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Highly diastereoselective multicomponent synthesis of polysubstituted 2-hydroxy-2-trifluoromethylpiperidines with four and five stereogenic centers

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1. Chemical Experimental Details

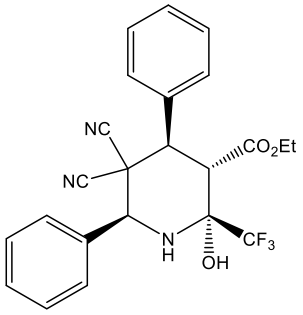
All melting points were measured with a Stuart SMP30 melting point apparatus and are uncorrected. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded with a Bruker AM300 and Bruker Avance-400 at ambient temperature in DMSO-d_6 or $CDCl_3$ solutions. Chemical shifts values are given in δ scale relative to Me_4Si. The *J* values are given in hertz. Only discrete or characteristic signals for the 1H NMR are reported. IR spectra were recorded with a Bruker ALPHA-T FT-IR spectrometer in KBr pellets. HR-ESI-MS was measured on a Bruker microTOF II instrument; external or internal calibration was done with electrospray calibrant solution (Fluka). All starting materials were obtained from commercial sources and used without purification.

2. Synthesis and Characterization Products

Synthesis of (3a-n):

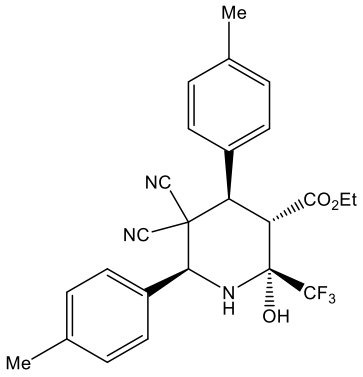
A mixture of arylidenemalononitriles or arylidenecyanoacetates **1** (3 mmol), aldehyde **2** (3 mmol), ethyl 4,4,4-trifluoro-3-oxobutanoate (3 mmol) and ammonium acetate (6 mmol) was refluxed in methanol (7 ml) for 2 h. After the reaction completion, the mixture was maintained at –10 °C for 30 min for the complete precipitation of the product. The precipitate was collected by filtration and dried to give piperidine **3**.

Ethyl (2*R,3*S**,4*R**,6*S**)-5,5-dicyano-2-hydroxy-4,6-diphenyl-2-(trifluoromethyl)-piperidine-3-carboxylate (3a)**



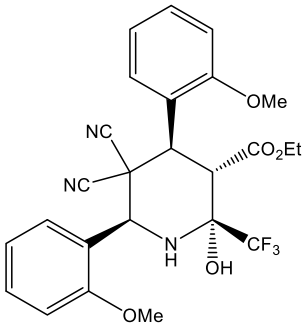
Yield 0.85 g (64%) white solid; M. p 175-177°C; ^{1}H-NMR ($CDCl_3$, 300.13 MHz): 0.86 (t, *J* = 7.1, Hz, 3H, CH_3), 2.90 (s, NH), 3.76 (d, *J* = 12.6 Hz, H, CH), 3.85 (d, *J* = 12.6 Hz, H, CH), 3.88-3.99 (m, 2H, CH_2), 4.89 (s, CH), 5.44 (s, OH), 7.41-7.60 (m, 8H, Ar), 7.67-7.74 (m, 2H, Ar) ppm; ^{13}C-NMR (DMSO-d_6, 75.47 MHz): 13.7, 45.8, 46.7, 48.7, 58.7, 61.1, 83.2 (q, J^2 = 29.5 Hz, C(CF_3)), 112.9, 113.4, 124.0 (q, J^1 = 287.8 Hz, CF_3), 128.8 (2C), 128.9 (2C), 129.4 (4C), 129.7, 130.3, 134.6, 135.9, 167.4 ppm; ^{19}F-NMR (DMSO-d_6, 282.4 MHz): -80.75 (s, 3F) ppm; IR (KBr): 3390, 3319, 2983, 1705, 1189 cm^{-1}; HRMS (ESI) m/z $(M + H)^+$ calcd for $C_{23}H_{20}F_3N_3O_3^+$: 444.1530; found: 444.1520

Ethyl (2*R,3*S**,4*R**,6*S**)-5,5-dicyano-2-hydroxy-4,6-bis(4-methylphenyl)-2-(trifluoromethyl)piperidine-3-carboxylate (3b)**



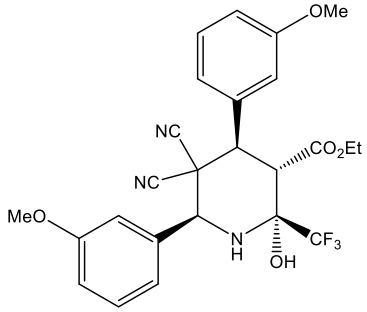
Yield 0.8 g (57%) white solid; M. p 92-95°C; ^{1}H-NMR ($CDCl_3$, 300.13 MHz): 0.89 (t, *J* = 7.1, Hz, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 2.85 (s, NH), 3.72 (d, *J* = 12.6 Hz, H, CH), 3.80 (d, *J* = 12.6 Hz, H, CH), 3.94 (q, *J* = 7,1 Hz, 2H, CH_2), 4.83 (s, CH), 5.45 (s, OH), 7.19-7.32 (m, 4H, Ar), 7.42 (d, *J* = 8 Hz, 2H, Ar), 7.57 (d, *J* = 8 Hz, 2H, Ar) ppm; ^{13}C-NMR($CDCl_3$, 75.47 MHz): 13.2, 21.2, 21.3, 44.4, 48.1, 48.3, 59.6, 62.6, 82.6 (q, J^2 = 30.4 Hz, C(CF_3)), 111.6, 112.7, 123.2 (q, J^1 = 286.7 Hz, CF_3), 128.2 (2C), 129.0, 129.3 (2C), 129.6 (2C), 129.7 (2C), 131.5, 140.0, 140.6, 172.1 ppm; ^{19}F-NMR ($CDCl_3$, 282.4 MHz): -83.91 (s, 3F) ppm; IR (KBr): 3435, 3326, 2984, 1714, 1198, 1185 cm^{-1}; HRMS (ESI) m/z $(M + H)^+$ calcd for $C_{25}H_{24}F_3N_3O_3^+$: 472.1843; found: 472.1847

Ethyl (2*R,3*S**,4*R**,6*S**)-5,5-dicyano-2-hydroxy-4,6-bis(2-methoxyphenyl)-2-(trifluoromethyl)piperidine-3-carboxylate (3c)**



Yield 0.98 g (65%) white solid; M. p 176-179°C; ^{1}H-NMR ($CDCl_3$, 300.13 MHz): 0.89 (t, *J* = 7.1 Hz, 3H, CH_3), 2.65 (s, NH), 3.71 (d, *J* = 12.8 Hz, H, CH), 3.89-3.98 (m, 2H, CH_2), 3.91 (s, 3H, CH_3), 3.92 (s, 3H, CH_3), 4.84 (d, *J* = 12.8 Hz, H, CH), 5.48 (s, CH), 5.61 (s, OH), 6.92-7.13 (m, 4H, Ar), 7.34-7.46 (m, 2H, Ar), 7.67 (dd, *J* = 7.7, 1.1, Hz, 1H, Ar), 7.85 (dd, *J* = 7.7, 1.1, Hz, 1H, Ar) ppm; ^{13}C-NMR($CDCl_3$, 75.47 MHz): 13.2, 38.5, 44.2, 46.6, 51.1, 55.5, 56.0, 62.4, 82.8 (q, J^2 = 30.1 Hz, C(CF_3)), 110.9, 111.4, 112.2, 112.3, 120.6, 120.7, 121.1, 123.3, 123.3 (q, J^1 = 286.4 Hz, CF_3), 128.2, 128.8, 130.8, 131.0, 157.2, 157.7, 172.2 ppm; ^{19}F-NMR (DMSO-d_6, 282.4 MHz): -80.94 (s, 3F) ppm; IR (KBr): 3399, 3308, 2983, 2257, 1700, 1600, 1252, 1203 cm^{-1}; HRMS (ESI) m/z $(M + H)^+$ calcd for $C_{25}H_{24}F_3N_3O_5^+$: 504.1741; found: 504.1733

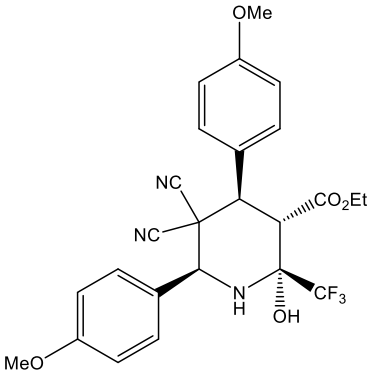
Ethyl (2*R,3*S**,4*R**,6*S**)-5,5-dicyano-2-hydroxy-4,6-bis(3-methoxyphenyl)-2-(trifluoromethyl)piperidine-3-carboxylate (3d)**



Yield 1.07 g (71%) white solid; M. p 164-167 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): 0.84 (t, J = 7.1 Hz, 3H, CH_3), 3.49 (d, J = 12.5 Hz, 1H,), 3.76 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 3.80 - 3.86 (m, 2H, CH_2), 3.87 (s, 1H, NH), 4.32 (d, J = 12.5 Hz, 1H), 4.97 (s, 1H), 7.07 – 6.96 (m, 4H, Ar), 7.10 (s, 1H, OH), 7.16 - 7.23 (m, 2H, Ar), 7.33 - 7.44 (m, 2H, Ar) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz): 13.3, 45.2, 46.2, 48.1, 55.1 (2C), 58.2, 60.6, 82.7 (q, J^2 = 29.4 Hz, C(CF_3)), 112.5, 112.9, 114.3 (2C), 114.8, 120.5, 123.5 (q, J^1 = 287.6 Hz, CF_3), 129.6, 129.8, 135.6, 136.9, 159.0, 159.1, 166.9 ppm; ^{19}F-NMR (DMSO-d_6, 282.4 MHz): -80.91 (s, 3F) ppm; IR (KBr): 3392, 3295, 2974, 1698, 1602, 1199cm^{-1}; HRMS (ESI) m/z (M + H)$^+$ calcd for $C_{25}H_{24}F_3N_3O_5^+$: 504.1735; found: 504.1741.

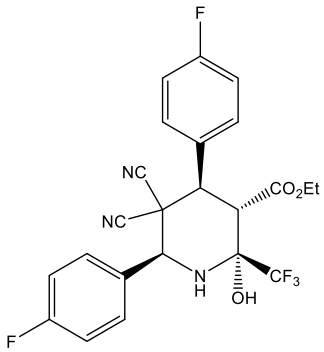
Two aromatic signals in carbon spectrum were missed due to large broadening because of restricted rotation of aryl moiety. A 13C NMR spectrum at 333K at 75 MHz was recorded to find them.

Ethyl (2*R,3*S**,4*R**,6*S**)-5,5-dicyano-2-hydroxy-4,6-bis(4-methoxyphenyl)-2-(trifluoromethyl)piperidine-3-carboxylate (3e)**



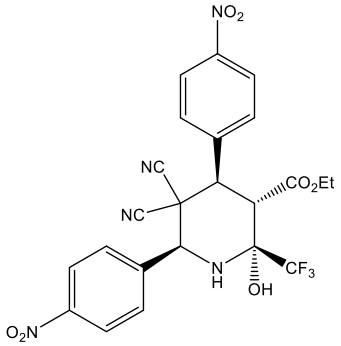
Yield 0.83 g (55%) white solid; M. p 156-158°C; ^{1}H-NMR ($CDCl_3$, 300.13 MHz): 0.92 (t, J = 7.1 Hz, 3H, CH_3), 2.83 (s, NH), 3.70 (d, J = 12.6 Hz, H, CH), 3.79 (d, J = 12.6 Hz, H, CH), 3.83 (s, 3H, CH_3), 3.85 (s, 3H, CH_3), 3.95 (q, J = 7,1 Hz, 2H, CH_2), 4.81 (s, CH), 5.44 (s, OH), 6.94 (d, J = 8.7 Hz, 2H, Ar), 6.99 (d, J = 8.7 Hz, 2H, Ar), 7.46 (d, J = 7.5 Hz, 2H, Ar), 7.61 (d, J = 8.7 Hz, 2H, Ar) ppm; ^{13}C-NMR (DMSO-d_6, 75.47 MHz): 13.8, 45.1; 46.8, 49.3, 55.6, 55.6, 58.2, 61.1, 83.1 (q, J^2 = 29.3 Hz, C(CF_3)), 113.1, 113.6, 114.3 (2C), 114.5 (2C), 124.0 (q, J^1 = 287.8 Hz, CF_3), 126.5, 127.9, 130.0 (2C), 130.5 (2C), 160.2, 160.7, 167.5 ppm; ^{19}F-NMR (DMSO-d_6, 282.4 MHz): -81.07 (s, 3F) ppm; IR (KBr): 3486, 3304, 2963, 2260, 1725, 1615, 1253, 1189 cm^{-1}; HRMS (ESI) m/z (M + H)$^+$ calcd for $C_{25}H_{24}F_3N_3O_5^+$: 504.1741; found: 504.1737

Ethyl (2*R,3*S**,4*R**,6*S**)-5,5-dicyano-4,6-bis(4-fluorophenyl)-2-hydroxy-2-(trifluoromethyl)piperidine-3-carboxylate (3f)**



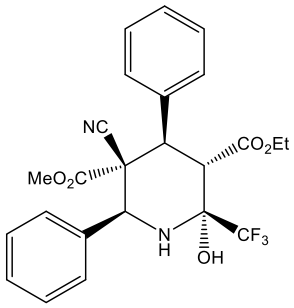
Yield 1.2 g (84%) white solid; M. p 148-151°C; ^{1}H-NMR ($CDCl_3$, 300.13 MHz): 0.93 (t, J = 7.1 Hz, 3H, CH_3), 2.86 (s, NH), 3.70 (d, J = 12.6 Hz, H, CH), 3.85 (d, J = 12.6 Hz, H, CH), 3.97 (q, J = 7,1 Hz, 2H, CH_2), 4.87 (s, CH), 5.43 (s, OH), 7.11-7.23 (m, 4H, Ar), 7.46-7.60 (m, 2H, Ar), 7.65-7.73 (m, 2H, Ar) ppm; ^{13}C-NMR ($CDCl_3$, 75.47 MHz): 13.3, 44.3, 47.8, 47.9, 59.2, 62.9, 82.5 (q, J^2 = 30.6 Hz, C(CF_3)), 111.2, 112.3, 116.2 (d, $J^2_{C\text{-}F}$ = 21.8 Hz, 2C), 116.2 (d, $J^2_{C\text{-}F}$ = 21.8 Hz, 2C), 123.0 (q, J^1 = 286.8 Hz, CF_3), 127.7 (d, $J^4_{C\text{-}F}$ = 3.1 Hz, 1C), 130.0 (d, $J^4_{C\text{-}F}$ = 3.1 Hz, 1C), 130.2 (d, $J^3_{C\text{-}F}$ = 8.4 Hz, 2C), 131.4 (d, $J^3_{C\text{-}F}$ = 8.4 Hz, 2C), 163.6 (d, $J^1_{C\text{-}F}$ = 250.5 Hz, 1C), 163.9 (d, $J^1_{C\text{-}F}$ = 250.5 Hz, 1C), 171.8 ppm; ^{19}F-NMR ($CDCl_3$, 282.4 MHz): -83.88 (s, 3F), -109.73 (s, F), -110.20 (s, F) ppm; IR (KBr): 3431, 3319, 2988, 1712, 1194, 1181 cm^{-1}; HRMS (ESI) m/z $(M + H)^+$ calcd for $C_{23}H_{18}F_5N_3O_3^+$: 480.1332; found: 480.1341

Ethyl (2*R,3*S**,4*R**,6*S**)-5,5-dicyano-2-hydroxy-4,6-bis(4-nitrophenyl)-2-(trifluoromethyl)piperidine-3-carboxylate (3g)**



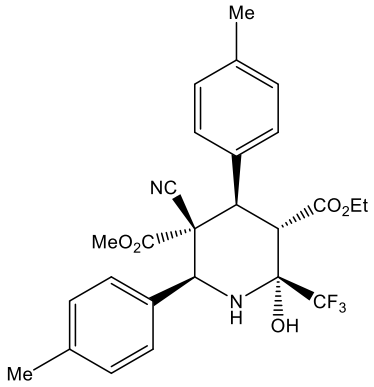
Yield 0.75 g (47%) white solid; M. p 184-187°C; ^{1}H-NMR (DMSO-d_6, 300.13 MHz): 0.86 (t, J = 7 Hz, 3H, CH_3), 3.58 (d, J = 12.6 Hz, H, CH), 3.84 (q, J = 7 Hz, 2H, CH_2), 4.37 (s, NH), 4.71 (d, J = 12.6 Hz, H, CH), 5.26 (s, CH), 7.30 (s, OH), 7.80 (d, J = 8.4 Hz, 2H, Ar), 7.89 (d, J = 8.4 Hz, 2H, Ar), 8.30-8.45 (m, 4H, Ar) ppm; ^{13}C-NMR (DMSO-d_6, 75.47 MHz): 13.8, 44.9, 46.7, 47.6, 58.1, 61.5, 83.2 (q, J^2 = 29.9 Hz, C(CF_3)), 112.2, 112.7, 123.8 (q, J^1 = 287.6Hz, CF_3), 124.1 (2C), 124.4 (2C), 130.4 (2C), 13.8 (2C), 141.6, 142.5, 148.6, 148.9, 167.0 ppm; IR (KBr): 3393, 3301, 2947, 1715, 1527, 1351, 1197 cm^{-1}; ^{19}F-NMR (DMSO-d_6, 282.4 MHz): -80.37 (s, 3F) ppm; HRMS (ESI) m/z $(M + Na)^+$ calcd for $C_{23}H_{18}F_3N_5O_7Na^+$: 556.1051; found: 556.1044

3-Ethyl 5-methyl (2*R,3*S**,4*R**,5*R**,6*S**)-5-cyano-2-hydroxy-4,6-diphenyl-2-(trifluoromethyl)piperidine-3,5-dicarboxylate (3h)**



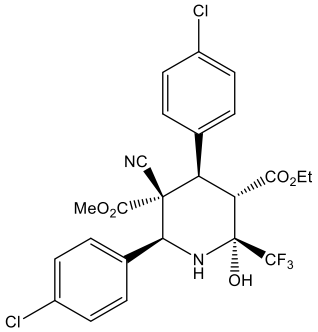
Yield 1.13 g (79%) white solid; M. p 162-163°C; ^{1}H-NMR ($CDCl_3$, 300.13 MHz): 0.82 (t, *J* = 7.1 Hz, 3H, CH_3), 2.71 (s, NH), 3.32 (s, 3H, CH_3), 3.80 (d, *J* = 12.7 Hz, H, CH), 3.89 (q, *J* = 6,7 Hz, 2H, CH_2), 4.05 (d, *J* = 12.7 Hz, H, CH), 5.01 (s, CH), 5.57 (s, OH), 7.29-7.49 (m, 8H, Ar), 7.50-7.58 (m, 2H, Ar) ppm; ^{13}C-NMR ($CDCl_3$, 75.47 MHz): 13.2, 44.7, 47.6, 53.1, 59.2, 59.6, 62.2, 82.9 (q, J^2 = 29.9 Hz, C(CF_3)), 115.1, 123.4 (q, J^1 = 286.5 Hz, CF_3), 127.9 (2C), 128.6 (2C), 128.8 (2C), 129.1, 129.4 (2C), 129.7, 133.2, 135.9, 165.8, 172.9 ppm; ^{19}F-NMR ($CDCl_3$, 282.4 MHz): -84.03 (s, 3F) ppm; IR (KBr): 3432, 3315, 2986, 1754, 1703, 1196, 1178 cm^{-1}; HRMS (ESI) m/z $(M + H)^+$ calcd for $C_{24}H_{23}F_3N_2O_5^+$: 477.1632; found: 477.1635

3-Ethyl 5-methyl (2*R,3*S**,4*R**,5*R**,6*S**)-5-cyano-2-hydroxy-4,6-bis(4-methylphenyl)-2-(trifluoromethyl)piperidine-3,5-dicarboxylate (3i)**



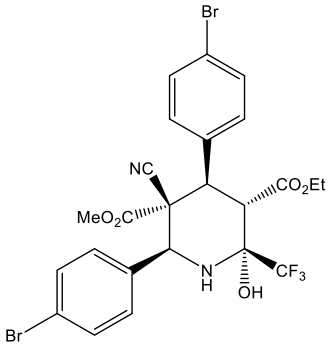
Yield 1.04 g (69%) white solid; M. p 138-141°C; ^{1}H-NMR ($CDCl_3$, 300.13 MHz): 0.85 (t, *J* = 7.1 Hz, 3H, CH_3), 2.32 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 2.66 (s, NH), 3.35 (s, 3H, CH_3), 3.77 (d, *J* = 12.7 Hz, H, CH), 3.90 (q, *J* = 7 Hz, 2H, CH_2), 4.00 (d, *J* = 12.7 Hz, H, CH), 4.96 (s, CH), 5.53 (s, OH), 7.12 (d, *J* = 7.8 Hz, 2H, Ar), 7.18 (d, *J* = 7.8 Hz, 2H, Ar), 7.27-7.35 (m, 2H, Ar), 7.42 (d, *J* = 5.9 Hz, 2H, Ar) ppm; ^{13}C-NMR ($CDCl_3$, 75.47 MHz): 13.2, 21.1, 21.2, 44.8, 47.2, 53, 58.9, 59.8, 62.1, 82.8 (q, J^2 = 30.1 Hz, C(CF_3)), 115.2, 123.4 (q, J^1 = 286.8 Hz, CF_3), 127.7 (2C), 129.2 (4C), 129.4 (2C), 130.2, 133.0, 138.9, 139.5, 165.9, 172.9 ppm; ^{19}F-NMR ($CDCl_3$, 282.4 MHz): -84. (s, 3F) ppm; IR (KBr): 3433, 3321, 2982, 2247, 1736, 1718, 1183cm^{-1}; HRMS (ESI) m/z $(M + H)^+$ calcd for $C_{26}H_{27}F_3N_2O_5^+$: 505.1945; found: 505.1953

3-Ethyl 5-methyl (2*R,3*S**,4*R**,5*R**,6*S**)-4,6-bis(4-chlorophenyl)-5-cyano-2-hydroxy-2-(trifluoromethyl)piperidine-3,5-dicarboxylate (3j)**



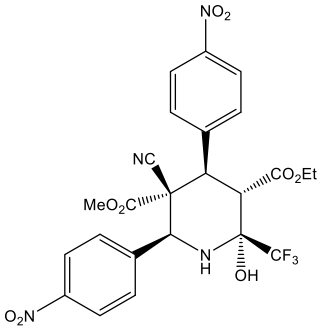
Yield 1.17 g (72%) white solid; M. p 165-168 °C; ^{1}H-NMR ($CDCl_3$, 300.13 MHz): 0.90 (t, *J* = 7.1 Hz, 3H, CH_3), 2.67 (s, NH), 3.37 (s, 3H, CH_3), 3.73 (d, *J* = 12.8 Hz, H, CH), 3.94 (q, *J* = 7,1 Hz, 2H, CH_2), 4.02 (d, *J* = 12.8 Hz, H, CH), 4.96 (s, CH), 5.50 (s, OH), 7.30-7.43 (m, 6H, Ar), 7.48 (d, *J* = 8.4 Hz, 2H, Ar) ppm; ^{13}C-NMR ($CDCl_3$, 75.47 MHz): 13.3, 44.6, 46.9, 53.4, 58.6, 59.3, 62.5, 82.8 (q, J^2 = 30.3 Hz, $C(CF_3)$), 114.6, 123.3 (q, J^1 = 286.5 Hz, CF_3), 128.9 (2C), 129.1 (2C), 129.3 (2C), 130.7 (2C), 131.5, 134.1, 135.4, 135.8, 165.6, 172.5 ppm; ^{19}F-NMR ($CDCl_3$, 282.4 MHz): -83.99 (s, 3F) ppm; IR (KBr): 3419, 3324, 2954, 1744, 1711, 1192 cm^{-1}; HRMS (ESI) m/z $(M + H)^+$ calcd (for ^{35}Cl) $C_{24}H_{21}Cl_2F_3N_2O_5^+$: 545.0852; found: 545.0845.

3-Ethyl 5-methyl (2*R,3*S**,4*R**,5*R**,6*S**)-4,6-bis(4-bromophenyl)-5-cyano-2-hydroxy-2-(trifluoromethyl)piperidine-3,5-dicarboxylate (3k)**



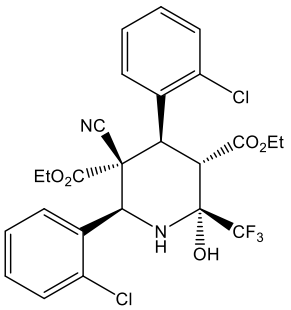
Yield 1.04 g (55%) white solid; M. p 187-190°C; ^{1}H-NMR ($CDCl_3$, 300.13 MHz): 0.91 (t, *J* = 7.1 Hz, 3H, CH_3), 2.66 (s, NH), 3.38 (s, 3H, CH_3), 3.73 (d, *J* = 12.8 Hz, H, CH), 3.94 (q, *J* = 7,1 Hz, 2H, CH_2), 4.01 (d, *J* = 12.8 Hz, H, CH), 4.95 (s, CH), 5.49 (s, OH), 7.31 (d, *J* = 8.4 Hz, 2H, Ar), 7.41 (d, *J* = 8.4 Hz, 2H, Ar), 7.49 (d, *J* = 8.5 Hz, 2H, Ar), 7.53 (d, *J* = 8.5 Hz, 2H, Ar) ppm; ^{13}C-NMR (DMSO-d_6, 75.47 MHz): 13.8, 45.2, 46.9, 54.0, 58.2, 60.4, 61.1, 83.3 (q, J^2 = 29.3 Hz, $C(CF_3)$), 115.2, 122.6, 123.0, 124.0 (q, J^1 = 288.2 Hz, CF_3), 130.3 (2C), 130.9 (2C), 132.0 (2C), 132.2 (2C), 134.5, 136.0, 165.9, 167.9 ppm; ^{19}F-NMR ($CDCl_3$, 282.4 MHz): -83.99 (s, 3F) ppm; IR (KBr): 3421, 3314, 2954, 2250, 1742, 1710, 1191 cm^{-1}; HRMS (ESI) m/z $(M + H)^+$ calcd (for ^{79}Br) $C_{24}H_{21}Br_2F_3N_2O_5^+$: 632.9842; found: 632.9841.

3-Ethyl 5-methyl (2*R,3*S**,4*R**,5*R**,6*S**)-5-cyano-2-hydroxy-4,6-bis(4-nitrophenyl)-2-(trifluoromethyl)piperidine-3,5-dicarboxylate (3l)**



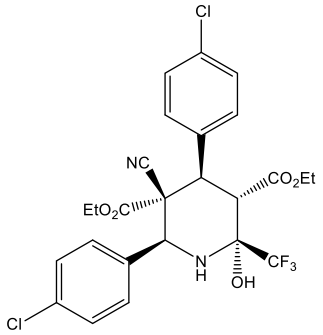
Yield 0.73 g (43%) white solid; M. p 203-206°C; ^{1}H-NMR ($CDCl_3$, 300.13 MHz): 0.92 (t, *J* = 7.1 Hz, 3H, CH_3), 2.77 (s, NH), 3.37 (s, 3H, CH_3), 3.82 (d, *J* = 12.8 Hz, H, CH), 3.87-4.04 (m, 2H, CH_2), 4.22 (d, *J* = 12.8 Hz, H, CH), 5.14 (s, CH), 5.45 (s, OH), 7.60-7.72 (m, 2H, Ar), 7.75 (d, *J* = 8.6 Hz, 2H, Ar), 8.23 (d, *J* = 8.9 Hz, 2H, Ar), 8.27 (d, *J* = 8.9 Hz, 2H, Ar) ppm; ^{13}C-NMR ($CDCl_3$, 75.47 MHz): 13.3, 44.5, 47.1, 53.7, 58.6, 58.7, 62.8, 82.7 (q, J^2 = 30.6 Hz, $C(CF_3)$), 114.0, 123.1 (q, J^1 = 287 Hz, CF_3) , 123.7 (2C), 124.0 (2C), 129.1 (2C), 130.3, 130.5, 139.8, 142.0, 148.4, 149.1, 165.2, 171.9 ppm; ^{19}F-NMR ($CDCl_3$, 282.4 MHz): -83.94 (s, 3F) ppm; IR (KBr): 3426, 3301, 2983, 1722, 1350, 1194 cm^{-1}; HRMS (ESI) m/z $(M + H)^+$ calcd for $C_{24}H_{21}F_3N_4O_9^+$: 567.1333; found: 567.1314.

