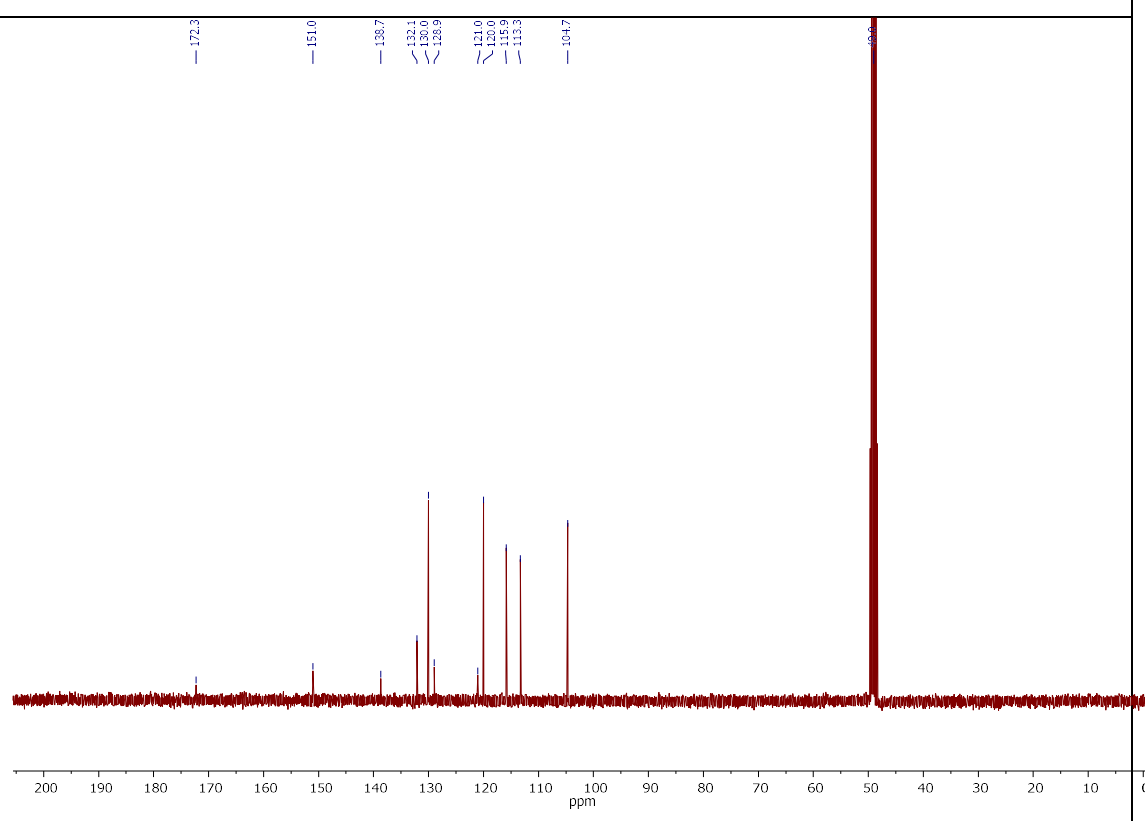
16, ¹³C RMN (101 MHz, CD₃OD)



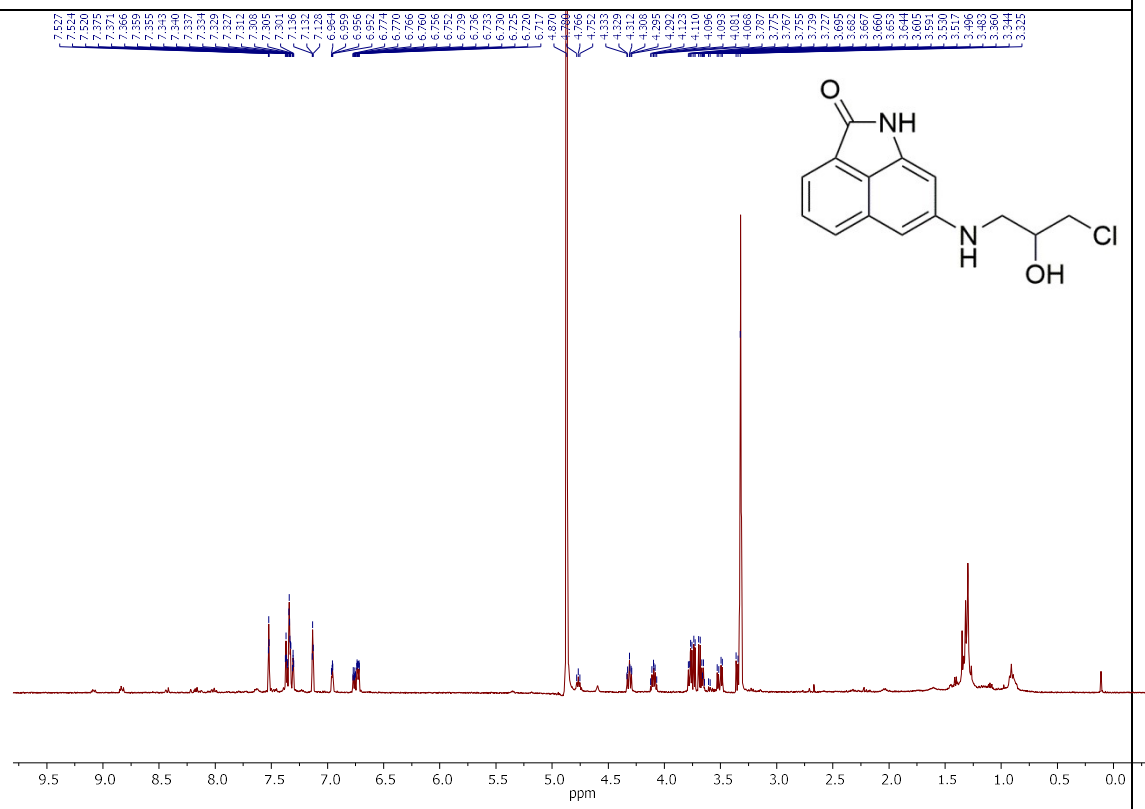
17, ¹H RMN (400 MHz, CD₃OD)



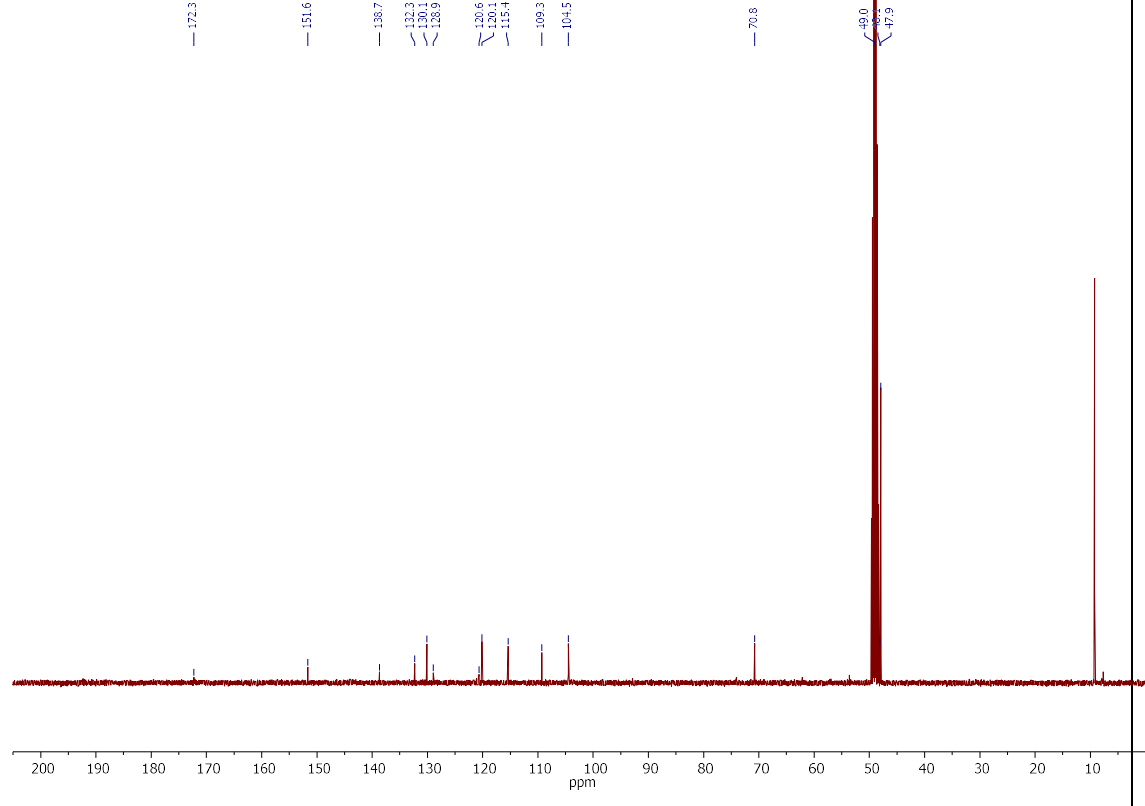
17, ¹³C RMN (101 MHz, CD₃OD)



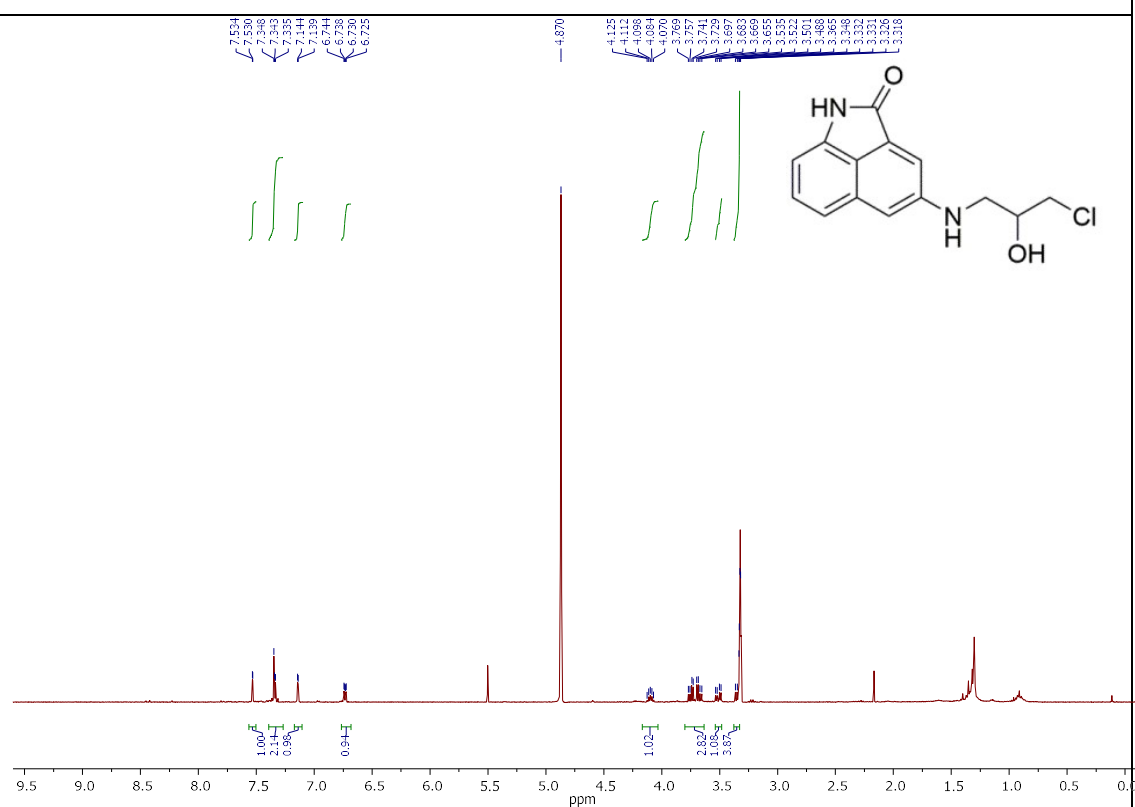
18, ¹H RMN (400 MHz, CD₃OD)



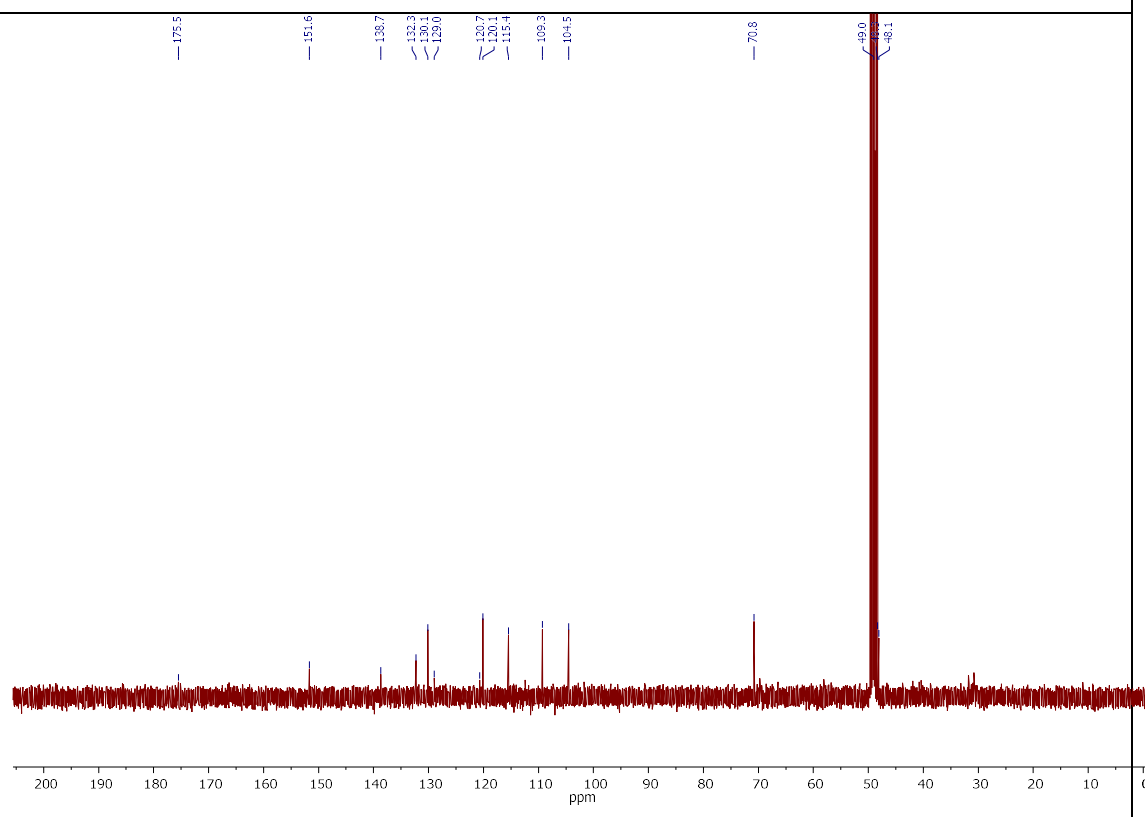
18, ¹³C RMN (101 MHz, CD₃OD)



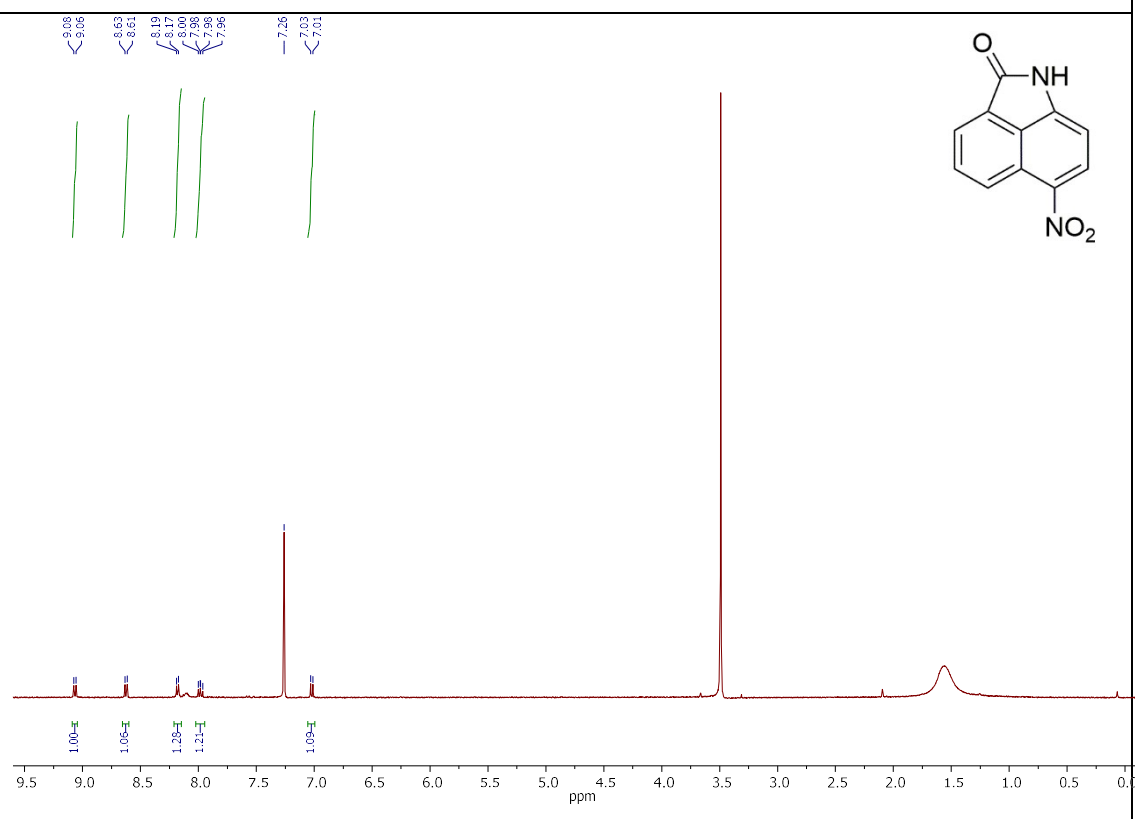
NSC611216, ¹H RMN (400 MHz, CD₃OD)



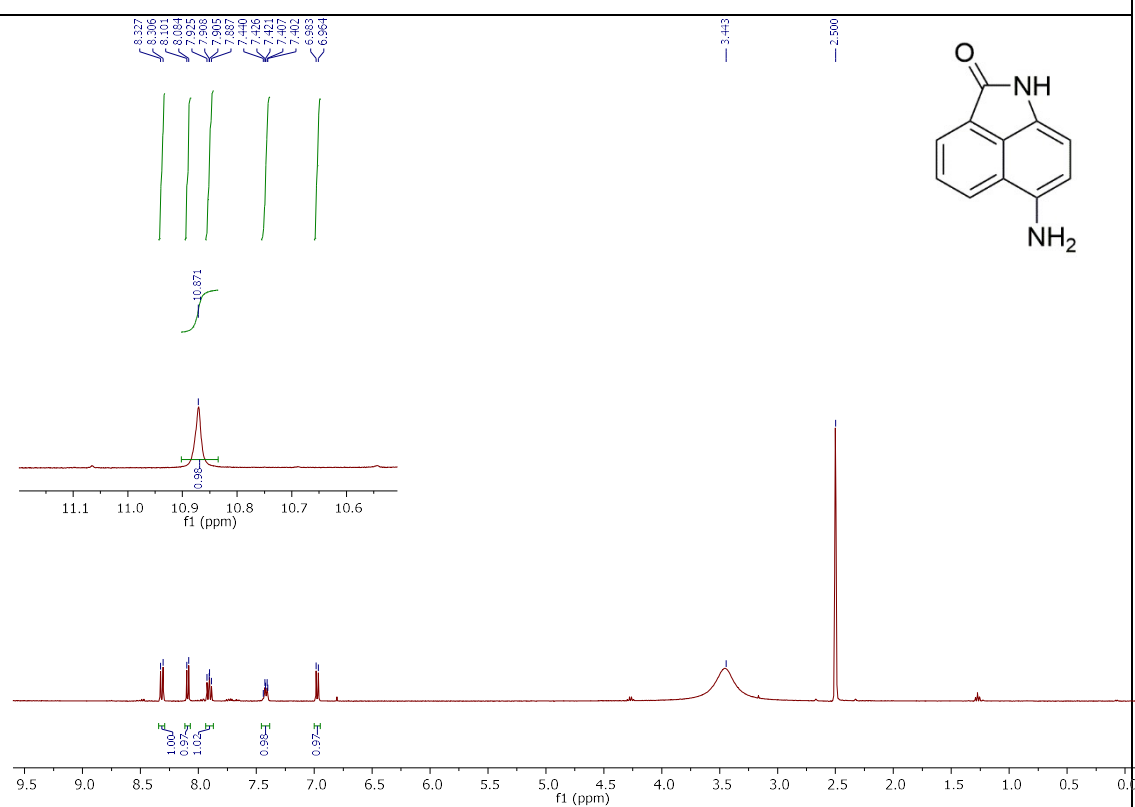
NSC611216, ¹³C RMN (101 MHz, CD₃OD)



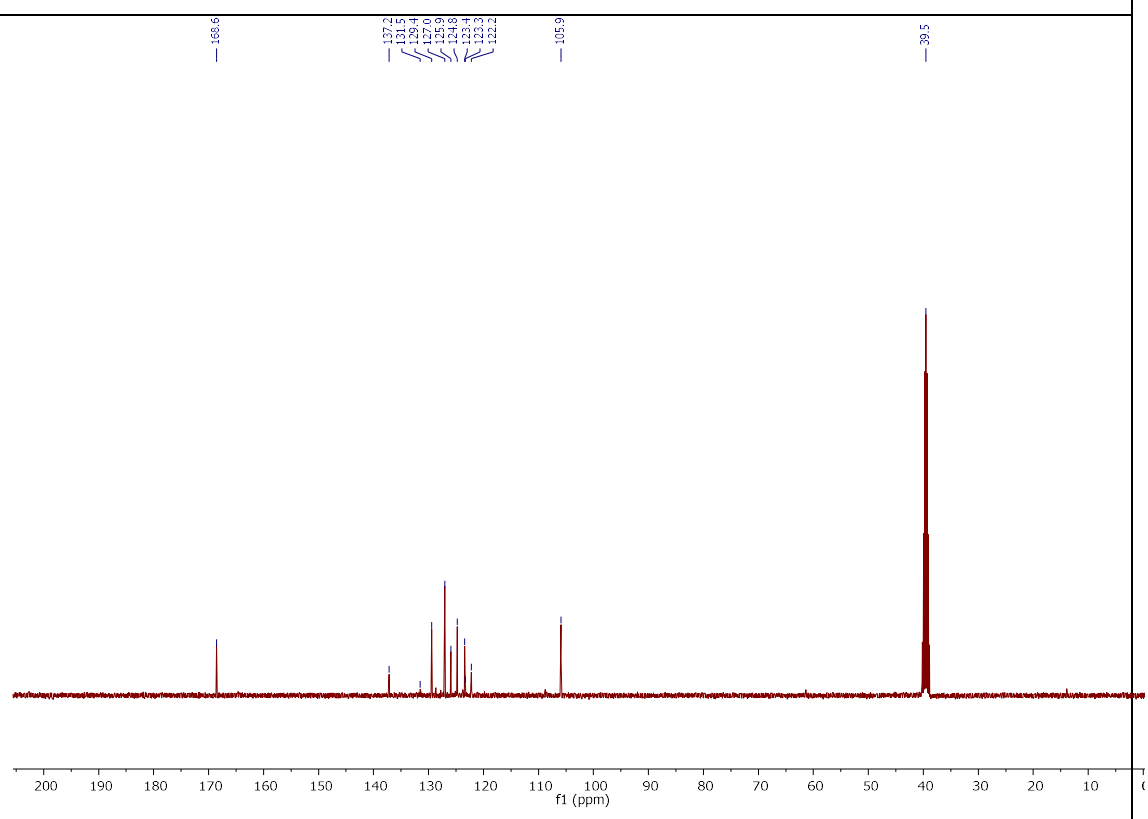
19, ¹H RMN (400 MHz, DMSO-d₆)



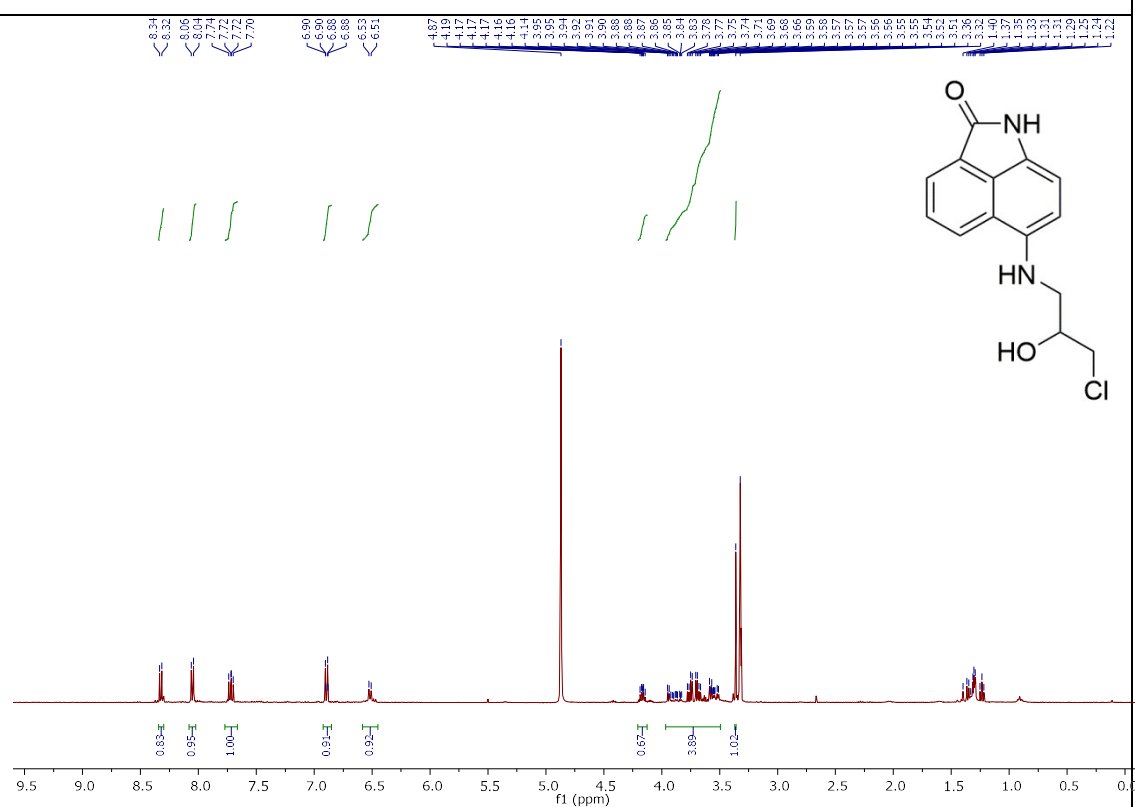
20, ¹H RMN (400 MHz, DMSO-d₆)



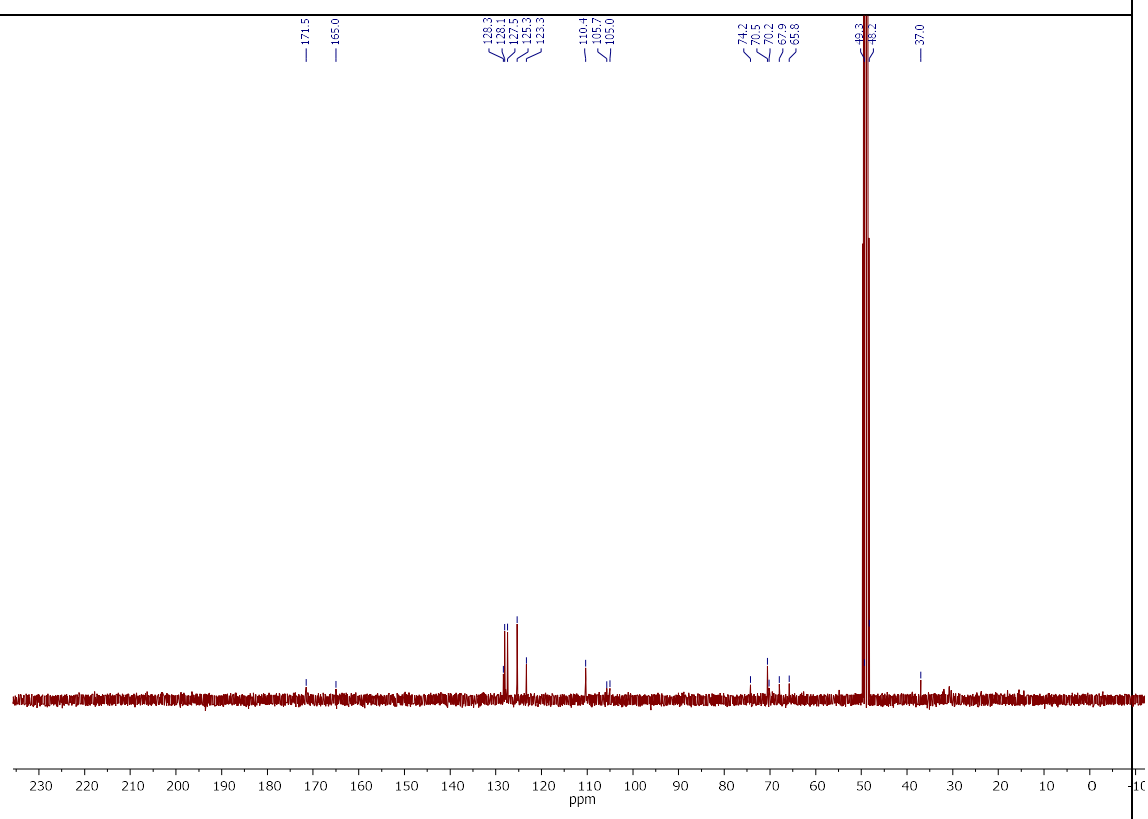
20, ¹³C RMN (101 MHz, DMSO-d₆)



