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Chemo- and regioselective reactions of 5-bromo enones/enaminones with pyrazoles

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Supporting Information

I - General considerations

Reagents were purchased and used without further purification. Flash chromatography was performed using silica gel (230–400 mesh) as stationary phase. The bromination reaction of enones for obtaining the 5-bromo enones **2a**–**d** was described in reference 1. The amination reaction of the 5-bromo enone **2a** for obtaining the 5-bromo enaminones **3a**–**f** was reported in reference 2. The pyrazoles **1a**–**j**, were synthesized in accordance to the reference 3. ^{1}H NMR spectra were recorded on a Bruker Avance III at 400 MHz using TMS as the internal standard. Chemical shifts δ are quoted in parts per million (ppm), and coupling constants *J* are given in hertz (Hz). ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$ solutions. ^{19}F NMR spectra were recorded at 565 MHz in $CDCl_3$ solutions on a Bruker Avance III spectrometer. The low-resolution mass spectra were recorded on a GC-MS Agilent 5975B using EI mode (70 eV) and high-resolution mass spectra (HRMS) were recorded on an ESI-TOF mass spectrometer for the oil products. All melting points were determined on a melting point apparatus and are uncorrected. The CHN microanalyses were performed for the solid compounds and they are within ±0.4 for all nuclei. Single crystal X-ray diffraction was recorded in a diffractometer equipped with a four circles KAPPA goniometer, PHOTON 100 CMOS array detector, graphite monochromator, and Mo-Kα (λ= 0.71073 Å) radiation source. The structure refinement was performed using the crystallographic software package WinGX

[1] (a) N. Zanatta, J. M. F. M. Schneider, P. H. Schneider, A. D. Wouters, H. G. Bonacorso, M. A. P. Martins and L. A. Wessjohann, *J. Org. Chem.,* 2006, **71**, 6996. (b) M. A. P. Martins, A. P. Sinhorin, N. E. K. Zimmermann, N. Zanatta and H. G. Bonacorso, *Synthesis*, 2001, 1959.

[2] (a) M. A. P. Martins, A. P. Sinhorin, A. da Rosa, A. F. C. Flores, A. D. Wastowski, C. M. P. Pereira, D. C. Flores, P. Beck, R. A. Freitag, S. Brondani, W. Cunico, H. G. Bonacorso and N. Zanatta, *Synthesis*, 2002, 2353. (b) E. C. Aquino, G. Leonel, V. C. Gariboti, C. P. Frizzo, M. A. P. Martins, H. G. Bonacorso and N. Zanatta *J. Org. Chem.*, 2015, **80**, 12453.

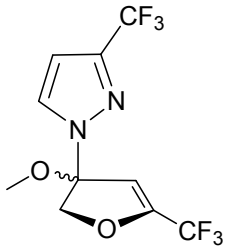
[3] (a) M. E. F. Braibante, M. A. P. Martins and G. Clar, *J. Heterocyclic Chem*., 1993, **30***,* 1159. (b) H. G. Bonacorso, M. A. P. Martins, S. R. T. Bittencourt, R. V. Lourega, N. Zanatta and A. F. C. Flores, *J. Fluorine Chem*., 1999, **99**, 177. (c) M. A. P. Martins, A. P. Sinhorin, C. P. Frizzo, L. Buriol, E. Scapin, N. Zanatta and H. G. Bonacorso, *J. Heterocycl. Chem.*, 2013, **50**, 71. (d) S. Fustero, M. Sanchez-Rosello, P. Barrio and A. Simon-Fuentes, *Chem. Rev.*, 2011, **111**, 6984.

from the SHELXS-97 and SHELXL-97 software.[4] Acetonitrile and dichloromethane were dried and purified by distillation as described by Perrin procedures.[5]

II - Experimental Procedures

General procedure for the synthesis of 1-(3-alkoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-1*H*-pyrazoles *4* and *5*. Pyrazoles **1a**–**j** (0.5 mmol) were added to the mixture of potassium carbonate (0.069 g, 0.5 mmol) in anhydrous acetonitrile (4 mL) and the mixture was kept under stirring at room temperature for 20 min. Then, a solution of the 5-bromo enones **2a**–**d** (0.6 mmol) in acetonitrile (1 mL) was added dropwise to the reaction vessel and the mixture was refluxed for 2 h. The solvent was removed under reduced pressure and to the residue was added chloroform (20 mL). The solution was filtered to remove the potassium bromide and the solvent was evaporated under reduced pressure. Dark oils were obtained, which were purified by a flash column chromatography using silica gel (230–400 mesh) and chloroform as the eluent.

*1-(3-Methoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-3-(trifluoromethyl)-1H-pyrazole (**4a**).*

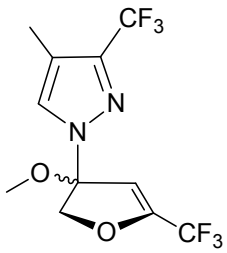


Brown oil (0.084 g, 55% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.87–7.86 (m, 1H), 6.58 (d, 1H, *J* = 2.4 Hz), 5.71–5.70 (m, 1H), 3.52–3.49, 3.48–3.45 (dm, 1H, *J* = 18.2 Hz), 3.35–3.32, 3.31–3.28 (dm, 1H, *J* = 18.2 Hz,) 3.28 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 144.8 (q, $^2J_{C\text{-}F}$ = 38.6 Hz), 143.1 (q, $^2J_{C\text{-}F}$ = 38.7 Hz), 130.1, 121.00 (q, $^1J_{C\text{-}F}$ = 265.3 Hz), 118.1 (q, $^1J_{C\text{-}F}$ = 266.3 Hz), 117.4, 104.7 (q, $^3J_{C\text{-}F}$ = 3.0 Hz), 104.5 (q, $^3J_{C\text{-}F}$ = 2.0 Hz), 51.3, 41.4. **GC-MS (EI, 70 eV)**: *m/z* (%) =

[4] WinGX Program version 1.80.05 *Single Crystal X-Ray Diffraction Data*, Farrugia L. J., *J. Appl. Cryst.*, 1999, **32**, 837.
[5] Perrin, D. D.; Armarego, L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: New York, 1996.

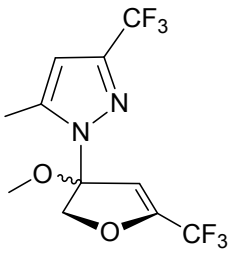
302 (2) [M$^+$], 287 (29), 271 (19), 223 (3) 167 (100), 151 (68). **HRMS (ESI$^+$)**: *m/z* calcd. for $C_{10}H_8F_6N_2O_2Na$ [M+Na]$^+$ 325.0388, found 325.0410.

*1-(3-Methoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-4-methyl-3-(trifluoromethyl)-1H-pyrazole (**4b**).*



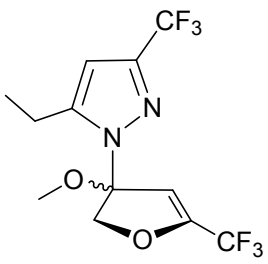
Brown oil (0.133 g, 84% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.66 (s, 1H), 5.69–5.67 (m, 1H), 3.50–3.47, 3.46–3.43 (dm, *J* = 18.2 Hz, 1H), 3.28 (s, 3H), 3.30–3.27, 3.26–3.23 (dm, *J* = 18.2 Hz, 1H), 2.17 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 143.1 (q, $^2J_{C\text{-}F}$ = 39.6 Hz), 142.9 (q, $^2J_{C\text{-}F}$ = 38.7 Hz), 129.3, 121.6 (q, $^1J_{C\text{-}F}$ = 266.3 Hz), 118.1 (q, $^1J_{C\text{-}F}$ = 265.3 Hz), 117.4, 115.7, 104.6 (q, $^3J_{C\text{-}F}$ = 3.0 Hz), 51.2, 41.2, 8.1. **GC-MS (EI, 70 eV)**: *m/z* (%) = 316 (2) [M$^+$], 301 (13), 285 (18), 151 (58), 167 (100), 151 (58). **HRMS (ESI$^+$)**: *m/z* calcd. for $C_{11}H_{10}F_6N_2O_2Na$ [M+Na]$^+$ 339.0544, found 339.0527.

*1-(3-Methoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-5-methyl-3-(trifluoromethyl)-1H-pyrazole (**4c**)*.



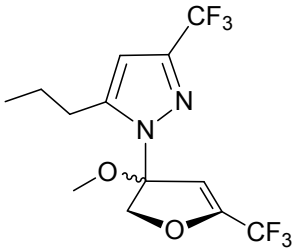
Brown oil (0.136 g, 86% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.34 (s, 1H), 5.73–5.71 (m, 1H), 4.02–3.99, 3.97–3.94 (dm, *J* = 18.5 Hz, 1H), 3.36 (s, 3H), 3.28–3.25, 3.23–3.20 (dm, *J* = 18.5 Hz, 1H), 2.50 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 142.9 (q, $^2J_{C\text{-}F}$ = 38.8 Hz), 142.4, 142.1 (q, $^2J_{C\text{-}F}$ = 38.6 Hz), 121.2 (q, $^1J_{C\text{-}F}$ = 266.7 Hz), 119.1, 118.1 (q, $^1J_{C\text{-}F}$ = 266,70 Hz), 106.5, 104.3 (q, $^3J_{C\text{-}F}$ = 4.0 Hz), 51.3, 39.2, 12.9. **^{19}F NMR (565 MHz, $CDCl_3$)**: δ -62.6 (CF_3), -69.8 (CF_3). **GC-MS (EI, 70 eV)**: *m/z* (%) = 316 (2) [M$^+$], 301 (22), 285 (17), 167 (100) 151 (63). HRMS (ESI$^+$): *m/z* calcd. for $C_{11}H_{11}F_6N_2O_2$ [M+H]$^+$ 317.0724, found 317.0716.

*5-Ethyl-1-(3-methoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-3-(trifluoromethyl)-1H-pyrazole (**4d**)*.



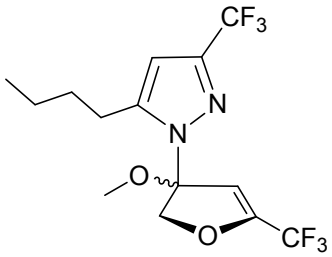
Brown oil (0.107 g, 65% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.39 (s, 1H), 5.73–5.71 (m, 1H), 4.07–4.04, 4.02–3.99 (dm, *J* = 18.6 Hz, 1H), 3.35 (s, 3H), 3.26–3.23, 3.21–3.18 (dm, *J* = 18.6 Hz, 1H), 2.89 (q, *J* = 7.5 Hz, 2H), 1.29 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 148.8, 143.0 (q, $^{2}J_{C\text{-}F}$ = 39.6 Hz), 142.0 (q, $^{2}J_{C\text{-}F}$ = 38.6 Hz), 121.3 (q, $^{1}J_{C\text{-}F}$ = 265.3 Hz), 119.2, 118.1 (q, $^{1}J_{C\text{-}F}$ = 266.3 Hz), 104.7, 104.3 (q, $^{3}J_{C\text{-}F}$ = 4.0 Hz), 51.2, 39.0, 20.1, 12.9. **GC-MS (EI, 70 eV)**: *m/z* (%) = 330 (3) [M^+], 315 (20), 299 (15), 167 (100), 151 (44). **HRMS (ESI^+)**: *m/z* calcd. for $C_{12}H_{12}F_6N_2O_2$ $[M+H]^+$ 331.0881, found 331.0890.

*1-(3-Methoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-5-propyl-3-(trifluoromethyl)-1H-pyrazole (**4e**)*.



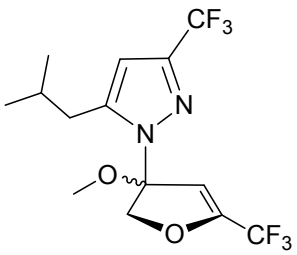
Brown oil (0.107 g, 62% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.37 (s, 1H), 5.73–5.71 (m, 1H), 4.05–4.02, 4.01–3.98 (dm, *J* = 18.5 Hz, 1H), 3.35 (s, 3H), 3.27–3.24, 3.22–3.19 (dm, *J* = 18.5 Hz, 1H), 2.82 (t, *J* = 6.9 Hz, 2H), 1.70 (sext, *J* = 7.9 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 147.3, 143.0 (q, $^{2}J_{C\text{-}F}$ = 39.6 Hz), 142.0 (q, $^{2}J_{C\text{-}F}$ = 38.6 Hz), 121.2 (q, $^{1}J_{C\text{-}F}$ = 265.3 Hz), 119.5, 118.1 (q, $^{1}J_{C\text{-}F}$ = 266.3 Hz), 105.2, 104.3 (q, $^{3}J_{C\text{-}F}$ = 4.0 Hz), 51.2, 39.1, 28.6, 22.0, 13.8. **GC-MS (EI, 70 eV)**: *m/z* (%) = 344 (3) [M^+], 329 (20), 313 (13) 167 (100), 151 (38). **HRMS (ESI^+)**: *m/z* calcd. for $C_{13}H_{15}F_6N_2O_2$ $[M+H]^+$ 345.1034, found 345.1037.

*5-Butyl-1-(3-methoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-3-(trifluoromethyl)-1H-pyrazole (**4f**)*.



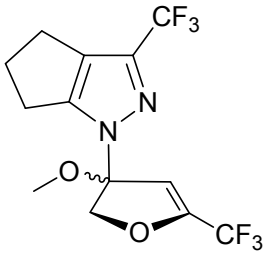
Brown oil (0.118 g, 66% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.38 (s, 1H), 5.73–5.71 (m, 1H), 4.06–4.03, 4.02–3.99 (dm, *J* = 18.5 Hz, 1H), 3.35 (s, 3H), 3.27–3.24, 3.22–3.19 (dm, *J* = 18.5 Hz, 1H), 2.85 (t, *J* = 7.0 Hz, 2H), 1.66 (qui, *J* = 7.7 Hz, 2H), 1.43 (sext, *J* = 7.6 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 147.5, 143.0 (q, $^{2}J_{C\text{-}F}$ = 39.6 Hz), 142.0 (q, $^{2}J_{C\text{-}F}$ = 38.6 Hz), 121.3 (q, $^{1}J_{C\text{-}F}$ = 265.3 Hz), 119.1, 118.1 (q, $^{1}J_{C\text{-}F}$ = 266.3 Hz), 105.1, 104.3 (q, $^{3}J_{C\text{-}F}$ = 4.0 Hz), 51.2, 39.0, 30.8, 26.3, 22.4, 13.7. **GC-MS (EI, 70 eV)**: *m/z* (%) = 358 (1) [M^+], 343 (17), 327 (10), 166 (100), 151 (29). **HRMS (ESI^+)**: *m/z* calcd. for $C_{14}H_{17}F_6N_2O_2$ $[M+H]^+$ 359.1194, found 359.1191.

*5-Isobutyl-1-(3-methoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-3-(trifluoromethyl)-1H-pyrazole (**4g**)*.



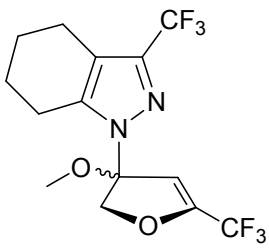
Brown oil (0.108 g, 60% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.36 (s, 1H), 5.73–5.71 (m, 1H), 4.08–4.05, 4.03–4.00 (dm, *J* = 18.6 Hz, 1H), 3.34 (s, 3H), 3.26–3.23, 3.21–3.18 (dm, *J* = 18.6 Hz, 1H), 2.77 (dd, *J* = 15,4; 7.1 Hz, 1H), 2.68 (dd, *J* = 15,4; 7.2 Hz, 1H), 1.99 (non, *J* = *7.2 Hz,* 1H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 146.4, 143.0 (q, $^{2}J_{C\text{-}F}$ = 39.6 Hz), 142.0 (q, $^{2}J_{C\text{-}F}$ = 38.6 Hz), 121.3 (q, $^{1}J_{C\text{-}F}$ = 265.3 Hz), 119.2, 118.1 (q, $^{1}J_{C\text{-}F}$ = 266.3 Hz), 106.0, 104.3 (q, $^{3}J_{C\text{-}F}$ = 4.0 Hz), 51.2, 39.0, 35.7, 28.1, 22.4. **GC-MS (EI, 70 eV)**: *m/z* (%) = 358 (1) [M^+], 343 (20), 327 (10) 166 (100), 151 (34). **HRMS (ESI^+)**: *m/z* calcd. for $C_{14}H_{17}F_6N_2O_2$ $[M+H]^+$ 359.1194, found 359.1191.

*1-(3-Methoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-3-(trifluoromethyl)-1,4,5,6-tetrahydrocyclopenta[c]pyrazole (**4h**)*.



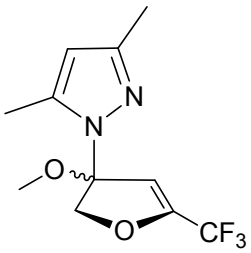
Yellow solid (0.127 g, 74% yield). **Mp**: 65–68 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 5.69–5.67 (m, 1H), 3.57–3.54, 3.53–3.50 (dm, *J* = 18.3 Hz, 1H), 3.31 (s, 3H), 3.31–3.28, 3.26–3.23 (dm, *J* = 18.3 Hz, 1H), 2.99–2.84 (m, 2H), 2.71–2.67 (m, 2H), 2.60–2.54 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 152.7, 142.9 (q, $^2J_{C\text{-}F}$ = 39.5 Hz), 137.8 (q, $^2J_{C\text{-}F}$ = 38.7 Hz), 126.2, 121.4 (q, $^1J_{C\text{-}F}$ = 265.3 Hz), 118.2 (q, $^1J_{C\text{-}F}$ = 266.3 Hz), 117.8, 104.5 (q, $^3J_{C\text{-}F}$ = 3.96 Hz), 51.1, 41.4, 30.4, 26.4, 22.4. **GC-MS (EI, 70 eV)**: m/z (%) = 342 (1) [M^+], 327 (3), 311 (9), 166 (100), 151 (23). **Anal. calcd. for $C_{13}H_{12}F_6N_2O_2$**: C, 45.62; H, 3.53; N, 8.19%. Found: C, 45.89; H, 3.72; N, 7.97%.

*1-(3-Methoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-3-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-indazole (**4i**)*.



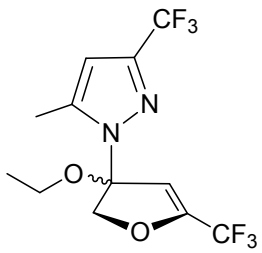
Brown oil (0.121 g, 68% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 5.71–5.69 (m, 1H), 3.88–3.85, 3.83–3.80 (dm, *J* = 18.4 Hz, 1H), 3.34 (s, 3H), 3.26–3.23, 3.21–3.18 (dm, *J* = 18.4 Hz, 1H), 2.91–2.75 (m, 2H), 2.60–2.57 (m, 2H), 1.80–1.74 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 142.9 (q, $^2J_{C\text{-}F}$ = 39.5 Hz), 141.8, 139.8 (q, $^2J_{C\text{-}F}$ = 38.7 Hz), 121.8 (q, $^1J_{C\text{-}F}$ = 265.3 Hz), 118.8, 118.2 (q, $^1J_{C\text{-}F}$ = 266.3 Hz), 116.9, 104,3 (q, $^3J_{C\text{-}F}$ = 4.0 Hz), 51.1, 39.6, 23.4, 22.4, 22.1, 20.2. **GC-MS (EI, 70 eV)**: *m/z* (%) = 356 (1) [M^+], 341 (6), 325 (8), 166 (100), 151 (23). **HRMS (ESI^+)**: *m/z* calcd. for $C_{14}H_{14}F_6N_2O_2Na$ $[M+Na]^+$ 379.0854, found 379.0840.

*1-(3-Methoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-3,5-dimethyl-1H-pyrazole (**4j**)*.



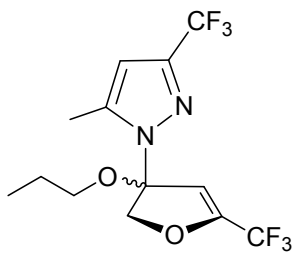
Brown oil (0.075 g, 57% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 5.85 (s, 1H), 5.68–5.66 (m, 1H), 3.82–3.79, 3.77–3.74 (dm, *J* = 18.2 Hz, 1H), 3.31 (s, 3H), 3.24–3.21, 3.19–3.16 (dm, *J* = 18.2 Hz, 1H), 2.37 (s, 3H), 2.21 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 148.8, 142.8 (q, $^2J_{C\text{-}F}$ = 38.6 Hz), 141.5, 118.4, 118.3 (q, $^1J_{C\text{-}F}$ = 266.3 Hz), 108.5, 104.2 (q, $^3J_{C\text{-}F}$ = 4.0 Hz), 50.8, 40.25, 13.6, 12.9. **GC-MS (EI, 70 eV)**: *m/z* (%) = 262 (3) [M^+], 247 (40), 231 (15), 166 (100), 151 (35). **HRMS (ESI^+)**: *m/z* calcd. for $C_{11}H_{13}F_3N_2O_2Na$ $[M+Na]^+$ 285.0827, found 285.0812.

*1-(3-Ethoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-5-methyl-3-(trifluoromethyl)-1H-pyrazole (**5a**)*.



Brown oil (0.125 g, 76% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.33 (s, 1H), 5.71–5.69 (m, 1H), 4.07–4.04, 4.02–3.99 (dm, *J* = 18.5 Hz, 1H), 3.64–3.55 (m, 2H), 3.25–3.22, 3.21–3.18 (dm, *J* = 18.5 Hz, 1H), 2.47 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 142.7 (q, $^2J_{C\text{-}F}$ = 38.8 Hz), 142.7, 141.8 (q, $^2J_{C\text{-}F}$ = 38.6 Hz), 121.2 (q, $^1J_{C\text{-}F}$ = 266.7 Hz), 118.8, 118.1 (q, $^1J_{C\text{-}F}$ = 266.70 Hz), 106.5, 104.2 (q, $^3J_{C\text{-}F}$ = 4.0 Hz), 60.2, 39.3, 14.8, 12.9. **GC-MS (EI, 70 eV)**: *m/z* (%) = 330 (2) [M^+], 301 (39), 285 (30), 180 (47), 153 (100), 151 (71), 131 (42). **HRMS (ESI^+)**: *m/z* calcd. for $C_{12}H_{13}F_6N_2O_2$ $[M+H]^+$ 331.0881, found 331.0890.

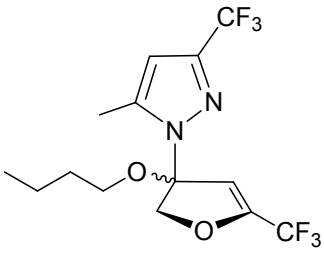
*5-Methyl-1-(3-propoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-3-(trifluoromethyl)-1H-pyrazole (**5b**)*.



Brown oil (0.138 g, 80% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.33 (s, 1H), 5.71–5.70 (m, 1H), 4.08–4.05, 4.04–4.01 (dm, *J* = 18.5 Hz, 1H), 3.51–3.45 (m, 2H), 3.26–3.23, 3.21–3.18 (dm, *J* = 18.5 Hz, 1H), 2.47 (s, 3H), 1.63 (sext, *J* = 7.4 Hz, 2H), 0.93 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR**

(100 MHz, $CDCl_3$): δ 142.8 (q, $^2J_{C\text{-}F}$ = 38.8 Hz), 142.1, 141.7 (q, $^2J_{C\text{-}F}$ = 38.6 Hz), 121.2 (q, $^1J_{C\text{-}F}$ = 266.7 Hz), 118.8, 118.1 (q, $^1J_{C\text{-}F}$ = 266.70 Hz), 106.4, 104.2 (q, $^3J_{C\text{-}F}$ = 4.0 Hz), 66.0, 39.1, 22.5, 12.9, 10.5. **GC-MS (EI, 70 eV)**: *m/z* (%) = 344 (2) [M^+], 301 (49), 285 (48), 153 (78), 151 (100), 131 (37). **HRMS (ESI^+)**: *m/z* calcd. for $C_{13}H_{15}F_6N_2O_2$ $[M+H]^+$ 345.1037, found 345.1032.

*1-(3-Butoxy-5-(trifluoromethyl)-2,3-dihydrofuran-3-yl)-5-methyl-3-(trifluoromethyl)-1H-pyrazole (**5c**)*.

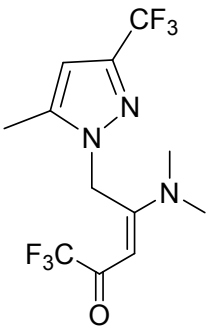


Brown oil (0.119 g, 66% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.33 (s, 1H), 5.71–5.70 (m, 1H), 4.07–4.04, 4.03–4.00 (dm, *J* = 18.5 Hz, 1H), 3.56–3.48 (m, 2H), 3.26–3.23, 3.21–3.18 (dm, *J* = 18.5 Hz), 2.47 (s, 3H), 1.59 (qui, *J* = 6.8 Hz, 2H), 1.38 (sext, *J* = 7.6 Hz, 2H), 0.89 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 142.8 (q, $^2J_{C\text{-}F}$ = 38.8 Hz), 142.1, 141.7 (q, $^2J_{C\text{-}F}$ = 38.6 Hz), 121.2 (q, $^1J_{C\text{-}F}$ = 266.7 Hz), 118.8, 118.1 (q, $^1J_{C\text{-}F}$ = 266.70 Hz), 106.4, 104.2 (q, $^3J_{C\text{-}F}$ = 4.0 Hz), 66.1, 39.2, 31.2, 19.1, 13.6, 12.9. **GC-MS (EI, 70 eV)**: *m/z* (%) = 352 (2) [M^+], 301 (43), 285 (45), 153 (64), 151 (100), 131 (34). **HRMS (ESI^+)**: *m/z* calcd. for $C_{14}H_{17}F_6N_2O_2$ $[M+H]^+$ 359.1194, found 359.1205.

General procedure for the synthesis of 4-(amino)-1,1,1-trifluoro-5-(5-methyl-3-trifluoromethyl)-1*H*-pyrazol-1-yl)pent-3-en-2-ones (6a–i). Pyrazoles **1b**-**c**/**1i**-**j** (0.5 mmol) were added to a mixture of potassium carbonate (0.069 g, 0.5 mmol) in anhydrous acetonitrile (4 mL) and the mixture was stirred at room temperature for 20 min. Then, a solution of the 5-bromo enaminones **3a**–**f** (0.6 mmol) in acetonitrile (1 mL) was added dropwise to the reaction vessel and the mixture was refluxed for 5 h. The solvent was removed under reduced pressure and to the residue was added chloroform (20 mL). The

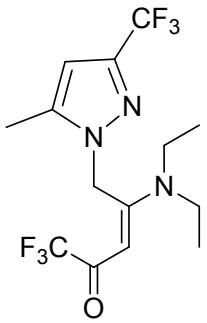
solution was filtered to remove the potassium bromide and the solvent was evaporated under reduced pressure for obtaining solid products, which were purified by recrystallization from hexane.

*(E)-4-(Dimethylamino)-1,1,1-trifluoro-5-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)pent-3-en-2-one (**6a**)*.



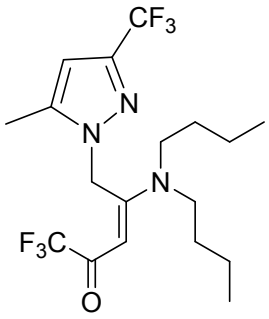
Brown solid (0.115 g, 70% yield). **Mp**: 126–129 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.27 (s, 1H), 5.74 (s, 2H), 5.35 (s, 1H), 3.19 (br s, 6H), 2.40 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 175.8 (q, $^{2}J_{C\text{-}F}$ = 31.8 Hz), 162.4, 141.9, 141.7 (q, $^{2}J_{C\text{-}F}$ = 39.8 Hz), 121.4 (q, $^{1}J_{C\text{-}F}$ = 266.7 Hz), 117.7 (q, $^{1}J_{C\text{-}F}$ = 289.6 Hz),104,3 (q, $^{3}J_{C\text{-}F}$ = 2.0 Hz), 88.7, 46.2, 41.5, 10.8. **^{19}F NMR (565 MHz, $CDCl_3$)**: δ -62.2 (CF_3, pirazole), -76.9 (CF_3, enaminone). **GC-MS (EI, 70 eV)**: *m/z* (%) = 329 (2) [M^+], 260 (14), 179 (100), 110 (39). **Anal. calcd. for $C_{12}H_{13}F_6N_3O$**: C, 43.78; H, 3.98; N, 12.76%. Found: C, 44.08; H, 4.06; N, 12.84%.

*(E)-4-(Diethylamino)-1,1,1-trifluoro-5-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)pent-3-en-2-one (**6b**)*.



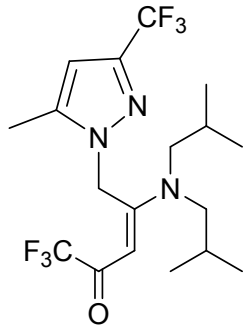
White Crystal (0.152 g, 85% yield). **Mp**: 70–75 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.27 (s, 1H), 5.78 (s, 2H), 5.39 (s, 1H), 3.62 (br s, 2H), 3.47 (br s, 2H), 2.40 (s, 3H), 1.28 (br s, 3H), 0.93 (br s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 175.6 (q, $^{2}J_{C\text{-}F}$ = 30.7 Hz), 160.8, 142.0, 141.7 (q, $^{2}J_{C\text{-}F}$ = 39.8 Hz), 121.4 (q, $^{1}J_{C\text{-}F}$ = 266.7 Hz), 117.7 (q, $^{1}J_{C\text{-}F}$ = 289.6 Hz), 104.3 (q, $^{3}J_{C\text{-}F}$ = 2.0 Hz), 88.8, 46.2, 45.4 (br s), 13.4 (br s), 10.7. **GC-MS (EI, 70 eV)**: *m/z* (%) = 357 (11) [M^+], 288 (17), 207 (100), 138 (68), 110 (65). **Anal. calcd. for $C_{14}H_{17}F_6N_3O$**: C, 47.06; H, 4.80; N, 11.76%. Found: C, 47.38; H, 4.83; N, 11.74%.

*(E)-4-(Dibutylamino)-1,1,1-trifluoro-5-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)pent-3-en-2-one (**6c**)*.



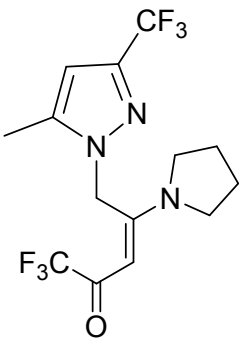
Brown oil (0.151 g, 73% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.26 (s, 1H), 5.76 (s, 2H), 5.38 (s, 1H), 3.51 (br s, 2H), 3.38 (br s, 2H), 2.40 (s, 3H), 1.41–1.25 (m, 8H), 0.87–0.98 (m, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 175.5 (q, $^{2}J_{C\text{-}F}$ = 30.7 Hz), 160.9, 142.0, 141.7 (q, $^{2}J_{C\text{-}F}$ = 39.8 Hz), 121.4 (q, $^{1}J_{C\text{-}F}$ = 266.7 Hz), 117.7 (q, $^{1}J_{C\text{-}F}$ = 289.6 Hz), 104.3 (q, $^{3}J_{C\text{-}F}$ = 2.0 Hz), 88.2, 52.2 (br s), 51.3 (br s), 46.2, 30.9 (br s), 27.5 (br s), 20.2 (br s), 13.6, 10.7. **GC-MS (EI, 70 eV)**: *m/z* (%) = 413 (16) [M^+], 344 (22), 250 (43), 179 (58), 166 (100), 152 (55). **HRMS (ESI^+)**: *m/z* calcd. for $C_{18}H_{26}F_6N_3O$ $[M+H]^+$ 414.1980, found 414.1971.

*(E)-4-(Diisobutylamino)-1,1,1-trifluoro-5-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)pent-3-en-2-one (**6d**)*.



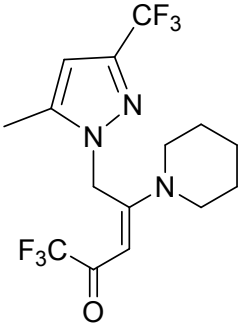
White solid (0.137 g, 66% yield). **Mp**: 96–98 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.26 (s, 1H), 5.67 (s, 2H), 5.39 (s, 1H), 3.47 (br s, 2H), 3.26 (br s, 2H), 2.46 (s, 3H), 2.28 (br s, 1H), 1.95 (br s, 1H), 0.95 (br s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 175.3 (q, $^{2}J_{C\text{-}F}$ = 30.9 Hz), 161.5, 141.8, 141.5 (q, $^{2}J_{C\text{-}F}$ = 39.8 Hz), 121.4 (q, $^{1}J_{C\text{-}F}$ = 266.7 Hz), 117.8 (q, $^{1}J_{C\text{-}F}$ = 289.6 Hz), 104.5 (q, $^{3}J_{C\text{-}F}$ = 2.0 Hz), 88.1, 60.2 (br s), 59.8 (br s), 45.2, 28.9 (br s), 25.5 (br s), 20.0 (br s), 10.9. **GC-MS (EI, 70 eV)**: *m/z* (%) = 413 (9) [M^+], 344 (10), 220 (36), 207 (100), 164 (67). **Anal. calcd. for $C_{18}H_{25}F_6N_3O$**: C, 52.30; H, 6.10; N, 10.16%. Found: C, 52.39; H, 6.19; N, 10.10%.

*(E)-1,1,1-Trifluoro-5-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-4-(pyrrolidin-1-yl)pent-3-en-2-one (**6e**)*.



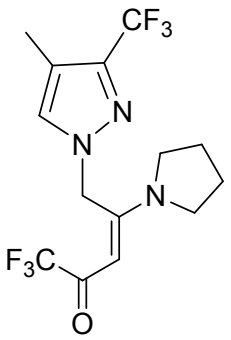
White crystal (0.138 g, 78% yield). **Mp**: 144–145 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.26 (s, 1H), 5.69 (s, 2H), 5.27 (s, 1H), 3.65 (t, *J* = 6,4 Hz, 2H), 3.45 (t, *J* = 6,4 Hz, 2H), 2.42 (s, 3H), 2.06–1.98 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 175.4 (q, $^{2}J_{C\text{-}F}$ = 30.9 Hz), 159.7, 141.9, 141.6 (q, $^{2}J_{C\text{-}F}$ = 39.8 Hz), 121.4 (q, $^{1}J_{C\text{-}F}$ = 266.7 Hz), 117.8 (q, $^{1}J_{C\text{-}F}$ = 289.6 Hz), 104.2 (q, $^{3}J_{C\text{-}F}$ = 2.0 Hz), 88.7, 50.3, 49.9, 47.6, 25.5, 24.5, 10.9. **GC-MS (EI, 70 eV)**: *m/z* (%) = 355 (6) [M^+], 286 (10), 205 (100), 136 (54). **Anal. calcd. for $C_{14}H_{15}F_6N_3O$**: C, 47.33; H, 4.26; N, 11.83%. Found: C, 47.54; H, 4.26; N, 11.78%.

*(E)-1,1,1-Trifluoro-5-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-4-(piperidin-1-yl)pent-3-en-2-one (**6f**)*.



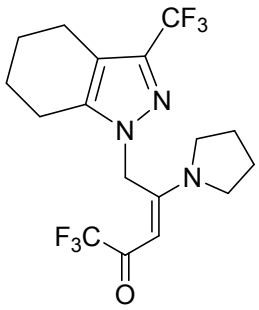
White solid (0.131 g, 71% yield). **Mp**: 148–149 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.27 (s, 1H), 5.84 (s, 2H), 5.47 (s, 1H), 3.59 (t, *J* = 5.2, 4H), 2.37 (s, 3H), 1.65–2.67 (m, 2H), 1.54 (br s, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 176.2 (q, $^{2}J_{C\text{-}F}$ = 30.9 Hz), 161.9, 141.9, 141.6 (q, $^{2}J_{C\text{-}F}$ = 39.8 Hz), 121.3 (q, $^{1}J_{C\text{-}F}$ = 266.7 Hz), 117.8 (q, $^{1}J_{C\text{-}F}$ = 289.6 Hz), 104.3 (q, $^{3}J_{C\text{-}F}$ = 2.0 Hz), 88.6, 50.1, 46.5, 25.7, 23.8, 10.7. **GC-MS (EI, 70 eV)**: *m/z* (%) = 369 (9) [M^+], 300 (12), 219 (98), 150 (100). **Anal. calcd. for $C_{15}H_{17}F_6N_3O$**: C, 48.78; H, 4.64; N, 11.38%. Found: C, 48.68; H, 4.59; N, 11.31%.

*(E)-1,1,1-Trifluoro-5-(4-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-4-(pyrrolidin-1-yl)pent-3-en-2-one (**6g**)*.



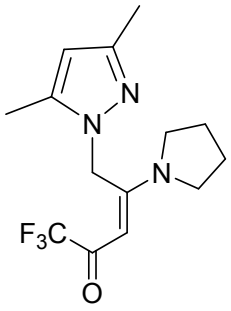
Brown solid (0.132 g, 74% yield). **Mp**: 149–151 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.66 (s, 1H), 5.63 (s, 2H), 5.22 (s, 1H), 4.02 (t, *J* = 6,4 Hz, 2H), 3.39 (t, *J* = 6,4 Hz, 2H), 2.12 (s, 3H), 2.05–2.03 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 175.7 (q, $^{2}J_{C\text{-}F}$ = 31.7 Hz), 160.2, 140.4 (q, $^{2}J_{C\text{-}F}$ = 39.8 Hz), 132.1, 121.9 (q, $^{1}J_{C\text{-}F}$ = 267.4 Hz), 117.9 (q, $^{1}J_{C\text{-}F}$ = 289.4 Hz), 115.7, 88.4, 50.1, 49.8, 49.4, 25.3, 24.6, 8.1. **GC-MS (EI, 70 eV)**: *m/z* (%) = 355 (7) [M^{+}], 286 (11), 205 (100), 136 (62). **Anal. calcd. for $C_{14}H_{15}F_6N_3O$**: C, 47.33; H, 4.26; N, 11.83%. Found: C, 47.36; H, 4.20; N, 11.58%.

*(E)-1,1,1-Trifluoro-4-(pyrrolidin-1-yl)-5-(3-(trifluoromethyl)-4,5,6,7-tetrahydro-1H-indazol-1-yl)pent-3-en-2-one (**6h**).*



White solid (0.138 g, 70% yield). **Mp**: 136–137 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 5.68 (s, 2H), 5.25 (s, 1H), 3.67 (t, *J* = 6,4 Hz, 2H), 3.44 (t, *J* = 6,4 Hz, 2H), 2.72 (t, *J* = 6,4 Hz, 2H), 2.56 (t, *J* = 6,4 Hz, 2H), 2.05–1.97 (m, 4H), 1.82–1.71 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 175.4 (q, $^{2}J_{C\text{-}F}$ = 30.9 Hz), 159.9, 141.8, 138.6 (q, $^{2}J_{C\text{-}F}$ = 35.9 Hz), 122.1 (q, $^{1}J_{C\text{-}F}$ = 267.7 Hz), 117.9 (q, $^{1}J_{C\text{-}F}$ = 290.7 Hz), 115.5, 88.7, 50.3, 50.1, 47.3, 25.5, 24.5, 22.3, 22.2, 21.0, 20.1. **GC-MS (EI, 70 eV)**: *m/z* (%) = 395 (1) [M^{+}], 205 (100), 136 (37). **Anal. calcd. for $C_{14}H_{15}F_6N_3O$**: C, 51.65; H, 4.84; N, 10.63%. Found: C, 51.45; H, 4.57; N, 10.39%.

*(E)-5-(*3,5-Dimethyl-1*H*-pyrazol-1-yl*)-1,1,1-Trifluoro-4-(pyrrolidin-1-yl)pent-3-en-2-one (**6i**)*.

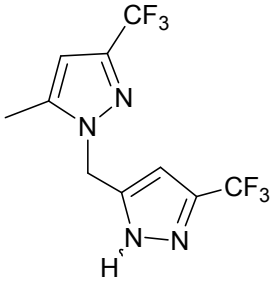


Brown solid (0.078 g, 52% yield). **Mp**: 140–141 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 5.78 (s, 1H), 5.66 (s, 2H), 5.26 (s, 1H), 3.52 (t, *J* = 6,4 Hz, 2H), 3.44 (t, *J* = 6,4 Hz, 2H), 2.27 (s, 3H), 2.16 (s, 3H), 2.01–1.92 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 175.1 (q, $^{2}J_{C\text{-}F}$ = 30.9 Hz), 161.7, 147.7, 140.6, 117.8 (q, $^{1}J_{C\text{-}F}$ = 289.6 Hz), 105.7, 88.5, 50.3, 49.8, 47.2, 25.6, 13.5, 10.8. **GC-MS (EI, 70 eV)**: *m/z* (%) = 301 (1) [M^+], 205 (100), 136 (46). **HRMS (ESI^+)**: *m/z* calcd. for $C_{14}H_{19}F_3N_3O$ $[M+H]^+$ 302.1480, found 302.1492.

