Supplemental Material

Design, synthesis and cholinesterase inhibitory properties of new oxazole benzylamine derivatives

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[§]These authors contributed equally.

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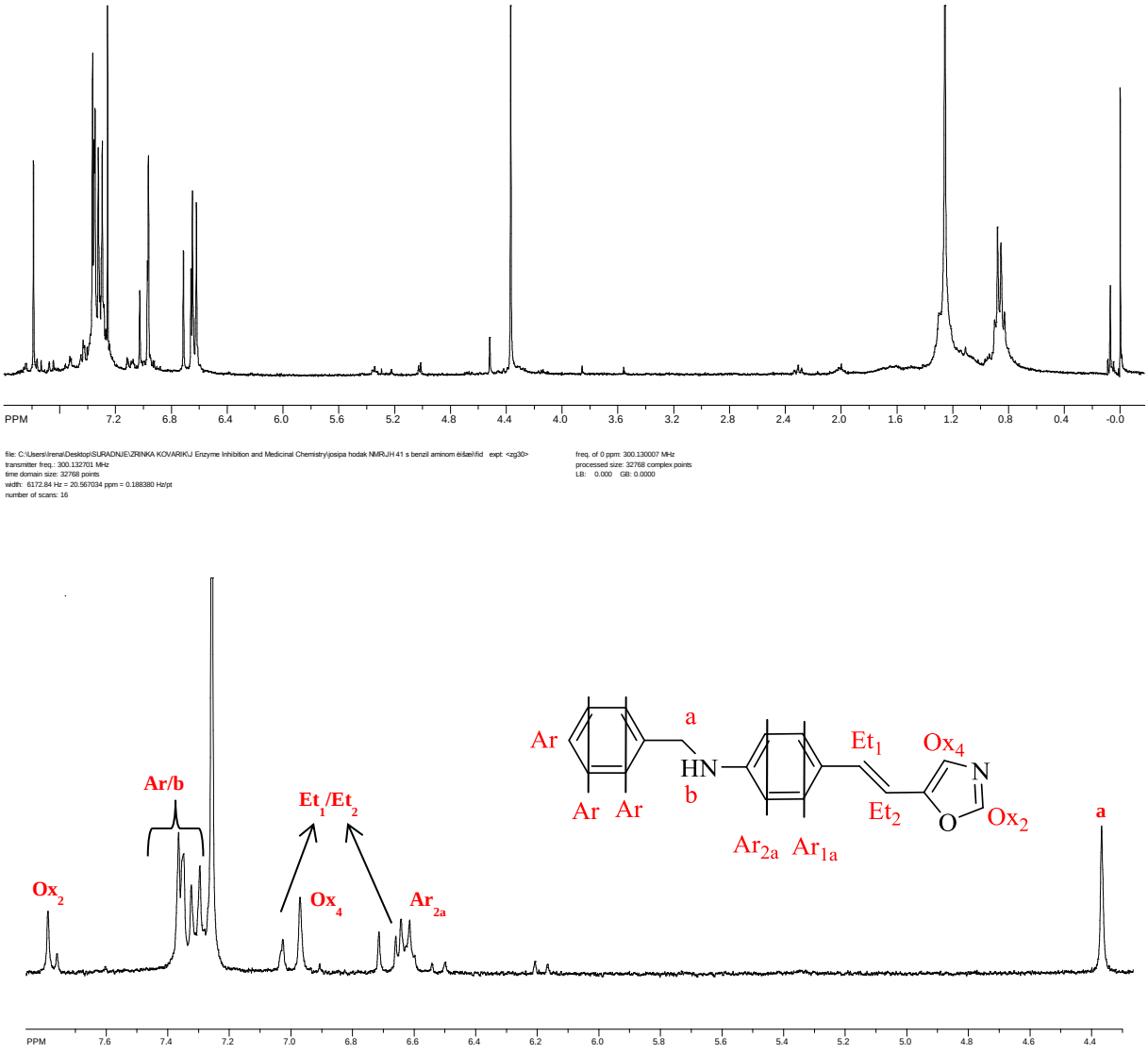
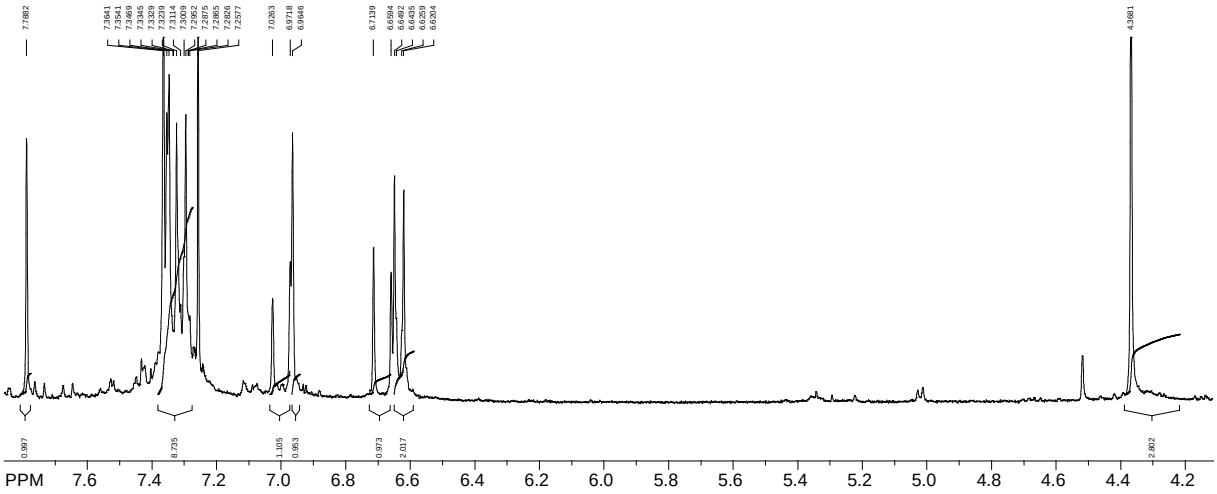
CONTENT

Figure S1. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-benzyl-4-(2-(oxazol-5-yl)vinyl)aniline **(*trans*-2)**

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7.3345
7.3239
7.3114
7.3009
7.2892
7.2805
7.2685
7.2626
7.2577
7.0263
6.9718
6.9646
6.7139
6.6984
6.6842
6.6435
6.6259
6.6204
4.3681
0.997
8.735
1.105
0.953
0.973
2.017
2.802
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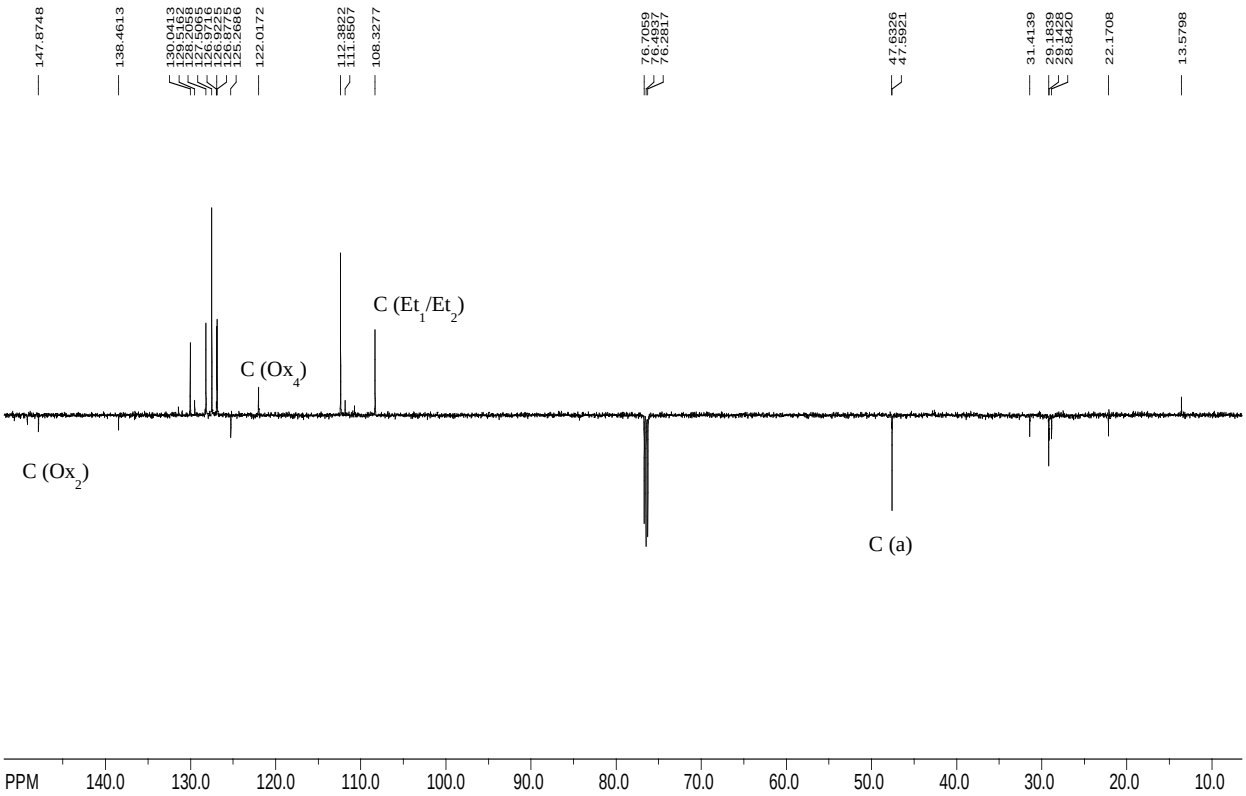
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129.6162
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126.9725
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122.0172
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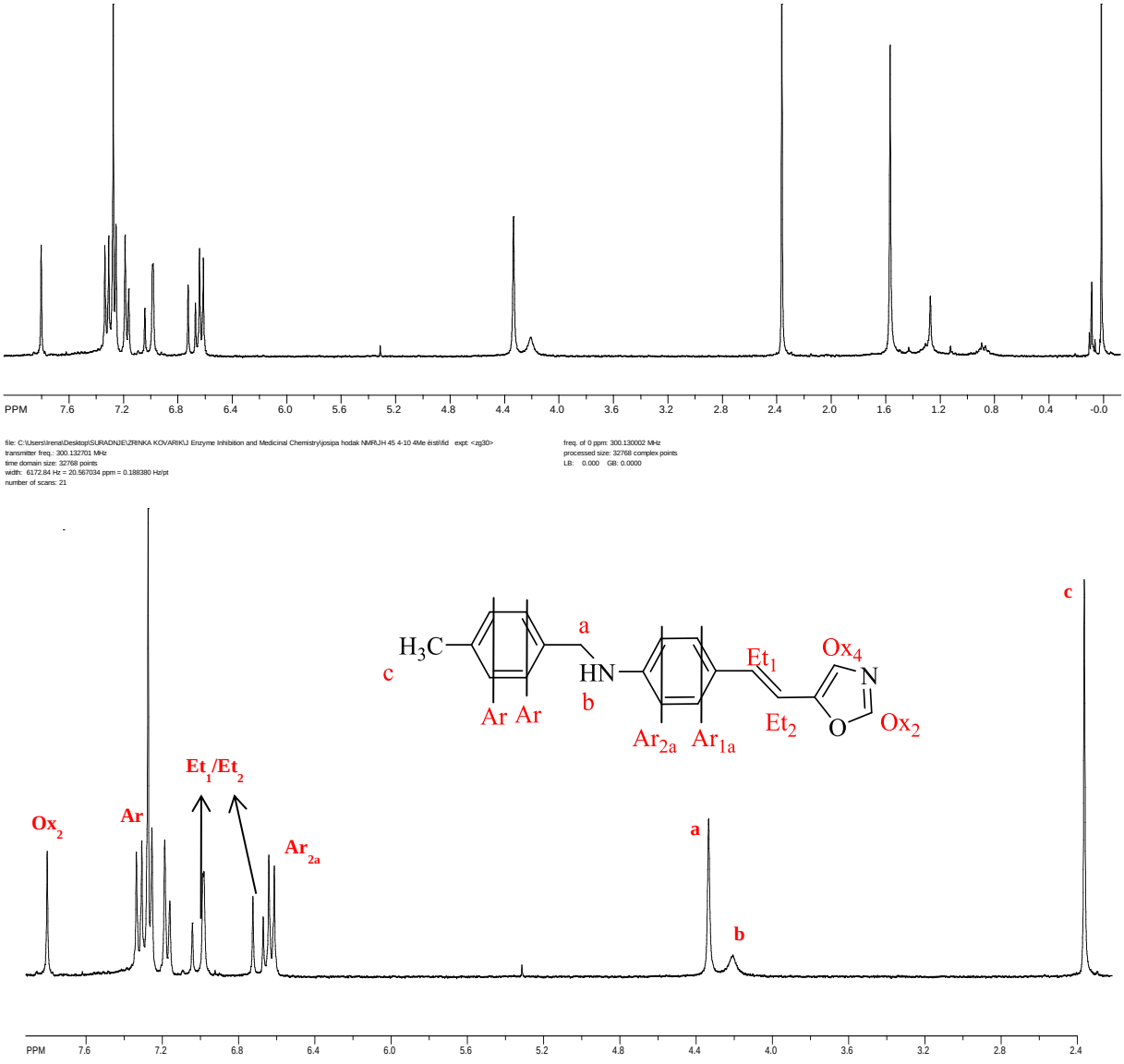
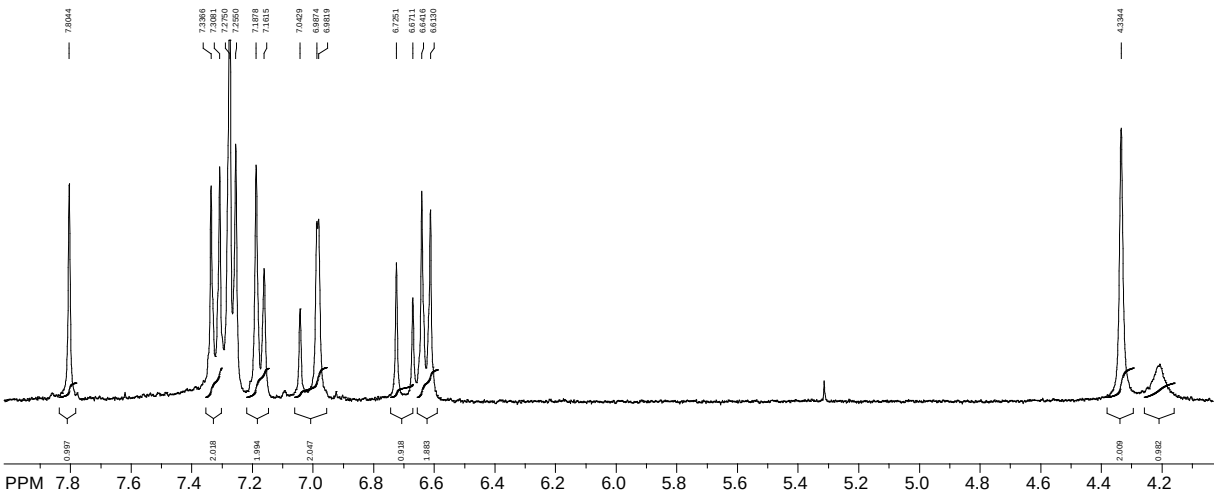
111.8507
108.3277
76.7059
76.2817
47.6326
47.5921
31.4139
29.1839
29.1428
28.8420
22.1708
13.5798
C (Et1/Et2)
C (Ox4)
C (Ox2)
C (a)
PPM 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0

Figure S2. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-(4-methylbenzyl)-4-(2-(oxazol-5-yl)vinyl)aniline **(*trans*-3)**

