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Trifluoroacetyl substituted pyrazolotriazines: synthesis and pathways of formation

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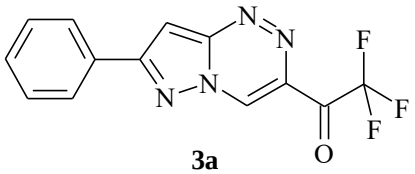
General information

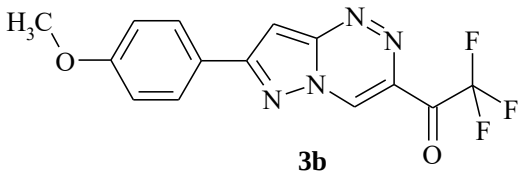
3-Aryl-1*H*-pyrazole-5-diazonium salts[S1,S2] **1a–d**, ethyl 5-diazopyrazole-4-carboxylate[S2,S3] **2'** and 4-dimethylamino-1,1,1-trifluorobut-3-en-2-one[S4] **4** were obtained as previously described.
IR spectra were recorded on a Bruker ALPHA FTIR spectrometer with a ZnSe ATR accessory for samples in the form of powders. ^{1}H (400.1 MHz), ^{13}C (101.6 MHz), ^{19}F (376.5 MHz) NMR spectra were recorded with a Bruker Avance II 400 spectrometer in DMSO-d_6 using TMS (^{1}H, ^{13}C), and $CFCl_3$ (^{19}F) as internal standards. The concerted application of ^{1}H–^{13}C 2D heteronuclear experiments HSQC and HMBC were used for the distinction of the carbon and proton resonances. Mass spectra were obtained on a Shimadzu GCMS-QP2010 Ultra instrument (EI ionization, 70 eV). Elemental analysis was performed on a PerkinElmer 2400 II CHNS-analyzer. Melting points were determined on a Stuart SMP-10 apparatus. Column chromatography was performed on SiO_2 (Merck 60 (0.063–0.2 mm)). Analytical TLC was performed using Silufol UV-254 plates (sorbent – silica gel CTX-1A) and solvent systems such as $CHCl_3$–EtOH (20:1); C_6H_{14}–EtOAc (1:3).
The NMR tubes (5 mm) were used for the monitoring of the reactions (**1b** → **3b**, **2'** → **7**). The amounts of each substance were determined by integration of the corresponding protone signals. A solutions of amino enone **4** (0.05 mmol), pyrazole-5-diazonium salt **1b** (0.05 mmol), 5-diazopyrazole **2'** (0.05 mmol) and hydrazone **6d** (0.05 mmol) in DMSO-d_6 were prepared and added to NMR tube. The ^{1}H NMR spectra were detected immediately after mixing. The time of each experiment depended on the reaction rate. The spectra obtained were analyzed in comparison with the spectra of pure compounds.

1-(7-Arylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)-2,2,2-trifluoroethan-1-ones 3a–d (general procedure). To a suspension of corresponding 3-aryl-1*H*-pyrazole-5-diazonium salt **1a–d** (1.0 mmol) in dry MeCN (3 ml) at 0°C was added a solution of 4-dimethylamino-1,1,1-trifluorobut-3-en-2-one **4** (167 mg, 1.0 mmol) in dry MeCN (2 ml). The mixture was allowed to warm up to room temperature and kept at this temperature and stirring for 1.5–2.0 h until the disappearance of the reactants (TLC). The resulting precipitate was filtered out; the filtrate was evaporated at reduced pressure. Chromatographic identical precipitates were combined and recrystallized from ethyl acetate–hexane mixture.



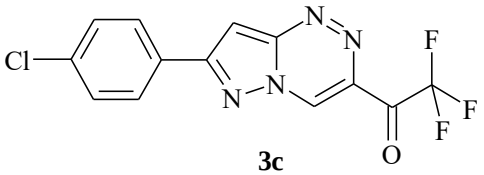
3a

2,2,2-Trifluoro-1-(7-phenylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)ethan-1-one (**3a**). Yield 200 mg (68%), yellow solid, mp 190–192 °C. IR spectrum, ν, cm^{-1}: 598, 675, 692, 707, 754, 772, 799, 837, 903, 932, 991, 1028, 1065, 1138, 1155, 1177, 1200, 1223, 1251, 1293, 1334, 1345, 1443, 1463, 1479, 1515, 1534, 1576, 1589, 1736, 3030, 3137, 3267, 3385. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 7.51–7.58 (3H, m, 3',4',5'-H); 8.04 (1H, s, 8-H); 8.17 (2H, d, *J* = 8.0, 2',6'-H); 9.25 (1H, s, 4-H). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm: -71.6 (s, CF_3). Mass spectrum, *m*/*z* (I_{rel}, %): 292 (85) $[M]^+$, 223 (68) $[M-CF_3]^+$ (68), 167 (3) $[M-N_2COCF_3]^+$, 143 (48) $[M-C_2N_2COCF_3]^+$. Found, %: C 53.32; H 2.57; N 18.95. $C_{13}H_7F_3N_4O$. Calculated, %: C 53.43; H 2.41; N 19.17.



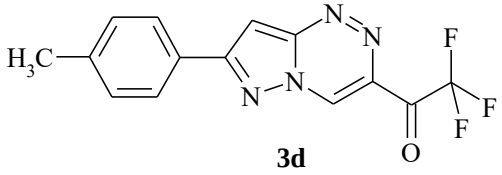
3b

2,2,2-Trifluoro-1-(7-(4-methoxyphenyl)pyrazolo[5,1-*c*][1,2,4]triazin-3-yl)ethan-1-one (**3b**). Yield 225 mg (70%), beige solid, mp 184–186 °C. IR spectrum, ν, cm^{-1}: 522, 545, 570, 667, 738, 750, 796, 836, 910, 929, 997, 1020, 1054, 1113, 1158, 1186, 1202, 1240, 1260, 1292, 1305, 1316, 1365, 1423, 1438, 1456, 1483, 1536, 1566, 1580, 1605, 1725, 2849, 2917, 2947, 2965, 2984, 3022, 3053, 3069, 3125, 3157. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 3.81 (3H, s, OCH_3); 6.93 (2H, d, *J* = 8.2, 3',5'-H); 7.88 (1H, s, 8-H); 8.02 (2H, d, *J* = 8.2, 2',6'-H); 9.24 (1H, s, 4-H). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm: -70.3 (s, CF_3). Mass spectrum, *m*/*z* (I_{rel}, %): 322 (100) $[M]^+$, 253 (24) $[M\text{-}CF_3]^+$, 197 (6) $[M\text{-}N_2COCF_3]^+$, 173 (33) $[M\text{-}C_2N_2COCF_3]^+$. Found, %: C 51.87; H 2.94; N 17.15. $C_{14}H_9F_3N_4O_2$. Calculated, %: 52.18; H 2.82; N 17.39.



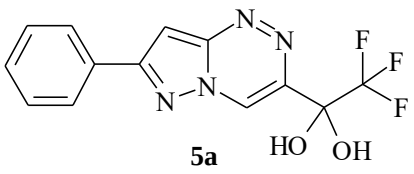
3c

1-(7-(4-Chlorophenyl)pyrazolo[5,1-*c*][1,2,4]triazin-3-yl)-2,2,2-trifluoroethan-1-one (**3c**). Yield 240 mg (73%), yellow solid, mp 130–135 °C. IR spectrum, ν, cm^{-1}: 512, 554, 557, 589, 634, 686, 736, 754, 793, 837, 911, 953, 987, 1012, 1069, 1092, 1115, 1174, 1213, 1250, 1295, 1326, 1360, 1409, 1453, 1487, 1507, 1527, 1552, 1586, 1601, 1709, 3059, 3141, 3203, 3216, 3255, 3267, 3294. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 7.64 (2H, d, *J* = 8.5, 3',5'-H); 8.07 (1H, s, 8-H); 8.18 (2H, d, *J* = 8.5, 2',6'-H); 9.26 (1H, s, 4-H). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 95.4 (s, C-8), 122.7 (s, C-4), 128.0 (q, *J* = 290.0, CF_3), 128.5 (s, C-2',6'), 129.2 (s, C-3',5'), 130.0 (s, C-1'), 134.8 (s, C-4'), 143.0 (s, C-3), 151.0 (s, C-9), 156.3 (s, C-7), 180.8 (q, *J* = 32.2, **C**OCF_3). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm: -70.2 (s, CF_3). Mass spectrum, *m*/*z* (I_{rel}, %): 326 (77) $[M]^+$, 257 (67) $[M\text{-}CF_3]^+$, 201 (3) $[M\text{-}N_2COCF_3]^+$, 177 (21) $[M\text{-}C_2N_2COCF_3]^+$. Found, %: C 47.34; H 2.03; N 17.29. $C_{13}H_6ClF_3N_4O$. Calculated, %: C 47.80; H 1.85; N 17.15.



3d

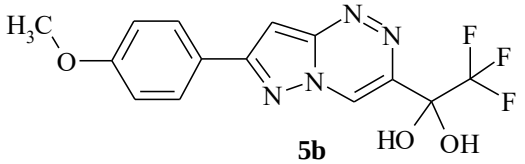
2,2,2-Trifluoro-1-(7-(*p*-tolyl)pyrazolo[5,1-*c*][1,2,4]triazin-3-yl)ethan-1-one (**3d**). Yield 190 mg (62%), beige solid, mp 206–207 °C. IR spectrum, ν, cm^{-1}: 593, 681, 692, 703, 758, 804, 835, 909, 934, 995, 1034, 1062, 1140, 1174, 1205, 1243, 1290, 1333, 1350, 1447, 1463, 1482, 1520, 1537, 1579, 1594, 1732, 3031, 3135, 3277, 3384. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 2.38 (3H, s, CH_3); 7.36 (2H, d, *J* = 7.9, 3',5'-H); 7.96 (1H, s, 8-H); 8.04 (2H, d, *J* = 7.9, 2',6'-H); 9.22 (1H, s, 4-H). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm: -70.5 (s, CF_3). Mass spectrum, *m*/*z* (I_{rel}, %): 306 (100) $[M]^+$ (100), 237 (65) $[M\text{-}CF_3]^+$, 181 (6) $[M\text{-}N_2COCF_3]^+$, 157 (56) $[M\text{-}C_2N_2COCF_3]^+$. Found, %: C 54.73; H 3.03; N 18.44. $C_{14}H_9F_3N_4O$. Calculated, %: C 54.91; H 2.96; N 18.29.



5a

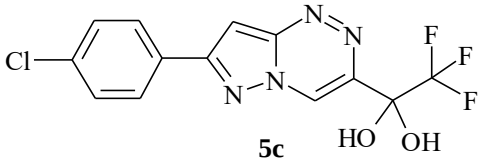
2,2,2-Trifluoro-1-(7-phenylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)ethane-1,1-diol (**5a**). Compound **3a** (60 mg, 0.2 mmol) was suspended in 5 ml of water at room temperature and mixed for 15 min. Precipitate was filtered out, dried in air. Yield 60 mg (94%), pale yellow solid, mp 166–168 °C. IR spectrum, ν, cm^{-1}: 555, 618, 672, 693, 707, 754, 772, 799, 853, 903, 933, 991, 1029, 1065, 1139, 1156, 1178, 1202, 1223, 1251, 1294, 1334, 1345, 1444, 1463, 1478, 1515, 1535, 1577, 1589, 3030, 3064, 3138, 3186, 3217, 3231,

3266, 3310, 3335, 3383. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 7.51–7.44 (3H, m, 3',4',5'-H); 7.84 (1H, s, 8-H); 8.06 (2H, s, 2OH); 8.11 (2H, d, *J* = 8.0, 2',6'-H); 9.05 (1H, s, 4-H). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 91.8 (q, *J* = 32.2, **C**$(OH)_2$), 95.1 (s, C-8), 122.7 (s, C-4), 126.8 (s, C-2',6'), 127.1 (q, *J* = 290.0, CF_3), 129.1 (s, C-3',5'), 130.1 (s, C-1'), 131.1 (s, C-4'), 142.9 (s, C-3), 151.0 (s, C-9), 157.6 (s, C-7). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm: -82.1 (s, CF_3). Mass spectrum, *m/z* (I_{rel}, %): 310 (5) $[M]^+$, 292 (95) $[M\text{-}H_2O]^+$, 241 (12), 224 (11), 223 (73) $[M\text{-}H_2OCF_3]^+$, 167 (4) $[M\text{-}N_2CH_2O_2CF_3]^+$, 143 (49) $[M\text{-}C_2N_2\ CH_2O_2CF_3]^+$, 142 (36), 128 (9), 116 (16), 112 (10), 103 (11), 102 (16), 89 (8), 78 (11), 77 (100), 76 (12), 69 (13), 64 (9), 53 (69), 51 (35), 50 (10), 39 (7). Found, %: C 50.57; H 2.73; N 18.25. $C_{13}H_9F_3N_4O_2$. Calculated, %: C 50.33; H 2.92; N 18.06.



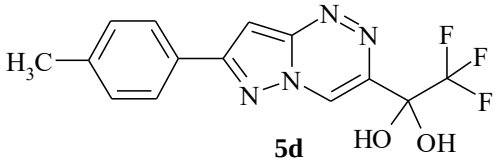
5b

2,2,2-Trifluoro-1-(7-(4-methoxyphenyl)pyrazolo[5,1-*c*][1,2,4]triazin-3-yl)ethane-1,1-diol (**5b**). It was registered in the NMR tube in DMSO-d_6. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 3.86 (3H, s, OCH_3); 7.01 (2H, d, *J* = 8.4, 3',5'-H); 7.72 (1H, s, 8-H); 8.04 (4H, m, 2',6'-H + 2OH); 9.01 (1H, s, 4-H). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 56.4 (s, OCH_3), 91.6 (q, *J* = 32.0, $C(OH)_2$), 95.2 (s, C-8), 116.2 (s, C-3',5'), 122.6 (s, C-4), 122.5 (s, C-1'), 124.2 (q, *J* = 290.0, CF_3), 128.0 (s, C-2',6'), 142.8 (s, C-3), 151.0 (s, C-9), 157.5 (s, C-7), 159.8 (s, C-4'). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm: -81.9 (s, CF_3).



5c

1-(7-(4-Chlorophenyl)pyrazolo[5,1-*c*][1,2,4]triazin-3-yl)-2,2,2-trifluoroethane-1,1-diol (**5c**). It was registered in the NMR tube in DMSO-d_6. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 7.53 (2H, d, *J* = 8.5, 3',5'-H); 7.90 (1H, s, 8-H); 8.07 (2H, br.s, 2OH); 8.13 (2H, d, *J* = 8.5, 2',6'-H); 9.05 (1H, s, 4-H). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 91.7 (q, *J* = 32.1, **C**$(OH)_2$), 94.9 (s, C-8), 122.5 (s, C-4), 123.0 (q, *J* = 290.0, CF_3), 128.2 (s, C-2',6'), 129.0 (s, C-3',5'), 130.0 (s, C-1'), 135.4 (s, C-4'), 143.0 (s, C-3), 151.1 (s, C-9), 157.3 (s, C-7). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm: -81.7 (s, CF_3).