Procedure for the synthesis of 5-methyl-3-(trifluoromethyl)-1-((3-(trifluoromethyl)-1*H*-pyrazol-5-yl)methyl)-1*H*-pyrazole *(7)*.

To a solution of hydrazine sulfate (0.130 g, 1.0 mmol) in anhydrous methanol (5 mL), pyrazole enaminone ***6e*** (0.178 g, 0.5 mmol) was added and the reaction mixture was stirred under reflux for 24 h. Then, the solvent was evaporated at reduced pressure, and the residue was dissolved in dichloromethane (10 mL), washed with water (3 x 10 mL), dried under magnesium sulfate, filtered, and the solvent was removed under reduced pressure, obtaining a brown solid, which was purified by flash column chromatography using silica gel (230–400 mesh) and chloroform as the eluent.

*5-Methyl-3-(trifluoromethyl)-1-((3-(trifluoromethyl)-1H-pyrazol-5-yl)methyl)-1H-pyrazole (**7**).*



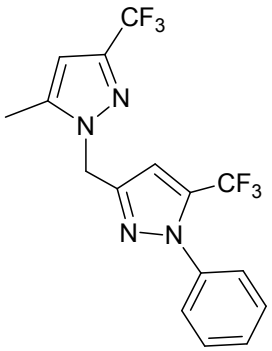
Brown solid (0.129 g, 87% yield). **Mp**: 76–78 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 12.04 (s, N-H), 6.48 (s, 1H), 6.32 (s, 1H), 5.34 (s, 2H), 2.34 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 142.6 (q, $^{2}J_{C\text{-}F}$ = 37.9 Hz), 140.8, 139.5, 121.9 (q, $^{1}J_{C\text{-}F}$ = 266.7 Hz), 120.9 (q, $^{1}J_{C\text{-}F}$ = 267.7 Hz), 104.7 (q, $^{3}J_{C\text{-}F}$ = 1.0 Hz), 103.5, 44.3, 11.1. **GC-MS (EI, 70 eV)**: *m/z* (%) = 298 (51) [M^+], 149 (100).

Anal. calcd. for $C_{14}H_{15}F_6N_3O$: C, 40.28; H, 2.70; N, 18.79%. Found: C, 40.83; H, 2.92; N, 18.14%.

Procedure for synthesis of 5-Methyl-1-((1-phenyl-5-(trifluoromethyl)-1*H*-pyrazol-3-yl)methyl)-3-(trifluoromethyl)-1*H*-pyrazole *(8)*.

To a solution of the pyrazole enaminone **6e** (0.178 g, 0.5 mmol), in anhydrous ethanol (5 mL), phenyl hydrazine (0.108 g, 1.0 mmol) was added dropwise at room temperature and the reaction mixture was refluxed for 24 h. After that, the solvent was evaporated at reduced pressure, and to the residue was added dichloromethane (5 mL) and sulfuric acid 96% (1 mL) and the mixture was stirred at 40 ºC for 2 h. Then, the residue was washed with water (3 x 10mL), dried under magnesium sulfate, filtered, and the solvent was removed under reduced pressure, to obtaining a brown solid, which was purified by a flash column chromatography using silica gel (230–400 mesh) and chloroform as the eluent.

*5-Methyl-1-((1-phenyl-5-(trifluoromethyl)-1H-pyrazol-3-yl)methyl)-3-(trifluoromethyl)-1H-pyrazole (**8**).*

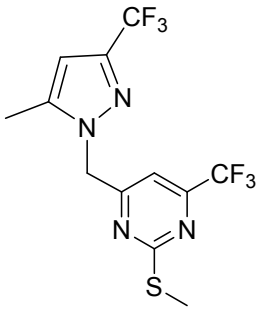


Brown solid (0.116 g, 62% yield). **Mp**: 47–49 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.49–7.44, (m, 5H, Ar), 6.67 (s, 1H), 6.31 (s, 1H), 5.37 (s, 2H), 2.35 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 147.9, 142.0 (q, $^2J_{C\text{-}F}$ = 37.9 Hz), 140.5, 138.8, 134.1 (q, $^2J_{C\text{-}F}$ = 38.9 Hz), 129.6, 129.2, 125.7 121.4 (q, $^1J_{C\text{-}F}$ = 266.7 Hz), 119.5 (q, $^1J_{C\text{-}F}$ = 268.7 Hz), 108.0 (q, $^3J_{C\text{-}F}$ = 2.9 Hz), 104.4 (q, $^3J_{C\text{-}F}$ = 2.0 Hz), 47.4, 11.3. **GC-MS (EI, 70 eV)**: *m/z* (%) = 374 (65) [M^+], 225 (100). **Anal. calcd. for $C_{14}H_{15}F_6N_3O$**: C, 51.34; H, 3.23; N, 14.97%. Found: C, 51.94; H, 3.25; N, 14.55%.

Procedure for synthesis of 4-((5-Methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)methyl)-2-(methylthio)-6-(trifluoromethyl)pyrimidine *(9)*.

A solution of sodium hydroxide (0.105 g in 1 mL of water, 1.0 mmol) was added to a solution 2-methyl-2-thiopseudourea sulfate (0.139 g, 1.0 mmol) in distilled water (3 mL). To this mixture was added a solution of pyrazole enaminone **6e** (0.178 g, 0.5 mmol) in methanol (7 mL) and the mixture was stirred under reflux for 24 h. Then, the methanol was evaporated under reduced pressure and the residue was dissolved in dichloromethane (10 mL), washed with water (3 x 10 mL), dried under magnesium sulfate, filtered, and the solvent was removed under reduced pressure, obtaining a brown oil, which was purified by a flash column chromatography using silica gel (230–400 mesh) and chloroform as the eluent.

*4-((5-Methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)methyl)-2-(methylthio)-6-(trifluoromethyl)pyrimidine (**9**).*



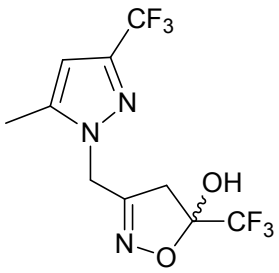
Brown oil (0.037 g, 20% yield). **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.83 (s, 1H), 6.40 (s, 1H), 5.40 (s, 2H), 2.55 (s, 3H), 2.32 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 174.9, 167.1, 156.9 (q, $^{2}J_{C\text{-}F}$ = 36.9 Hz), 142.9 (q, $^{2}J_{C\text{-}F}$ = 38.0 Hz), 141.4, 121.2 (q, $^{1}J_{C\text{-}F}$ = 266.7 Hz), 120.1 (q, $^{1}J_{C\text{-}F}$ = 274.7 Hz), 108.8 (q, $^{3}J_{C\text{-}F}$ = 3.0 Hz), 104.8 (q, $^{3}J_{C\text{-}F}$ = 1.0 Hz), 54.1, 14.2, 11.2.

GC-MS (EI, 70 eV): *m/z* (%) = 356 (100) [M^+], 206 (80), 163 (27). **HRMS (ESI^+)**: *m/z* calcd. for $C_{12}H_{11}F_6N_4S$ $[M+H]^+$ 357.0608, found 357.0612.

Procedure for the synthesis of 3-((5-Methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)methyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-5-ol *(10)*.

A solution of pyrazole enaminone ***6e*** (0.178 g, 0.5 mmol), hydroxylamine hydrochloride (0.070 g, 1.0 mmol), and pyridine (0.05 mL, 1.0 mmol) in anhydrous methanol (5 mL), was refluxed under magnetic stirring for 24 h. After, the solvent was evaporated at reduced pressure and the residue was dissolved in dichloromethane (10 mL), washed with acidic water solution HCl 3% (1 × 10 mL) and water (3 x 10 mL), dried under magnesium sulfate, filtered, and the solvent was removed under reduced pressure, obtaining a white solid, which was purified by recrystallization from hexane/$CHCl_3$ (3:1).

*3-((5-Methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)methyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-5-ol (**10**).*



White solid (0.124 g, 70% yield). **Mp**: 131–133 °C. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 6.34 (s, 1H), 5.07 (s, 2H), 3.26 (d, *J* = 18.7 Hz, 1H), 3.05 (d, *J* = 18.9 Hz, 1H), 2.33 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 154.7, 142.8 (q, $^2J_{C\text{-}F}$ = 37.9 Hz), 141.3, 121.7 (q, $^1J_{C\text{-}F}$ = 281.7 Hz), 121.0 (q, $^1J_{C\text{-}F}$ = 266.7 Hz), 104.9 (q, $^3J_{C\text{-}F}$ = 2.0 Hz), 103.9 (q, $^2J_{C\text{-}F}$ = 33.9 Hz), 46.3, 43.0, 10.9. **GC-MS (EI, 70 eV)**: *m/z* (%) = 317 (20) [M^+], 163 (100). **Anal. calcd. for $C_{14}H_{15}F_6N_3O$**: C, 37.87; H, 2.86; N, 13.25%. Found: C, 37.95; H, 2.89; N, 12.91%.

III - ^{1}H, ^{13}C, ^{19}F and two-dimensional NMR experiments such as COSY HH, HSQC, HMBC, NOESY and GC-MS spectra of compounds 4a–j

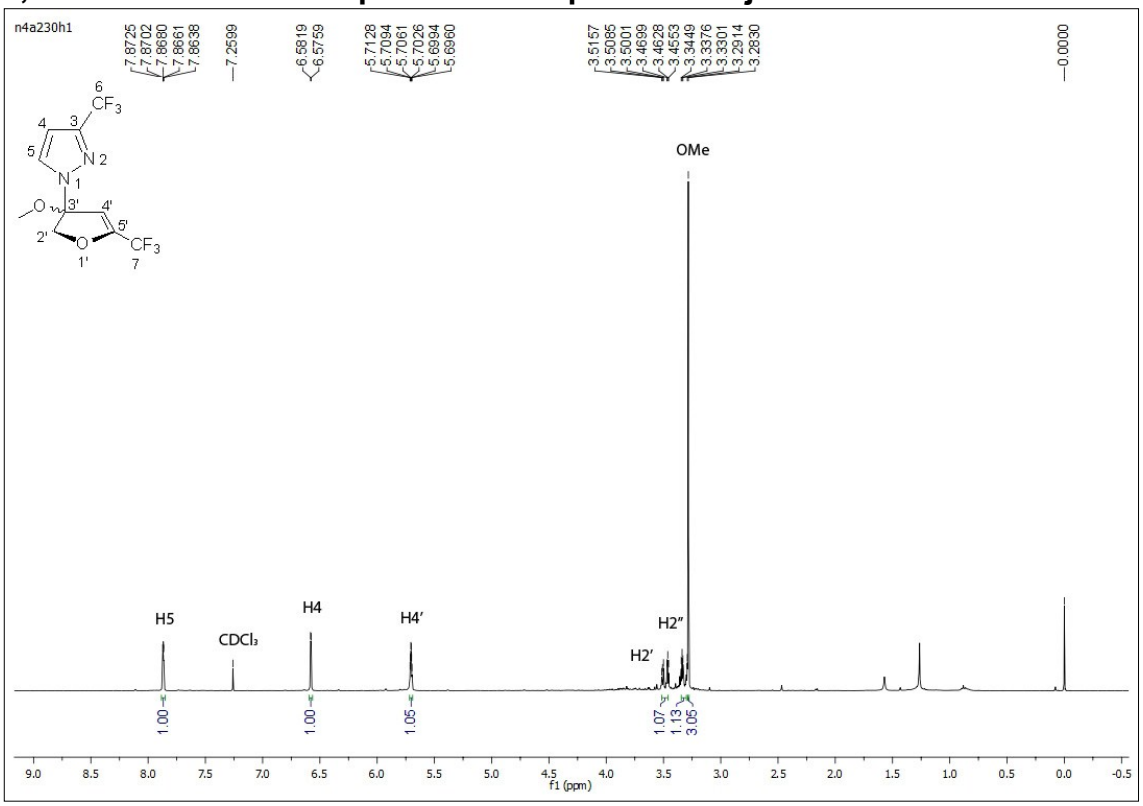


Figure 1 - ^{1}H NMR spectrum of compound **4a** in $CDCl_3$ at 400 MHz.

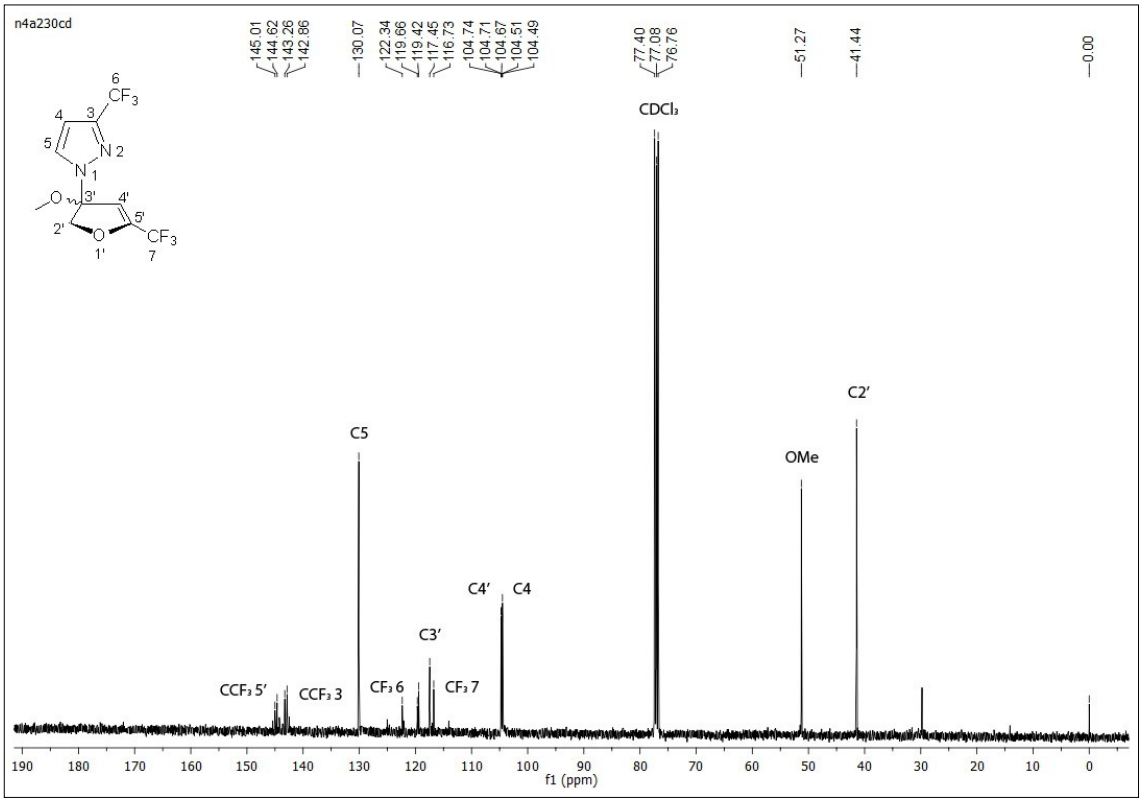


Figure 2 - ^{13}C NMR spectrum of compound **4a** in $CDCl_3$ at 100 MHz.

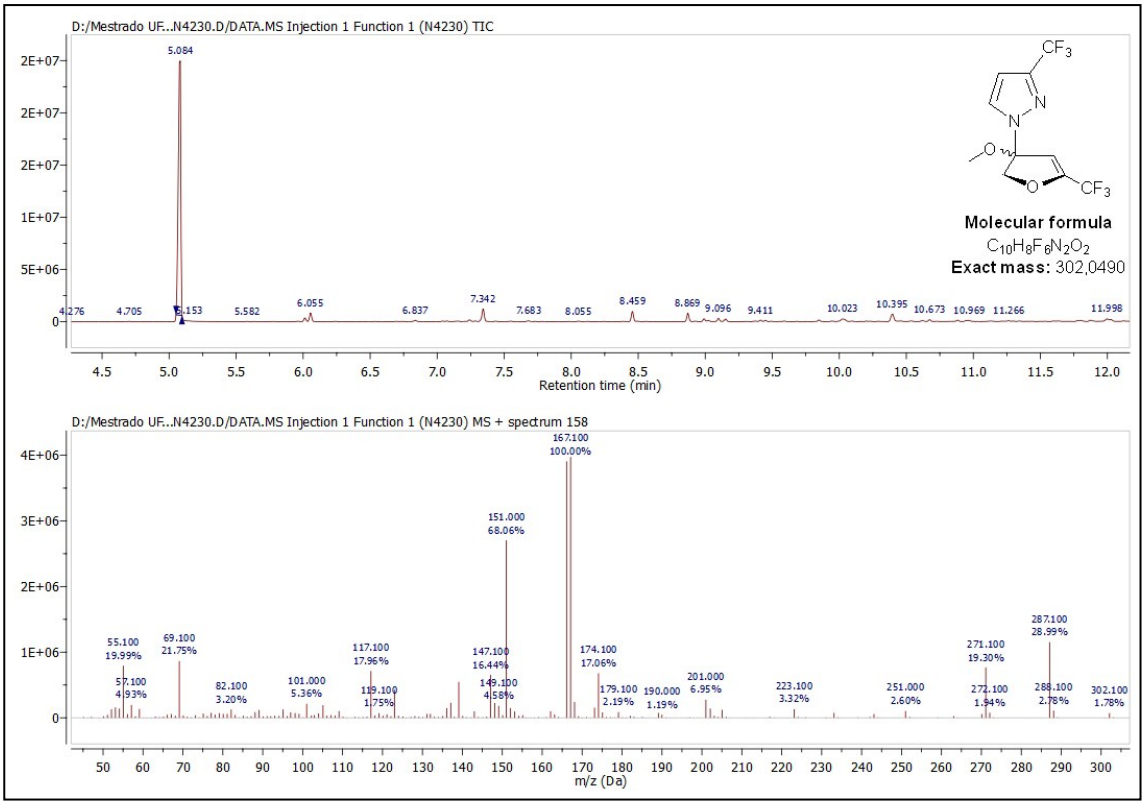


Figure 3 - Chromatogram and mass spectrum (EI, 70 eV) of compound **4a**.

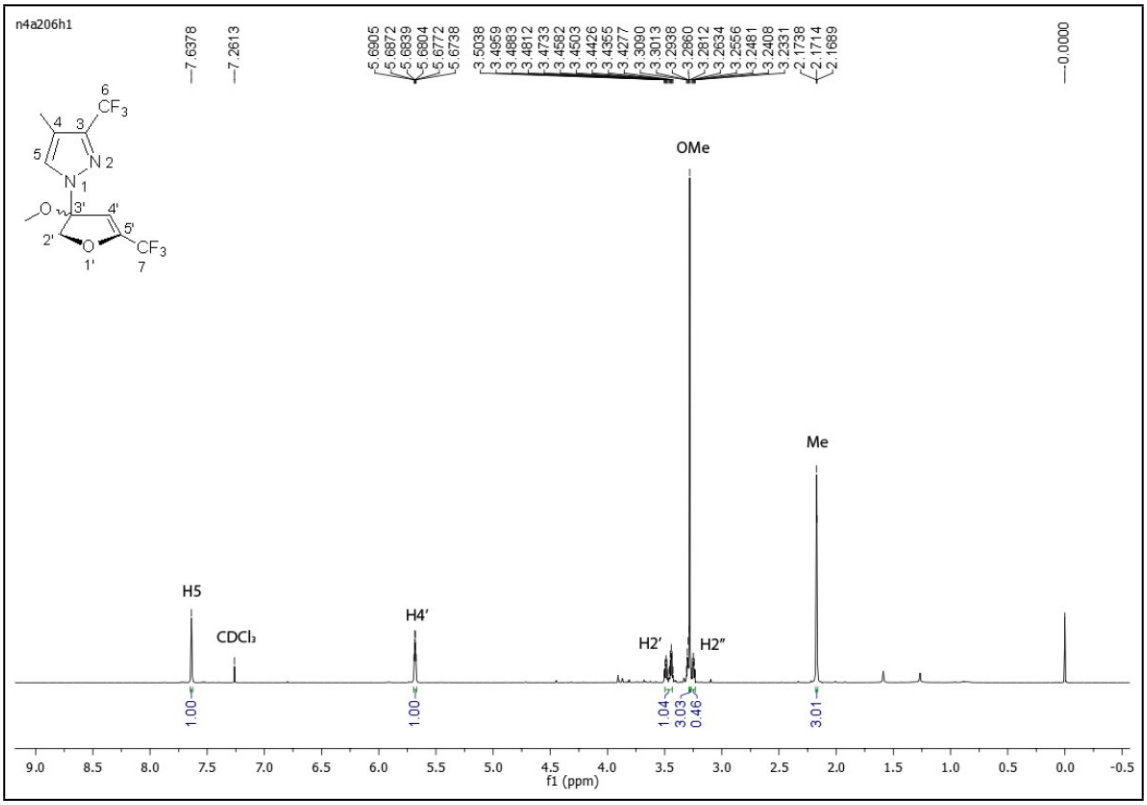


Figure 4 - ^{1}H NMR spectrum of compound **4b** in $CDCl_3$ at 400 MHz.

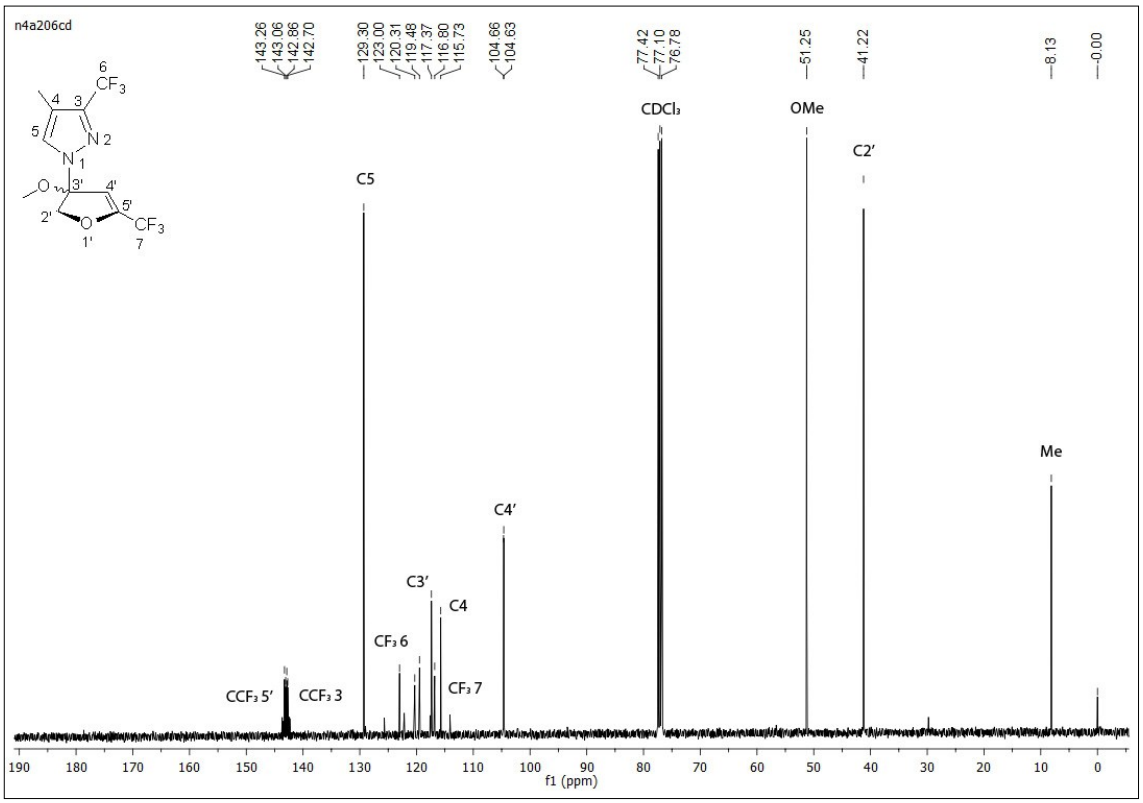


Figure 5 - ^{13}C NMR spectrum of compound **4b** in $CDCl_3$ at 100 MHz.

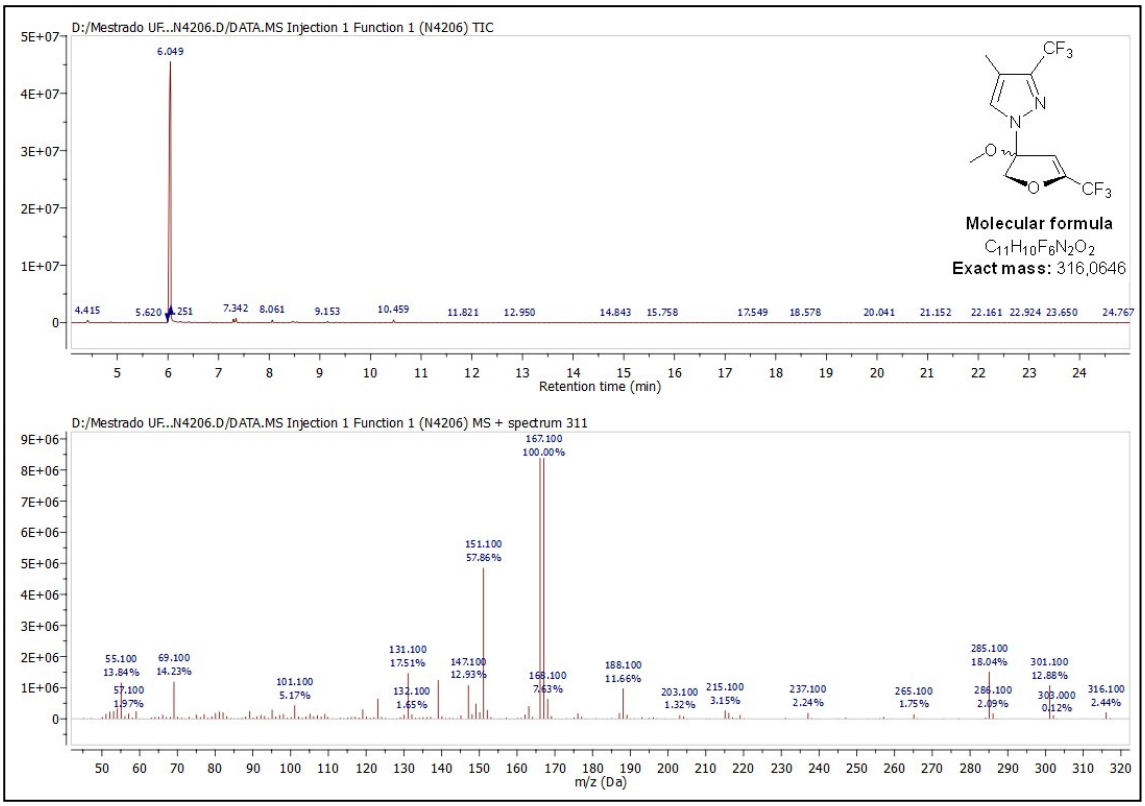


Figure 6 - Chromatogram and mass spectrum (EI, 70 eV) of compound **4b**.

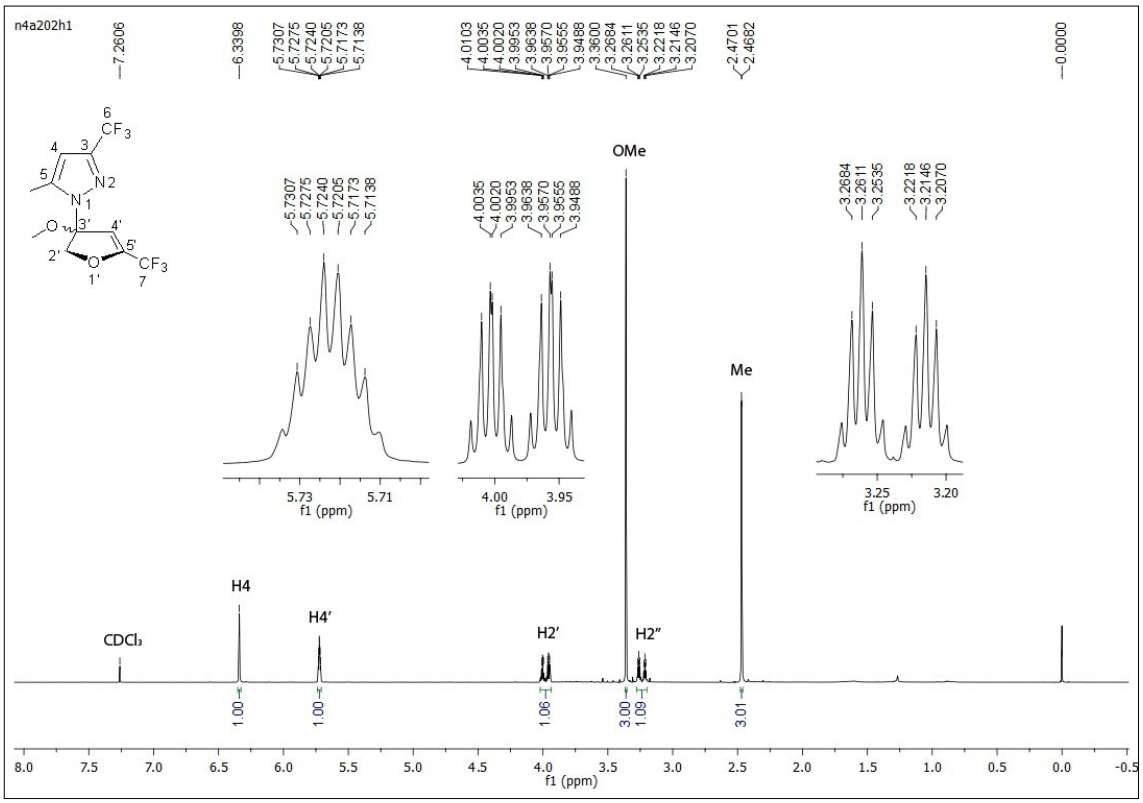


Figure 7 - ^{1}H NMR spectrum of compound **4c** in $CDCl_3$ at 400 MHz.

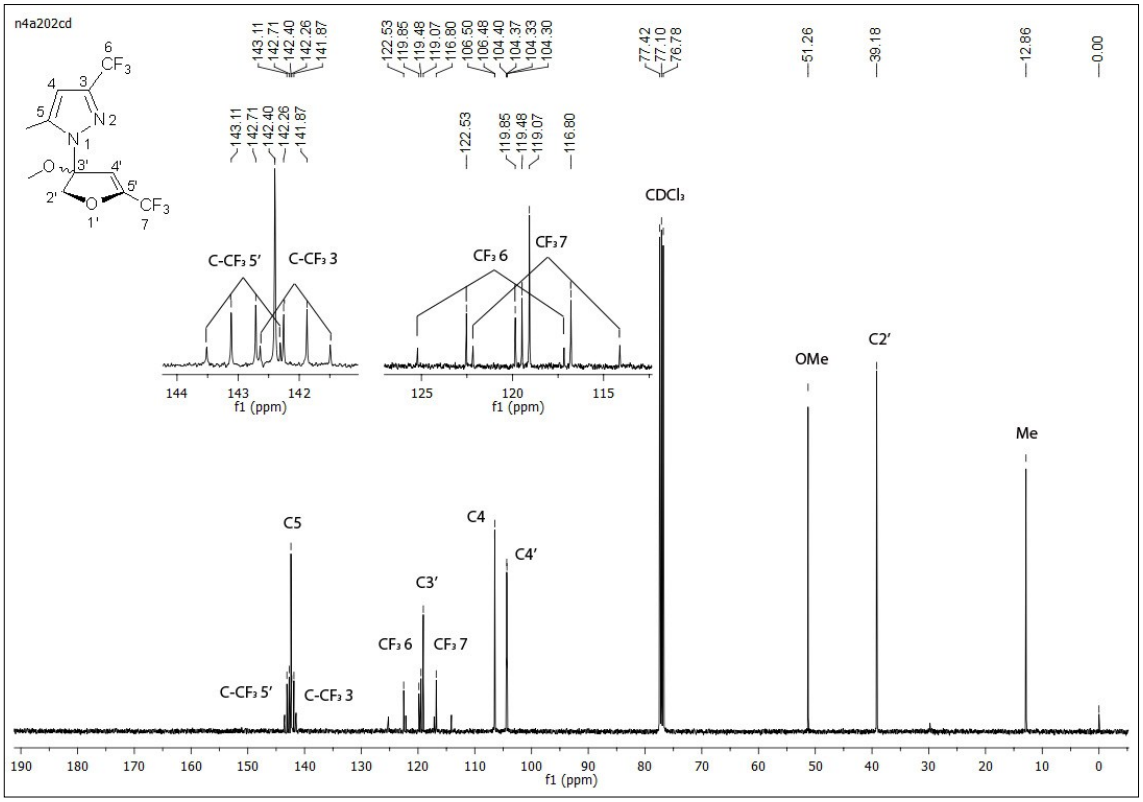


Figure 8 - ^{13}C NMR spectrum of compound **4c** in $CDCl_3$ at 100 MHz.

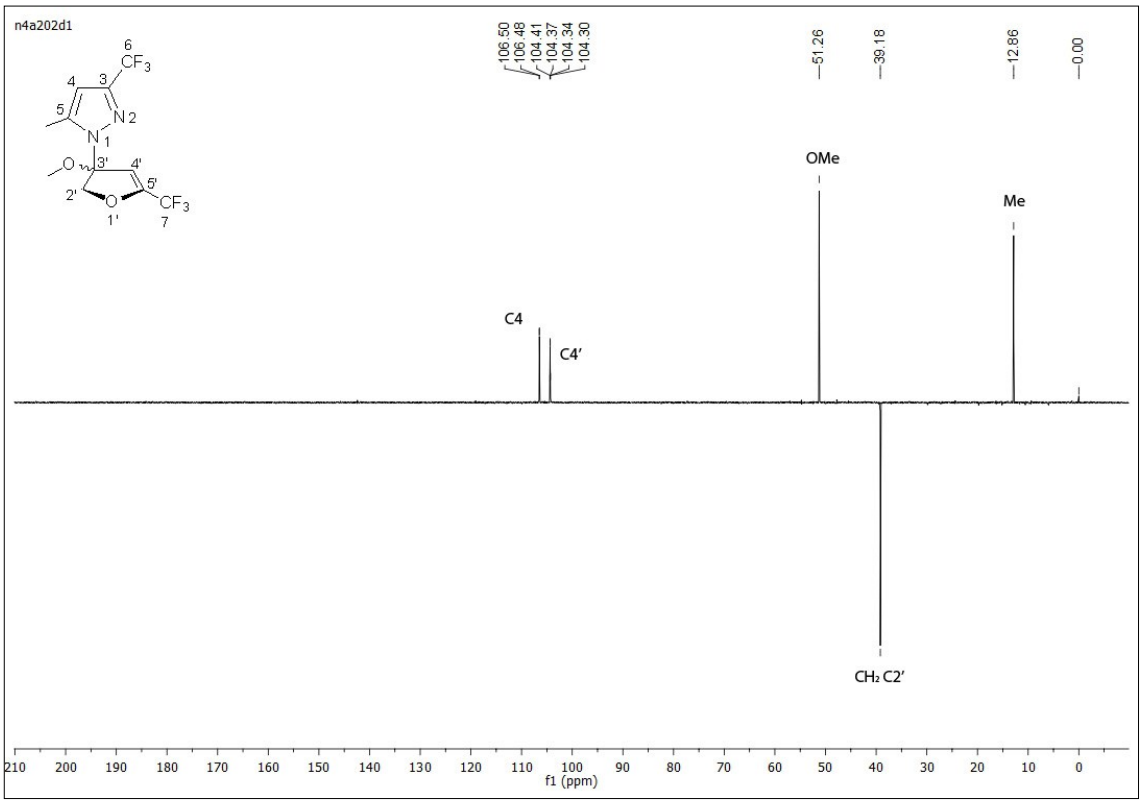


Figure 9 - DEPT 135 NMR spectrum of compound **4c** in $CDCl_3$ at 100 MHz.

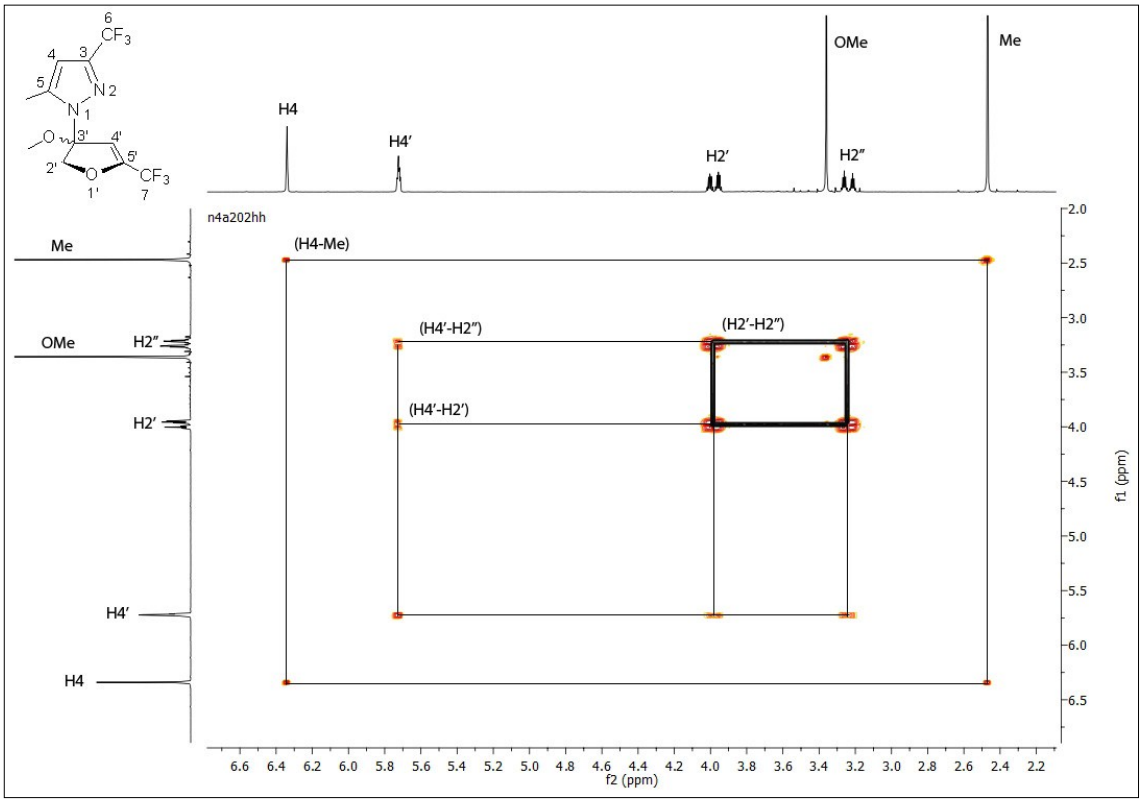


Figure 10 - COSY NMR spectrum of compound **4c** in $CDCl_3$ at 400 MHz.

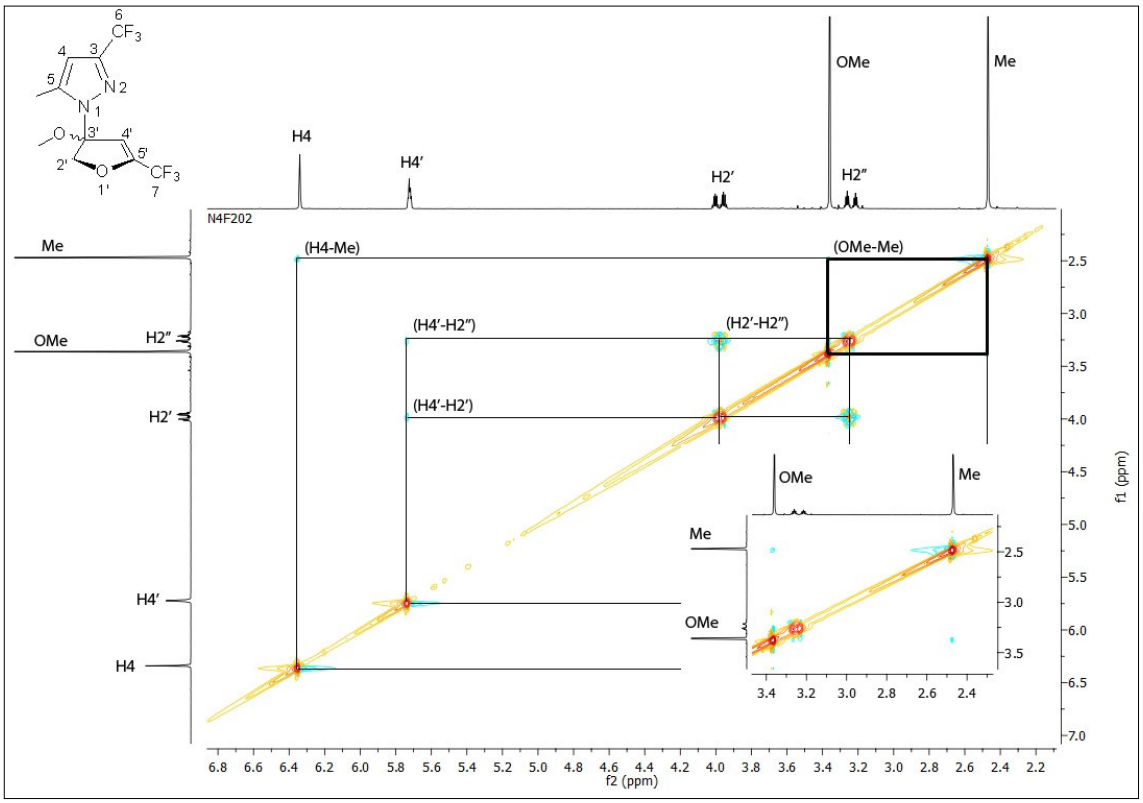


Figure 11 - NOESY NMR spectrum of compound **4c** in $CDCl_3$ at 400 MHz.

