



ESTUDIS SINTÈTICS DIRIGITS ALS ALCALOIDES STENINA I SESSILIFOLIAMIDES B I C

TESI DOCTORAL

Javier Alonso Fernández

2012

Dirigida per:

Marta Figueredo i Galimany

Pau Bayón Rueda

Programa de Doctorat en Química

Departament de Química

Facultat de Ciències

5. Referències

¹ (a) Götz, M.; Edwards, O. E. *Alkaloids*; Manske, R. H. F., Ed.; Academic Press: New York, **1967**; Vol 9, 545-551. (b) Götz, M.; Strunz, G. M. en *Alkaloids*; Wiesner, K., Ed.; MTP International Review of Sciences, Organic Chemistry, Series One; Butterworths: London, **1973**; Vol. 9, 143-160.

² A internet existeixen un elevat nombre de portals on es descriuen l'ús i comercialització de productes que contenen extractes d'aquestes plantes.

³ (a) Pilli, R. A.; Rosso, G. B.; de Oliveira, M. C. F. *The Alkaloids* (Ed.: G. A. Cordell), Elsevier, New York, **2005**, Vol. 62, 77-173. (b) Greger, H.; *Planta Med.* **2006**, 72, 99-113. (c) Alibés, R.; Figueredo, M.; *Eur. J. Org. Chem.* **2009**, 2421-2435. (d) Pilli, R. A.; Rosso, G. B.; de Oliveira, M.C.F. *Nat. Prod. Rep.* **2010**, 27, 1908-1937.

⁴ (a) Gaw, H. Z.; Wang, H. P. *Science* **1949**, 110, 11-12. (b) Yang, H.-C.; Chang, H.-H.; Weng, T.-C. *J. Formosan Med. Assoc.* **1953**, 52, 109-112.

⁵ Wang, K. W.; Wu, J. S. *Zhong Erke Z* **1960**, 11, 143.

⁶ Huang, Y.; Xie, S.; Zhang, Y. *Zhongcaoyao* **2001**, 32, 127-128.

⁷ (a) Liren, Z.; Yuebin, Z. CN 1054349 A 19910911. (b) Changan, W.; Zhaoming, W.; Na, L.; Xueling, R.; Bangai, Z. CN 1120890 A 19960424. (c) Jinfeng, G. CN 1176742 A 19980325. (d) Maoxuan, L.; Guangyu, Y. CN 1308871 A 20010822.

⁸ Ahaoli, C. CN 1129733 A 19960828.

⁹ (a) Xianliang, H. CN 1247893 A 20000322. (b) Xianliang, H. CN 1280176 A 20010117. (c) Xianliang, H. CN 280174 A 20010117. (d) Minqui, D.; Jihua, X.; Chengjing, W. CN 1301533 A 20010704.

¹⁰ (a) Chunxu, C. CN 1094105 A 19941026. (b) Shuili, X. CN 1186604 A 19980708.

¹¹ Hongfen, L. WO 2002078723 A1 20021010.

¹² Junrui, M. CN 1265315 A 20000906.

¹³ Aproximacions sintètiques:

(a) Xiang, L.; Kozikowski, A. P.; *Synlett* **1990**, 279-281. (b) Wipf, P.; Kim, Y. *Tetrahedron Lett.* **1992**, 33, 5477-5480. (c) Beddoes, R. L.; Davies, M. P. H.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1992**, 538-540. (d) Martin, S. F.; Corbett, J. W. *Synthesis* **1992**, 55-57. (e) Morimoto, Y.; Nishida, K.; Hayashi, Y.; Shirahama, H. *Tetrahedron Lett.* **1993**, 34, 5773-5776. (f) Morimoto, Y.; Iwahashi, M. *Synlett* **1995**, 1221-1222. (g) Wipf, P.; Goldstein, D. M. *Tetrahedron Lett.* **1996**, 37, 739-742. (h) Martin, S. F.; Bur, S. K. *Tetrahedron Lett.* **1997**, 38, 7641-7644. (i) Rigby, J. H.; Laurent, S.; Cavezza, A.; Heeg, M. *J. Org. Chem.* **1998**, 63, 5587-5591. (j) Wipf, P.; Li, W. *J. Org. Chem.* **1999**, 64, 4576-4577. (k) Pearson, W. H.; Hutta, D. A.; Fang, W-K. *J. Org. Chem.* **2000**, 65, 8326-8332. (l) Jung, S. H.; Lee, J. E.; Joo, H. J.; Kim, S. H.; Koh, H. Y. *Bull. Korean Chem. Soc.* **2000**, 21, 159-160. (m) Pearson, W. H.; Walavalkar, R. *Tetrahedron* **2001**, 57, 5081-5089. (n) Hinmnar, M. M.; Heathcock, C. H. *J. Org. Chem.* **2001**, 66, 7751-7756. (o) Velázquez, F.; Olivo, H. F. *Org. Lett.* **2002**, 4, 3175-3178. (p) Booker-Milburn, K. I.; Hirst, P.; Charmant, J. P. H.; Taylor, L. H. *J. Angew. Chem. Int. Ed.* **2003**, 42, 1642-1644. (q) Lindsay, K. B.; Pyne, S. G. *Synlett* **2004**, 779-782. (r) Cid, P.; Closa, M.; de March, P.; Figueredo, M.; Font, J.; Sanfeliu, E.; Soria, A. *Eur. J. Org. Chem.* **2004**, 4215-4233. (s) Roberts, E.; Samçon, J. P.; Sweeney, J. B. *Org. Lett.* **2005**, 7, 2075-2078. (t) Alibés, R.; Blanco, P.; Casas, E.; Closa, M.; de March, P.; Figueredo, M.; Font, J.; Sanfeliu, E.; Álvarez-Larena, A. *J. Org. Chem.* **2005**, 70, 3157-3167. (u) Gu, P.; Zhao Y. -M.; Tu, Y. Q.; Ma, Y.; Zhang, F. *Org. Lett.* **2006**, 8, 5271-5273. (v) Antoline, J. E.; Hsung, R. P.; Huang, J.; Song, Z.; Li, G. *Org. Lett.* **2007**, 9, 1275-1278. (w) Zhu, L.; Lauchli, R.; Loo, M.; Shea, K. J. *Org. Lett.* **2007**, 9, 2269-2271. (x) Frankowski, K. J.; Neuenswander, B.; Aubé, J. *J. Comb. Chem.* **2008**, 10, 721-725. (y) Yaji, K.; Shindo, M. *Tetrahedron Lett.* **2010**, 51, 5469-5472. (z) Burrell, A.; Watson, L.; Martin, N. G.; Oram, N.; Coldham, I. *Org. Biomol. Chem.* **2010**, 8, 4530-4532. (aa) Dietz, J.; Martin, S. F. *Tetrahedron Lett.*, **2011**, 52, 2048-2050. (ab) Bates, R. W.; Sridhar, S. *J. Org. Chem.* **2011**, 76, 5026-5035.

¹⁴⁻³⁵ Síntesis totals:

¹⁴ (+)-**Croomina**: (a) Williams, D. R.; Brown, D. L.; Benbow, J. W. *J. Am. Chem. Soc.* **1989**, 111, 1923-1925. (b) Martin, S. F.; Barr, K. J. *J. Am. Chem. Soc.* **1996**, 118, 3299-3300. (c) Martin, S. F.; Barr, K. J.; Smith, D. W.; Bur, S. K. *J. Am. Chem. Soc.* **1999**, 121, 6990-6997.

¹⁵ (±)-**Stenina**: (a) Chen, C. Y.; Hart, D. J. *J. Org. Chem.* **1990**, 55, 6236-6240. (b) Chen, C.Y.; Hart, D. J. *J. Org. Chem.* **1993**, 58, 3840-3849. (c) Ginn, J. D.; Padwa, A. *Org. Lett.* **2002**, 4, 1515-1517. (d) Golden, J. E.; Aubé, J. *Angew. Chem. Int. Ed.* **2002**, 41, 4316-4318. (e) Zeng, Y.; Aubé, J. *J. Am. Chem. Soc.* **2005**, 127, 15712-15713.

5. REFERÈNCIES

- ¹⁶ (-)-**Stenina**: (a) Wipf, P.; Kim, Y.; Goldstein, D. M. *J. Am. Chem. Soc.* **1995**, *117*, 11106-11112. (b) Morimoto, Y.; Iwahashi, M.; Nishida, K.; Hayashi, Y.; Shirahama, H. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 904-906. (c) Morimoto, Y.; Iwahashi, M.; Kinoshita, T.; Nishida, K. *Chem. Eur. J.* **2001**, *7*, 4107-4116.
- ¹⁷ (\pm)-**Stemoamida**: (a) Kohno, Y.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2063-2070. (b) Jacobi, P. A.; Lee, K. *J. Am. Chem. Soc.* **1997**, *119*, 3409-3410. (c) Jacobi, P. A.; Lee, K. *J. Am. Chem. Soc.* **2000**, *122*, 4295-4303. (d) Bogliotti, N.; Dalko, P. I.; Cossy, J. *J. Org. Chem.* **2006**, *71*, 9528-9531. (e) Honda, T.; Matsukawa, T.; Takahashi, K. *Org. Biomol. Chem.* **2011**, *9*, 673-675.
- ¹⁸ (-)-**Stemoamida**: (a) Williams, D. R.; Reddy, J. P.; Amato, G. S. *Tetrahedron Lett.* **1994**, *35*, 6417-6420. (b) Kinoshita, A.; Mori, M. *J. Org. Chem.* **1996**, *61*, 8356-8357. (c) Kinoshita, A.; Mori, M. *Heterocycles* **1997**, *46*, 287-299. (d) mireu ref. 17c. (e) Gurjar, M. K.; Reddy, D. S. *Tetrahedron Lett.* **2002**, *43*, 295-298. (f) Sibi, M. P.; Subramanian, T. *Synlett* **2004**, 1211-1214. (g) Olivo, H. F.; Tovar-Miranda, R.; Barragán, E. *J. Org. Chem.* **2006**, *71*, 3287-3290. (h) Torsell, S.; Wanngren, E.; Somfai, P.; *J. Org. Chem.* **2007**, *72*, 4246-4249.
- ¹⁹ (+)-**Stemoamida**: Bogliotti, N.; Dalko, P. I.; Cossy, J. *Synlett*, **2006**, 2664-2666.
- ²⁰ (-)-**9,10-epi-Stemoamida**: Khim, S.-K.; Schultz, A. G.; *J. Org. Chem.* **2004**, *69*, 7734-7736.
- ²¹ (\pm)-**9,10-epi-Stemoamida**: mireu ref. 17d.
- ²² (\pm)-**Isostemofolina**: Kende, A. S.; Smalley, Jr T. L.; Huang, H. *J. Am. Chem. Soc.* **1999**, *121*, 7431-7432.
- ²³ (\pm)-**Stemonamida i (\pm)-isostemonamida**: (a) Kende, A. S.; Hernando, J. I. M.; Milbank, J. B. *J. Org. Lett.* **2001**, *3*, 2505-2508. (b) Kende, A. S.; Hernando, J. I. M.; Milbank, J. B. *Tetrahedron* **2002**, *58*, 61-74. (c) Taniguchi, T.; Tanabe, O.; Muraoka, O.; Ishibashi, H. *Org. Lett.* **2008**, *10*, 197-199. (d) Taniguchi, T.; Ishibashi, H. *Tetrahedron* **2008**, *64*, 8773-8779. (e) Chen, Z. -H.; Zhang, Y.; Chen, Z.; Tu, Y.; Zhang, F. *Chem. Comm.* **2011**, *47*, 1836-1838.
- ²⁴ (-)-**Stemospironina**: Williams, D. R.; Fromhold, M. G.; Earley, J. D. *Org. Lett.* **2001**, *3*, 2721-2724.
- ²⁵ (-)-**Tuberostemonina**: (a) Wipf, P.; Rector, S. R.; Takahashi, H. *J. Am. Chem. Soc.* **2002**, *124*, 14848-14849. (b) Wipf, P.; Spencer, S. R. *J. Am. Chem. Soc.* **2005**, *127*, 225-235.
- ²⁶ (-)-**Stemonina**: Williams, D. R.; Shamim, K.; Reddy, J. P.; Amato, G. S.; Shaw, S. M. *Org. Lett.* **2003**, *5*, 3361-3364.
- ²⁷ (\pm)-**Didehidrostemofolina (asparagamina A) i (\pm)-isodidehidrostemofolina**: Brüggemann, M.; McDonald, A. I.; Overman, L. E.; Rosen, M. D.; Schwink, L.; Scott, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 15284-15285.
- ²⁸ (-)-**Didehidrotuberostemonina**: mireu ref 25b.
- ²⁹ (\pm)-**Neostenina**: (a) Lainchbury, M. D.; Medley, M. I.; Taylor, P. M.; Hirst, P.; Dohle, W.; Booker-Milburn, K. I. *J. Org. Chem.* **2008**, *73*, 6497-6505. (b) Frankowski, K. J.; Golden, J. E.; Zeng, Y.; Lei, Y.; Aubé, J. *J. Am. Chem. Soc.* **2008**, *130*, 6018-6024.
- ³⁰ (\pm)-**Stemonamina i (\pm)-isostemonamina**: (a) mireu ref 23d. (b) Zhao, Y.-M.; Gu, P.; Tu, Y.-Q.; Fan, C.-A.; Zhang, Q. *Org. Lett.* **2008**, *10*, 1763-1766. (c) Zhao, Y.-M.; Gu, P.; Zhang, H.-J.; Zhang, Q.-W.; Fan, C.-A.; Tu, Y.-Q.; Young-Qiang; Zhang, F.-M. *J. Org. Chem.* **2009**, *74*, 3211-3213.
- ³¹ (\pm)-**Cephalotaxina**: mireu ref. 30c.
- ³² **Oxistemofolina i metoxistemofolina**: Sastraruji, K.; Pyne, S. G.; Ung, A. T.; Jatisatiens, A.; Lie, W. *J. Nat. Prod.* **2010**, *73*, 935-941.
- ³³ (-)-**Sessilifoliamida C i (-)-8-epi-stemoamida**: Hoye, A. T.; Wipf, P. *Org. Lett.* **2011**, *13*, 2634-2637.
- ³⁴ (\pm)-**Maistemonine**: mireu ref 23e
- ³⁵ **Stemonidine** (Estructura proposada): Sánchez-Izquierdo, F.; Blanco, P.; Busqué, F.; Alibés, R.; de March, P.; Figueredo, M.; Font, J.; Parella, T. *Org. Lett.* **2007**, *9*, 1769-1772.
- ³⁶ **Nitrones enantiomèricament pures**:
- (a) Golik, J.; Wong, H.; Krishnan, B.; Vyas, D. M.; Doyle, T. W. *Tetrahedron Lett.* **1991**, *32*, 1851-1854. (b) Ballini, R.; Marcantoni, E.; Petrini, M. *J. Org. Chem.* **1992**, *57*, 1316-1318. (c) Oppolzer, W.; Bochet, C. G.; Merifield, E. *Tetrahedron Lett.* **1994**, *35*, 7015-7018. (d) Cicchi, S.; Goti, A.; Brandi, A. *J. Org. Chem.* **1995**, *60*, 4743-4748. (e) de March, P.; Figueredo, M.; Font, J.; Gallagher, T.; Milán, S. *Chem. Commun.* **1995**, 2097-2098. (f) Ishikawa, T.; Tajima, Y.; Fukui, M.; Saito, S. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1863-1864. (g) Hall, A.; Meldrum, K. P.; Therond, P. R.; Wightman, R. H. *Synlett* **1997**, 123-125. (h) Closa, M.; de March, P.; Figueredo, M.; Font, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1031-1037.

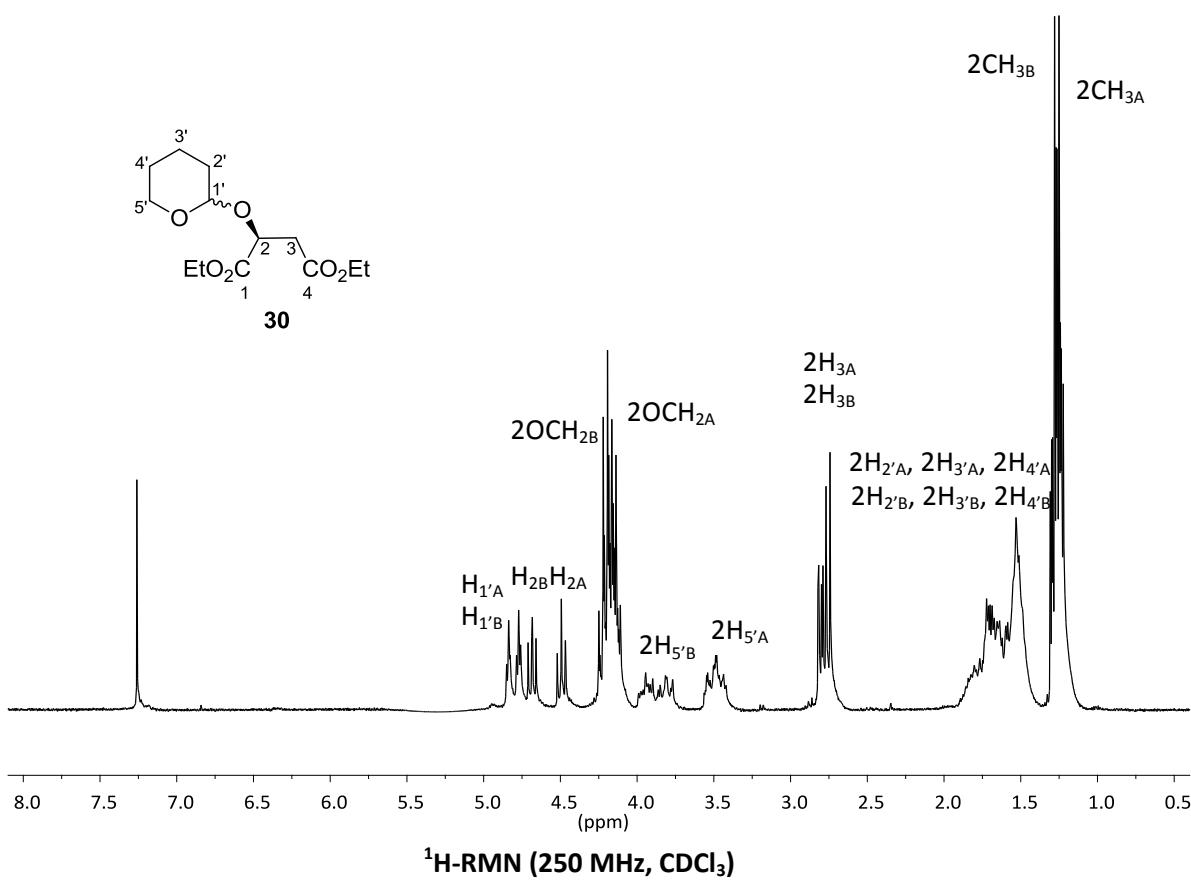
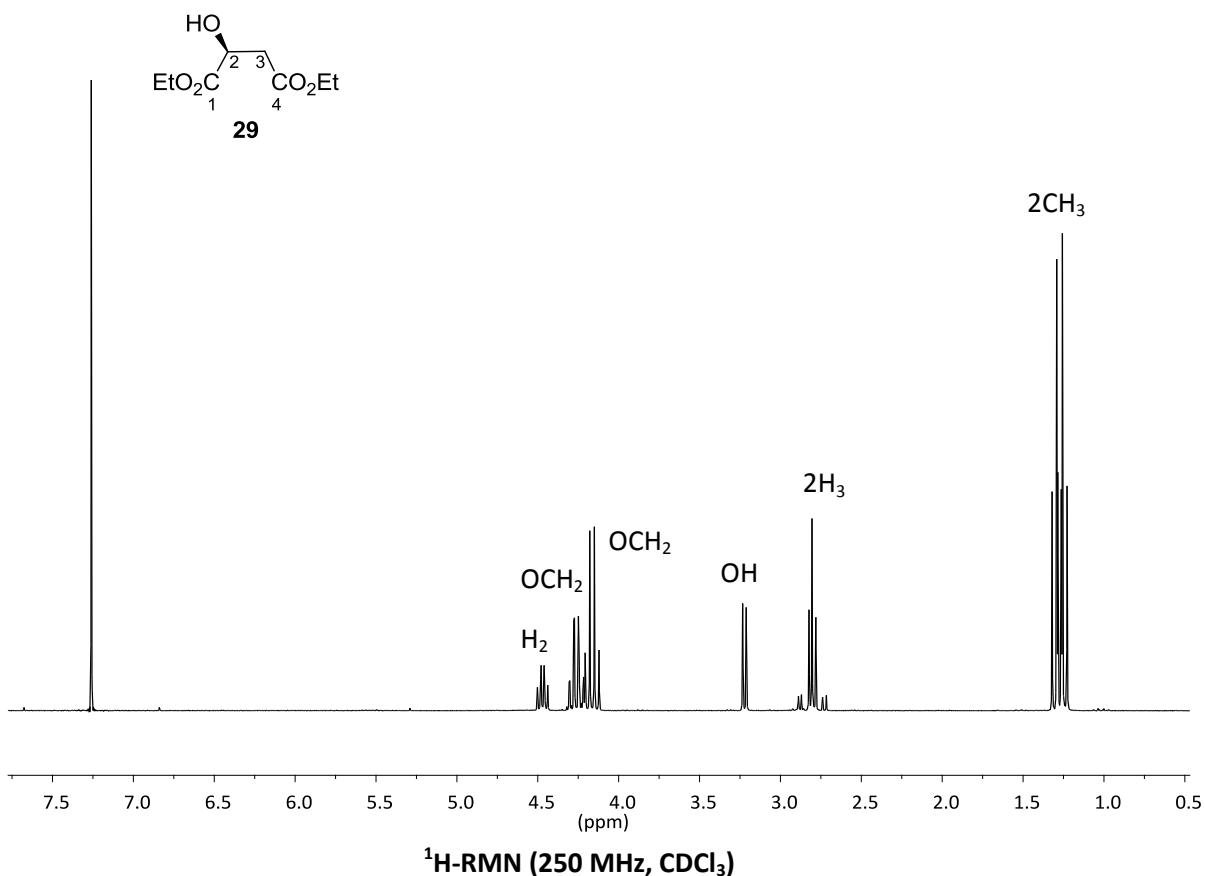
- (i) Merino, P.; Franco, S.; Merchan, F. L.; Tejero, T. *Tetrahedron: Asymmetry* **1997**, *8*, 3489-3496. (j) Goti, A.; Cicchi, S.; Fedi, V.; Nannelli, L.; Brandi, A. *J. Org. Chem.* **1997**, *62*, 3119-3125. (k) Closa, M.; Wightman, R. H. *Synth. Commun.* **1998**, *28*, 3443. (l) Murahashi, S.-I.; Ohtake, H.; Imada, Y. *Tetrahedron Lett.* **1998**, *39*, 2765-2766. (m) Cicchi, S.; Nunes, Jr., J.; Goti, A.; Brandi, A. *Eur. J. Org. Chem.* **1998**, *419*-421. (n) Goti, A.; Cacciarini, M.; Cardona, F.; Brandi, A. *Tetrahedron Lett.* **1999**, *40*, 2853-2856. (o) Chiacchio, U.; Corsaro, A.; Gumina, G.; Rescifina, A.; Iannazzo, D.; Piperno, A.; Romeo, G.; Romeo, R. *J. Org. Chem.* **1999**, *64*, 9321-9327. (p) Carda, M.; Portolés, R.; Murga, J.; Uriel, S.; Marco, J. A.; Domingo, L. R.; Zaragoza, R. J.; Röper, H. *J. Org. Chem.* **2000**, *65*, 7000-7009. (q) Cordero, F. M.; Gensini, M.; Goti, A.; Brandi, A. *Org. Lett.* **2000**, *2*, 2475-2477. (r) Cicchi, S.; Marradi, M.; Goti, A.; Brandi, A. *Tetrahedron Lett.* **2001**, *42*, 6503-6505. (s) Busqué, F.; de March, P.; Figueredo, M.; Font, J.; Gallagher, T.; Milán, S. *Tetrahedron: Asymmetry* **2002**, *13*, 437-445. (t) Cordero, F. M.; Pisaneschi, F.; Gensini, M.; Goti, A.; Brandi, A. *Eur. J. Org. Chem.* **2002**, *12*, 1941-1951. (u) Alibés, R.; Blanco, P.; de March, P.; Figueredo, M.; Font, J.; Álvarez-Larena, A.; Piniella, J. F. *Tetrahedron Lett.* **2003**, *44*, 523-525. (v) Gella, C.; Ferrer, E.; Alibés, R.; Busqué, F.; de March, P.; Figueredo, M.; Font, J. *J. Org. Chem.* **2009**, *74*, 6365-6367. (w) Brandi, A.; Cardona, F.; Cicchi, S.; Cordero, F.; Goti, A. *Chem. Eur. J.* **2009**, *15*, 7808-7821.
- ³⁷ Eva Casas, *Tesi Doctoral*, Universitat Autònoma de Barcelona, **2005**.
- ³⁸ Kakuta, D.; Hitotsuyanagi, Y.; Matsuura, N.; Fukaya, H.; Takeya, K.; *Tetrahedron*, **2003**, *59*, 7779-7786.
- ³⁹ Miura, K.; Fujisawa, N.; Saito, H.; Wang, D.; Hosomi, A. *Org. Lett.* **2001**, *3*, 2591-2594.
- ⁴⁰ Raghavan, S.; Reddy, S. R.; Tony, K.A.; Kumar, C. N.; Varma, A. K.; Nangia, A. *J. Org. Chem.* **2002**, *67*, 5838-5841.
- ⁴¹ Alonso-Perarnau, D.; de March, P.; Figueredo, M.; Font, J.; Soria, A. *Tetrahedron* **1993**, *49*, 4267-4274.
- ⁴² (a) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574-1585. (b) Barton, D. H. R. ; Dorchak, J. ; Jaszberenyl, J. C. *Tetrahedron* **1992**, *48*, 7435-7446.
- ⁴³ Lainchbury, M. D.; Medley, M. I.; Taylor, P. M.; Hirst, P.; Dohle, W.; Booker-Milburn, K. *J. Org. Chem.* **2008**, *73*, 6497-6505.
- ⁴⁴ a) Roy, B. G.; Maity, J. K.; Drew, M. G.; Achari, B.; Mandal, S. B. *Tetrahedron Lett.* **2006**, *47*, 8821-8825. b) Roy, B. G.; Jana, P. K.; Achari, B.; Mandal, S. B. *Tetrahedron Lett.* **2007**, *48*, 1563-1566.
- ⁴⁵ (a) Dupont, C.; Guénard, D.; Tchertanov, L.; Thoret, S.; Guérinne, F. *Bioorg. Med. Chem.* **1999**, *7*, 2961-2969. (b) Kornet, M. J.; Thio, P. A.; Tan, S. I. *J. Org. Chem.* **1968**, *33*, 3637-3639.
- ⁴⁶ González-Gálvez, D.; García-García, E.; Alibés, R.; Bayón, P.; de March, P.; Figueredo, M.; Font, J. *J. Org. Chem.* **2009**, *34*, 6199-6211.
- ⁴⁷ Giraud, L.; Huber, V.; Jenny, T. *Tetrahedron*, **1998**, *54*, 11899-11906.
- ⁴⁸ Yamazaki, N.; Atobe, M.; Kibayashi, C. *Tetrahedron Lett.* **2001**, *42*, 5029-5032.
- ⁴⁹ (a) Gazak, R.; Kren, V.; Sedmera, P.; Passarella, D; Novotna, M.; Danieli, B. *Tetrahedron* **2007**, *63*, 10466-10447. (b) Zou, M.-F.; Cao, J.; Kopajtic, T.; Desai, R. I.; Katz, J. L.; Newman, A. H. *J. Med. Chem.* **2006**, *49*, 6391-6399. (c) Biel, M.; Deck, P.; Giannis, A.; Waldmann, H. *Chem. Eur. J.* **2006**, *12*, 4121-43. (d) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155-4156. (e) Appell, R. B.; Duguid, R. J. *Org. Process Res. Dev.* **2000**, *4*, 172-174.
- ⁵⁰ Jacobi, P. A.; Blum, C. A.; DeSimone, R. W.; Udodong, U. E. S. *J. Am. Chem. Soc.* **1991**, *113*, 5384-5392.
- ⁵¹ Meltzer, P. C.; Wang, B.; Chen, Z.; Blundell, P.; Jayaraman, M.; Gonzalez, M. D.; George, C.; Madras, B. K. *J. Med. Chem.* **2001**, *44*, 2619-2635.
- ⁵² Koskinen, A. P.; Helaja, J.; Kumpulainen, E. T.; Koivisto, J.; Mansikkamäki, H.; Rissanen, K. *J. Org. Chem.* **2005**, *70*, 6447-6453.
- ⁵³ Boers, R., B.; Pazos Randulfe, Y.; van der Haas, H.; van Rossum-Baan, M.; Lugtenburg, J. *Eur. J. Org. Chem.* **2002**, 2094-2108.
- ⁵⁴ Aggarwal, V. K.; Eames, J.; de las Heras, M. A.; McIntyre, S.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4456-4461.
- ⁵⁵ Chorki, F.; Grellepois, F.; Crousse, B.; Hoang, V. D. ; Hung, N. V. ; Bonnet-Delpont, D.; Bégué, J. P. *Org. Lett.* **2002**, *4*, 757-759.
- ⁵⁶ Jas, G. *Synthesis*, **1991**, *11*, 965-966.
- ⁵⁷ Brown, S. P.; Goodwin, N. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2003**, *125*, 1192-1194.

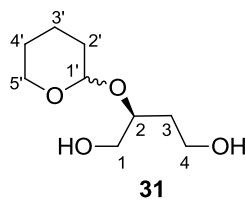
5. REFERENCES

- ⁵⁸ (a) Mangion, I. K.; Northrup, A. B.; MacMillan, D. W. C. *Angew. Chem. Int. Ed.* **2004**, *41*, 6722-6724. (b) Huang, Y.; Walji, A. M.; Larsen, C. H.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2005**, *127*, 15051-15053. (c) Chen, Y. K.; Yoshida, M.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2006**, *128*, 0328-9329. (d) Jang, H.-Y.; Hong, J.-B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2007**, *129*, 7004-7005. (e) Borths, C. J.; Carrera, D. E.; MacMillan, D. W. C. *Tetrahedron* **2009**, *65*, 6746-6753.
- ⁵⁹ (a) Kurasaki, H.; Okamoto, I.; Morita, N.; Tamura, O. *Org. Lett.* **2009**, *11*, 1179-1181. (b) Kurasaki, H.; Okamoto, I.; Morita, N.; Tamura, O. *Chem. Eur. J.* **2009**, *15*, 12754-12763.
- ⁶⁰ Mhaske, S. B.; Argade, N. P. *J. Org. Chem.* **2001**, *66*, 9038-9040.
- ⁶¹ Zabawa, T. P.; Chemler, S. R. *Org. Lett.* **2007**, *9*, 2035-2038.
- ⁶² Gagné, M. R.; Stern, C. L.; Marks, T. J.; *J. Am. Chem. Soc.* **1992**, *114*, 275-294.
- ⁶³ (a) Martin, S. F.; Chen, H.-J.; Courtney, A. K.; Liao, Y.; Pitzel, M.; Ramser, M. N.; Wagman, A. S. *Tetrahedron* **1996**, *52*, 7251-7264. (b) Kumareswaran, R.; Shin, S.; Gallou, I.; RajanBabu, T. V. *J. Org. Chem.* **2004**, *21*, 7157-7170. (c) Chevallier, F.; Grogne, E. L.; Beaudet, I.; Fliegel, F.; Evain, M.; Quintard, J.-P. *Org. Biomol. Chem.* **2004**, *2*, 3128-3133.
- ⁶⁴ (a) Tarling, C. A.; Holmes, A. B.; Markwell, R. E.; Pearson, N. D. *J. Chem. Soc., Perkin Trans. 1*, **1999**, 1695-1701. (b) Marhold, M.; Buer, A.; Hiemstra, H.; Maarseveen, J.H.; Haufe, G. *Tetrahedron Lett.* **2004**, *45*, 57-60. (c) Marsden, S. P.; McElhinney, A. D. *Synlett* **2005**, *16*, 2528-2530. (d) Marsden, S. P.; McElhinney, A. D. *Beilstein J. Org. Chem.* **2008**, *4*, 8.
- ⁶⁵ Koseki, Y.; Fujino, K.; Takeshita, A.; Sato, H.; Nagasaka, T. *Tetrahedron: Asymmetry* **2007**, *18*, 1533-1539.
- ⁶⁶ (a) Rassu, G.; Zanardi, F.; Battistini, L.; Casiraghi, G. *Synlett* **1999**, 1333-1350. (b) Szloseck, M.; Franck, X.; Figadère, B.; Clavé, A. *J. Org. Chem.* **1998**, *63*, 5169-5172. (c) Franck, X.; Vaz Araujo, M. E.; Jullian, J.-C.; Hocquemiller, R.; Figadère, B. *Tetrahedron Lett.* **2001**, *42*, 2801-2803. (d) Busqué, F.; de March, P.; Figueiredo, M.; Font, J.; Sanfeliu, E. *Tetrahedron Lett.* **2002**, *43*, 5583-5585.
- ⁶⁷ Parés, S. Tesis Doctoral, Universitat Autònoma de Barcelona, **2010**.
- ⁶⁸ (a) Molander, G. A.; Quirmbach, M. S.; Silva, L. F.; Spencer, K. C.; Balsells, J. *Org. Lett.* **2001**, *3*, 2257-2260. (b) Shigehisa, H.; Mizutani, T.; Tosaki, S.; Ohshima, T.; Shibasaki, M.; *Tetrahedron* **2005**, *61*, 5057-5065. (c) Yamashita, S.; Iso, K.; Hirama, M. *Org. Lett.* **2008**, *10*, 3413-3415. (d) Nicolau, K. C.; Ding, H.; Richard, J.-A.; Chen, D. Y.-K. *J. Am. Chem. Soc.* **2010**, *132*, 3815-3818.
- ⁶⁹ Yadav, J. S.; Reddy, B. V.; Narasimhulu, G.; Reddy, N. S.; Reddy, P. J. *Tetrahedron Lett.* **2009**, *50*, 3760-3762.
- ⁷⁰ Grieco, P. A.; Dubay, W. J.; Todd, L. J. *Tetrahedron Lett.* **1996**, *48*, 8707-8710.
- ⁷¹ Pearson, W. H.; Schkeryantz, J. M.; *J. Org. Chem.* **1992**, *57*, 2986-2987.
- ⁷² Clarke, P. A.; Cridland, A. P.; Rolla, G. A.; Iqbal, M.; Bainbridge, N. P.; Whitwood, A. C.; Wilson, C. *J. Org. Chem.* **2009**, *74*, 7812-7821.
- ⁷³ Liu, G.; Meng, J.; Feng, C.-G.; Huang, P.-Q. *Tetrahedron: Asymmetry* **2008**, *19*, 1297-1303.
- ⁷⁴ Ray, D.; Paul, S.; Brahma, S.; Ray, J. *Tetrahedron Lett.* **2007**, *48*, p. 8005-8008.
- ⁷⁵ Nakata, K.; Kobayashi, Y. *Org. Lett.* **2005**, *7*, 1319-1322.
- ⁷⁶ (a) Lamblin, M; Nassar-Hardly, L.; Hieso, J.-C.; Fouquet, F.-X.; Felpin, F.-X. *Adv. Synth. Catal.* **2010**, *352*, 33-79. (b) Webber, P.; Krische, M. J. *J. Org. Chem.* **2008**, *73*, 9379-9387. (c) Braun, M.; Meier, T. *Angew. Chem. Int. Ed.* **2006**, *45*, 6952-6955. (d) Norsikian, S.; Lubineau, A. *Org. Biomol. Chem.* **2005**, 4089-94. (e) Ogasawara, M.; Ngo, H. L.; Sakamoto, T.; Takahashi, T.; Lin, W. *Org. Lett.* **2005**, *7*, 2881-2884. (f) Ikeda, S.-I.; Sanuki, R.; Miyachi, H.; Miyashita, H.; Taniguchi, M.; Odashima, K. *J. Am. Chem. Soc.* **2004**, *126*, 10331-10338. (g) Trost, B. M.; Shi, Y. *J. Am. Chem. Soc.* **1993**, *115*, 9421-9438.
- ⁷⁷ (a) Molander, G. A.; McWilliams, J. C.; Noll, B. C. *J. Am. Chem. Soc.* **1997**, *119*, 1265-1276. (b) Märkl, G.; Sauer, H.; Kreitmeier, P.; Burgemeister, T.; Kastner, F. *Tetrahedron*, **1999**, *55*, 13407-13416. (c) Park, J.; Fu, H.; Pei, D. *Biochemistry*, **2003**, *42*, 5159-5167. (d) Kuerschner, L.; Ejsing, C. S.; Ekroos, K.; Schevchenko, A.; Anderson, K. I.; Thiele, C. *Nature Methods* **2005**, 39-45. (e) Liao, W.-W.; Ibrahim, I.; Córdova, A. *Chem. Commun.* **2006**, 674-676. (f) Figueiredo, R. M.; Berner, R.; Julis, J.; Liu, T.; Türp, D.; Christmann, M. *J. Org. Chem.* **2007**, *72*, 640-642. (g) Hsu, D. S.; Liao, C.-C. *Org. Lett.* **2007**, *9*, 4563-4565. (h) Sisa, M.; Pla, D.; Altuna, M.; Francesch, A.; Cuervas, C.; Albericio, F.; Alvarez, M. *J. Med. Chem.* **2009**, *52*, 6217-6223.
- ⁷⁸ Valenta, P.; Drucker, N. A.; Bode, J. W.; Walsh, P. J. *Org. Lett.* **2009**, *11*, 2117-2119.

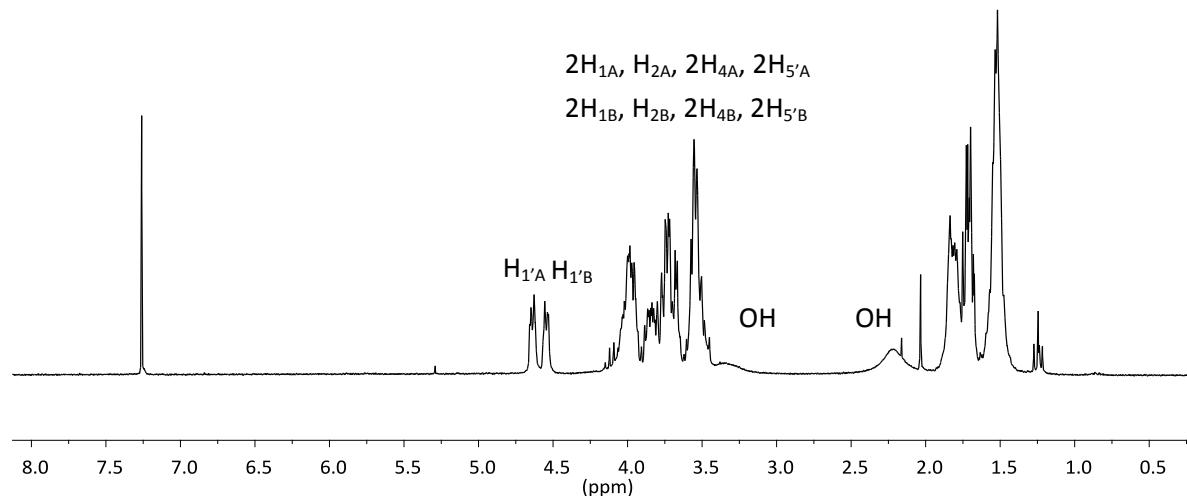
- ⁷⁹ Quintard, A.; Lefranc, A.; Alexakis, A. *Org. Lett.* **2011**, *13*, 1540-1543.
- ⁸⁰ Evans, A. D.; Kværnø, L.; Dunn, T. V.; Beauchemin, A.; Raymer, B.; Mulder, J. A.; Olhava, E. J.; Juhl, M.; Kagechika, K.; Favor, D. A. *J. Am. Chem. Soc.* **2008**, *130*, 16295–16309.
- ⁸¹ (a) Piers, E.; Renaud, J. *J. Chem. Soc., Chem. Commun.* **1990**, 1324-1326. (b) Bull, J. R.; Thomson, R. I. *J. Chem. Soc., Perkin Trans. 1*, **1990**, 241-251. (c) Ermolenko, M. S. *Tetrahedron Lett.* **1996**, *37*, 6711-6712. (d) Njardarson, J. T.; McDonald, I. M.; Spiegel, D. A.; Inoue, M.; Wood, J. *Org. Lett.* **2001**, *3*, 2435-2438. (e) Lassaletta, J. M.; Vázquez, J.; Prieto, A.; Fernández, R.; Raabe, G.; Enders, D. *J. Org. Chem.* **2003**, *68*, 2698-2703. (f) Ma, B.; Snyder, J. K. *Tetrahedron Lett.* **2005**, *46*, 703-706. (g) Joseph-Nathan, P.; Reyes-Trejo, B.; Morales-Ríos, M. S. *J. Org. Chem.* **2006**, *71*, 4411-4417. (h) Snyder, S. A.; Corey, E. J. *J. Am. Chem. Soc.* **2006**, *128*, 740-742. (i) Corbu, A.; Castro, J. M.; Aquino, M.; Gandara, Z.; Retailleau, P.; Arseniyadis, S. *Eur. J. Org. Chem.* **2010**, 1483-1493.
- ⁸² (a) Gutierrez, C. G.; Stringham, R. A.; Nitashaka, T.; Glasscock, K. G. *J. Org. Chem.* **1980**, *45*, 3393-3395. (b) Kiyooka, S.; Hena, M. A.; Goto, F. *Tetrahedron: Asymmetry*, **1999**, *10*, 2871-2879. (c) Kim, S.; Oh, D. H.; Yoon, J.-Y.; Cheong, J. H. *J. Am. Chem. Soc.* **1999**, *121*, 5330-5331. (d) Davis, F. A.; Fang, T.; Goswami, R. *Org. Lett.* **2002**, *4*, 1599-1602. (e) Pandey, G.; Raikar, S. B. *Tetrahedron Lett.* **2006**, *47*, 2029-2032. (f) Davis, F.; Santhanaraman, M. *J. Org. Chem.* **2006**, *71*, 4222-4226. (g) Miyagawa, T.; Nagai, K.; Yamada, A.; Sugihara, Y.; Fukuda, T.; Fukuda, T.; Uchida, R.; Tomoda, H.; Omura, S.; Nagamitsu, T. *Org. Lett.* **2011**, *13*, 1158-1161.

6. Recull d'espectres

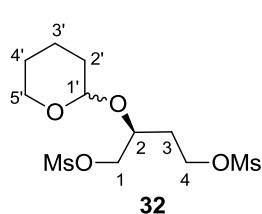




2H_{3A}, 2H_{2'A}, 2H_{3'A}, 2H_{4'A}
2H_{3A}, 2H_{2'A}, 2H_{3'A}, 2H_{4'A}



¹H-RMN (250 MHz, CDCl₃)



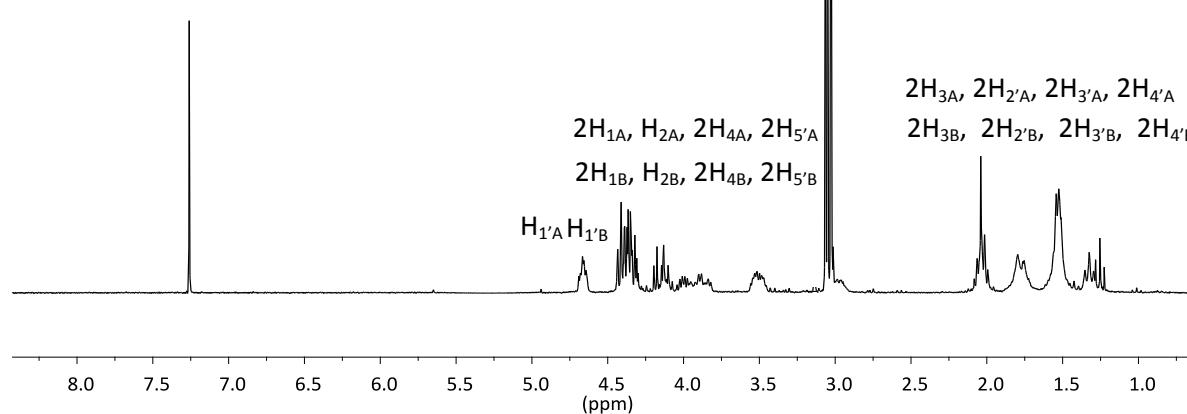
2CH_{3A}
2CH_{3B}

2H_{3A}, 2H_{2'A}, 2H_{3'A}, 2H_{4'A}
2H_{3B}, 2H_{2'B}, 2H_{3'B}, 2H_{4'B}

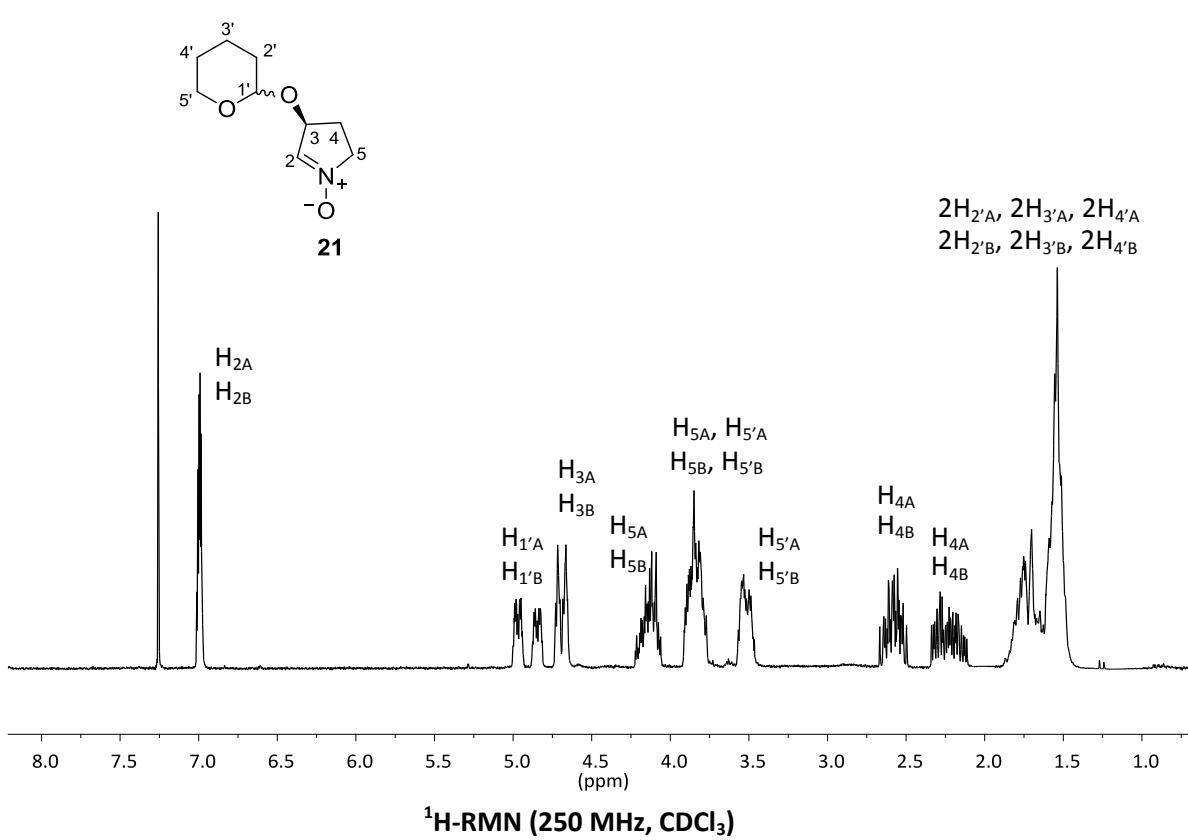
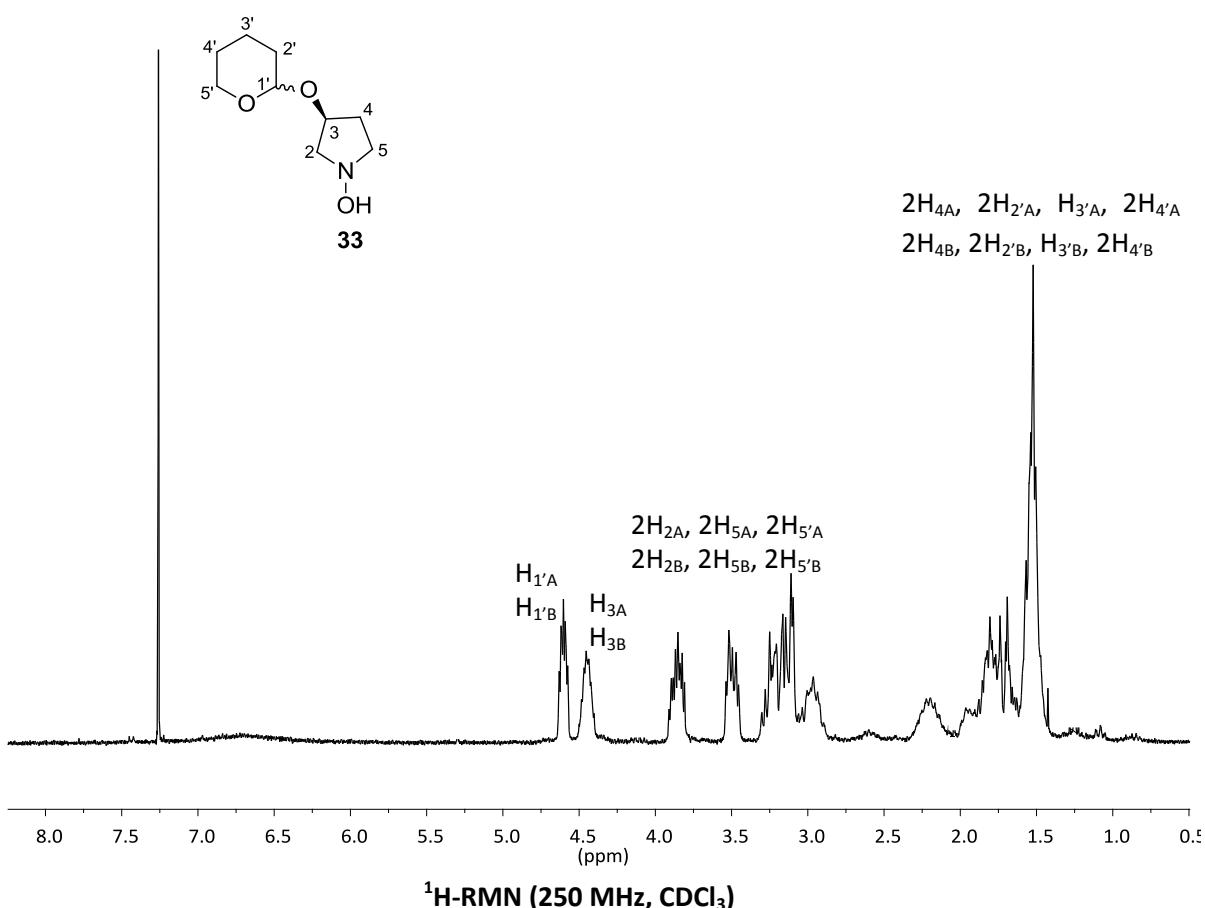
2H_{1A}, H_{2A}, 2H_{4A}, 2H_{5'A}

2H_{1B}, H_{2B}, 2H_{4B}, 2H_{5'B}

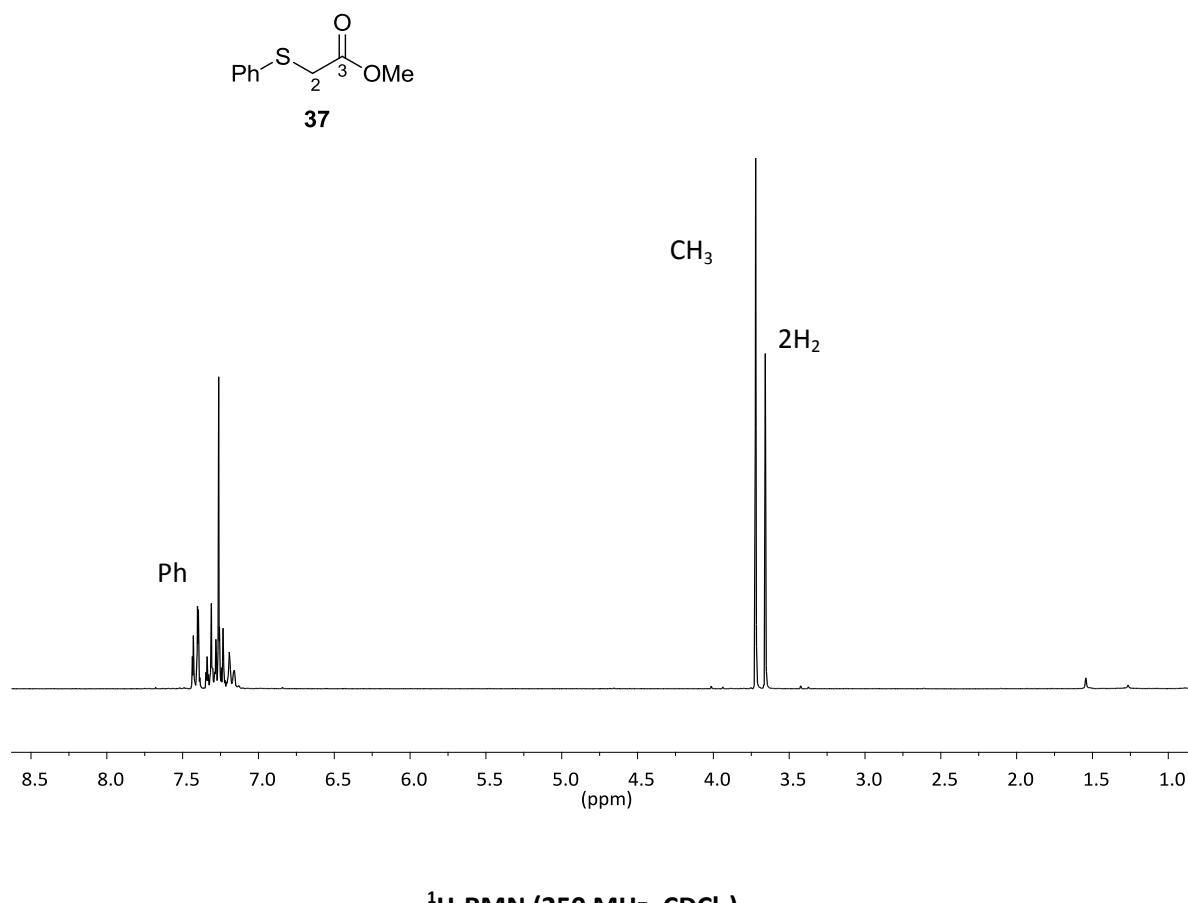
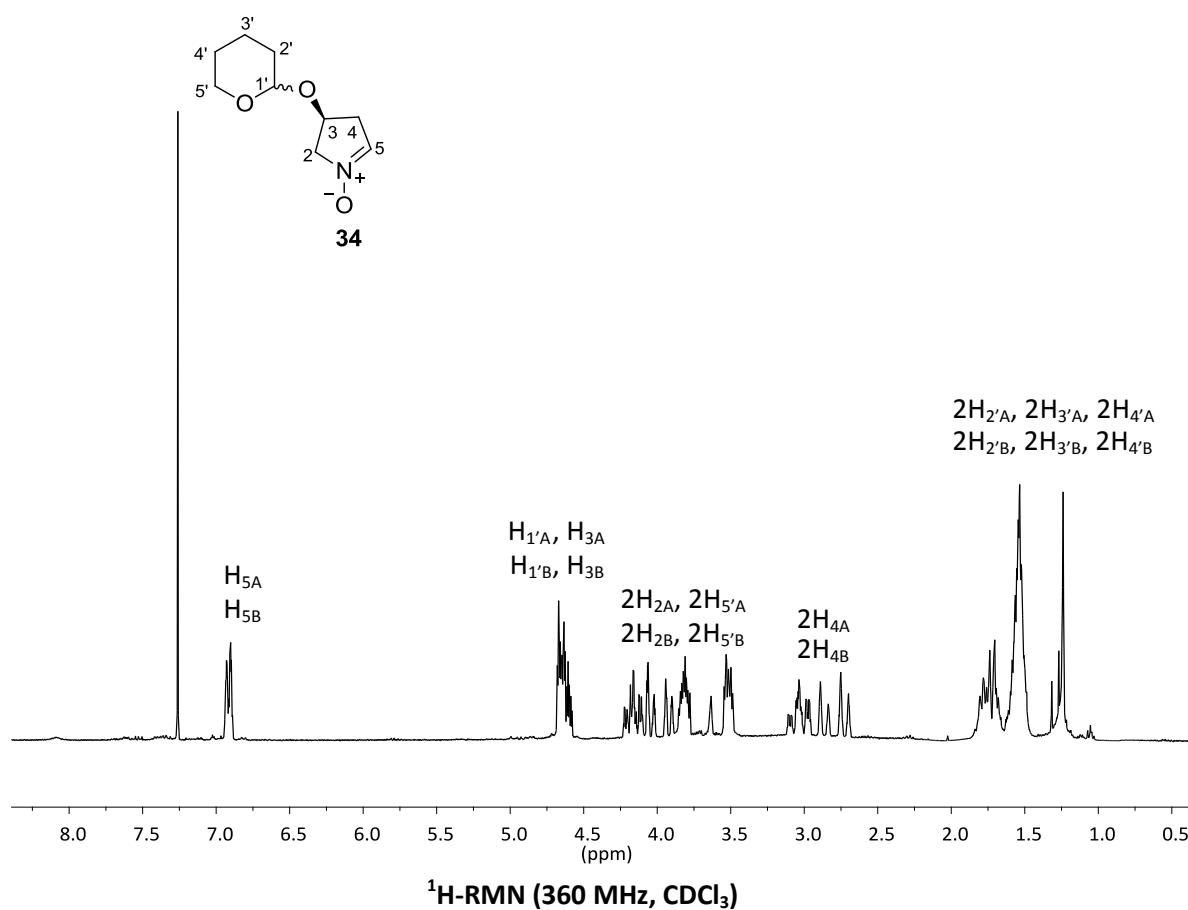
H_{1'A} H_{1'B}

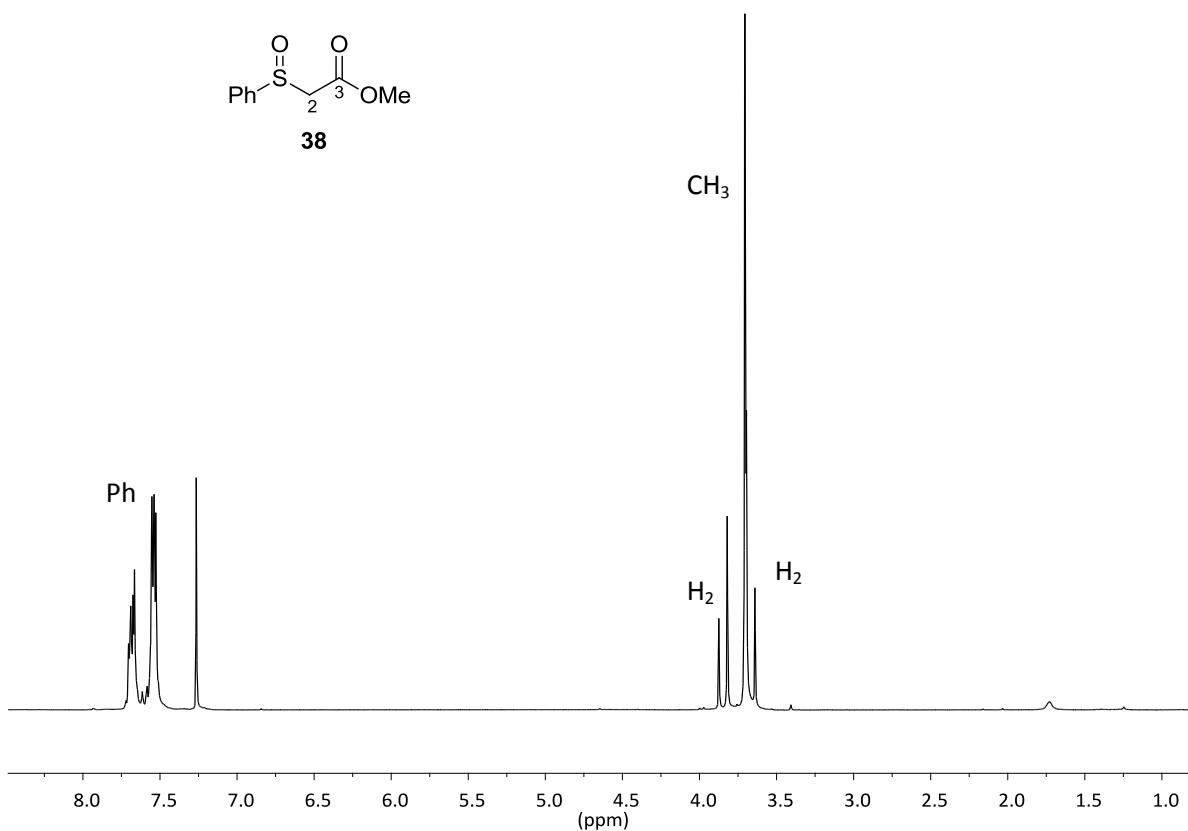
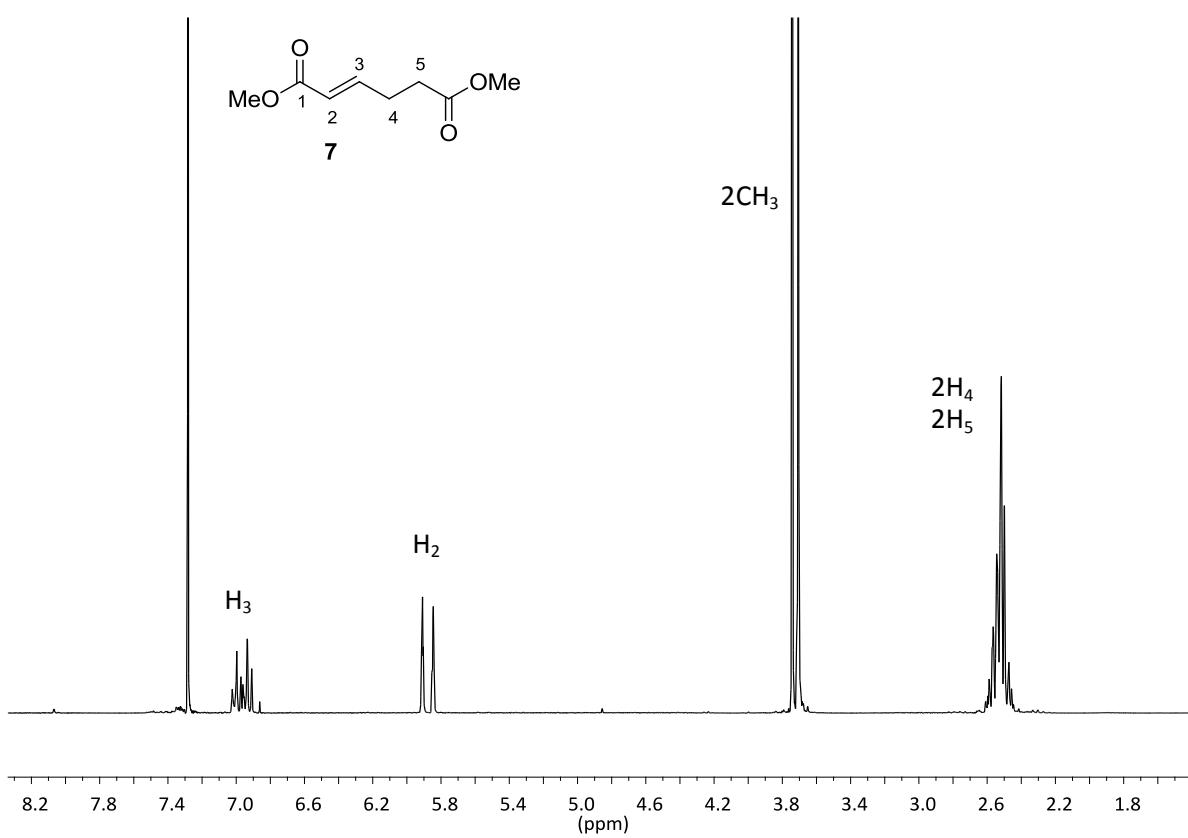


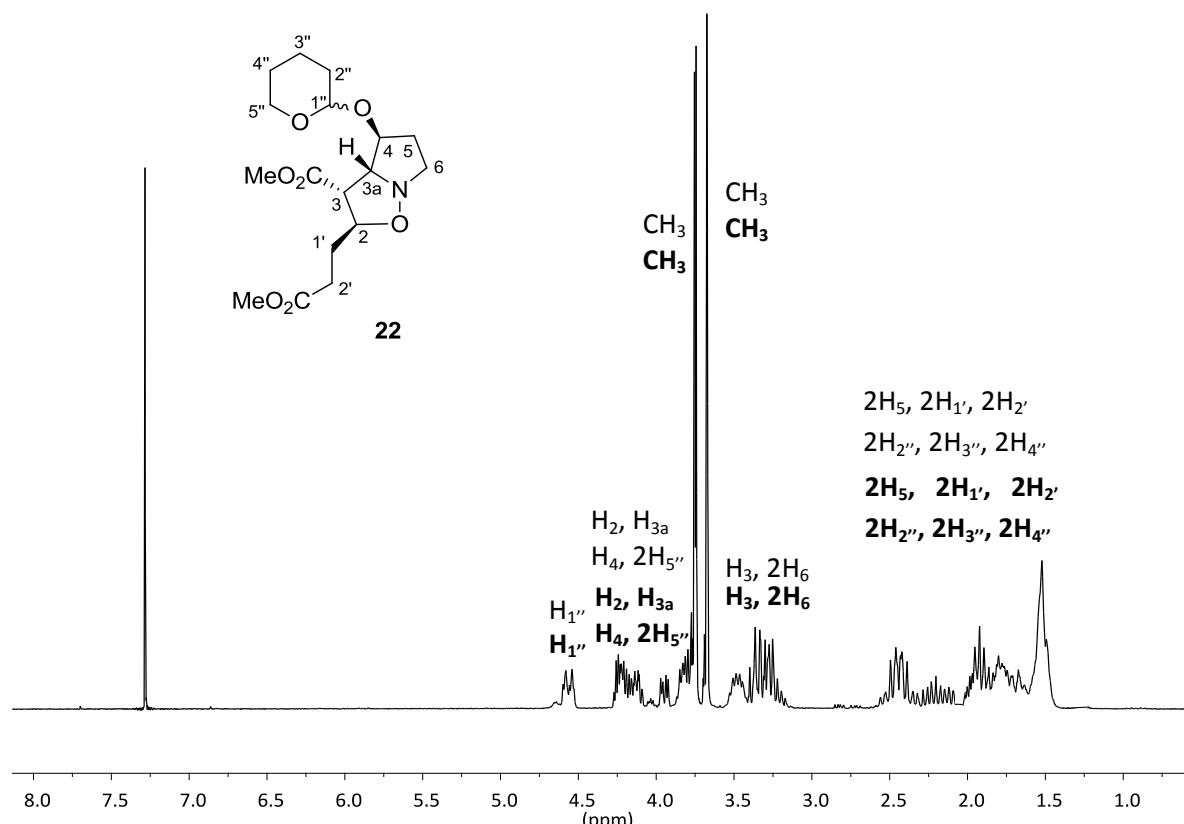
¹H-RMN (250 MHz, CDCl₃)



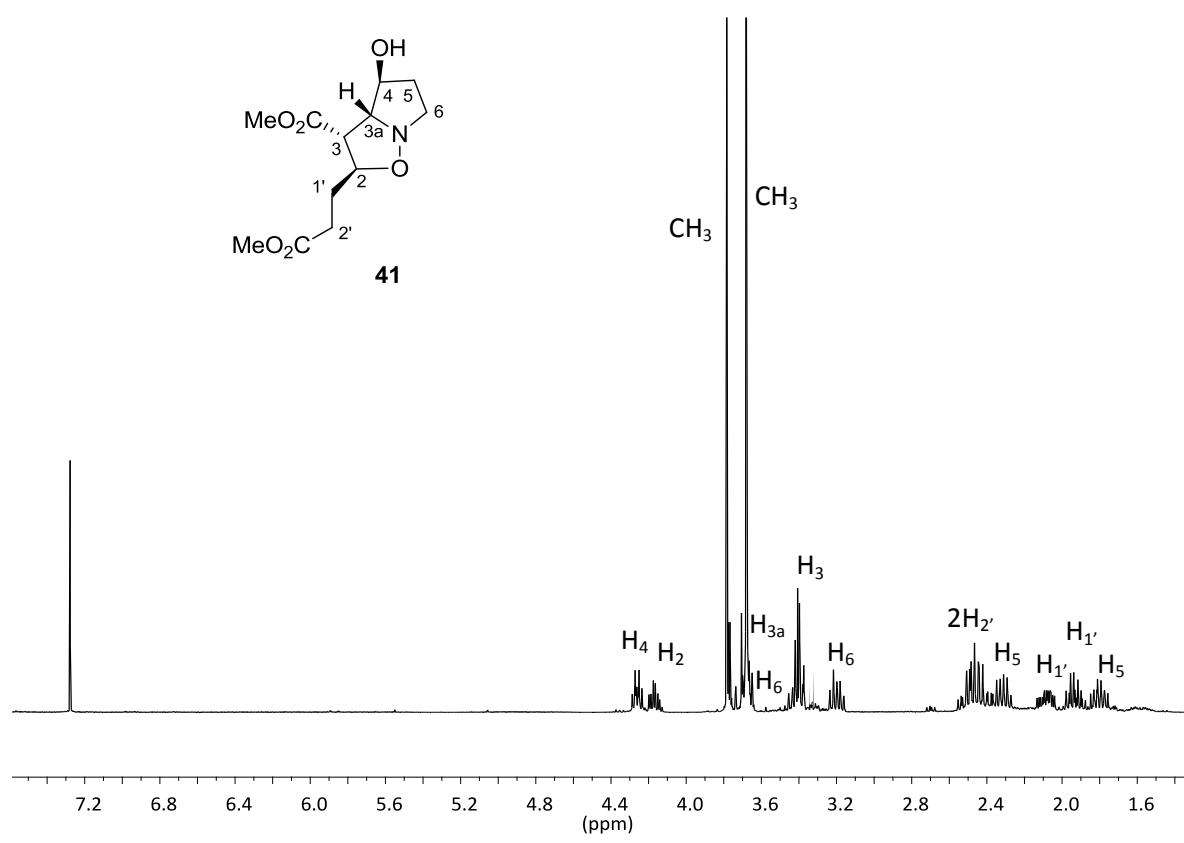
6. RECULL D'ESPECTRES



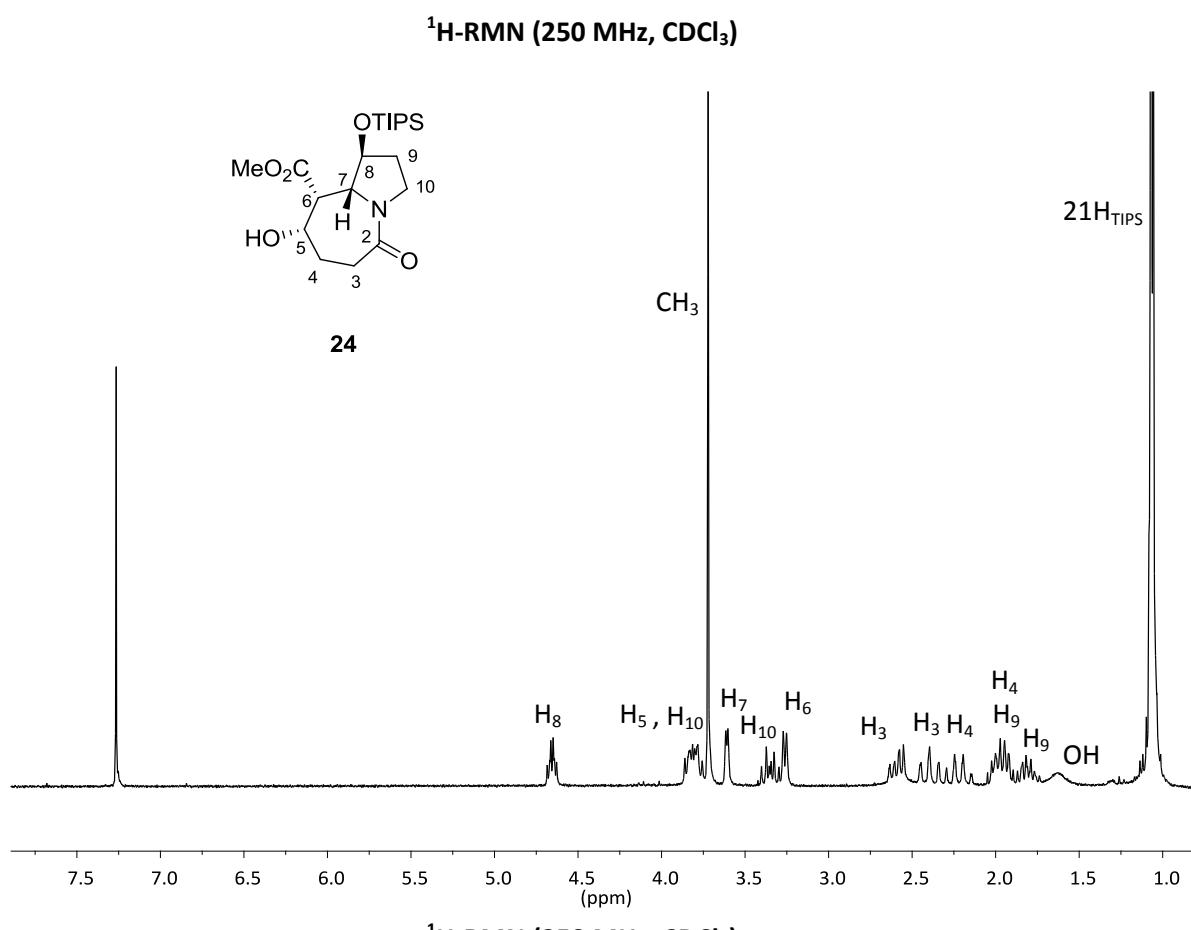
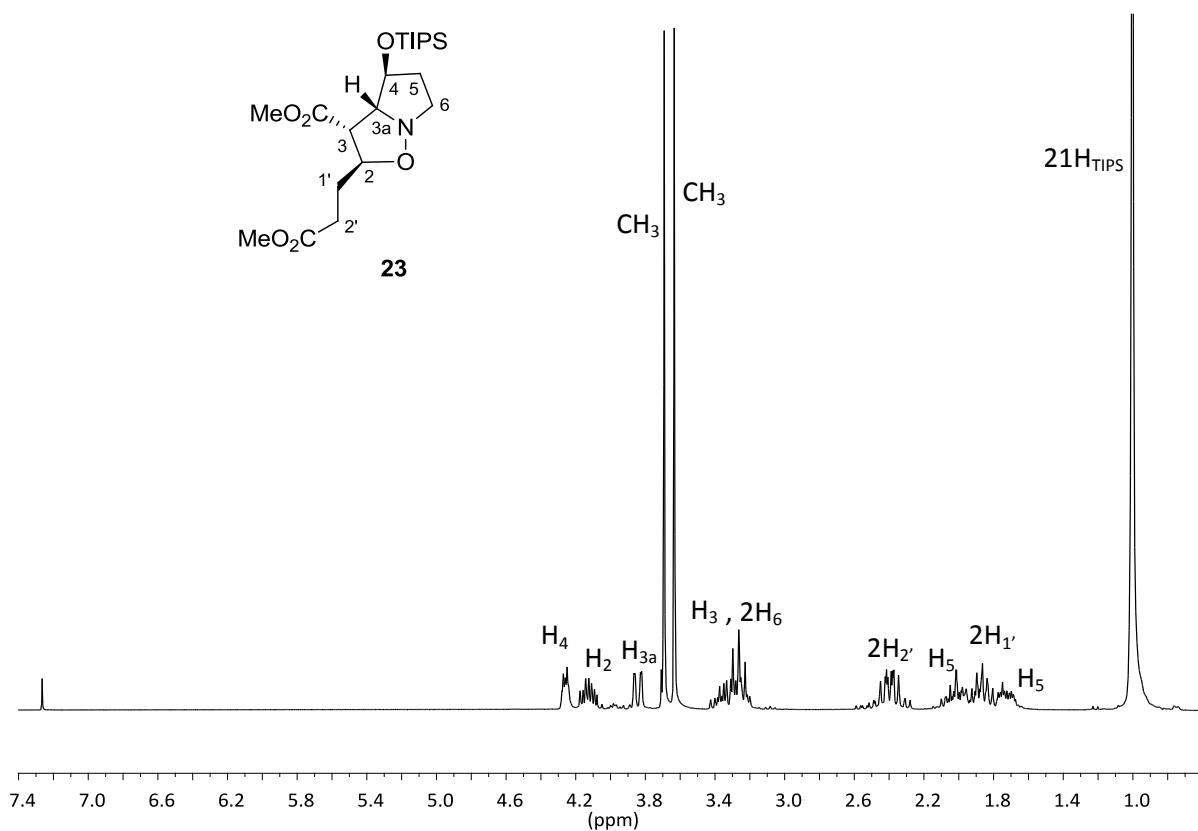
 **^1H -RMN (250 MHz, CDCl_3)** **^1H -RMN (250 MHz, CDCl_3)**

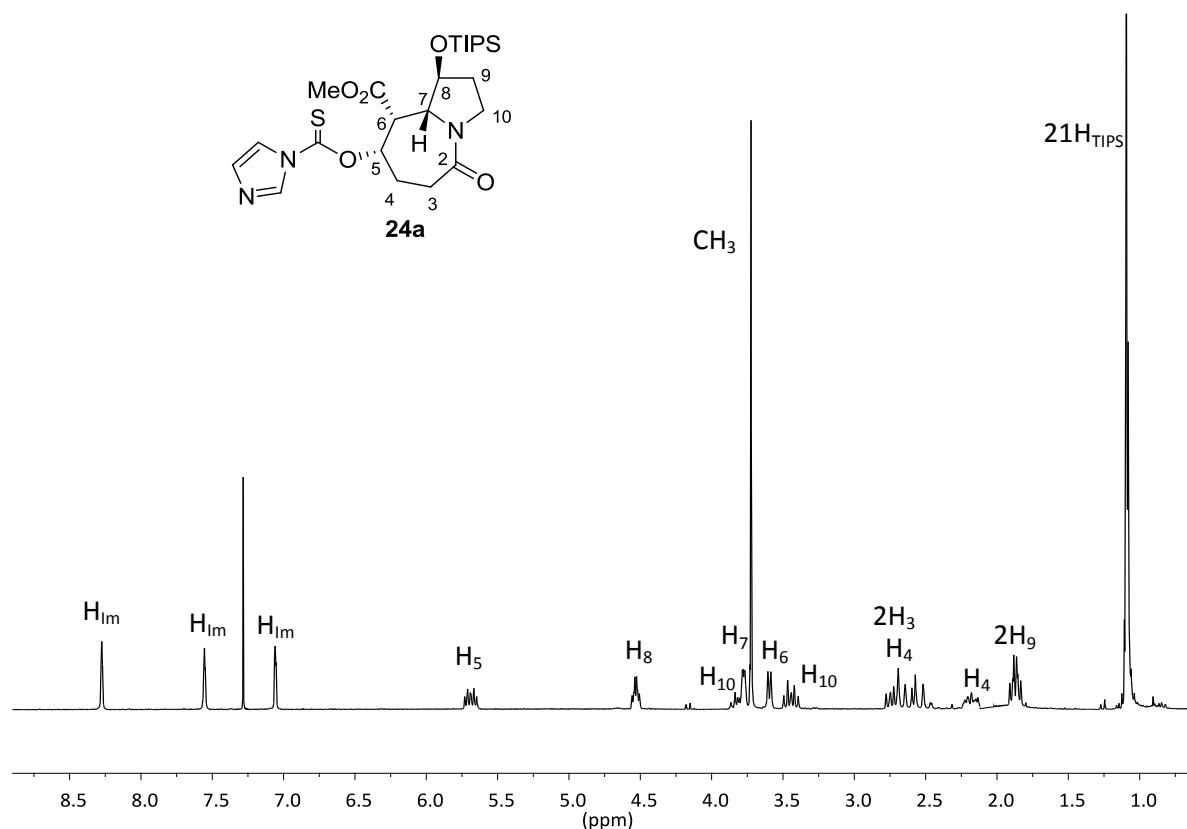


¹H-RMN (250 MHz, CDCl₃)

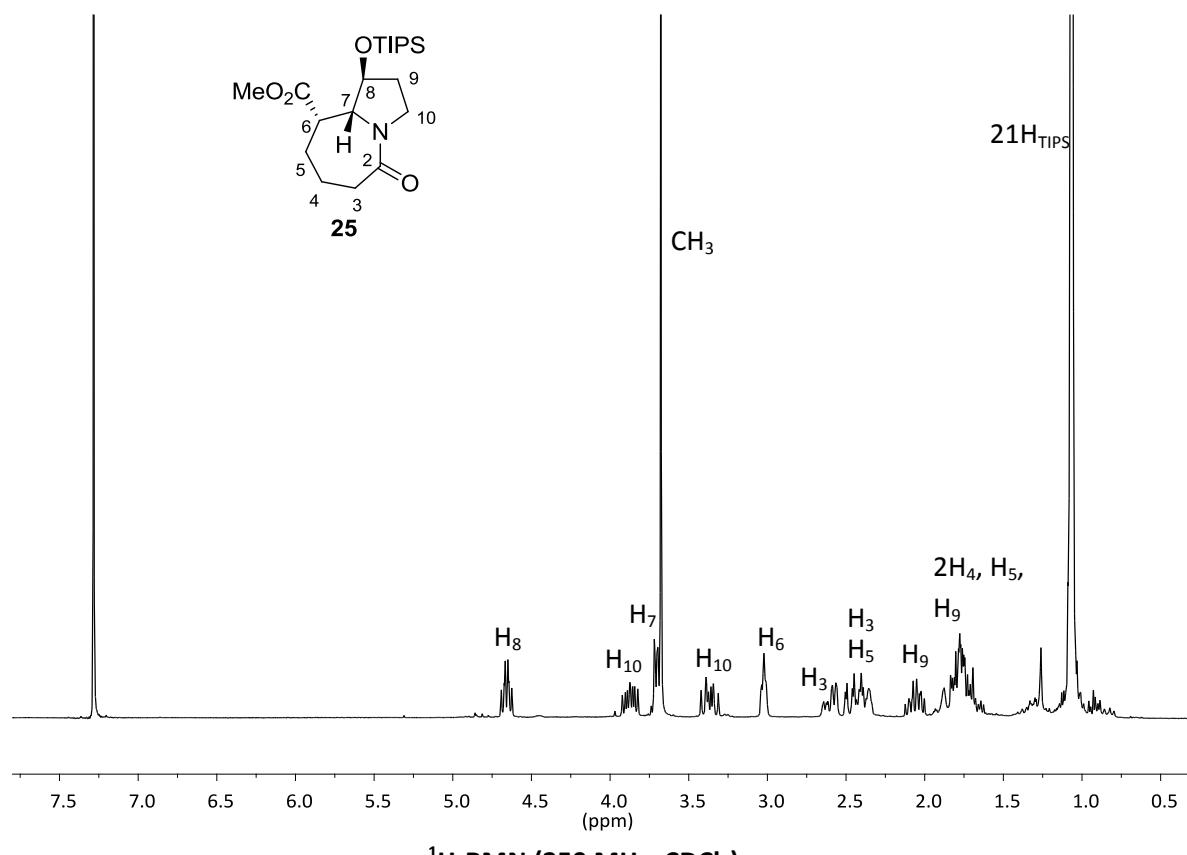


¹H-RMN (360 MHz, CDCl₃)

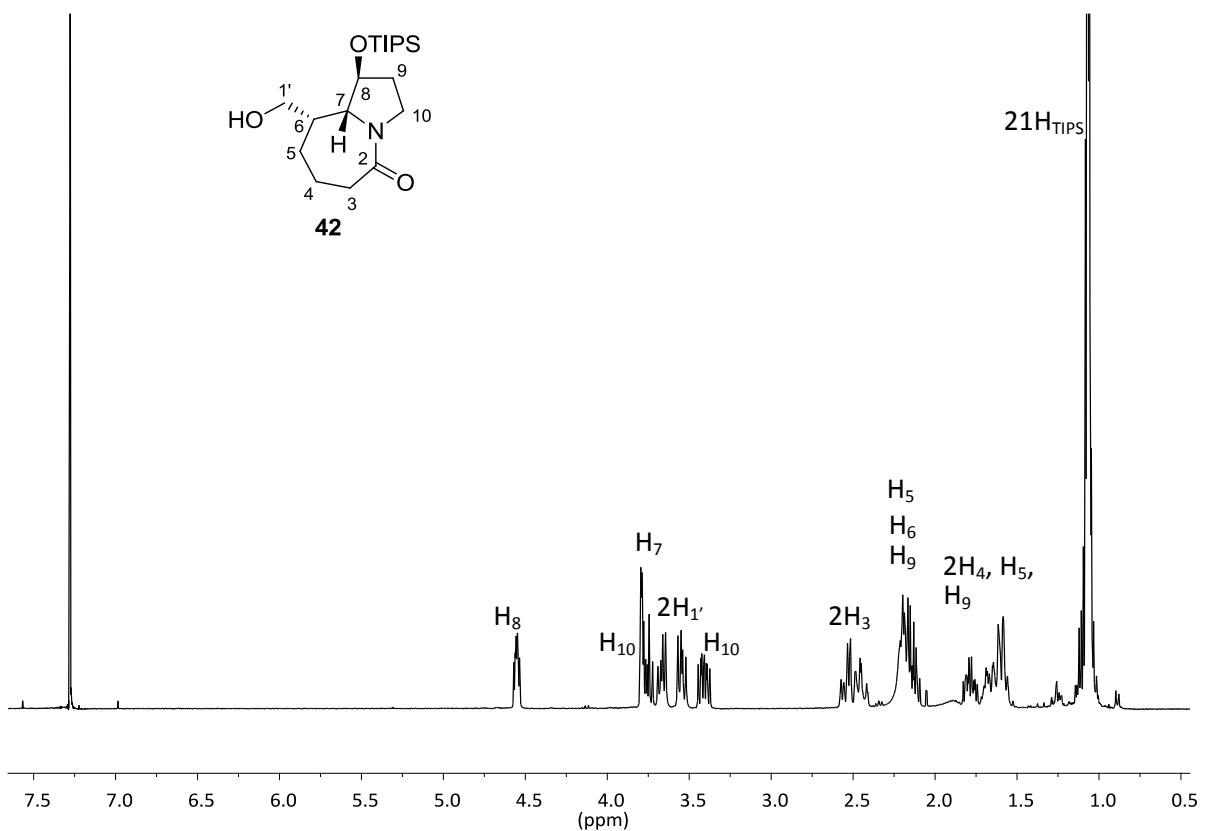
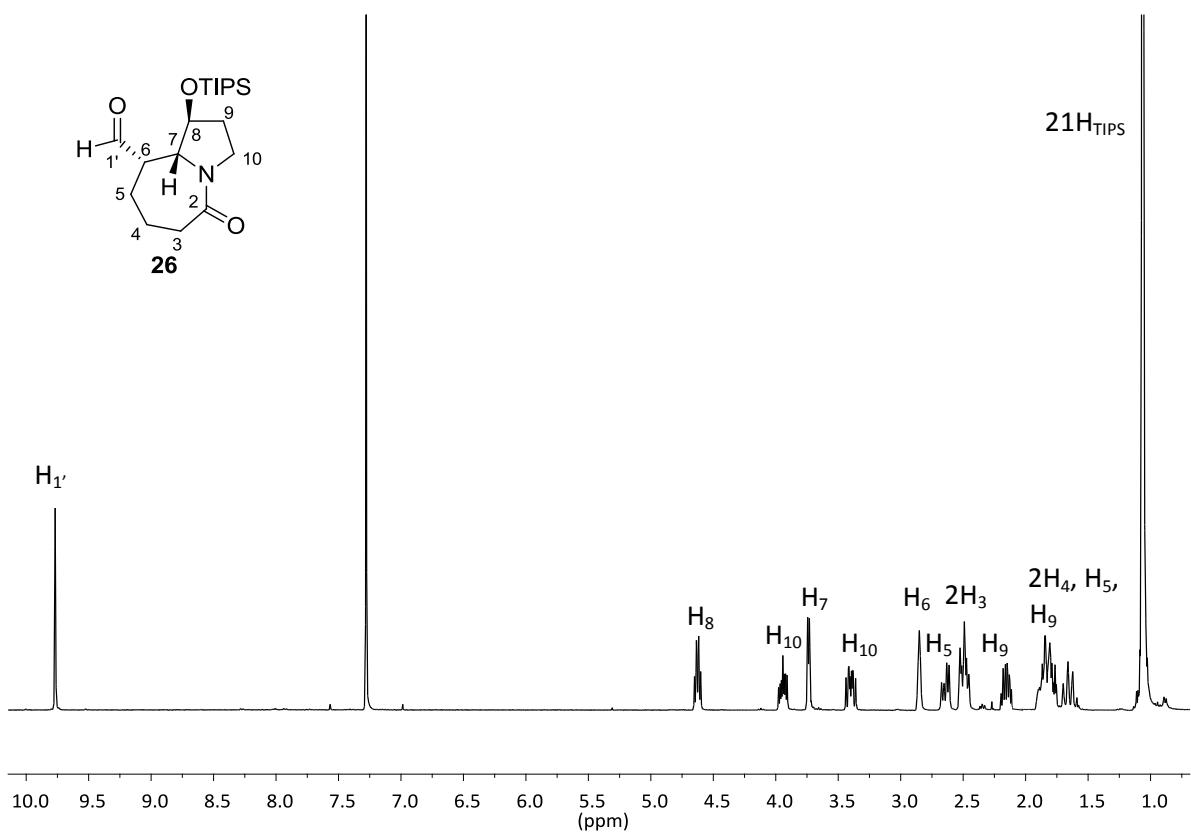