3,5-Diethyl (2*R,3*S**,4*R**,5*R**,6*S**)-4,6-bis(2-chlorophenyl)-5-cyano-2-hydroxy-2-(trifluoromethyl)piperidine-3,5-dicarboxylate (3m)**



Yield 0.59 g (35%) white solid; M. p 144-147°C; ^{1}H-NMR ($CDCl_3$, 300.13 MHz): 0.79 (t, *J* = 7.1 Hz, 3H, CH_3), 0.82 (t, *J* = 7.1 Hz, 3H, CH_3), 2.60 (s, NH), 3.71 (d, *J* = 12.6 Hz, H, CH), 3.78-3.98 (m, 4H, $2CH_2$), 4.99 (d, *J* = 12.6 Hz, H, CH), 5.65 (s, CH), 5.79 (s, OH), 7.17-7.49 (m, 6H, Ar), 8.10 (dd, *J* = 7.9, 1.4, Hz, 1H, Ar), 8.17 (dd, *J* = 7.9, 1.4, Hz, 1H, Ar) ppm; ^{13}C-NMR ($CDCl_3$, 75.47 MHz): 13.2, 13.3, 41.5, 46.0, 54.7, 57.7, 62.3, 63.3, 82.8 (q, J^2 = 30.2 Hz, $C(CF_3)$), 116.2, 123.3 (q, J^1 = 286.7 Hz, CF_3), 127.3, 127.6, 129.8, 129.8, 130.0 (2C), 130.1, 130.6, 131.8, 133.3, 134.1, 135.3, 163.7, 172.0 ppm; ^{19}F-NMR ($CDCl_3$, 282.4 MHz): -83.90 (s, 3F) ppm; IR (KBr): 3438, 3319, 2987, 2258, 1748, 1711, 1193 cm^{-1}; HRMS (ESI) m/z $(M + H)^+$ (for ^{35}Cl) $C_{25}H_{23}Cl_2F_3N_2O_5^+$: 559.1009; found: 559.1004.

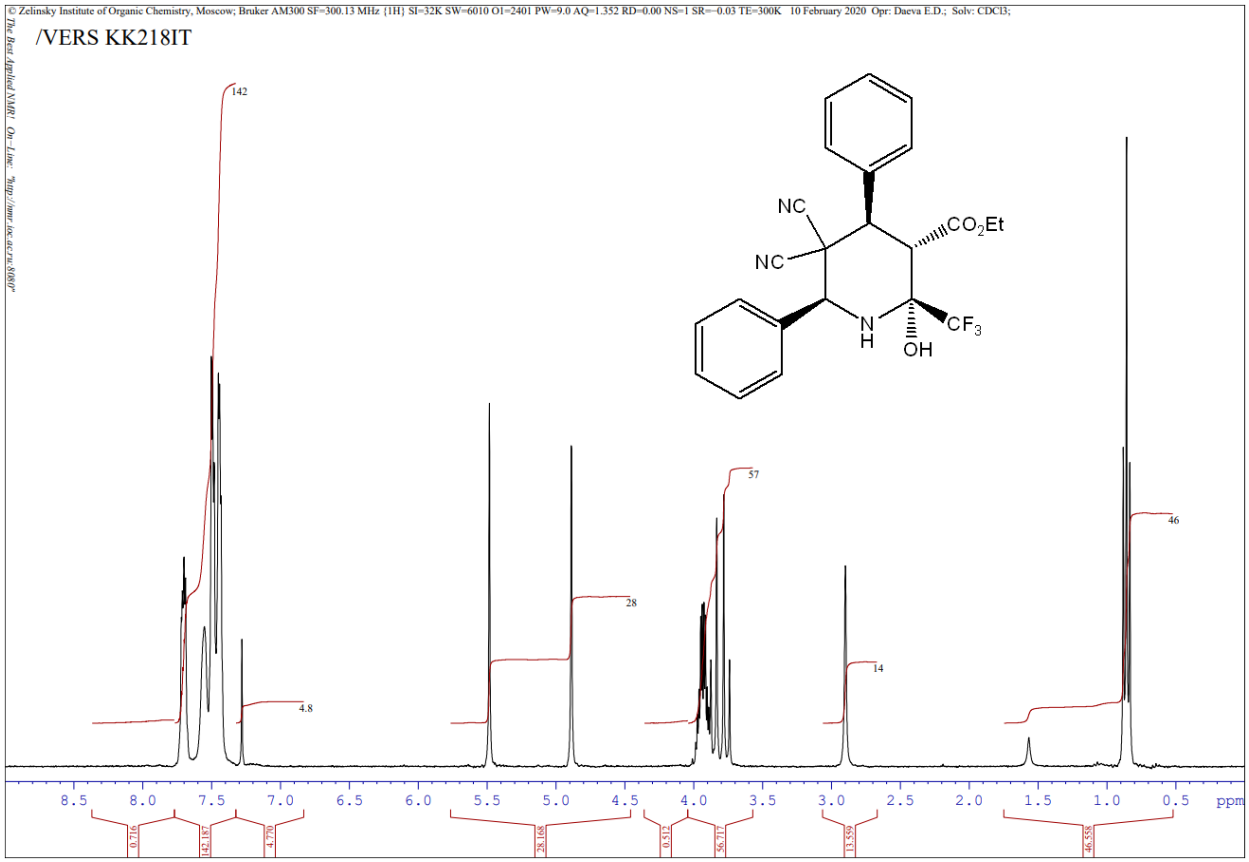
3,5-Diethyl (2*R,3*S**,4*R**,5*R**,6*S**)-4,6-bis(4-chlorophenyl)-5-cyano-2-hydroxy-2-(trifluoromethyl)piperidine-3,5-dicarboxylate (3n)**

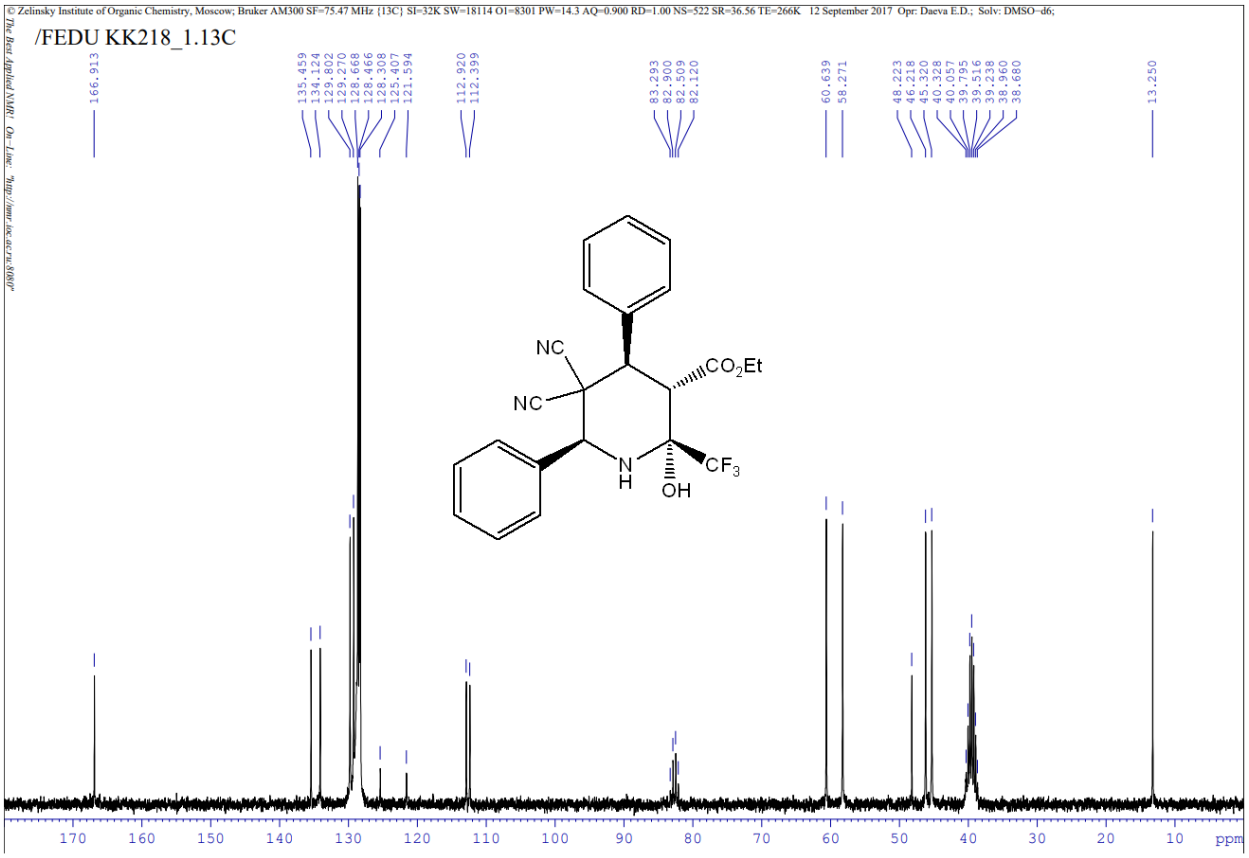


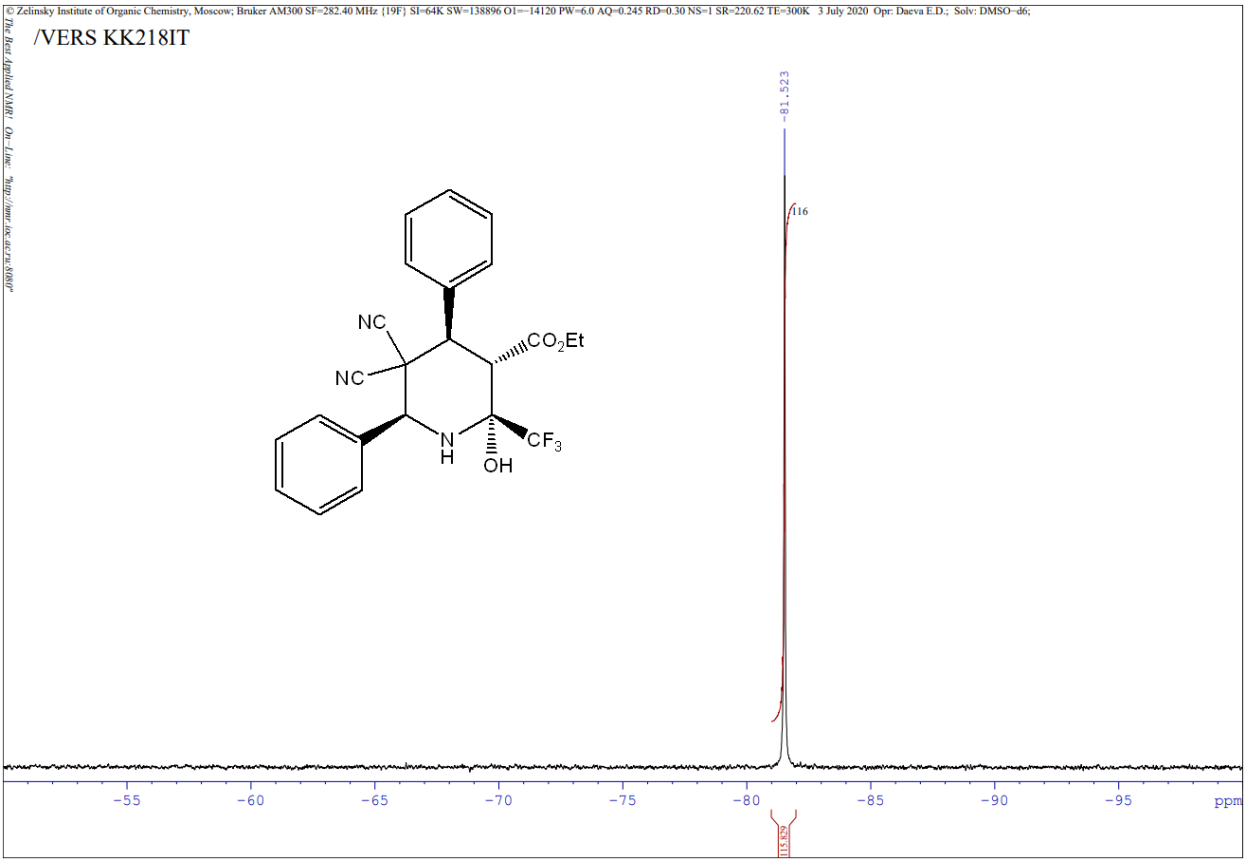
Yield 0.92 g (55%) white solid; M. p 145-148°C; ^{1}H NMR (DMSO-d_6, 400 MHz) : 0.82 (t, J = 7.1 Hz, 3H, CH_3), 0.90 (t, J = 7.1 Hz, 3H, CH_3), 2.65 (s, NH), 3.73 (d, J = 12.8 Hz, H, CH), 3.77-3.88 (m, 2H, CH_2), 3.93 (q, J = 7,1 Hz, 2H, CH_2), 4.01 (d, J = 12.8 Hz, H, CH), 4.96 (s, CH), 5.51 (s, OH), 7.29-7.45 (m, 6H, Ar), 7.50 (d, J = 8.5 Hz, 2H, Ar) ppm; ^{13}C-NMR($CDCl_3$, 75.47 MHz): 13.3, 13.5, 44.7, 46.9, 58.6, 59.1, 62.5, 63.0, 82.8 (q, J^2 = 30.3 Hz, C(CF_3)), 114.8, 123.3 (q, J^1 = 286.6 Hz, CF_3), 128.8 (2C), 129.0 (2C), 129.4 (2C), 130.8 (2C), 131.6, 134.2, 135.3, 135.7, 165.0, 172.5 ppm; ^{19}F-NMR (DMSO-d_6, 282.4 MHz): -81.19 (s, 3F) ppm; IR (KBr): 3433, 3326, 2981, 2253, 1744, 1717, 1193 cm^{-1}; HRMS (ESI) m/z $(M + H)^+$ (for^{35}Cl) $C_{25}H_{23}Cl_2F_3N_2O_5^+$: 559.1009; found: 559.1000.

3. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR Spectra

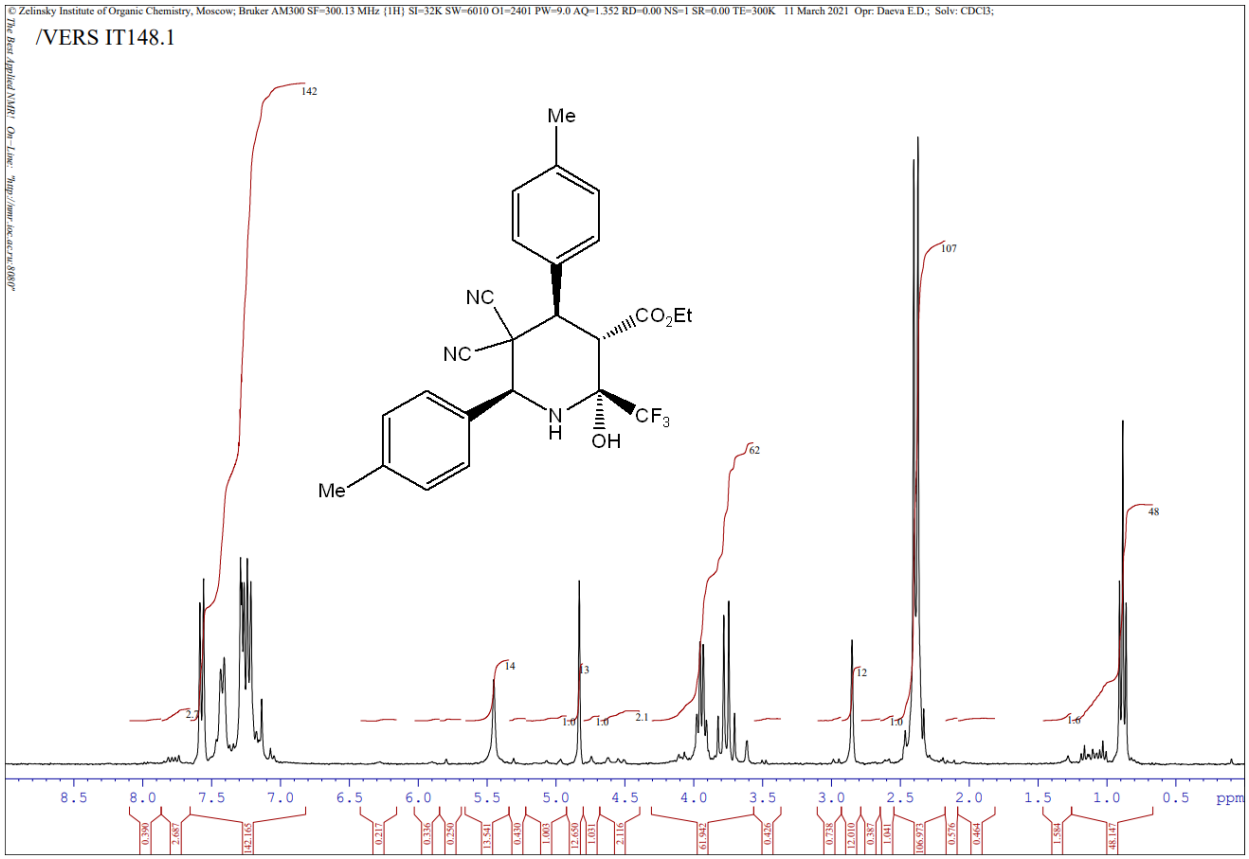
3a

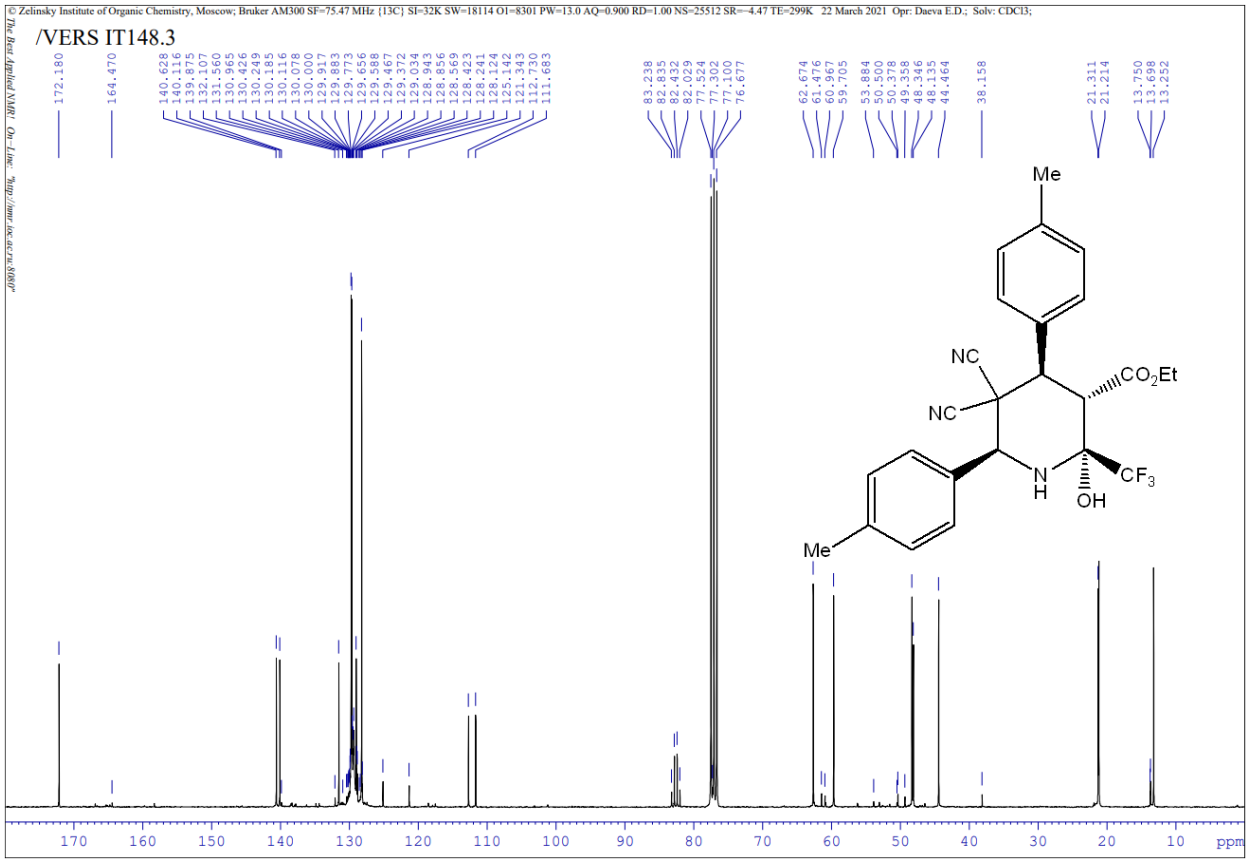


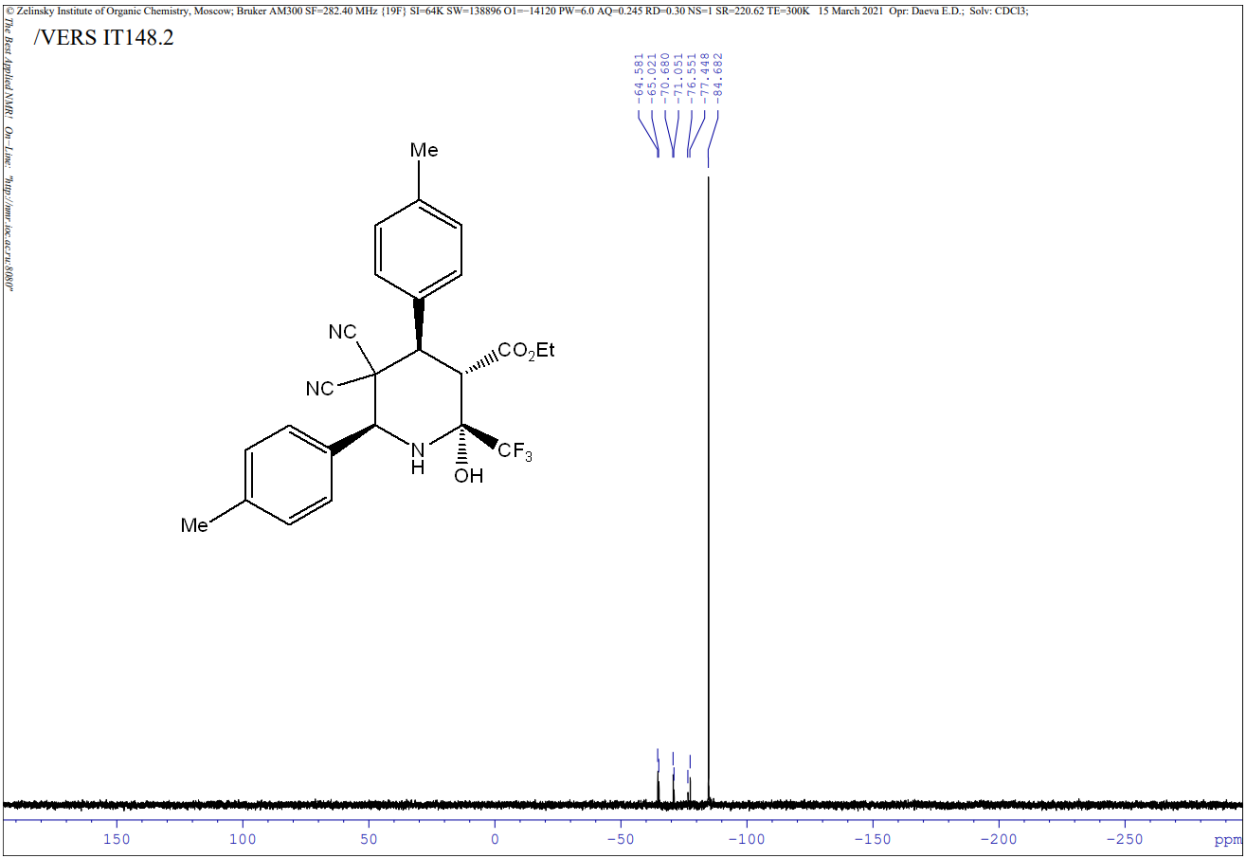



© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=−14120 PW=6.0 AQ=0.245 RD=0.30 NS=1 SR=220.62 TE=300K 3 July 2020 Opr: Daeva E.D.; Solv: DMSO−d6;
"The Best Applied NMR On Line" http://nmr.ioc.ac.ru:8080/
/VERS KK218IT
-81.523
1.16
NC
NC
CO2Et
N
H
CF3
OH
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm
116.869

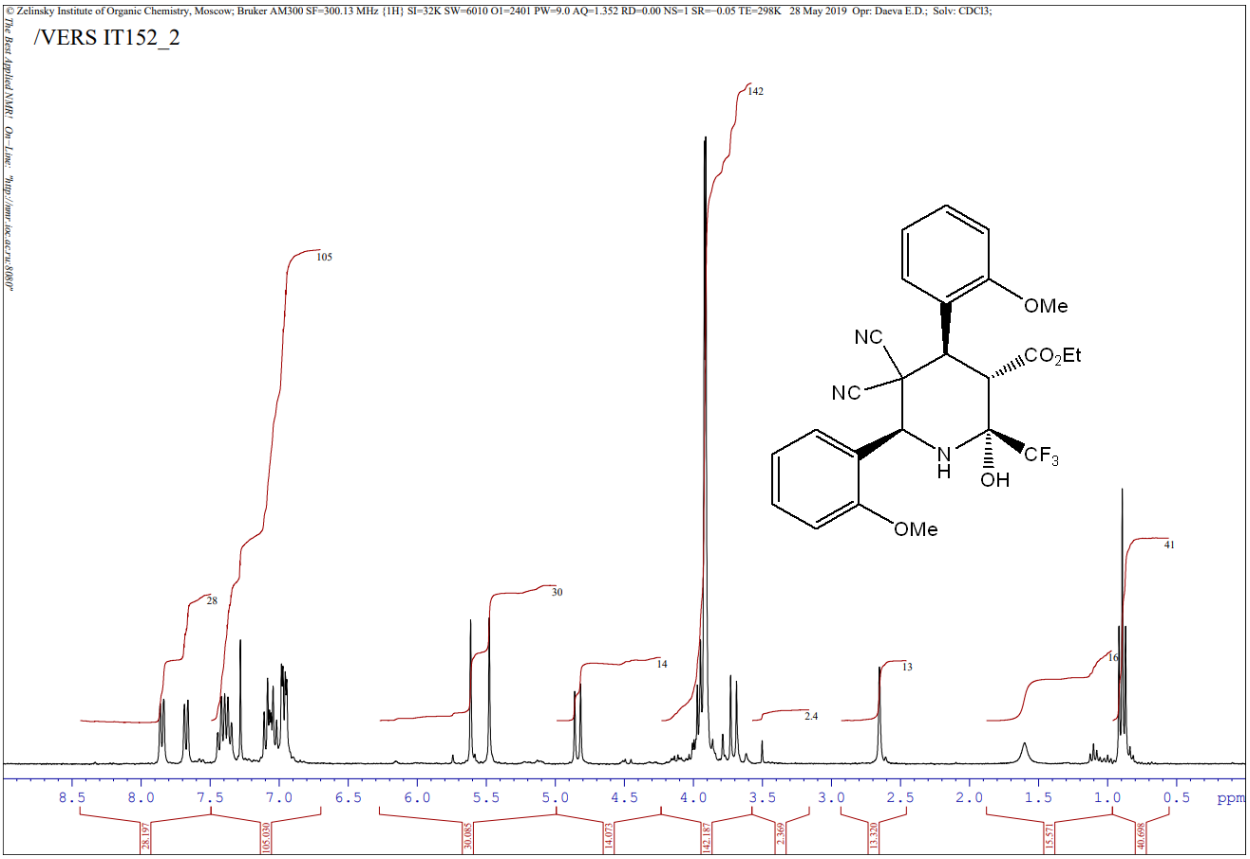
3b


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=32K SW=6010 O1=2401 PW=9.0 AQ=1.352 RD=0.00 NS=1 SR=0.00 TE=300K 11 March 2021 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT148.1
Me
NC
NC
CO2Et
N
H
CF3
OH
Me
142
107
62
48
14
13
12
2.7
1.0
1.0
2.1
1.0
1.0
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.399 2.687 142.165 0.217 0.336 0.250 13.341 0.449 1.665 12.650 1.051 2.116 61.942 0.426 0.758 12.010 0.387 1.041 106.973 0.576 0.464 1.584 48.147