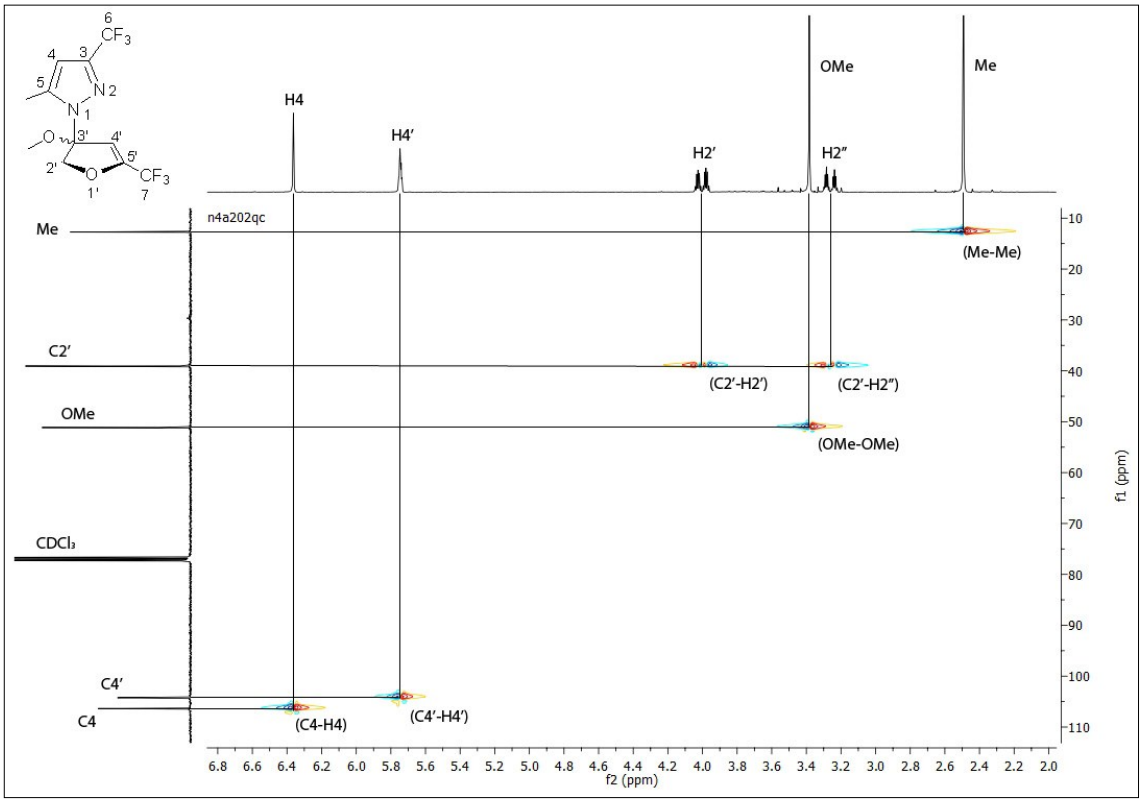


Figure 12 - HMQC NMR spectrum of compound **4c** in $CDCl_3$ at 400 MHz.

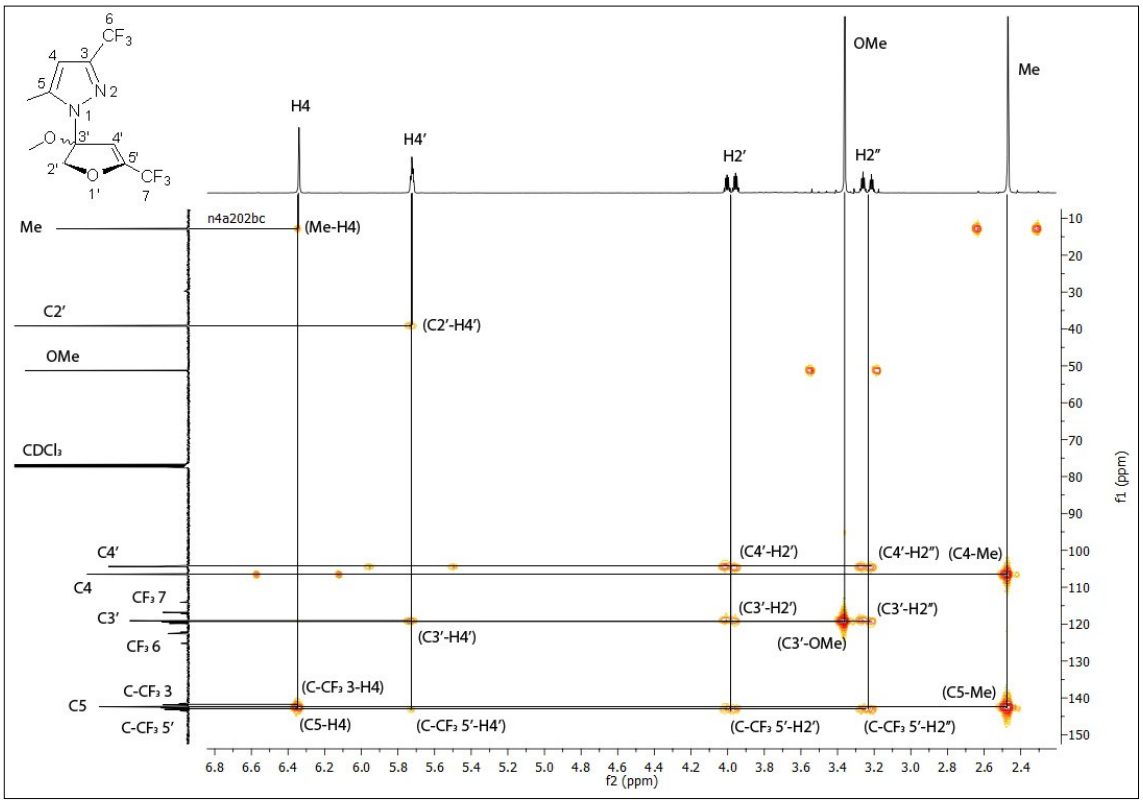


Figure 13 - HMBC NMR spectrum of compound **4c** in $CDCl_3$ at 400 MHz.

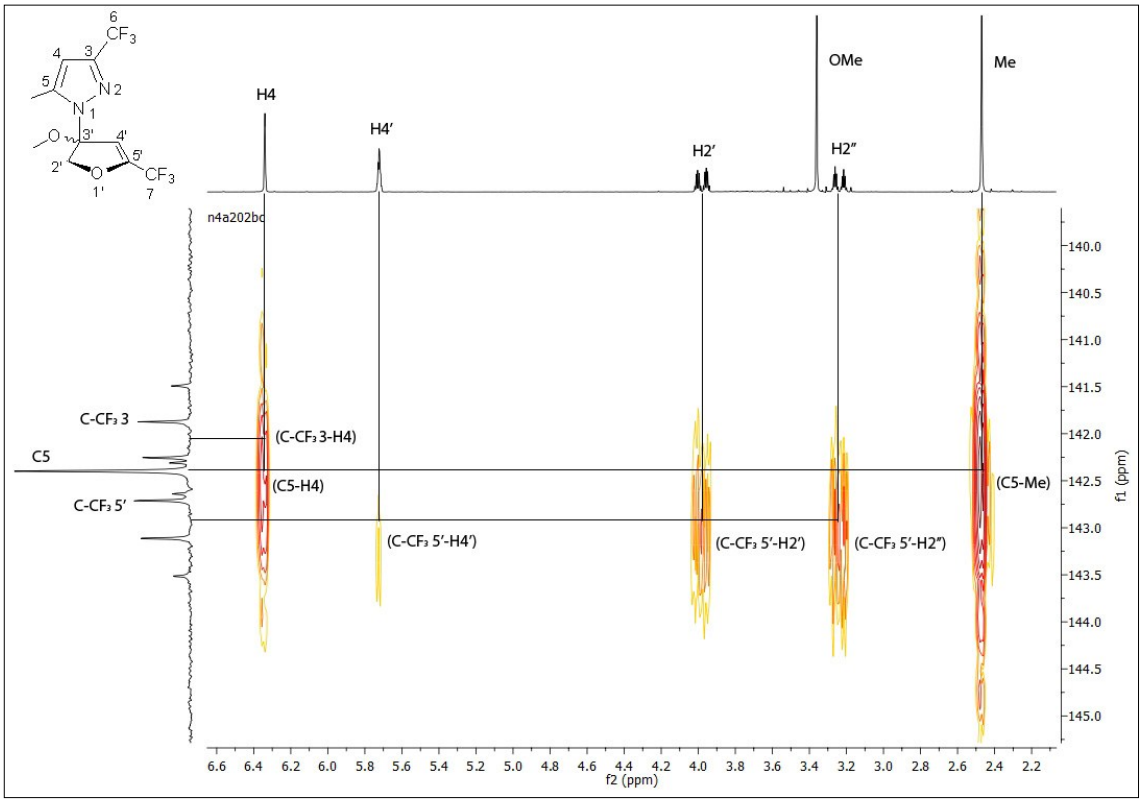


Figure 14 - HMBC NMR spectrum (Expansion) of compound **4c** in $CDCl_3$ at 400 MHz.

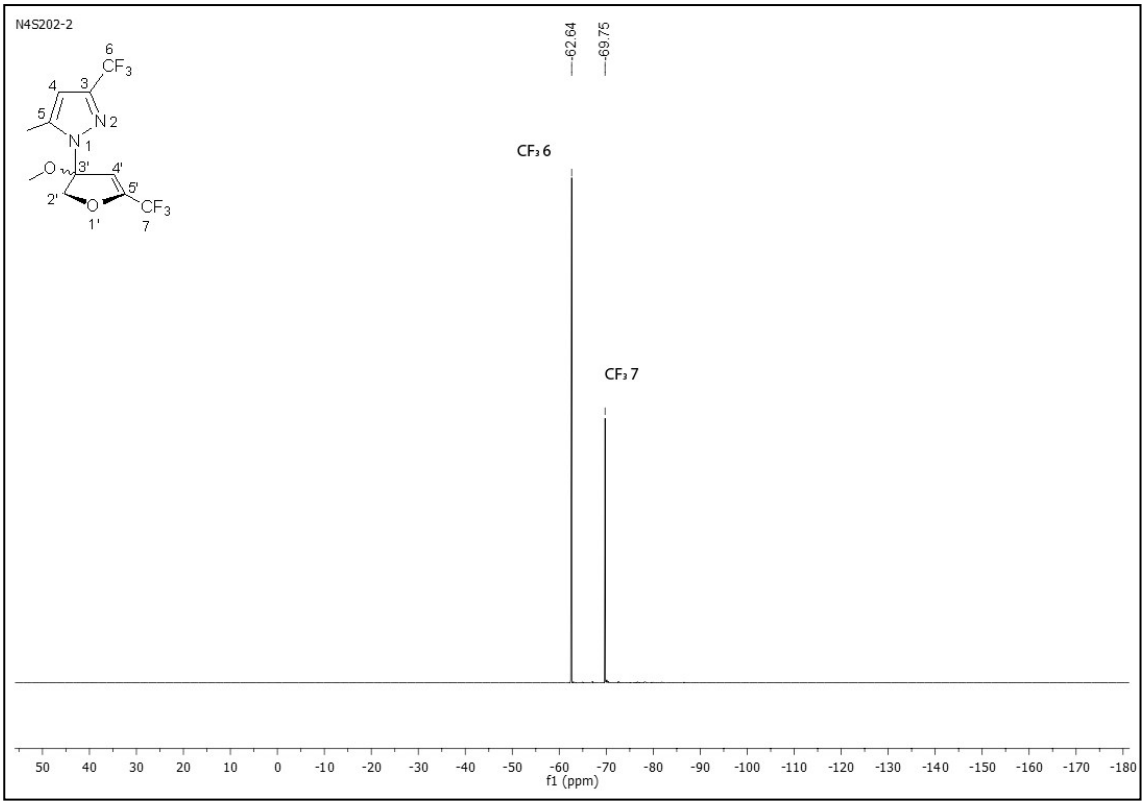


Figure 15 - ^{19}F NMR spectrum of compound **4c** in $CDCl_3$ at 100 MHz.

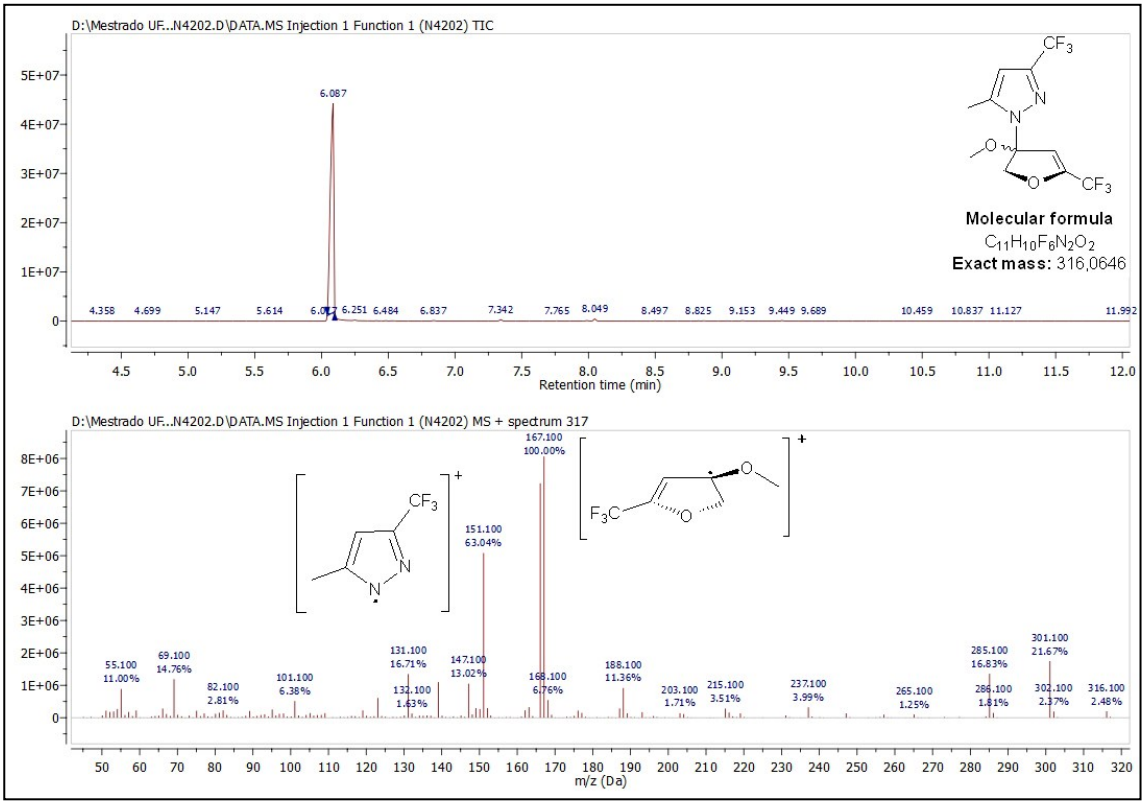


Figure 16 - Chromatogram and mass spectrum (EI, 70 eV) of compound **4c**.

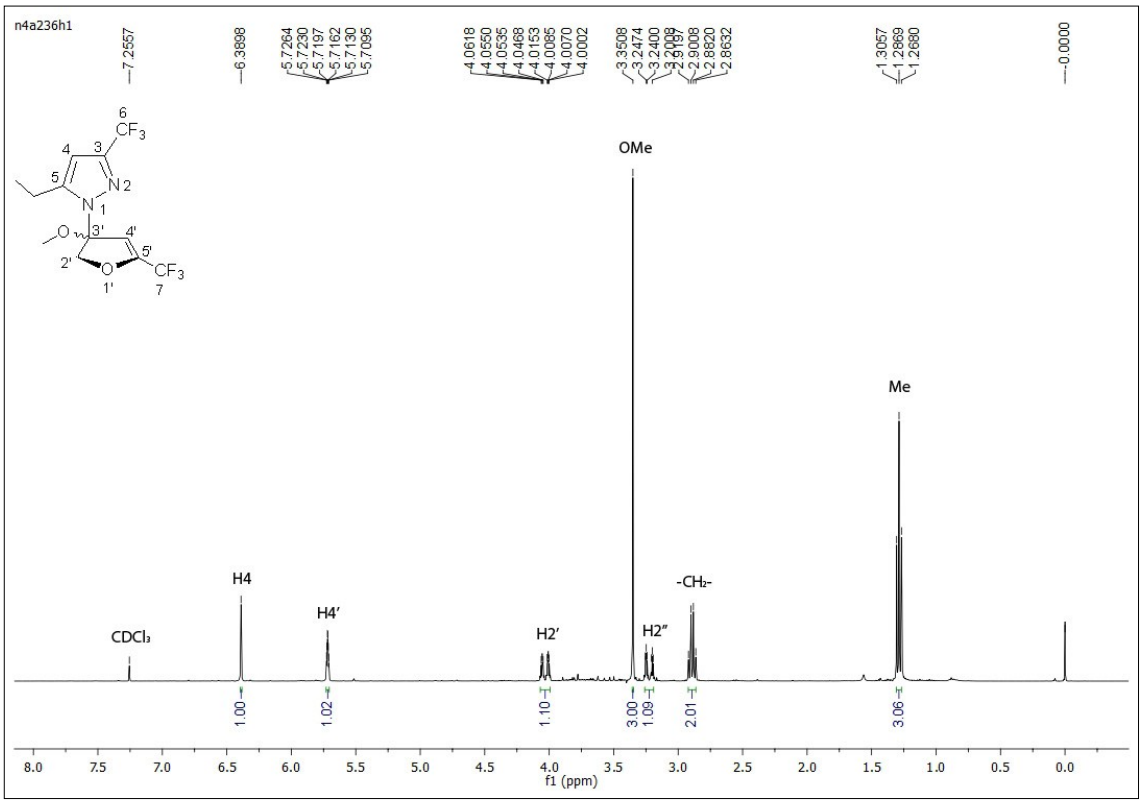


Figure 17 - ^{1}H NMR spectrum of compound **4d** in $CDCl_3$ at 400 MHz.

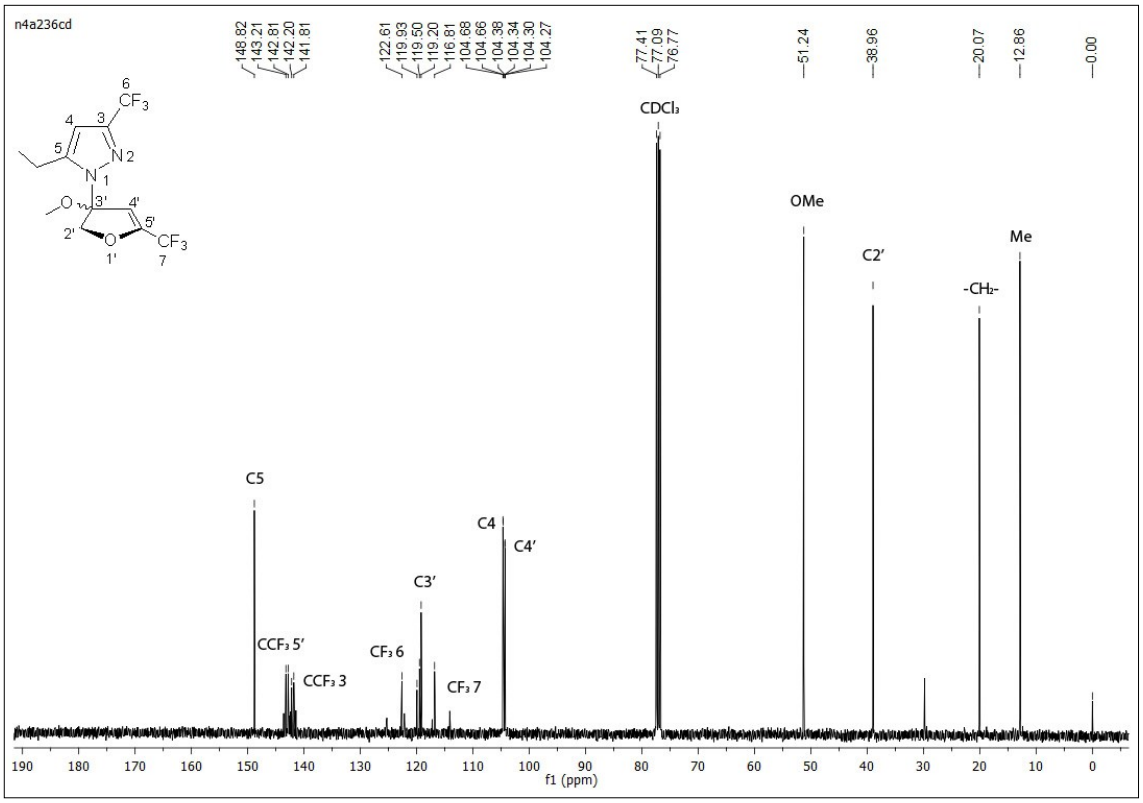


Figure 18 - ^{13}C NMR spectrum of compound **4d** in $CDCl_3$ at 100 MHz.

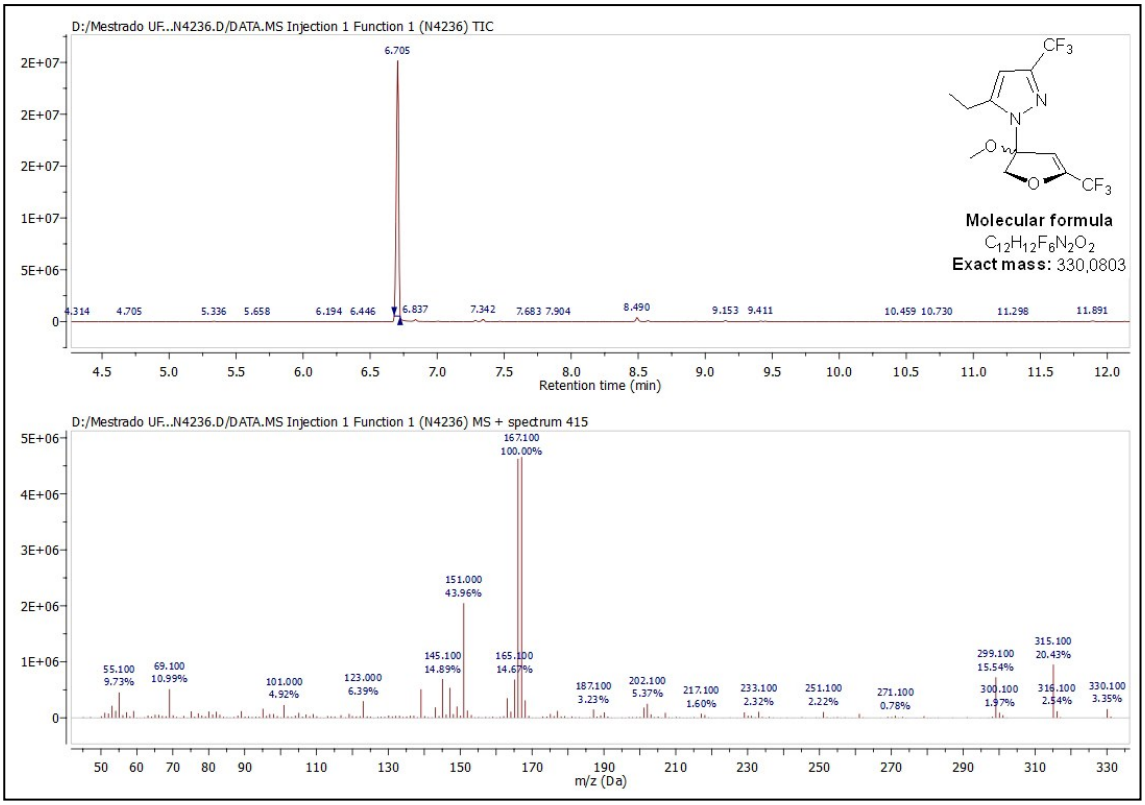


Figure 19 - Chromatogram and mass spectrum (EI, 70 eV) of compound **4d**.

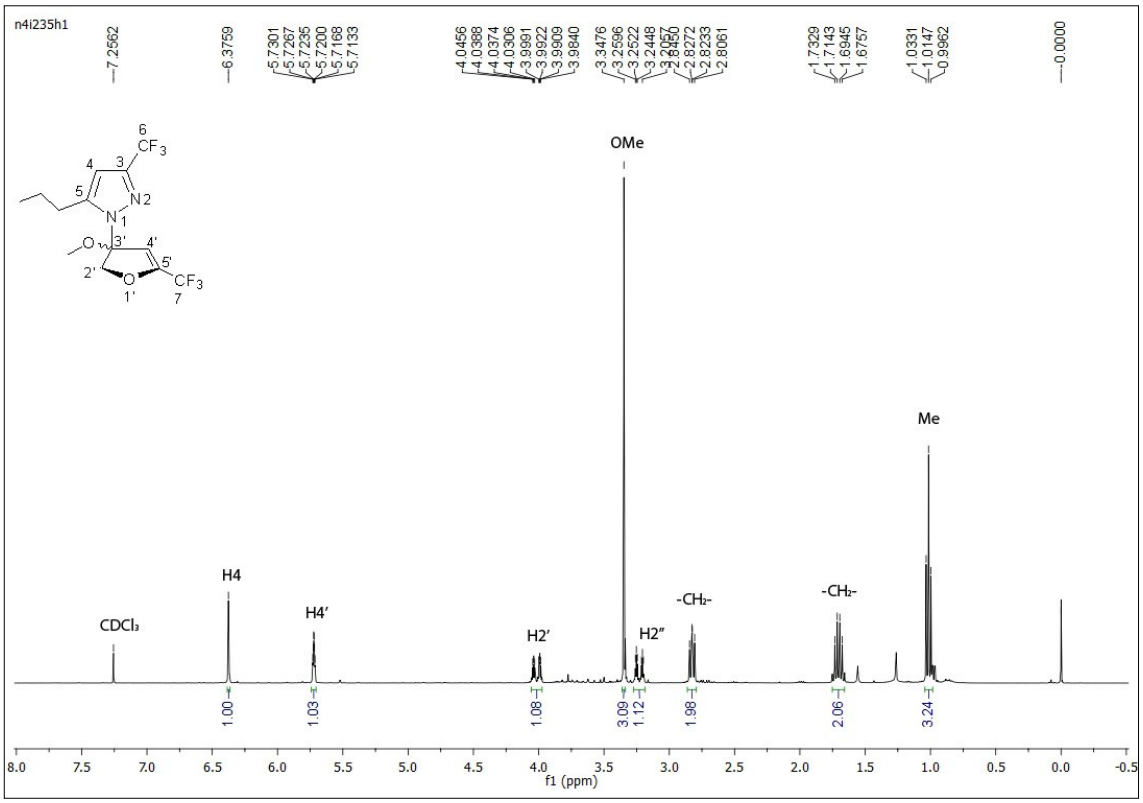


Figure 20 - ^{1}H NMR spectrum of compound **4e** in $CDCl_3$ at 400 MHz.

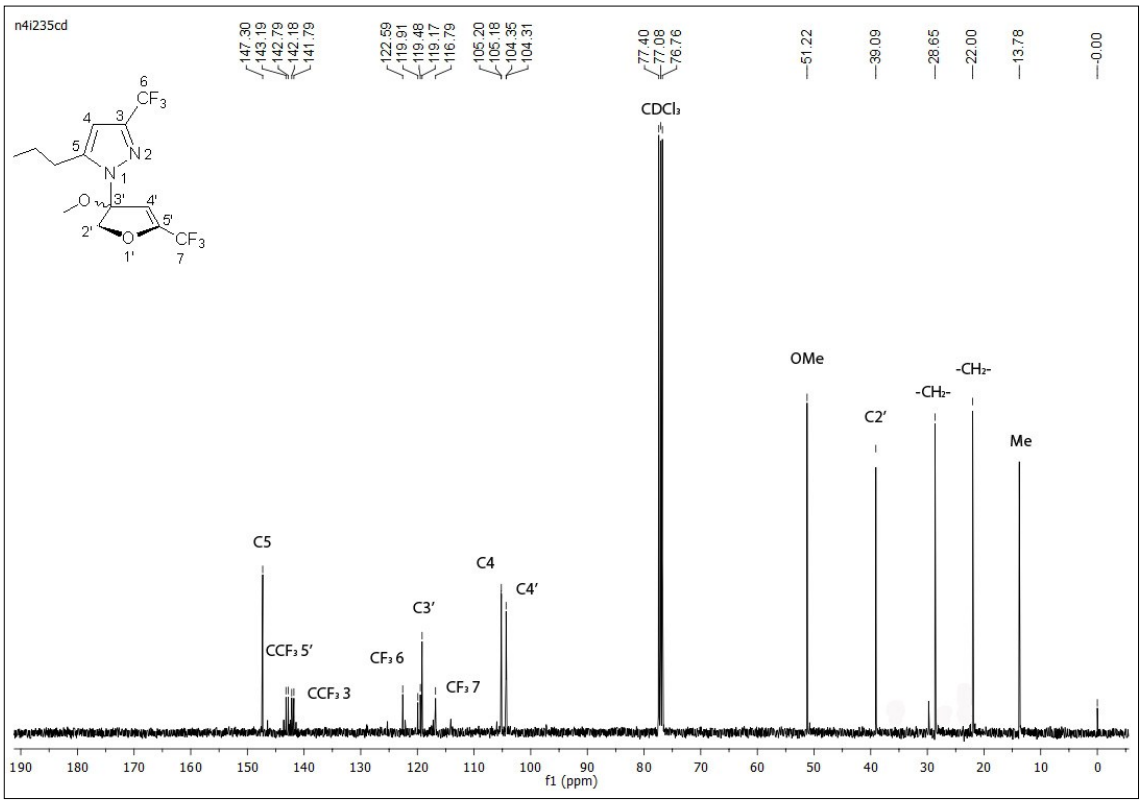


Figure 21 - ^{13}C NMR spectrum of compound **4e** in $CDCl_3$ at 100 MHz.

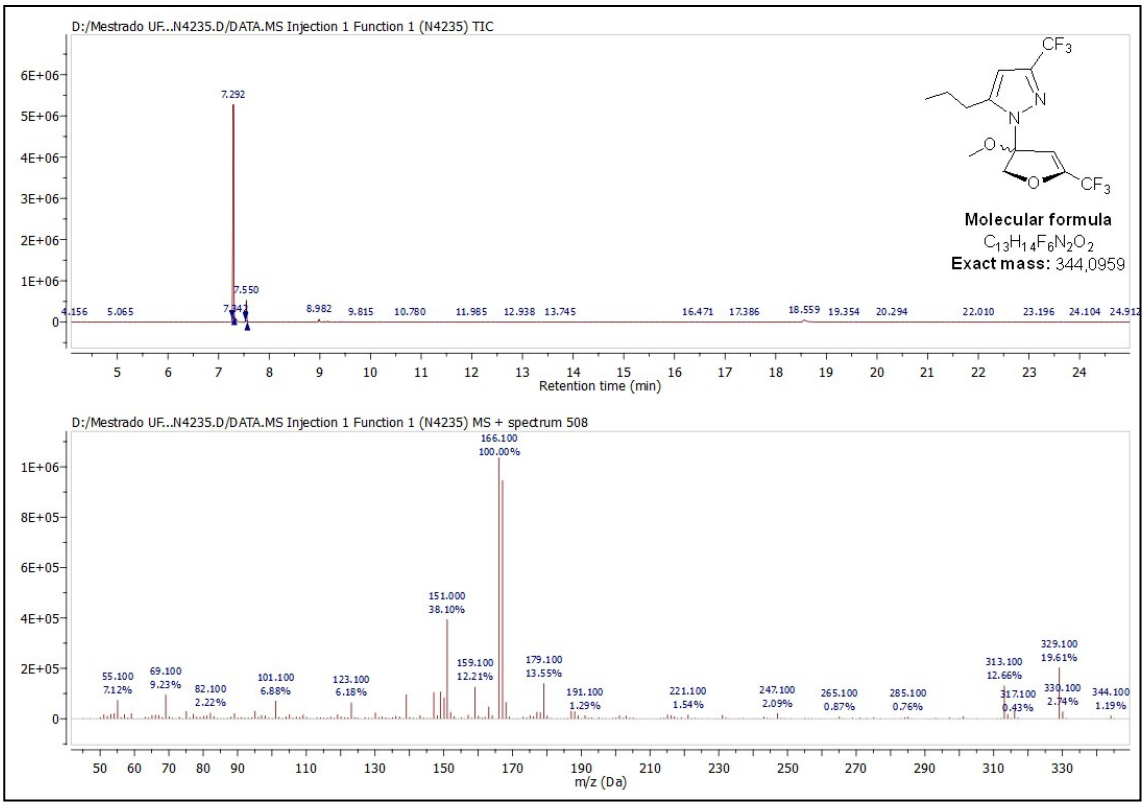


Figure 22 - Chromatogram and mass spectrum (EI, 70 eV) of compound **4e**.

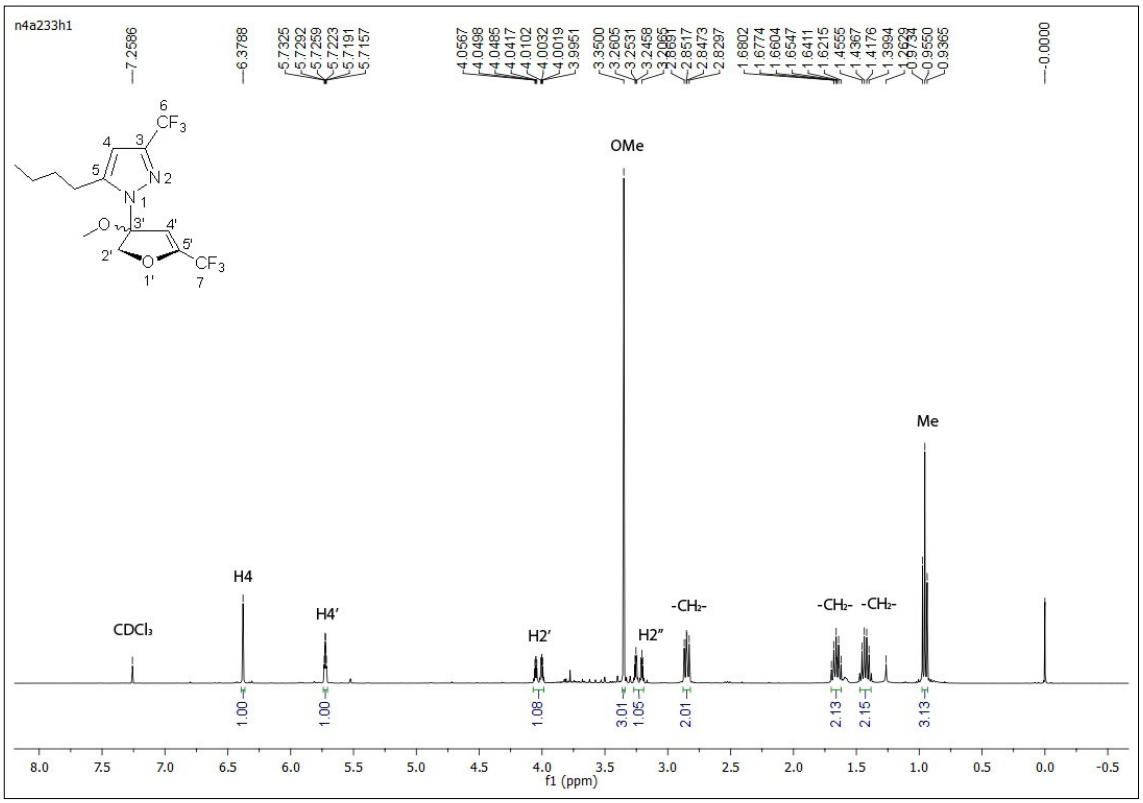


Figure 23 - ^{1}H NMR spectrum of compound **4f** in $CDCl_3$ at 400 MHz.

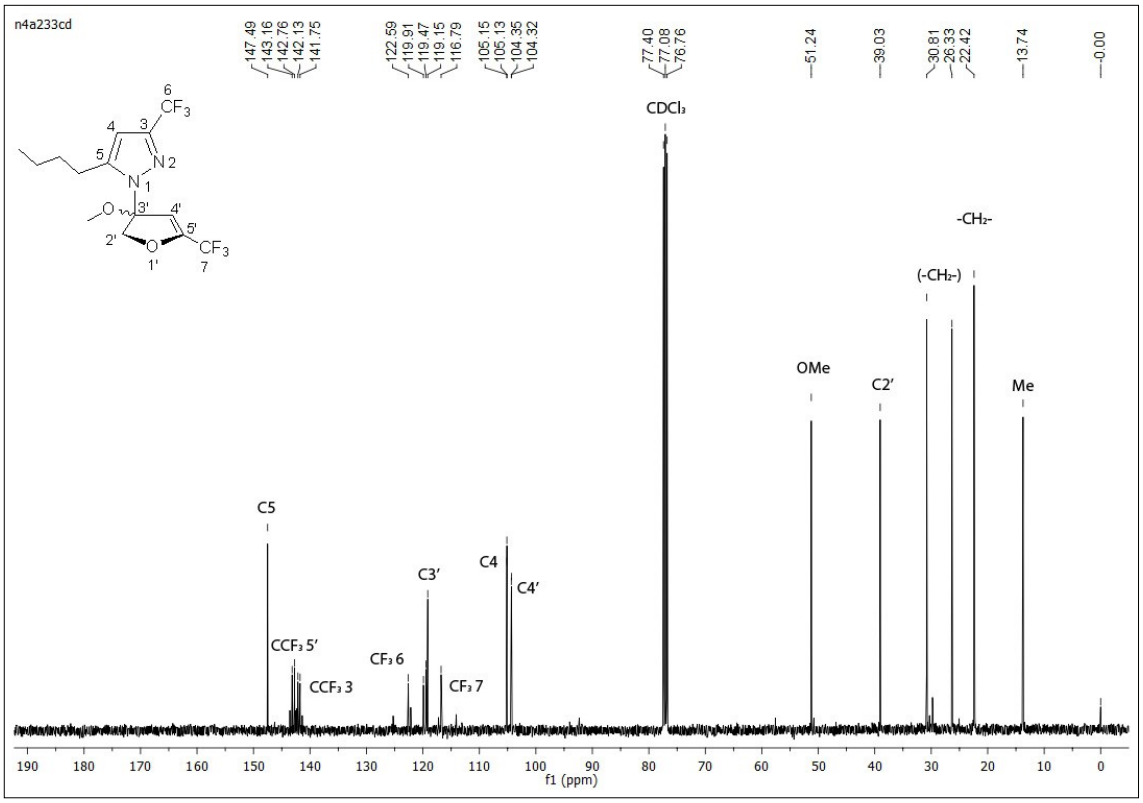


Figure 24 - ^{13}C NMR spectrum of compound **4f** in $CDCl_3$ at 100 MHz.

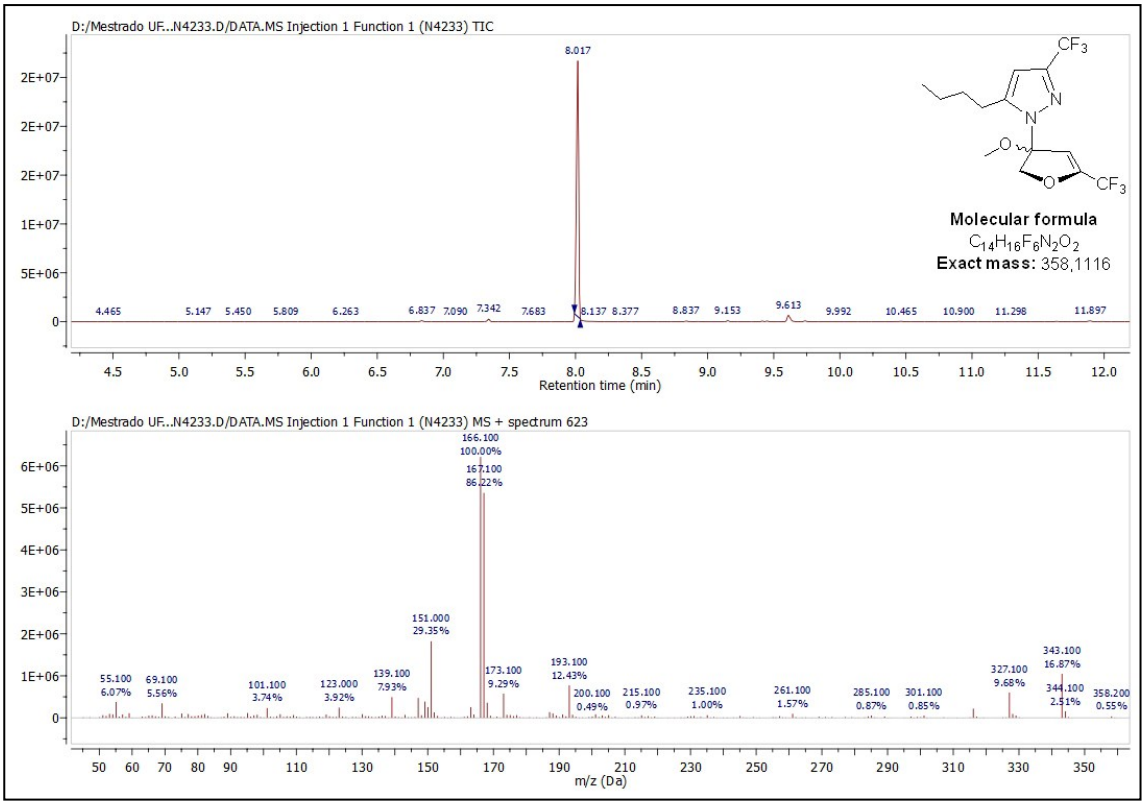


Figure 25 - Chromatogram and mass spectrum (EI, 70 eV) of compound **4f**.

