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Aryne approach towards 2,3-difluoro-10-(1*H*-1,2,3-triazol-1-yl)pyrido-[1,2-*a*]indoles

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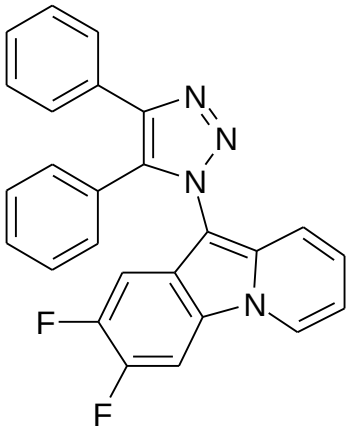
General. Unless otherwise indicated, all common reagents and solvents were used from commercial suppliers without further purification. Melting points were measured on the instrument Boetius. ^{1}H, ^{13}C and ^{19}F NMR spectra were acquired on a Bruker Avance-400 spectrometer, 298 K, digital resolution ± 0.01 ppm, using TMS as internal reference for ^{1}H and ^{13}C NMR or $CFCl_3$ for ^{19}F NMR. Mass spectra were recorded on MicrOTOF-Q II (Bruker Daltonics), electrospray as a method of ionization. Microanalyses (C, H, N) were performed using a Perkin–Elmer 2400 elemental analyzer. The structure of compound **4b** was determined on an Xcalibur E X-ray diffractometer.

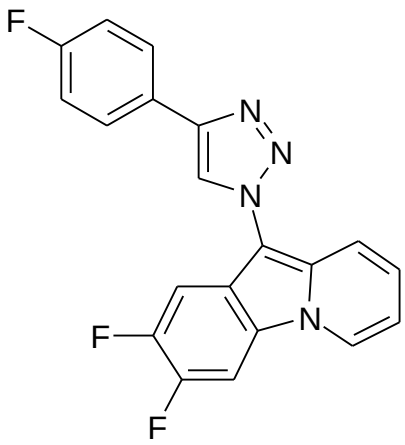
Starting triazines **3a**,[1] **3b**,[2] **3c**,[3] 5,6-difluoro-1*H*-indole-2,3-dione **2**[4] were synthesized as described in literature.

2-Amino-4,5-difluorobenzoic acid (1). A mixture of 5,6-difluoro-1*H*-indole-2,3-dione **2** (10 g, 54.6 mmol) and water solution of NaOH (2.5N, 90 ml) was stirred at room temperature until homogeneous red solution formed. Water solution of H_2O_2 (30%, 16.2 ml) was added for 20 min at temperature below 45 ^{0}C. The reaction mass was heated at 50-55 ^{0}C for 2 h. The resulting mixture was cooled to 15 ^{0}C. 6N HCl was added at 15-20 ^{0}C to adjust pH = 4.5. The obtaining precipitate was filtered off and dried. Yield 8.99 g (51.9 mmol, 95%). Mp 180-182 $^{\circ}$C. ^{1}H NMR (DMSO-d_6): 6.71 (m, 1H, H-3), 7.59 (m, 1H, H-6). ^{13}C NMR (DMSO-d_6): 103.8 (d, *J* 20.3 Hz), 105.6 (m), 119.0 (dd, *J* 17.6, 2.9 Hz), 140.3 (dd, *J* 233.6, 13.3 Hz), 150.1 (d, *J* 11 Hz), 153.8 (dd, *J* 250.6, 13.8 Hz), 168.5 (d, *J* 1.5 Hz, C=O). ^{19}F NMR (DMSO-d_6): -154.86 (d, 1F, ^{3}J 23.9 Hz), -130.93 (d, 1F, ^{3}J 23.9 Hz). ESI-MS, *m/z*: found 172.0, calculated 172.0 $(M-H)^{-}$.

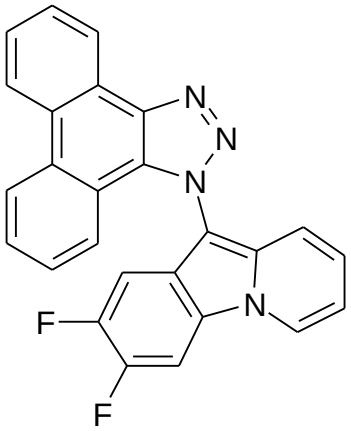
*General procedure for the preparation of 2,3-difluoro-10-(1*H*-1,2,3-triazol-1-yl)pyrido[1,2-*a*]indoles* **4**. Corresponding triazine **3** (3 mmol) was suspended in dry toluene (130 ml). Isoamyl nitrite (1.61 ml, 12 mmol) was added to this mixture. The resulting mixture was stirred under reflux while solution of 3,4-difluoroanthranilic acid (2.08 g, 12 mmol) in dry 1,4-dioxane (15 ml) was added from dropping funnel for 30 min. The reaction mixture was heated under reflux for 1 h and then cooled to room temperature. Then the reaction mass was washed with potassium hydroxide solution (3M, 3 x 75 ml), dried with anhydrous sodium sulfate. The solvents were removed under reduced pressure. Products **4** were separated by column chromatography (Silica gel, mixture of ethyl acetate and dichloromethane (3:1) as eluent, Rf = 0.8). Analytical samples of products **4** were obtained by recrystallization from acetonitrile.