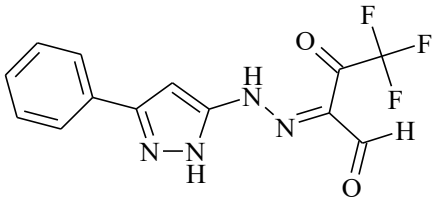


5d

2,2,2-Trifluoro-1-(7-(*p*-tolyl)pyrazolo[5,1-*c*][1,2,4]triazin-3-yl)ethane-1,1-diol (**5d**). It was registered in the NMR tube in DMSO-d_6. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 2.42 (3H, s, CH_3); 7.30 (2H, d, *J* = 8.0, 3',5'-H); 7.73 (1H, s, 8-H); 7.98 (2H, d, *J* = 8.0, 2',6'-H); 8.02 (2H, br.s, 2OH); 8.99 (1H, s, 4-H). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 20.9 (s, CH_3), 91.8 (q, *J* = 32.2, **C**$(OH)_2$), 94.6 (s, C-8), 122.4 (s, C-4), 123.1 (q, *J* = 290.0, CF_3), 126.6 (s, C-2',6'), 128.2 (s, C-1'), 129.6 (s, C-3',5'), 139.8 (s, C-4'), 142.7 (s, C-3), 151.0 (s, C-9), 157.7 (s, C-7). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm: -82.2 (s, CF_3).

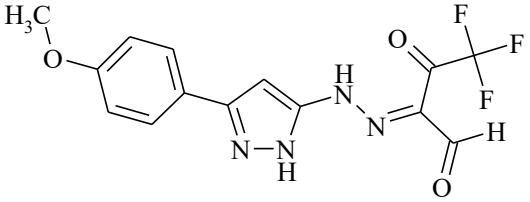
5-[*N*'-(3,3,3-Trifluoro-1-formyl-2-oxopropylidene)hydrazino]-3-*R*-4-*R*'-1*H*-pyrazoles 6a–d (general procedure). To a cooled mixture of the appropriate 5-aminopyrazole (1.0 mmol) in 48% HBF_4 (3 ml, for 3-aryl-5-amino-1*H*-pyrazole) or 10% HCl (5 ml, for ethyl 5-amino-1*H*-pyrazole-4-carboxylate) at 0°C was slowly added an ice solution of sodium nitrite (83 mg, 1.2 mmol) of in water (3 ml). The resulting mixture was stirred at -5–0°C for 30–45 min, and then a solution of 4-dimethylamino-1,1,1-trifluorobut-3-en-2-one **4** (167 mg, 1.0 mmol) in water (2 ml) was added. The mixture was allowed to warm up to room temperature and kept at this temperature and stirring for 30–36 h until the disappearance of the reactants (TLC), then neutralized with saturated $NaHCO_3$ solution to pH 7. The product was extracted with chloroform (3 x 30

ml), the combined extract was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography (eluent ethyl acetate : hexane = 5 : 1).



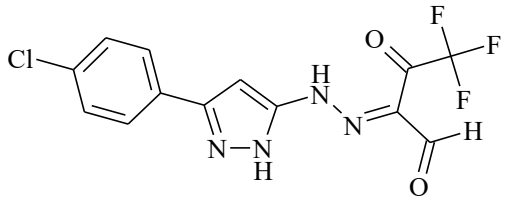
6a

3-Phenyl-5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole (**6a**). Yield 180 mg (58%), orange solid, mp 166–168 °C. IR spectrum, ν, cm^{-1}: 514, 555, 619, 646, 691, 707, 770, 841, 904, 927, 959, 978, 1028, 1066, 1103, 1139, 1157, 1178, 1252, 1268, 1295, 1355, 1383, 1415, 1452, 1463, 1534, 1599, 1664, 1697, 3029, 3061, 3096, 3154, 3204, 3223, 3238, 3295, 3360, 3385. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 6.34 (1H, s, 4-H), 7.39–7.42 (3H, m, 3',4',5'-H), 7.86 (2H, d, *J* = 8.0, 2',6'-H), 8.72 (1H, br.s, NH), 9.57 (1H, br.s, COH), 12.98 (1H, br.s, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 96.7 (s, C-4), 115.8 (q, *J* = 287.0, CF_3), 125.1 (s, C-2',6'), 128.0 (s, C-4'), 128.5 (s, C-3',5'), 129.9 (s, C-1'), 140.3 (s, C-3), 153.4 (s, C-5), 158.3 (s, C=N), 176.7 (q, *J* = 32.0, **C**OCF_3), 187.3 (s, **C**OH). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm: -77.8 (s, CF_3). Found, %: C 50.47; H 2.87; N 17.89. $C_{13}H_9F_3N_4O_2$. Calculated, %: C 50.33; H 2.92; N 18.06.



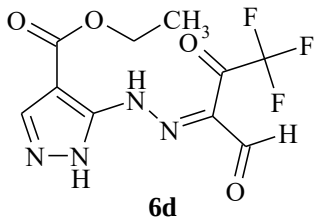
6b

3-(4-Methoxyphenyl)-5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole (**6b**). Yield 194 mg (57%), beige solid, mp 170–172 °C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 6.26 (1H, s, 4-H), 7.77 (2H, d, *J* = 8.5, 3',5'-H), 7.93 (2H, d, *J* = 8.5, 2',6'-H), 8.68 (1H, br.s, NH), 9.57 (1H, br.s, COH), 12.64 (1H, s, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 55.9 (s, OCH_3), 96.7 (s, C-4), 116.2 (q, *J* = 287.0, CF_3), 117.2 (s, C-3',5'), 123.6 (s, C-1'), 127.7 (s, C-2',6'), 142.4 (s, C-3), 155.1 (s, C-5), 157.6 (s, C=N), 159.2 (s, C-4'), 176.6 (q, *J* = 31.0, **C**OCF_3), 187.4 (s, **C**OH). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm (*J*, Hz): -77.7 (s, CF_3). Found, %: C 49.62; H 3.37; N 16.28. $C_{14}H_{11}F_3N_4O_3$. Calculated, %: C 49.42; H 3.26; N 16.47.



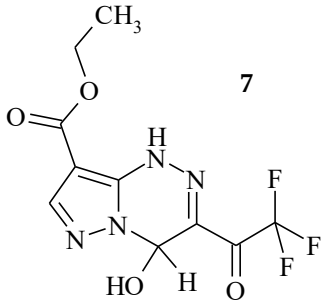
6c

3-(4-Chlorophenyl)-5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole (**6c**). Yield 210 mg (61%), pale brown solid, mp 162–163 °C. IR spectrum, ν, cm^{-1}: 539, 553, 601, 639, 714, 773, 797, 836, 904, 918, 957, 980, 1014, 1091, 1138, 1259, 1315, 1418, 1453, 1472, 1510, 1539, 1602, 1683, 1697, 3020, 3044, 3110, 3149, 3257, 3384. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 6.38 (1H, s, 4-H), 7.41 (2H, d, *J* = 8.5, 3',5'-H), 7.88 (2H, d, *J* = 8.5, 2',6'-H), 8.75 (1H, br.s, NH), 9.57 (1H, br.s, COH), 13.00 (1H, s, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 97.3 (s, C-4), 116.5 (q, *J* = 288.0, CF_3), 128.8 (s, C-2',6'), 129.7 (s, C-3',5'), 131.2 (s, C-1'), 134.8 (s, C-4'), 142.6 (s, C-3), 156.5 (s, C-5), 157.8 (s, C=N), 176.8 (q, *J* = 32.0, **C**OCF_3), 187.4 (s, **C**OH). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm (*J*, Hz): -77.5 (s, CF_3). Found, %: C 45.42; H 2.47; N 16.17. $C_{13}H_8ClF_3N_4O_2$. Calculated, %: C 45.30; H 2.34; N 16.25.



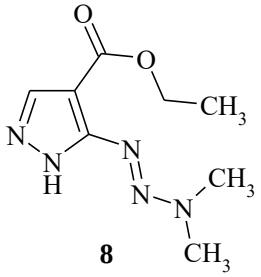
6d

Ethyl 5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole-4-carboxylate (**6d**). Yield 159 mg (52%), beige solid, mp 198–200 °C. IR spectrum, ν, cm^{-1}: 518, 571, 606, 633, 650, 683, 722, 744, 770, 818, 844, 875, 893, 902, 920, 1010, 1054, 1088, 1177, 1211, 1244, 1307, 1348, 1374, 1464, 1543, 1586, 1600, 1622, 1677, 1695, 1713, 2722, 2841, 2951, 3003, 3088, 3107, 3123, 3166, 3195, 3246. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.33 (3H, t, *J* = 7.0, $COOCH_2C\mathbf{H}_3$); 4.30 (2H, q, *J* = 7.0, $COOC\mathbf{H}_2CH_3$); 7.97 (1H, s, 3-H), 9.12 (1H, br.s, NH), 9.62 (1H, br.s, C(O)H), 13.03 (1H, s, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.4 (s, $OCH_2\mathbf{C}H_3$); 59.9 (s, $O\mathbf{C}H_2CH_3$); 96.1 (s, C-4); 116.3 (q, *J* = 288.0, CF_3); 132.9 (s, C-3); 137.7 (s, C-5); 141.9 (s, C=N); 161.2 (s, **C**OOEt); 175.8 (q, *J* = 32.0, $\mathbf{C}OCF_3$); 186.7 (s, **C**OH). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm: -77.7 (s, CF_3). Mass spectrum, *m*/*z* (I_{rel}, %): 306 (23) $[M]^+$, 261 (11), 238 (11), 237 (99), 192 (8), 191 (100), 163 (30), 136 (8), 135 (17), 111 (9), 110 (16), 109 (17), 107 (8), 93 (4), 80 (5), 69 (24), 68 (11), 65 (7), 54 (11), 53 (19), 52 (36), 43 (6). Found, %: C 39.54; H 2.84; N 18.18. $C_{10}H_9F_3N_4O_4$. Calculated, %: C 39.23; H 2.96; N 18.30.



7

Ethyl 4-hydroxy-3-trifluoroacetyl-1,4-dihydropyrazolo[5,1-*c*][1,2,4]triazin-8-carboxylate (**7**). To a solution of ethyl 5-diazopyrazole-4-carboxylate **2'** (200 mg, 1.2 mmol) in dry MeCN (3 ml) at 0°C was added a solution of 4-dimethylamino-1,1,1-trifluorobut-3-en-2-one **4** (200 mg, 1.2 mmol) in dry MeCN (2 ml). The mixture was allowed to warm up to room temperature and kept at this temperature and stirring for 48 h until the disappearance of the reactants (TLC). The resulting precipitate was filtered off to afford product **7** in 24% yield. Additional crop of **7** and triazene **8** were isolated by column chromatography (eluent ethyl acetate : hexane = 6 : 1). Yield of **7** – 210 mg (57%), white solid, mp 206–208 °C. IR spectrum, ν, cm^{-1}: 580, 619, 639, 647, 682, 738, 752, 773, 808, 837, 863, 883, 910, 930, 958, 1050, 1081, 1157, 1200, 1210, 1235, 1294, 1359, 1383, 1420, 1484, 1521, 1566, 1607, 1683, 1713, 2731, 2839, 2954, 2998, 3017, 3091, 3131, 3197, 3226, 3240, 3252. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.29 (3H, t, *J* = 7.0, $OCH_2\underline{CH_3}$); 4.29 (2H, q, *J* = 7.0, $O\underline{CH_2}CH_3$); 6.53 (1H, d, *J* = 7.2, 4-H); 7.76 (1H, d, *J* = 7.2, C-OH); 8.00 (1H, s, 7-H); 13.04 (1H, s, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.4 (s, $OCH_2\mathbf{C}H_3$); 59.9 (s, $O\mathbf{C}H_2CH_3$); 69.3 (s, C-4); 96.9 (s, C-8); 116.4 (q, *J* = 289.0, CF_3); 133.9 (s, C-3); 136.9 (s, C-9); 141.1 (s, C-7); 161.2 (s, **C**OOEt); 175.6 (q, *J* = 32.4, $\mathbf{C}OCF_3$). ^{19}F NMR (376 MHz, DMSO-d_6), δ, ppm: -70.7 (s, CF_3). Mass spectrum, *m*/*z* (I_{rel}, %): 306 (100) $[M]^+$, 289 (12), 288 (6), 278 (9), 261 (21), 260 (45), 244 (17), 243 (69), 216 (11), 192 (6), 191 (66), 163 (16), 139 (7), 138 (20), 136 (9), 135 (7), 120 (12), 111 (7), 110 (32), 109 (57), 93 (6), 80 (5), 69 (31), 68 (10), 67 (13), 65 (9), 54 (13), 53 (36), 52 (45), 39 (5). Found, %: C 39.44; H 3.04; N 18.10. $C_{10}H_9F_3N_4O_4$. Calculated, %: C 39.23; H 2.96; N 18.30. Yield of triazene **8** was 84 mg (33%), pale yellow solid, mp 112–113 °C.



8

Ethyl 3-(3,3-dimethyltriaz-1-en-1-yl)pyrazole-4-carboxylate (**8**), **independent synthesis**. To a solution of ethyl 5-diazopyrazole-4-carboxylate **2'** (100 mg, 0.6 mmol) in dry MeCN (3 ml) at 0°C was added a 33% aqueous solution of dimethylamine (70 μl, 0.6 mmol). The mixture was allowed to warm up to room temperature and kept at this temperature and stirring for 2.0 h until the disappearance of reactant **2'** (TLC). Then the mixture was evaporated at reduced pressure; the residue was treated with diethyl ether. The resulting precipitate was filtered off and washed with diethyl ether. Yield 100 mg (79%), pale yellow solid, mp 112–113 °C (mp 113–115 °C[S5]). IR spectrum, ν, cm^{-1}: 608, 623, 643, 698, 775, 833, 874, 896, 950, 1020, 1079, 1120, 1133. 1187, 1243, 1277, 1334, 1373, 1404, 1439, 1478, 1498, 1572, 1684, 1710, 2769, 2813, 2901, 2982, 3034, 3095, 3134, 3153. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 1.23 (3H, t, *J* = 7.0, $COOCH_2C\mathbf{H}_3$); 3.18 (3H, s, NCH_3); 3.51 (3H, s, NCH_3); 4.14 (2H, q, *J* = 7.0, $COOC\mathbf{H}_2CH_3$); 7.81 (1H, br.s, 3-H); 12.94 (1H, br.s, NH). ^{13}C NMR spectrum (100 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 13.8 (s, $OCH_2\mathbf{C}H_3$), 35.5 (br.s, NCH_3), 42.7 (br.s, NCH_3), 58.6 (s, $O\mathbf{C}H_2CH_3$), 99.3 (s, C-4), 141.0 (s, C-3), 141.1 (s, C-5), 162.1 (s, C=O). Found, %: C 45.28; H 6.33; N 32.95. $C_8H_{13}N_5O_2$. Calculated, %: C 45.49; H 6.20; N 33.16.