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=13.0 AQ=0.900 RD=1.00 NS=25512 SR=-4.47 TE=299K 22 March 2021 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT148.3
172.180 164.470
140.628 140.116 139.875 132.107 131.560 130.965 130.426 130.249 130.185 130.116 130.078 130.000 129.917 129.893 129.753 129.656 129.588 129.467 129.372 129.034 128.943 128.856 128.569 128.423 128.241 128.124 125.142 121.343 112.730 111.683
83.238 82.835 82.432 82.029 77.524 77.302 77.100 76.677
62.674 61.476 60.967 59.705
53.884 50.500 50.378 49.358 48.346 48.135 44.464
38.158
21.311 21.214
13.750 13.698 13.252
Me
NC
NC
CO2Et
N
H
CF3
OH
Me
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=-14120 PW=6.0 AQ=0.245 RD=0.30 NS=1 SR=220.62 TE=300K 15 March 2021 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT148.2
-64.581
-65.021
-70.680
-71.051
-76.551
-77.448
-84.682
Me
NC
NC
CO2Et
N
H
CF3
OH
Me
150
100
50
0
-50
-100
-150
-200
-250
ppm

3c


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=32K SW=6010 O1=2401 PW=9.0 AQ=1.352 RD=0.00 NS=1 SR=-0.05 TE=298K 28 May 2019 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT152_2
OMe
NC
CO2Et
NC
N
H
CF3
OH
OMe
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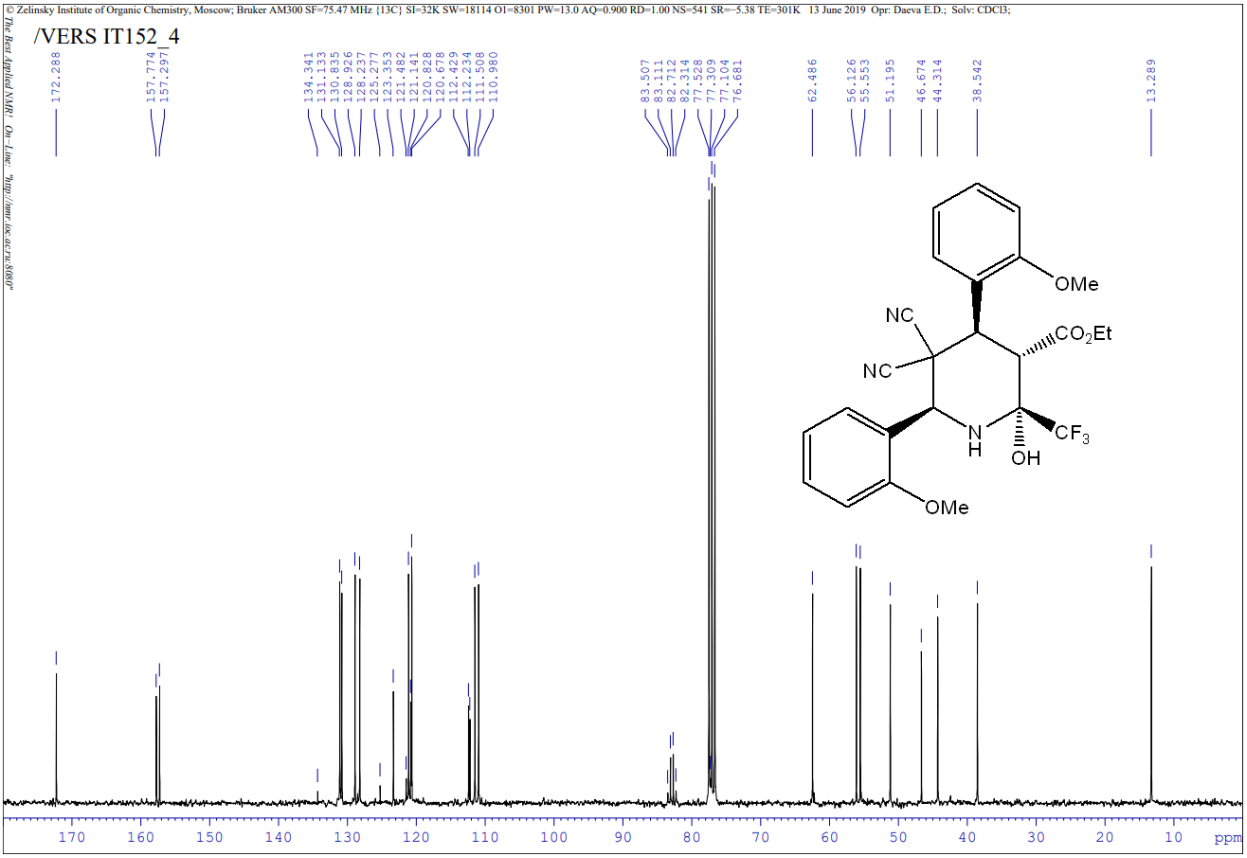
© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=13.0 AQ=0.900 RD=1.00 NS=541 SR=-5.38 TE=301K 13 June 2019 Opr: Daeva E.D.; Solv: CDCl3;
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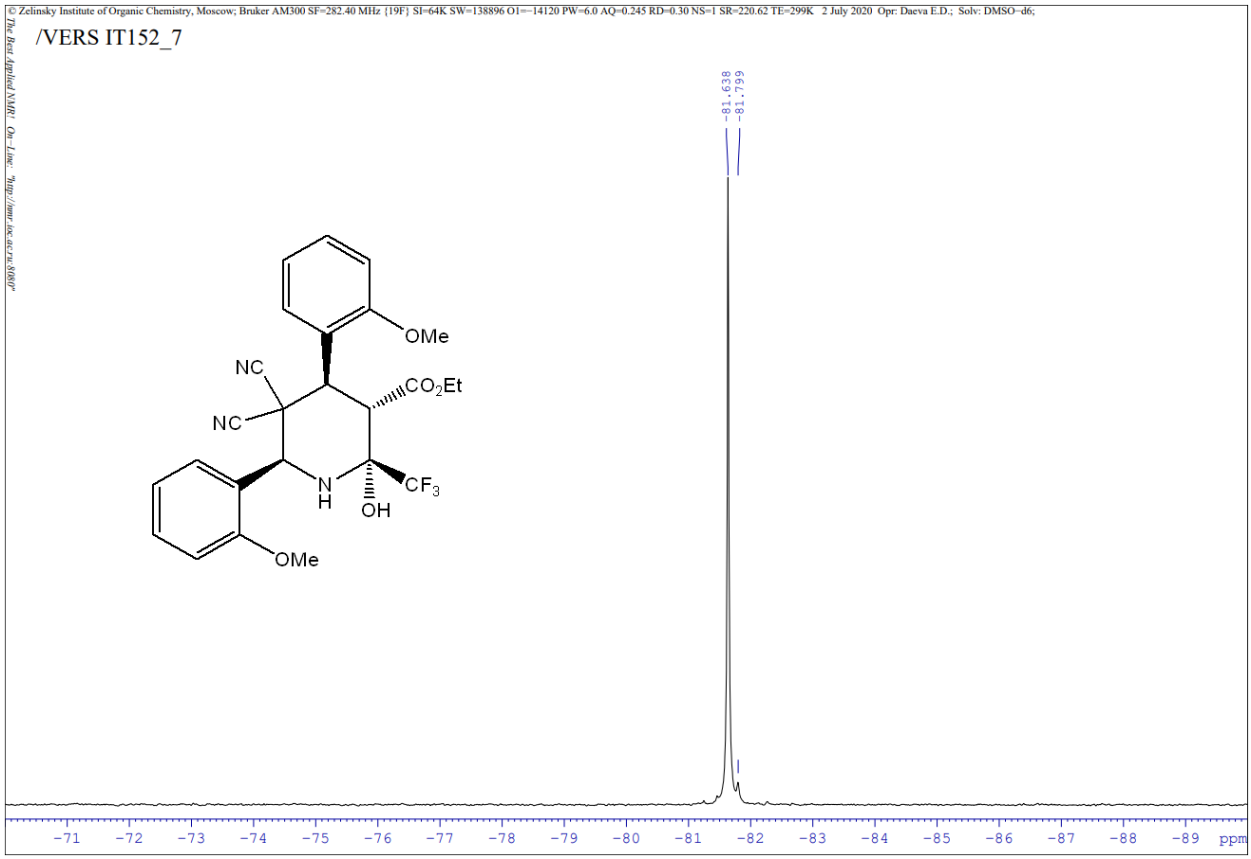
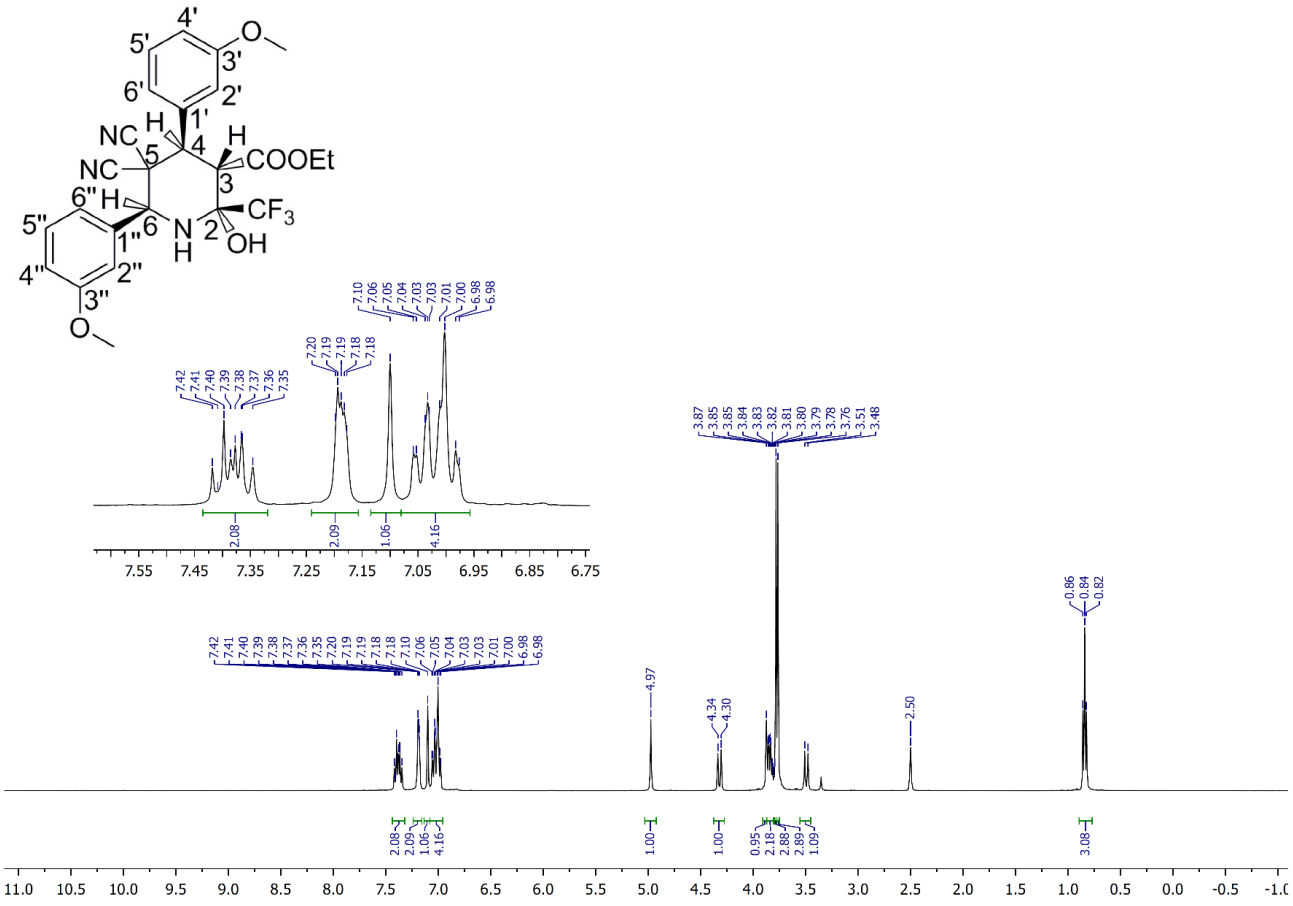
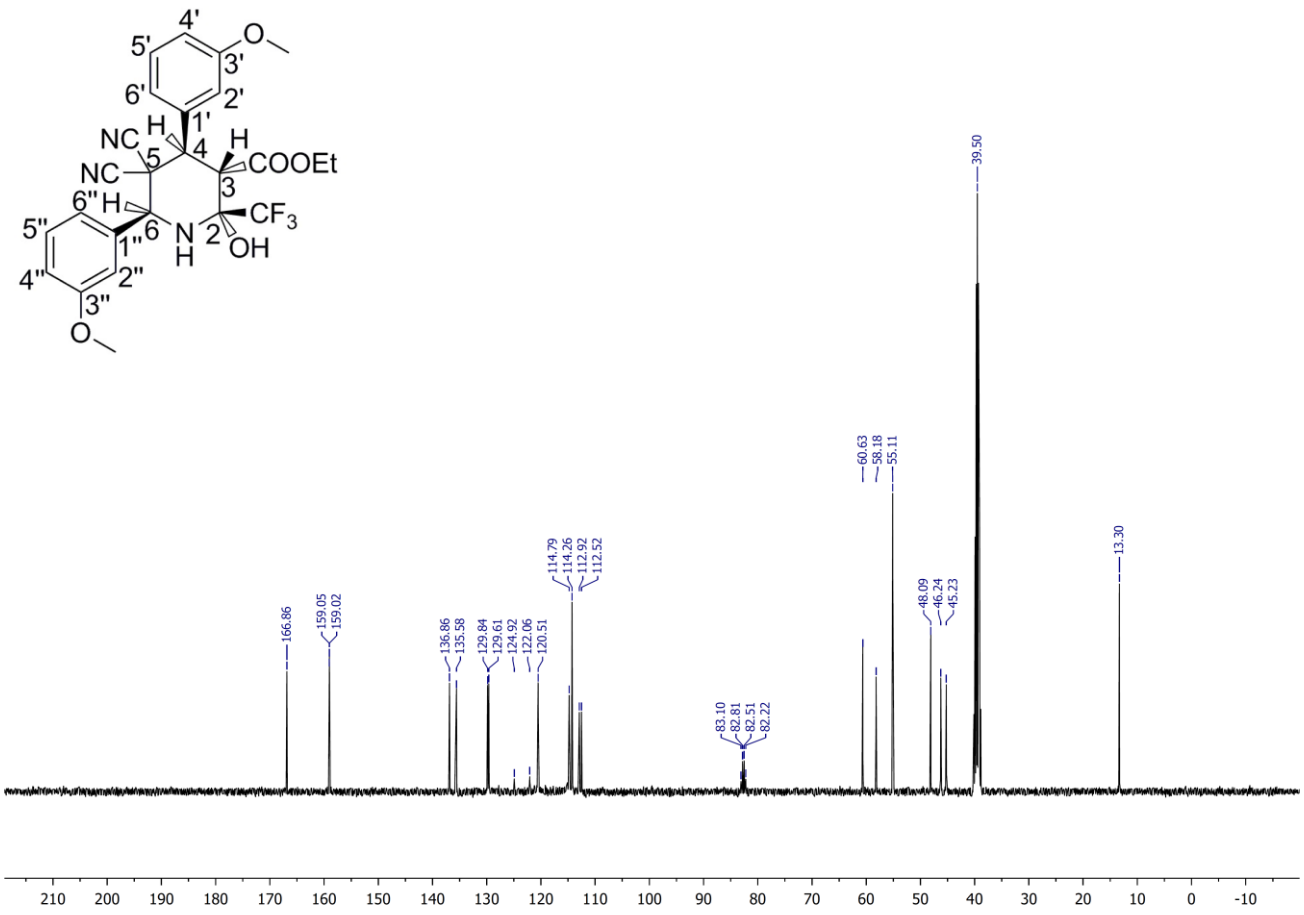
157.774
157.297
134.341
131.133
130.835
128.926
128.277
123.353
121.482
121.141
120.828
120.678
112.429
112.234
111.508
110.980
83.507
83.111
82.712
82.314
77.328
77.109
76.894
76.681
62.486
56.126
55.553
51.195
46.674
44.314
38.542
13.289
OMe
NC
CO2Et
NC
N
H
CF3
OH
OMe
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=-14120 PW=6.0 AQ=0.245 RD=0.30 NS=1 SR=220.62 TE=299K 2 July 2020 Opr: Daeva E.D.; Solv: DMSO-d6;
/VERS IT152_7
-81.638
-81.799
OMe
NC
CO2Et
NC
N
H
CF3
OH
OMe
-71 -72 -73 -74 -75 -76 -77 -78 -79 -80 -81 -82 -83 -84 -85 -86 -87 -88 -89 ppm

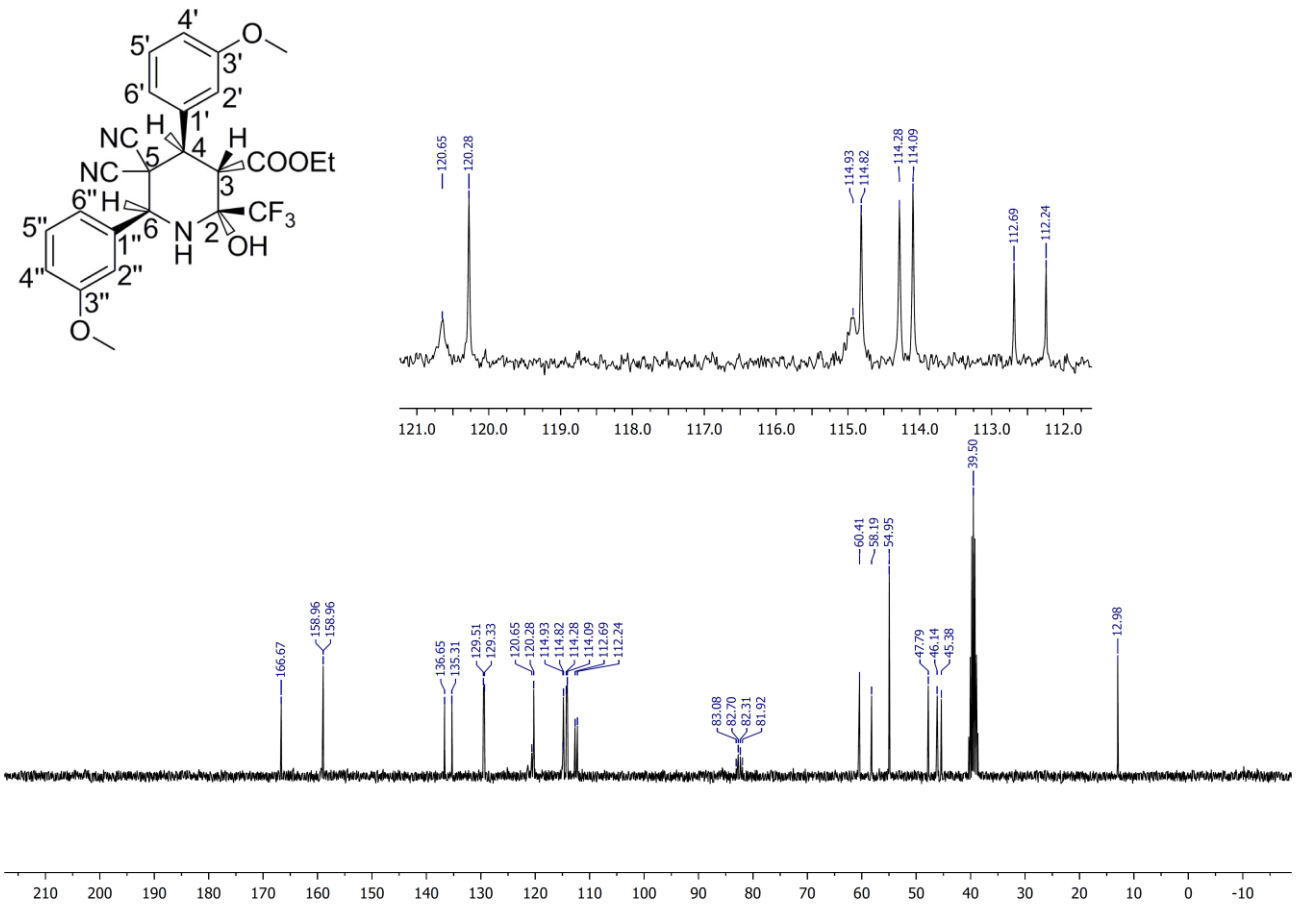
3d



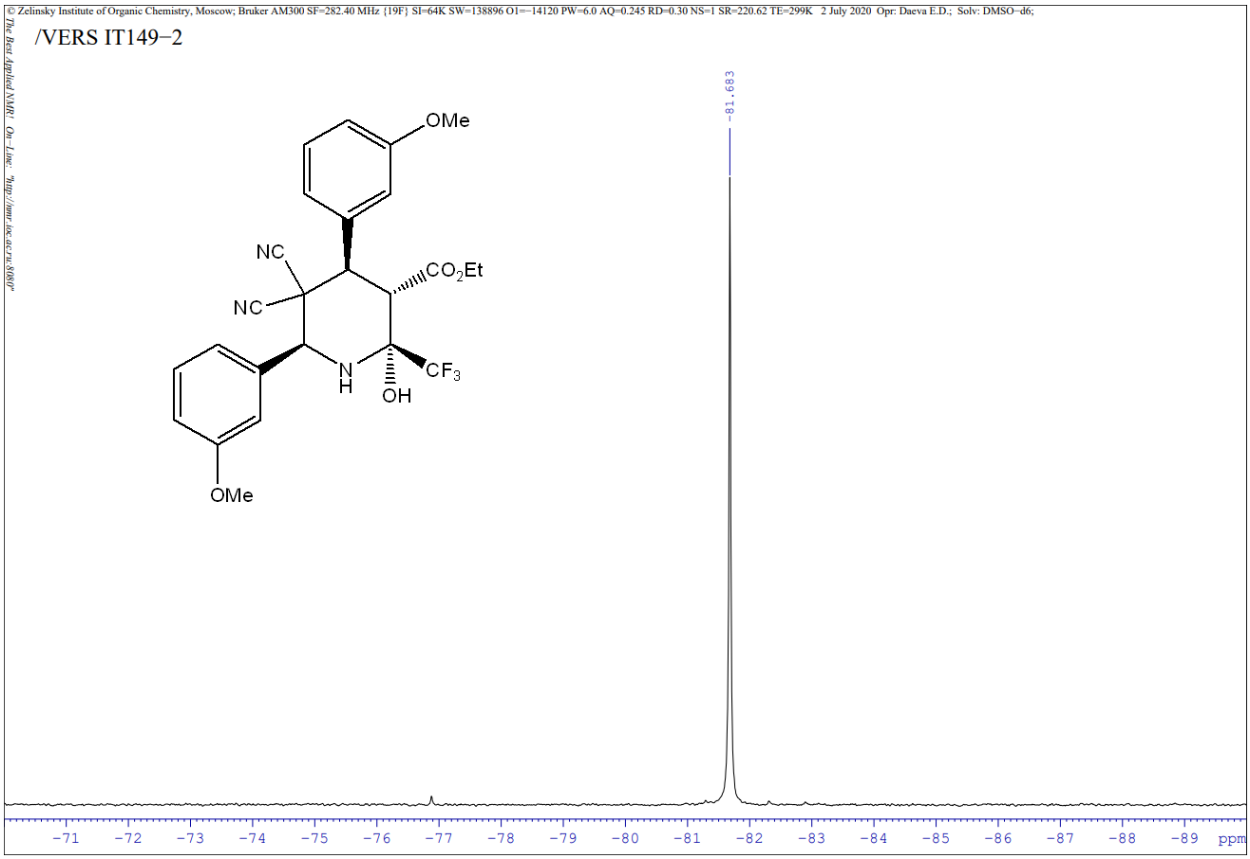
^{1}H NMR spectrum of the compound **3d**, 400MHz, DMSO-d_6, 298 K.



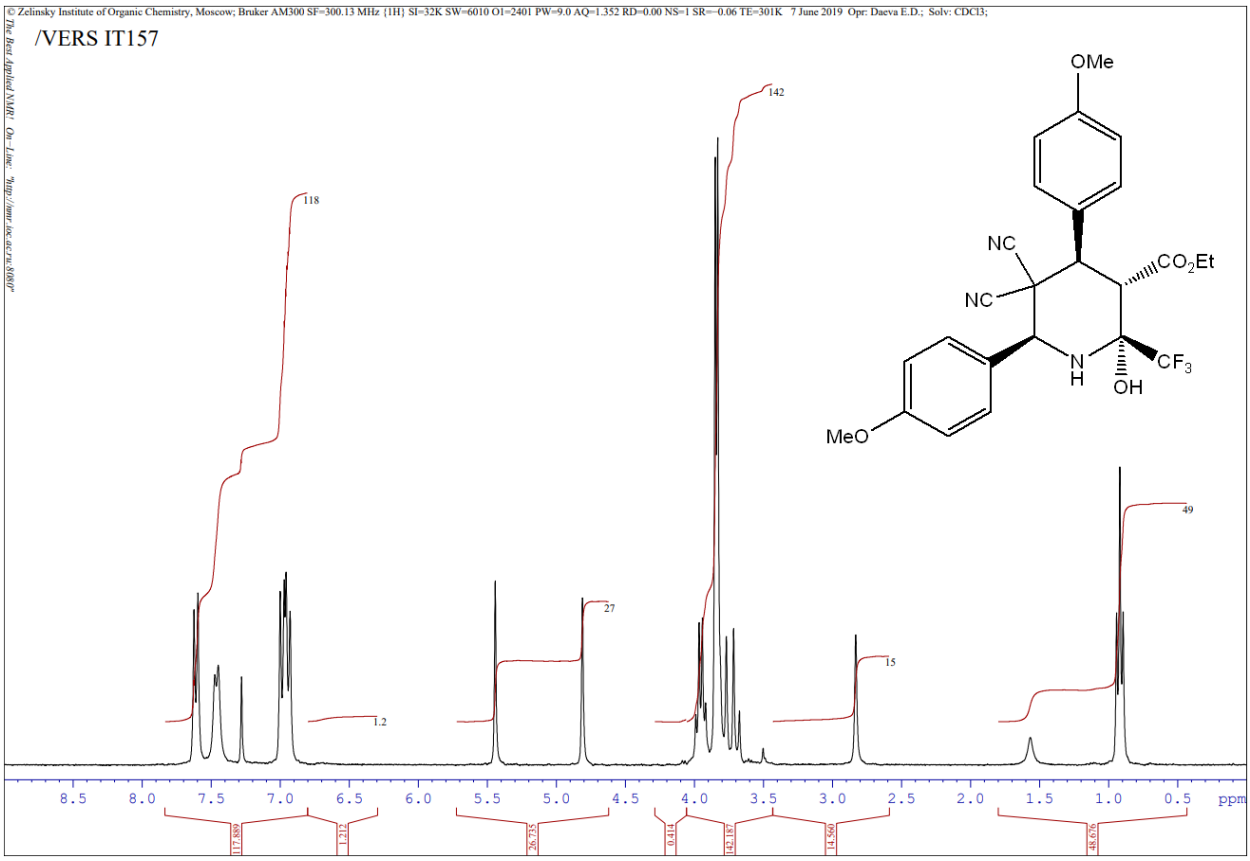
^{13}C NMR spectrum of the compound **3d**, 100 MHz, DMSO-d_6, 298 K.