2,3-Difluoro-10-(4,5-diphenyl-1*H*-1,2,3-triazol-1-yl)pyrido[1,2-*a*]indole (4a). Yield 0.46 g (1.1 mmol, 37%). ^{1}H NMR ($CDCl_3$): 6.64 (ddd, 1H, ^{3}J 7.5, 6.8, ^{4}J 1.3 Hz), 6.99 (ddd, 1H, ^{3}J 9.8, 6.5 ^{4}J 1.0 Hz), 7.13 (dd, ^{3}J 10.4, 7.6 Hz), 7.19 (m, 4H), 7.21-7.26 (m, 2H), 7.30-7.39 (m, 3H), 7.63-7.72 (m, 3H), 8.17 (dd, 1H, ^{3}J 8.2, ^{4}J 1.0 Hz). ^{13}C NMR ($CDCl_3$): 99.0 (d, *J* 21.3 Hz), 103.9 (d, *J* 21.3 Hz), 109.9, 115.9, 120.7 (d, *J* 8.5 Hz), 122.5 (d, *J* 8.5 Hz), 123.9, 124.6, 127.4, 127.5, 128.0, 128.6, 128.9, 129.3, 129.3, 130.9, 133.4 (d, *J* 3.2 Hz), 135.8, 144.1, 147.0 (dd, *J* 220.8, 14.6 Hz), 149.4 (dd, *J* 222.4, 15.4 Hz). ^{19}F NMR ($CDCl_3$): -141.95 (d, 1F, *J* 20.7 Hz), -138.97 (d, 1F, *J* 20.7 Hz). ESI-MS, *m/z*: found 423.1, calculated 423.1 $(M+H)^+$. Calcd for $C_{26}H_{16}F_2N_4$: C 73.93; H 3.82; N 13.26. Found: C 73.78; H 3.72; N 12.99.



2,3-Difluoro-10-[4-(4-fluorophenyl)-1*H*-1,2,3-triazol-1-yl]pyrido[1,2-*a*]indole (4b). Yield 0.38 g (1.05 mmol, 35%). ^{1}H NMR ($CDCl_3$): 6.71 (ddd, 1H, ^{3}J 6.9, 6.9, ^{4}J 1.0 Hz), 7.12 (ddd, 1H, ^{3}J 9.5, 6.6 ^{4}J 1.2 Hz), 7.18 (m, 2H, 4-FC_6H_5), 7.55-7.65 (m, 2H), 7.76 (dd, ^{3}J 9.8, 6.4 Hz), 7.94 (m, 2H, 4-FC_6H_5), 8.13 (s, 1H, H-4), 8.25 (m, 1H). ^{19}F NMR ($CDCl_3$): -141.25 (d, 1F, *J* 20.4 Hz), -138.46 (d, 1F, *J* 20.4 Hz), -113.18 (s, 1F). ESI-MS, *m/z*: found 365.1, calculated 365.1 $(M+H)^+$. Calcd for $C_{20}H_{11}F_3N_4$: C 65.94; H 3.04; N 15.38. Found: C 65.82; H 2.89; N 15.13.