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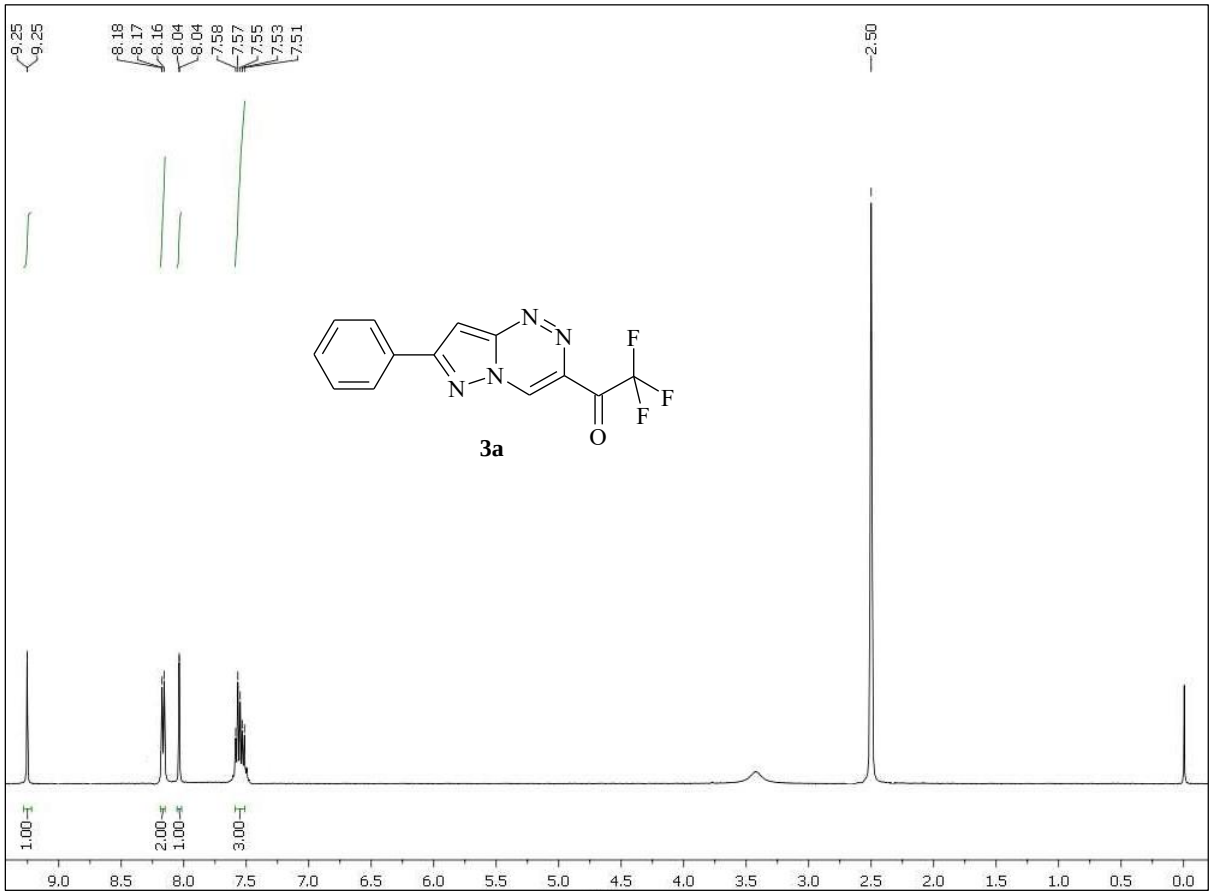


Figure S1. ^{1}H NMR of 2,2,2-trifluoro-1-(7-phenylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)ethan-1-one (**3a**)

Figure S2. ^{19}F NMR of 2,2,2-trifluoro-1-(7-phenylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)ethan-1-one (**3a**)

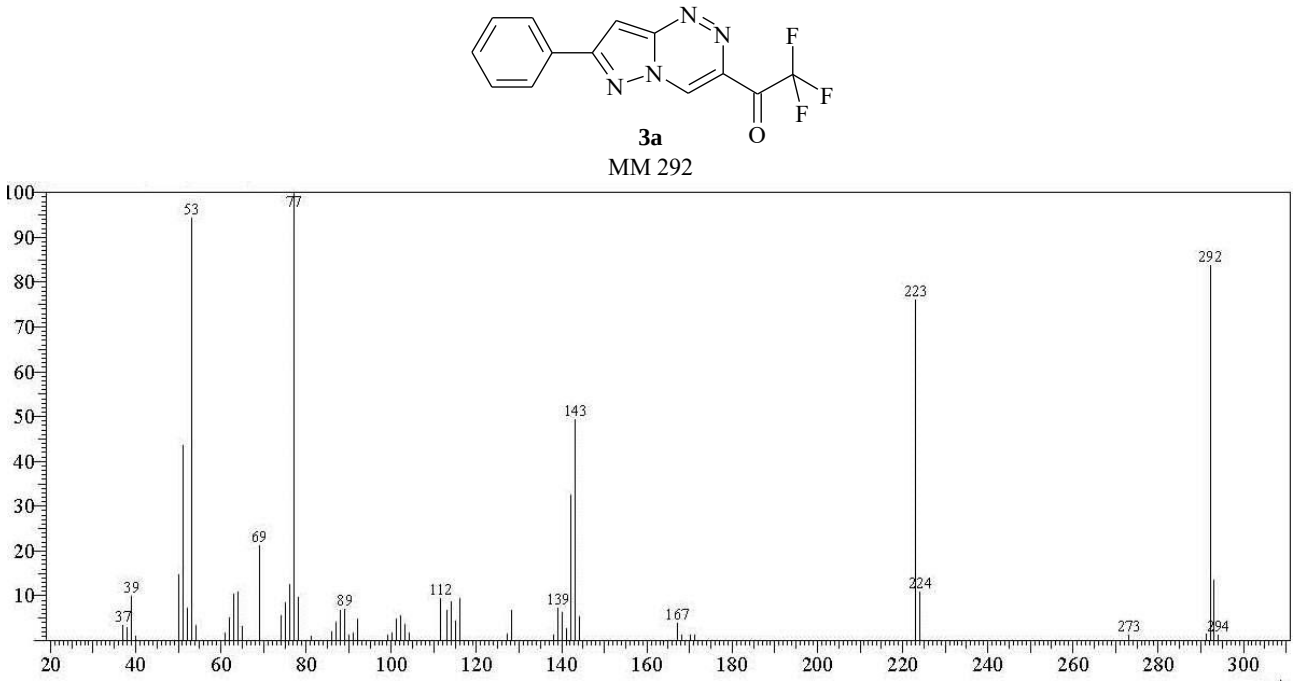


Figure S3. Mass-spectrum of compound **3a**

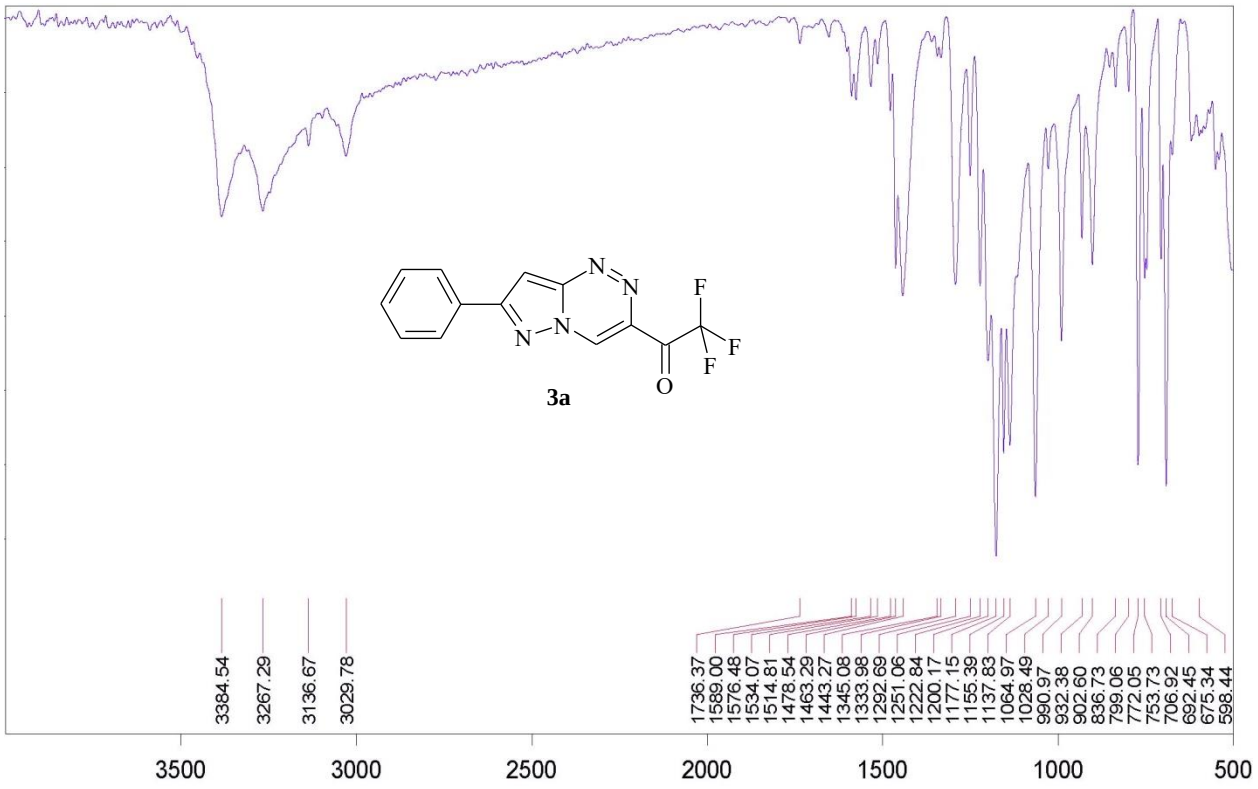


Figure S4. IR spectrum of 2,2,2-trifluoro-1-(7-phenylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)ethan-1-one (**3a**)

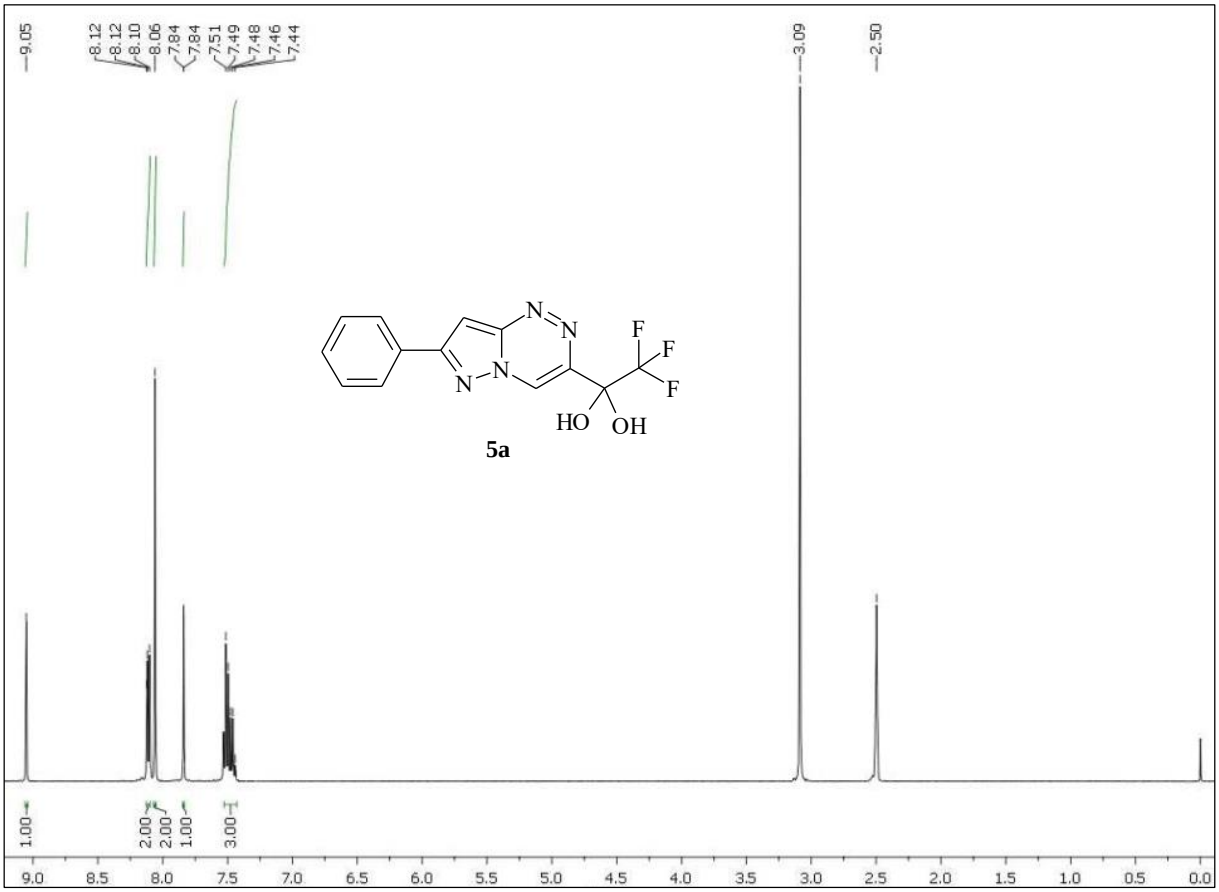


Figure S5. ^{1}H NMR of 2,2,2-trifluoro-1-(7-phenylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)ethane-1,1-diol (**5a**)