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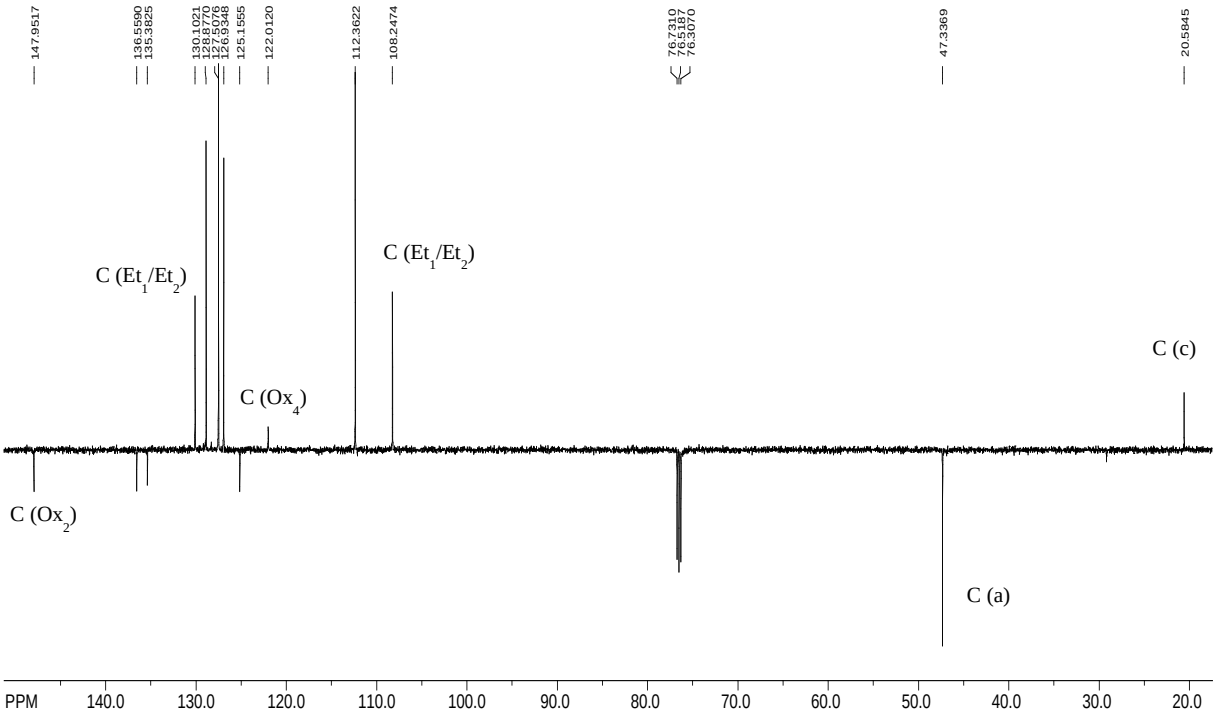
7.3081
7.2750
7.2560
7.1878
7.1615
7.0429
6.9974
6.9819
6.7251
6.6711
6.6416
6.6130
4.3344
0.997
2.018
1.994
2.047
0.918
1.883
2.009
0.982
PPM 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2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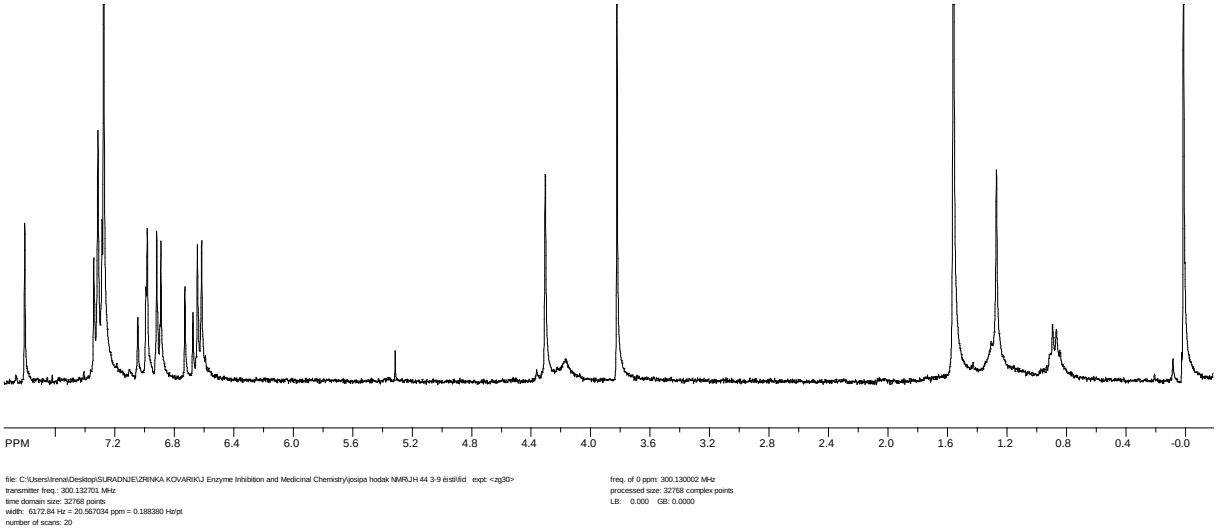
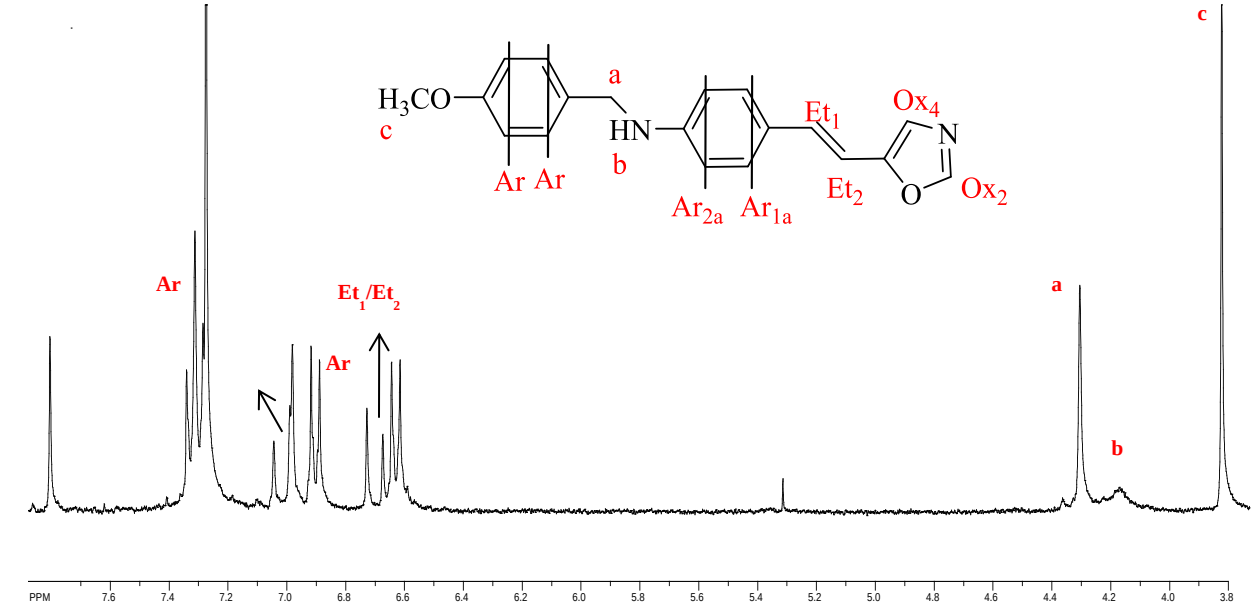
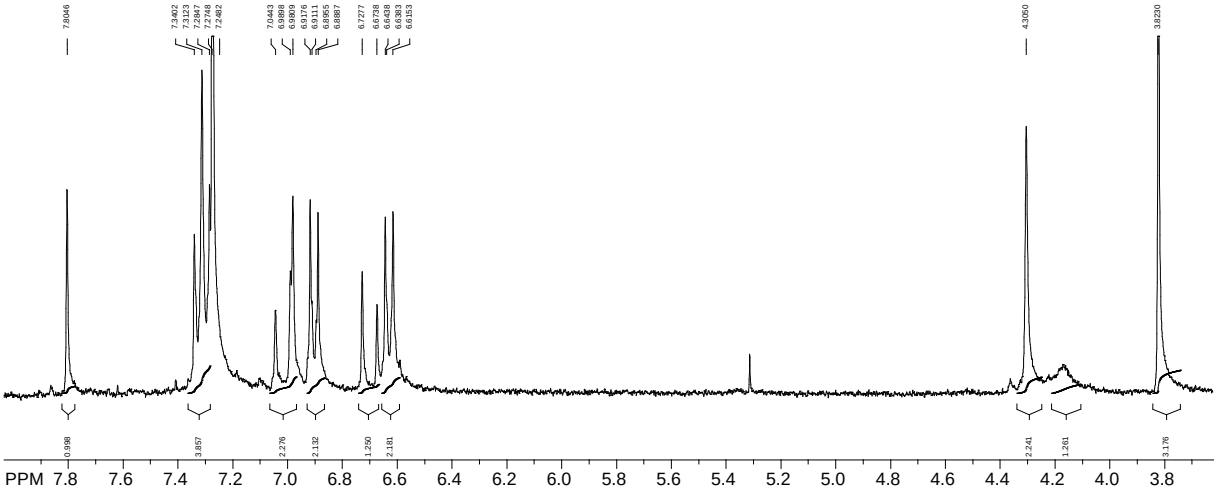
127.5076
126.9348
125.1555
122.0120
112.3622
108.2474
76.7310
76.5187
76.3070
47.3369
20.5845
C (Et1/Et2)
C (Et1/Et2)
C (Ox4)
C (c)
C (Ox2)
C (a)
PPM 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0

Figure S3. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-(4-methoxybenzyl)-4-(2-(oxazol-5-yl)vinyl)aniline **(*trans*-4)**



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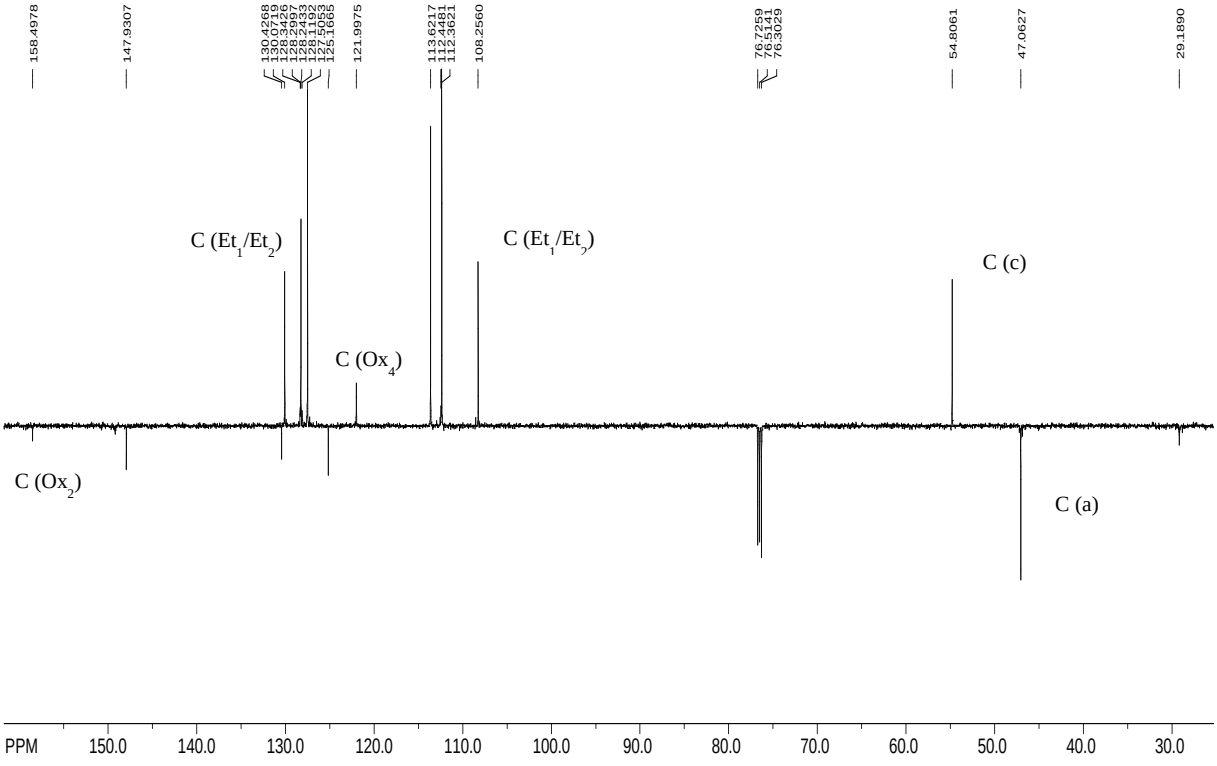
7.3402
7.3123
7.2847
7.2749
7.2482
7.0443
6.9898
6.9699
6.9376
6.9111
6.8955
6.8887
6.7277
6.6738
6.6438
6.6383
6.6153
4.3050
3.8220
0.998
3.857
2.276
2.132
1.250
2.101
2.241
1.261
3.176
PPM 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8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128.3426
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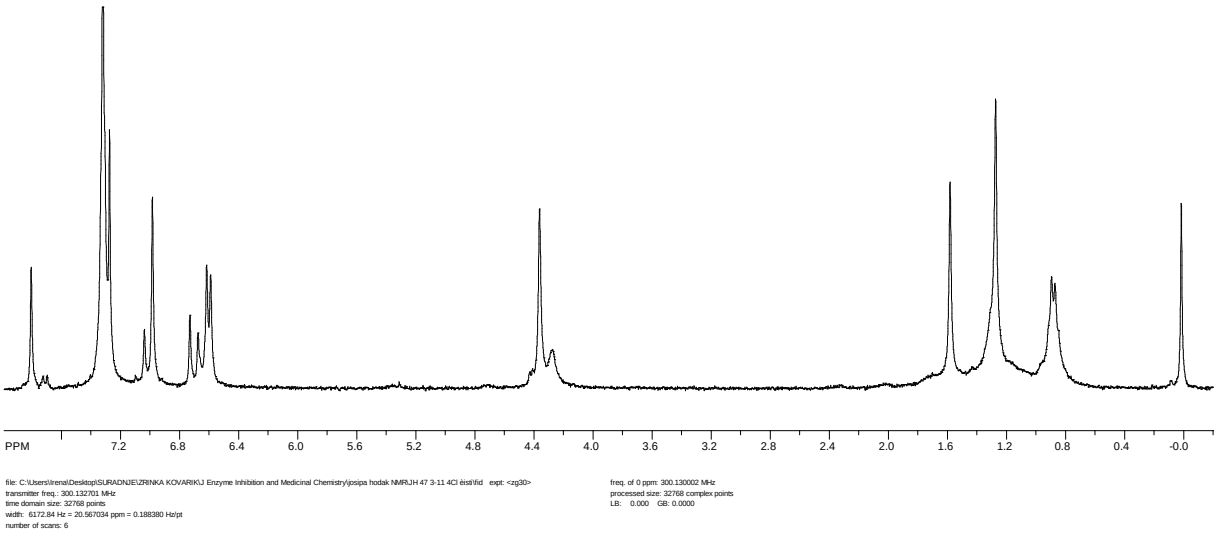
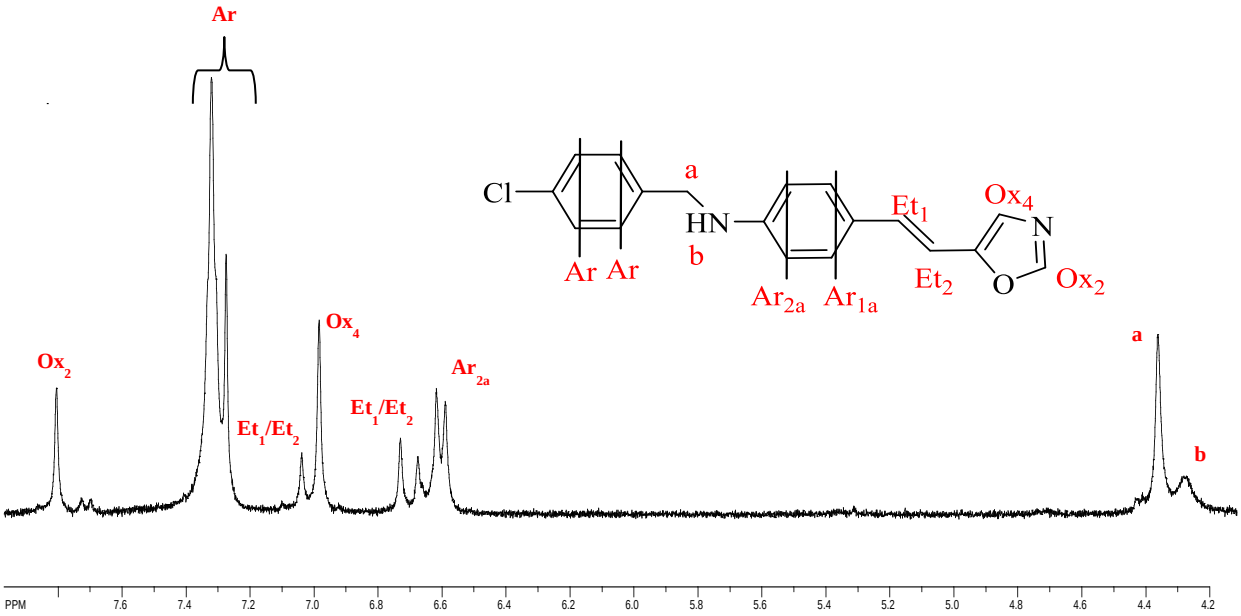
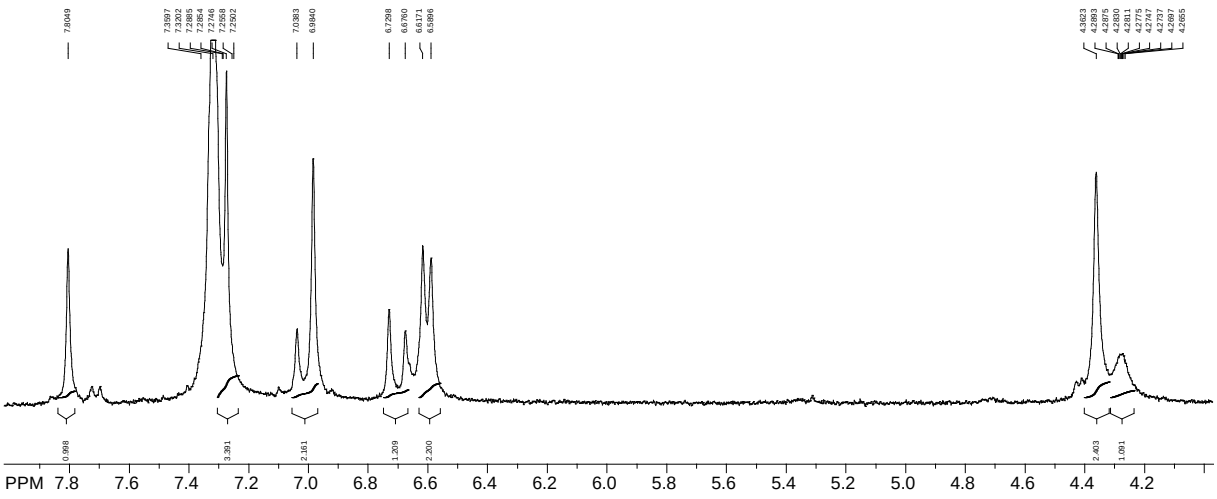
127.5063
125.1665
121.9975
113.6217
112.4481
112.3621
108.2560
76.7259
76.5141
76.3029
54.8061
47.0627
29.1890
C (Et1/Et2)
C (Et1/Et2)
C (c)
C (Ox4)
C (Ox2)
C (a)
PPM 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0

Figure S4. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-(4-chlorobenzyl)-4-(2-(oxazol-5-yl)vinyl)aniline **(*trans*-5)**