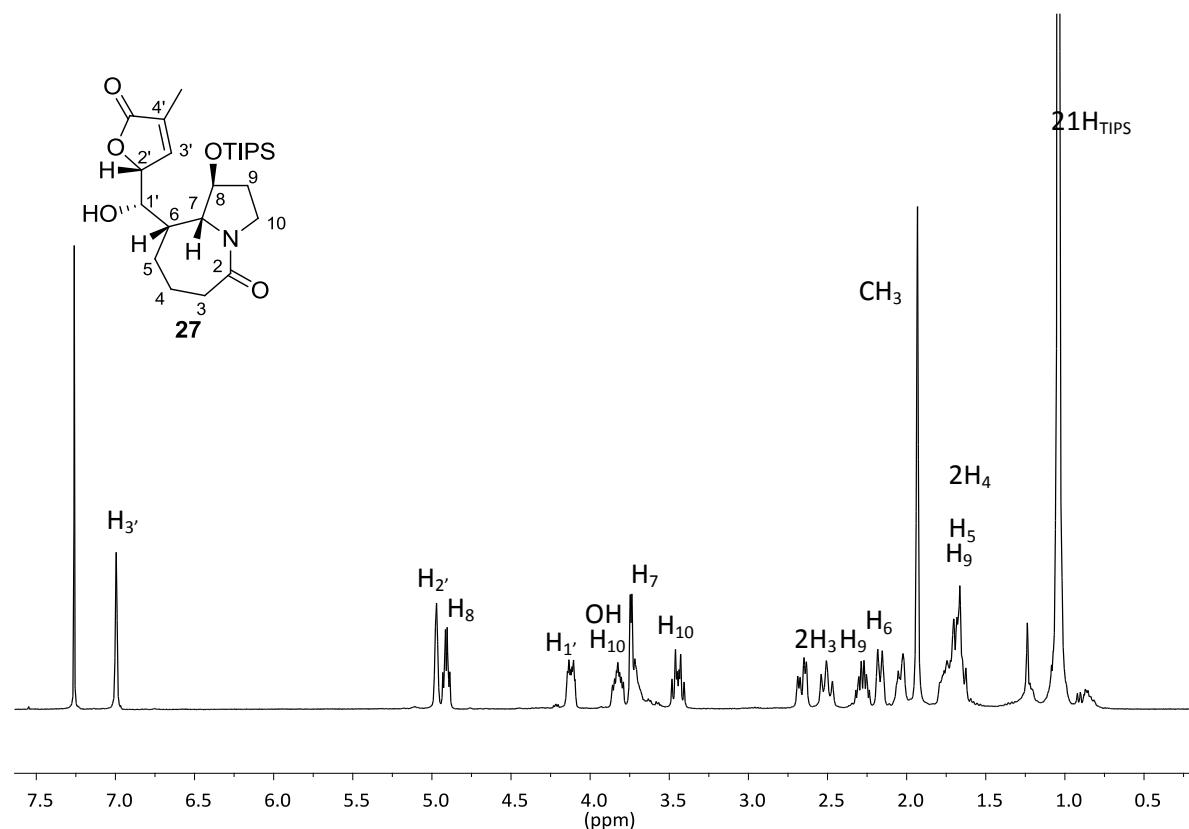


^1H -RMN (250 MHz, CDCl_3)

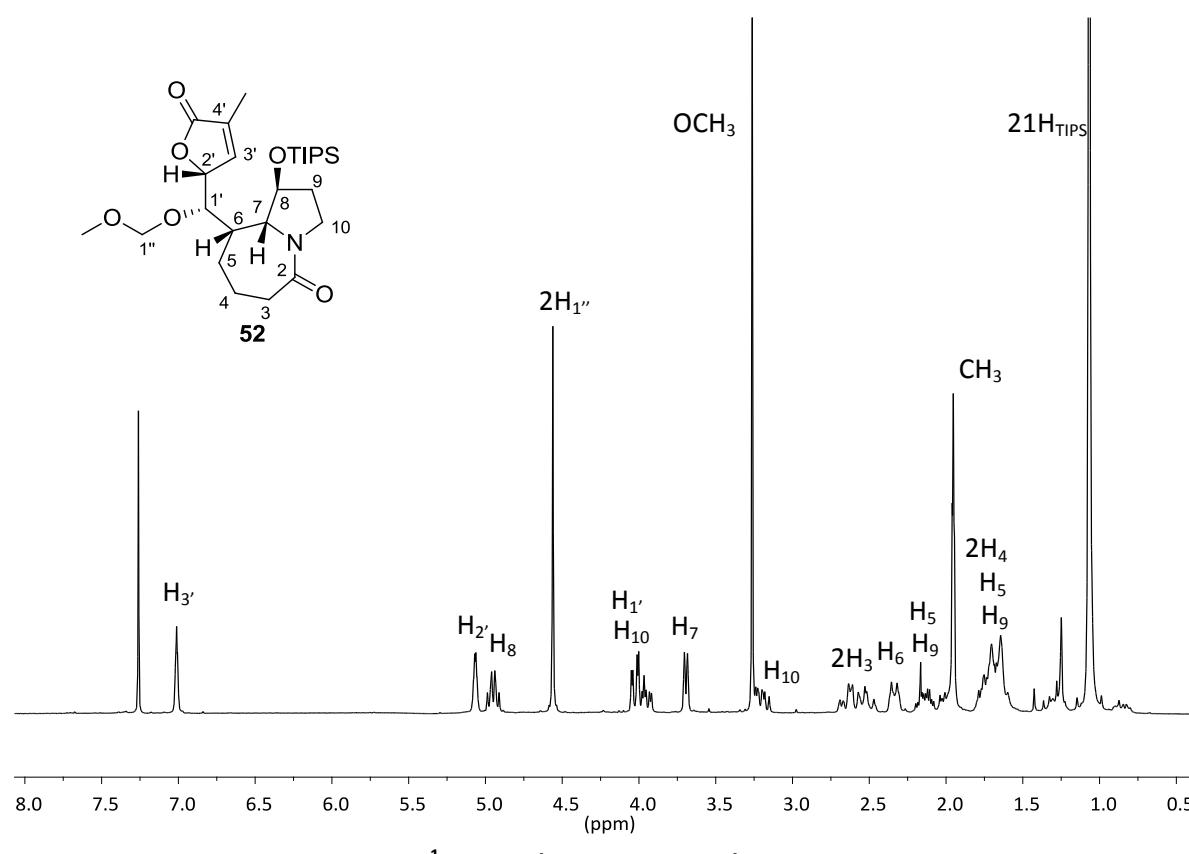


^1H -RMN (250 MHz, CDCl_3)

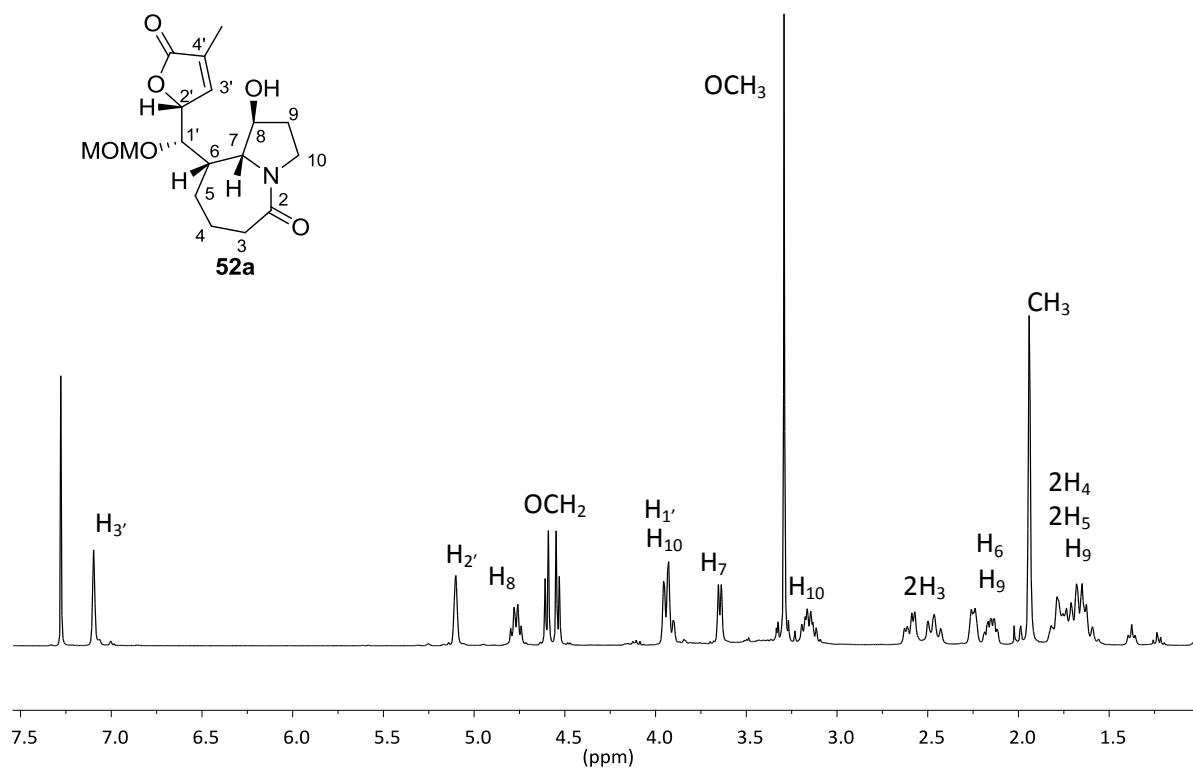
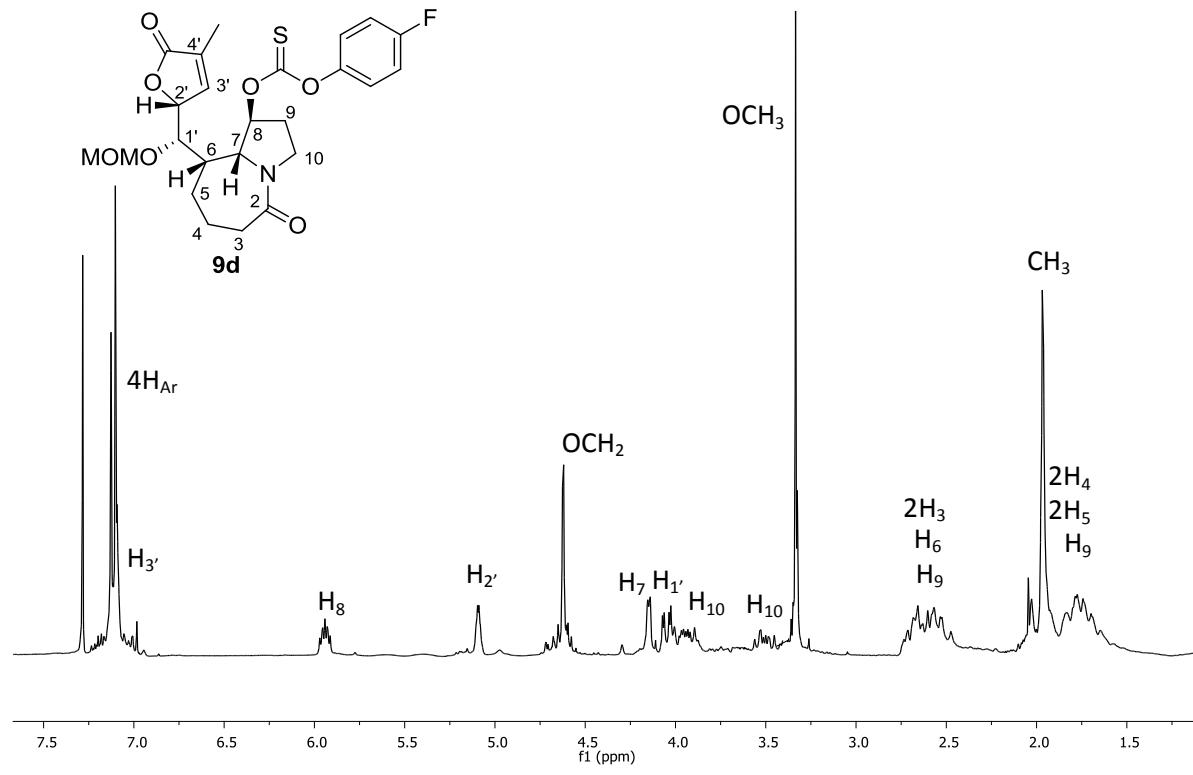
 $^1\text{H-RMN}$ (360 MHz, CDCl_3) $^1\text{H-RMN}$ (360 MHz, CDCl_3)

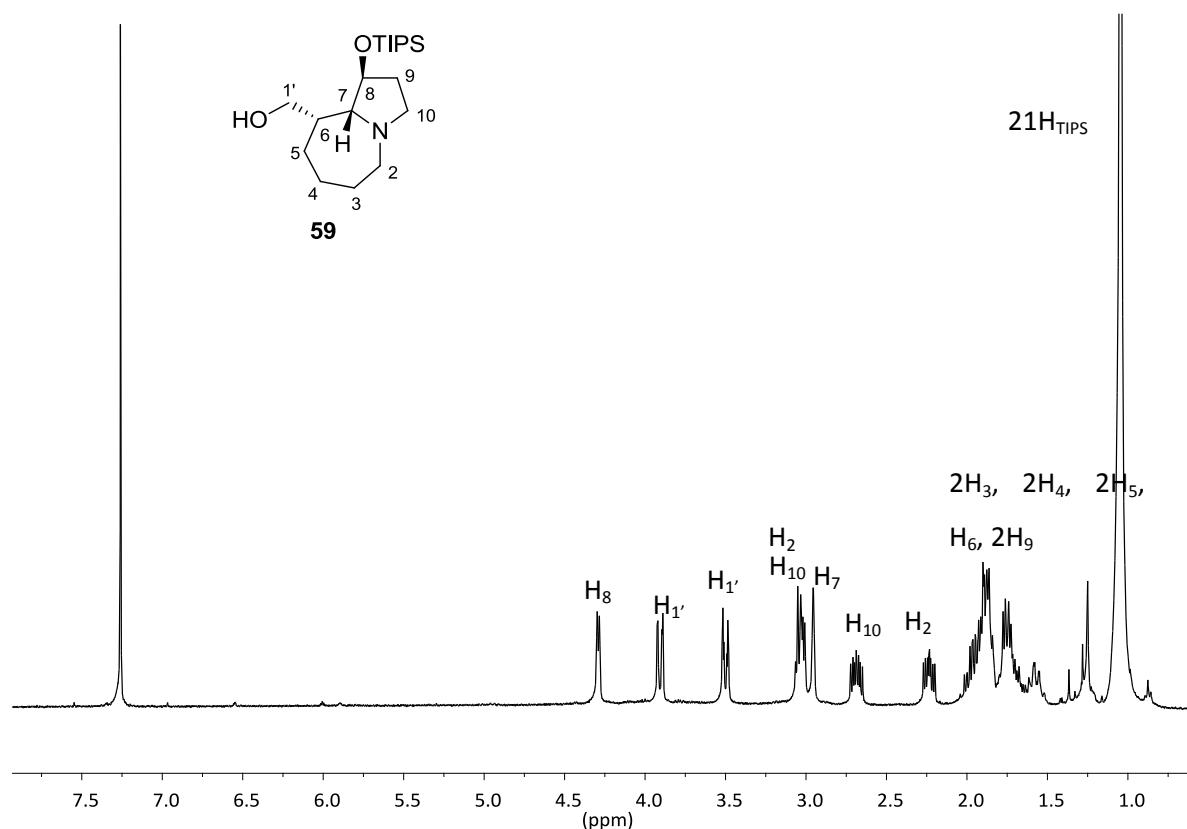


¹H-RMN (360 MHz, CDCl₃)

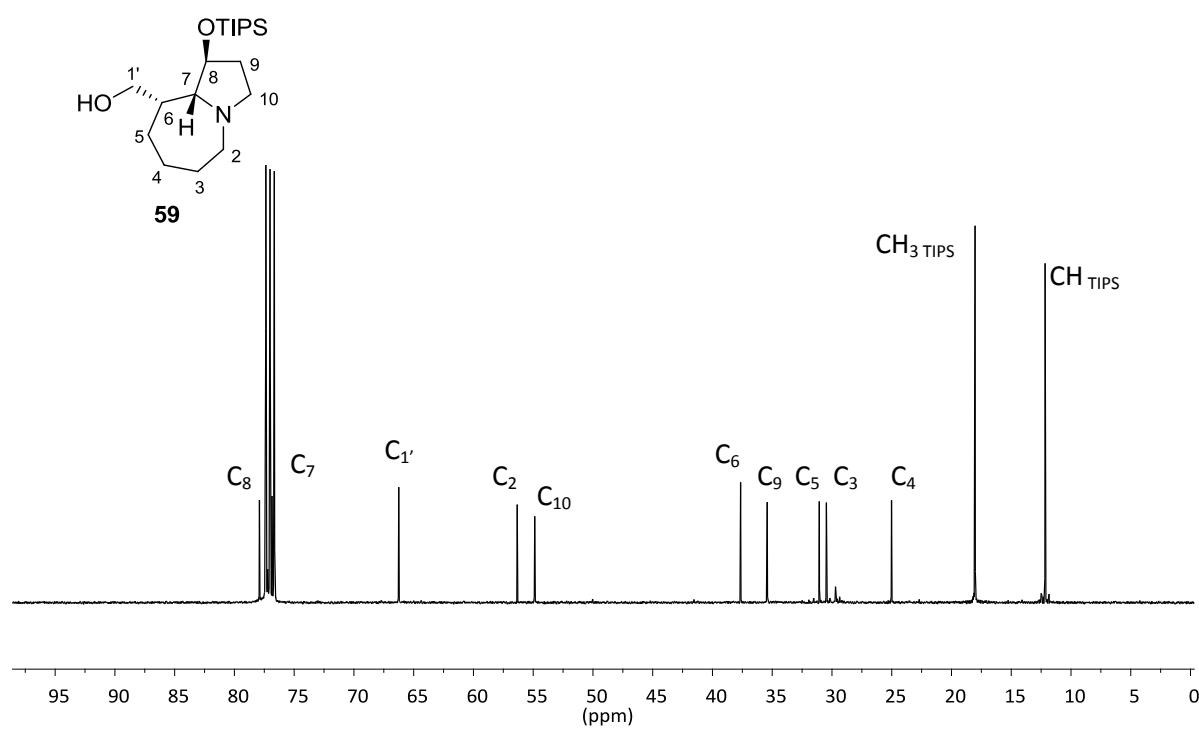


¹H-RMN (250 MHz, CDCl₃)

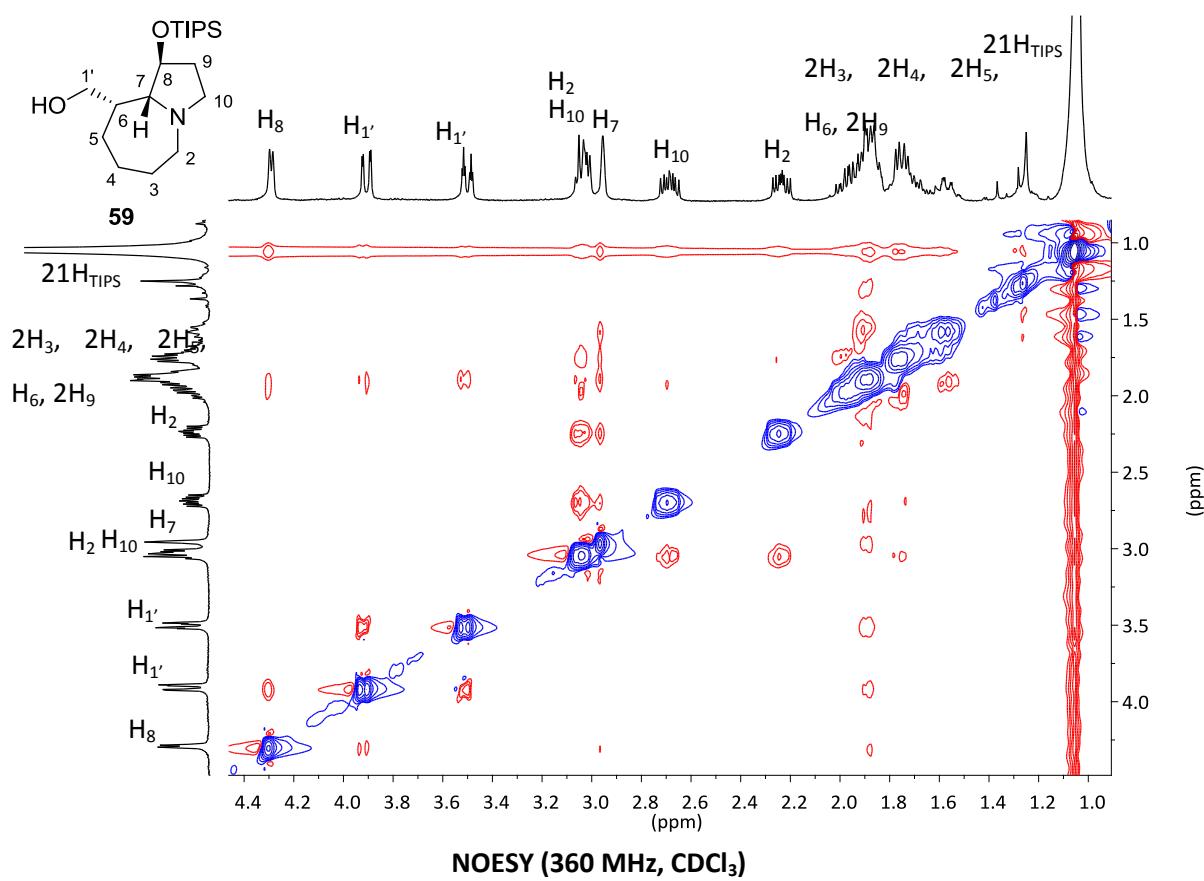
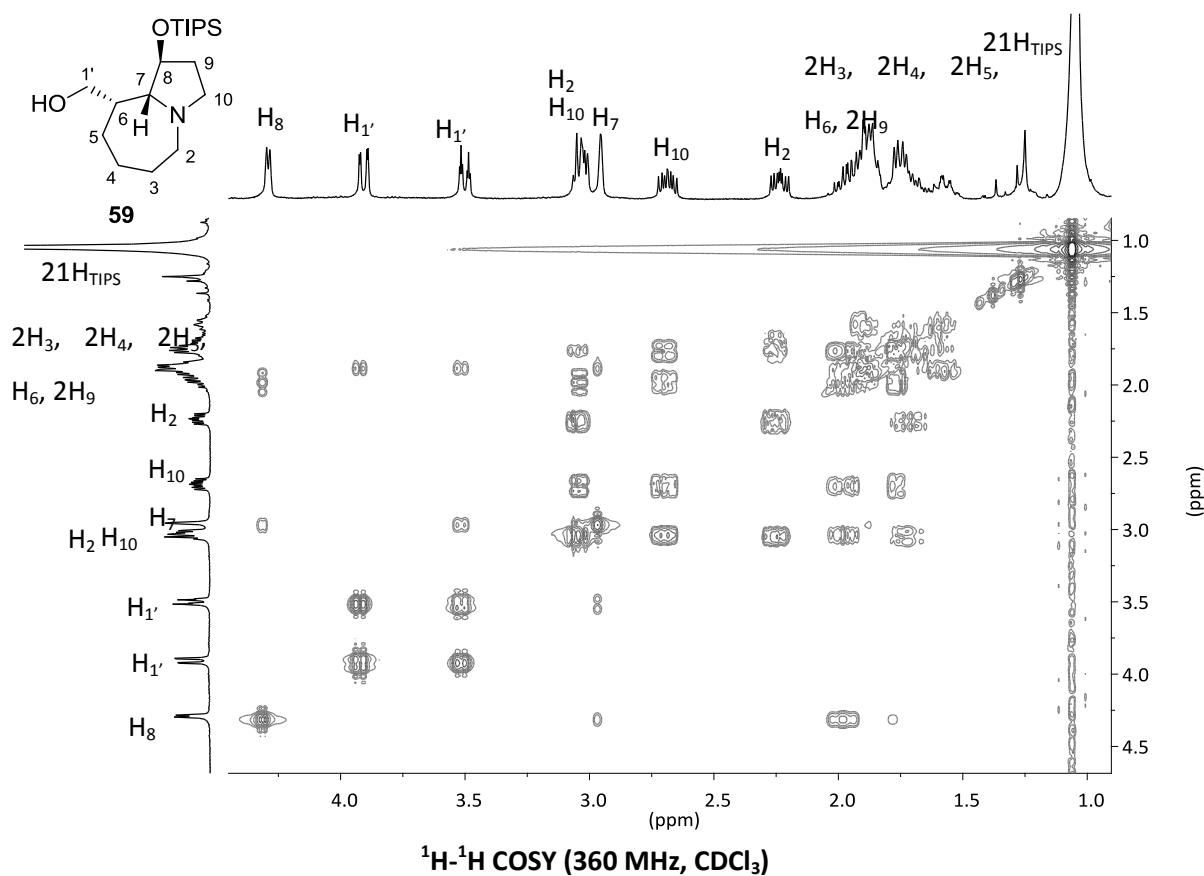
**¹H-RMN (360 MHz, CDCl₃)****¹H-RMN (250 MHz, CDCl₃)**



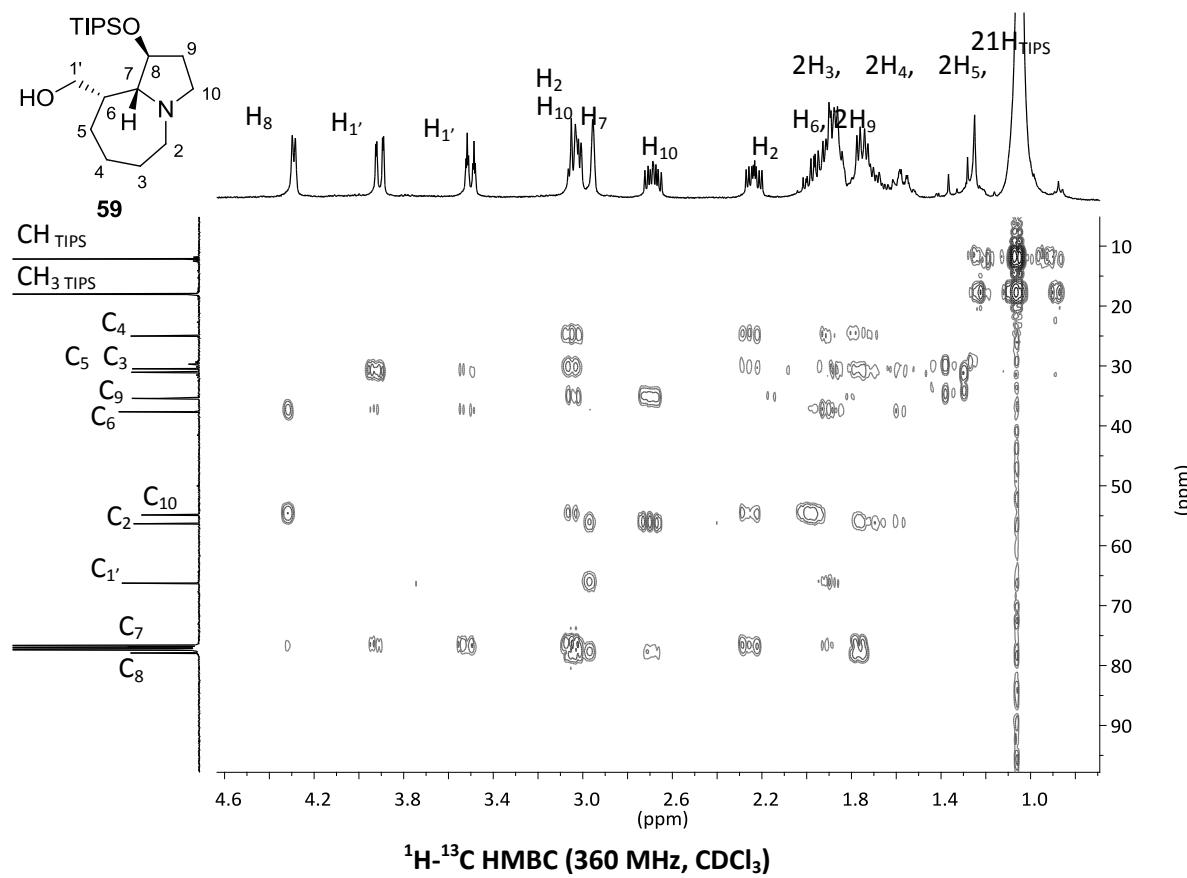
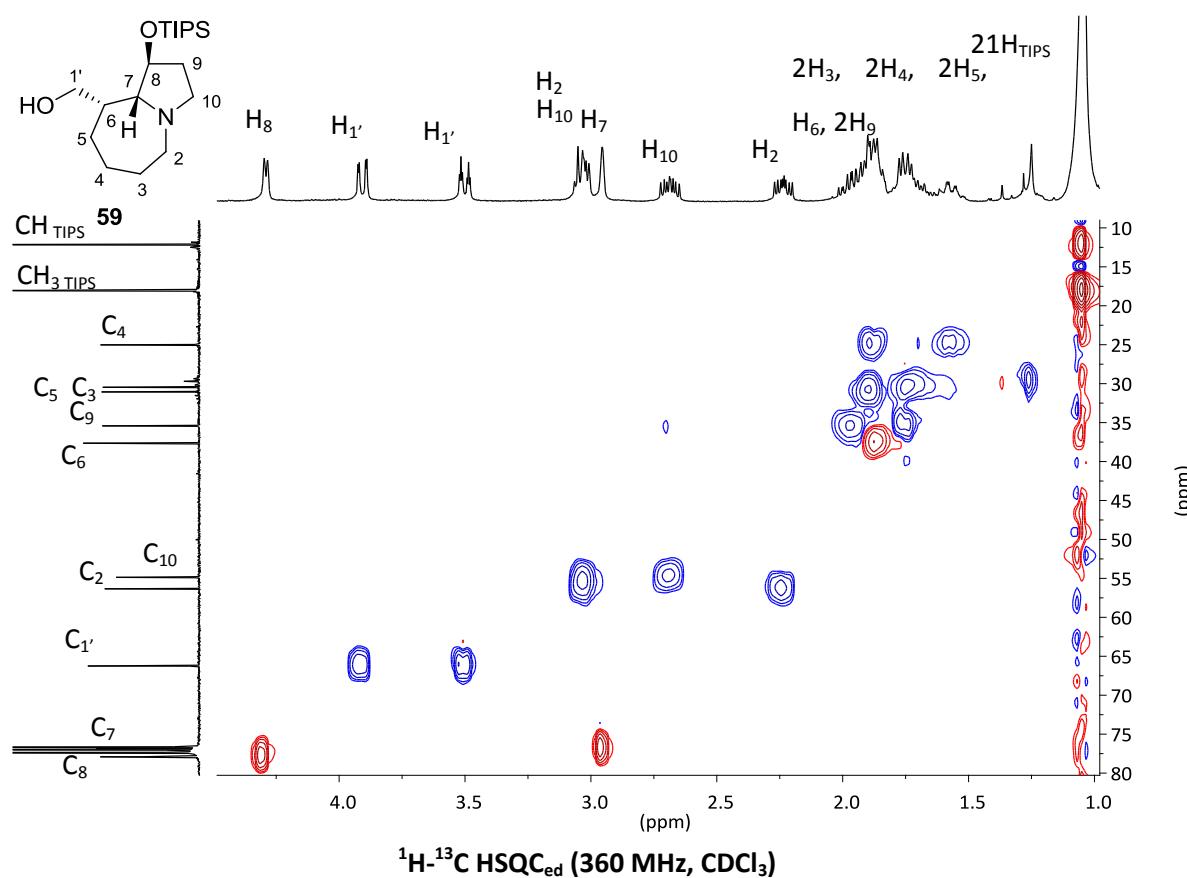
^1H -RMN (360 MHz, CDCl_3)

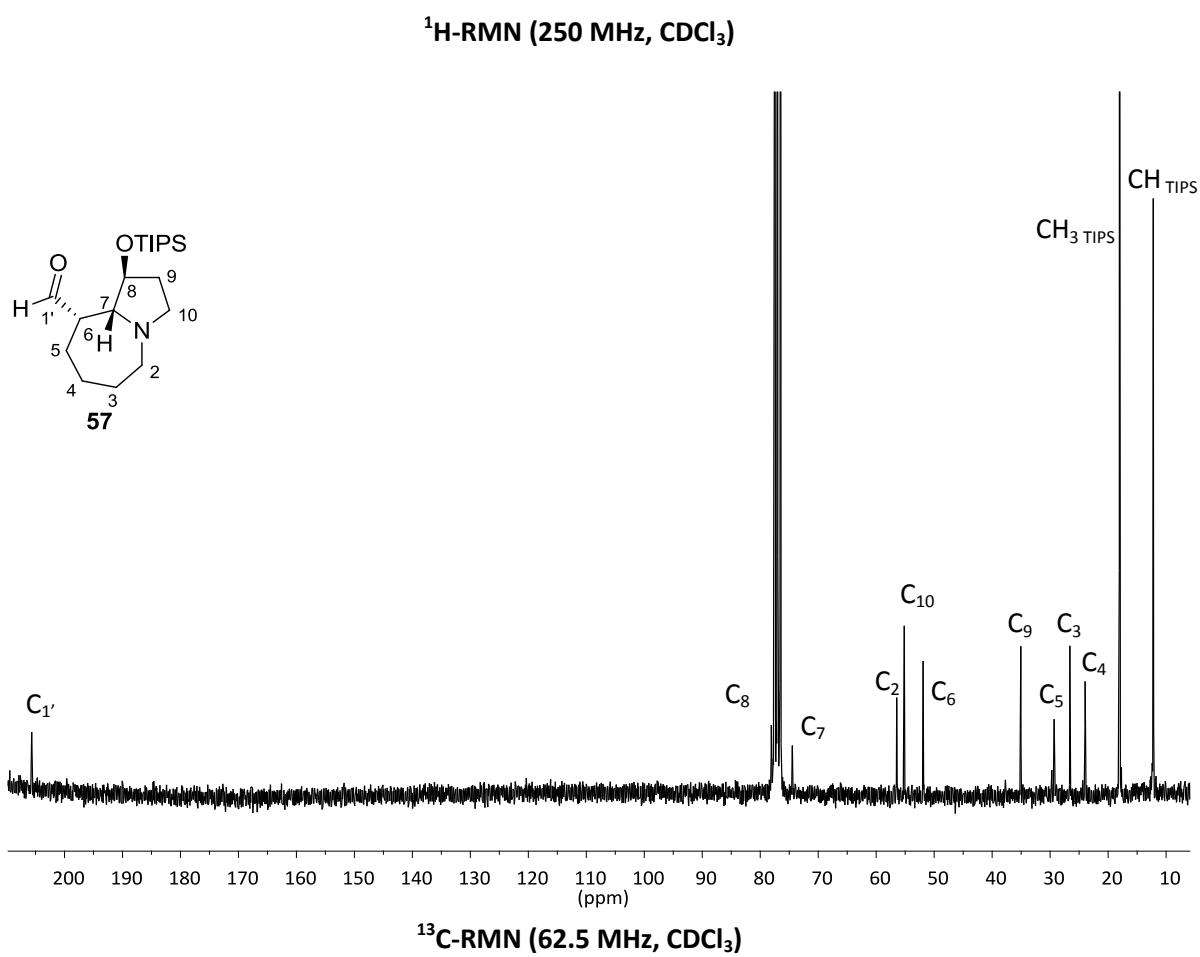
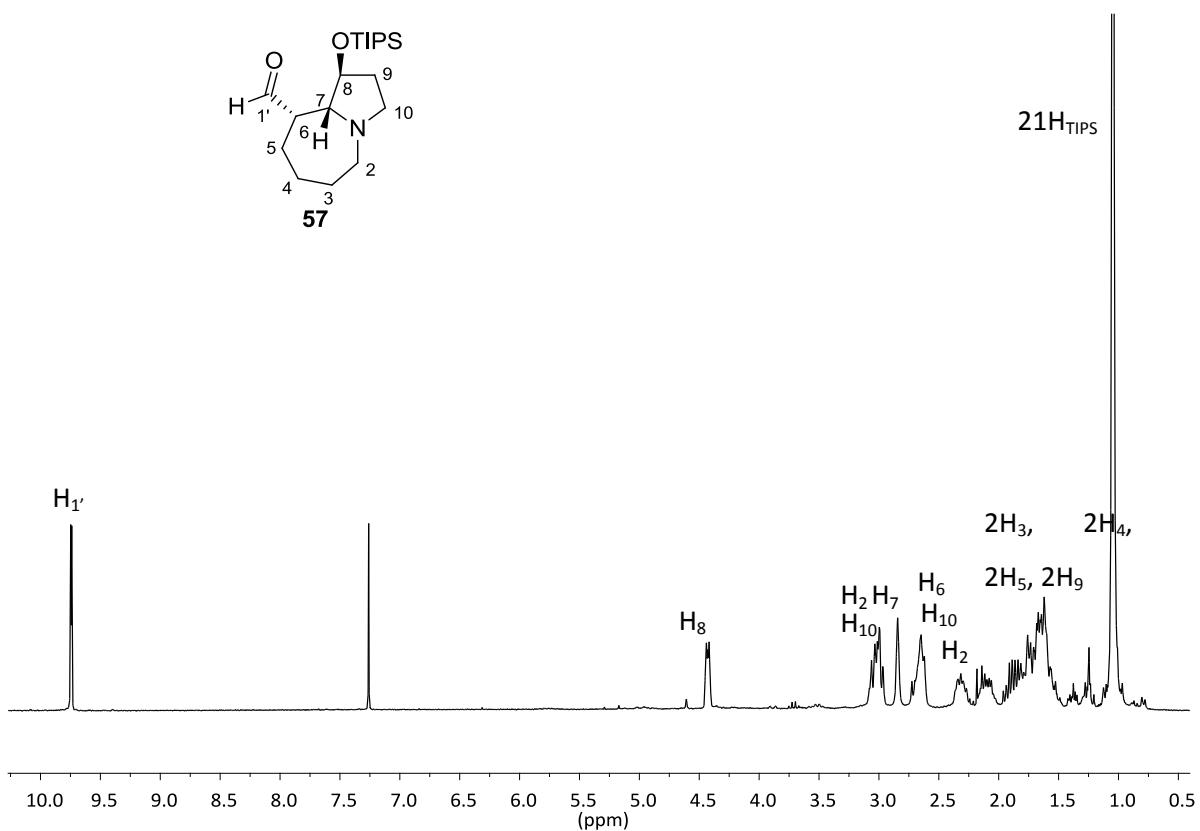


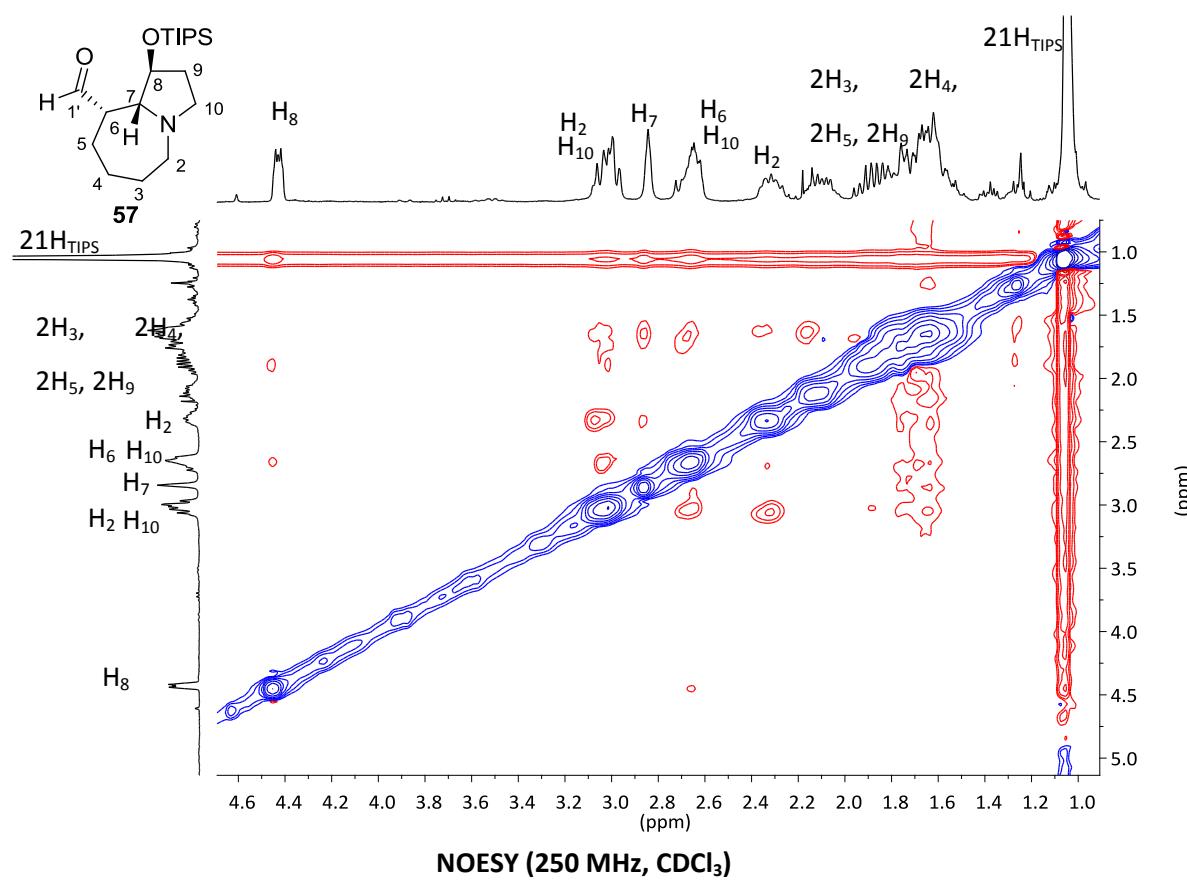
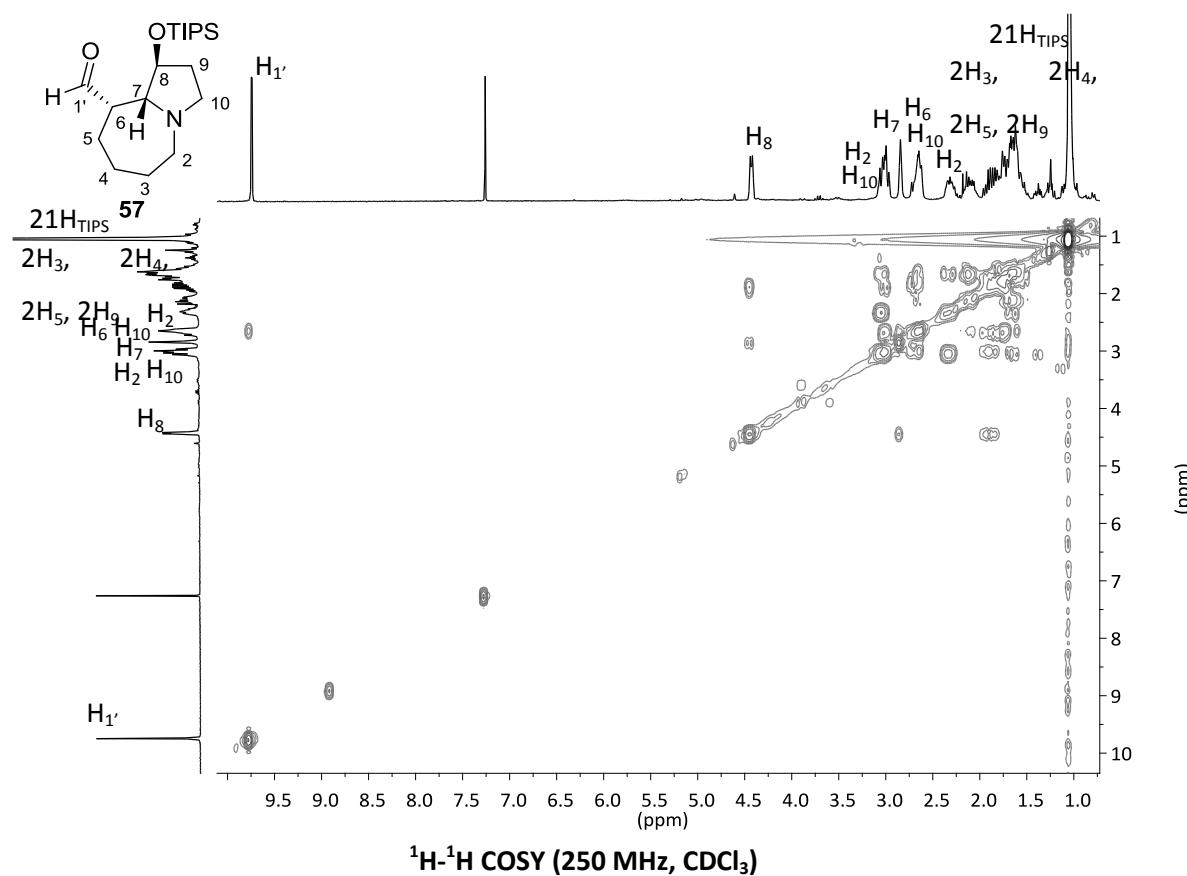
^{13}C -RMN (90 MHz, CDCl_3)

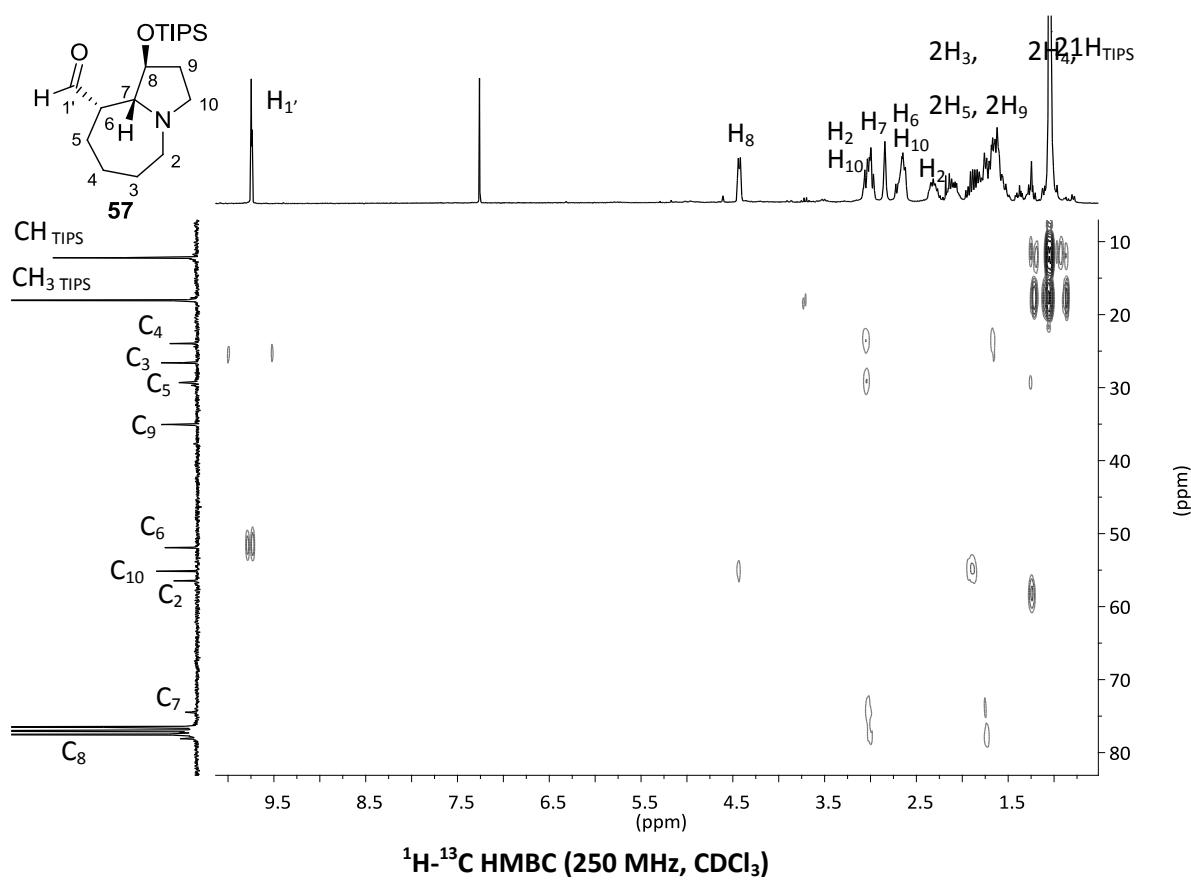
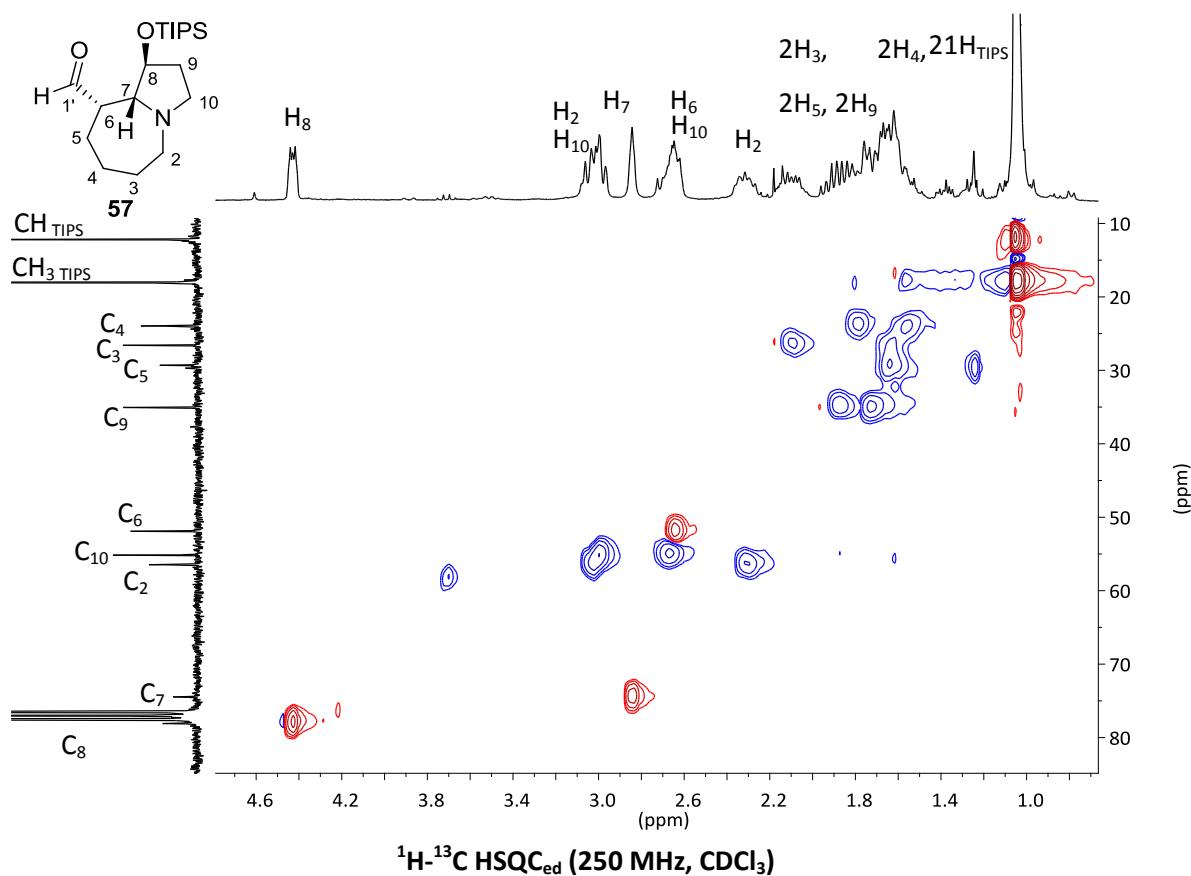


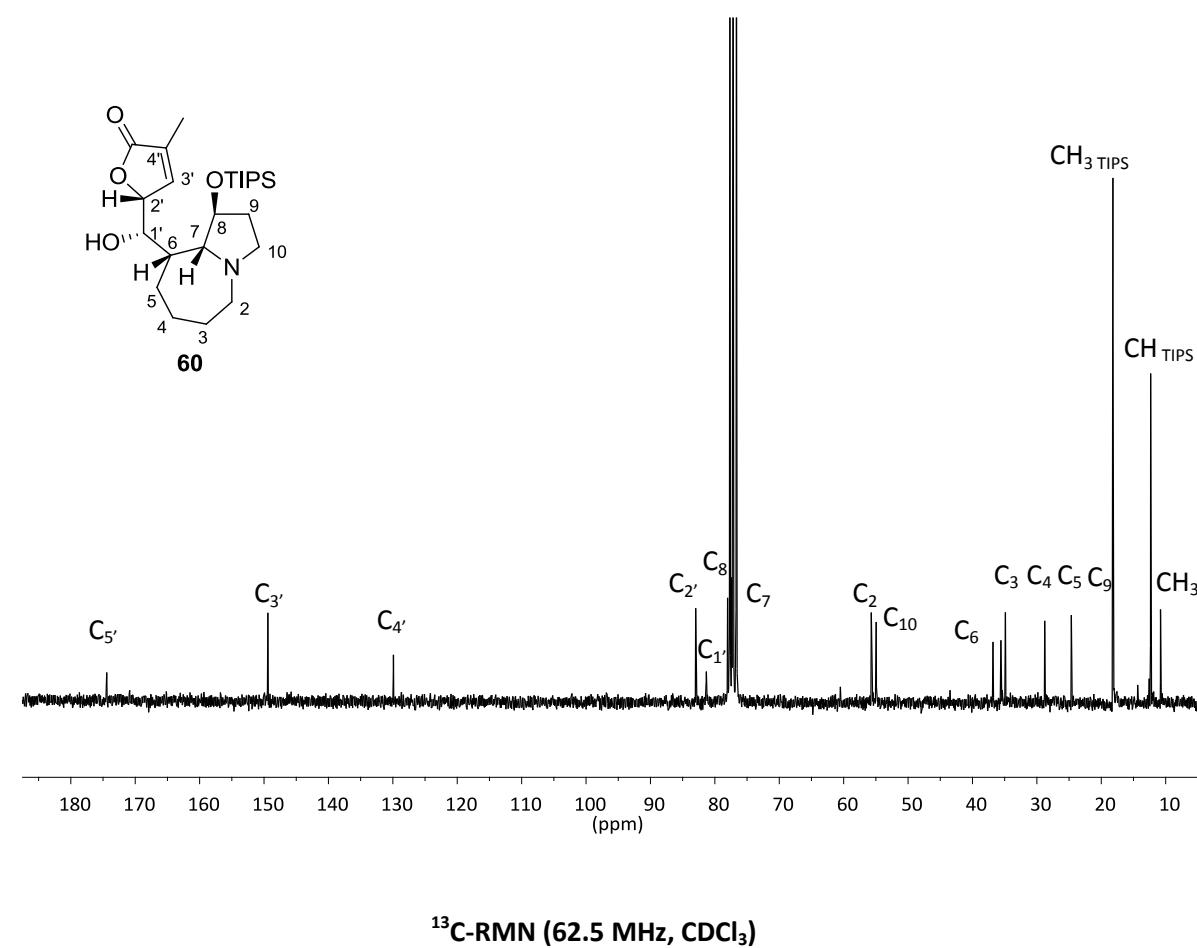
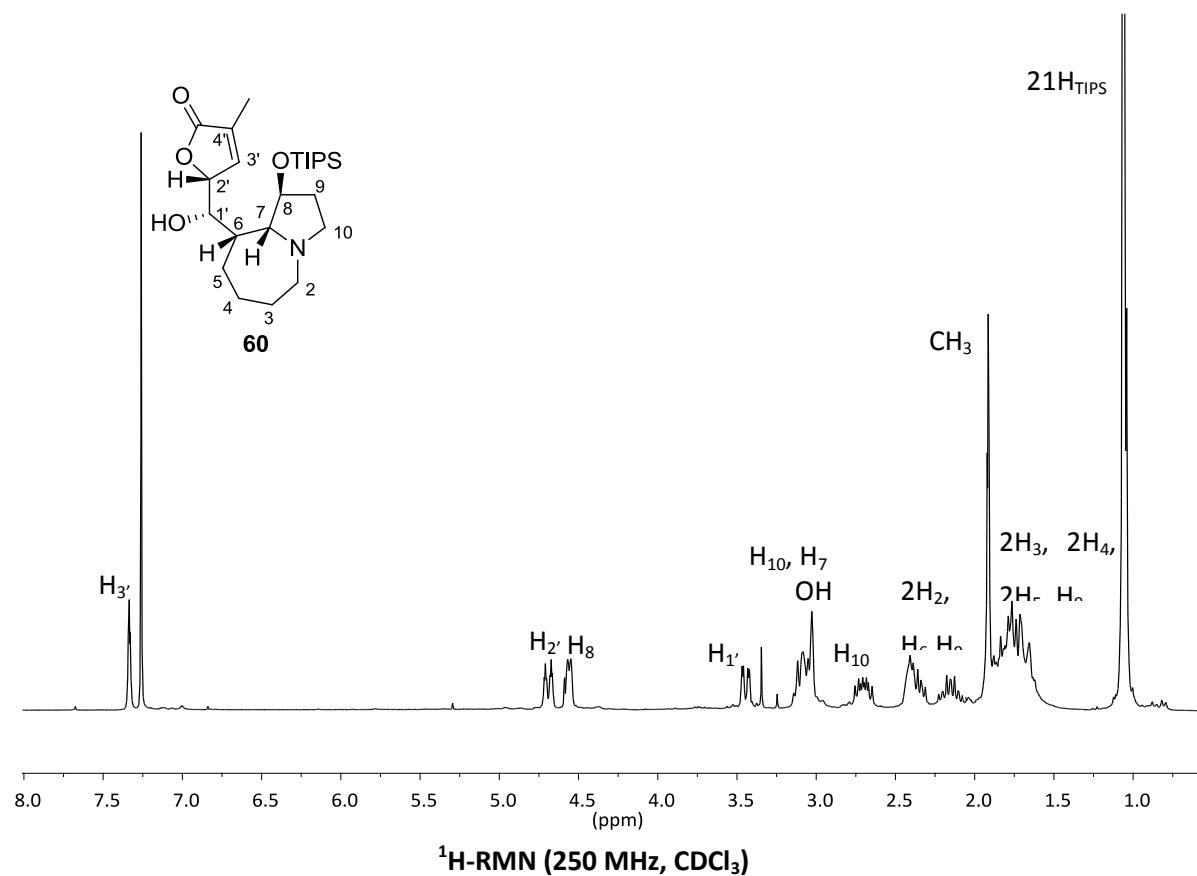
6. RECULL D'ESPECTRES

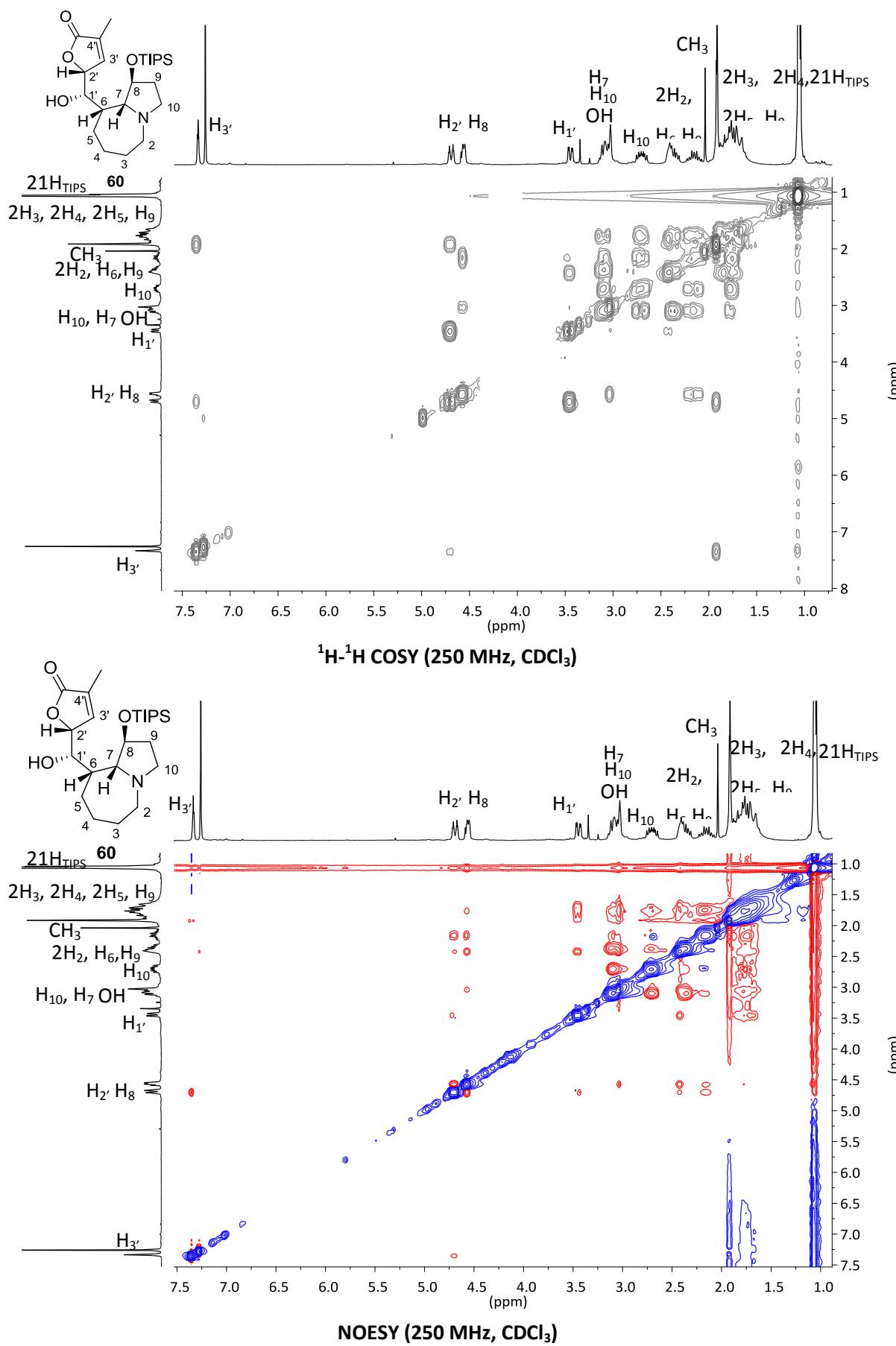




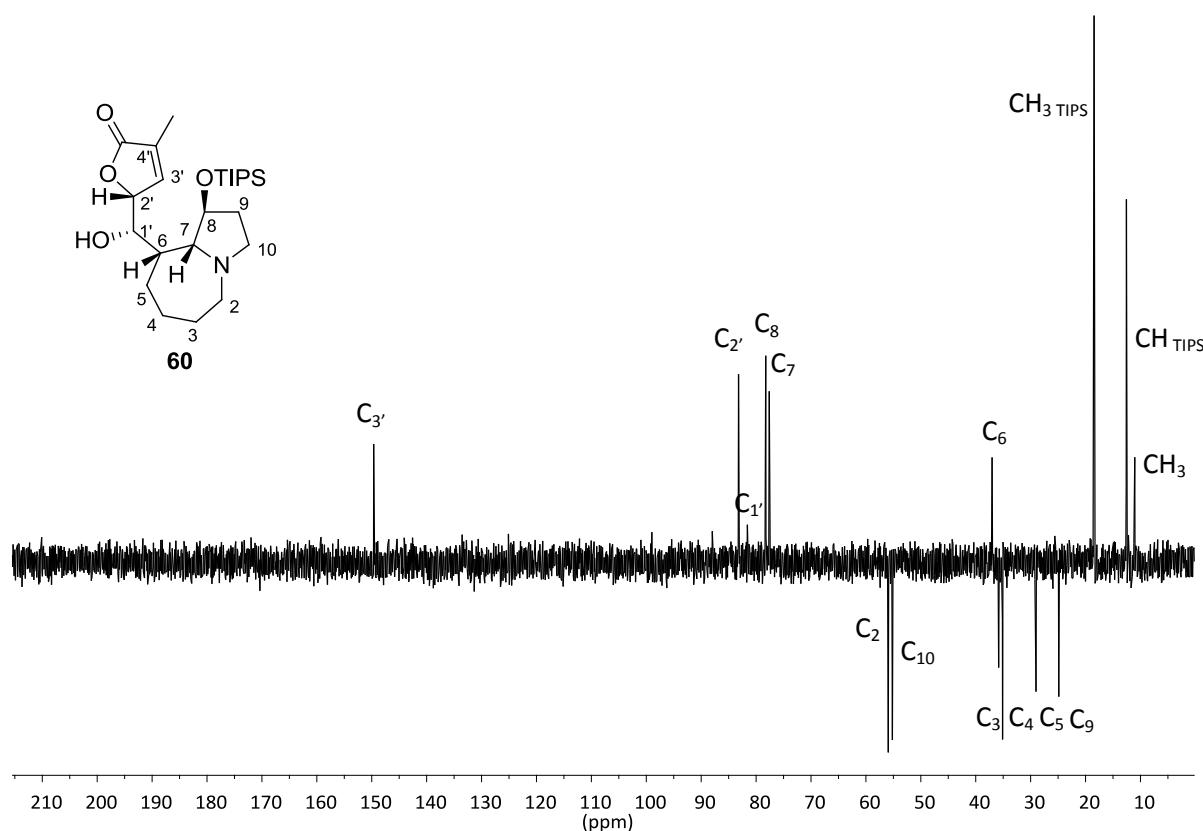
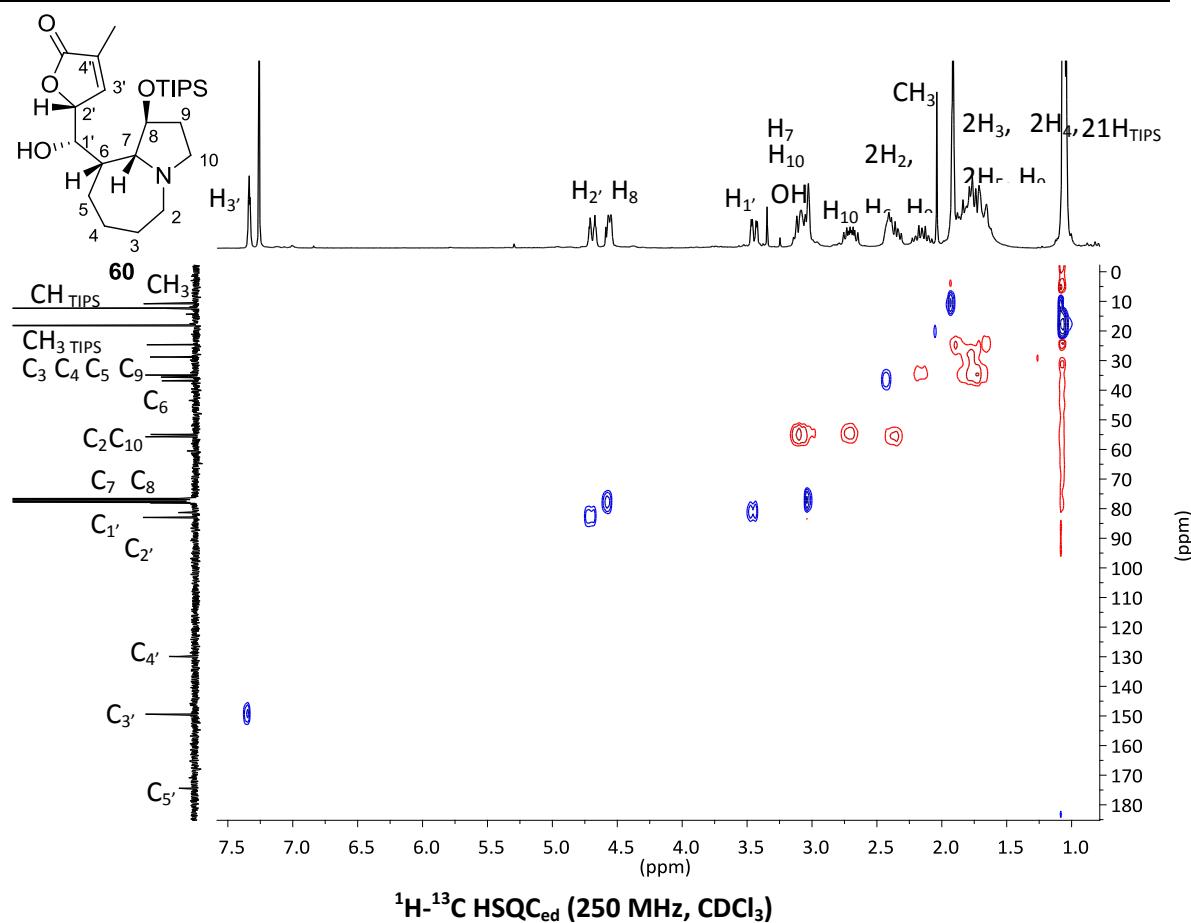


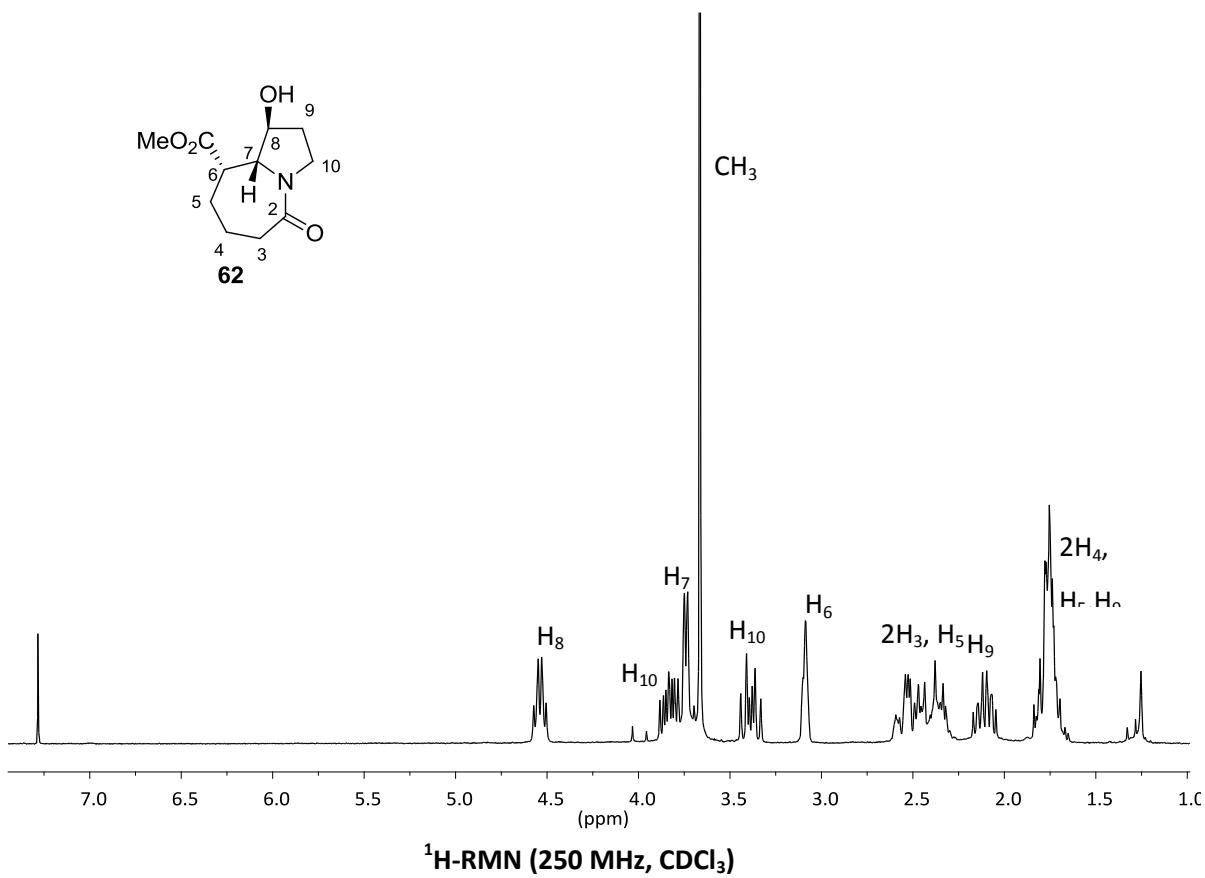
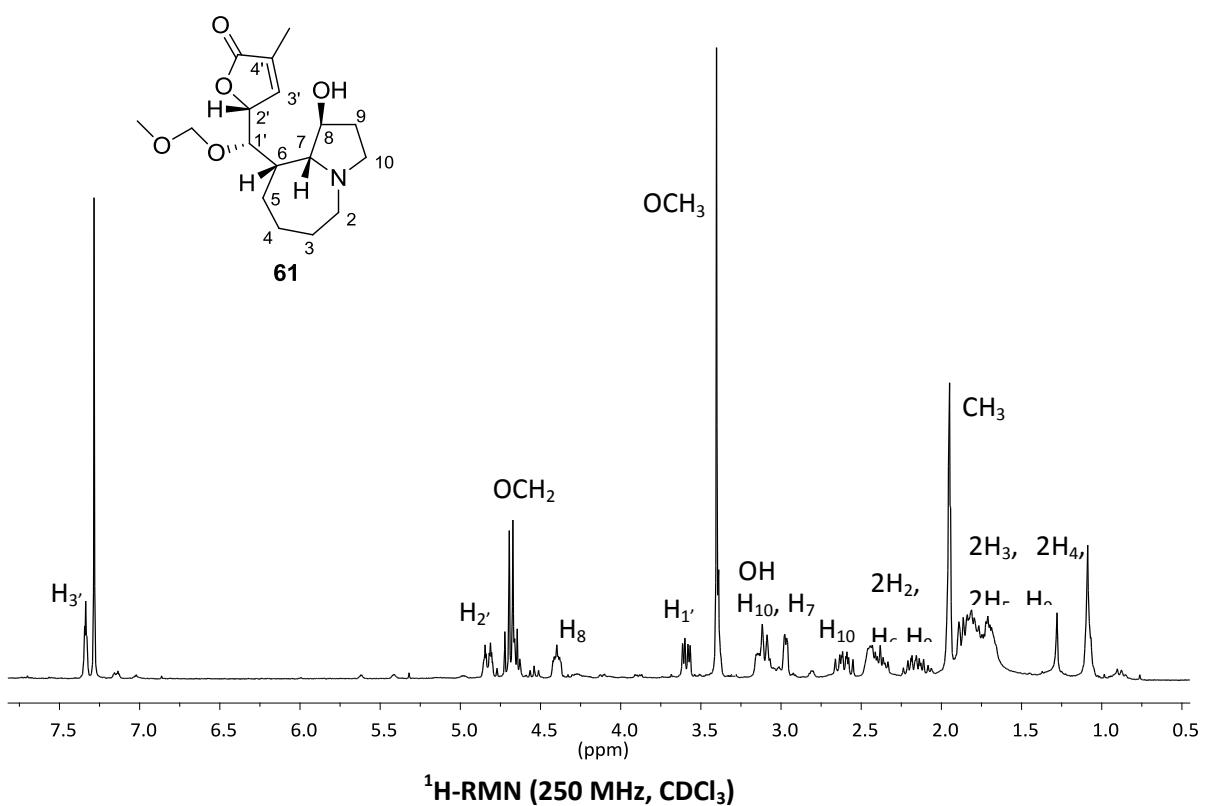


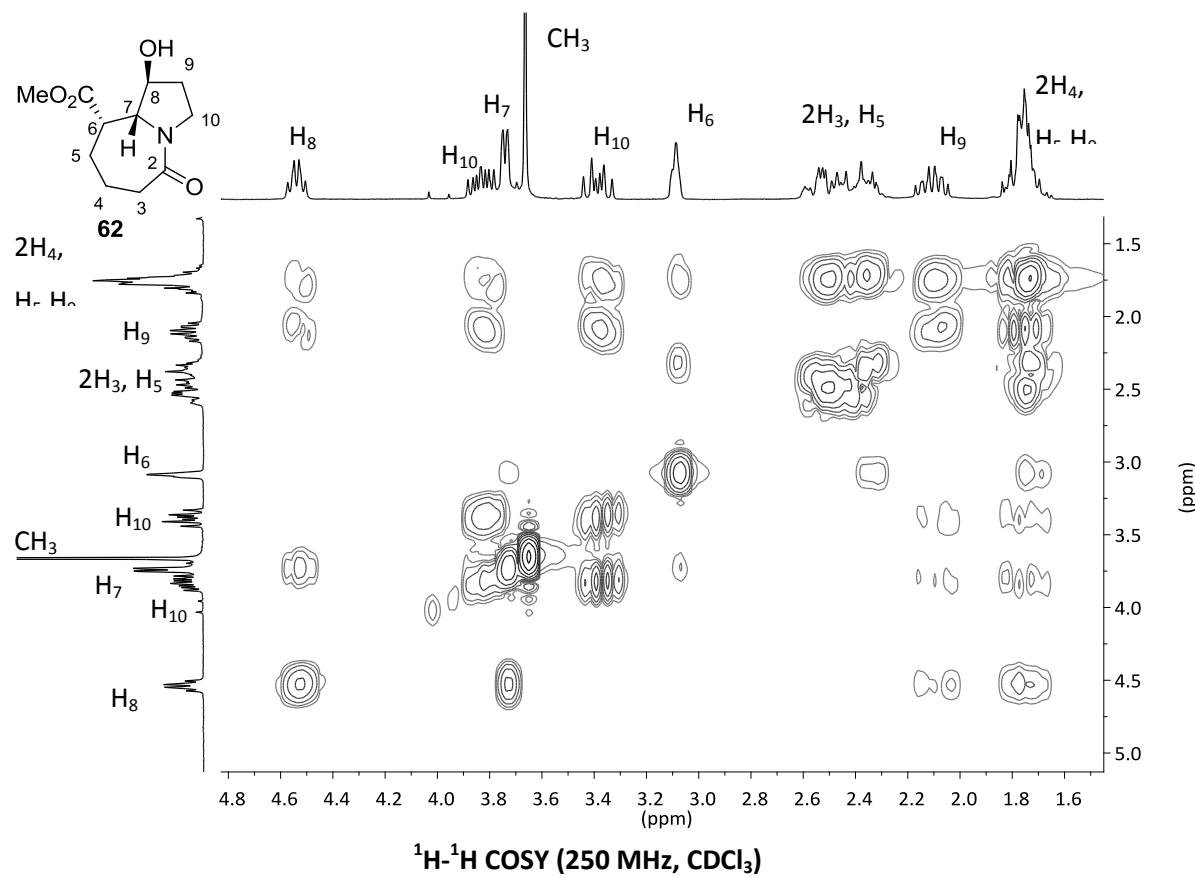
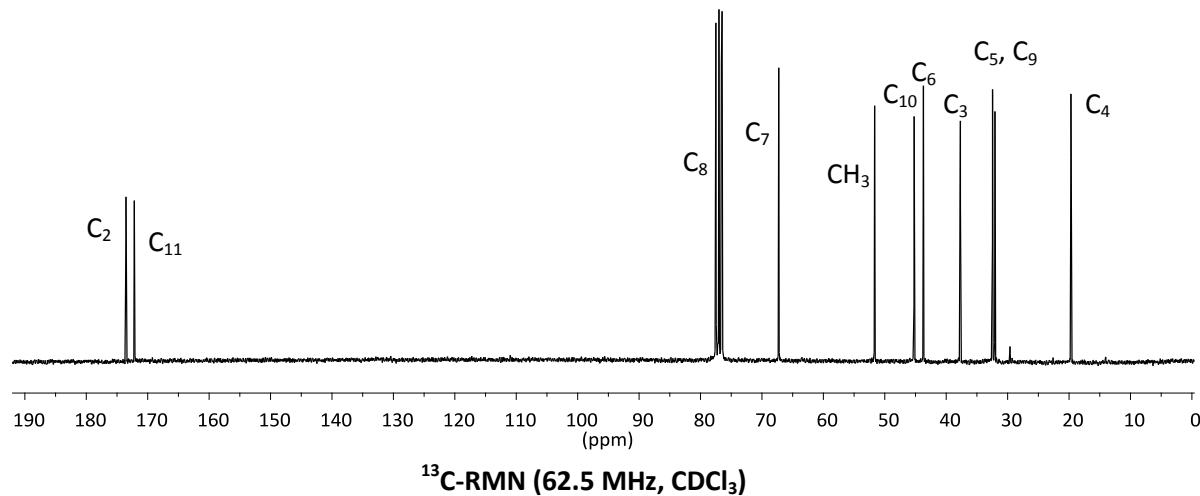
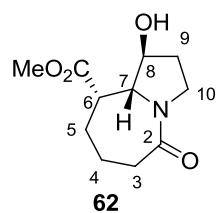


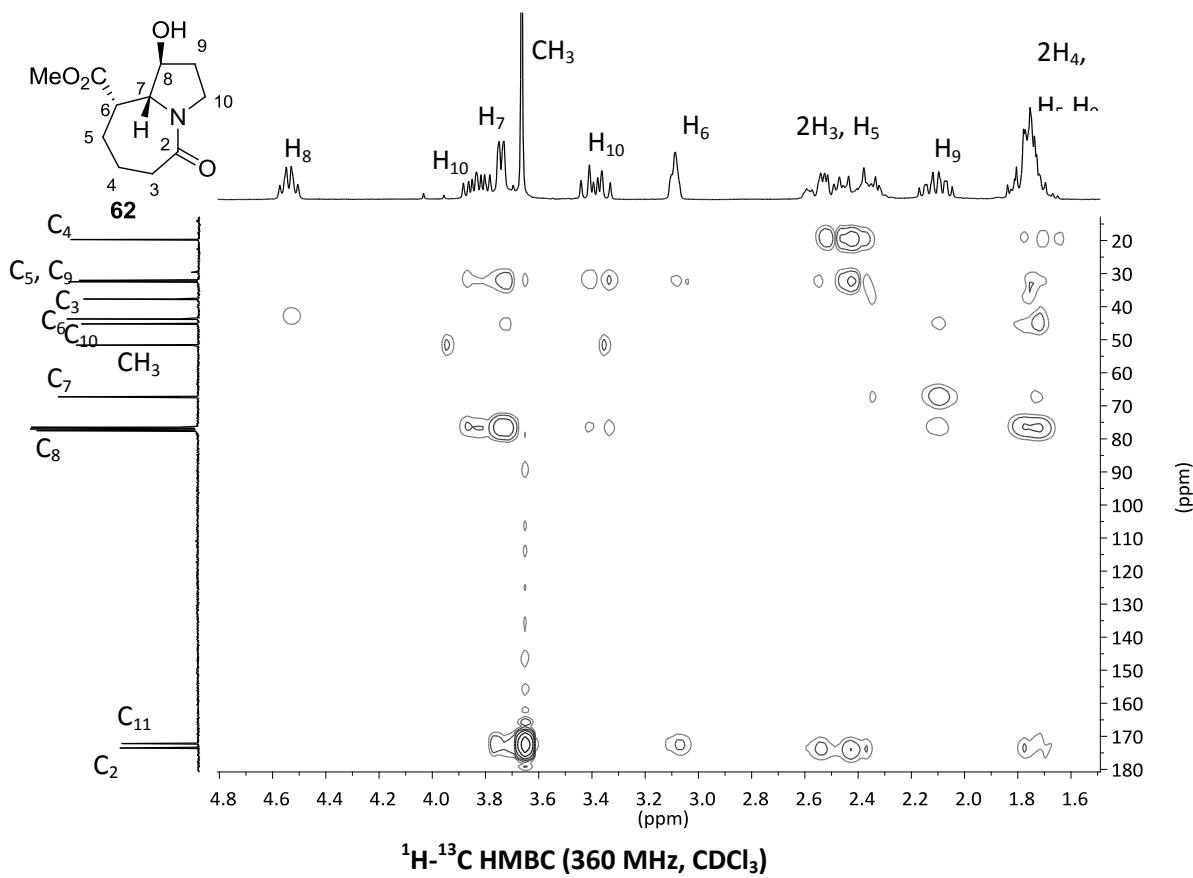
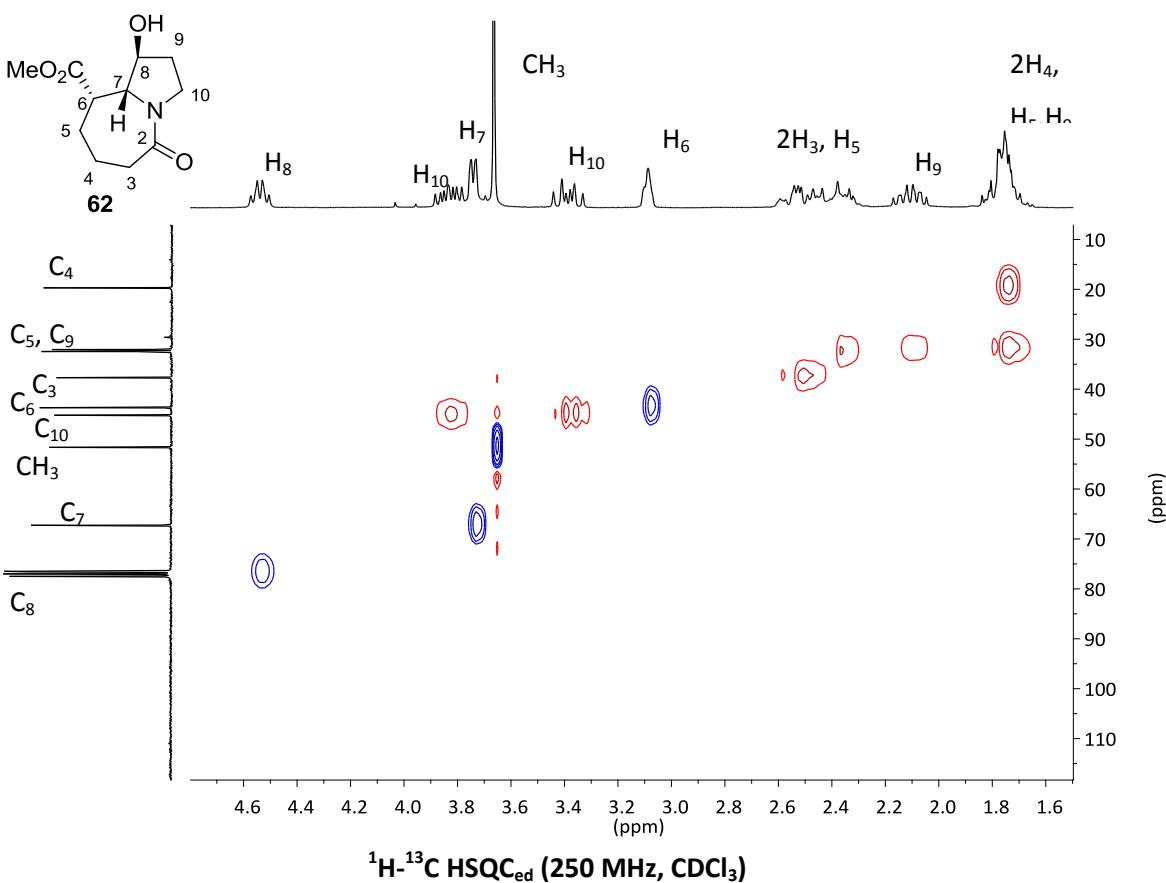