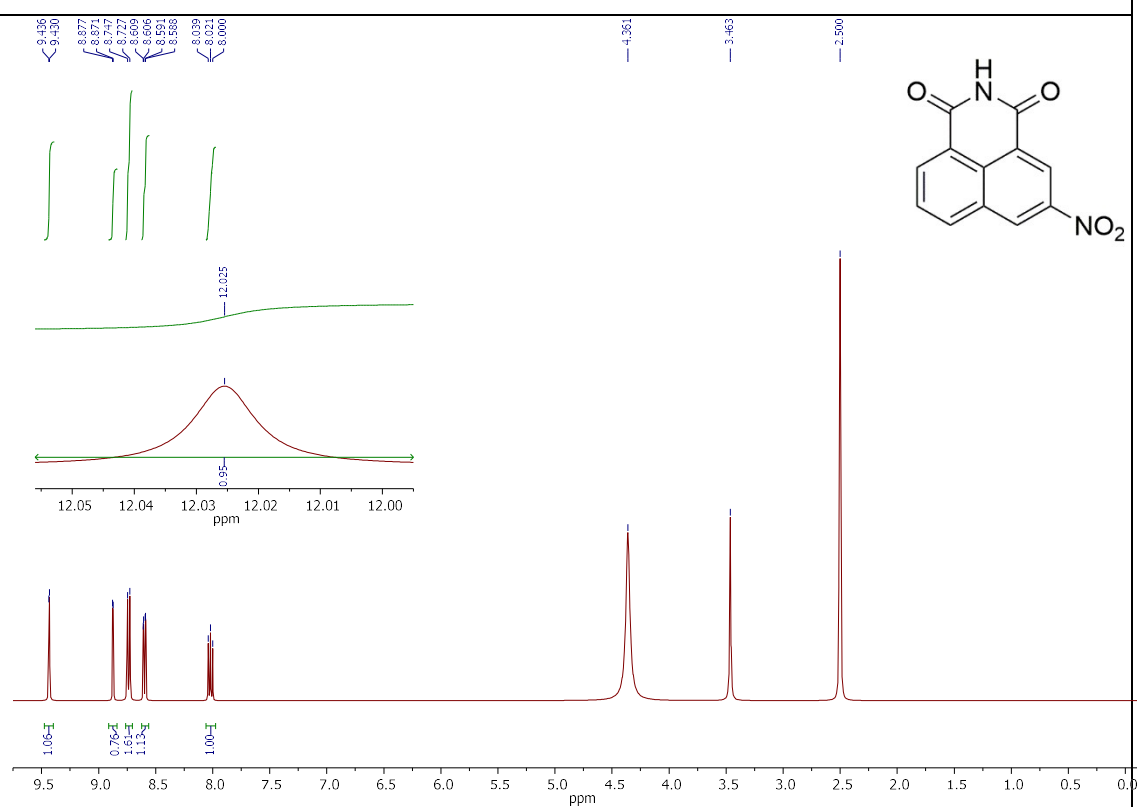
21, ¹H RMN (400 MHz, CD₃OD)



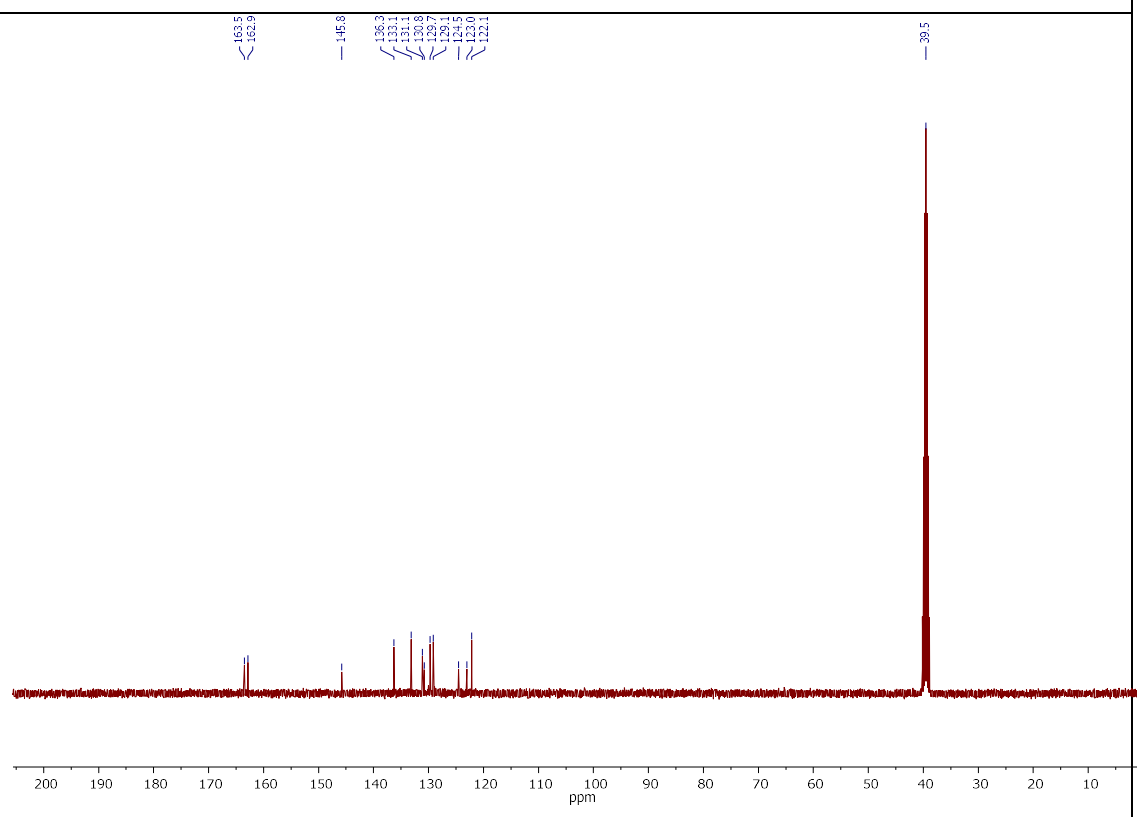
21, ¹³C RMN (101 MHz, CD₃OD)



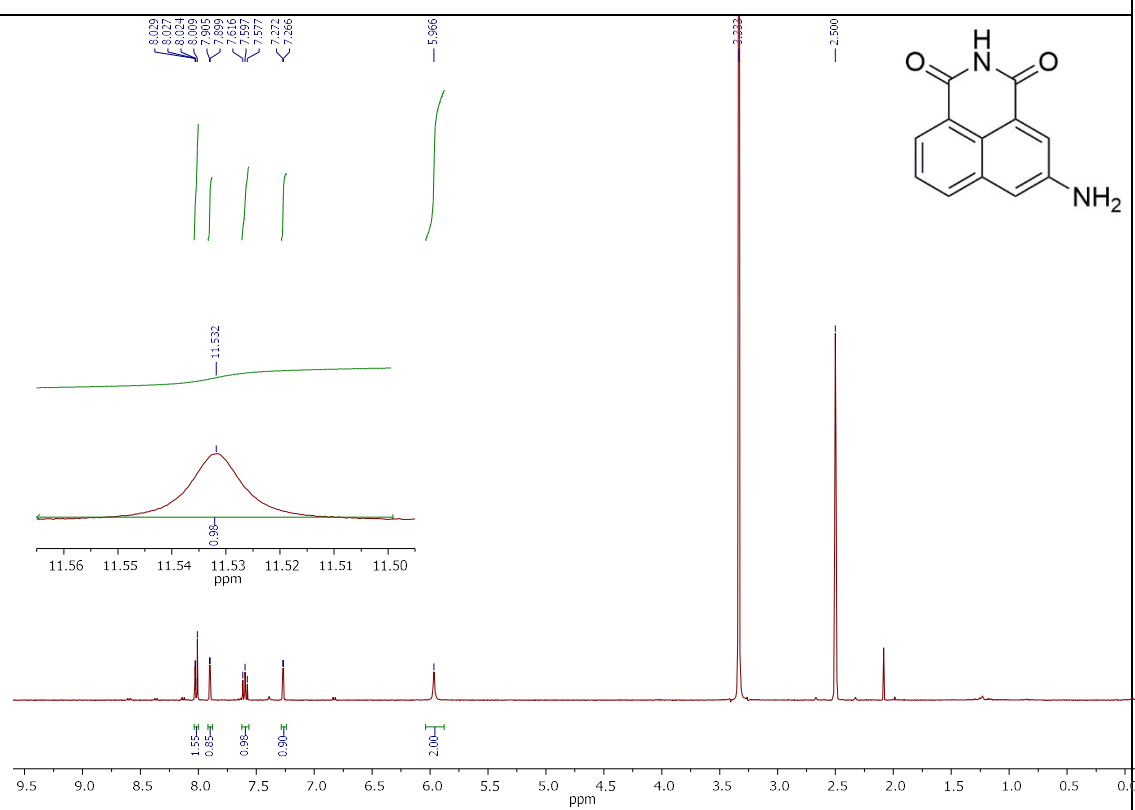
22, ¹H RMN (400 MHz, DMSO-d₆)



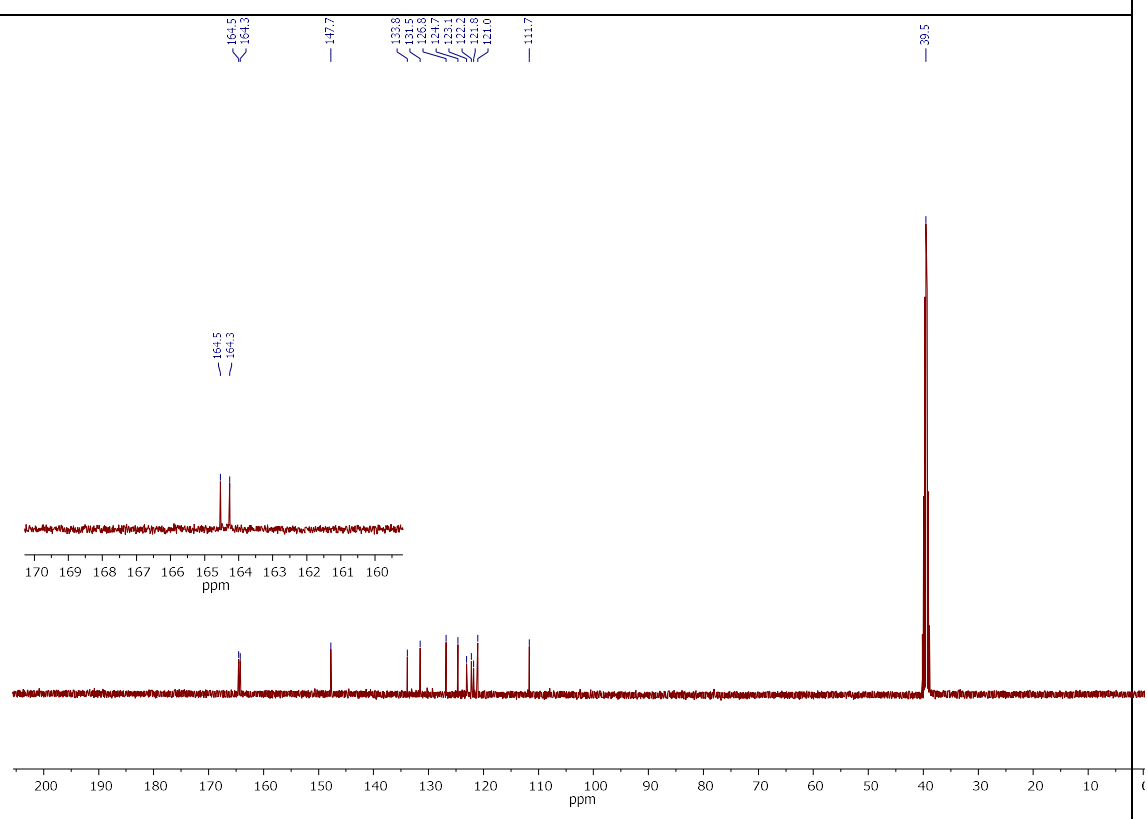
22, ¹³C RMN (101 MHz, DMSO-d₆)



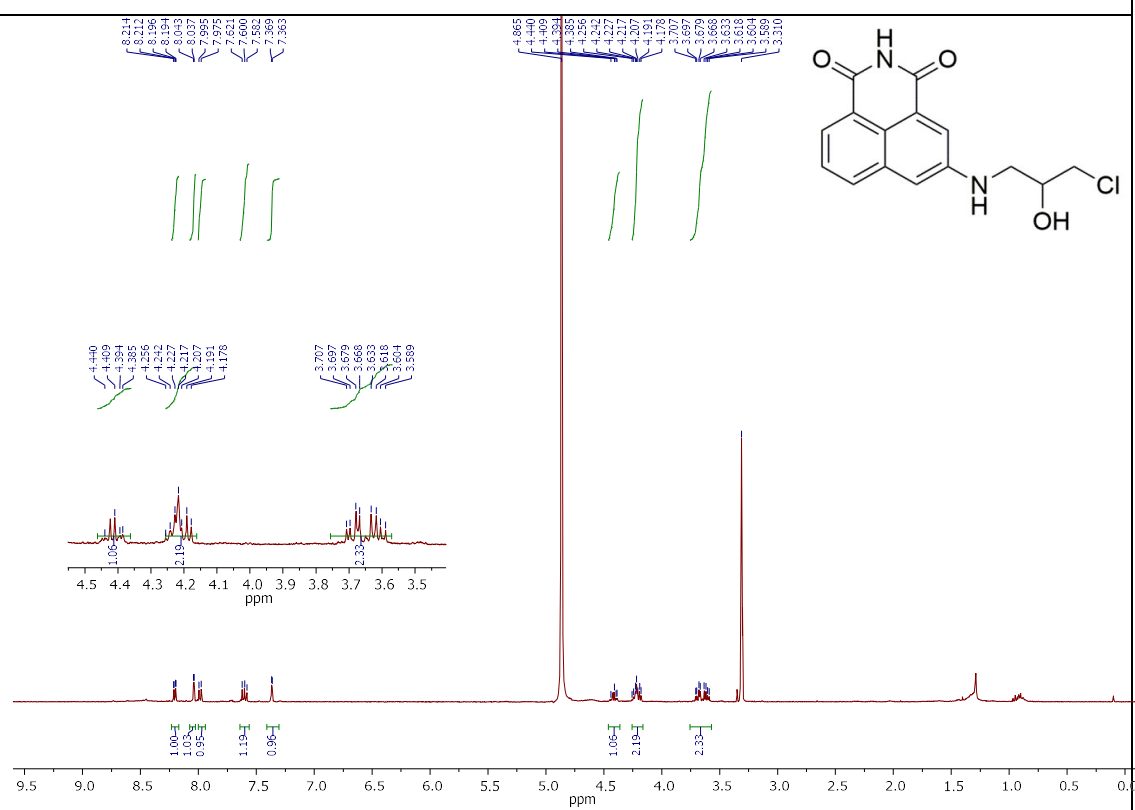
23, ¹H RMN (400 MHz, DMSO-d₆)



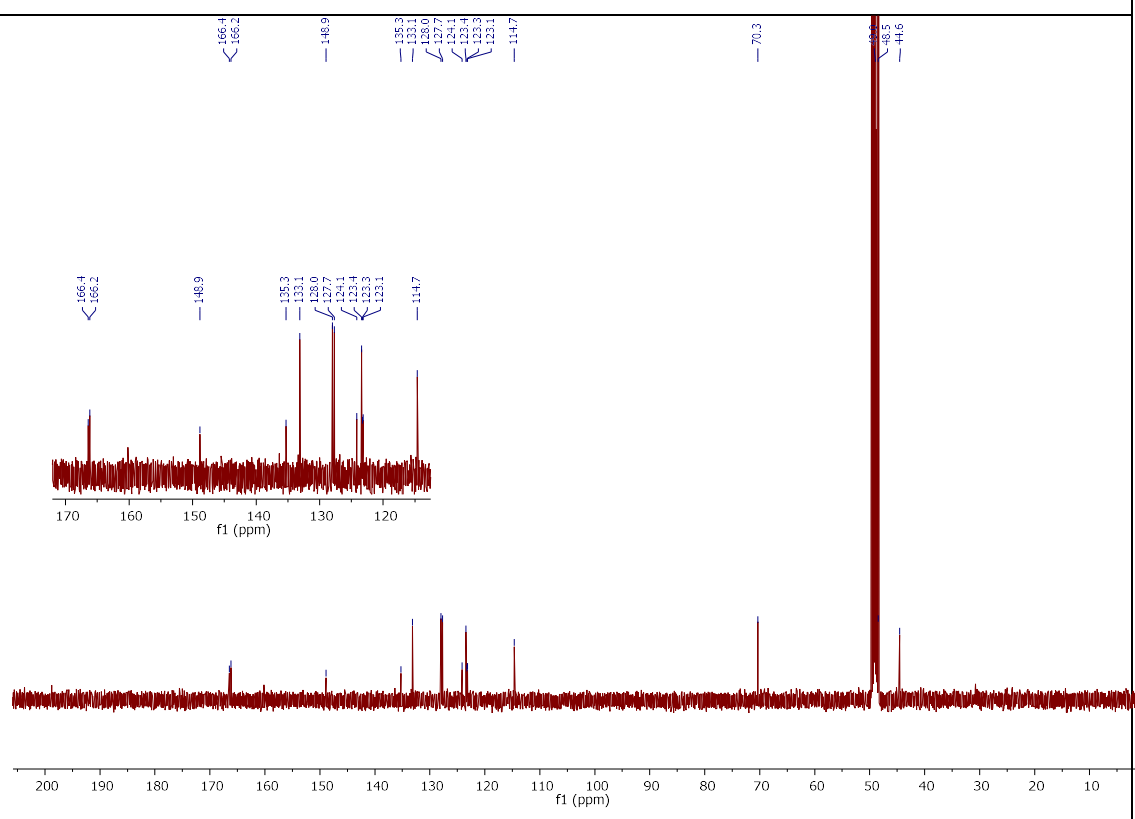
23, ¹³C RMN (101 MHz, DMSO-d₆)



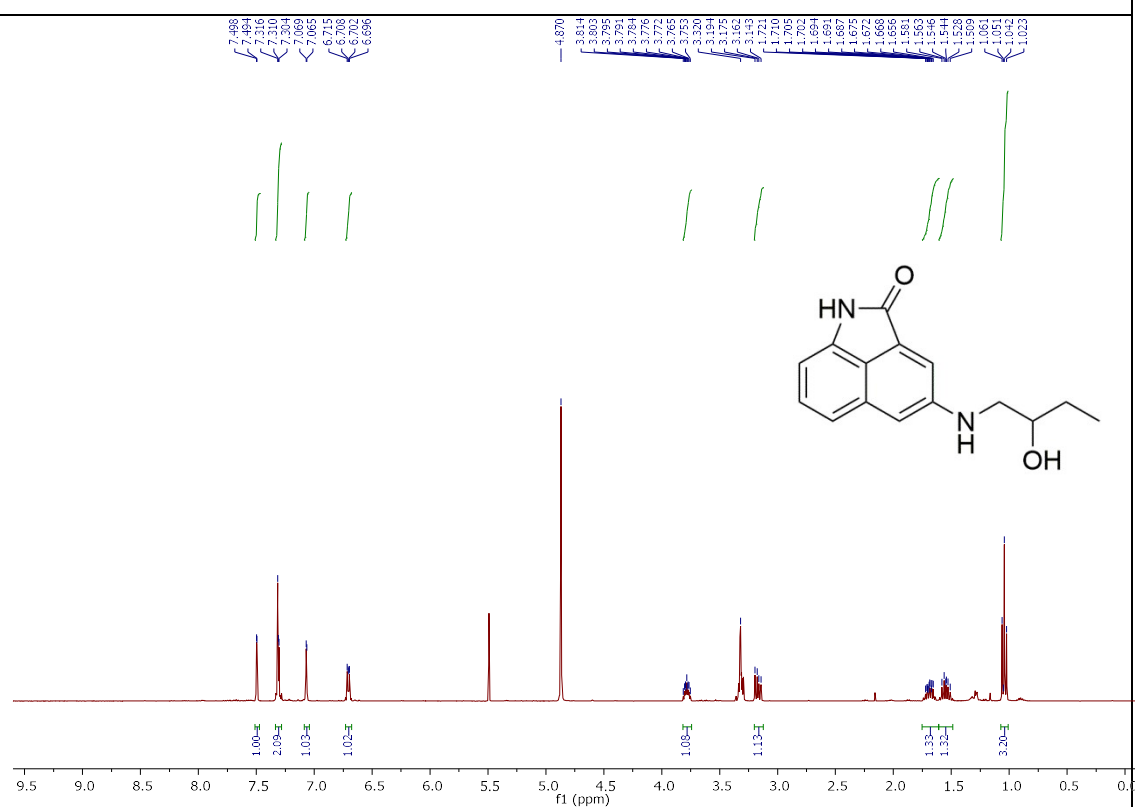
24, ¹H RMN (400 MHz, CD₃OD)



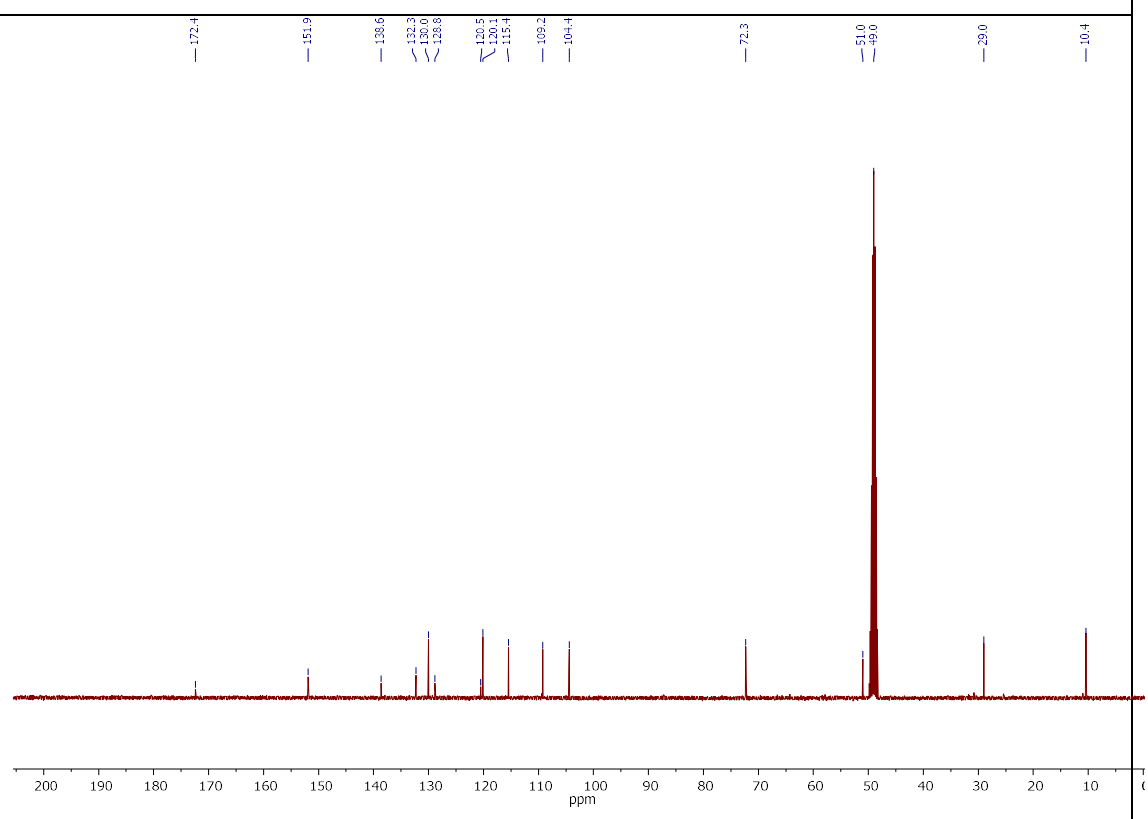
24, ¹³C RMN (101 MHz, CD₃OD)



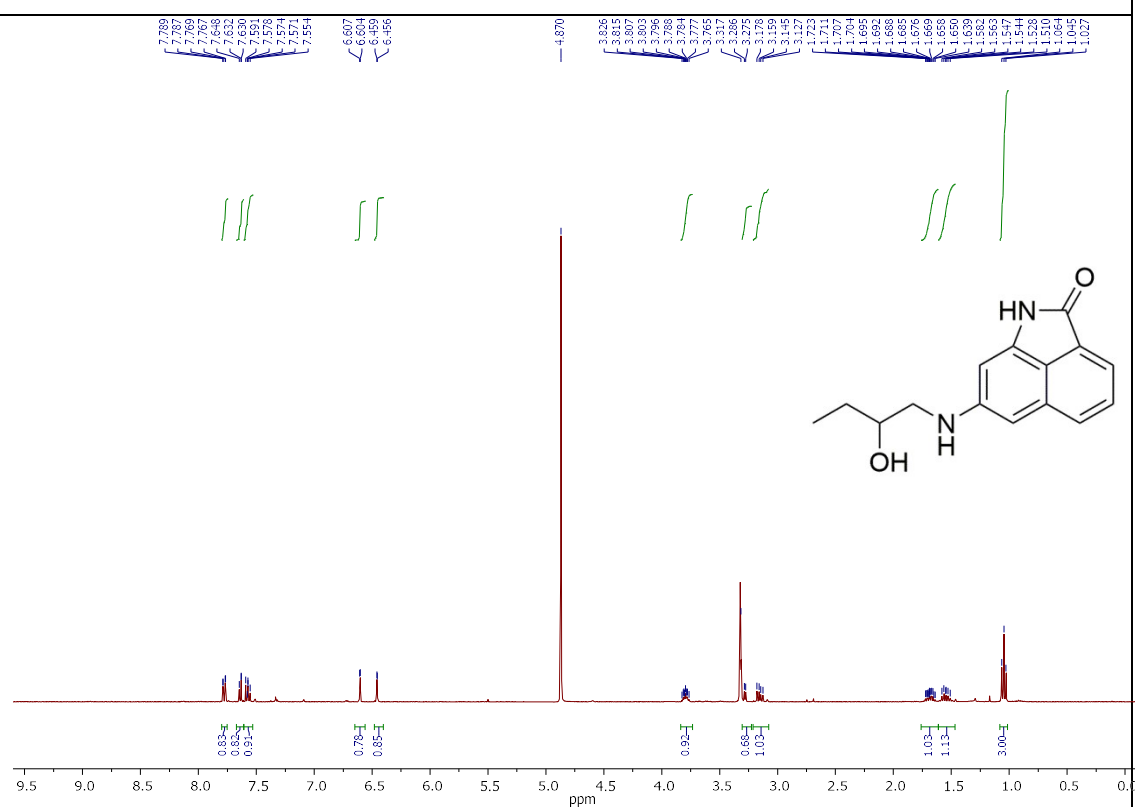
25, ¹H RMN (400 MHz, CD₃OD)