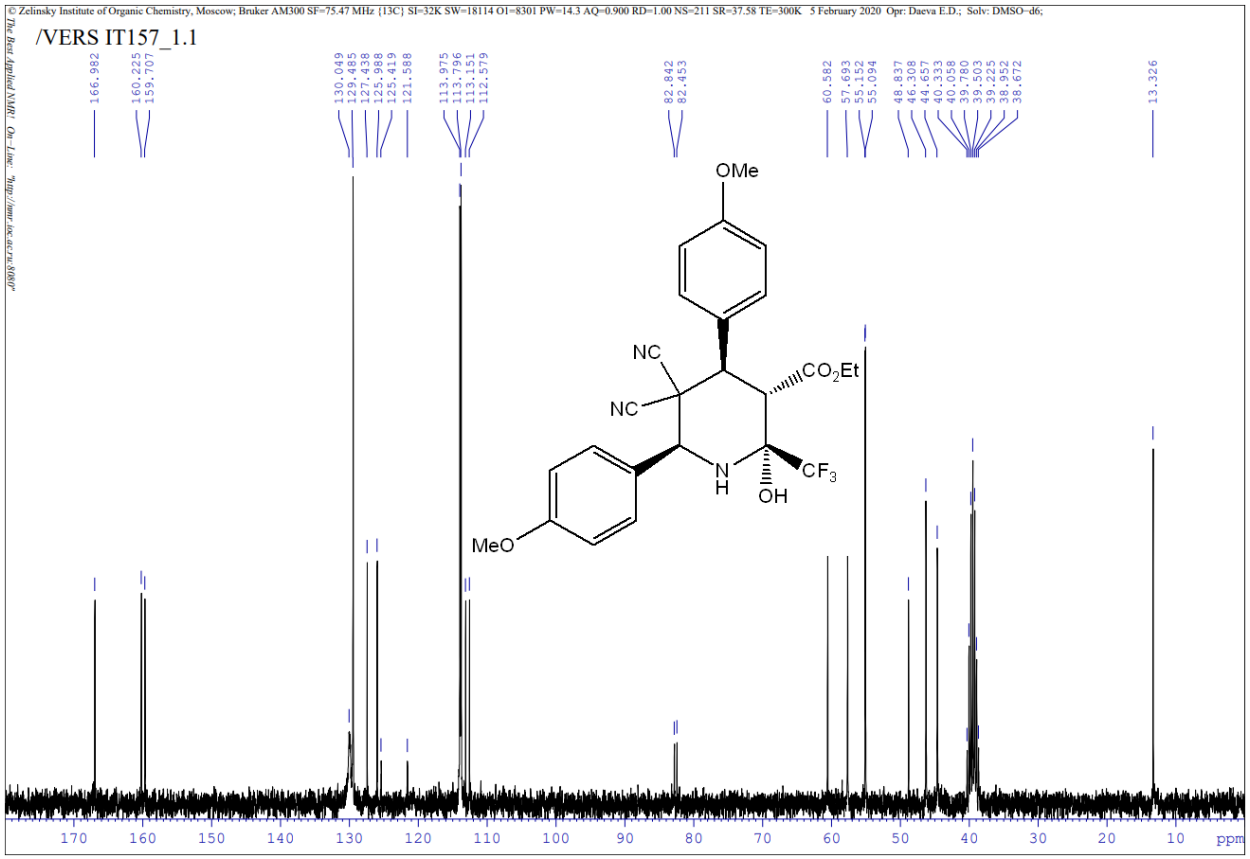


^{13}C NMR spectrum of the compound **3d**, 75 MHz, DMSO-d_6, 333 K. Two broad signals at δ 120.65 and 114.93 ppm appeared.


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=-14120 PW=6.0 AQ=0.245 RD=0.30 NS=1 SR=220.62 TE=299K 2 July 2020 Opr: Daeva E.D.; Solv: DMSO-d6;
"The Best Applied NMR On Line" "http://nmr.ioc.ac.ru:8080/"
/VERS IT149-2
OMe
NC
NC
CO2Et
N
H
CF3
OH
OMe
-81.683
-71 -72 -73 -74 -75 -76 -77 -78 -79 -80 -81 -82 -83 -84 -85 -86 -87 -88 -89 ppm

3e


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=32K SW=6010 O1=2401 PW=9.0 AQ=1.352 RD=0.00 NS=1 SR=-0.06 TE=301K 7 June 2019 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT157
OMe
NC
NC
CO2Et
CF3
N
H
OH
MeO
118
142
27
15
49
1.2
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm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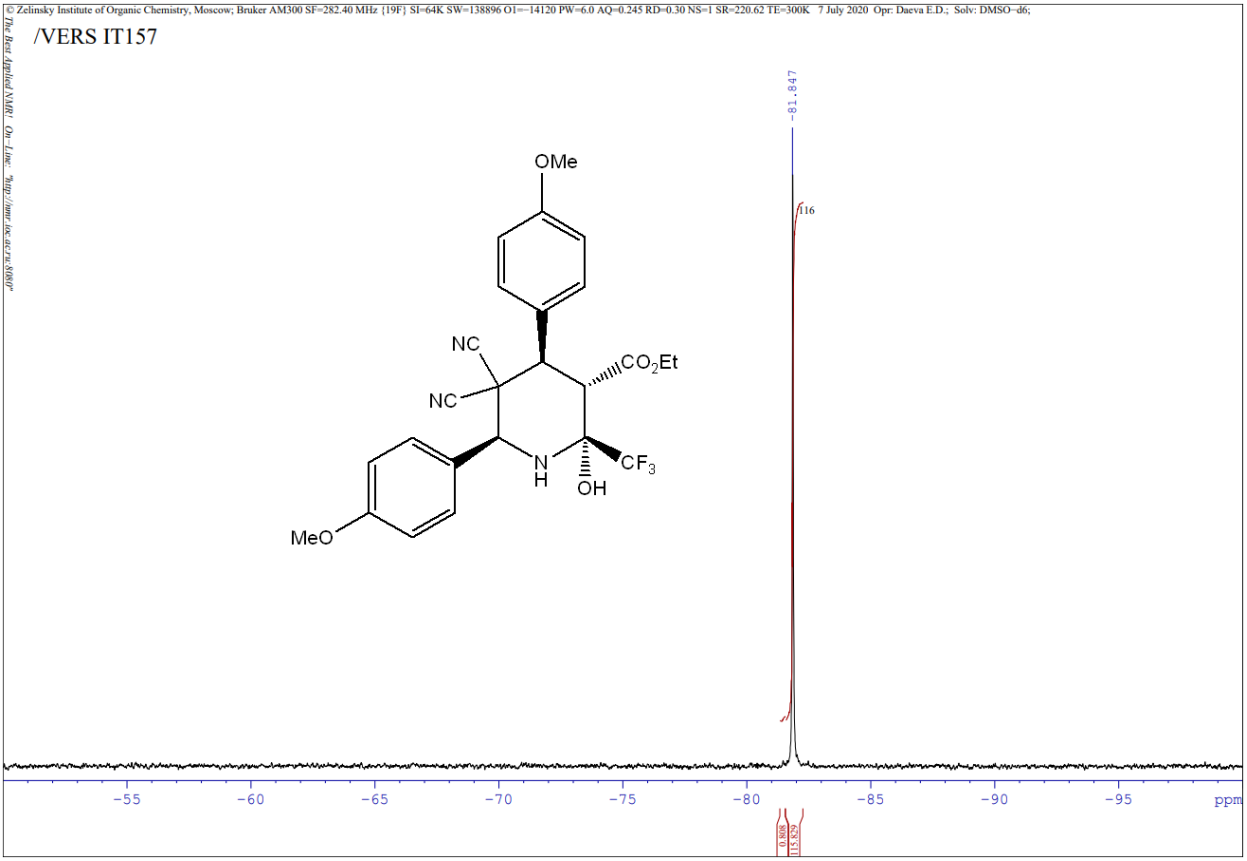
160.225
159.707
130.049
129.485
127.438
125.988
125.419
121.588
113.975
113.796
113.151
112.579
82.842
82.453
60.582
57.693
55.152
55.094
48.837
46.308
44.657
40.333
40.158
39.780
39.503
39.225
38.952
38.672
13.326
OMe
NC
NC
CO2Et
CF3
N
H
OH
MeO
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=−14120 PW=6.0 AQ=0.245 RD=0.30 NS=1 SR=220.62 TE=300K 7 July 2020 Opr: Daeva E.D.; Solv: DMSO−d6;
/VERS IT157
-81.847
1.16
OMe
NC
NC
CO2Et
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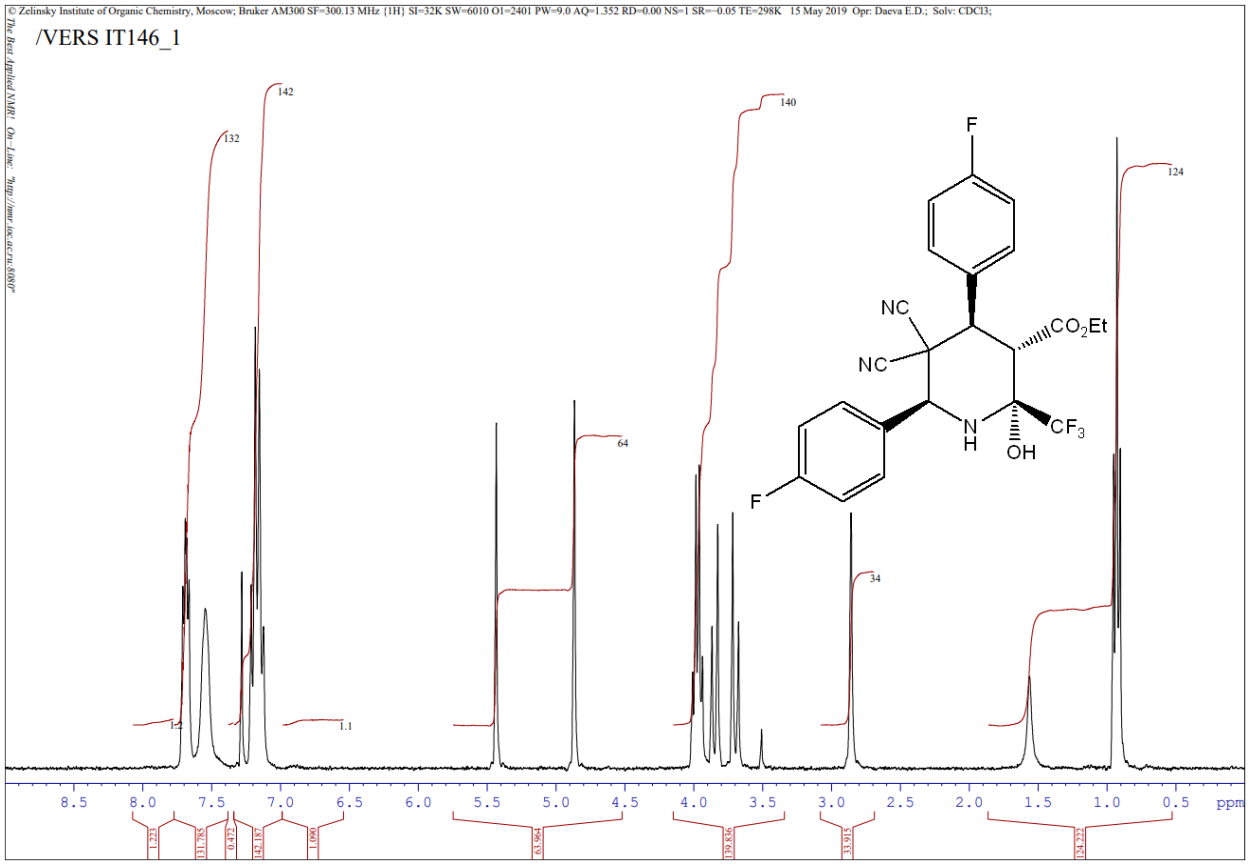
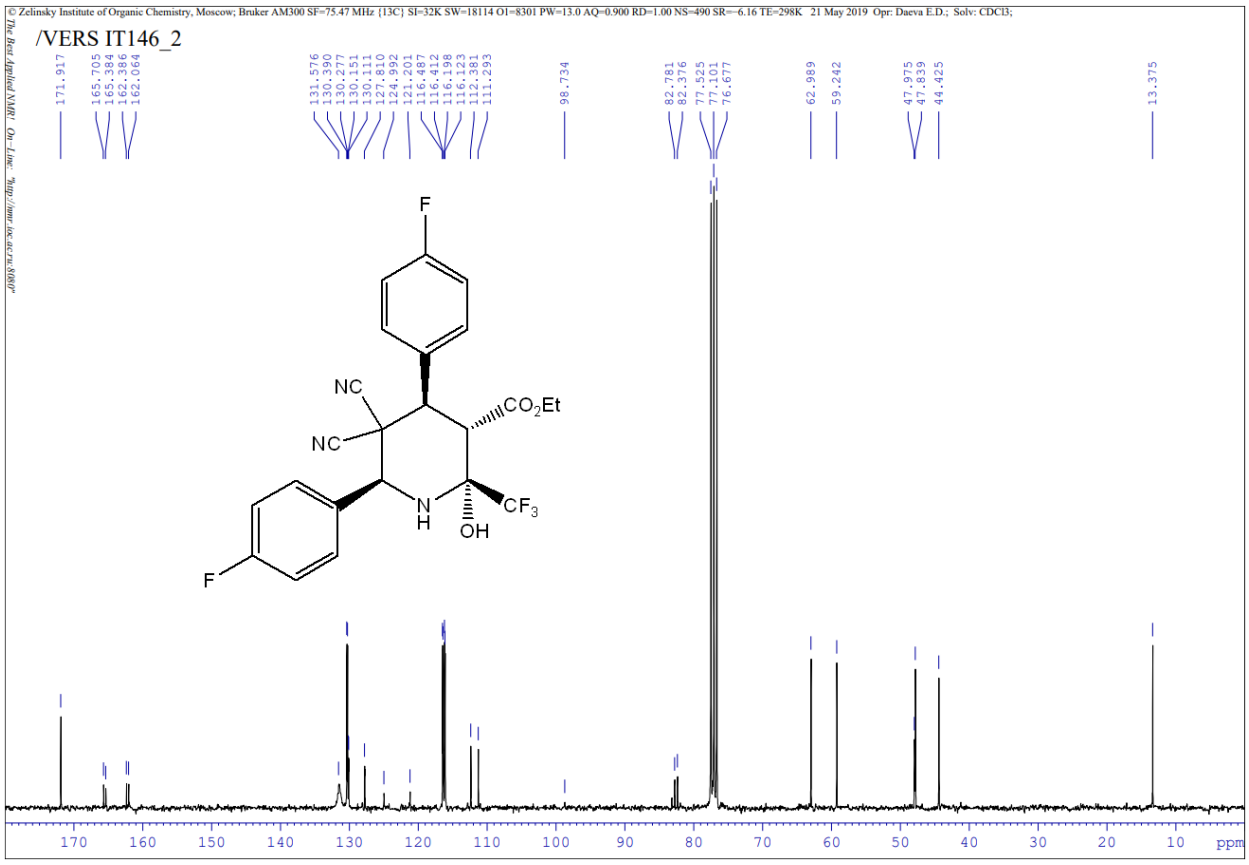
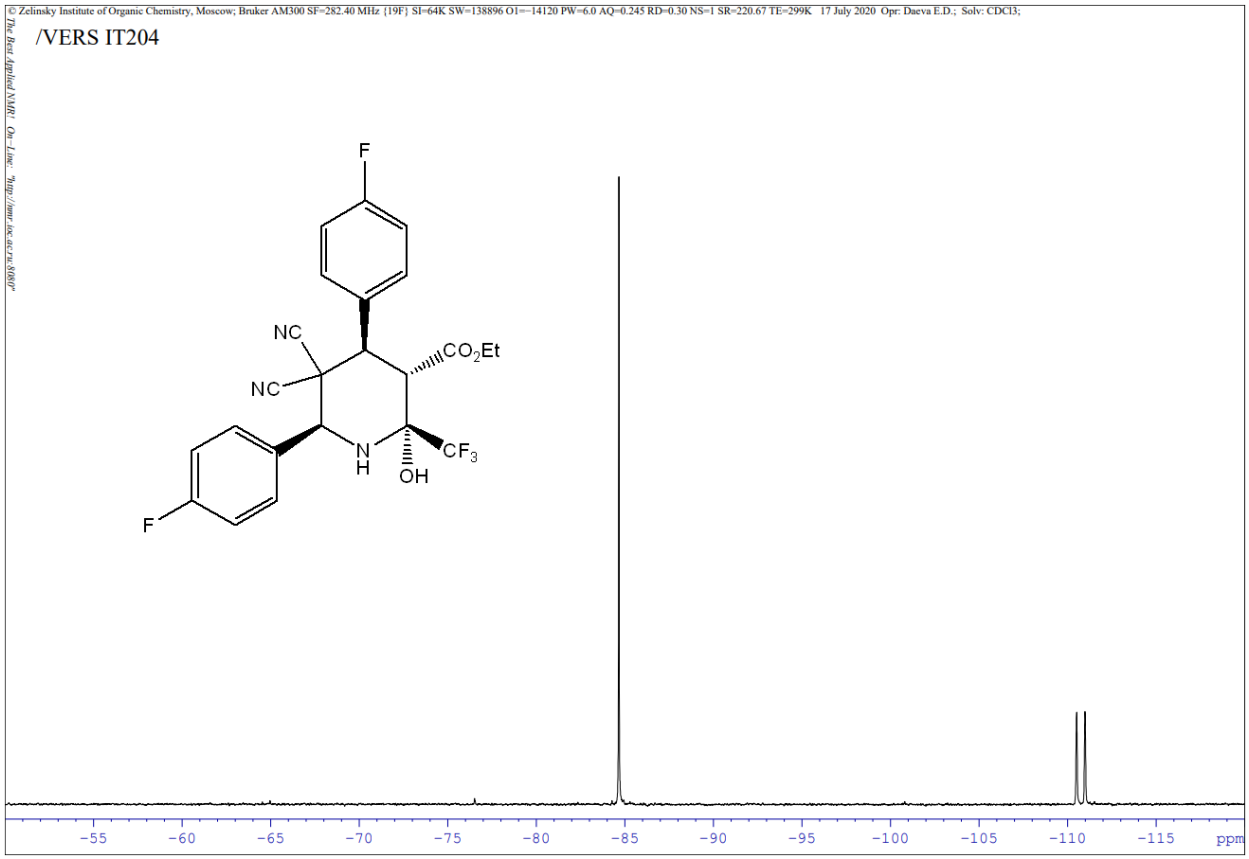
−70
−75
−80
−85
−90
−95
ppm

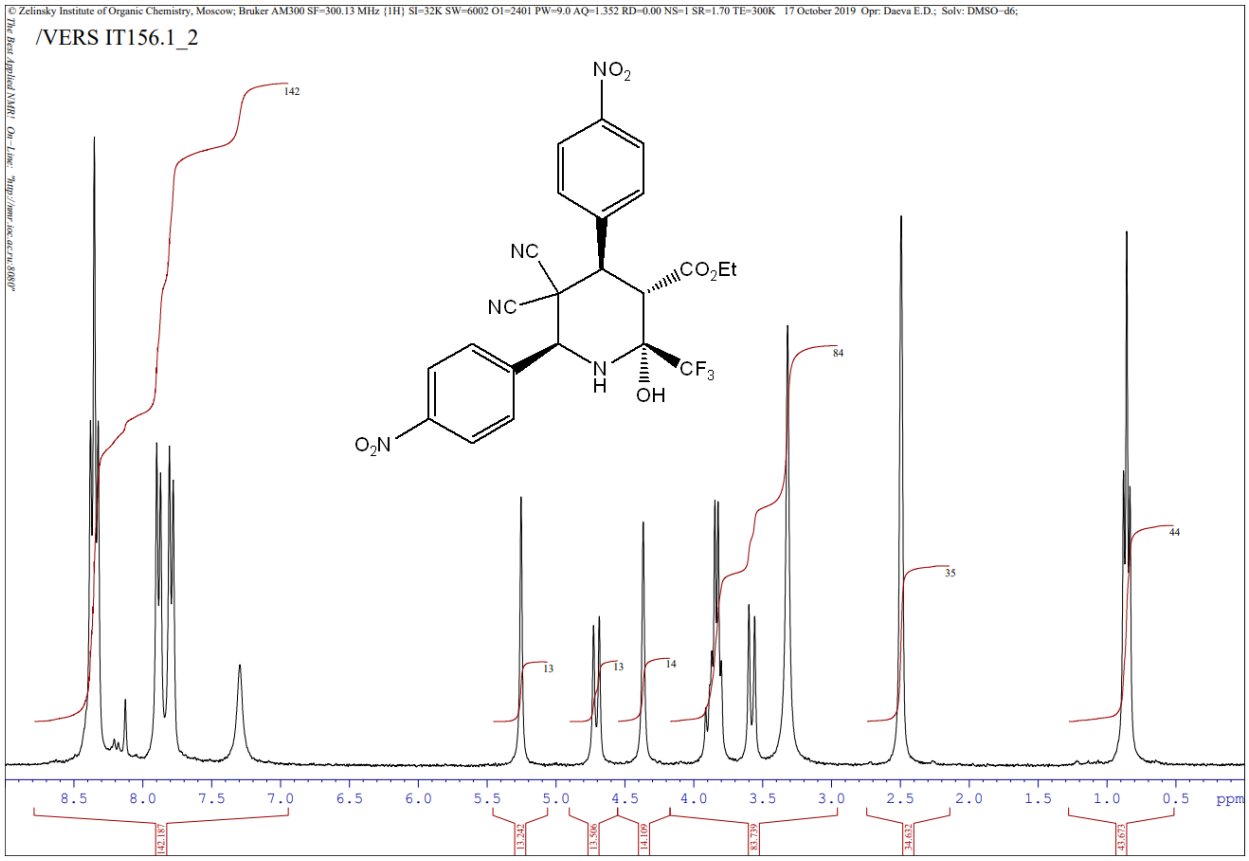
3f

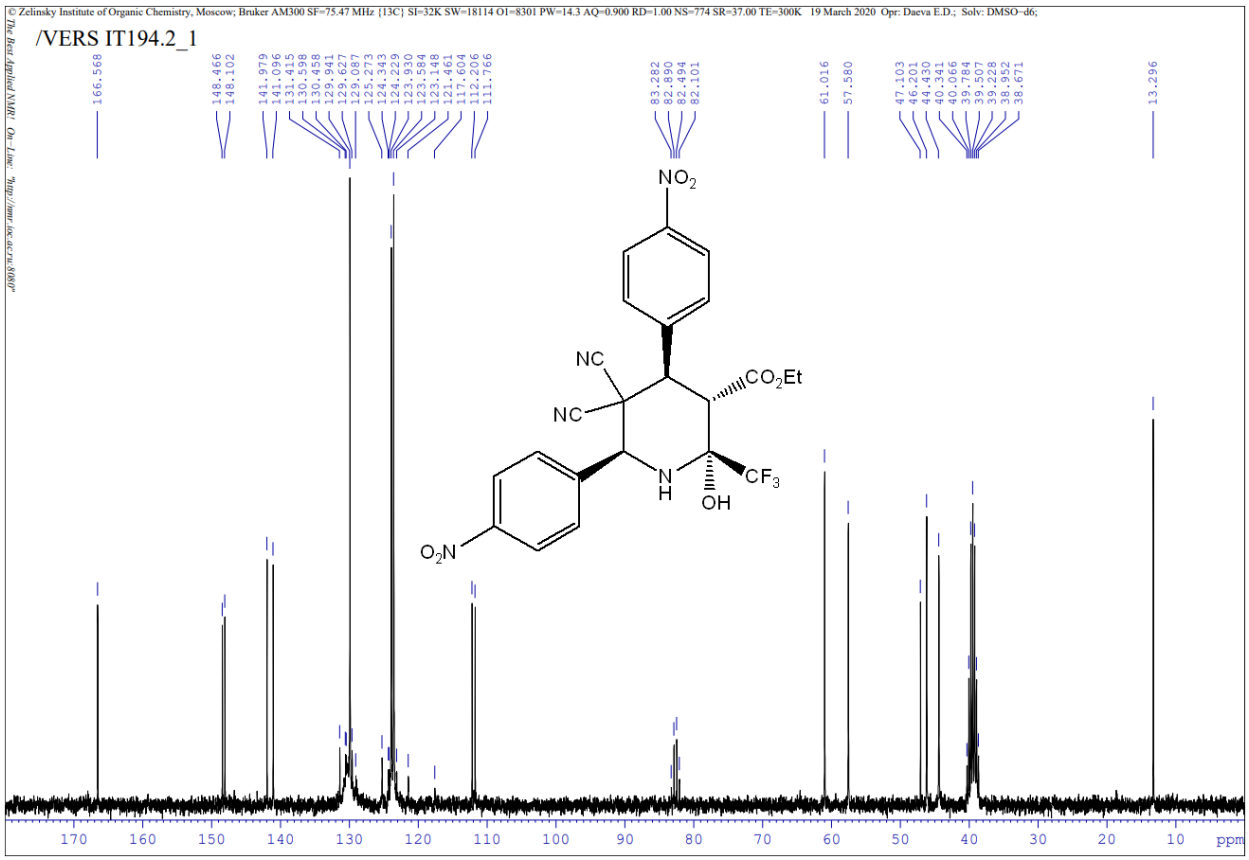

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=32K SW=6010 O1=2401 PW=9.0 AQ=1.352 RD=0.00 NS=1 SR=-0.05 TE=298K 15 May 2019 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT146_1
142
132
140
124
64
34
1.4
1.1
F
NC
NC
CO2Et
N
H
CF3
OH
F
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
7.235
131.785
0.472
142.187
1.000
63.964
139.836
33.915
134.222

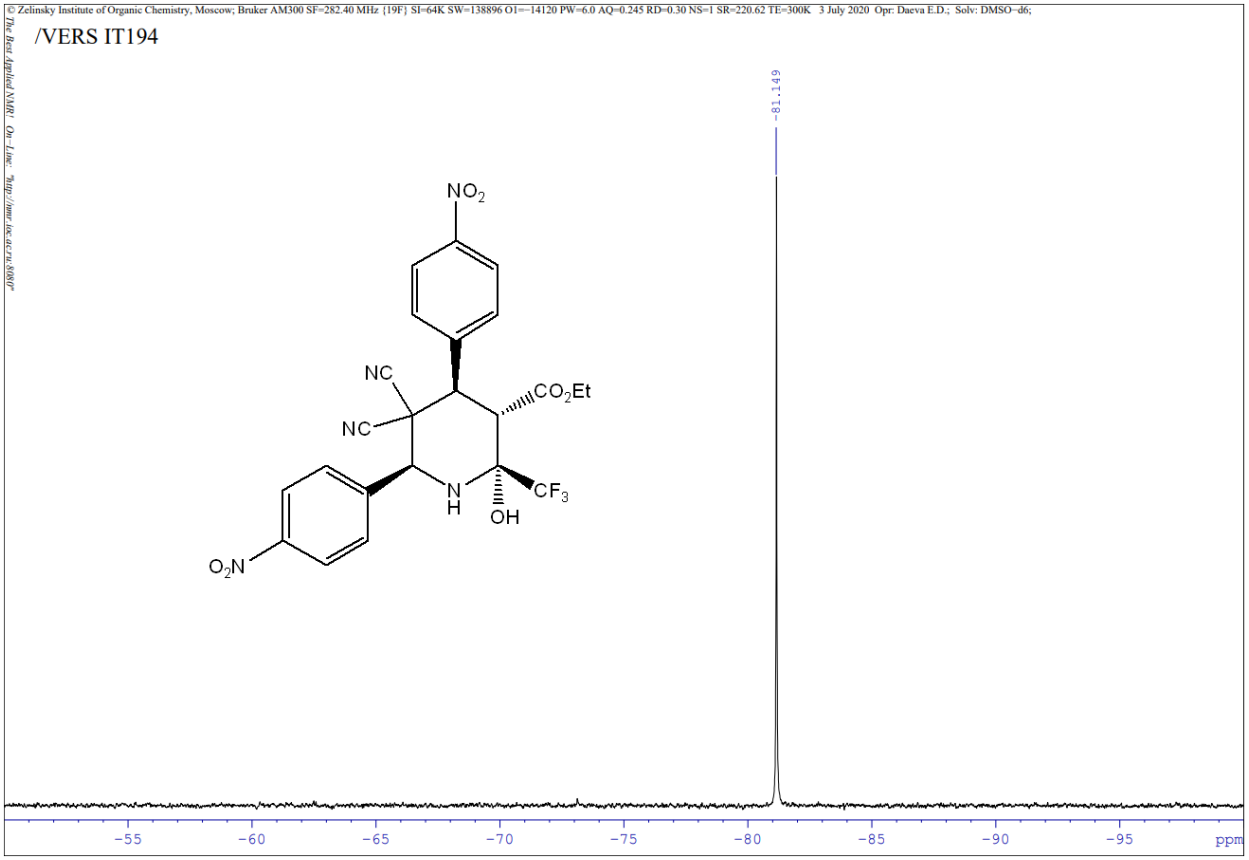

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=13.0 AQ=0.900 RD=1.00 NS=490 SR=-6.16 TE=298K 21 May 2019 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT146_2
171.917
165.705
165.384
162.386
162.064
131.576
130.390
130.277
130.151
130.111
127.810
124.992
121.201
116.487
116.412
116.198
116.123
112.381
112.293
98.734
82.781
82.376
77.525
77.201
76.877
62.989
59.242
47.975
47.839
44.425
13.375
F
NC
NC
CO2Et
N
H
CF3
OH
F
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=−14120 PW=6.0 AQ=0.245 RD=0.30 NS=1 SR=220.67 TE=299K 17 July 2020 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT204
F
NC
NC
CO2Et
N
H
CF3
OH
F
−55
−60
−65
−70
−75
−80
−85
−90
−95
−100
−105
−110
−115
ppm