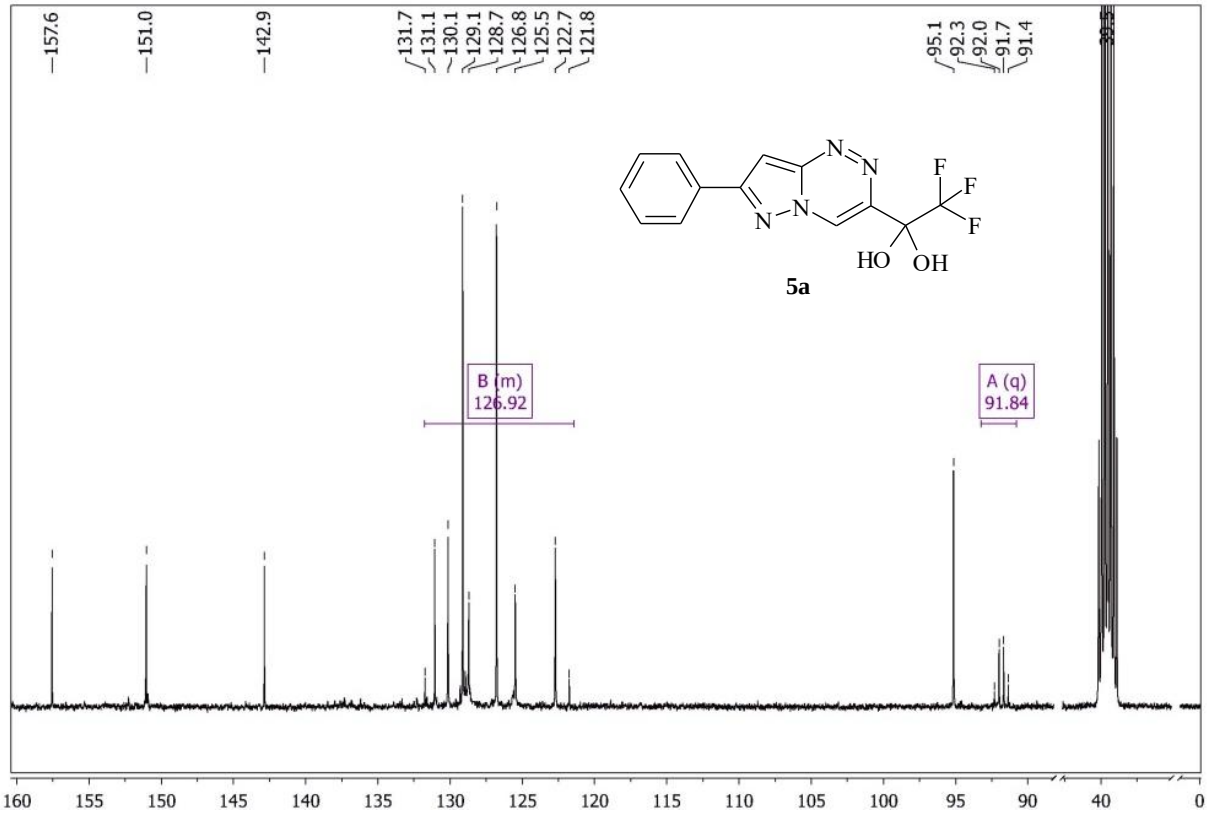


Figure S6. ^{13}C NMR of 2,2,2-trifluoro-1-(7-phenylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)ethane-1,1-diol (**5a**)

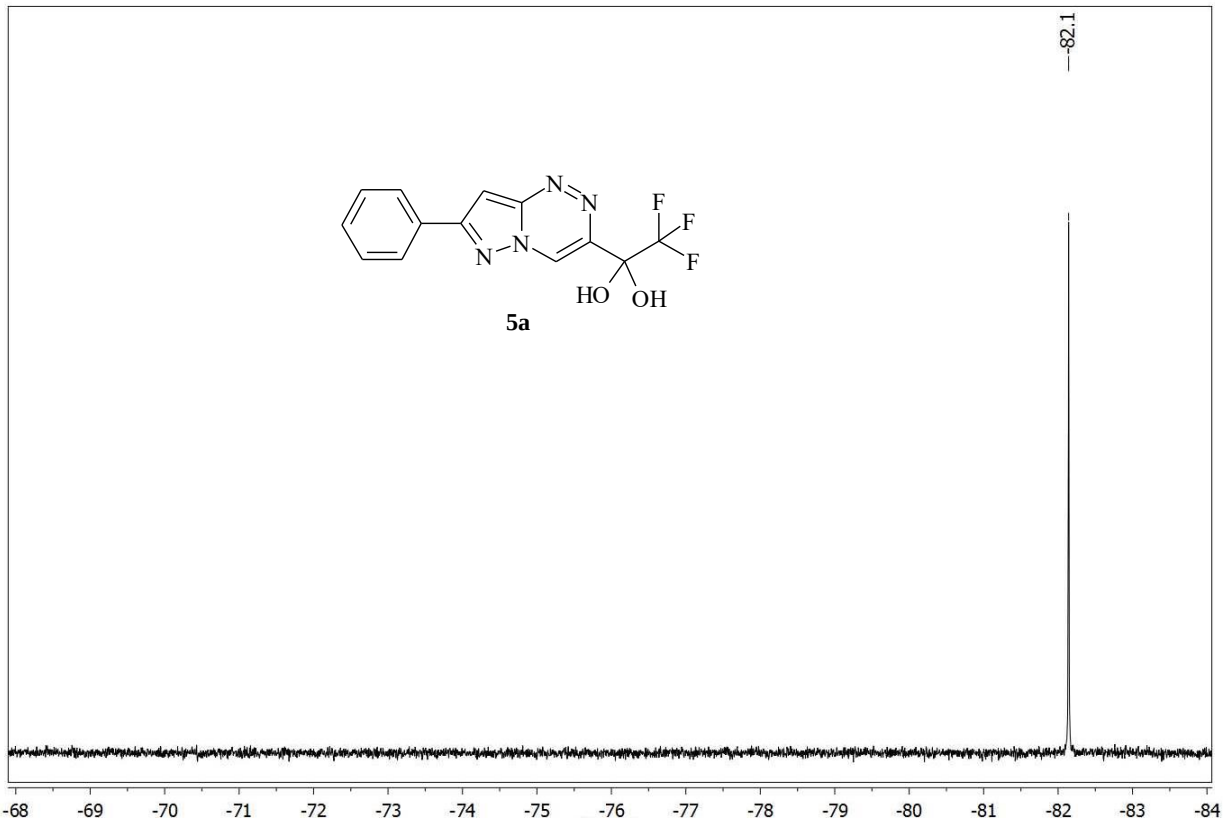


Figure S7. ^{19}F NMR of 2,2,2-trifluoro-1-(7-phenylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)ethane-1,1-diol (**5a**)

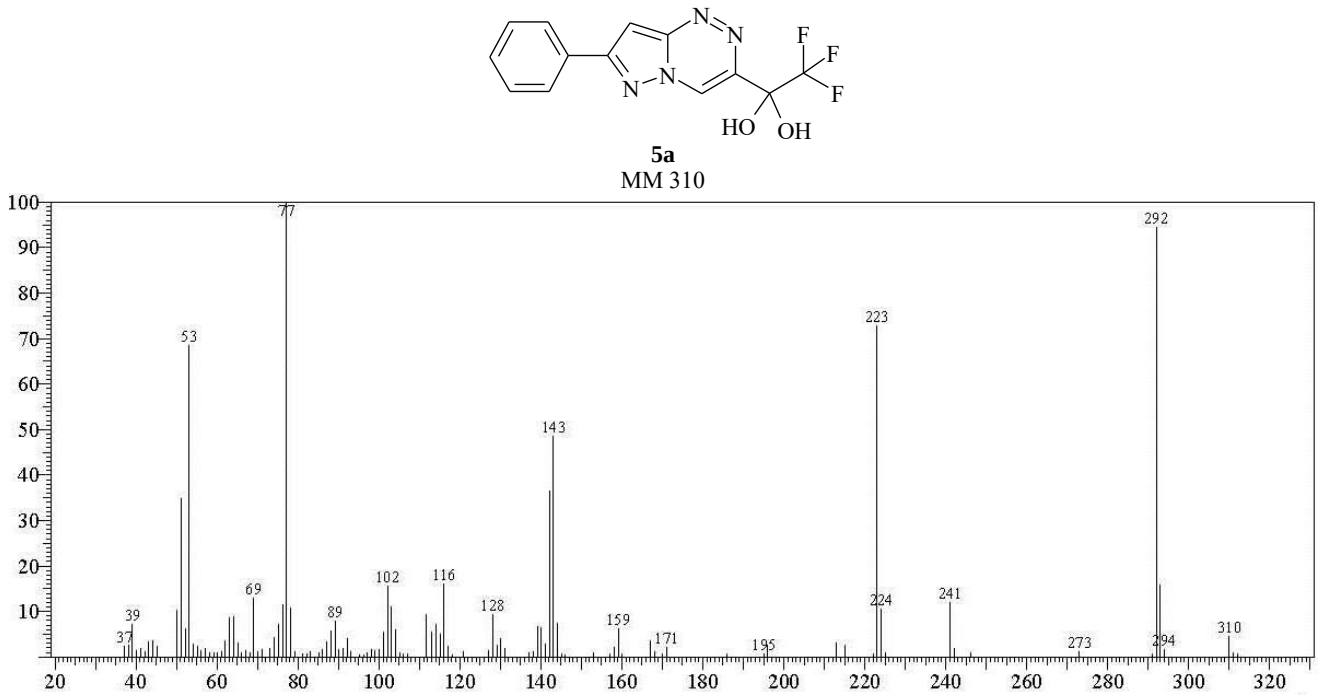
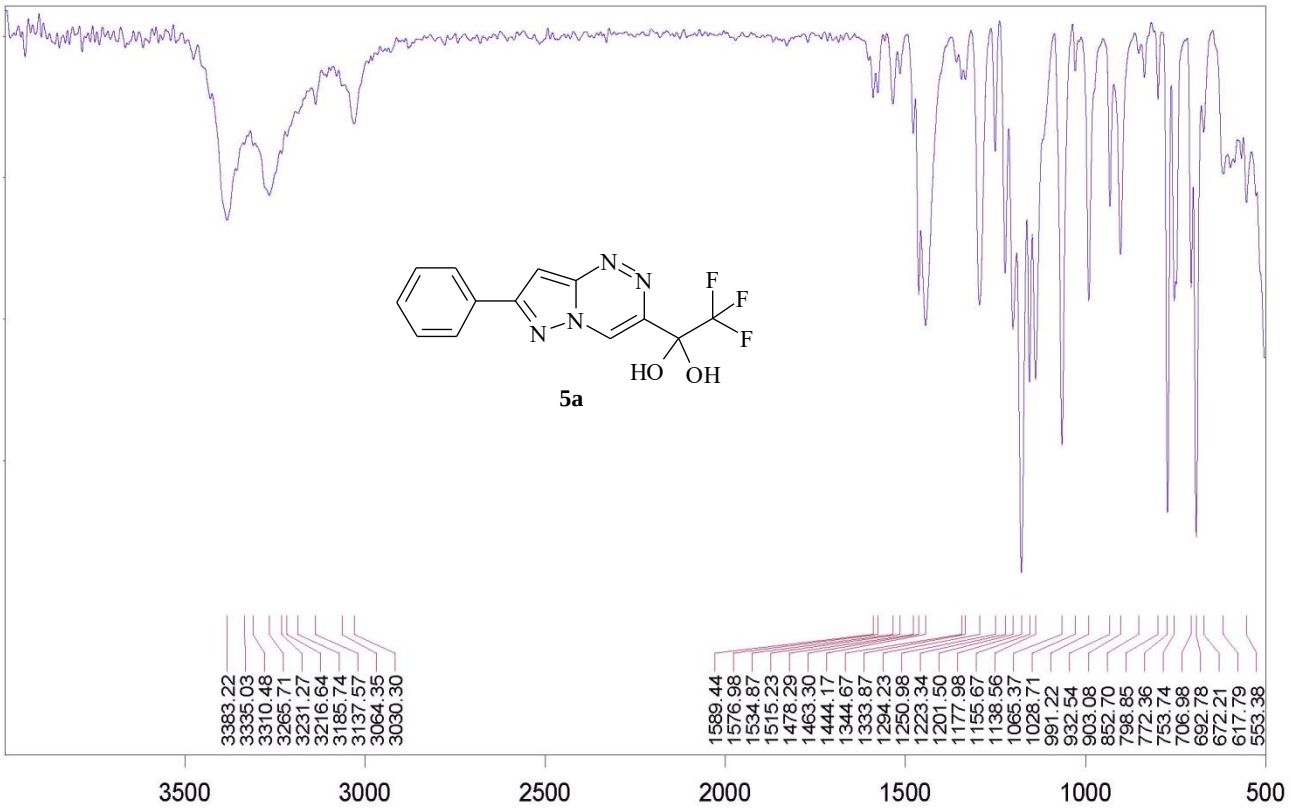
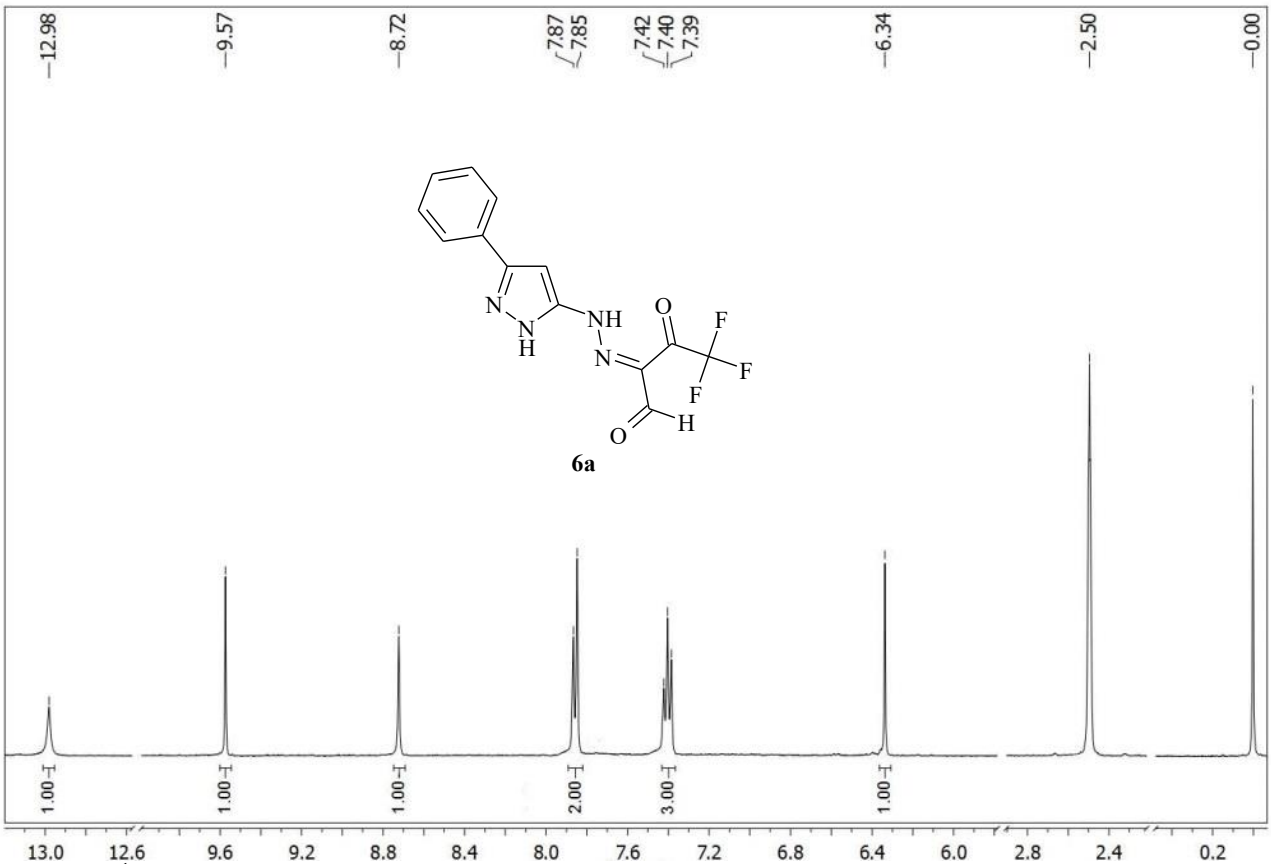