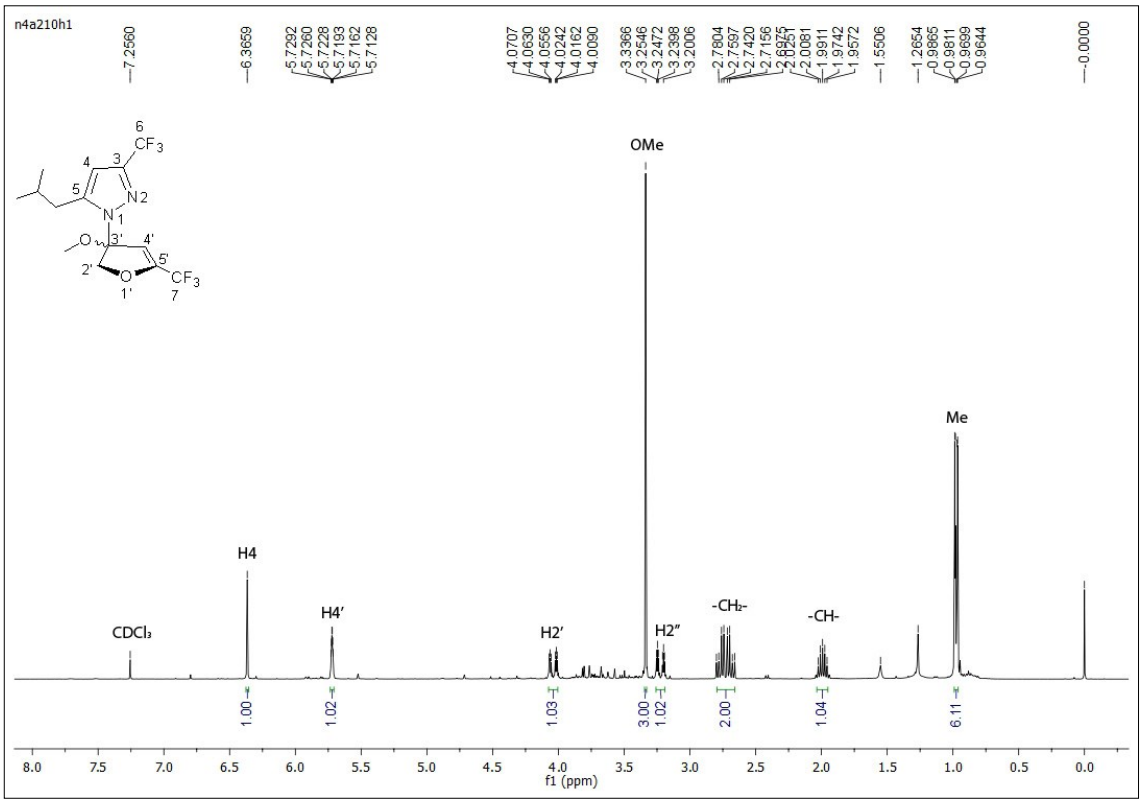


Figure 26 - ^{1}H NMR spectrum of compound **4g** in $CDCl_3$ at 400 MHz.

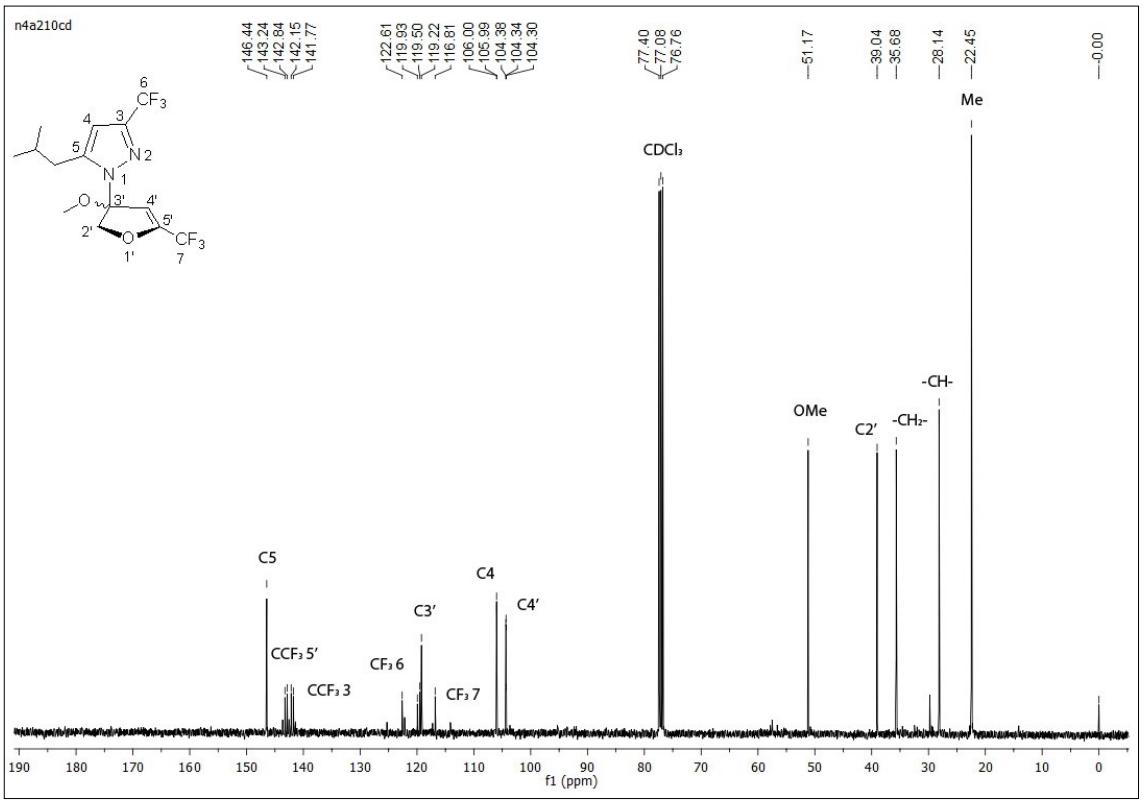


Figure 27 - ^{13}C NMR spectrum of compound **4g** in $CDCl_3$ at 100 MHz.

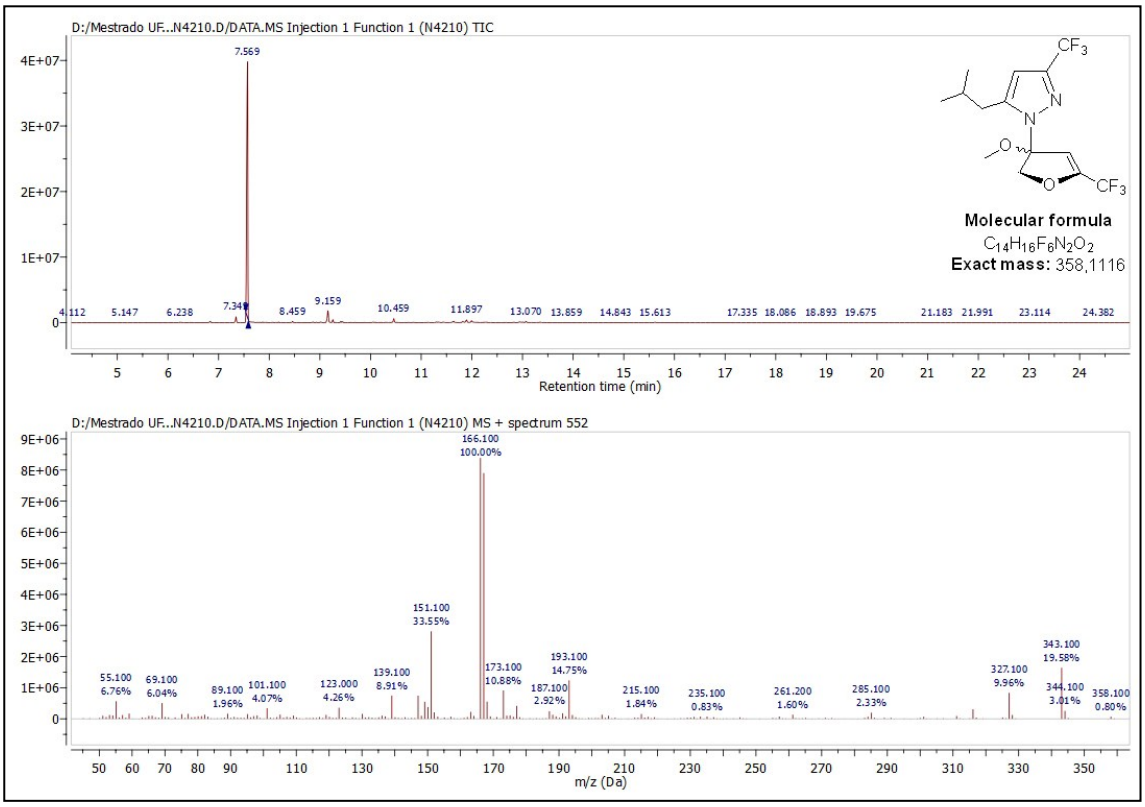


Figure 28 - Chromatogram and mass spectrum (EI, 70 eV) of compound **4g**.

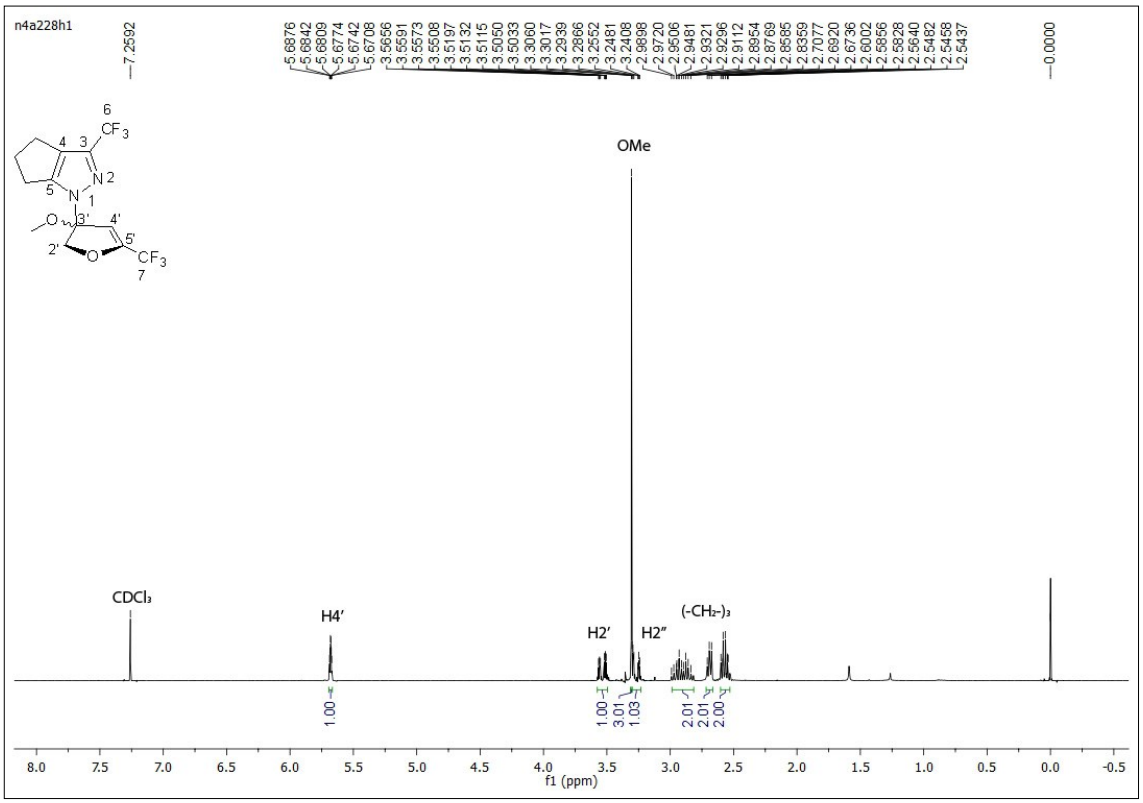


Figure 29 - ^{1}H NMR spectrum of compound **4h** in $CDCl_3$ at 400 MHz.

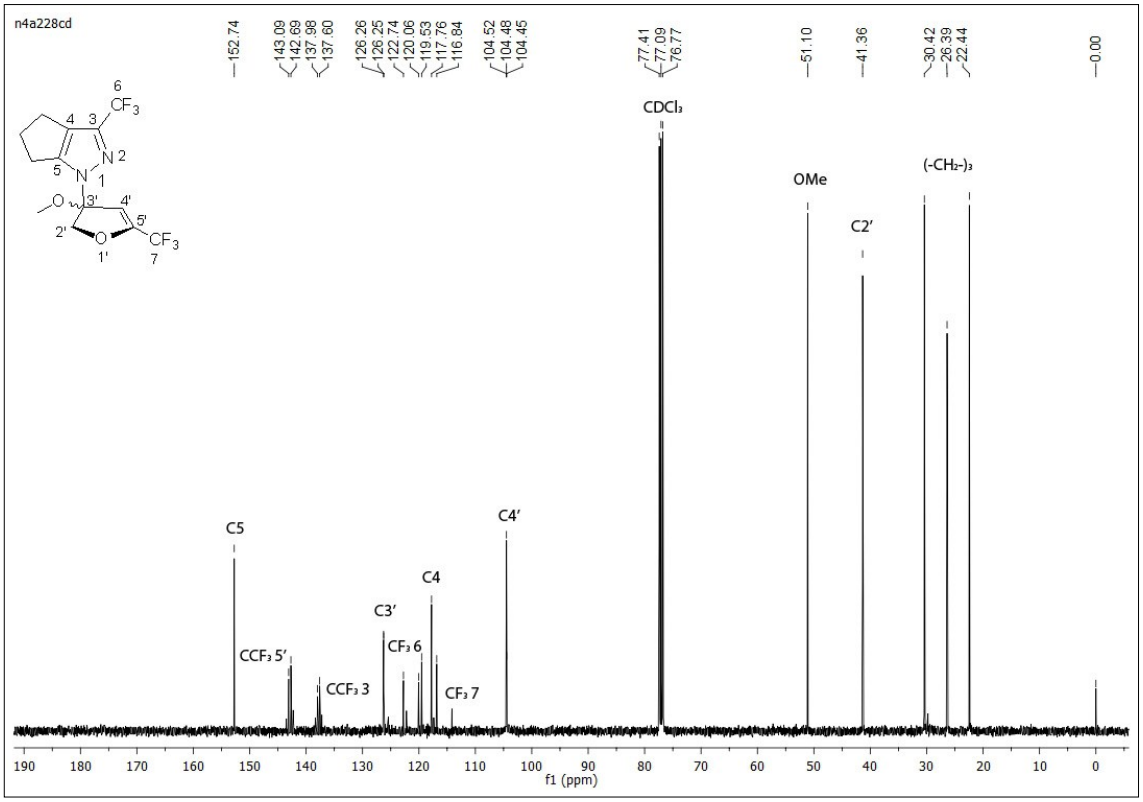


Figure 30 - ^{13}C NMR spectrum of compound **4h** in $CDCl_3$ at 100 MHz.

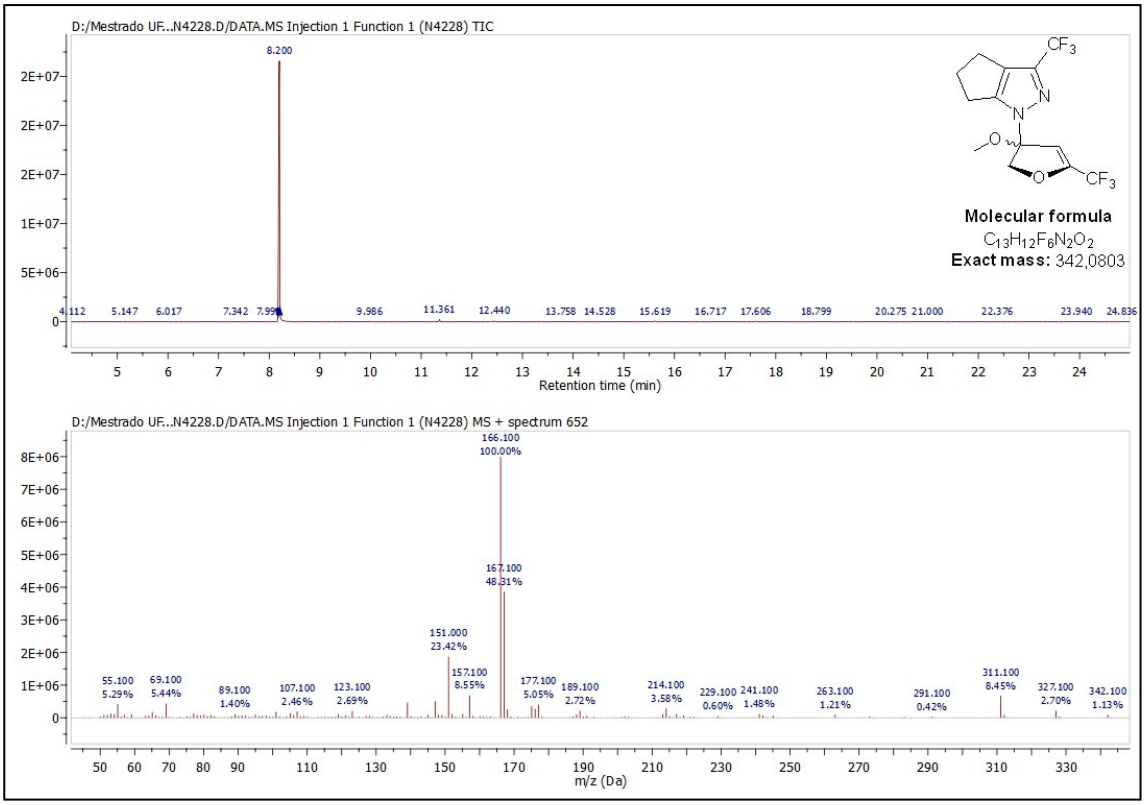


Figure 31 - Chromatogram and mass spectrum (EI, 70 eV) of compound **4h**.

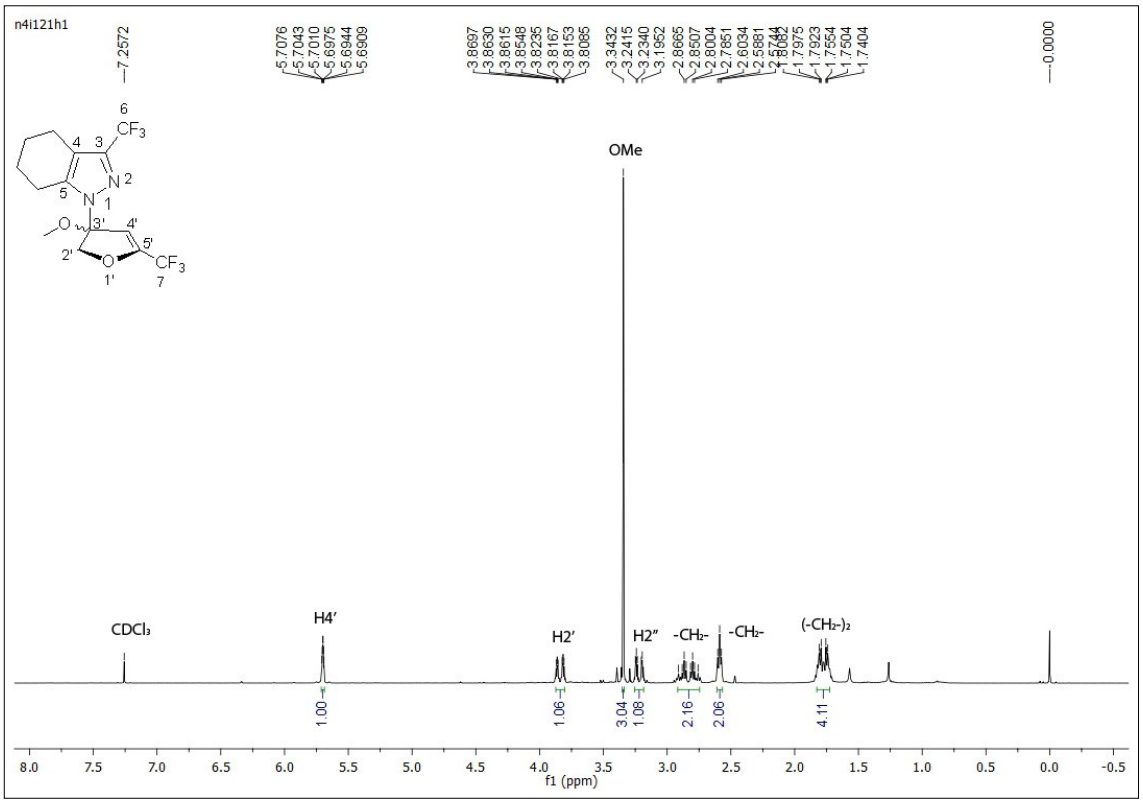


Figure 32 - ^{1}H NMR spectrum of compound **4i** in $CDCl_3$ at 400 MHz.

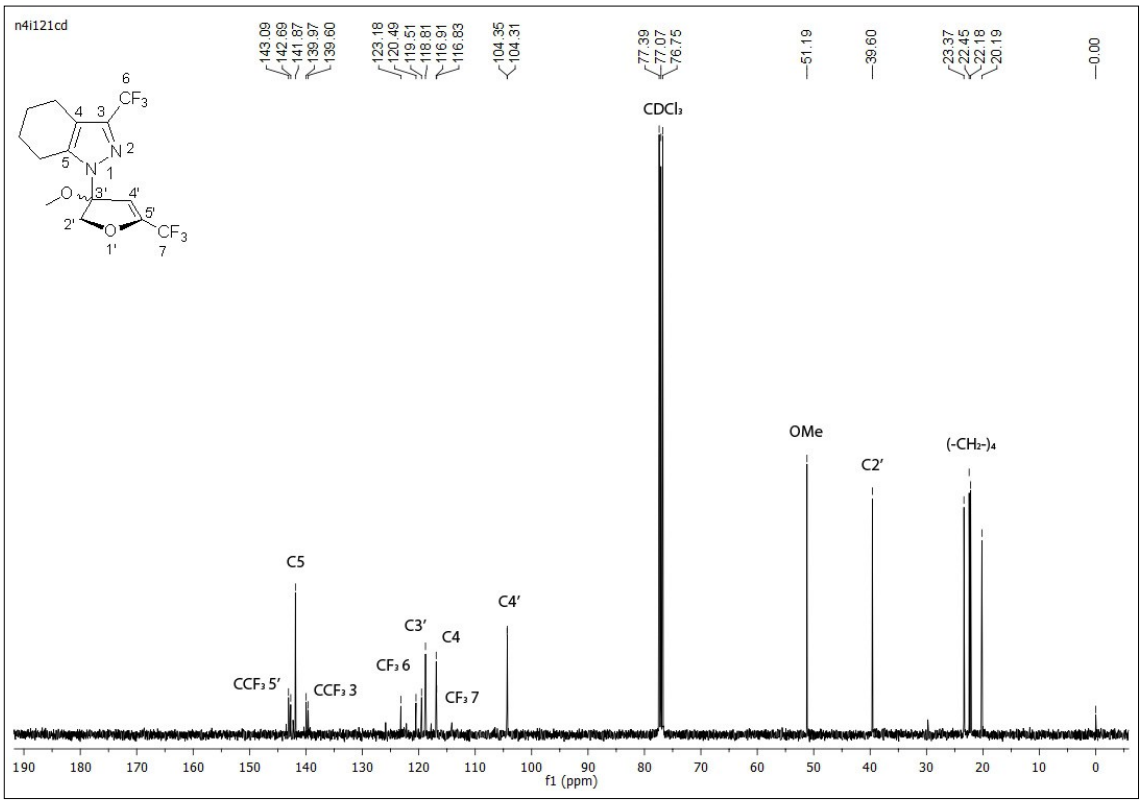


Figure 33 - ^{13}C NMR spectrum of compound **4i** in $CDCl_3$ at 100 MHz.

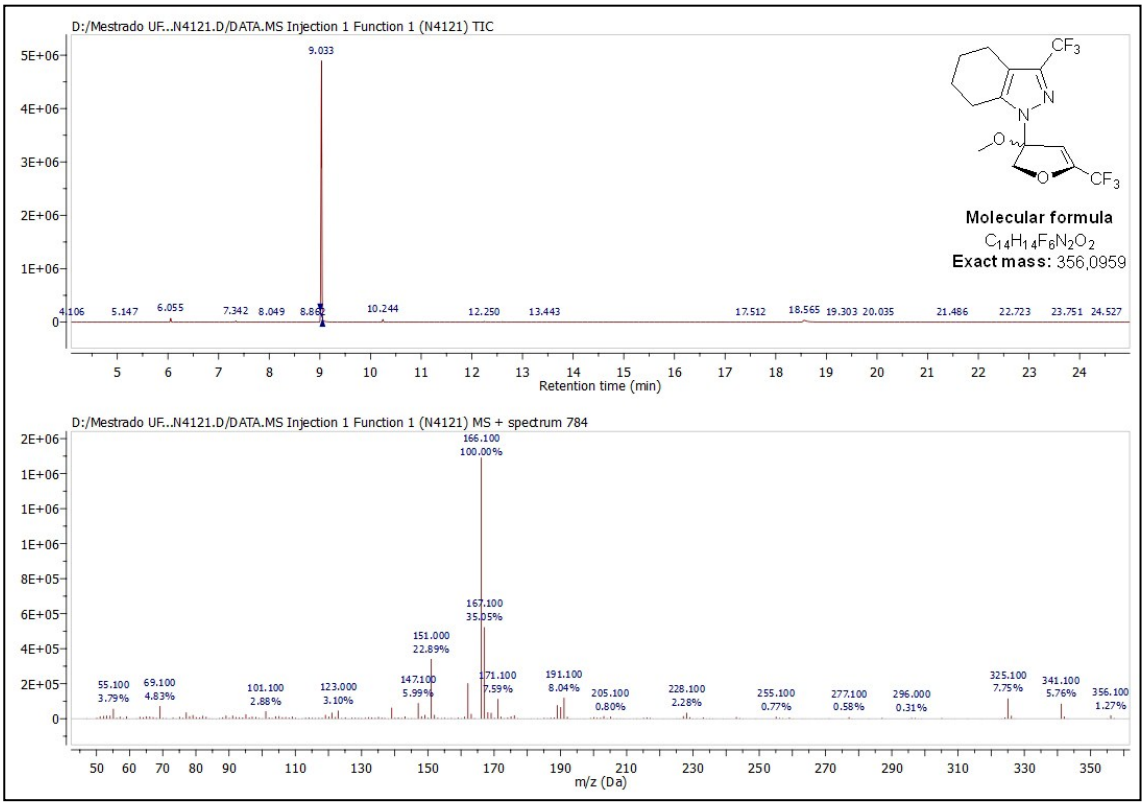


Figure 34 - Chromatogram and mass spectrum (EI, 70 eV) of compound **4i**.

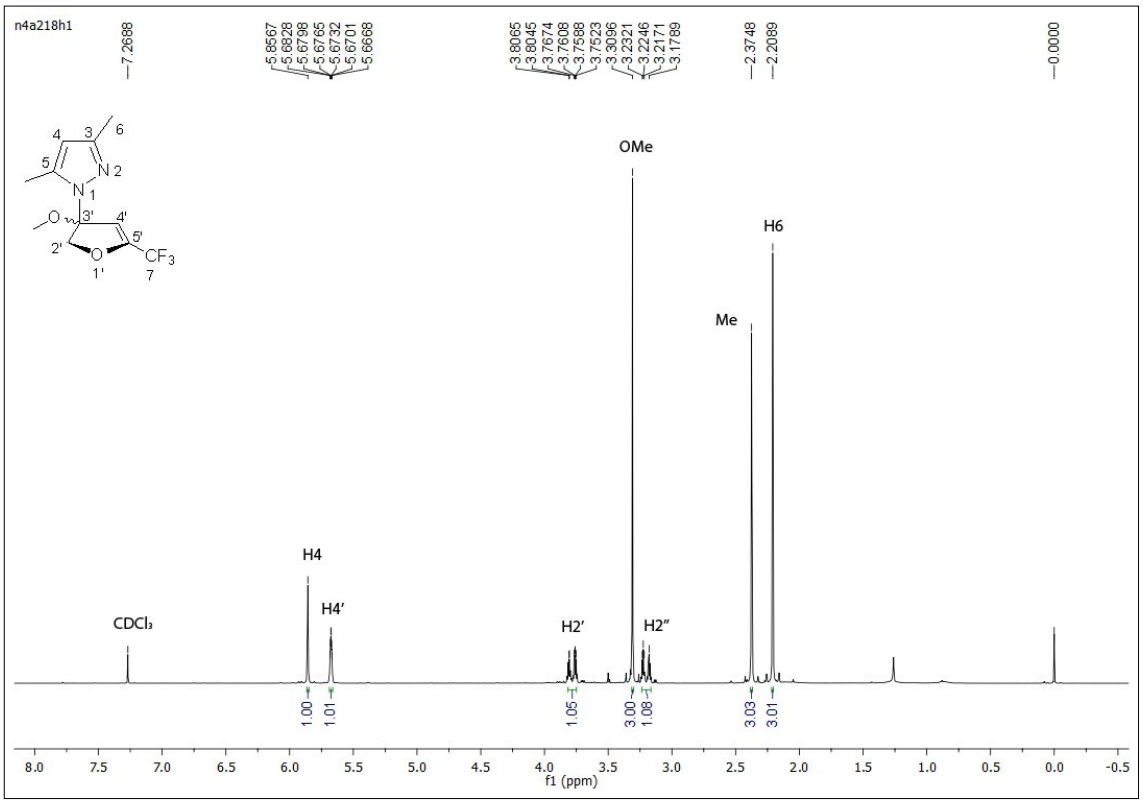


Figure 35 - ^{1}H NMR spectrum of compound **4j** in $CDCl_3$ at 400 MHz.

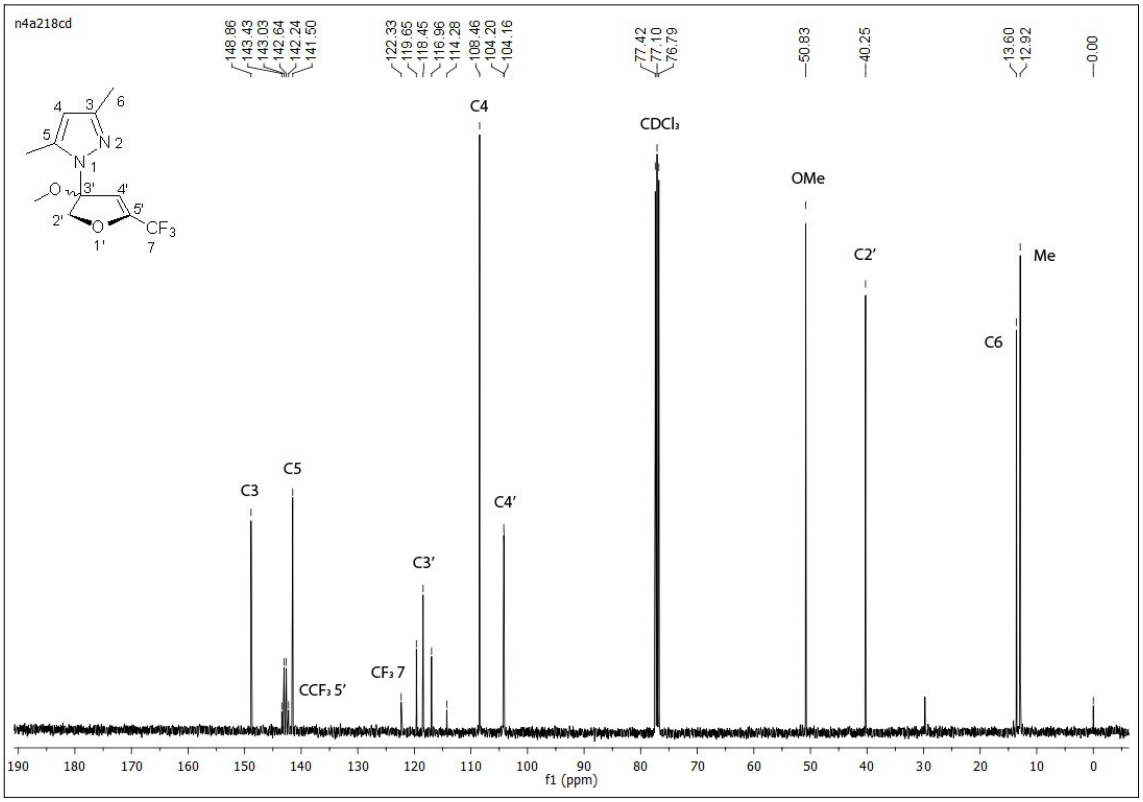


Figure 36 - ^{13}C NMR spectrum of compound **4j** in $CDCl_3$ at 100 MHz.

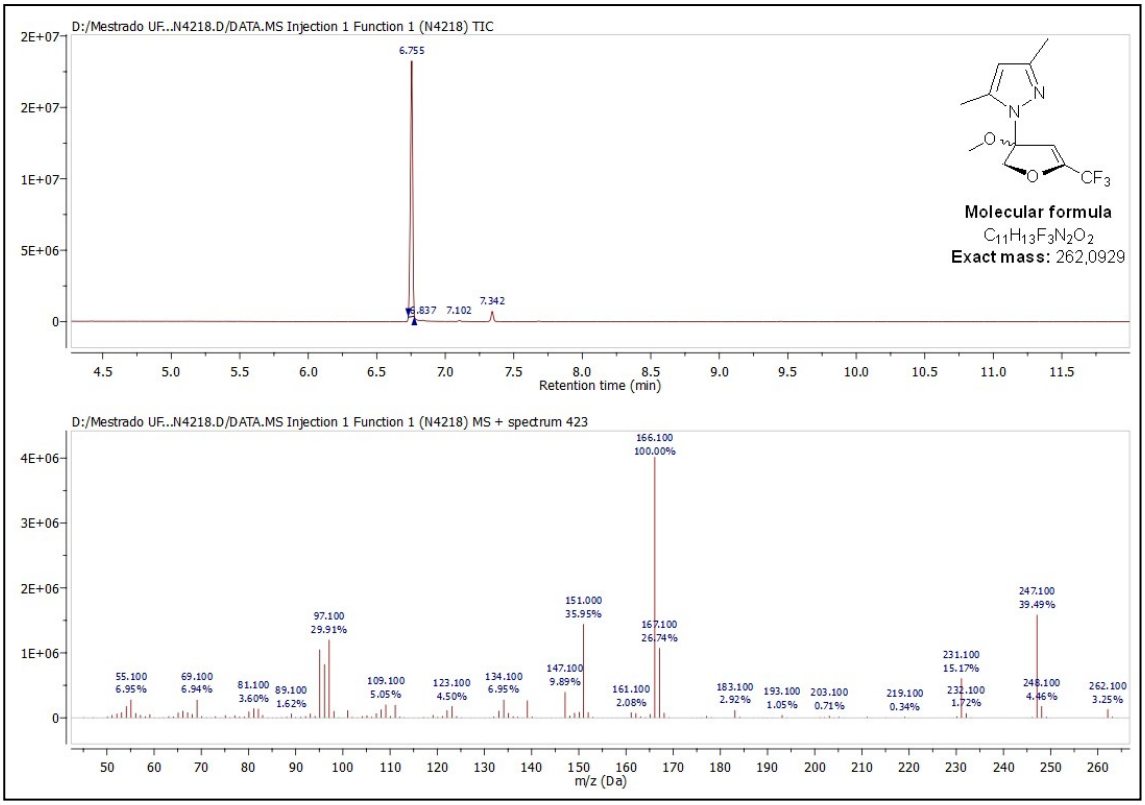


Figure 37 - Chromatogram and mass spectrum (EI, 70 eV) of compound **4j**.

IV - ^{1}H, ^{13}C NMR and GC-MS spectra of compounds 5a–c

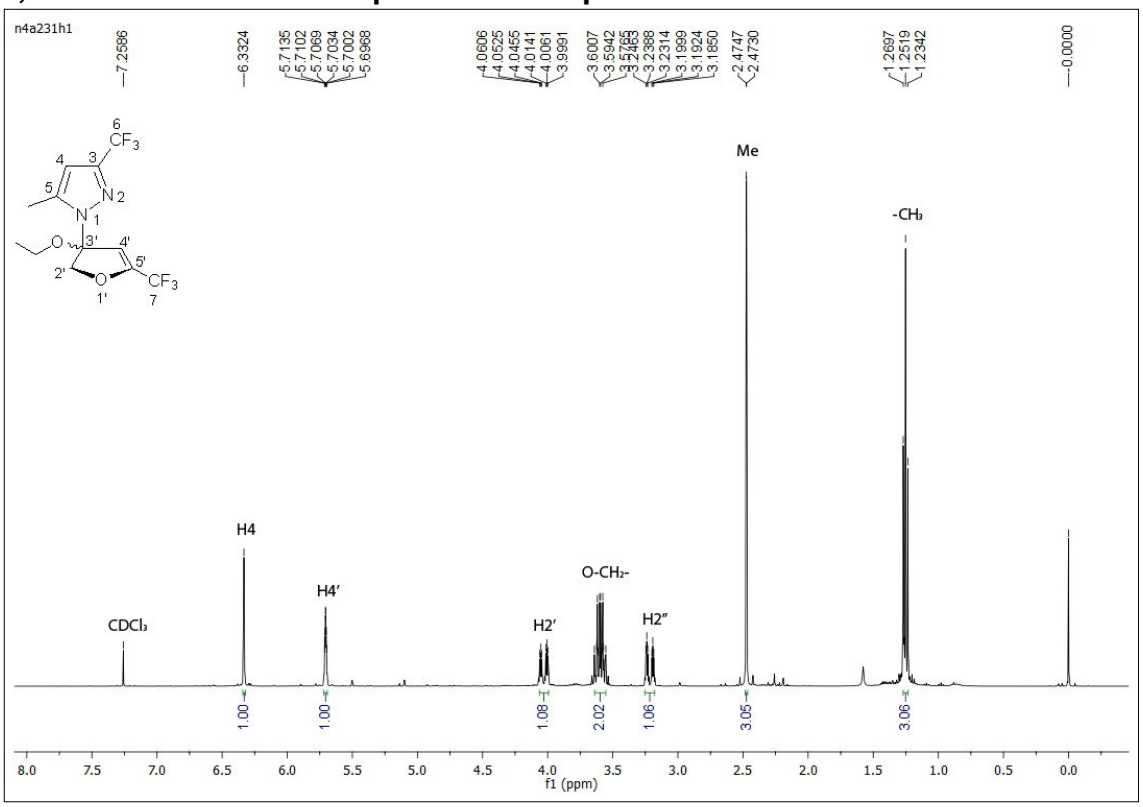


Figure 38 - ^{1}H NMR spectrum of compound **5a** in $CDCl_3$ at 400 MHz.