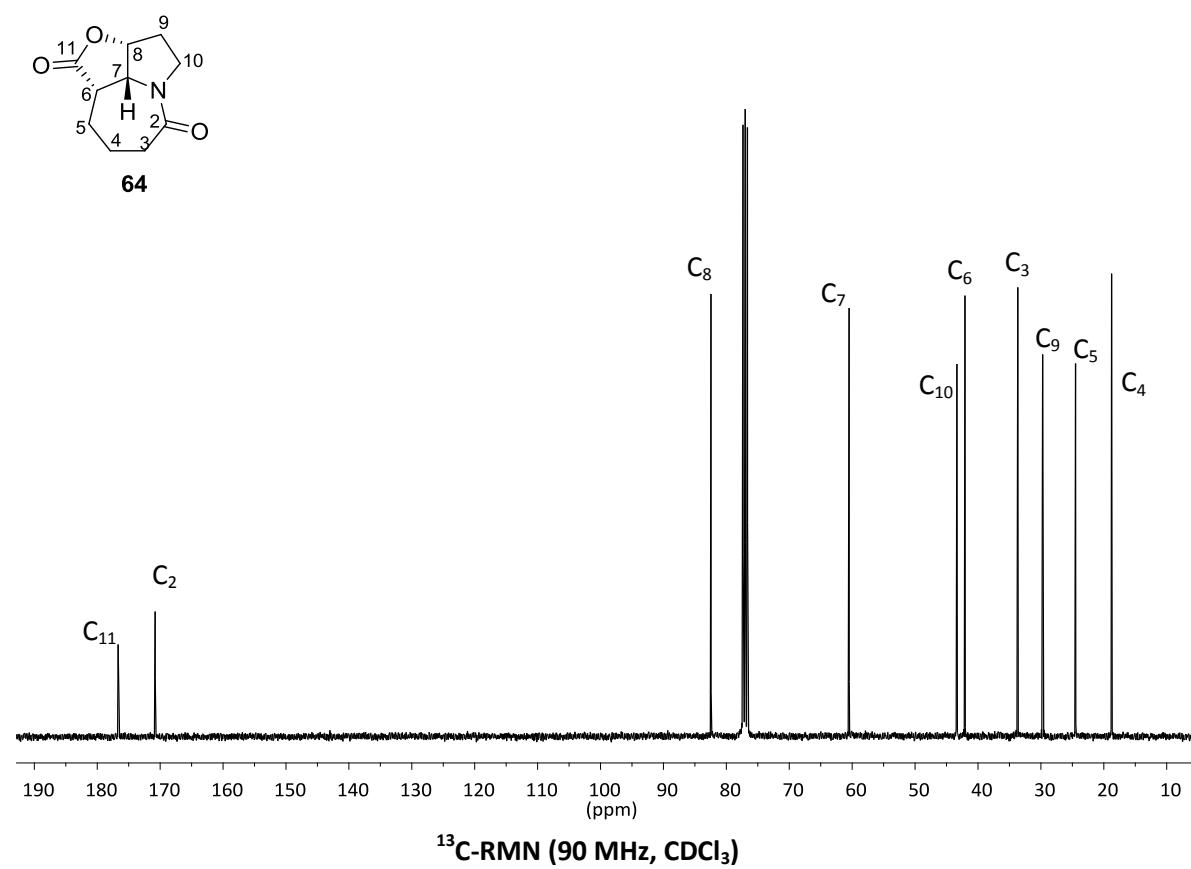
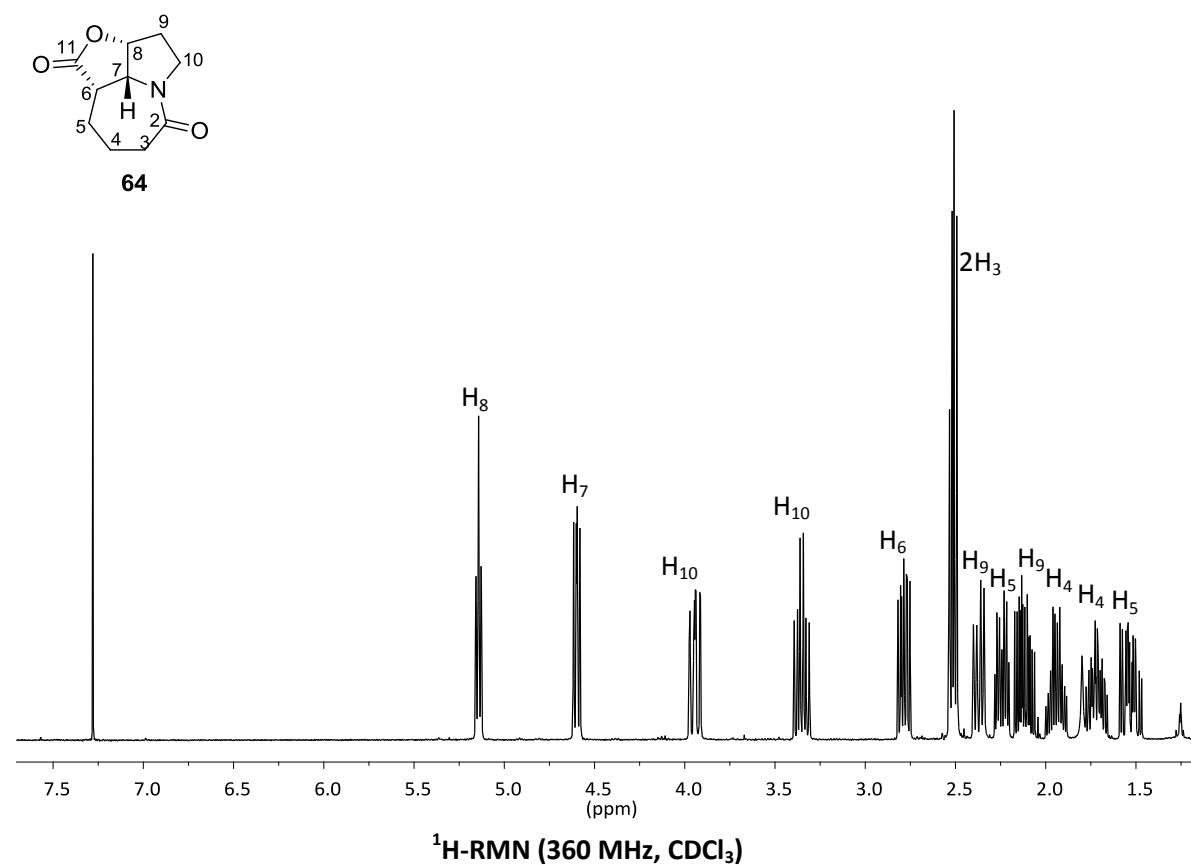
6. RECULL D'ESPECTRES

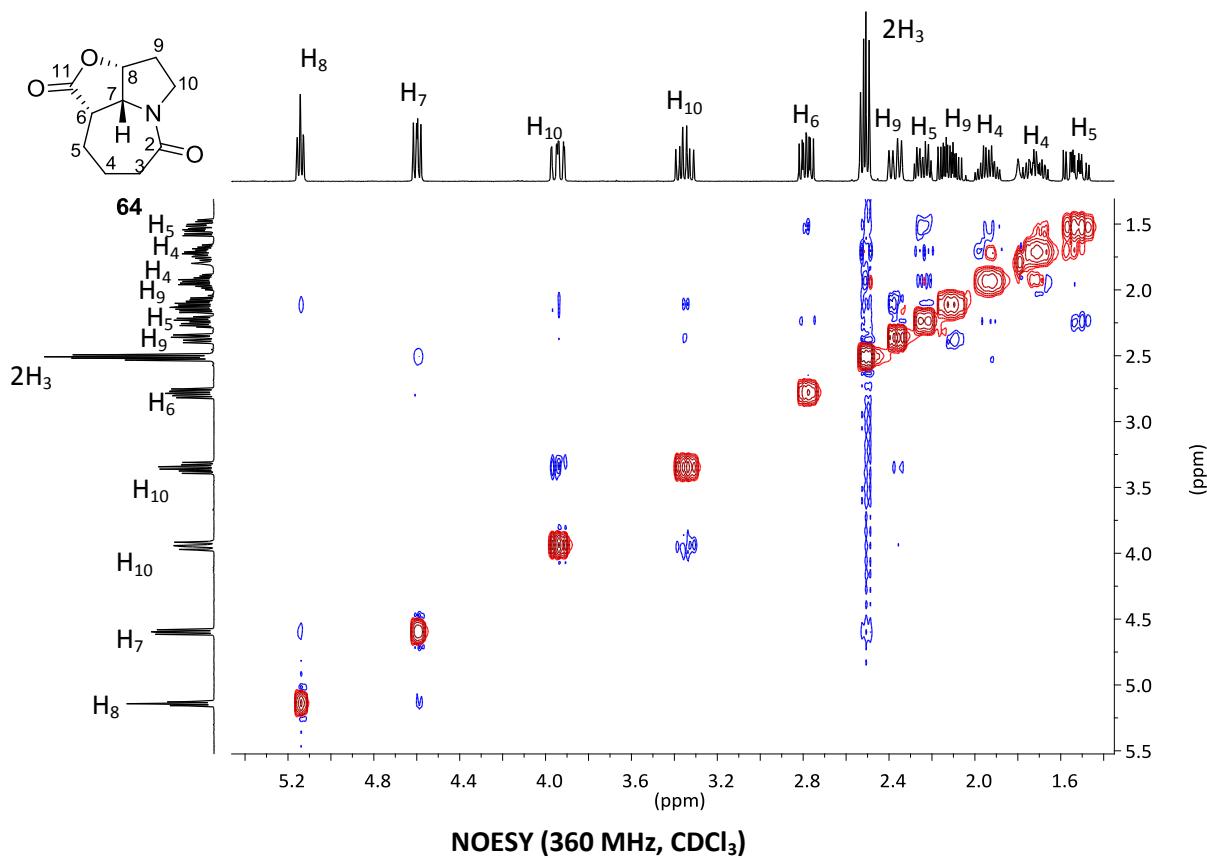
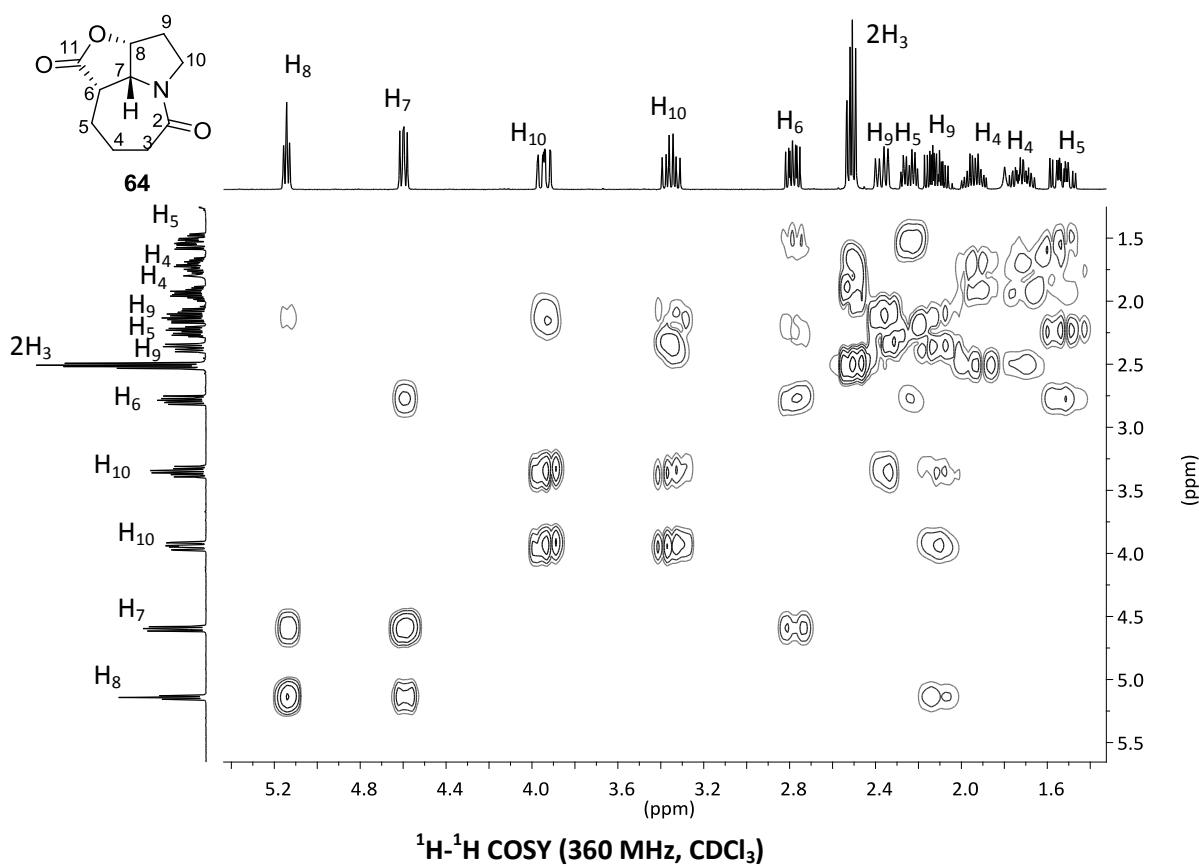


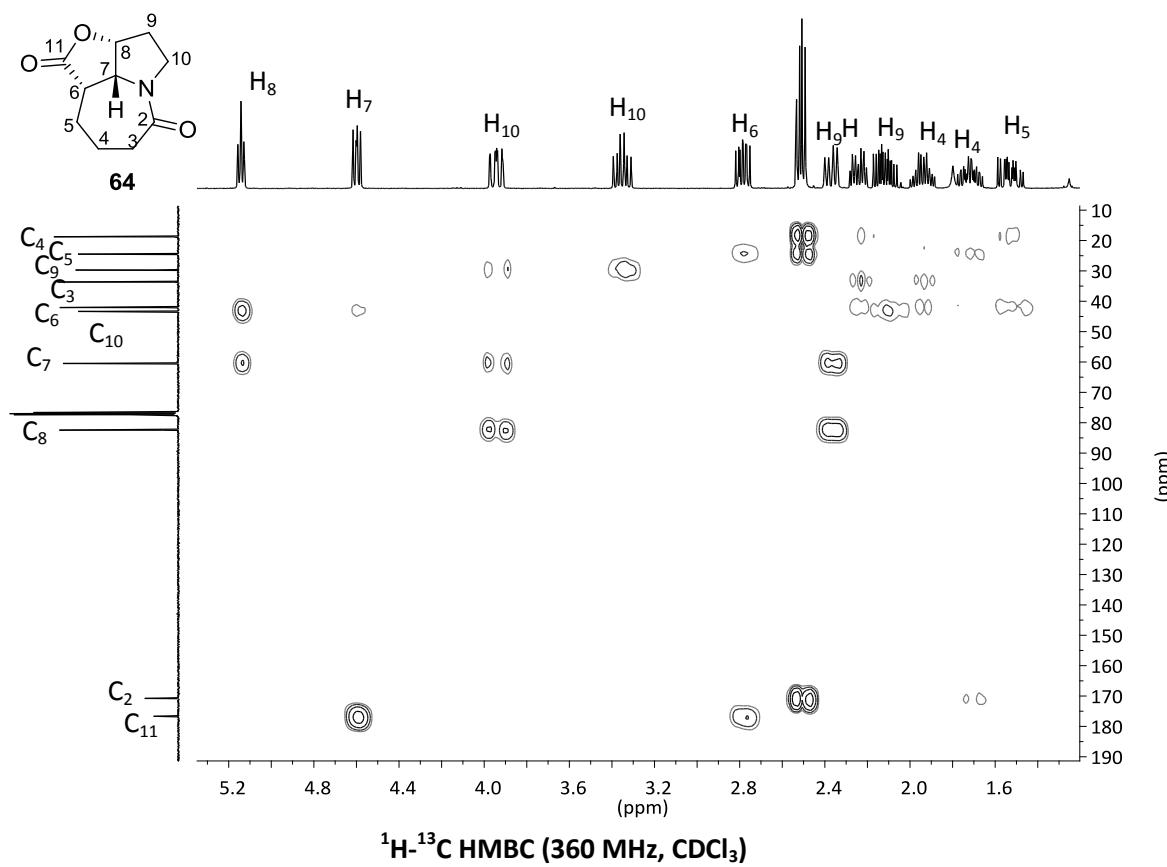
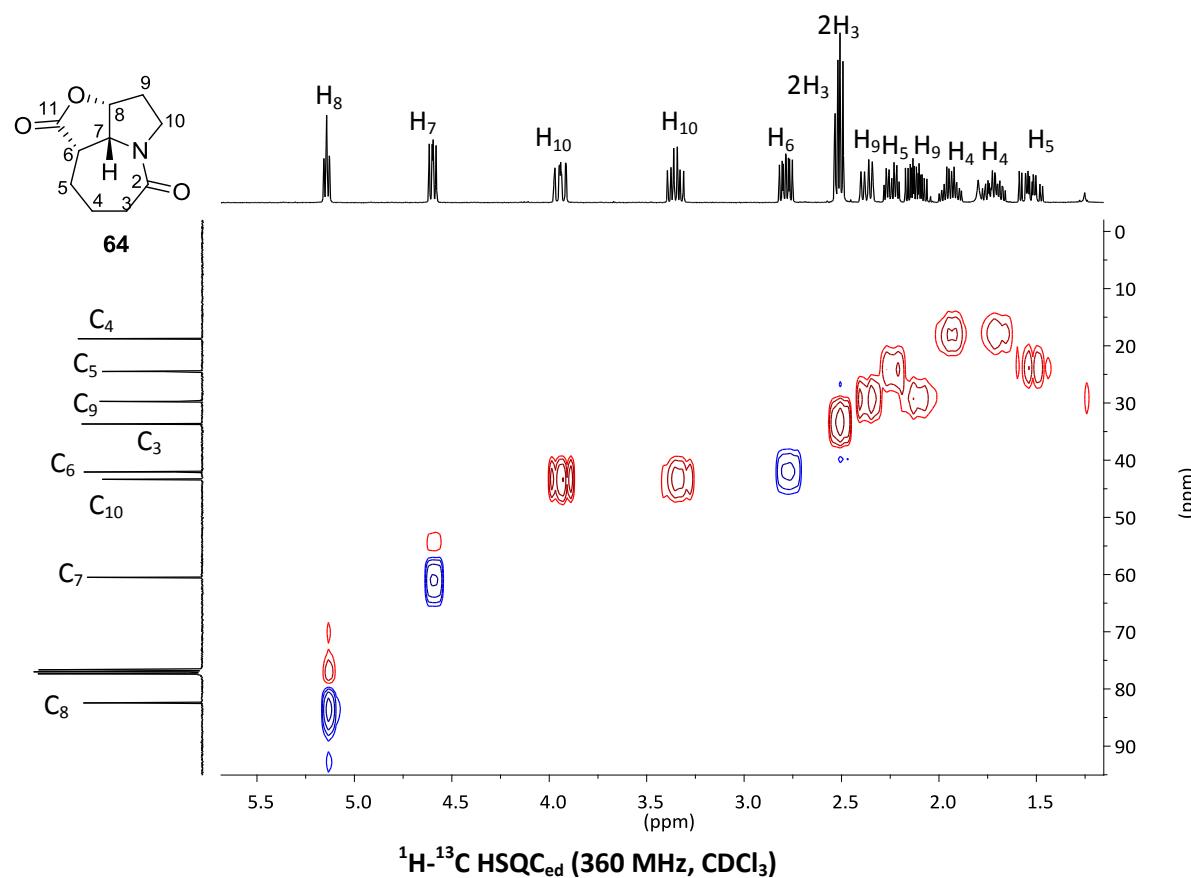


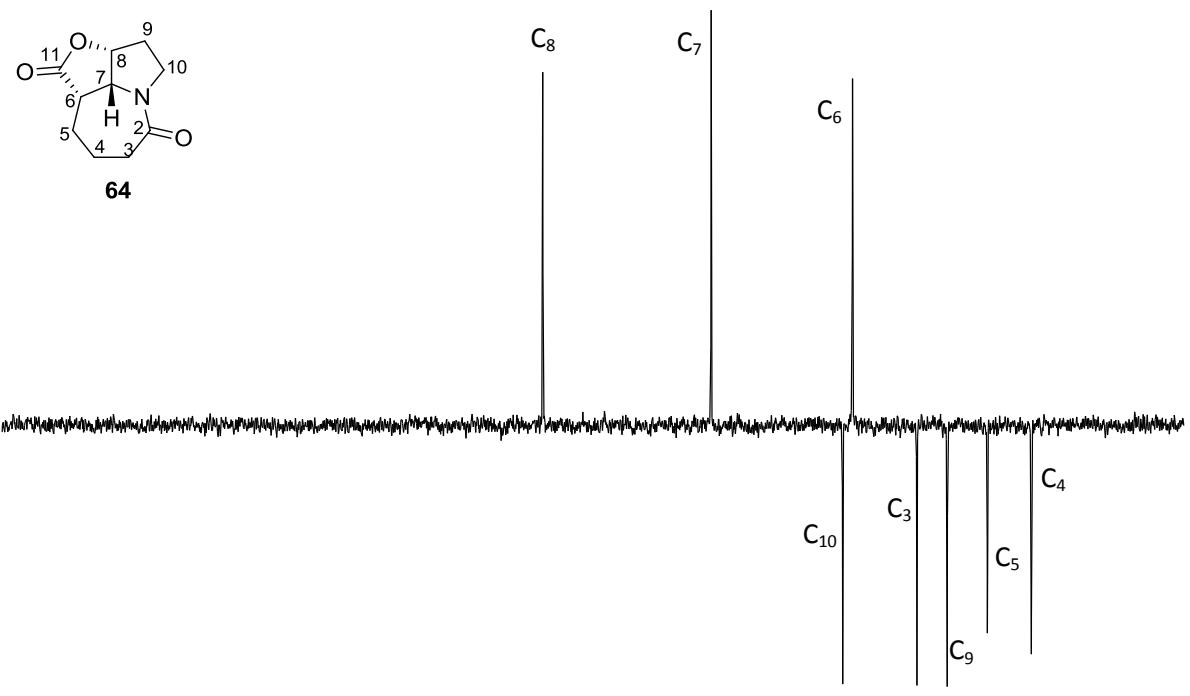
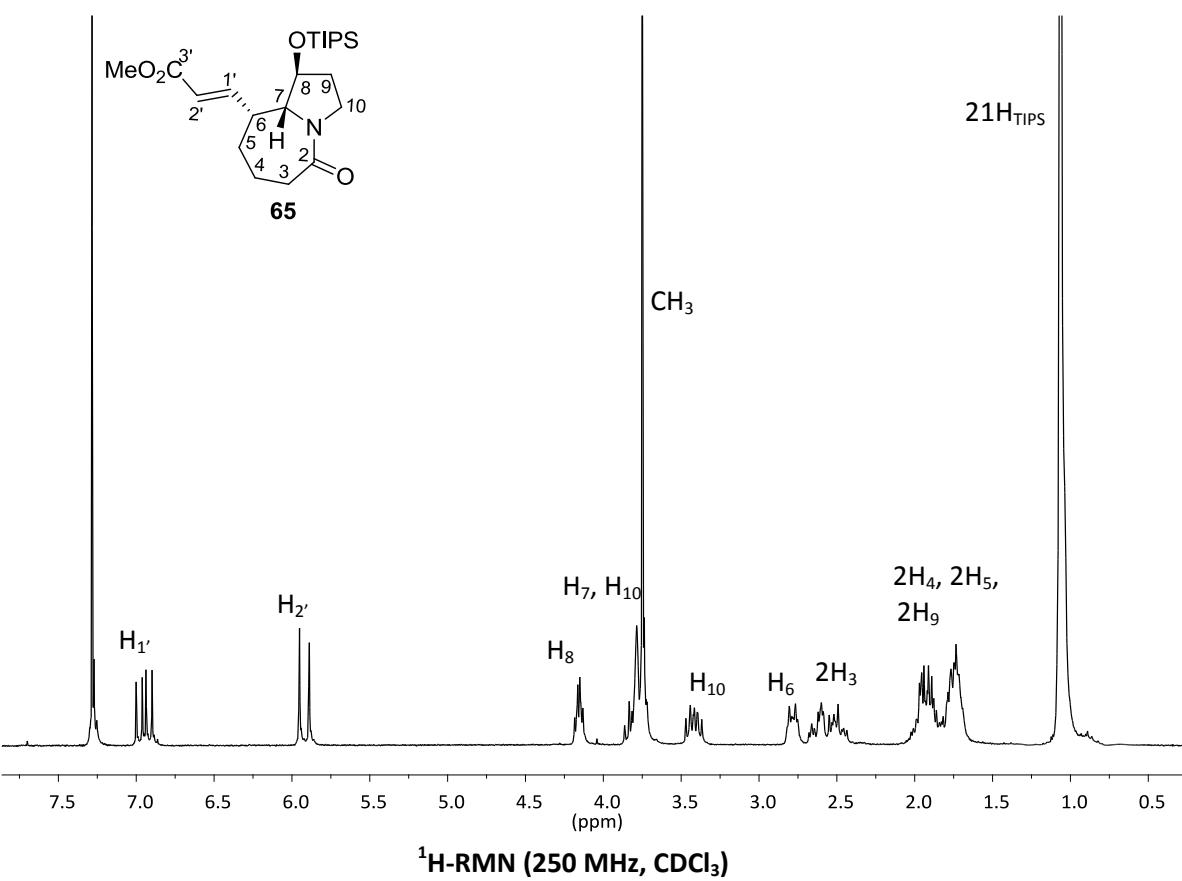


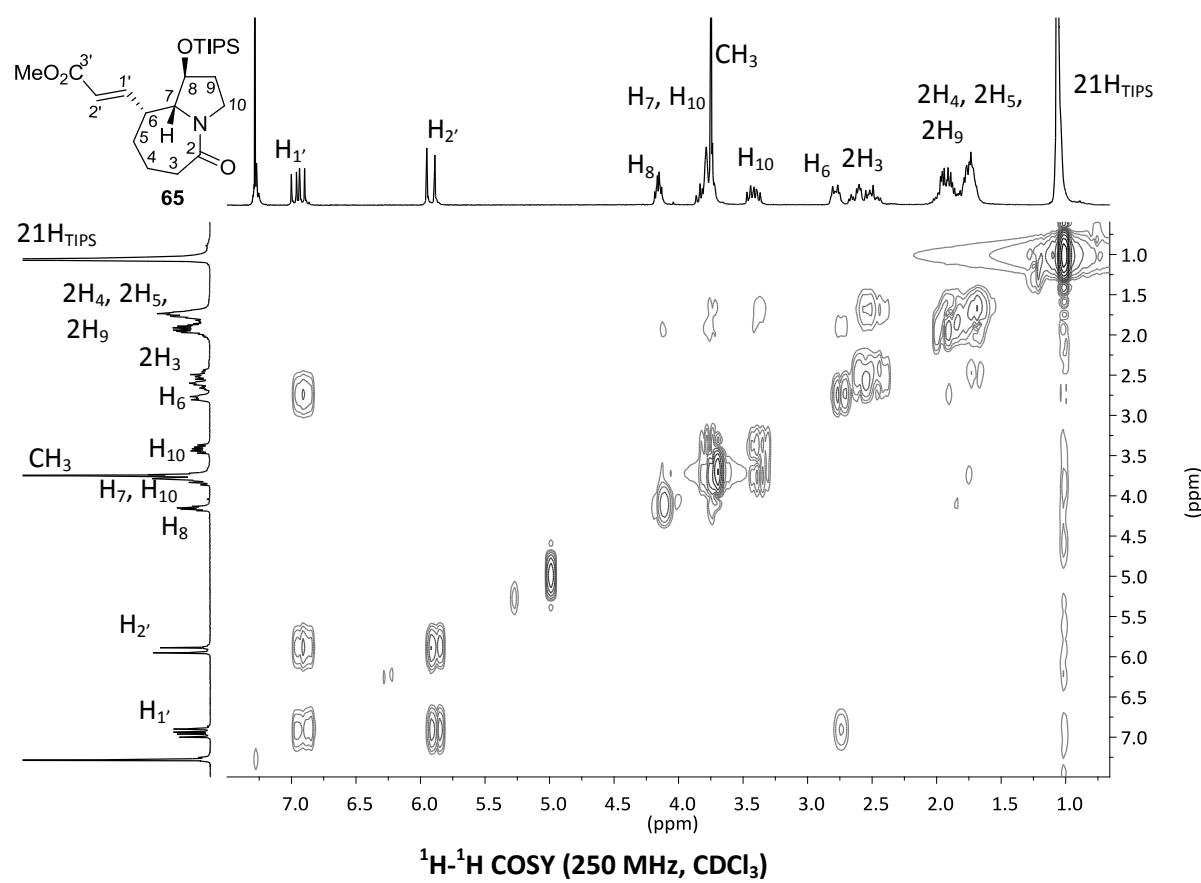
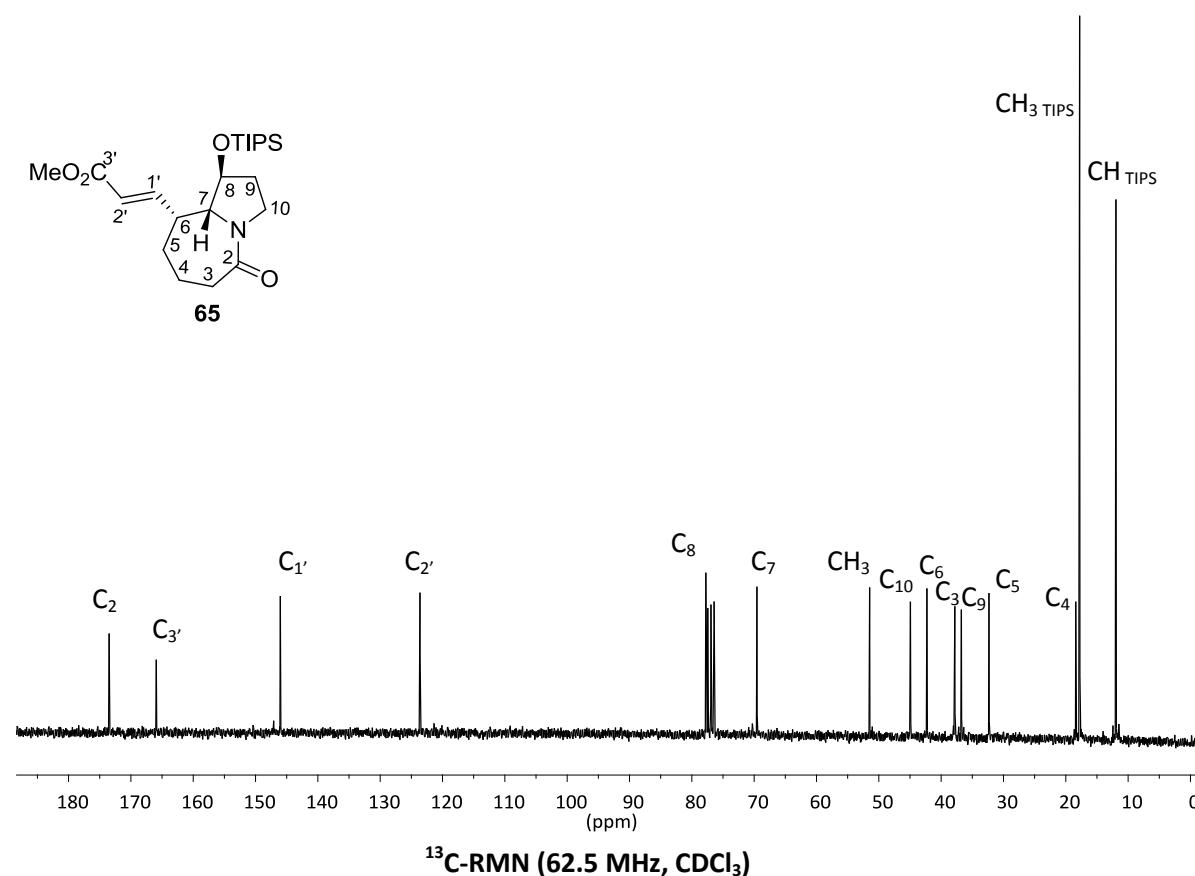


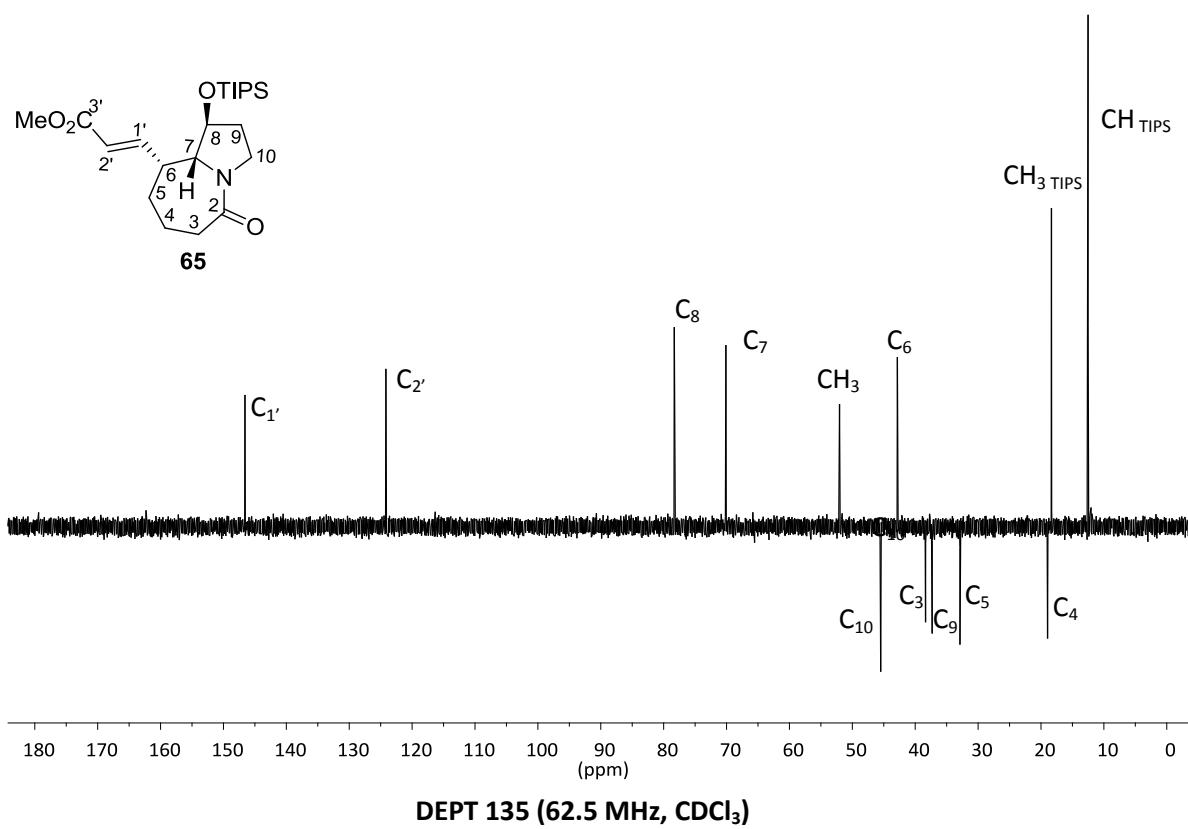
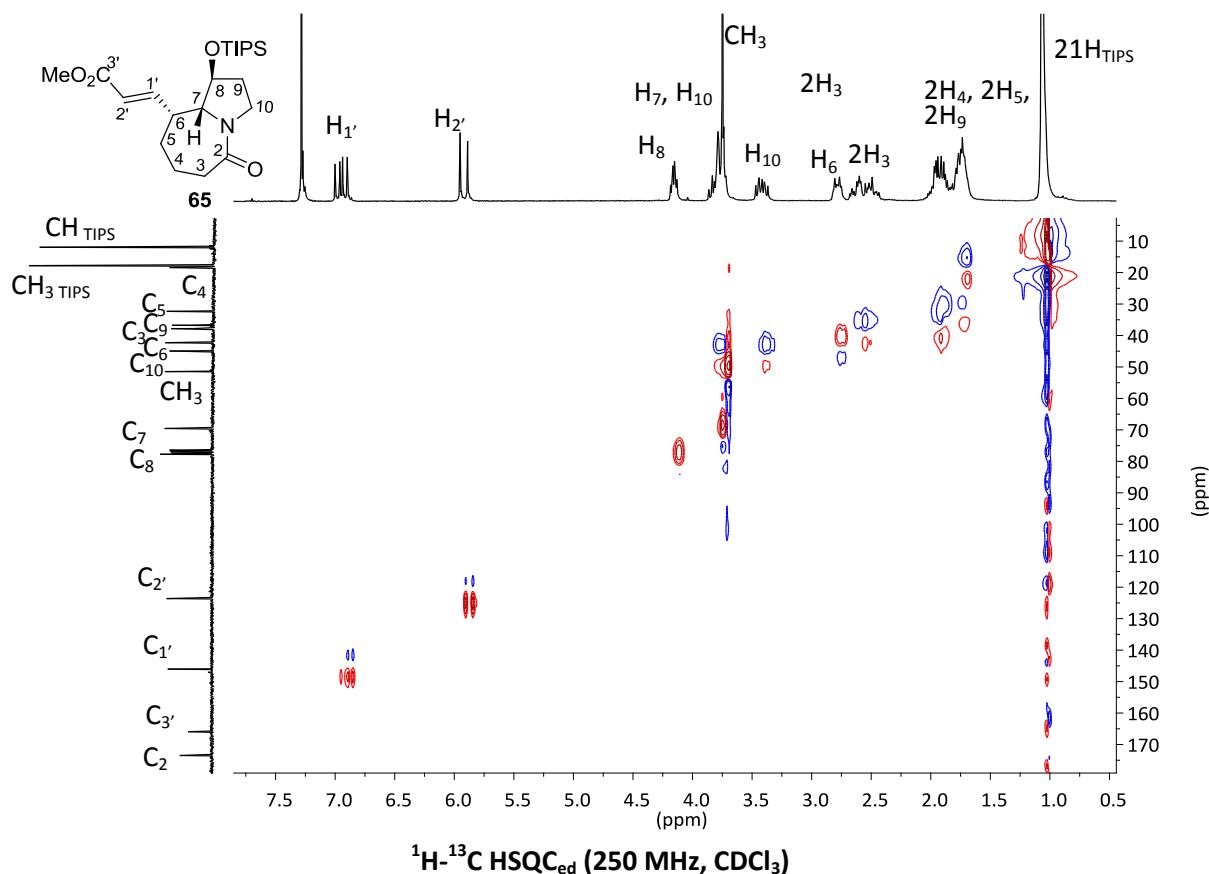


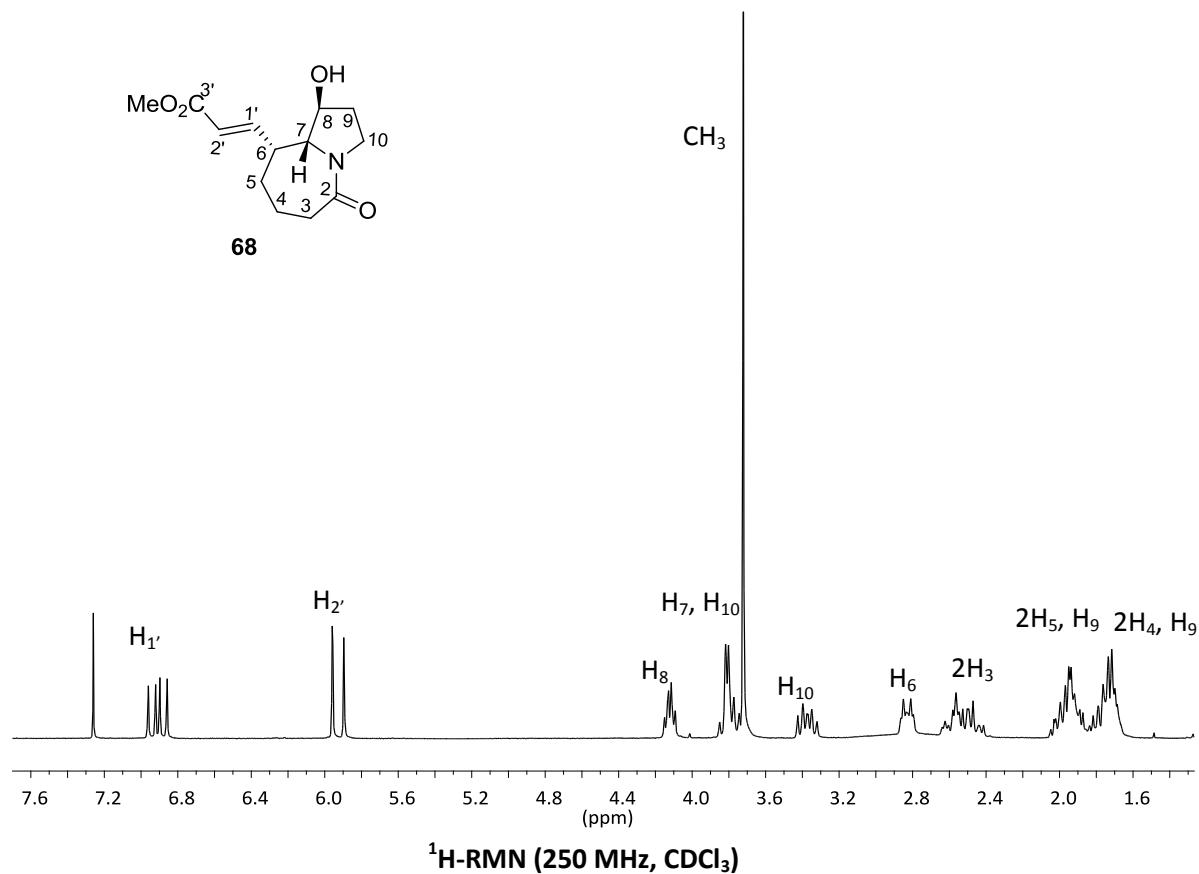




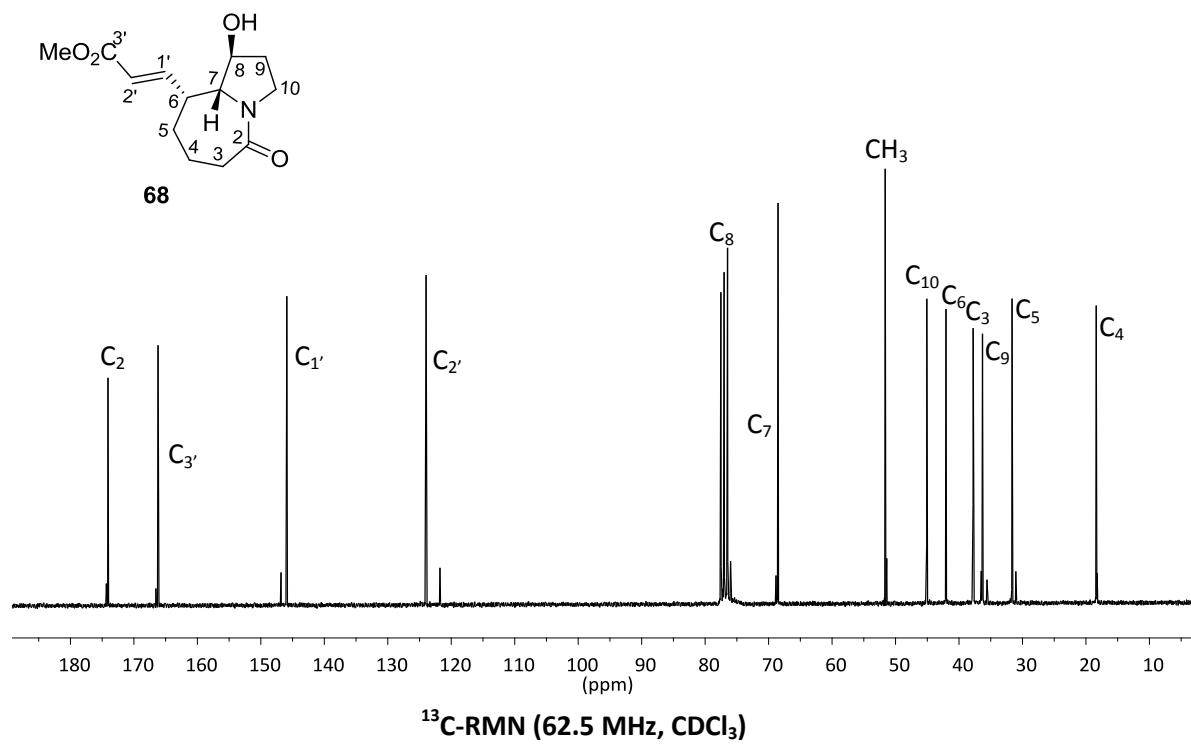
DEPT 135 (90 MHz, CDCl₃)¹H-RMN (250 MHz, CDCl₃)



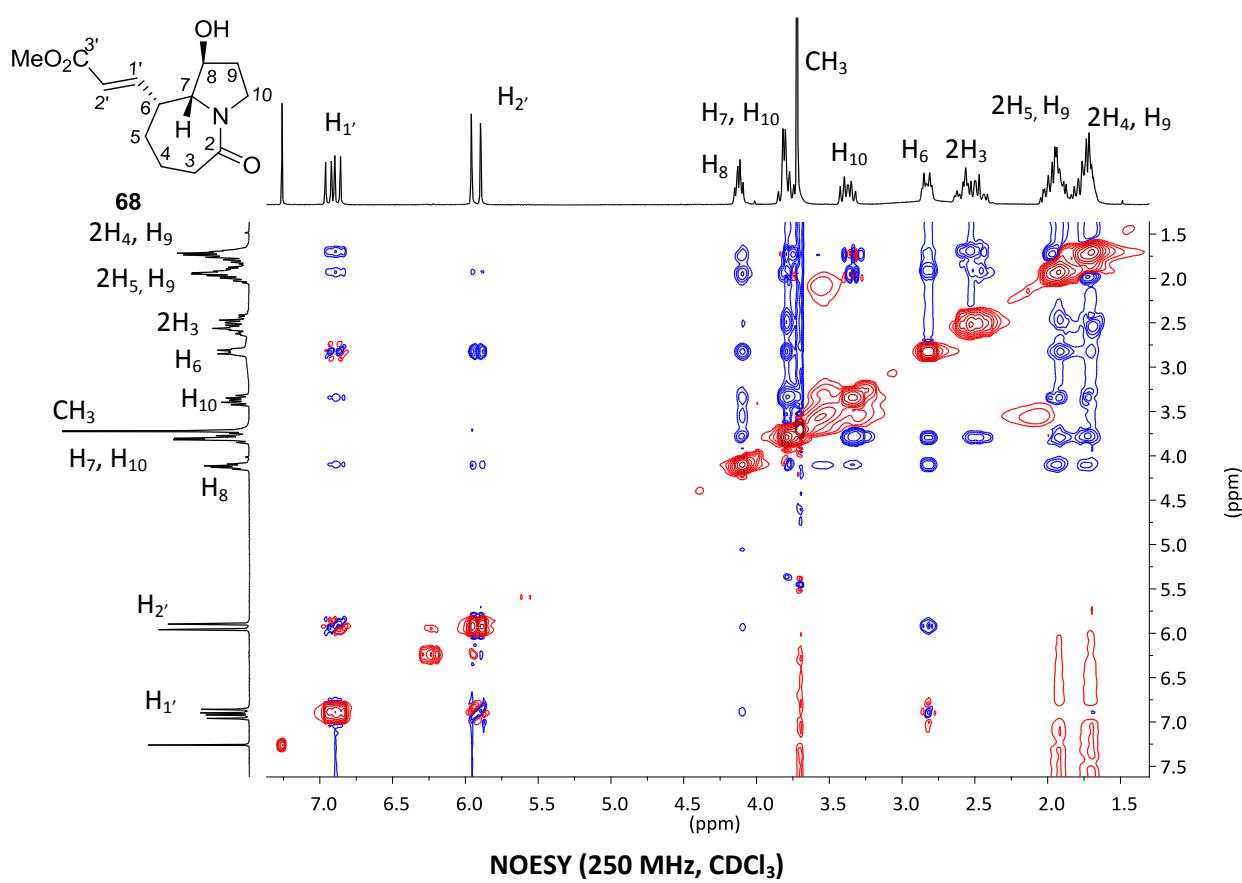
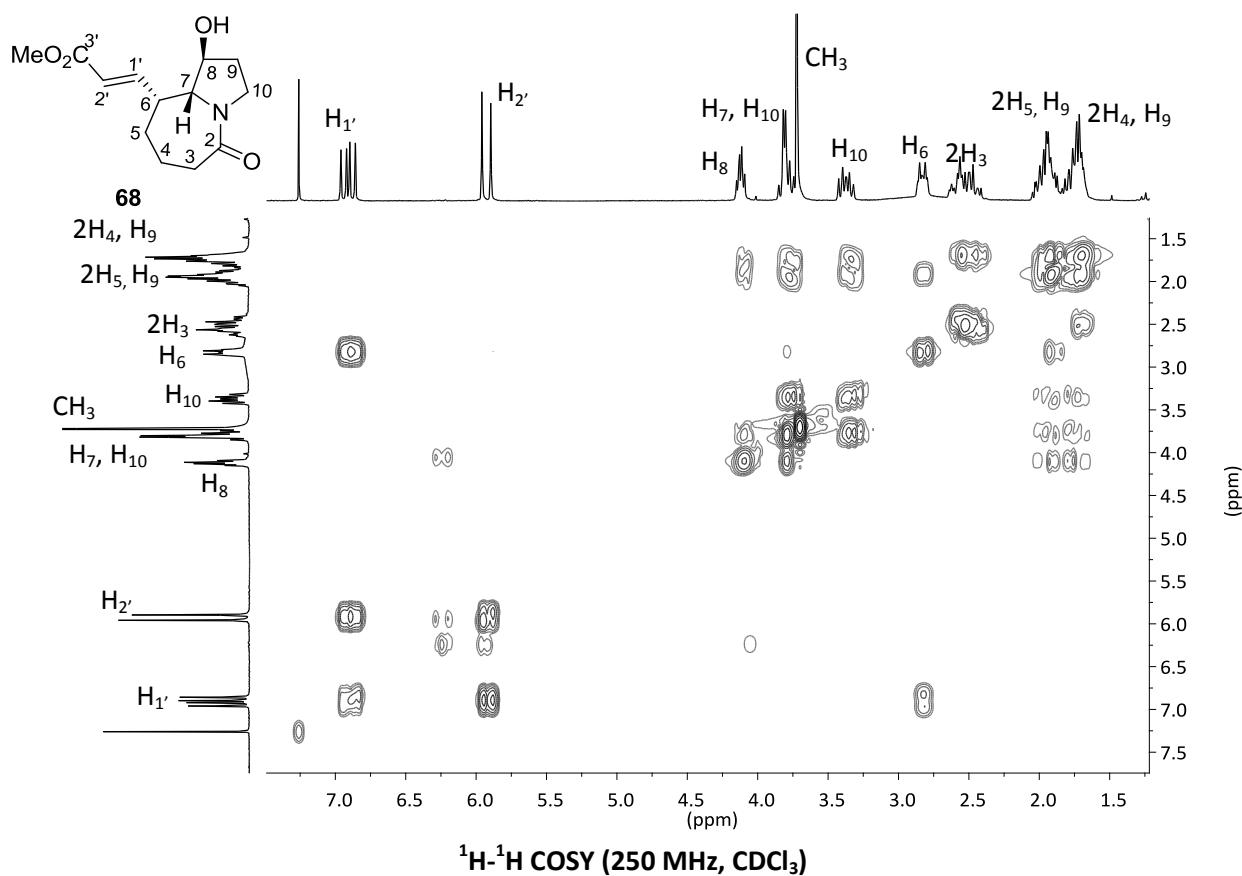


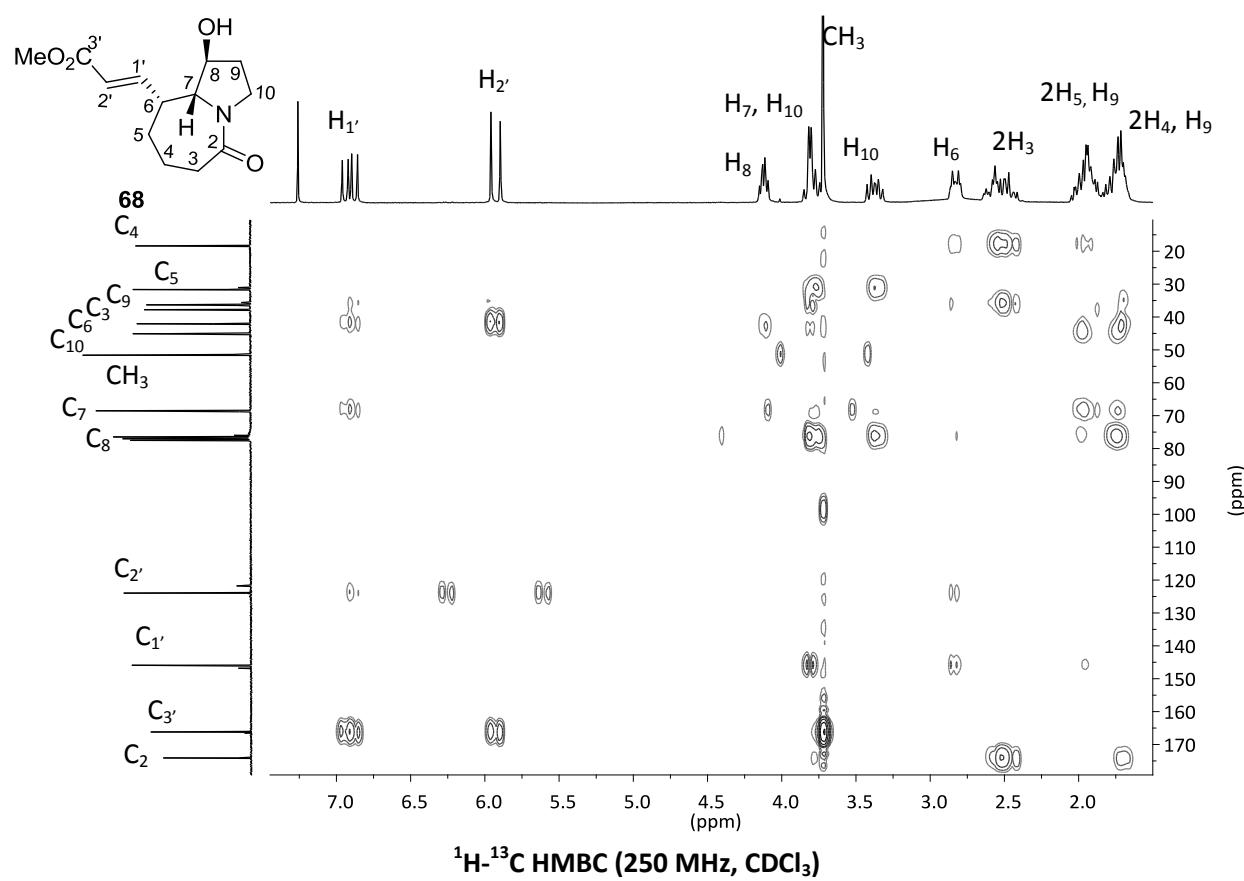
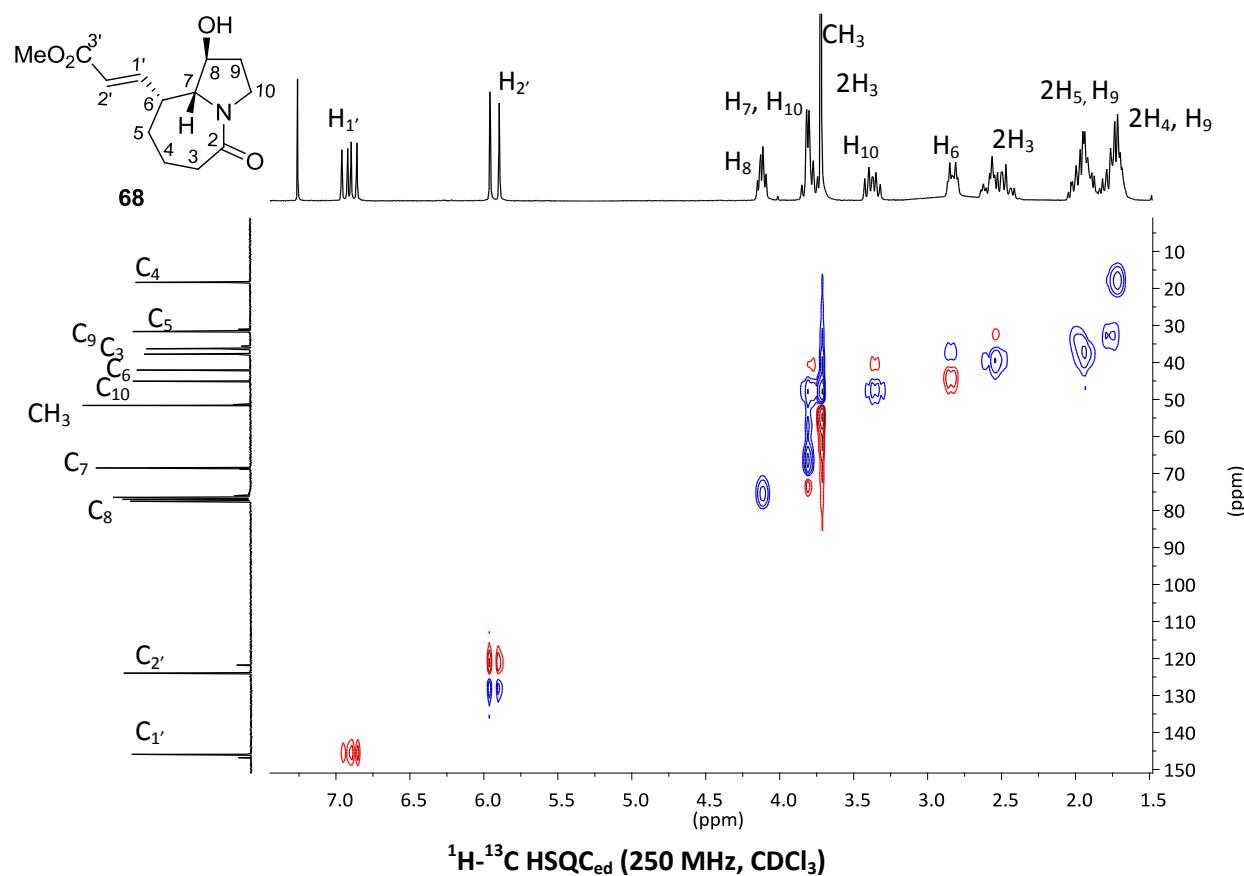


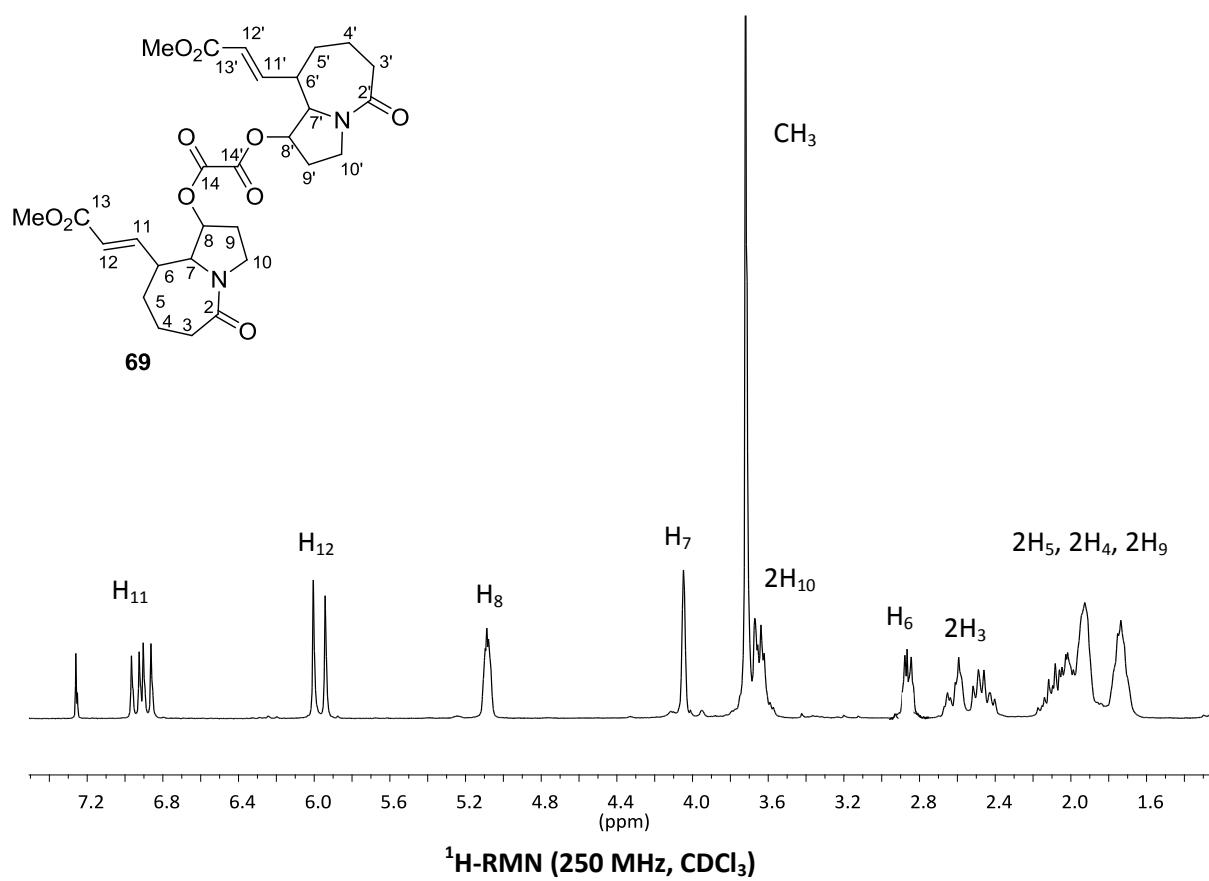
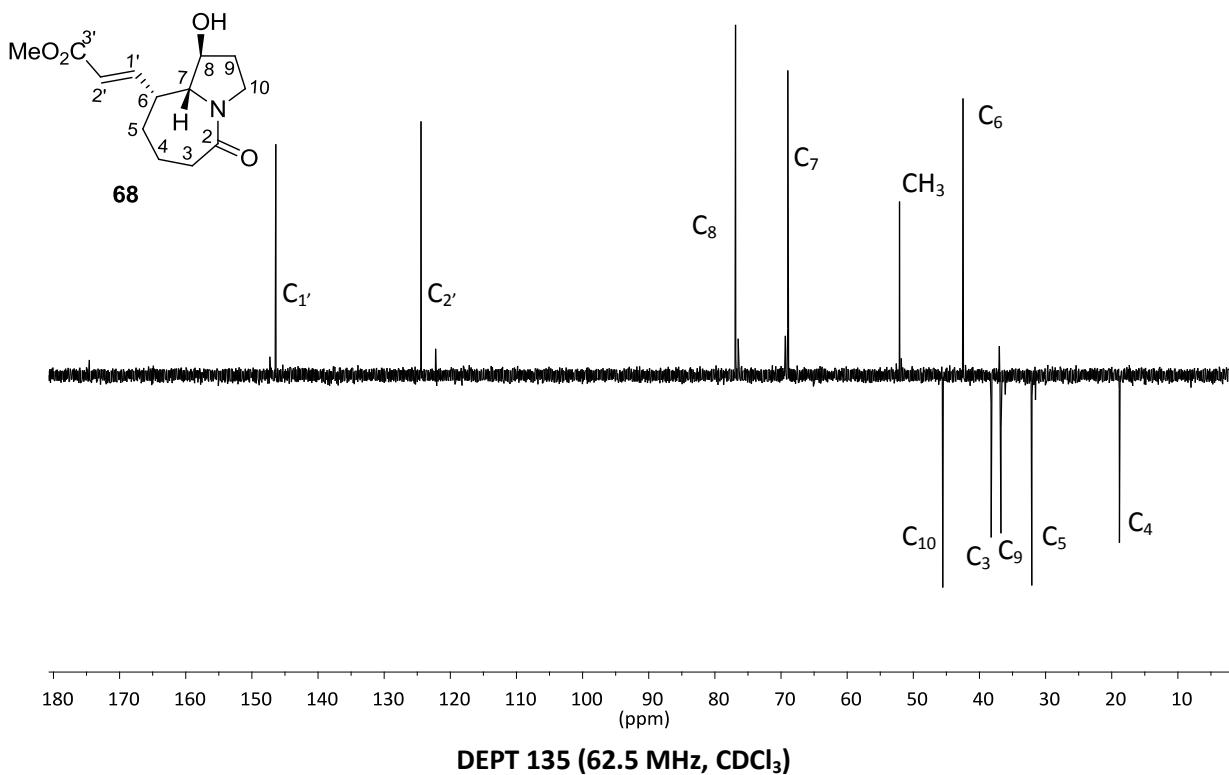
^1H -RMN (250 MHz, CDCl_3)



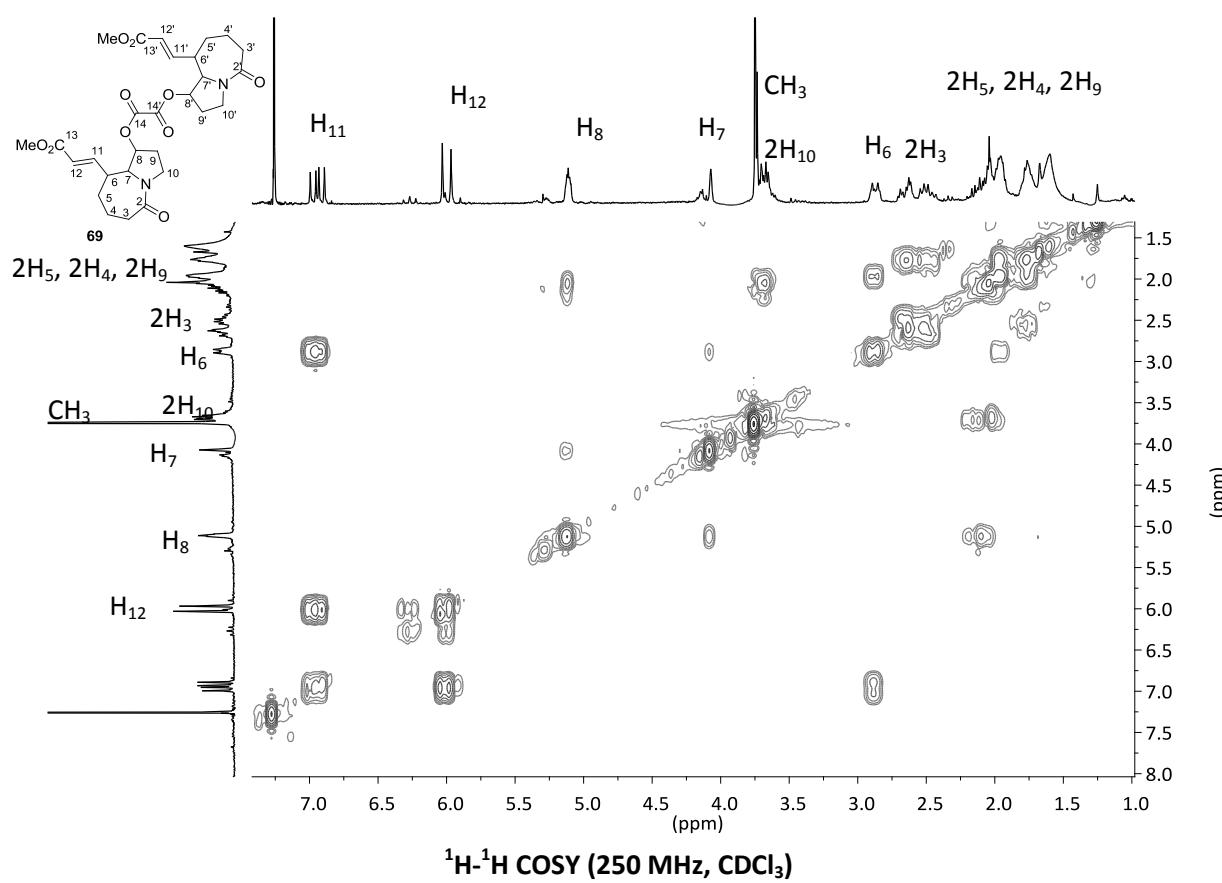
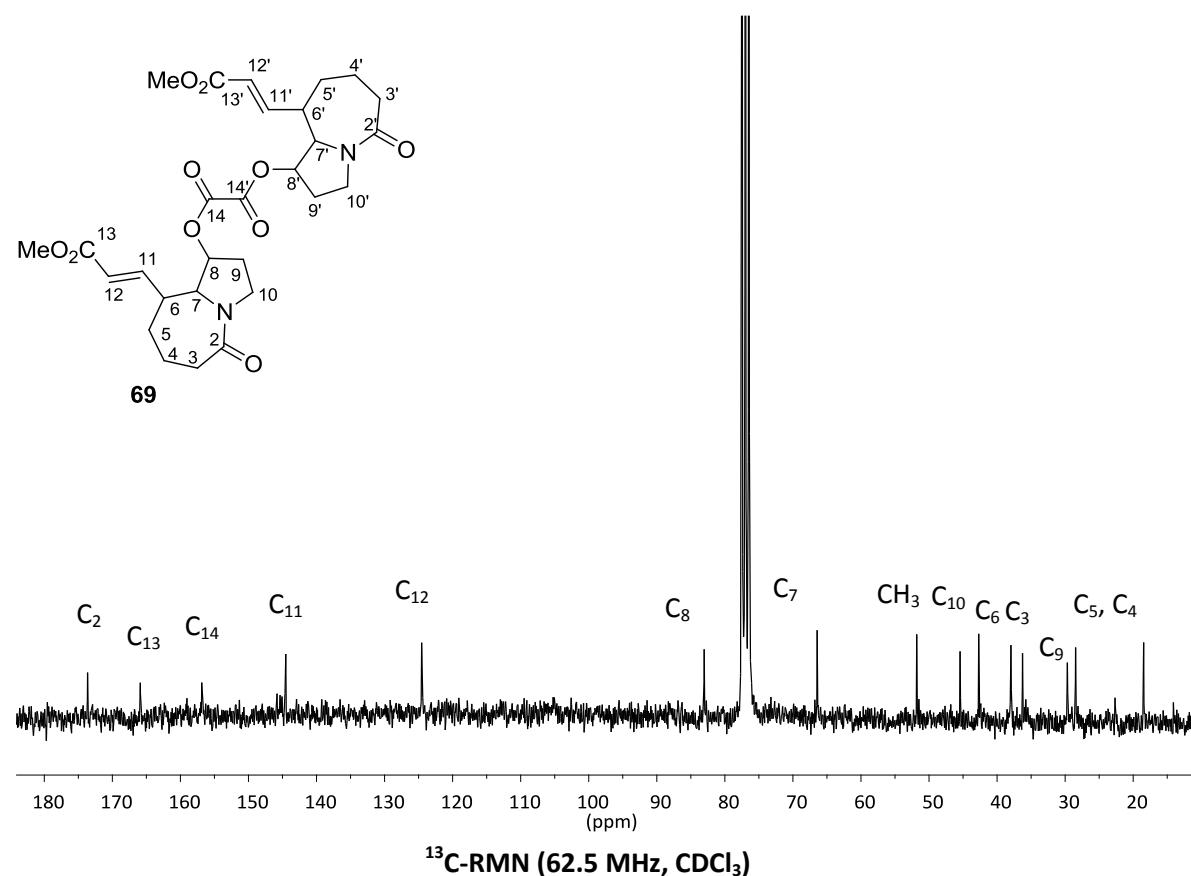
^{13}C -RMN (62.5 MHz, CDCl_3)

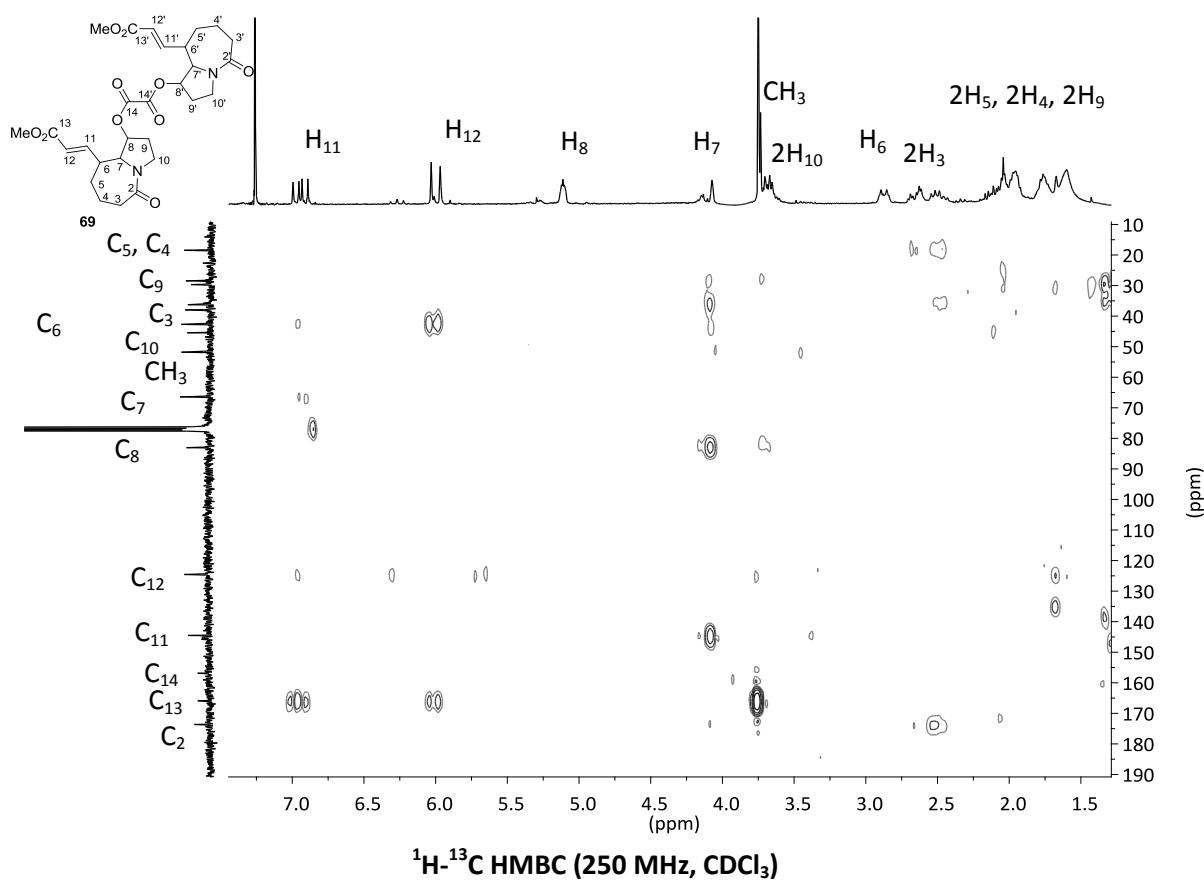
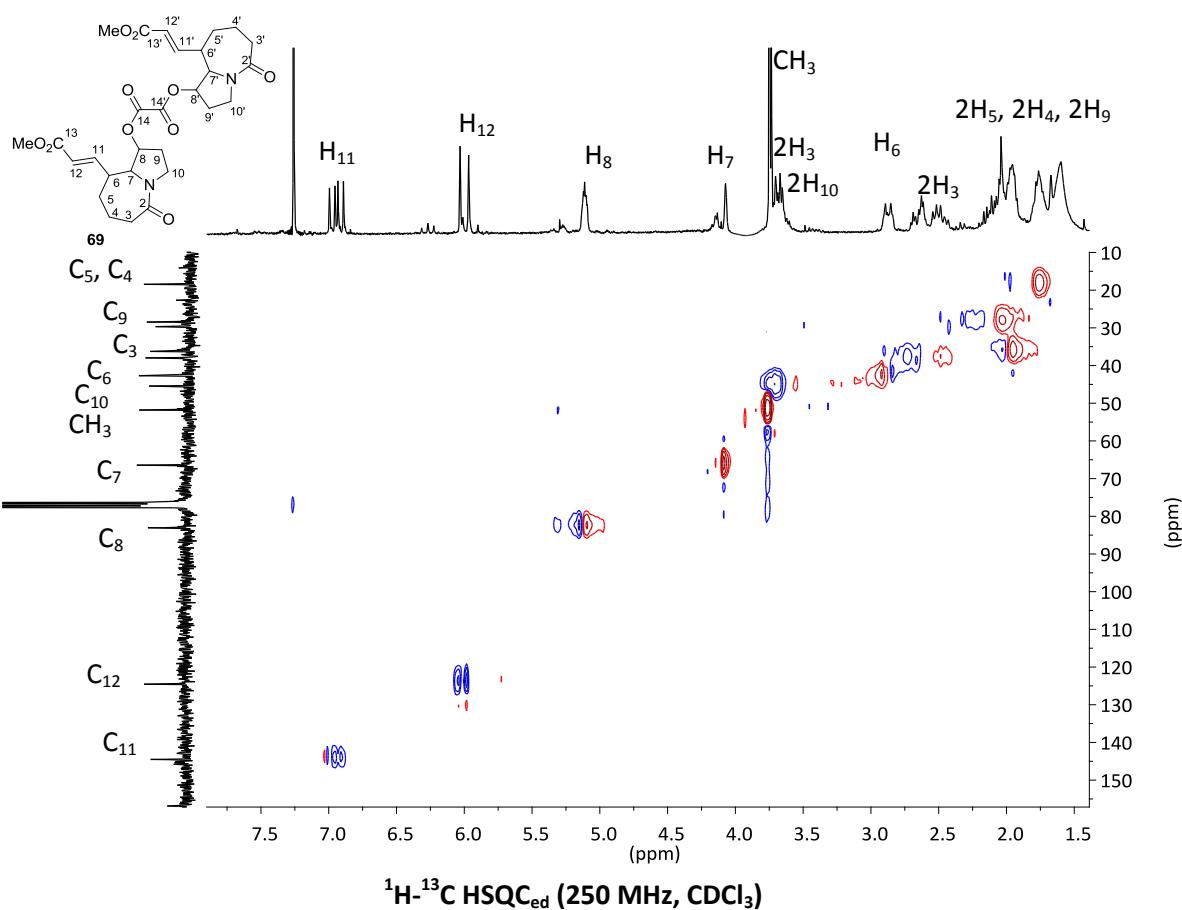


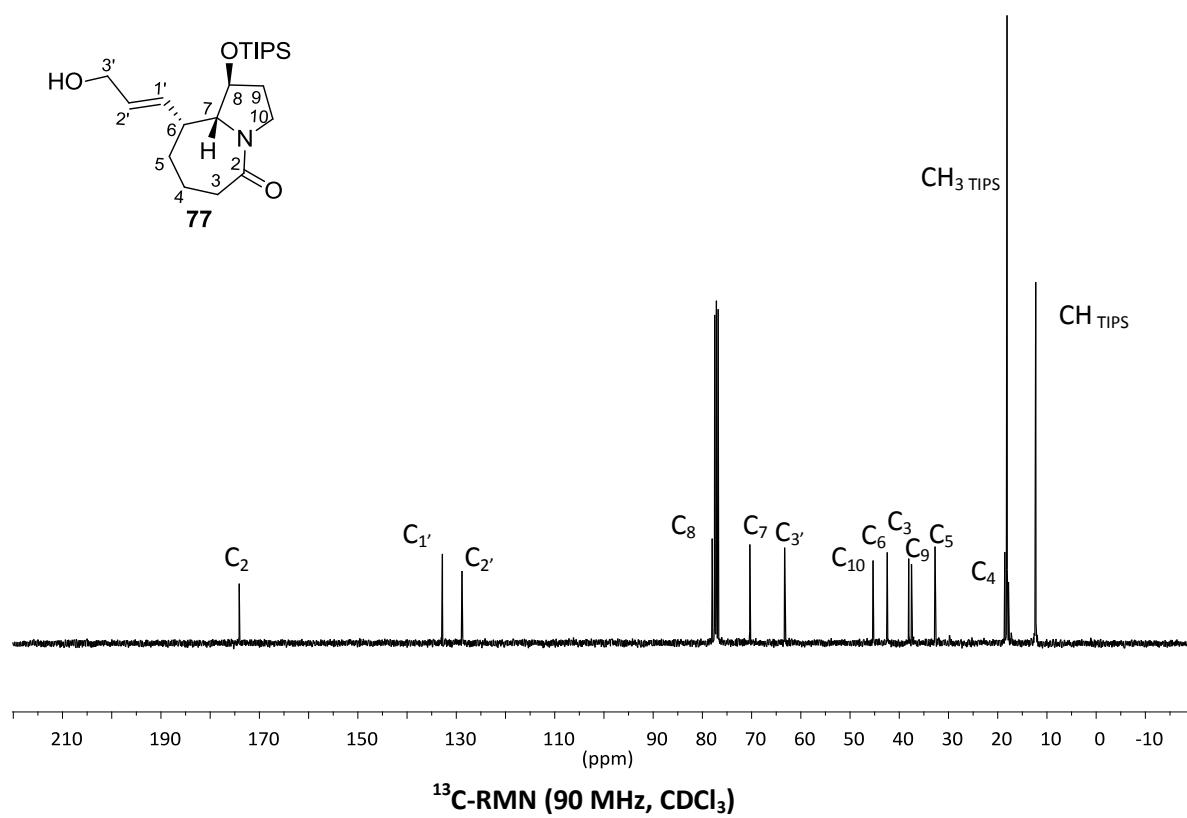
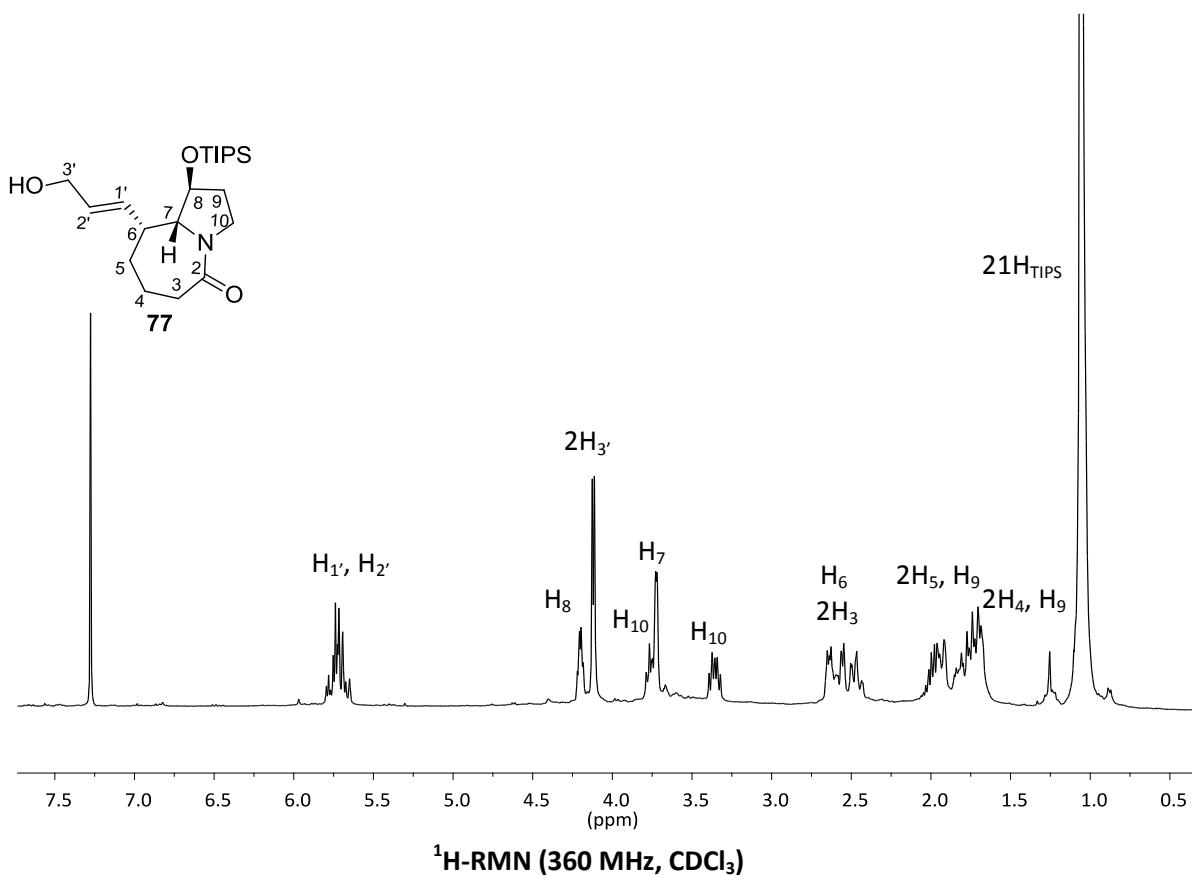