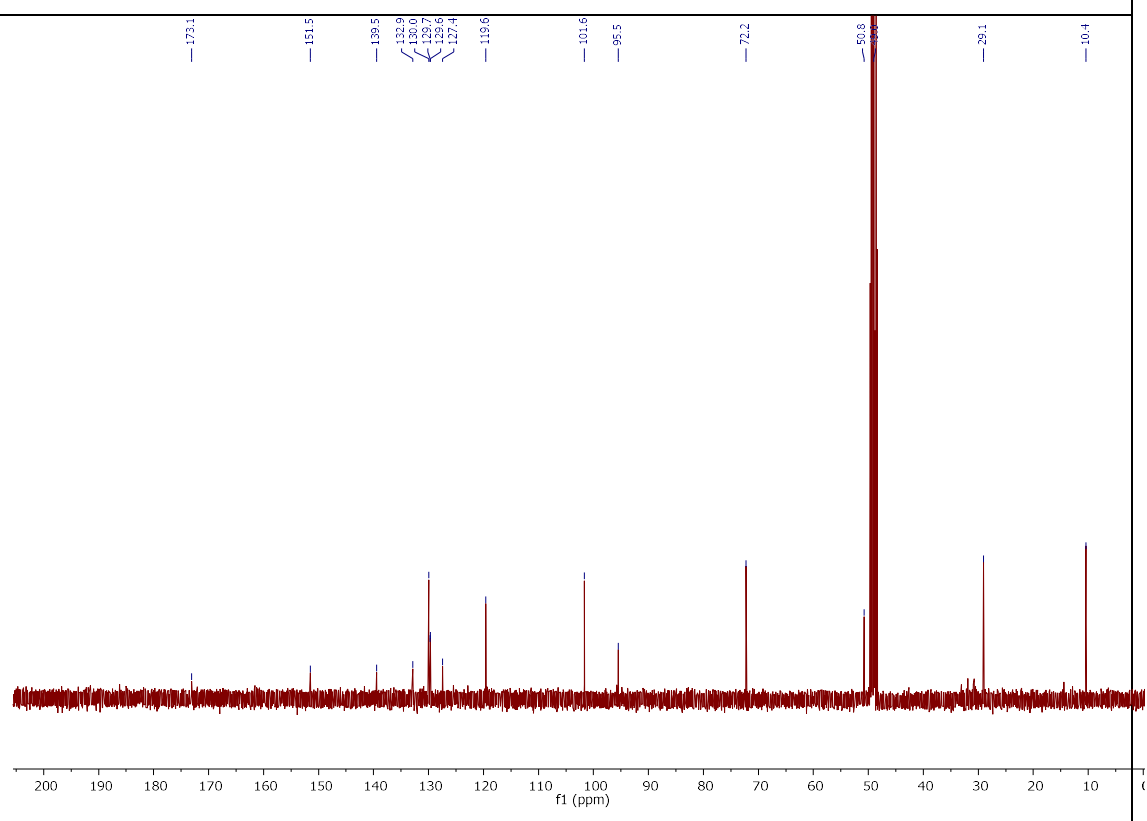
25, ¹³C RMN (101 MHz, CD₃OD)



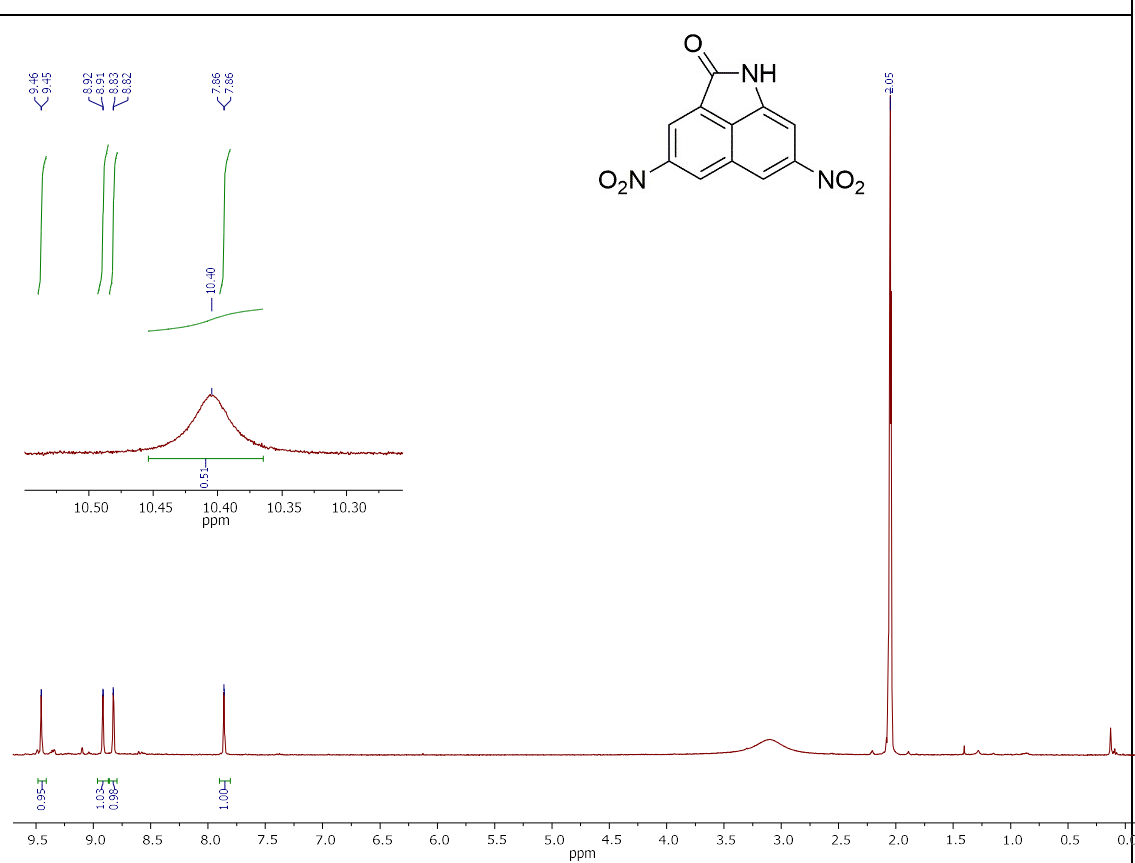
26, ¹H RMN (400 MHz, CD₃OD)



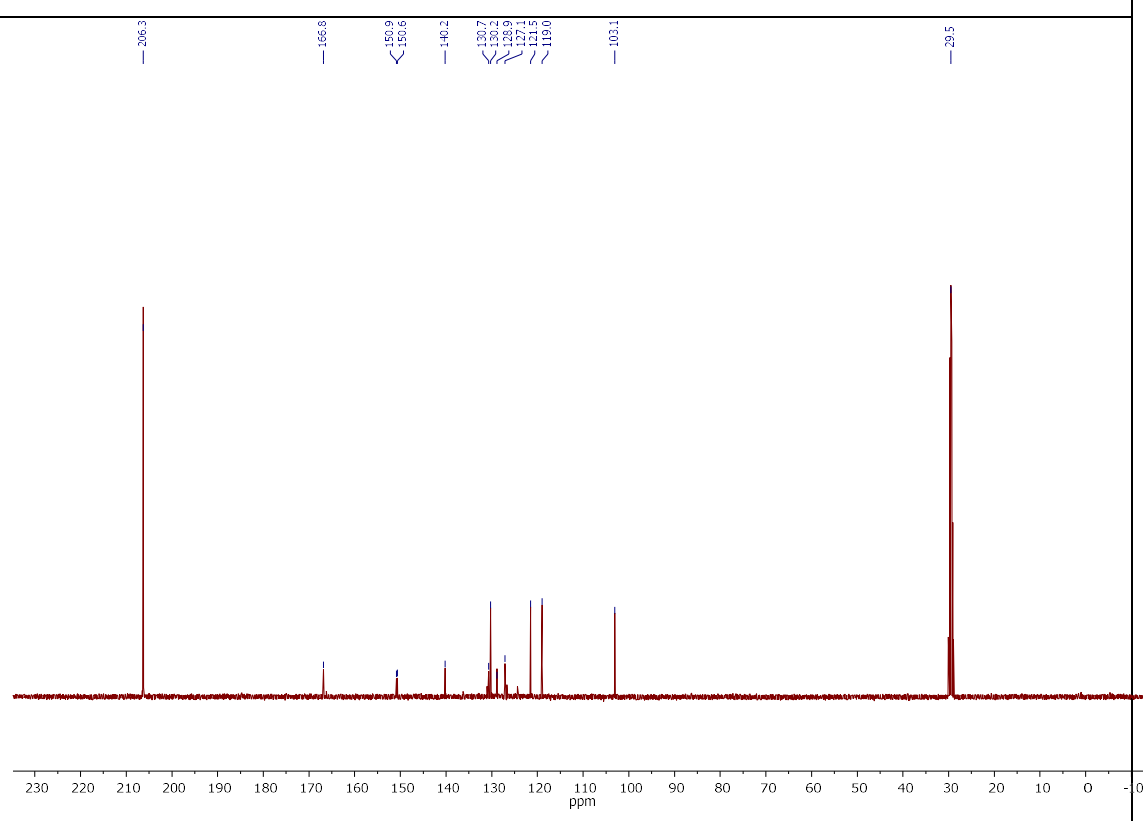
26, ¹³C RMN (101 MHz, CD₃OD)



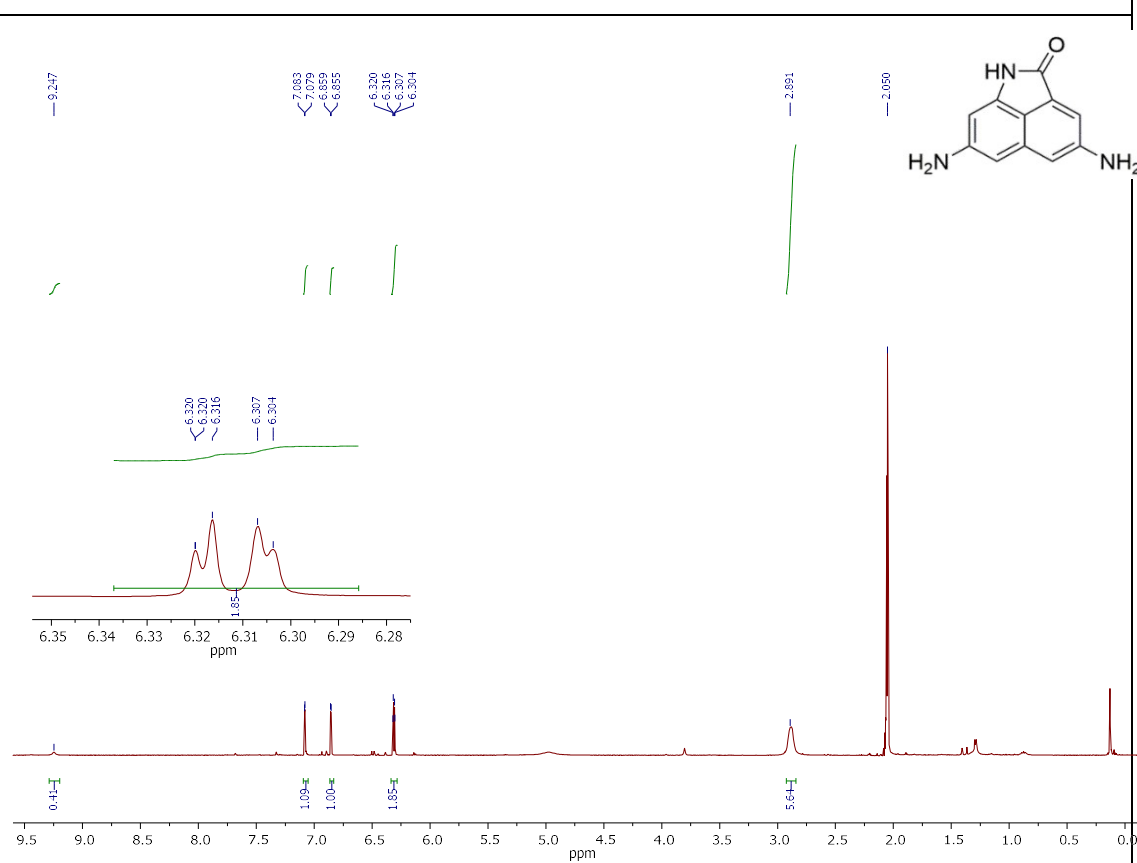
27, ¹H RMN (400 MHz, acetona-d₆)



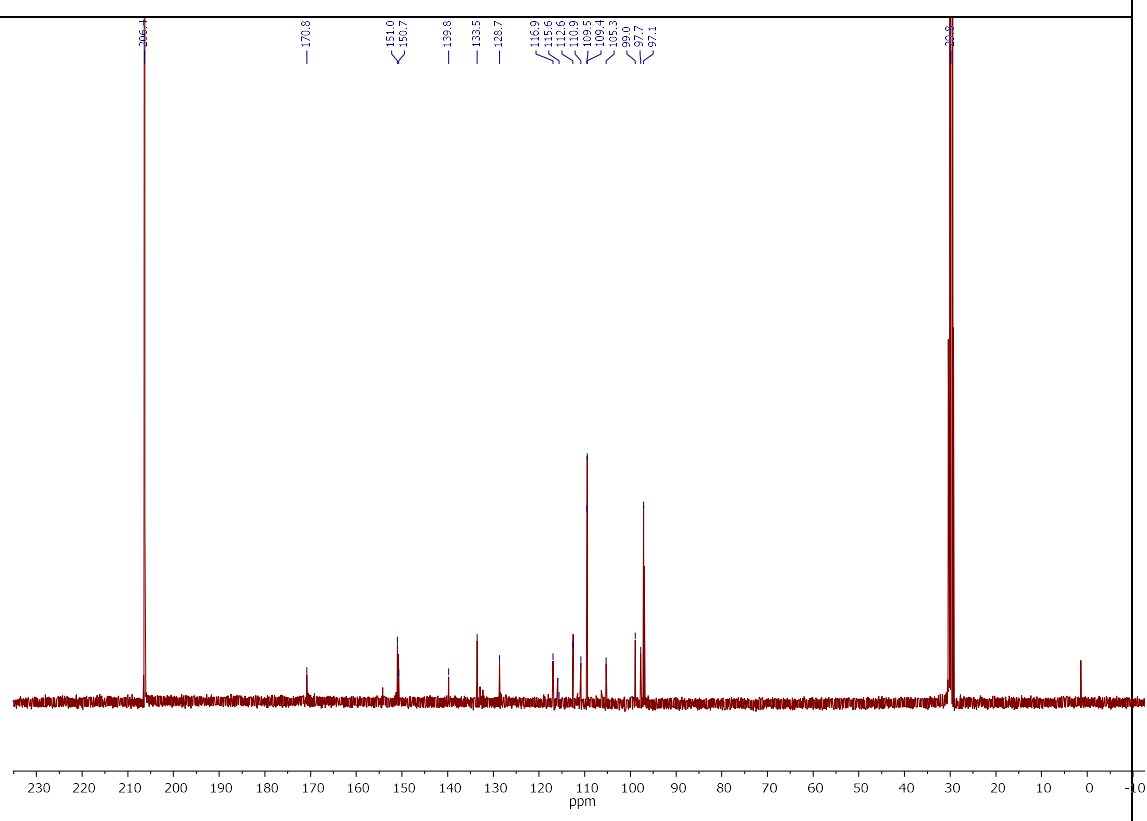
27, ¹³C RMN (101 MHz, acetona-d₆)



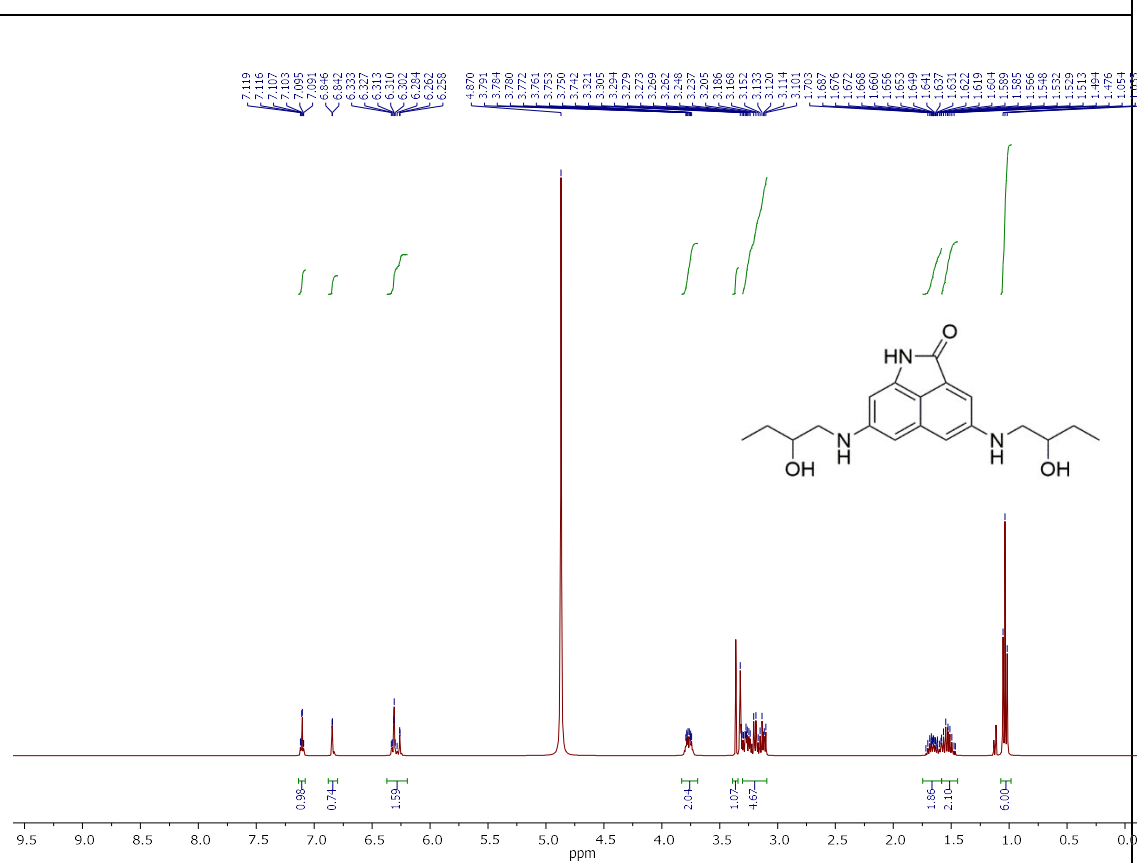
28, ¹H RMN (400 MHz, acetona-d₆)



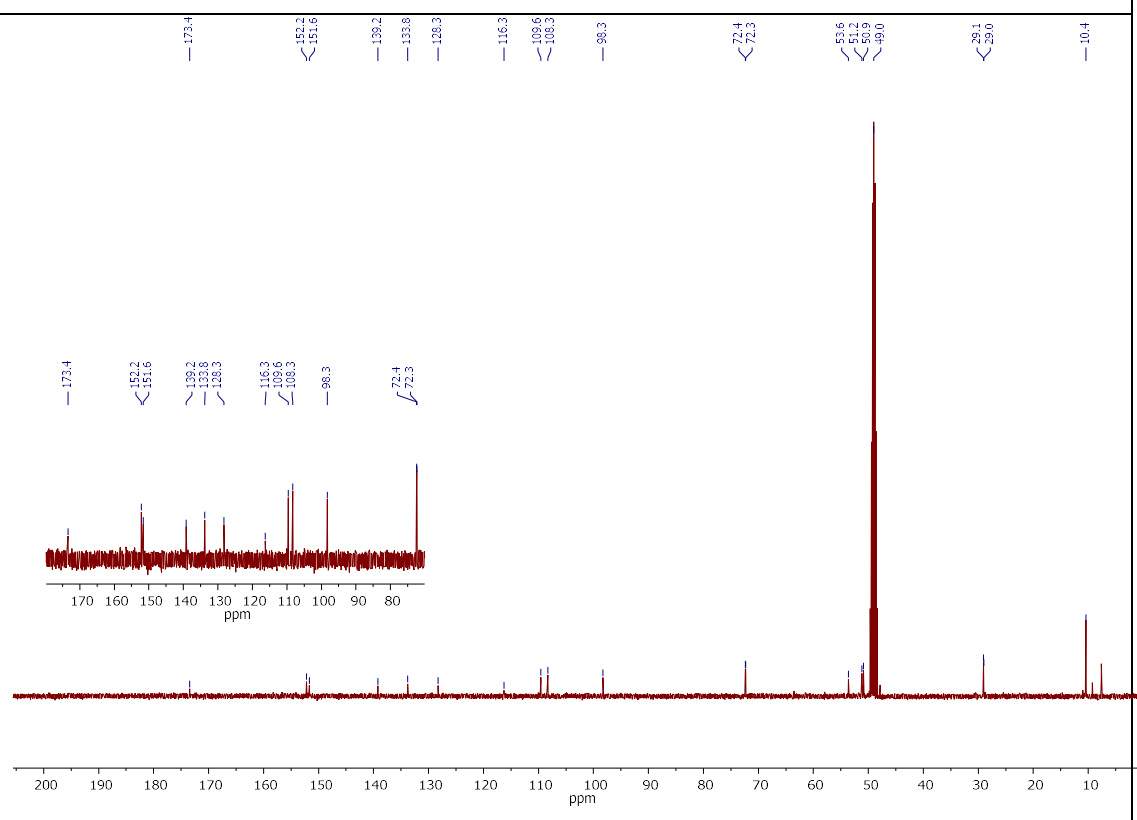
28, ¹³C RMN (101 MHz, acetona-d₆)



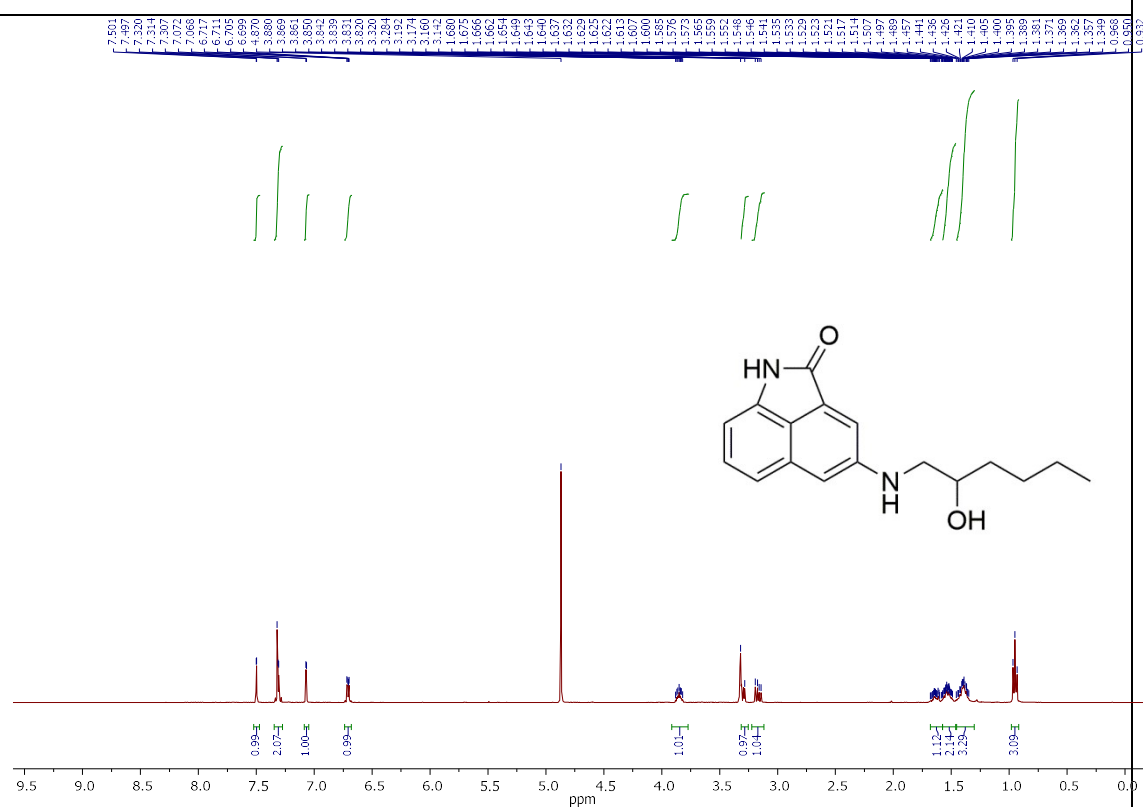
29, ¹H RMN (400 MHz, CD₃OD)



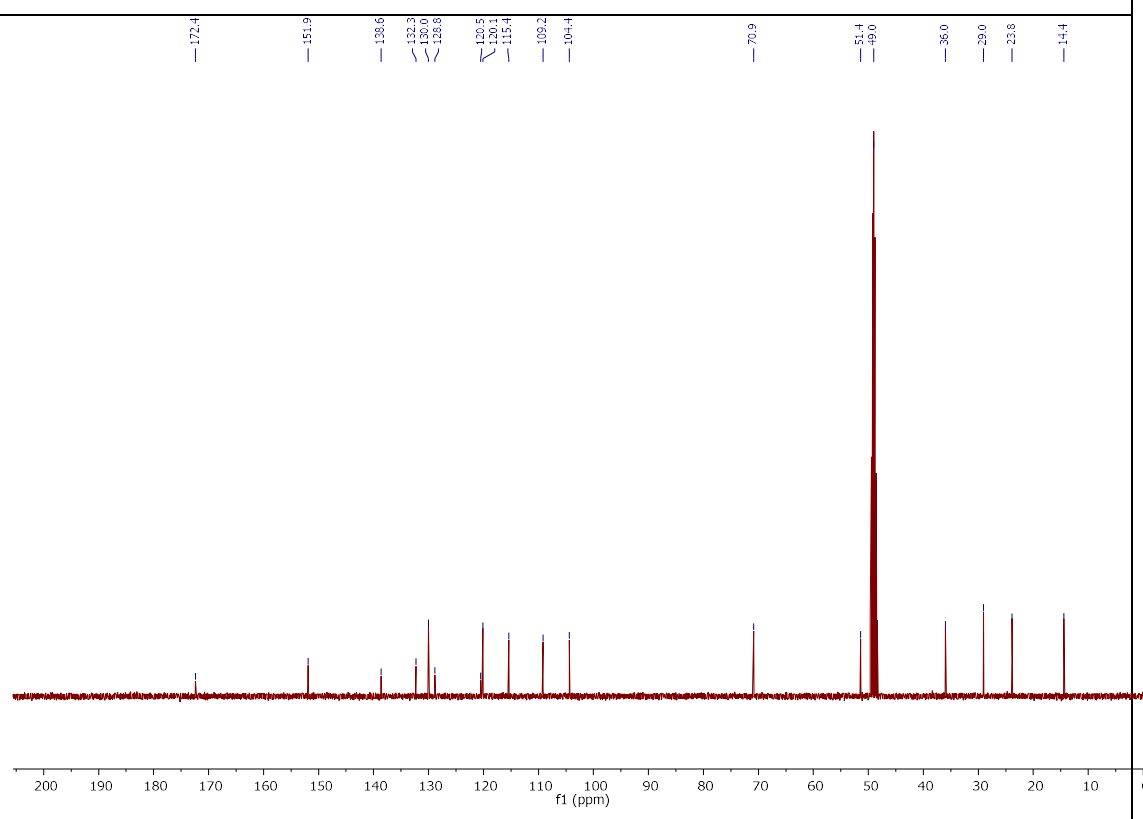
29, ¹³C RMN (101 MHz, CD₃OD)



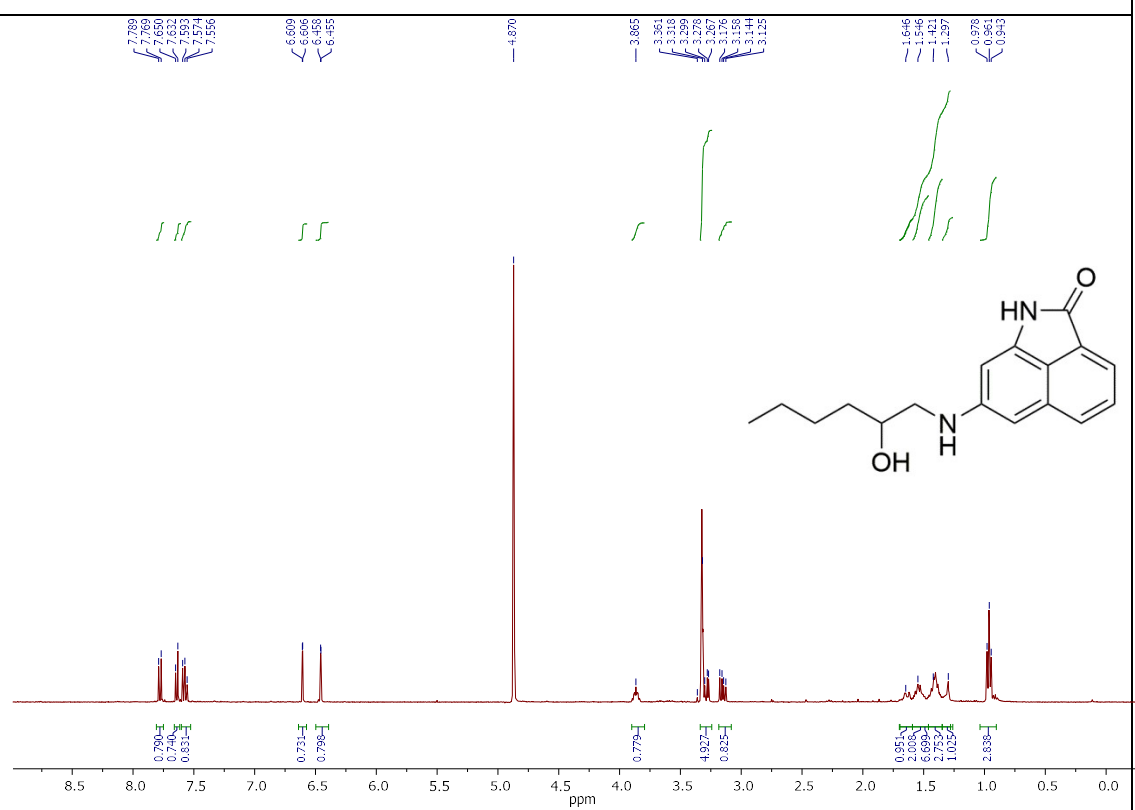
30, ¹H RMN (400 MHz, CD₃OD)