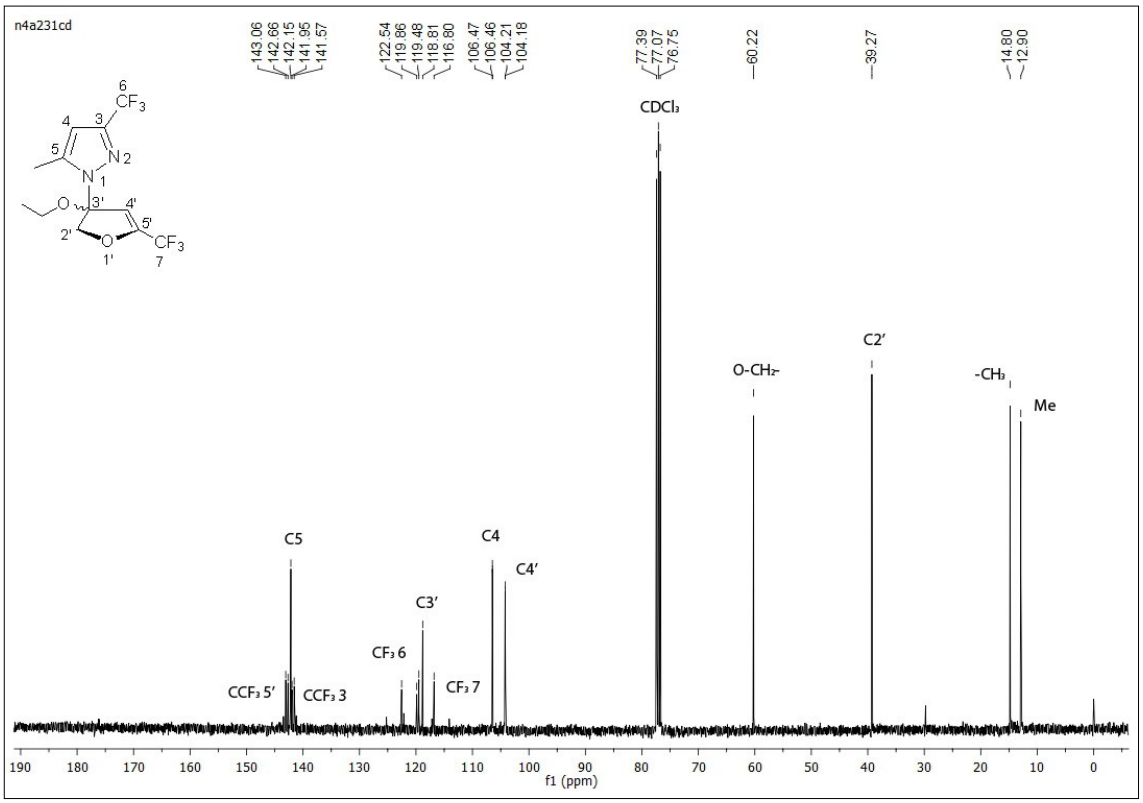


Figure 39 - ^{13}C NMR spectrum of compound **5a** in $CDCl_3$ at 100 MHz.

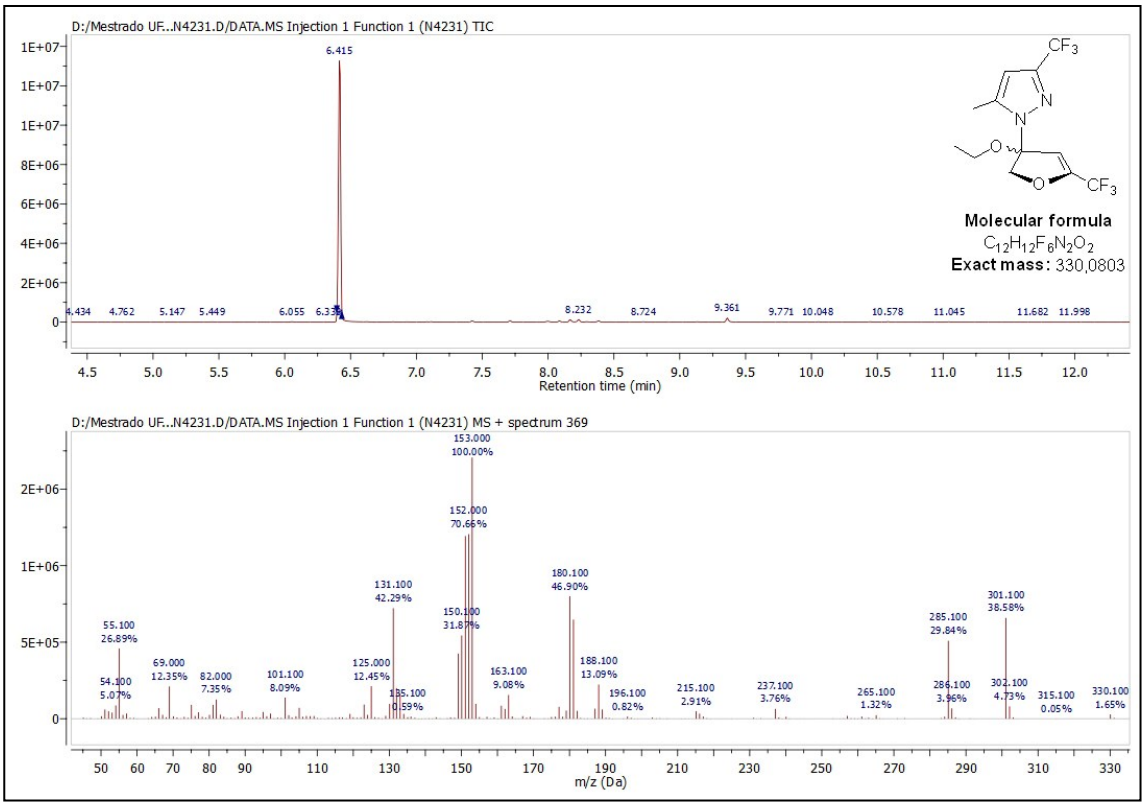


Figure 40 - Chromatogram and mass spectrum (EI, 70 eV) of compound **5a**.

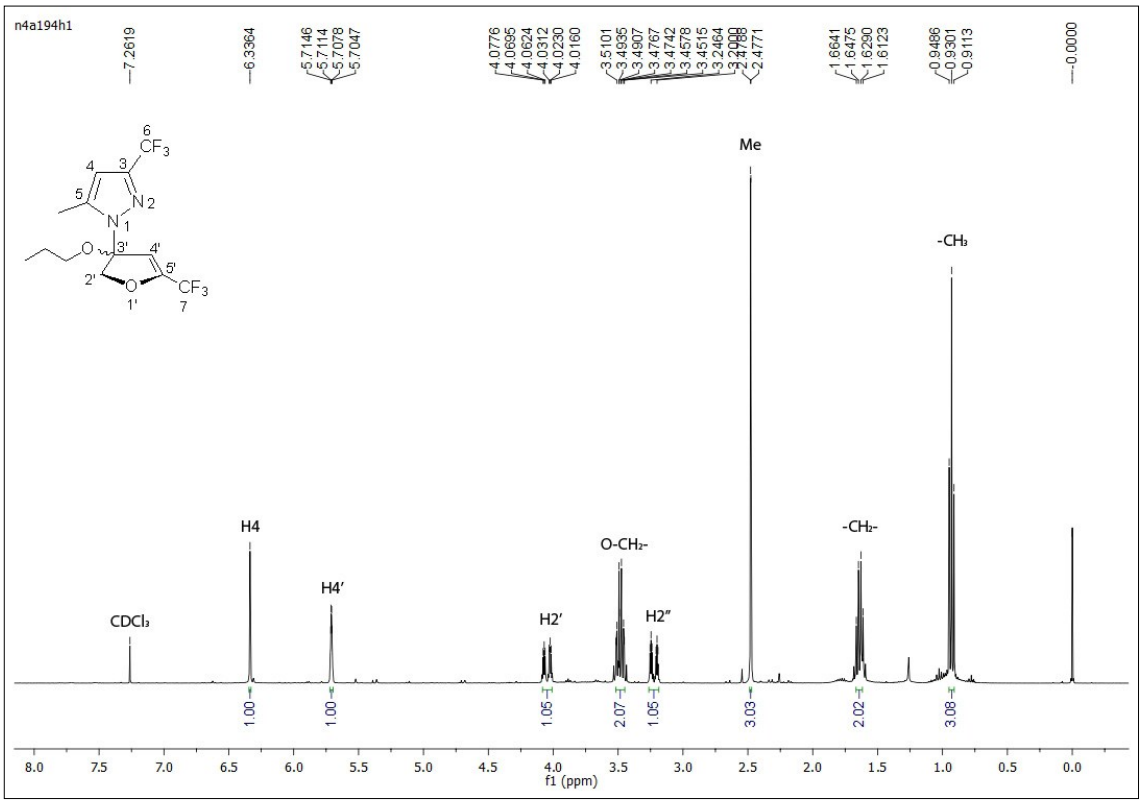


Figure 41 - ^{1}H NMR spectrum of compound **5b** in $CDCl_3$ at 400 MHz.

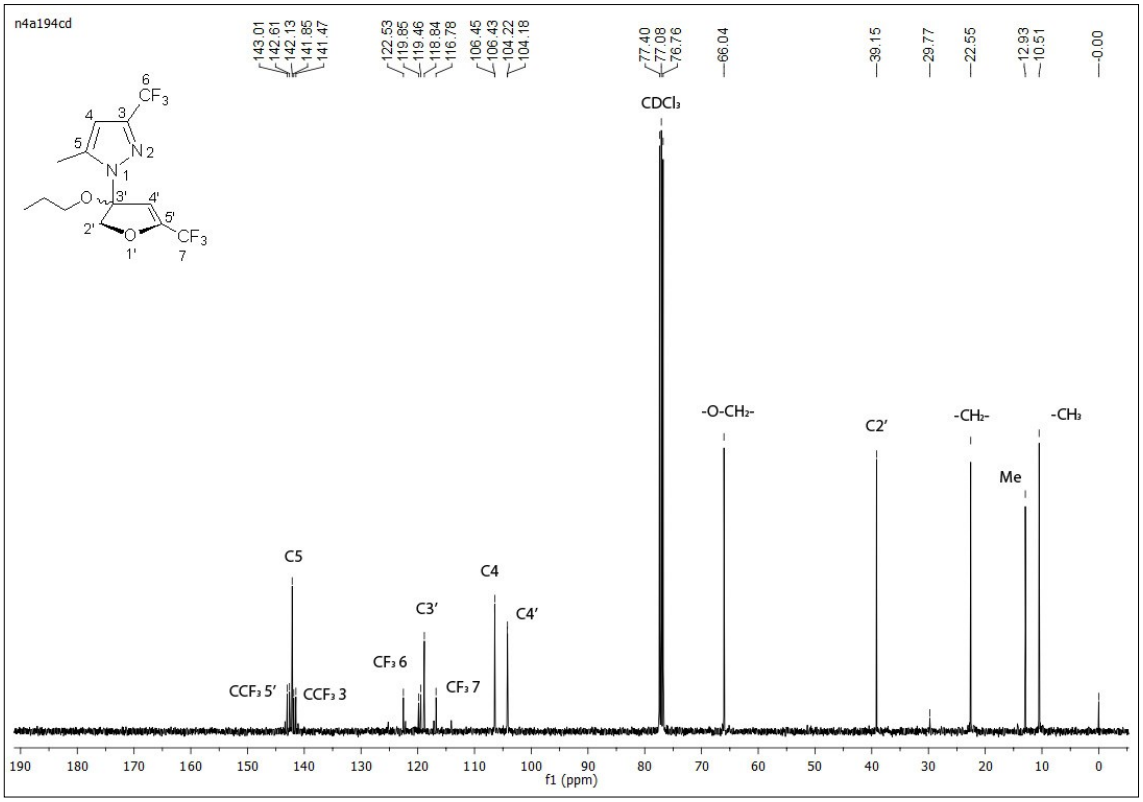


Figure 42 - ^{13}C NMR spectrum of compound **5b** in $CDCl_3$ at 100 MHz.

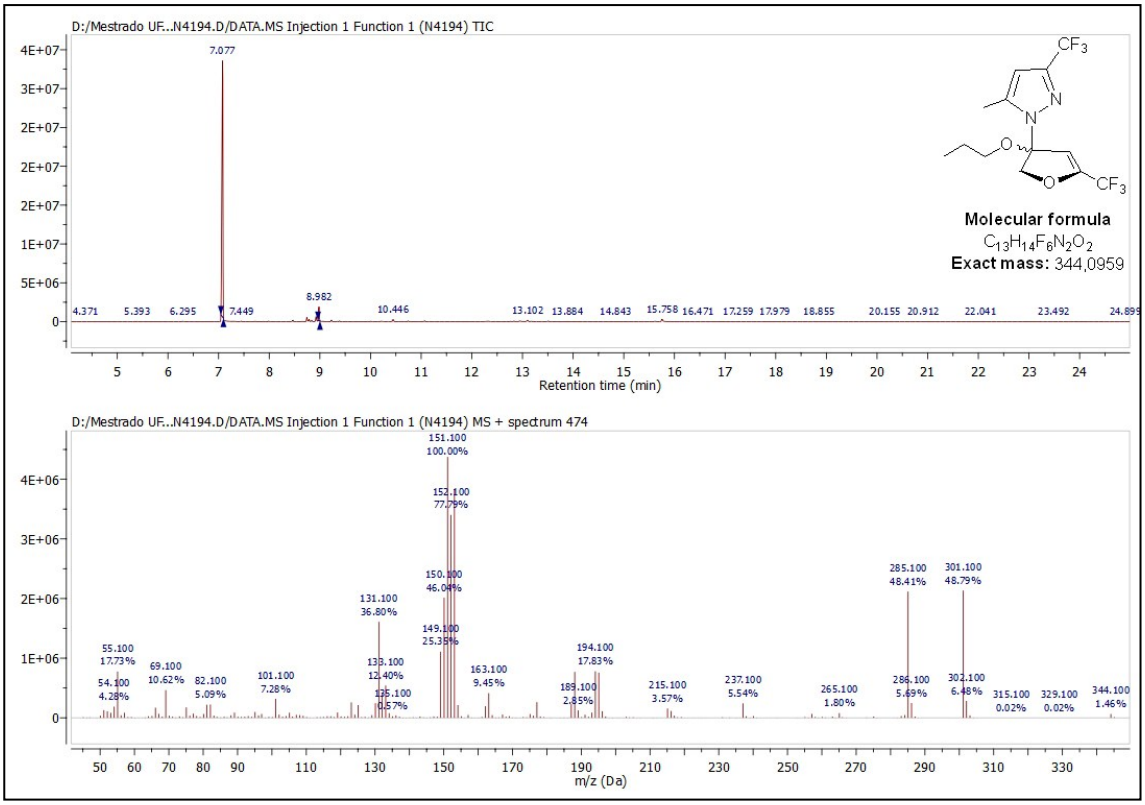


Figure 43 - Chromatogram and mass spectrum (EI, 70 eV) of compound **5b**.

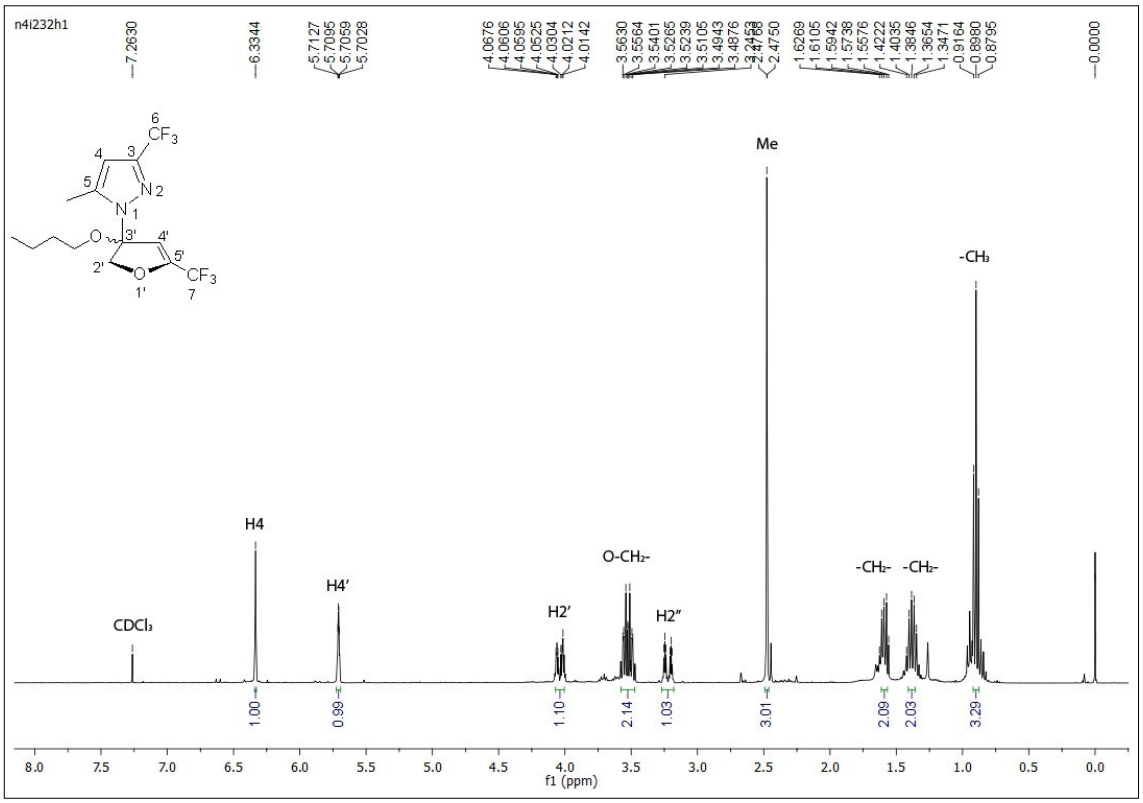


Figure 44 - ^{1}H NMR spectrum of compound **5c** in $CDCl_3$ at 400 MHz.

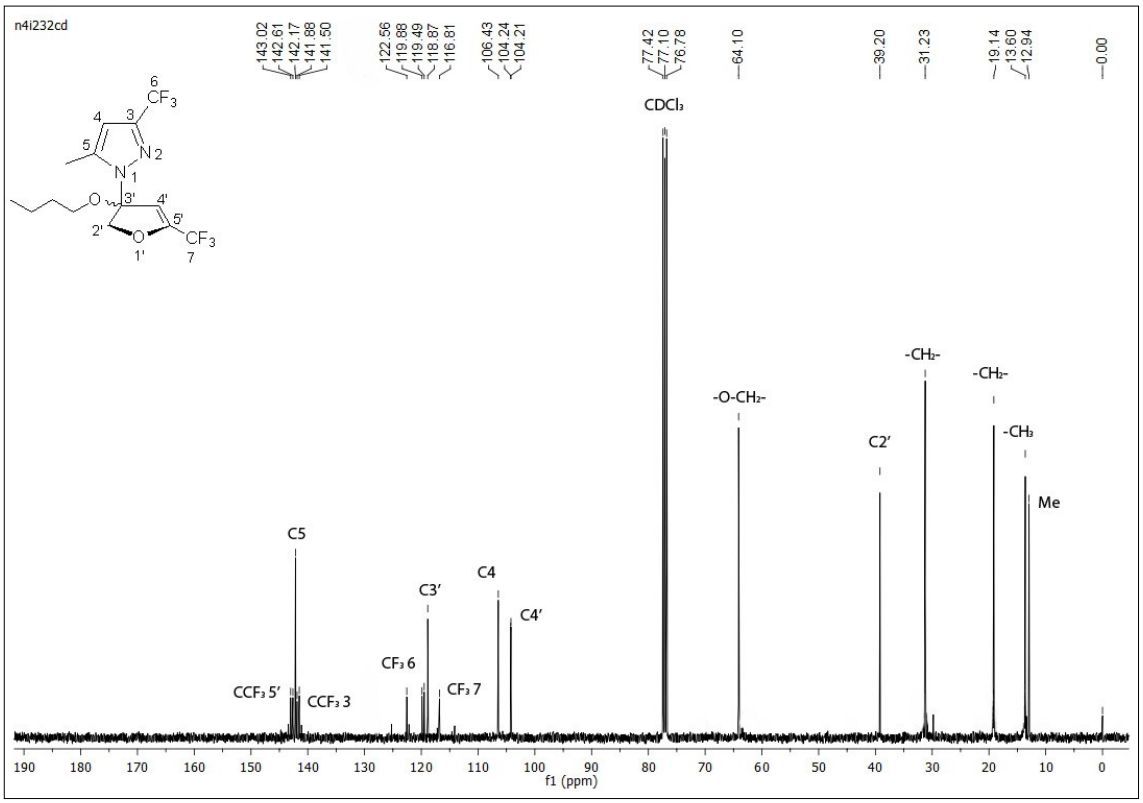


Figure 45 - ^{13}C NMR spectrum of compound **5c** in $CDCl_3$ at 100 MHz.

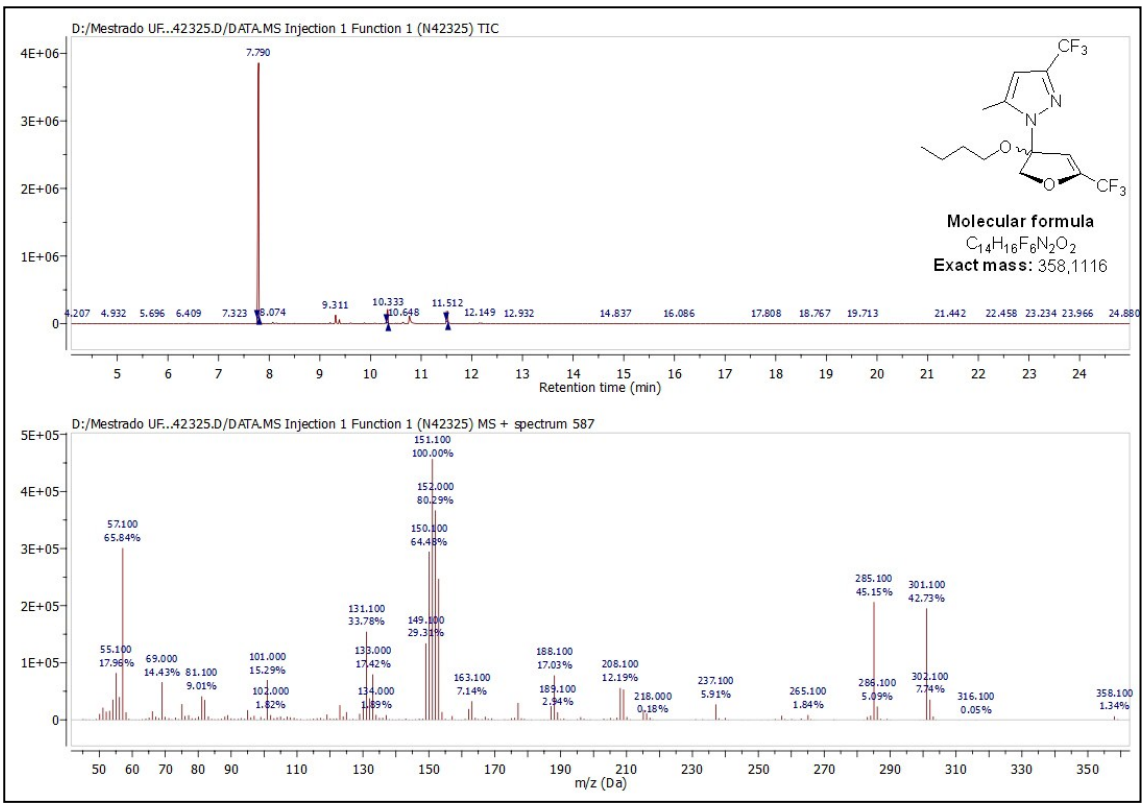


Figure 46 - Chromatogram and mass spectrum (EI, 70 eV) of compound **5c**.

V - ^{1}H, ^{13}C, ^{19}F and two-dimensional NMR experiments such as COSY HH, HSQC, HMBC, GC-MS and X-ray diffraction spectra of compounds 6a–i

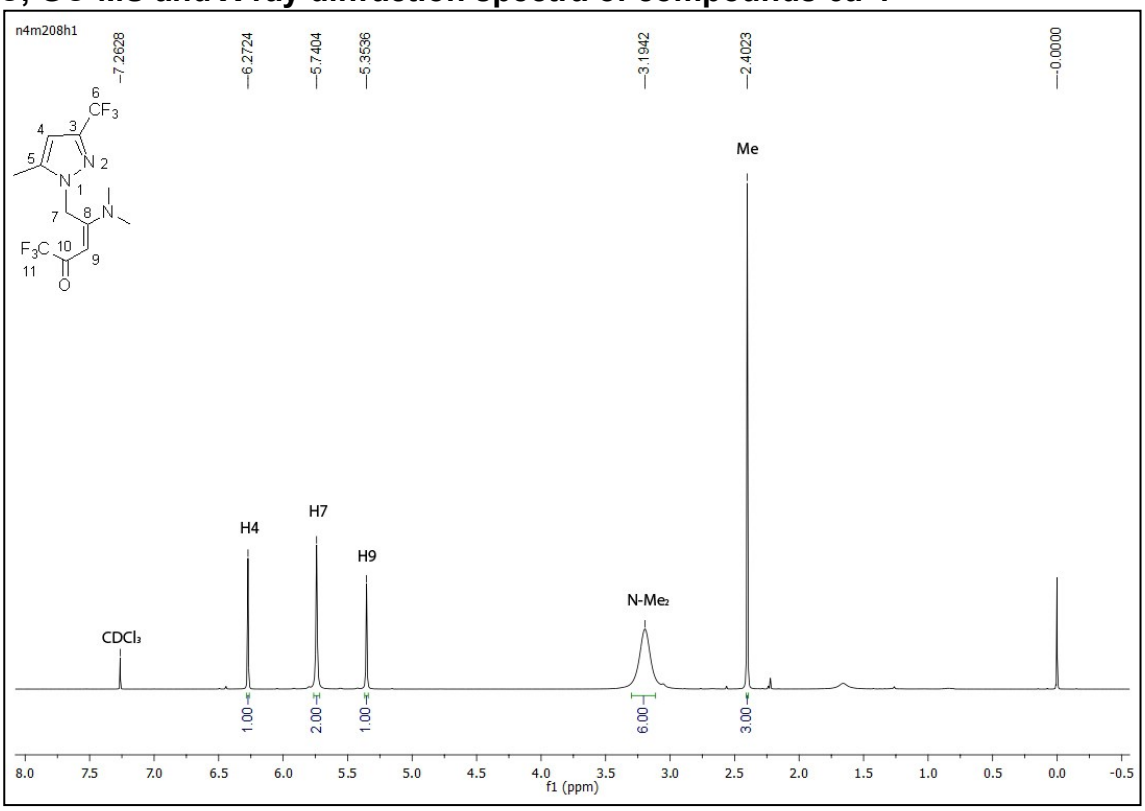


Figure 47 - ^{1}H NMR spectrum of compound **6a** in $CDCl_3$ at 400 MHz.

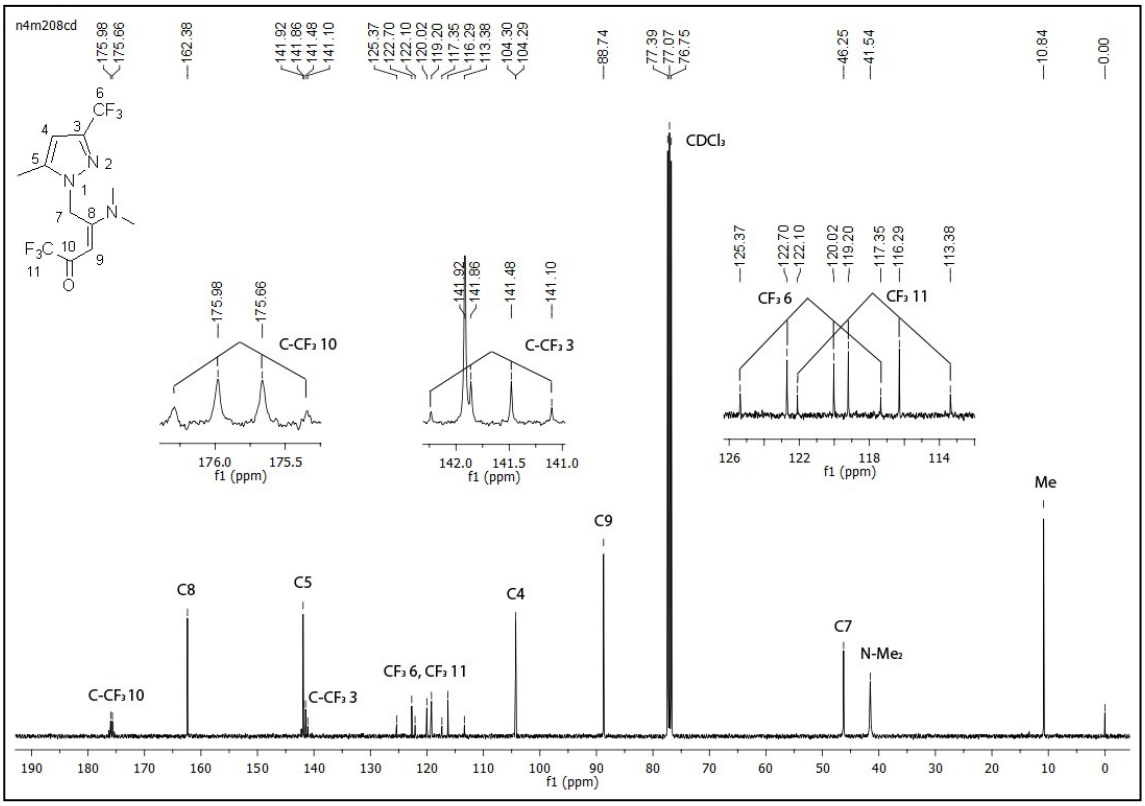


Figure 48 - ^{13}C NMR spectrum of compound **6a** in $CDCl_3$ at 100 MHz.

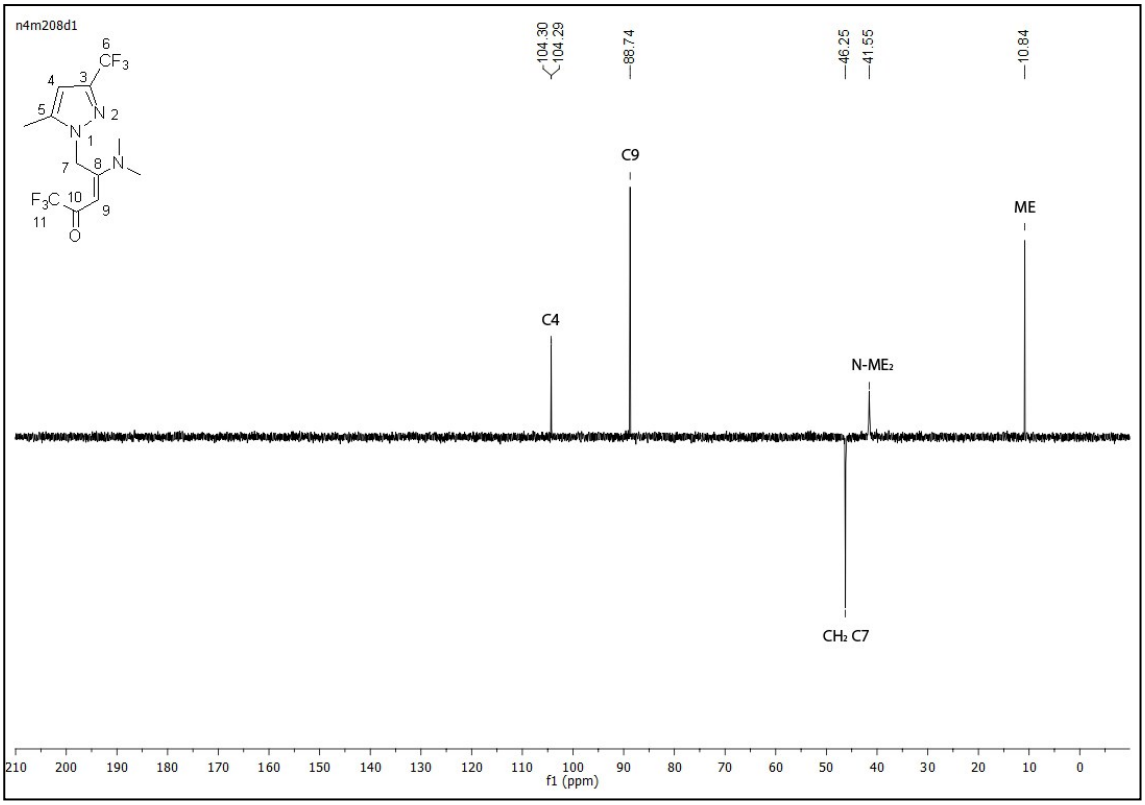


Figure 49 - DEPT 135 NMR spectrum of compound **6a** in $CDCl_3$ at 100 MHz.

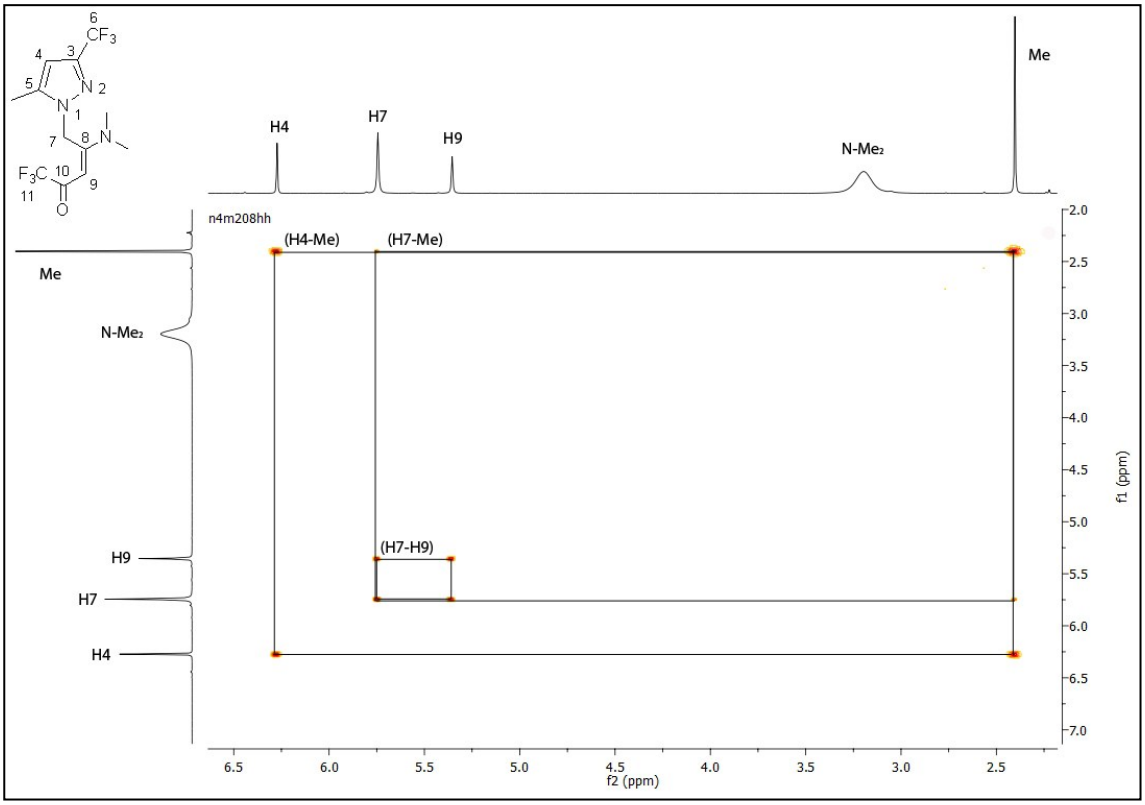


Figure 50 - COSY NMR spectrum of compound **6a** in $CDCl_3$ at 400 MHz.

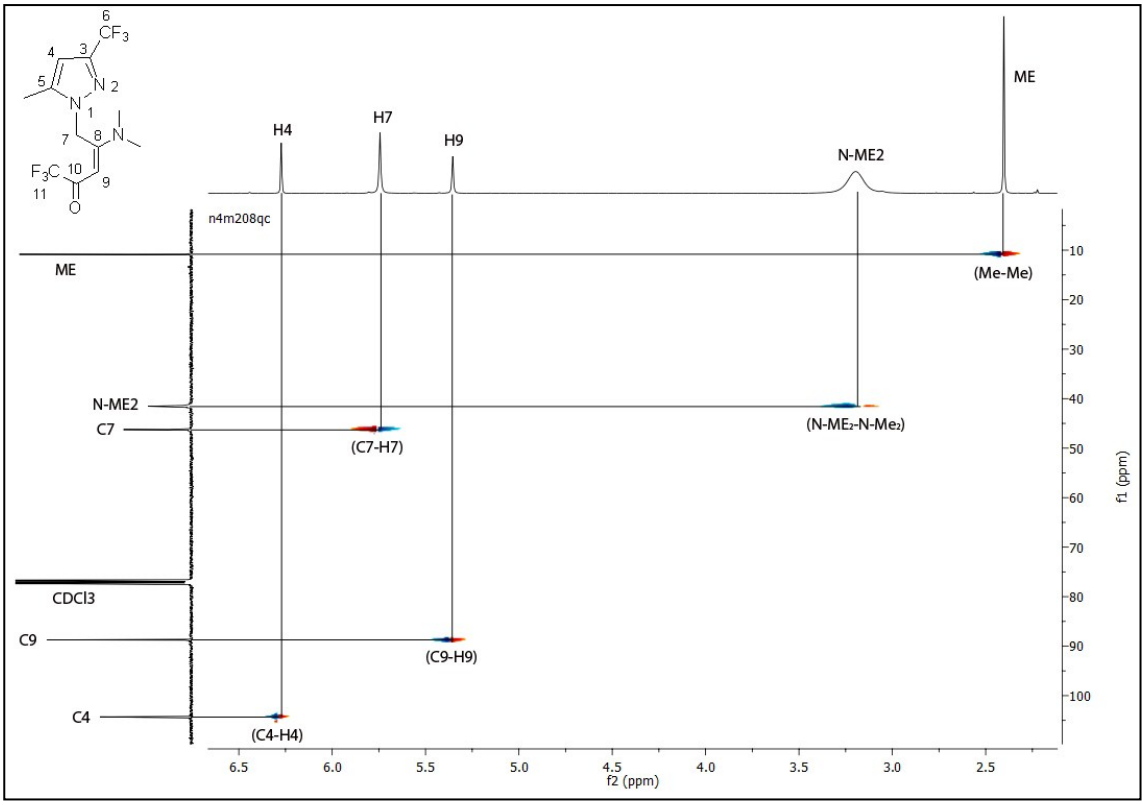


Figure 51 - HMQC NMR spectrum of compound **6a** in $CDCl_3$ at 400 MHz.

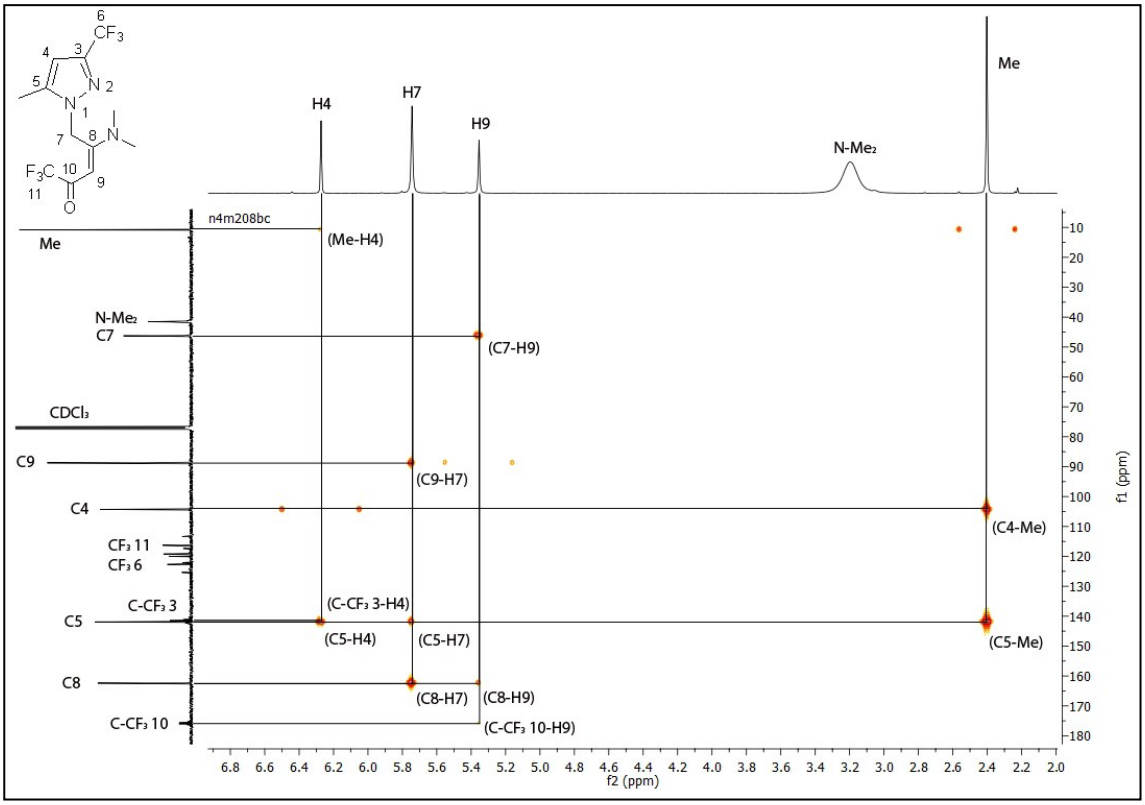


Figure 52 - HMBC NMR spectrum of compound **6a** in $CDCl_3$ at 400 MHz.