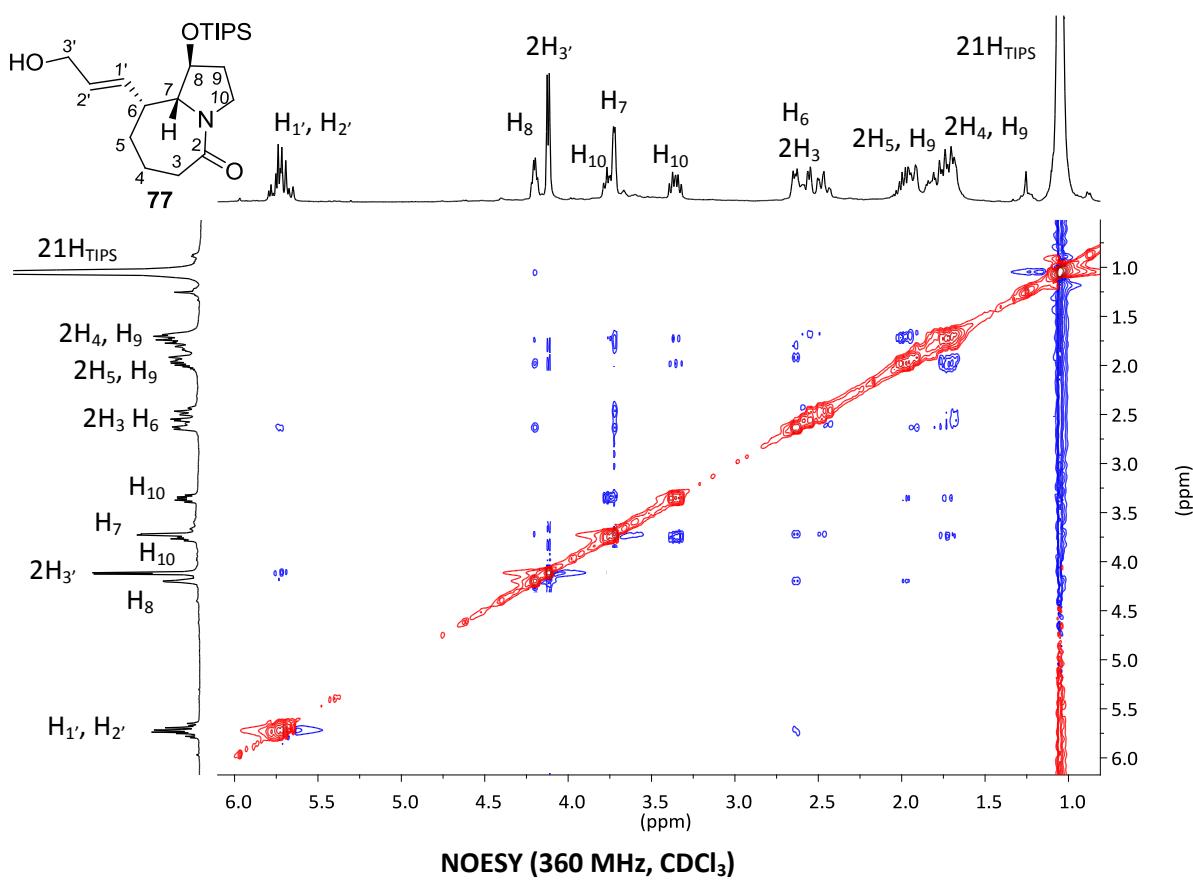
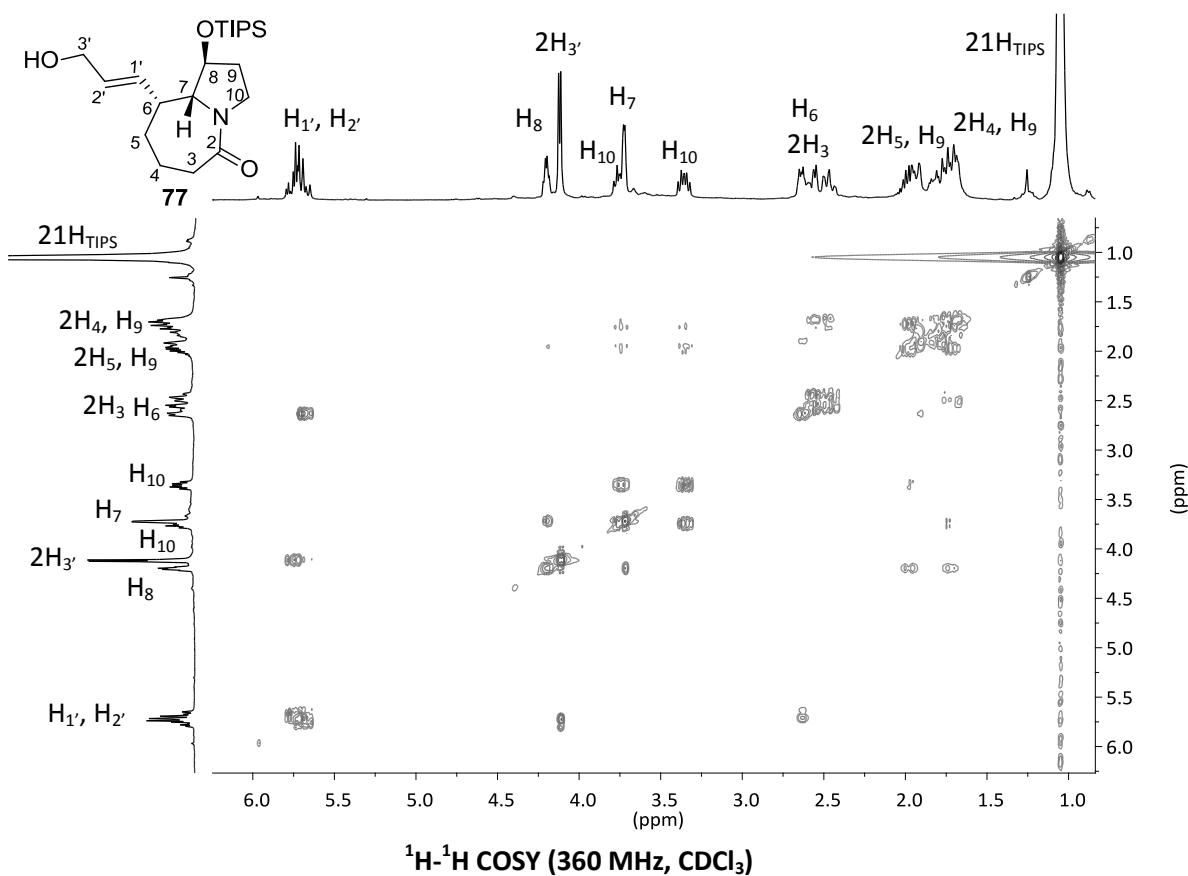


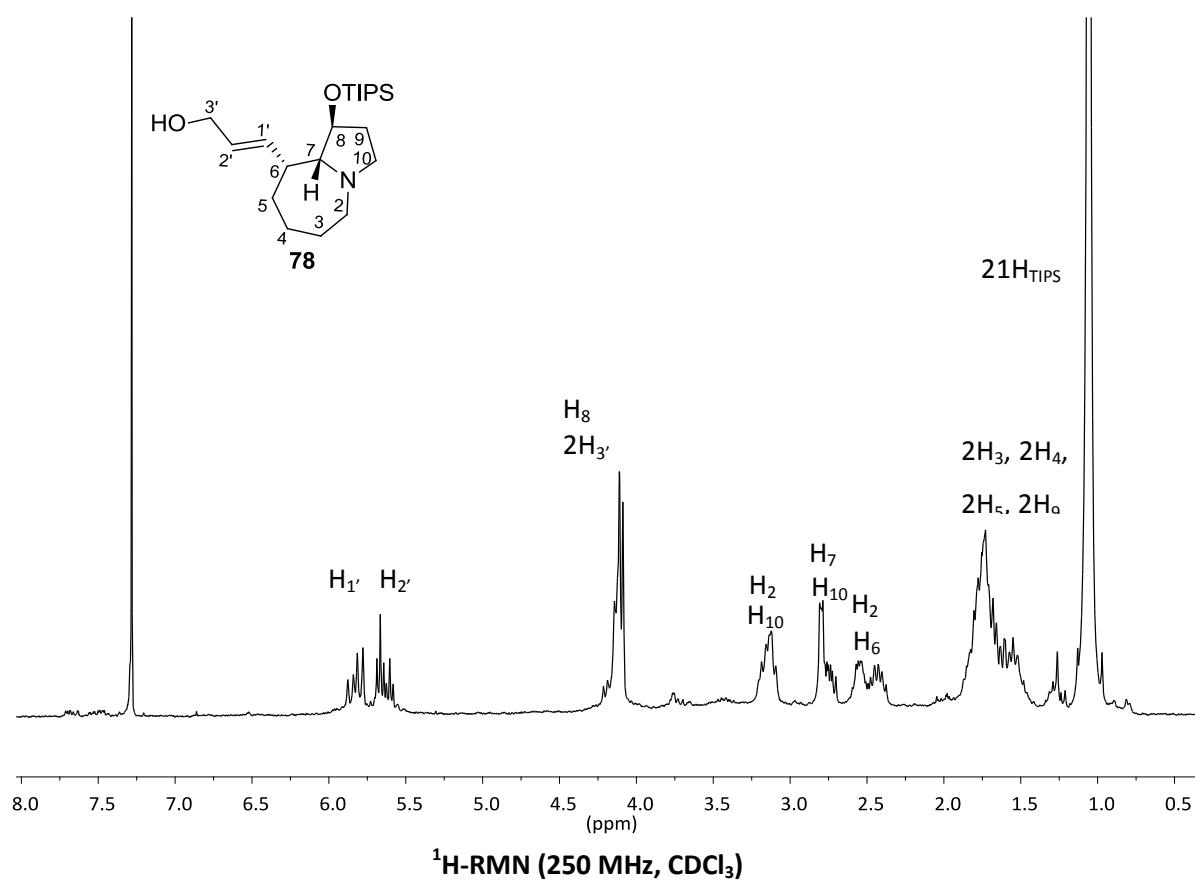
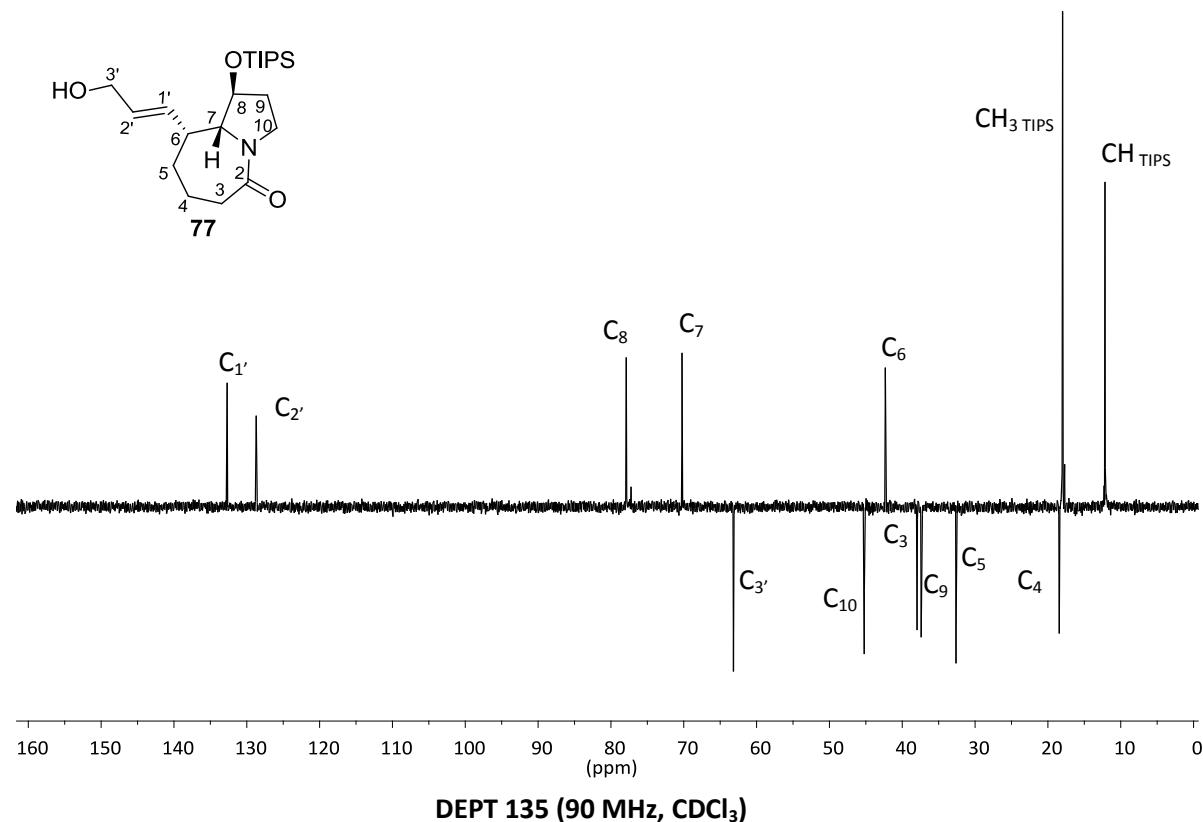
6. RECULL D'ESPECTRES

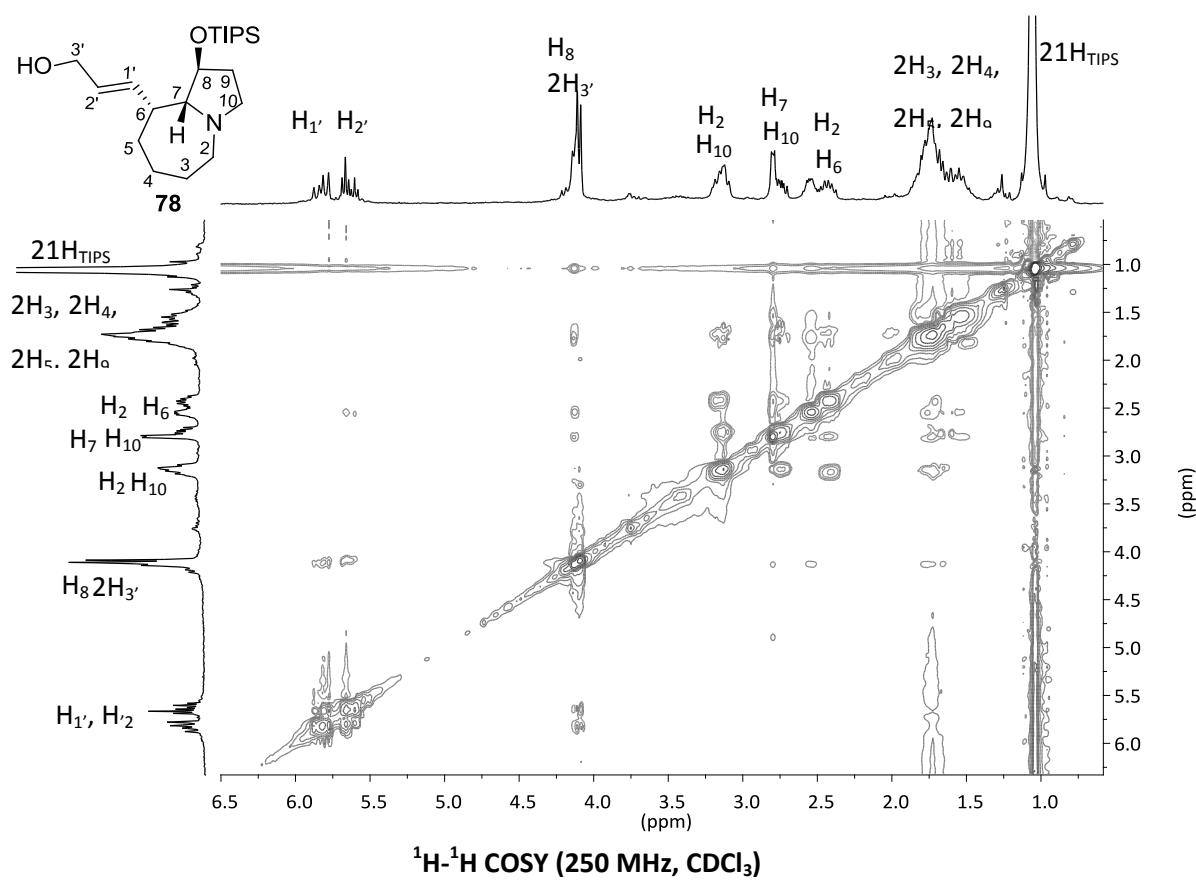
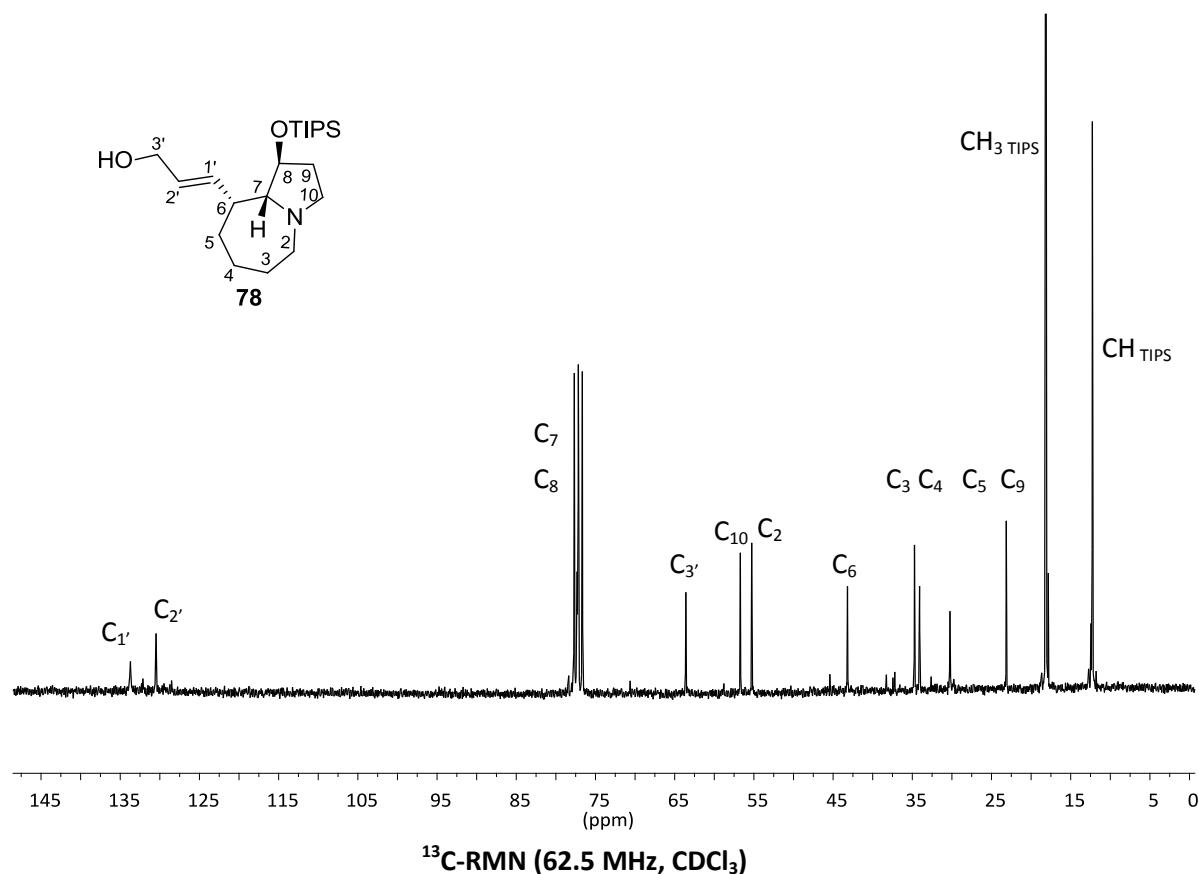


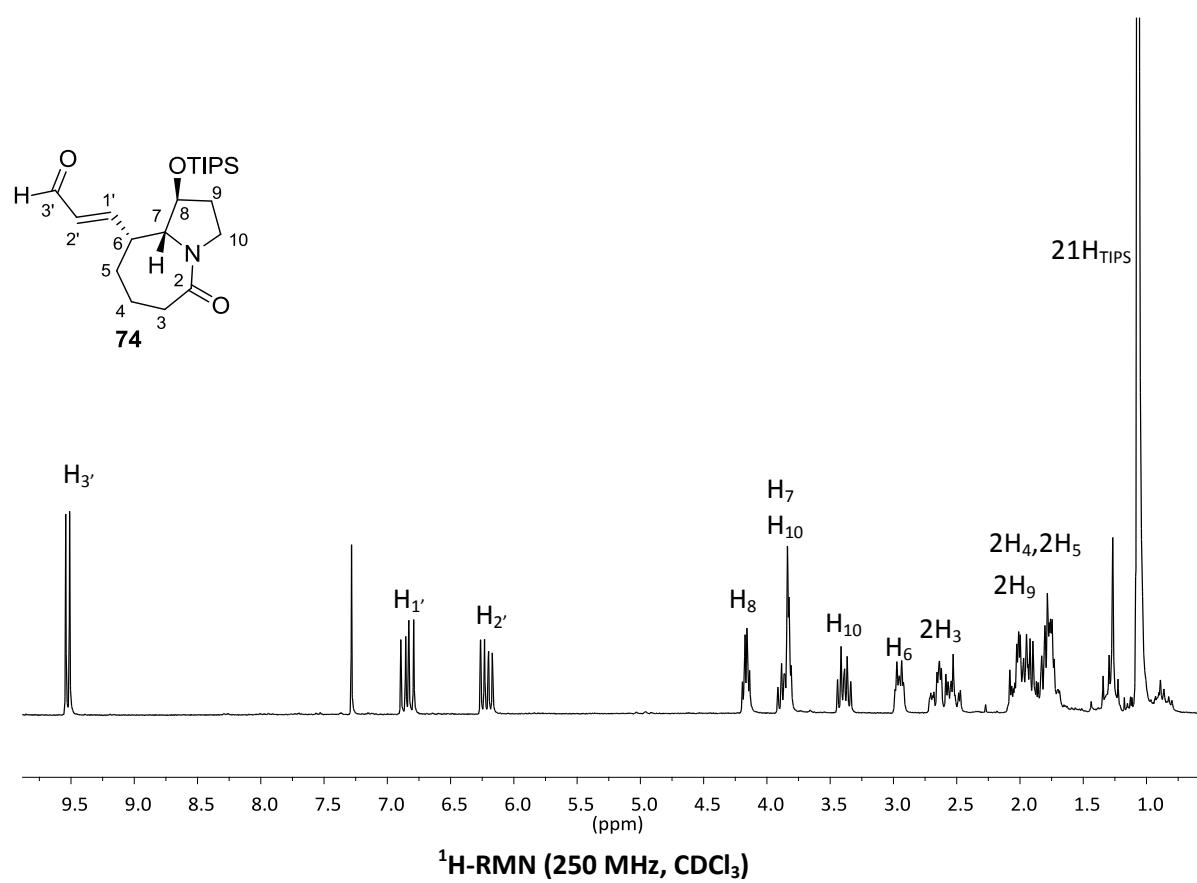
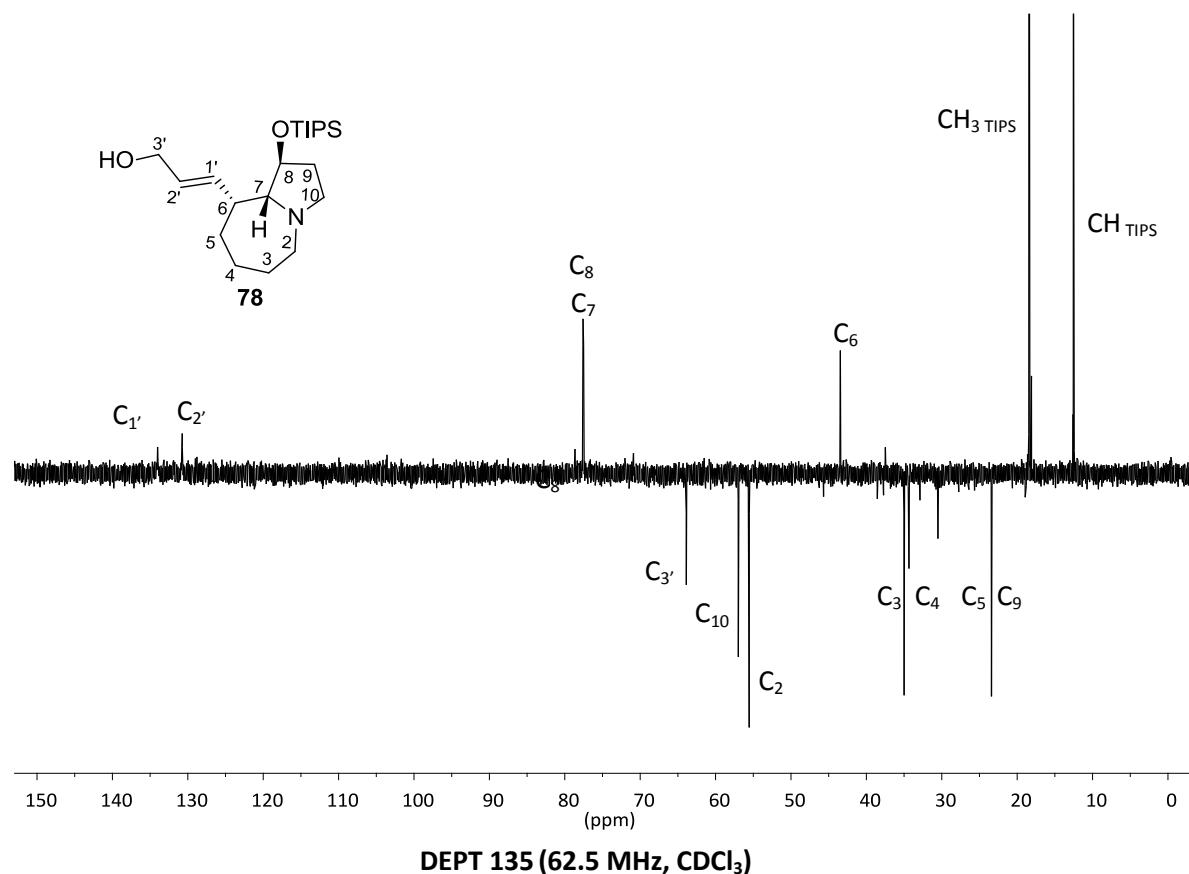


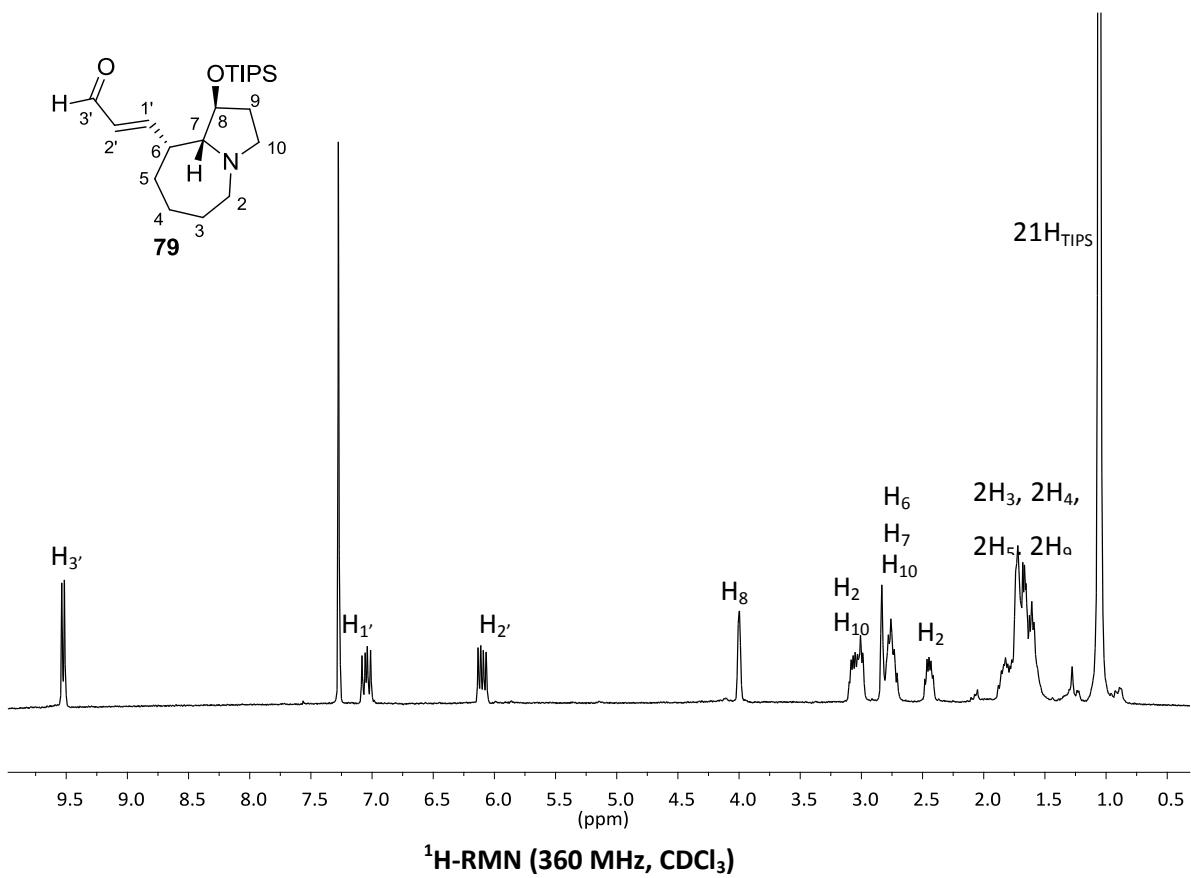
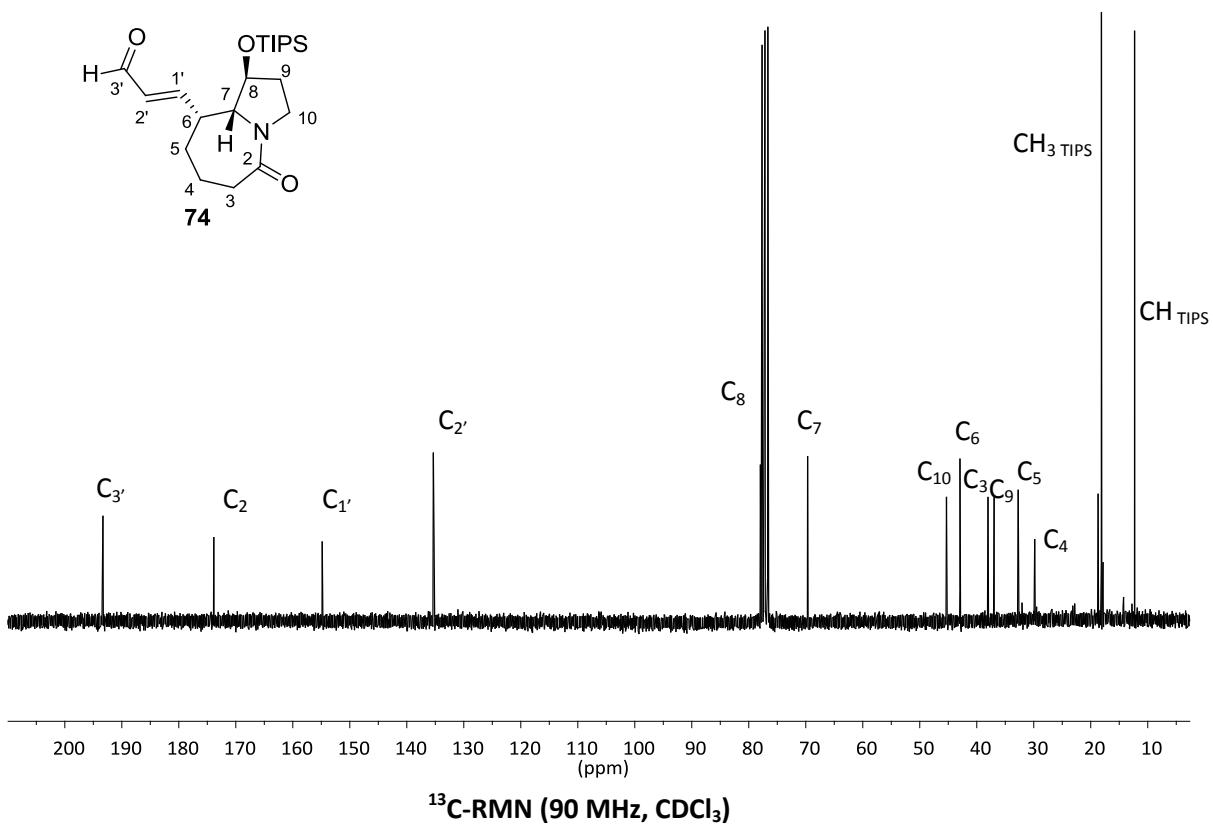


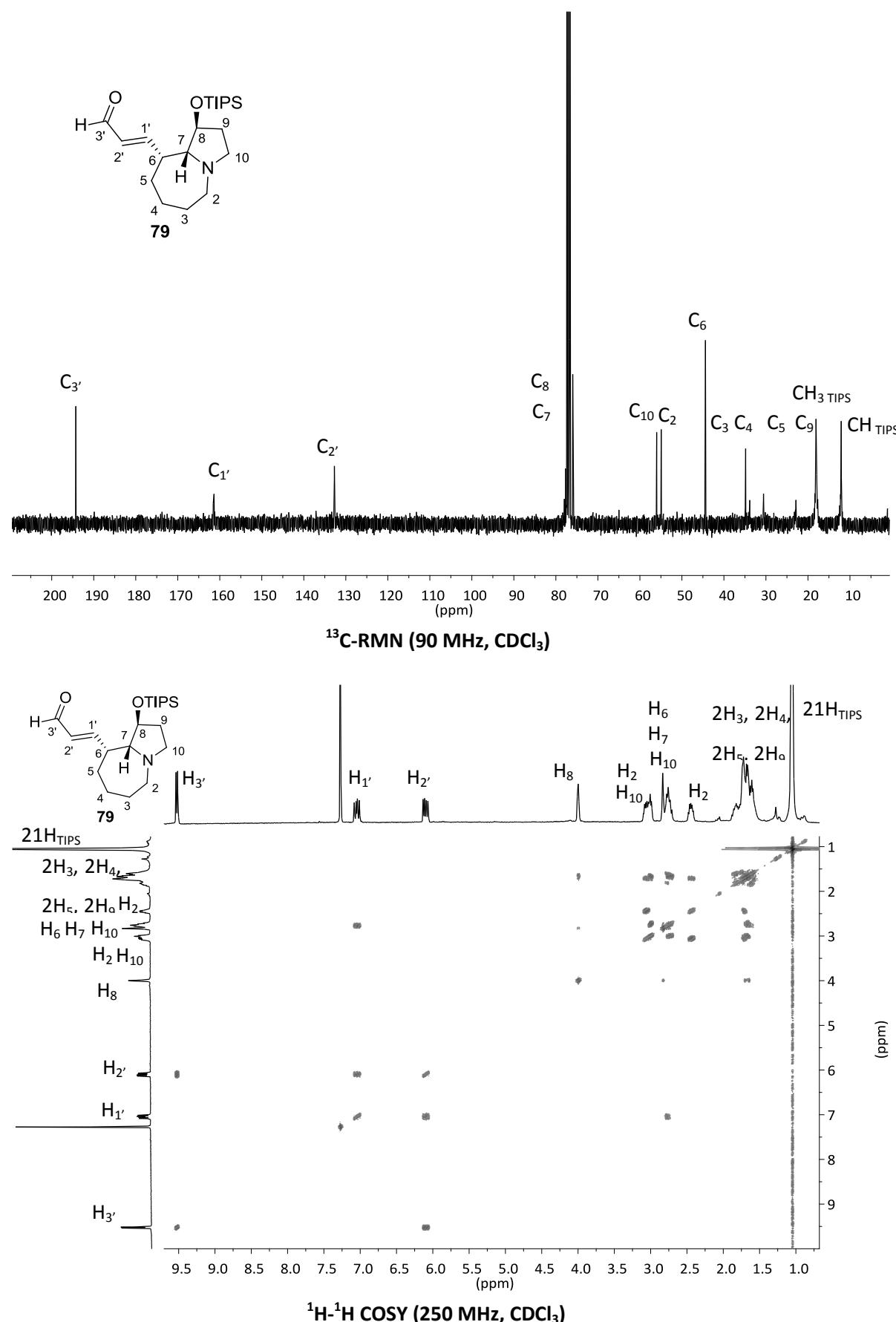


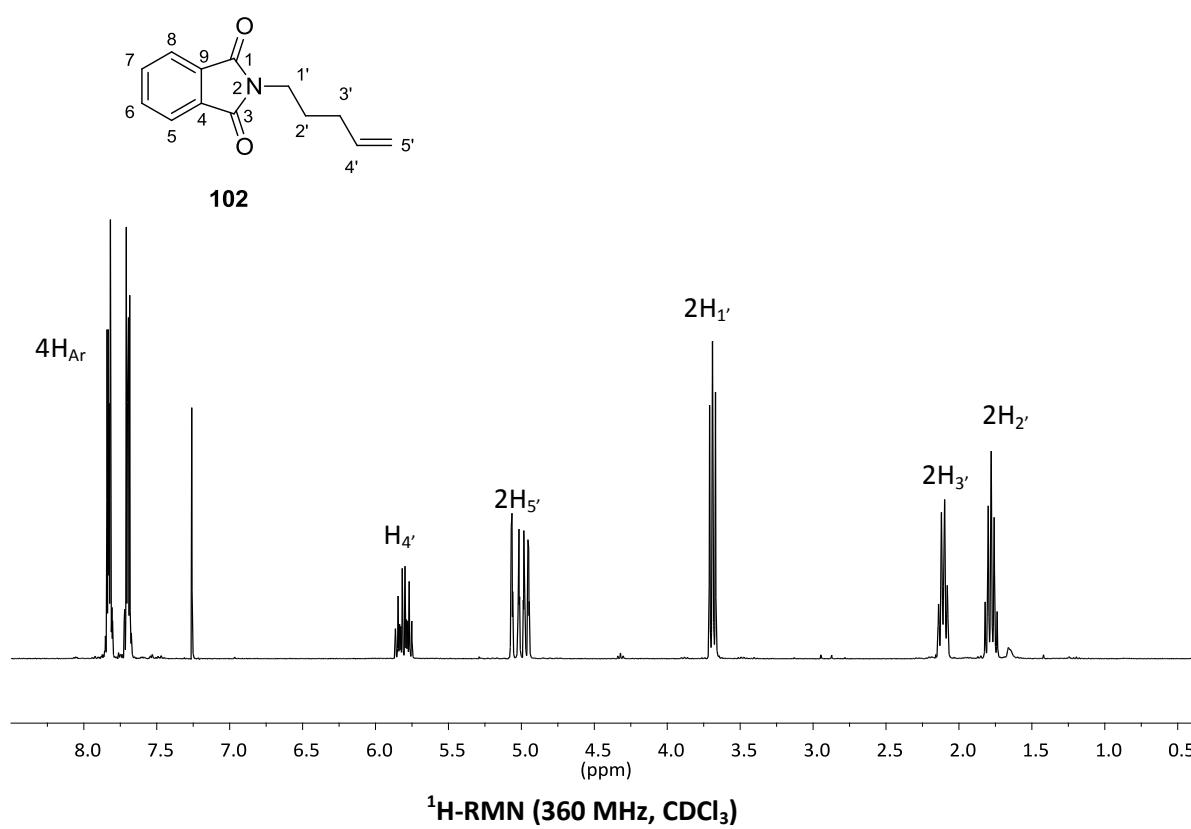
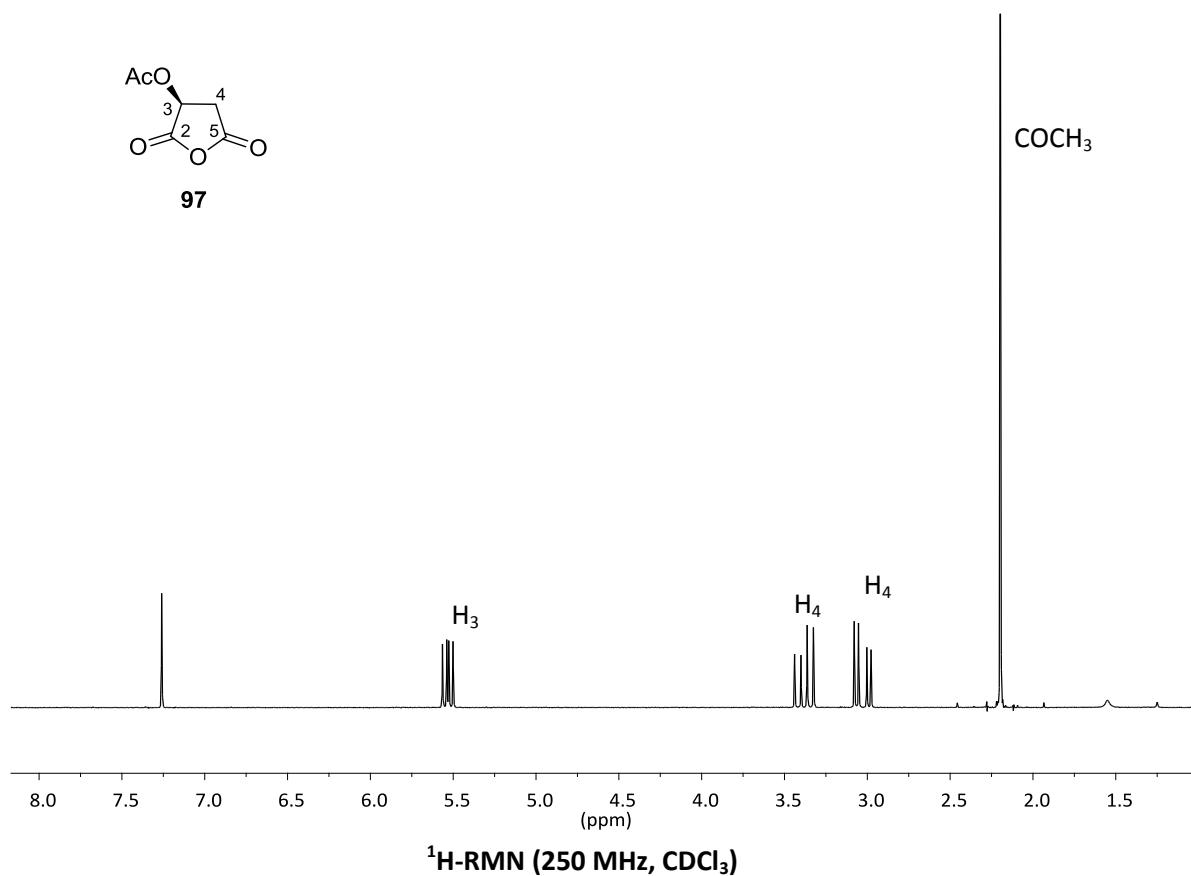


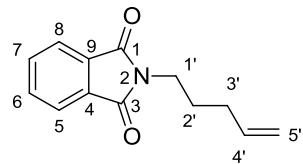




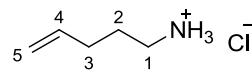
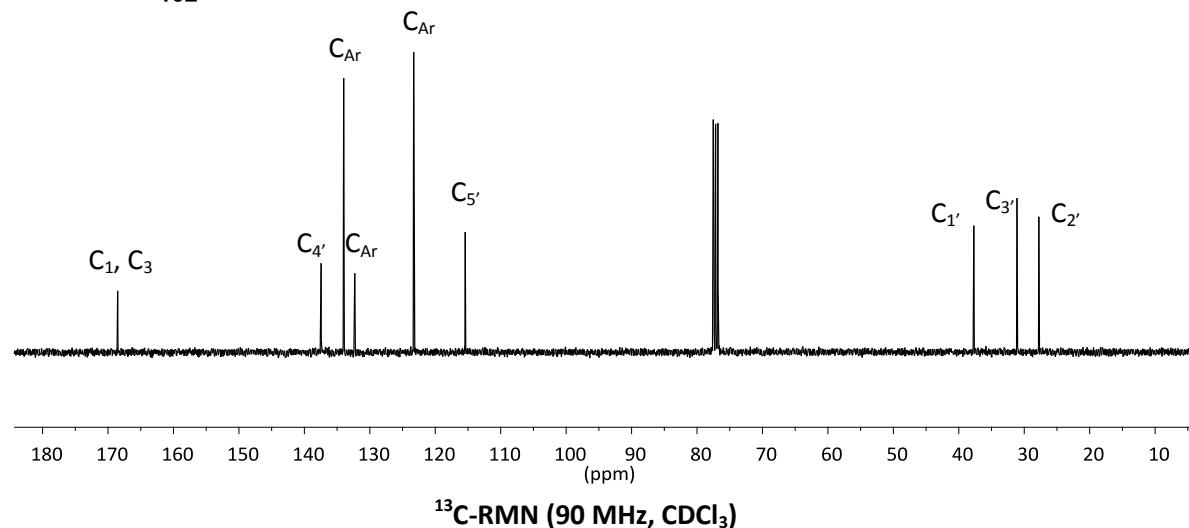




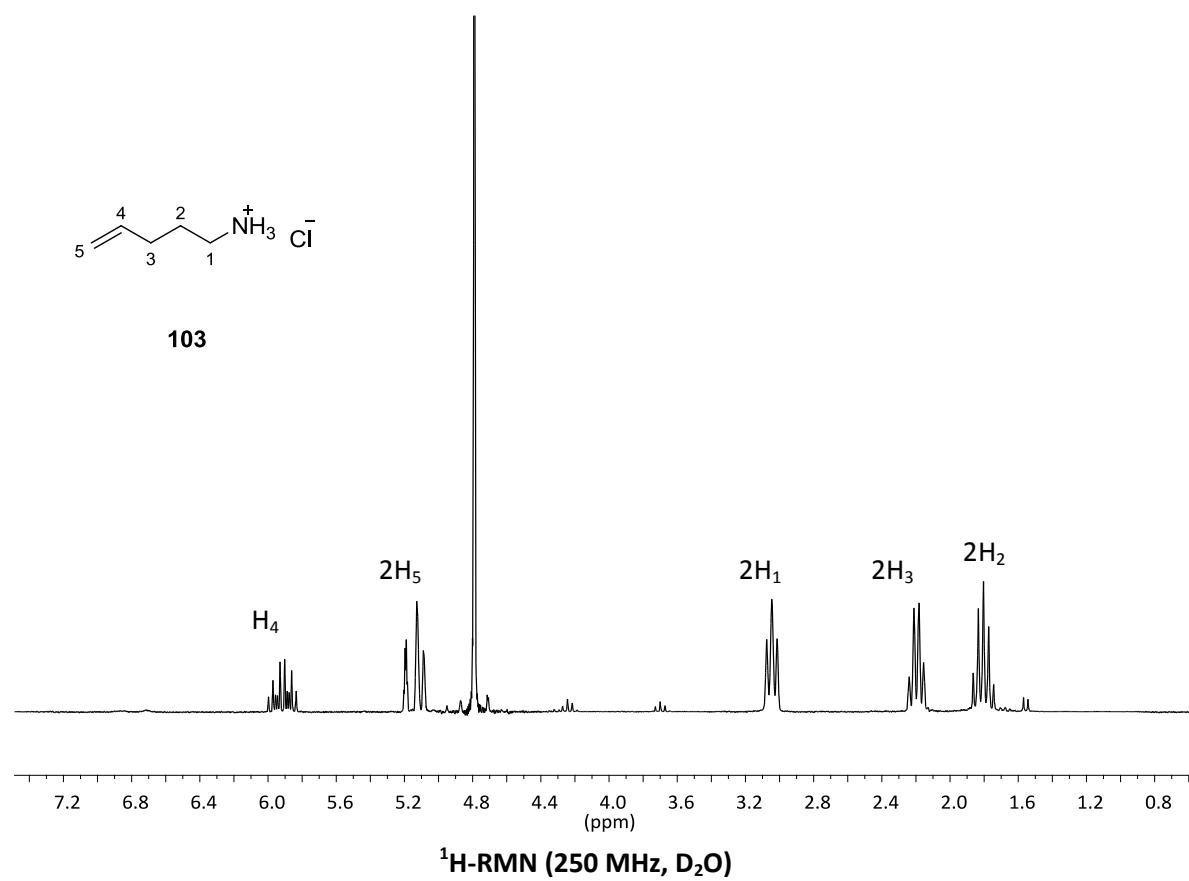


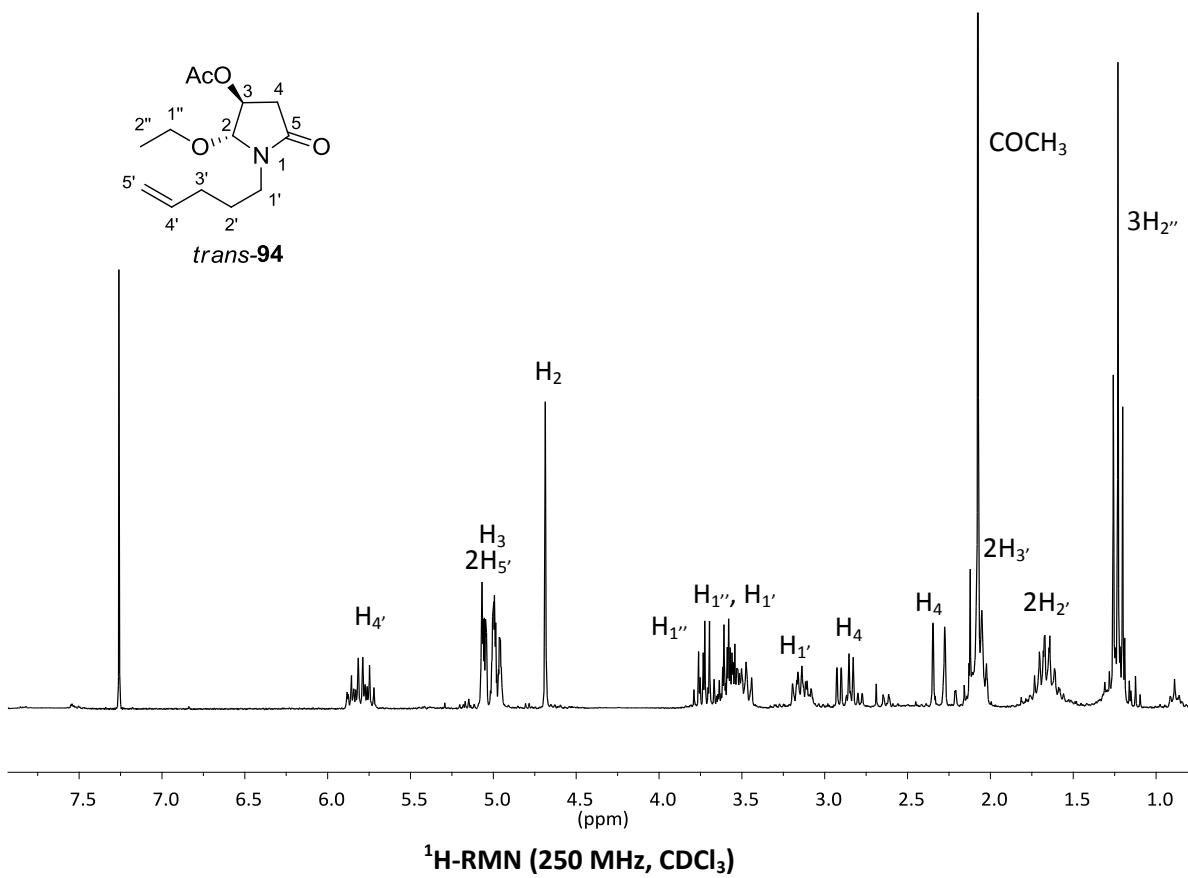
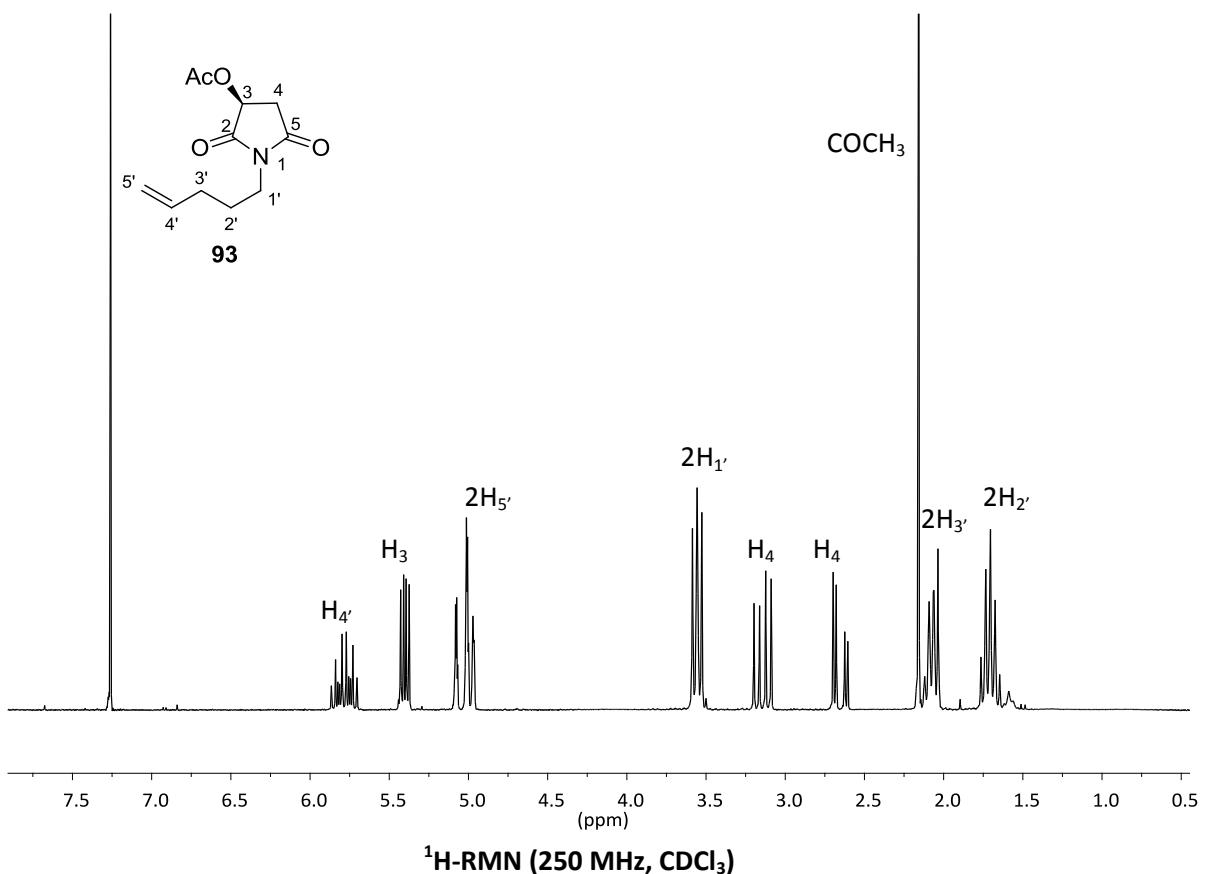


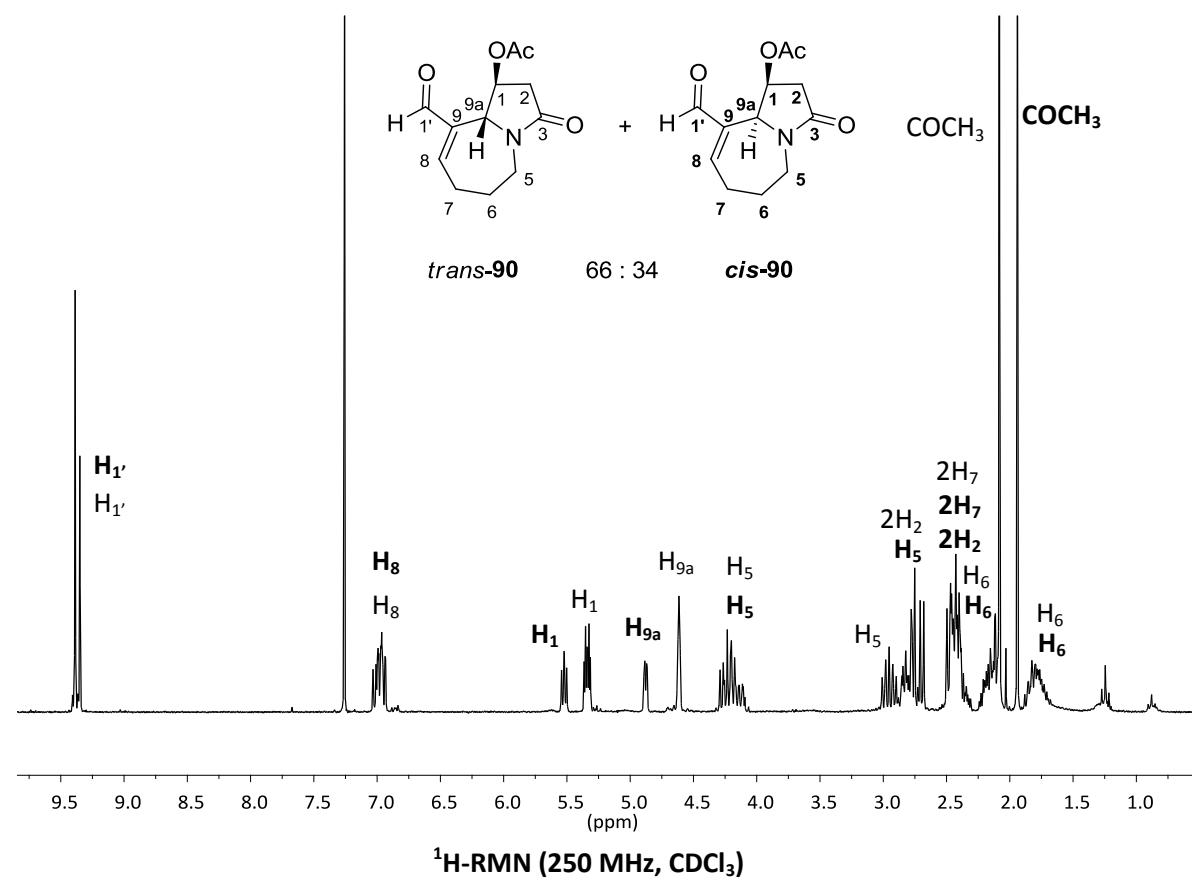
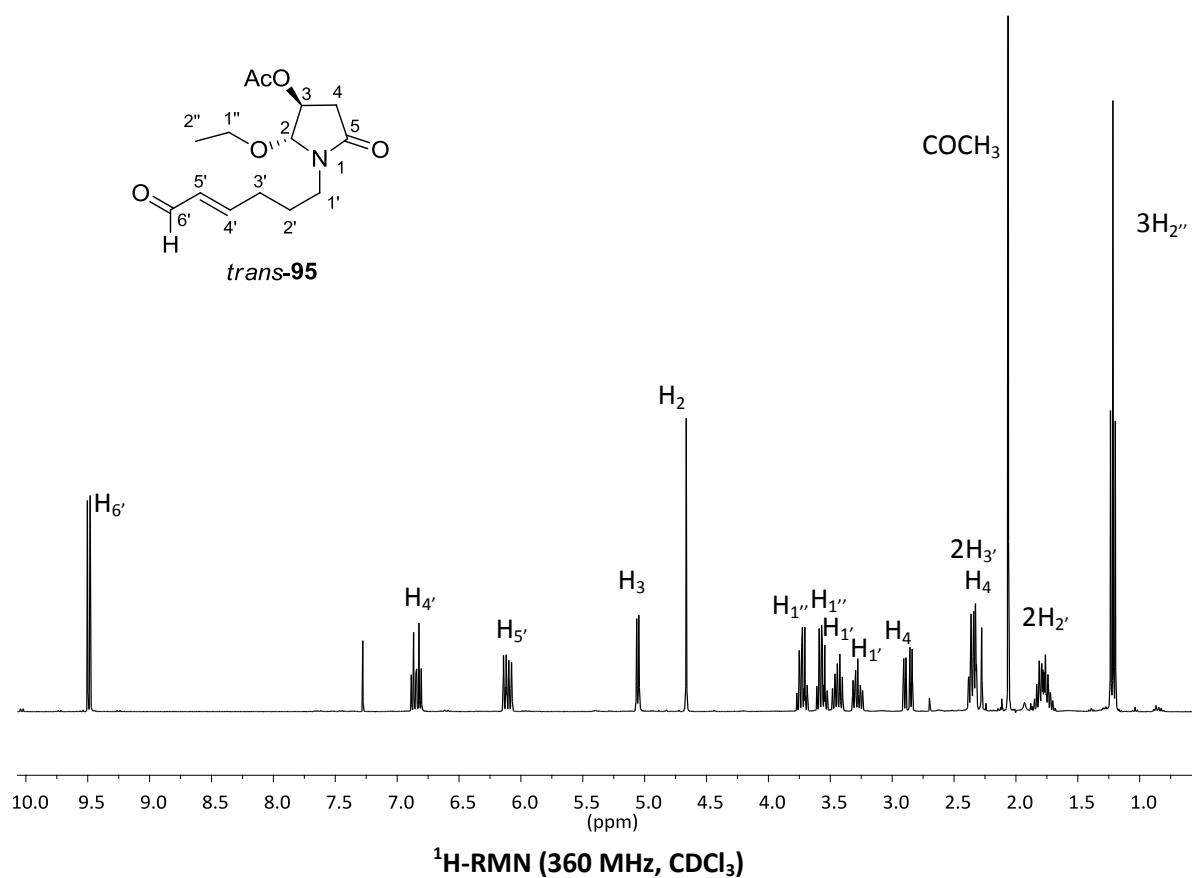
102

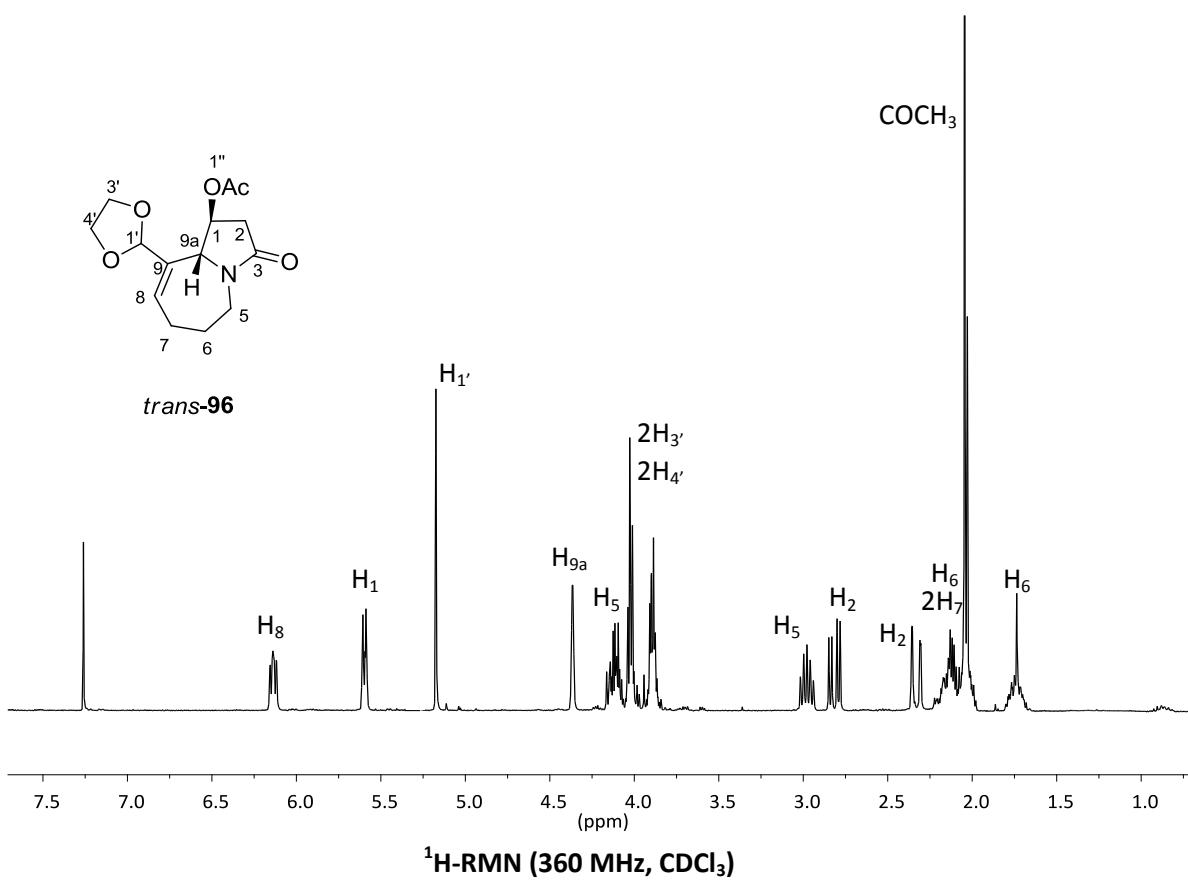
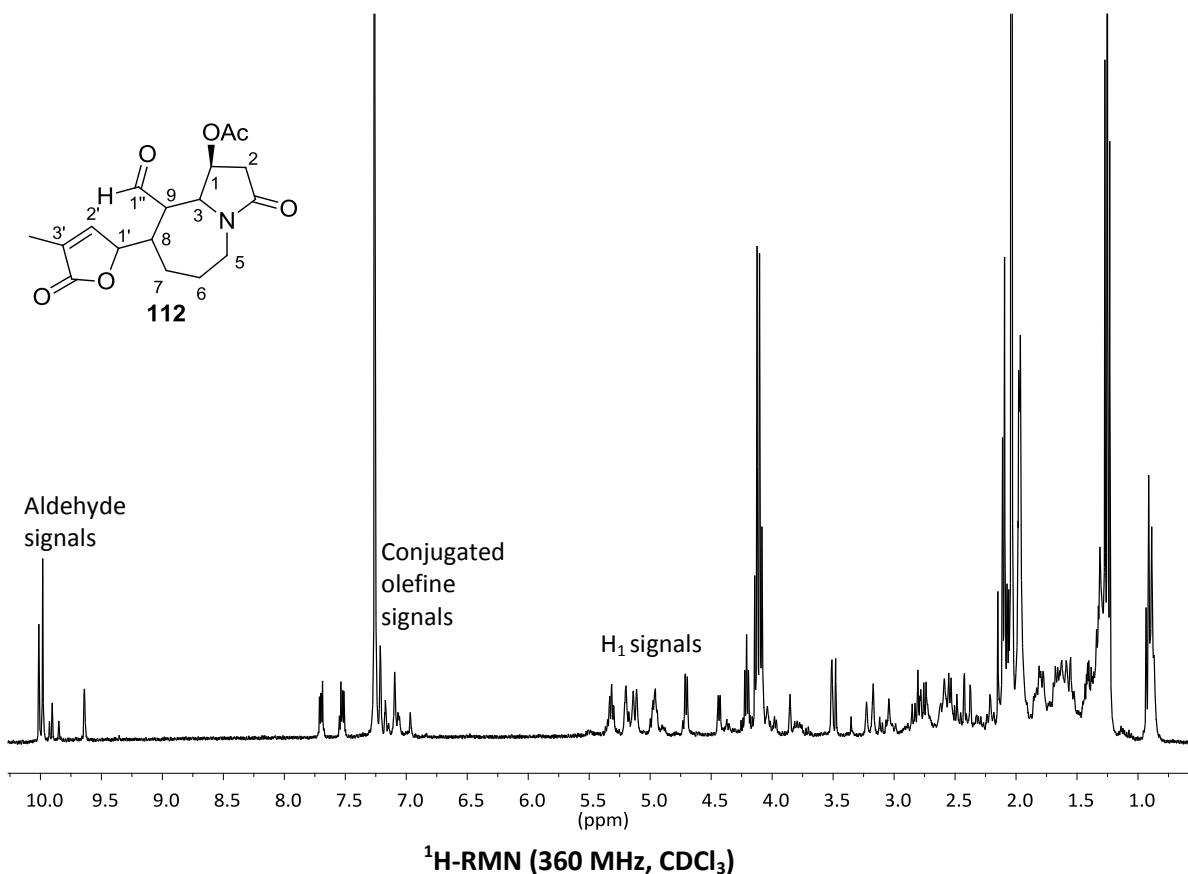


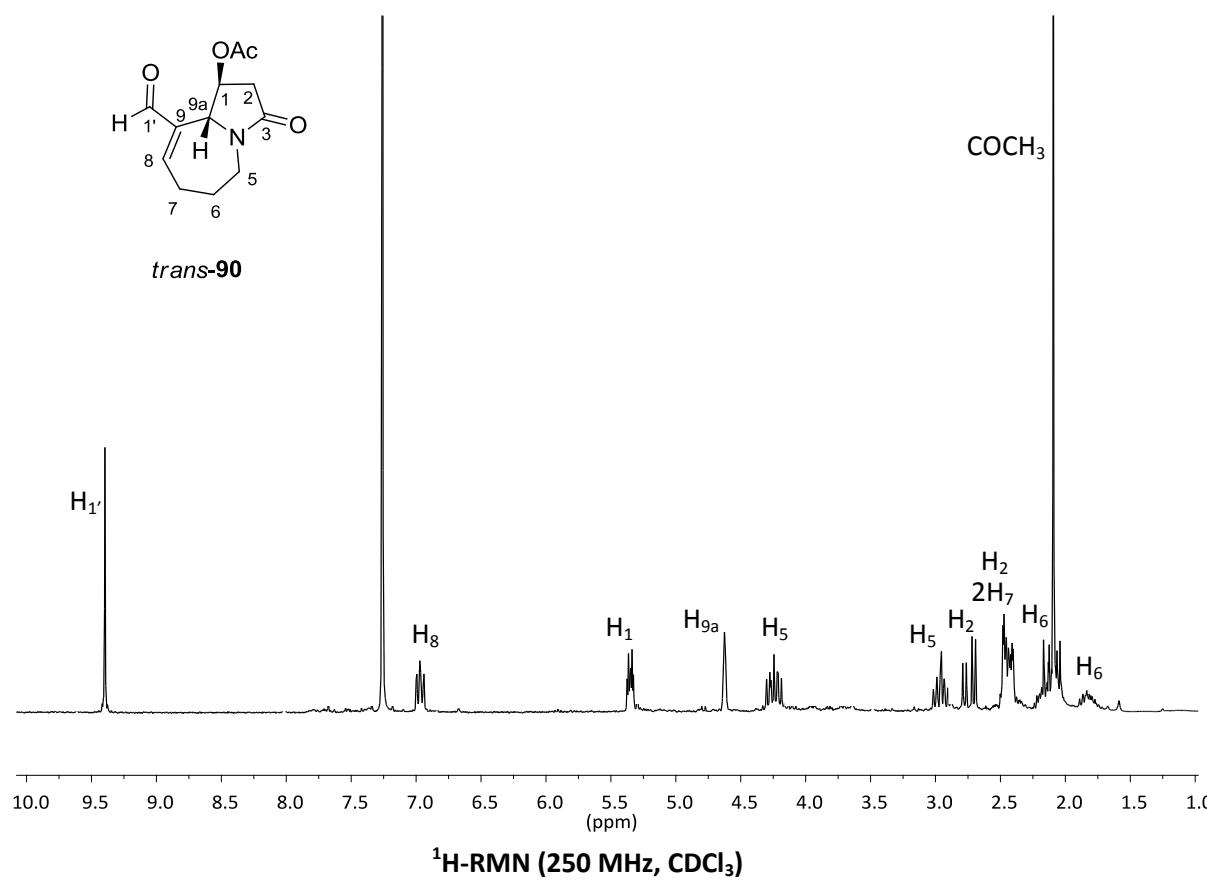
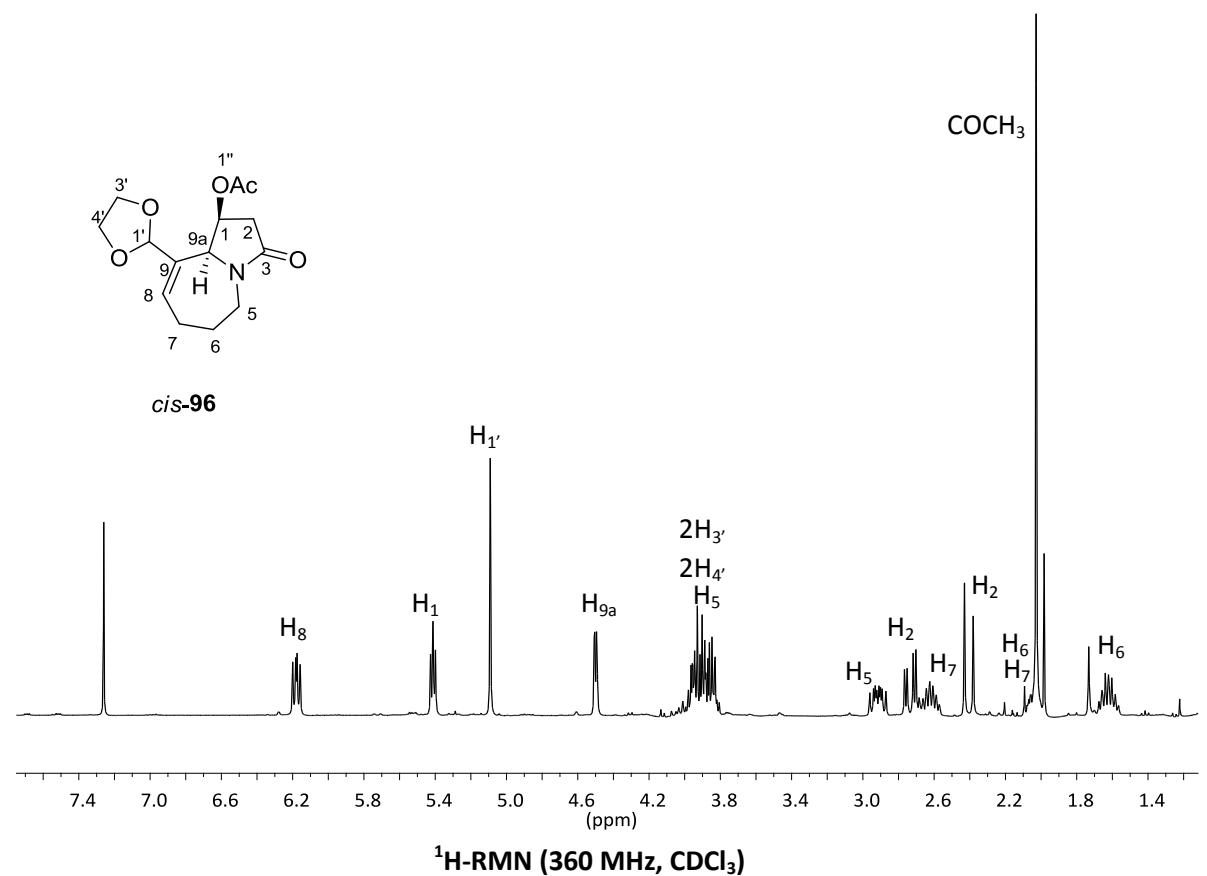
103

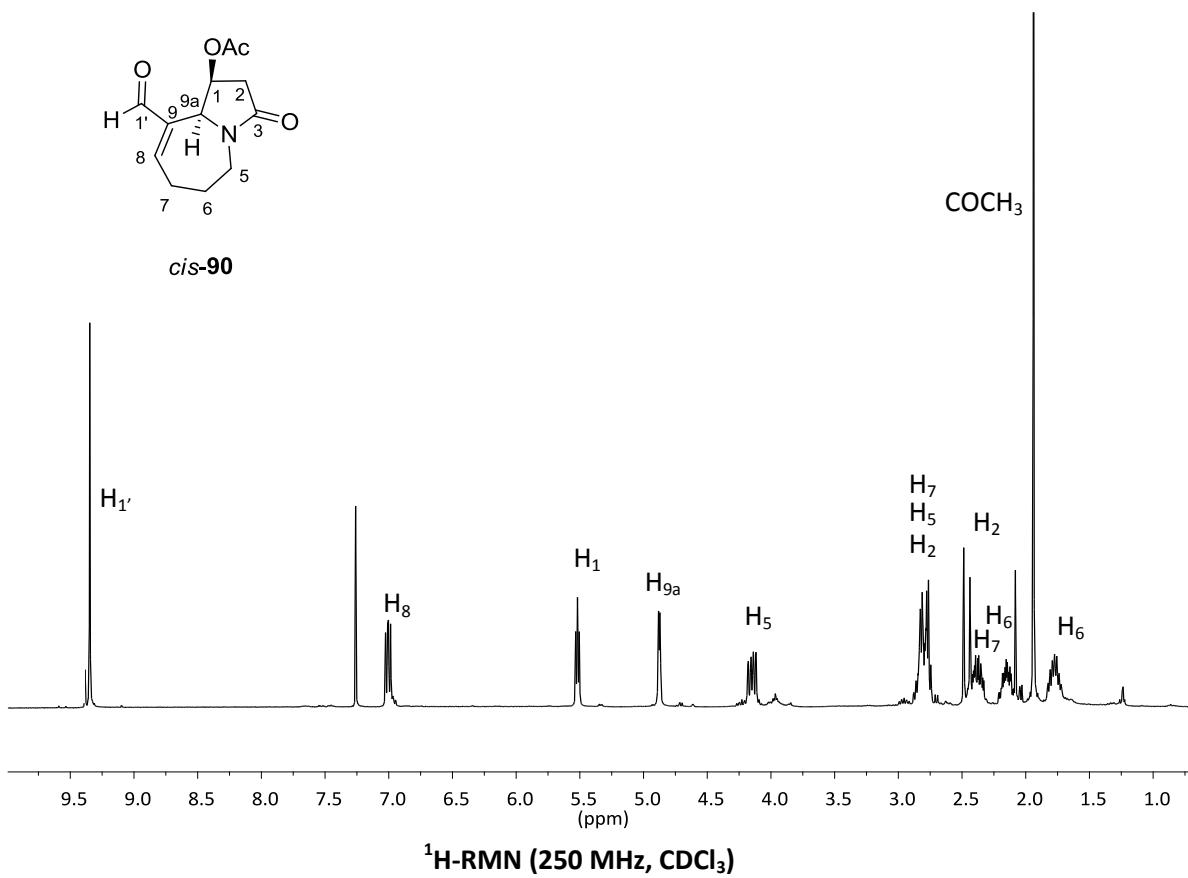
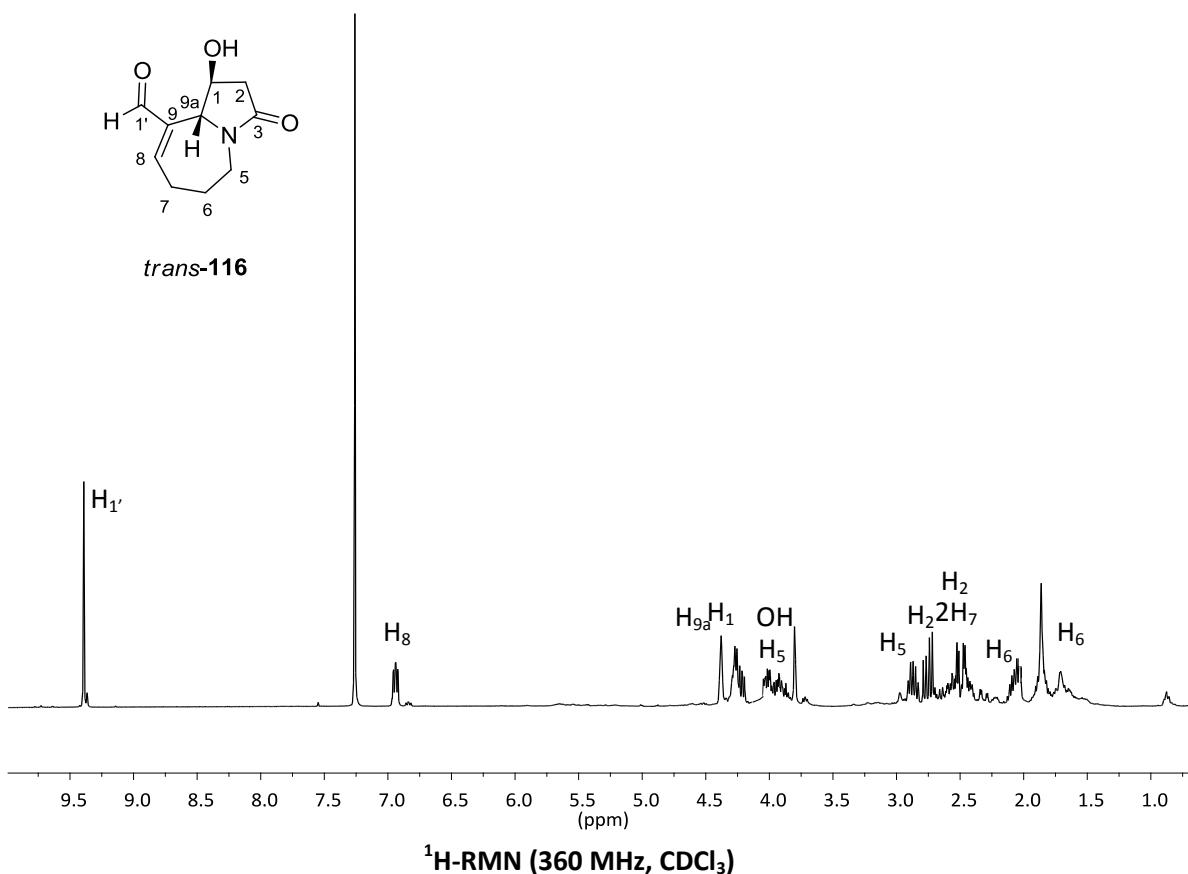


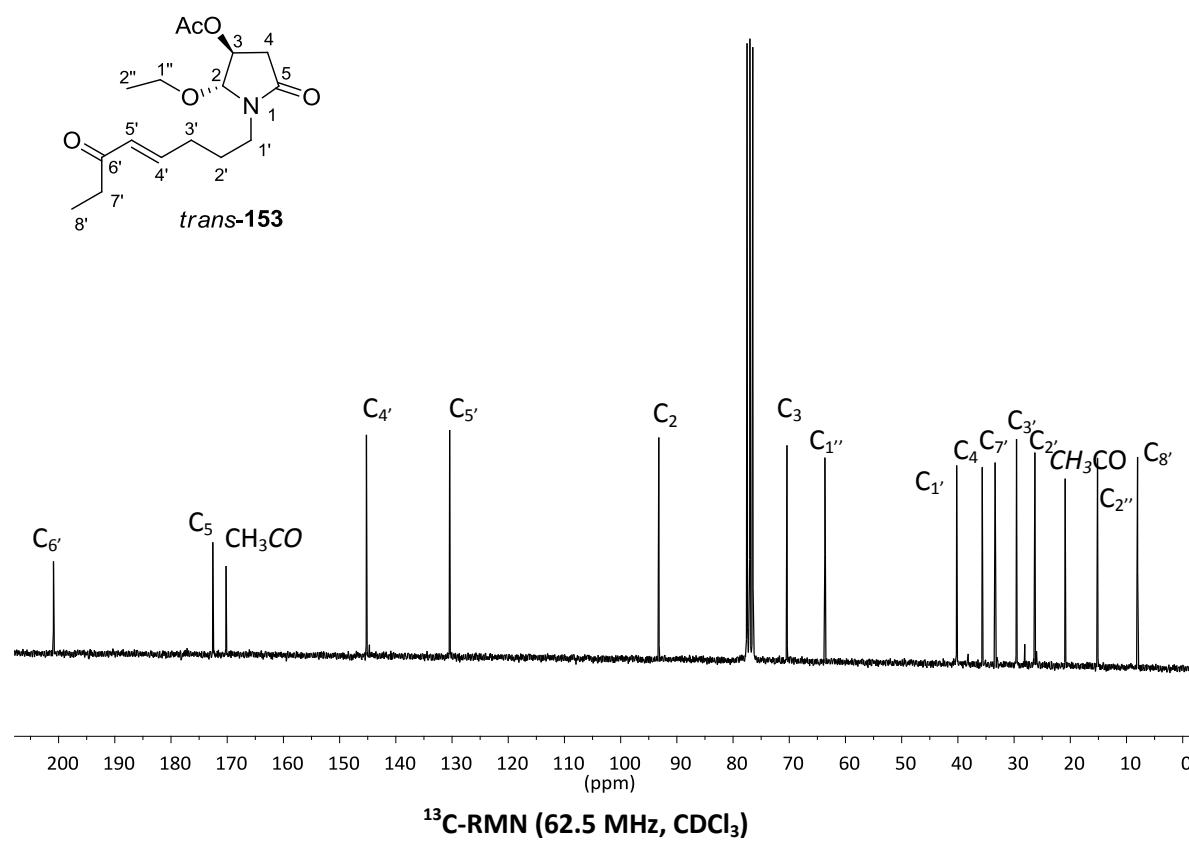
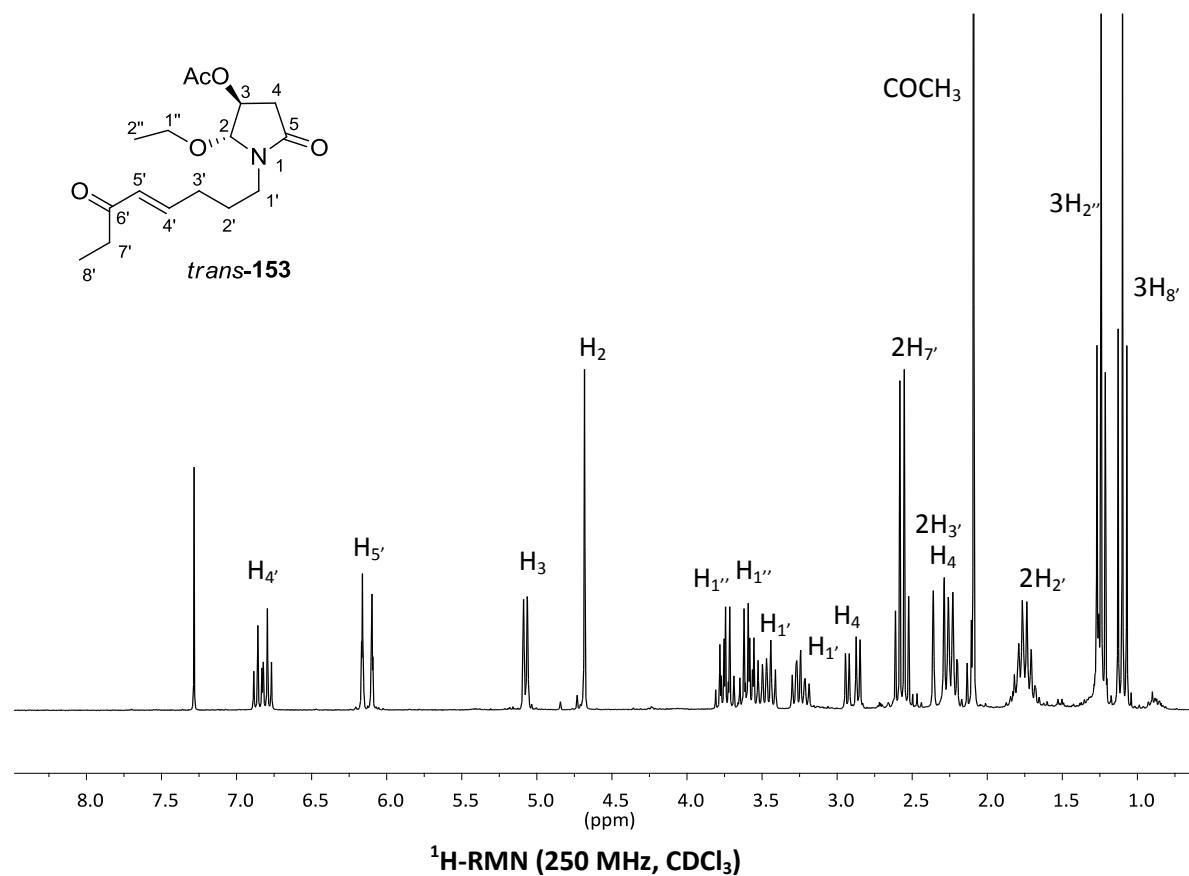