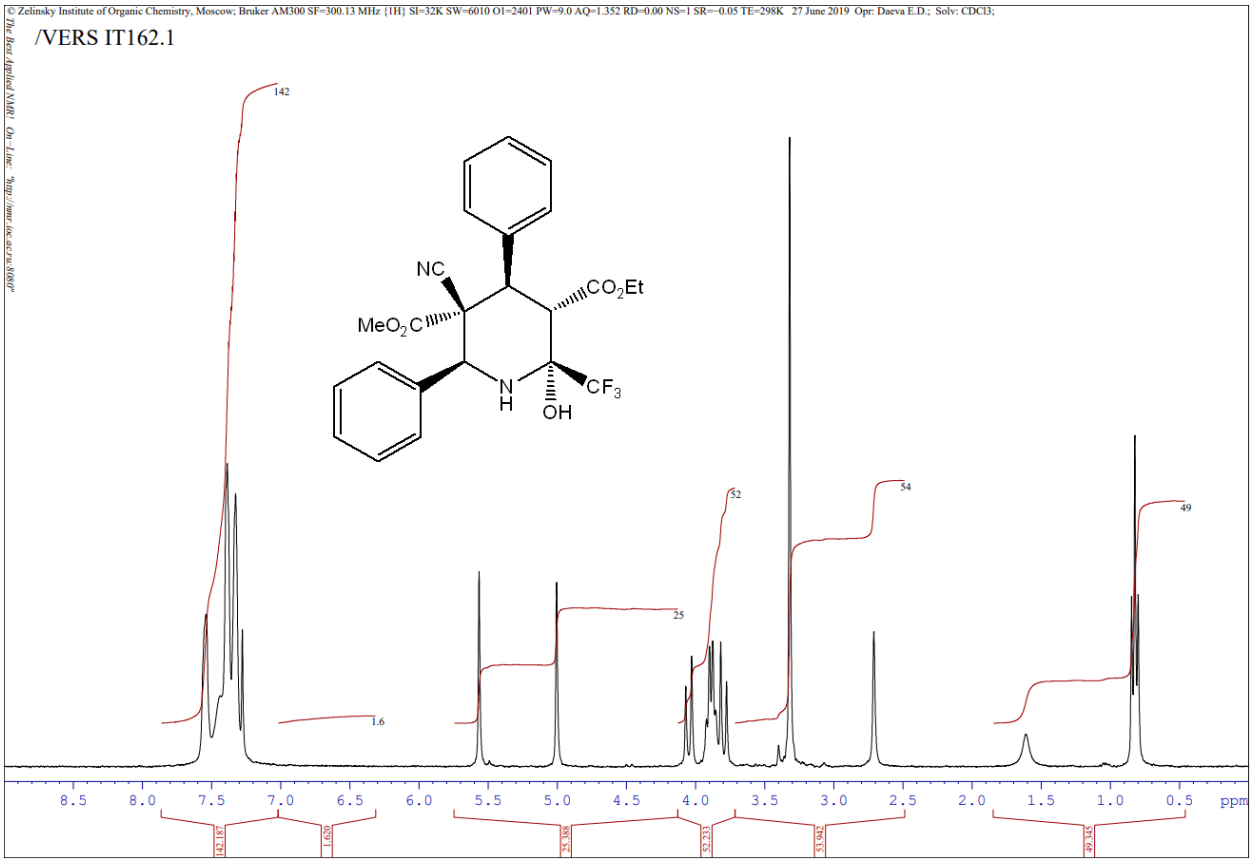
3g

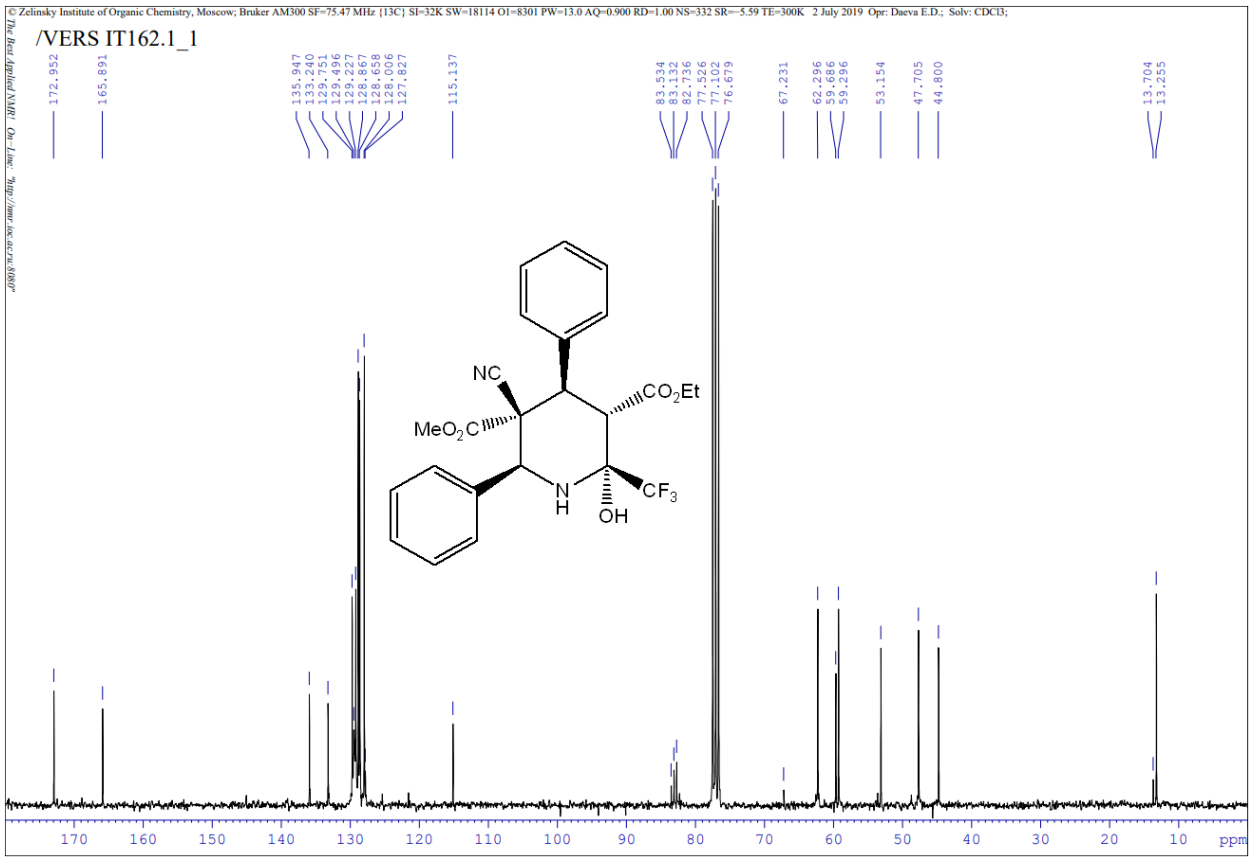

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=32K SW=6002 O1=2401 PW=9.0 AQ=1.352 RD=0.00 NS=1 SR=1.70 TE=300K 17 October 2019 Opr: Daeva E.D.; Solv: DMSO-d6;
/VERS IT156.1_2
NO2
NC
NC
CO2Et
CF3
N
H
OH
O2N
142
84
44
35
13
13
14
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

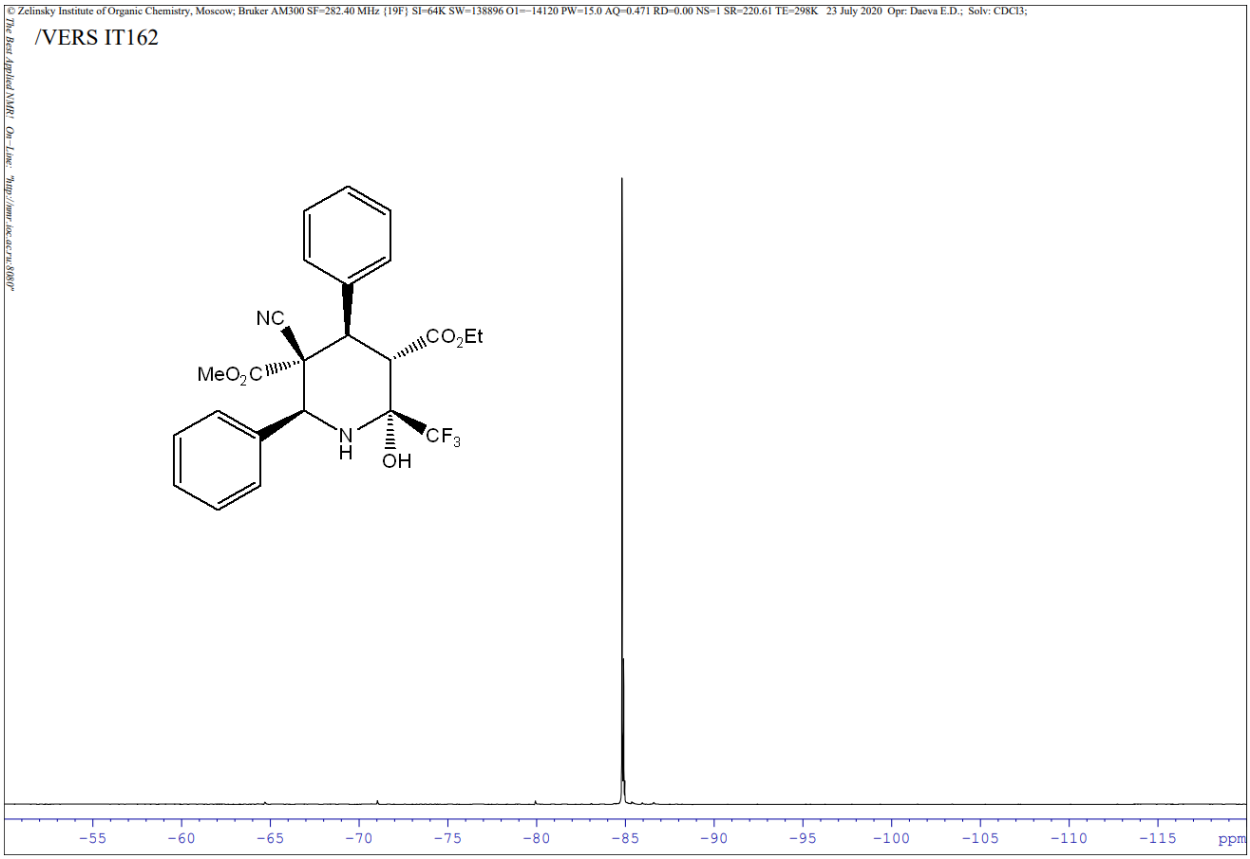

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=14.3 AQ=0.900 RD=1.00 NS=774 SR=37.00 TE=300K 19 March 2020 Opr: Daeva E.D.; Solv: DMSO-d6;
/VERS IT194.2_1
166.568
148.466
148.102
141.979
141.096
131.415
130.598
130.458
129.941
129.627
129.087
125.273
124.343
124.229
123.930
123.584
123.148
121.461
117.604
112.206
111.766
83.282
82.890
82.494
82.101
61.016
57.580
47.103
46.201
44.430
40.341
40.066
39.784
39.497
39.210
38.952
38.671
13.296
NO2
NC
NC
CO2Et
CF3
N
H
OH
O2N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=−14120 PW=6.0 AQ=0.245 RD=0.30 NS=1 SR=220.62 TE=300K 3 July 2020 Opr: Daeva E.D.; Solv: DMSO−d6;
/VERS IT194
-81.149
NO2
NC
NC
CO2Et
N
H
CF3
OH
O2N
−55
−60
−65
−70
−75
−80
−85
−90
−95
ppm

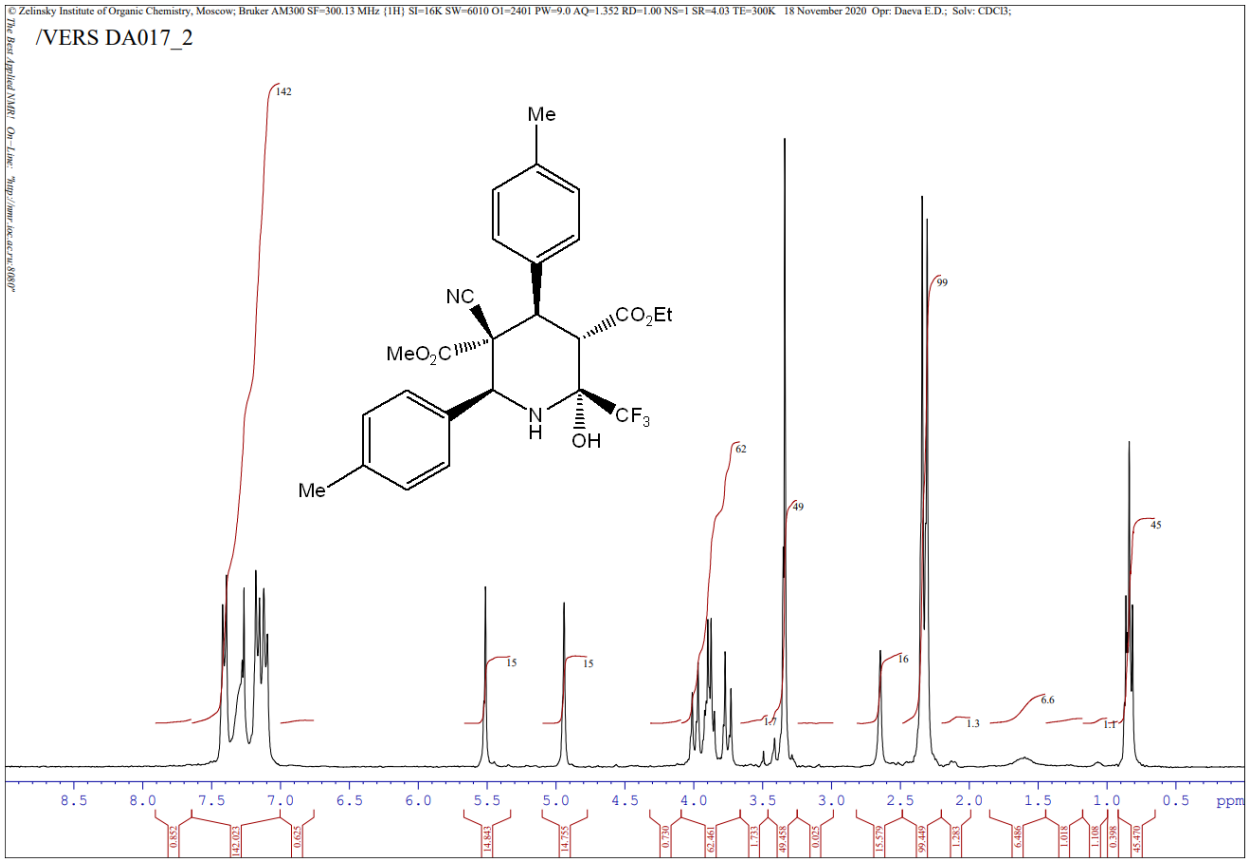
3h

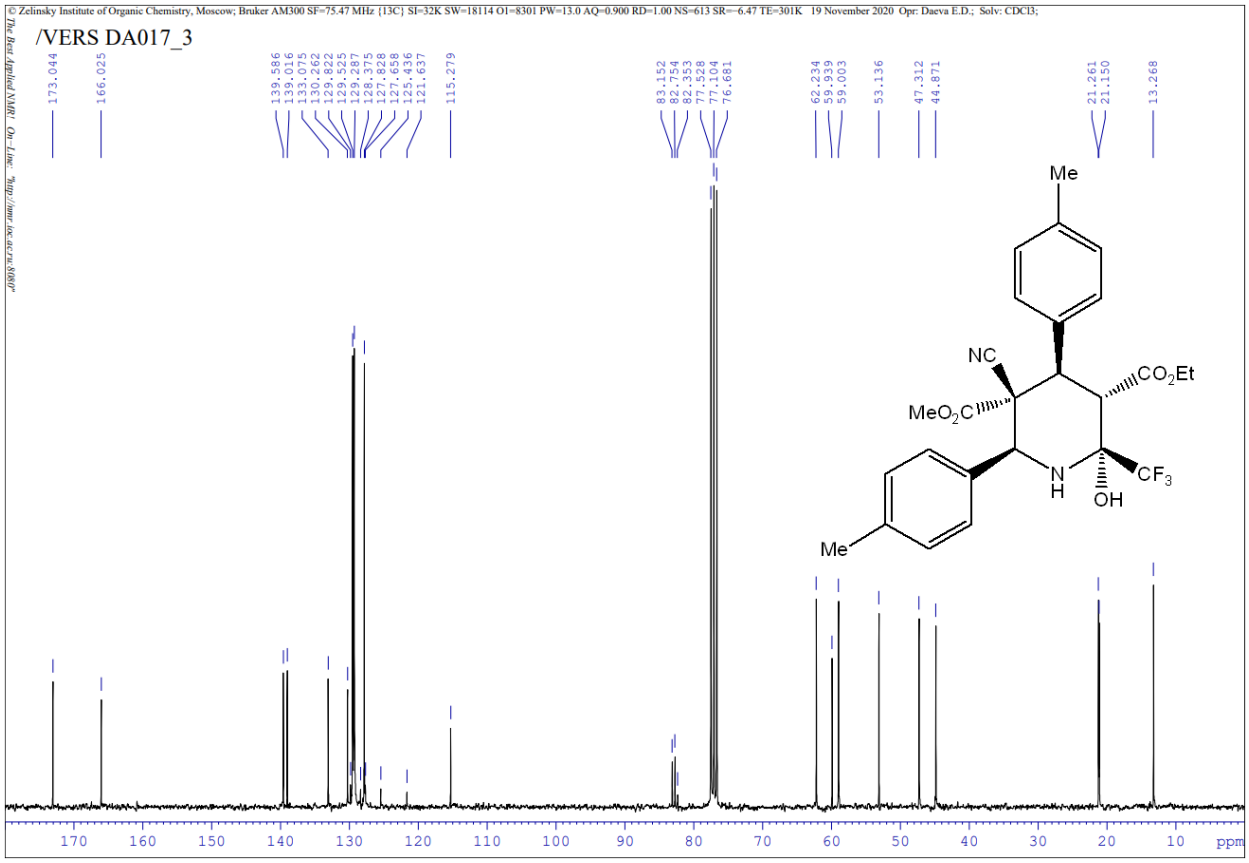

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=32K SW=6010 O1=2401 PW=9.0 AQ=1.352 RD=0.00 NS=1 SR=-0.05 TE=298K 27 June 2019 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT162.1
NC
CO2Et
MeO2C
CF3
N
H
OH
142
52
54
49
25
1.6
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
142.187
1.600
25.388
52.233
53.942
49.345

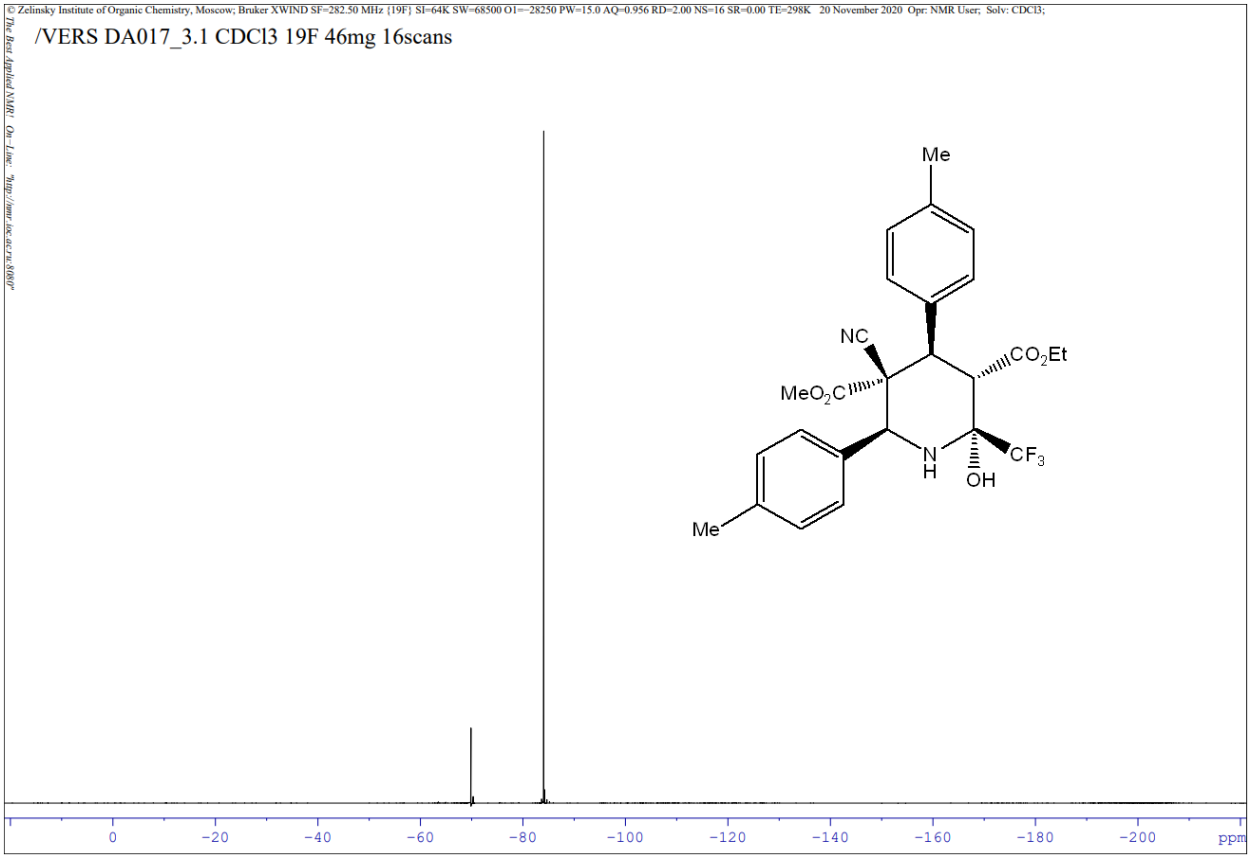

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=13.0 AQ=0.900 RD=1.00 NS=332 SR=-5.59 TE=300K 2 July 2019 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT162.1_1
172.952
165.891
135.947
133.240
131.731
129.496
129.227
128.867
128.658
128.006
127.827
115.137
83.534
83.132
82.736
77.526
77.202
76.879
67.231
62.296
59.686
59.296
53.154
47.705
44.800
13.704
13.255
NC
CO2Et
MeO2C
CF3
N
H
OH
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

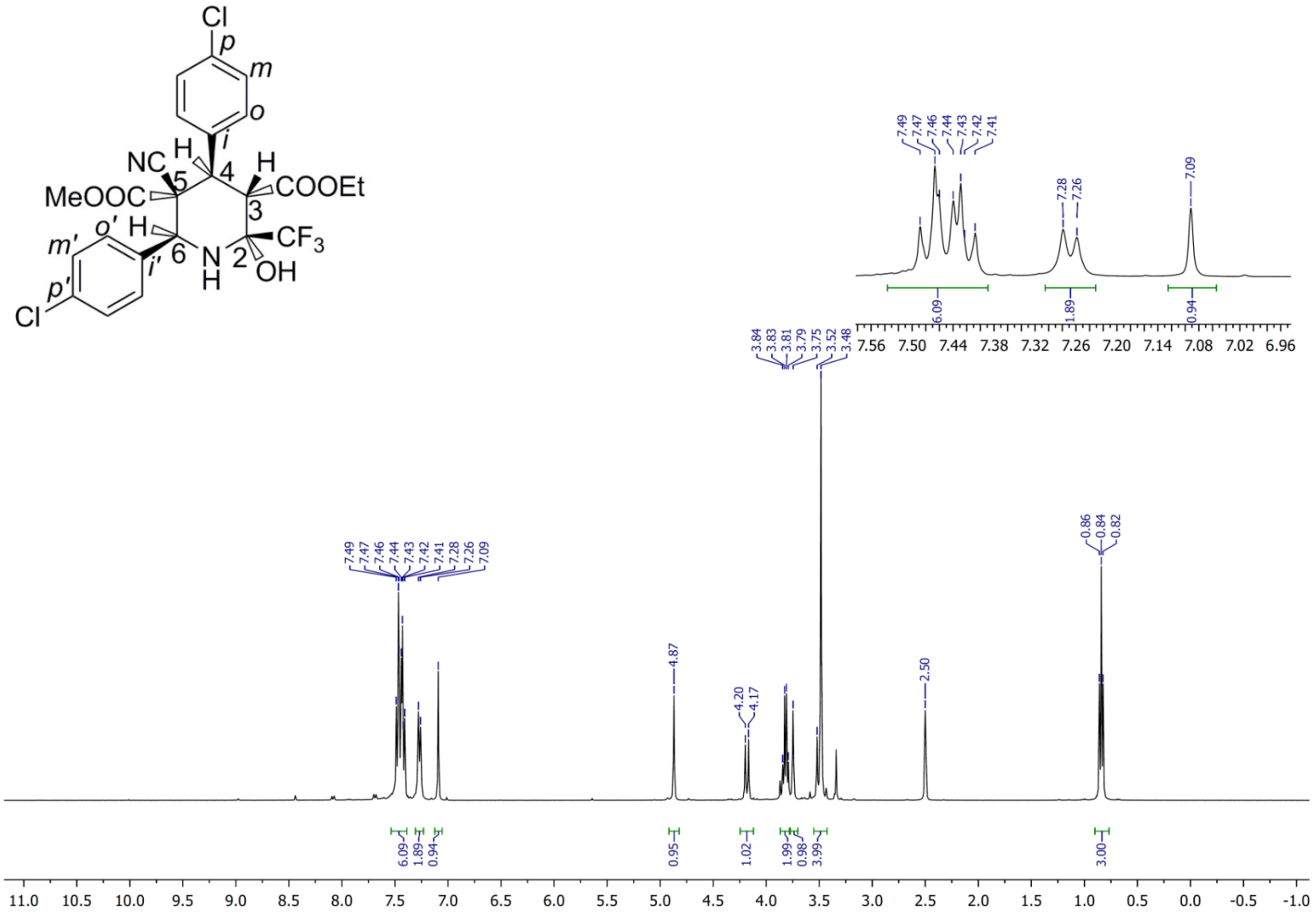

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=-14120 PW=15.0 AQ=0.471 RD=0.00 NS=1 SR=220.61 TE=298K 23 July 2020 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT162
NC
CO2Et
MeO2C
N
H
CF3
OH
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
ppm