Figure S8. Mass-spectrum of compound **5a**



5a

Figure S9. IR spectrum of 2,2,2-trifluoro-1-(7-phenylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)-ethane-1,1-diol (**5a**)



6a

Figure S10. ^{1}H NMR of 3-phenyl-5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole (**6a**)

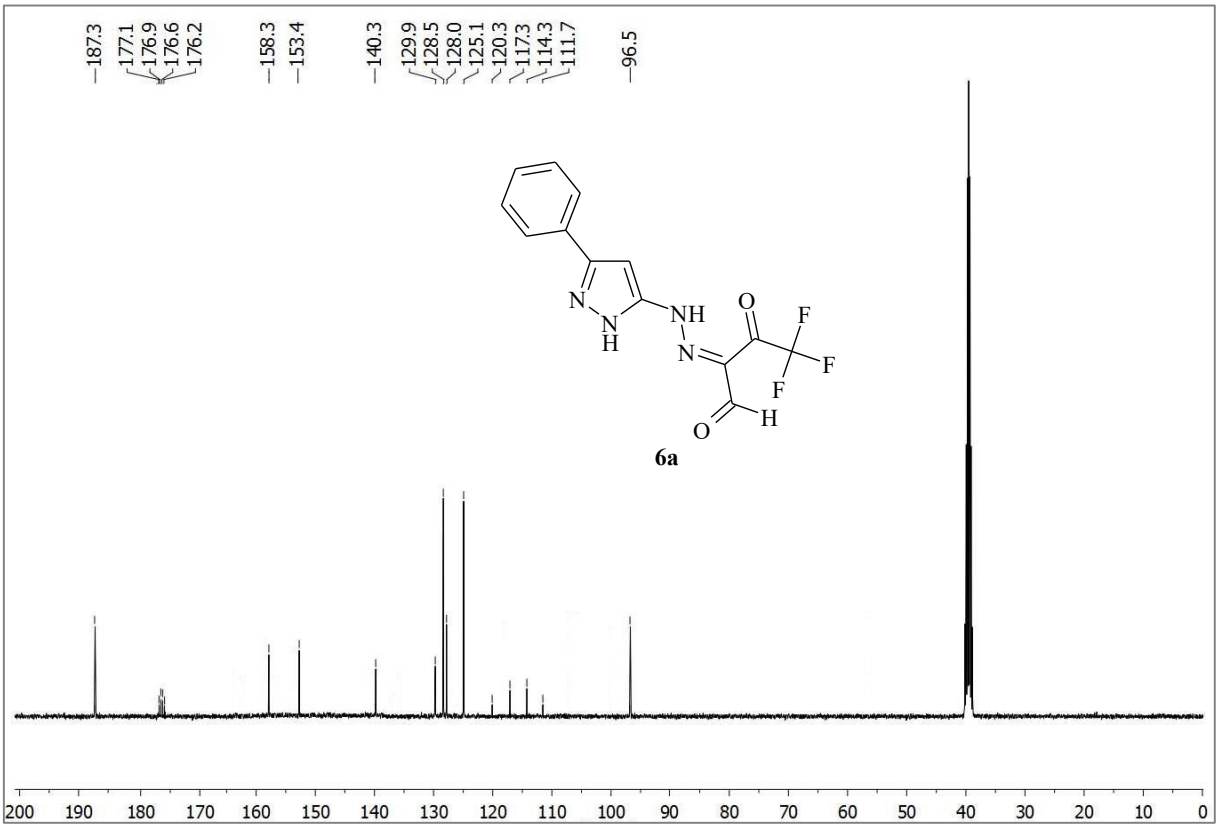


Figure S11. ^{13}C NMR of 3-phenyl-5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole (**6a**)

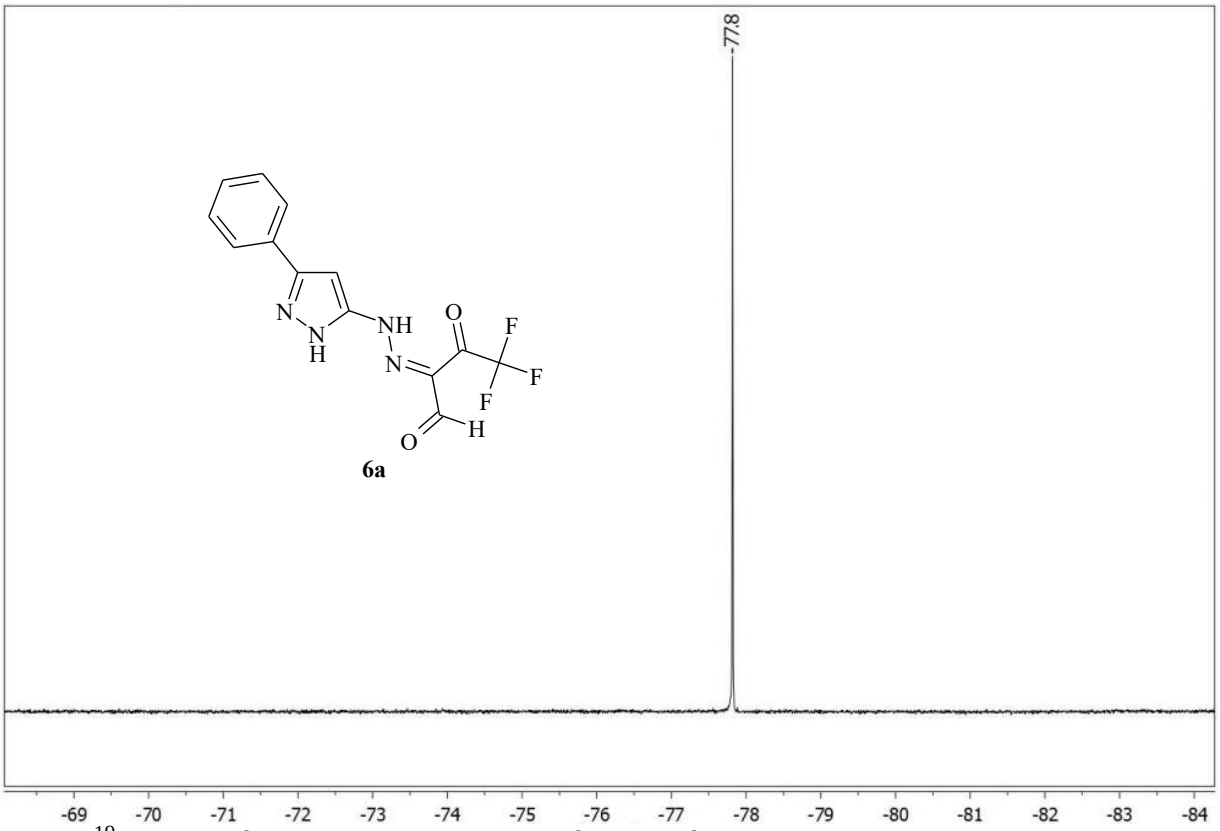


Figure S12. ^{19}F NMR of 3-phenyl-5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole (**6a**)

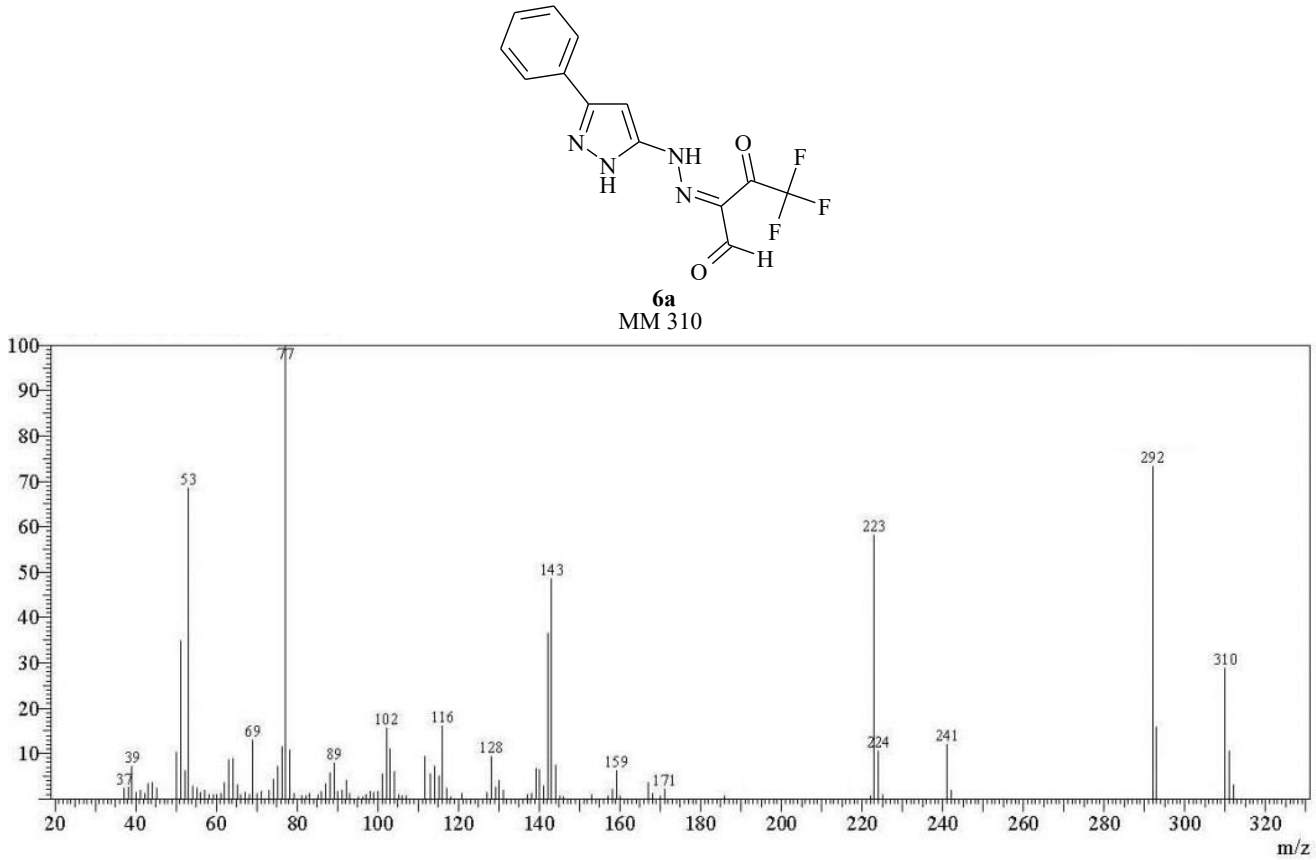


Figure S13. Mass-spectrum 3-phenyl-5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole (**6a**)

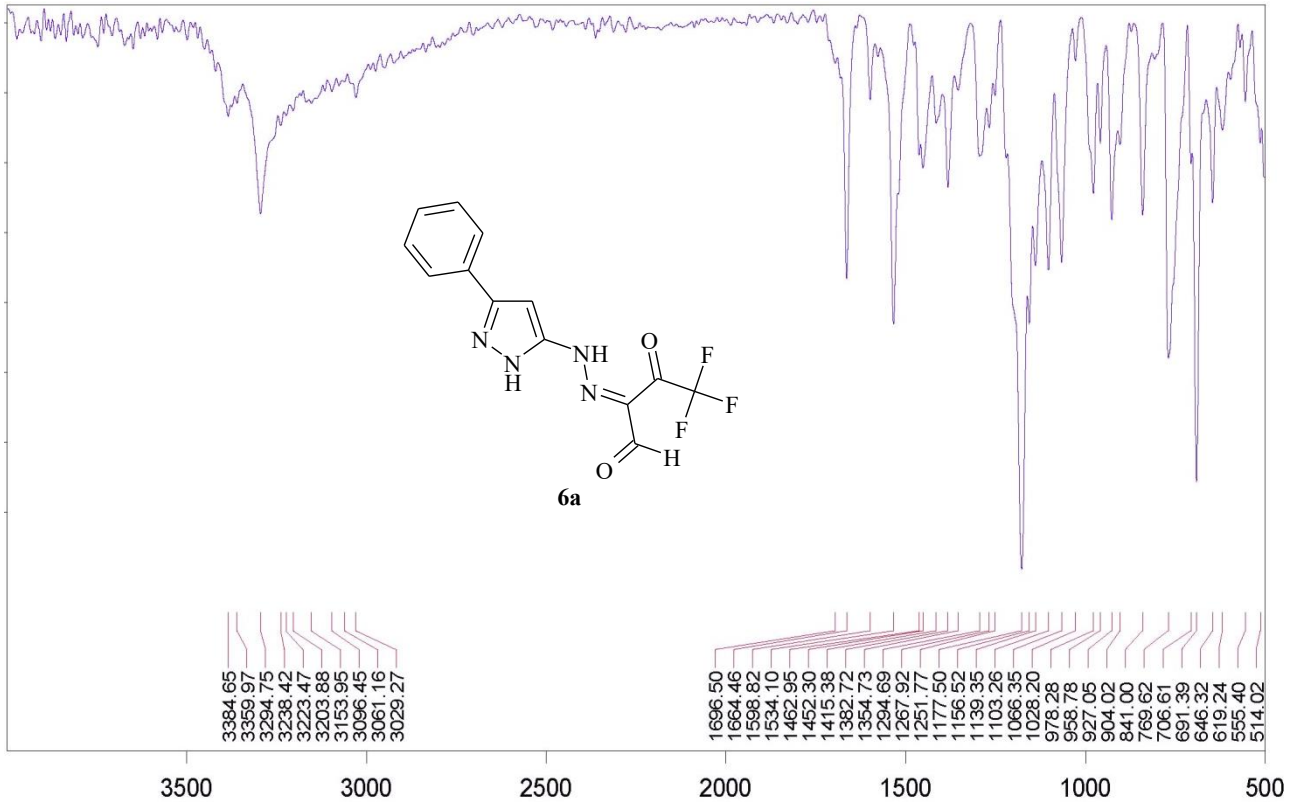


Figure S14. IR spectrum of 3-phenyl-5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole (**6a**)