1-(2,3-Difluoropyrido[1,2-*a*]indol-10-yl)-1*H*-phenanthro[9,10-*d*][1,2,3]triazole (4c). Yield 0.57 g (1.35 mmol, 45%). ^{1}H NMR ($CDCl_3$): 6.76 (m, 1H), 7.06 (m, 1H), 7.12-7.28 (m, 3H), 7.52 (m, 1H), 7.63 (m, 1H), 7.75 (m, 1H), 7.80-7.90 (m, 2H), 8.38 (dt, ^{3}J 7.4, ^{4}J 1.0, 1.0 Hz), 8.70 (d, 1H, ^{3}J 8.2 Hz), 8.74 (d, 1H, ^{3}J 8.2 Hz), 8.96 (dd, 1H, ^{3}J 8.2, ^{4}J 1.0 Hz). ^{13}C NMR ($CDCl_3$): 99.5 (d, *J* 22.8 Hz), 104.4 (d, *J* 21.6 Hz), 105.2, 110.3, 116.3, 120.4, 121.0 (d, *J* 8.5 Hz), 122.5, 122.9 (d, *J* 8.5 Hz), 123.0, 123.4, 124.2, 125.2 (d, *J* 3.7 Hz), 127.2, 127.3, 127.9, 128.3, 129.1, 130.1, 131.2, 134.0 (d, *J* 3.0 Hz), 136.1, 141.5, 147.3 (dd, *J* 221.0, 16.8 Hz), 149.1, 149.8 (dd, *J* 223.0, 15.3 Hz). ^{19}F NMR ($CDCl_3$): -141.29 (d, 1F, *J* 20.4 Hz), -138.18 (d, 1F, *J* 20.4 Hz). ESI-MS, *m/z*: found 421.1, calculated 421.1 $(M+H)^+$. Calcd for $C_{26}H_{14}F_2N_4$: C 74.28; H 3.36; N 13.33. Found: C 74.11; H 3.18; N 12.95.

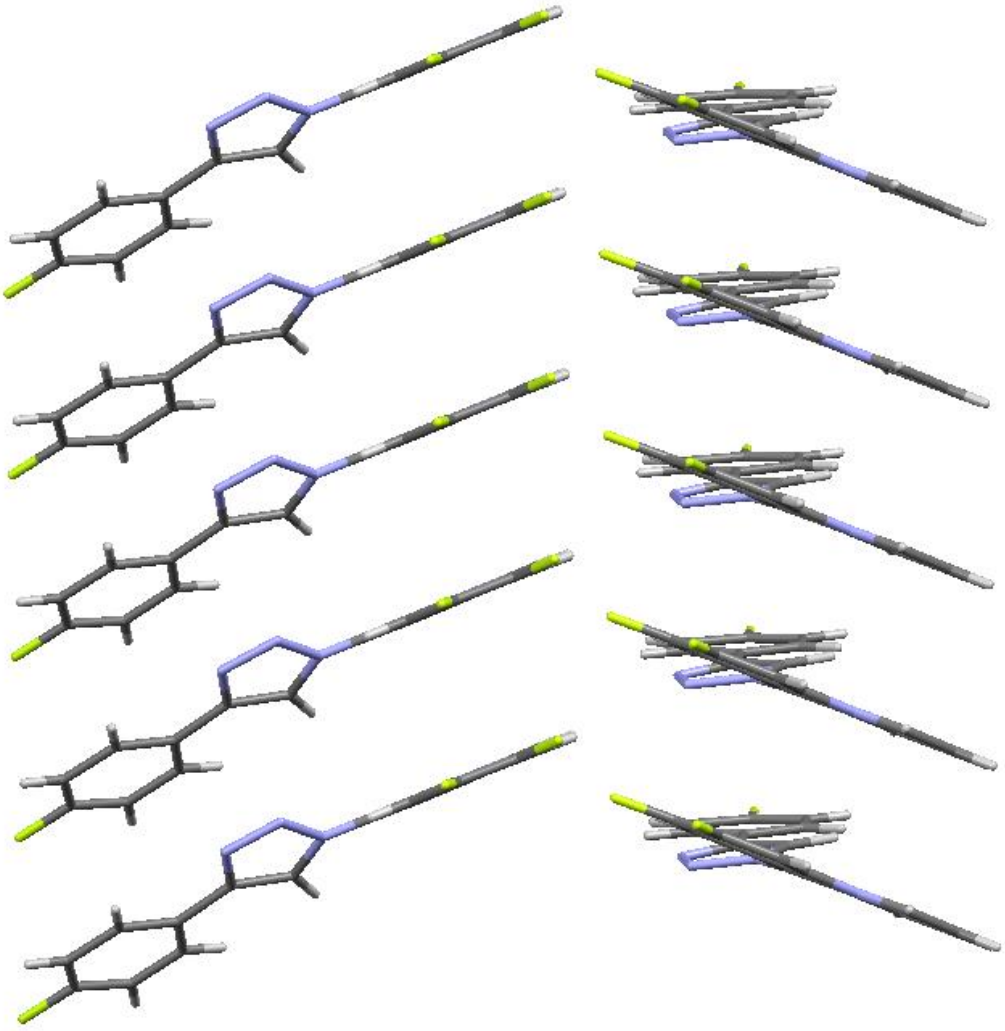


Figure S1 Stacking in crystals of compound **4b**.