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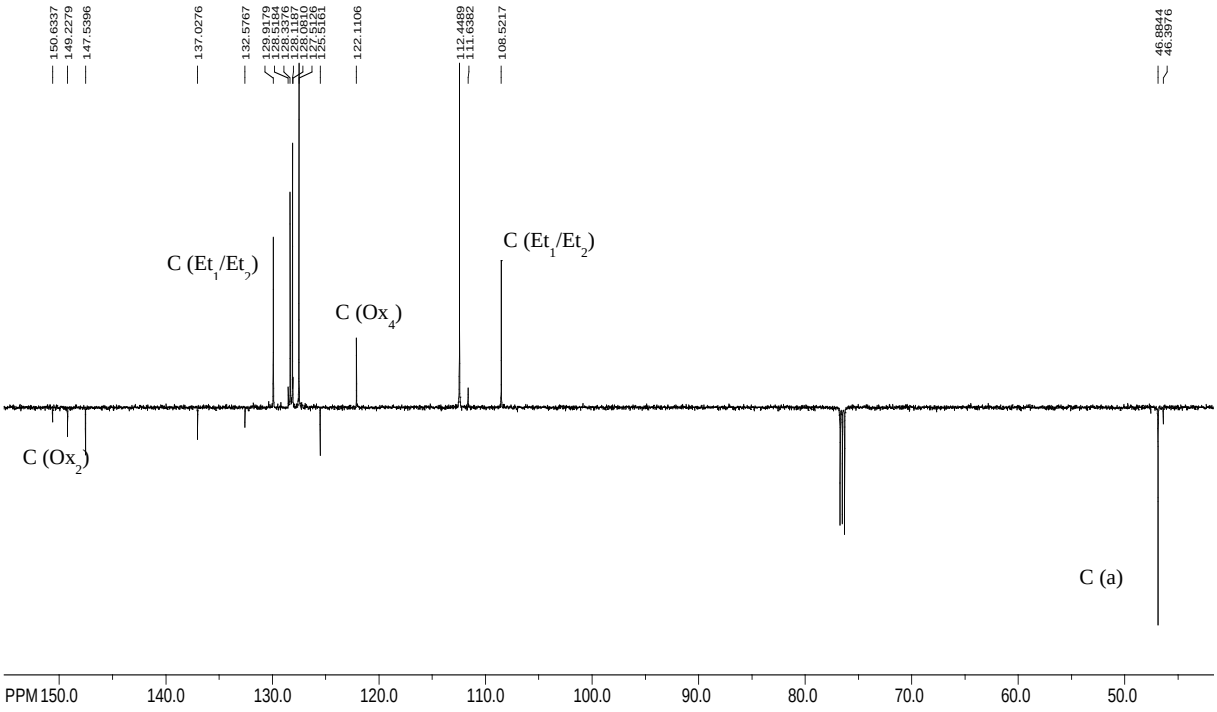
7.3923
7.3885
7.2854
7.2746
7.2588
7.2502
7.0383
6.9940
6.7298
6.6760
6.6171
6.5866
4.3623
4.2883
4.2875
4.2831
4.2811
4.2775
4.2747
4.2737
4.2697
4.2665
0.998
3.391
2.161
1.209
2.200
2.403
1.091
PPM 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2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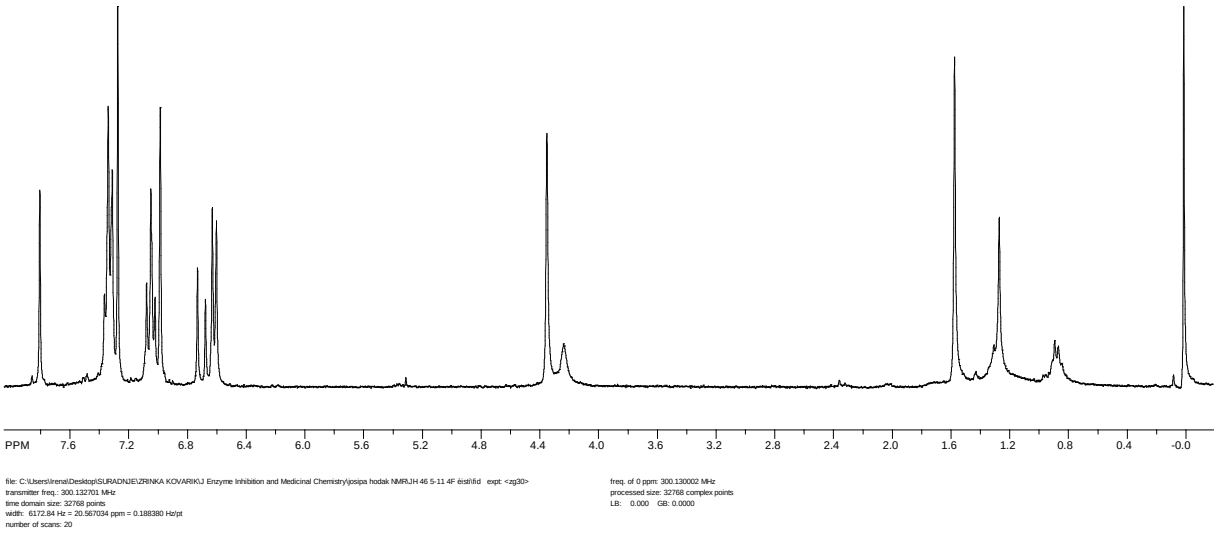
147.5396
137.0276
132.5767
129.9179
129.5154
128.3376
128.1187
128.0810
127.5126
125.5161
122.1106
112.4489
111.6382
108.5217
46.8844
46.3976
C (Et1/Et2)
C (Ox4)
C (Et1/Et2)
C (Ox2)
C (a)
PPM 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0

Figure S5. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-(4-fluorobenzyl)-4-(2-(oxazol-5-yl)vinyl)aniline **(*trans*-6)**



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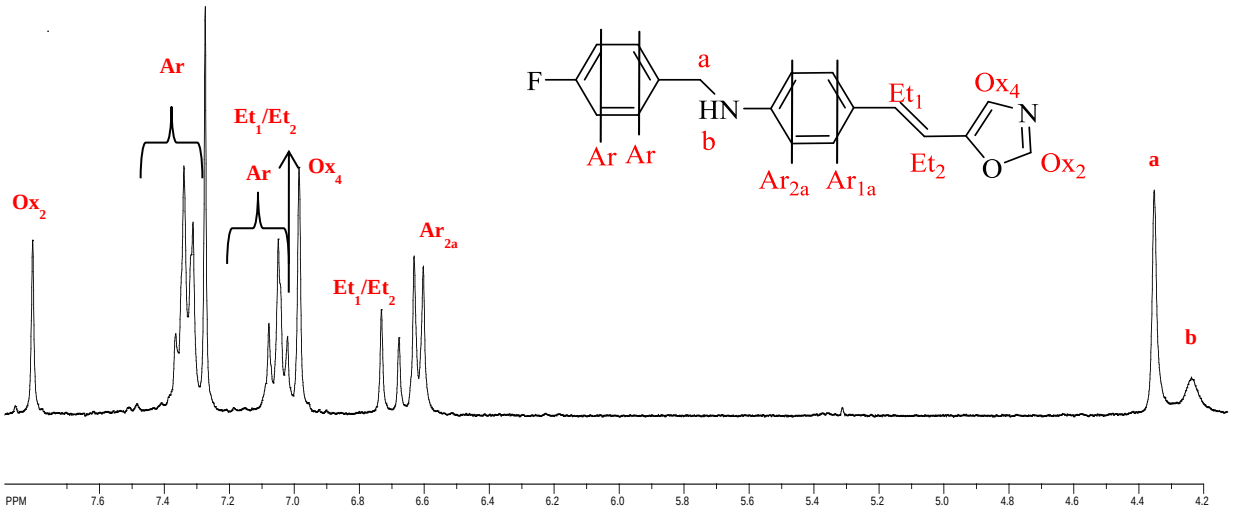
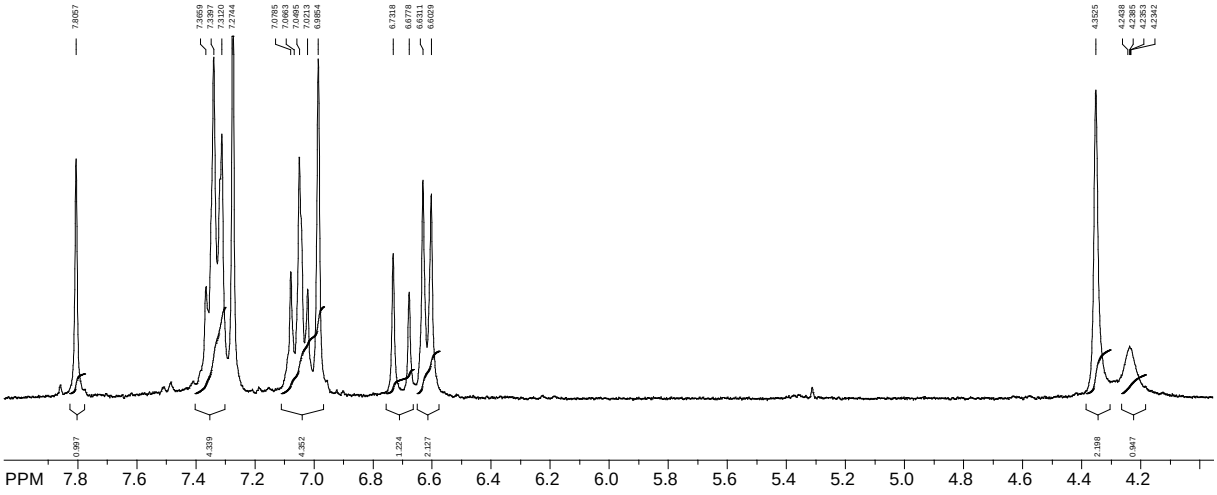
time domain size: 32768 points
width: 6172.84 Hz = 20.567034 ppm = 0.188380 Hz/pt
number of scans: 20

freq. of 0 ppm: 300.130002 MHz
processed size: 32768 complex points
LB: 0.000 GB: 0.0000

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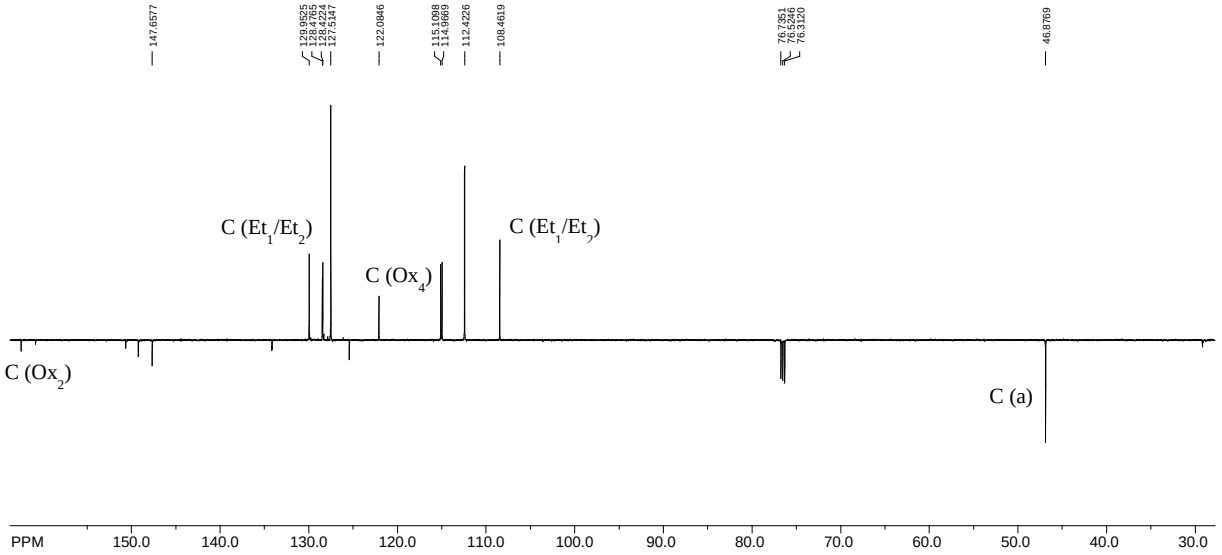
7.3659
7.3397
7.3130
7.2744
7.0785
7.0663
7.0495
7.0213
6.6954
6.7318
6.6778
6.6631
6.6029
4.3525
4.2438
4.2385
4.2053
4.2342
0.997
4.339
4.352
1.224
2.127
2.198
0.947
PPM 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2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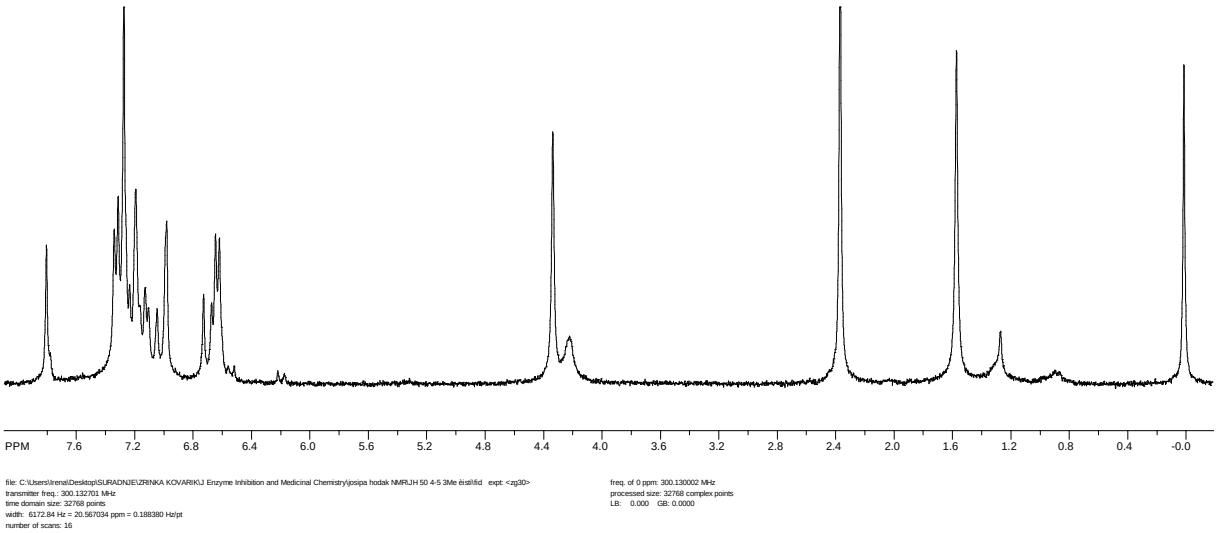
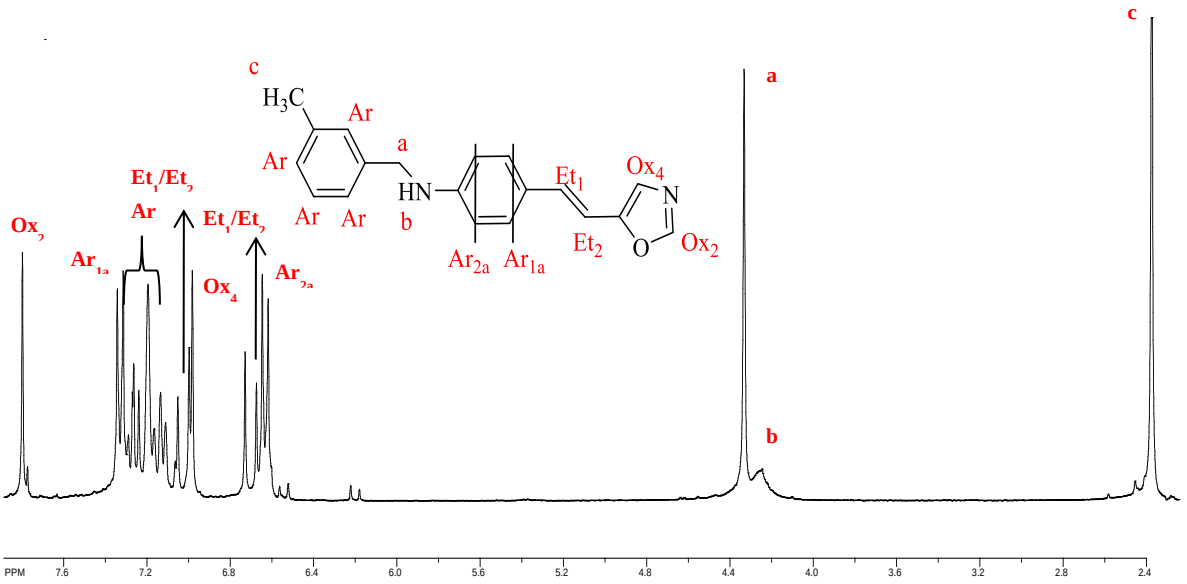
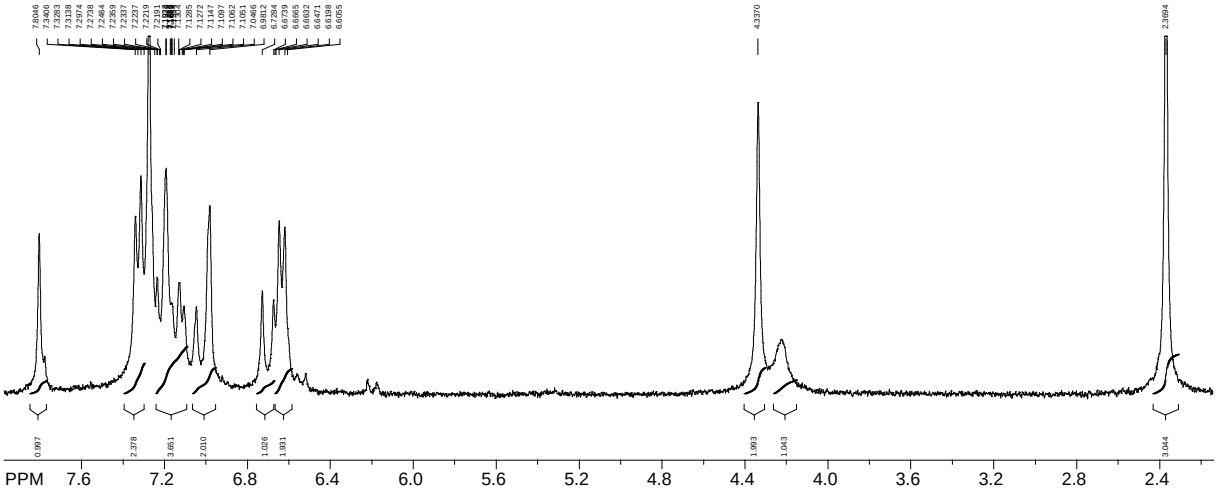
129.9525
128.4755
128.4224
127.5147
122.0846
115.1098
114.9669
112.4226
108.4619
76.7351
76.5246
76.3120
46.8769
C (Et1/Et2)
C (Ox4)
C (Et1/Et2)
C (Ox2)
C (a)
PPM 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0