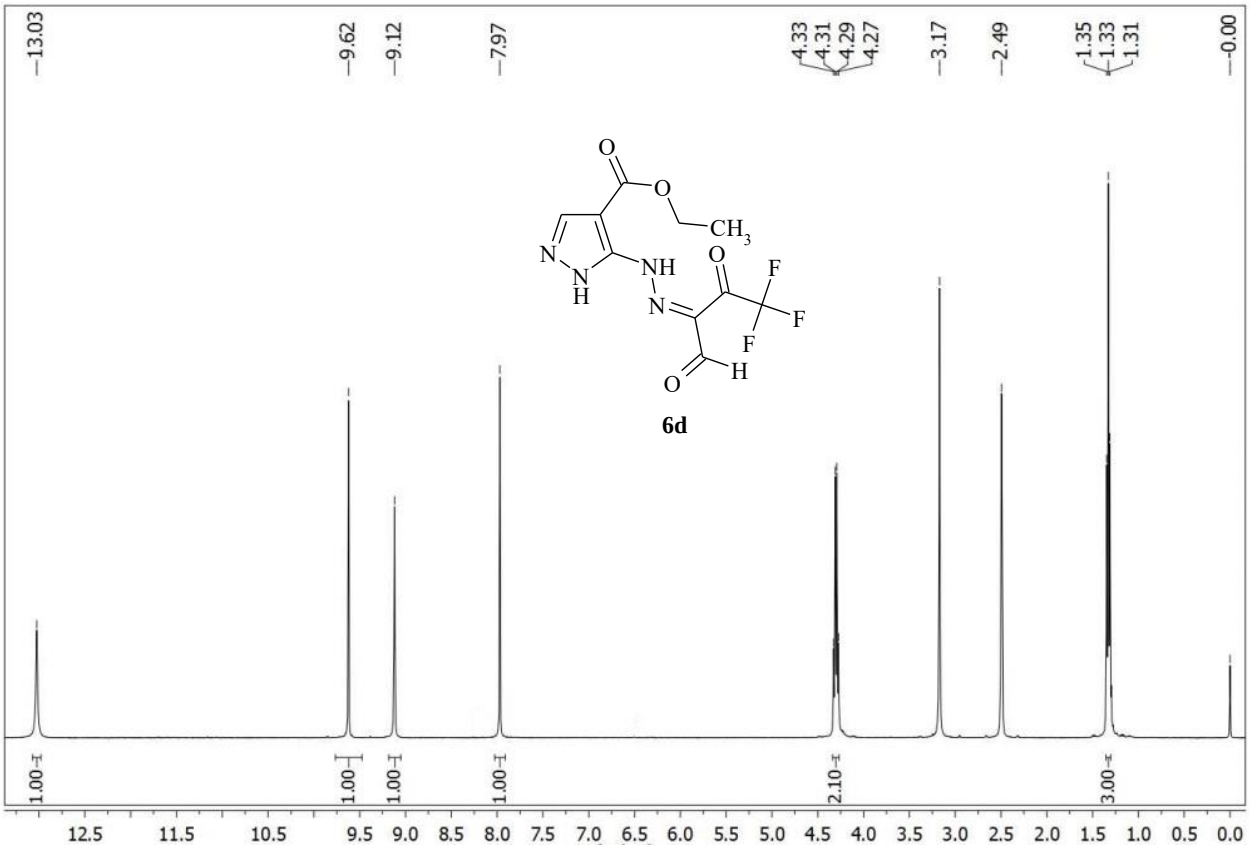


Figure S15. ^{1}H NMR of ethyl 5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole-4-carboxylate (**6d**)

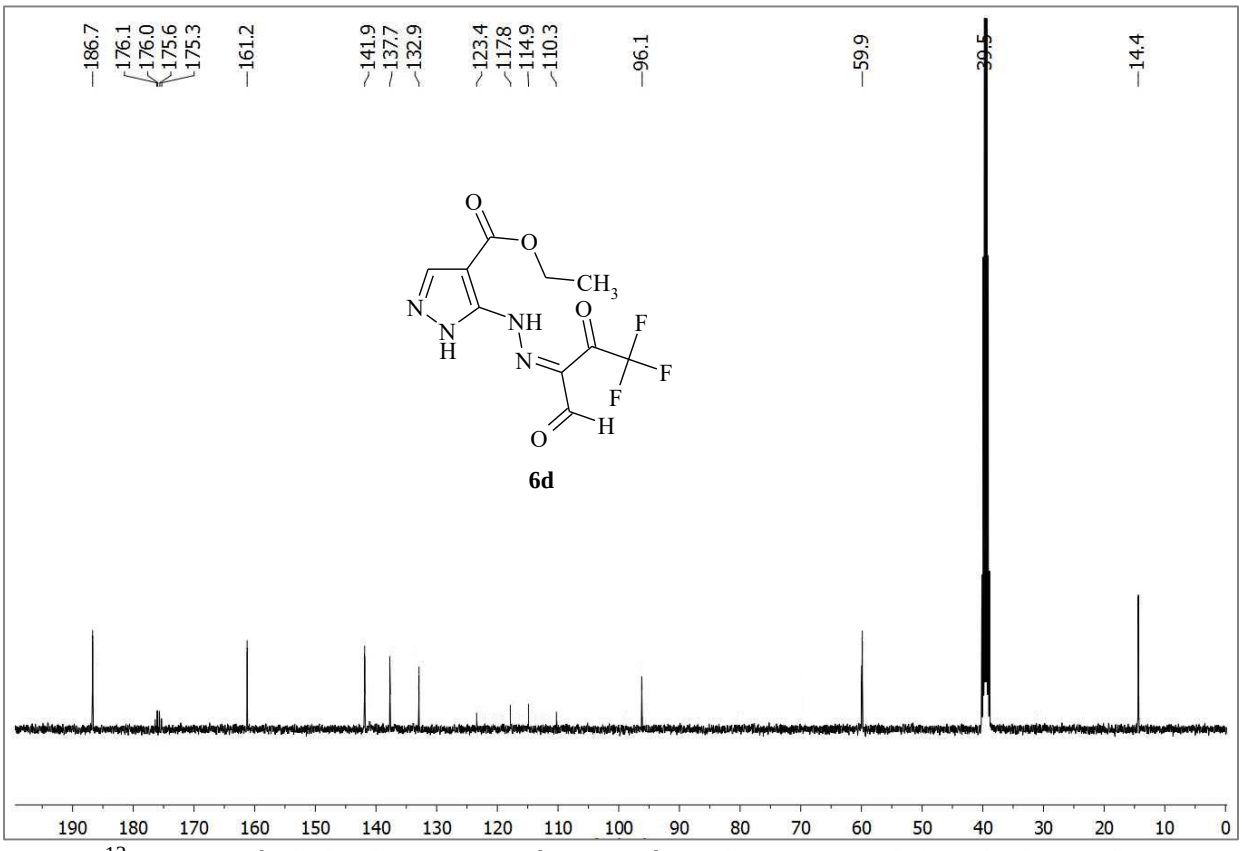


Figure S16. ^{13}C NMR of ethyl 5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole-4-carboxylate (**6d**)

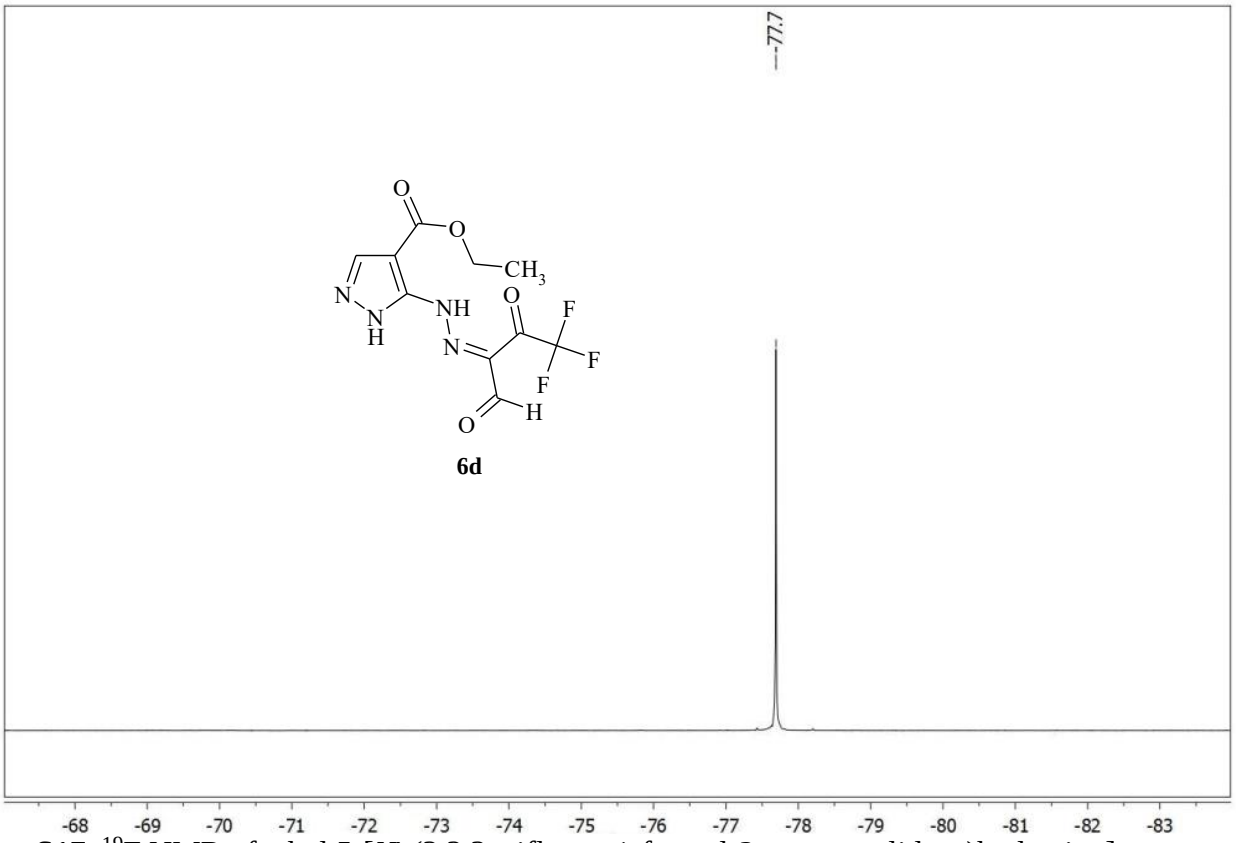


Figure S17. ^{19}F NMR of ethyl 5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole-4-carboxylate (**6d**)

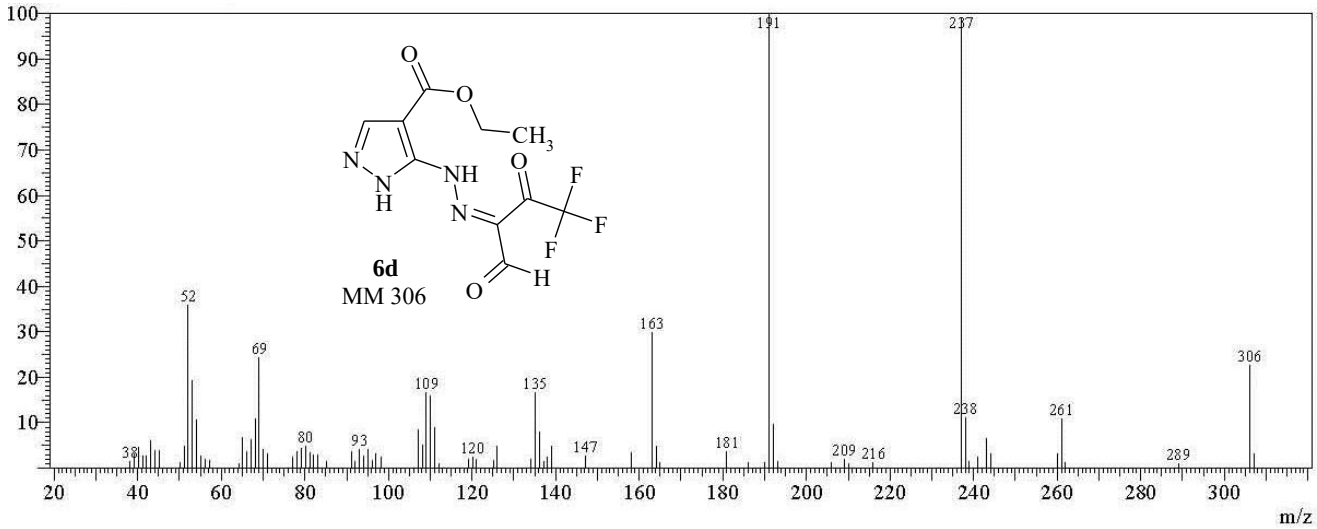


Figure S18. Mass-spectrum of ethyl 5-[*N*'-(3,3,3-trifluoro-1-formyl-2-oxopropylidene)hydrazino]-1*H*-pyrazole-4-carboxylate (**6d**)

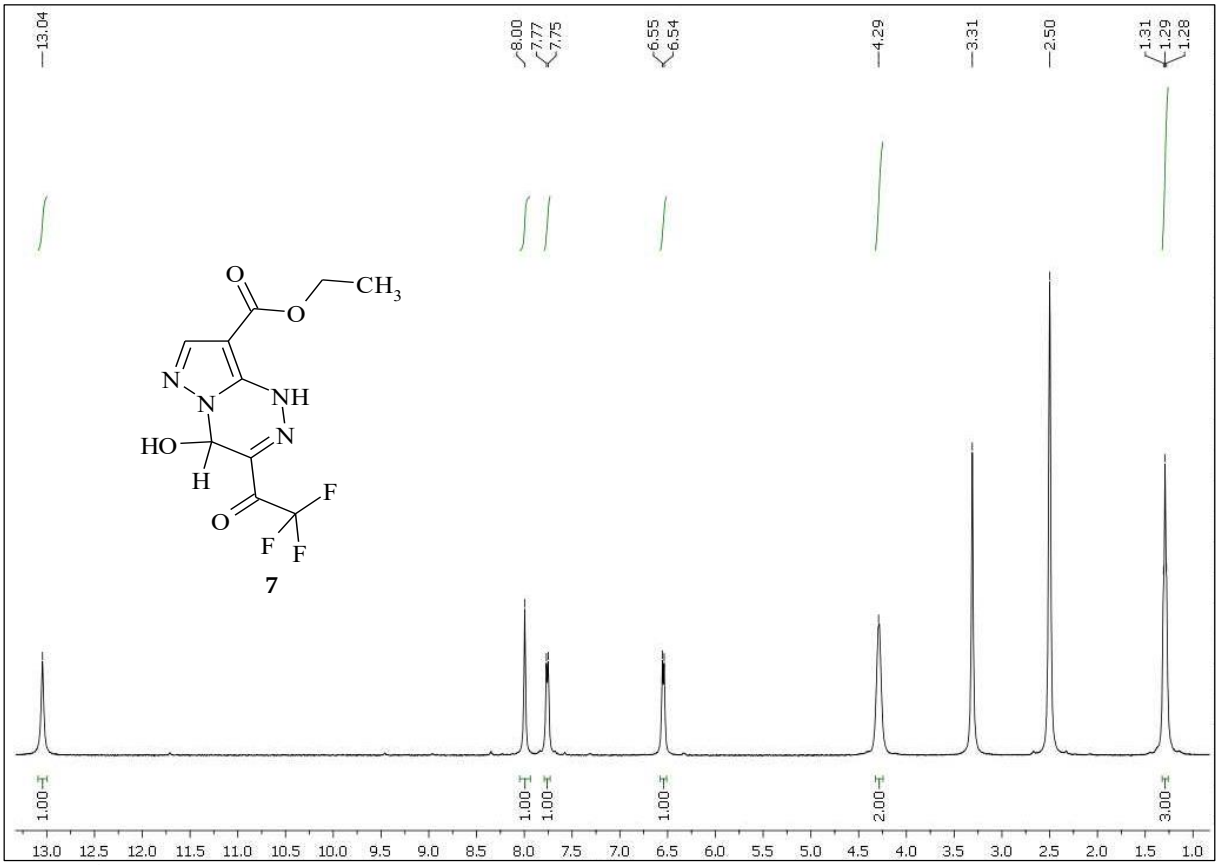


Figure S19. ^{1}H NMR of ethyl 4-hydroxy-3-trifluoroacetyl-1,4-dihydropyrazolo-[5,1-*c*][1,2,4]triazine-8-carboxylate (**7**)