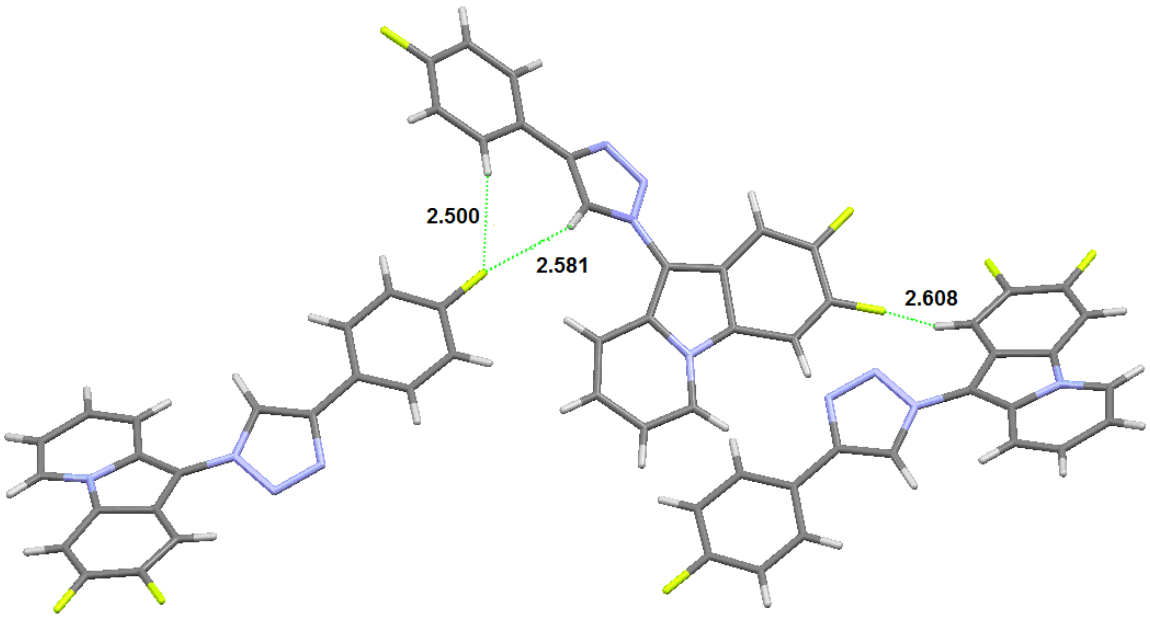
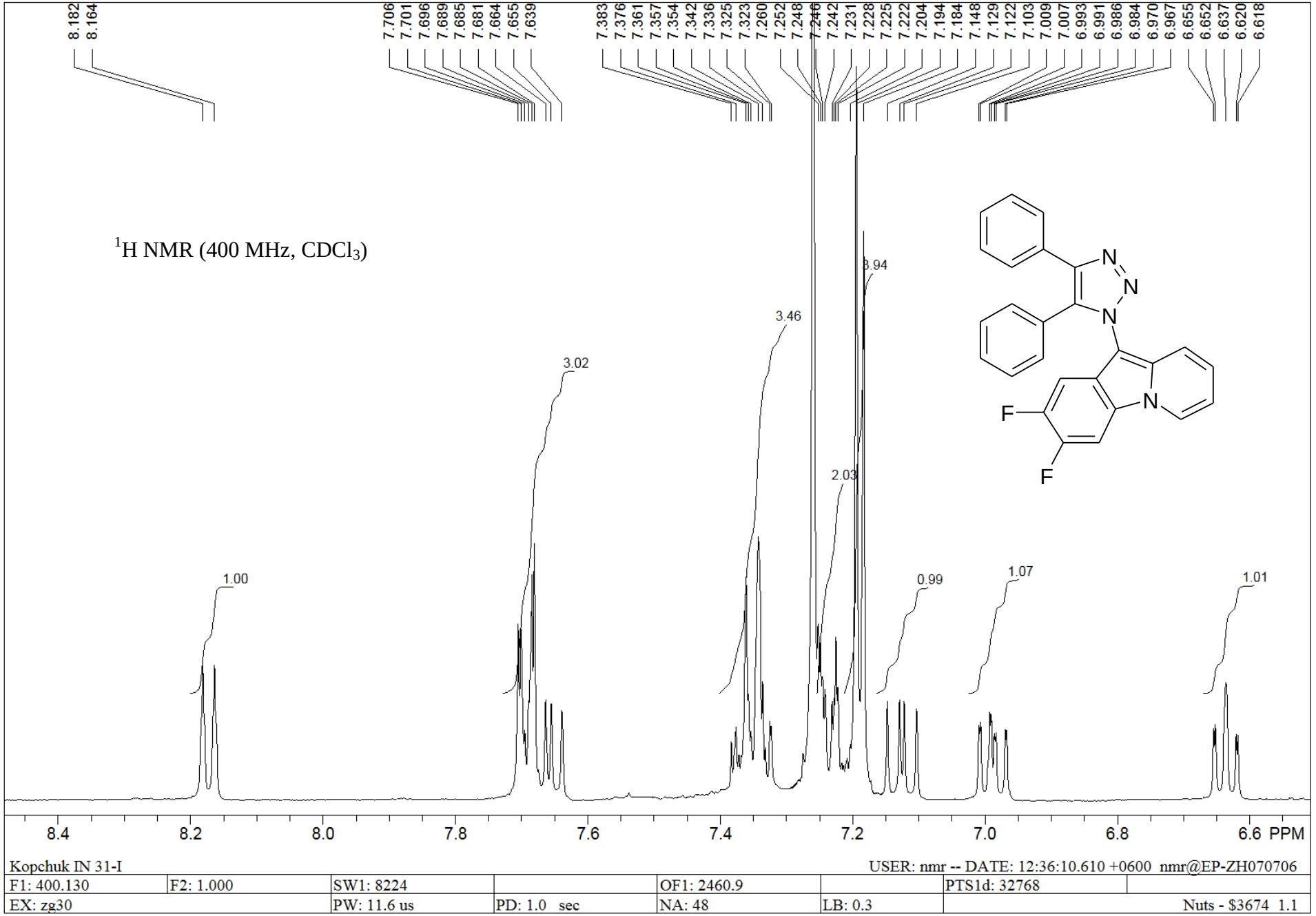