3i

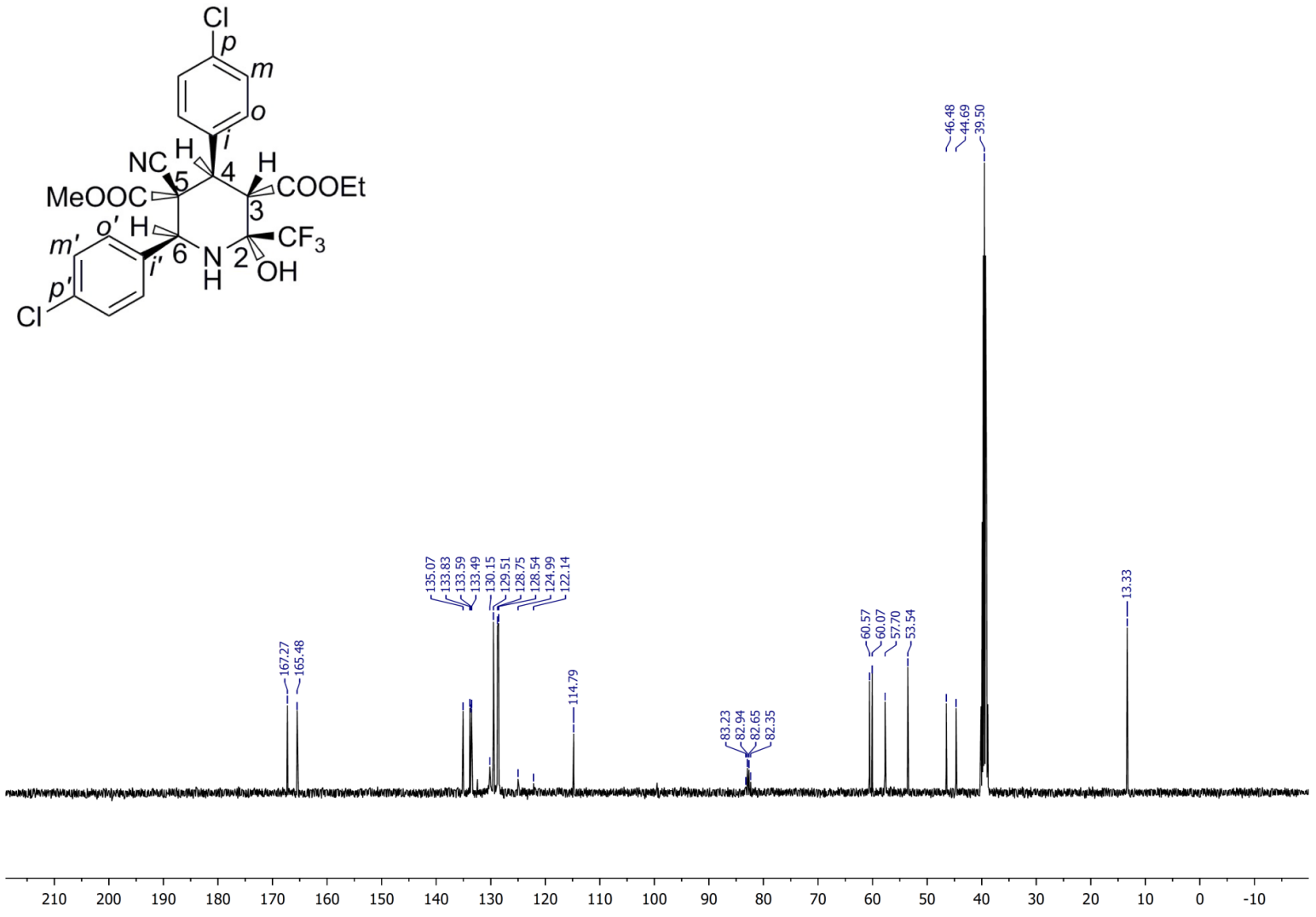

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=16K SW=6010 O1=2401 PW=9.0 AQ=1.352 RD=1.00 NS=1 SR=4.03 TE=300K 18 November 2020 Opr: Daeva E.D.; Solv: CDCl3;
/VERS DA017_2
Me
NC
CO2Et
MeO2C
N
H
CF3
OH
Me
142
62
49
99
45
15
15
16
6.6
1.3
1.7
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=13.0 AQ=0.900 RD=1.00 NS=613 SR=-6.47 TE=301K 19 November 2020 Opr: Daeva E.D.; Solv: CDCl3;
/VERS DA017_3
173.044
166.025
139.586
139.016
133.075
130.262
129.822
129.525
129.287
128.375
127.828
127.658
125.436
121.637
115.279
83.152
82.754
82.353
77.528
77.104
76.681
62.234
59.939
59.003
53.136
47.312
44.871
21.261
21.150
13.268
Me
NC
CO2Et
MeO2C
N
H
CF3
OH
Me
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

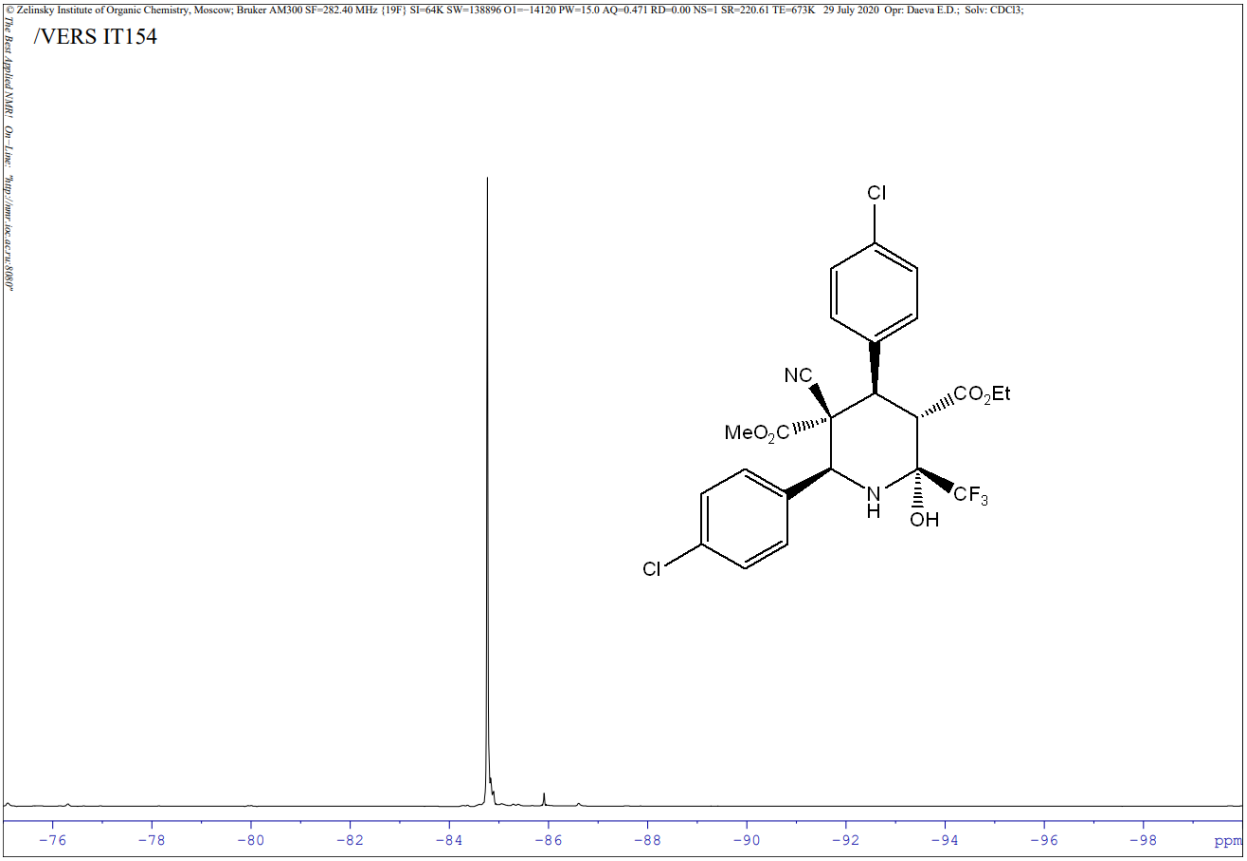

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker XWIND SF=282.50 MHz {19F} SI=64K SW=68500 O1=-28250 PW=15.0 AQ=0.956 RD=2.00 NS=16 SR=0.00 TE=298K 20 November 2020 Opr: NMR User; Solv: CDCl3;
/VERS DA017_3.1 CDCl3 19F 46mg 16scans
Me
NC
CO2Et
MeO2C
N
H
CF3
OH
Me
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm



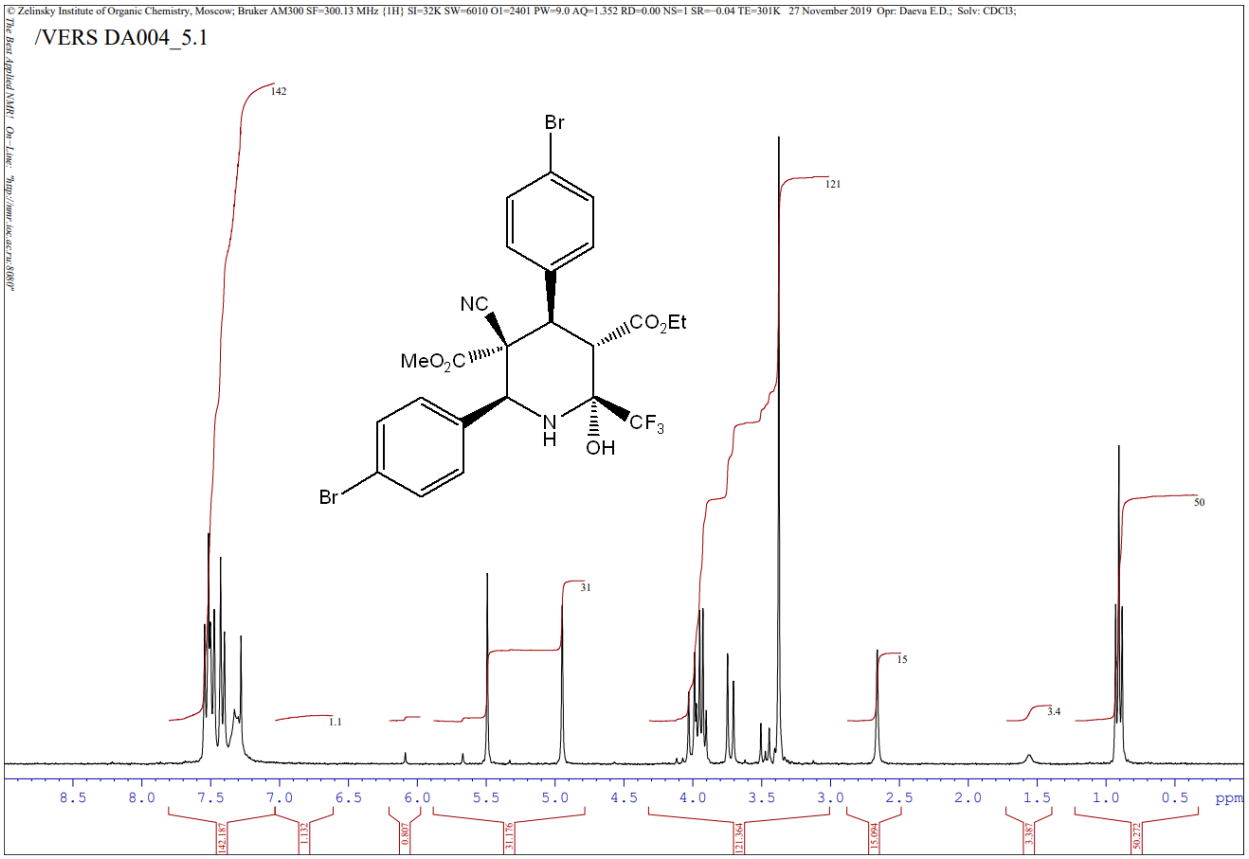
^{1}H NMR spectrum of the compound 3j, 400MHz, DMSO-d_6, 298 K.

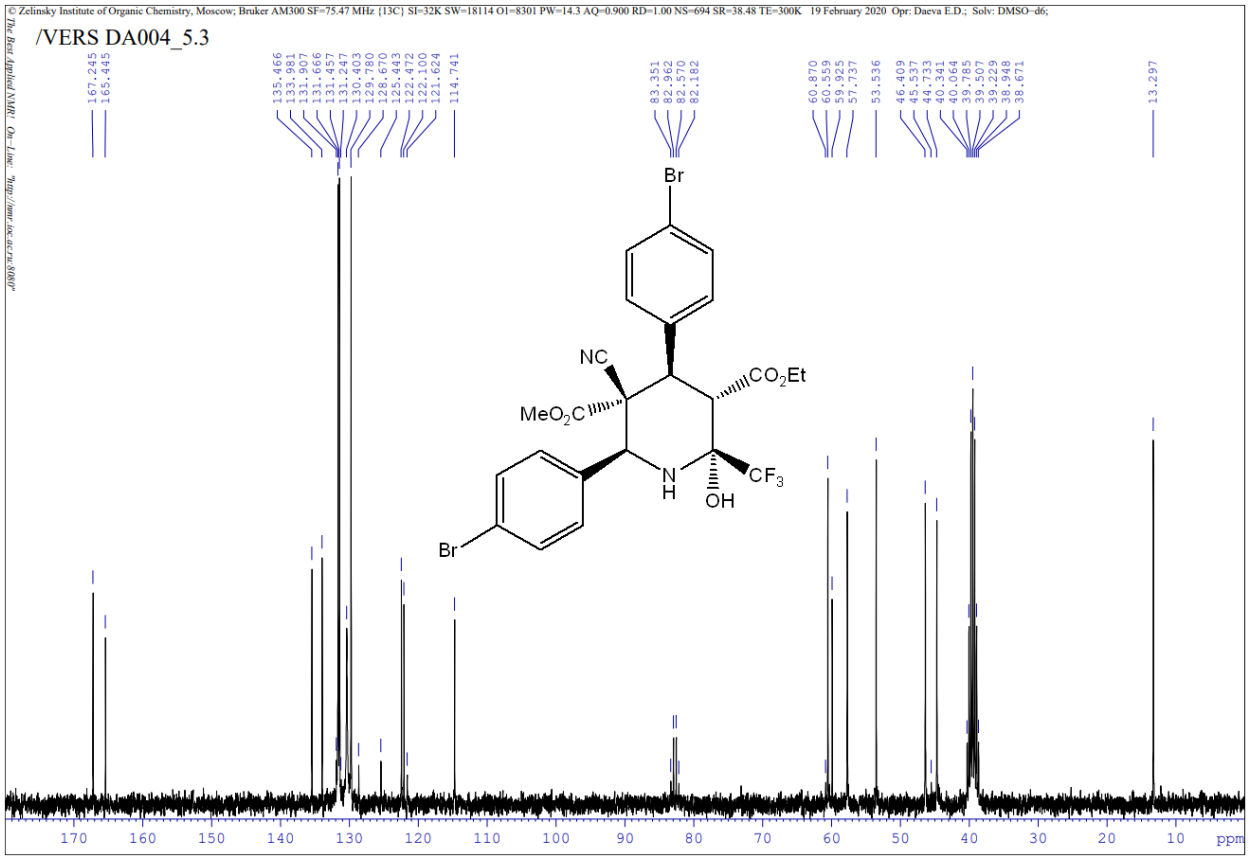


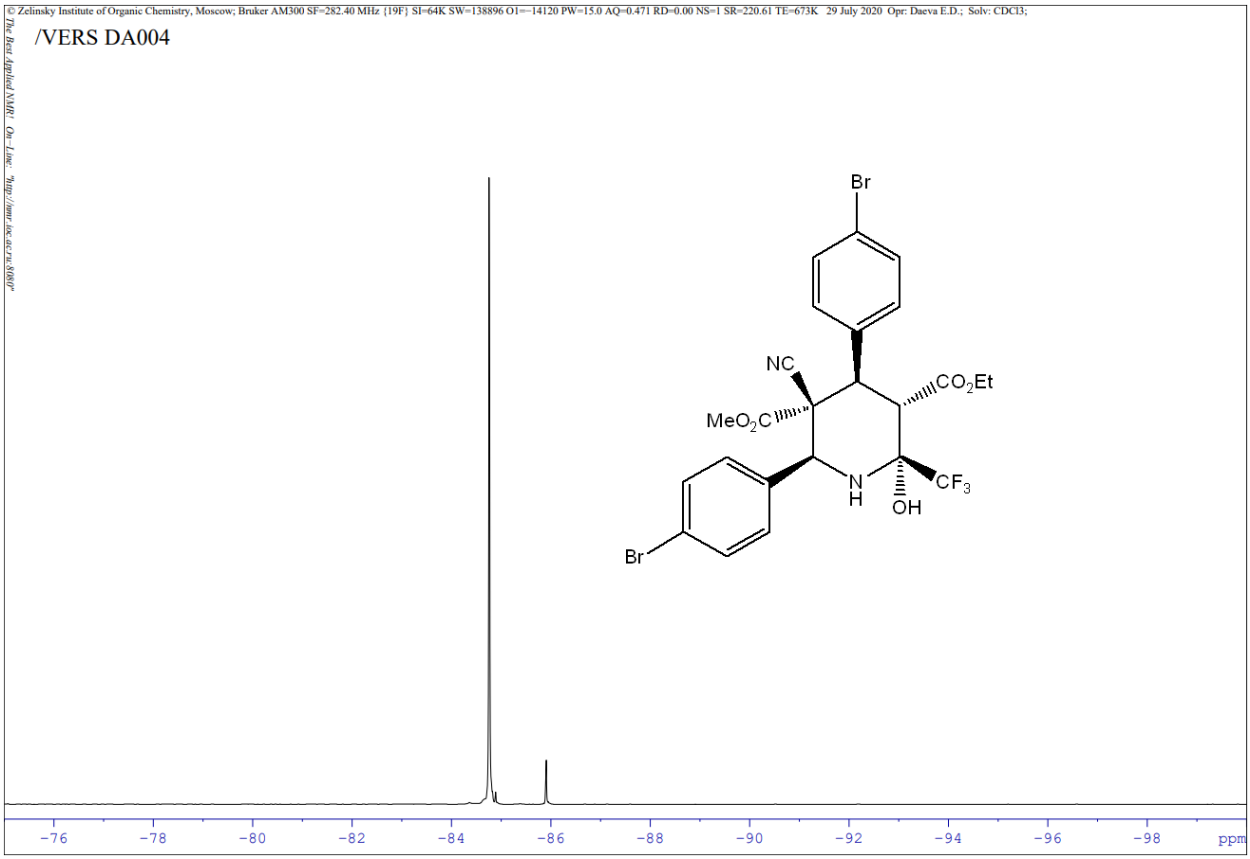
^{13}C NMR spectrum of the compound **3j**, 100 MHz, DMSO-d_6, 298 K.


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=−14120 PW=15.0 AQ=0.471 RD=0.00 NS=1 SR=220.61 TE=673K 29 July 2020 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT154
Cl
NC
CO2Et
MeO2C
N
H
CF3
OH
Cl
−76
−78
−80
−82
−84
−86
−88
−90
−92
−94
−96
−98
ppm

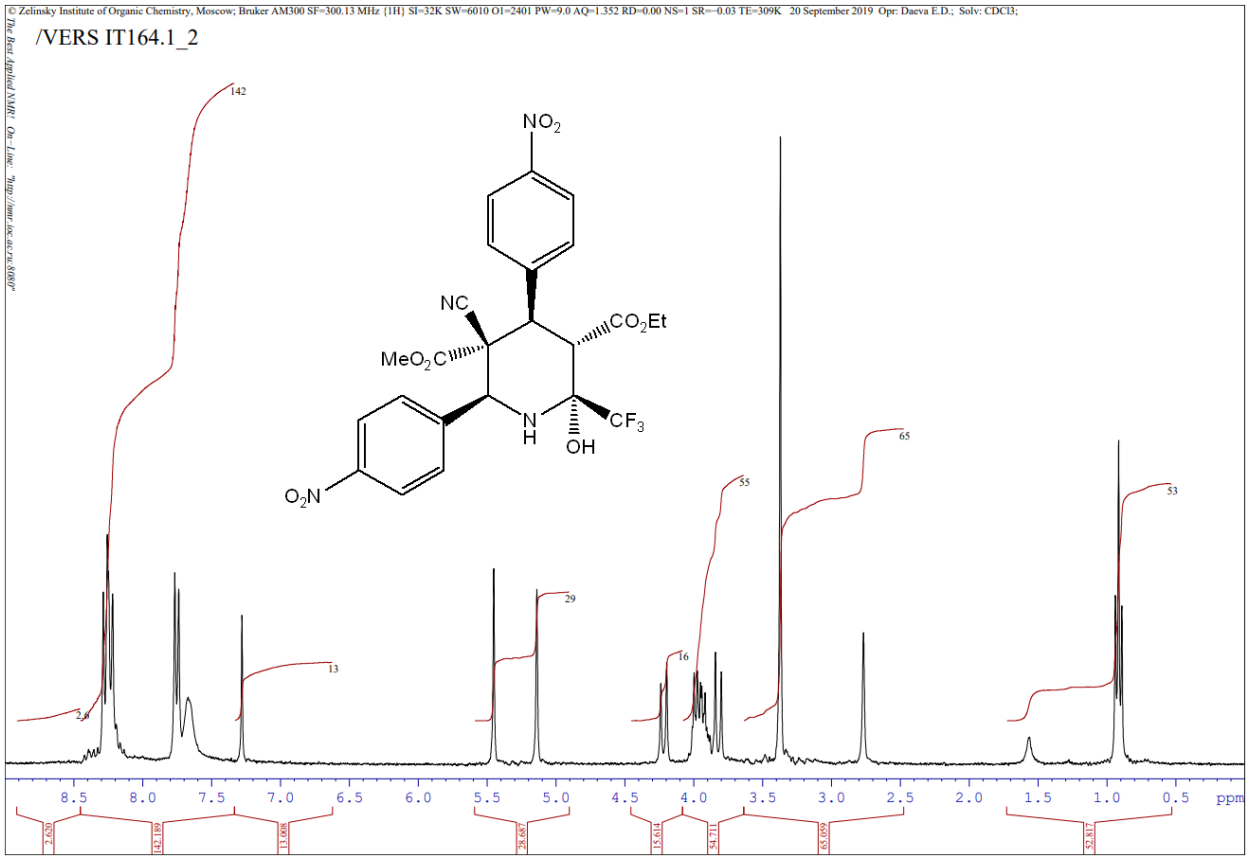
3k

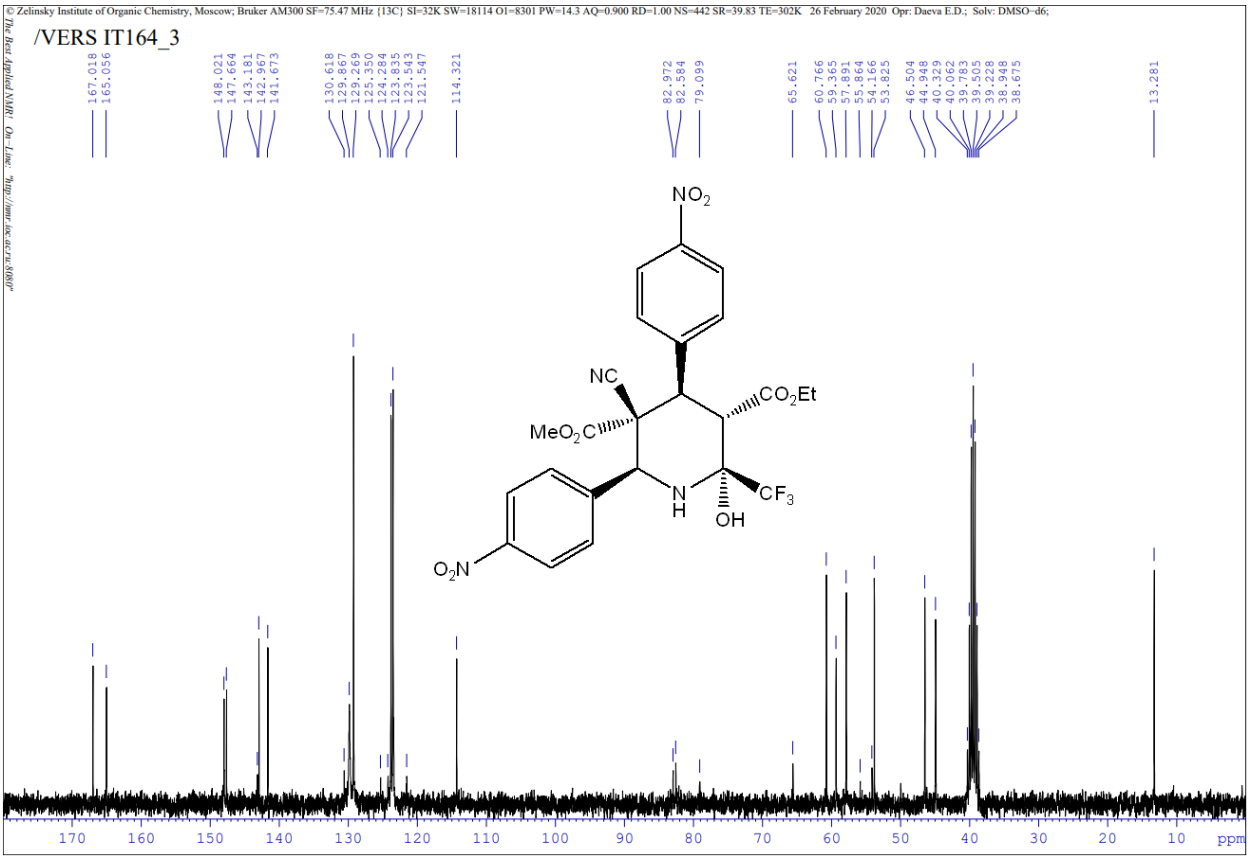

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=32K SW=6010 O1=2401 PW=9.0 AQ=1.352 RD=0.00 NS=1 SR=-0.04 TE=301K 27 November 2019 Opr: Daeva E.D.; Solv: CDCl3;
/VERS DA004_5.1
Br
NC
CO2Et
MeO2C
N
H
CF3
OH
Br
142
121
50
31
15
3.4
1.1
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

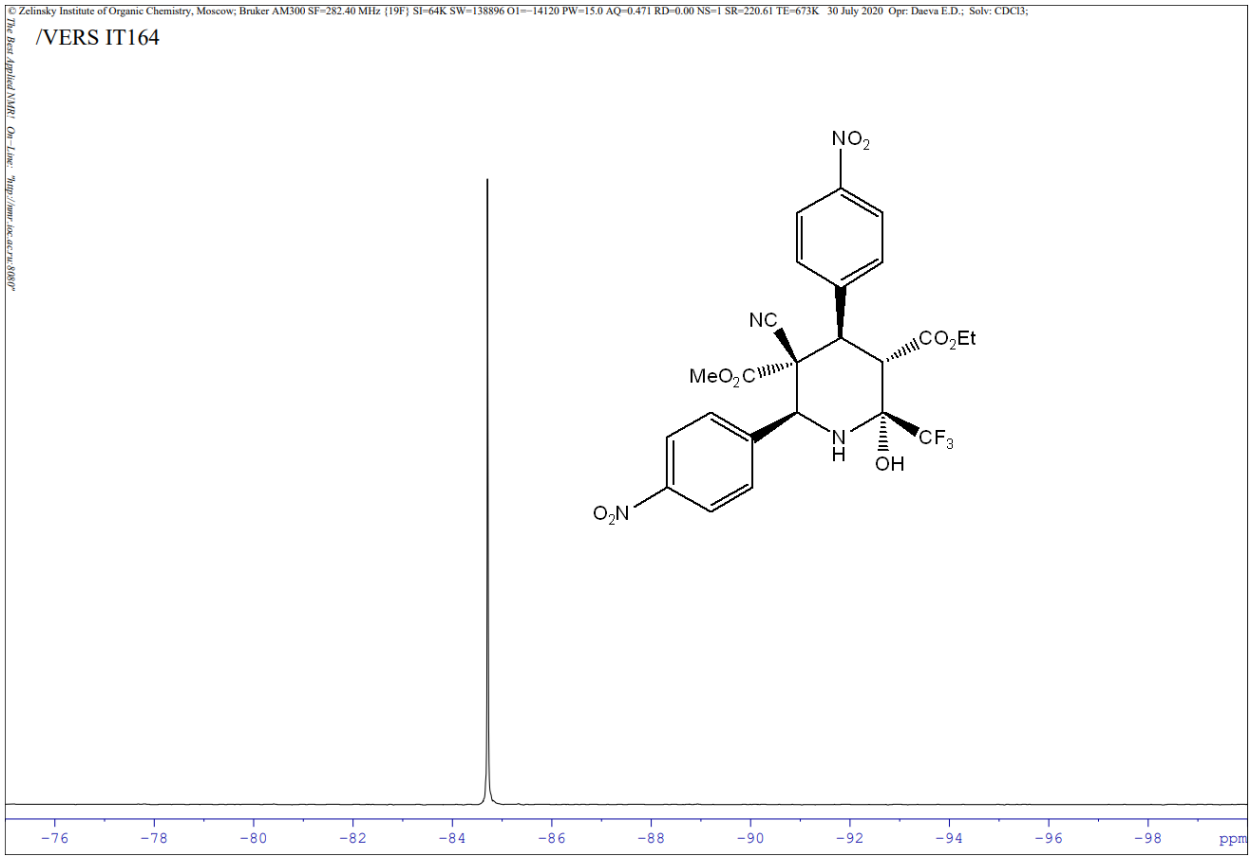

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=14.3 AQ=0.900 RD=1.00 NS=694 SR=38.48 TE=300K 19 February 2020 Opr: Daeva E.D.; Solv: DMSO-d6;
/VERS DA004_5.3
167.245
165.445
135.466
133.981
131.907
131.666
131.457
131.247
130.403
129.780
128.670
125.443
122.472
122.100
121.624
114.741
83.351
82.962
82.570
82.182
60.870
60.559
59.925
57.737
53.536
46.409
45.537
44.733
40.341
40.064
39.785
39.507
39.229
38.948
38.671
13.297
Br
NC
CO2Et
MeO2C
N
H
CF3
OH
Br
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=-14120 PW=15.0 AQ=0.471 RD=0.00 NS=1 SR=220.61 TE=673K 29 July 2020 Opr: Daeva E.D.; Solv: CDCl3;
/VERS DA004
Br
NC
CO2Et
MeO2C
N
H
CF3
OH
Br
-76
-78
-80
-82
-84
-86
-88
-90
-92
-94
-96
-98
ppm