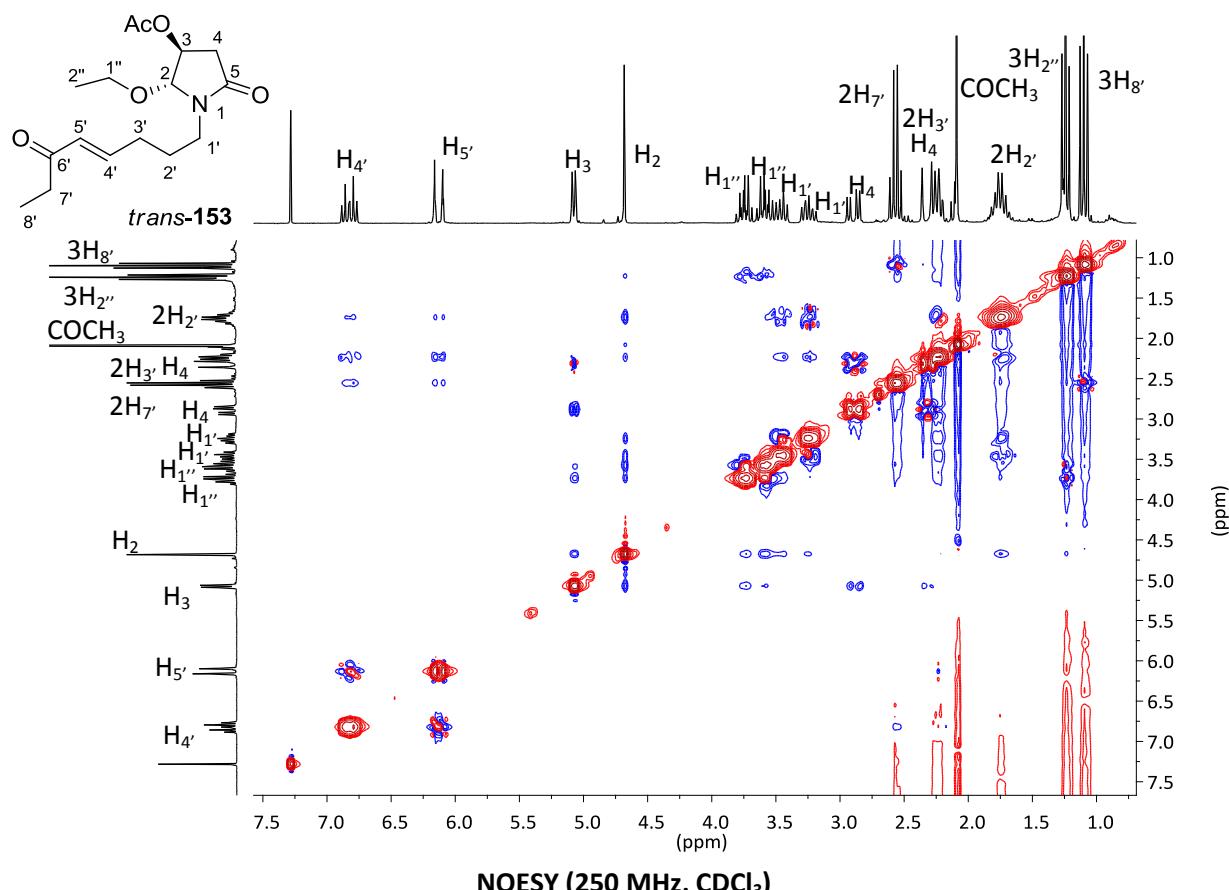
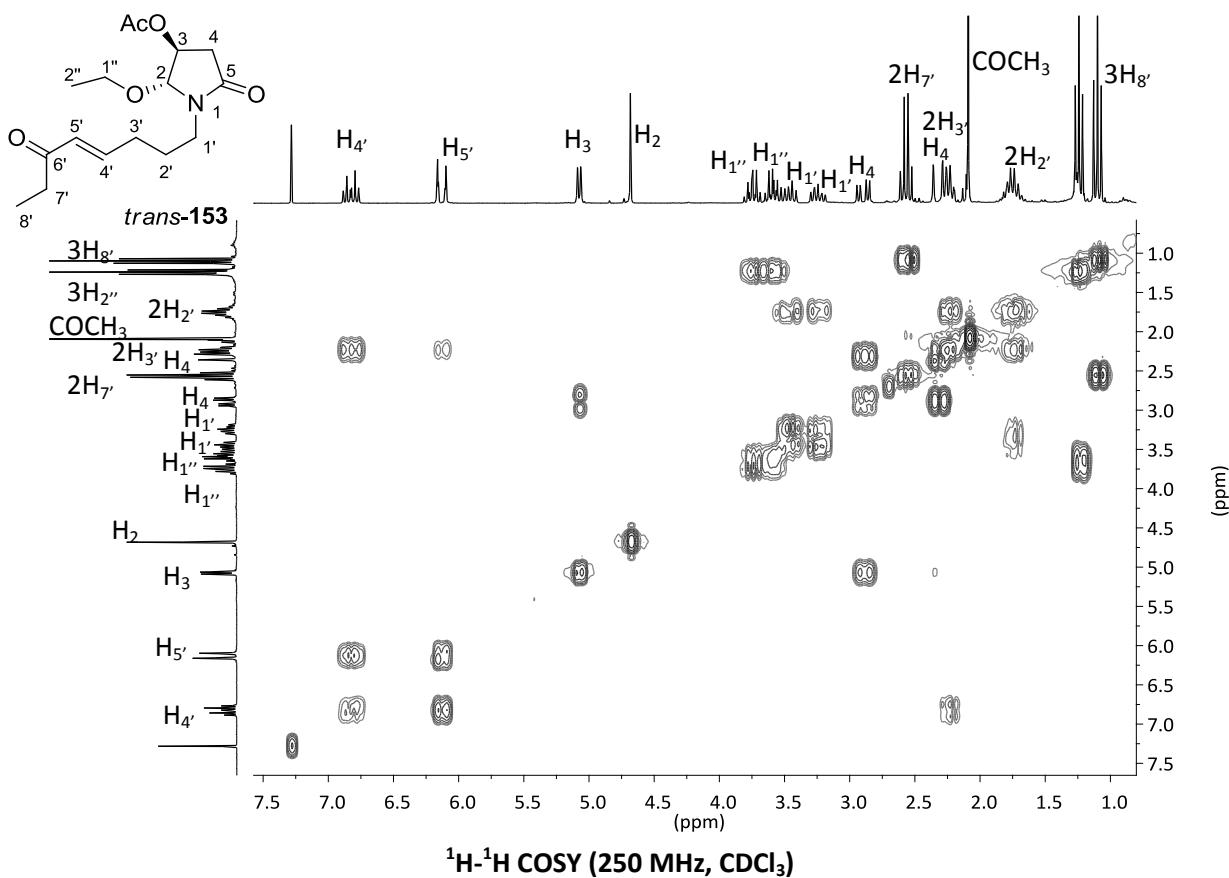




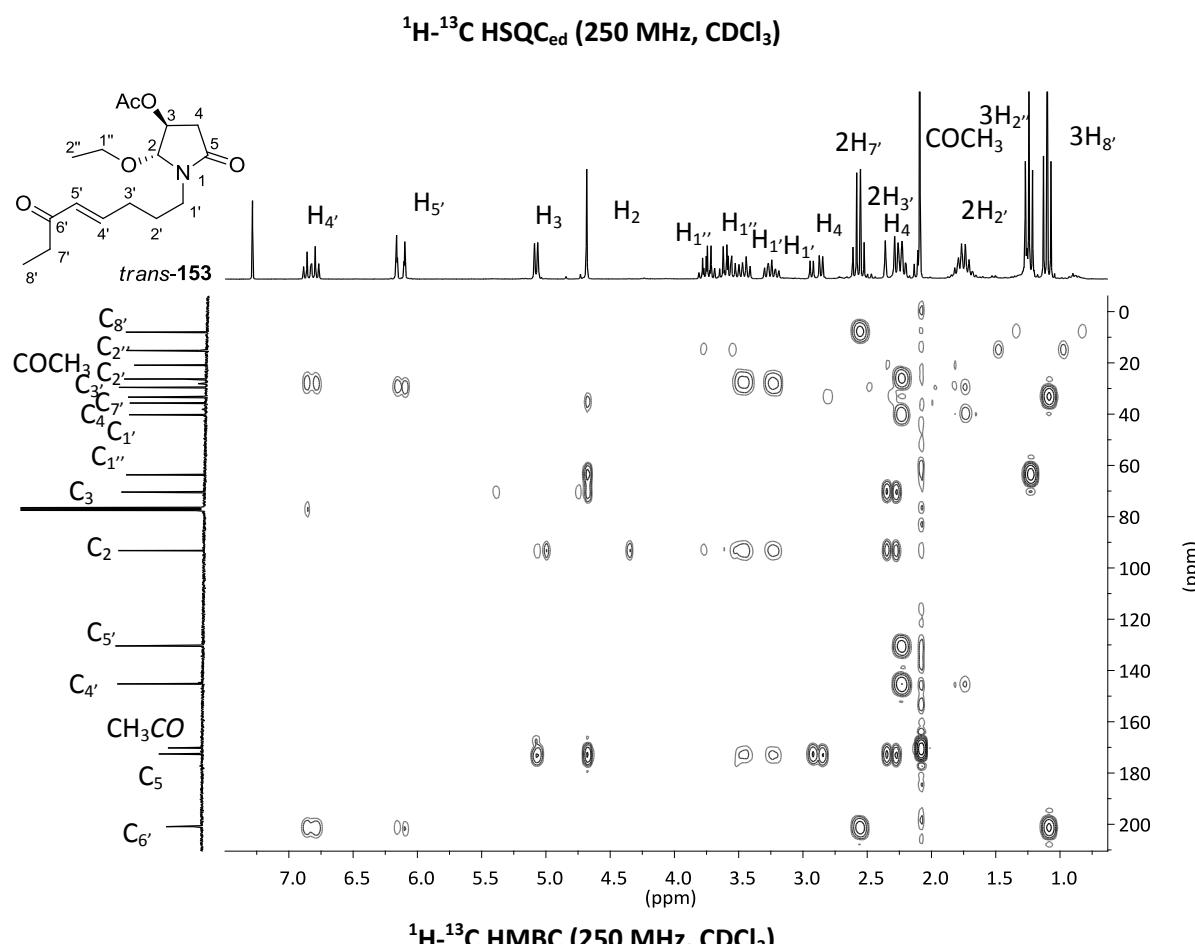
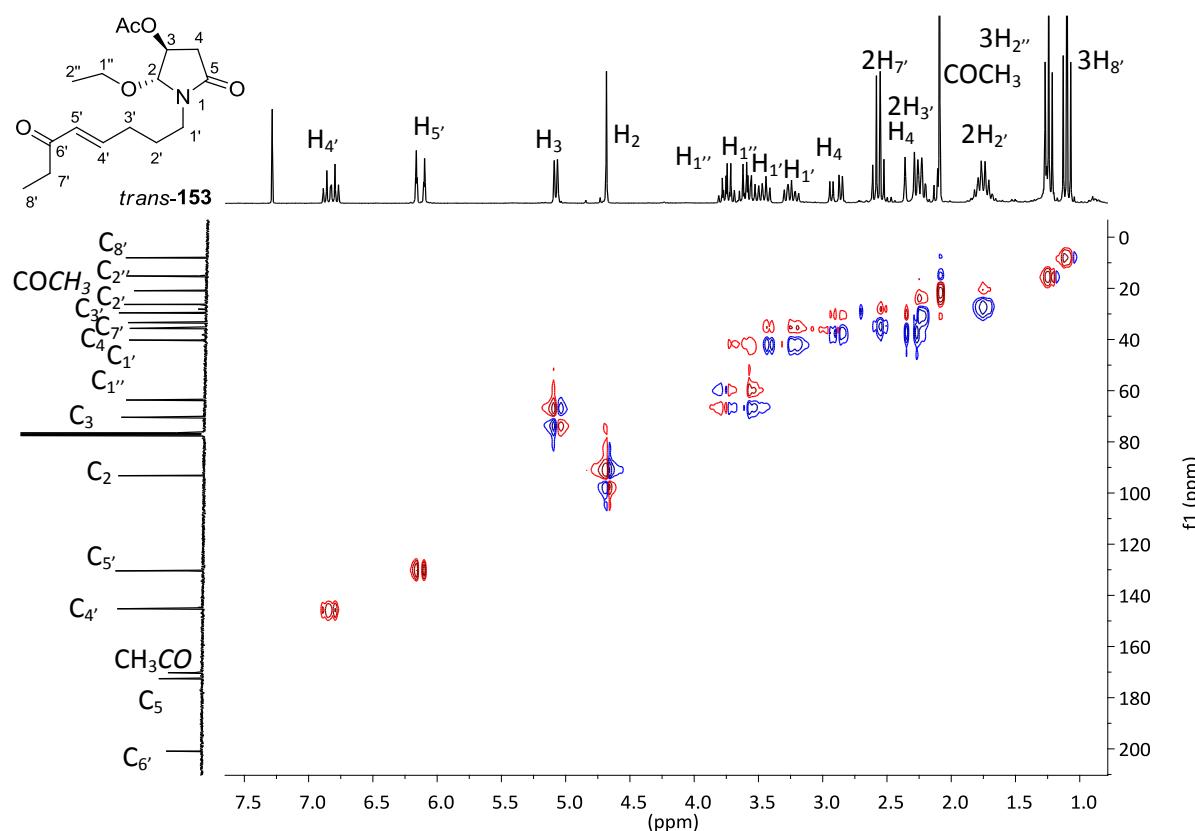


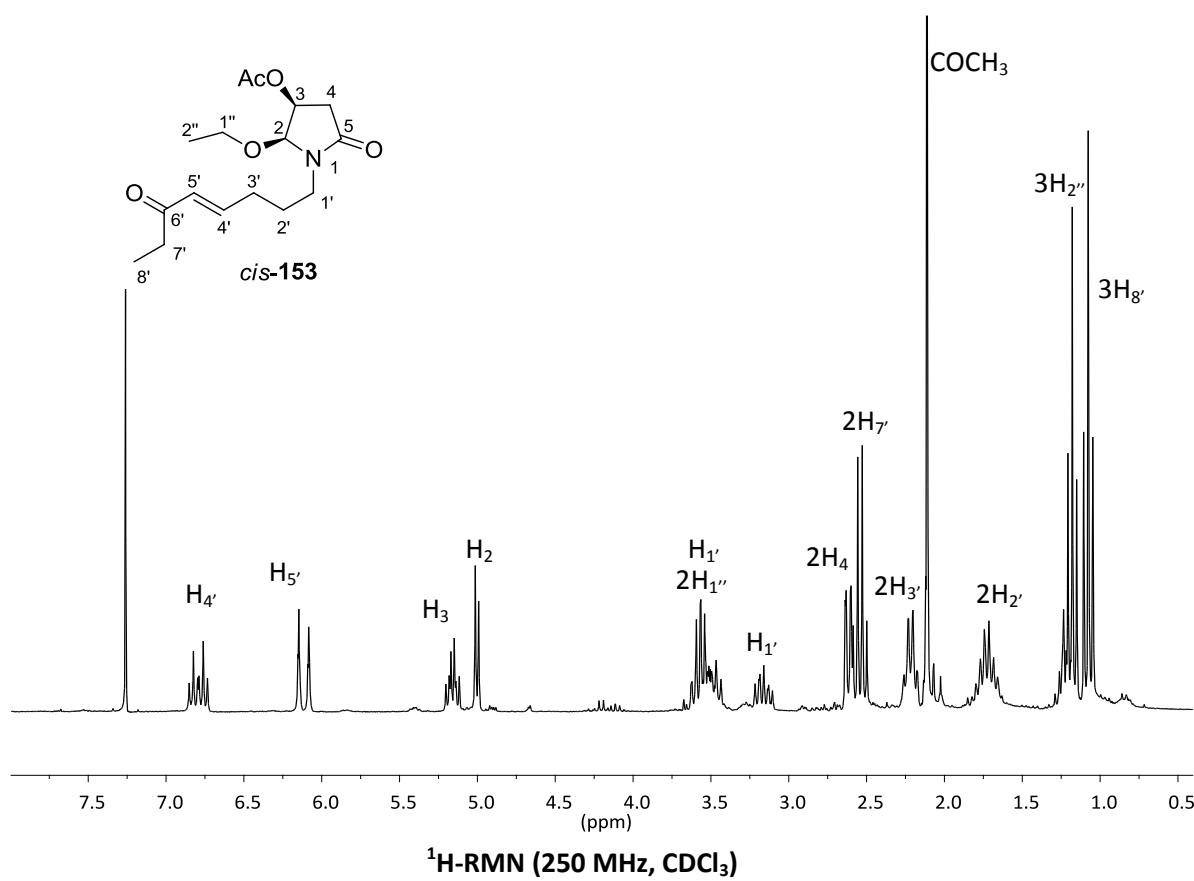
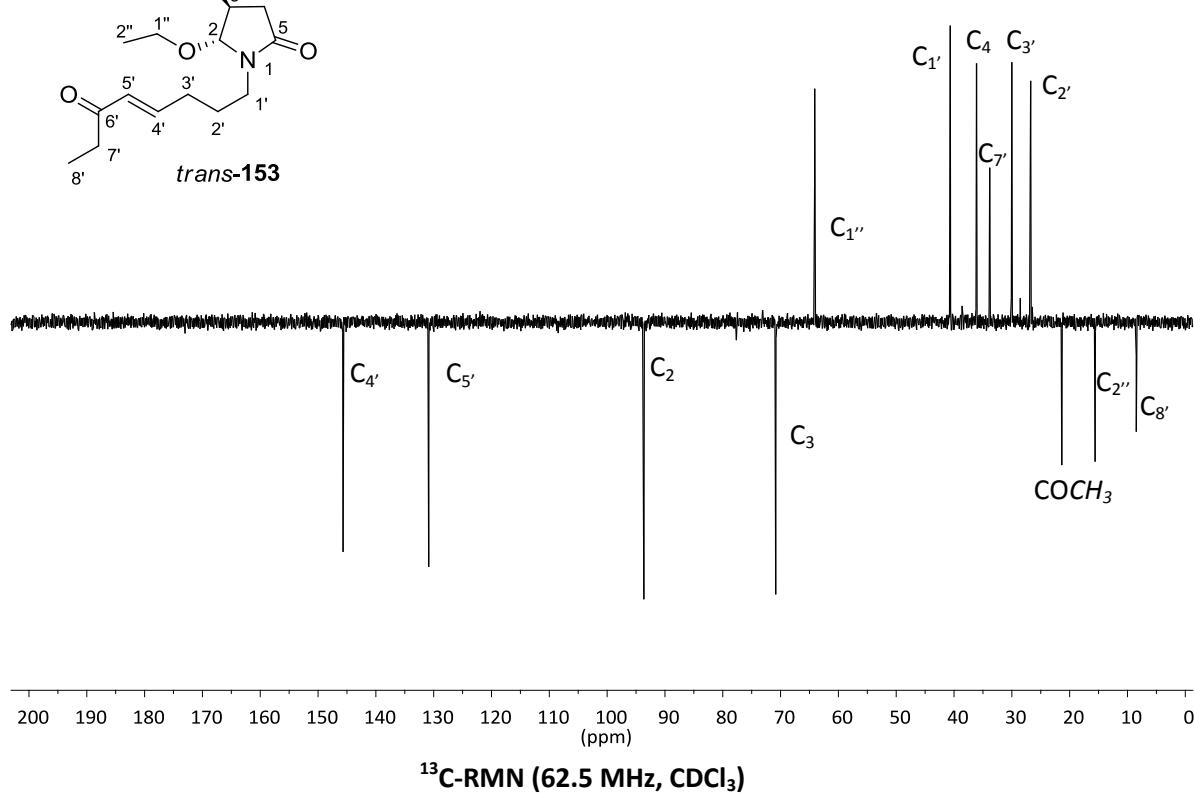
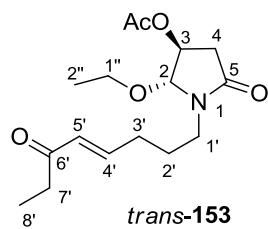


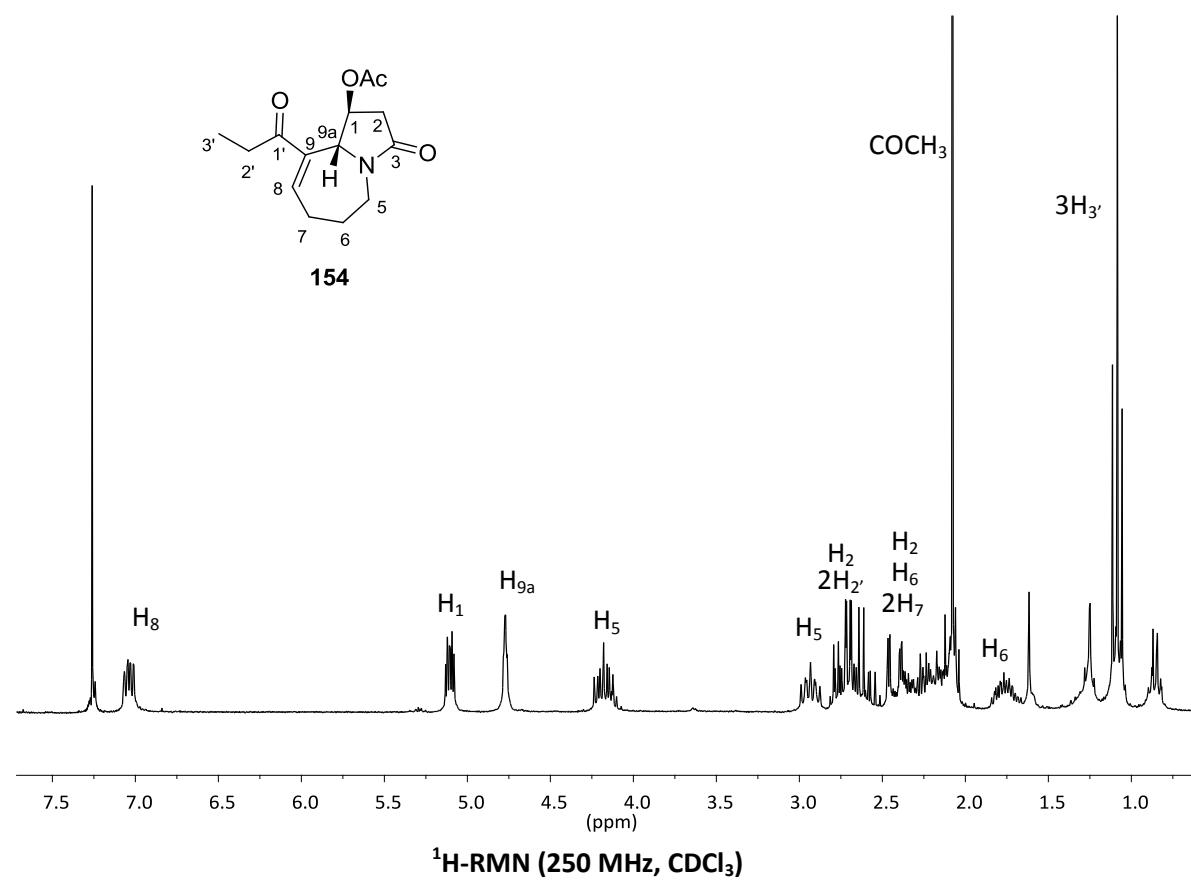
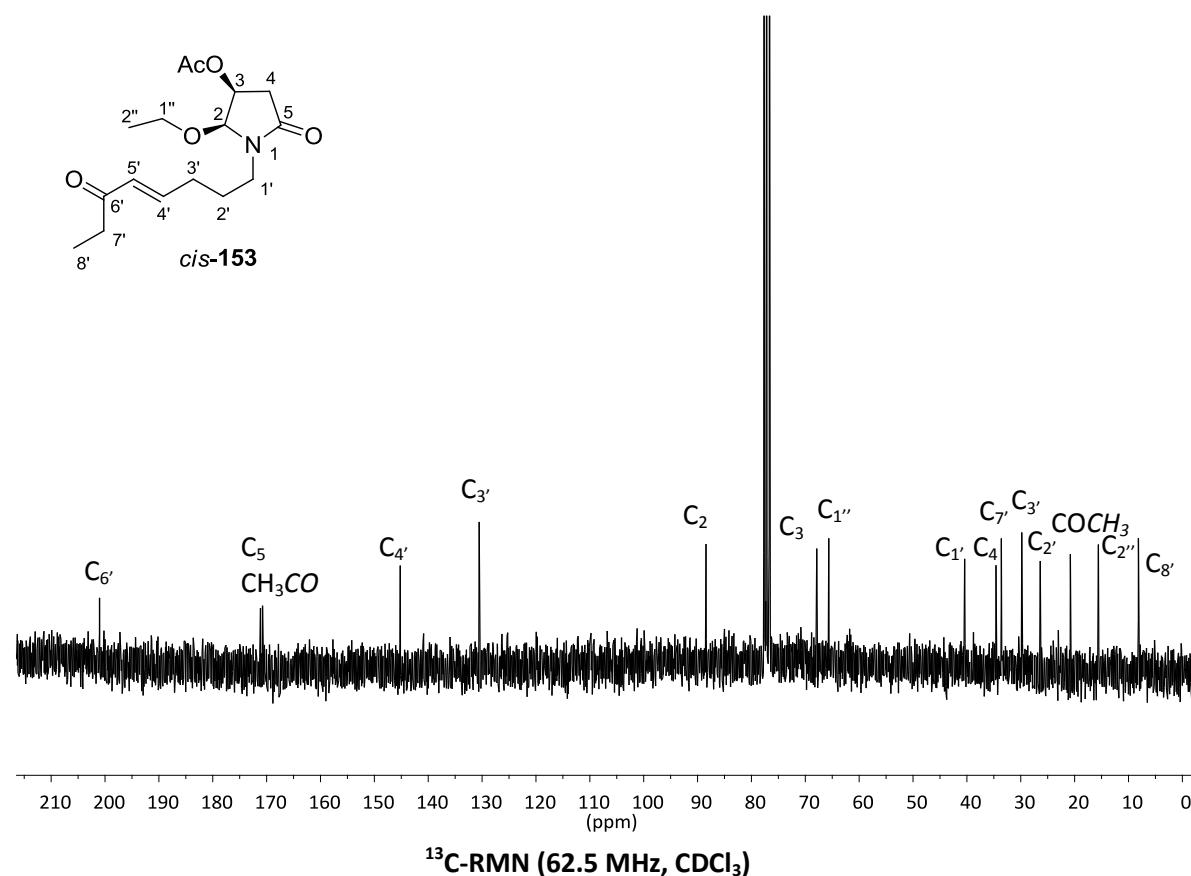


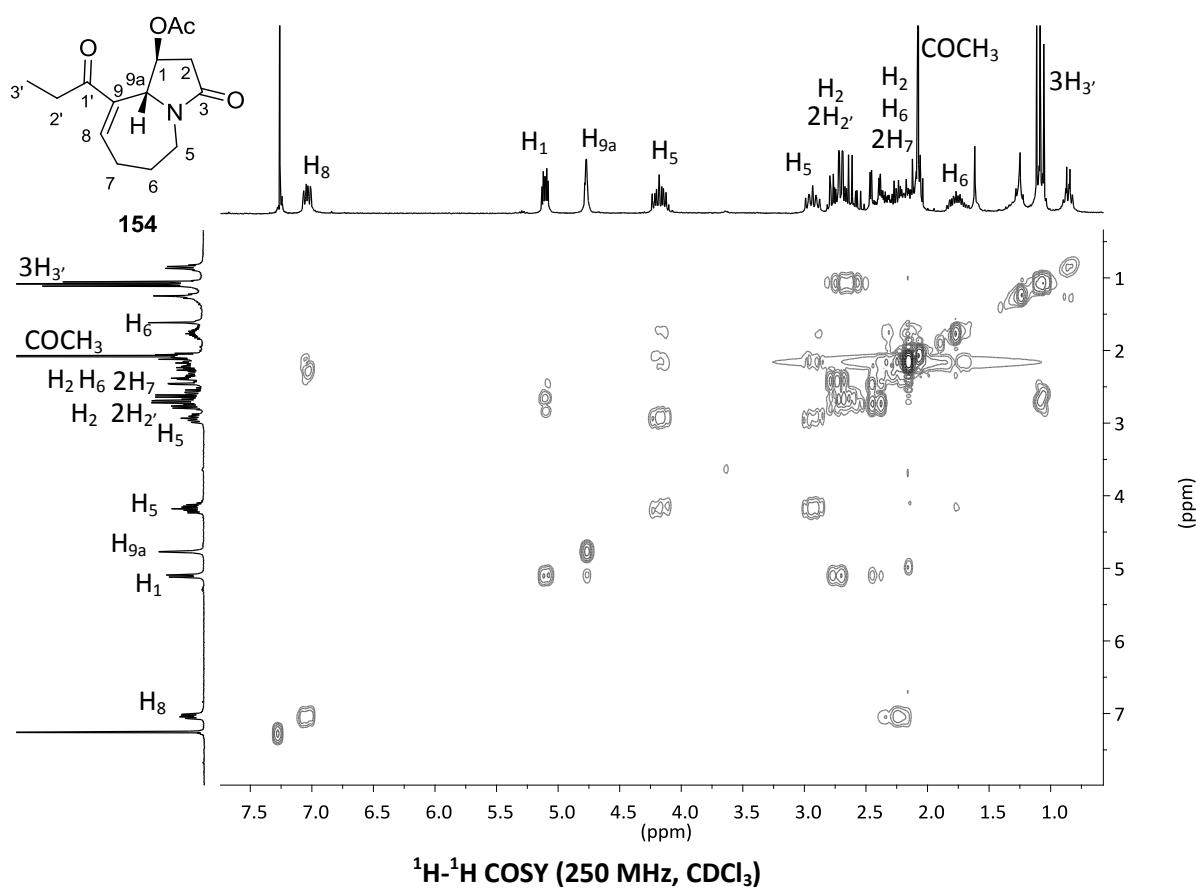
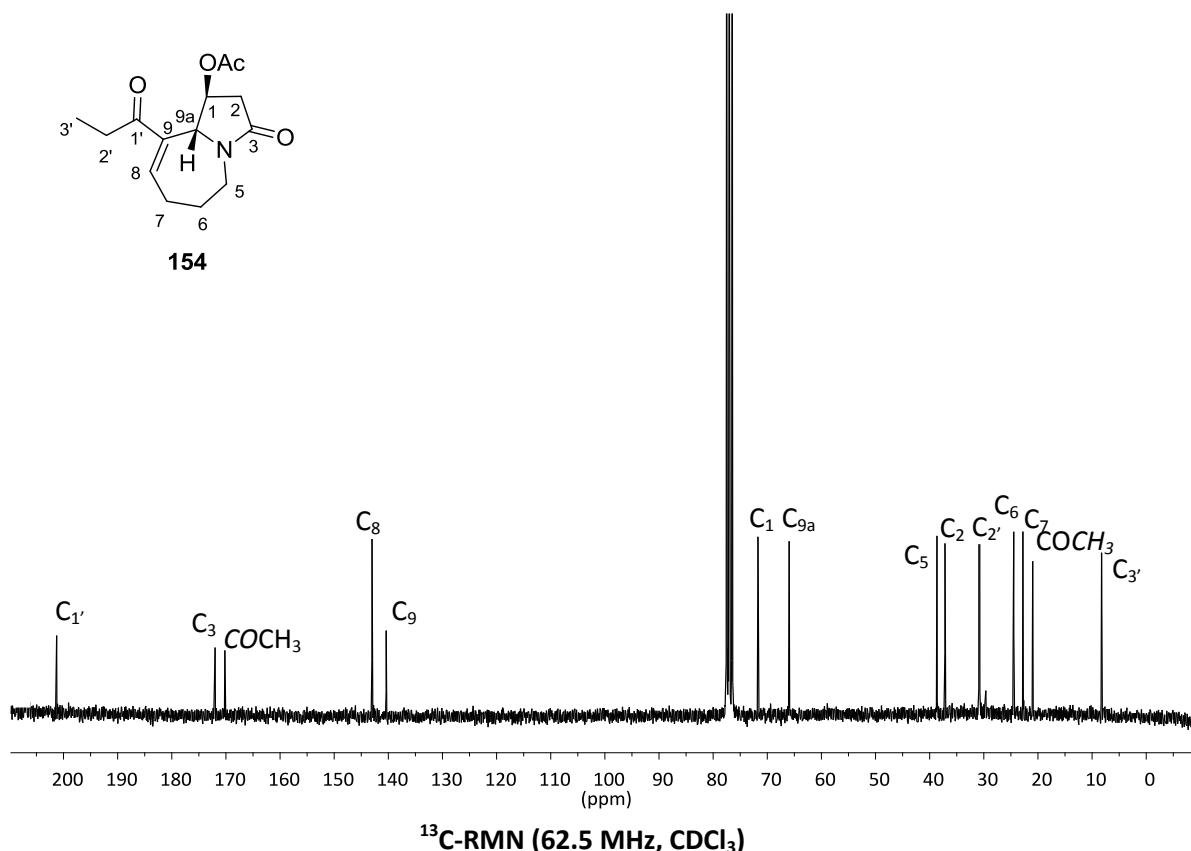


6. RECULL D'ESPECTRES

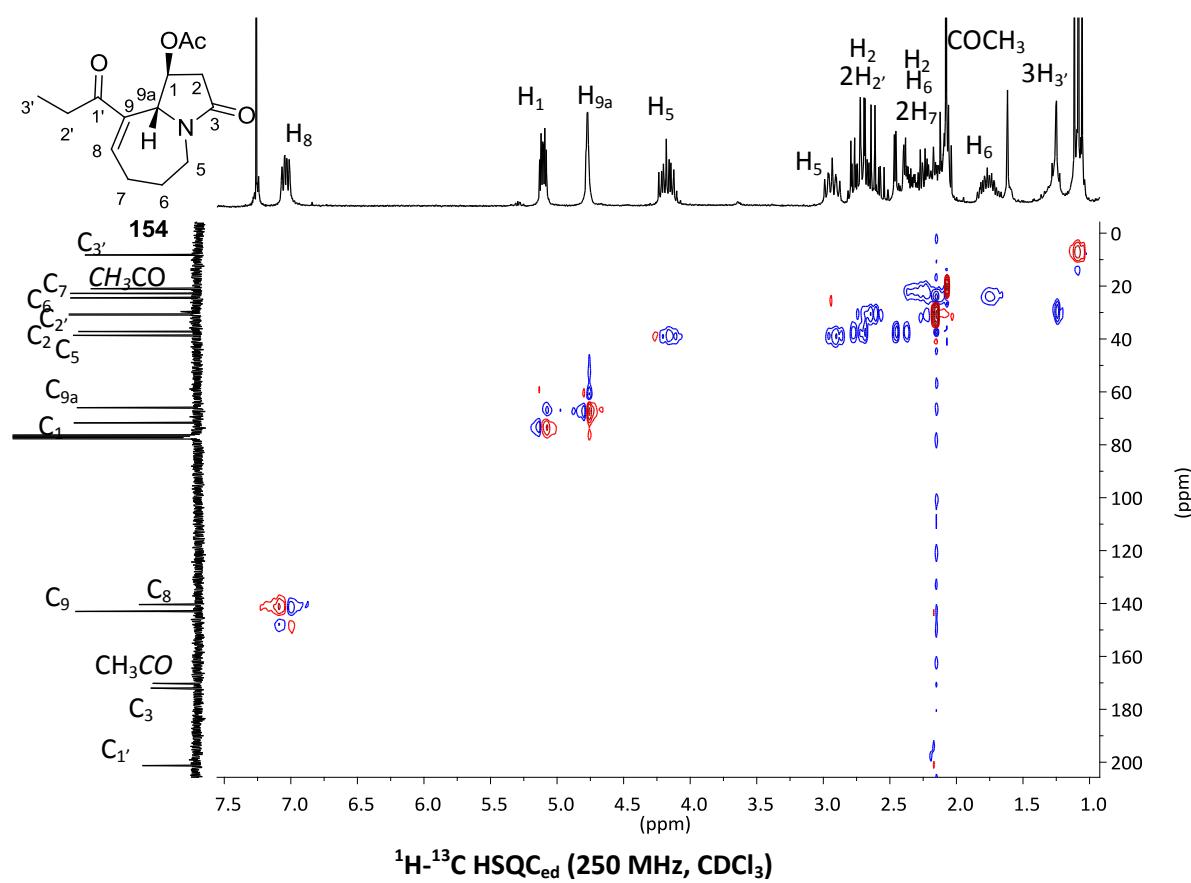
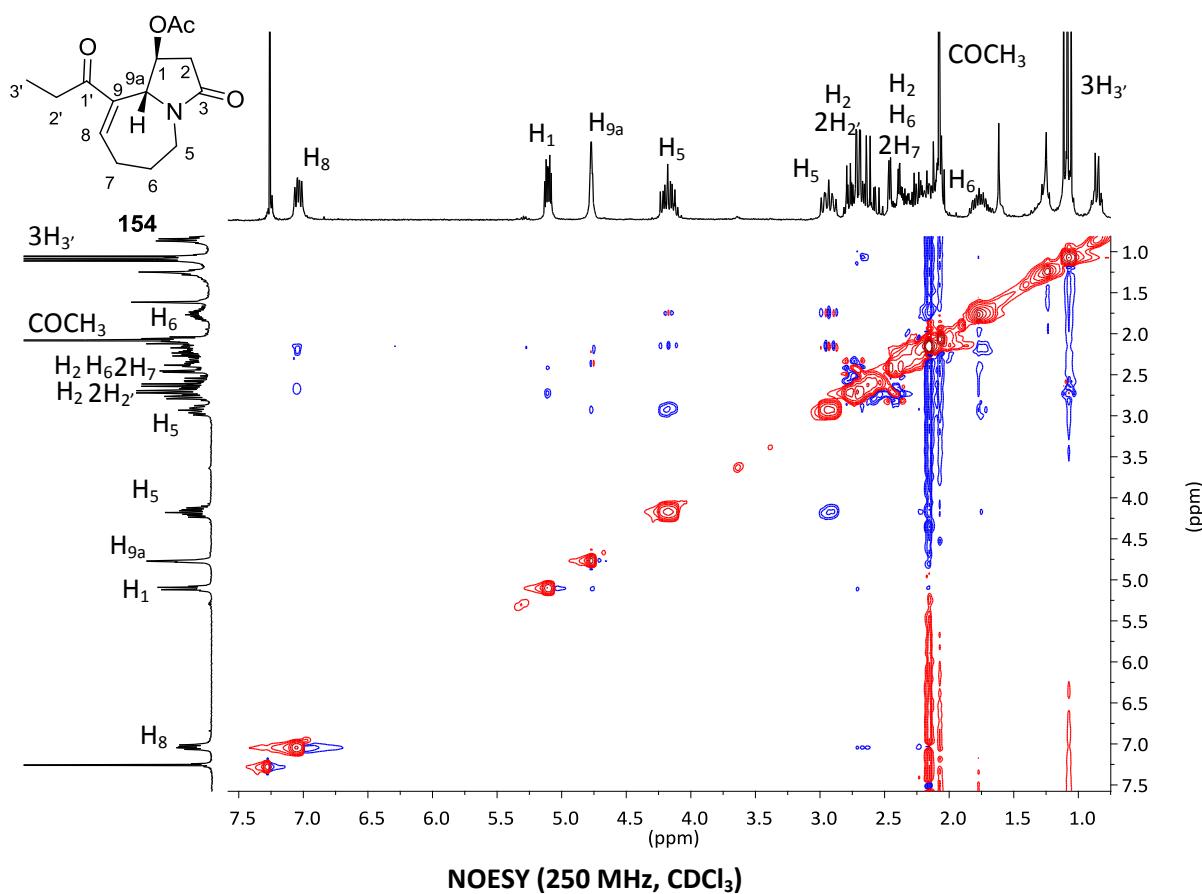


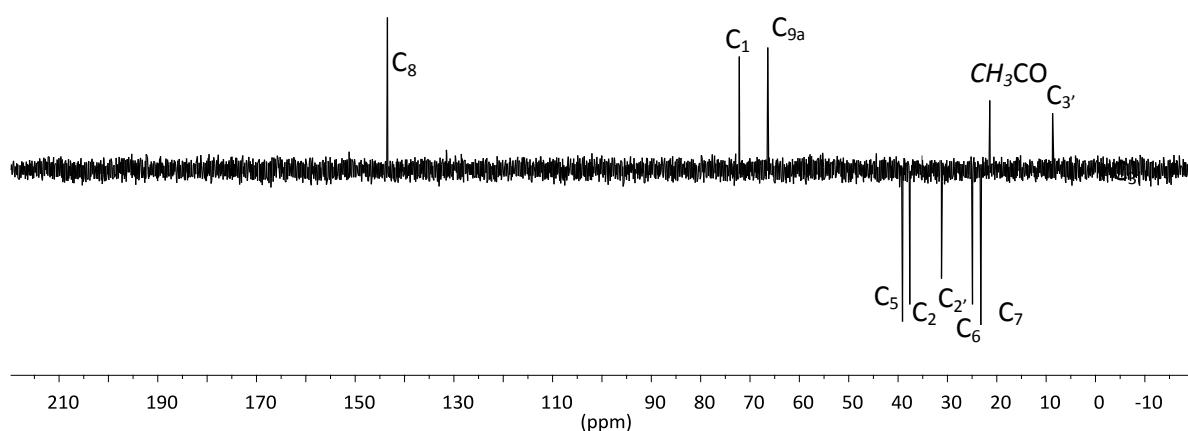
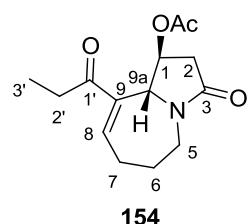
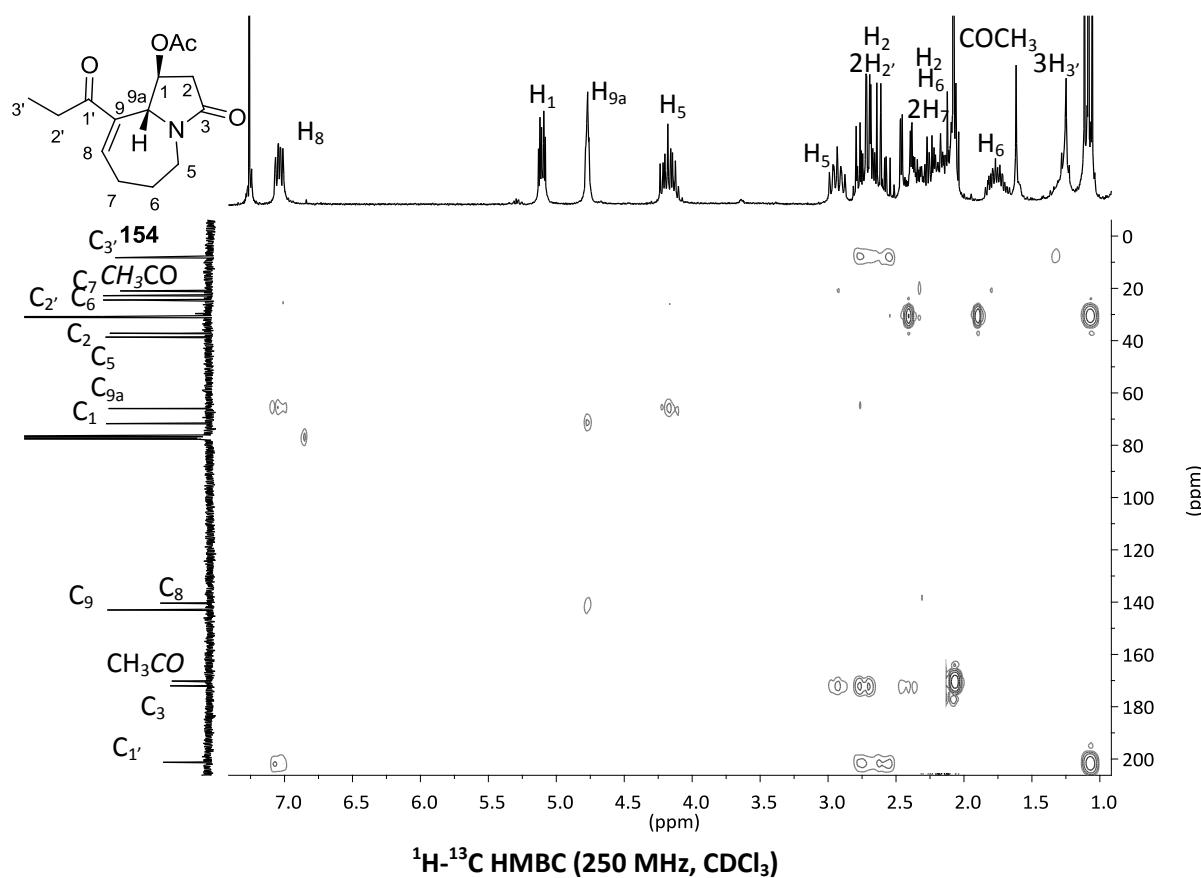


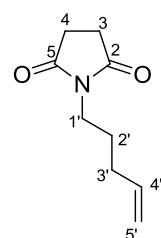




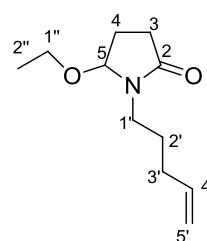
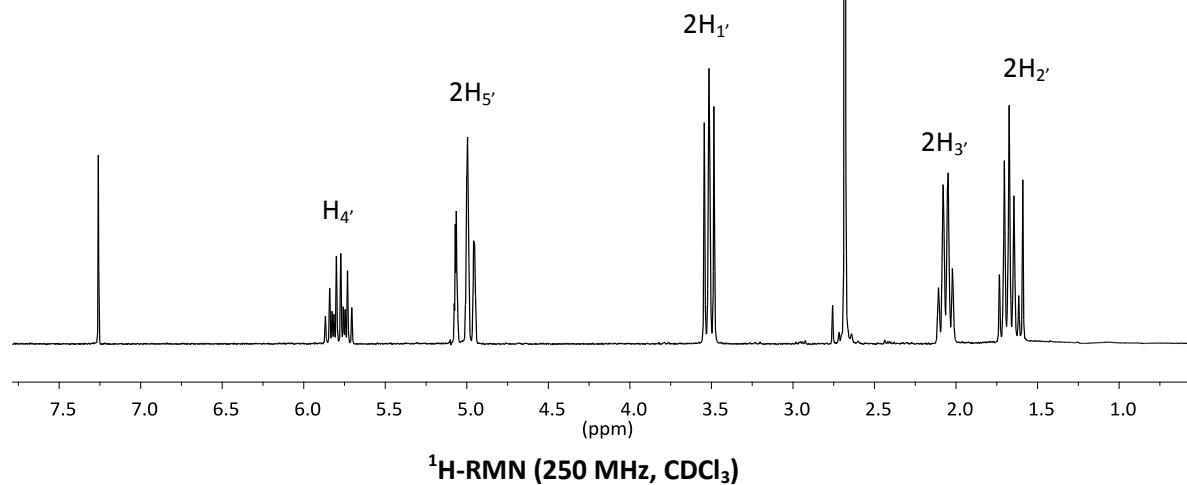
6. RECULL D'ESPECTRES



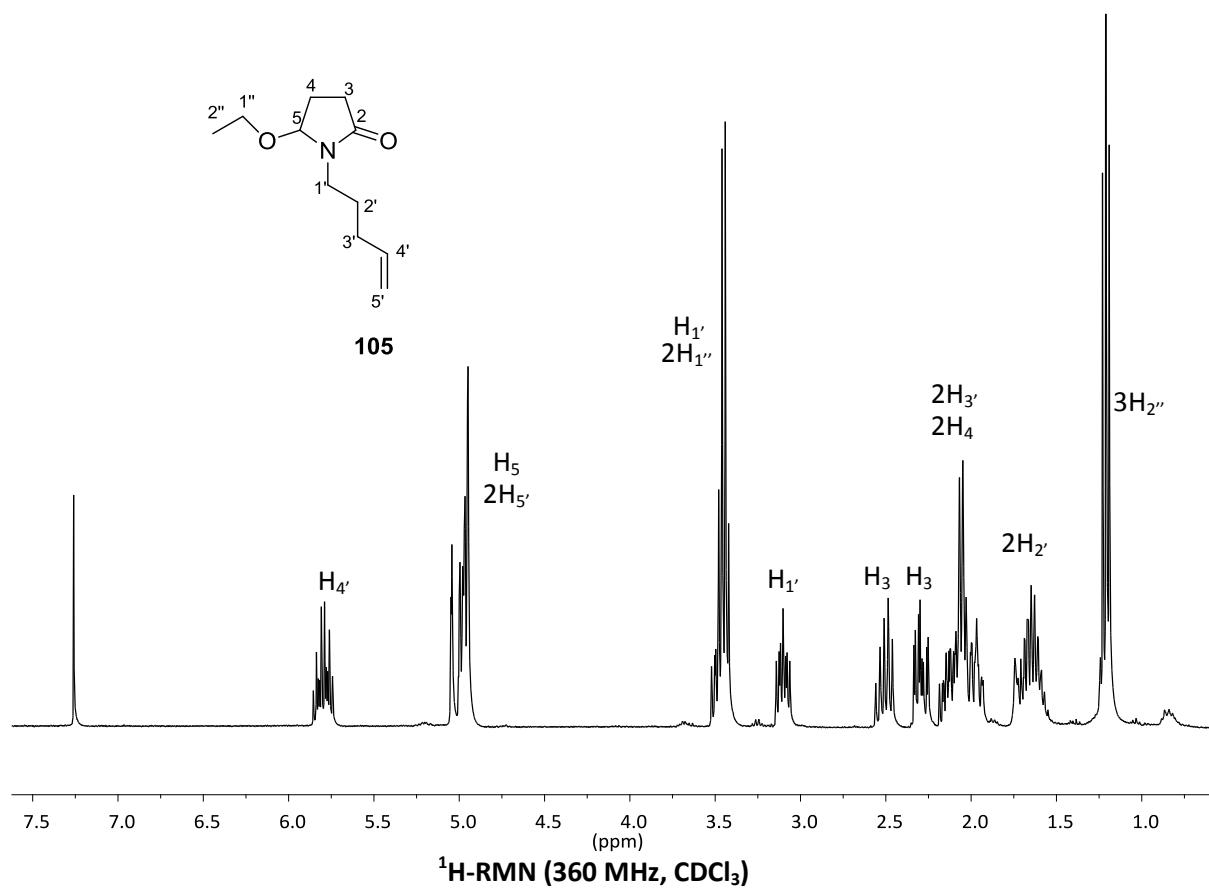
DEPT 135 (62.5 MHz, CDCl₃)

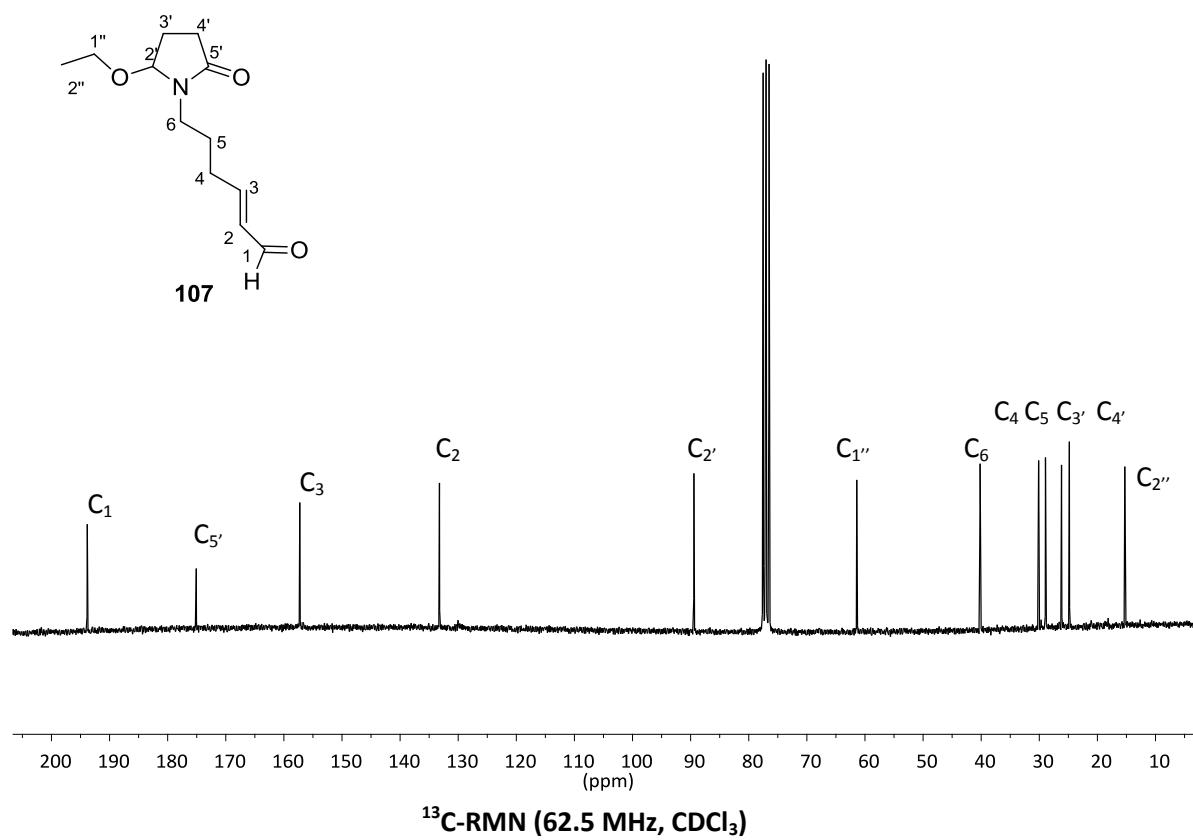
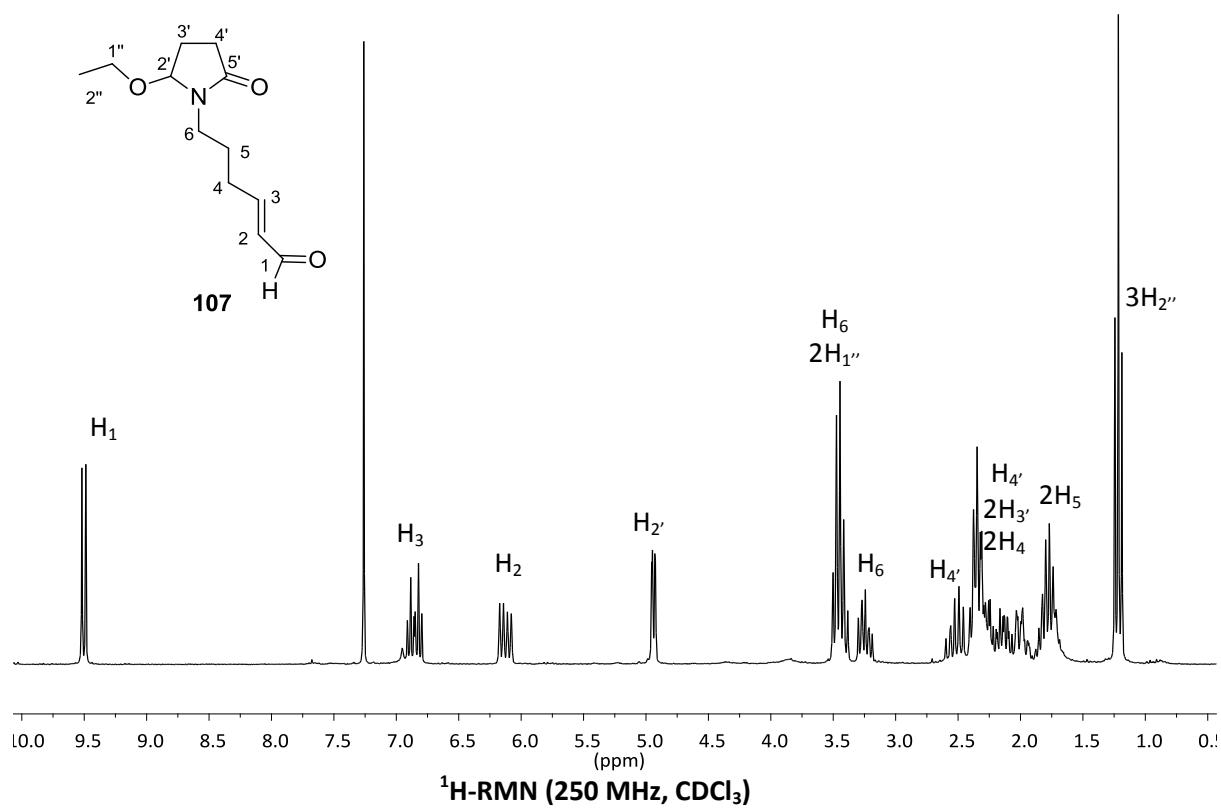


104

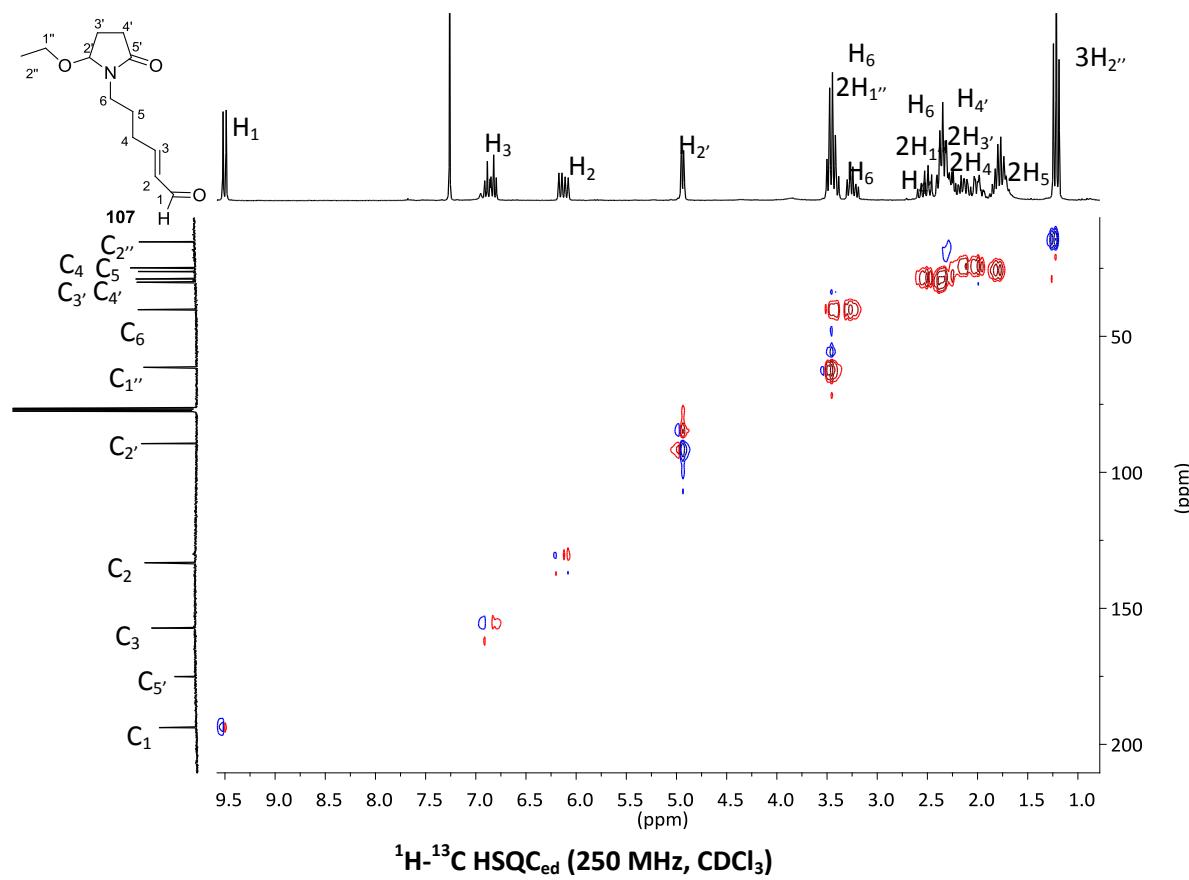
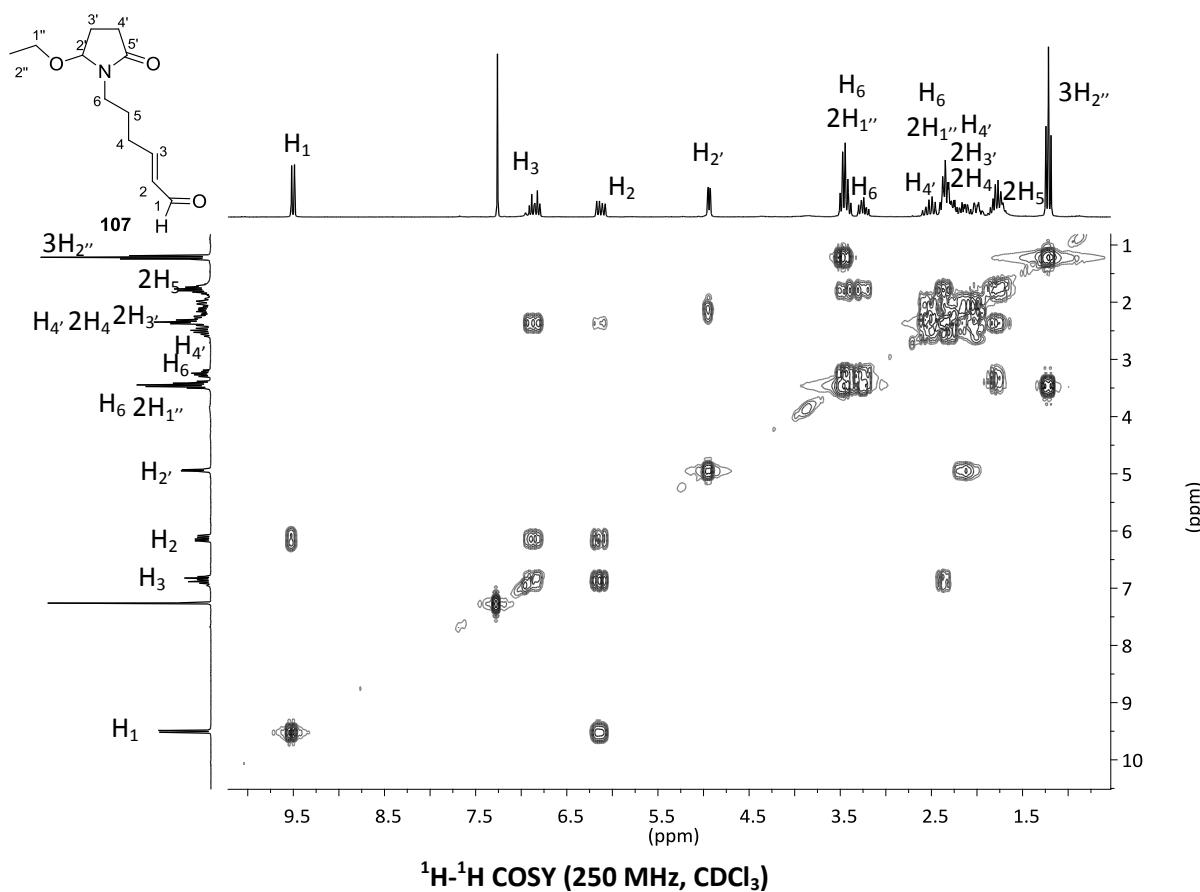


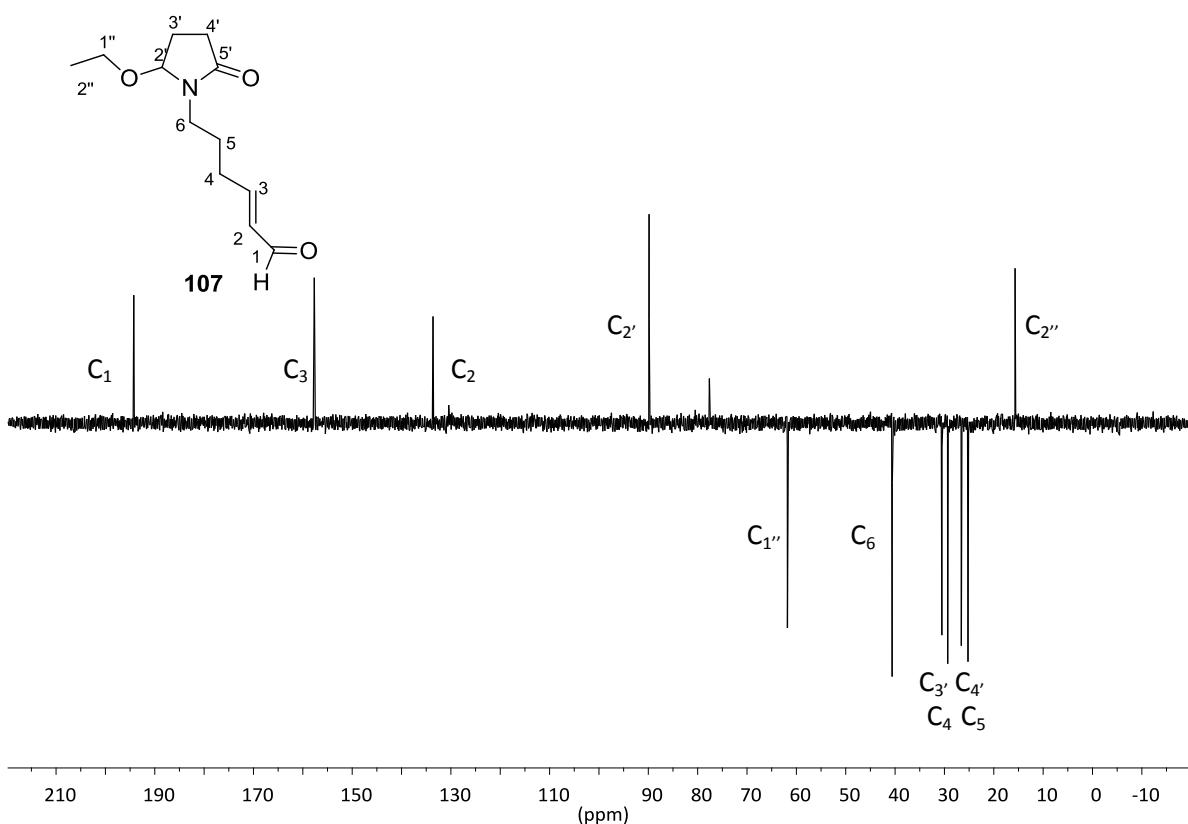
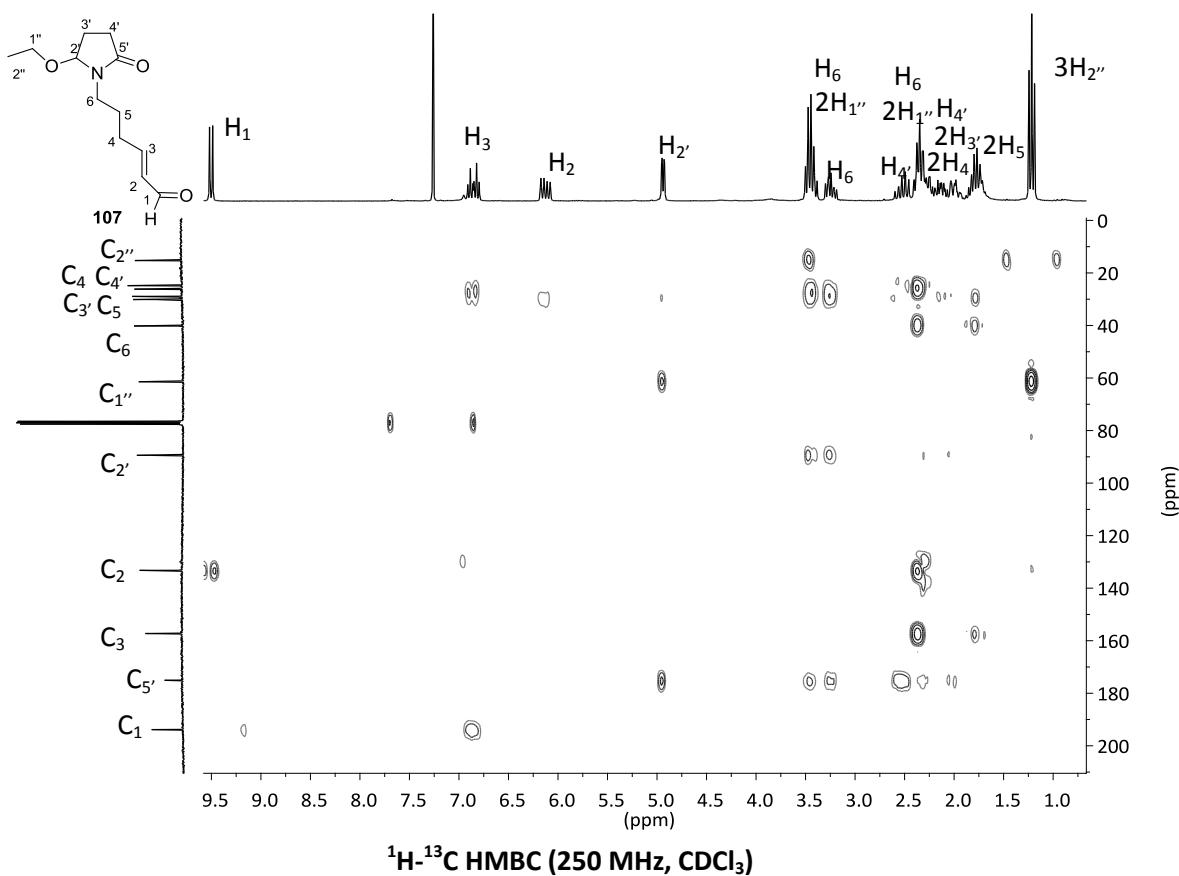
105

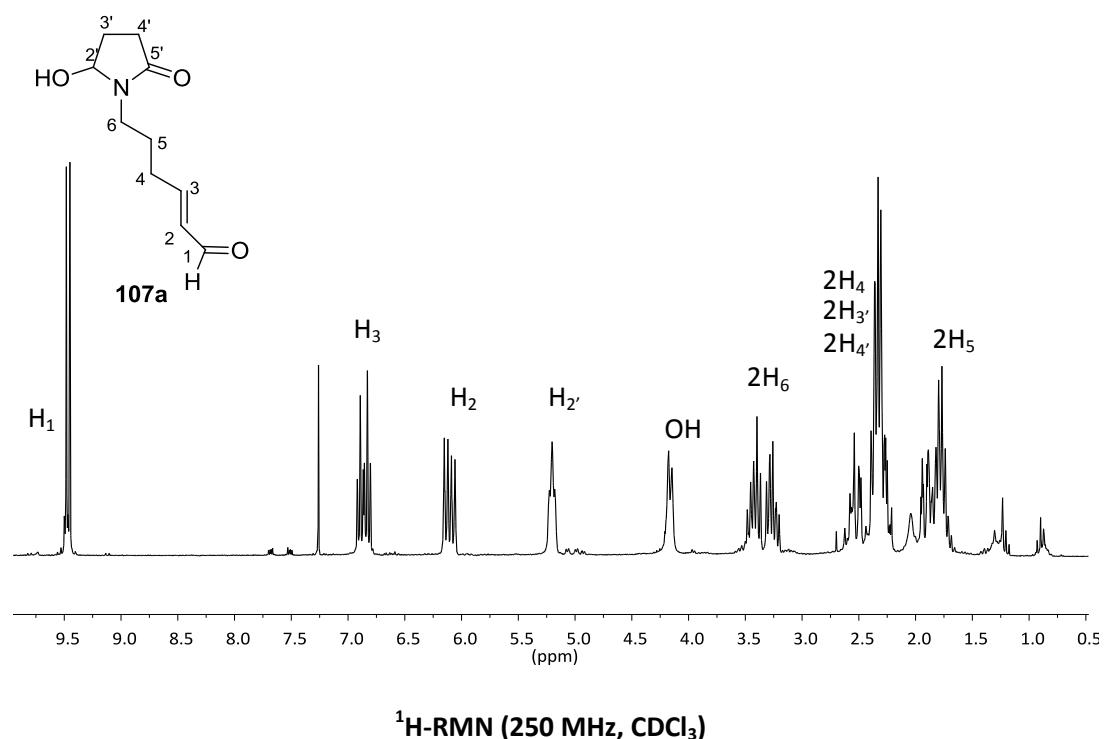




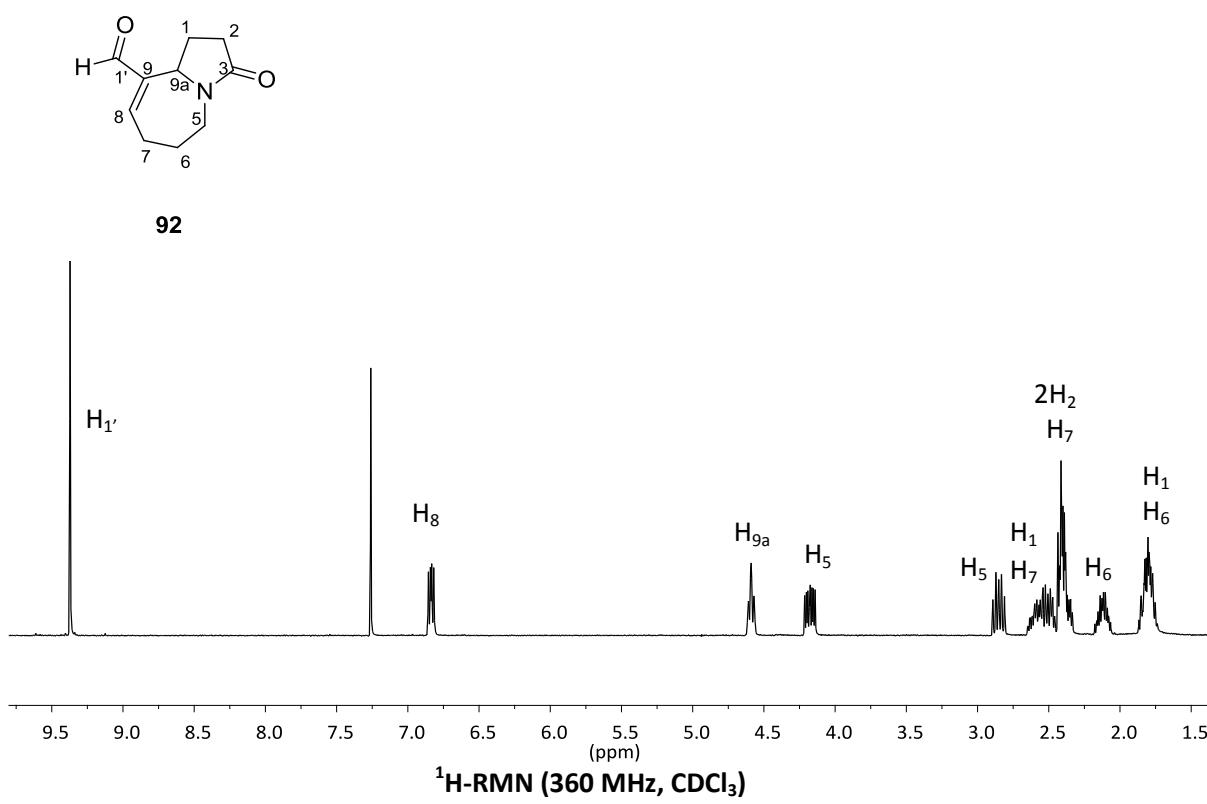
6. RECULL D'ESPECTRES

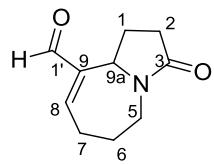




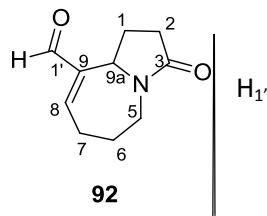
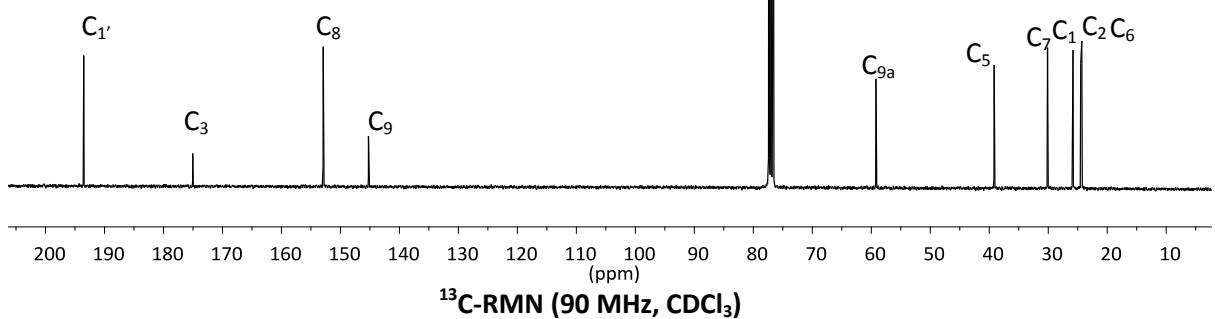


¹H-RMN (250 MHz, CDCl₃)

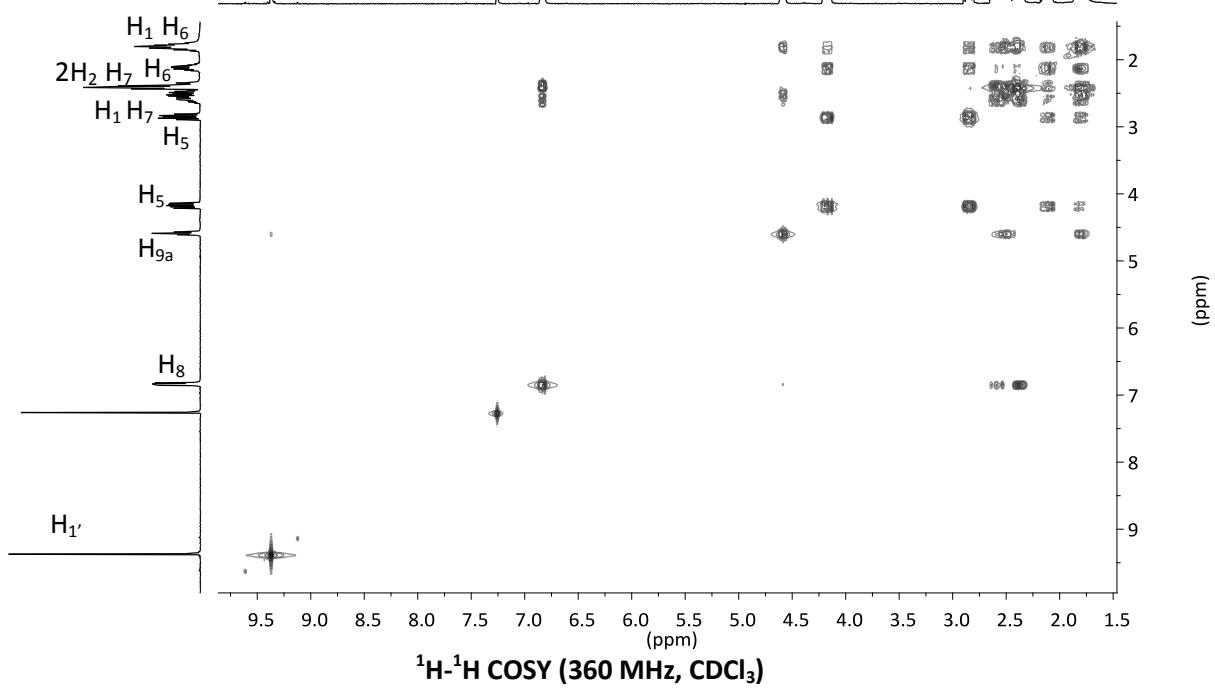




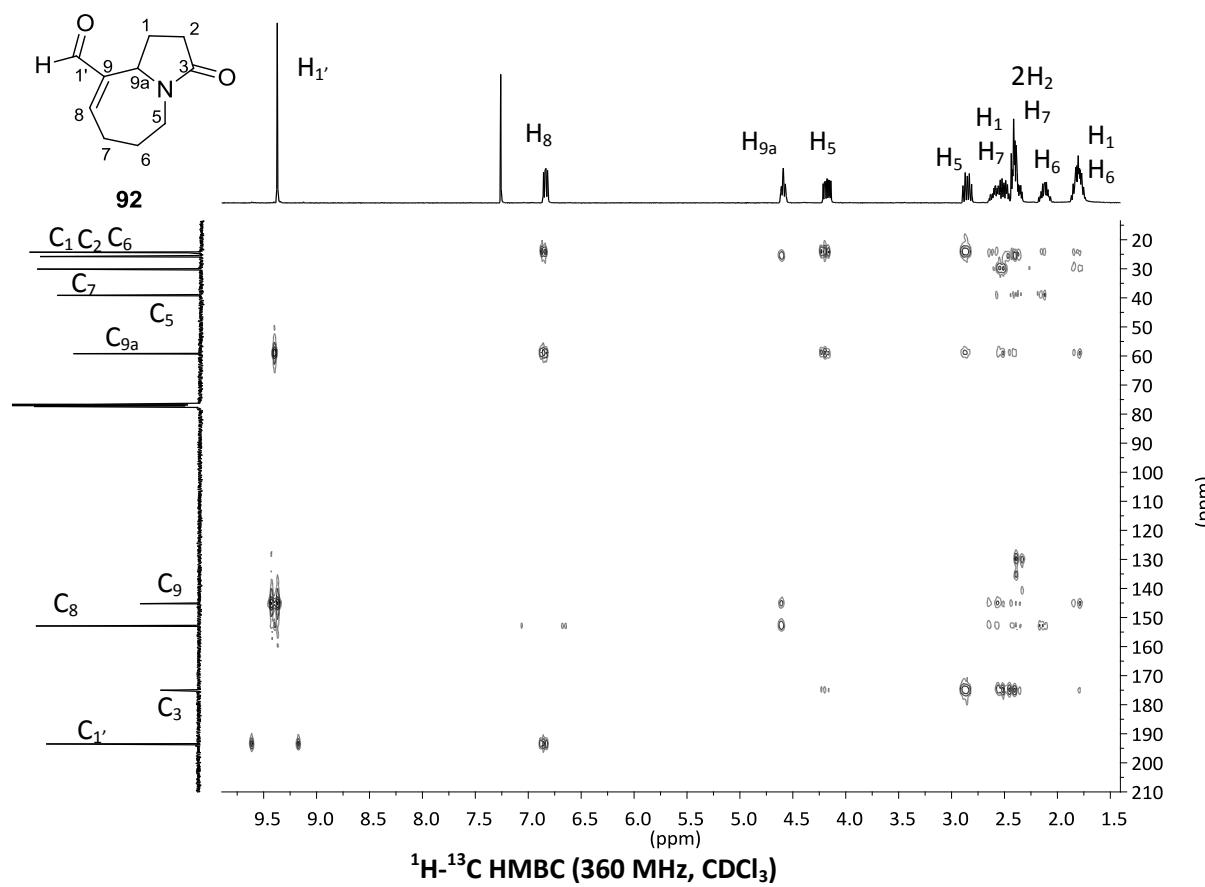
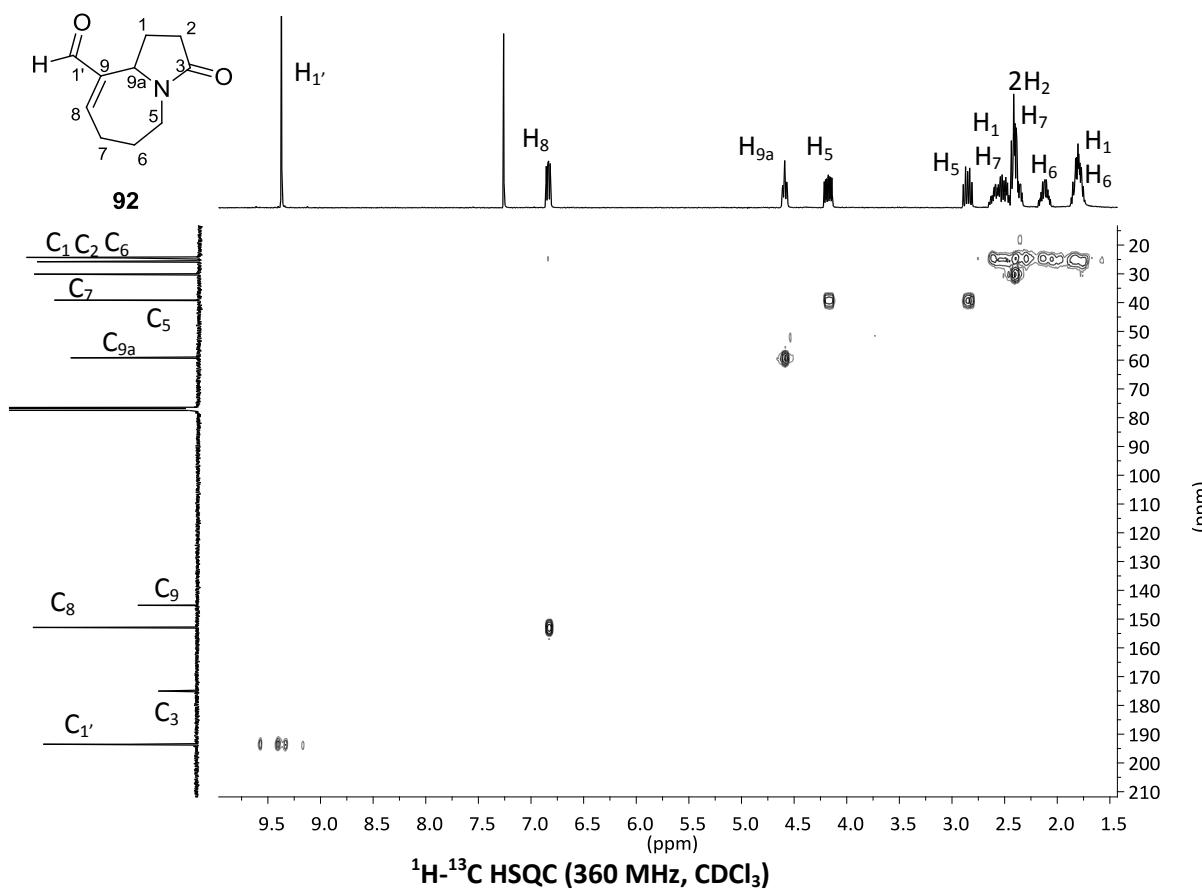
92