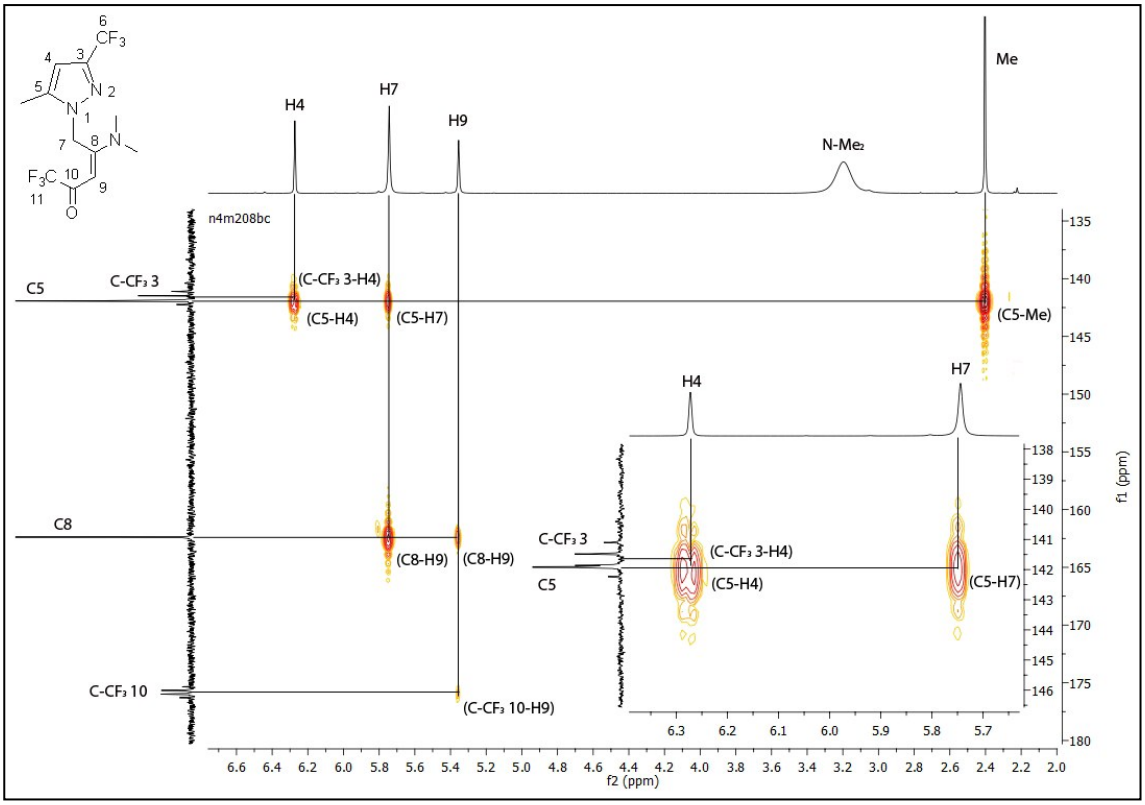


Figure 53 - HMBC NMR spectrum (Expansion) of compound **6a** in $CDCl_3$ at 400 MHz.

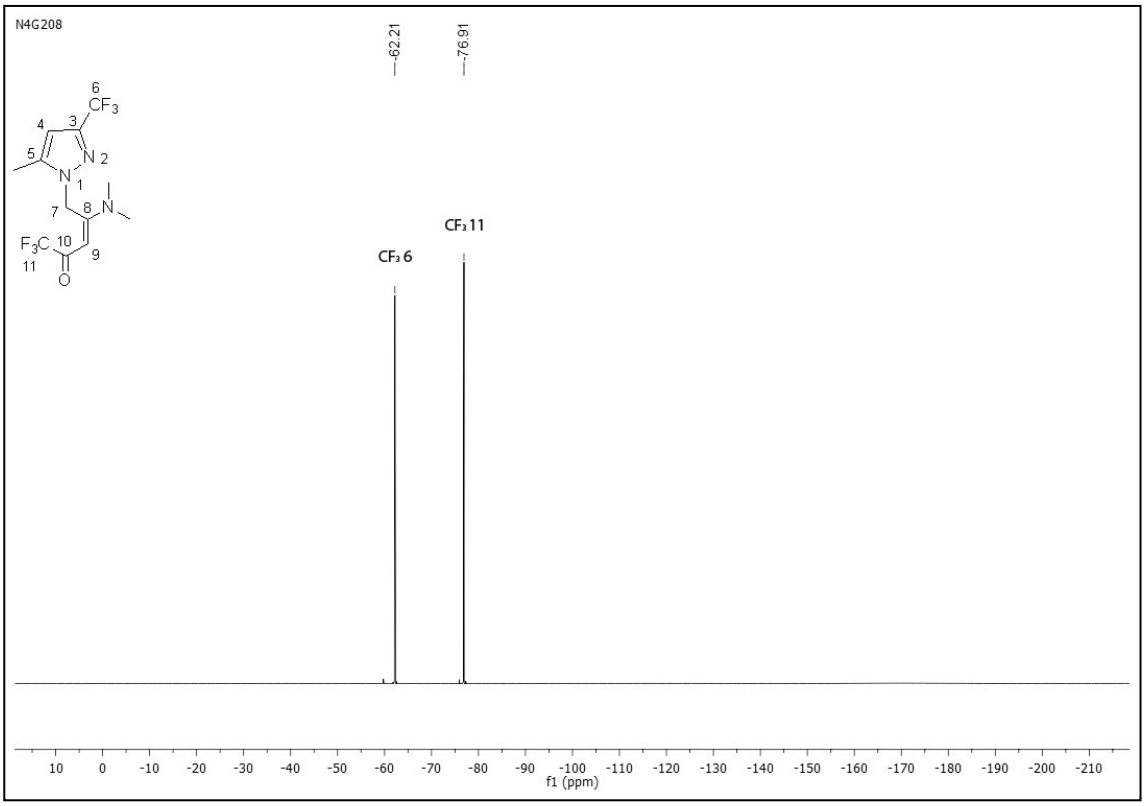


Figure 54 – ^{19}F NMR spectrum of compound **6a** in $CDCl_3$ at 100 MHz.

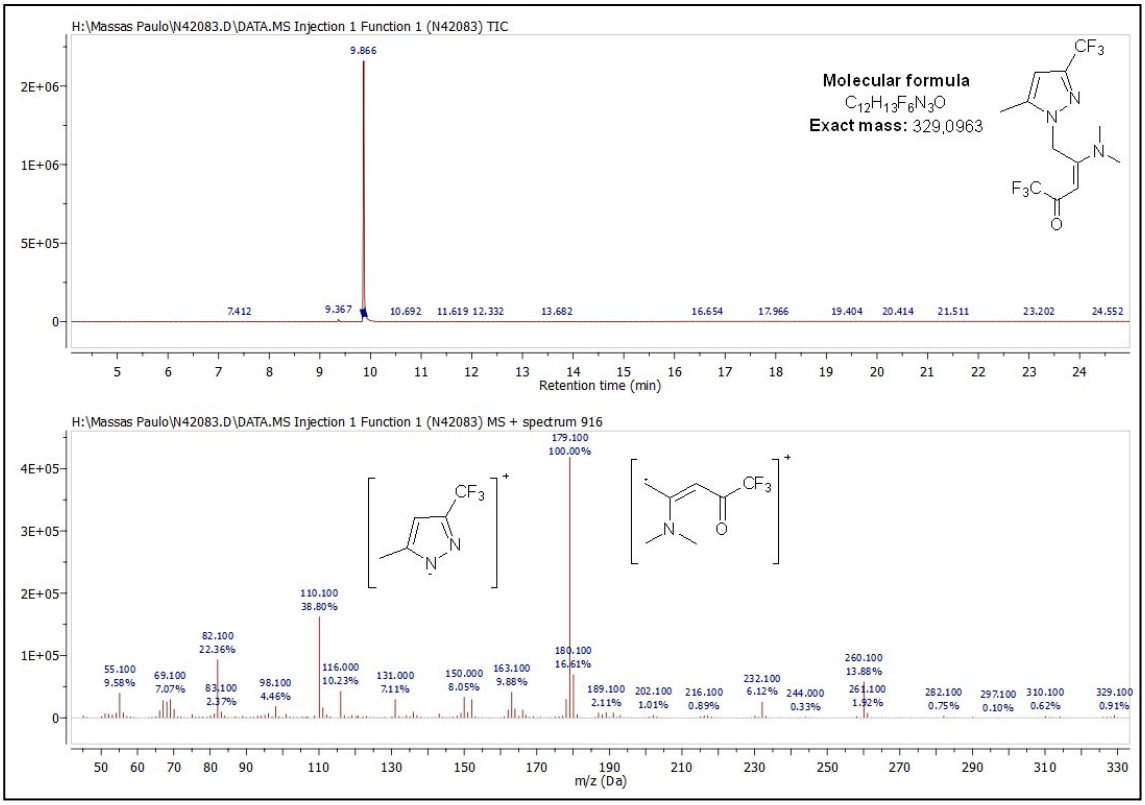


Figure 55 - Chromatogram and mass spectrum (EI, 70 eV) of compound **6a**.

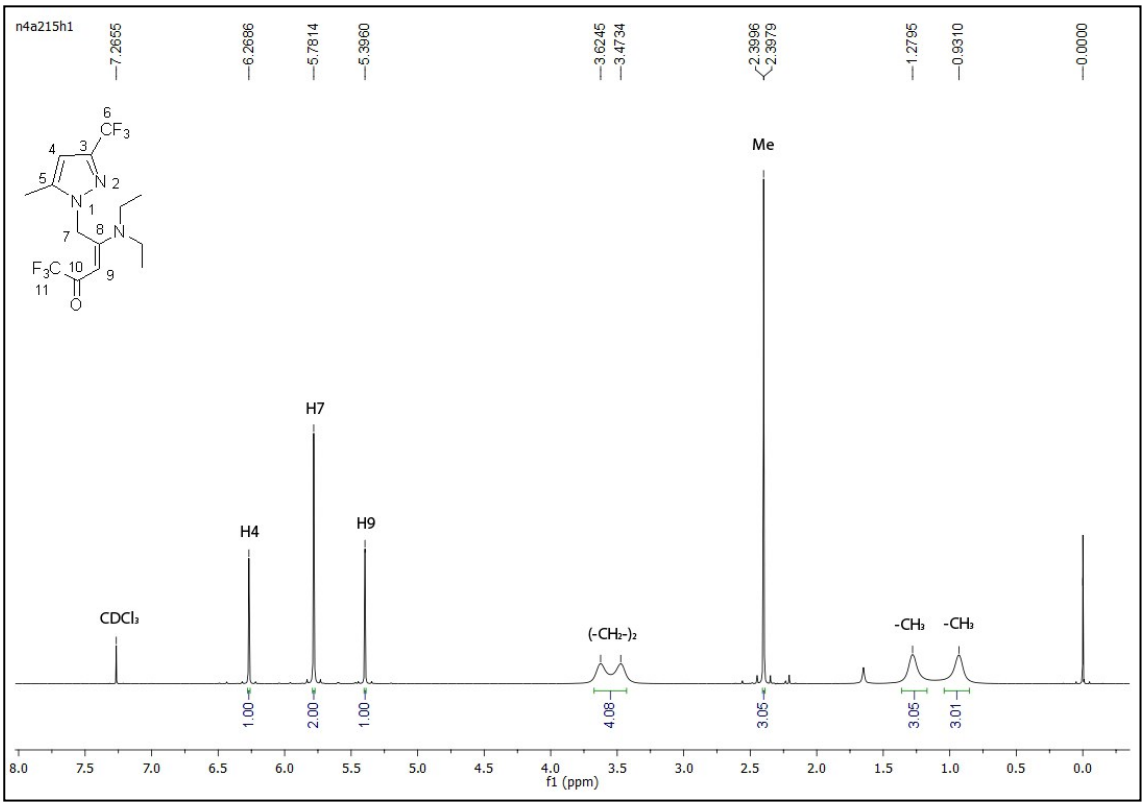


Figure 56 - ^{1}H NMR spectrum of compound **6b** in $CDCl_3$ at 400 MHz.

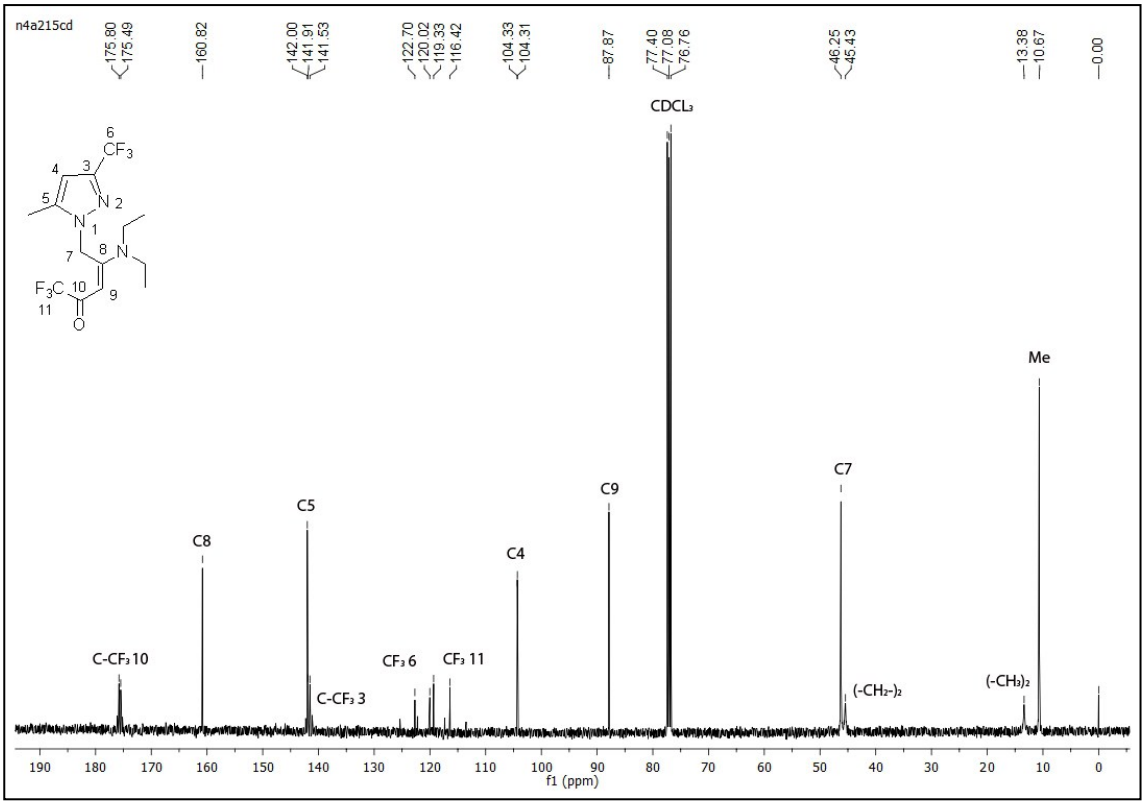


Figure 57 - ^{13}C NMR spectrum of compound **6b** in $CDCl_3$ at 100 MHz.

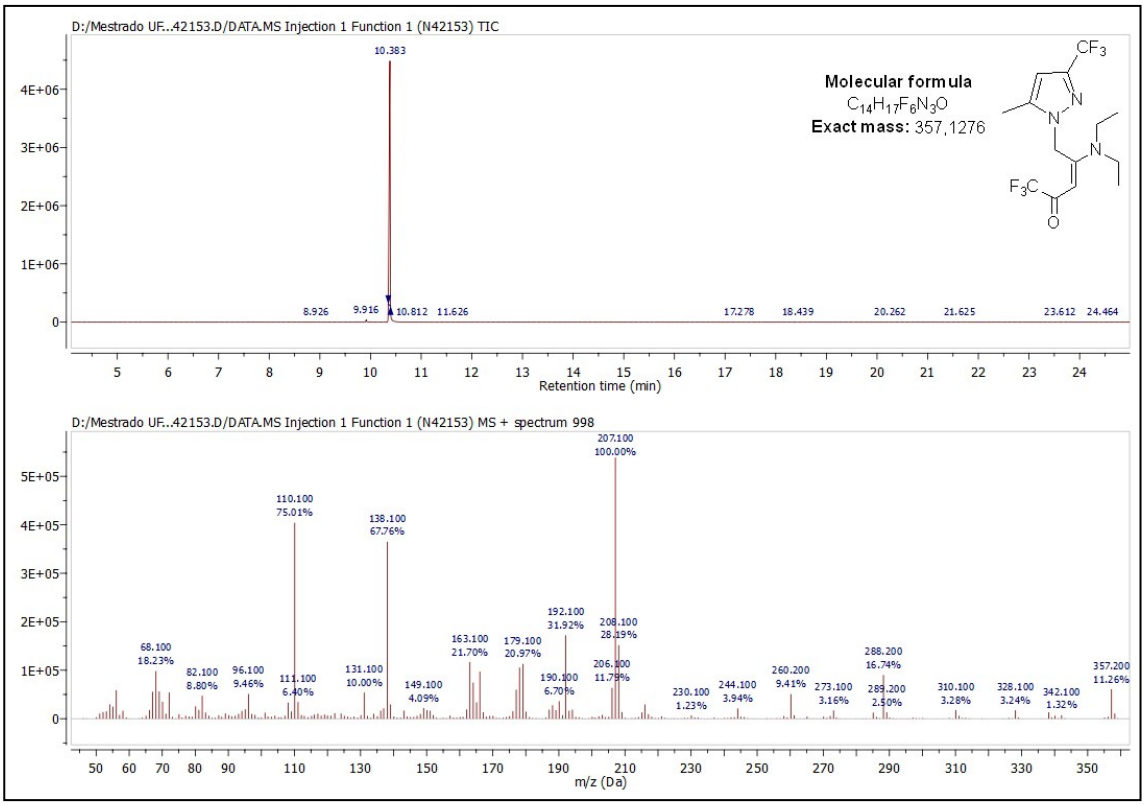


Figure 58 - Chromatogram and mass spectrum (EI, 70 eV) of compound **6b**.

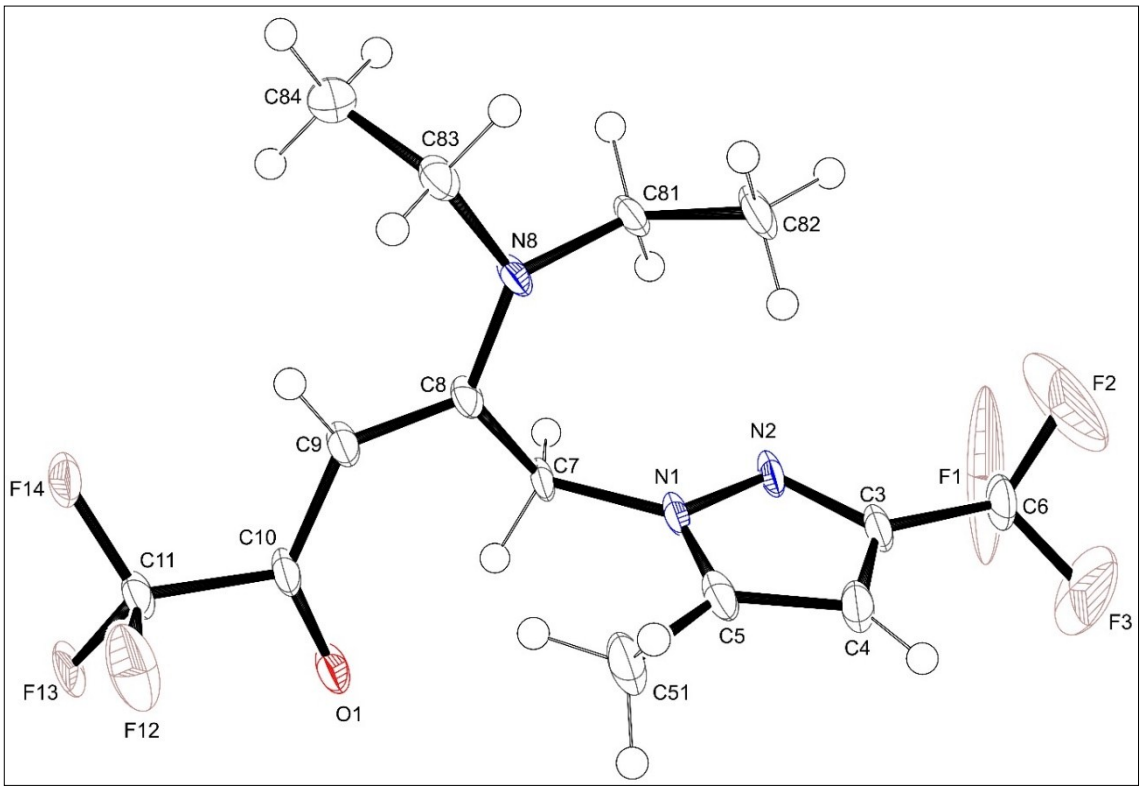


Figure 59 - X-ray diffraction of compound **6b**, CCDC number 1487398.

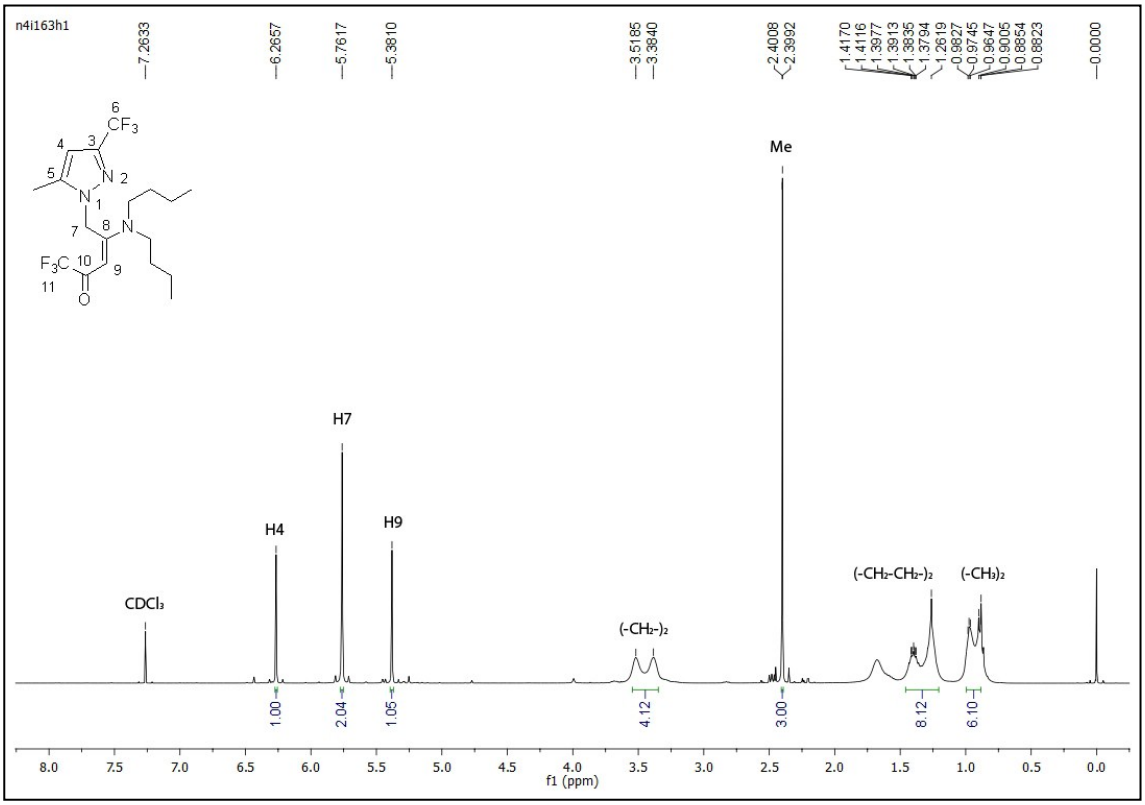


Figure 60 - ^{1}H NMR spectrum of compound **6c** in $CDCl_3$ at 400 MHz.

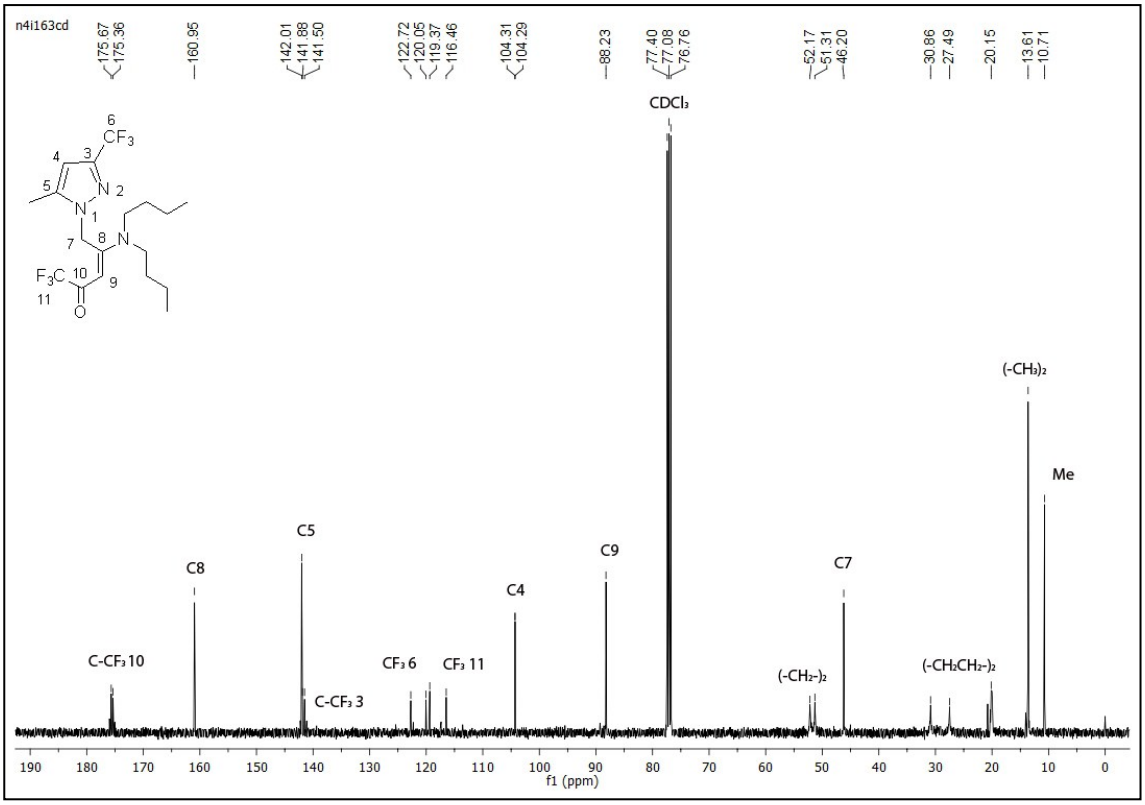


Figure 61 - ^{13}C NMR spectrum of compound **6c** in $CDCl_3$ at 100 MHz.

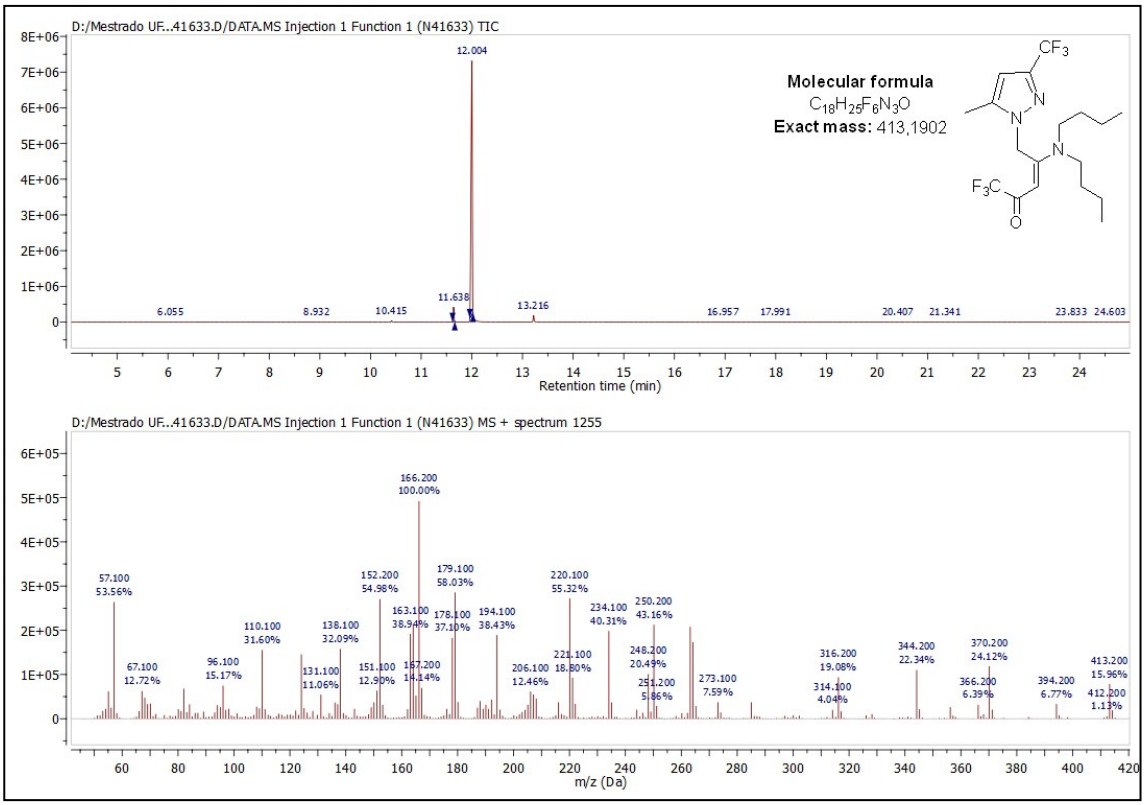


Figure 62 - Chromatogram and mass spectrum (EI, 70 eV) of compound **6c**.

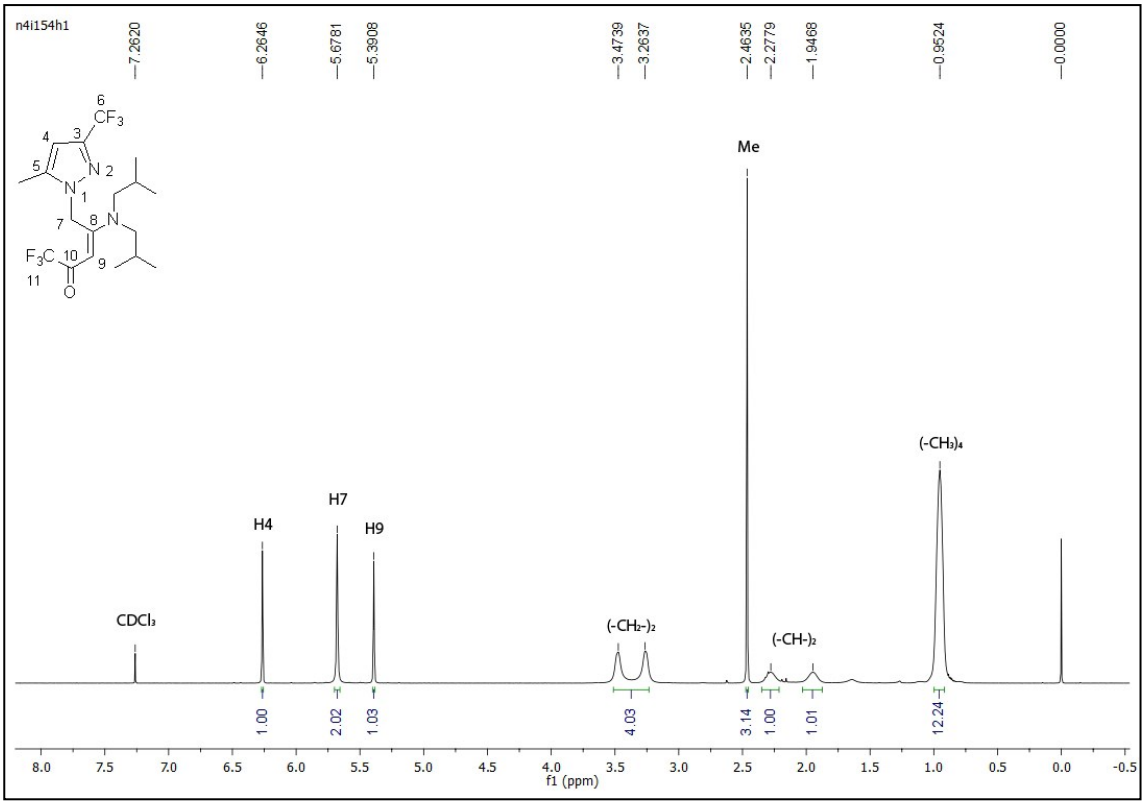


Figure 63 - ^{1}H NMR spectrum of compound **6d** in $CDCl_3$ at 400 MHz.

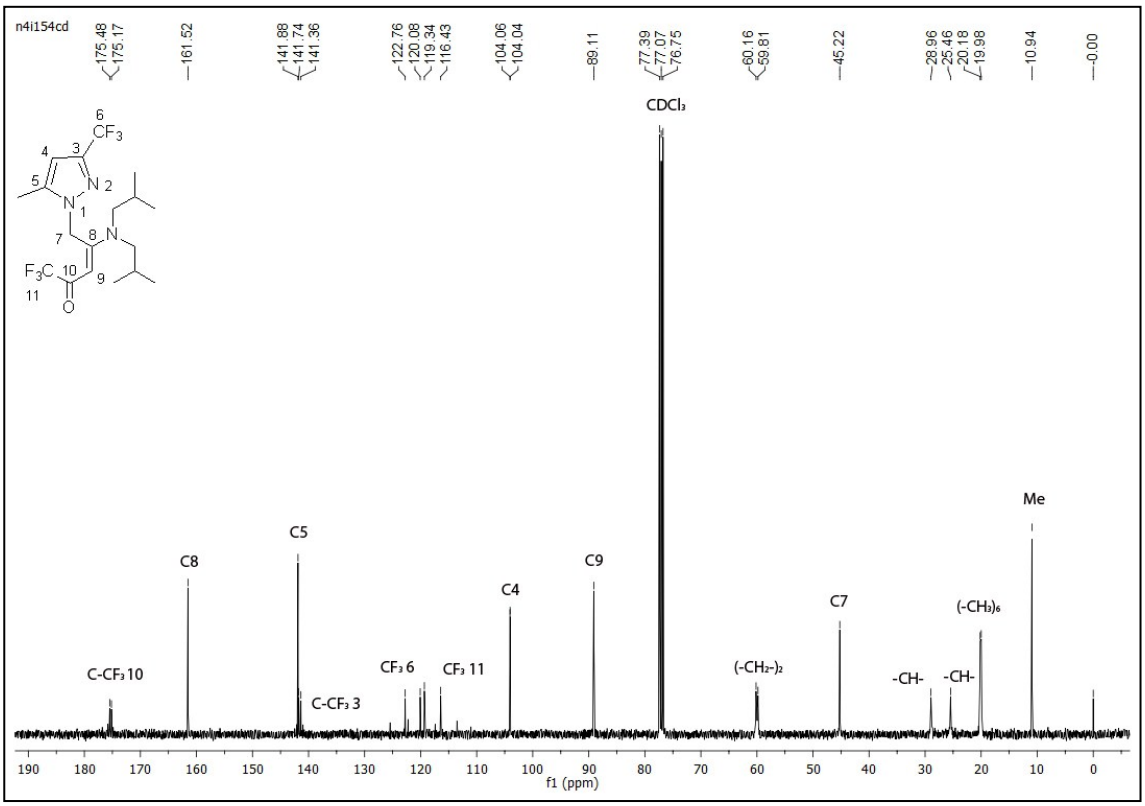


Figure 64 - ^{13}C NMR spectrum of compound **6d** in $CDCl_3$ at 100 MHz.

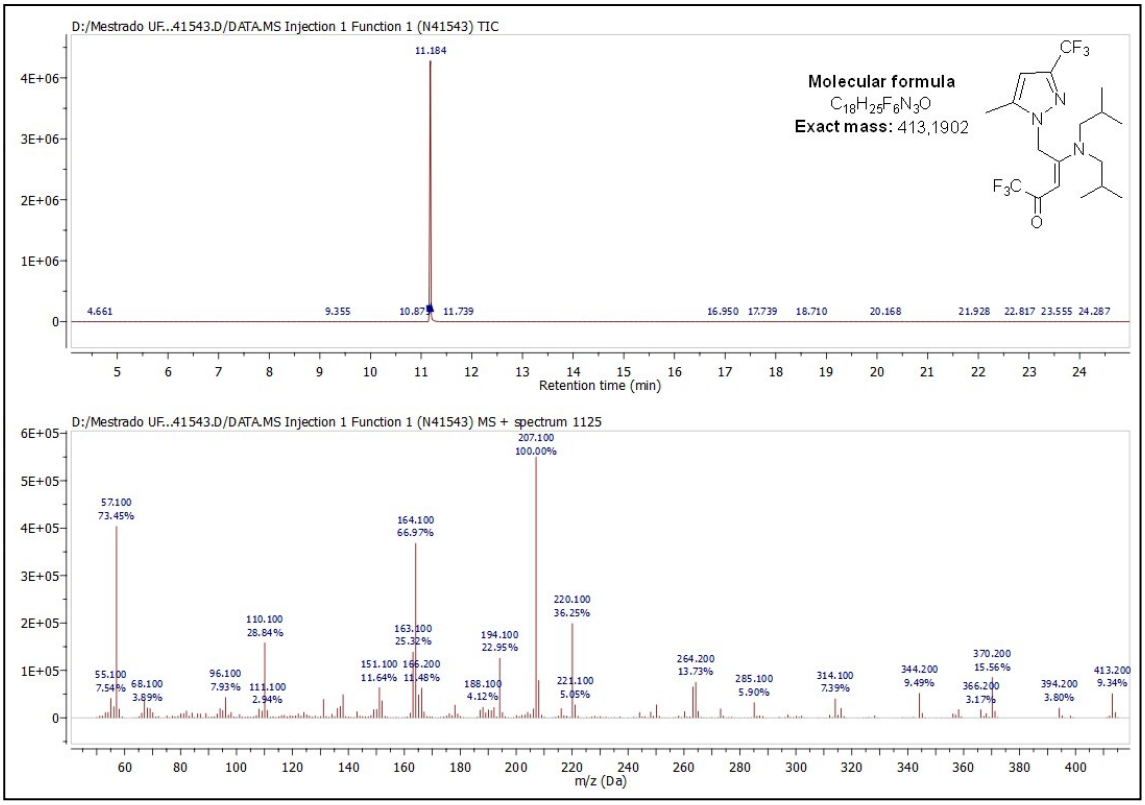


Figure 65 - Chromatogram and mass spectrum (EI, 70 eV) of compound **6d**.

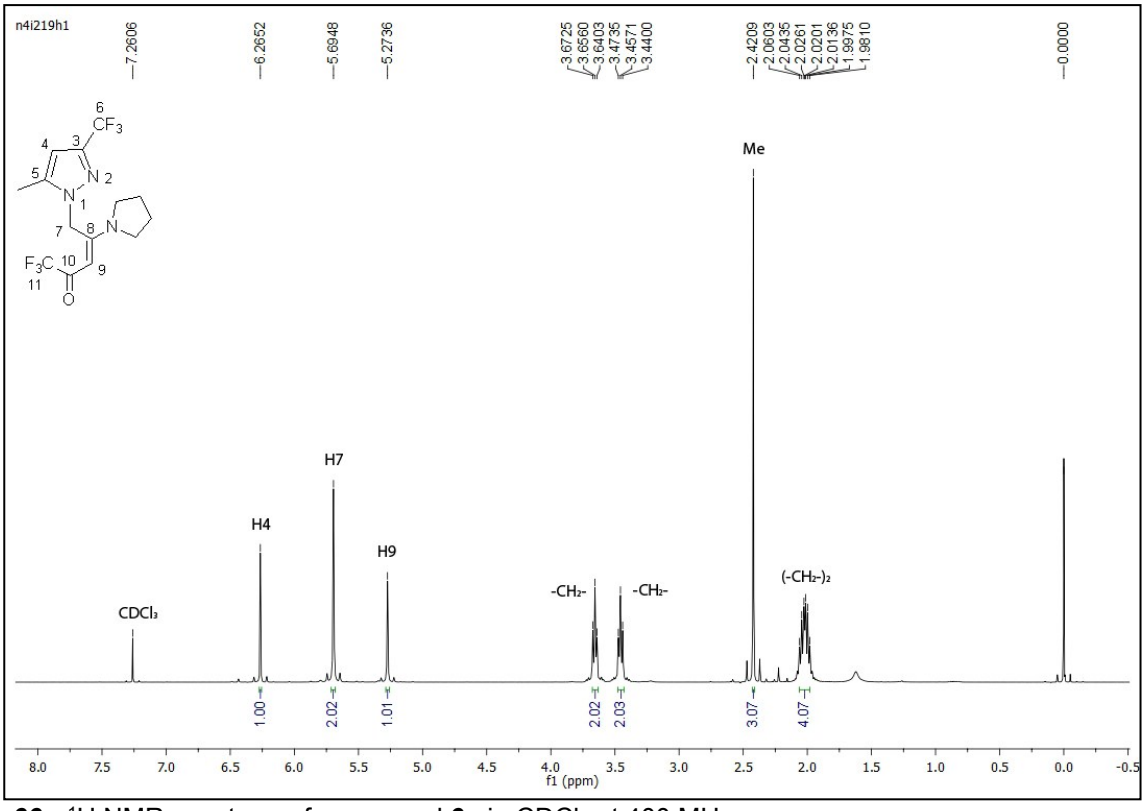


Figure 66 - ^{1}H NMR spectrum of compound **6e** in $CDCl_3$ at 400 MHz.