Figure S6. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-(3-methylbenzyl)-4-(2-(oxazol-5-yl)vinyl)aniline **(*trans*-7)**



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6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4

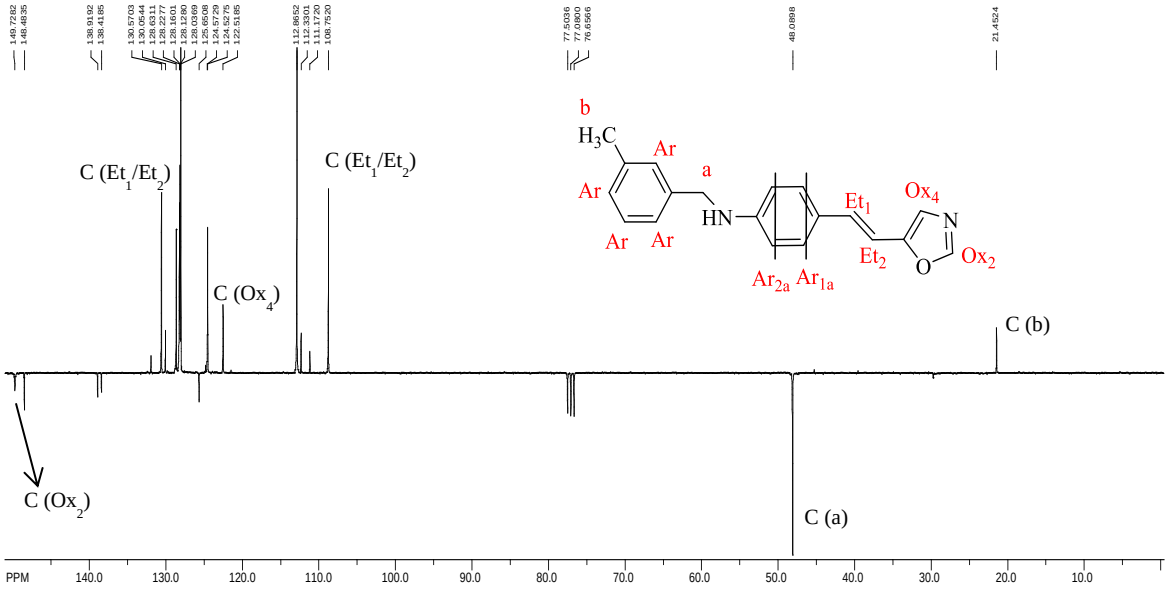

C (Et1/Et2)
C (Et1/Et2)
C (Ox4)
C (Ox2)
C (b)
C (a)
b
H3C
Ar
a
HN
Et1
Ox4
N
Et2
O
Ox2
Ar2a
Ar1a
PPM
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0

Figure S7. COSY spectra of (*E*)-*N*-(3-methylbenzyl)-4-(2-(oxazol-5-y)vinyl)aniline (*trans*-**7**)

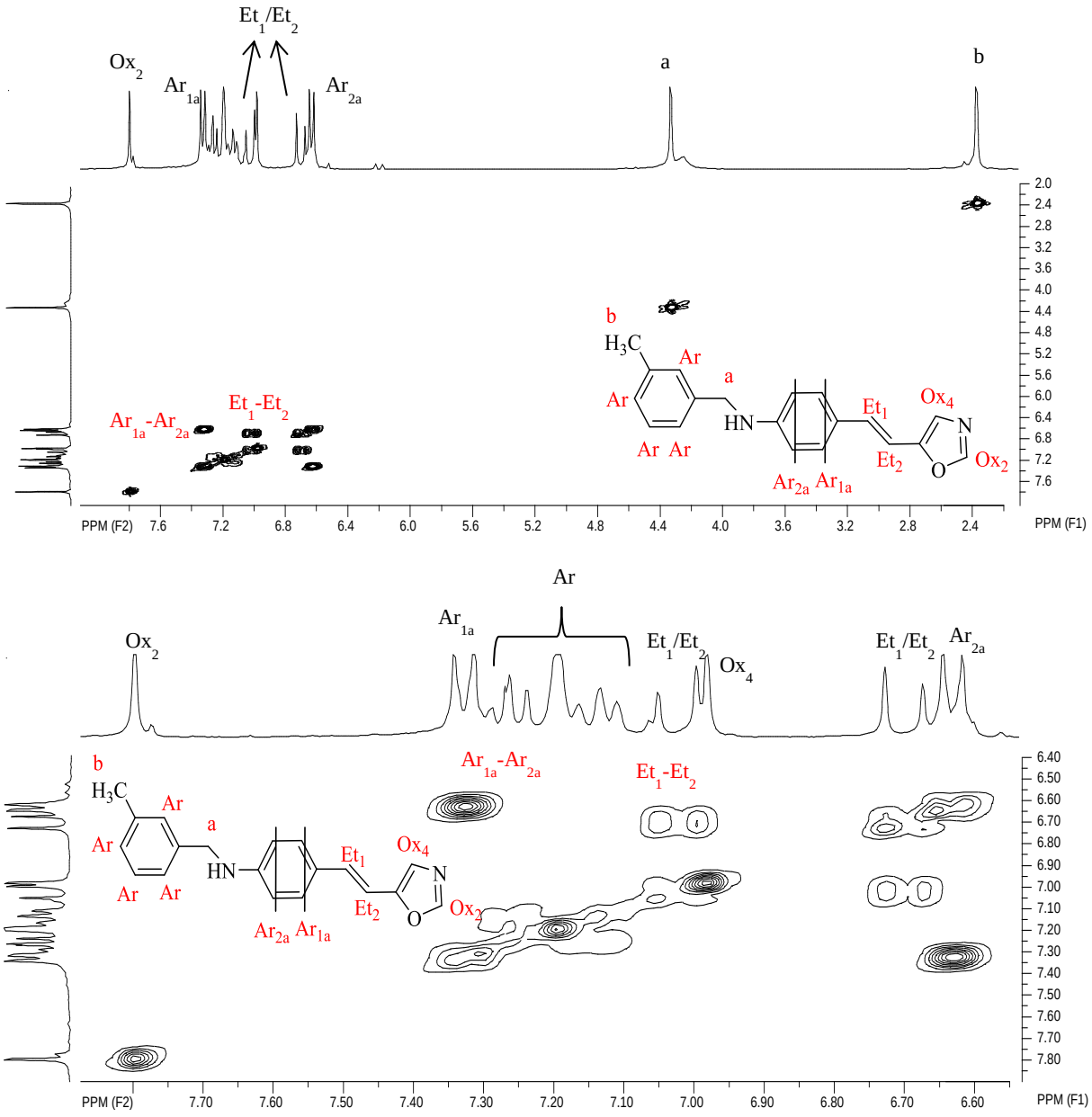


Figure S8. HETCOR spectra of (*E*)-*N*-(3-methylbenzyl)-4-(2-(oxazol-5-il)vinil)aniline (*trans*-**7**)

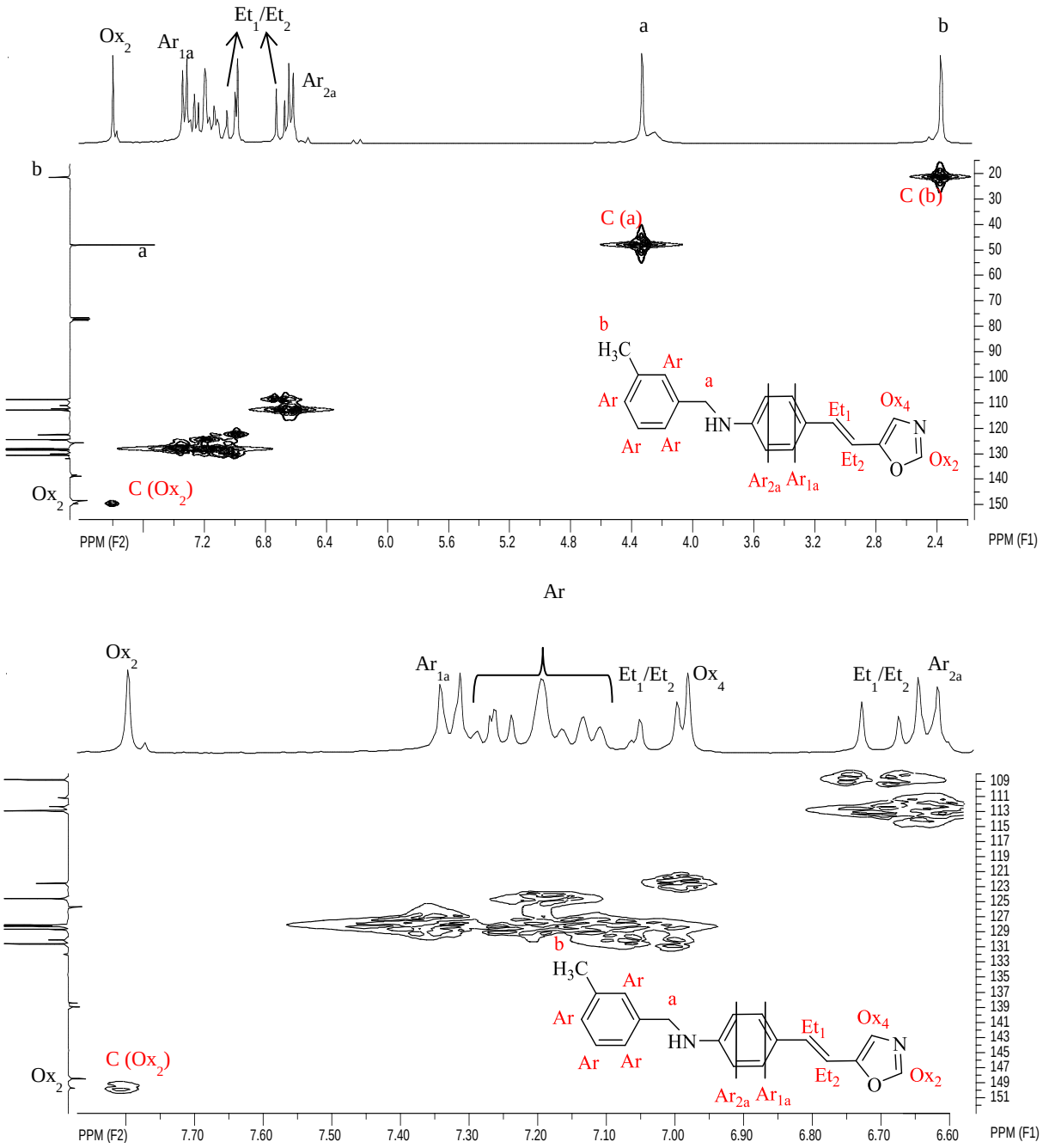
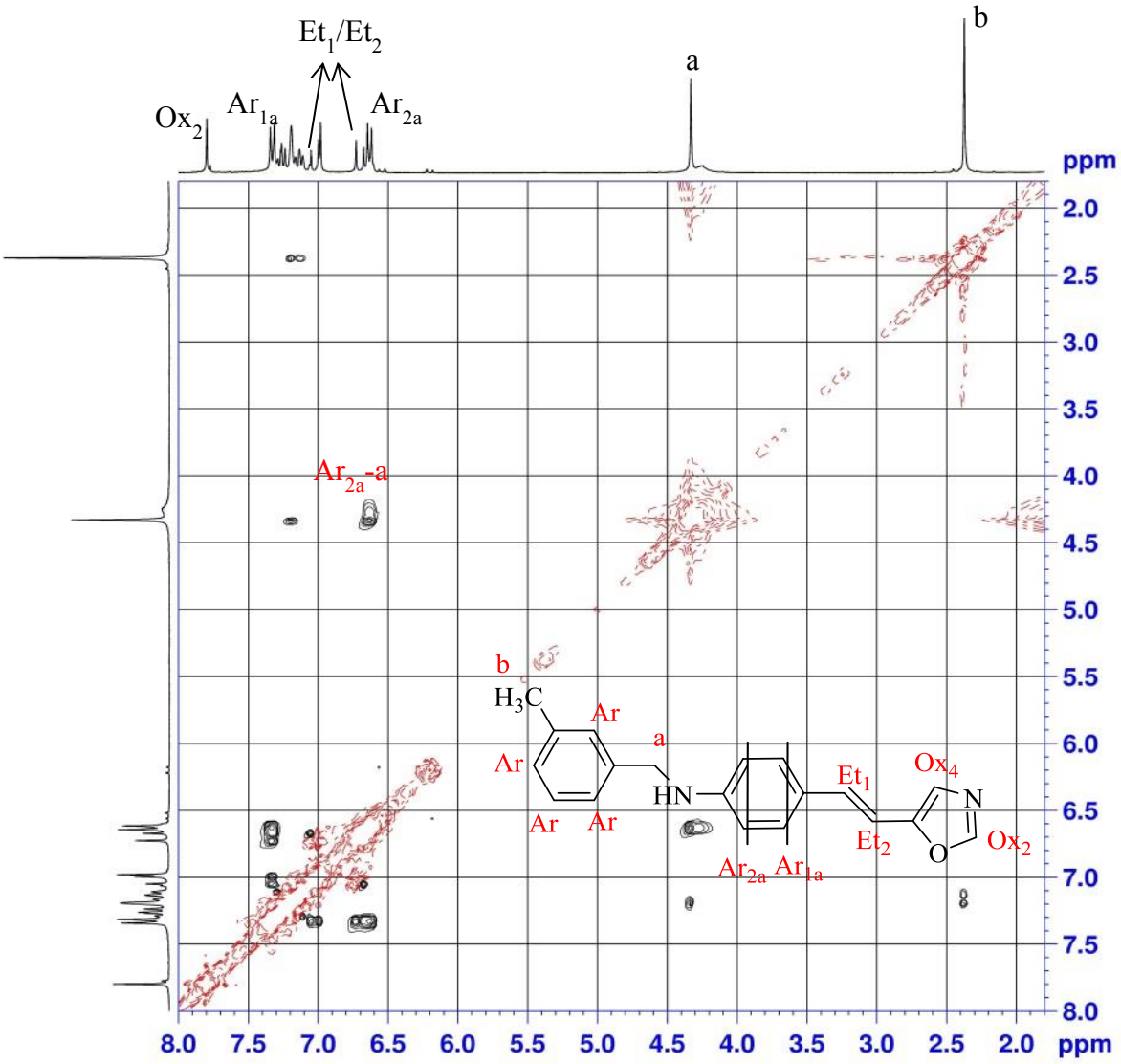


Figure S9. NOESY spectra of (*E*)-*N*-(3-methylbenzyl)-4-(2-(oxazol-5-yl)vinyl)aniline (*trans*-**7**)