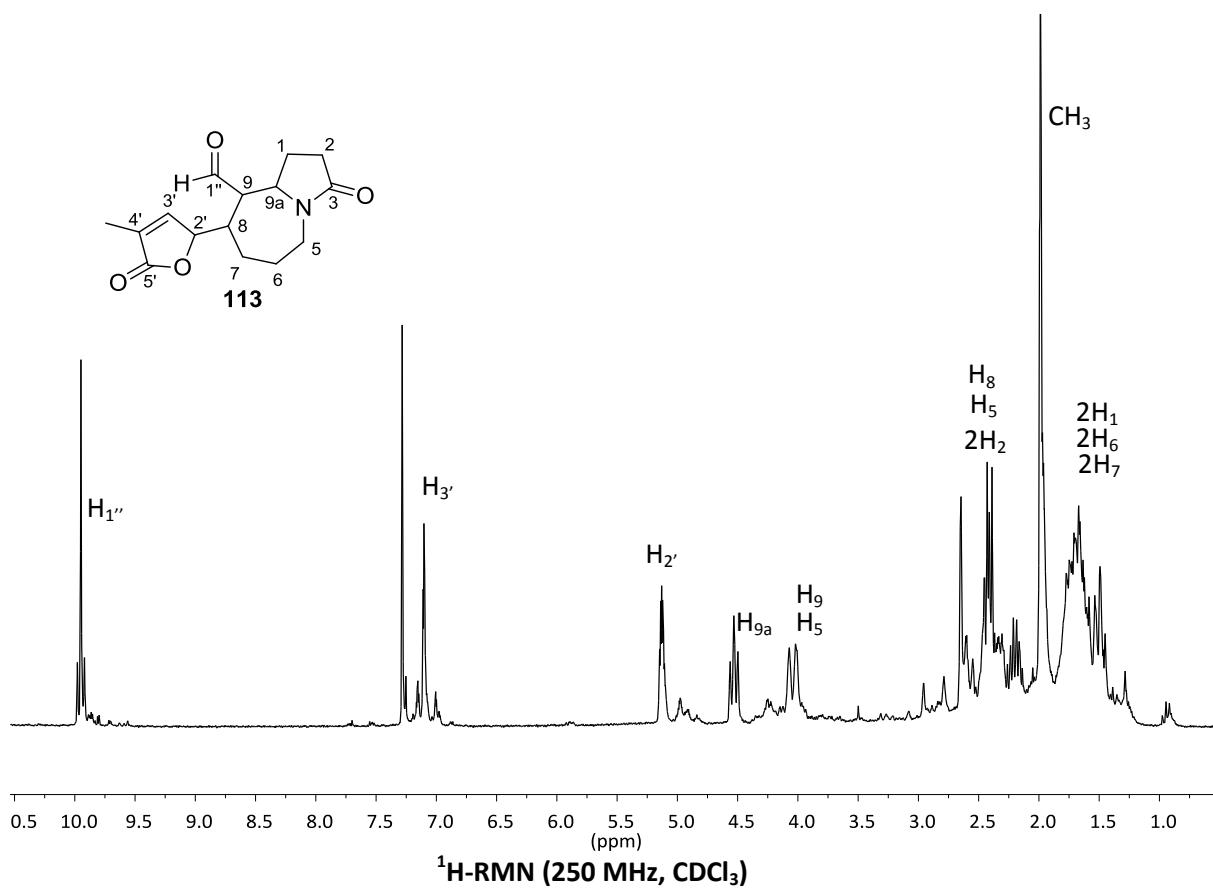
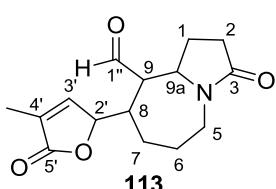
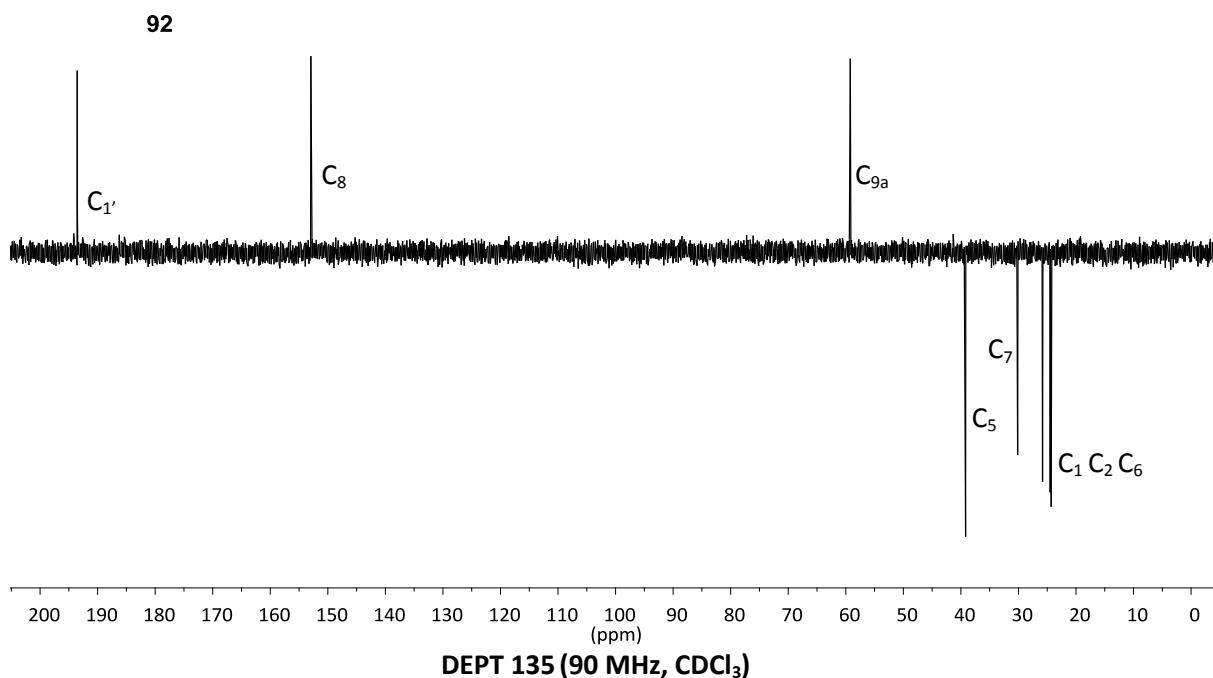
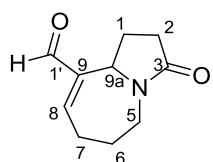


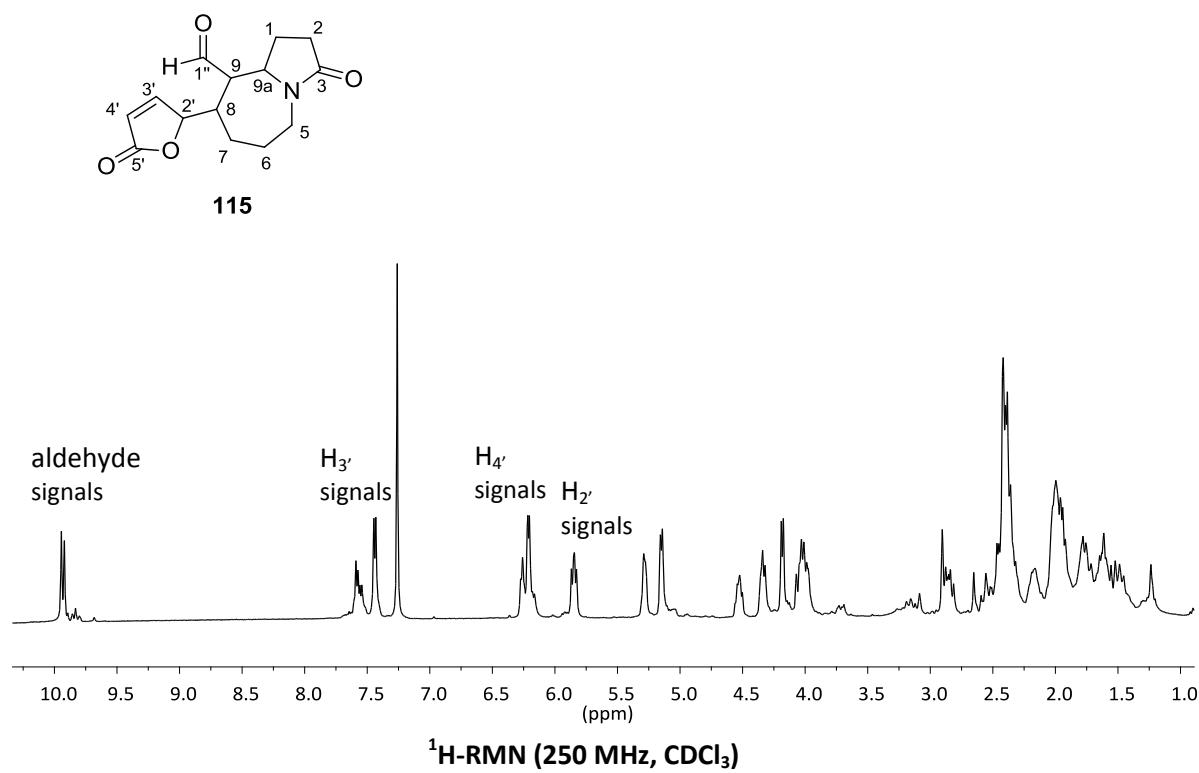
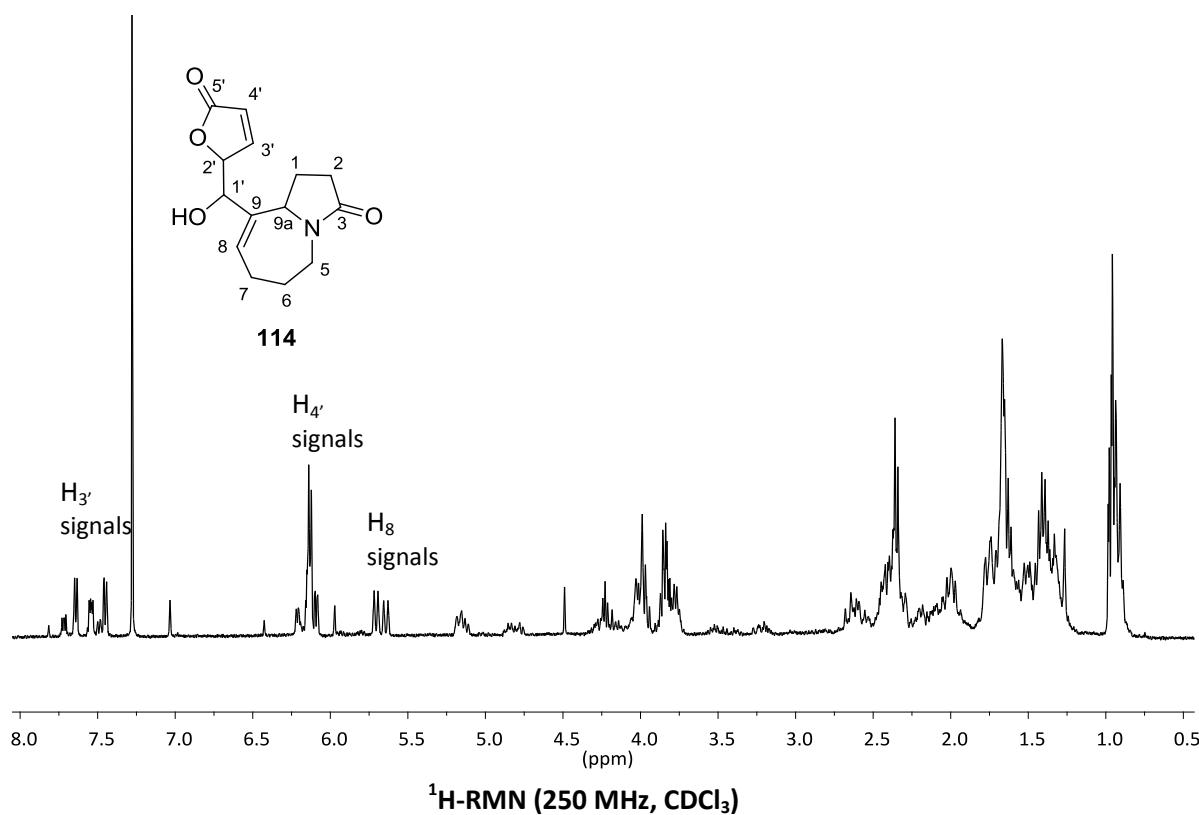
92

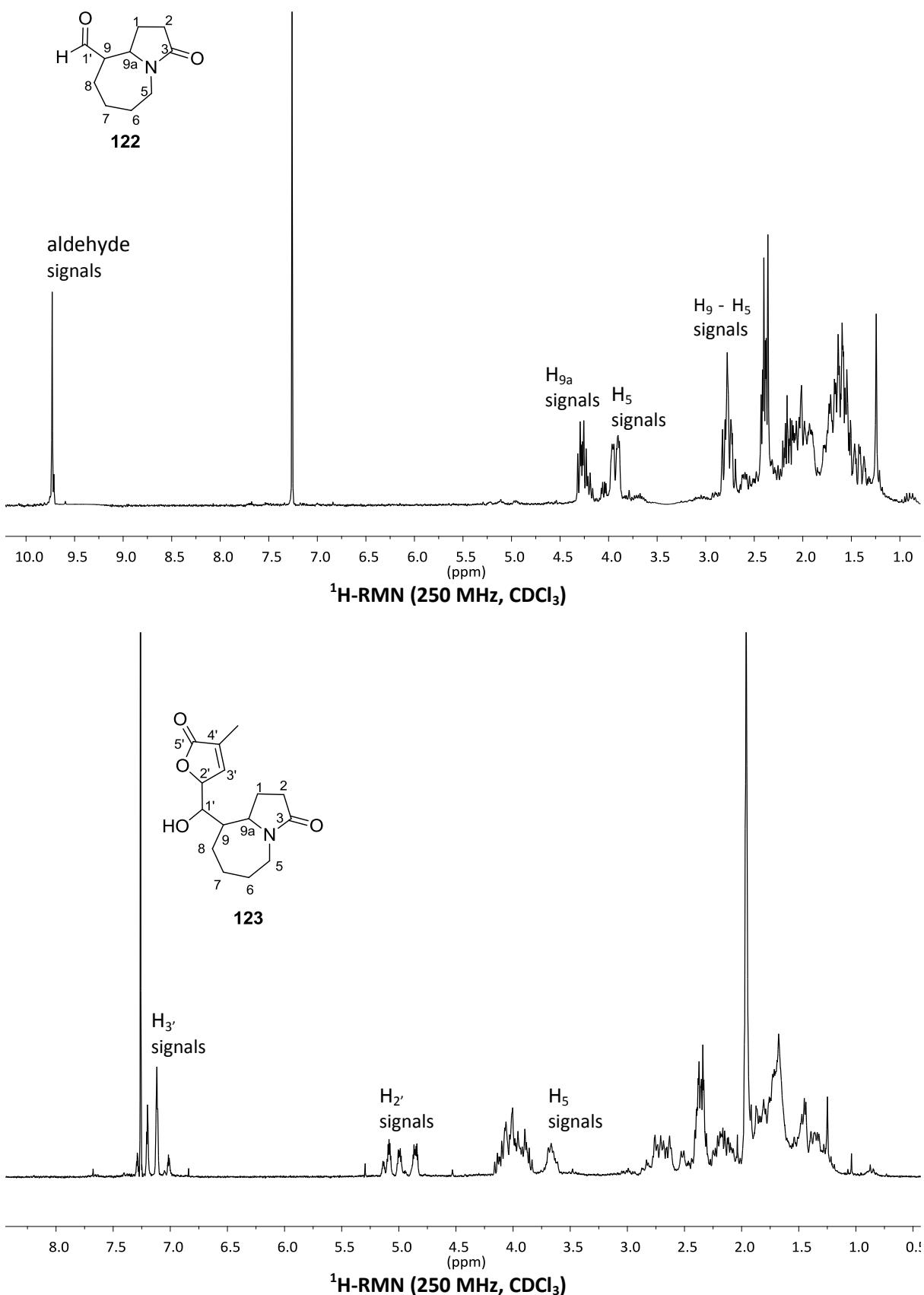


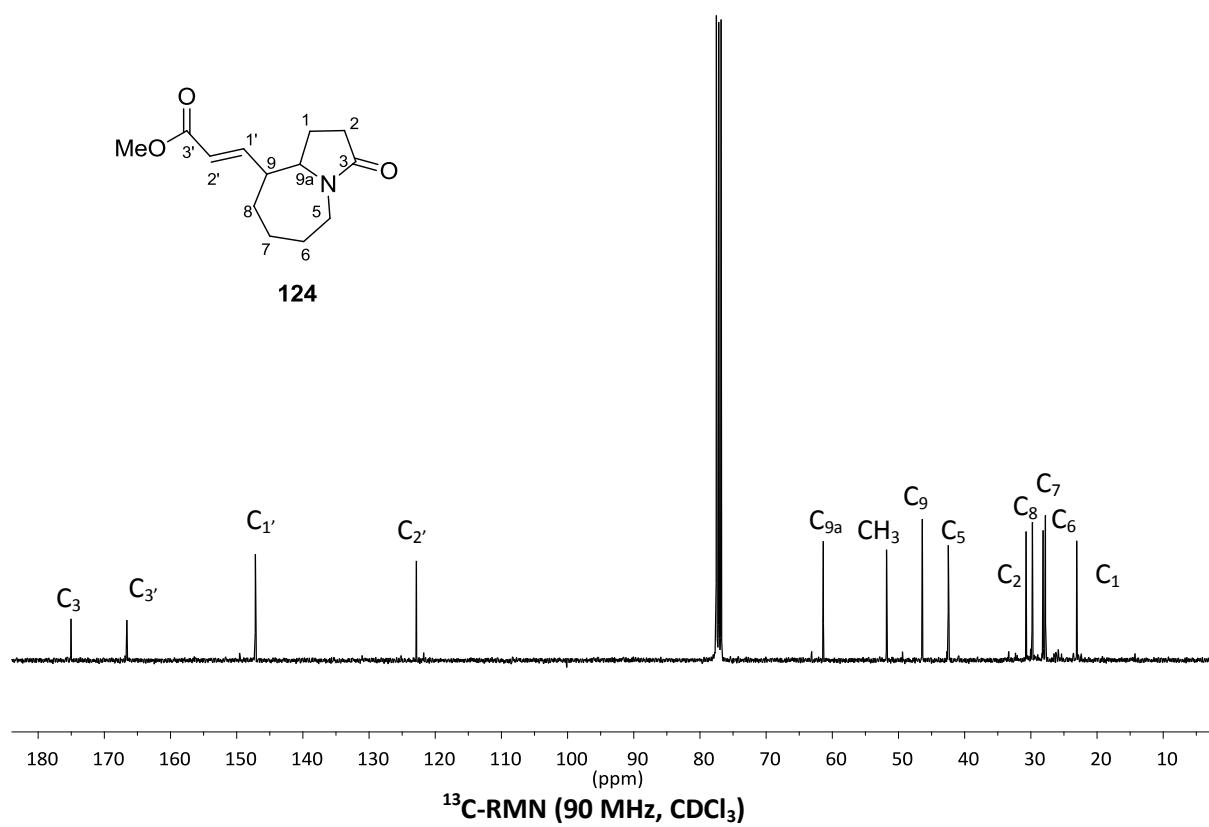
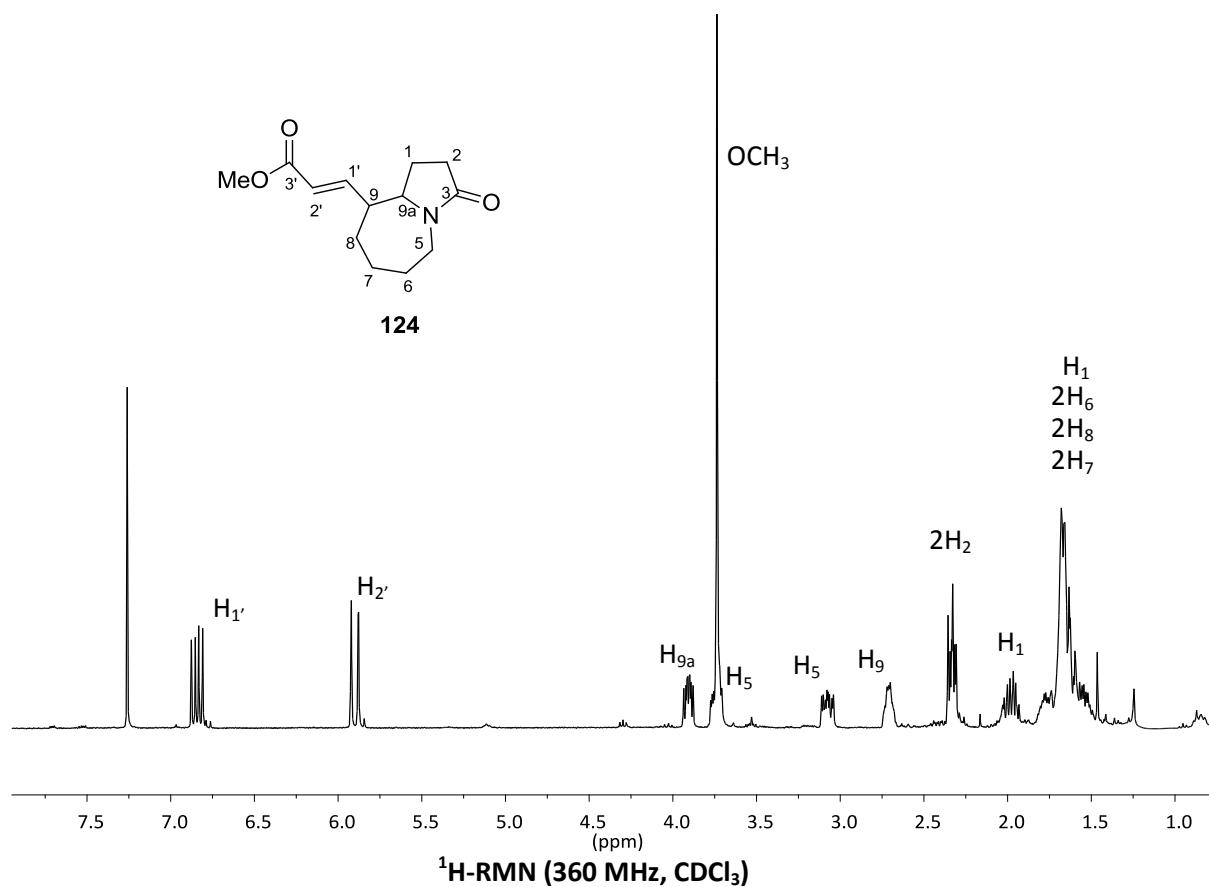
6. RECULL D'ESPECTRES

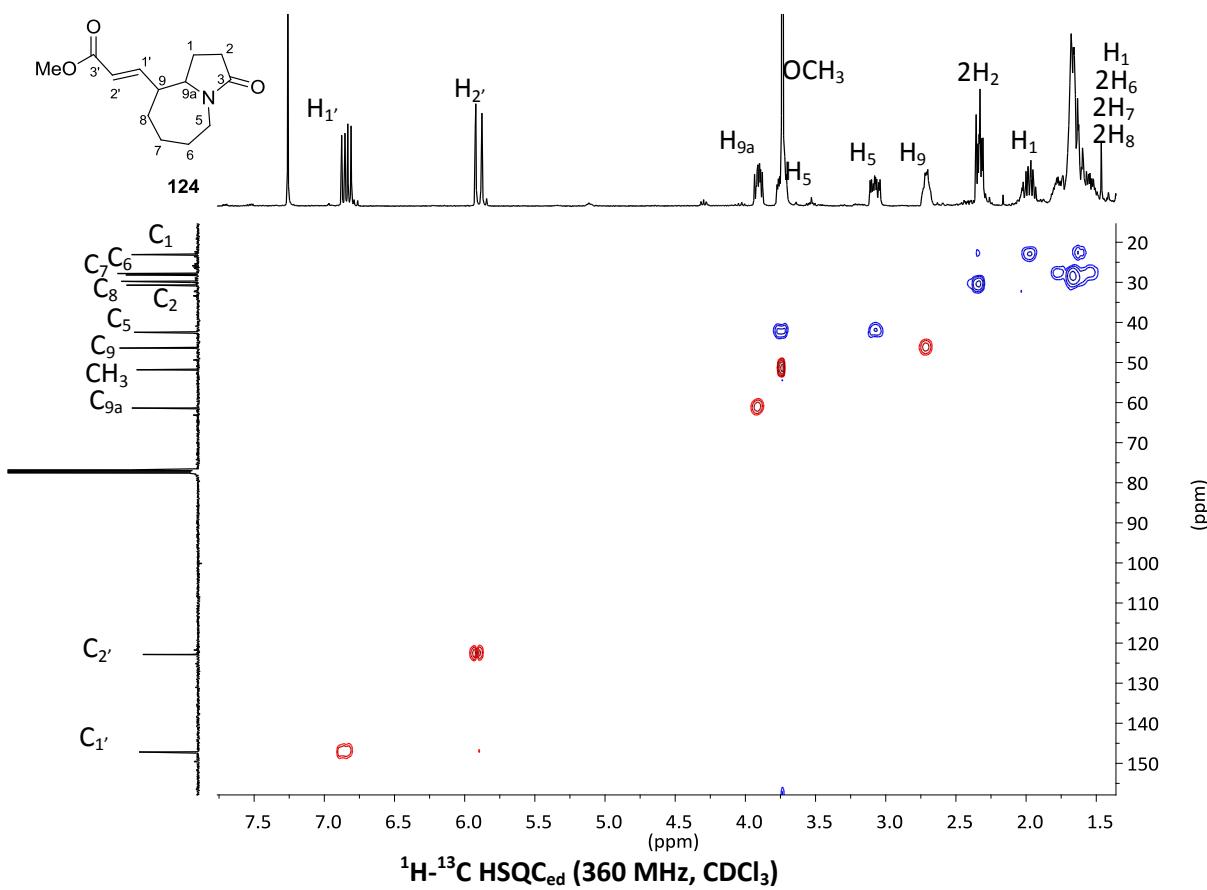
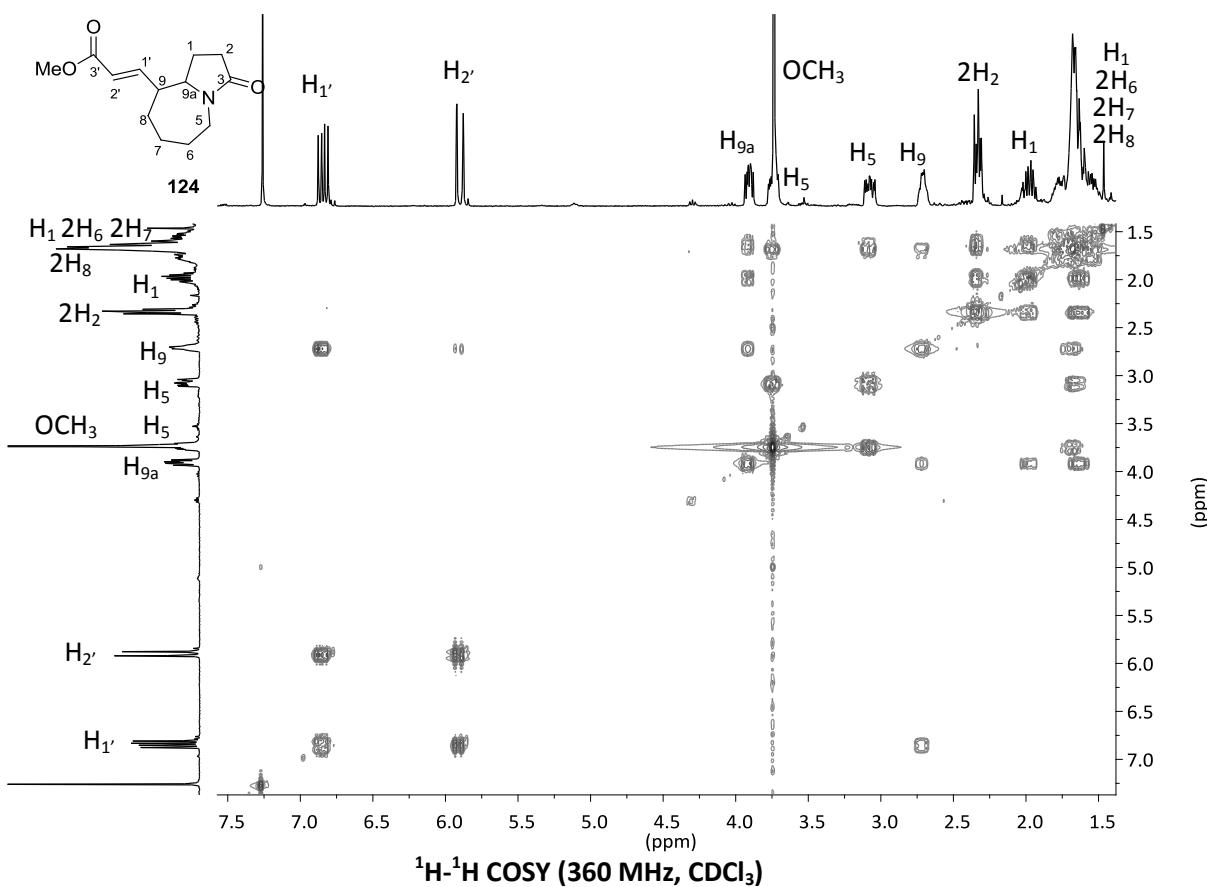




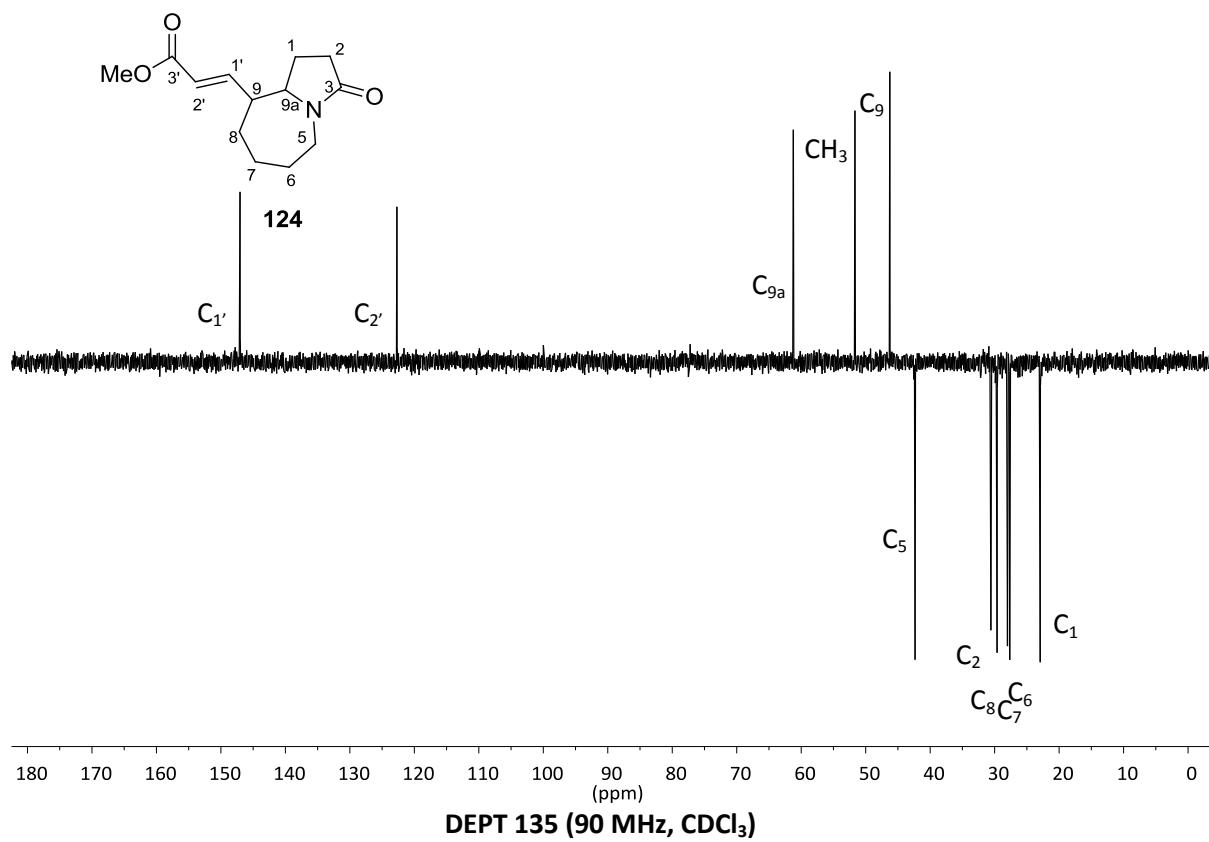
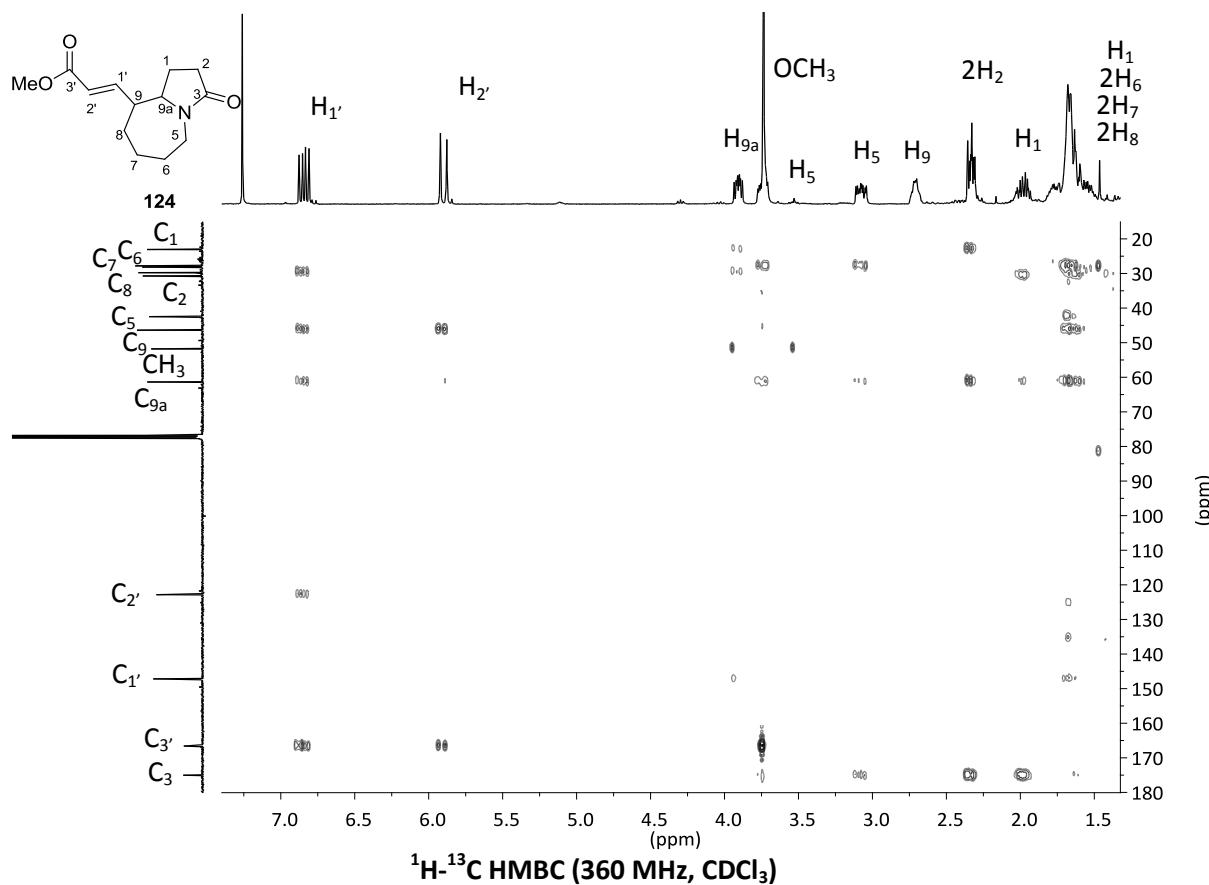


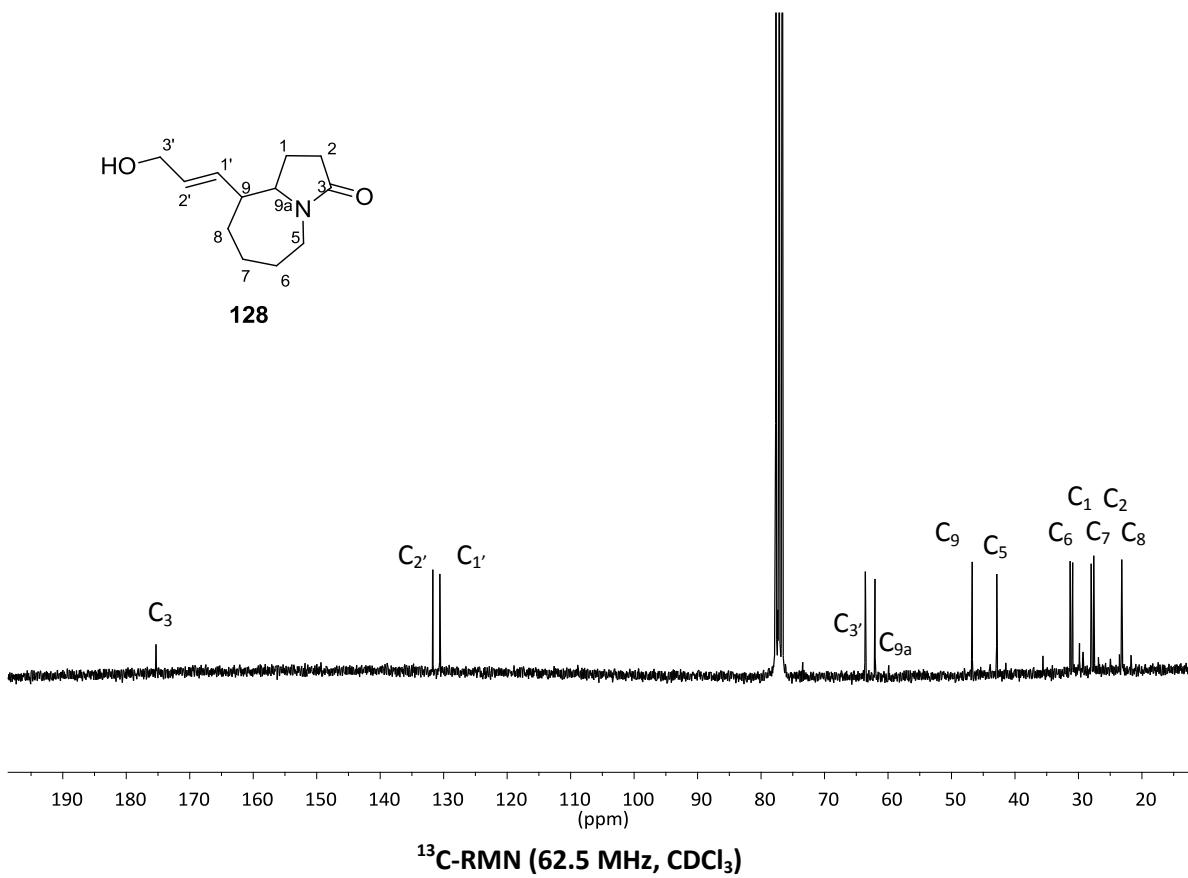
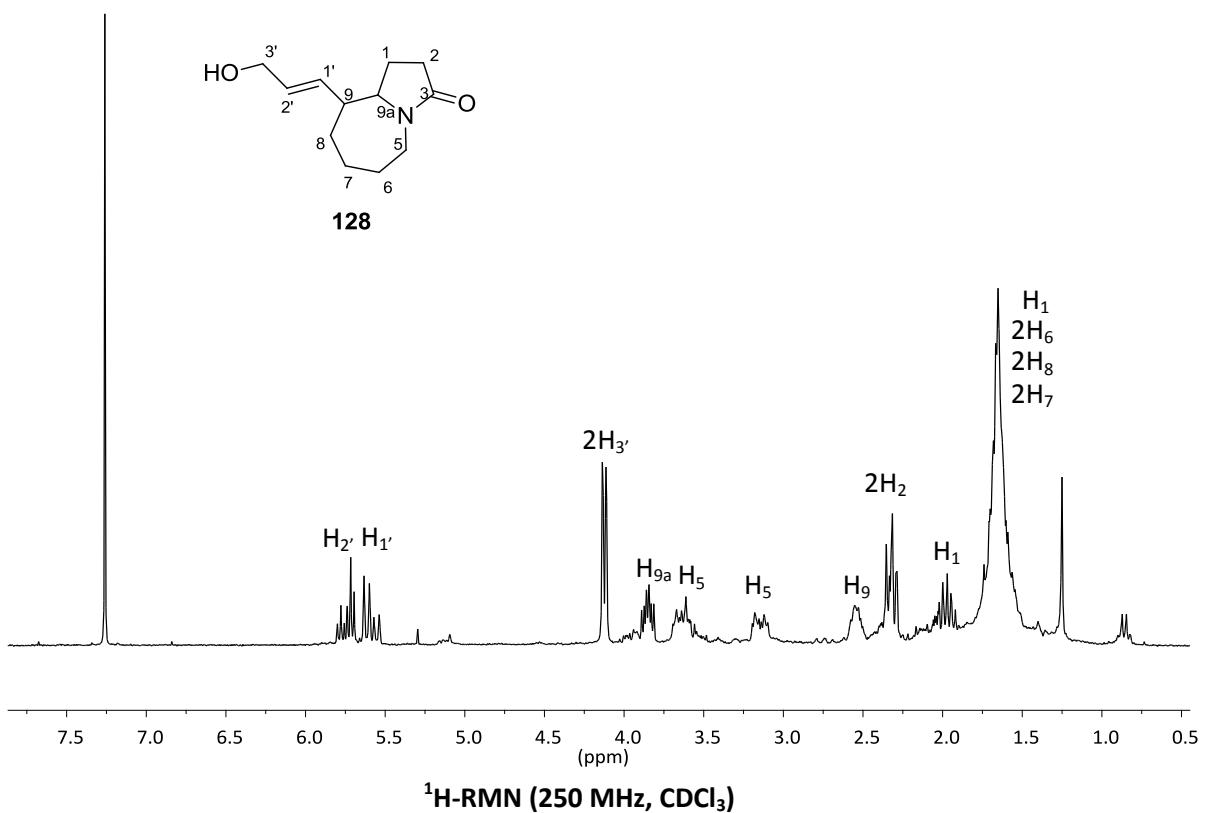




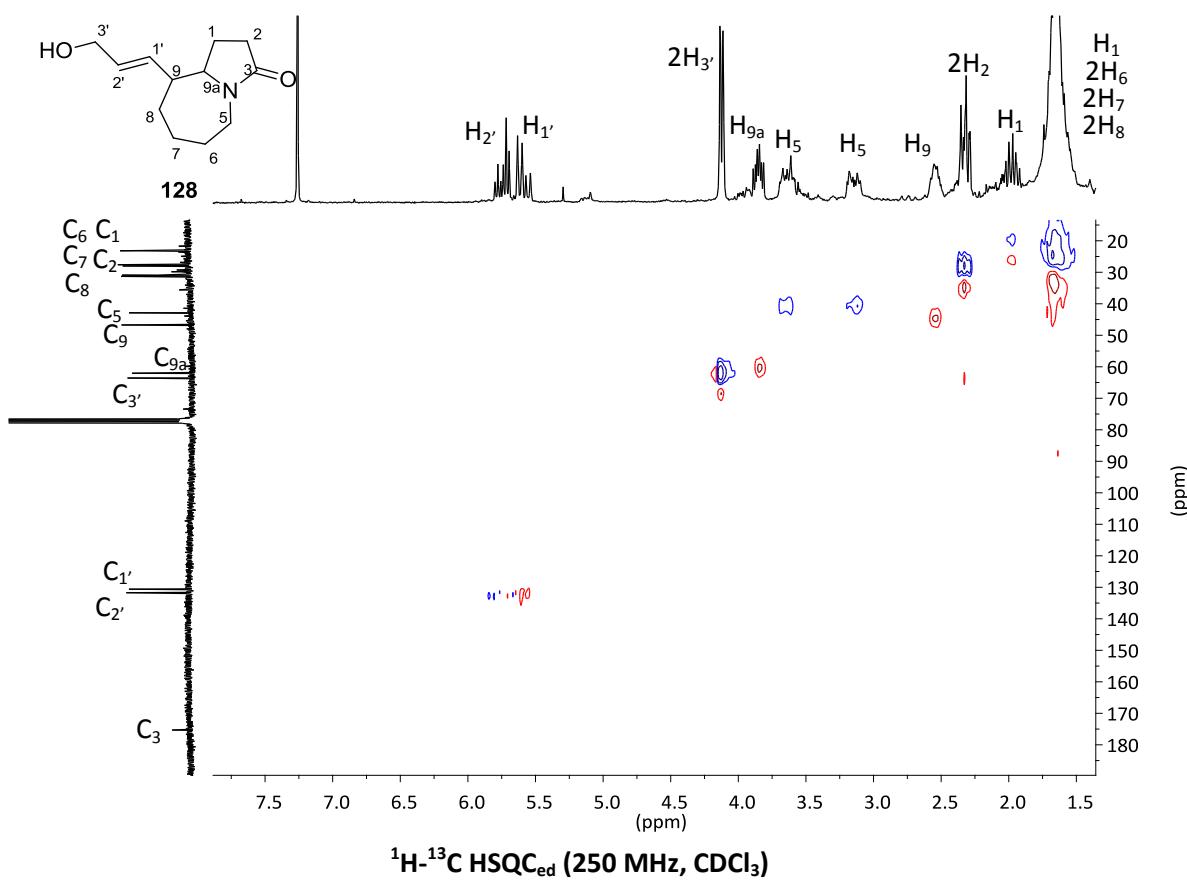
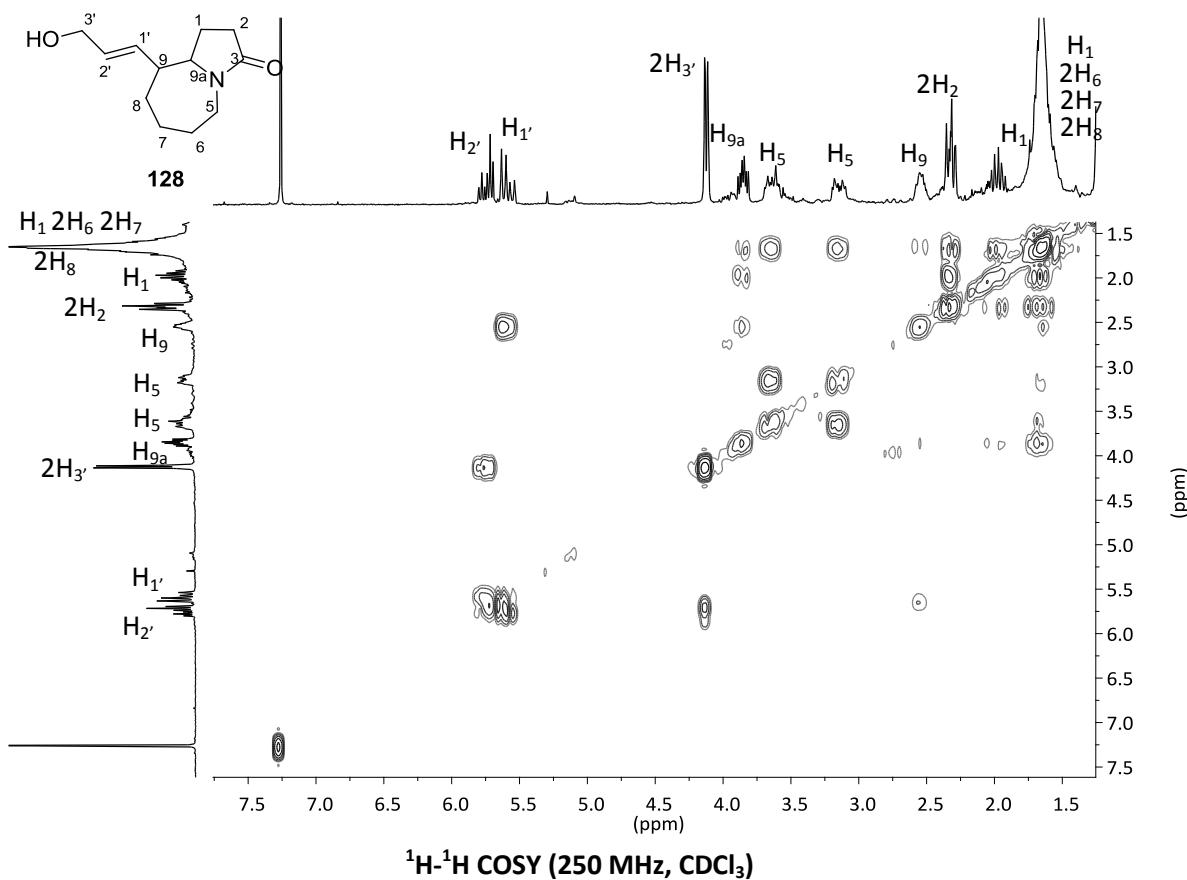


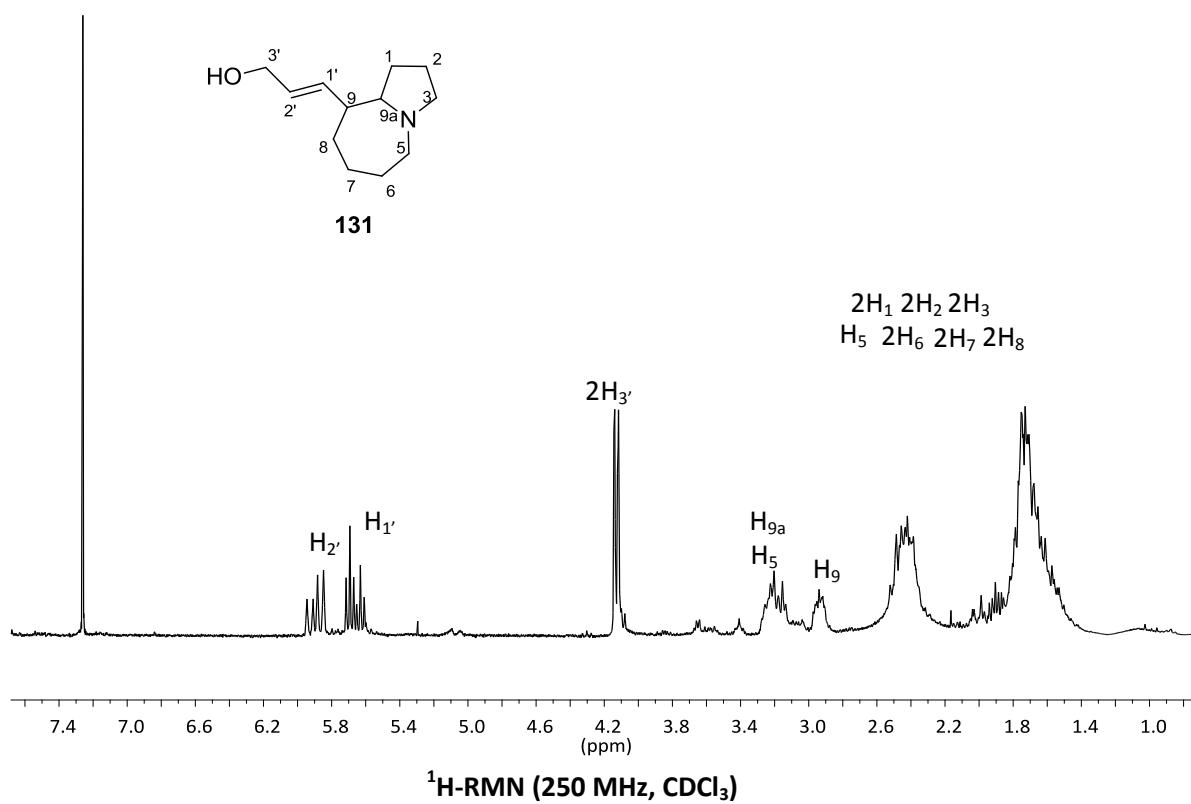
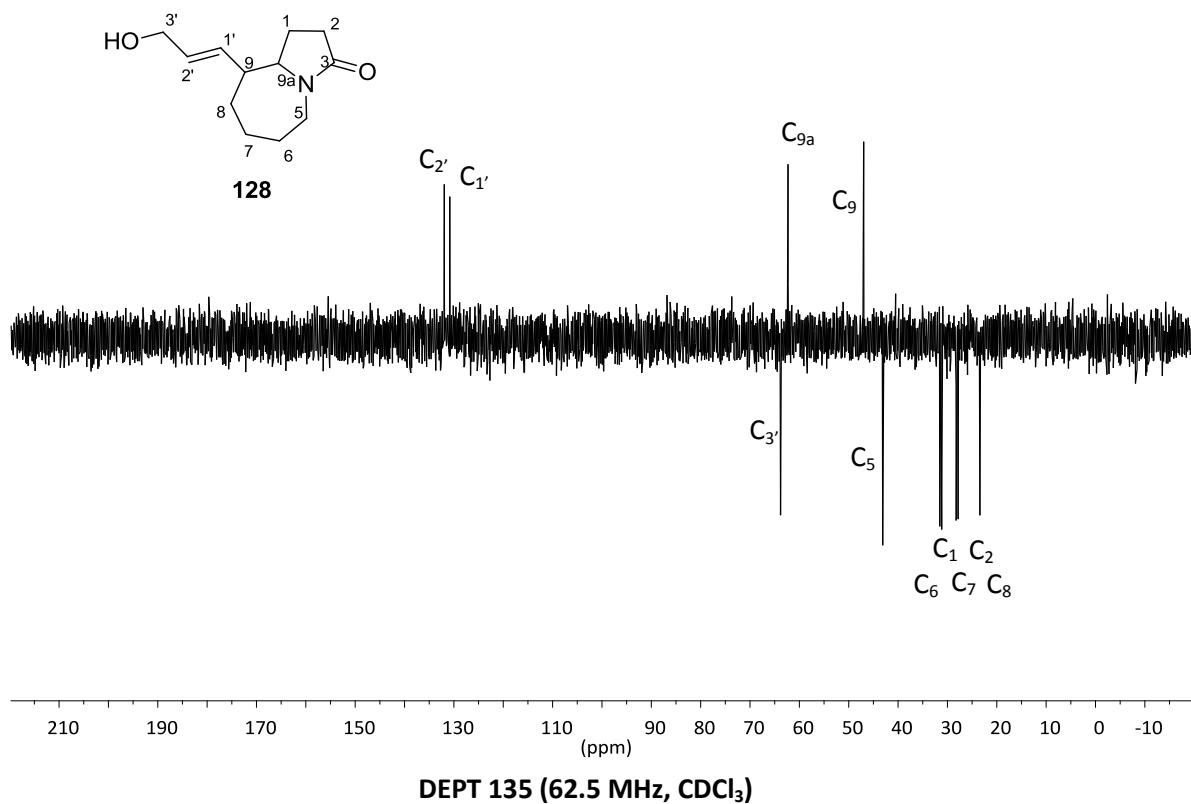
6. RECULL D'ESPECTRES

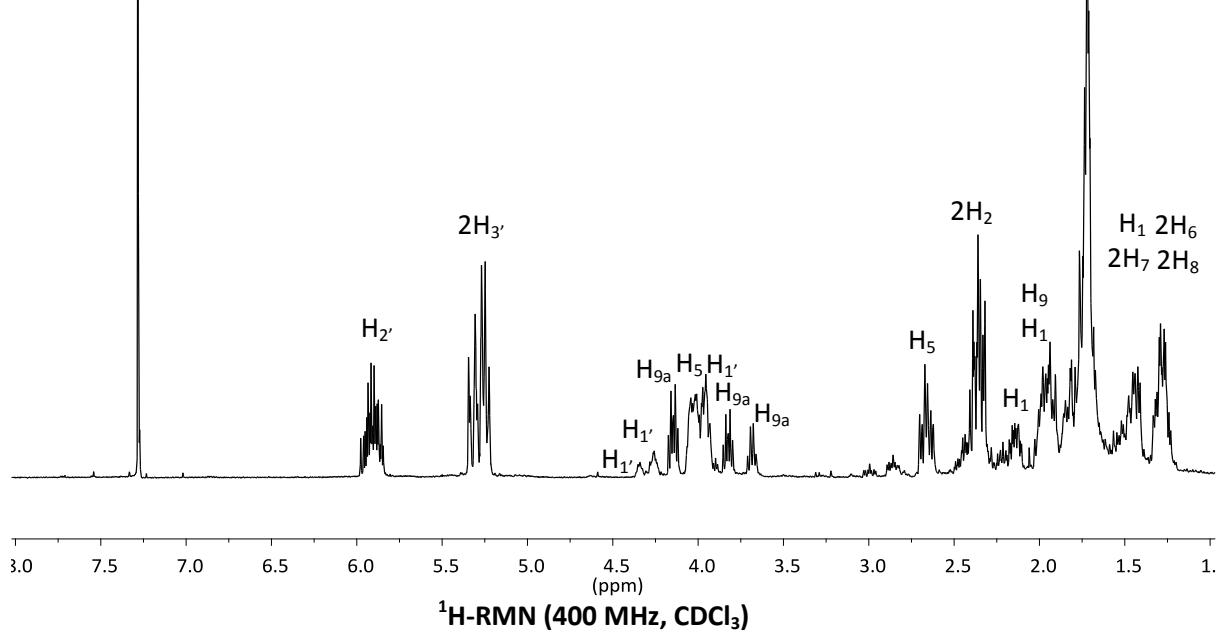
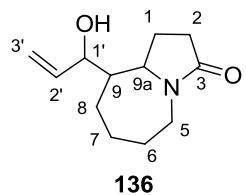
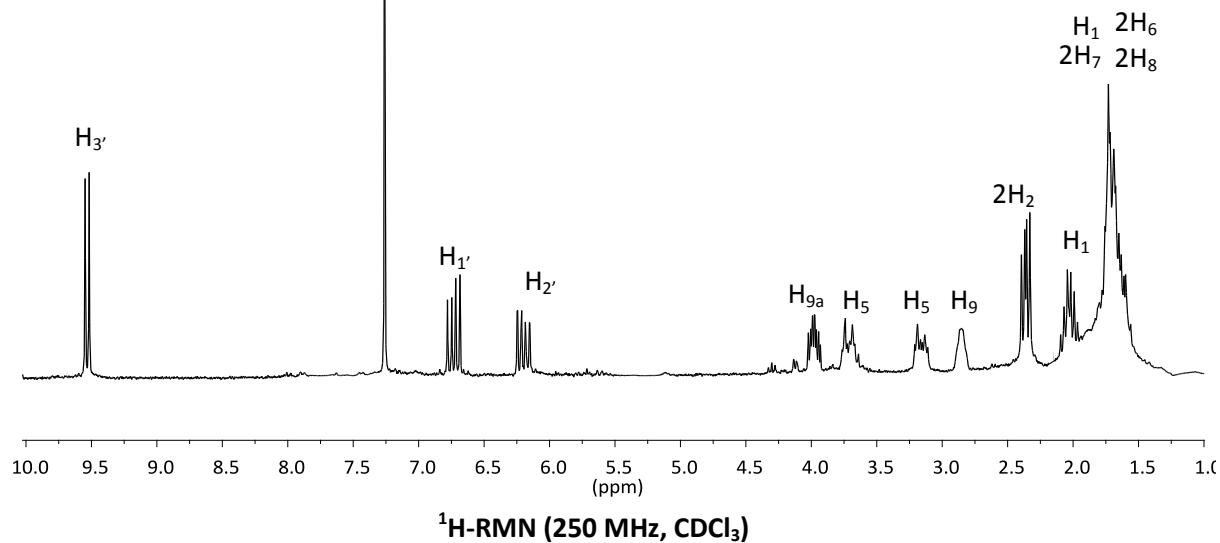
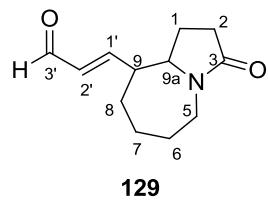


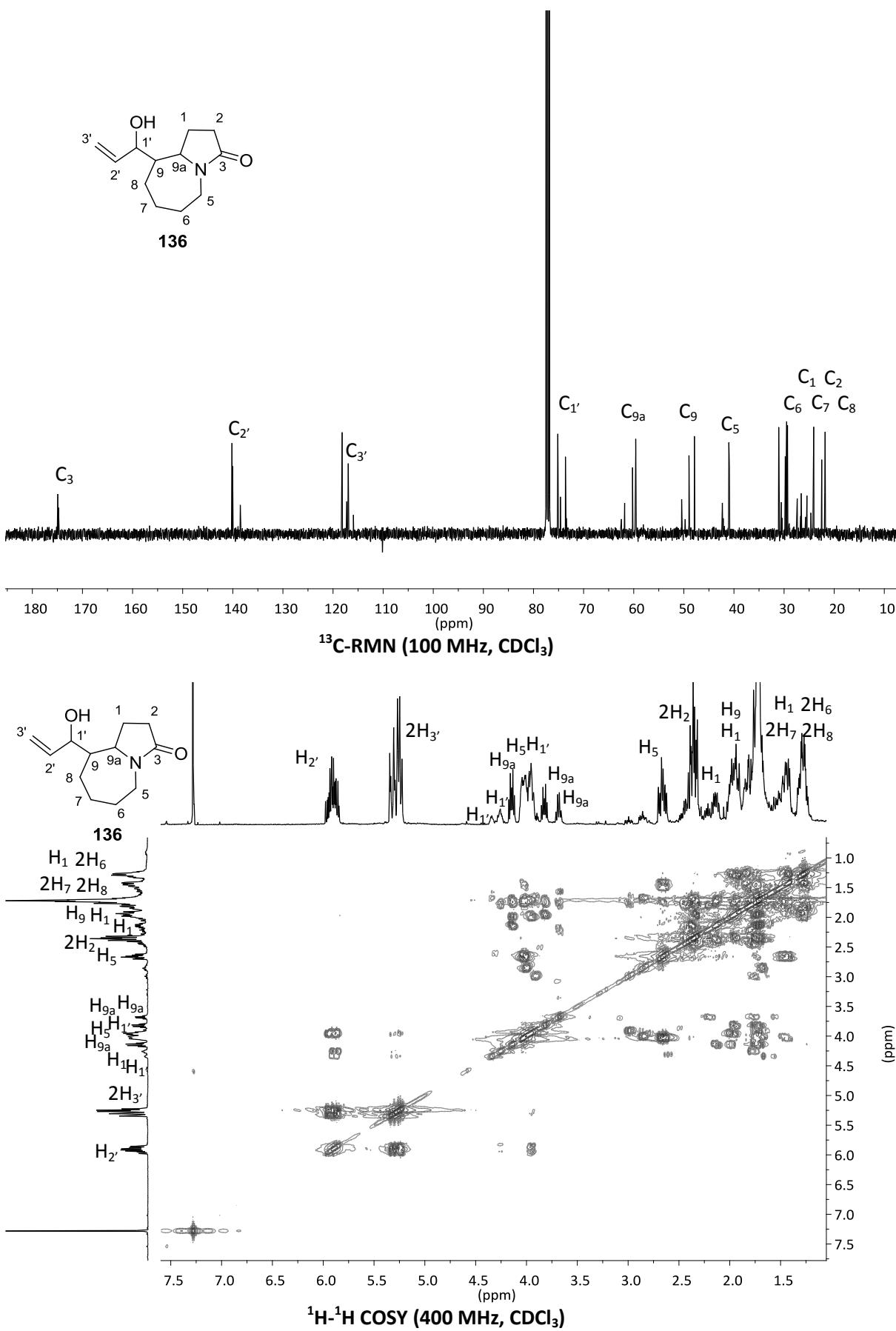


6. RECULL D'ESPECTRES

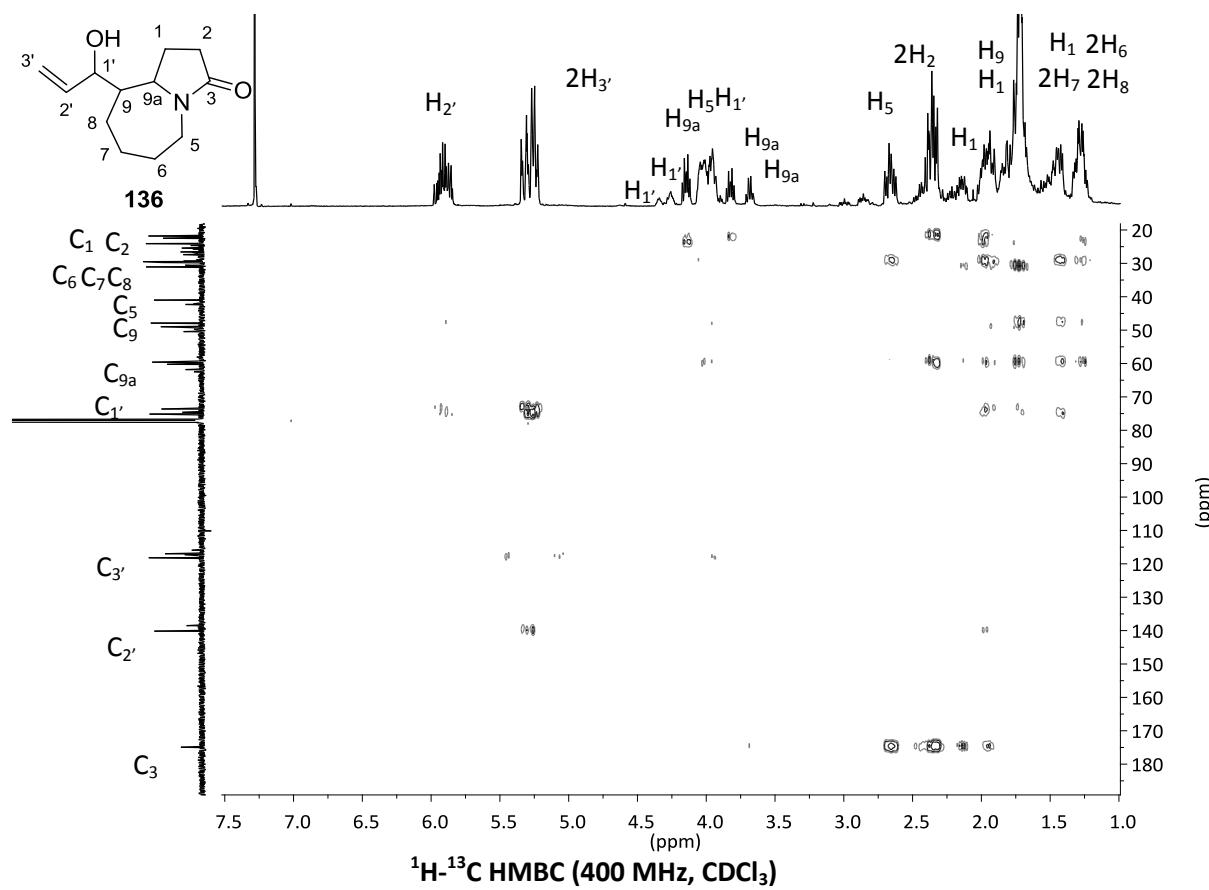
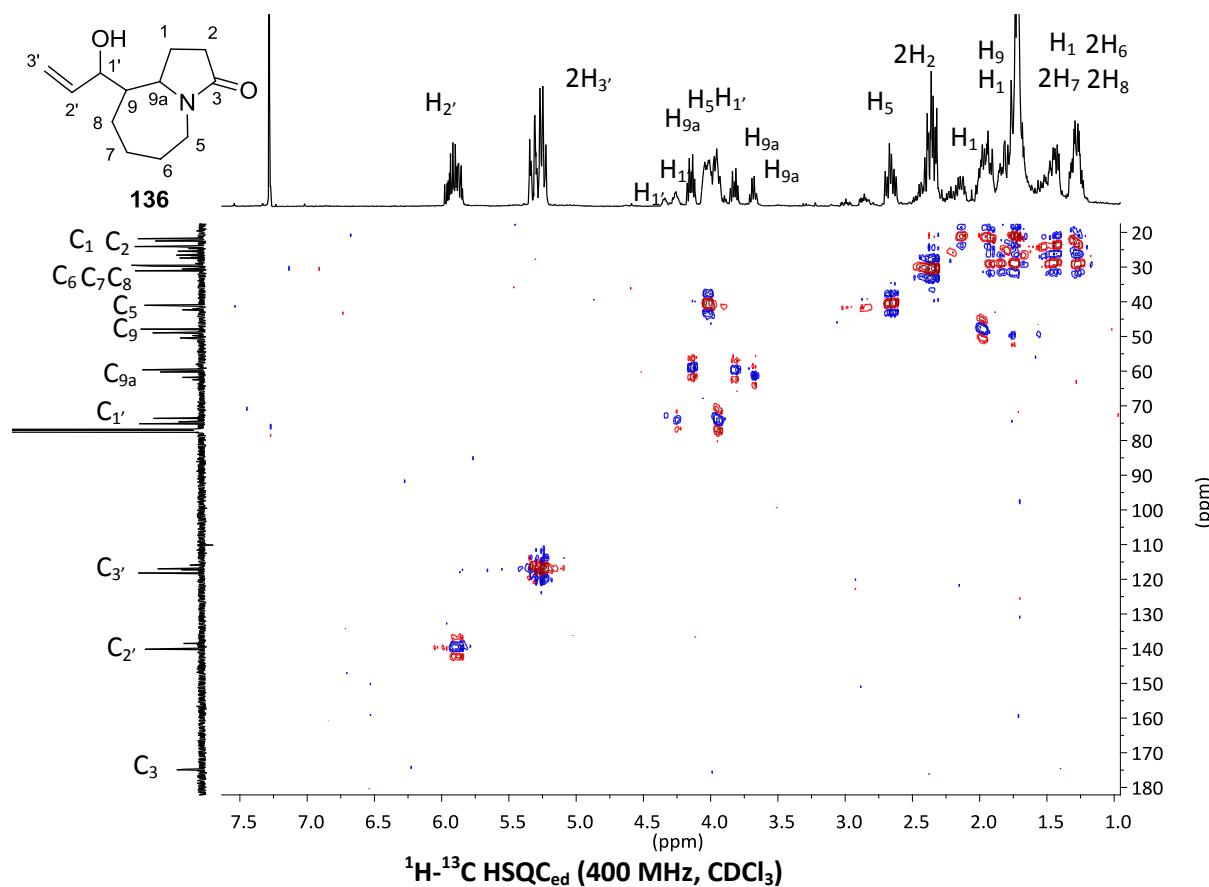


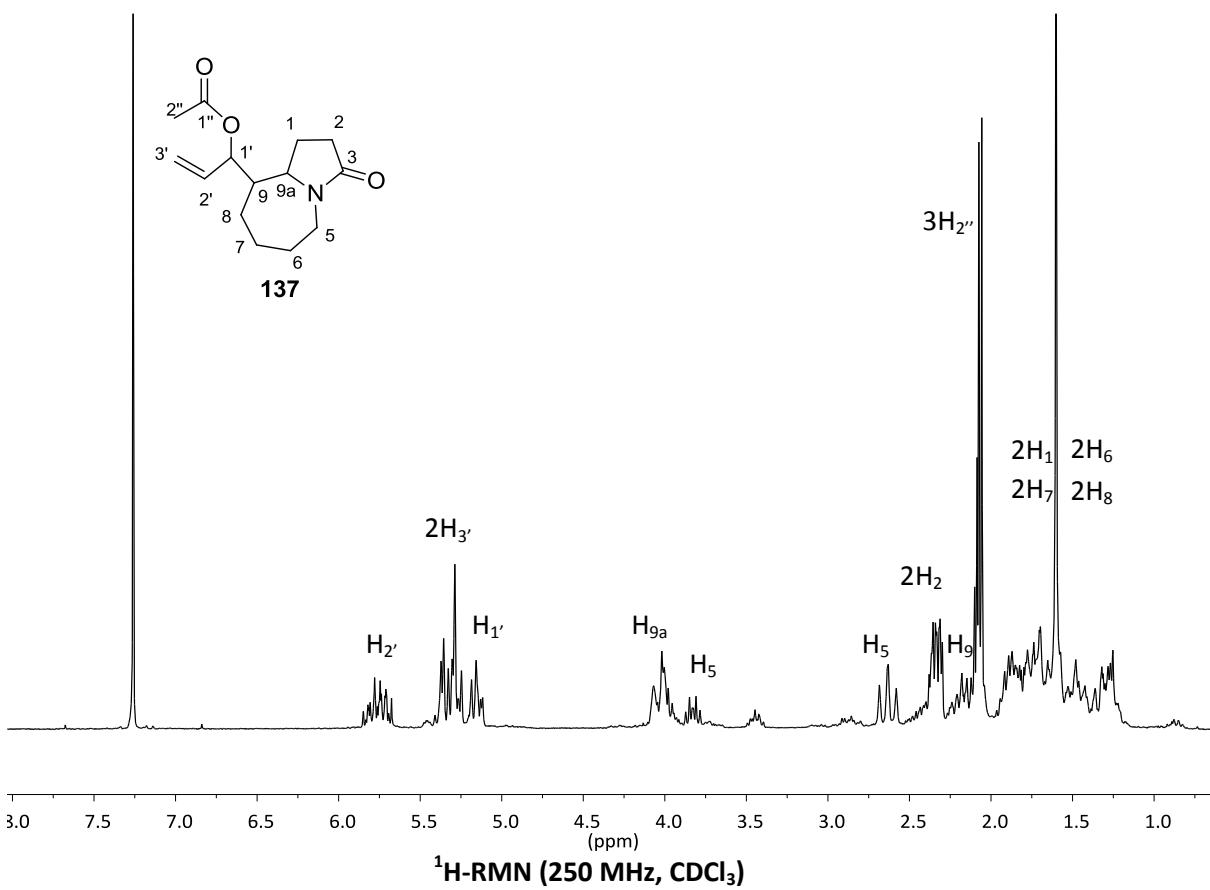
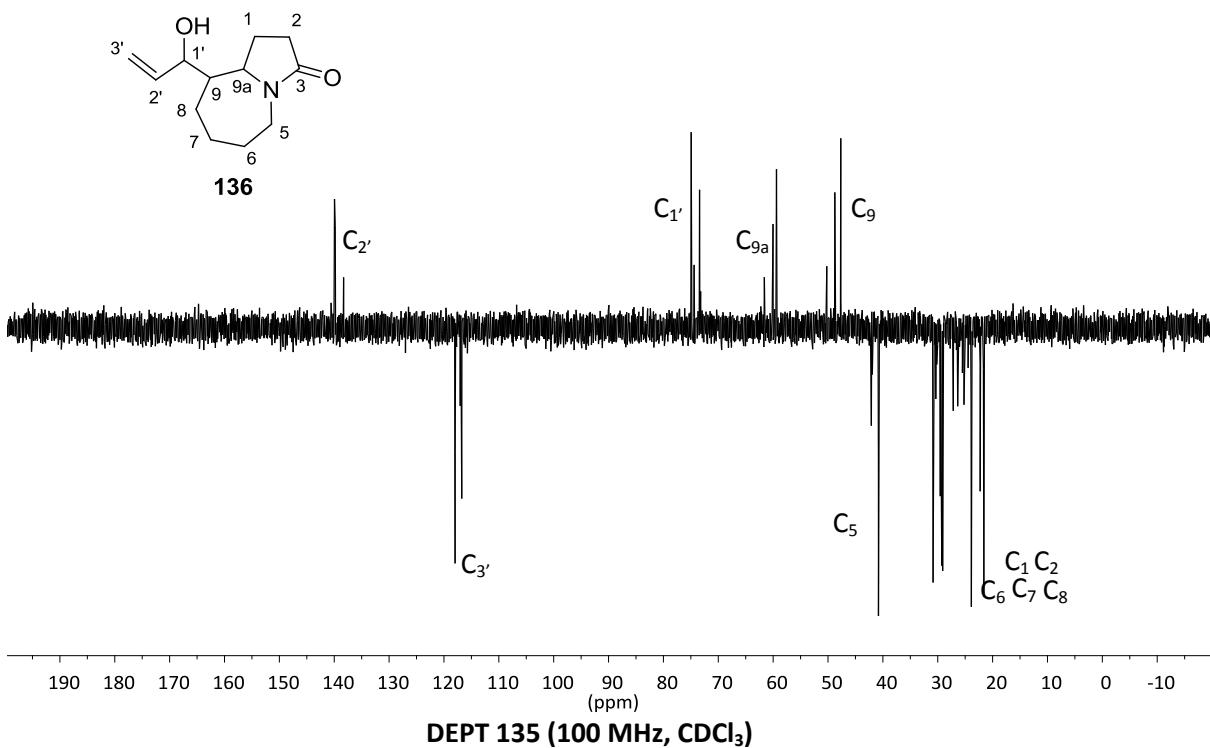


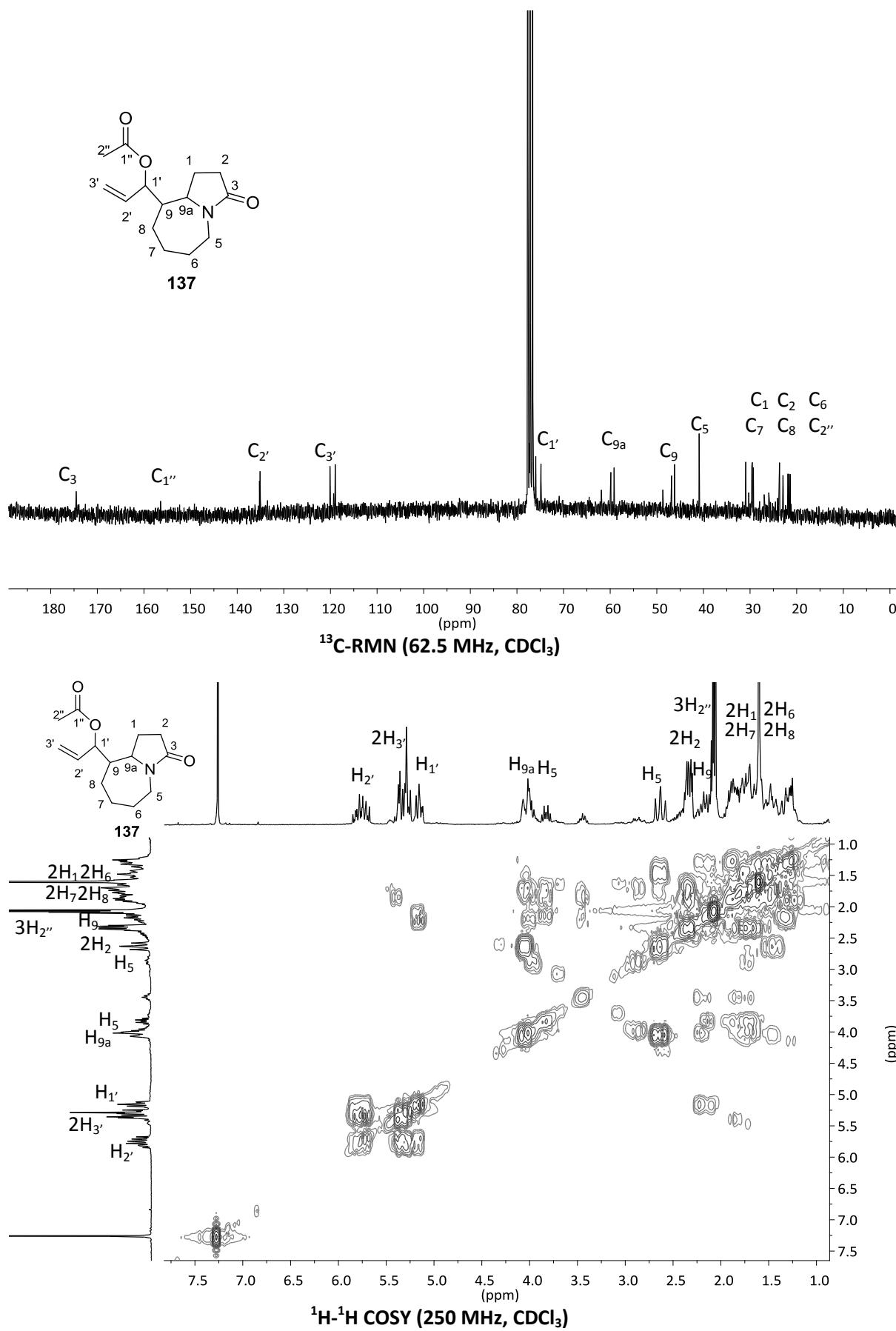


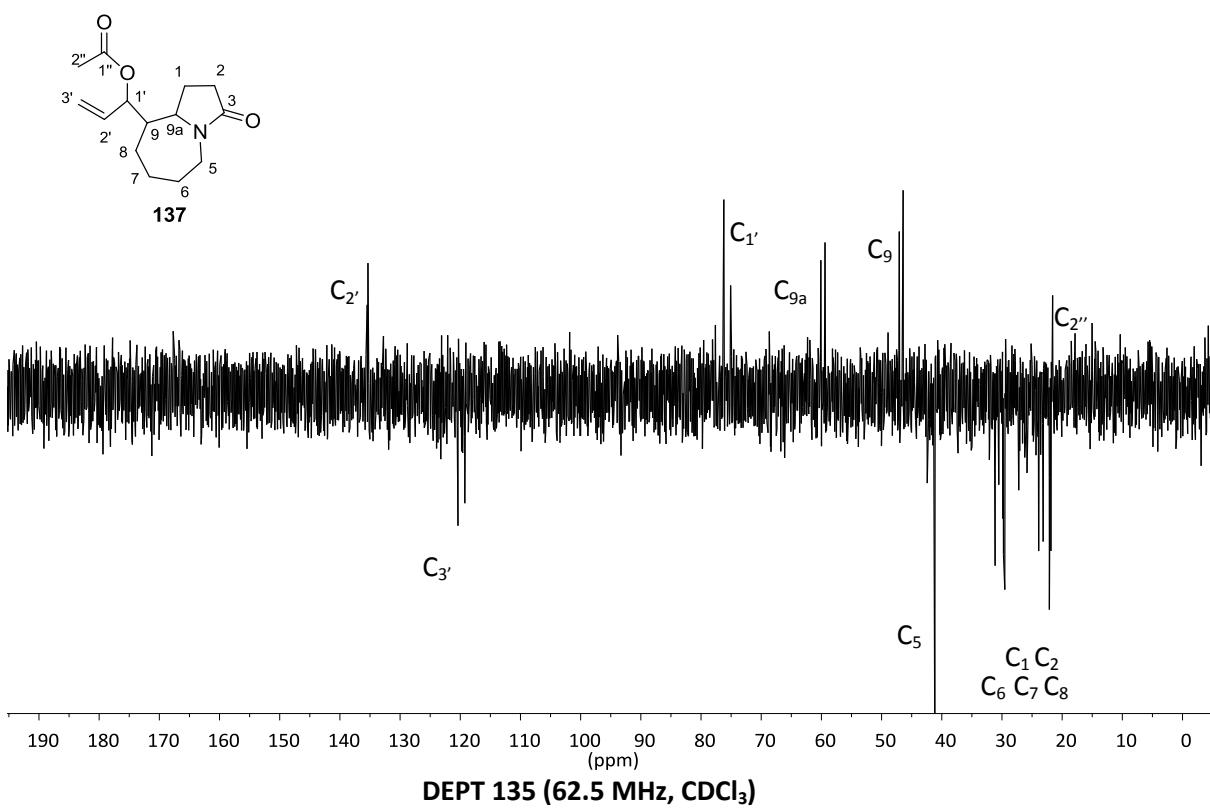
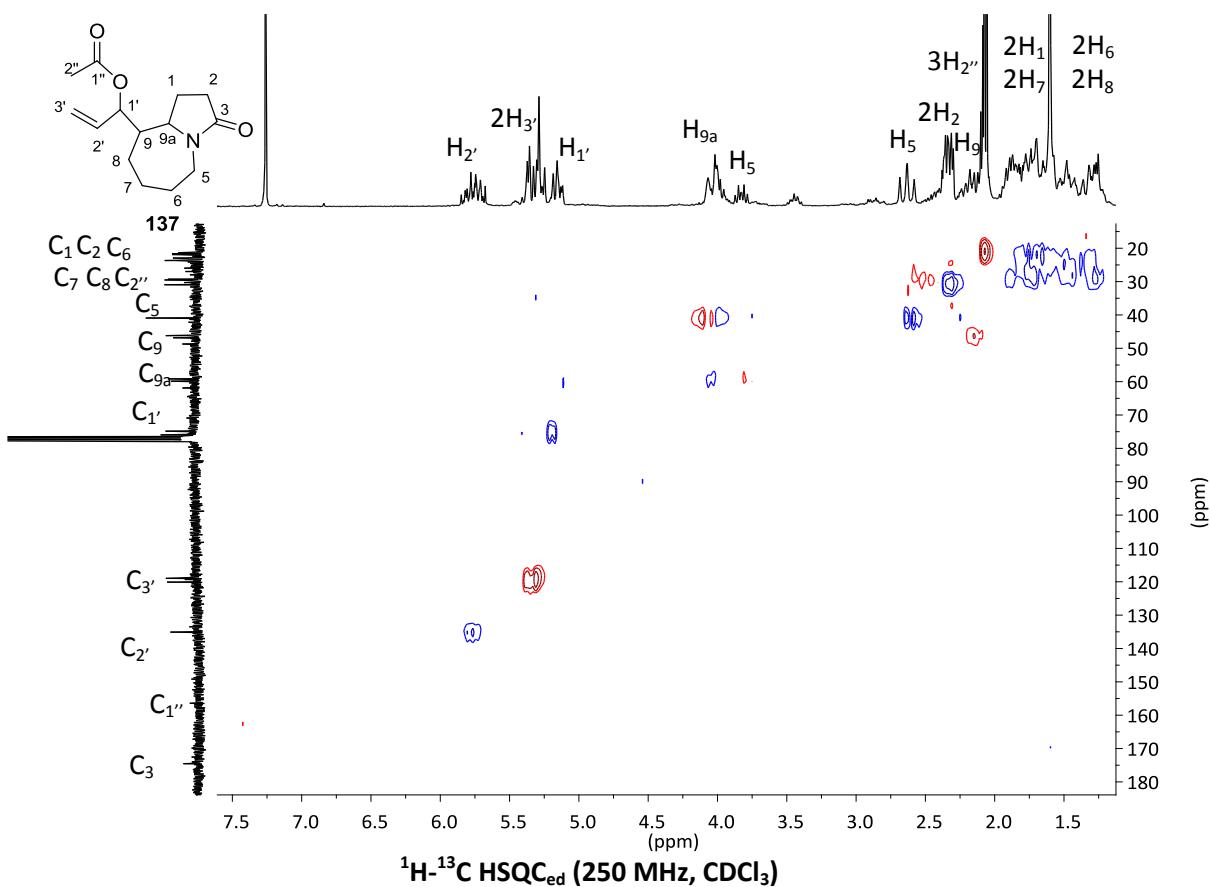