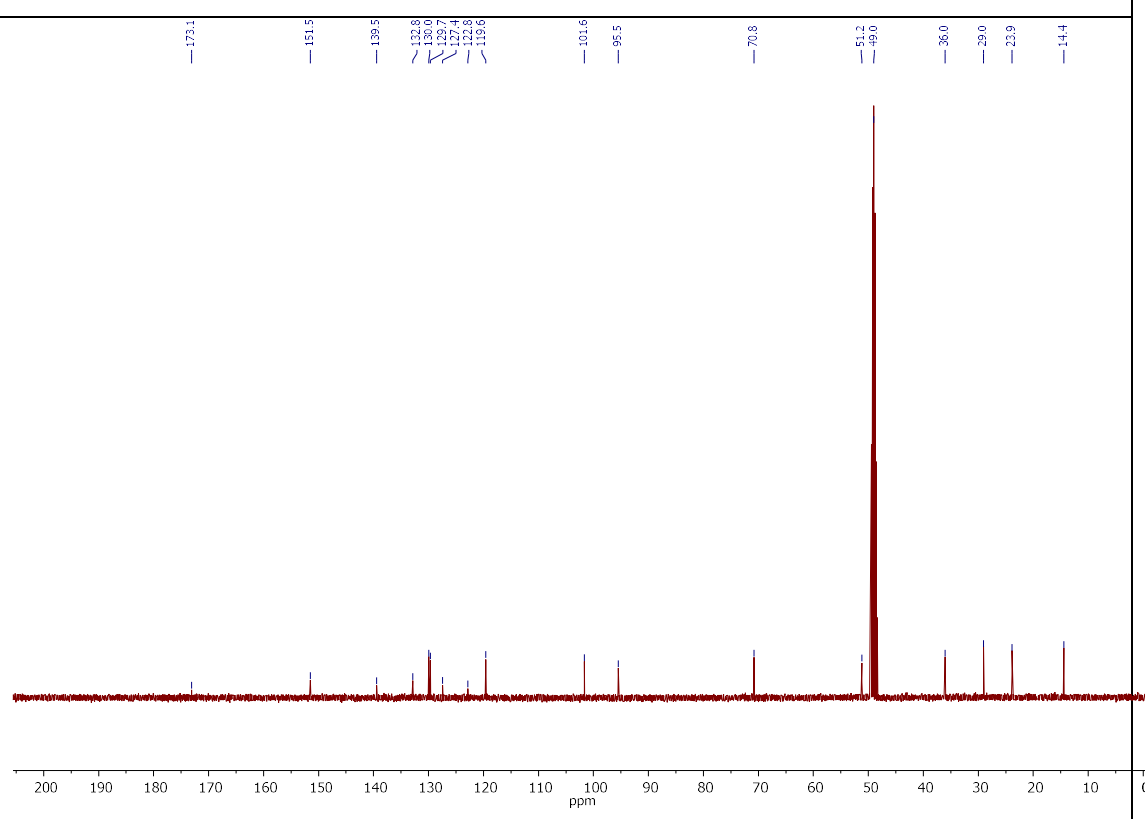
30, ¹³C RMN (101 MHz, CD₃OD)



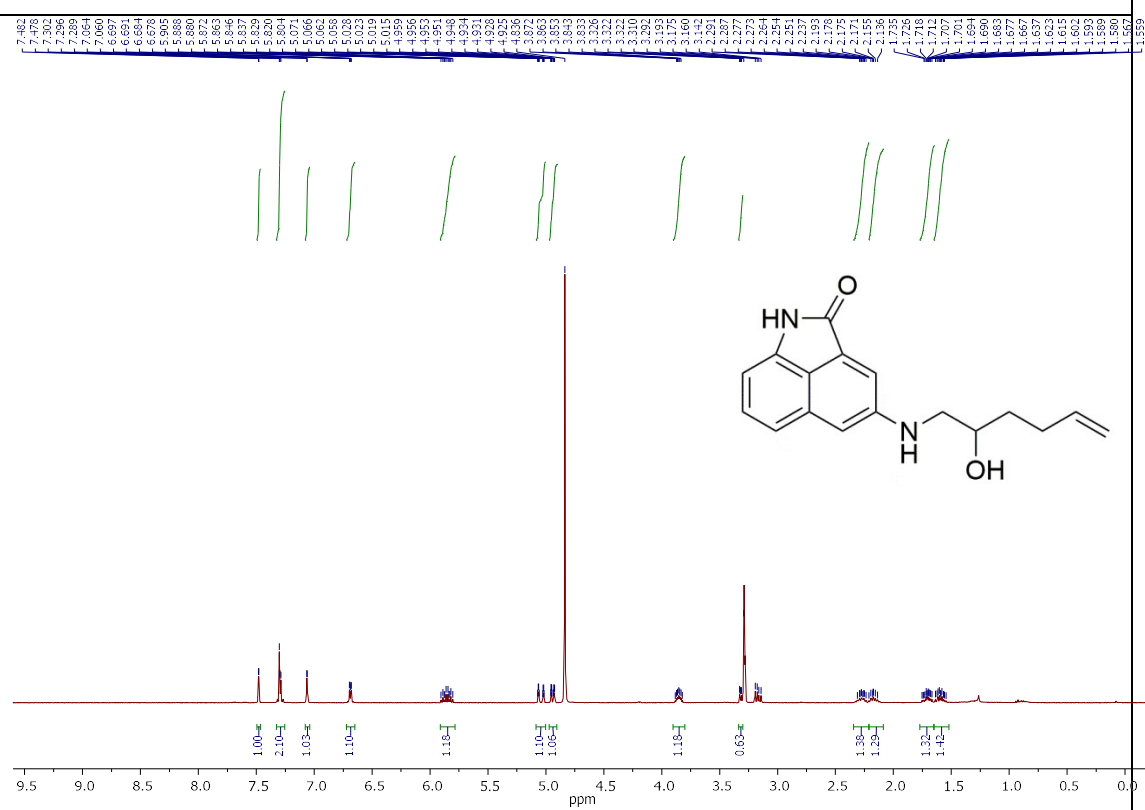
31, ¹H RMN (400 MHz, CD₃OD)



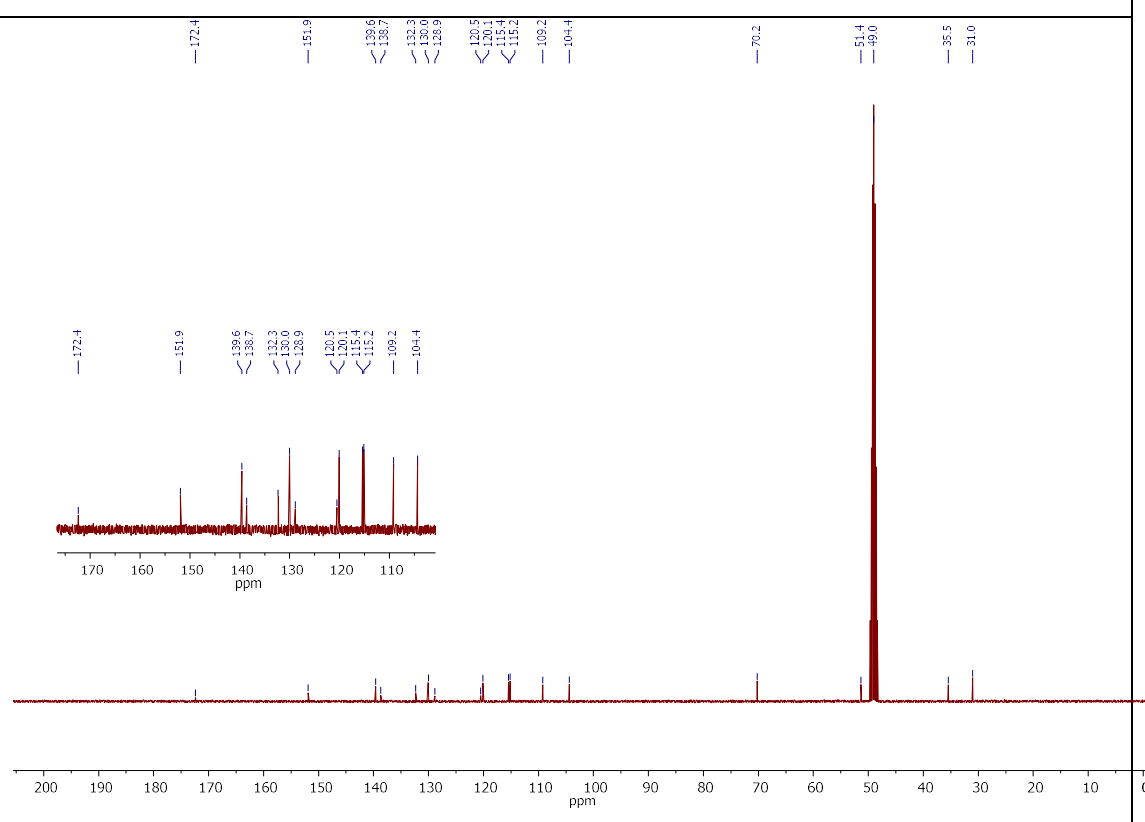
31, ¹³C RMN (101 MHz, CD₃OD)



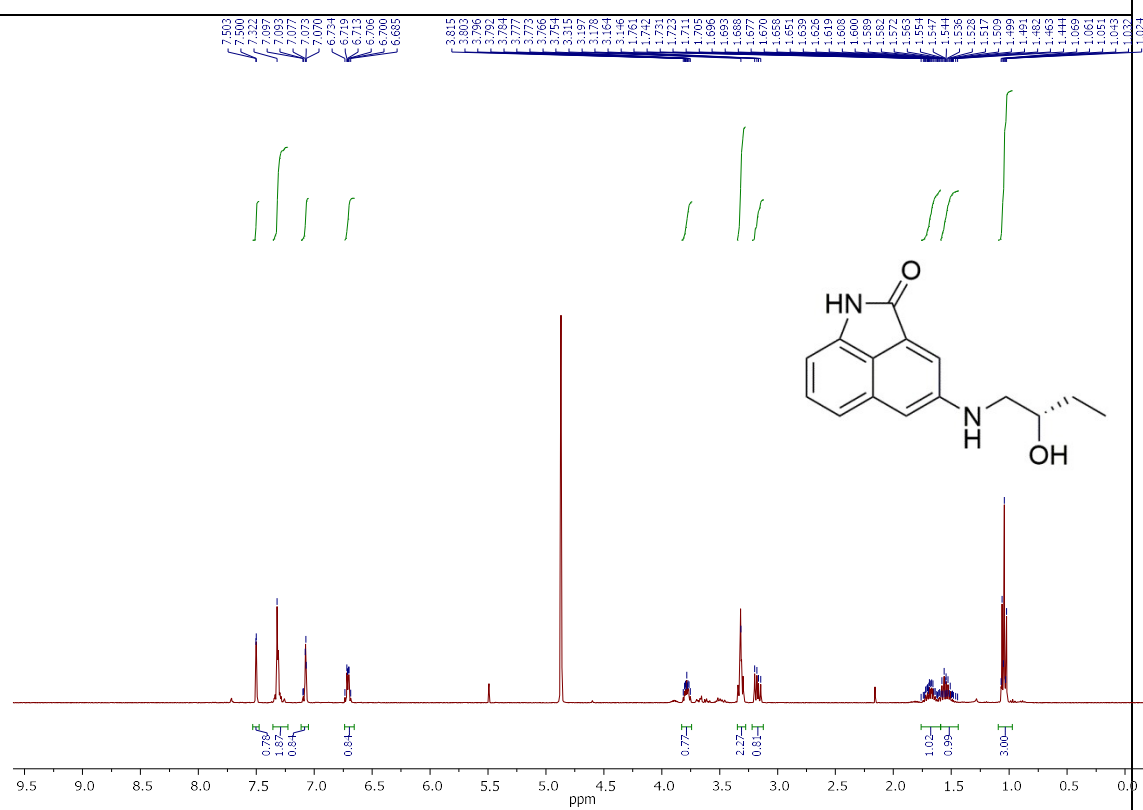
32, ¹H RMN (400 MHz, CD₃OD)



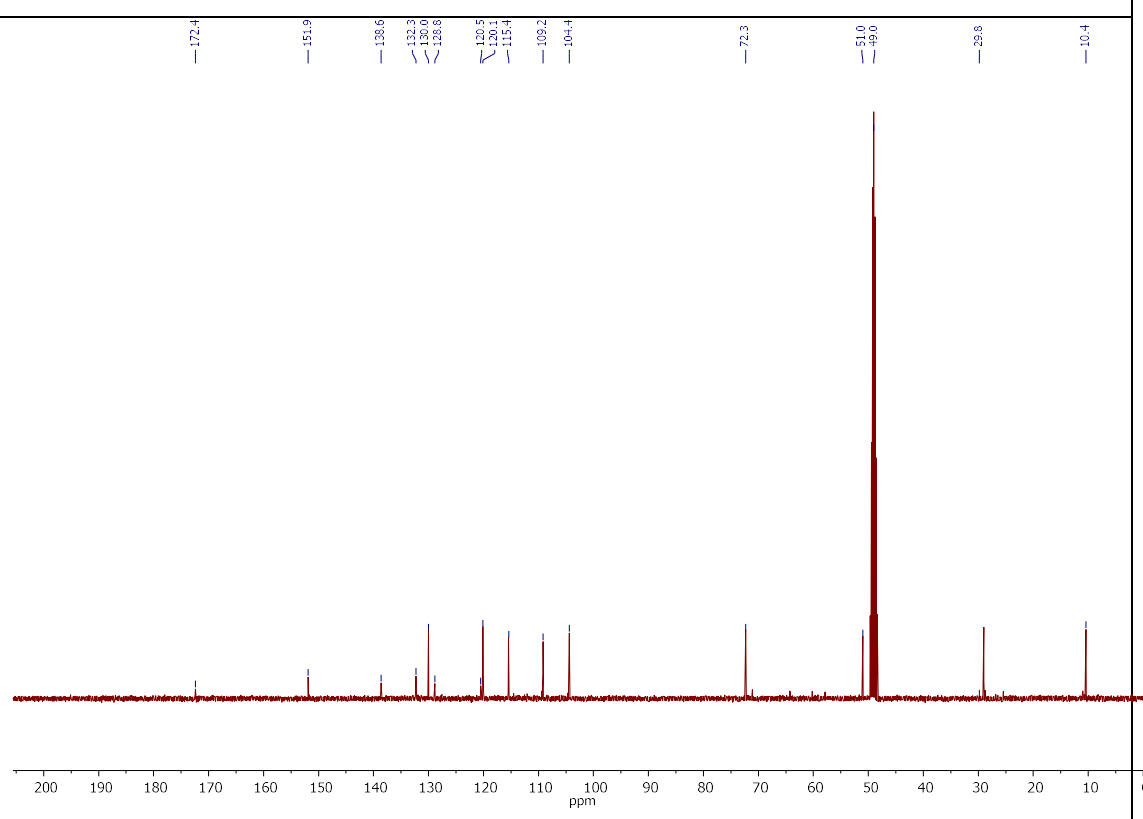
32, ¹³C RMN (101 MHz, CD₃OD)



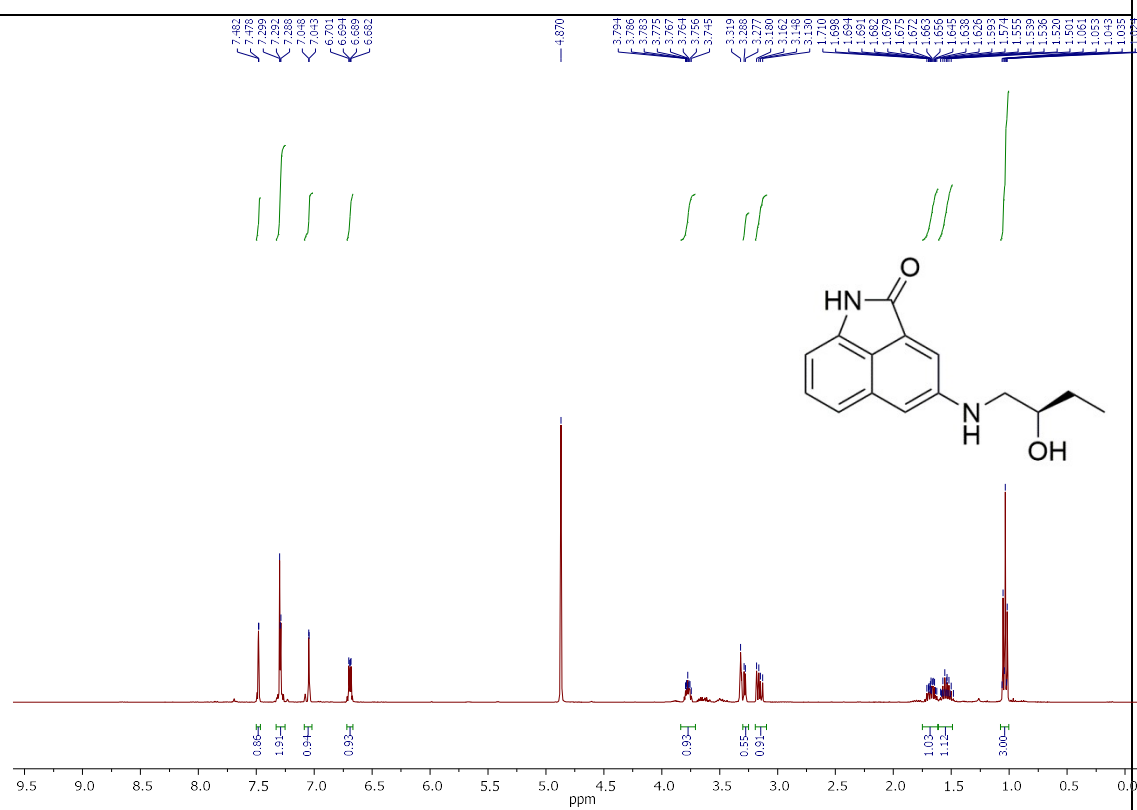
33, ¹H RMN (400 MHz, CD₃OD)



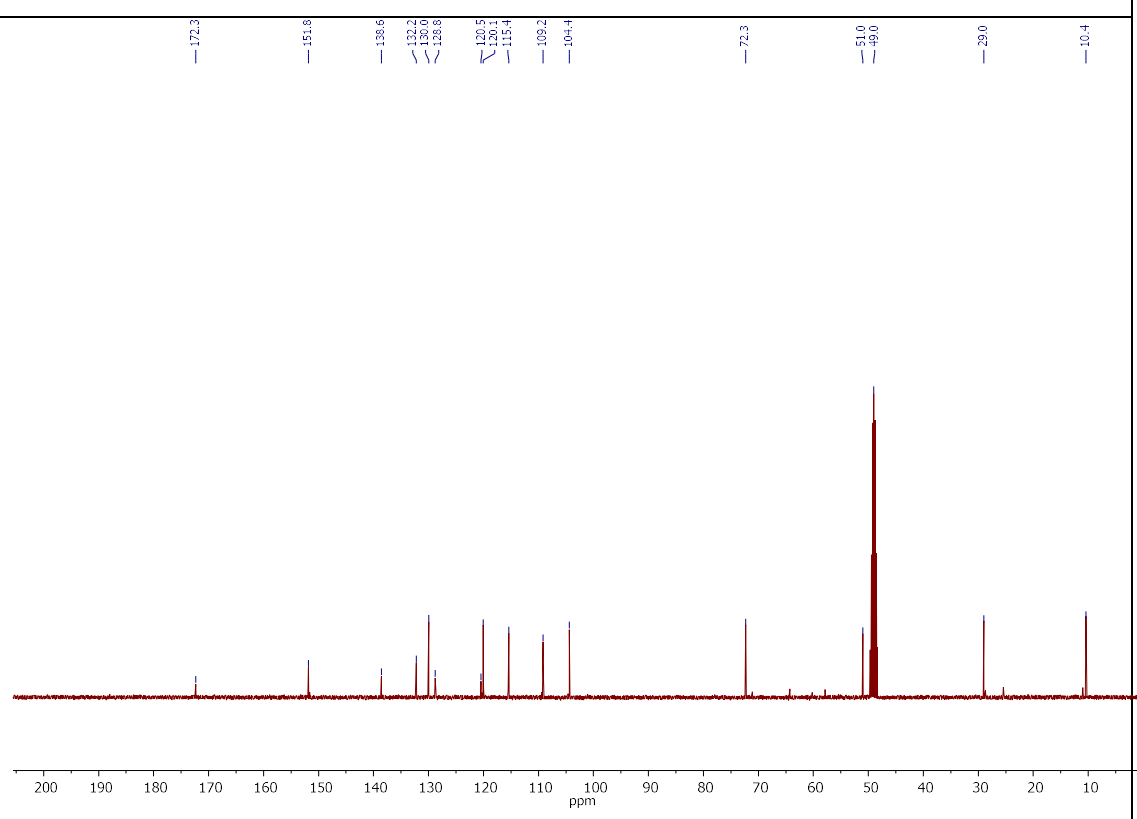
33, ¹³C RMN (101 MHz, CD₃OD)



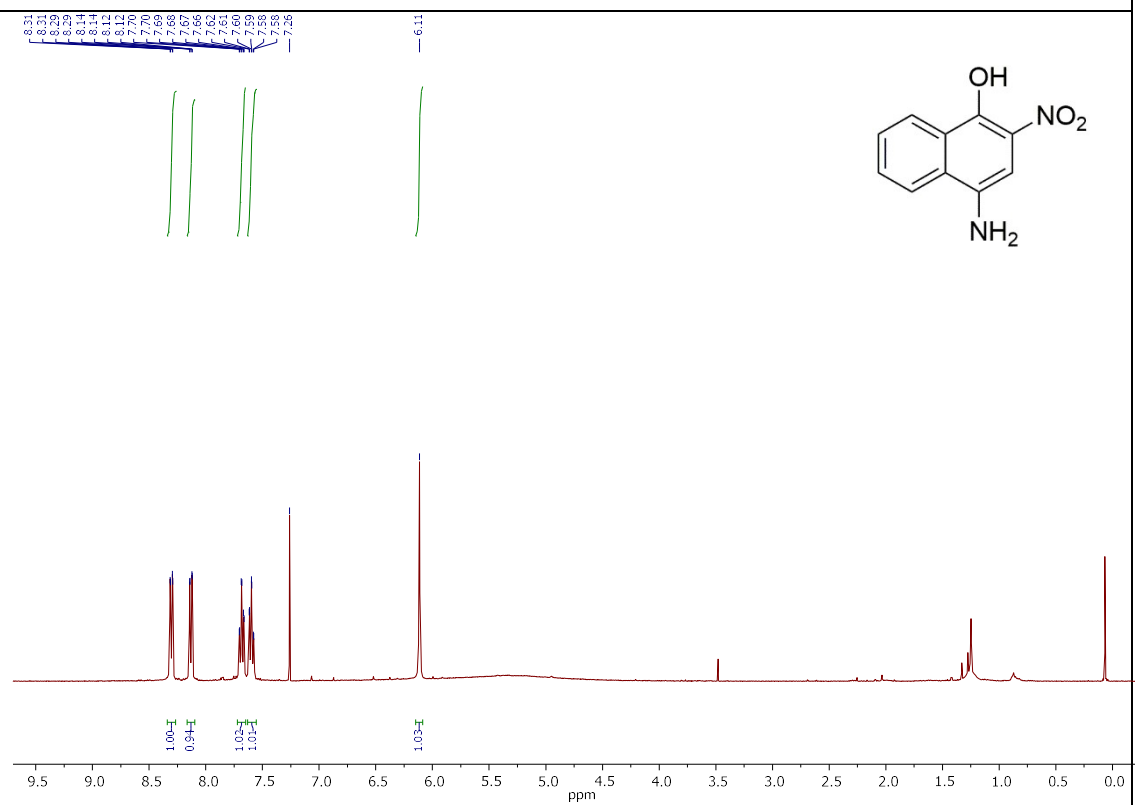
34, ¹H RMN (400 MHz, CD₃OD)



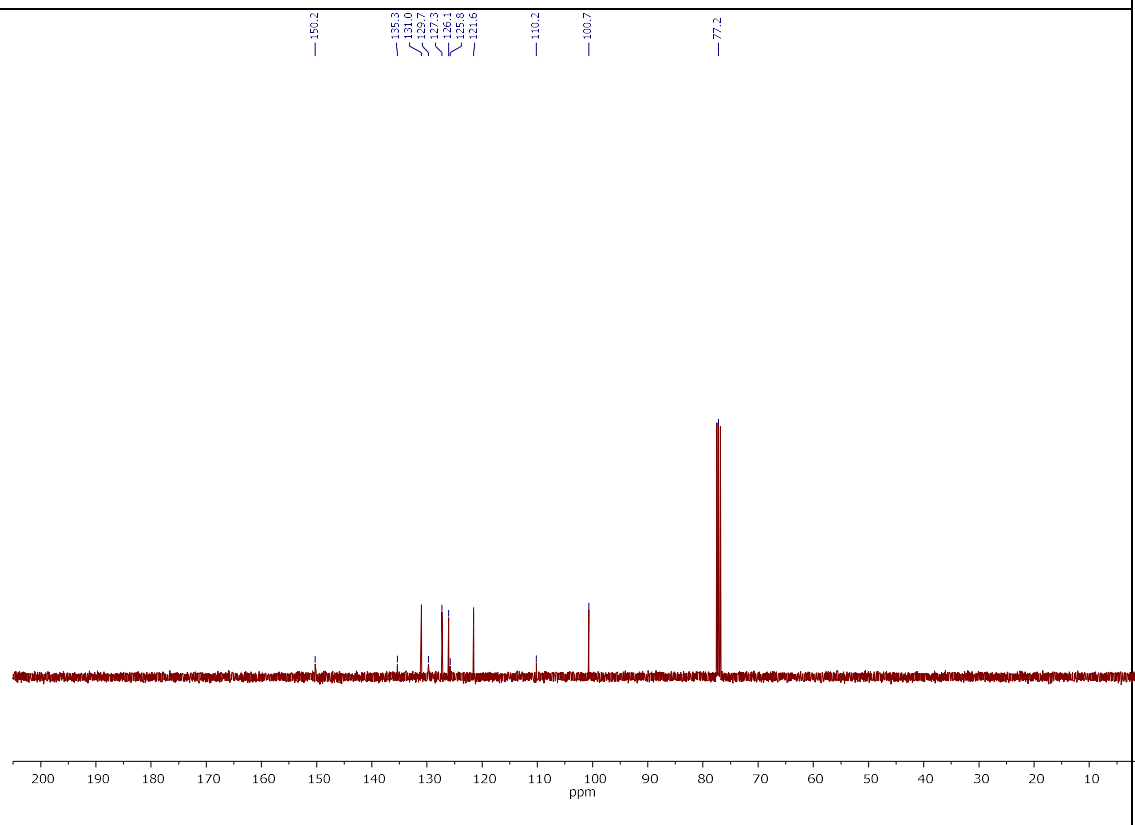
34, ¹³C RMN (101 MHz, CD₃OD)