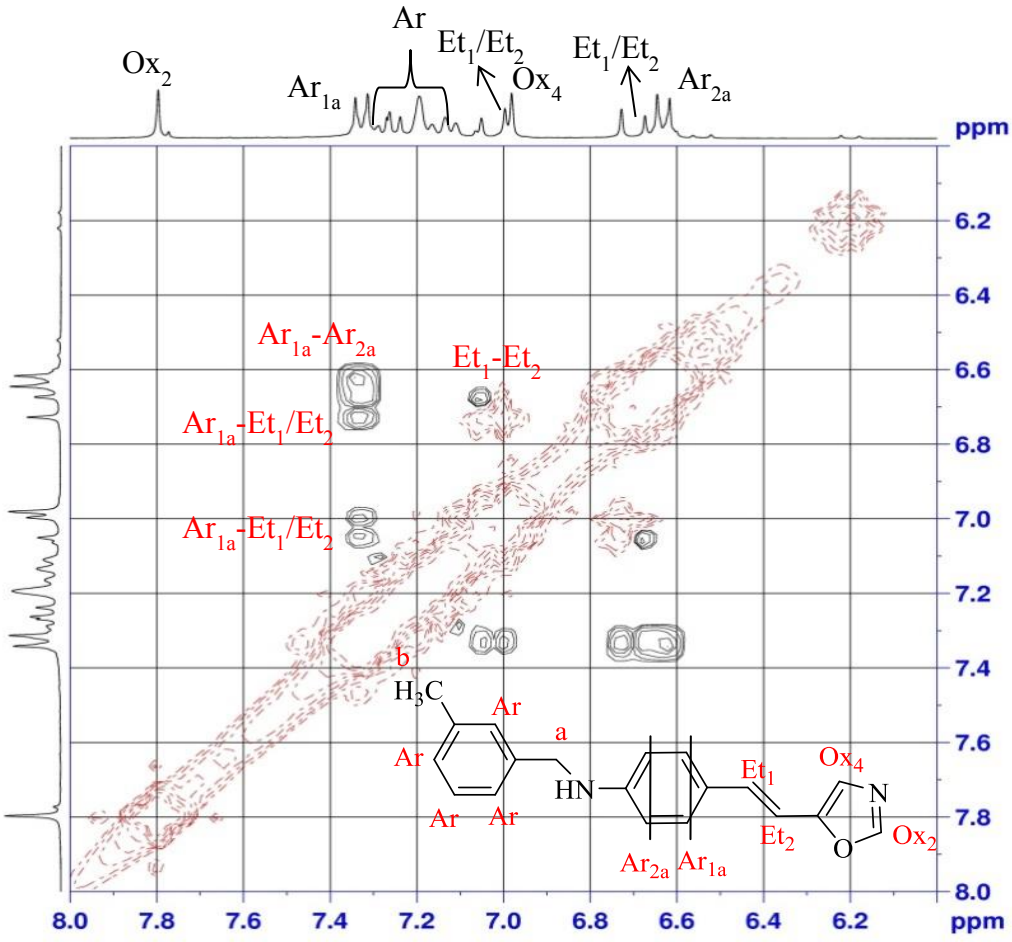
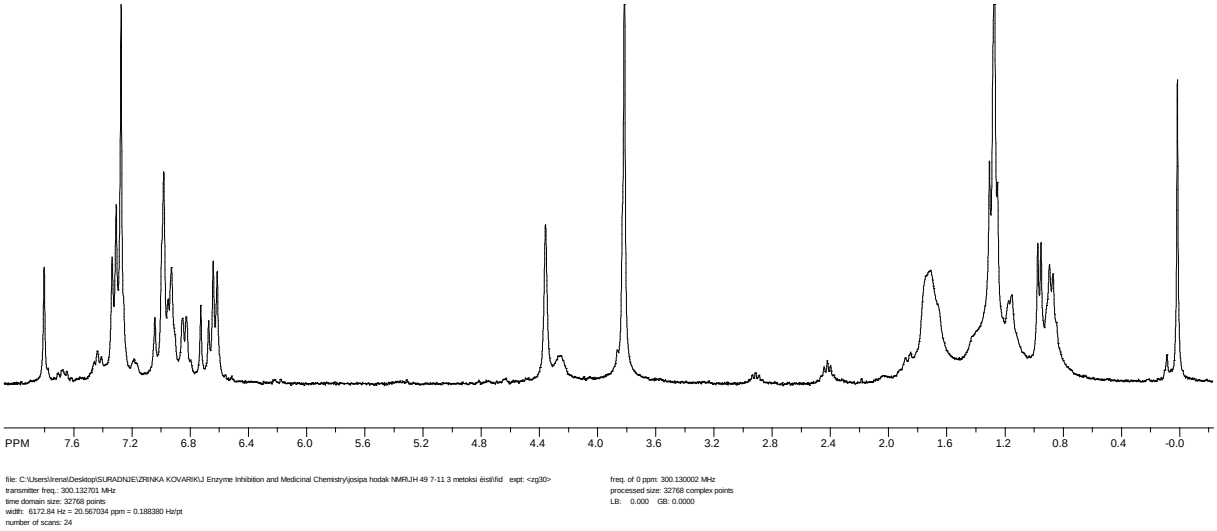
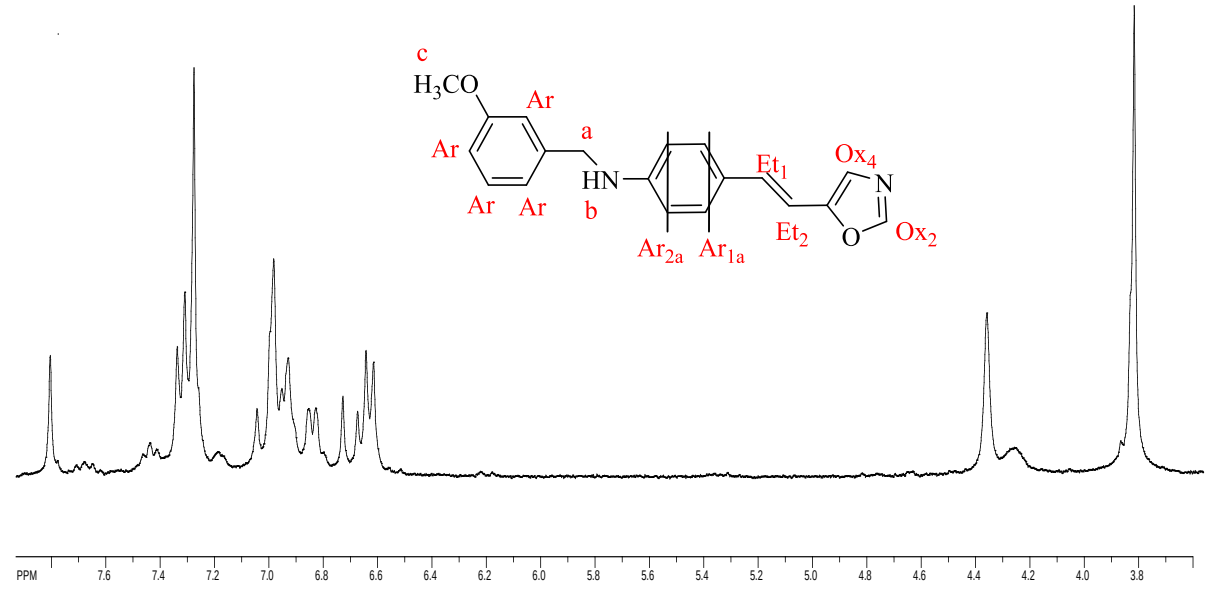
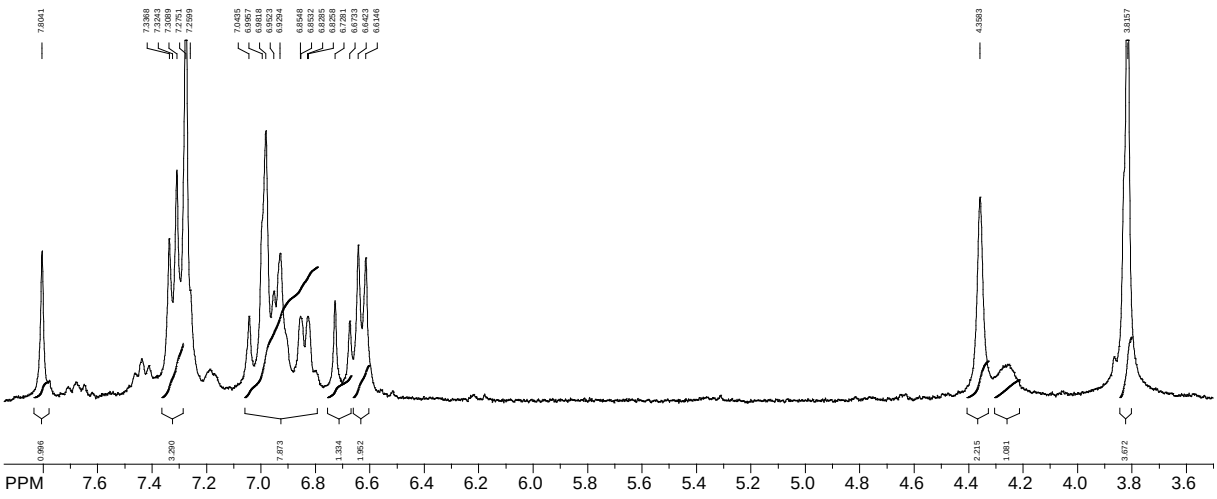

Ox2
Ar1a
Ar
Et1/Et2
Ox4
Et1/Et2
Ar2a
ppm
6.2
6.4
6.6
6.8
7.0
7.2
7.4
7.6
7.8
8.0
Ar1a-Ar2a
Et1-Et2
Ar1a-Et1/Et2
Ar1a-Et1/Et2
b
H3C
Ar
a
Ar
HN
Et1
Ox4
N
Et2
O
Ox2
Ar2a
Ar1a

Figure S10. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-(3-methoxybenzyl)-4-(2-(oxazol-5-yl)vinyl)aniline **(*trans*-8)**



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7.3368
7.3243
7.3089
7.2975
7.2599
7.0435
6.9927
6.9811
6.9923
6.9294
6.8548
6.8832
6.8285
6.8060
6.7281
6.6733
6.6423
6.6146
4.3983
3.8157
0.996
3.200
7.873
1.334
1.952
2.215
1.081
3.672
PPM
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6

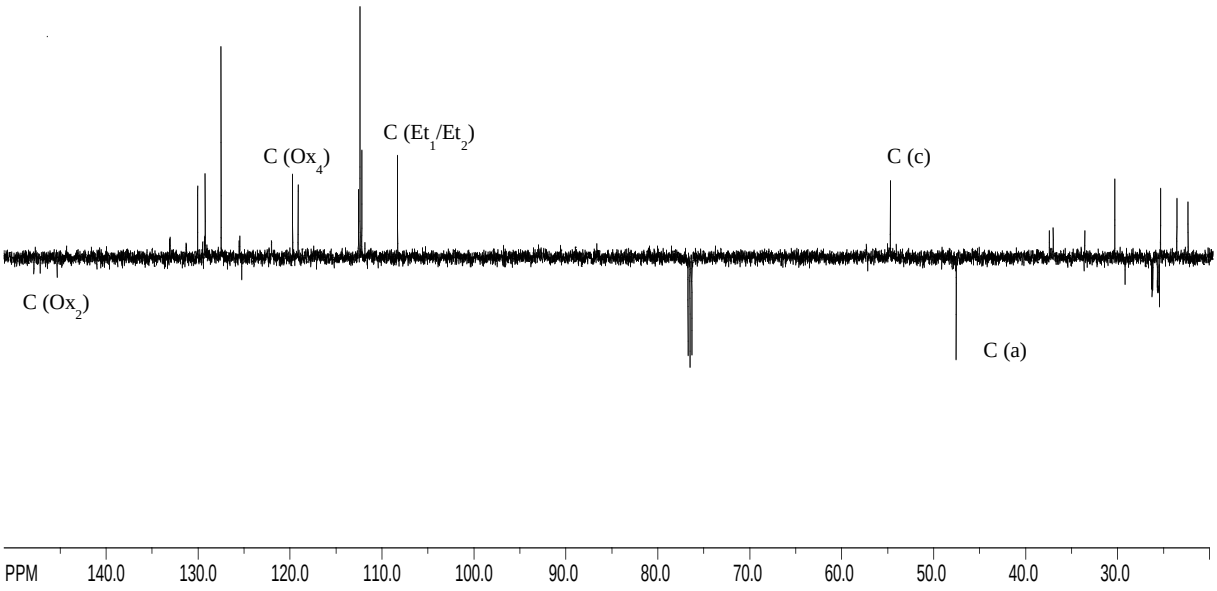
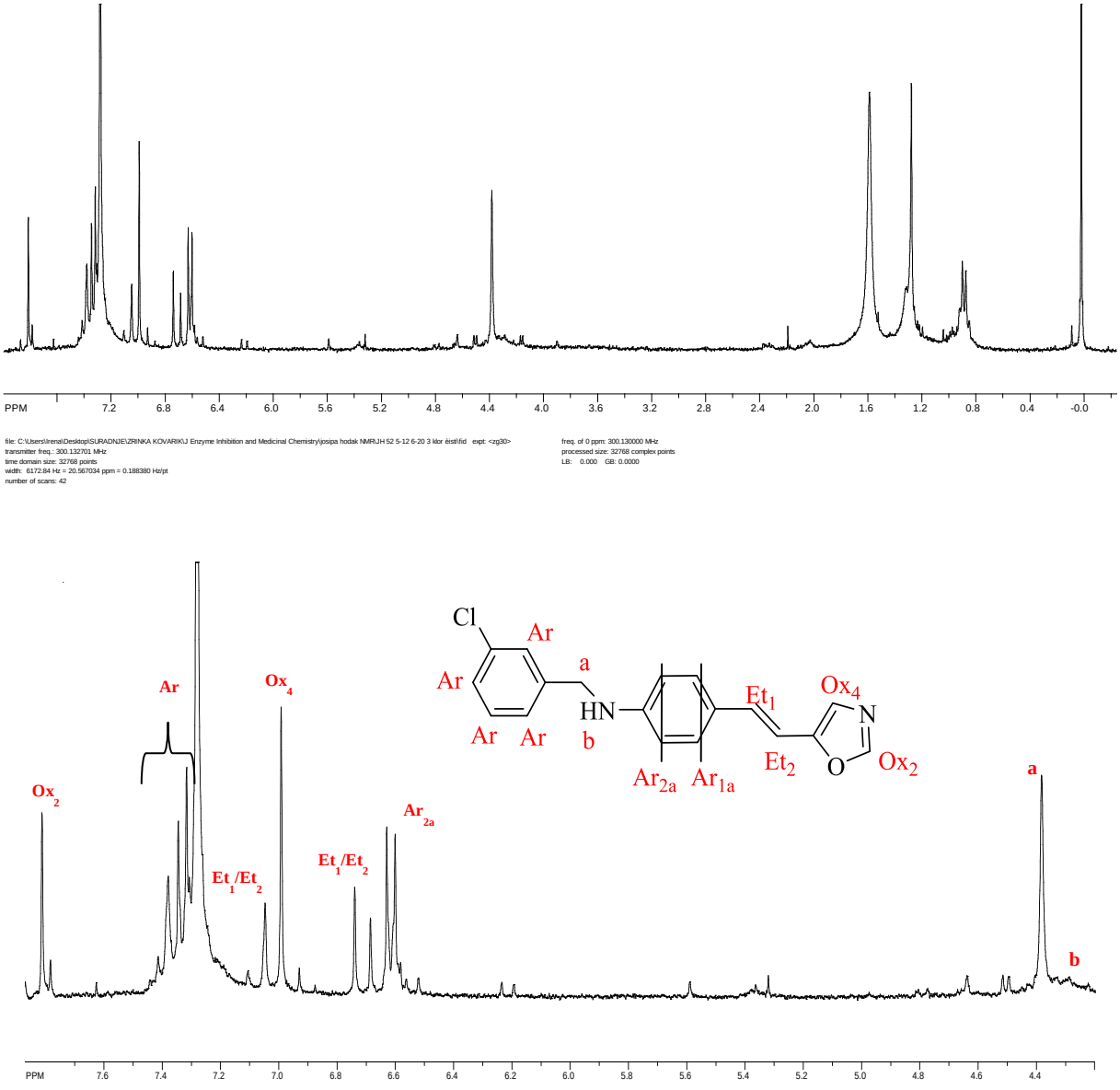
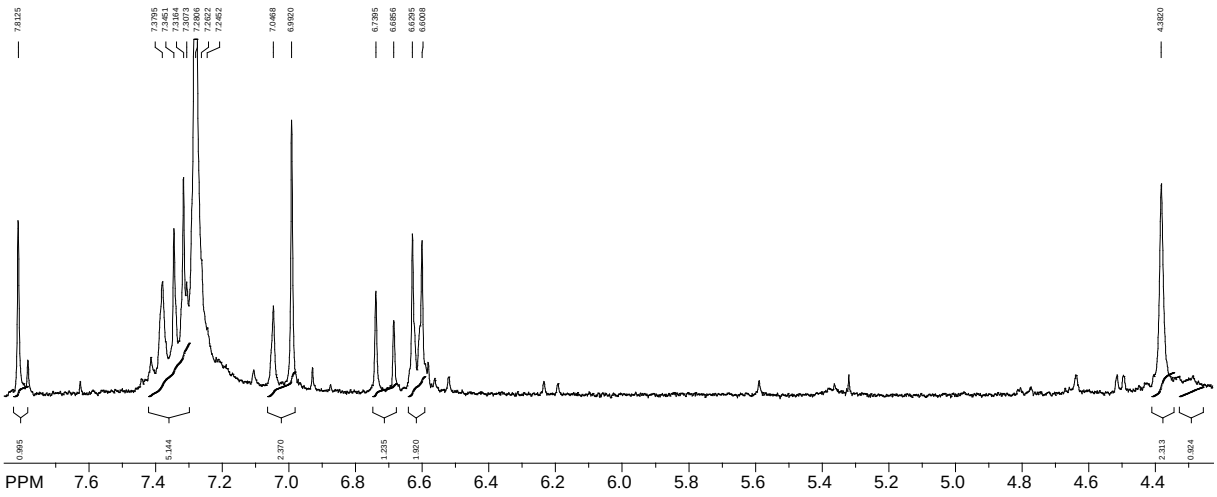

C (Ox4)
C (Et1/Et2)
C (c)
C (Ox2)
C (a)
PPM
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0

Figure S11. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-(3-chlorobenzyl)-4-(2-(oxazol-5-yl)vinyl)aniline **(*trans*-9)**

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7.3795
7.3641
7.3184
7.3073
7.2806
7.2652
7.2462
7.0468
6.9920
6.7395
6.6856
6.6295
6.6008
4.3820
0.995
5.144
2.370
1.235
1.920
2.313
0.924
PPM 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4