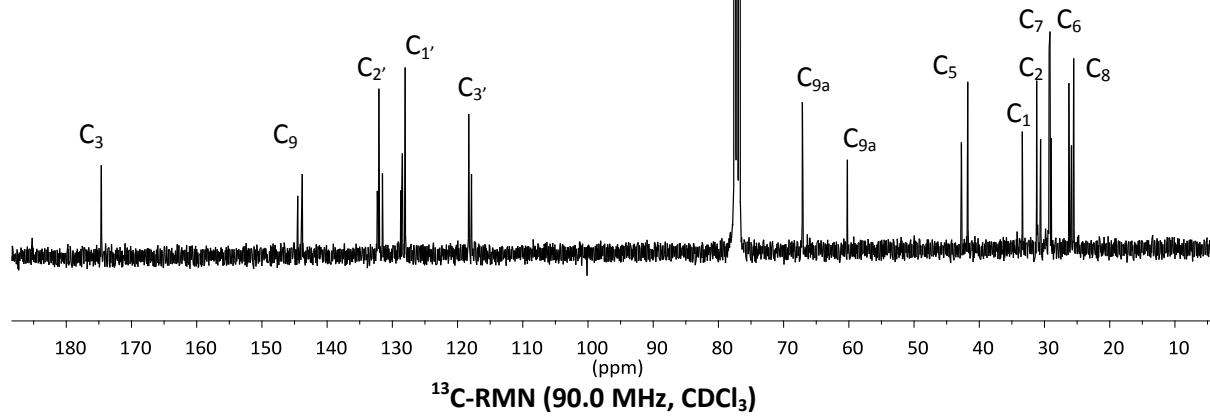
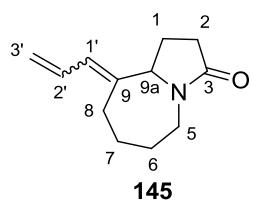
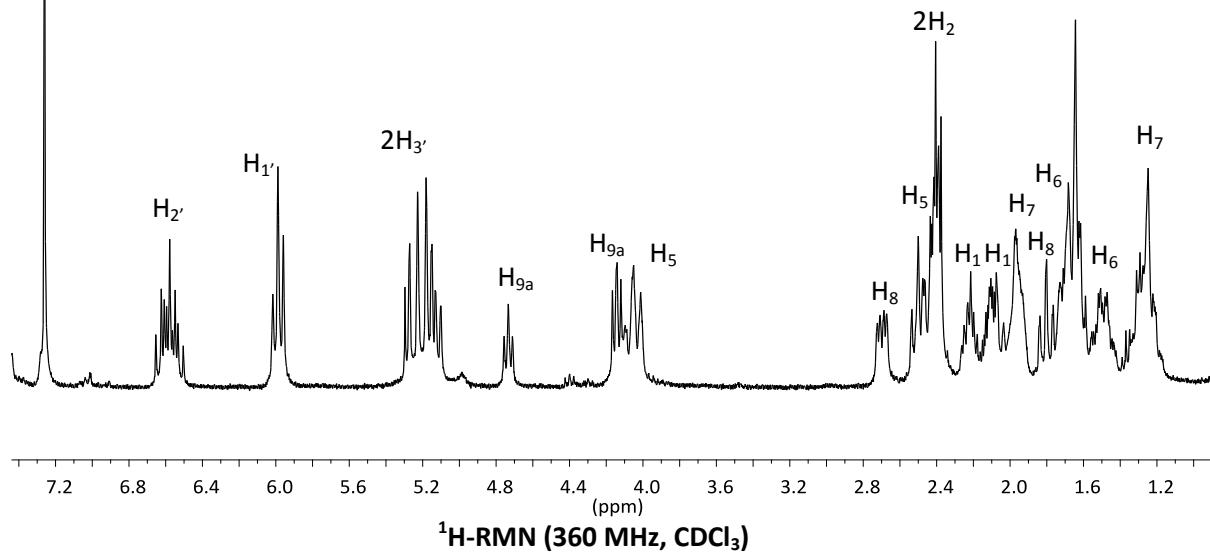
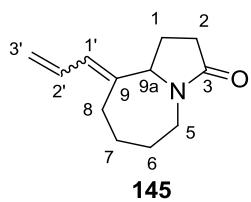
6. RECULL D'ESPECTRES

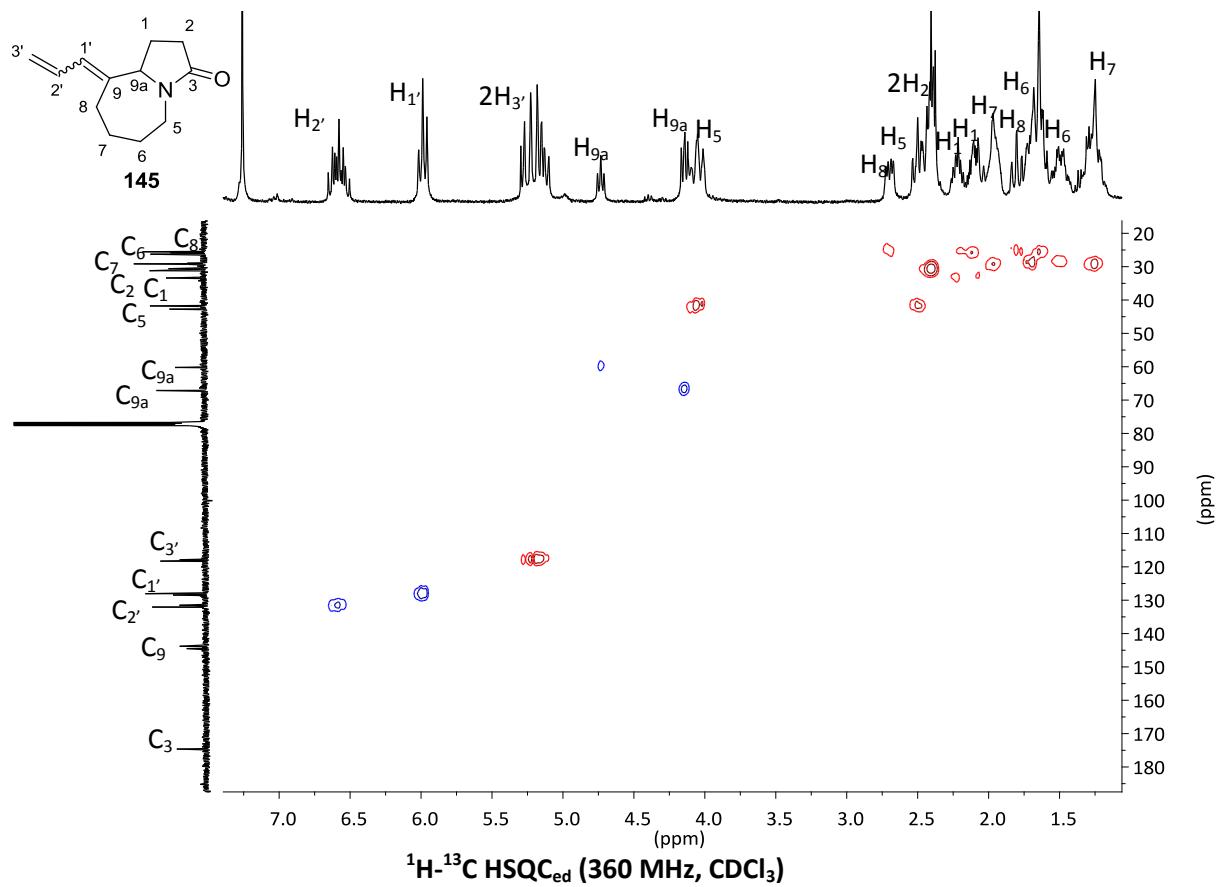
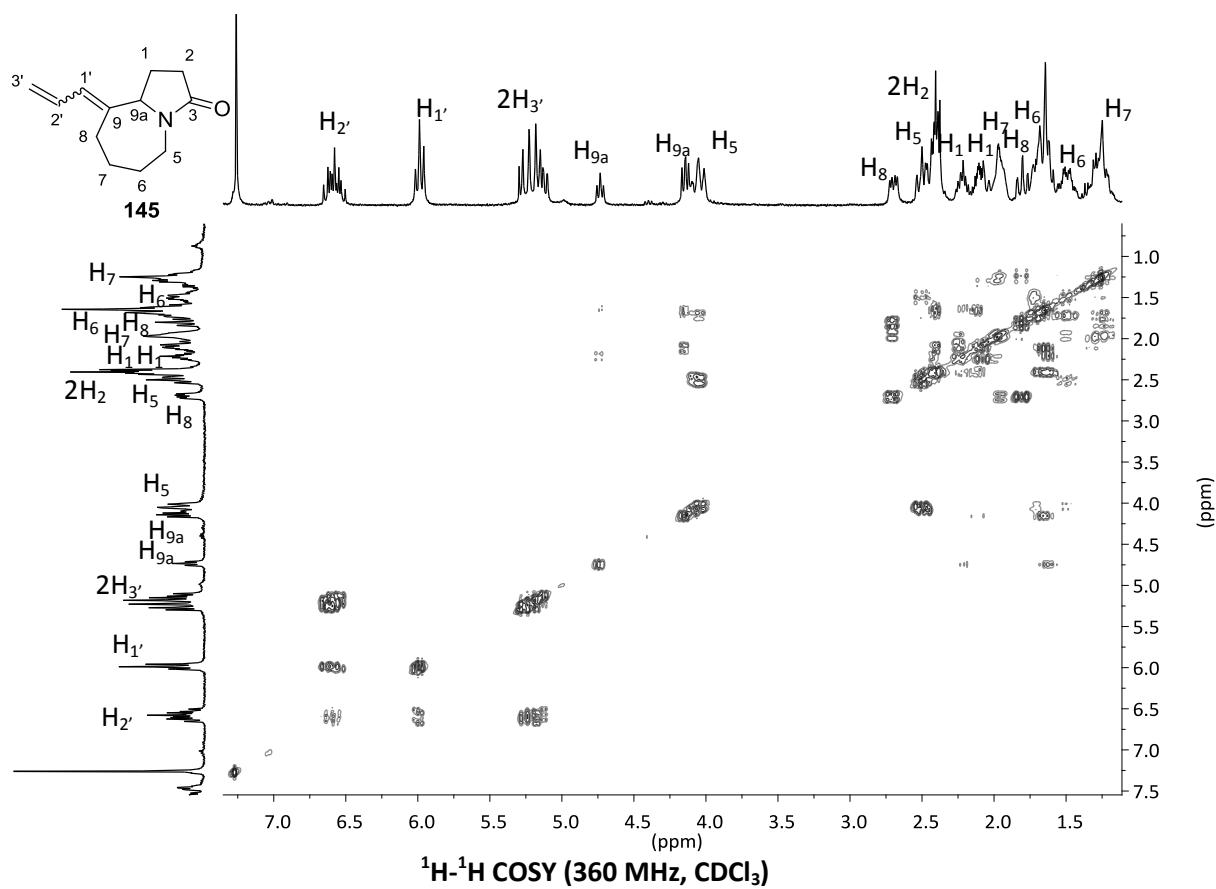


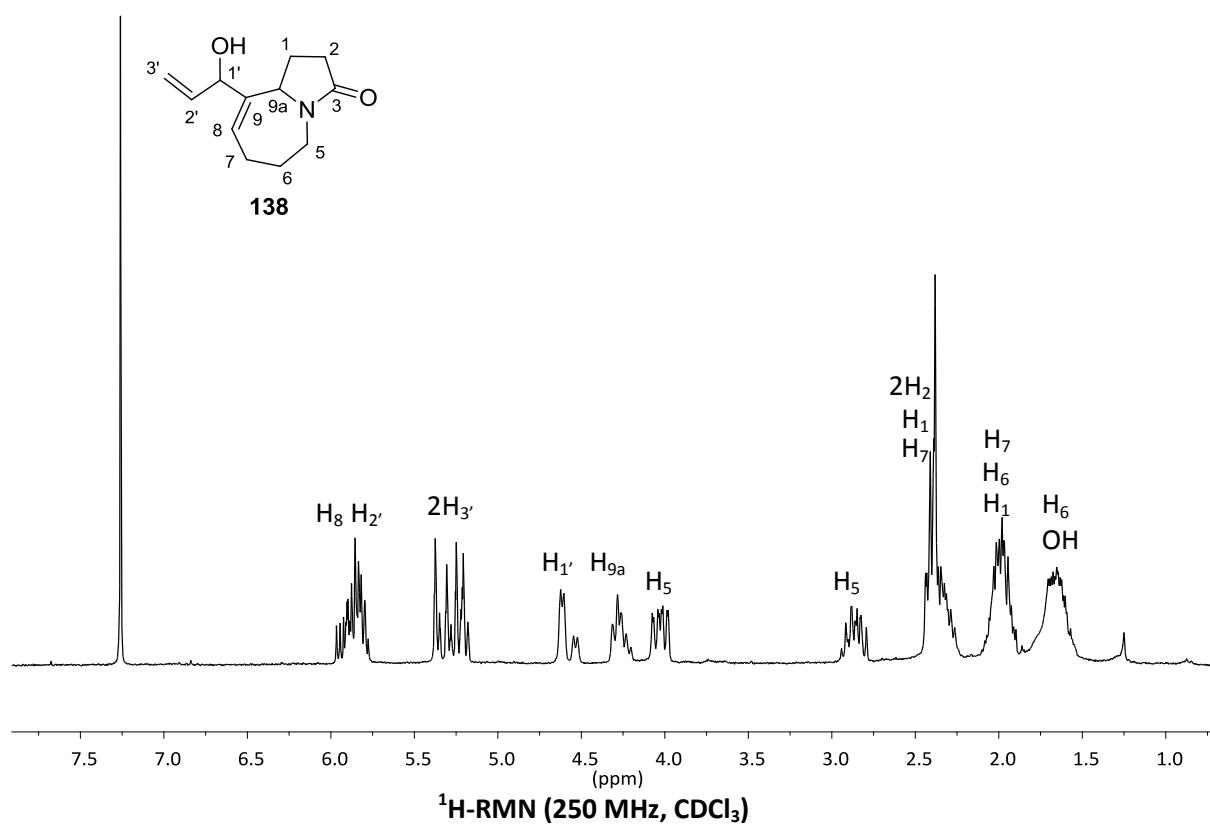
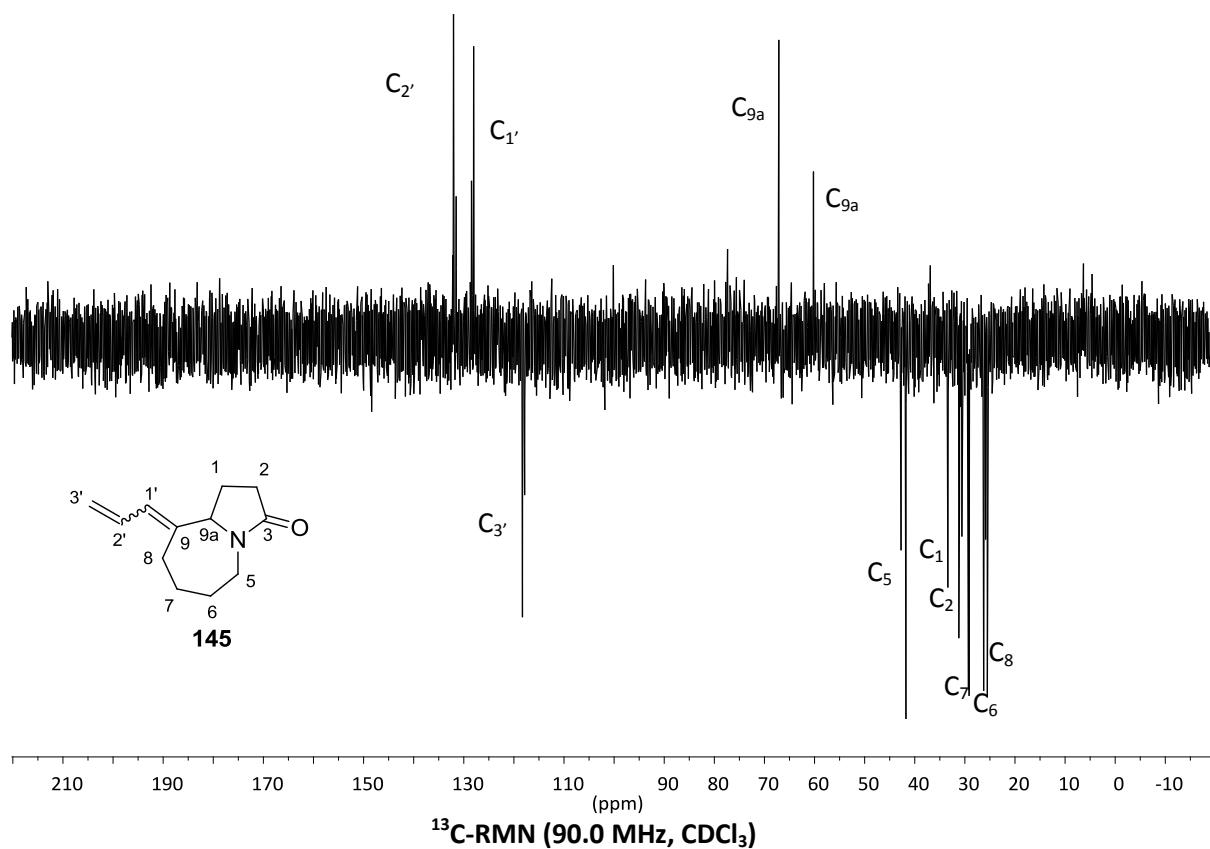


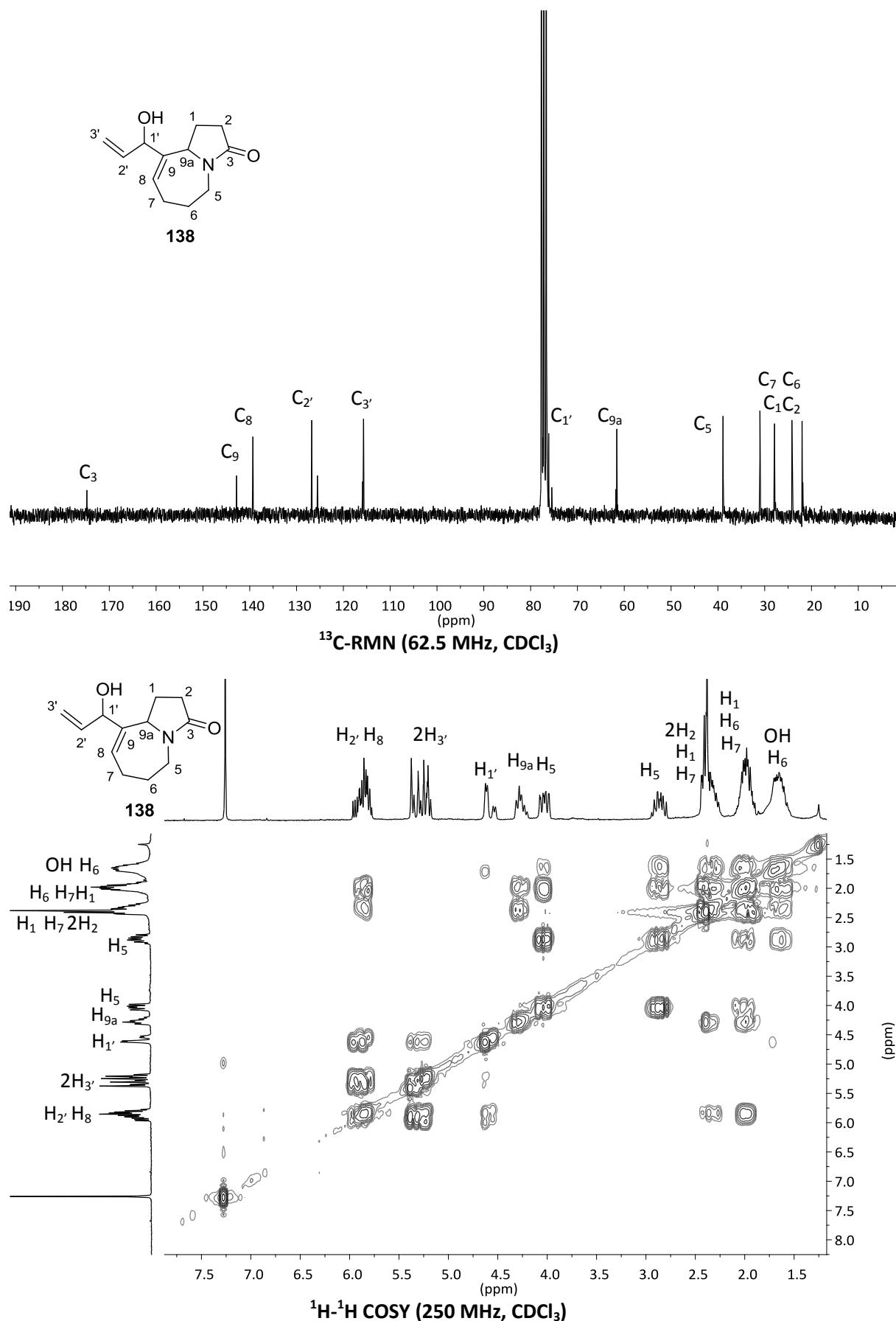




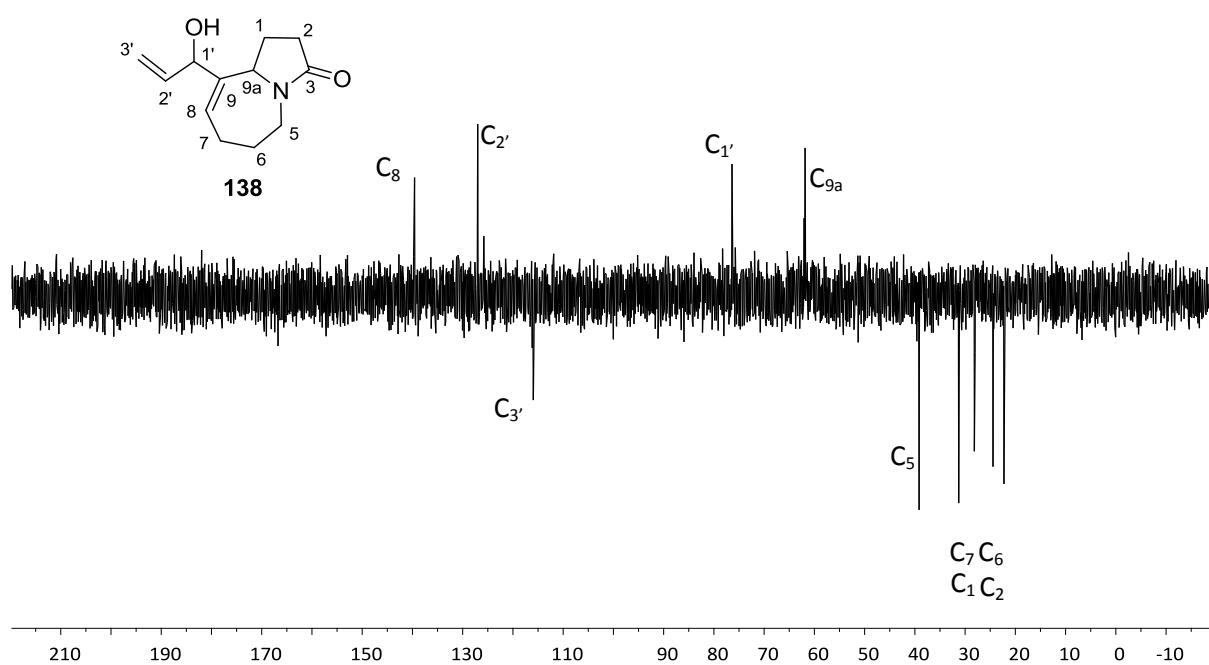
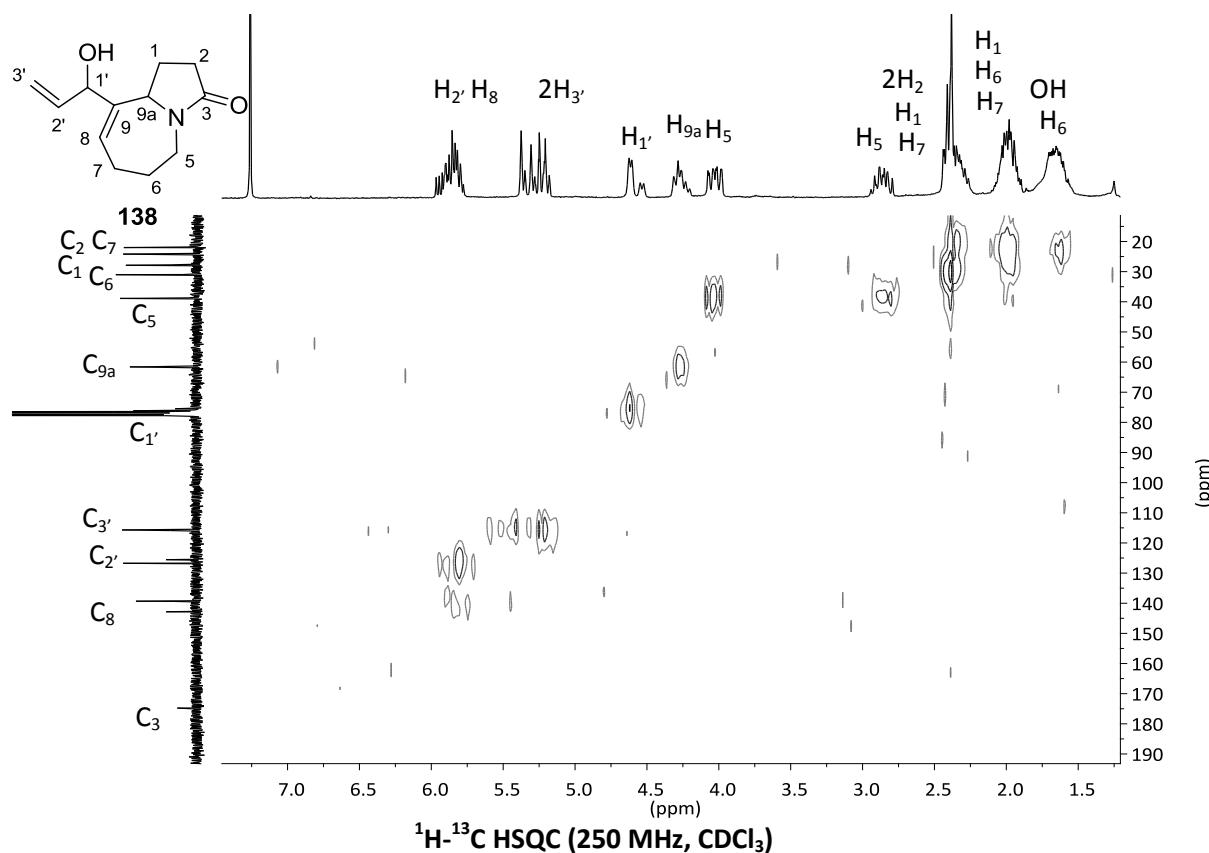


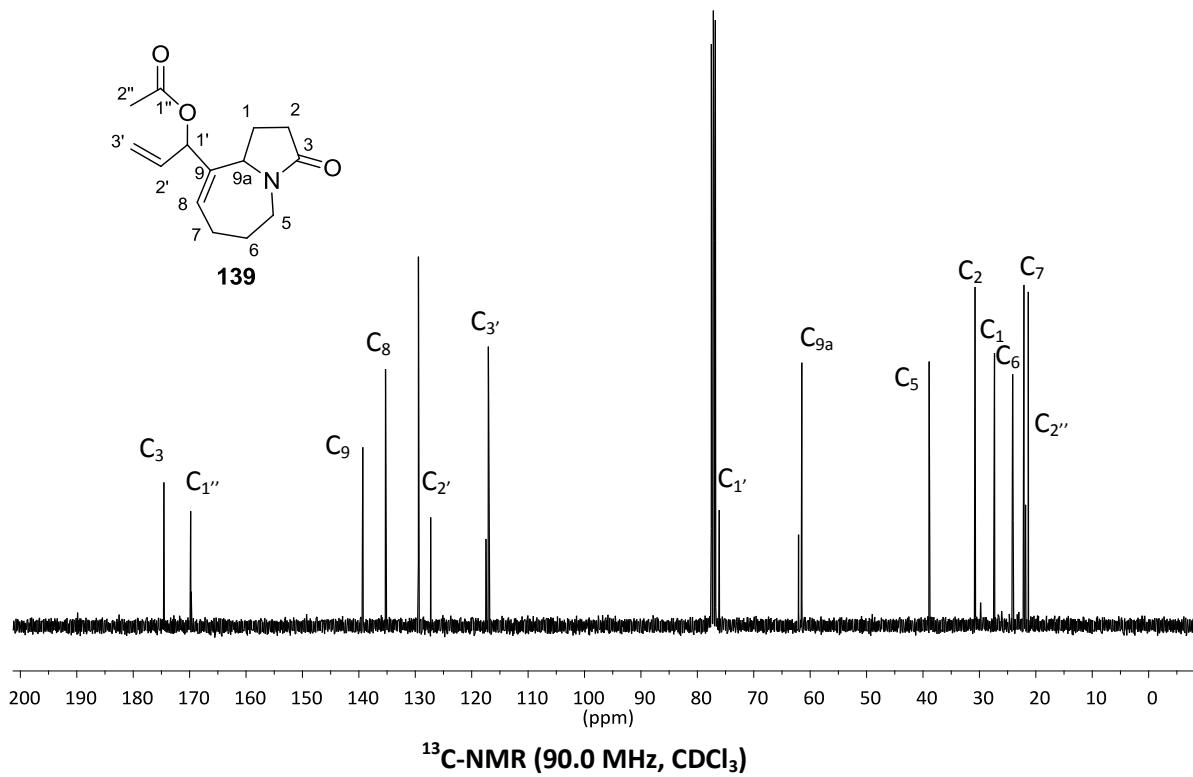
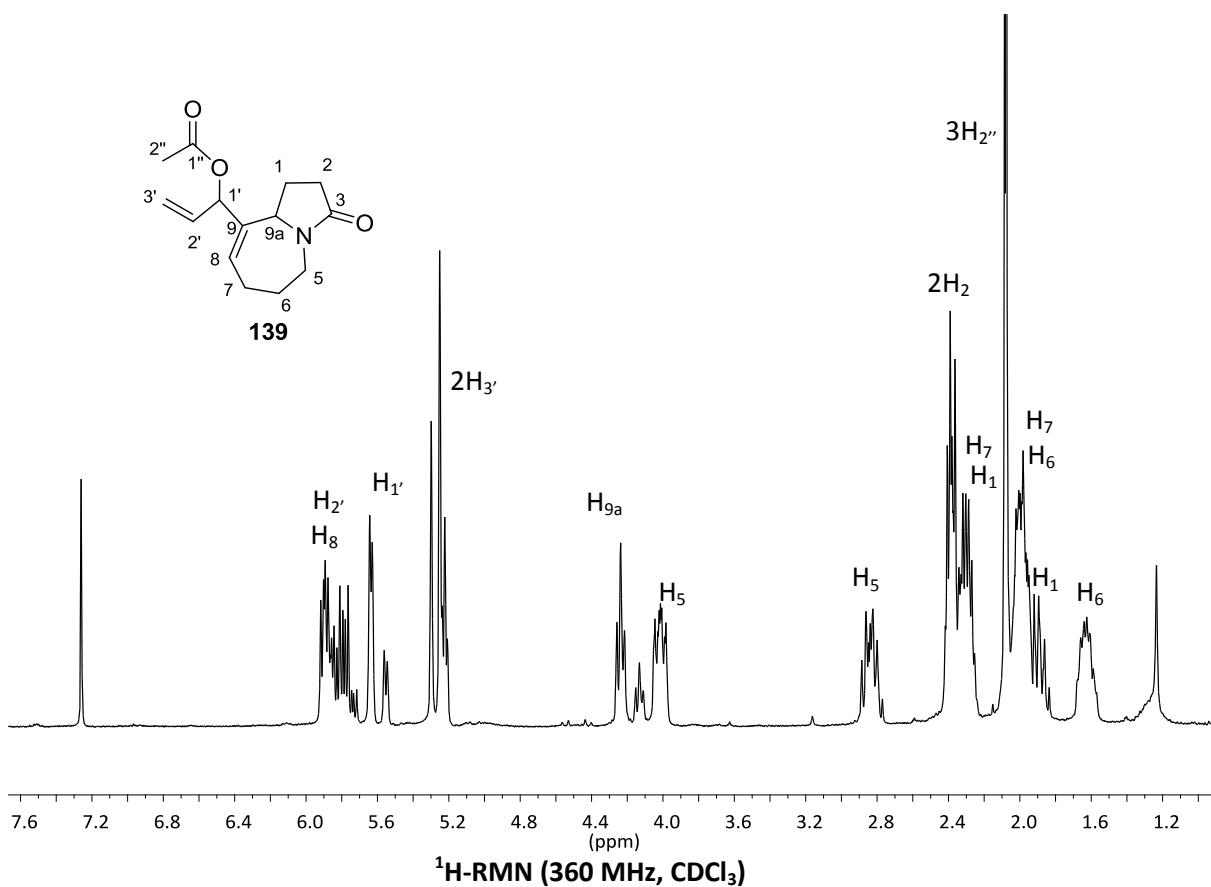




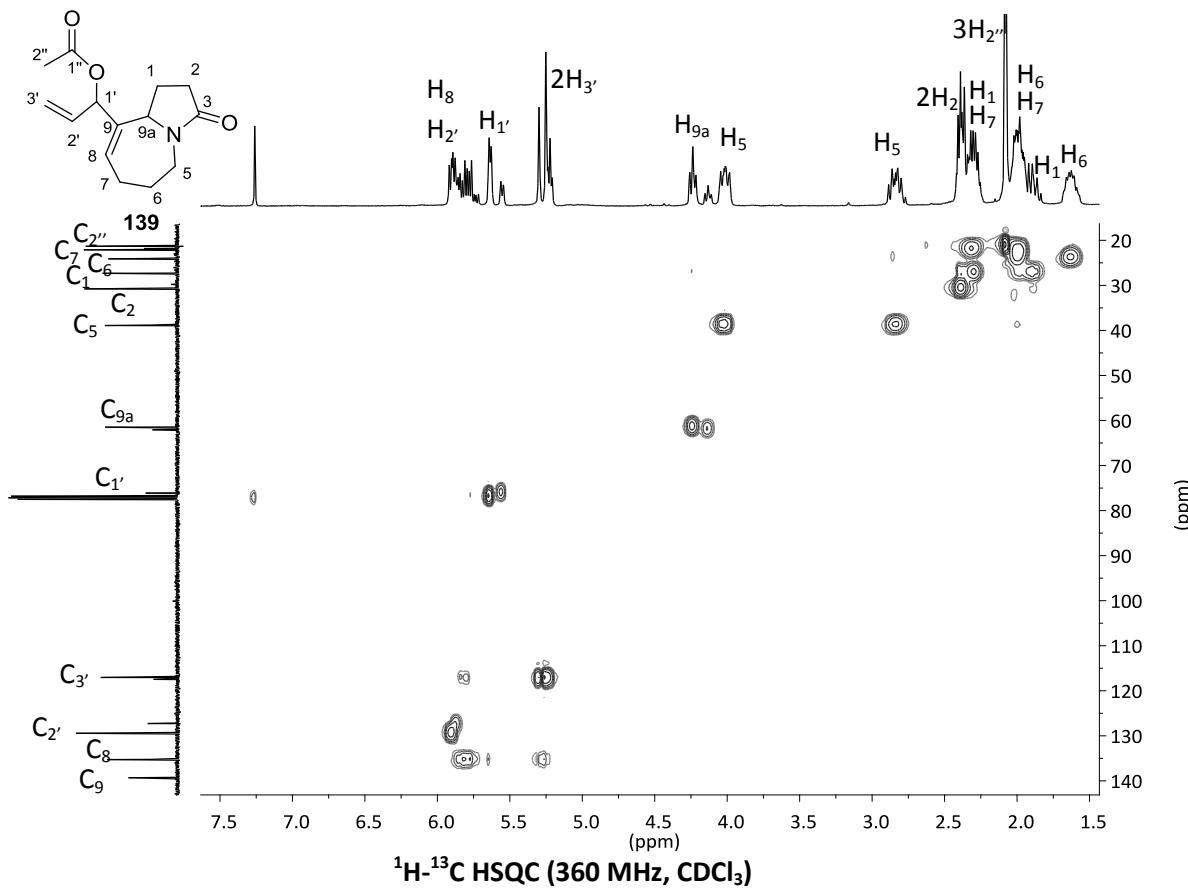
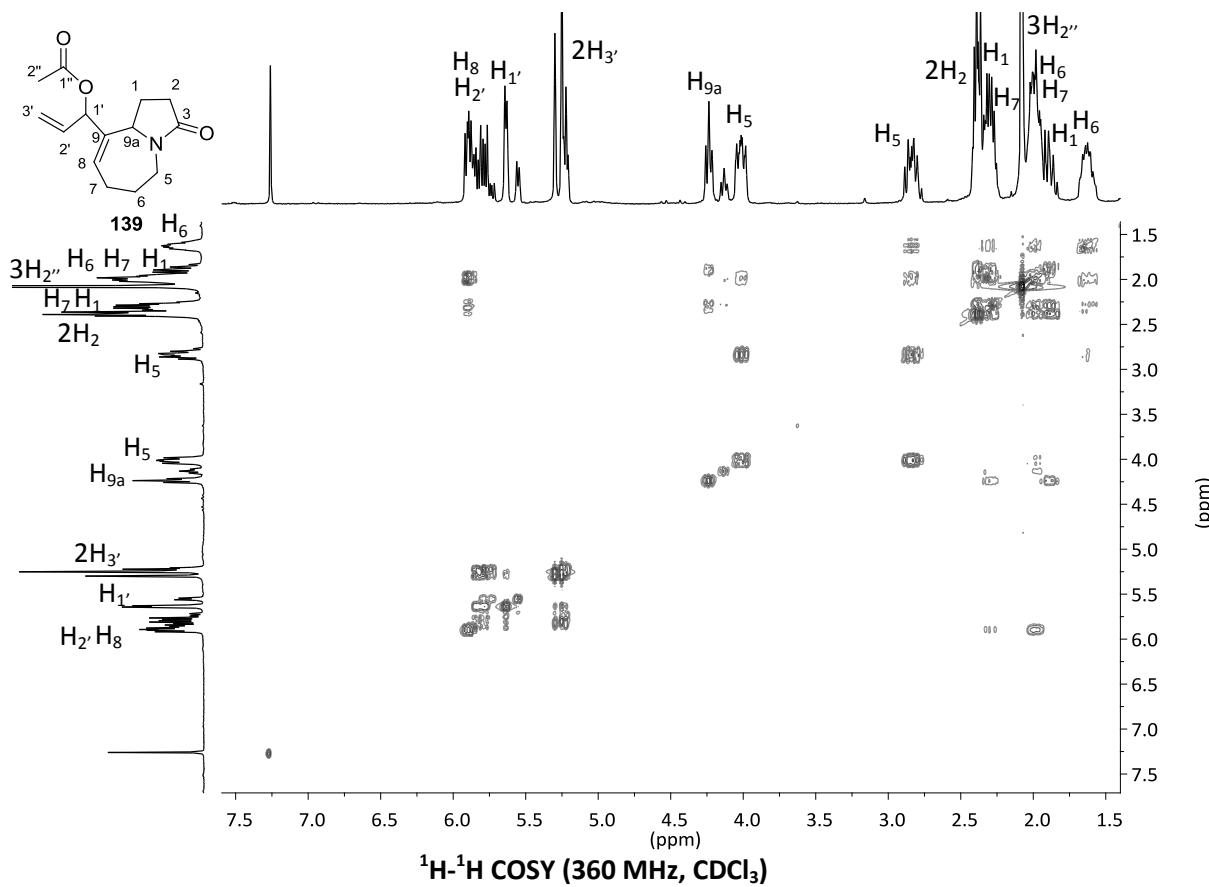


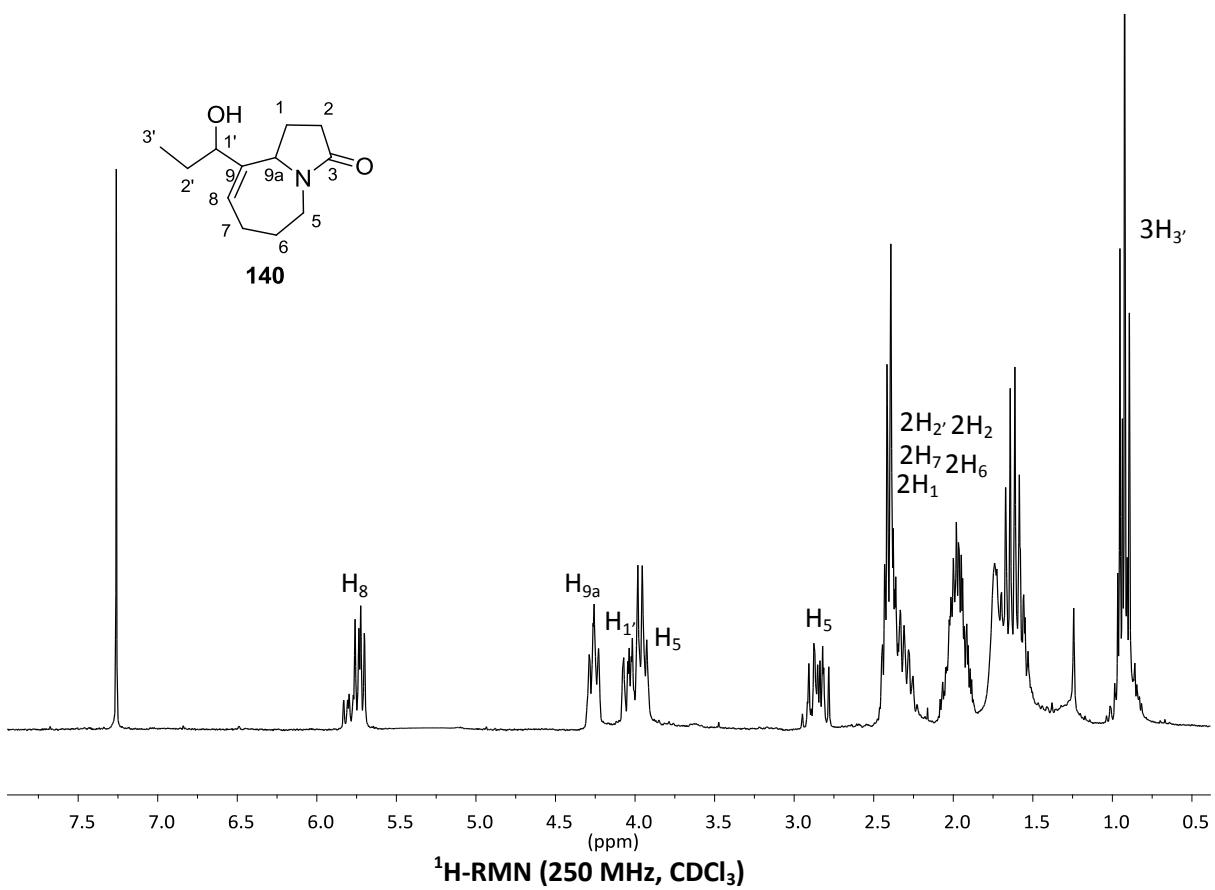
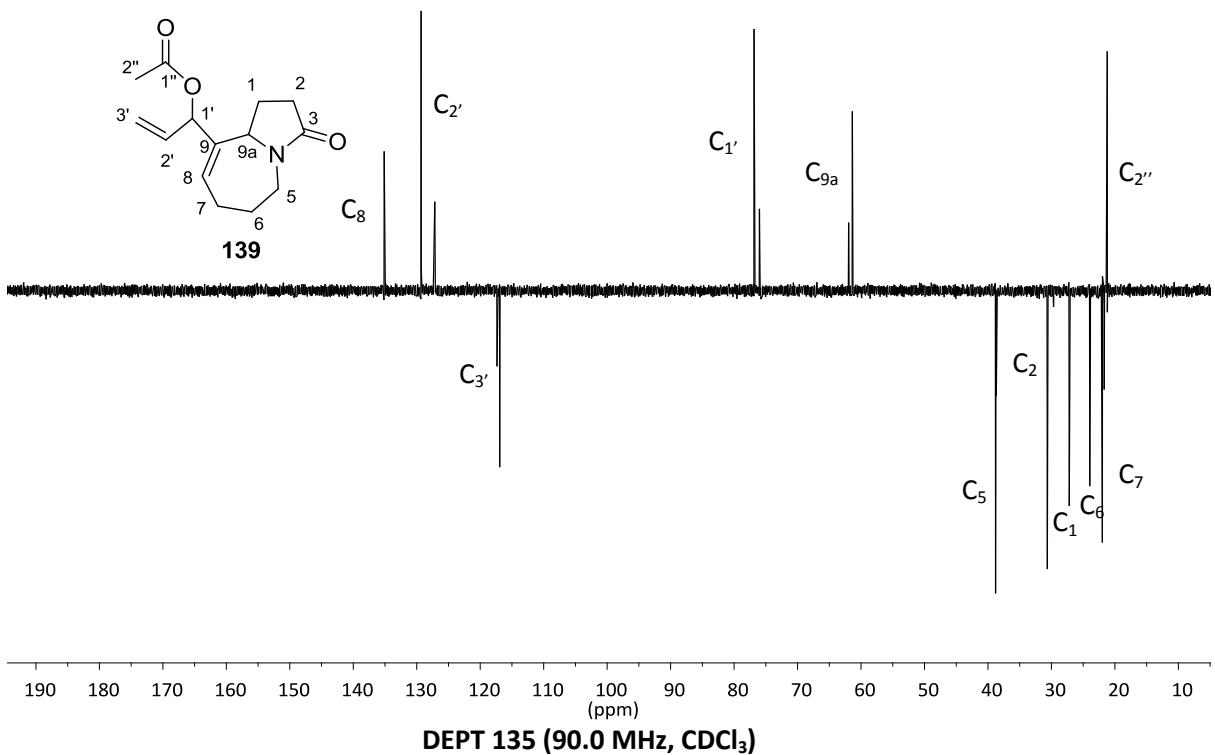
6. RECULL D'ESPECTRES

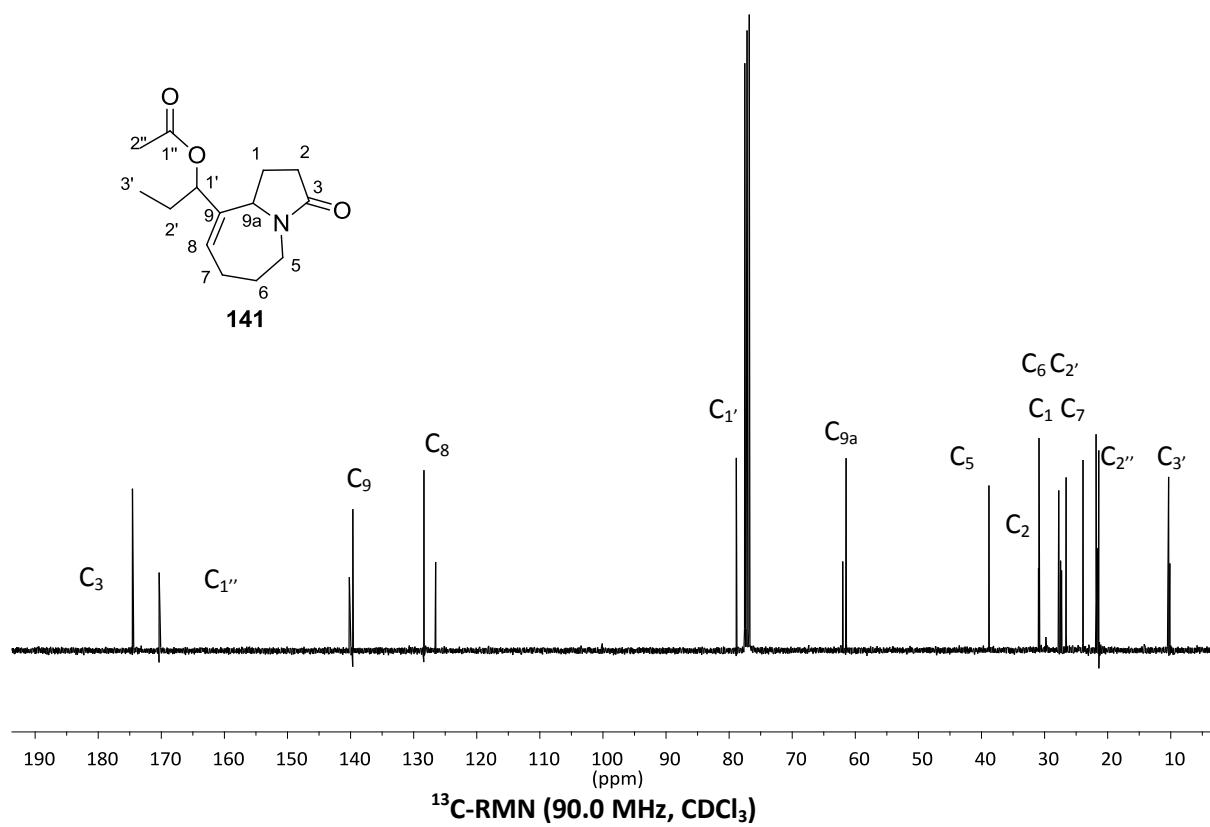
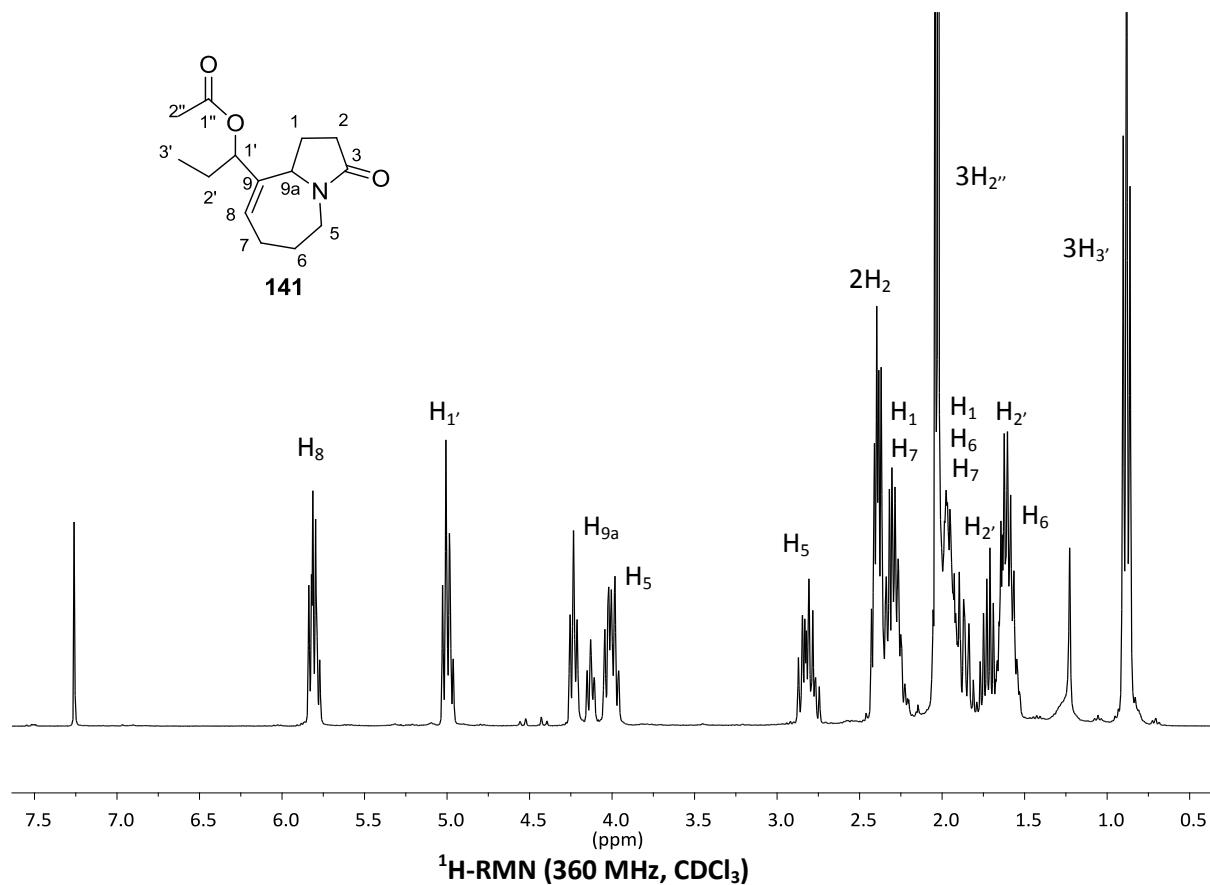


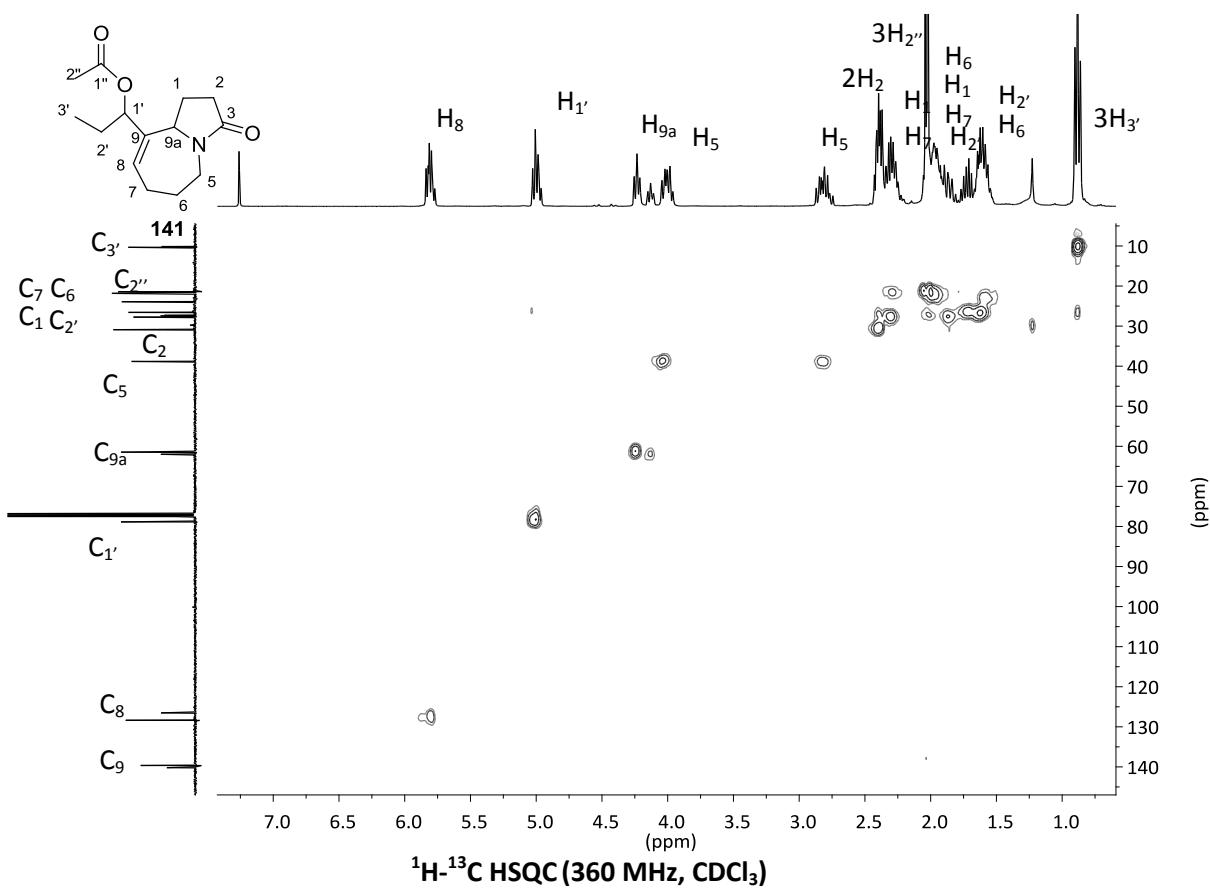
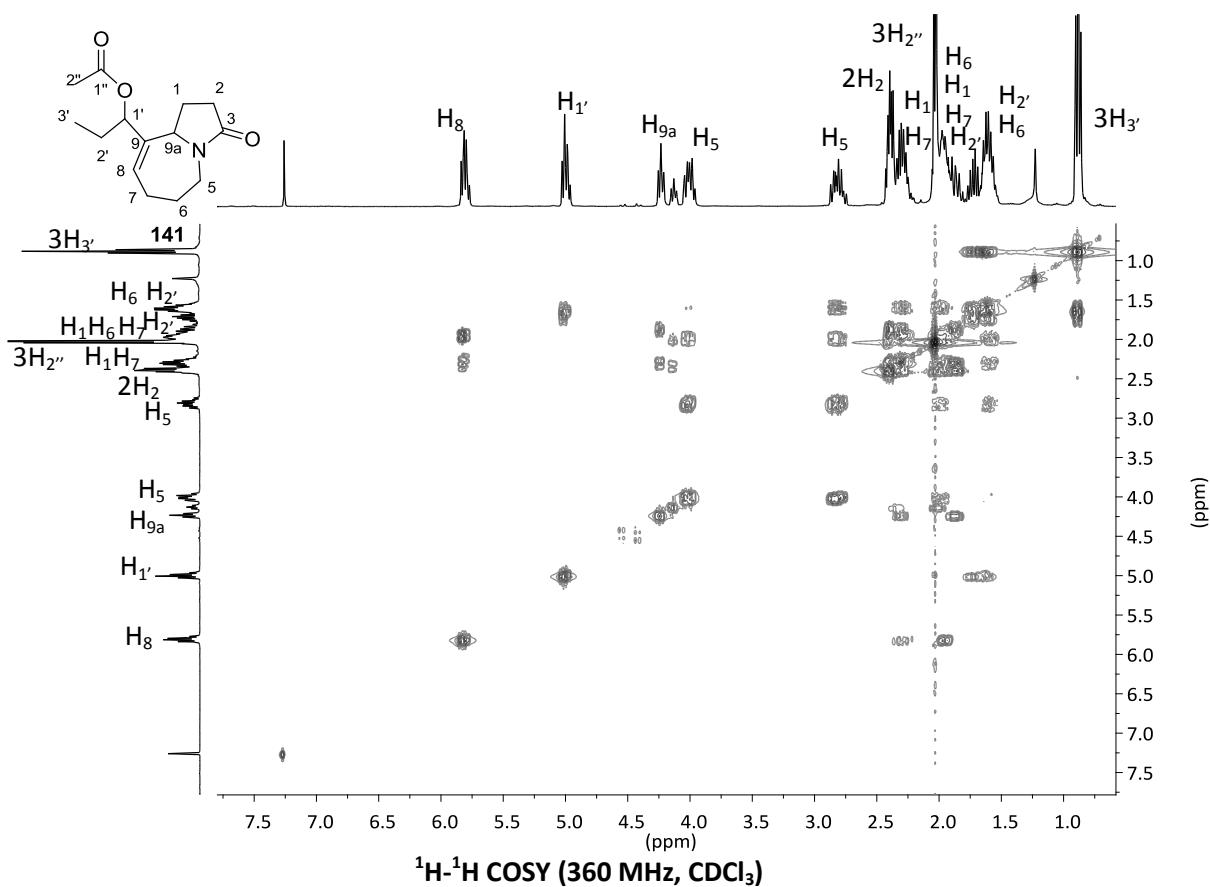


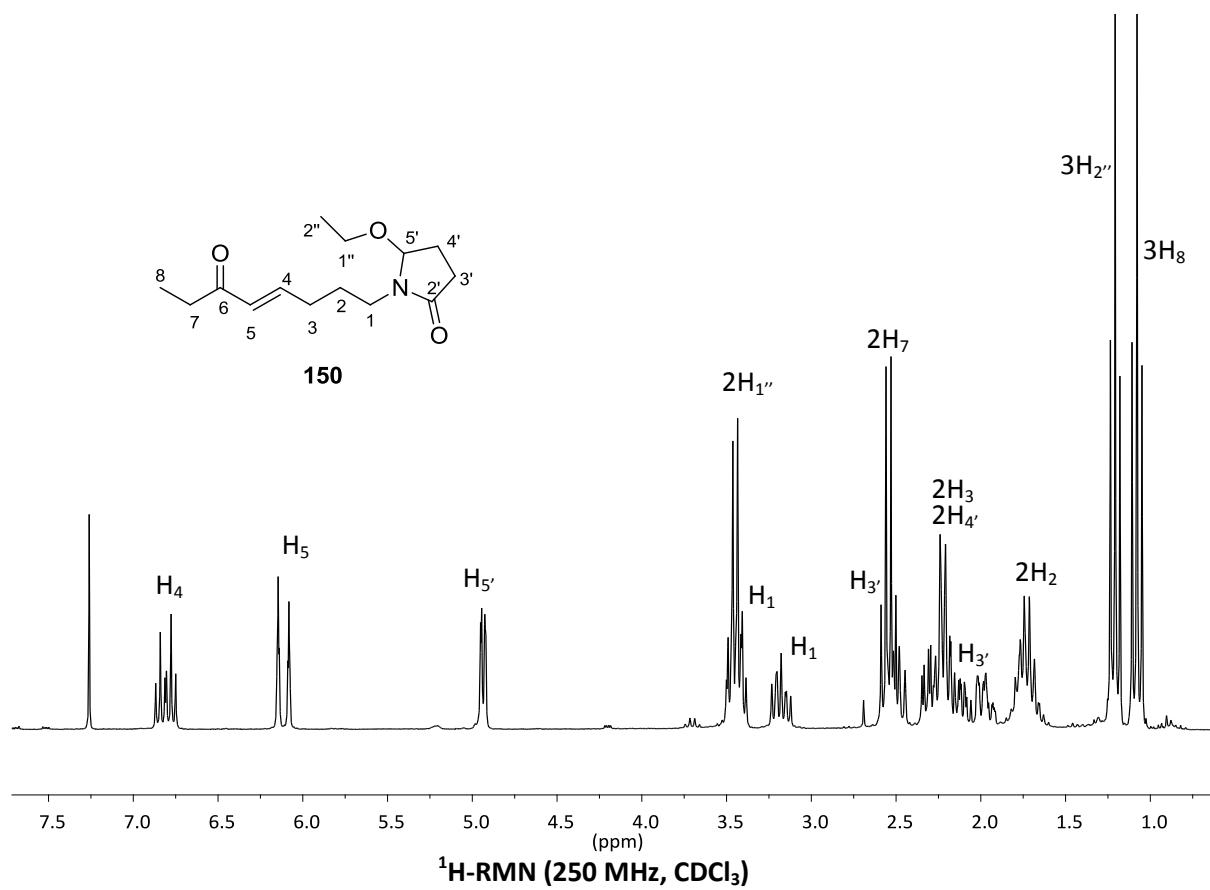
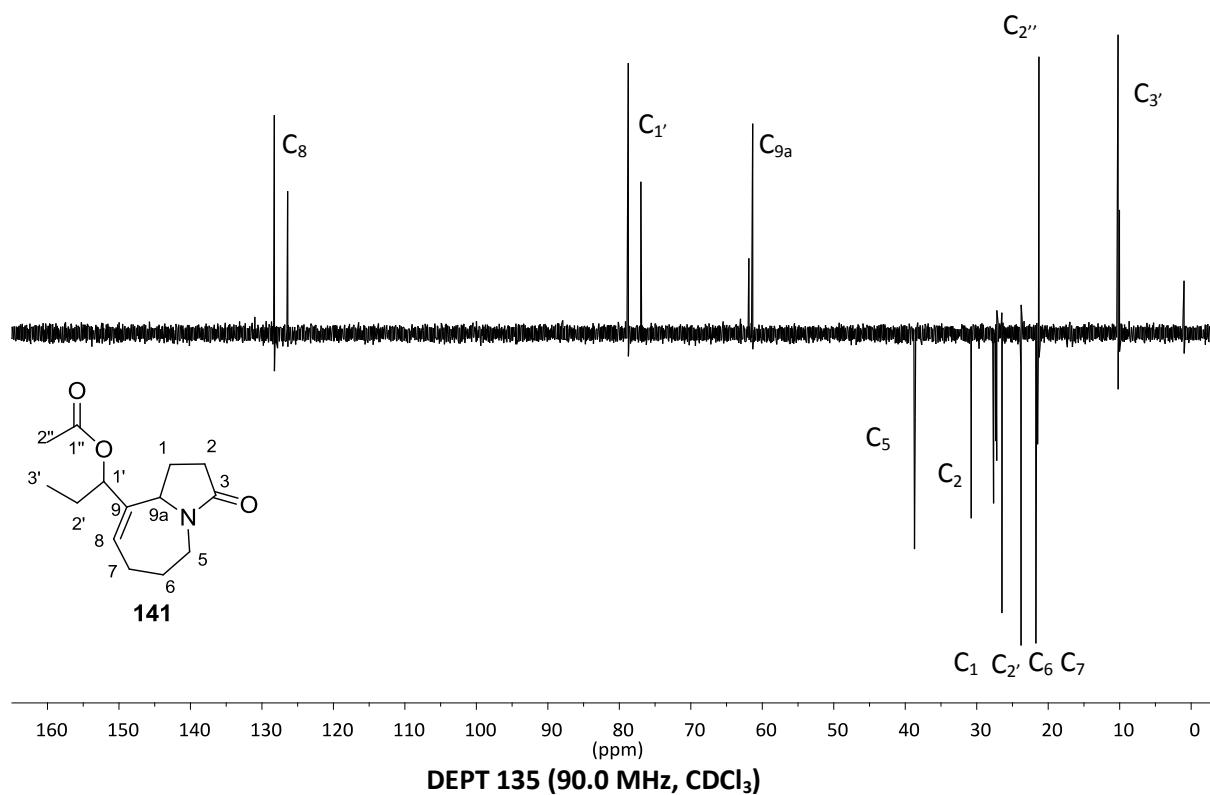
6. RECULL D'ESPECTRES

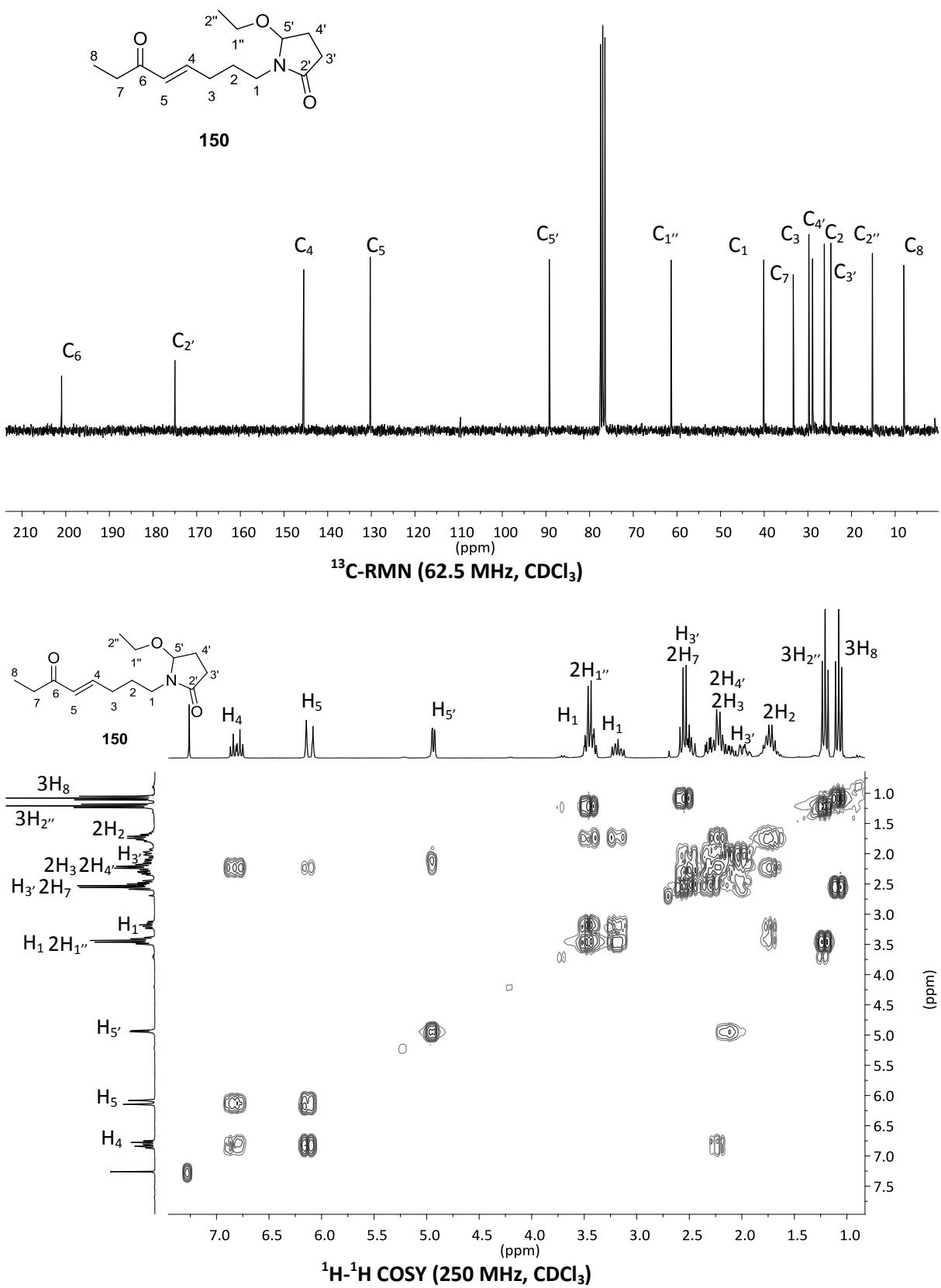




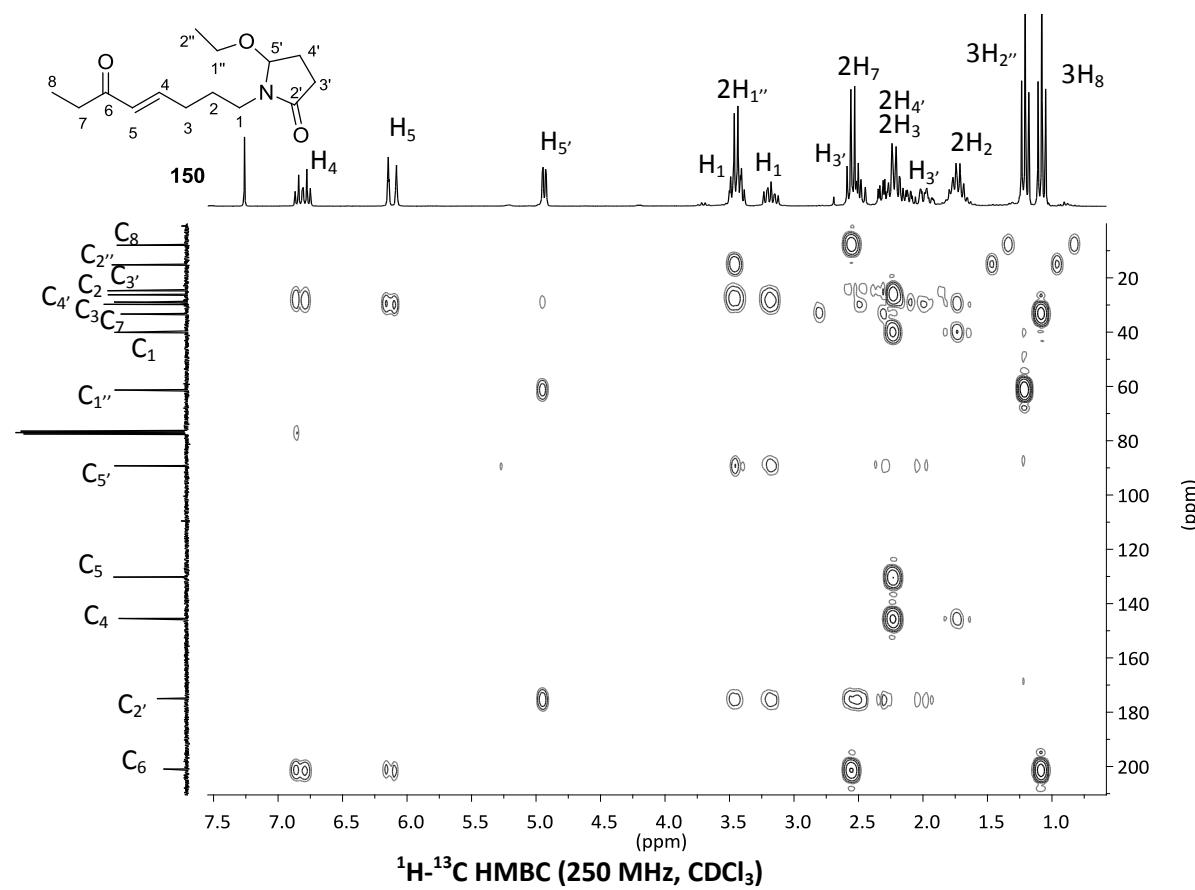
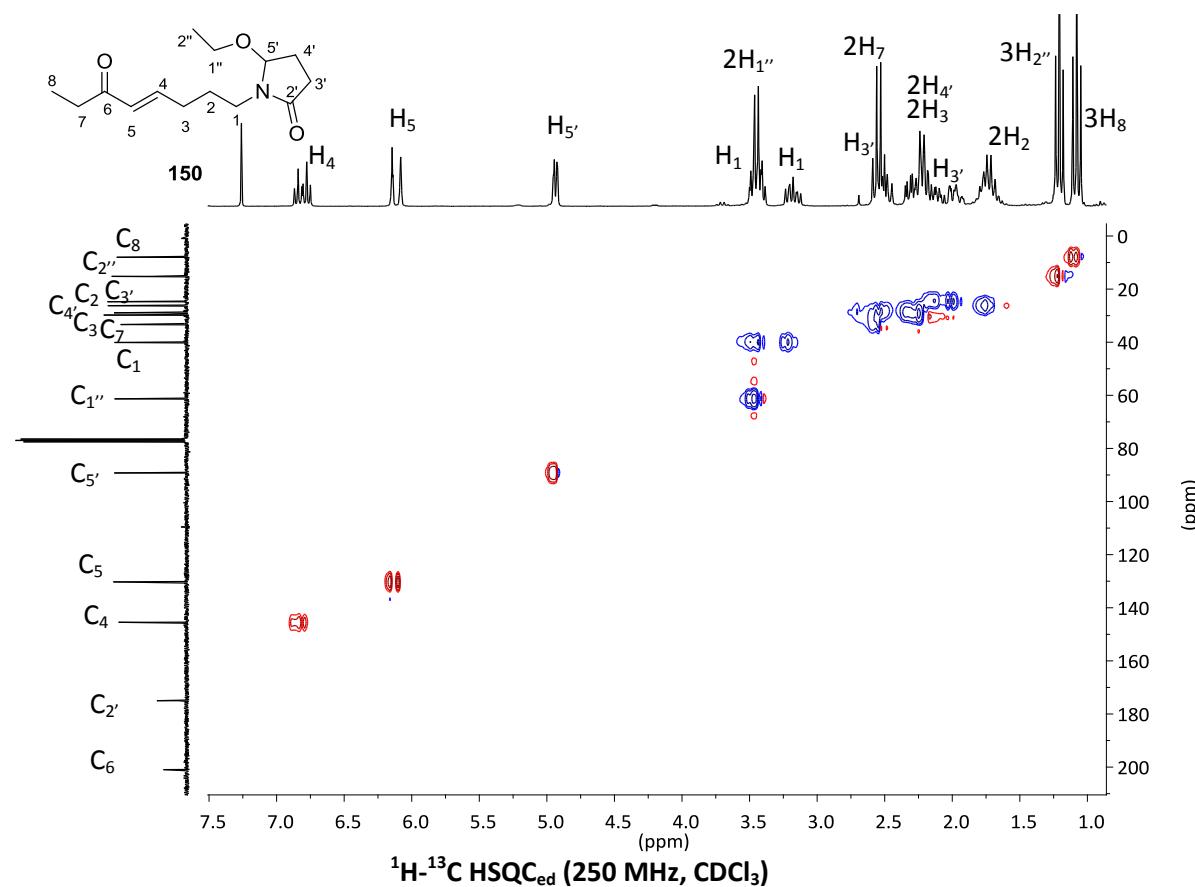


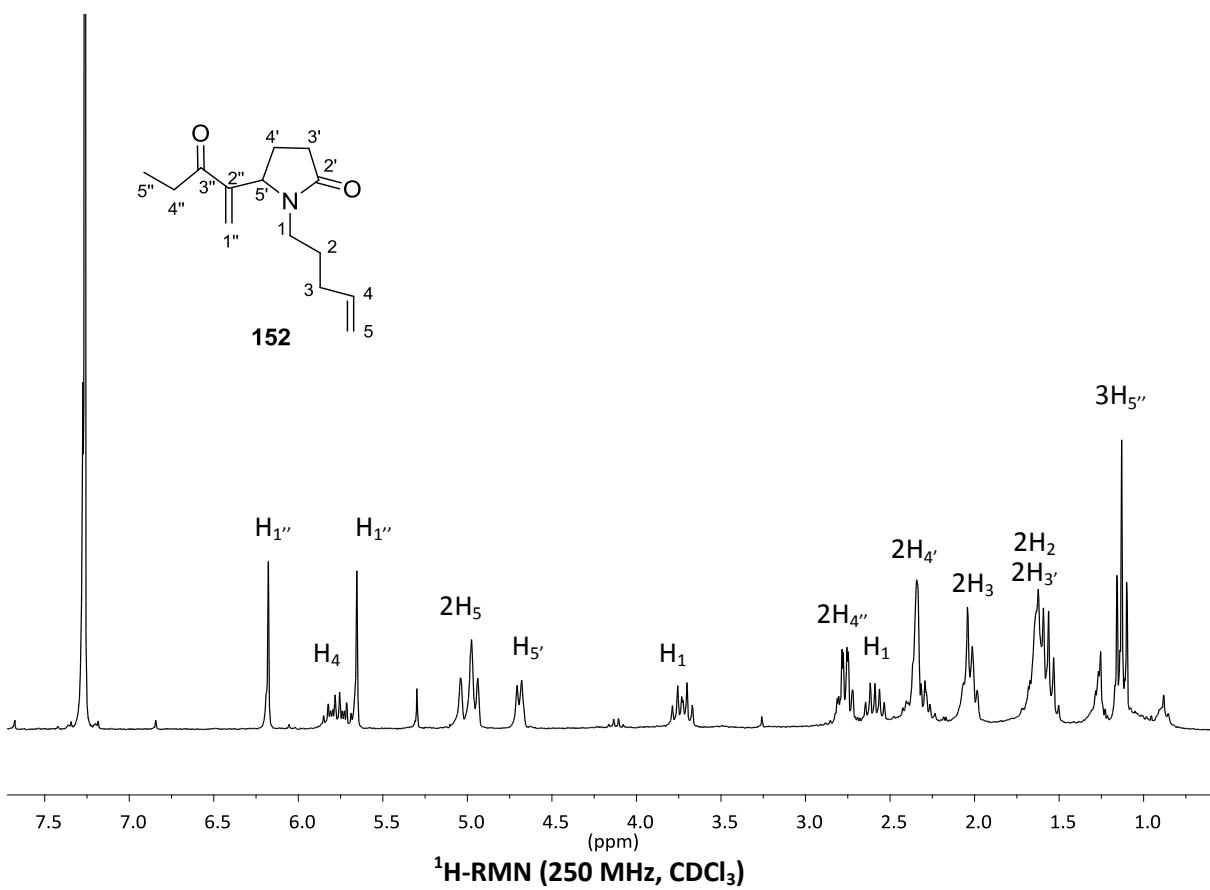
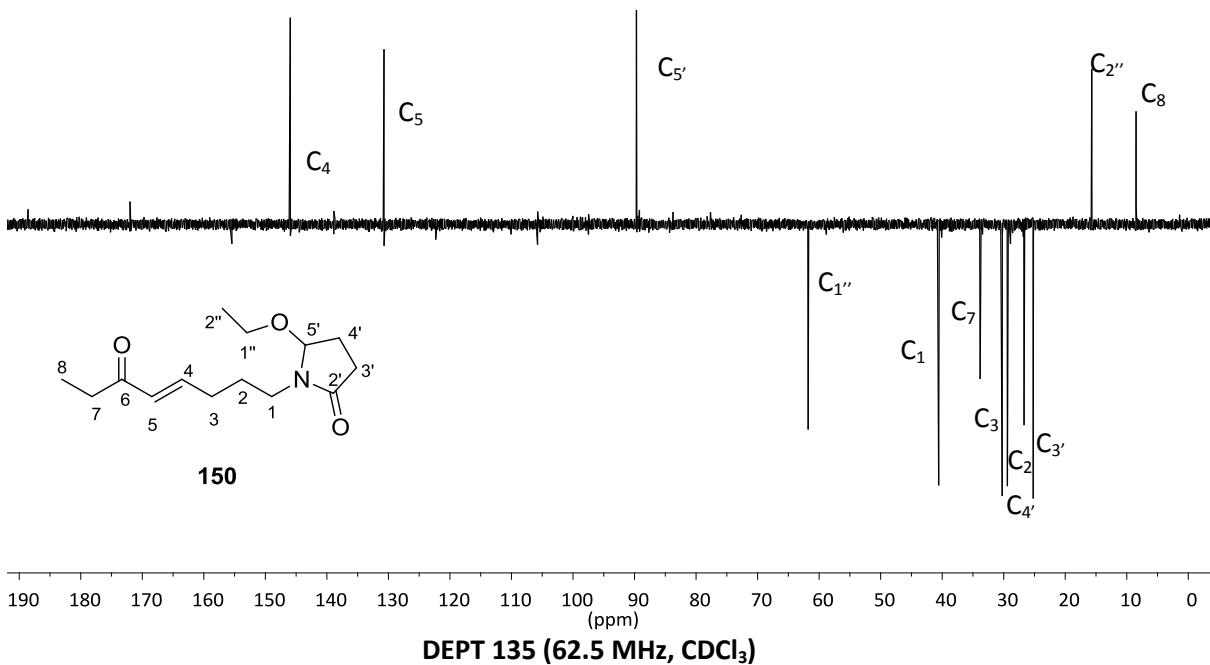


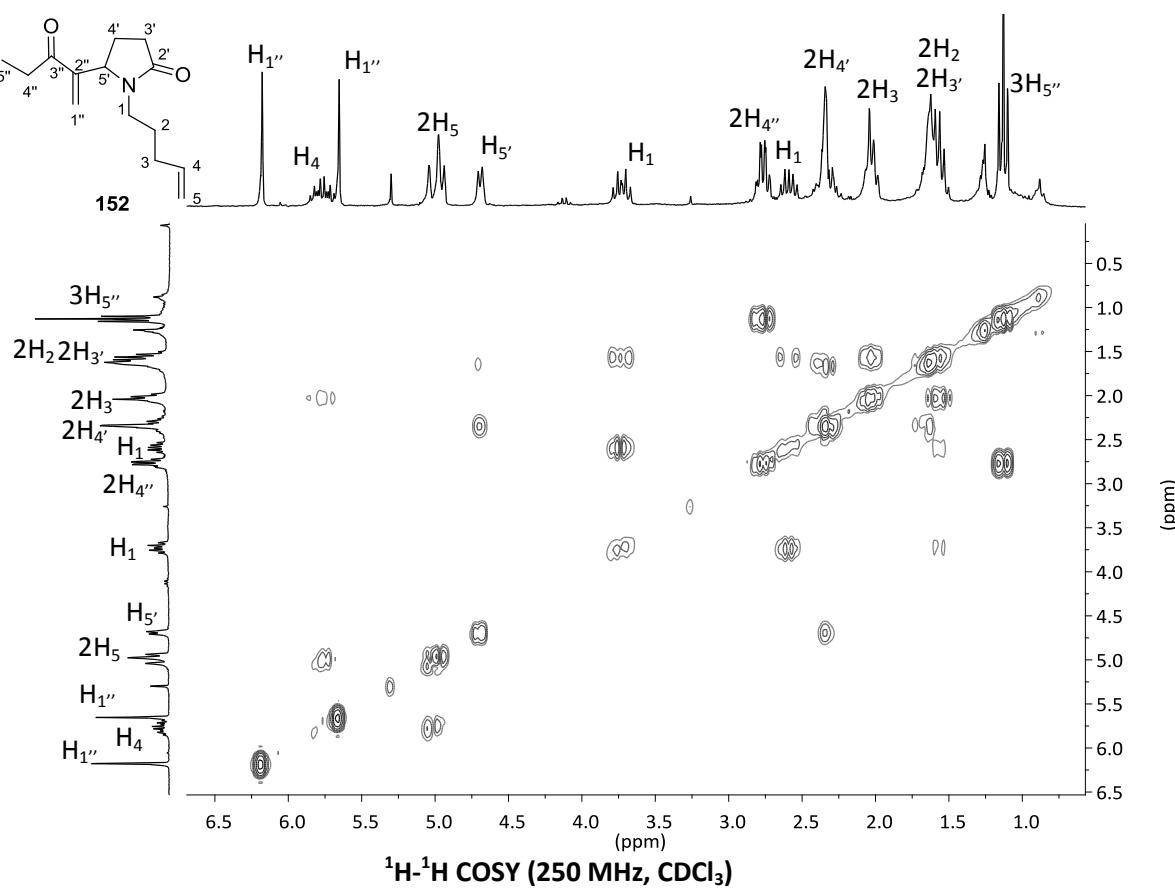
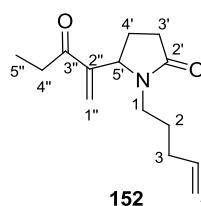
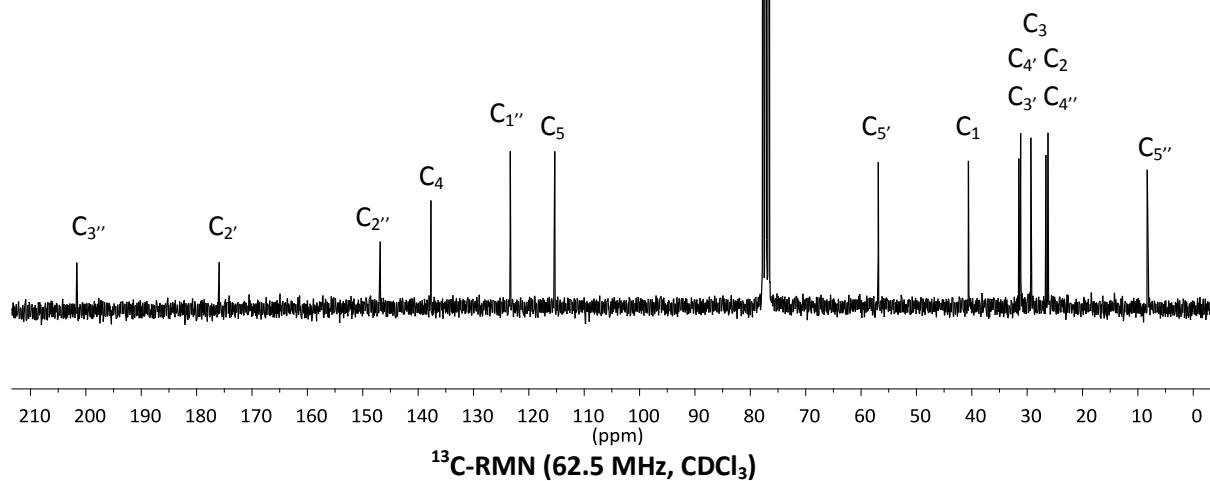
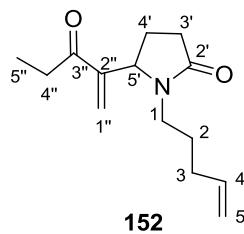