Figure S2 Hydrogen bonds in crystals of product **4b** (distances are shown in Angstroms).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7.706
7.701
7.696
7.689
7.685
7.681
7.664
7.655
7.639
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7.361
7.357
7.354
7.342
7.336
7.325
7.323
7.260
7.252
7.248
7.246
7.242
7.231
7.228
7.225
7.222
7.204
7.194
7.184
7.148
7.129
7.122
7.103
7.009
7.007
6.993
6.991
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6.655
6.652
6.637
6.620
6.618
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3.02
3.46
3.94
2.03
0.99
1.07
1.01
N
N
N
N
F
F
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6 PPM
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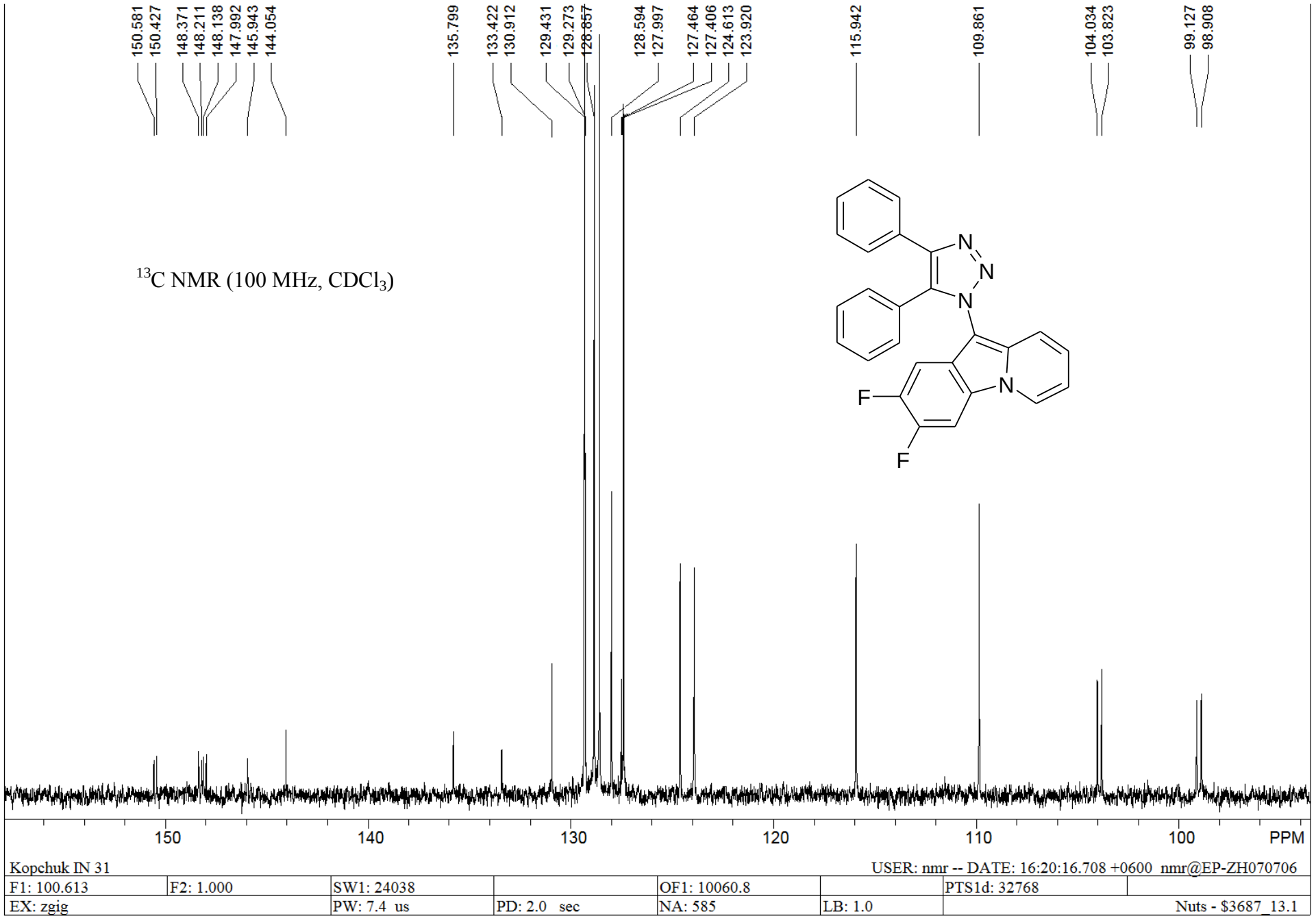
Nuts - $3674 1.1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148.138
147.992
145.943
144.054
135.799
133.422
130.912
129.431
129.273
128.857
128.594
127.997
127.464
127.406
124.613
123.920
115.942
109.861
104.034
103.823
99.127
98.908
^{13}C NMR (100 MHz, $CDCl_3$)
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N
N
N
F
F
150
140
130
120
110
100
PPM
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OF1: 10060.8
PTS1d: 32768
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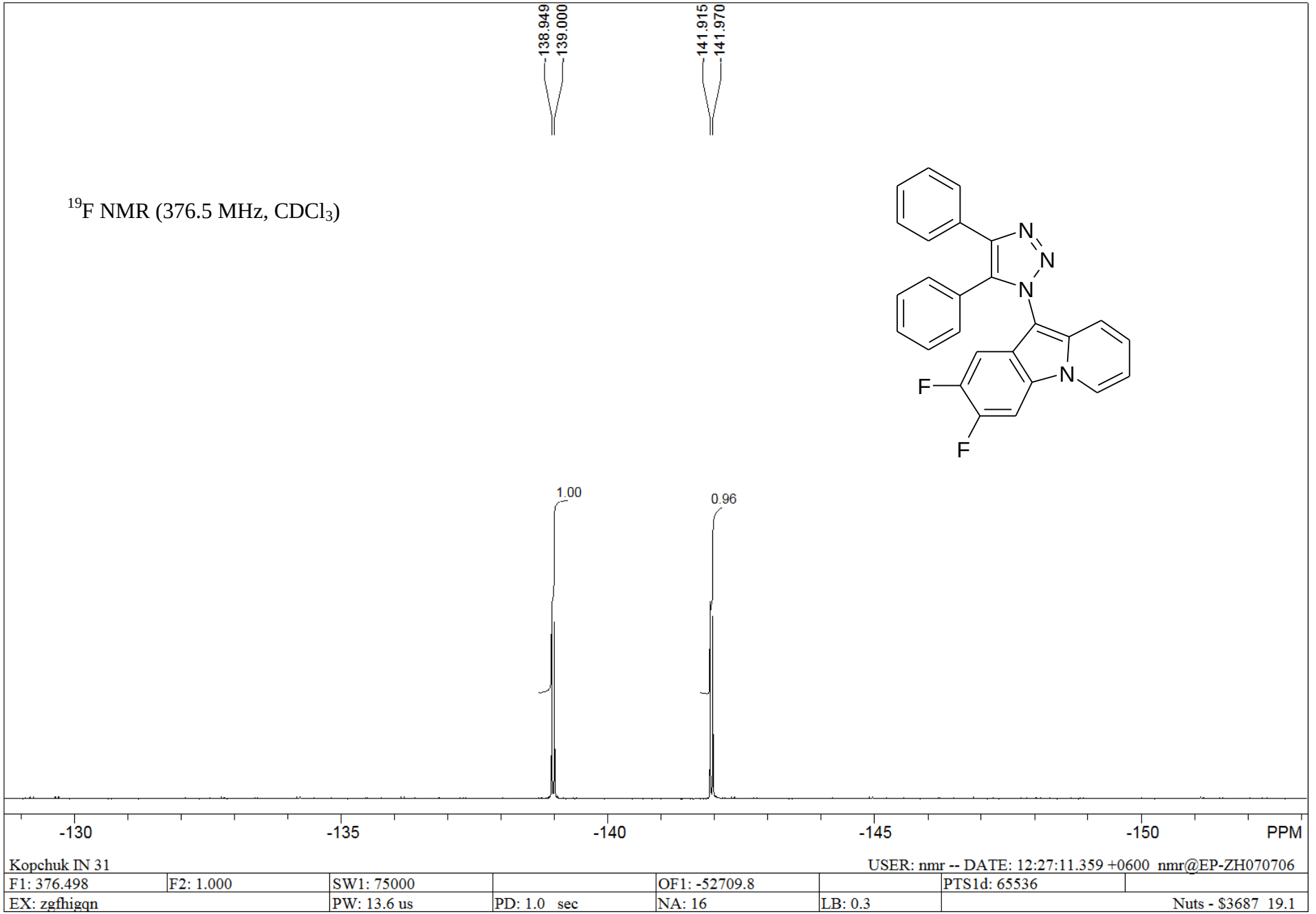
LB: 1.0
Nuts - $3687_13.1