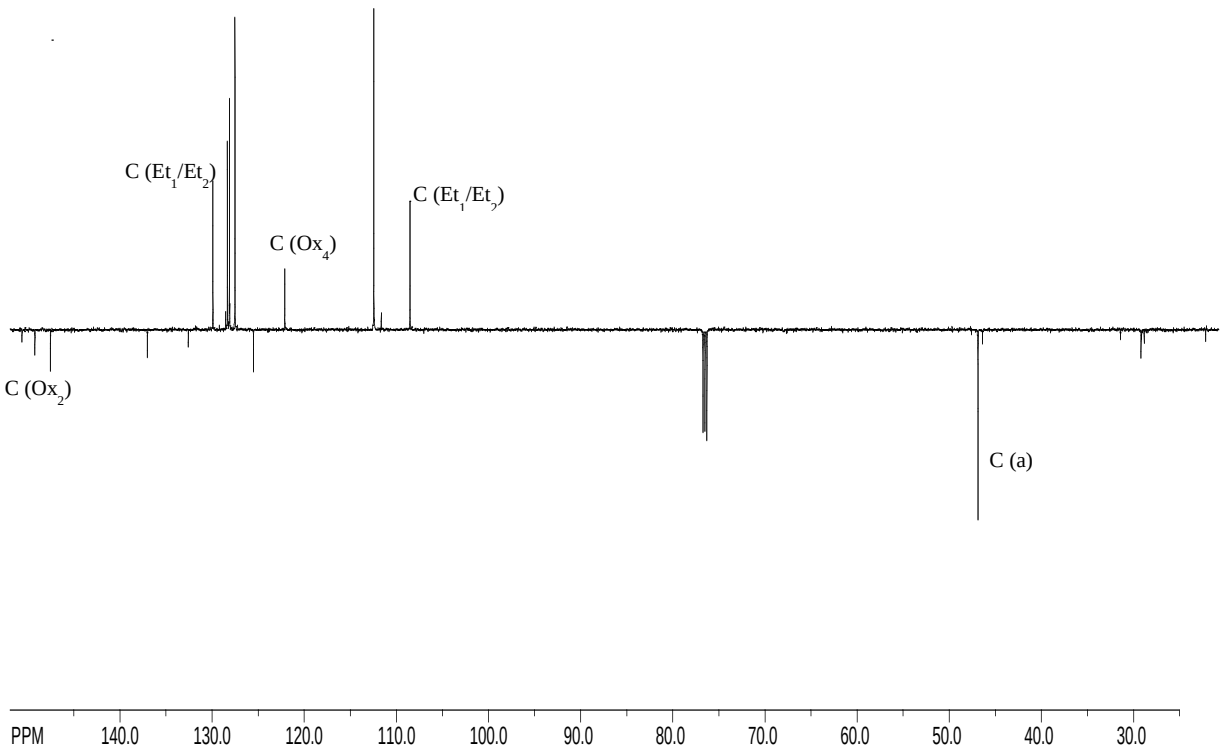
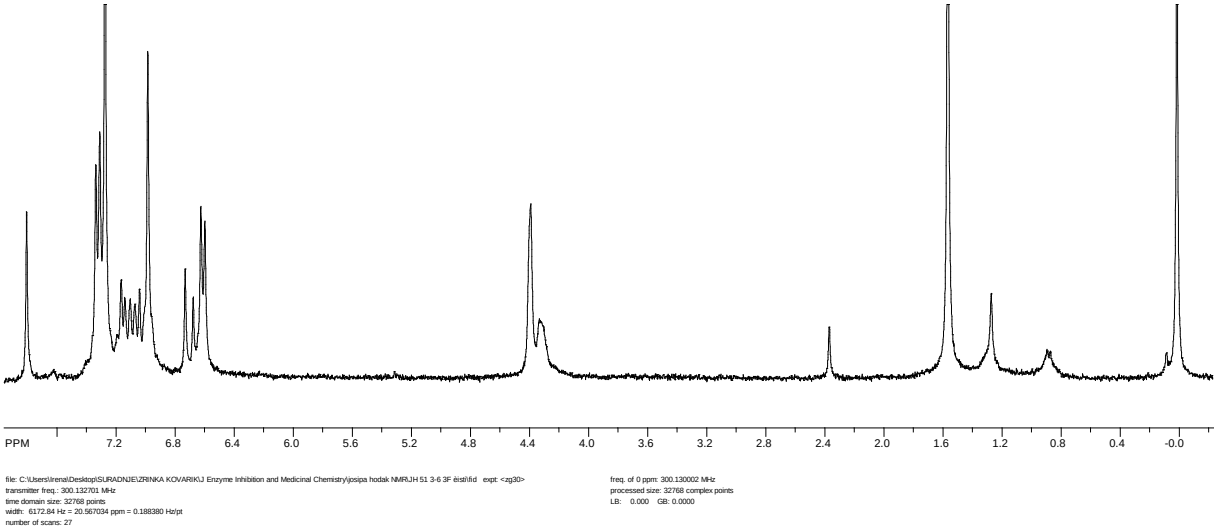
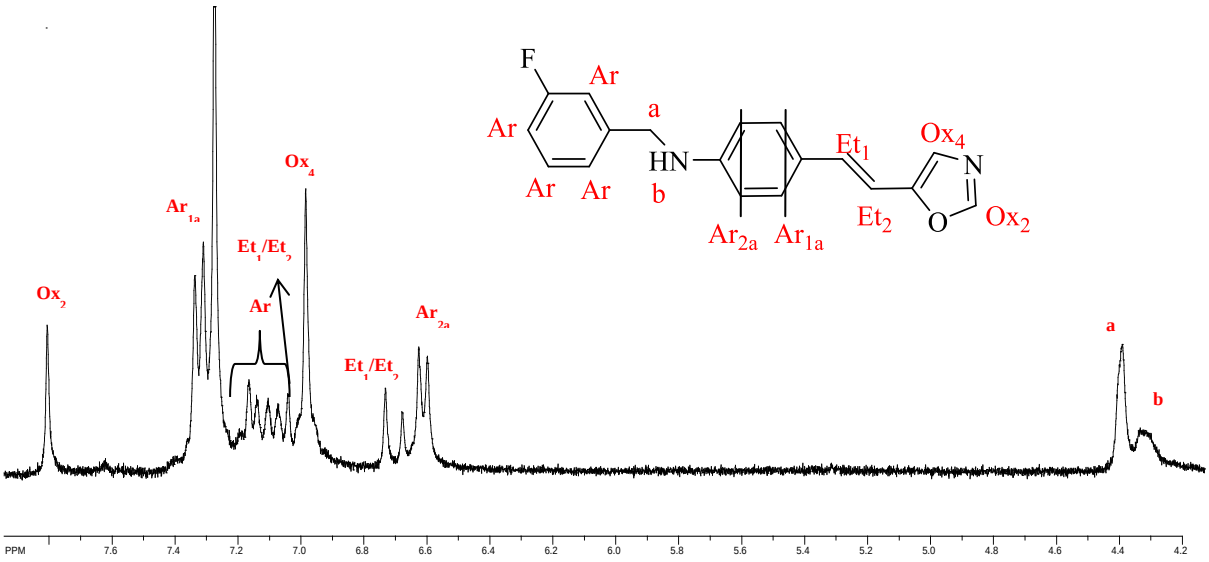
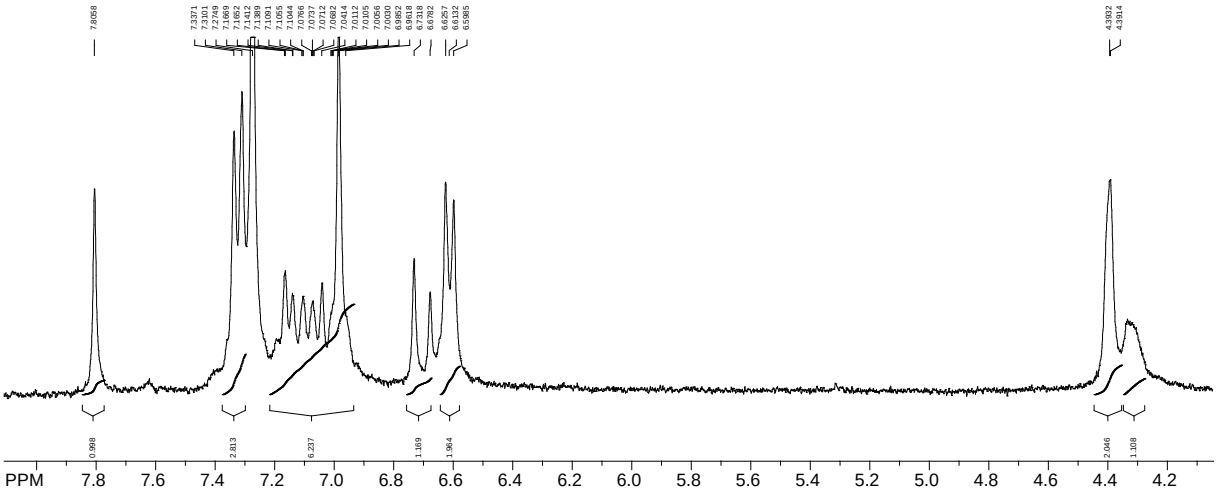

C (Et1/Et2)
C (Ox4)
C (Et1/Et2)
C (Ox2)
C (a)
PPM 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0

Figure S12. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-(3-fluorobenzyl)-4-(2-(oxazol-5-yl)vinyl)aniline **(*trans*-10)**






7.8058
7.3371
7.3301
7.2749
7.1669
7.1652
7.1457
7.1389
7.1091
7.1055
7.1044
7.0766
7.0737
7.0712
7.0688
7.0414
7.0112
7.0105
7.0056
7.0000
6.9982
6.9618
6.7318
6.6928
6.6257
6.6132
6.5985
4.3932
4.3914
0.998
2.813
6.237
1.169
1.964
2.046
1.108
PPM
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2

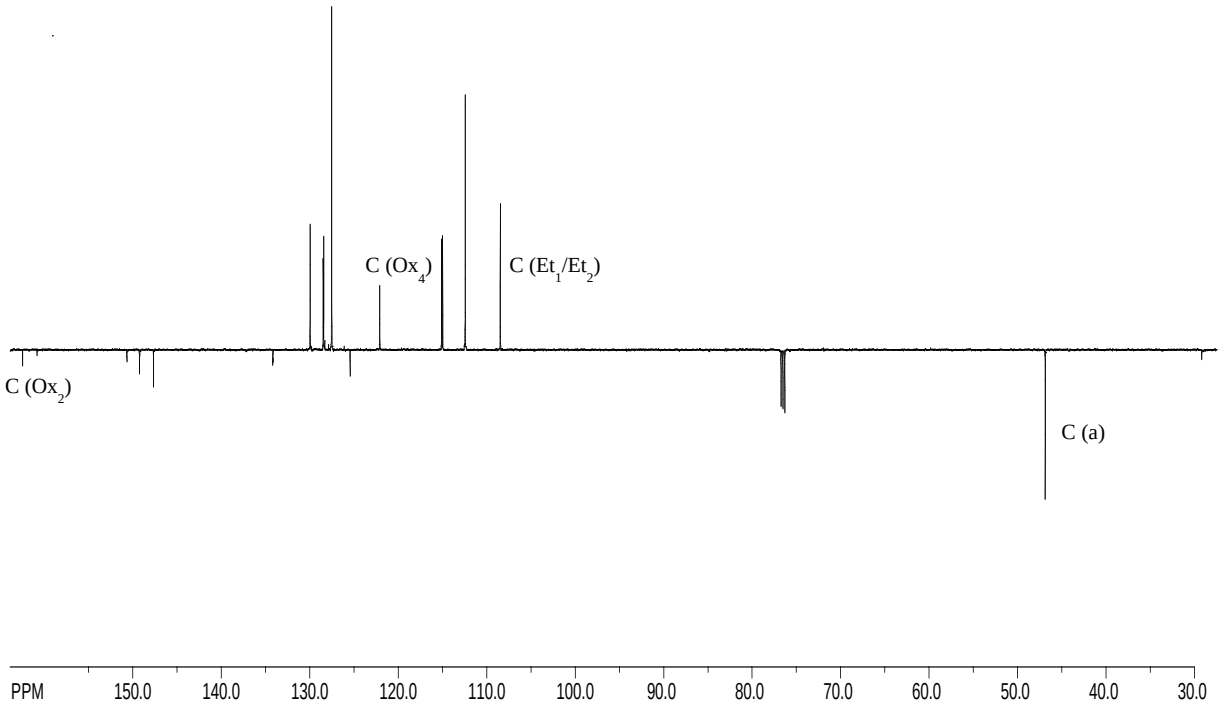
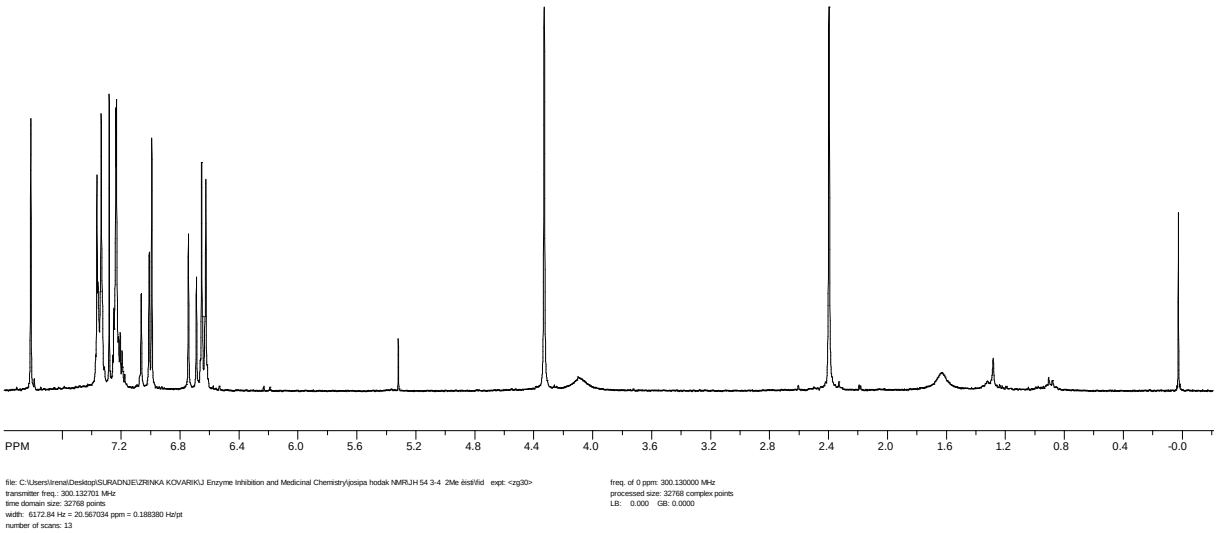
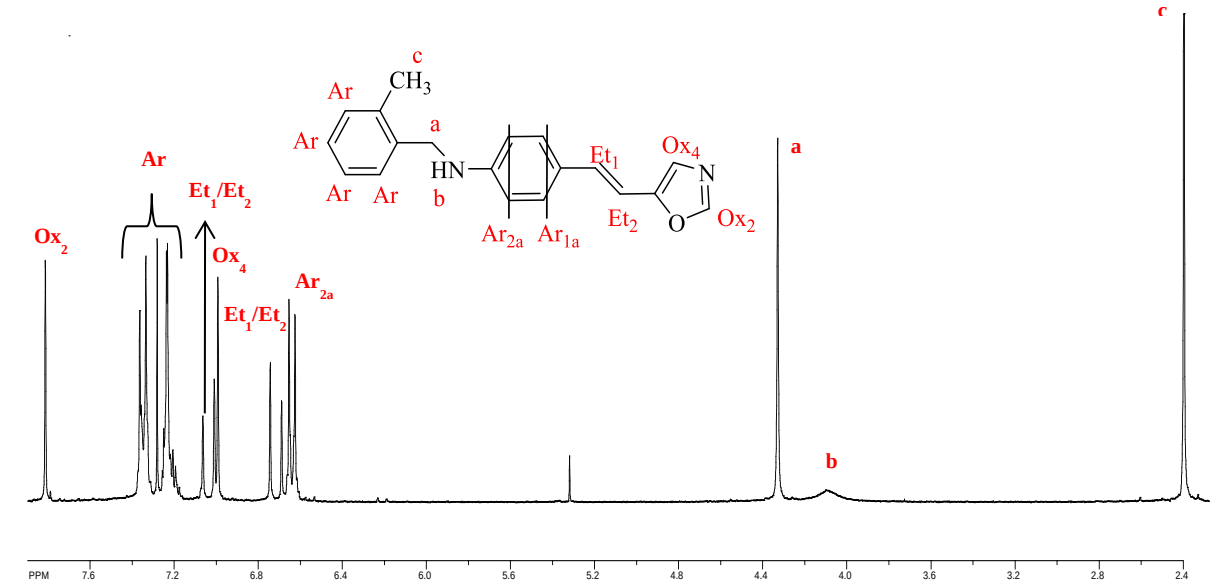
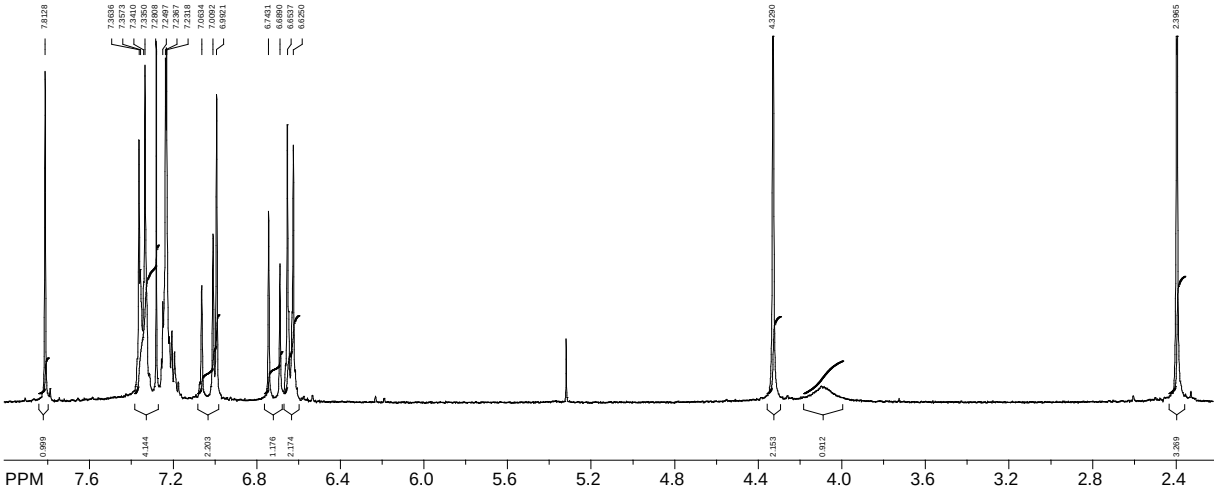

C (Ox4)
C (Et1/Et2)
C (Ox2)
C (a)
PPM
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0

Figure S13. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-(2-methylbenzyl)-4-(2-(oxazol-5-yl)vinyl)aniline (***trans*-11**)






7.8128
7.3636
7.3523
7.3410
7.3380
7.2808
7.2697
7.2387
7.2318
7.0634
7.0092
6.9921
6.7451
6.6880
6.6577
6.6250
4.3290
2.3965
0.999
4.144
2.203
1.176
2.174
2.153
0.912
3.269
PPM
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4