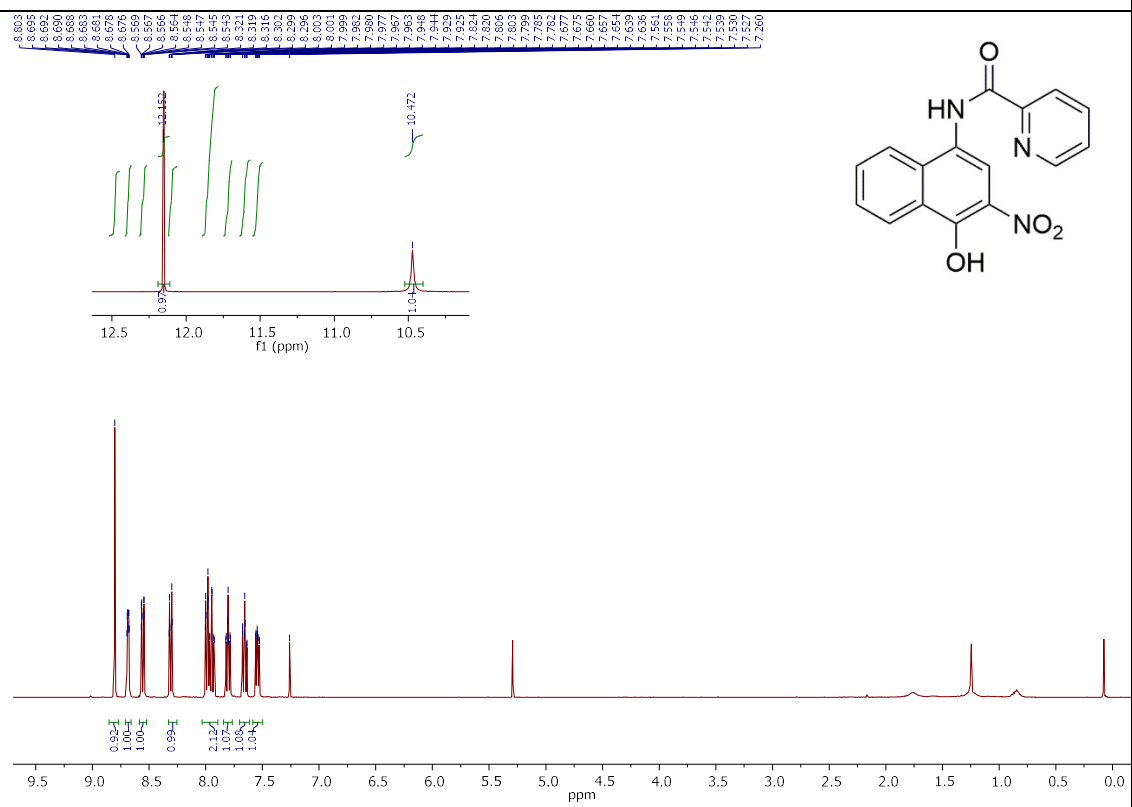
35, ¹H RMN (400 MHz, CDCl₃)



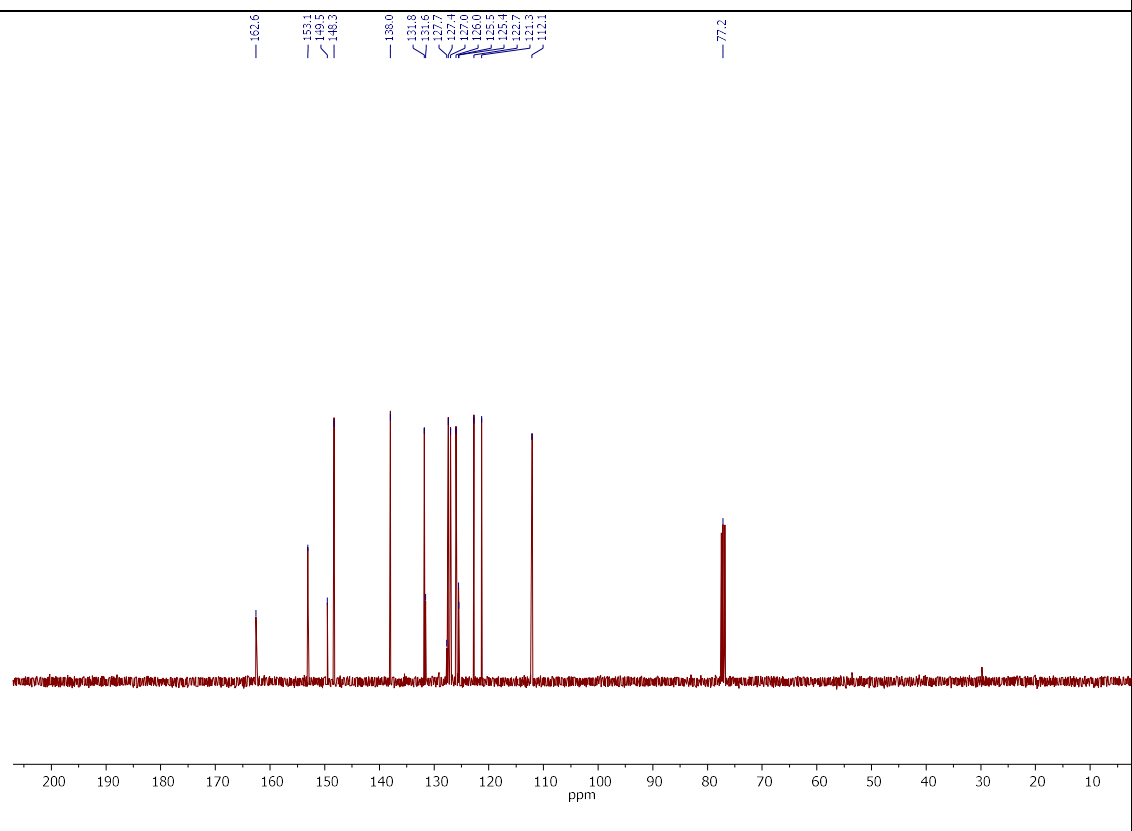
35, ¹³C RMN (101 MHz, CDCl₃)



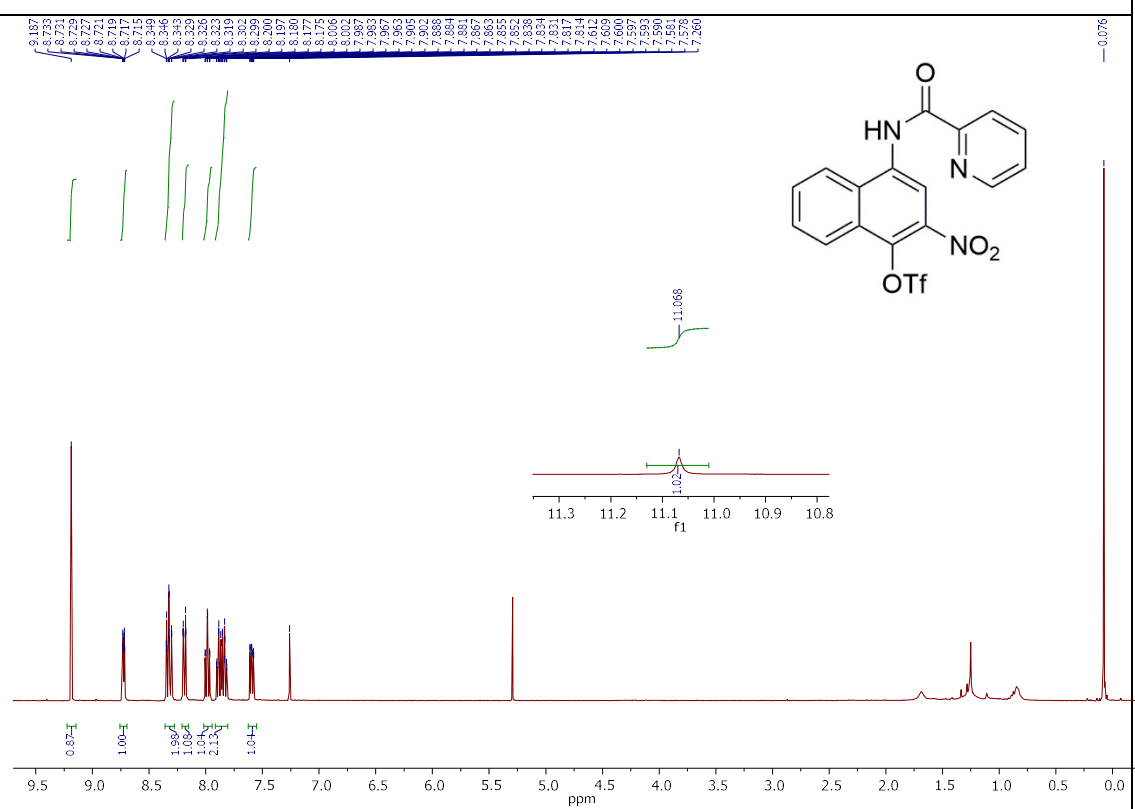
36, ^1H RMN (400 MHz, CDCl_3)



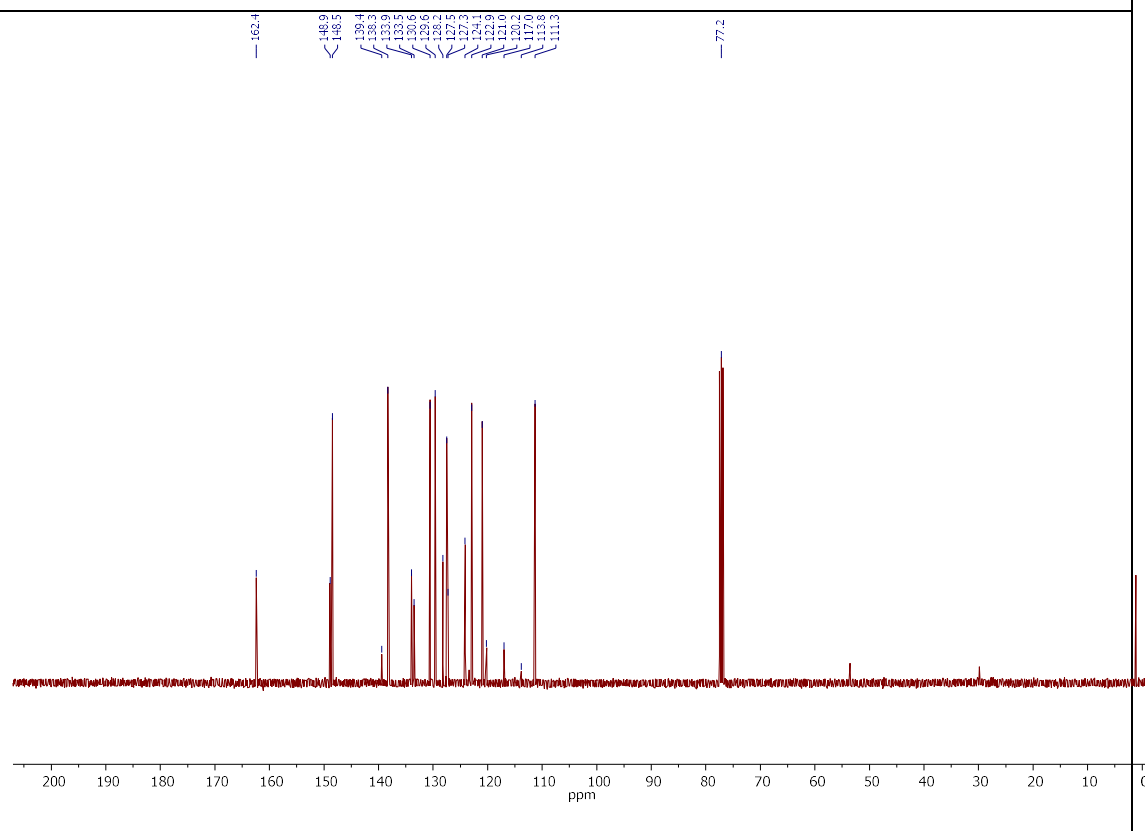
36, ^{13}C RMN (101 MHz, CDCl_3)



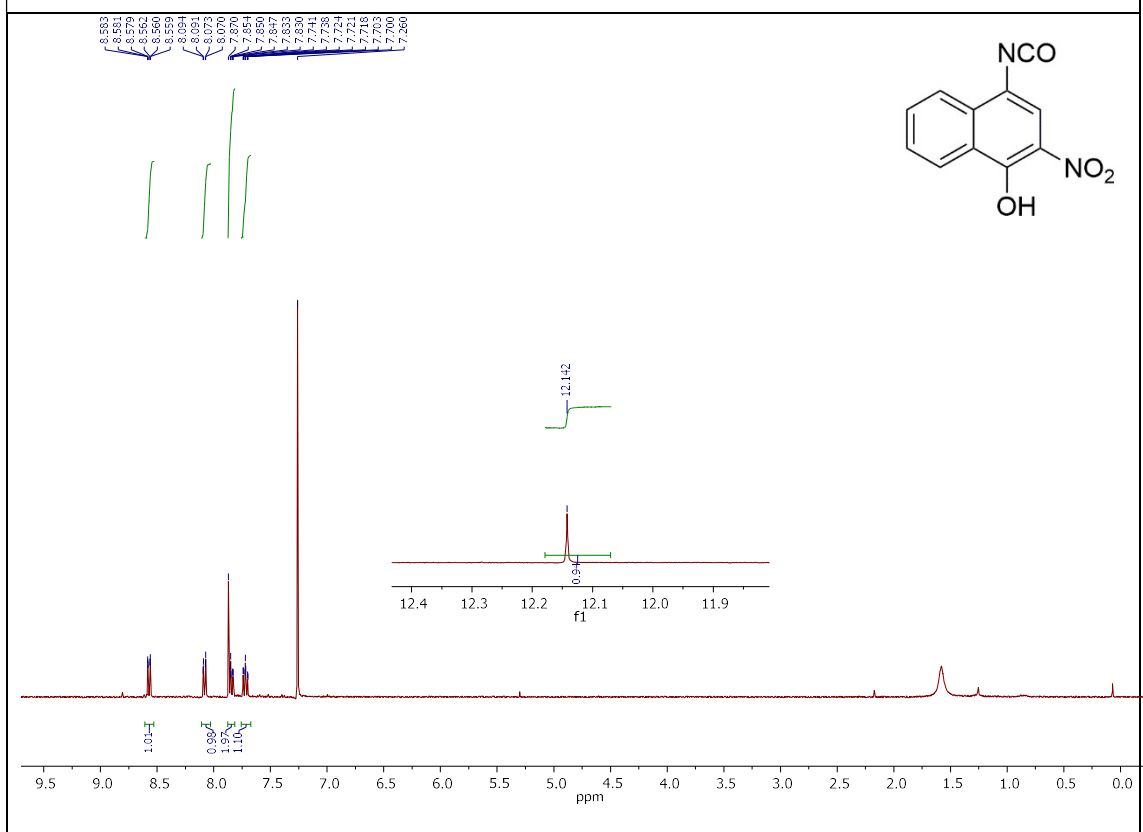
37, ¹H RMN (400 MHz, CDCl₃)



37, ¹³C RMN (101 MHz, CDCl₃)

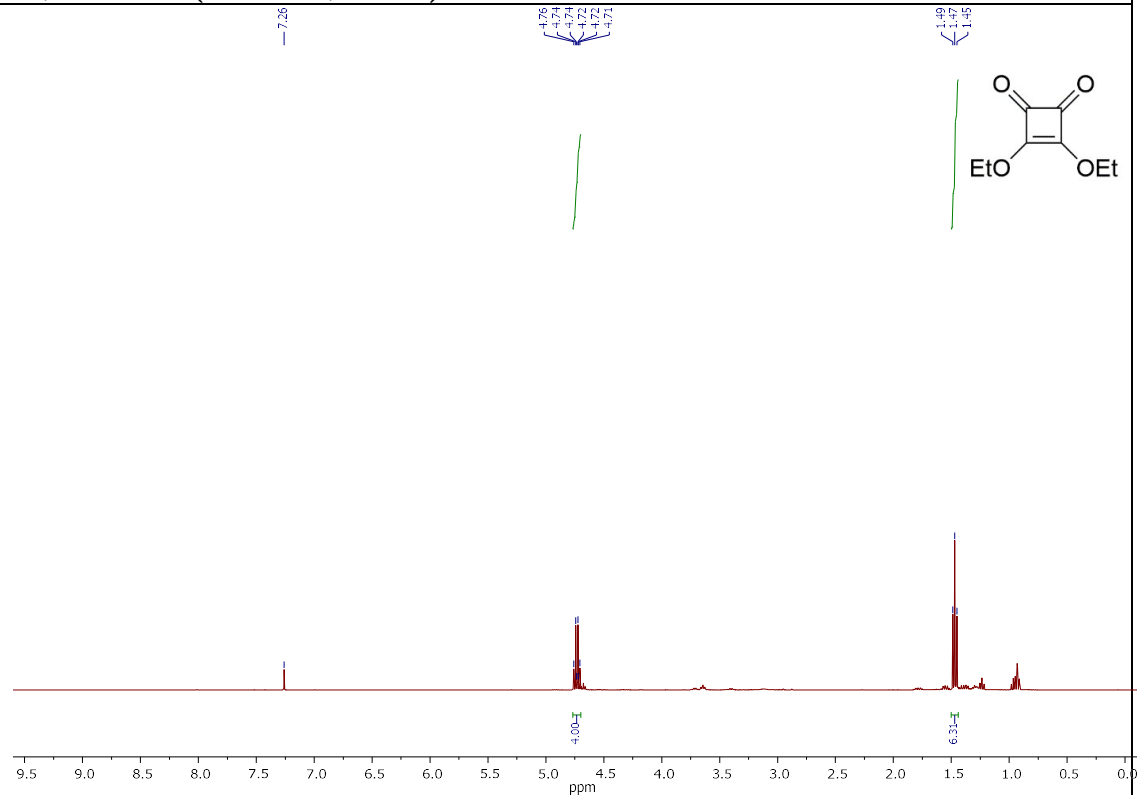


38, ¹H RMN (400 MHz, CDCl₃)

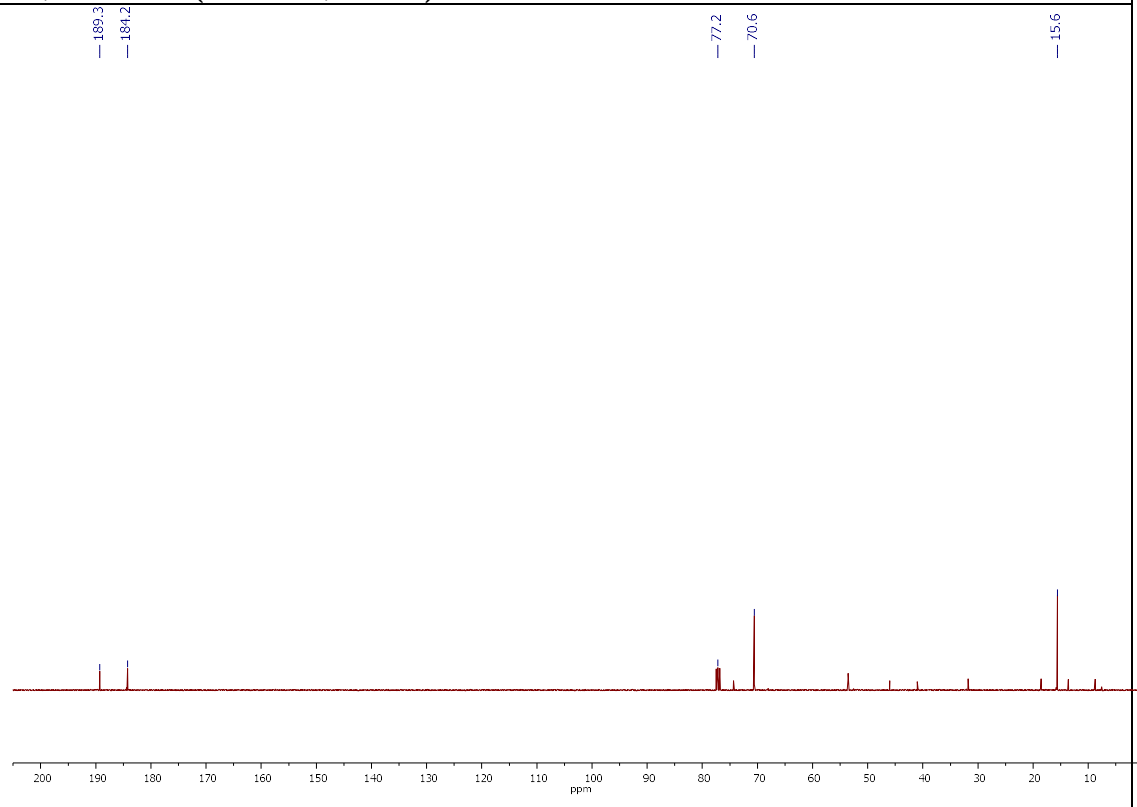


Espectros de RMN Capítulo 2

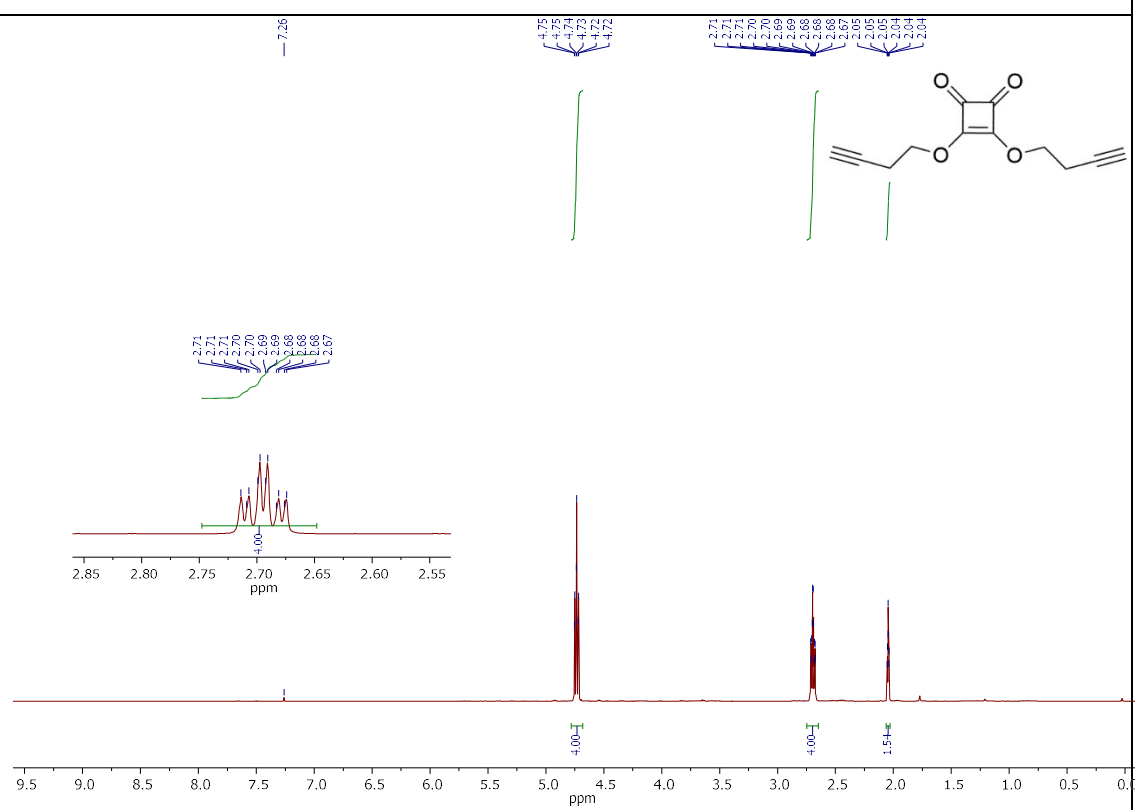
40, ^1H RMN (400 MHz, CDCl_3)



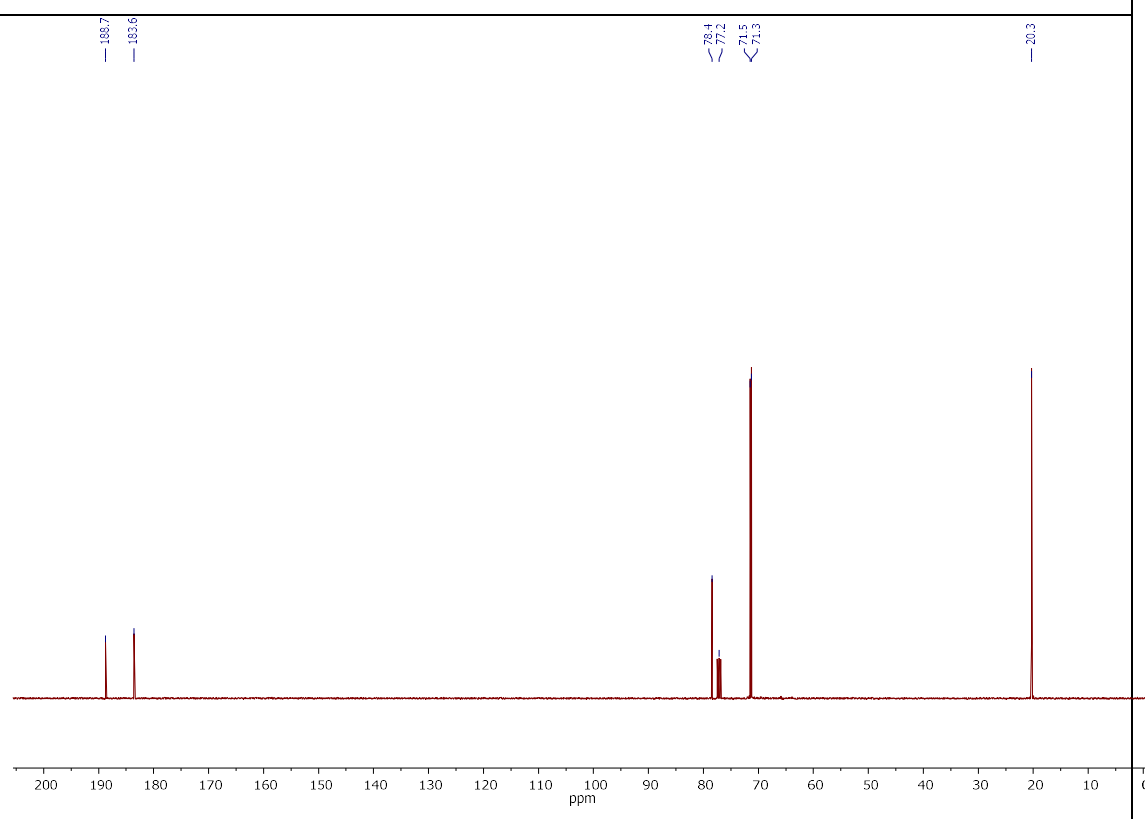
40, ^{13}C RMN (101 MHz, CDCl_3)



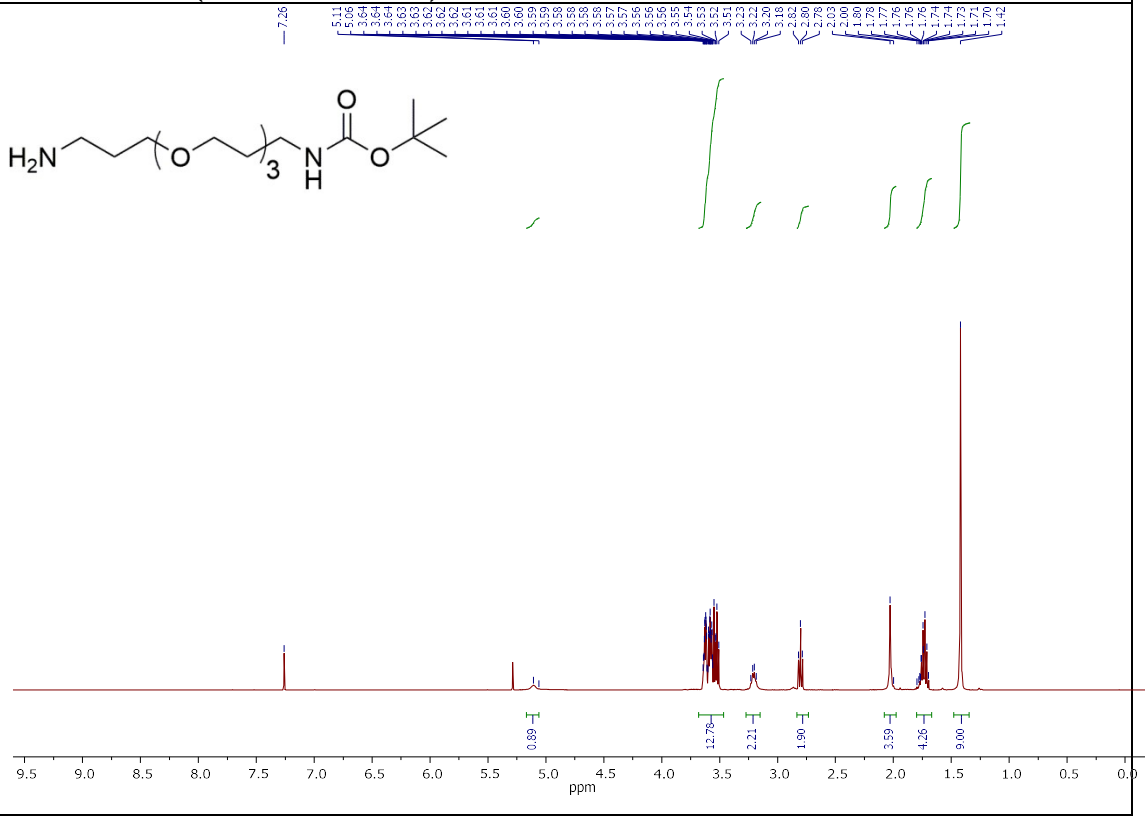
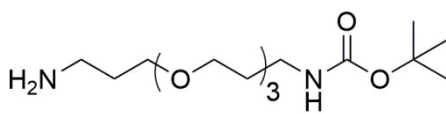
41, ¹H RMN (400 MHz, CDCl₃)