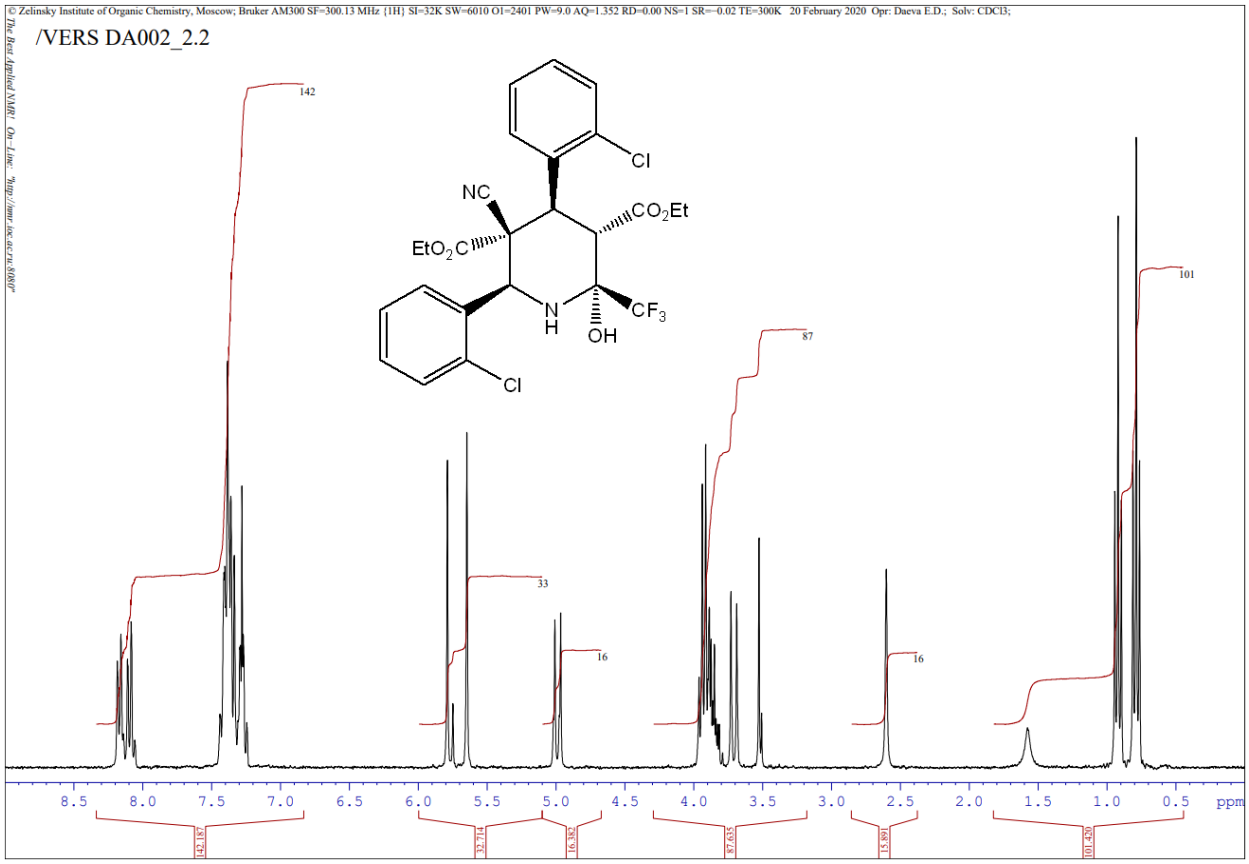
3l

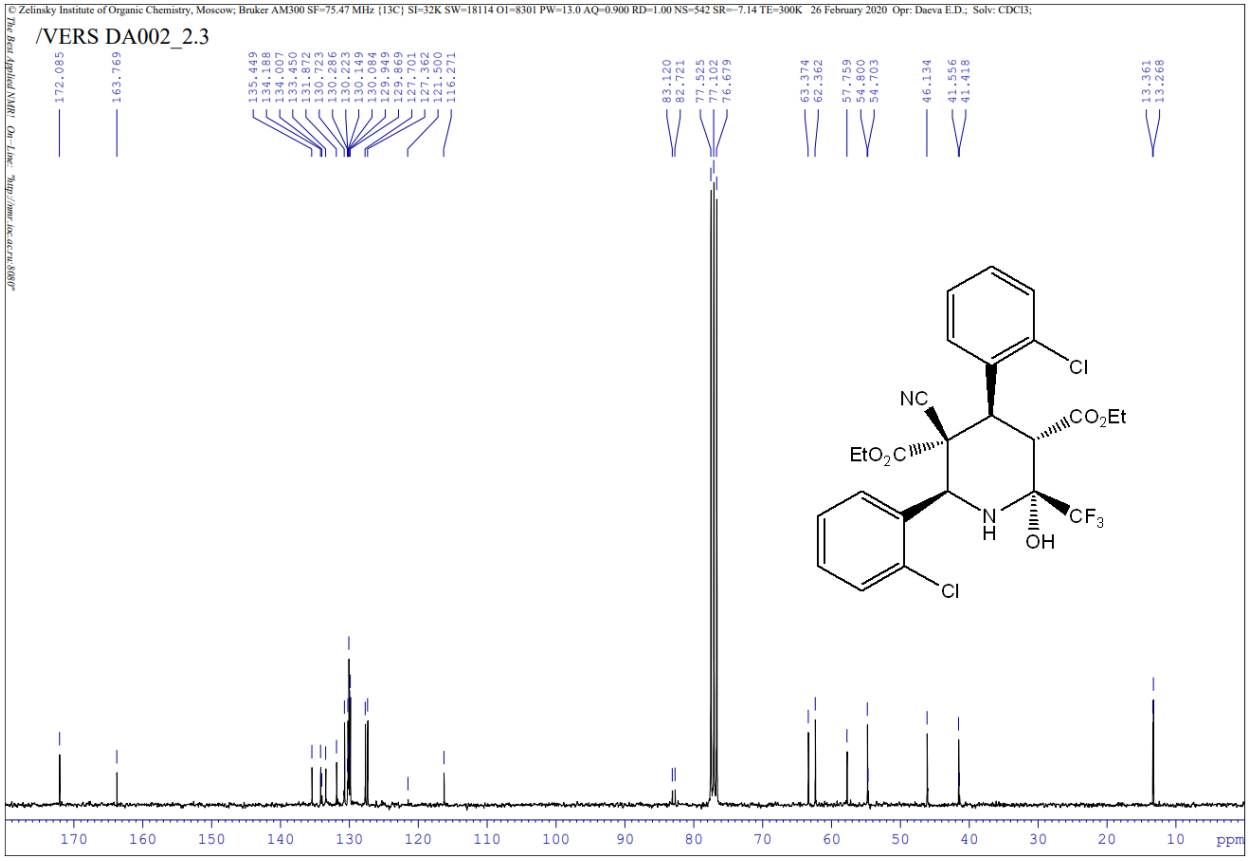

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=32K SW=6010 O1=2401 PW=9.0 AQ=1.352 RD=0.00 NS=1 SR=-0.03 TE=309K 20 September 2019 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT164.1_2
NO2
NC
CO2Et
MeO2C
N
H
CF3
OH
O2N
142
65
55
53
29
16
13
2.0
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

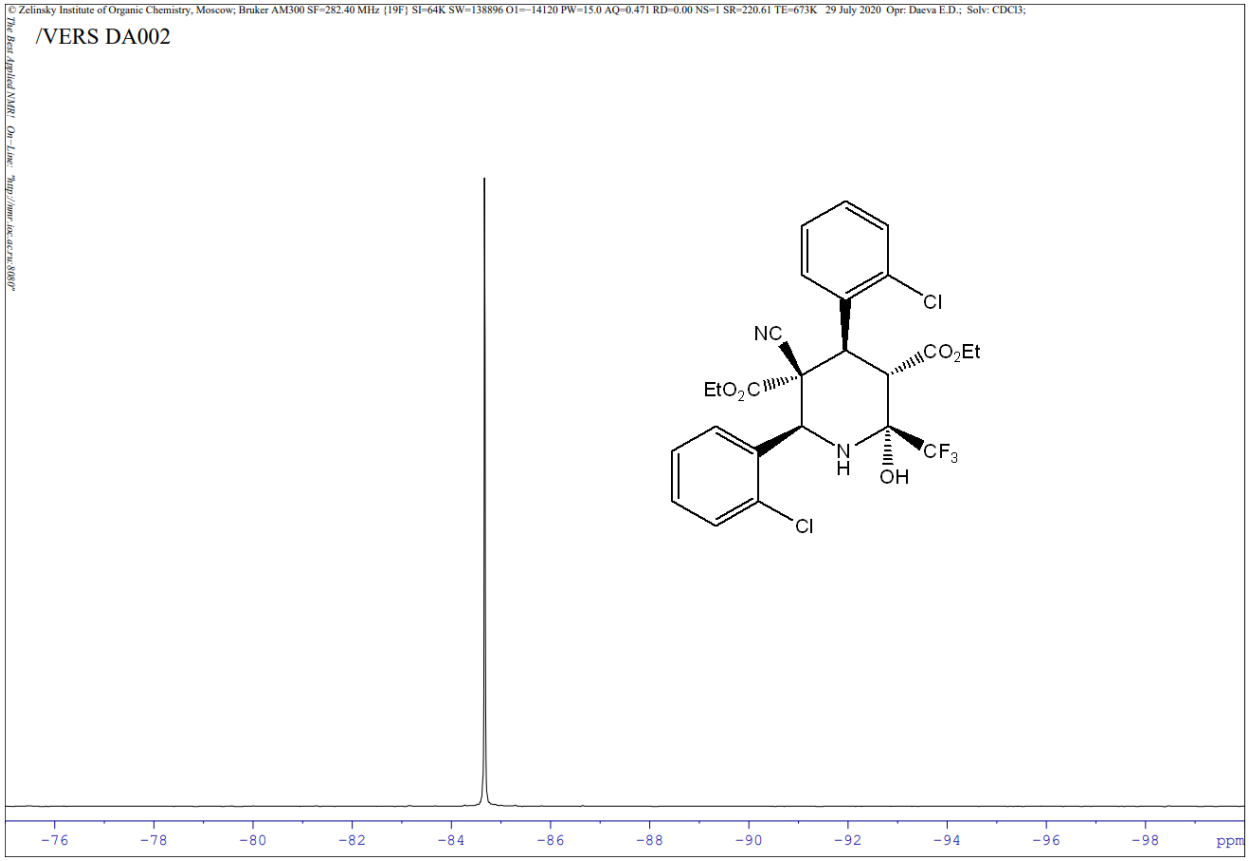

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=14.3 AQ=0.900 RD=1.00 NS=442 SR=39.83 TE=302K 26 February 2020 Opr: Daeva E.D.; Solv: DMSO-d6;
/VERS IT164_3
167.018
165.056
148.021
147.664
143.181
142.967
141.673
130.618
129.867
129.269
125.350
124.284
123.835
123.543
121.547
114.321
82.972
82.584
79.099
65.621
60.766
59.365
57.891
55.864
54.166
53.825
46.504
44.948
40.329
39.922
39.783
39.505
39.228
38.948
38.675
13.281
NO2
NC
CO2Et
MeO2C
N
H
CF3
OH
O2N
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=-14120 PW=15.0 AQ=0.471 RD=0.00 NS=1 SR=220.61 TE=673K 30 July 2020 Opr: Daeva E.D.; Solv: CDCl3;
"The Best Applied NMR On Line" "http://nmr.ioc.ac.ru:8080"
/VERS IT164
NO2
NC
CO2Et
MeO2C
N
H
CF3
OH
O2N
-76
-78
-80
-82
-84
-86
-88
-90
-92
-94
-96
-98
ppm

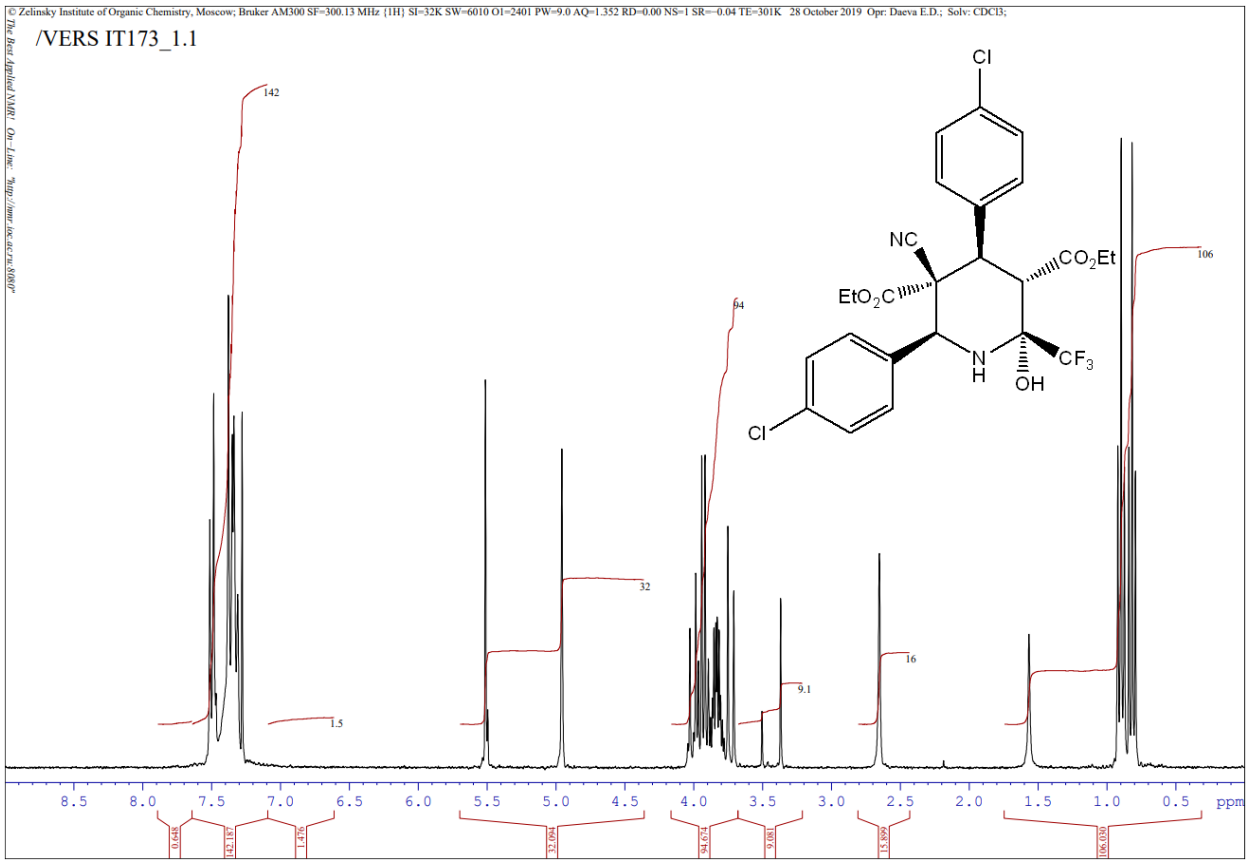
3m

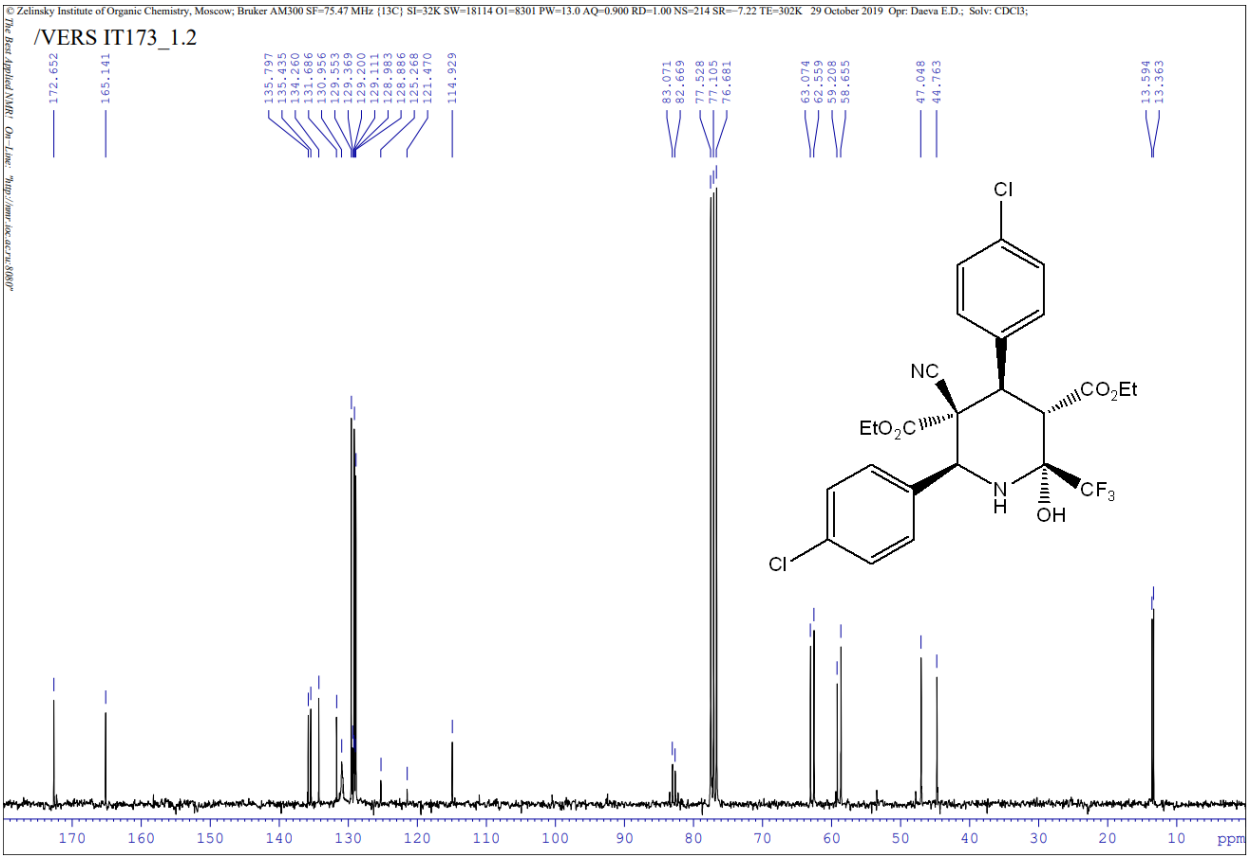

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=32K SW=6010 O1=2401 PW=9.0 AQ=1.352 RD=0.00 NS=1 SR=-0.02 TE=300K 20 February 2020 Opr: Daeva E.D.; Solv: CDCl3;
/VERS DA002_2.2
142
33
16
87
16
101
Cl
NC
CO2Et
EtO2C
N
H
CF3
OH
Cl
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
142.187
32.714
16.382
87.635
15.891
101.420

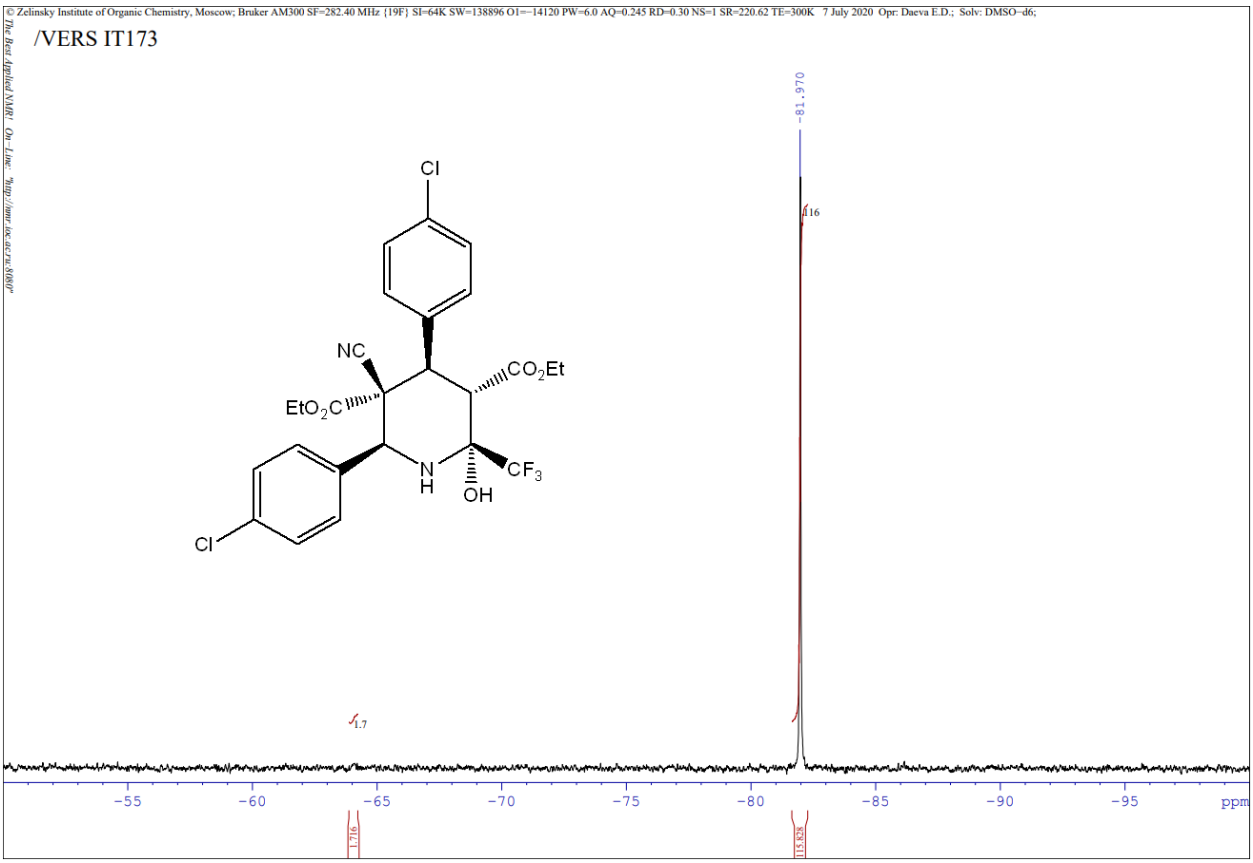

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=13.0 AQ=0.900 RD=1.00 NS=542 SR=-7.14 TE=300K 26 February 2020 Opr: Daeva E.D.; Solv: CDCl3;
/VERS DA002_2.3
172.085
163.769
135.449
134.188
134.007
133.450
131.372
130.723
130.286
130.223
130.149
130.084
129.949
129.869
127.701
127.362
121.500
116.271
83.120
82.721
77.525
77.102
76.679
63.374
62.362
57.759
54.800
54.703
46.134
41.556
41.418
13.361
13.268
Cl
NC
CO2Et
EtO2C
N
H
CF3
OH
Cl
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=−14120 PW=15.0 AQ=0.471 RD=0.00 NS=1 SR=220.61 TE=673K 29 July 2020 Opr: Daeva E.D.; Solv: CDCl3;
/VERS DA002
Cl
NC
CO2Et
EtO2C
N
H
CF3
OH
Cl
−76
−78
−80
−82
−84
−86
−88
−90
−92
−94
−96
−98
ppm

3n


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=300.13 MHz {1H} SI=32K SW=6010 O1=2401 PW=9.0 AQ=1.352 RD=0.00 NS=1 SR=-0.04 TE=301K 28 October 2019 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT173_1.1
142
94
106
32
16
9.1
1.5
Cl
NC
CO2Et
EtO2C
N
H
CF3
OH
Cl
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.648
42.187
1.476
32.094
34.674
9.081
15.899
106.000