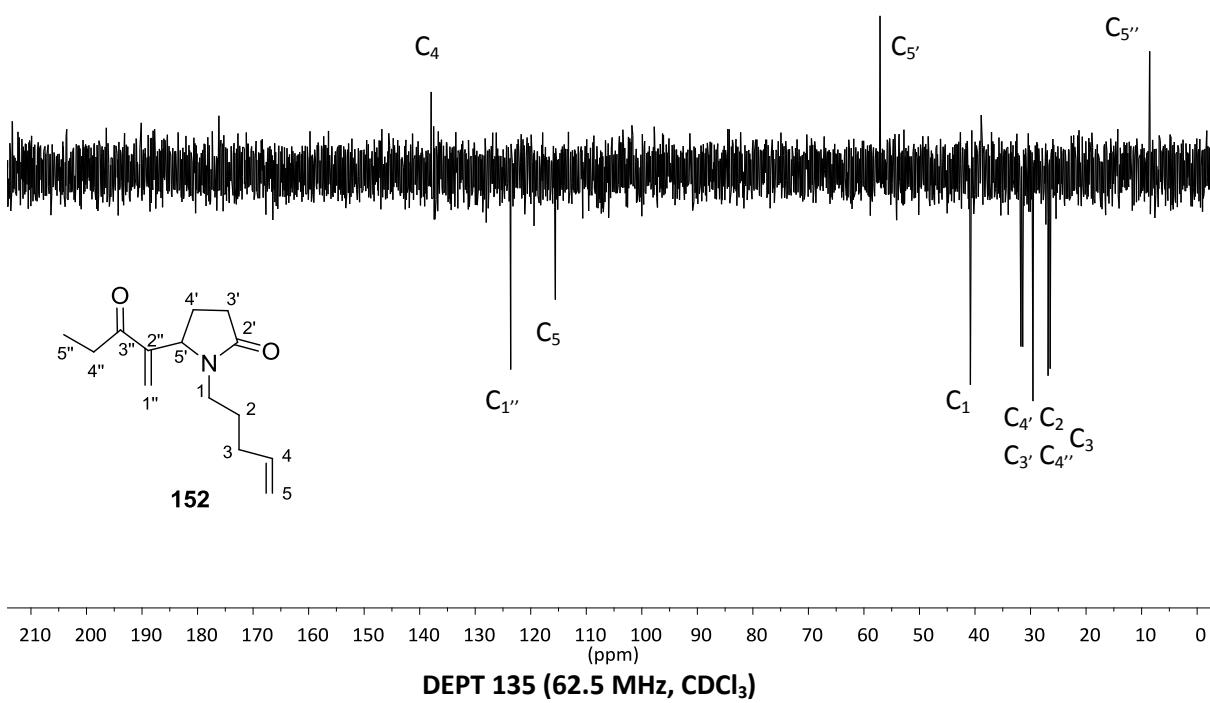
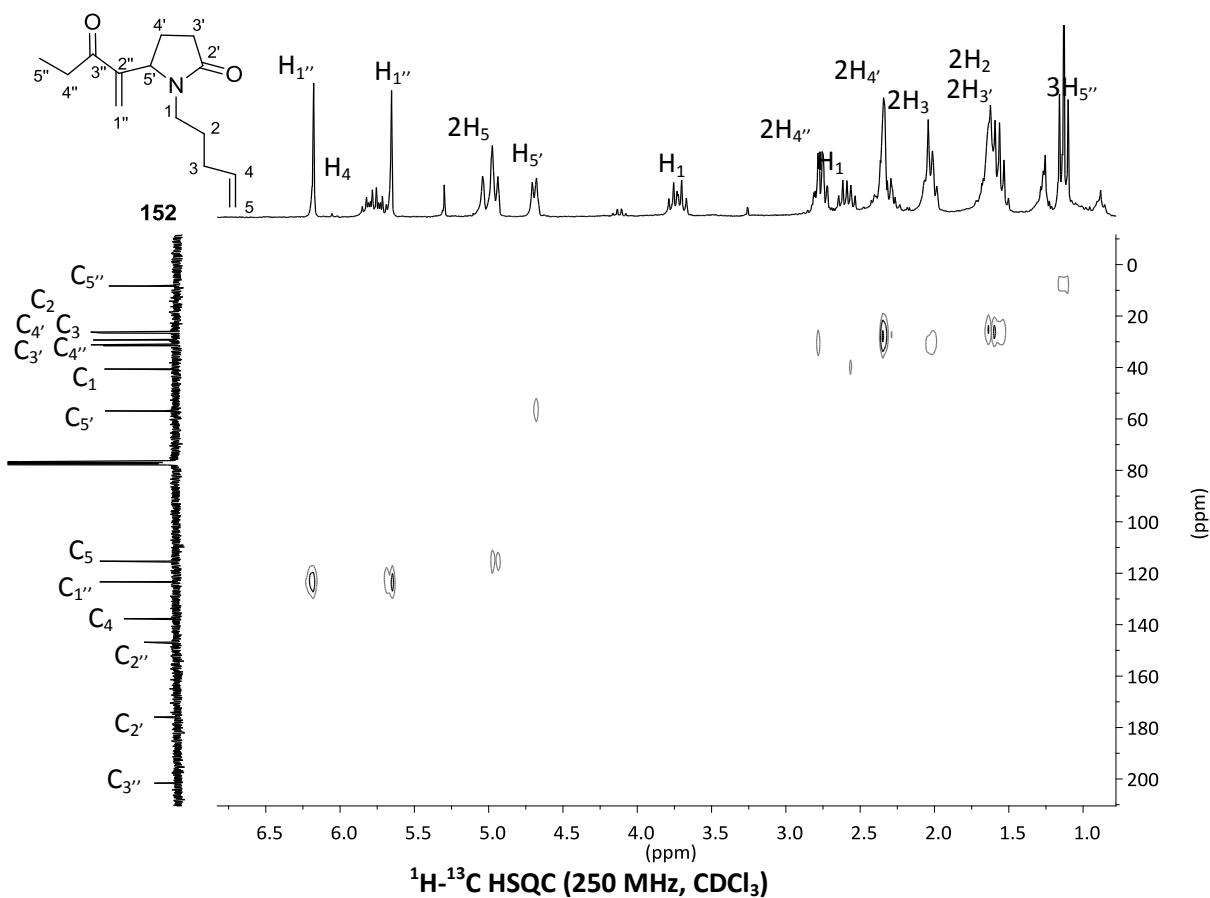


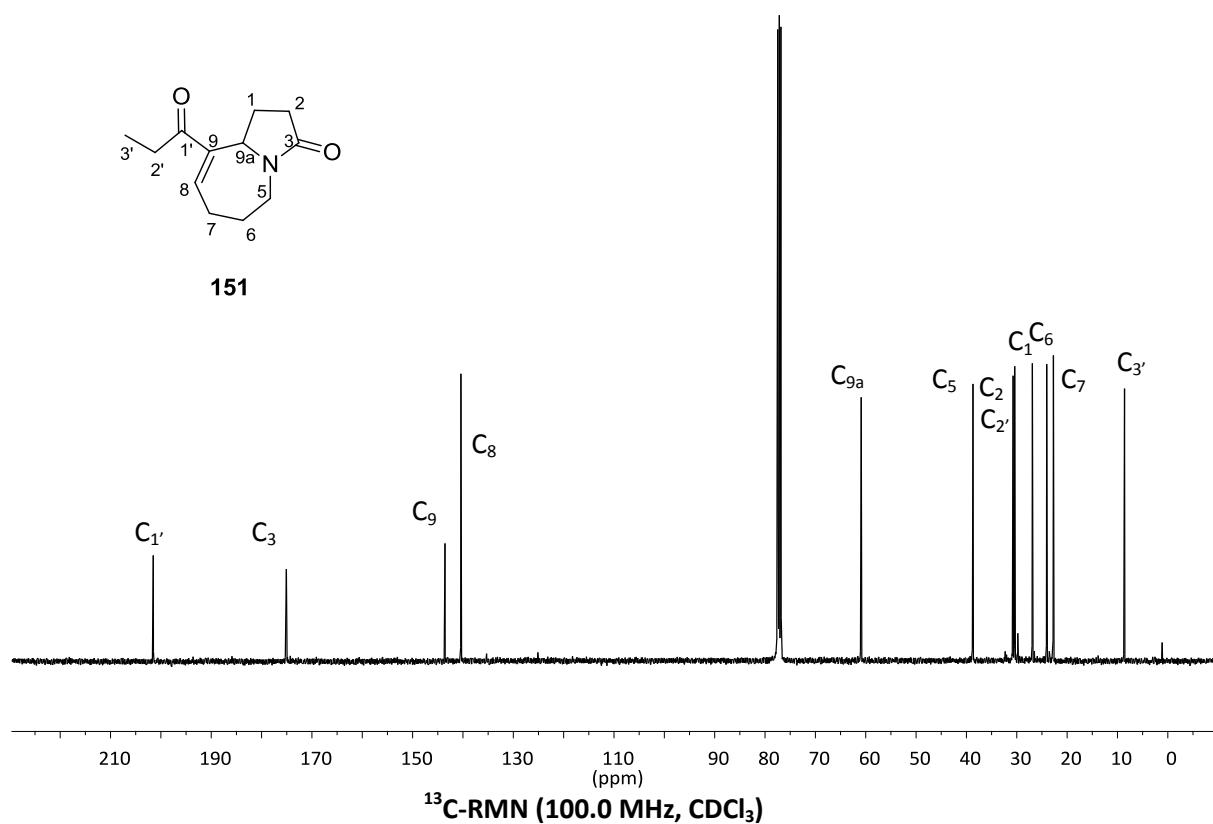
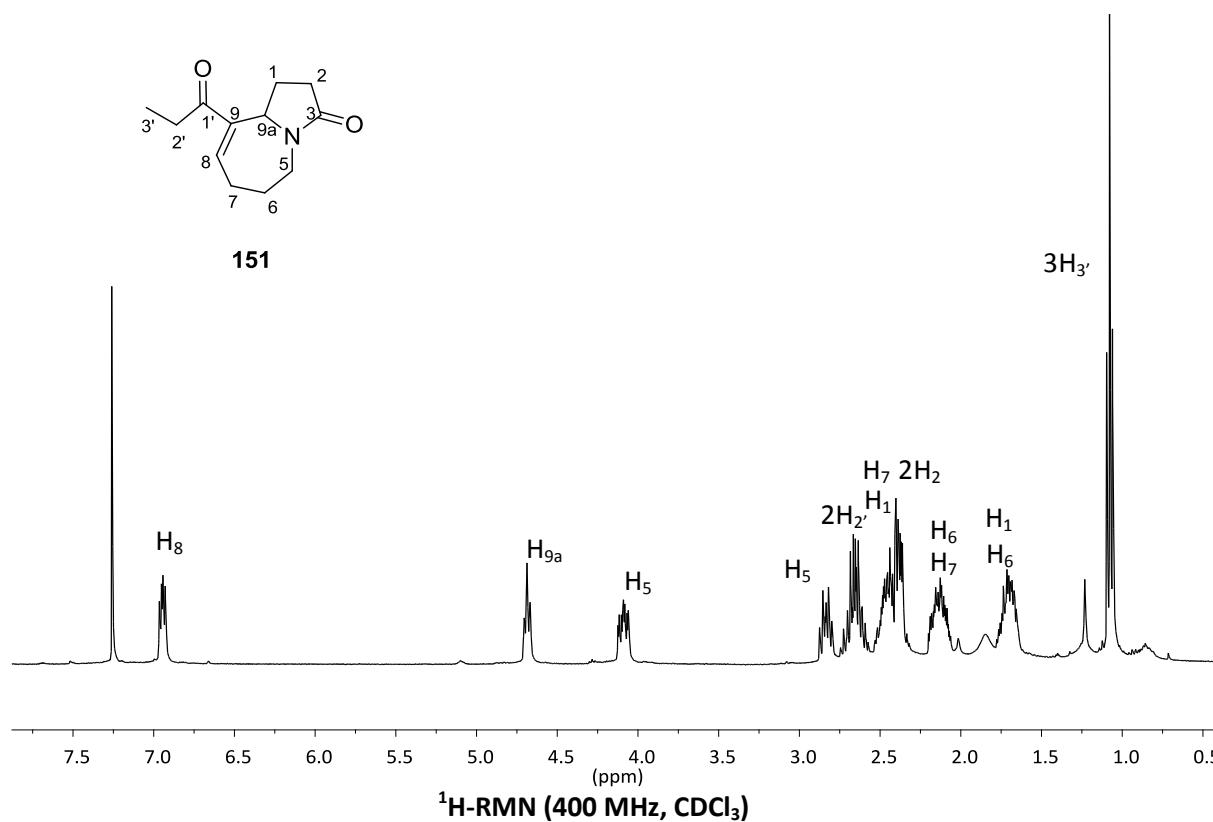
6. RECULL D'ESPECTRES

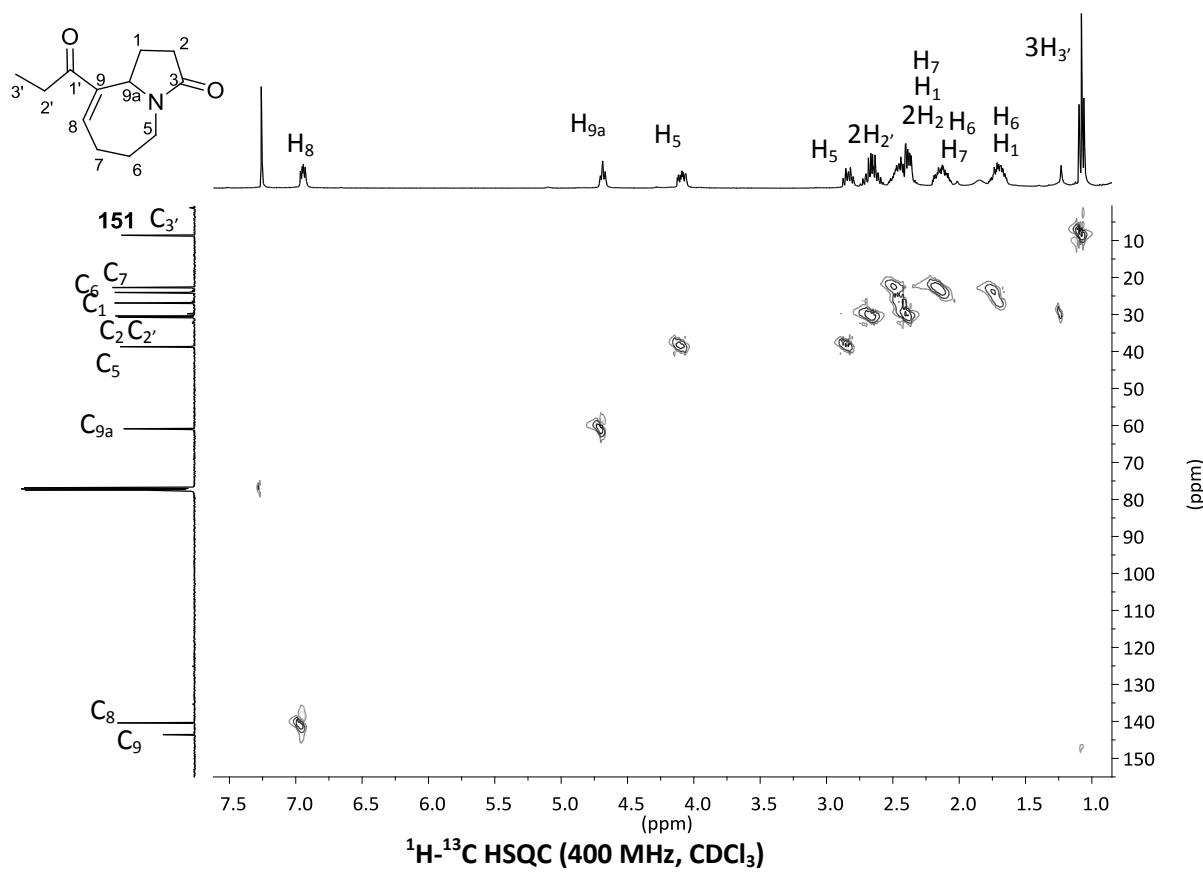
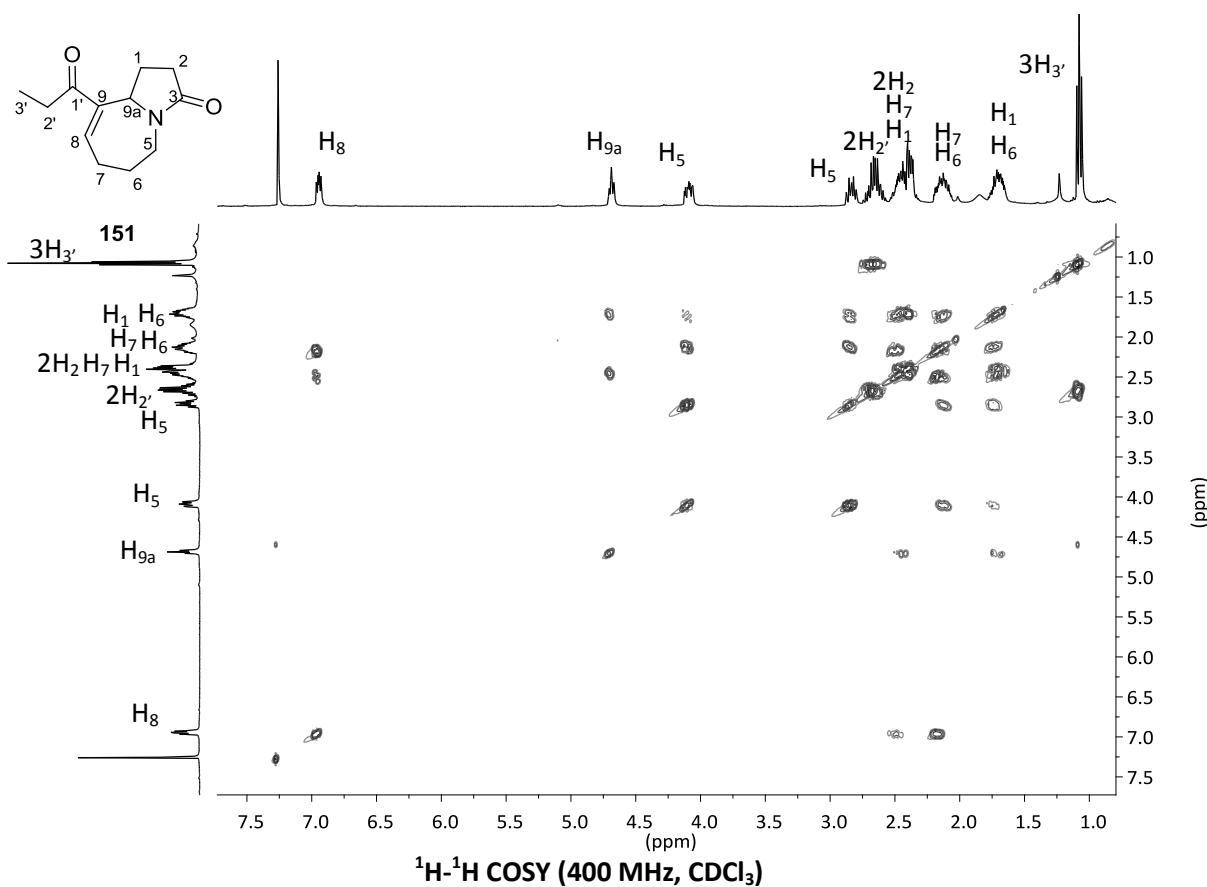


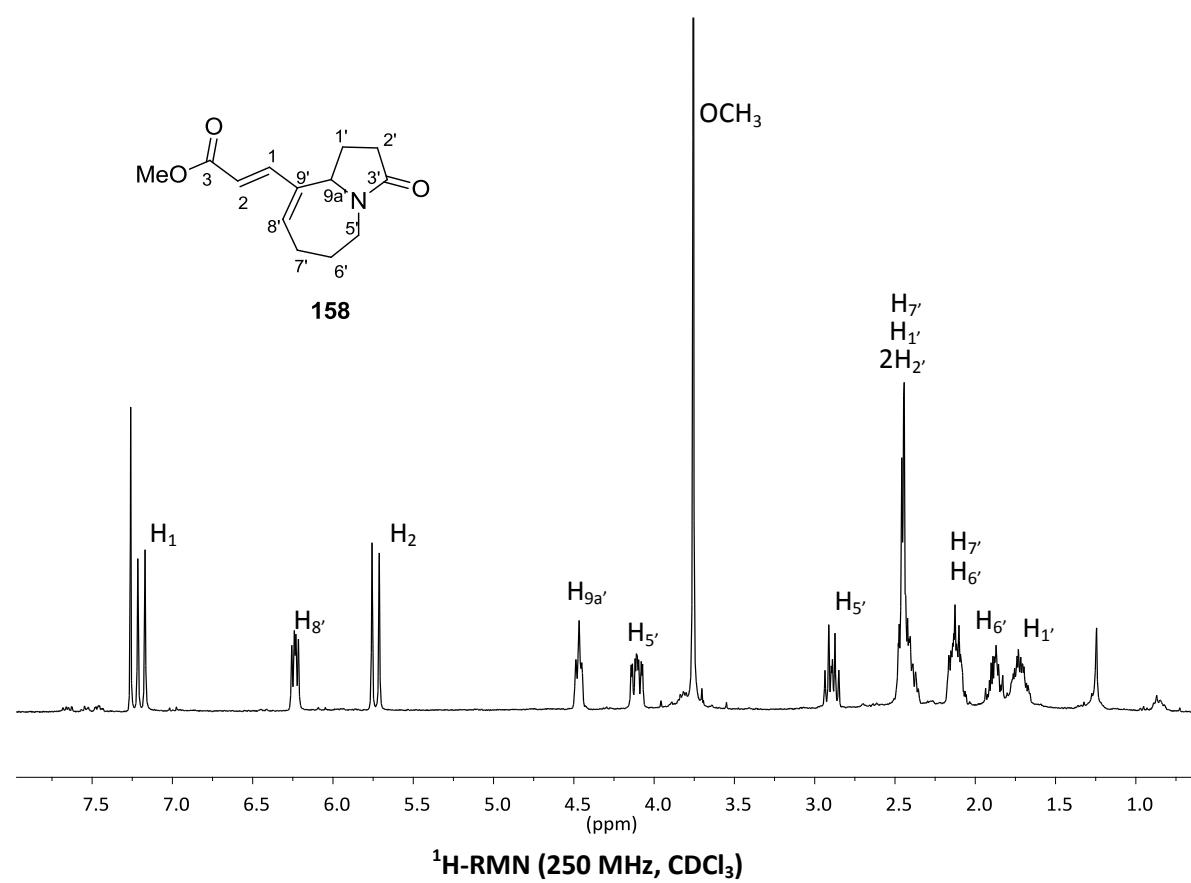
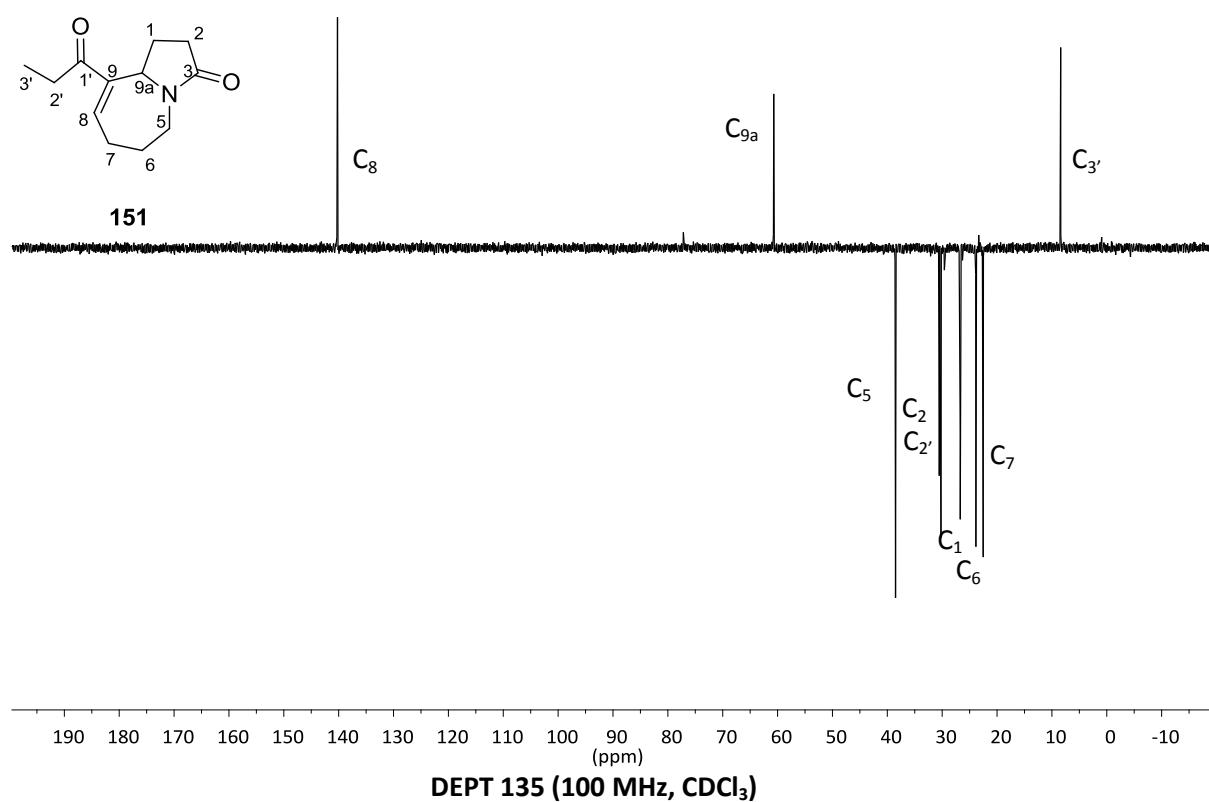


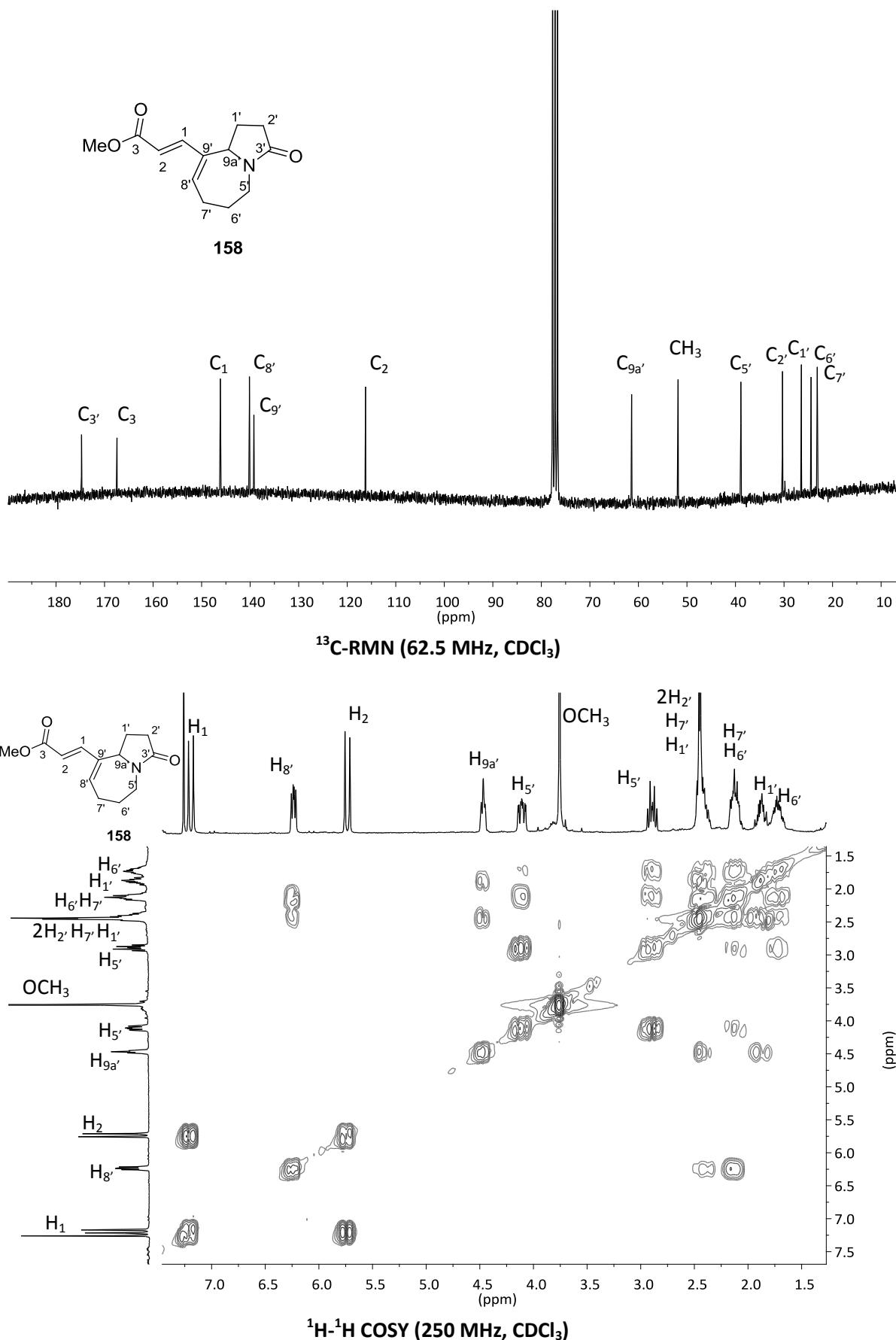




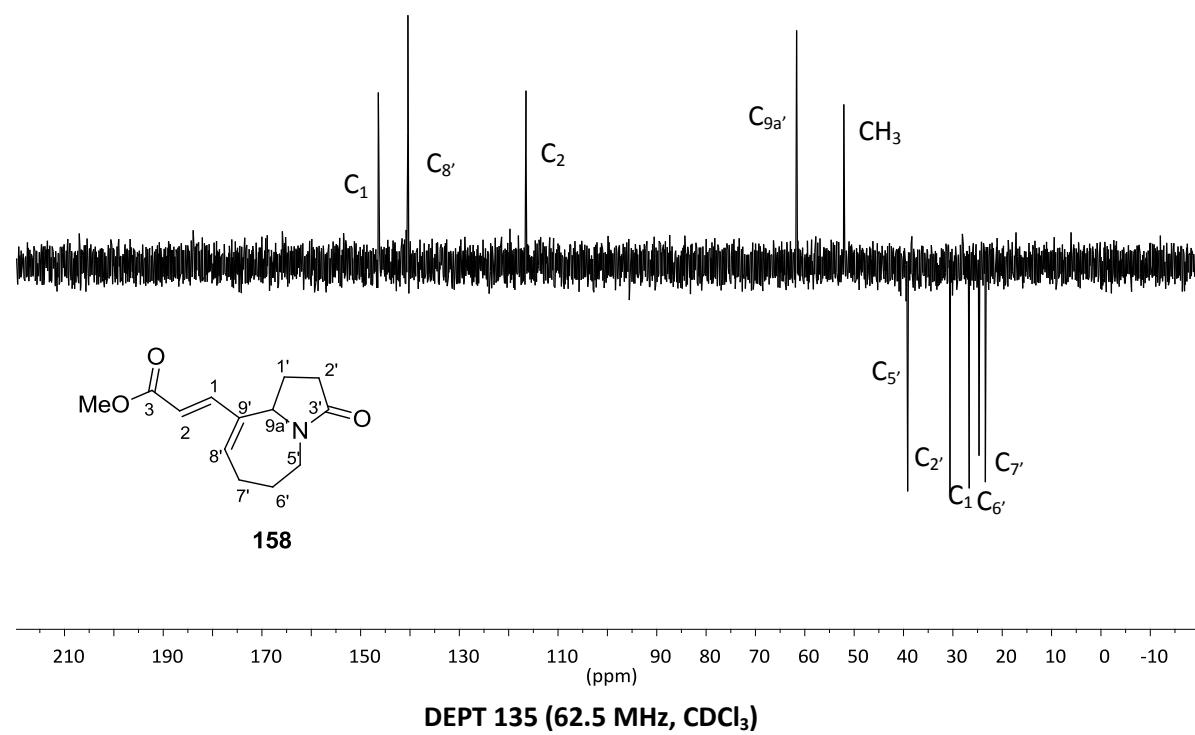
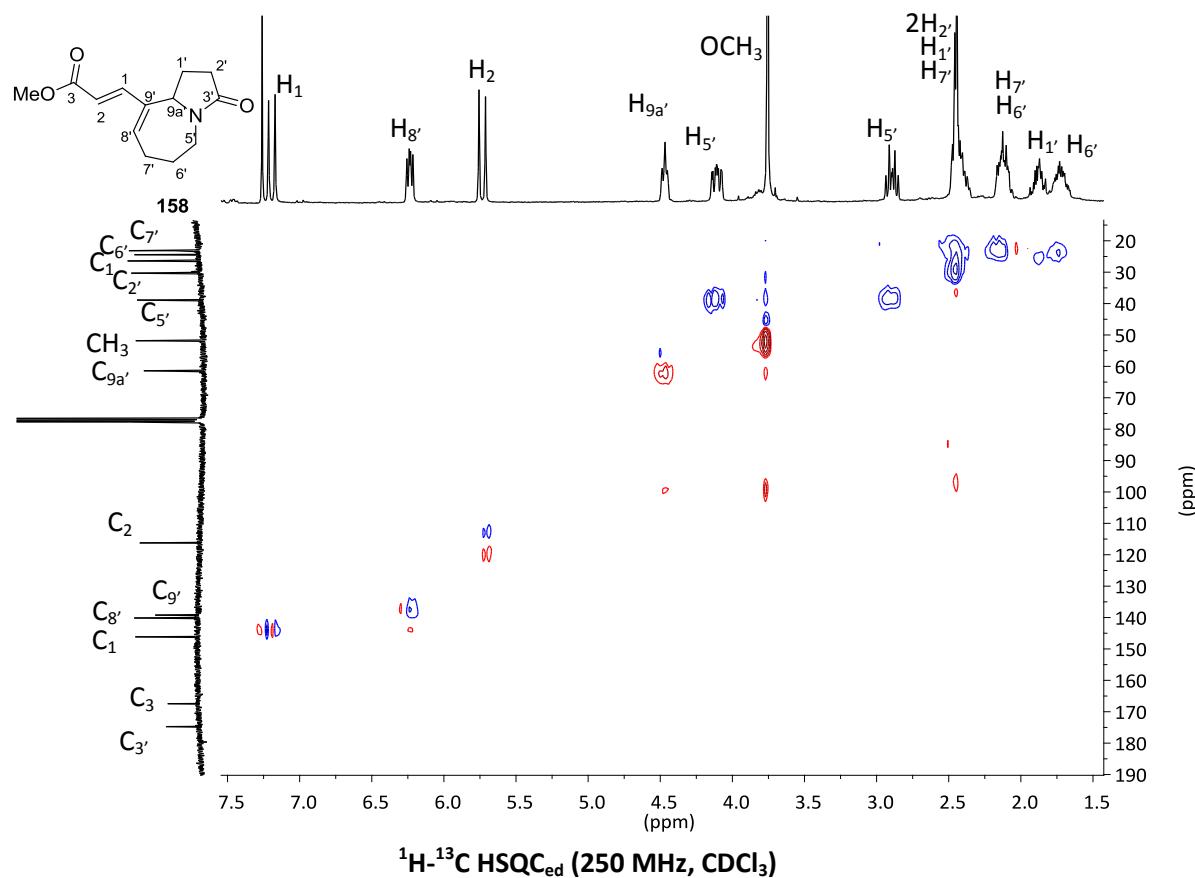


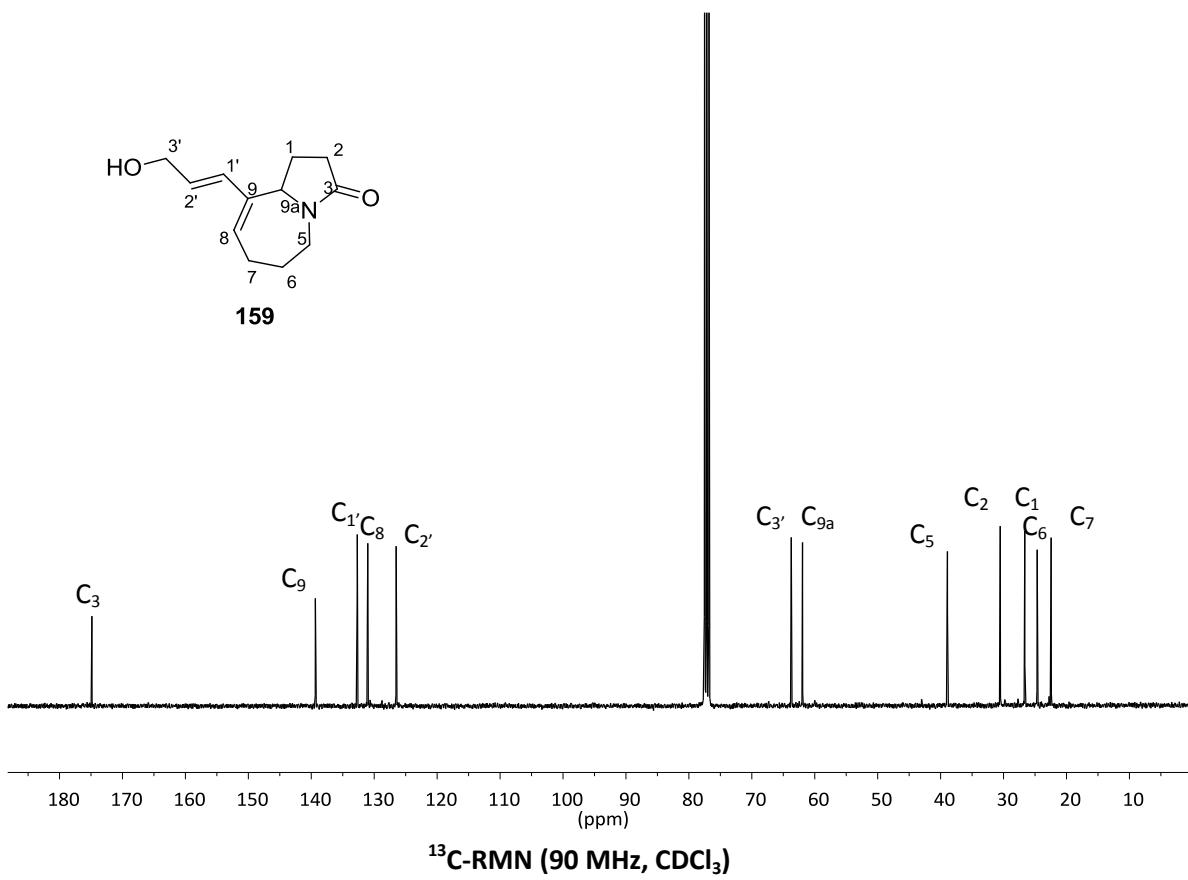
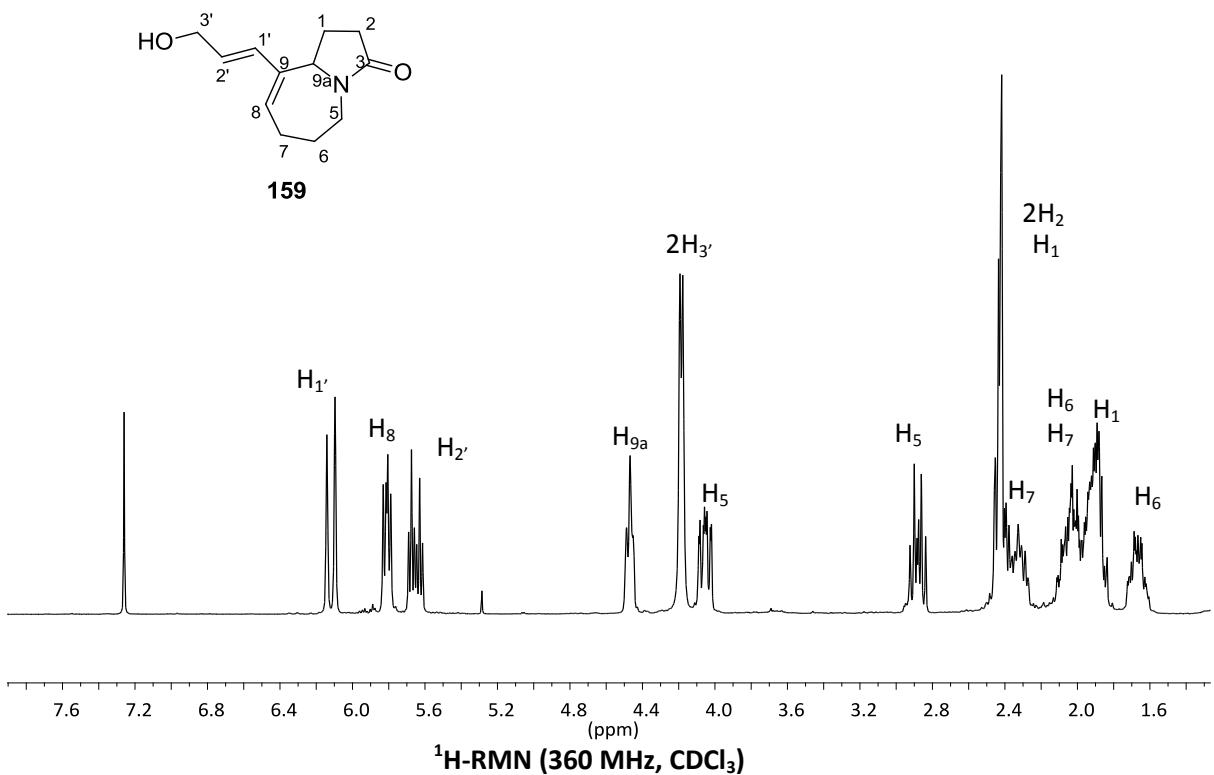


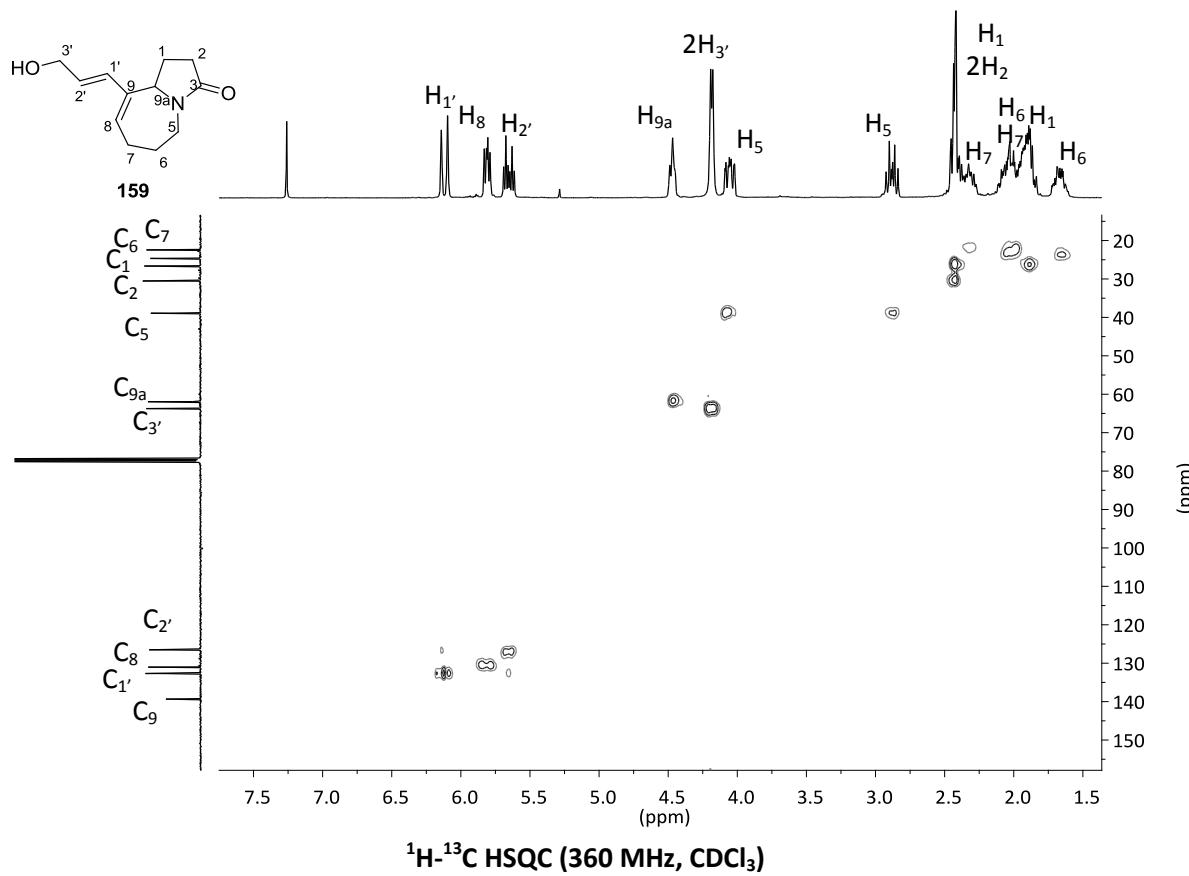
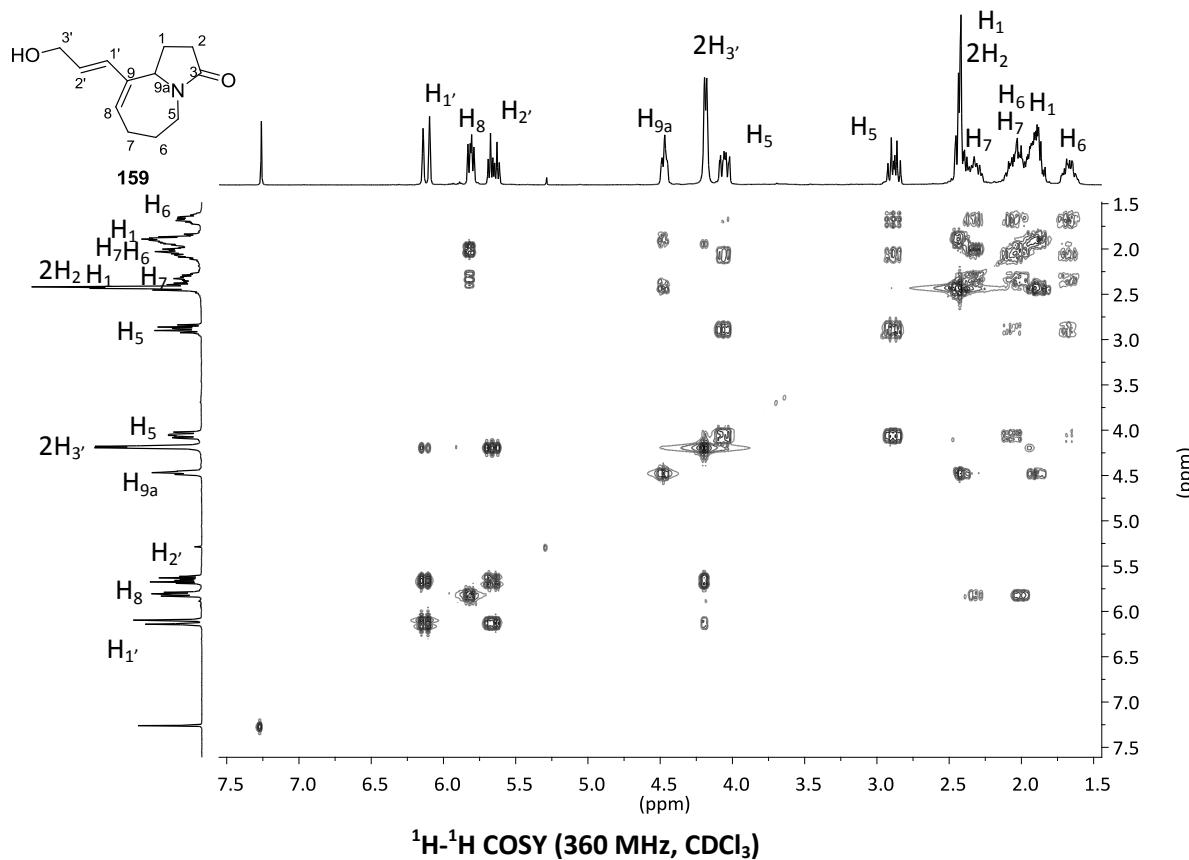


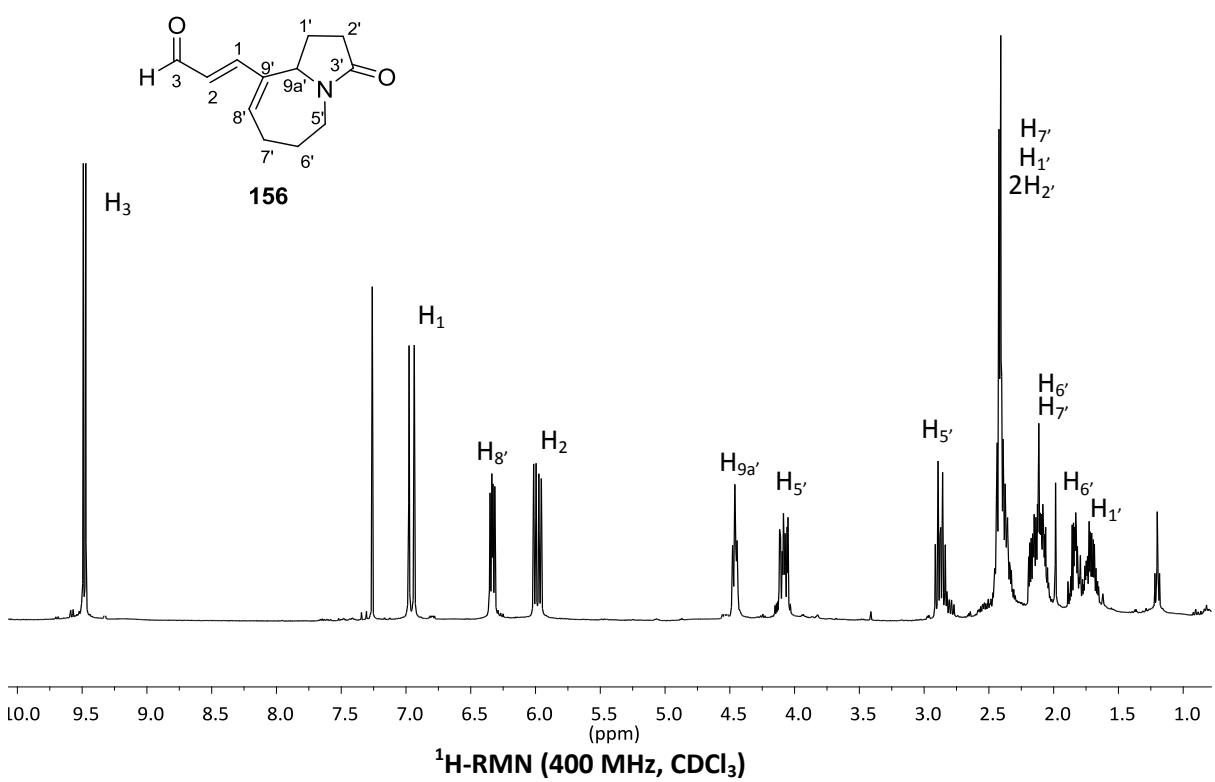
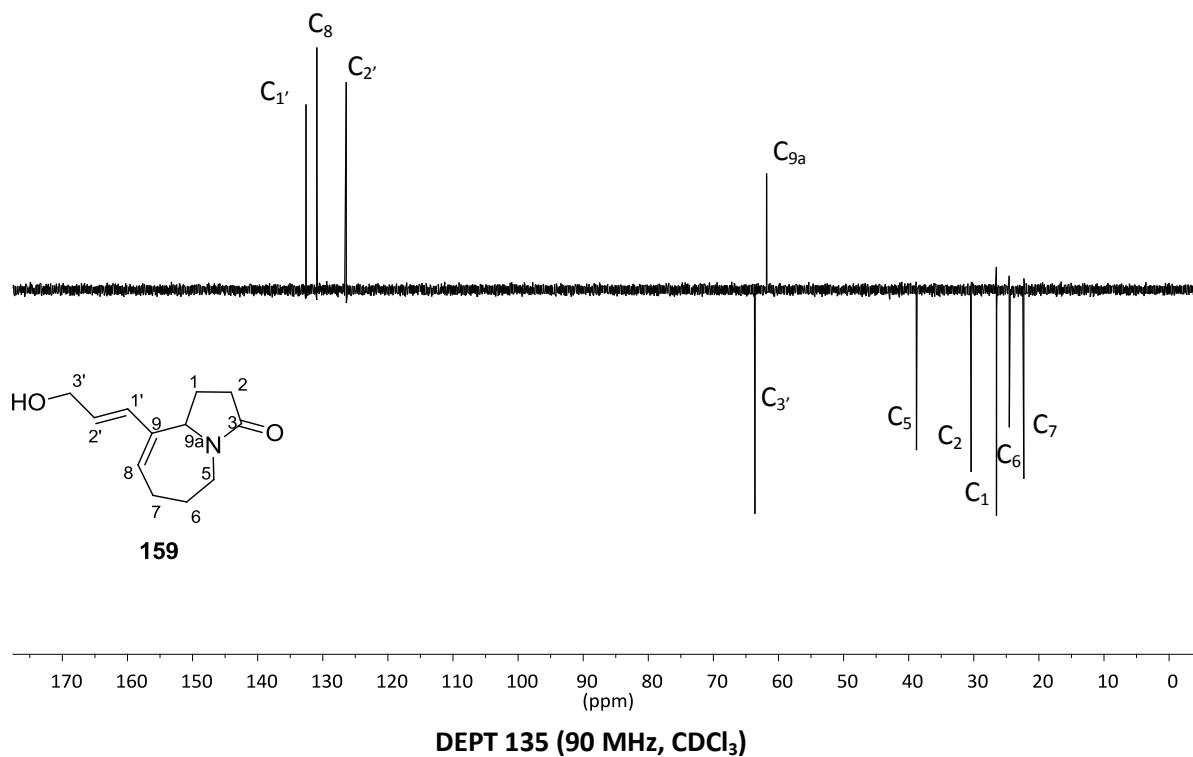


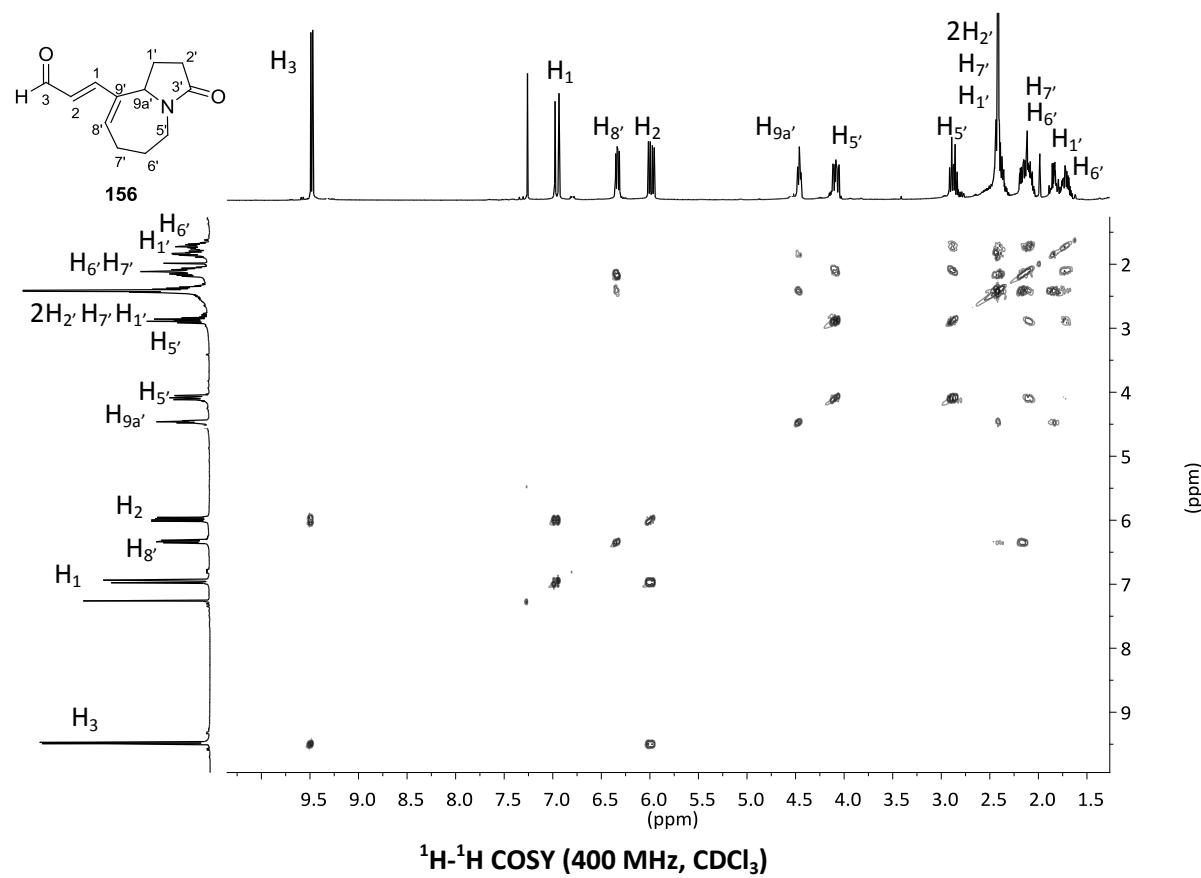
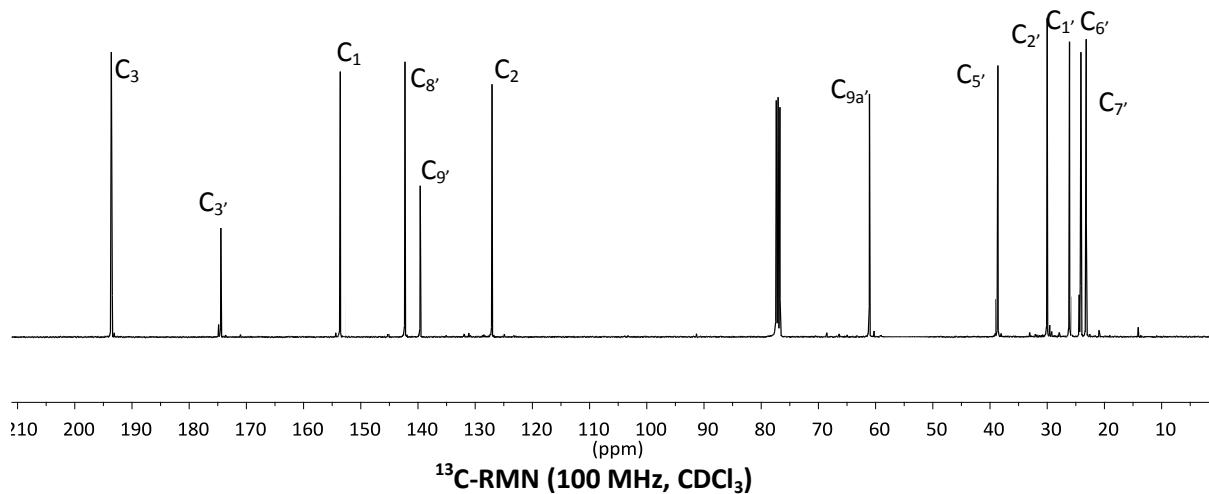
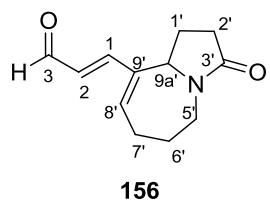
6. RECULL D'ESPECTRES

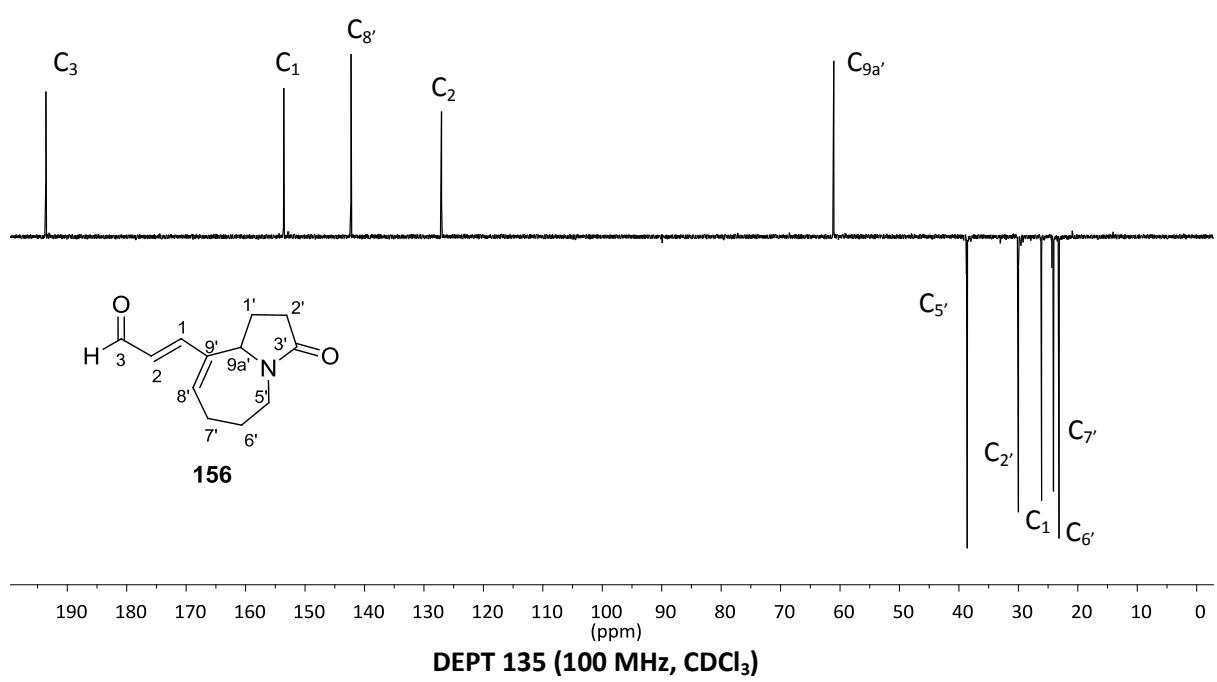
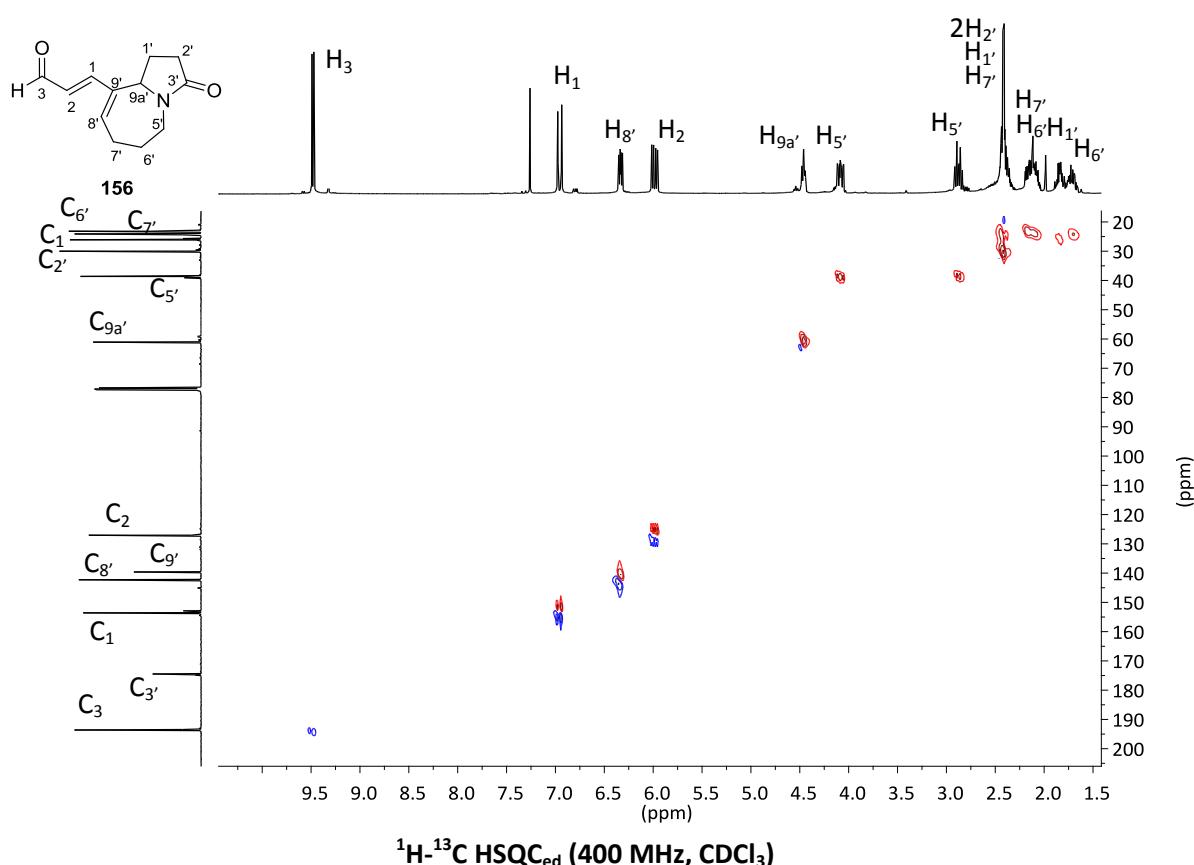


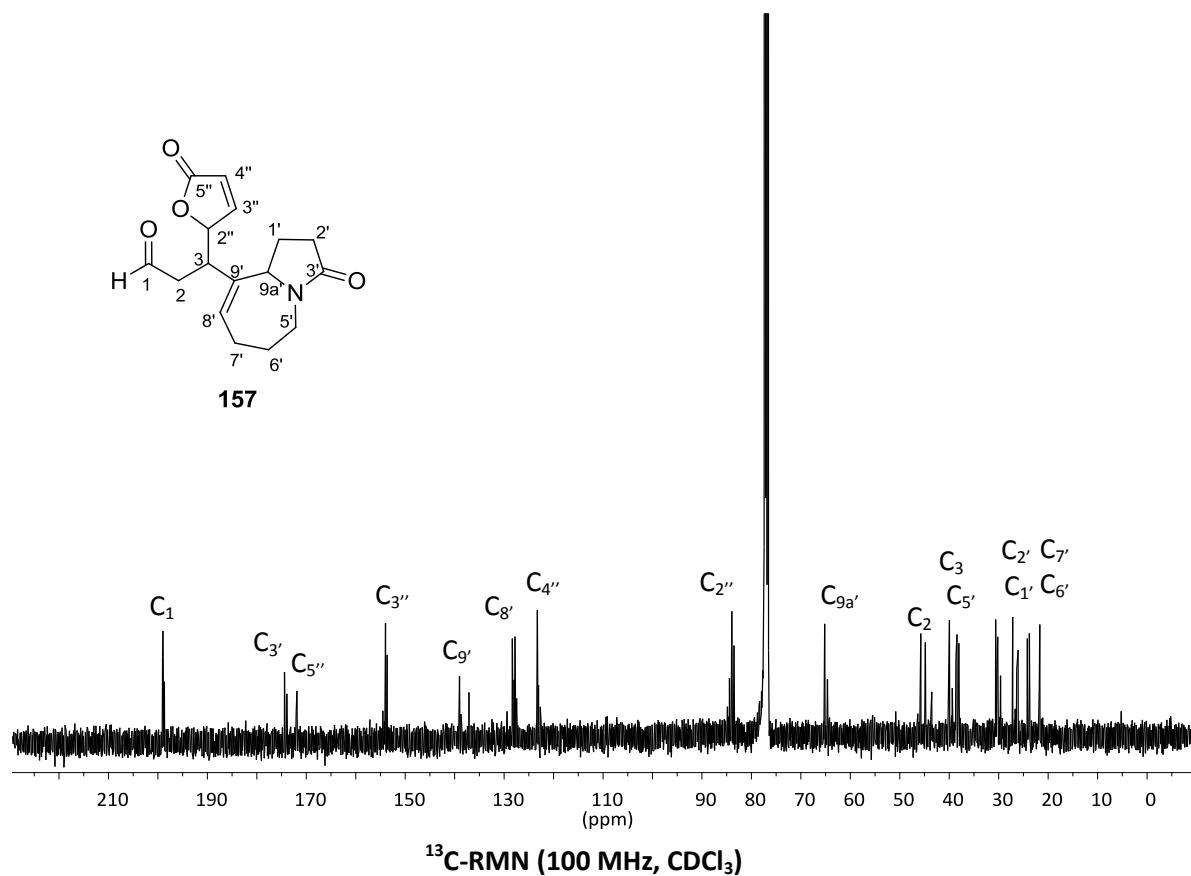
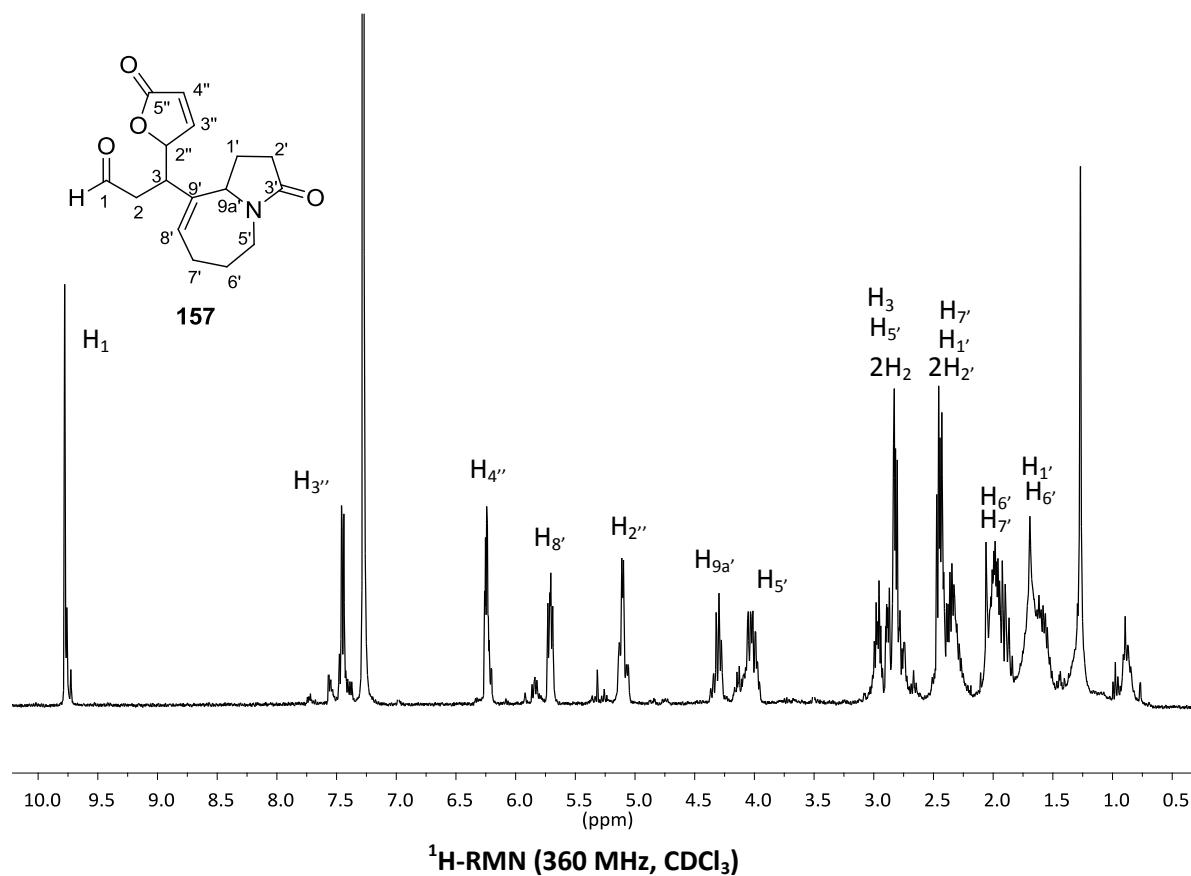


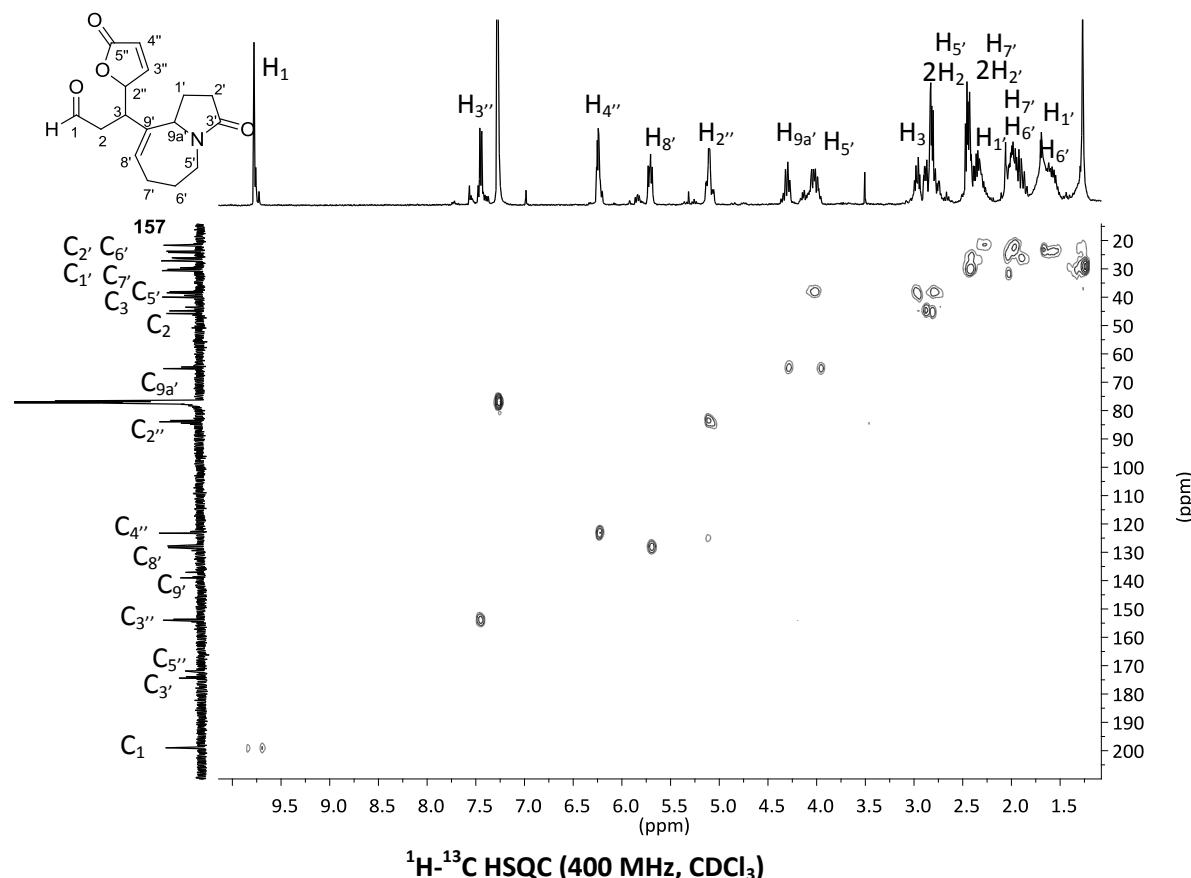
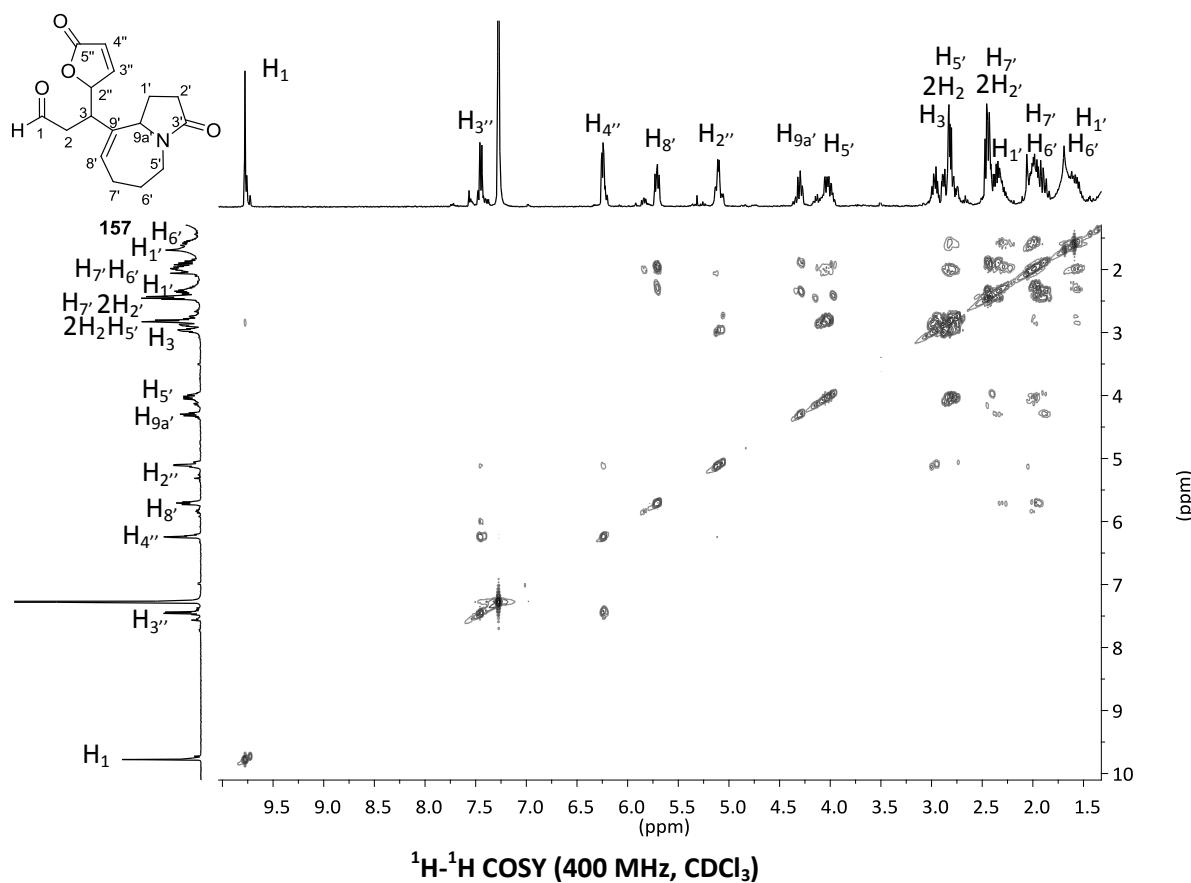


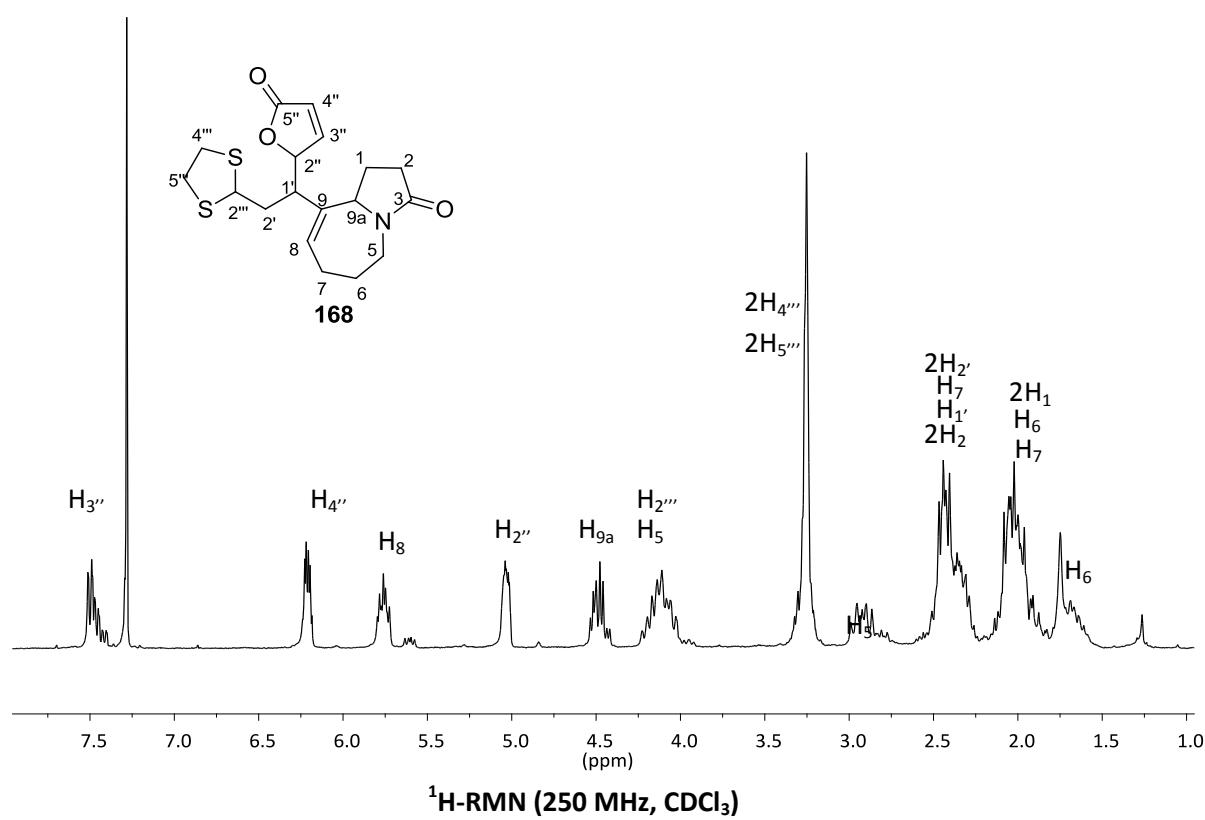
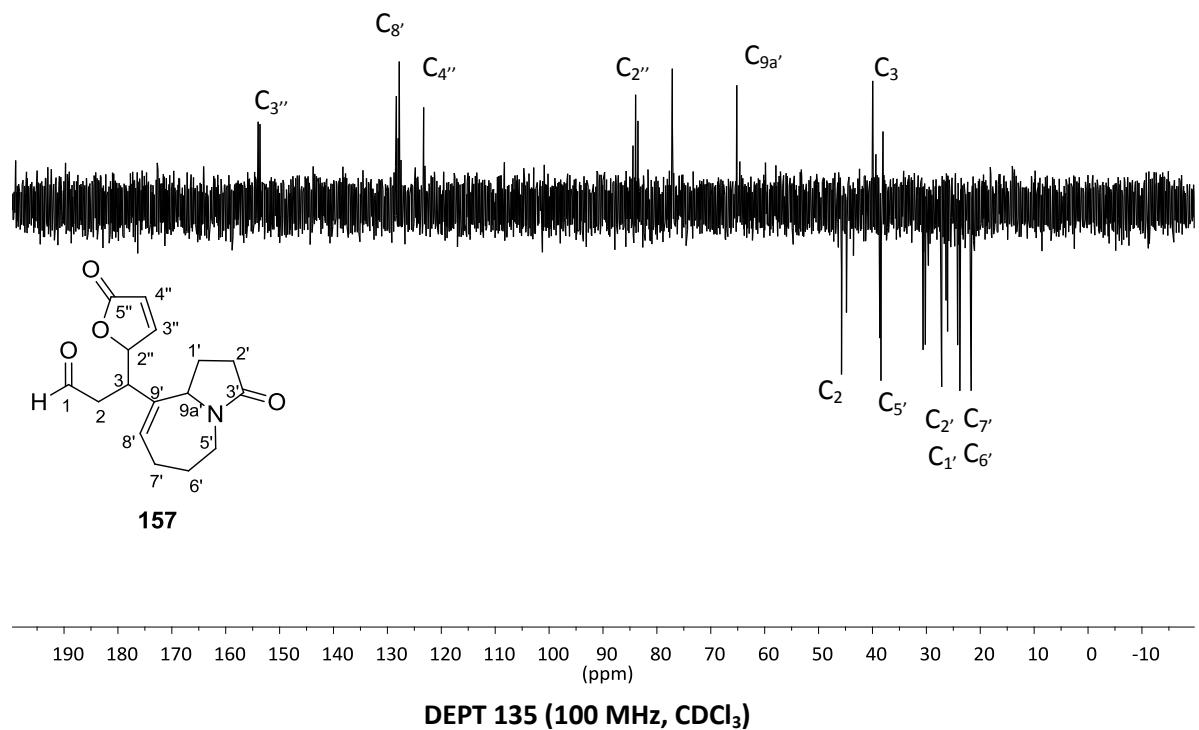


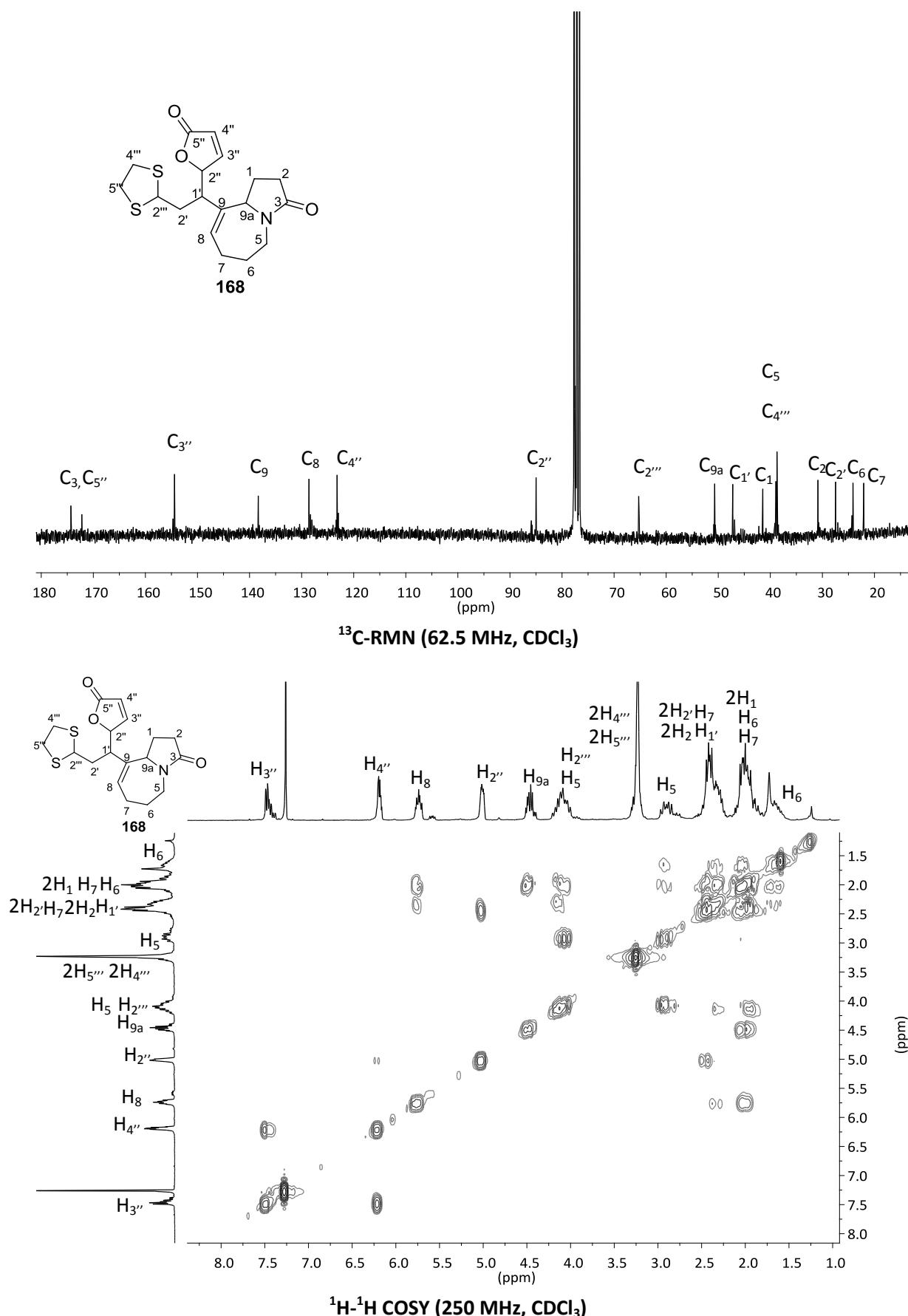












6. RECULL D'ESPECTRES