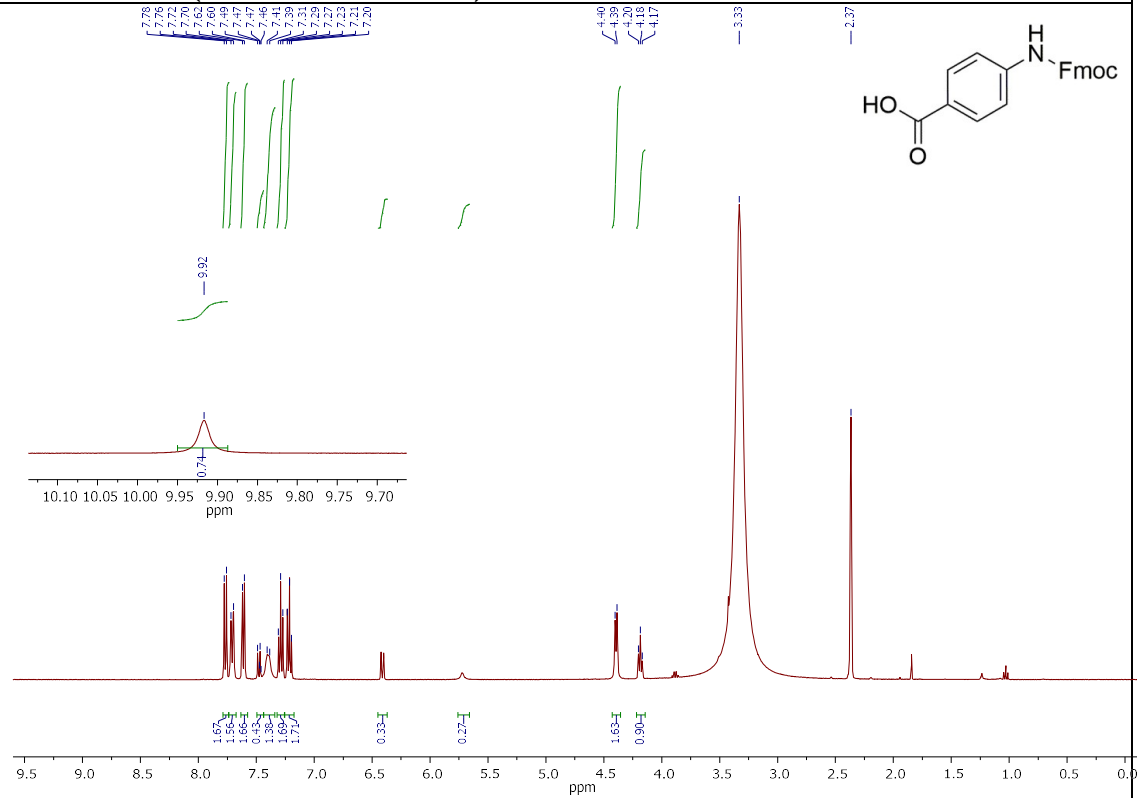
41, ¹³C RMN (101 MHz, CDCl₃)



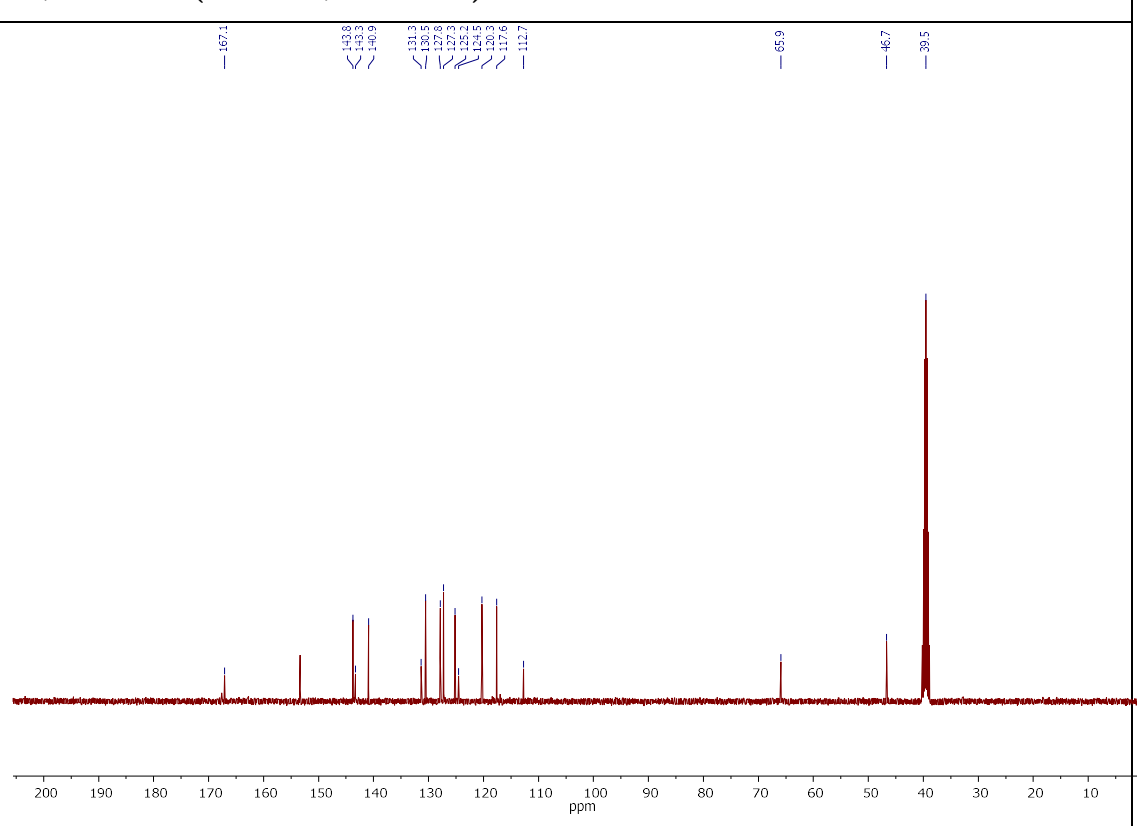
42, ¹H RMN (400 MHz, CDCl₃)



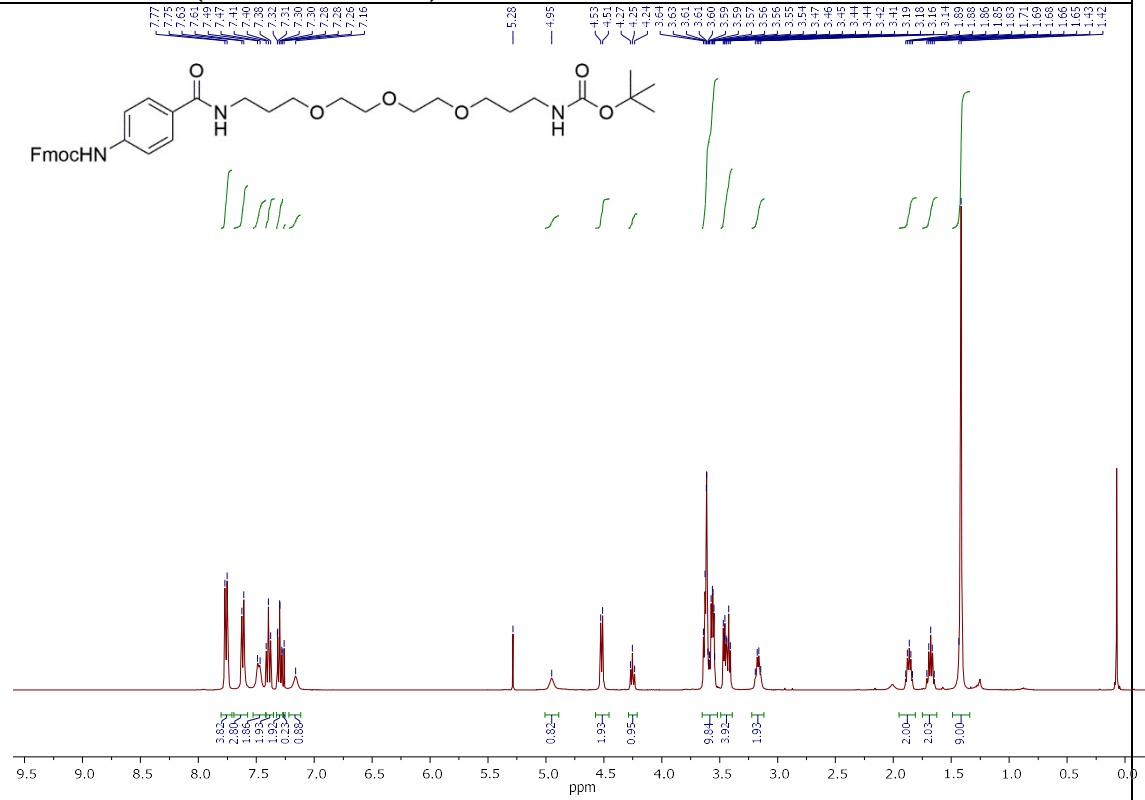
43, ¹H RMN (400 MHz, DMSO-d₆)



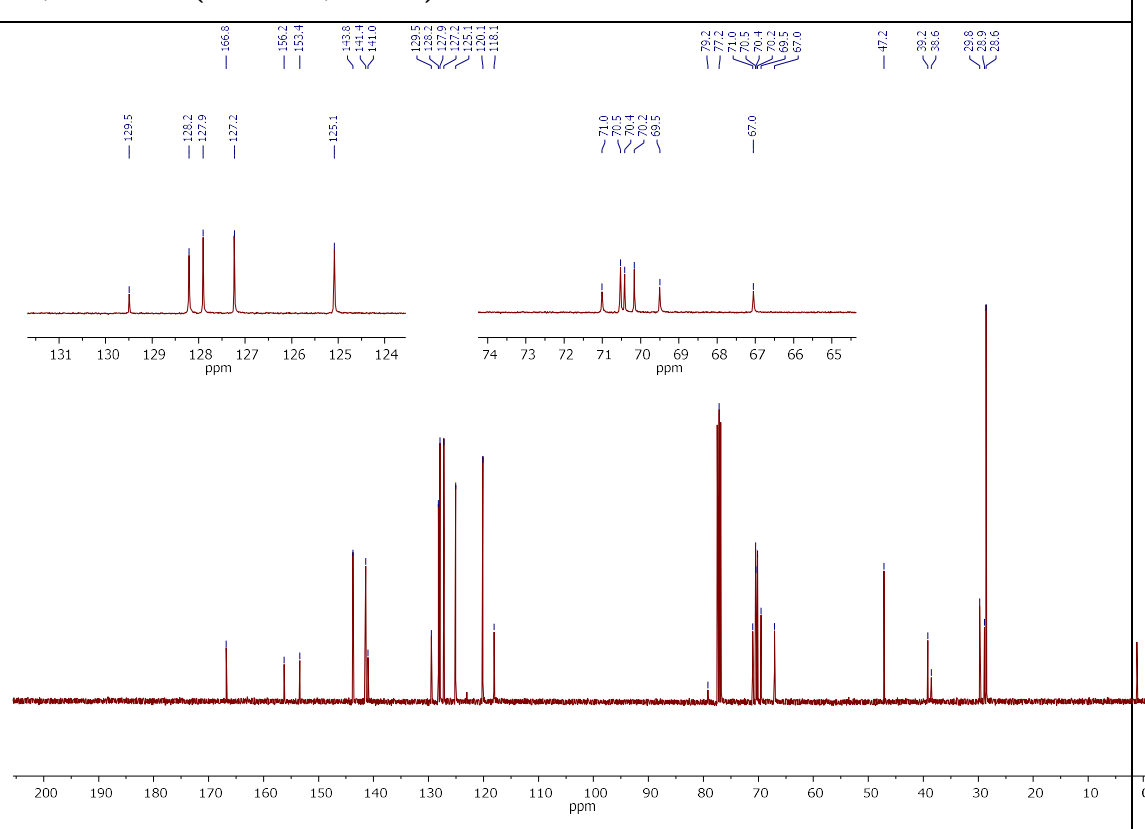
43, ¹³C RMN (101 MHz, DMSO-d₆)



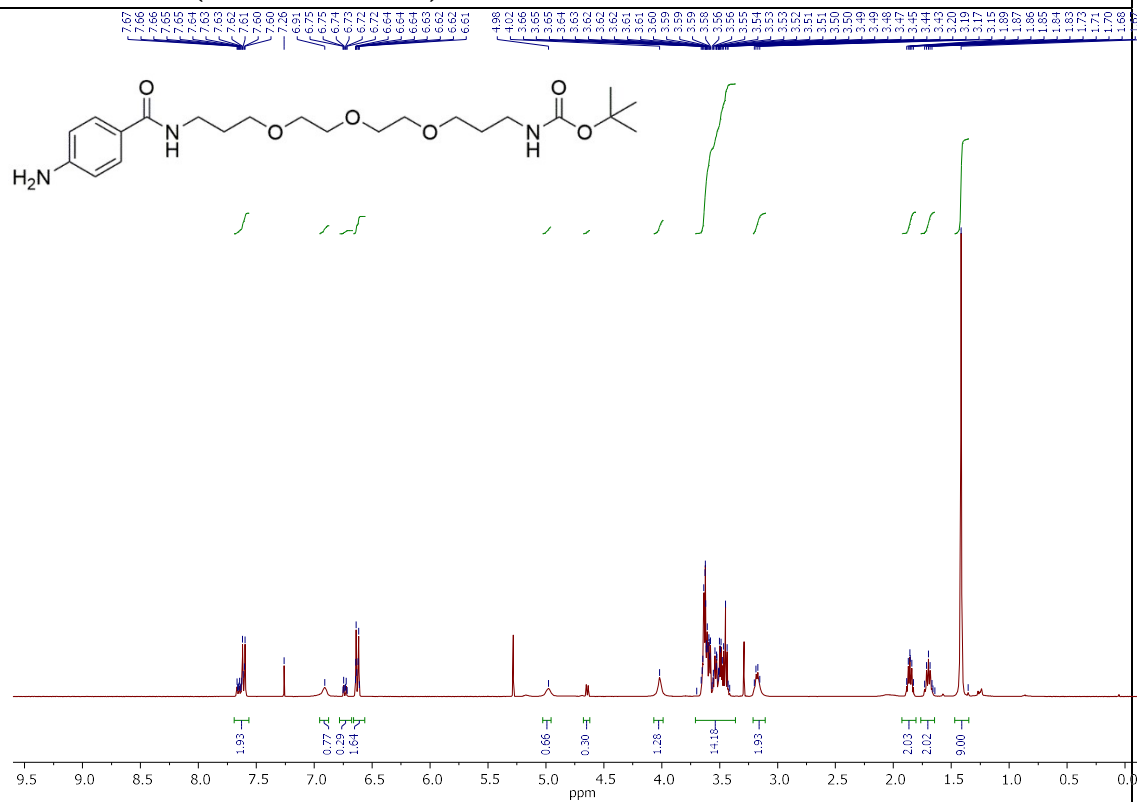
44, ¹H RMN (400 MHz, CDCl₃)



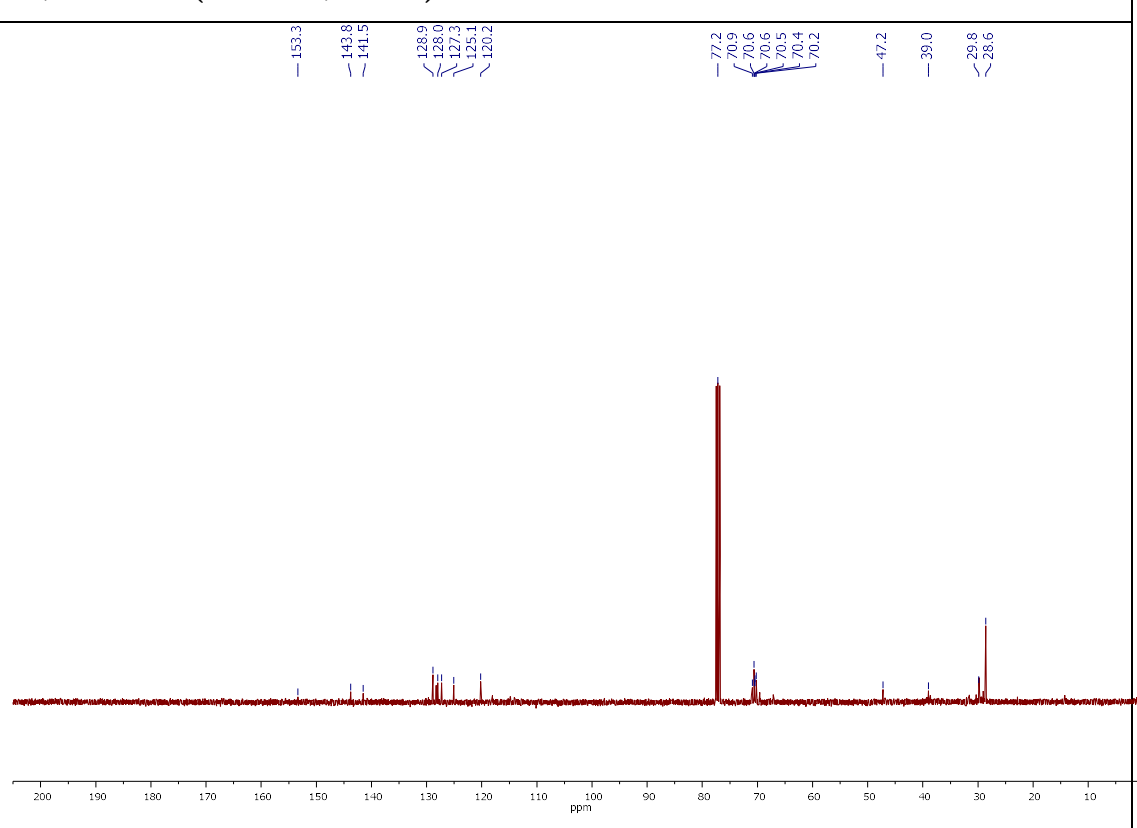
44, ¹³C RMN (101 MHz, CDCl₃)



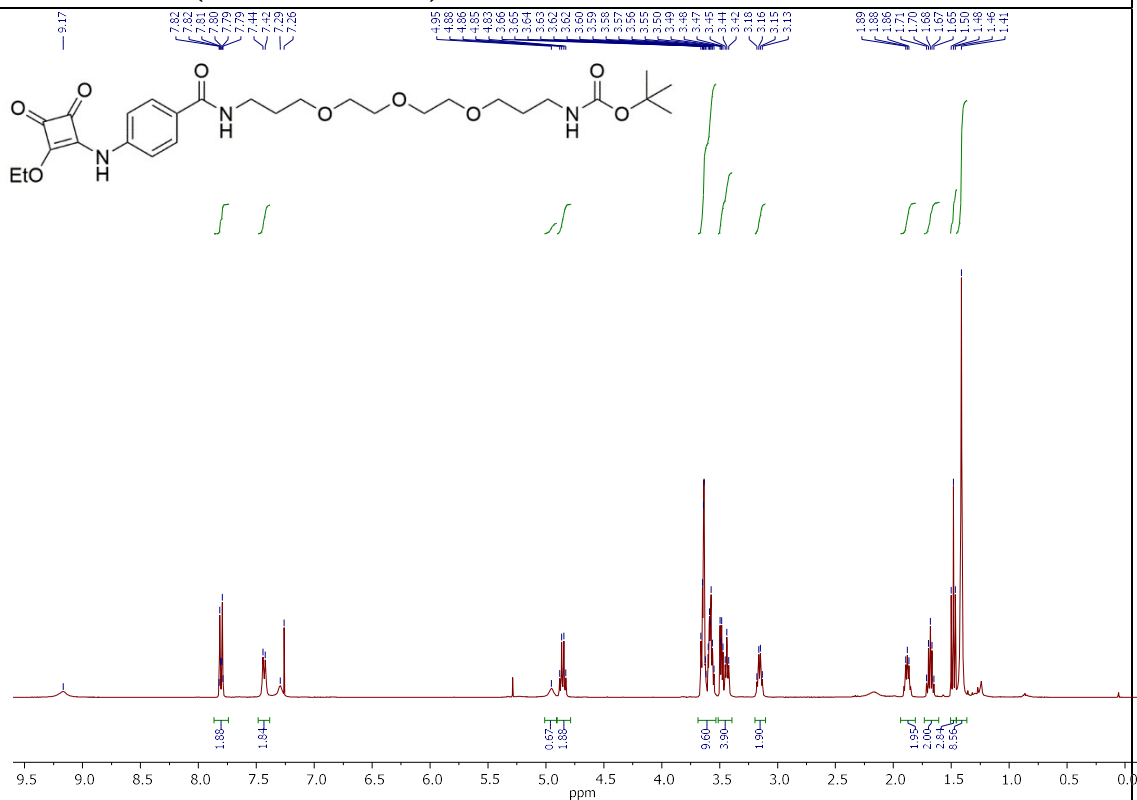
45, ¹H RMN (400 MHz, CDCl₃)



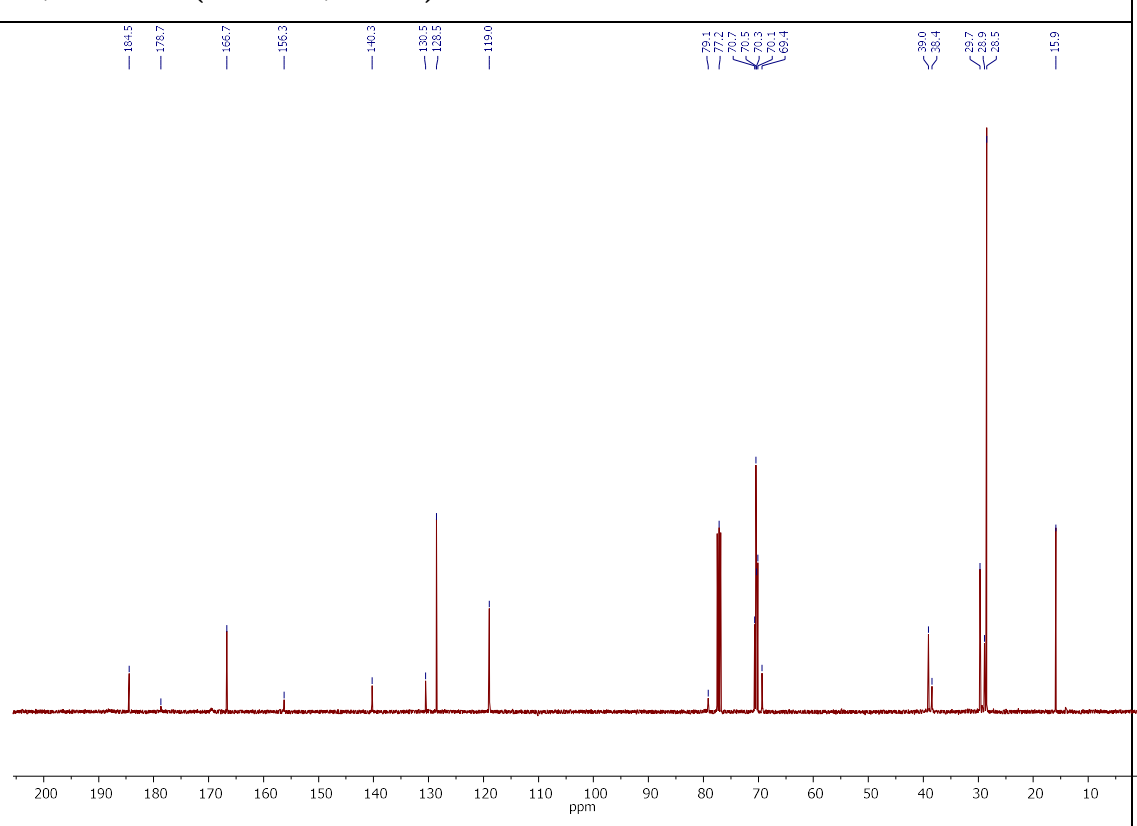
45, ¹³C RMN (101 MHz, CDCl₃)



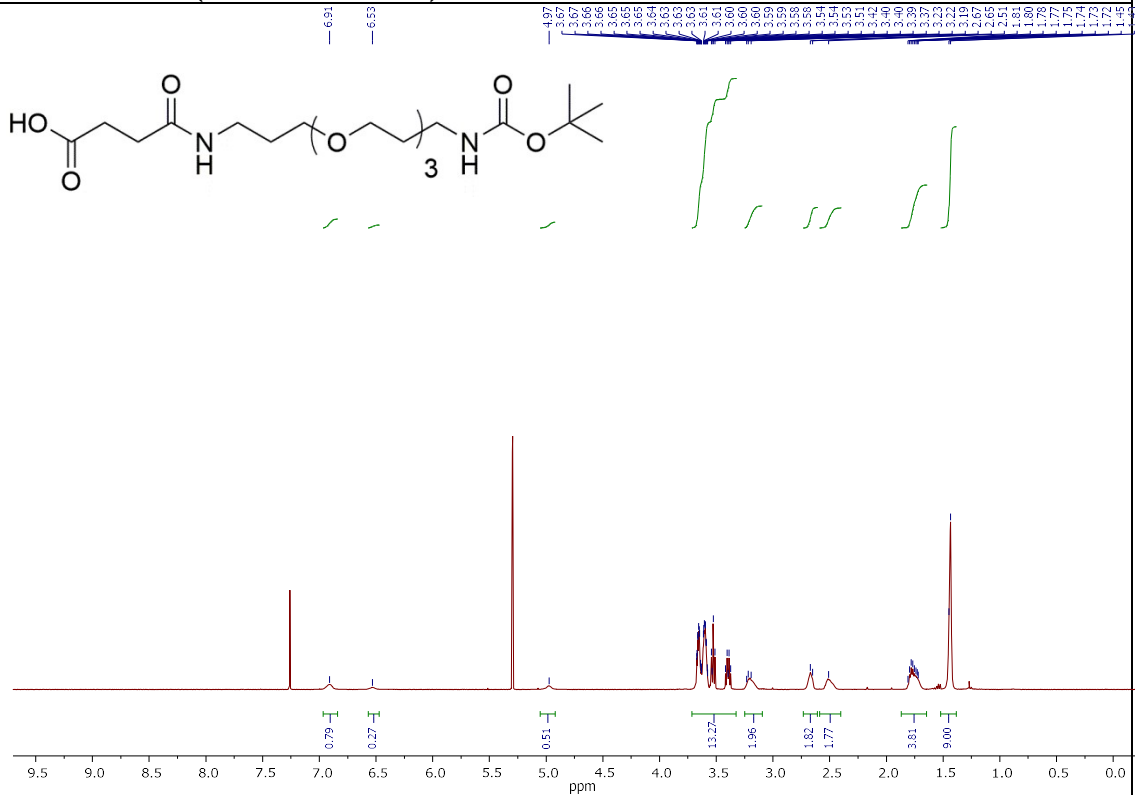
46, ¹H RMN (400 MHz, CDCl₃)



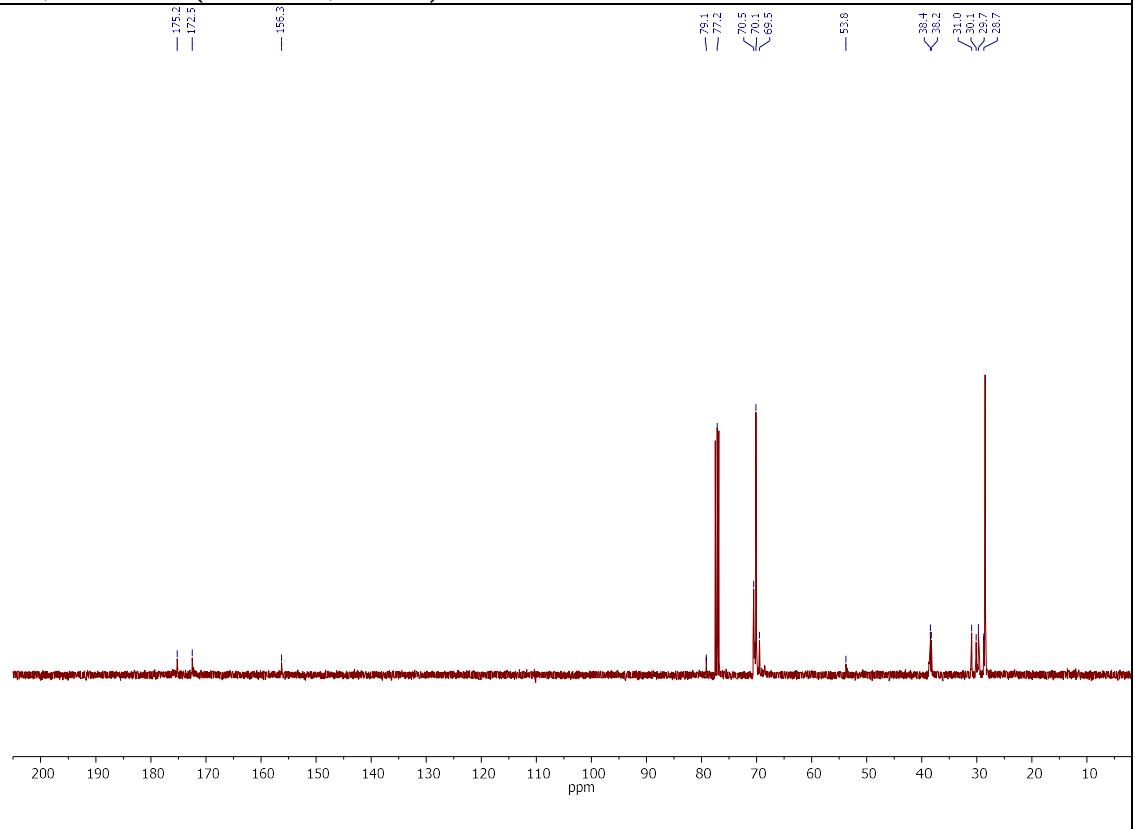
46, ¹³C RMN (101 MHz, CDCl₃)