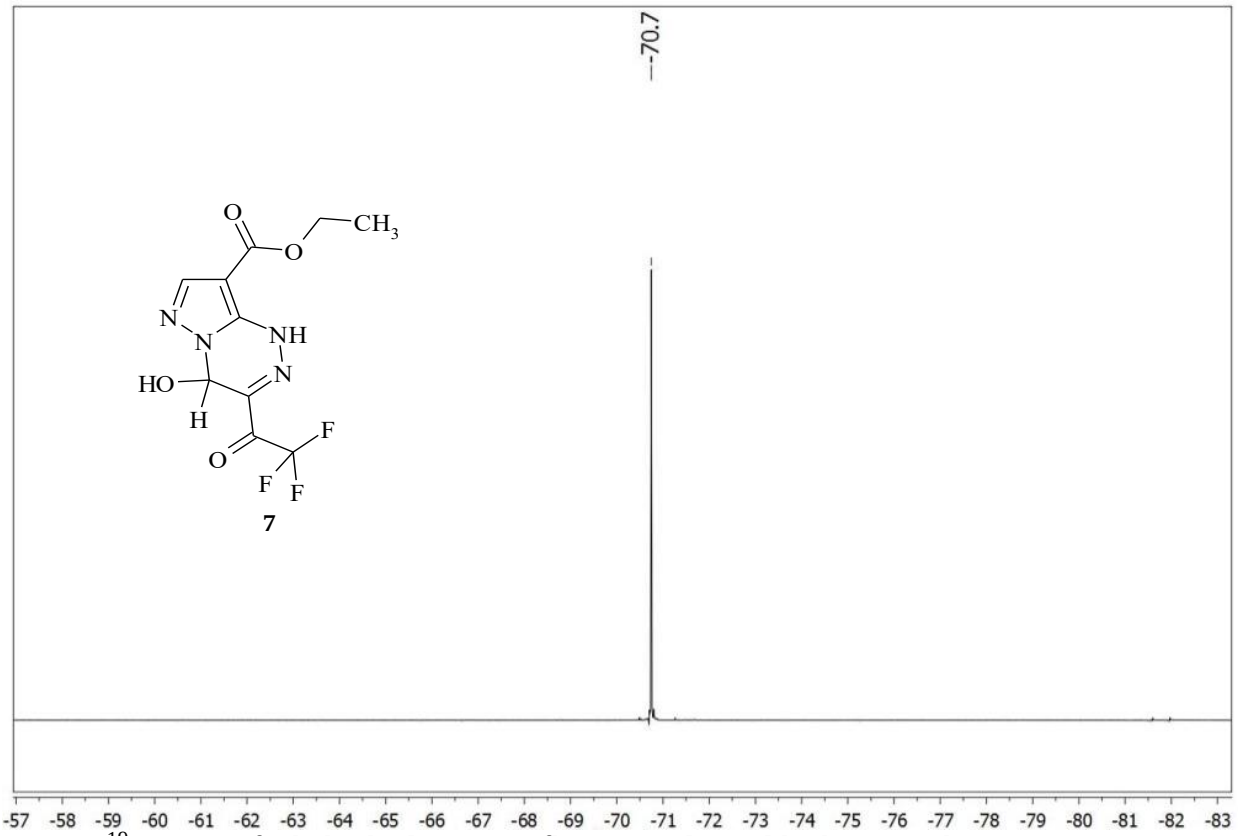


Figure S20. ^{19}F NMR of ethyl 4-hydroxy-3-trifluoroacetyl-1,4-dihydropyrazolo-[5,1-*c*][1,2,4]triazine-8-carboxylate (**7**)

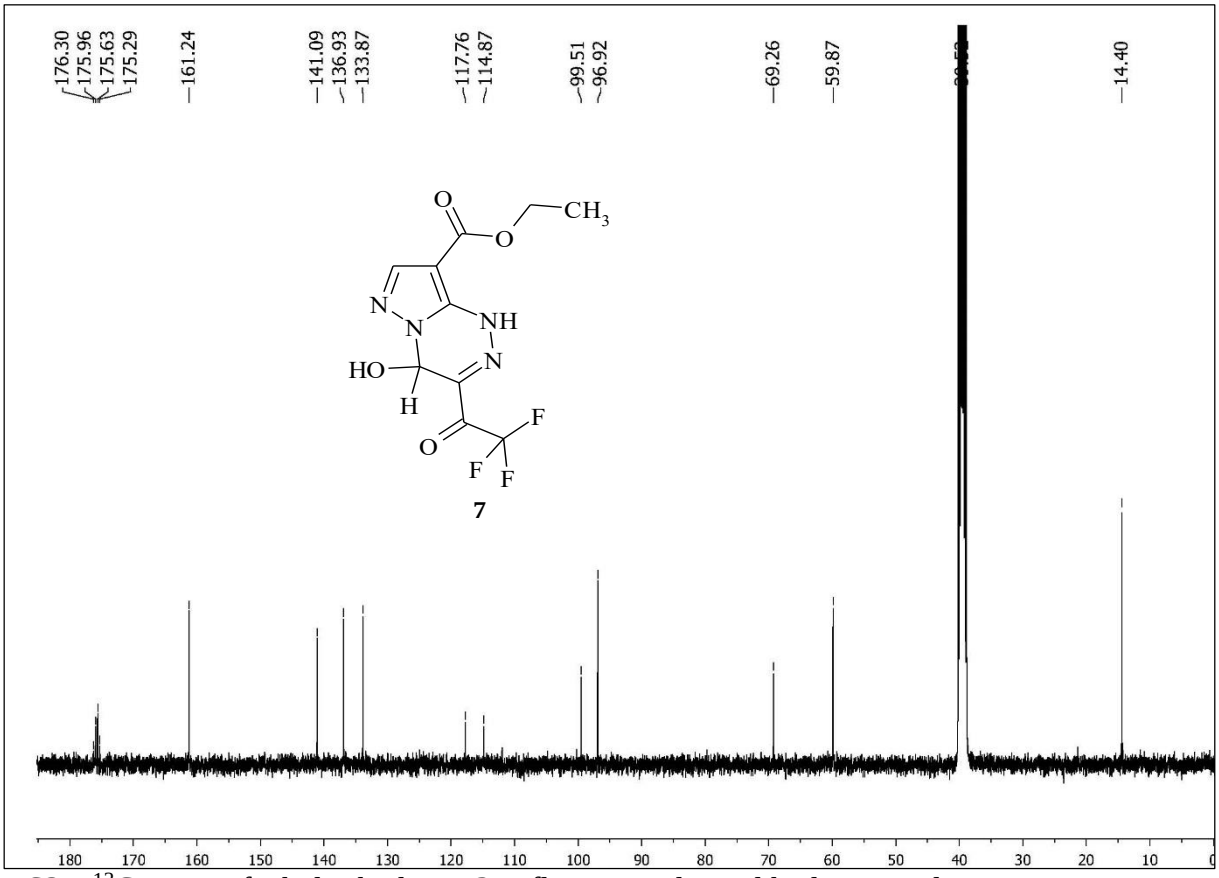


Figure S21. ^{13}C NMR of ethyl 4-hydroxy-3-trifluoroacetyl-1,4-dihydropyrazolo-[5,1-*c*][1,2,4]triazin-8-carboxylate (**7**)

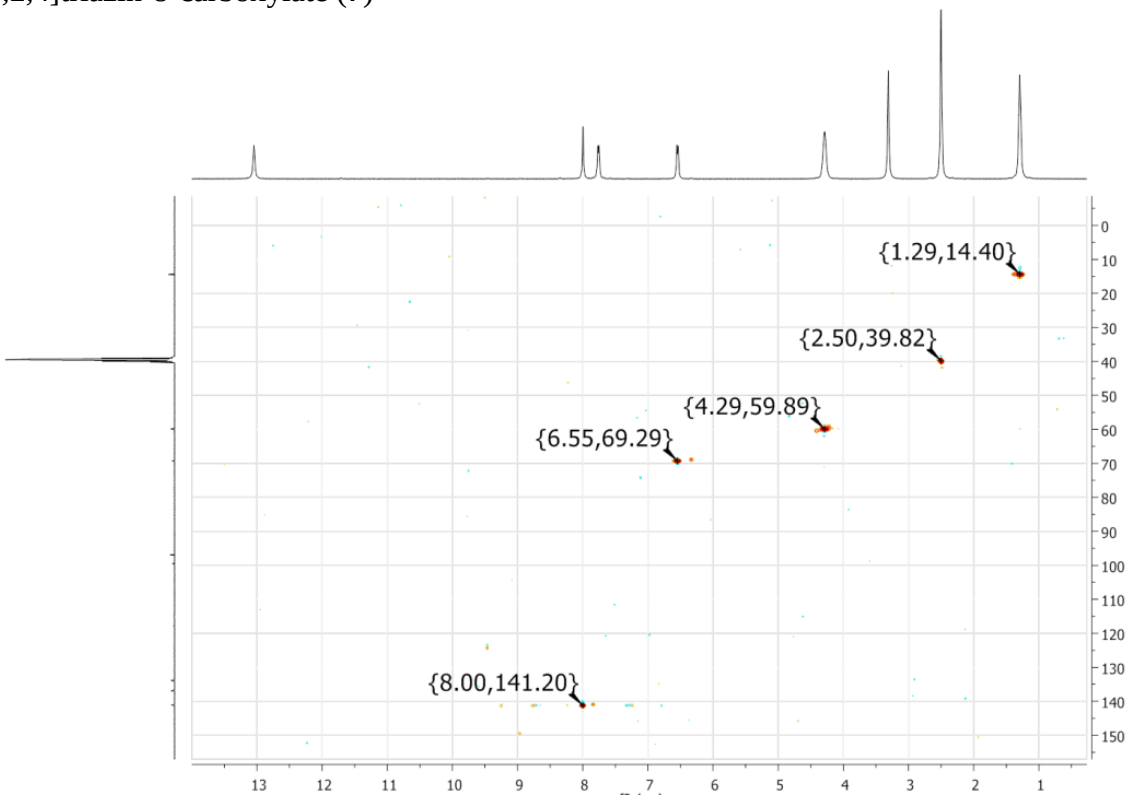


Figure S22. HMBC of ethyl 4-hydroxy-3-trifluoroacetyl-1,4-dihydropyrazolo-[5,1-*c*][1,2,4]triazine-8-carboxylate (**7**)

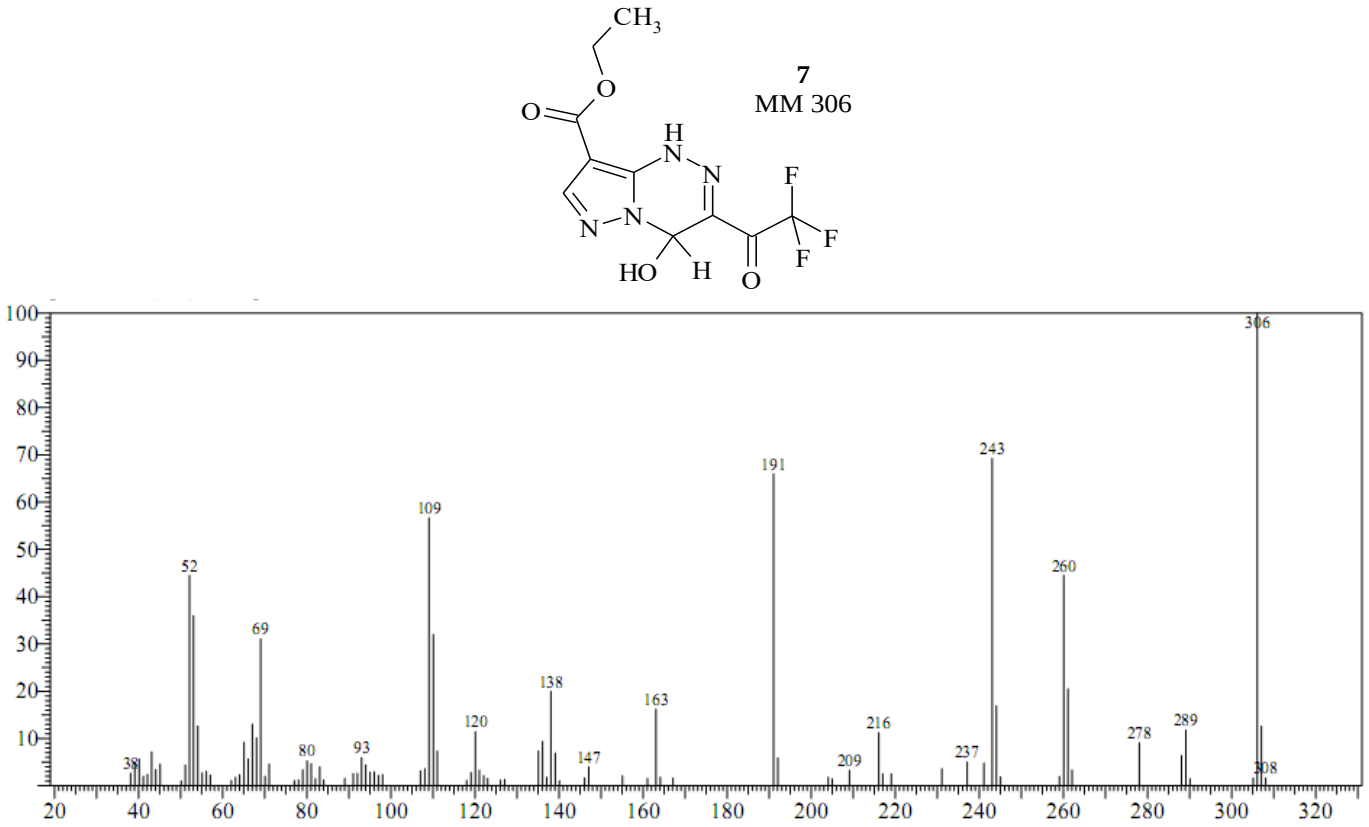


Figure S23. Mass-spectrum of ethyl 4-hydroxy-3-trifluoroacetyl-1,4-dihydropyrazolo-[5,1-*c*][1,2,4]triazine-8-carboxylate (**7**)