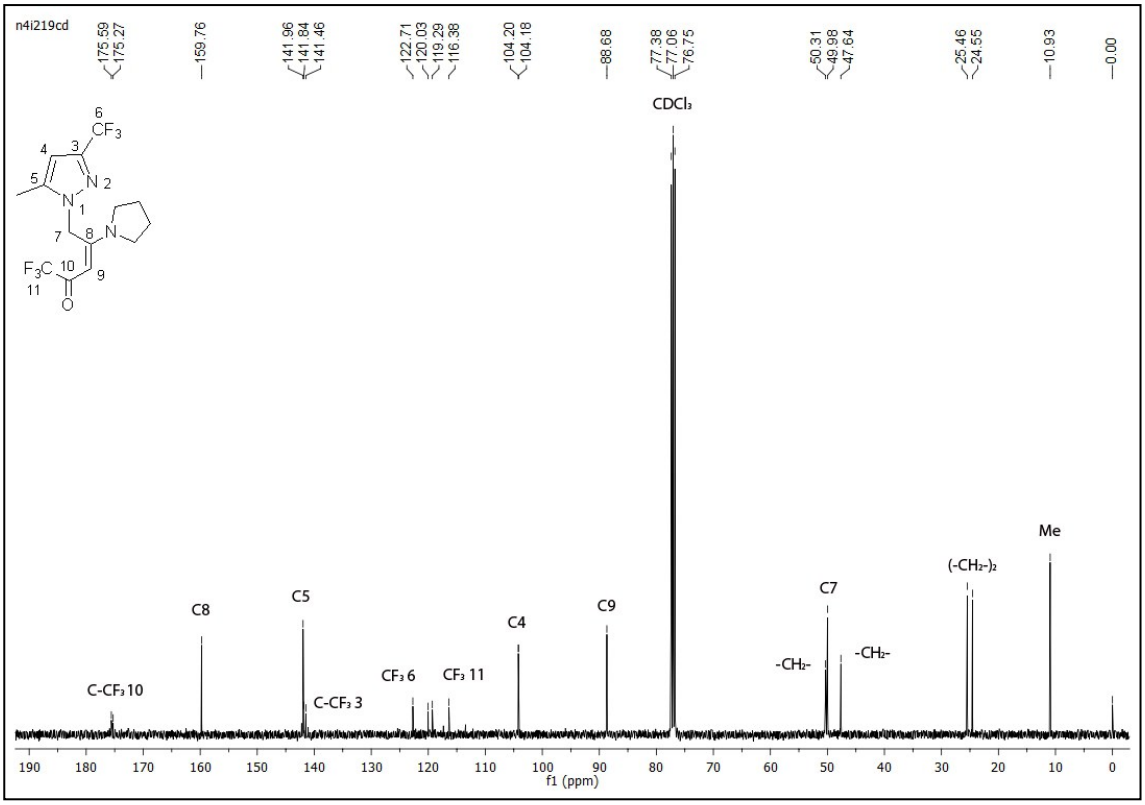


Figure 67 - ^{13}C NMR spectrum of compound **6e** in $CDCl_3$ at 100 MHz.

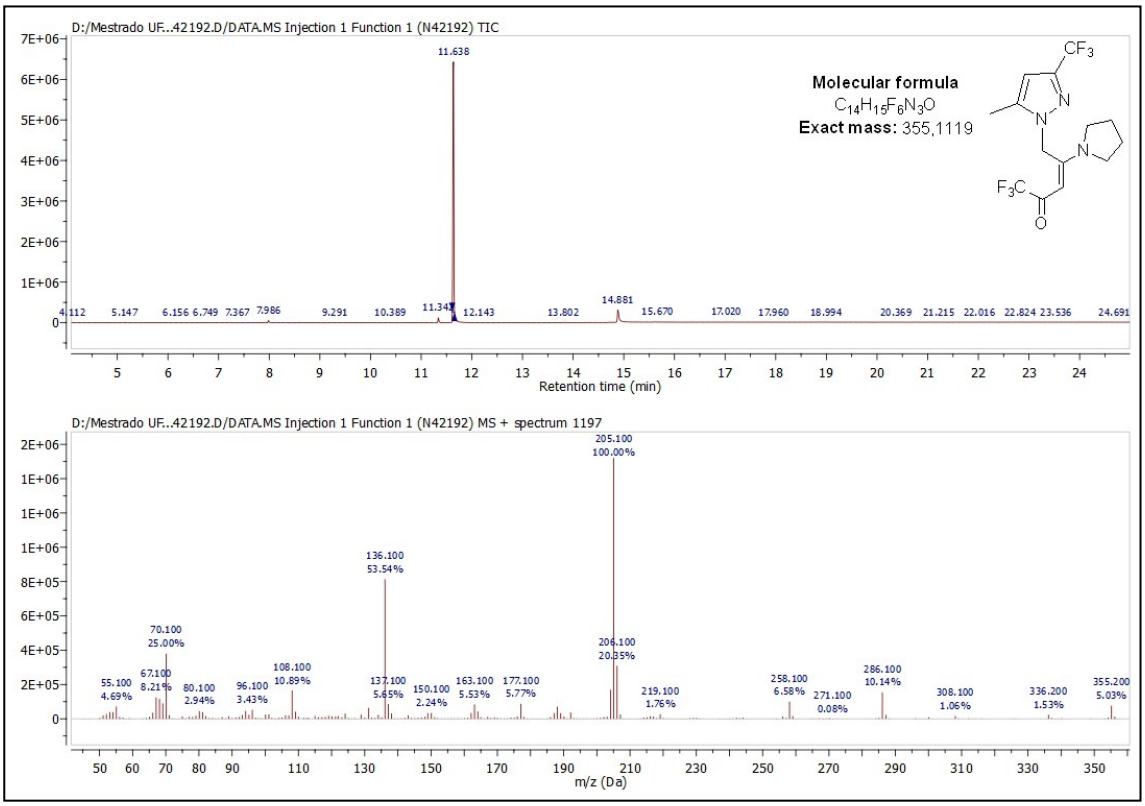


Figure 68 - Chromatogram and mass spectrum (EI, 70 eV) of compound **6e**.

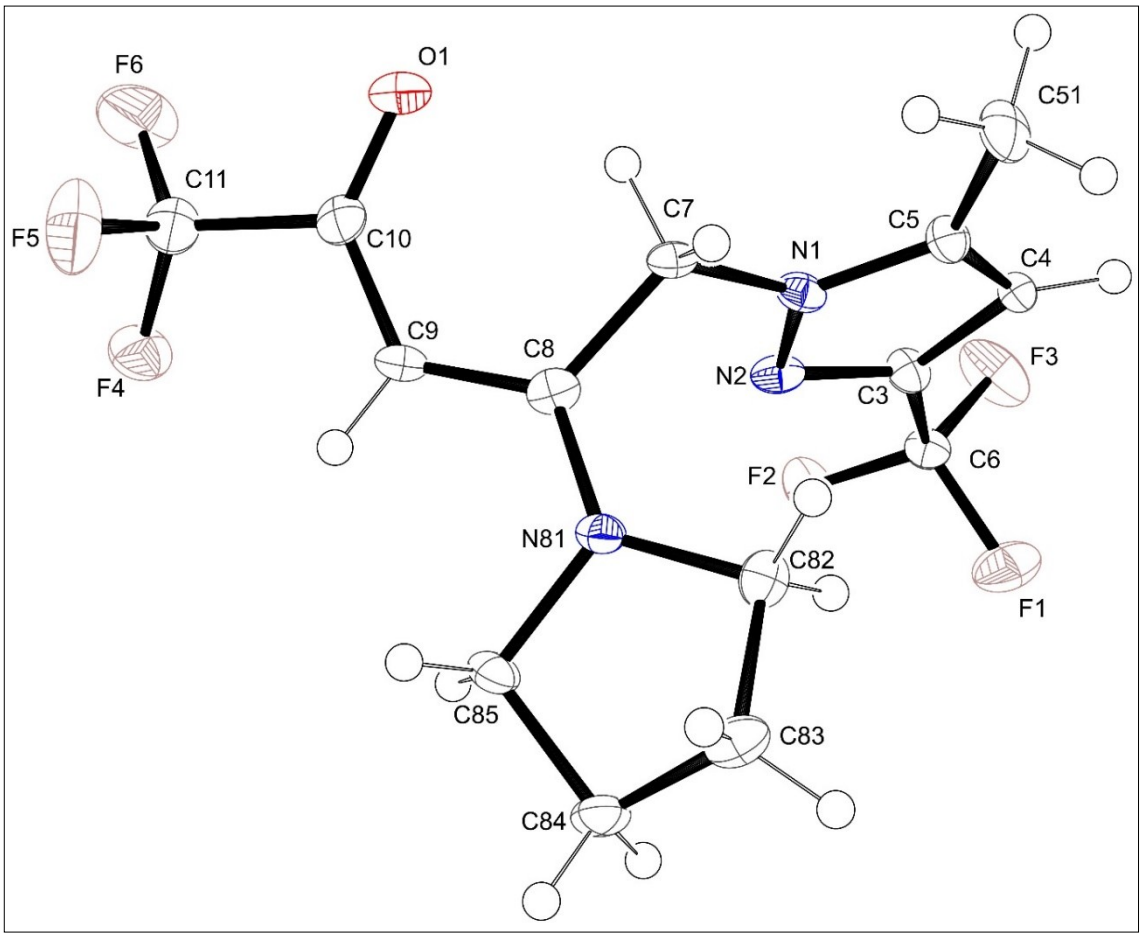


Figure 69 - X-ray diffraction of compound **6e**, CCDC number 1487390.

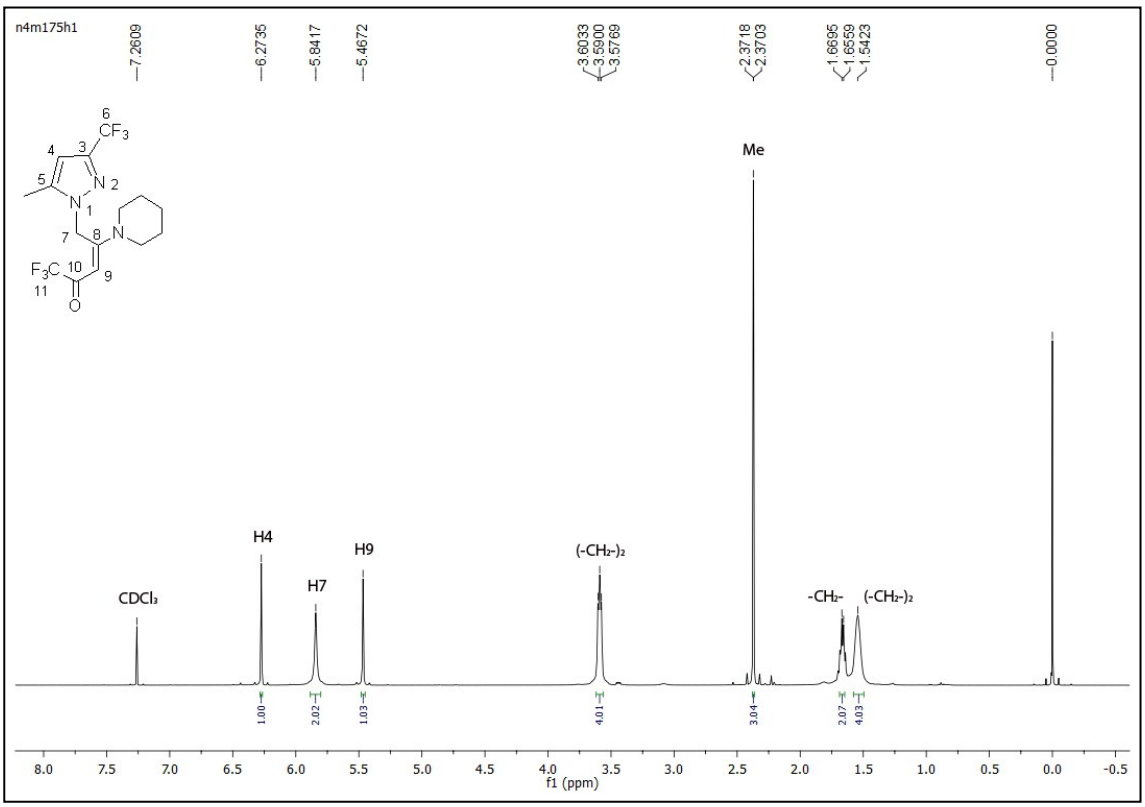


Figure 70 - ^{1}H NMR spectrum of compound **6f** in $CDCl_3$ at 400 MHz.

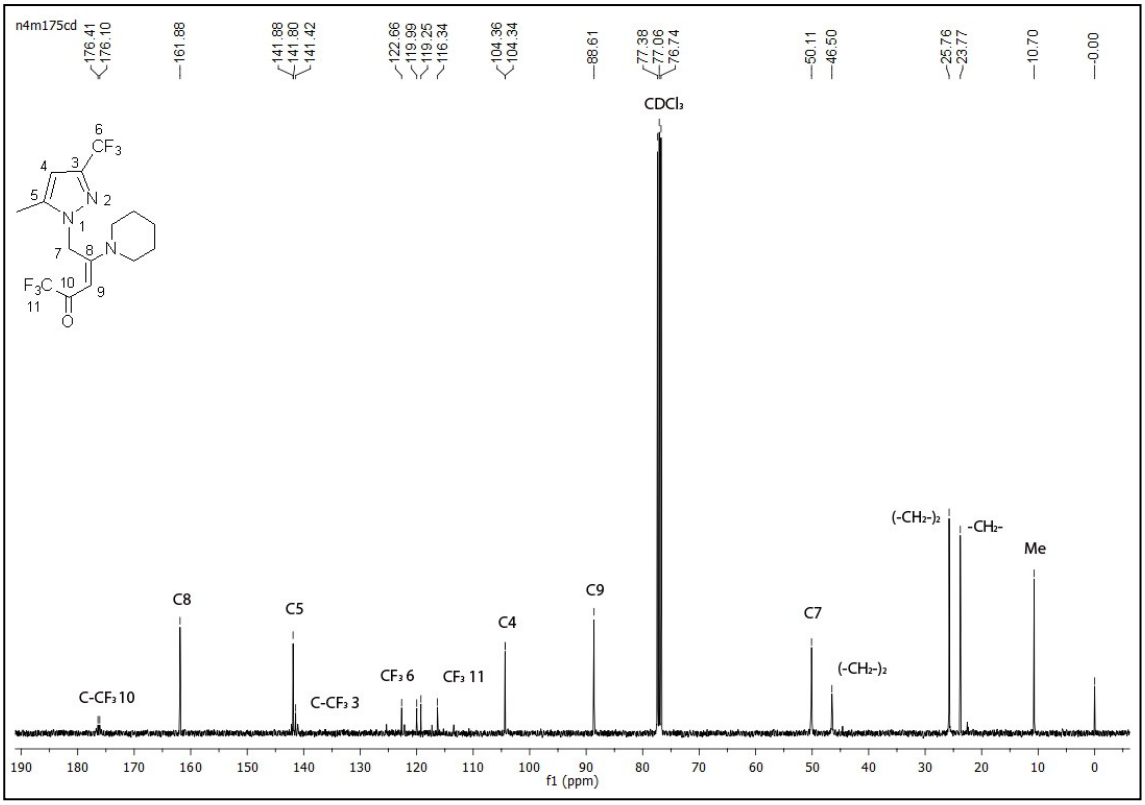


Figure 71 - ^{13}C NMR spectrum of compound **6f** in $CDCl_3$ at 100 MHz.

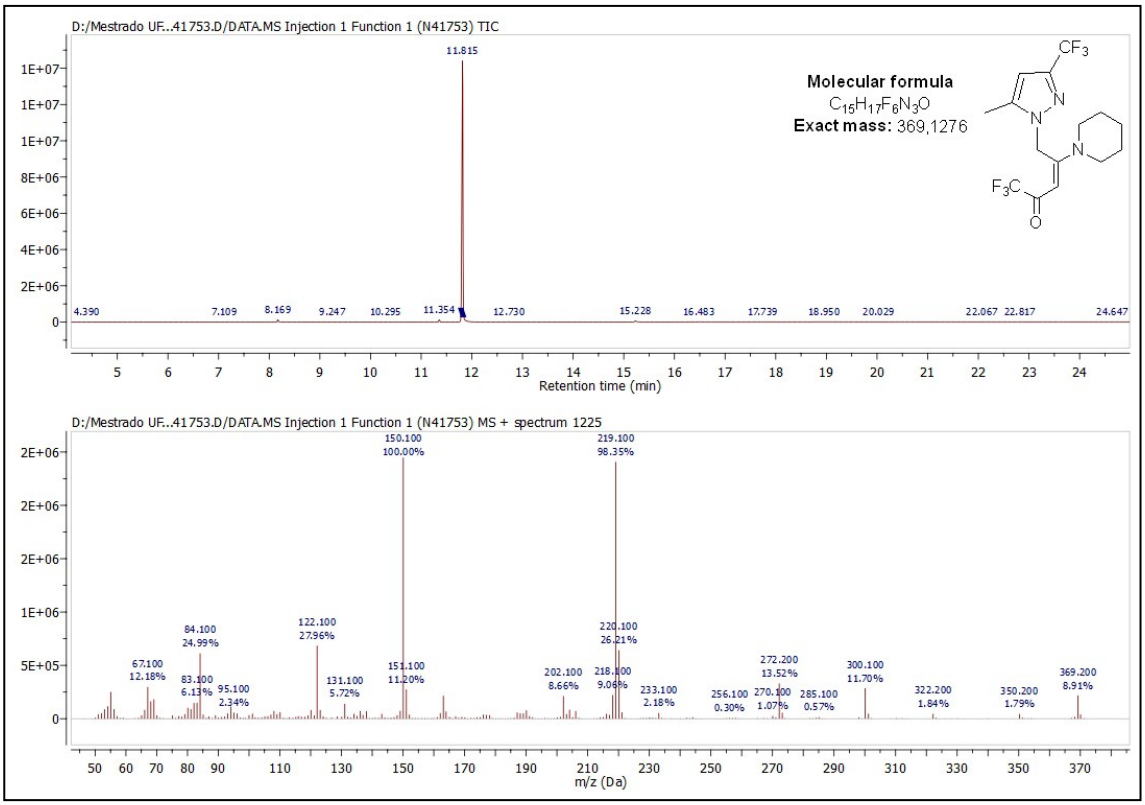


Figure 72 - Chromatogram and mass spectrum (EI, 70 eV) of compound **6f**.

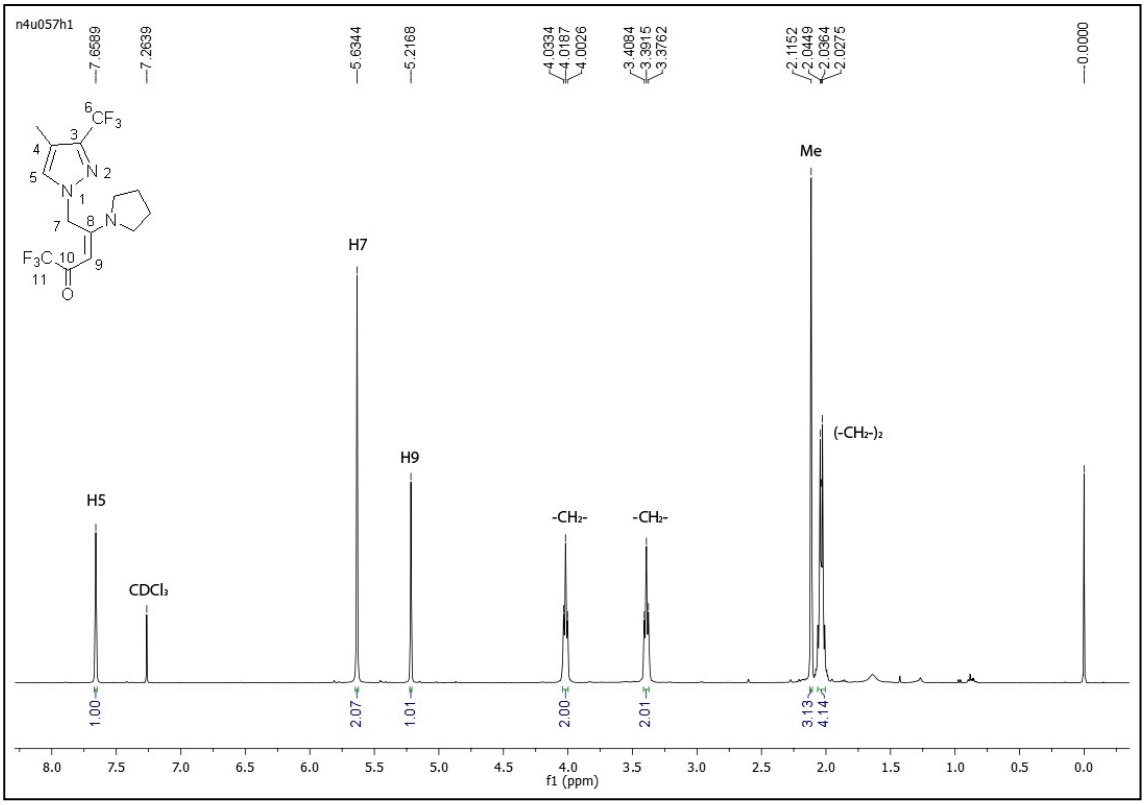


Figure 73 - ^{1}H NMR spectrum of compound **6g** in $CDCl_3$ at 400 MHz.

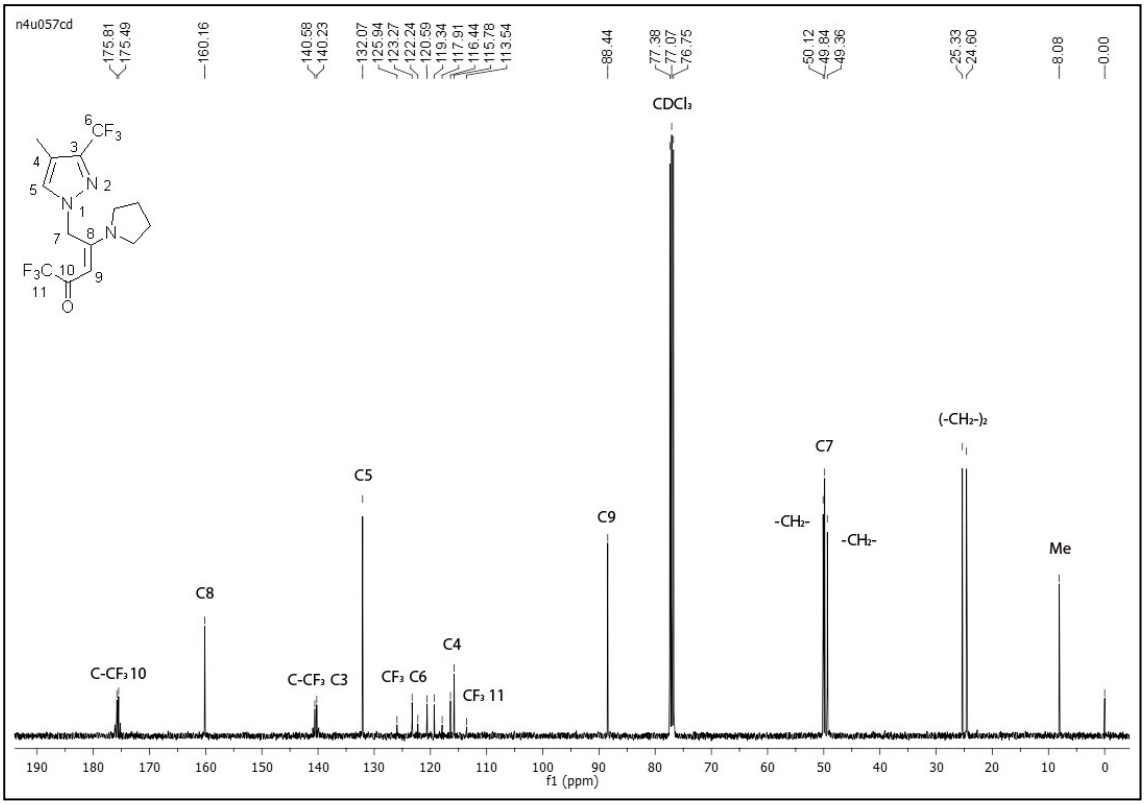


Figure 74 - ^{13}C NMR spectrum of compound **6g** in $CDCl_3$ at 100 MHz.

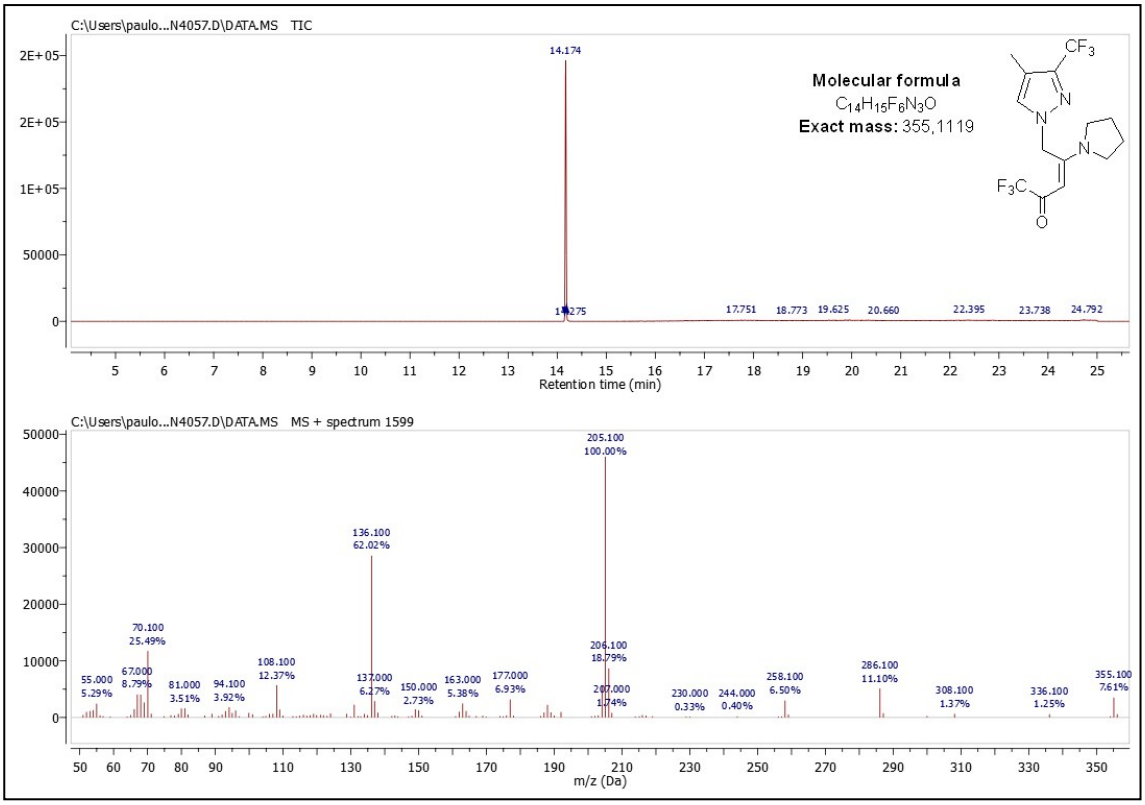


Figure 75 - Chromatogram and mass spectrum (EI, 70 eV) of compound **6g**.

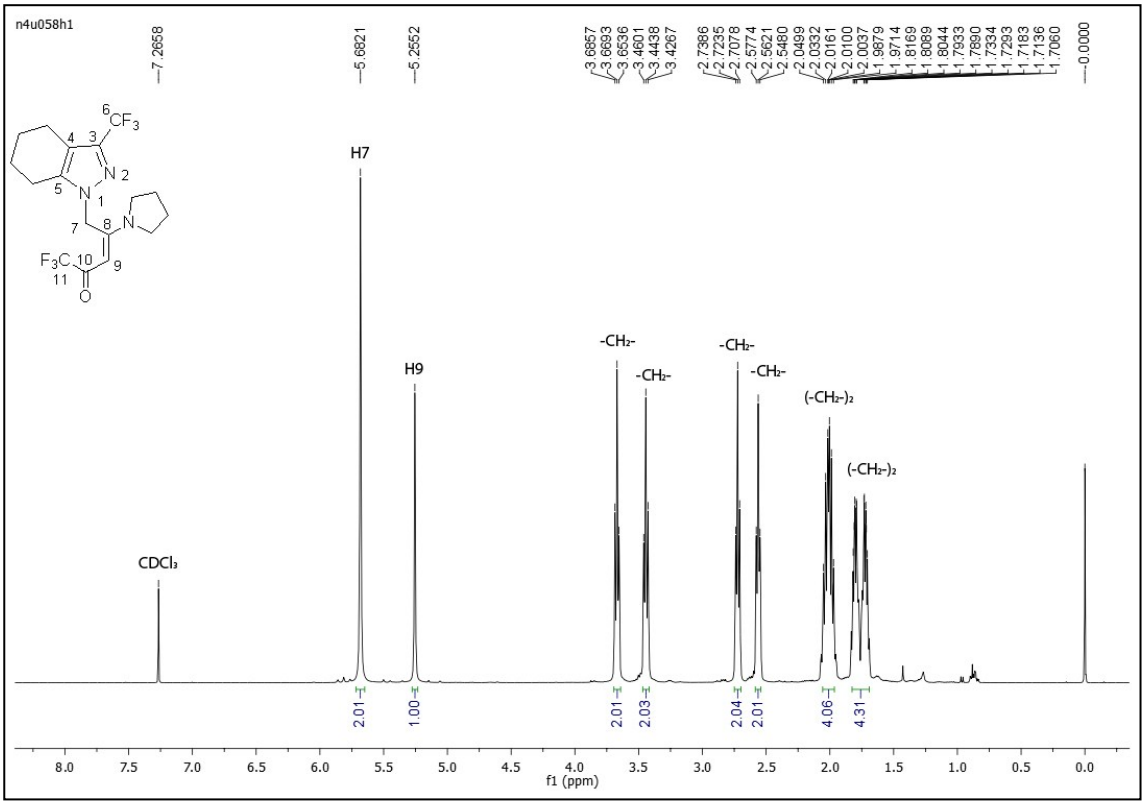


Figure 76 - ^{1}H NMR spectrum of compound **6h** in $CDCl_3$ at 400 MHz.

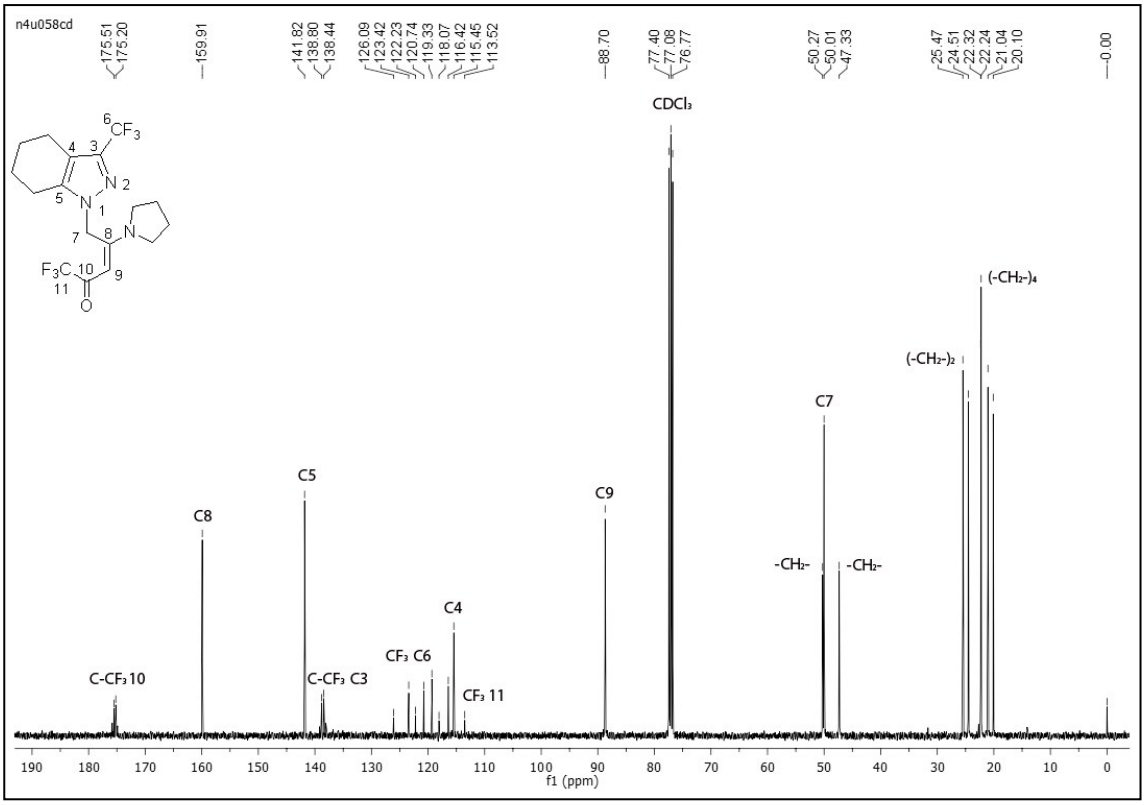


Figure 77 - ^{13}C NMR spectrum of compound **6h** in $CDCl_3$ at 100 MHz.

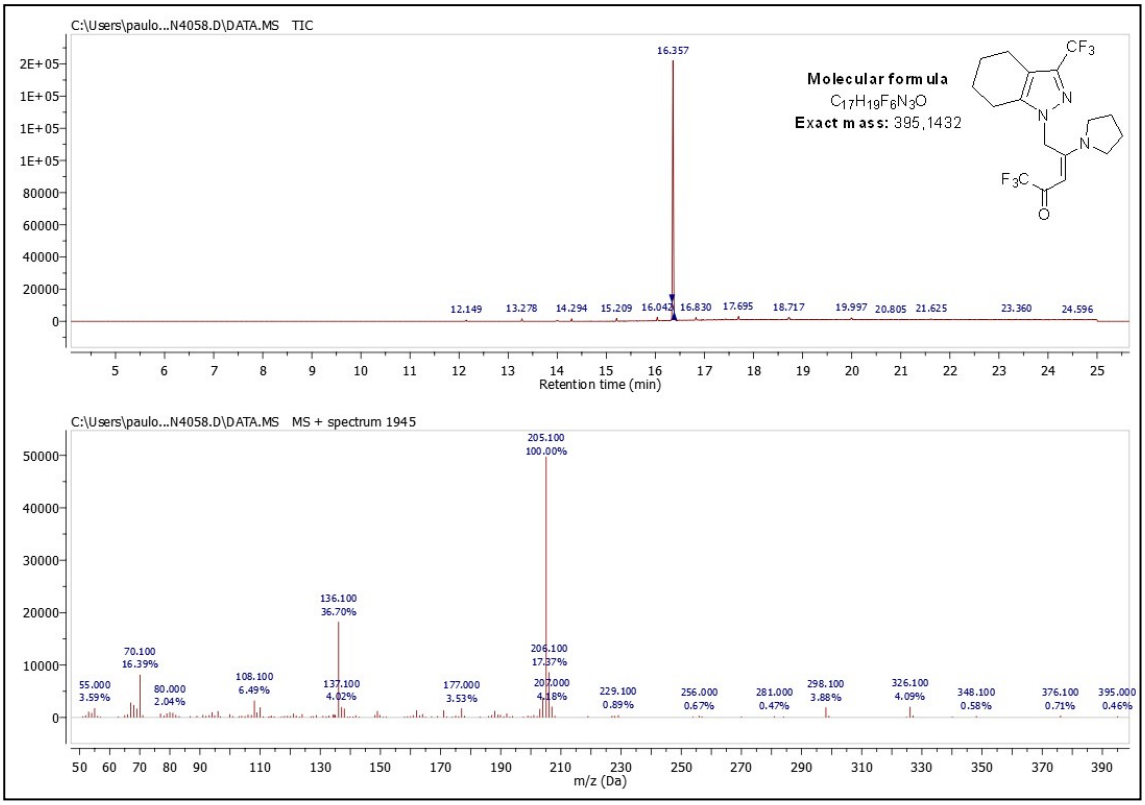


Figure 78 - Chromatogram and mass spectrum (EI, 70 eV) of compound **6h**.

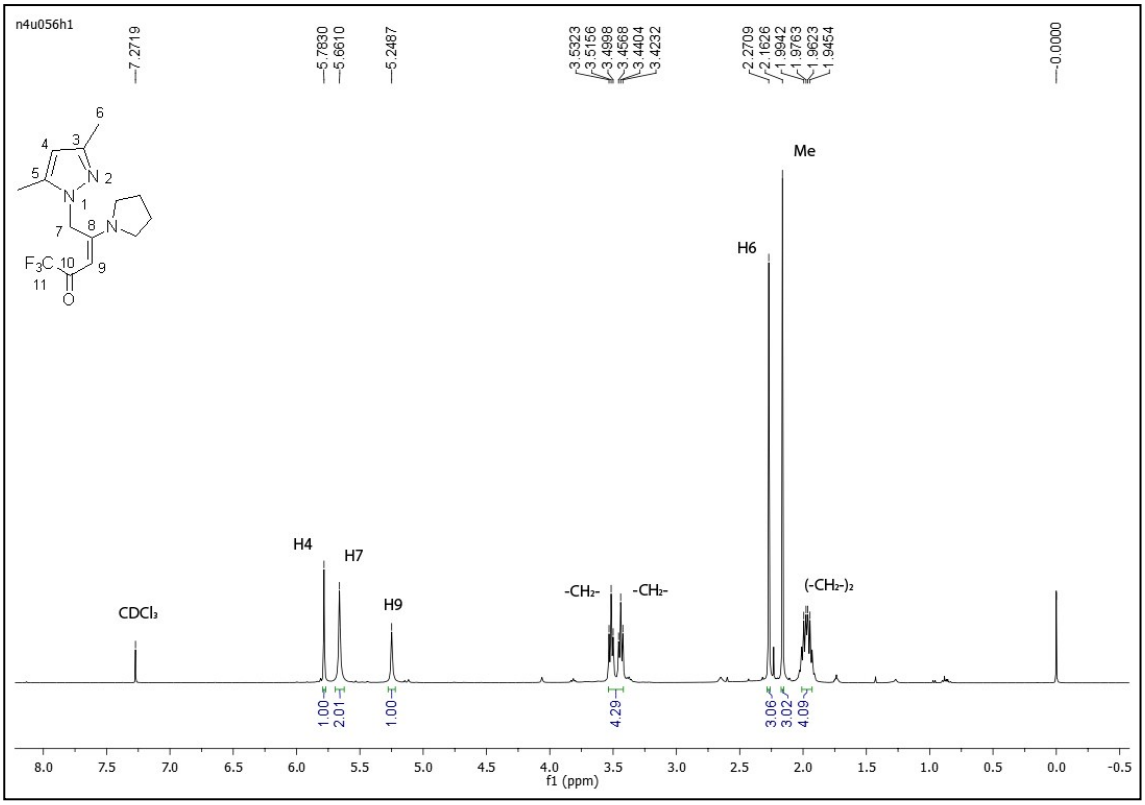


Figure 79 - ^{1}H NMR spectrum of compound **6i** in $CDCl_3$ at 400 MHz.