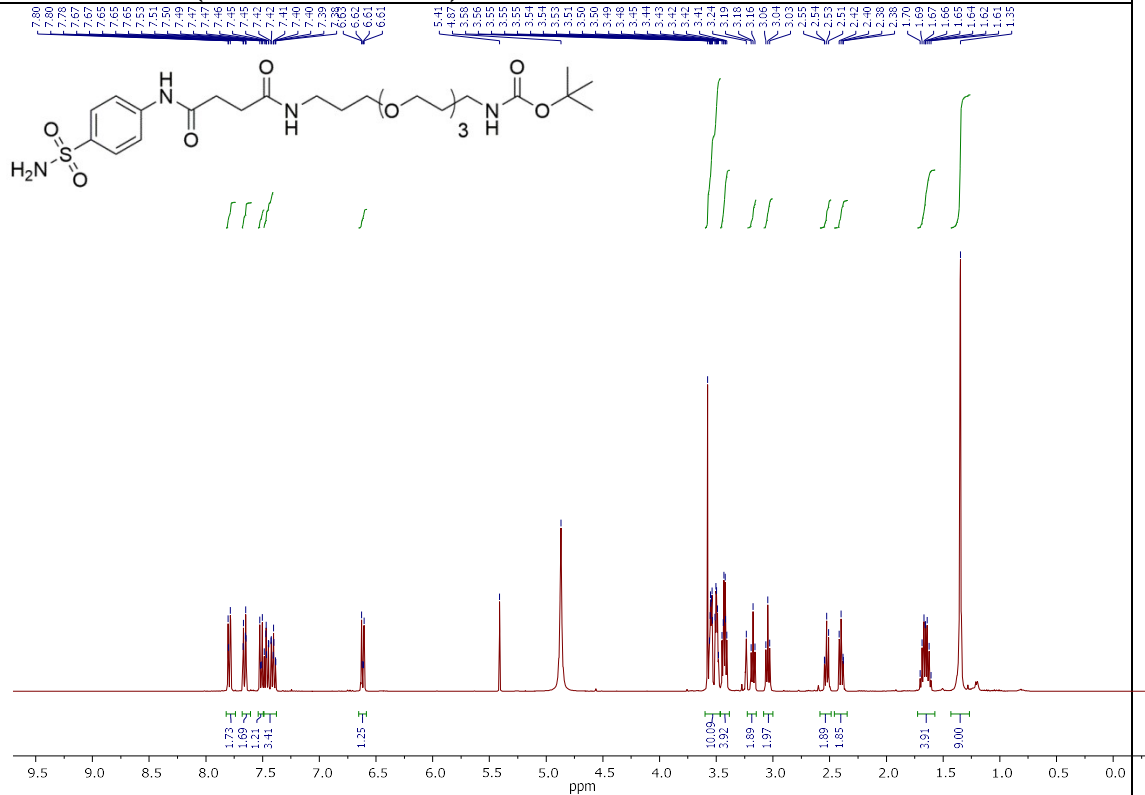
47, ¹H RMN (400 MHz, CDCl₃)



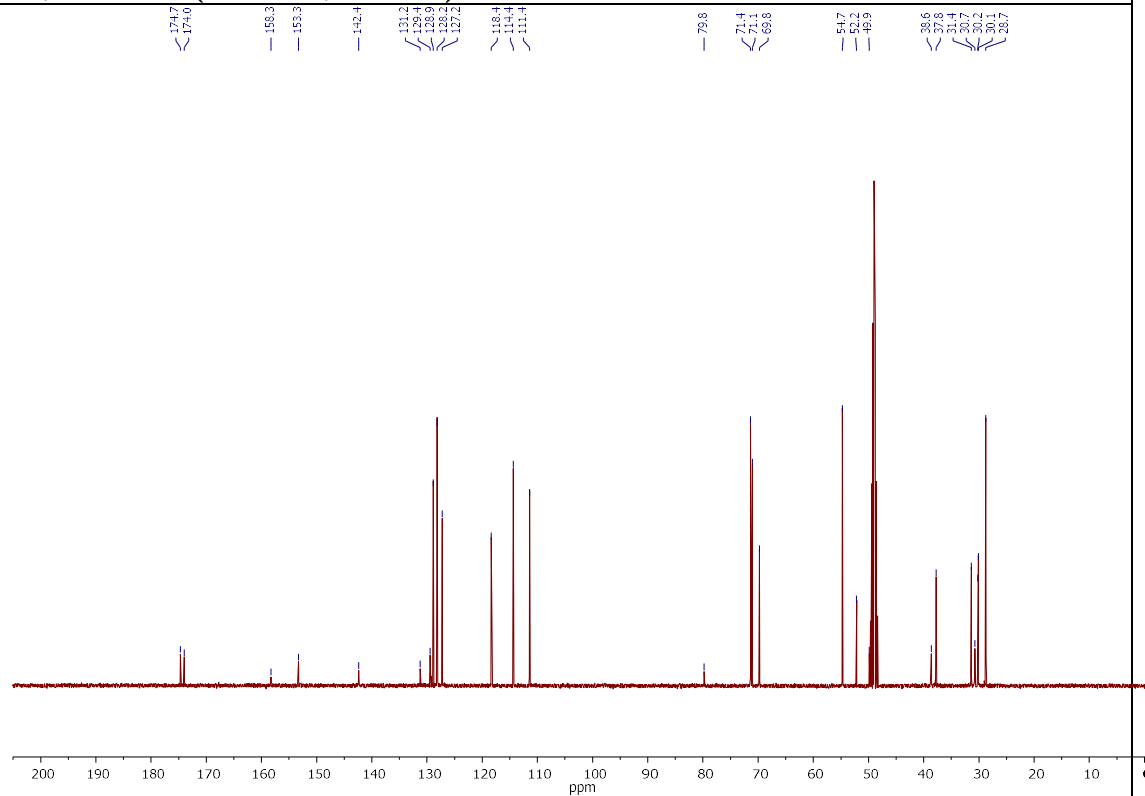
47, ¹H RMN (400 MHz, CDCl₃)



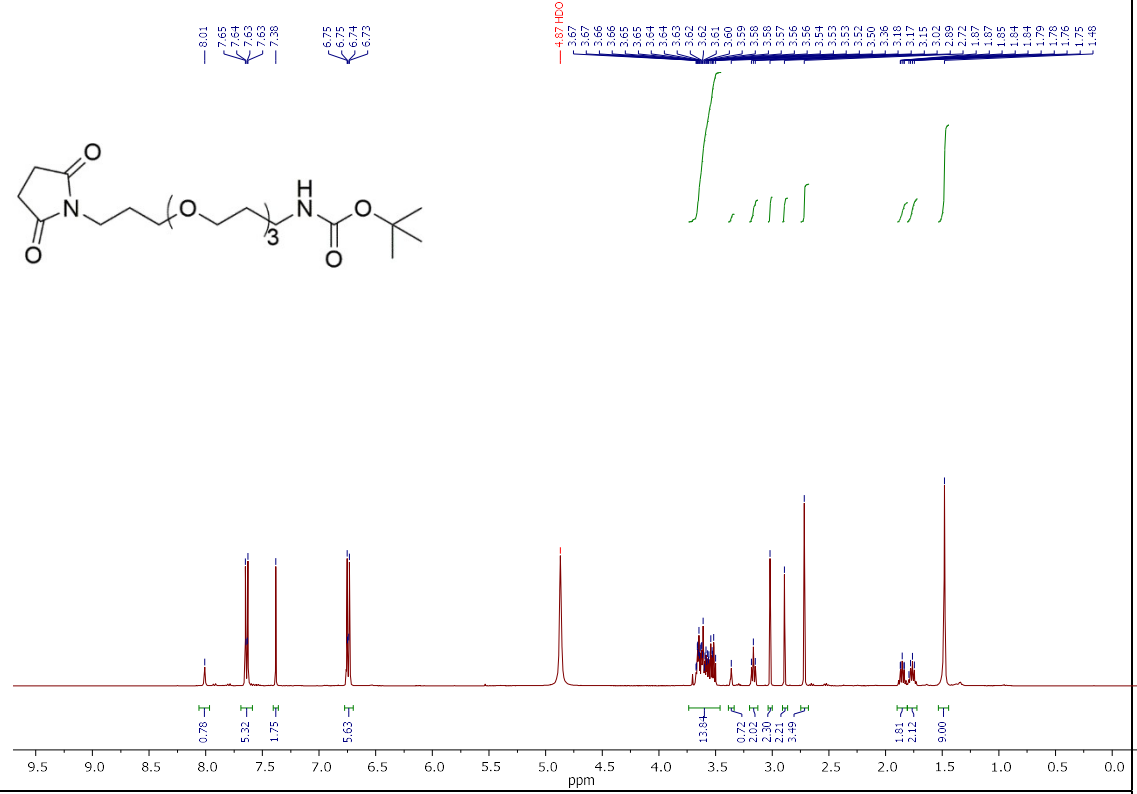
48, ¹H RMN (400 MHz, CD₃OD)



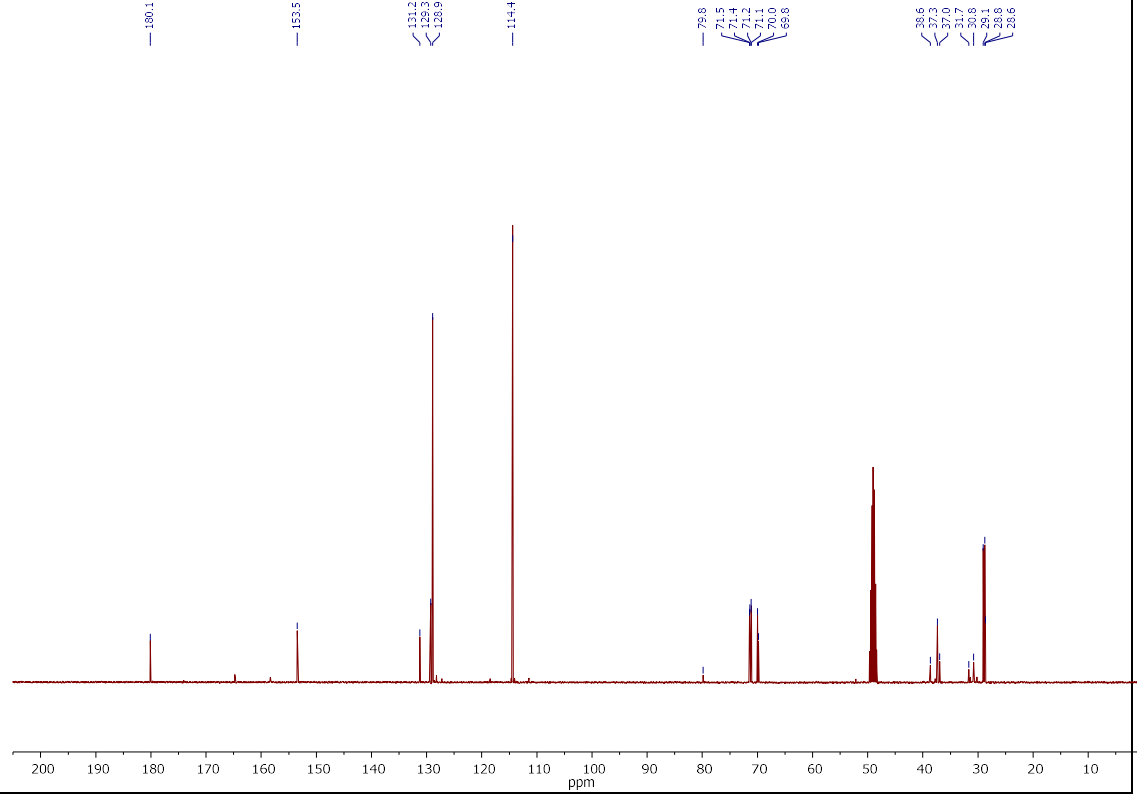
48, ¹³C RMN (101 MHz, CD₃OD)



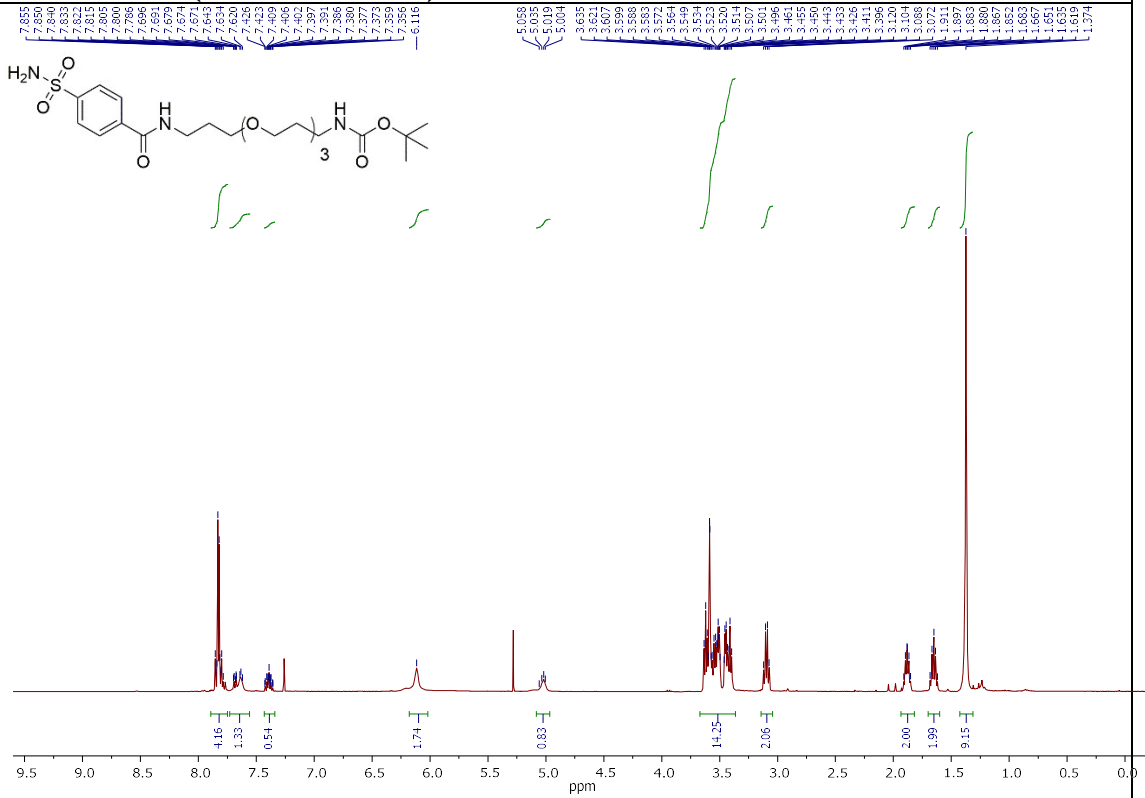
50, ^1H RMN (400 MHz, CD_3OD)



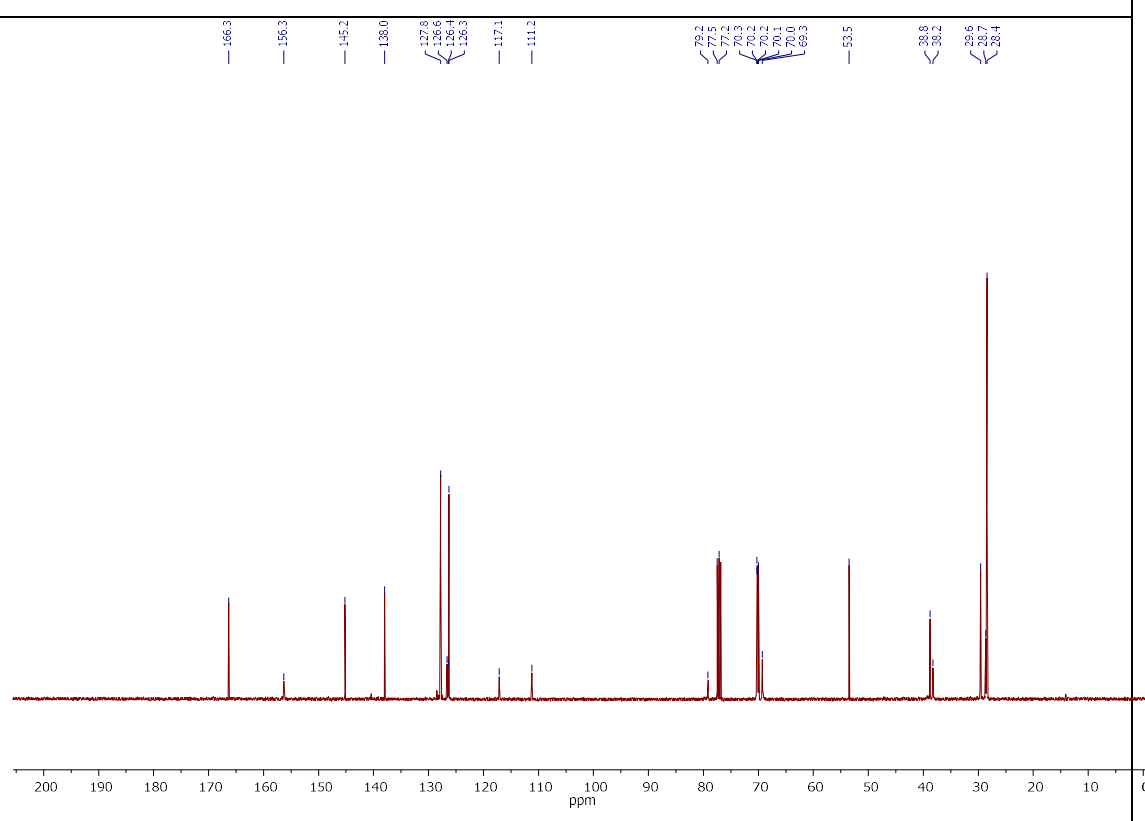
50, ^{13}C RMN (101 MHz, MeOD)



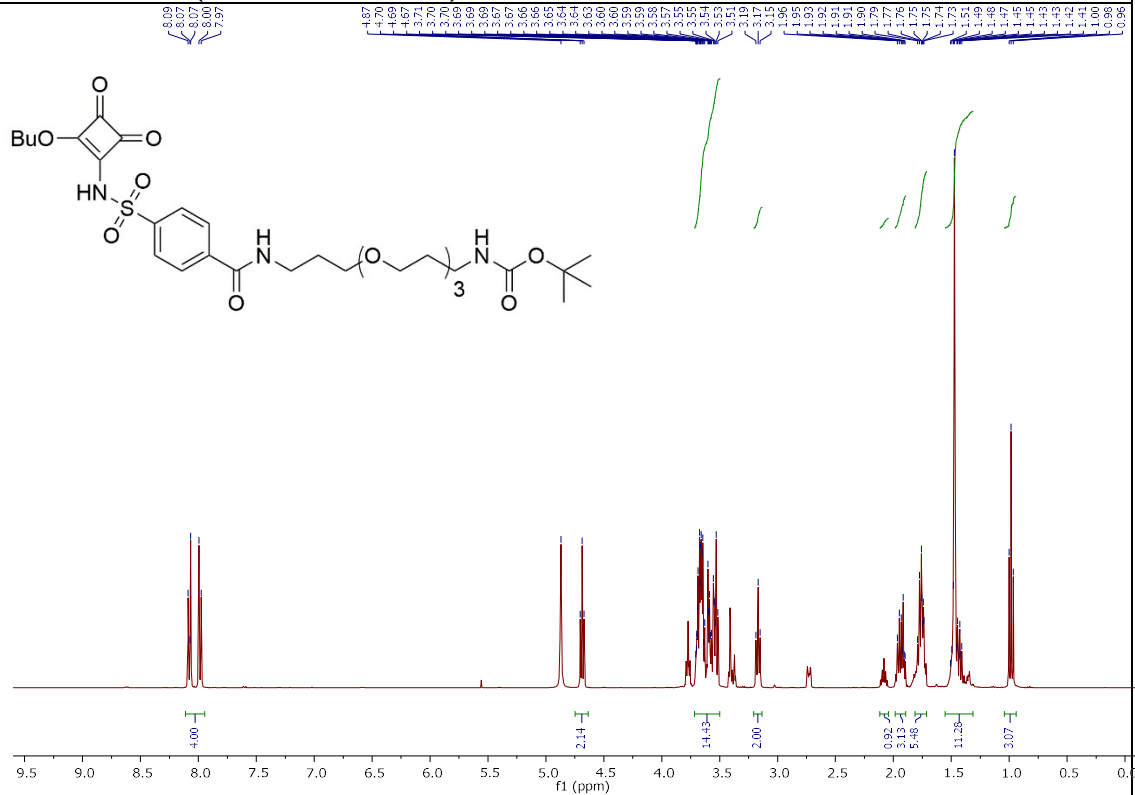
51, ¹H RMN (400 MHz, CDCl₃)



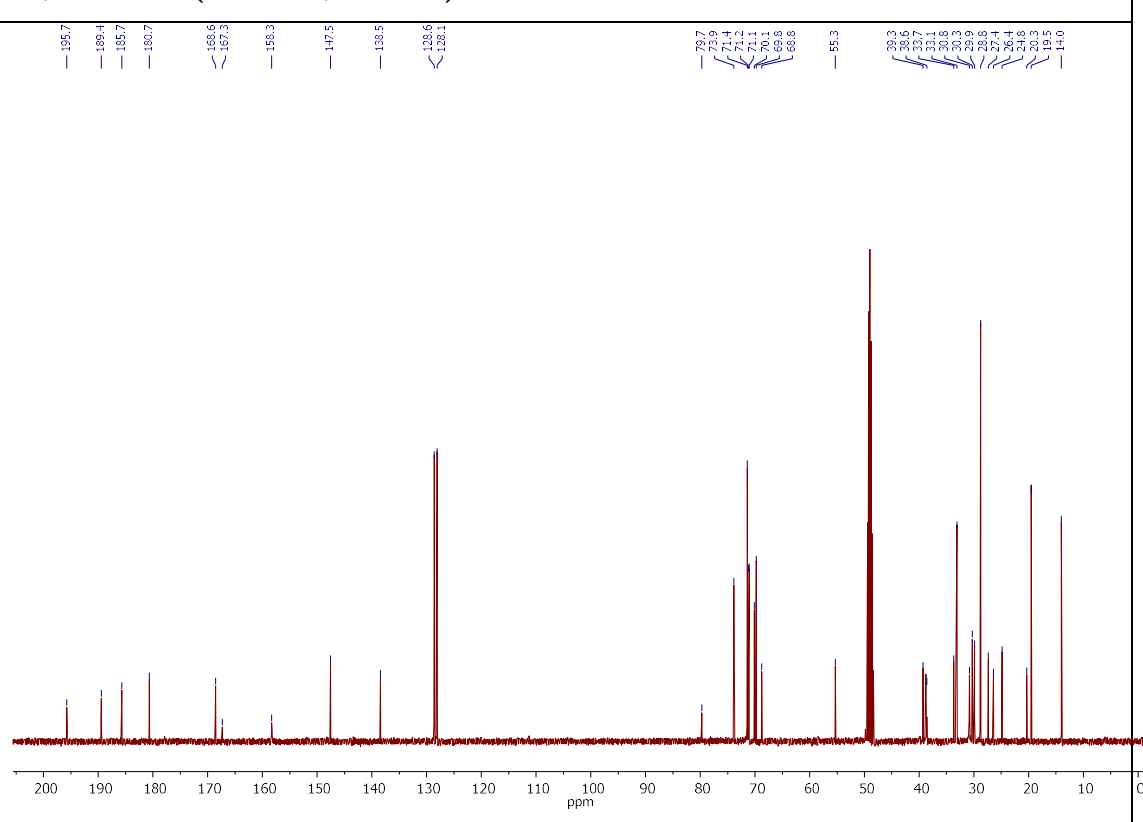
51, ¹³C RMN (101 MHz, CDCl₃)



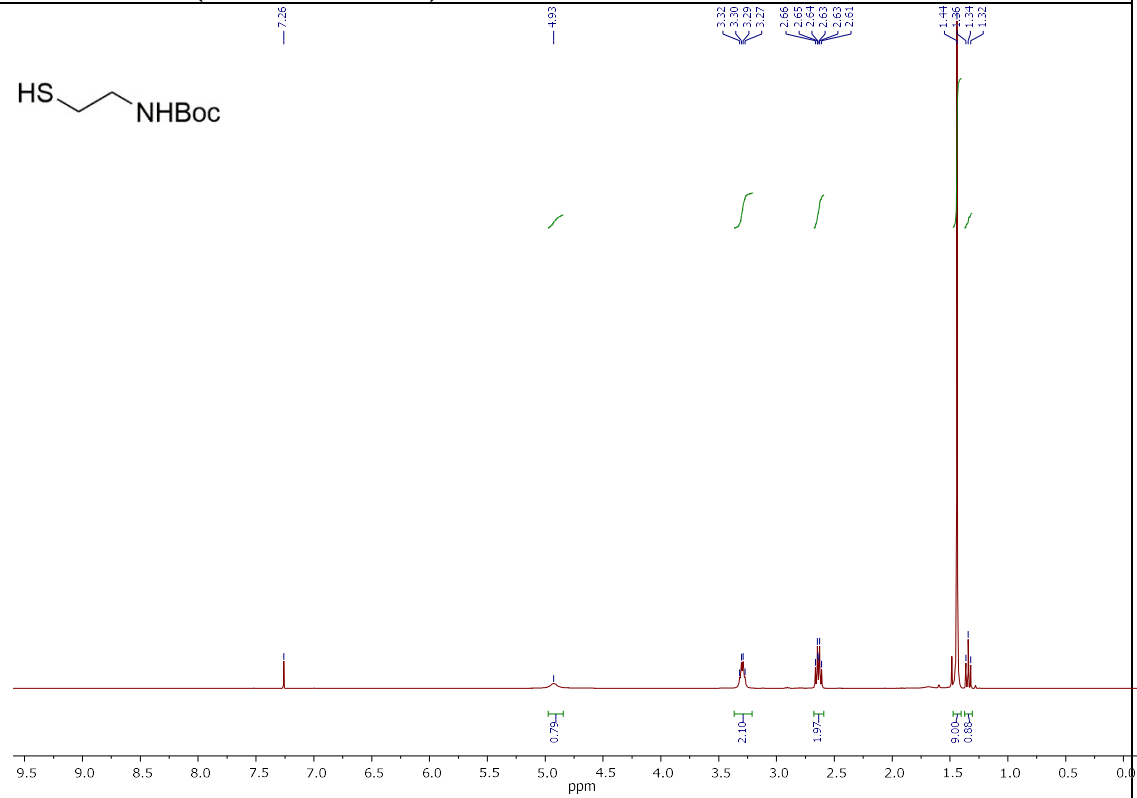
52, ¹H RMN (400 MHz, CD₃OD)