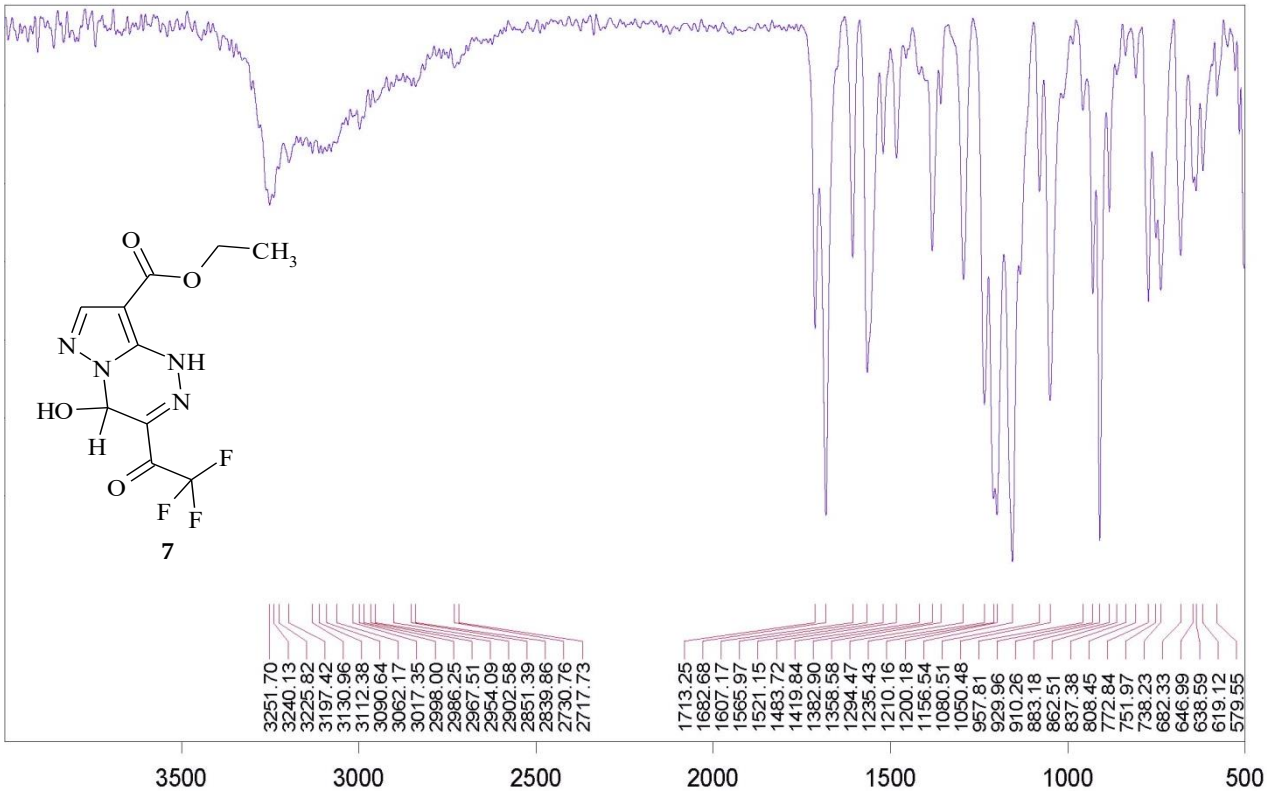


Figure S24. IR spectrum of ethyl 4-hydroxy-3-trifluoroacetyl-1,4-dihydropyrazolo-[5,1-*c*][1,2,4]triazine-8-carboxylate (**7**)

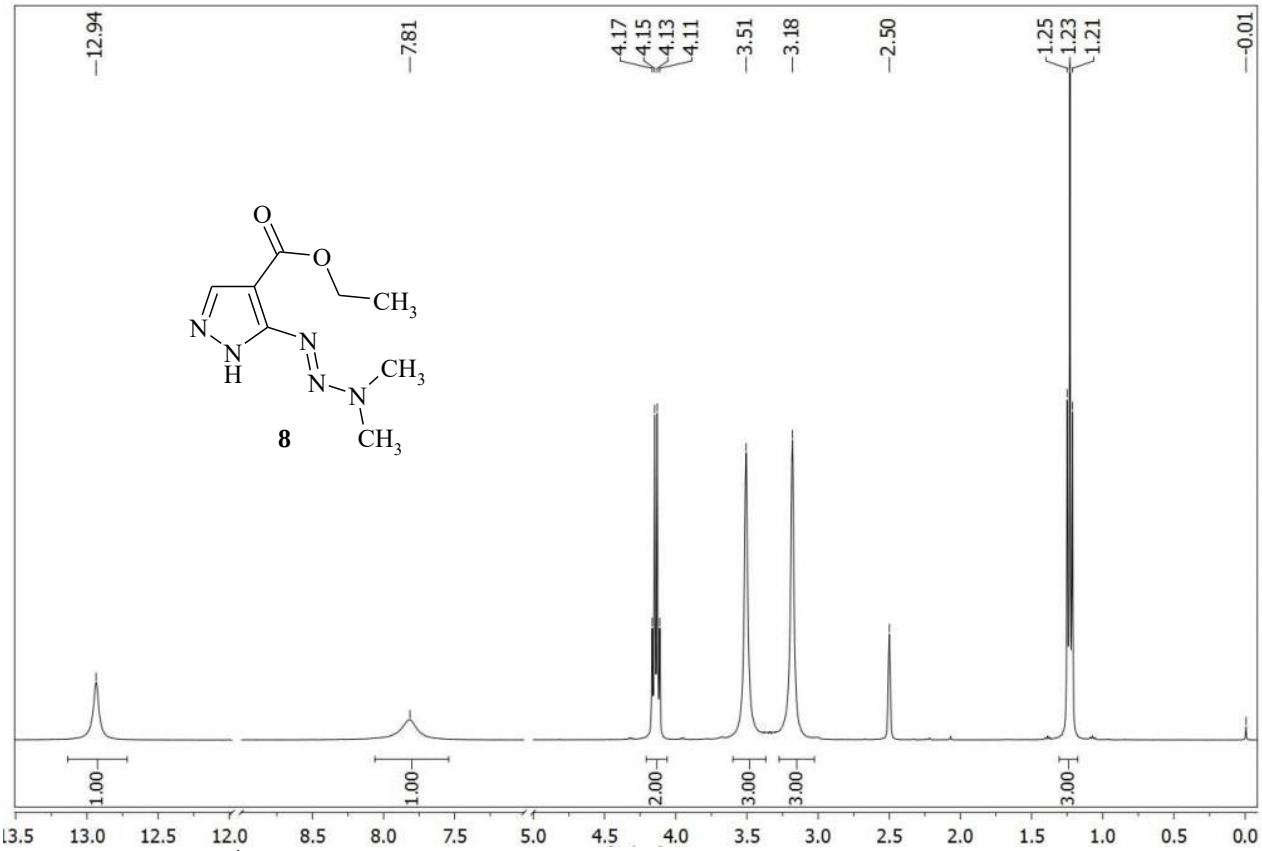


Figure S25. ^{1}H NMR of ethyl 3-(3,3-dimethyltriaz-1-en-1-yl)pyrazole-4-carboxylate (**8**)

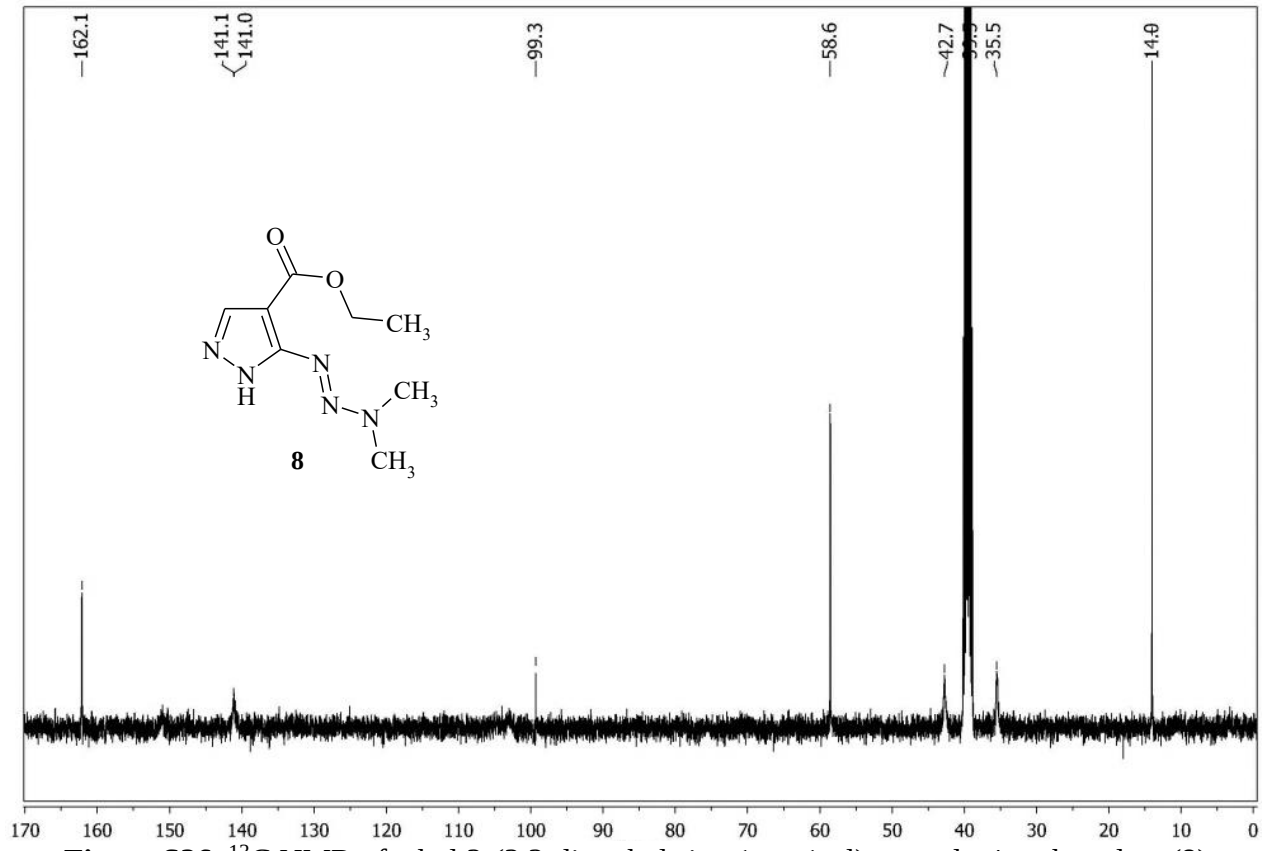
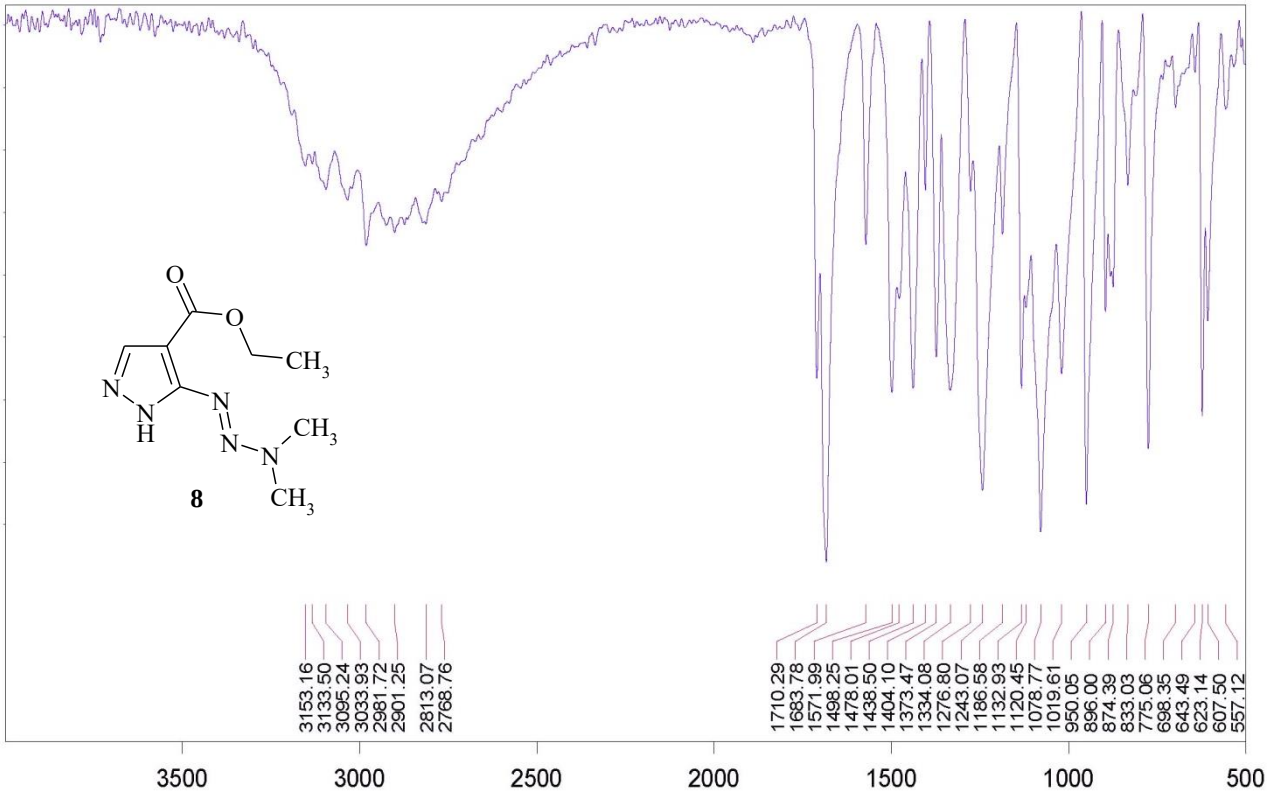


Figure S26. ^{13}C NMR of ethyl 3-(3,3-dimethyltriaz-1-en-1-yl)pyrazole-4-carboxylate (**8**)



8

Figure S27. IR spectrum of ethyl 3-(3,3-dimethyltriaz-1-en-1-yl)pyrazole-4-carboxylate (**8**)