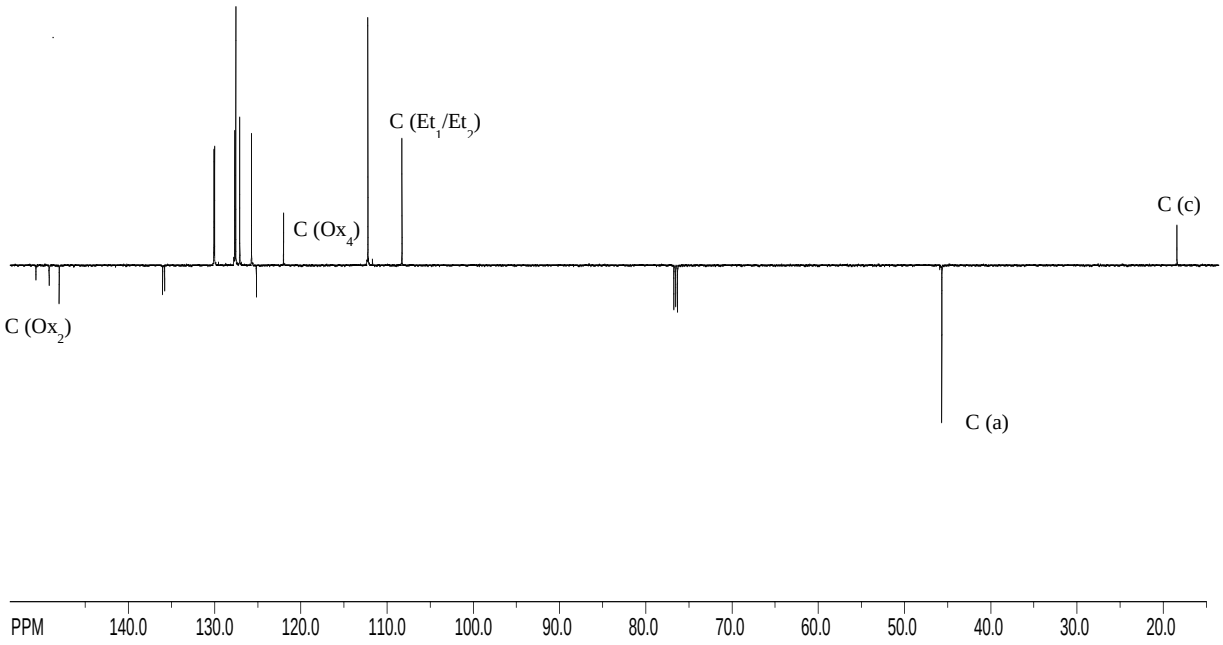
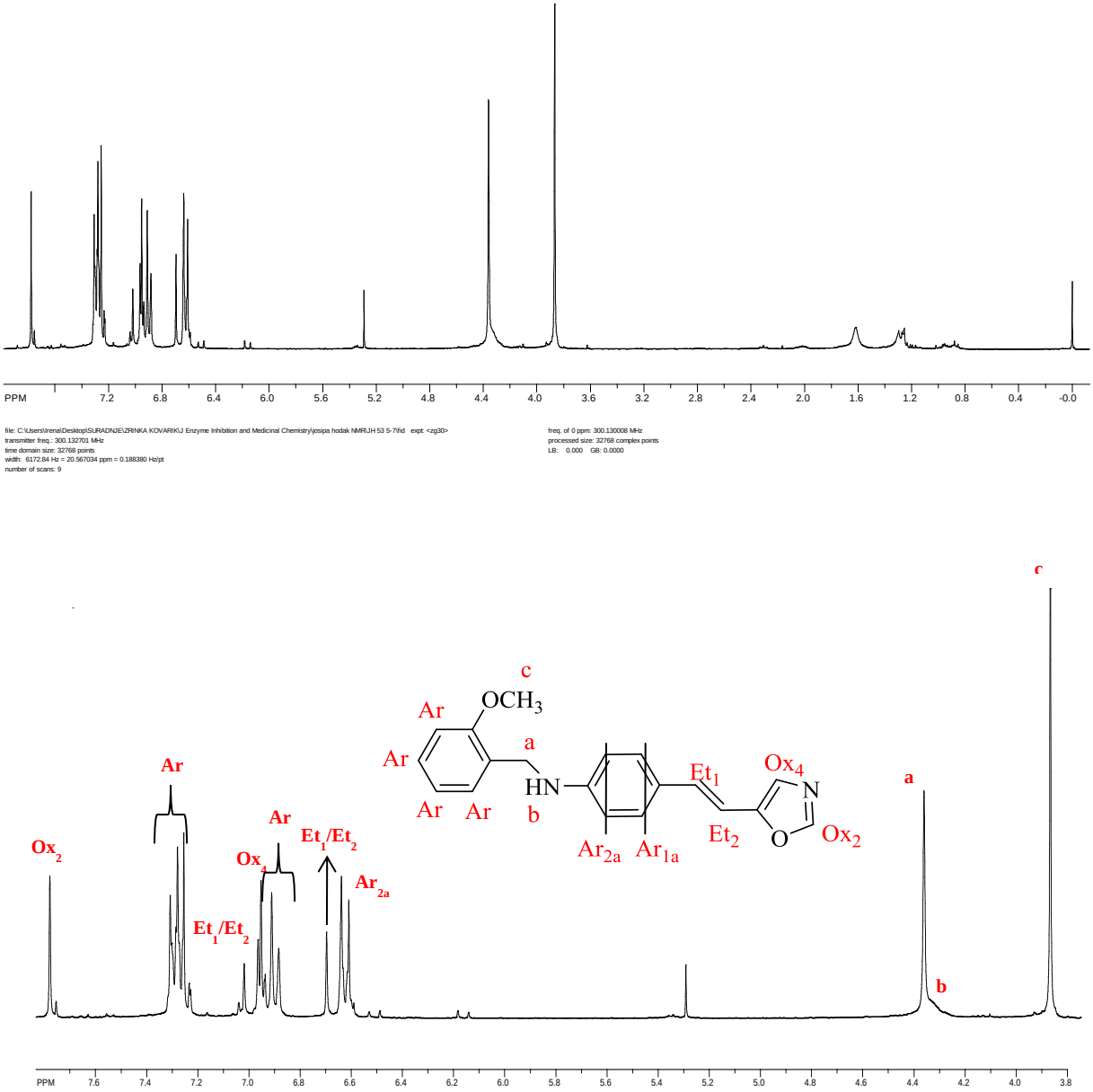
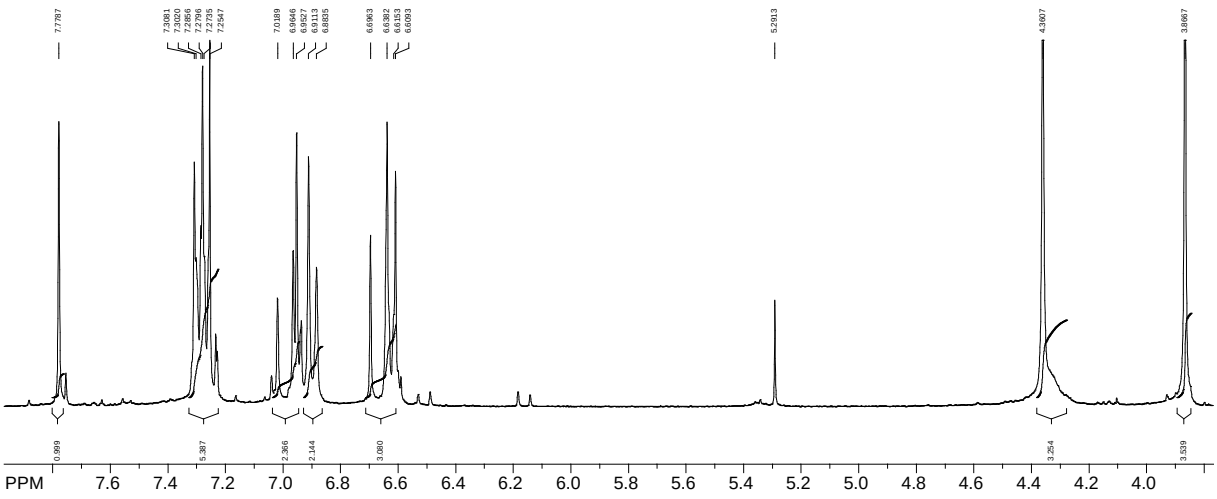

C (Et1/Et2)
C (Ox4)
C (c)
C (Ox2)
C (a)
PPM
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0

Figure S14. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-(2-methoxybenzyl)-4-(2-(oxazol-5-yl)vinyl)aniline (***trans*-12**)




7.7787
7.3081
7.2920
7.2856
7.2796
7.2735
7.2647
7.0189
6.9646
6.9527
6.9113
6.8835
6.6963
6.6382
6.6153
6.6093
5.2913
4.3607
3.8667
0.999
5.387
2.366
2.144
3.080
3.254
3.539
PPM
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0

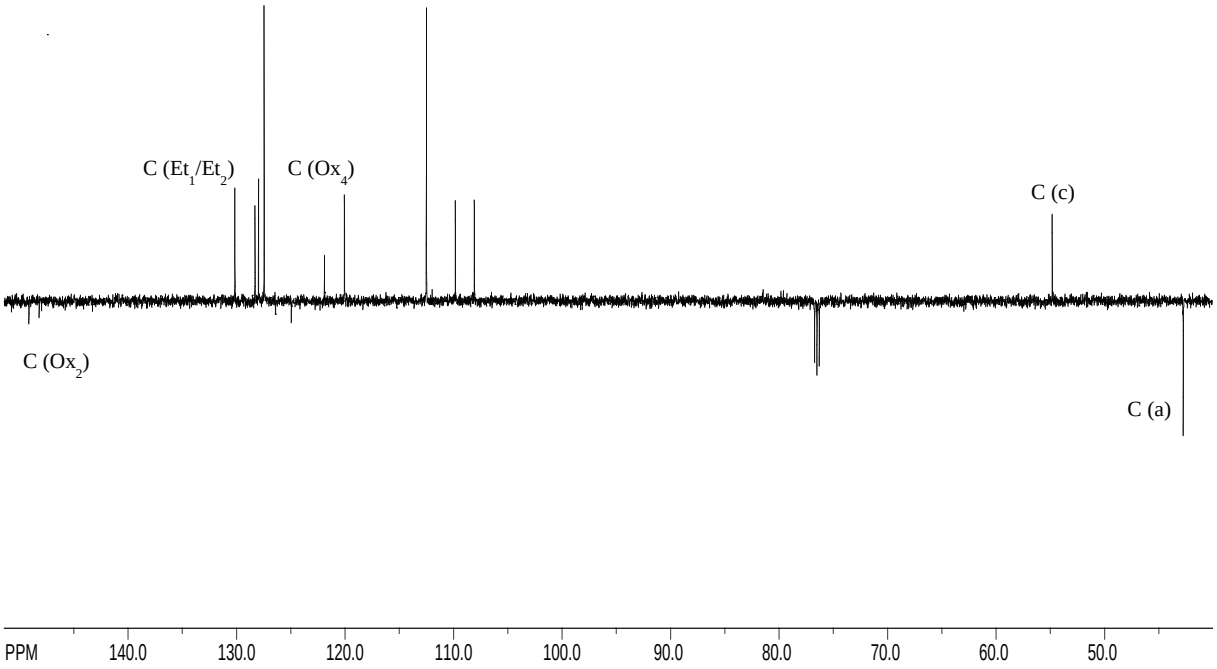
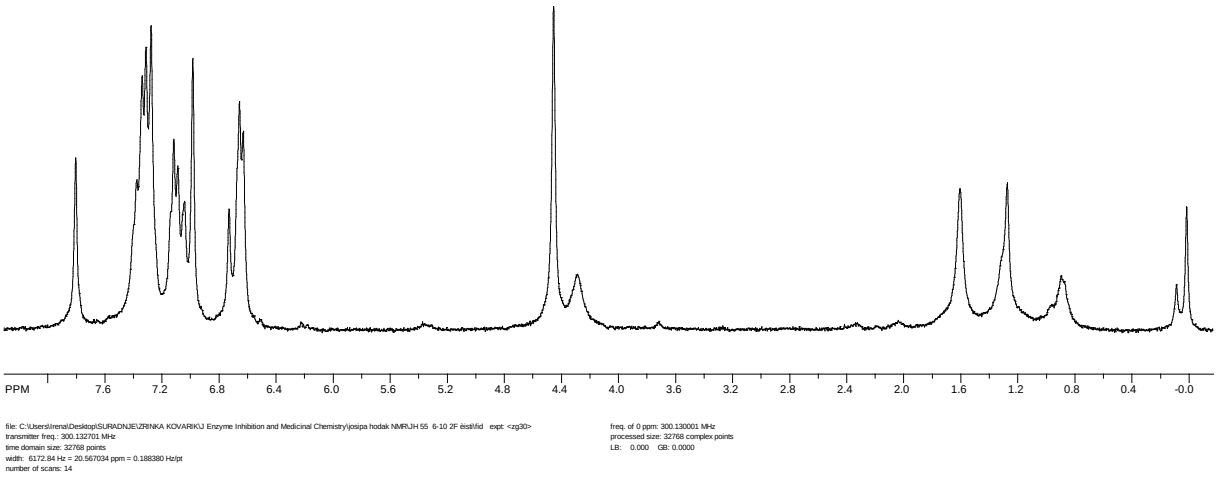
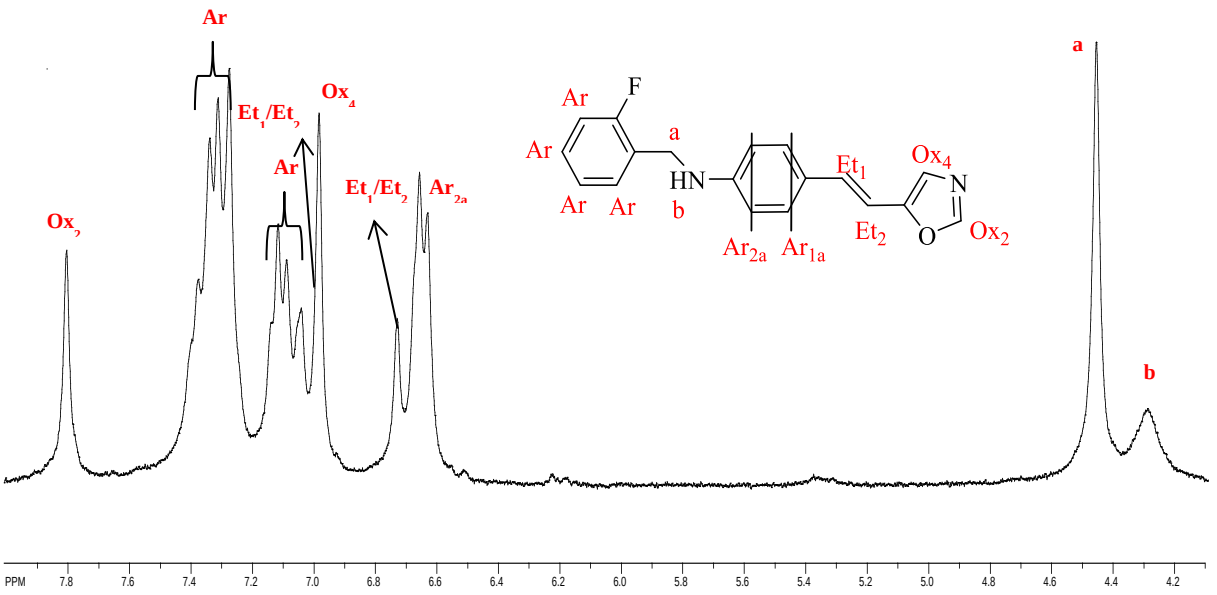
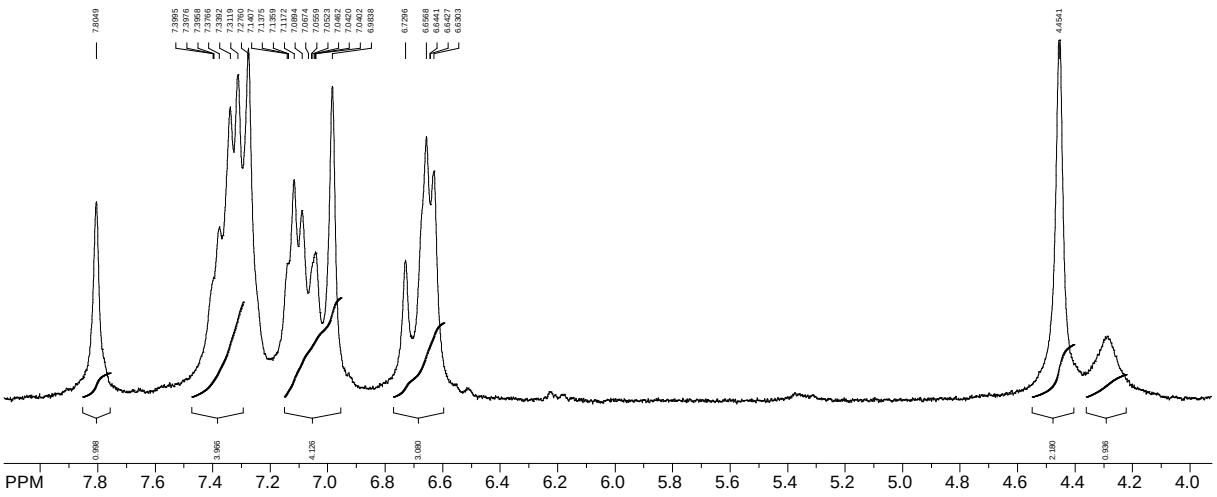
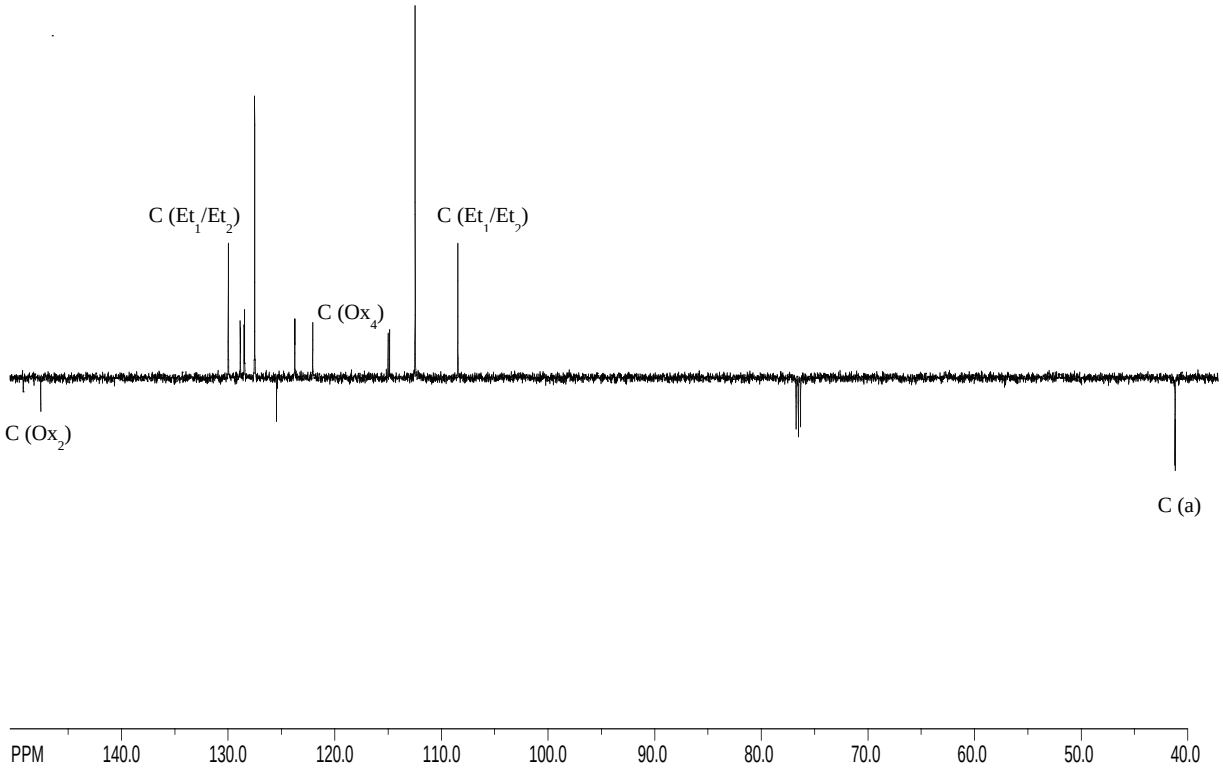