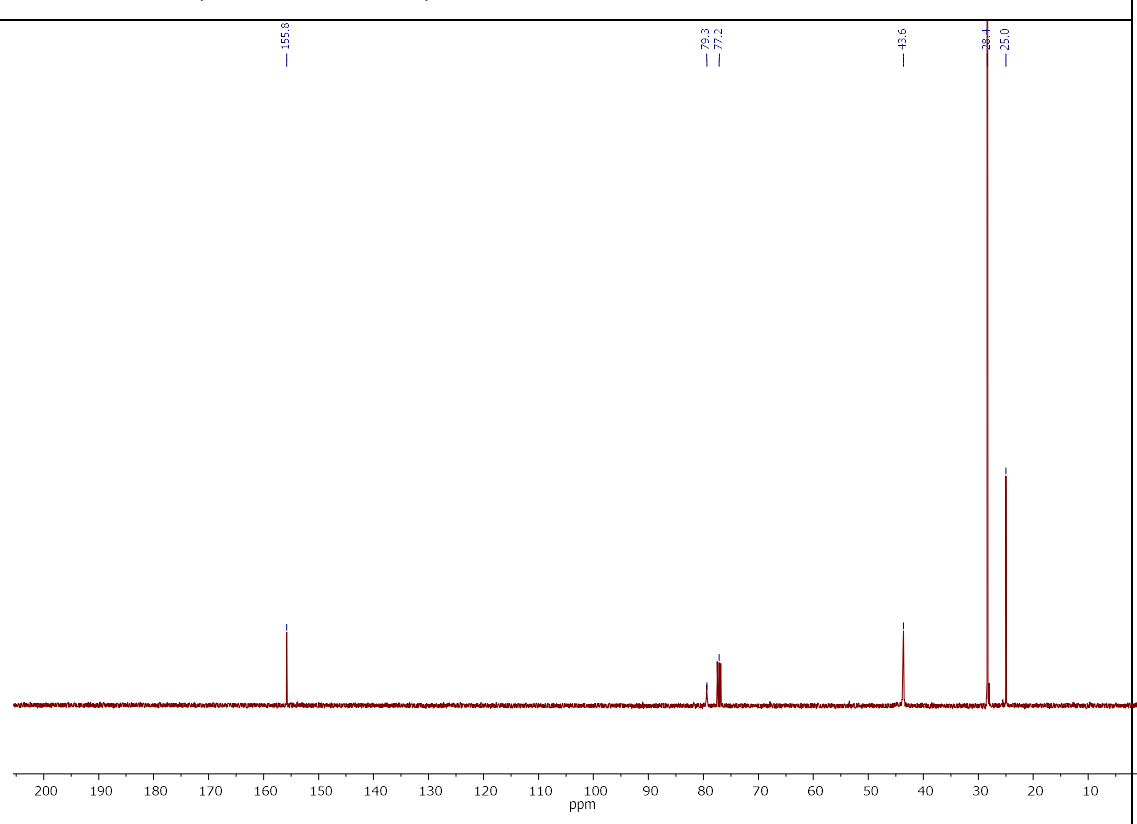
52, ¹³C RMN (101 MHz, CD₃OD)



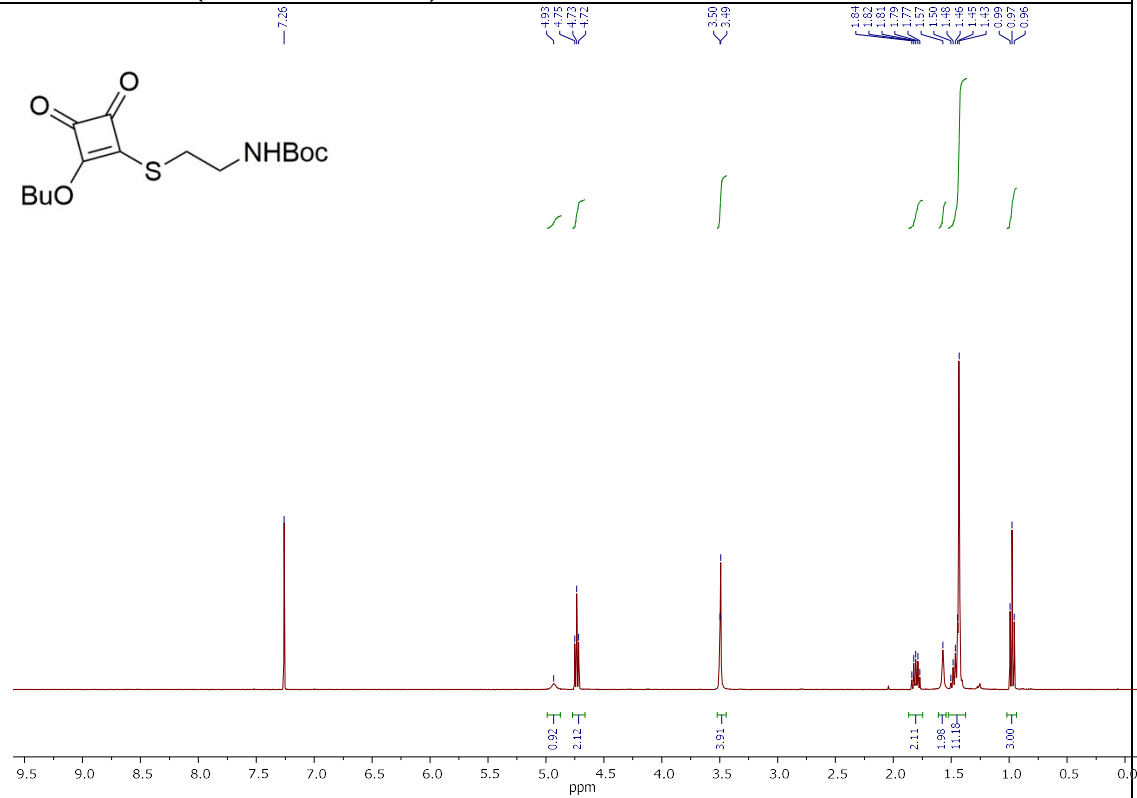
53, ¹H RMN (400 MHz, CDCl₃)



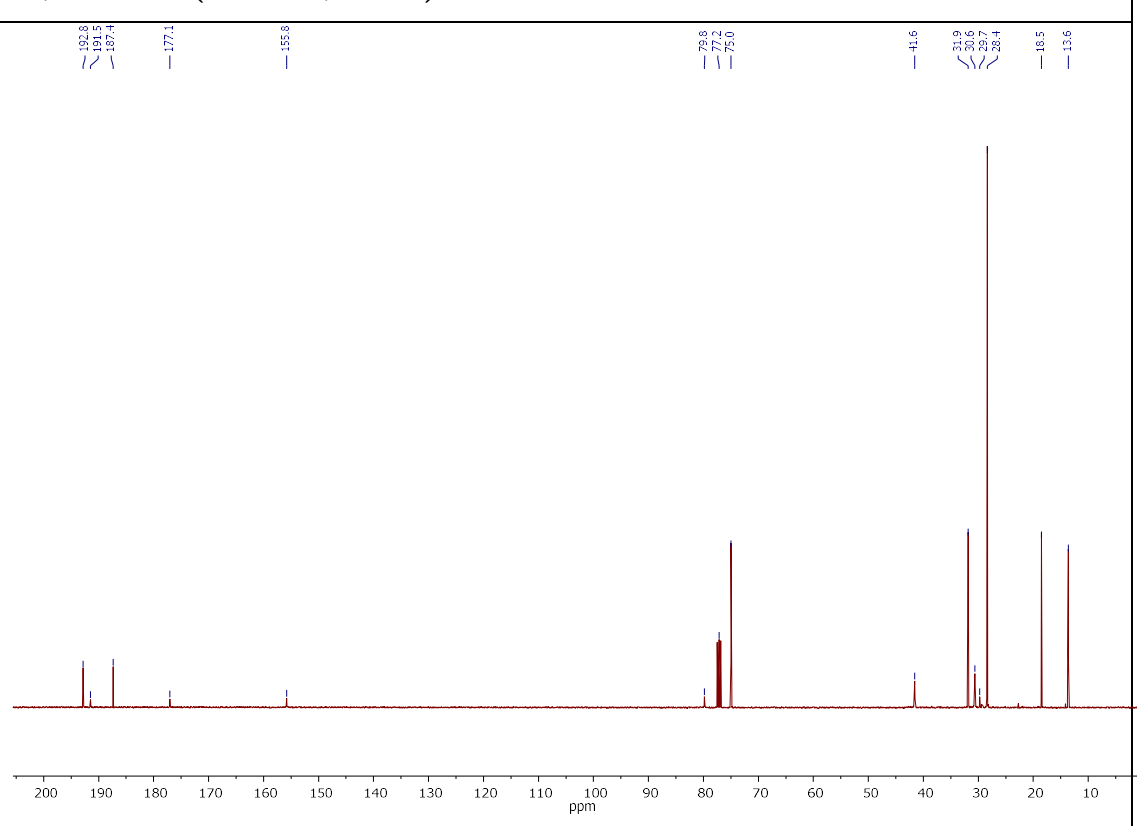
53, ¹³C RMN (101 MHz, CDCl₃)



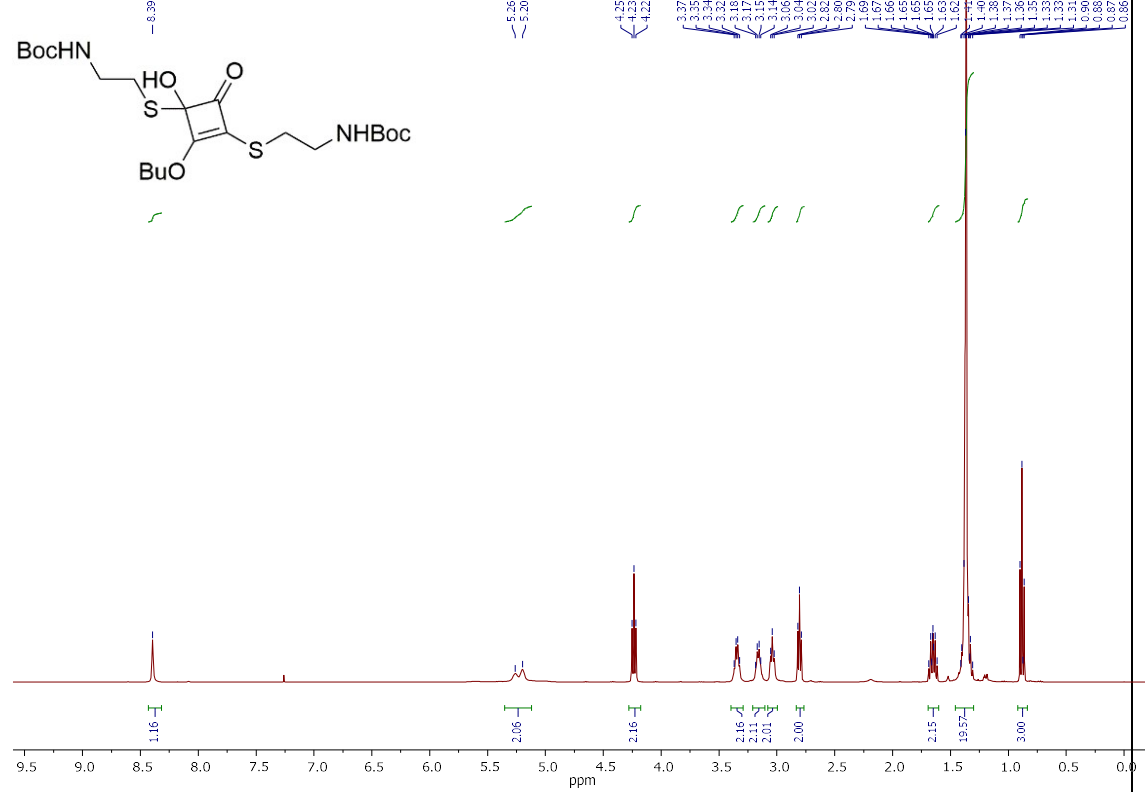
54, ¹H RMN (400 MHz, CDCl₃)



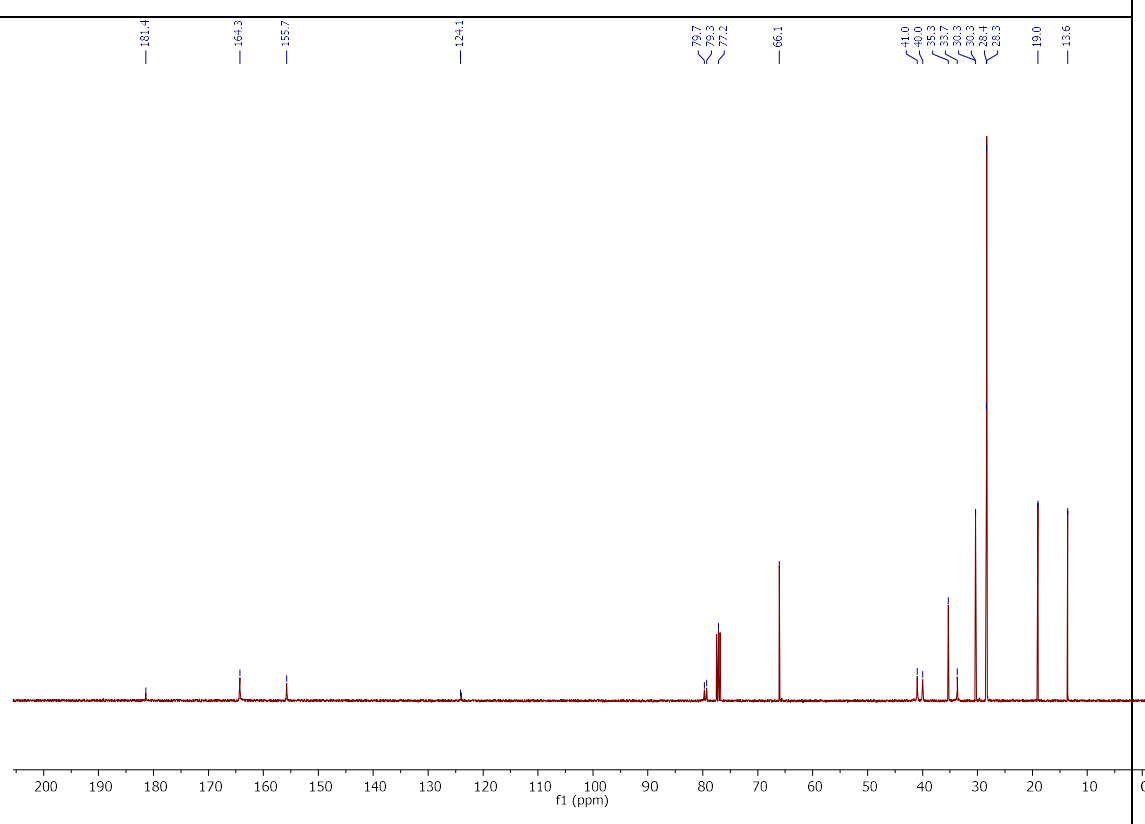
54, ¹³C RMN (101 MHz, CDCl₃)



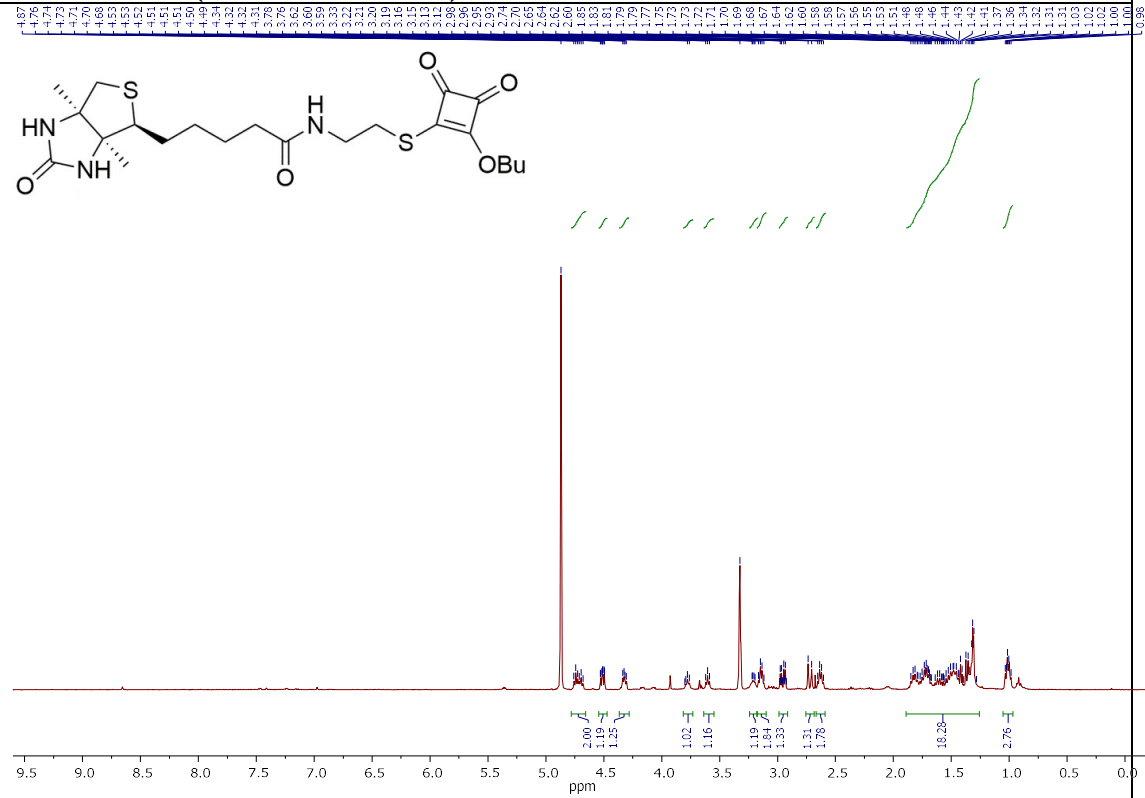
55, ¹H RMN (400 MHz, CDCl₃)



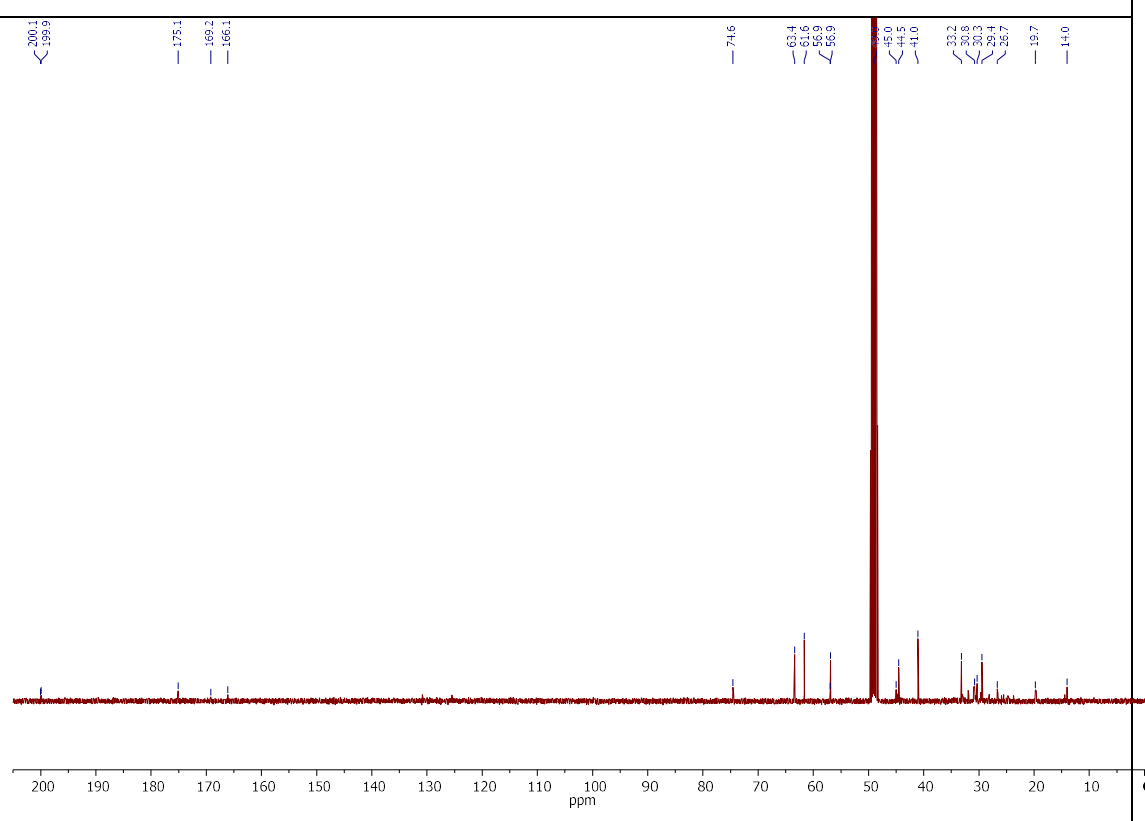
55, ¹³C RMN (101 MHz, CDCl₃)



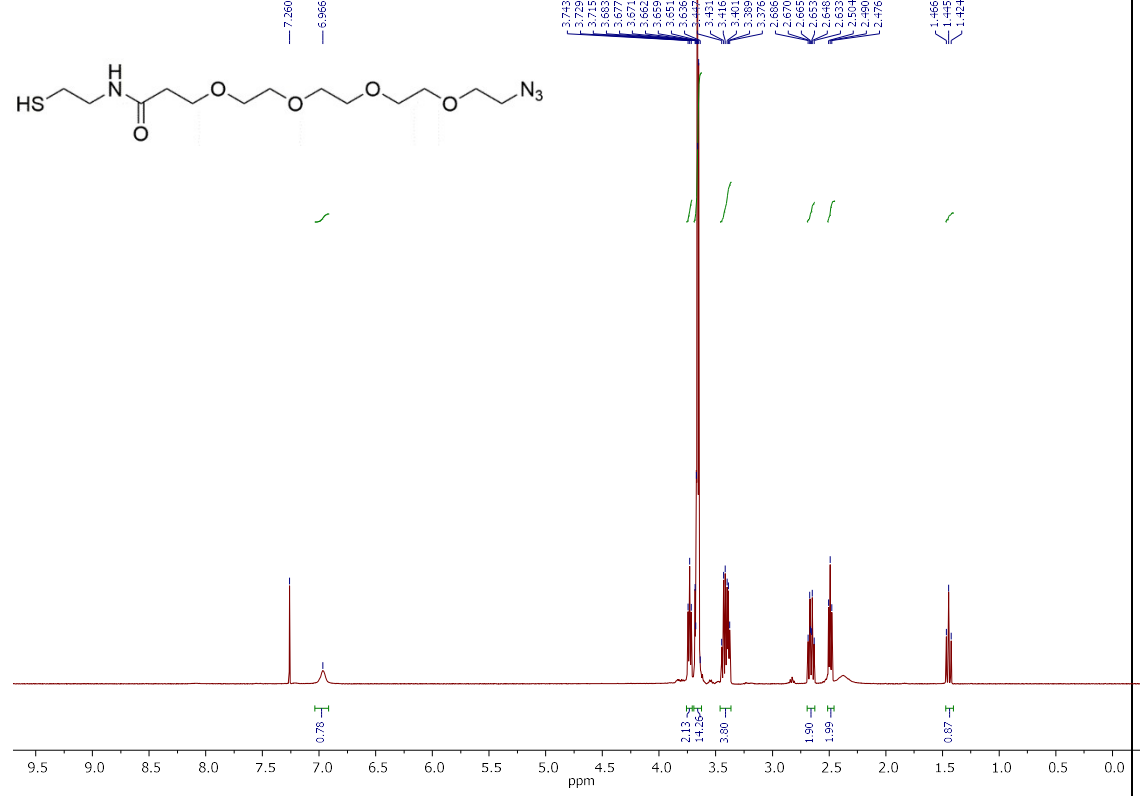
57, ¹H RMN (400 MHz, CD₃OD)



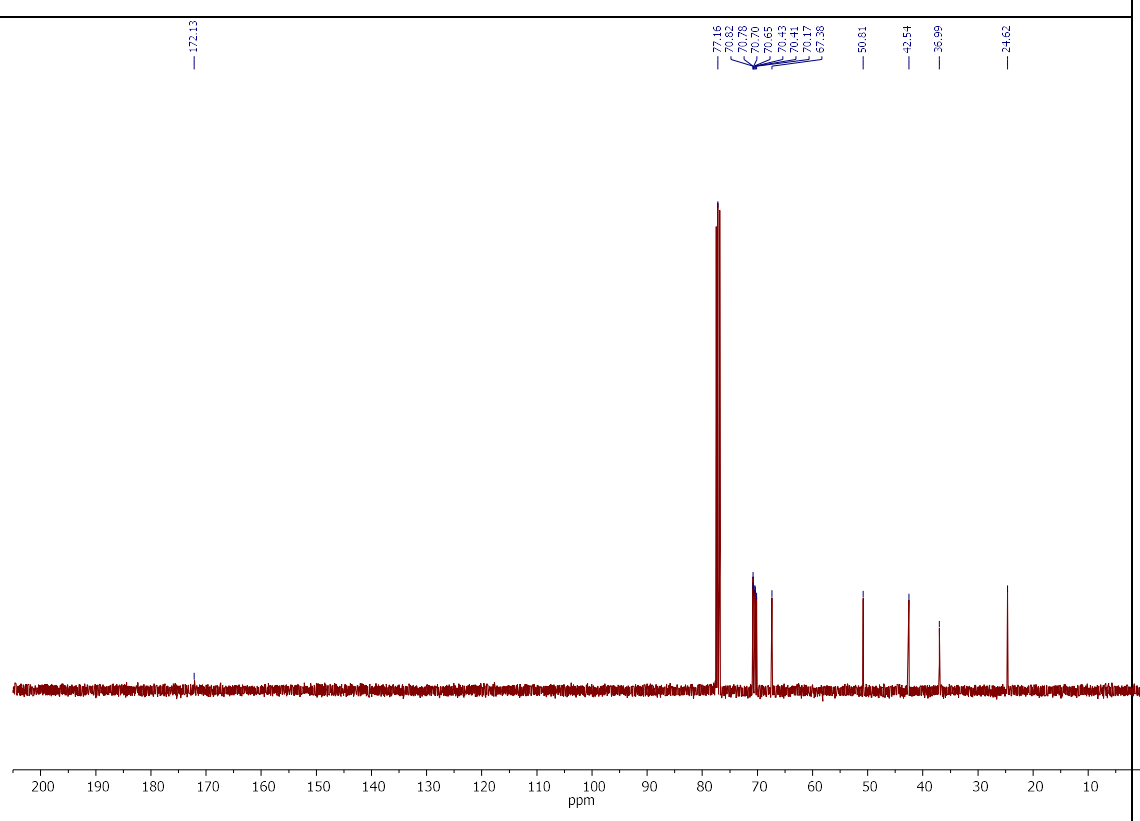
57, ¹³C RMN (101 MHz, CD₃OD)



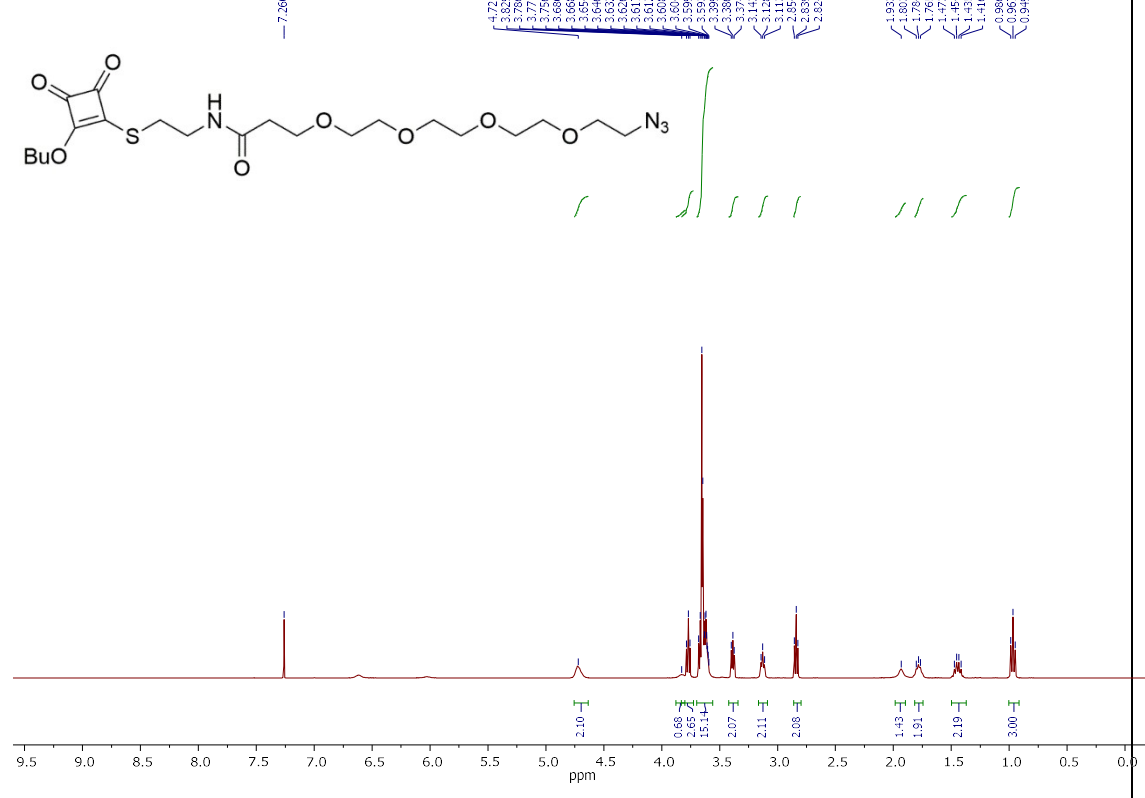
59, ¹H RMN (400 MHz, CDCl₃)



59, ¹³C RMN (101 MHz, CDCl₃)



60, ¹H RMN (400 MHz, CDCl₃)



60, ¹³C RMN (101 MHz, CDCl₃)