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=13.0 AQ=0.900 RD=1.00 NS=214 SR=-7.22 TE=302K 29 October 2019 Opr: Daeva E.D.; Solv: CDCl3;
/VERS IT173_1.2
172.652
165.141
135.797
135.435
134.260
131.666
130.956
129.553
129.369
129.200
129.111
128.983
128.886
125.268
121.470
114.929
83.071
82.669
77.528
77.105
76.681
63.074
62.559
59.208
58.655
47.048
44.763
13.594
13.363
Cl
NC
CO2Et
EtO2C
N
H
CF3
OH
Cl
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=282.40 MHz {19F} SI=64K SW=138896 O1=−14120 PW=6.0 AQ=0.245 RD=0.30 NS=1 SR=220.62 TE=300K 7 July 2020 Opr: Daeva E.D.; Solv: DMSO−d6;
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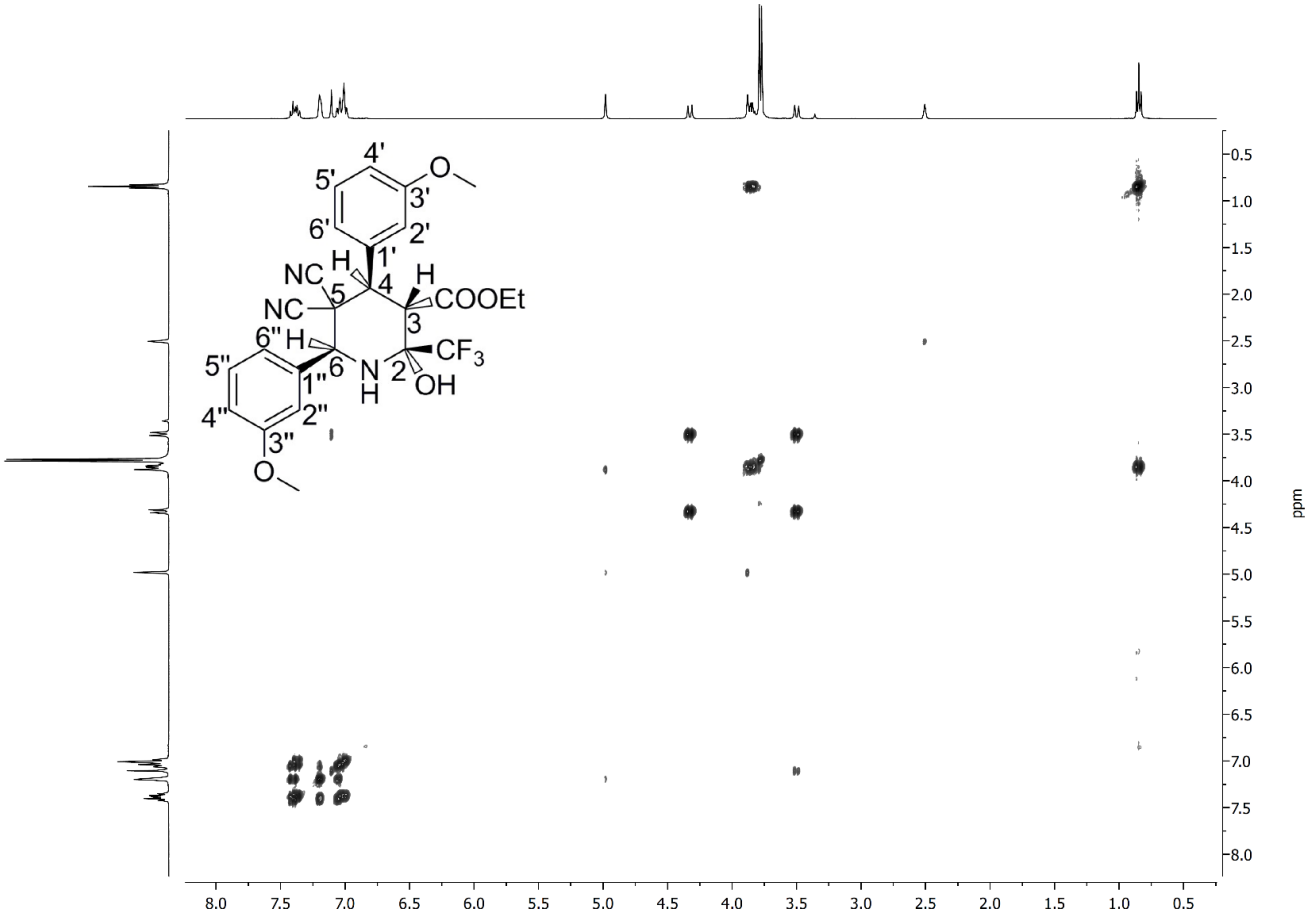
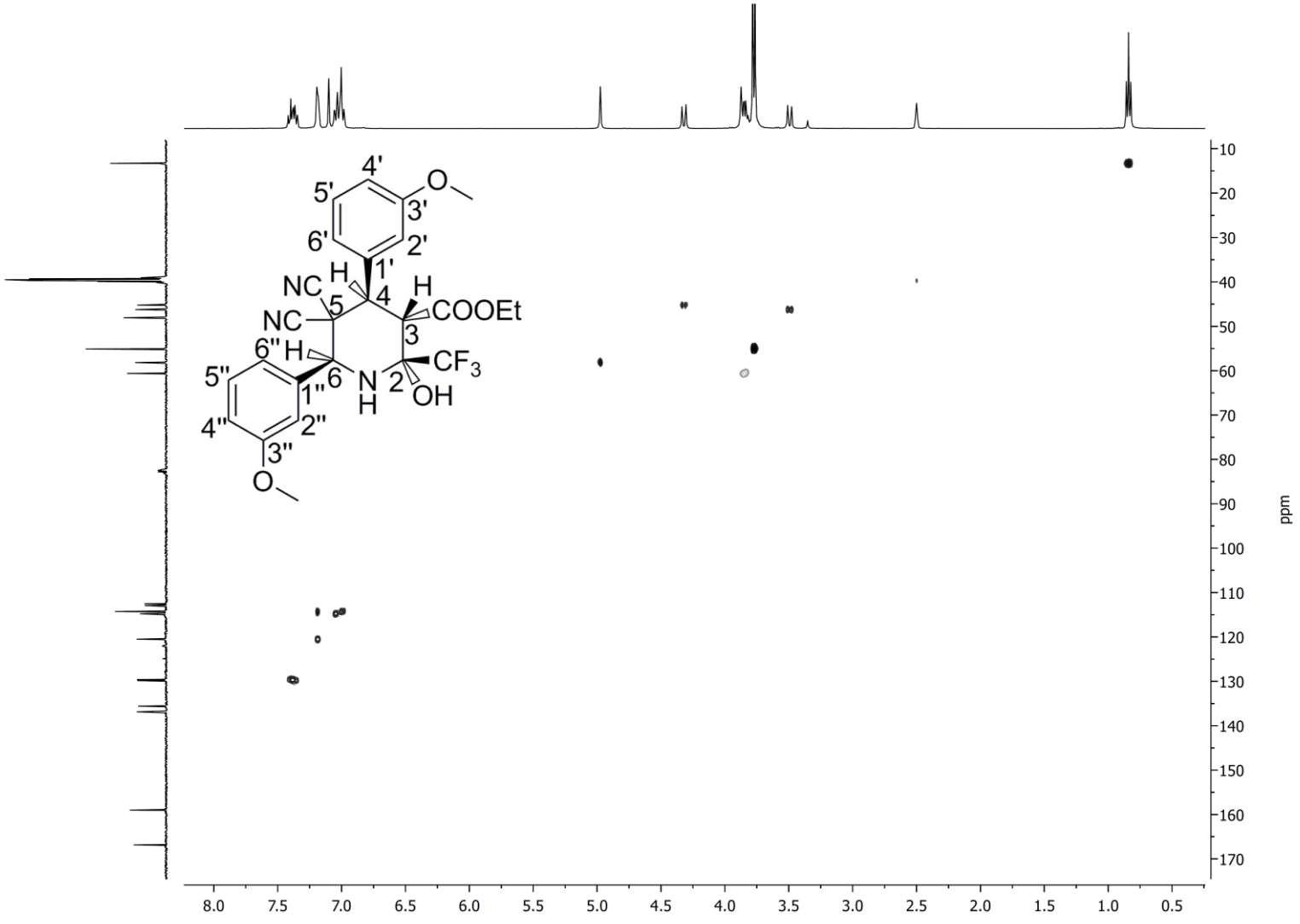
1.16
1.7
Cl
NC
CO2Et
EtO2C
N
H
CF3
OH
Cl
−55
−60
−65
−70
−75
−80
−85
−90
−95
ppm
1.716
15.828

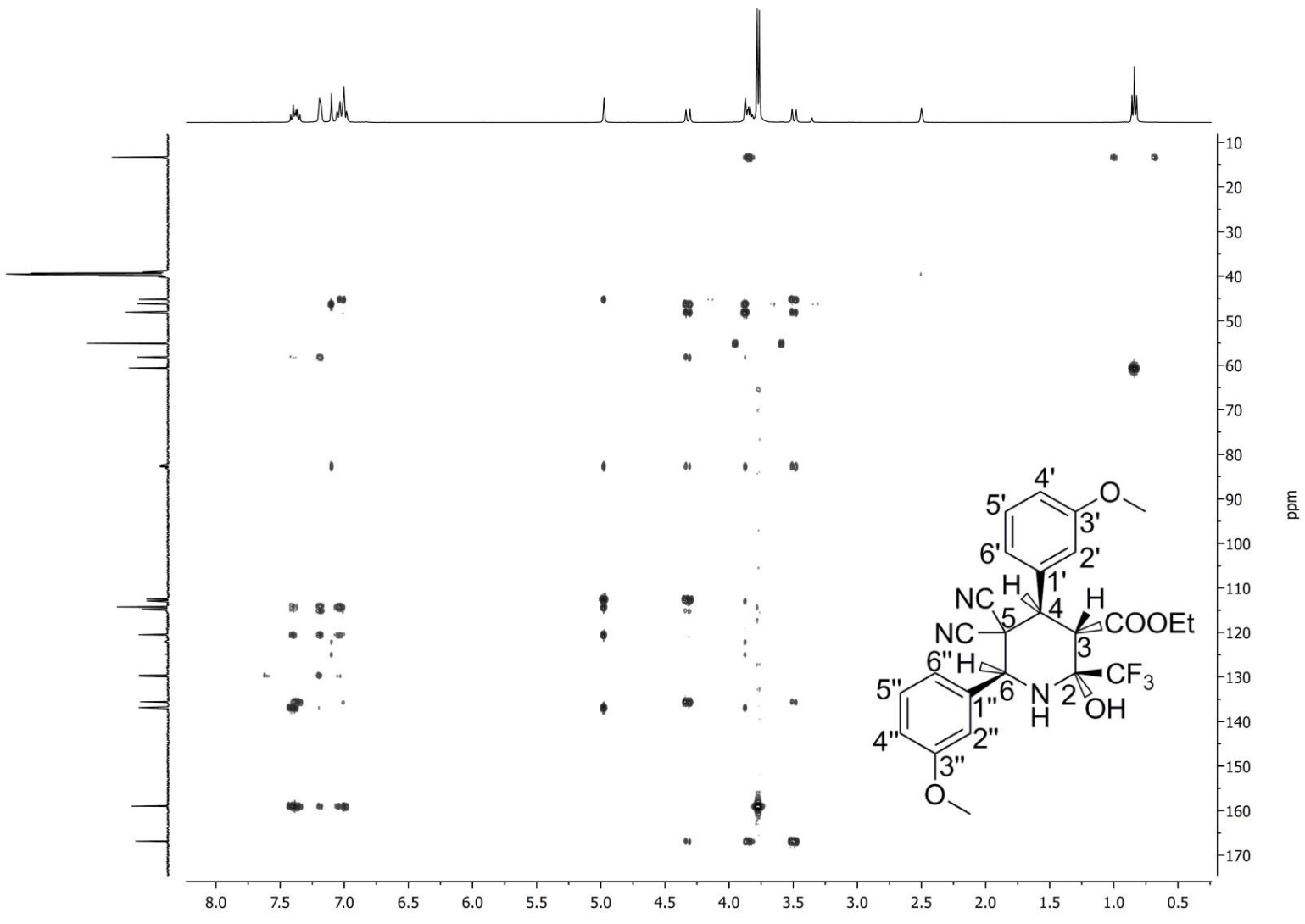
4. ^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H NOESY spectra for compounds 3d, 3j



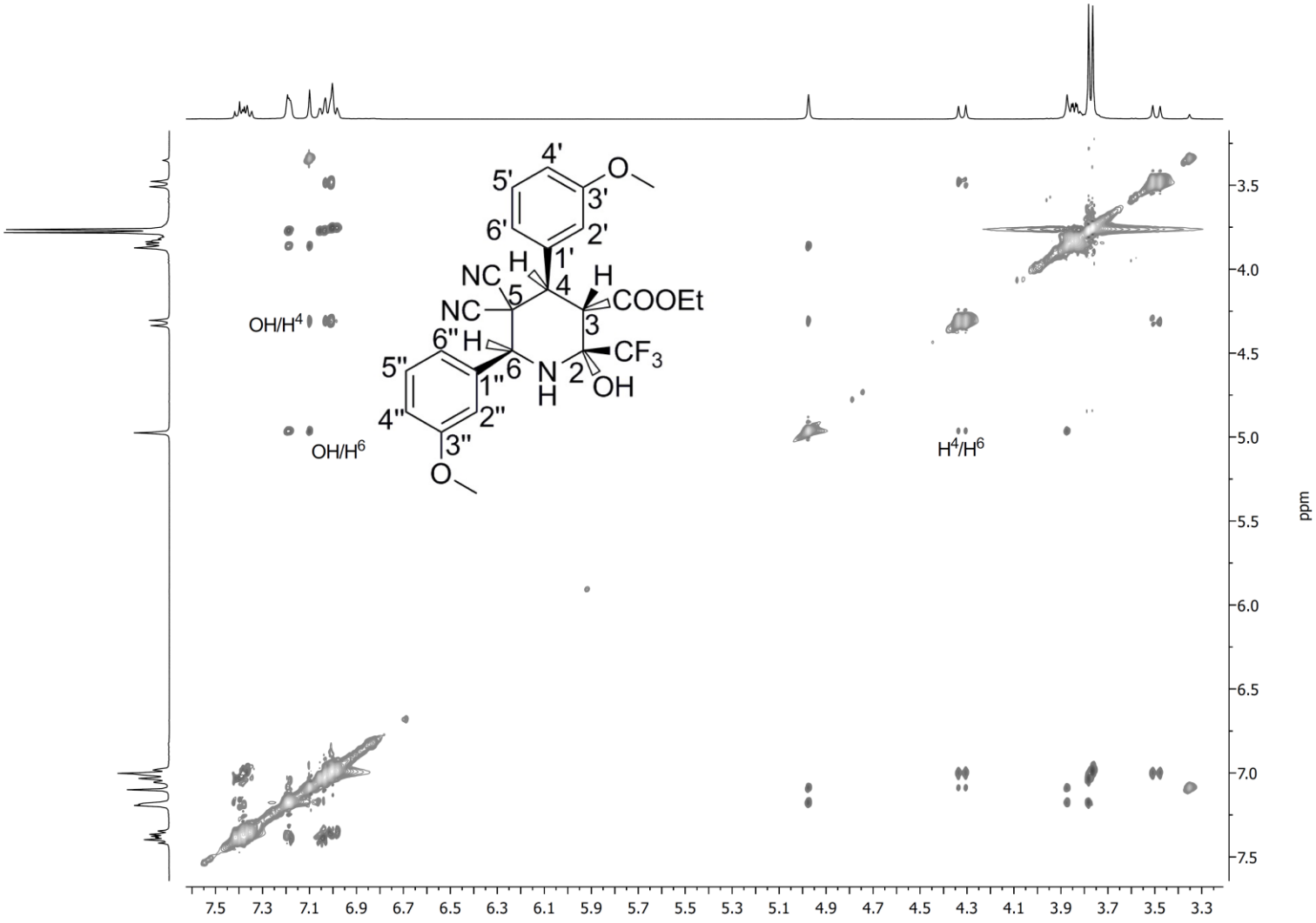
^{1}H-^{1}H COSY NMR spectrum of the compound **3d**, 400MHz, DMSO-d_6, 298 K.



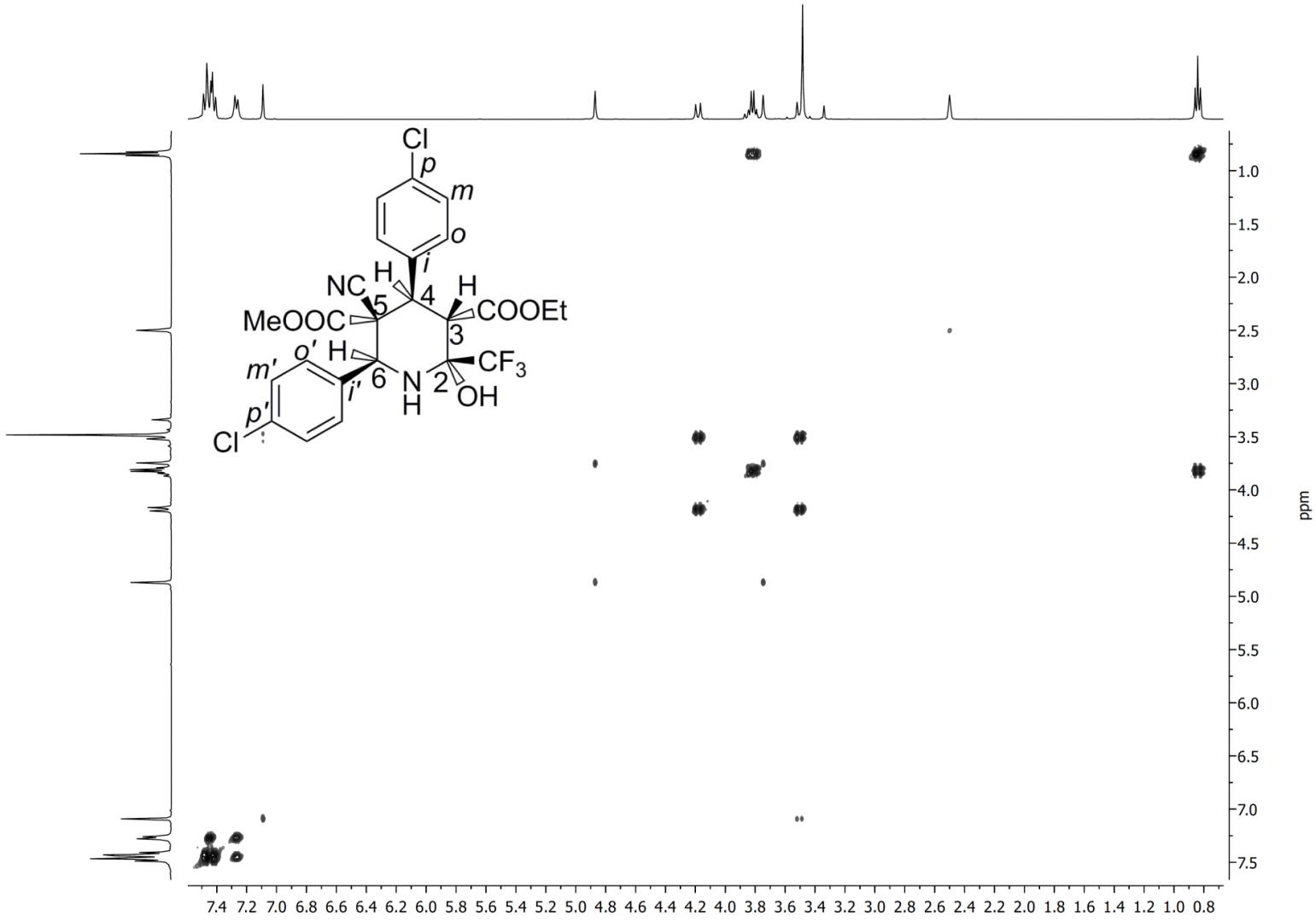
^{1}H-^{13}C HSQC NMR spectrum of the compound **3d**, 400MHz, DMSO-d_6, 298 K.



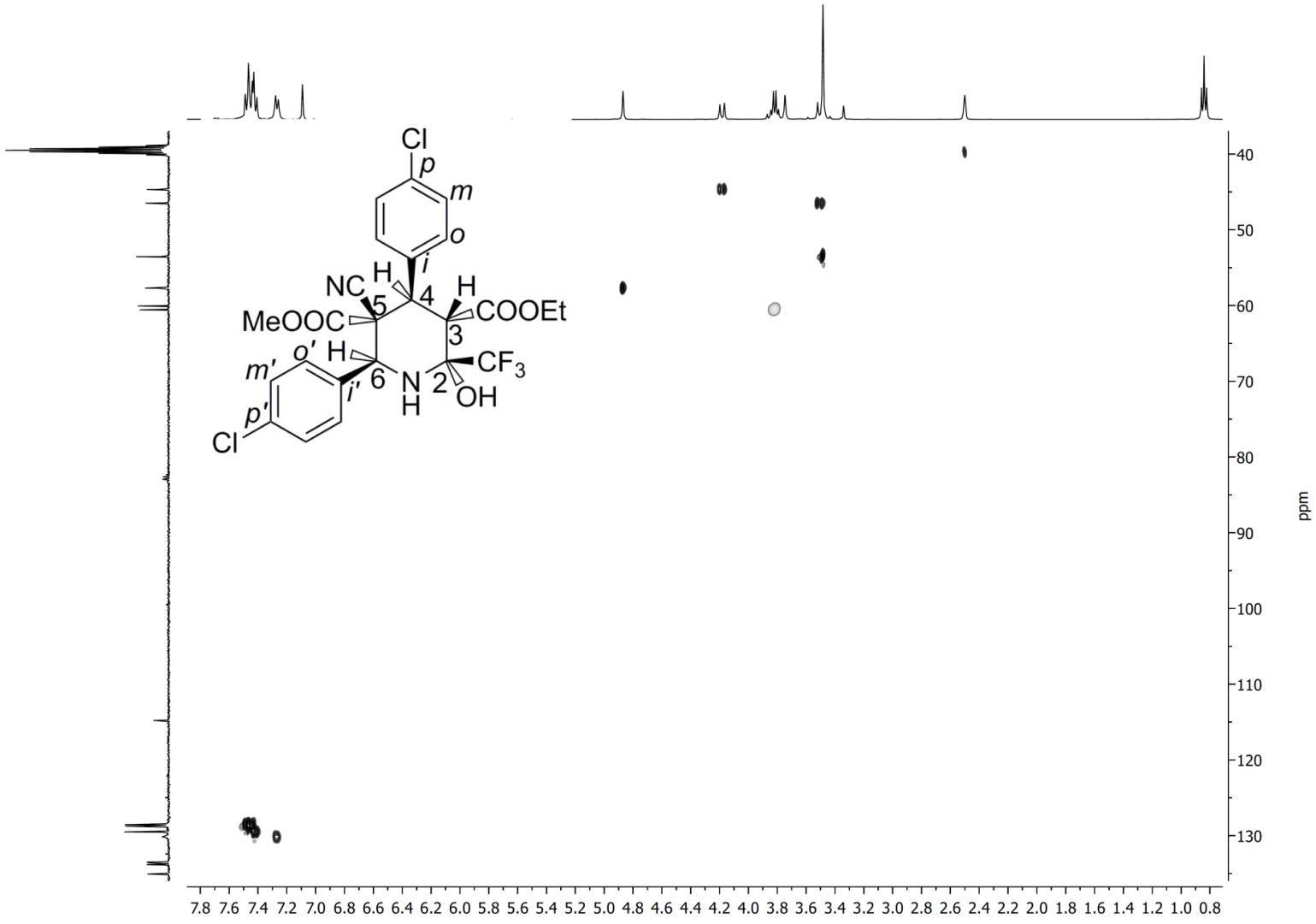
^{1}H-^{13}C HMBC NMR spectrum of the compound **3d**, 400MHz, DMSO-d_6, 298 K.



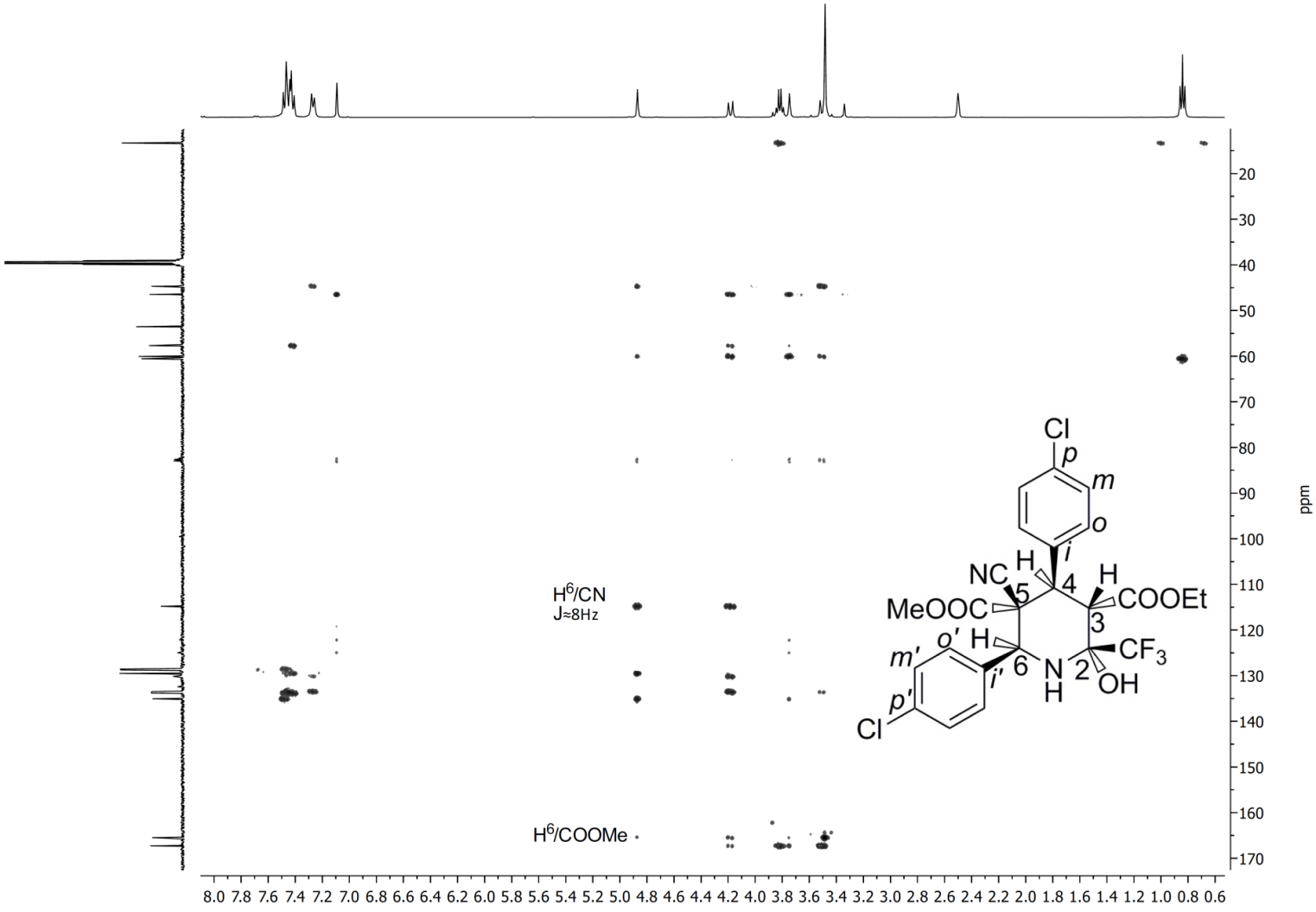
^{1}H-^{1}H NOESY NMR spectrum of the compound **3d**, 400MHz, DMSO-d_6, 298 K. The key correlations are subscribed.



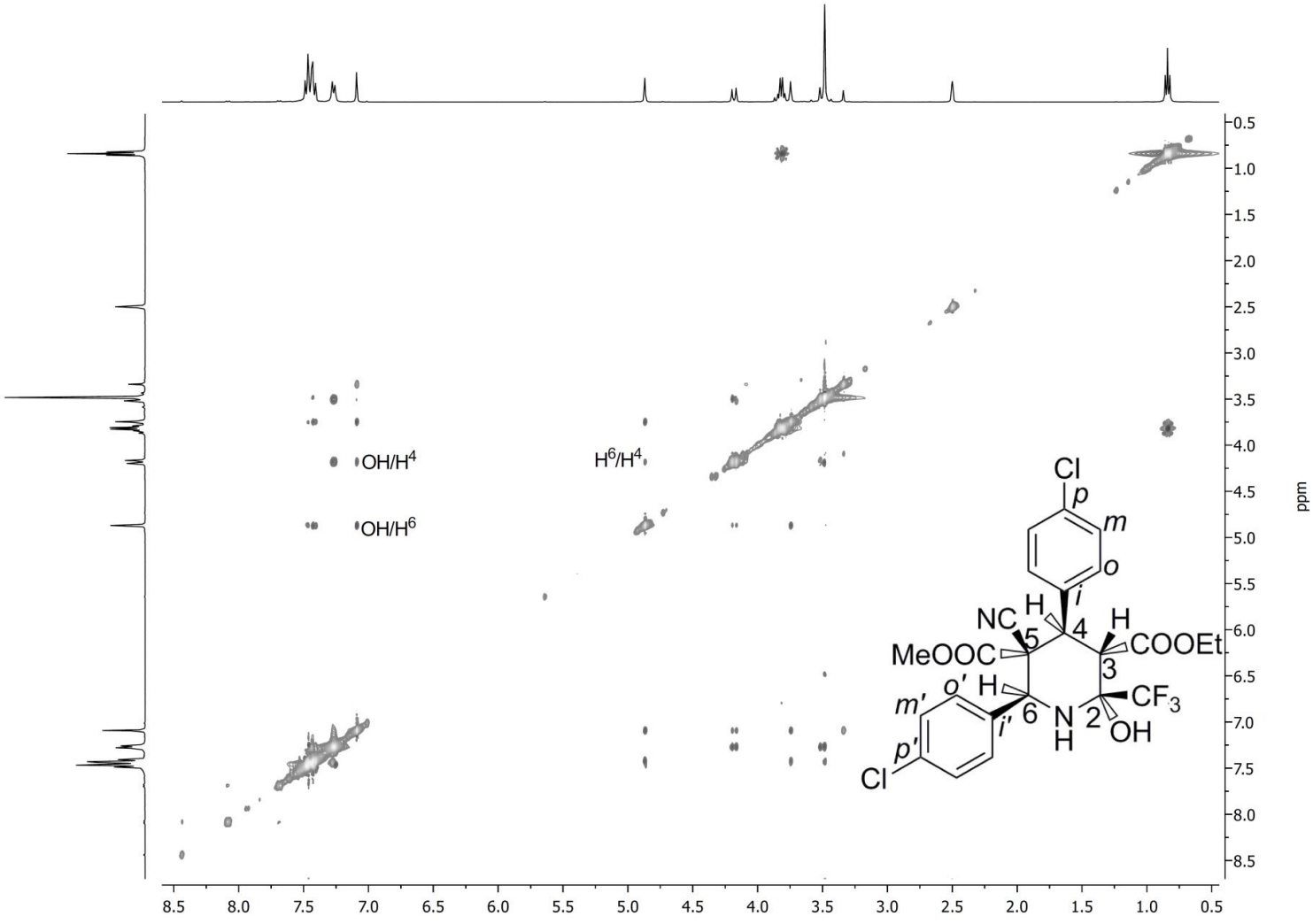
^{1}H-^{1}H COSY NMR spectrum of the compound **3j**, 400MHz, DMSO-d_6, 298 K.



The fragment of ^{1}H-^{13}CHSQC NMR spectrum of the compound **3j**, 400MHz, DMSO-d_6, 298 K.



^{1}H-^{13}CHMBC NMR spectrum of the compound **3j**, 400MHz, DMSO-d_6, 298 K.



^{1}H-^{1}H NOESY NMR spectrum of the compound **3j**, 400MHz, DMSO-d_6, 298 K. The key correlations are subscribed