^{19}F NMR (376.5 MHz, $CDCl_3$)



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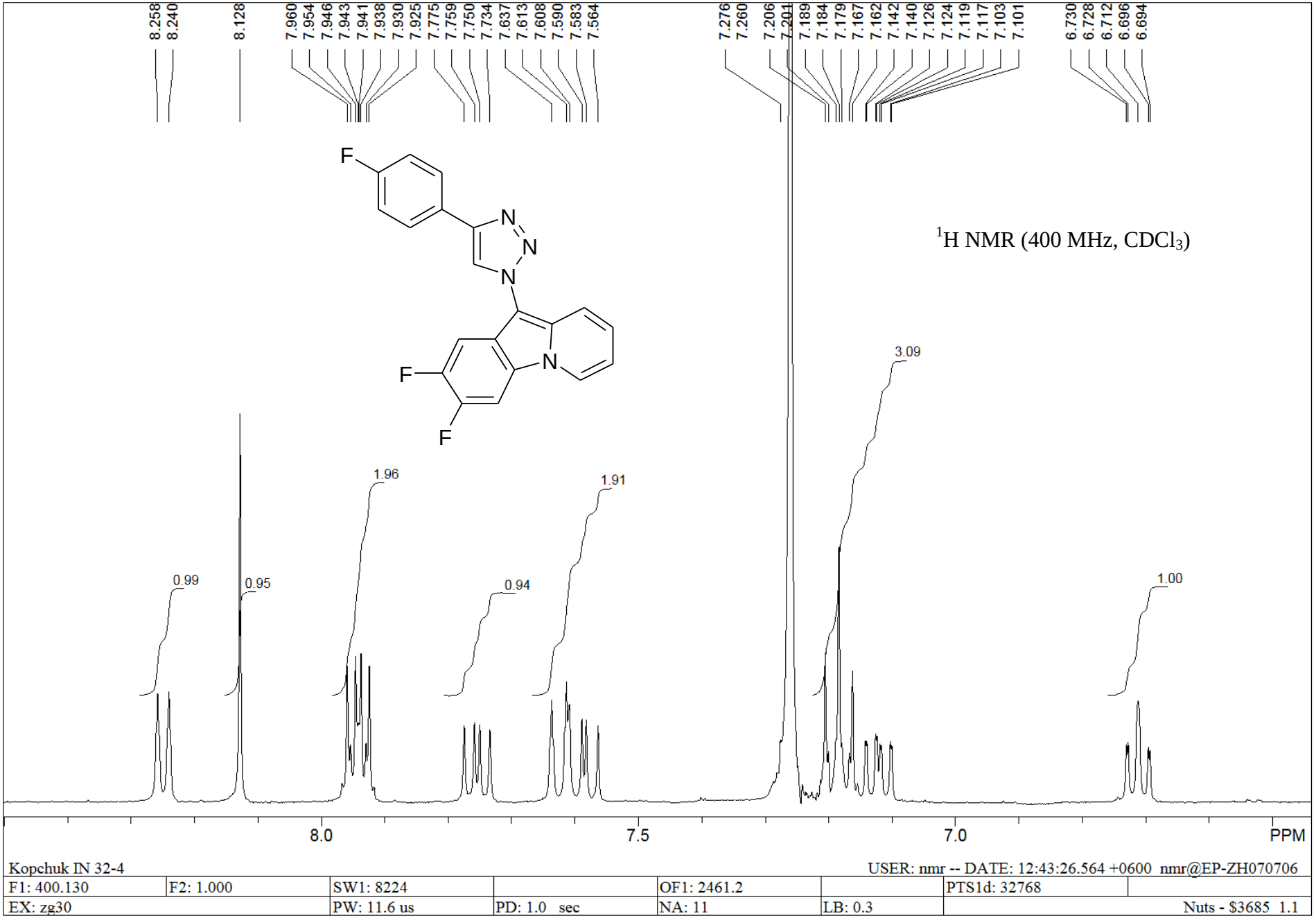
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7.946
7.943
7.941
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7.925
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7.608
7.590
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7.260
7.206
7.201
7.189
7.184
7.179
7.167
7.162
7.142
7.140
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7.103