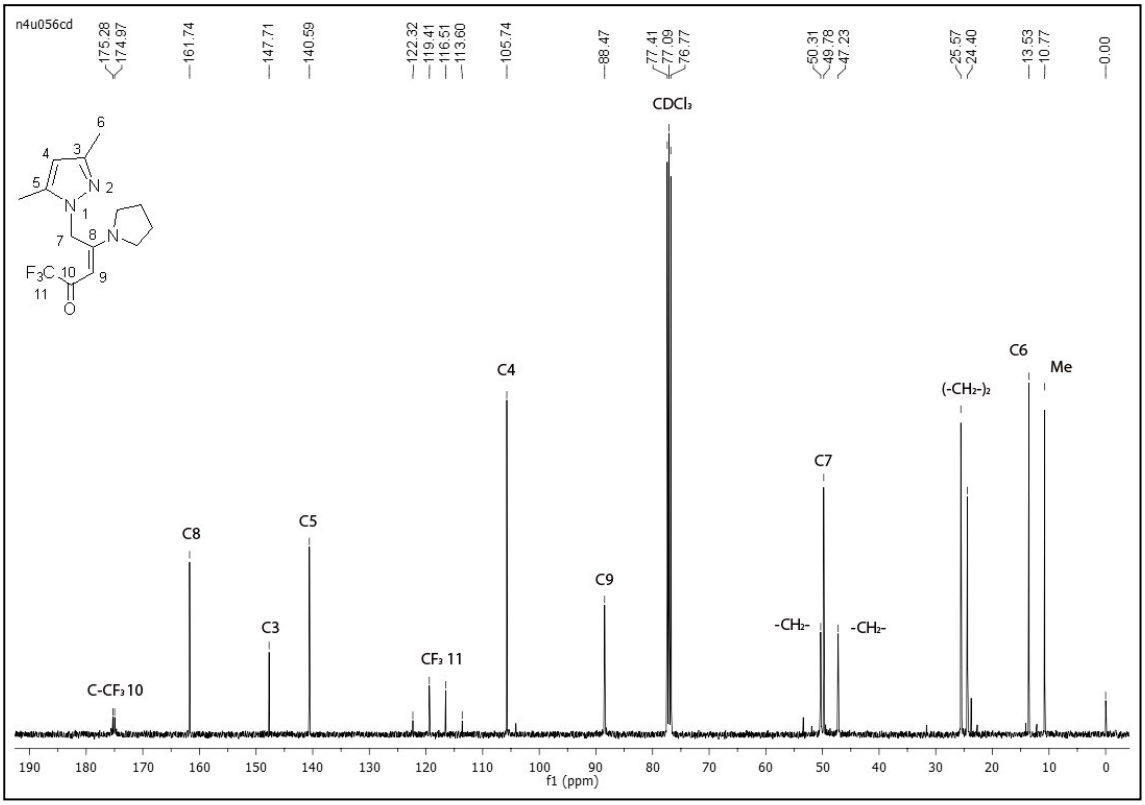


Figure 80 - ^{13}C NMR spectrum of compound **6i** in $CDCl_3$ at 100 MHz.

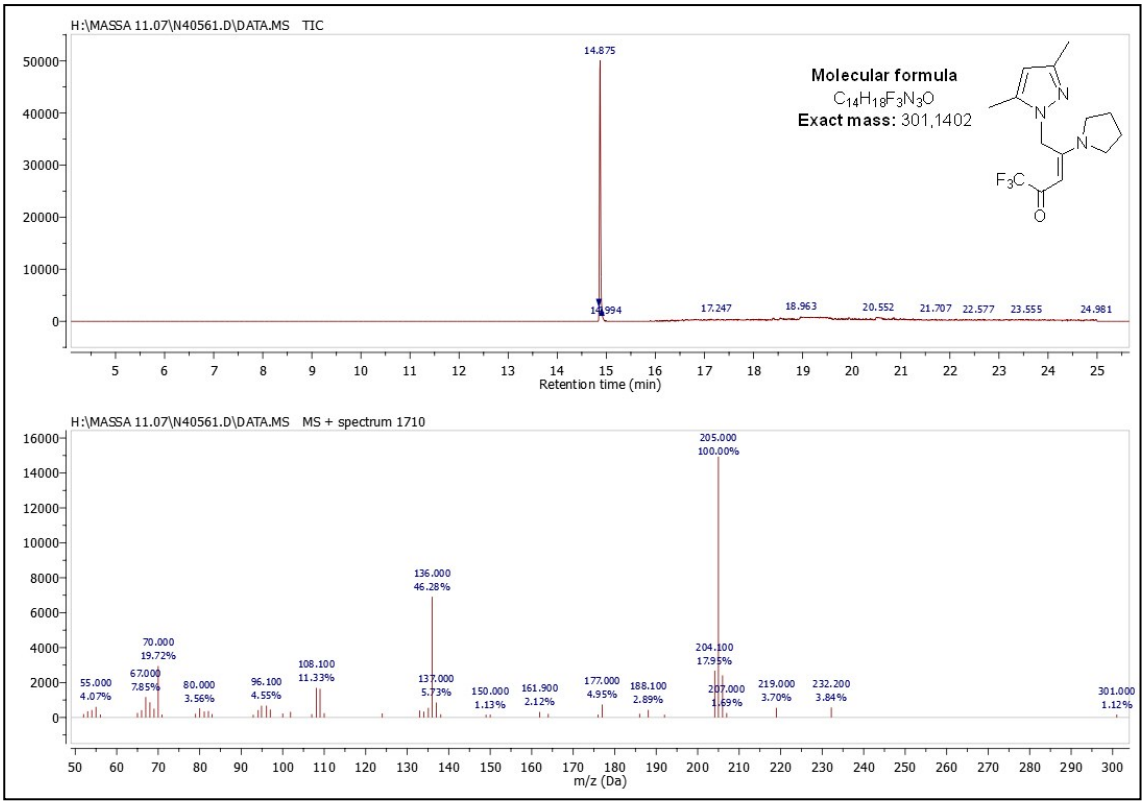


Figure 81 - Chromatogram and mass spectrum (EI, 70 eV) of compound **6i**.

VI - ^{1}H, ^{13}C NMR and GC-MS spectra of compounds 7–10

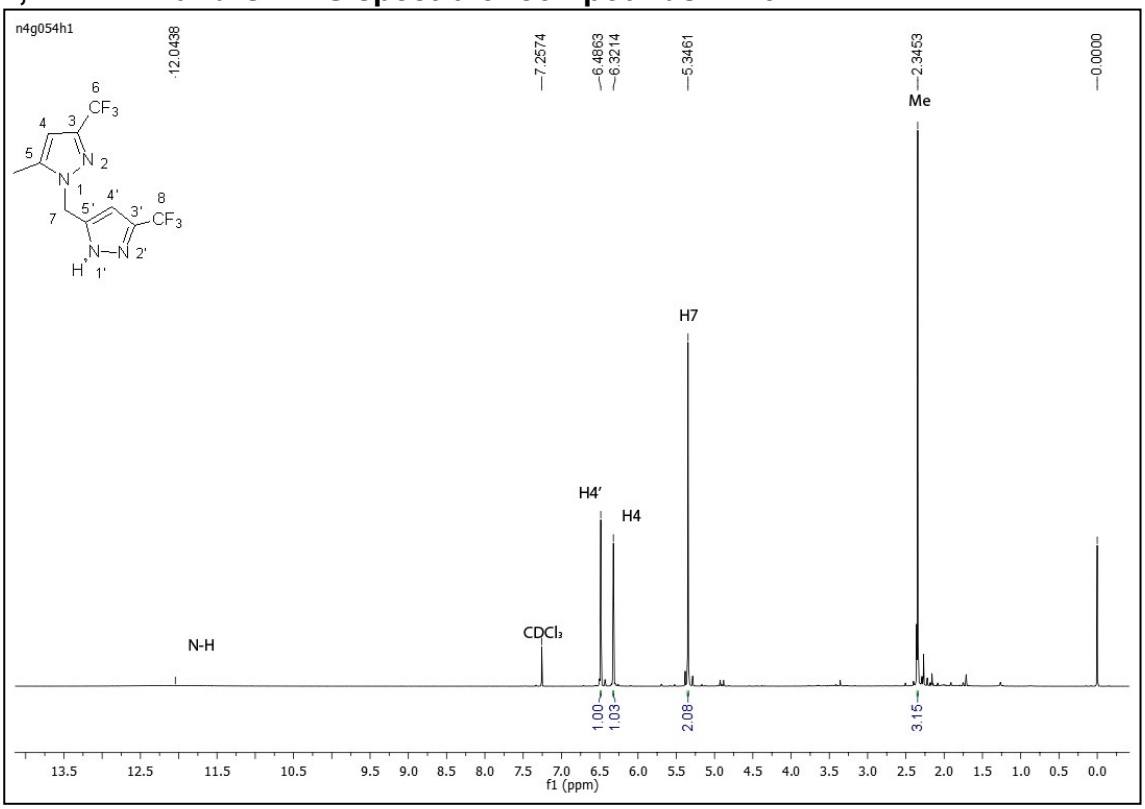


Figure 82 - ^{1}H NMR spectrum of compound **7** in $CDCl_3$ at 400 MHz.

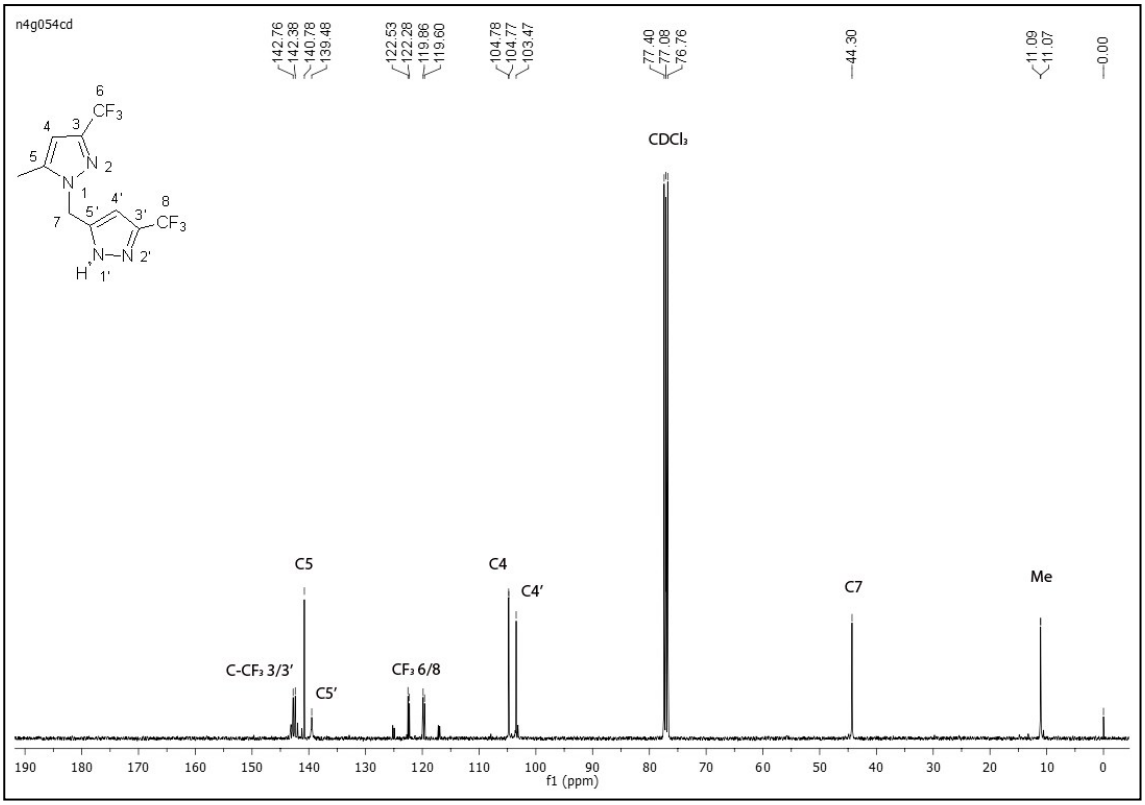


Figure 83 - ^{13}C NMR spectrum of compound **7** in $CDCl_3$ at 100 MHz.

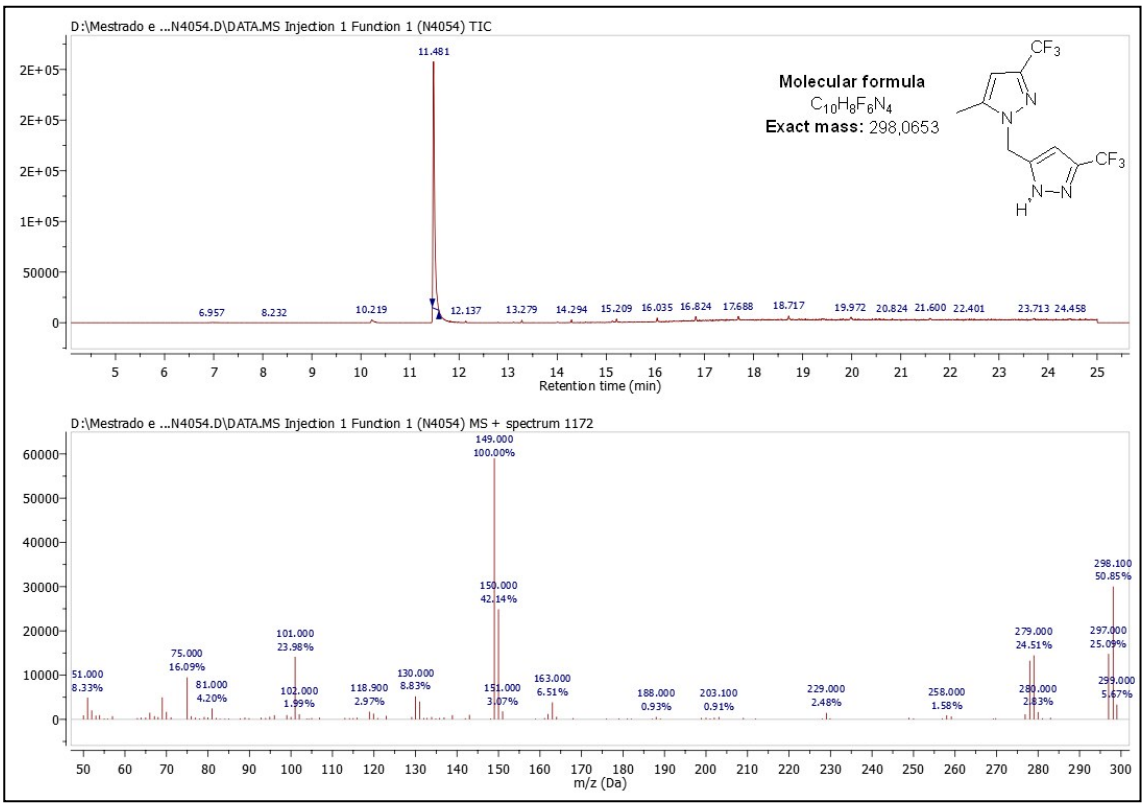


Figure 84 - Chromatogram and mass spectrum (EI, 70 eV) of compound **7**.

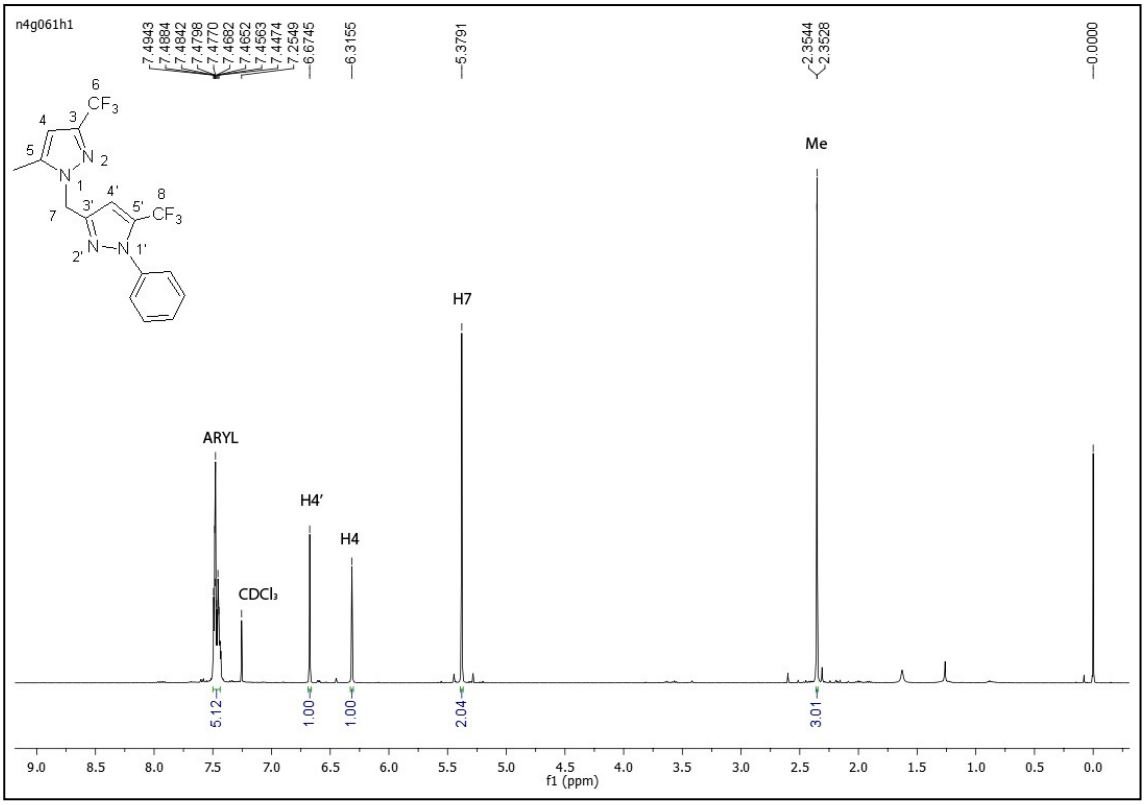


Figure 85 - ^{1}H NMR spectrum of compound **8** in $CDCl_3$ at 400 MHz.

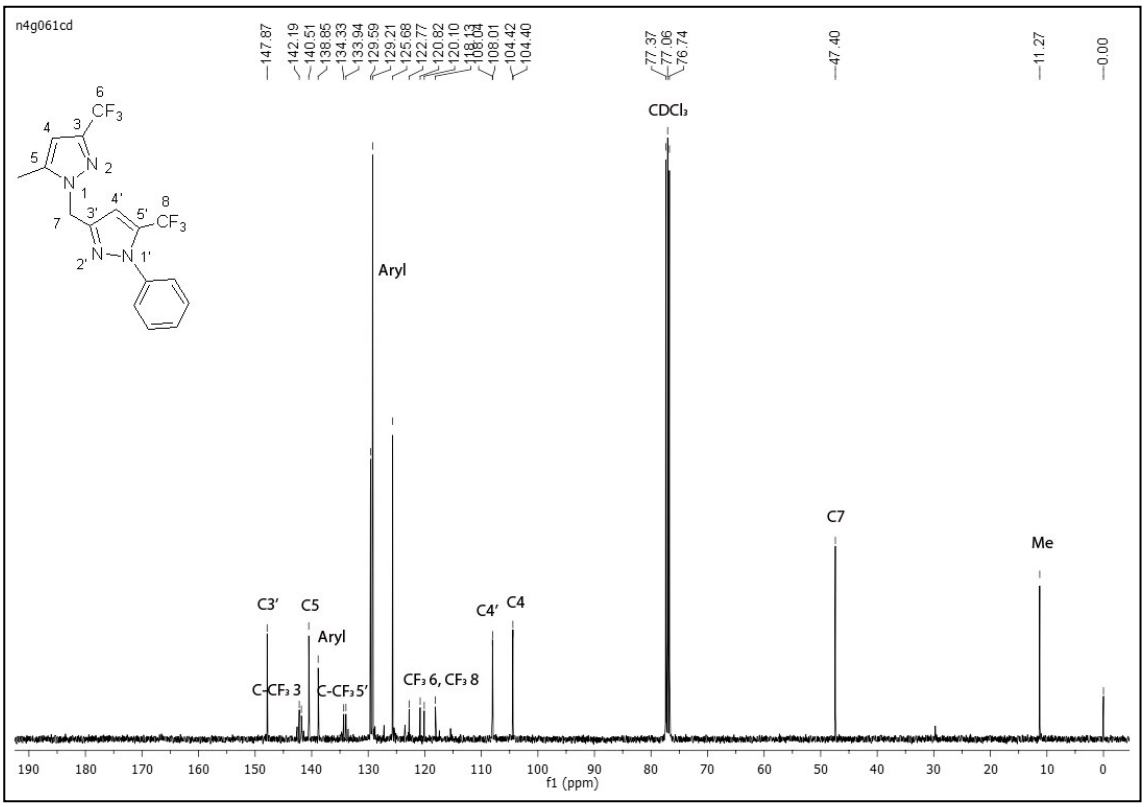


Figure 86 - ^{13}C NMR spectrum of compound **8** in $CDCl_3$ at 100 MHz.

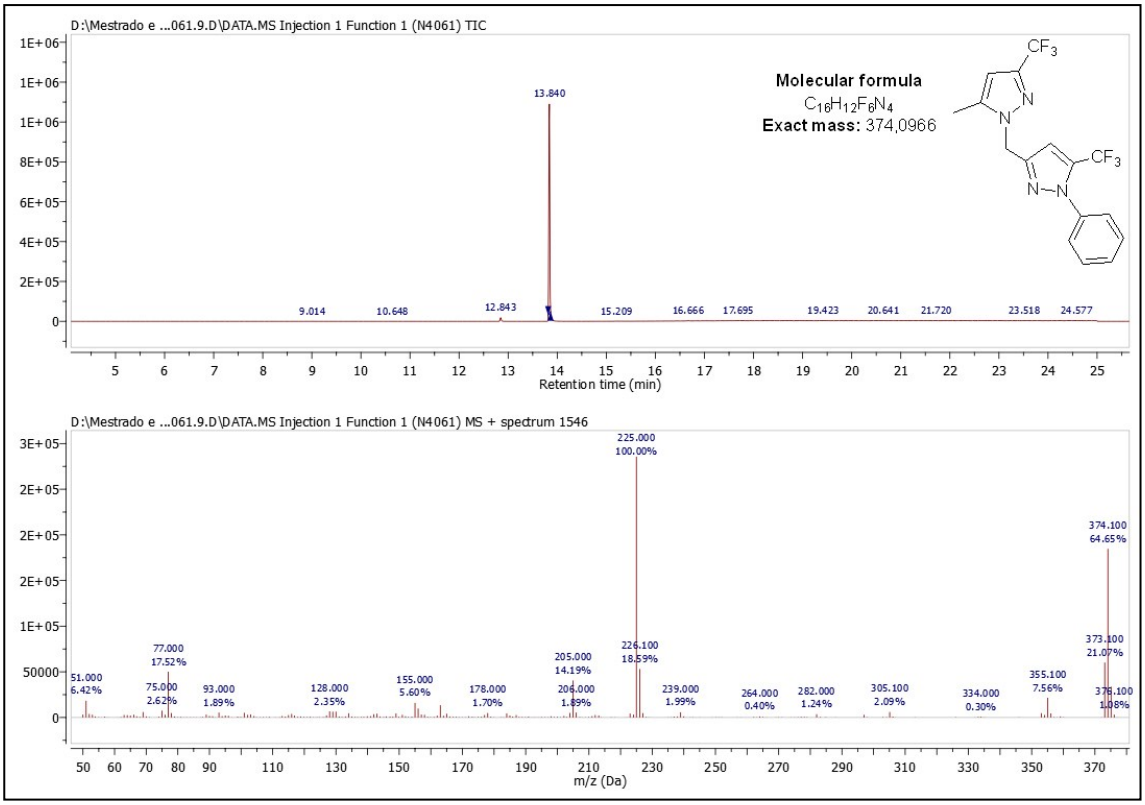


Figure 87 - Chromatogram and mass spectrum (EI, 70 eV) of compound **8**.

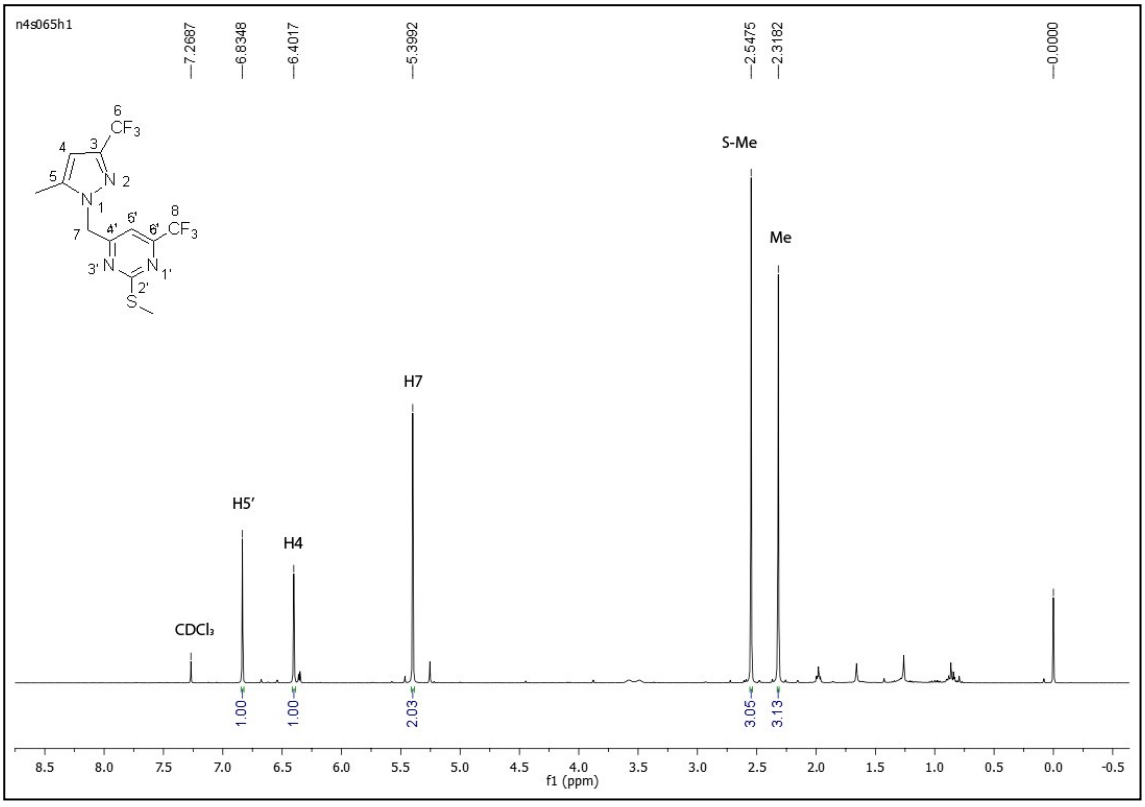


Figure 88 - ^{1}H NMR spectrum of compound **9** in $CDCl_3$ at 400 MHz.

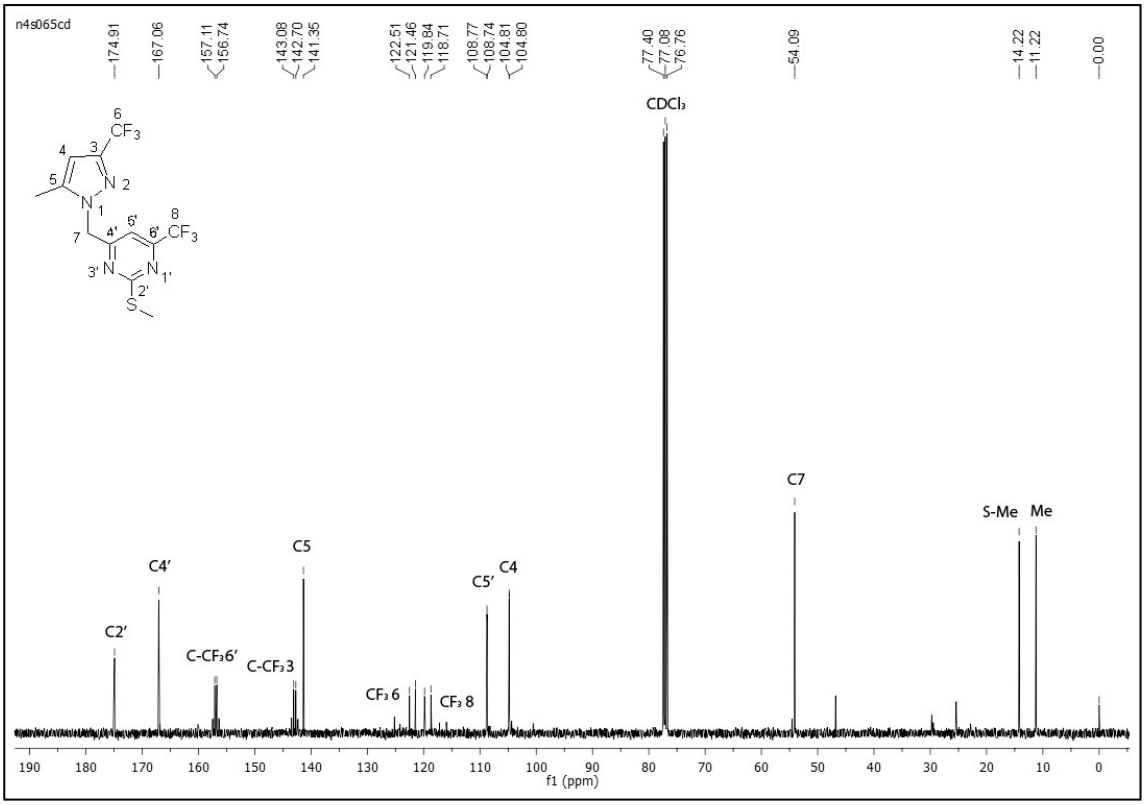


Figure 89 - ^{13}C NMR spectrum of compound **9** in $CDCl_3$ at 100 MHz.

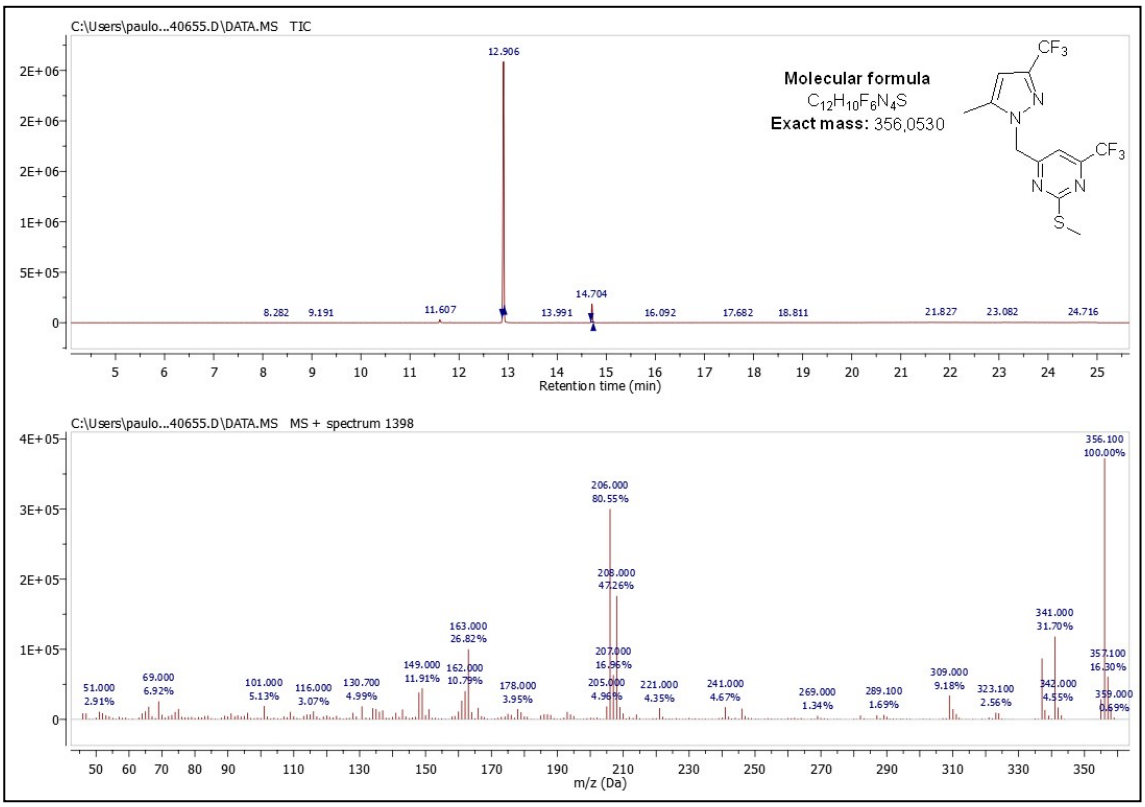


Figure 90 - Chromatogram and mass spectrum (EI, 70 eV) of compound **9**.

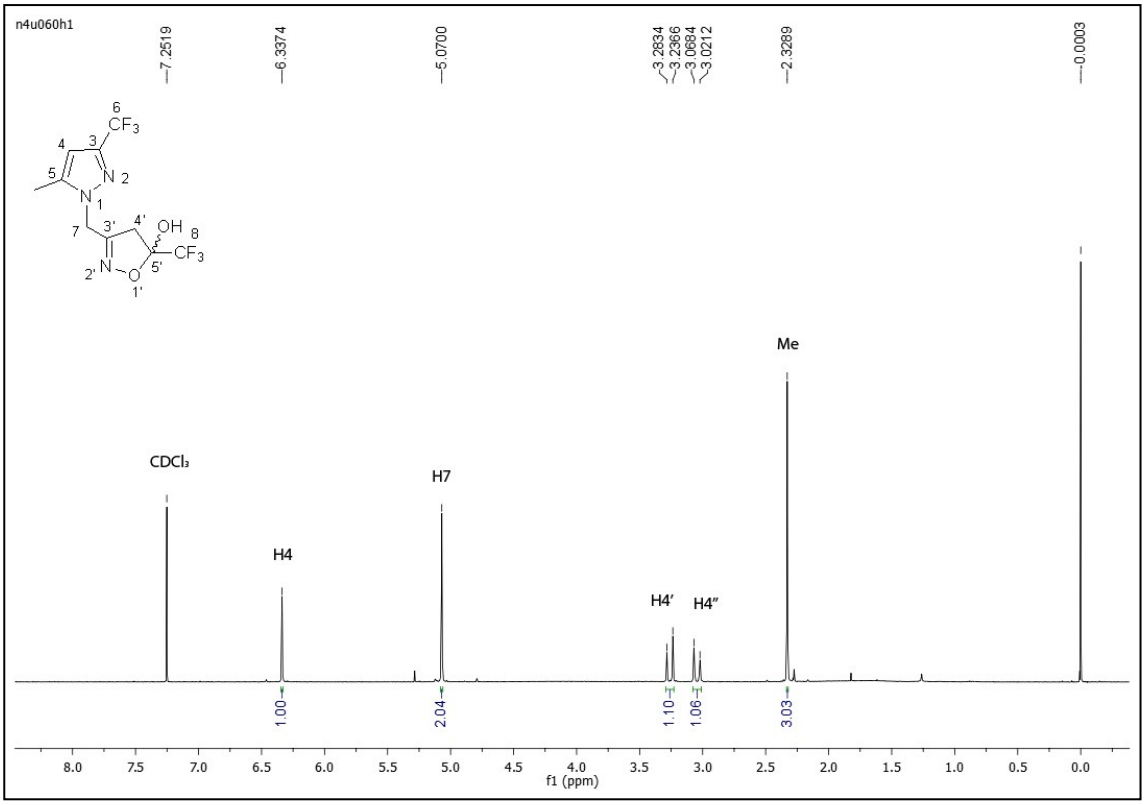


Figure 91 - ^{1}H NMR spectrum of compound **10** in $CDCl_3$ at 400 MHz.

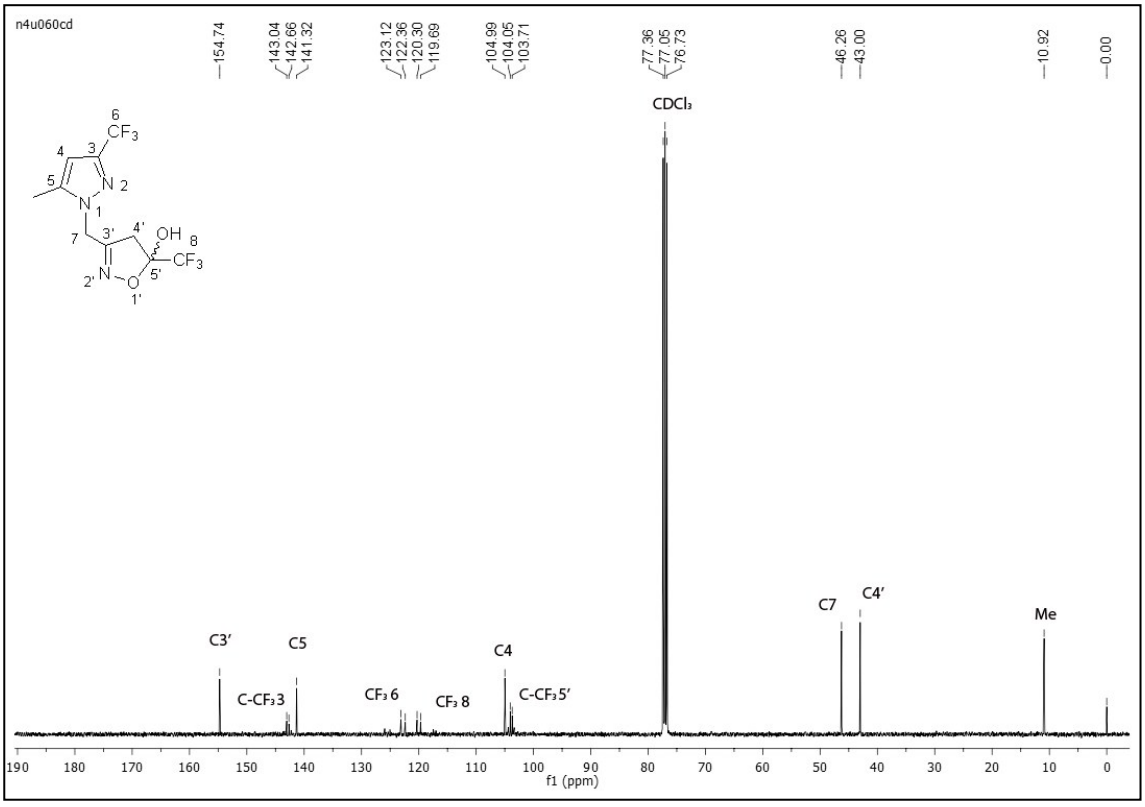


Figure 92 - ^{13}C NMR spectrum of compound **10** in $CDCl_3$ at 100 MHz.

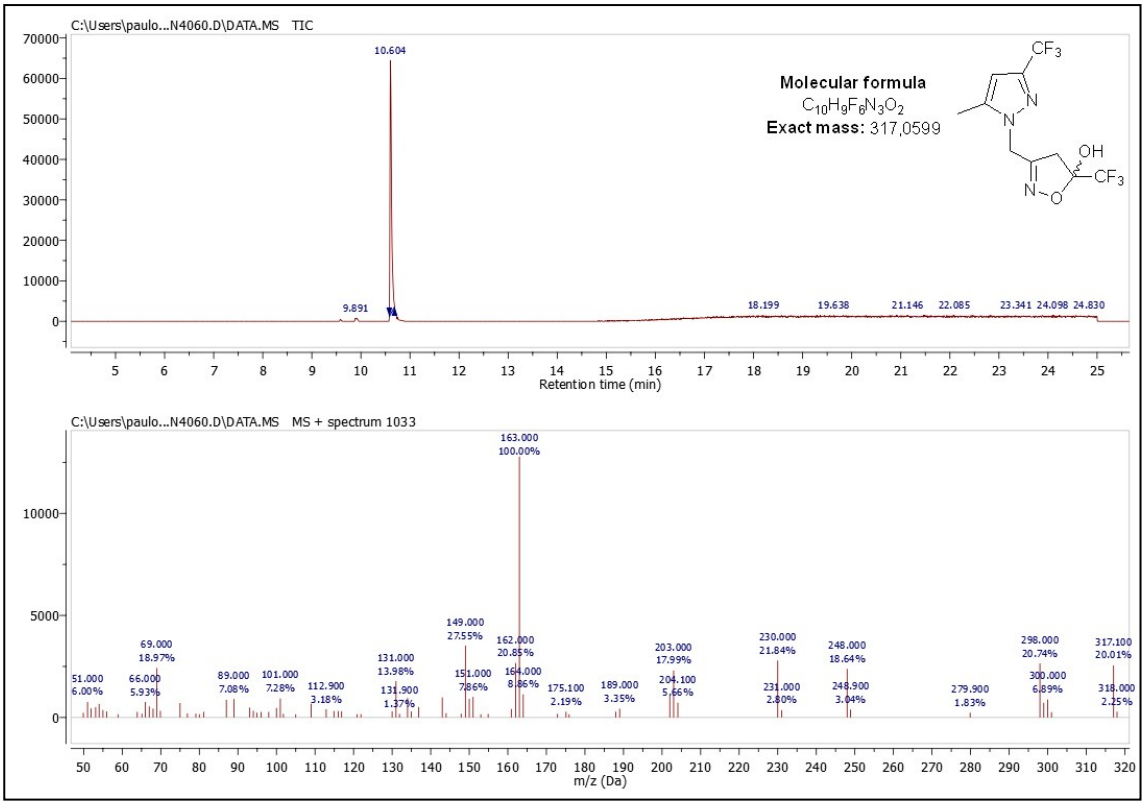


Figure 93 - Chromatogram and mass spectrum (EI, 70 eV) of compound **10**.