7.101
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6.728
6.712
6.696
6.694
F
N
N
N
F
F
N
^{1}H NMR (400 MHz, $CDCl_3$)
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0.95
1.96
0.94
1.91
3.09
1.00
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7.5
7.0
PPM
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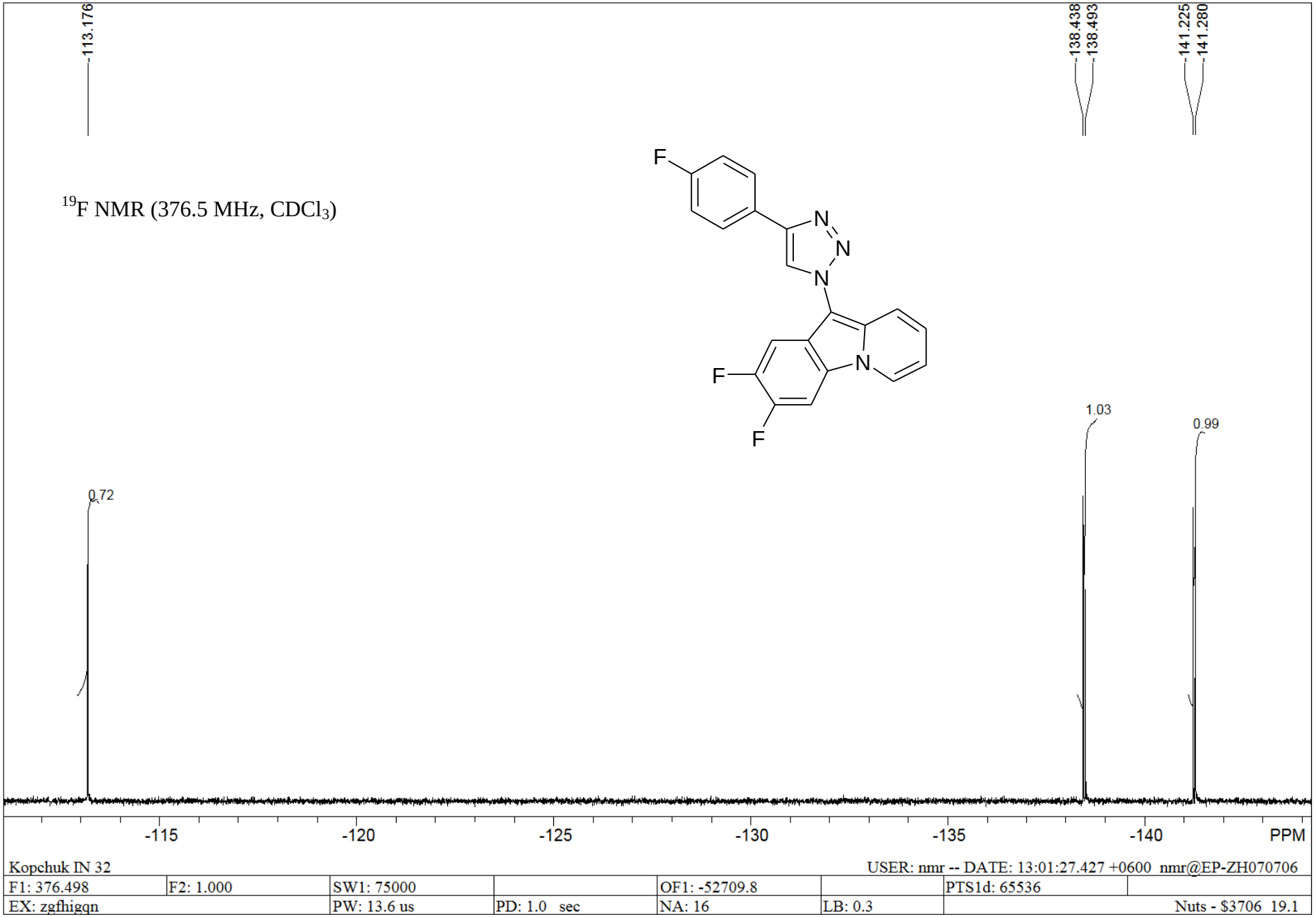
Nuts - $3685 1.1

^{19}F NMR (376.5 MHz, $CDCl_3$)



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