C (Et1/Et2)
C (Ox4)
C (c)
C (Ox2)
C (a)
PPM
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0

Figure S15. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-(2-fluorobenzyl)-4-(2-(oxazol-5-yl)vinyl)aniline **(*trans*-14)**



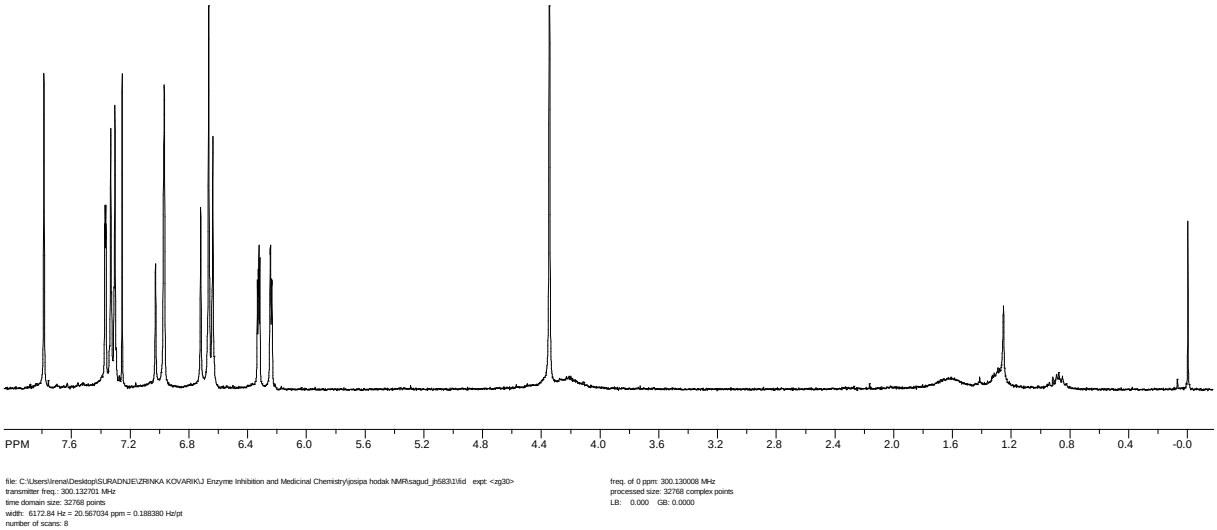


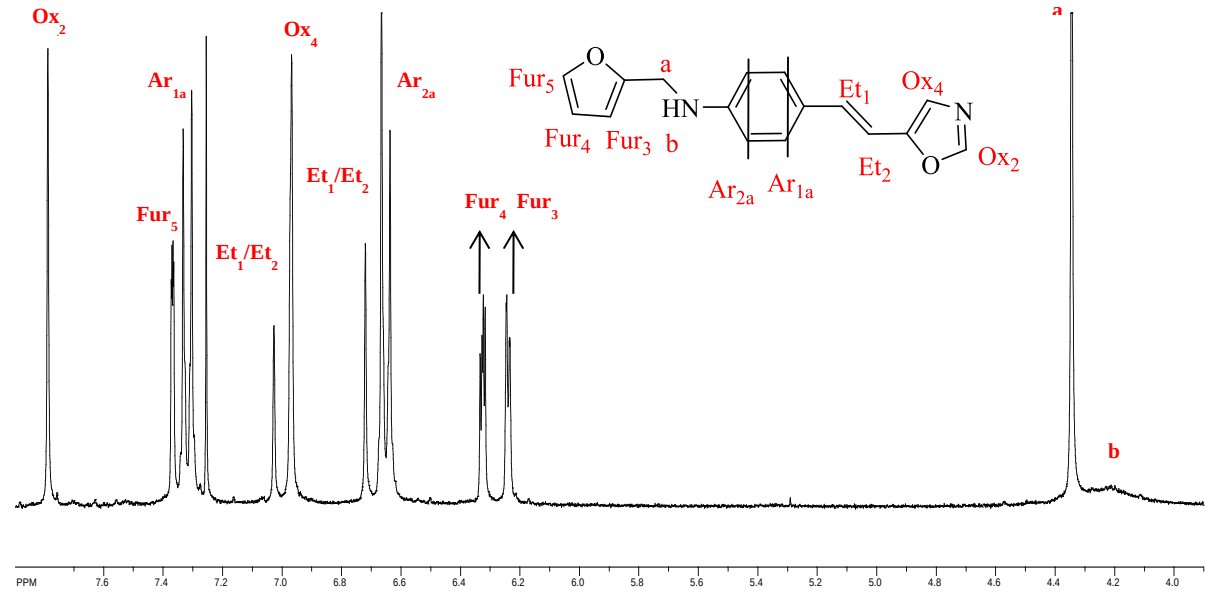

7.8049
7.3995
7.3976
7.3958
7.3796
7.3782
7.3119
7.2760
7.1497
7.1375
7.1359
7.1172
7.0894
7.0714
7.0553
7.0523
7.0462
7.0420
7.0402
6.9838
6.7296
6.6568
6.6441
6.6427
6.6303
4.4541
0.998
3.966
4.126
3.000
2.180
0.936
PPM
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0

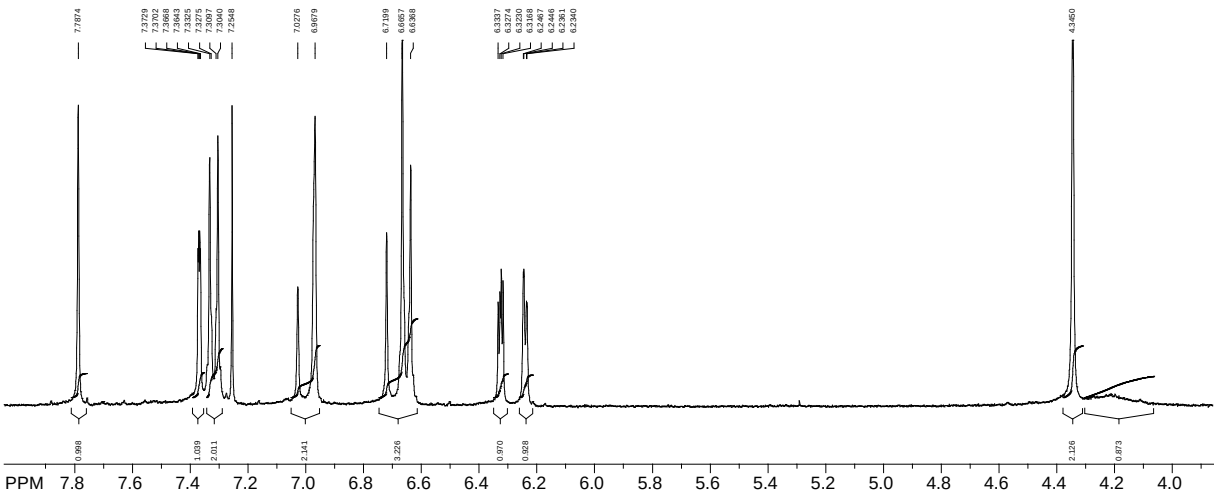

C (Et1/Et2)
C (Et1/Et2)
C (Ox4)
C (Ox2)
C (a)

PPM
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0

Figure S16. ^{1}H and ^{13}C NMR spectra of (*E*)-*N*-(furan-2-ylmethyl)-4-(2-(oxazol-5-yl)vinyl)aniline **(*trans*-17)**






7.7874
7.3729
7.3702
7.3681
7.3643
7.3325
7.3275
7.3097
7.2940
7.2548
7.0276
6.9979
6.7199
6.6957
6.6368
6.3337
6.3274
6.3230
6.2467
6.2446
6.2361
6.2340
4.3460
0.998
1.039
2.011
2.141
3.226
0.970
0.928
2.126
0.873
PPM 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0

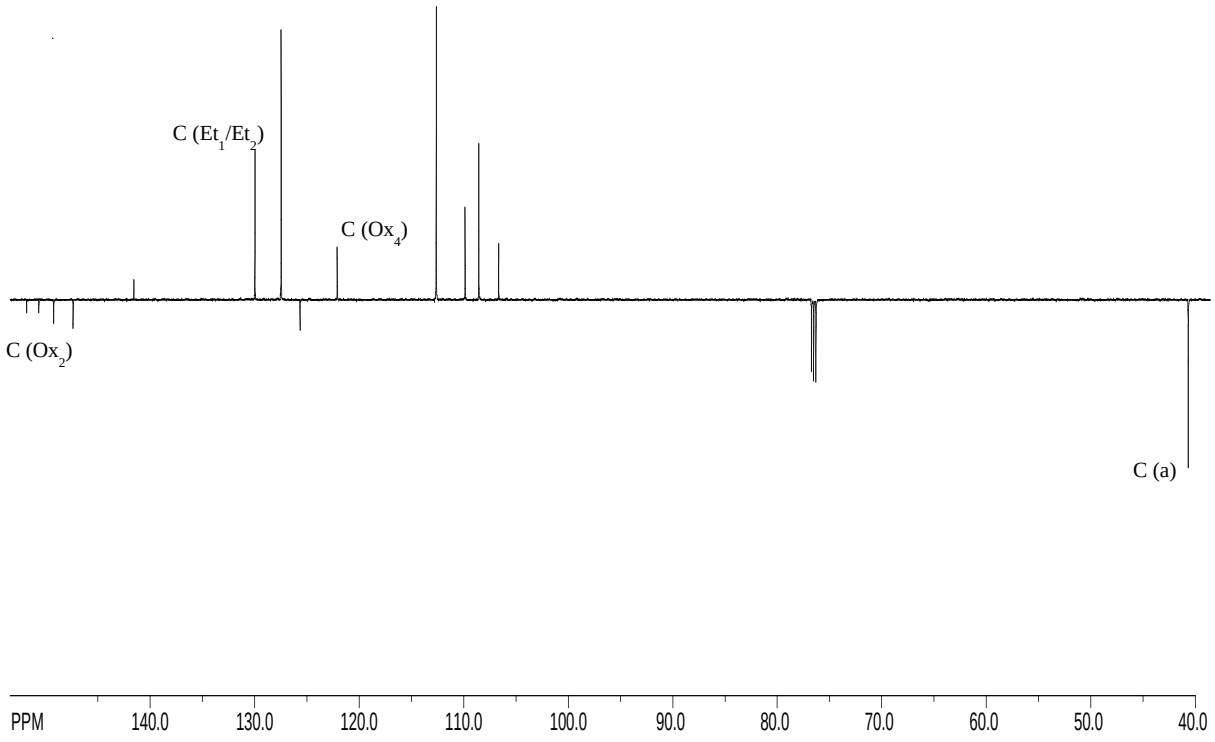
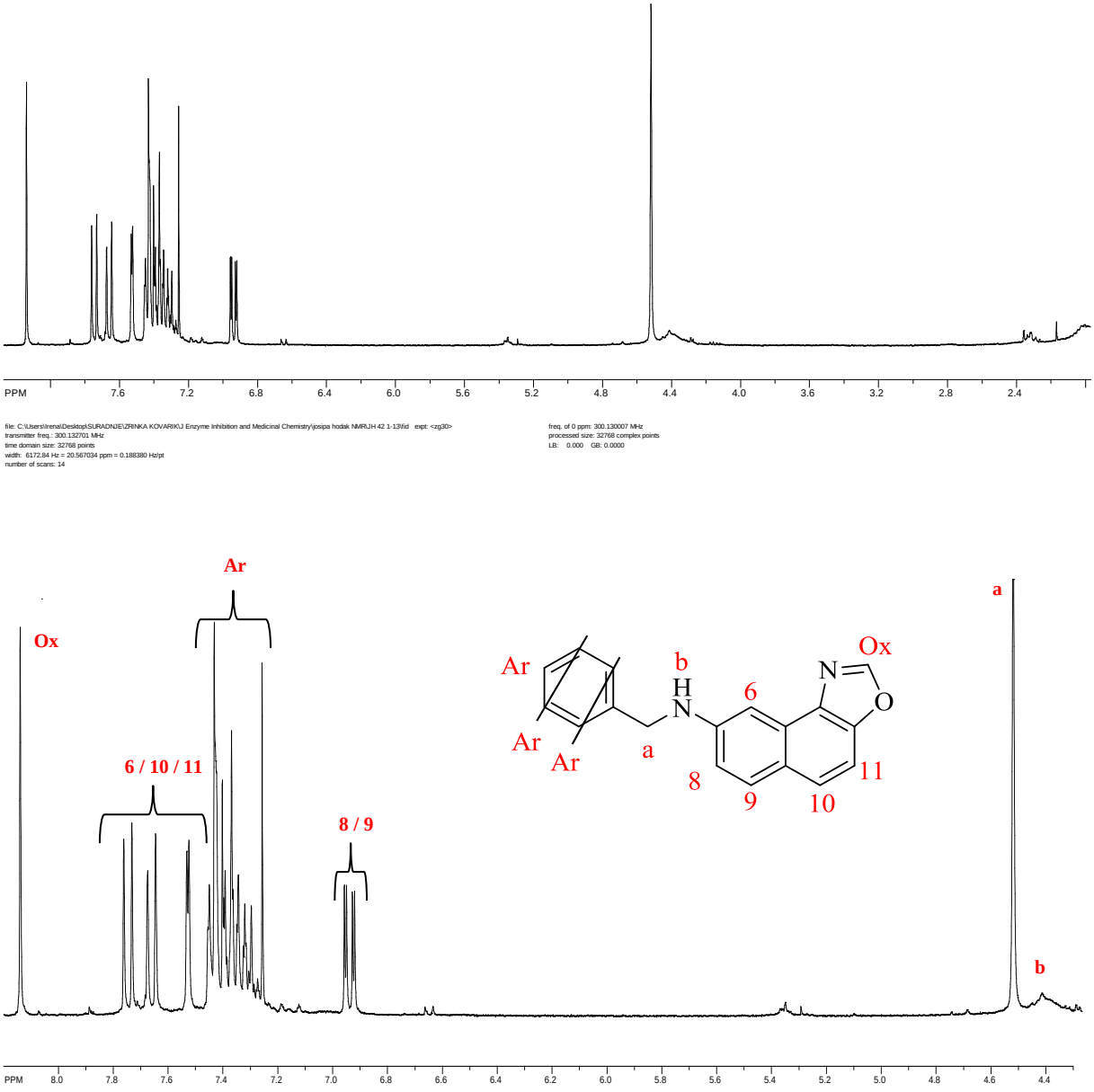
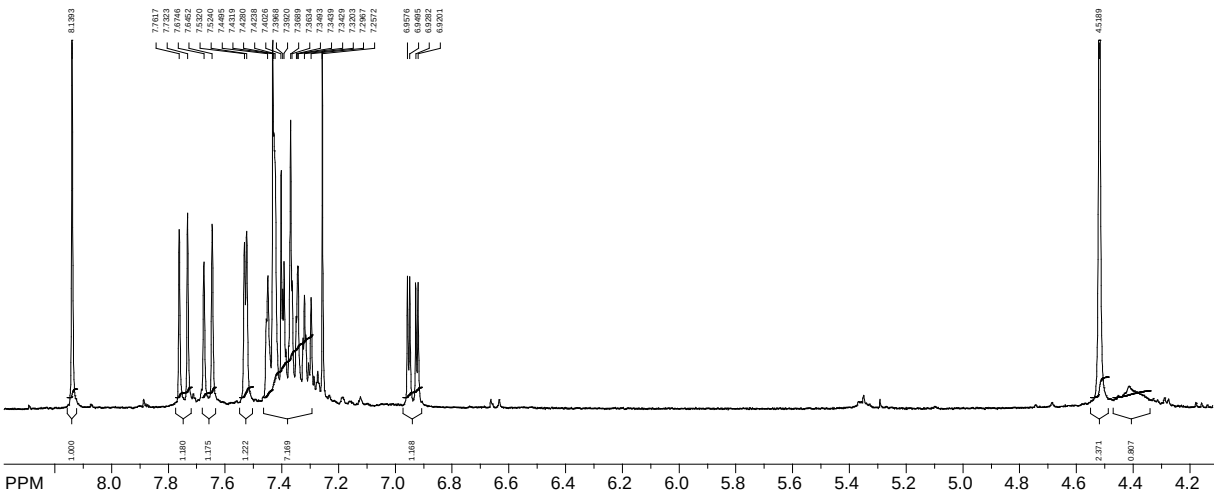
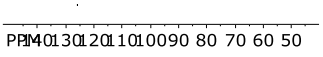

C (Et1/Et2)
C (Ox4)
C (Ox2)
C (a)
PPM 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0

Figure S17. ^{1}H and ^{13}C NMR spectra of *N*-benzylnaphtho[1,2-*d*]oxazol-8-amine **(19)**




8.1393
7.7617
7.7323
7.7046
7.6452
7.5320
7.5240
7.4645
7.4513
7.4280
7.4238
7.4026
7.3968
7.3920
7.3689
7.3634
7.3483
7.3459
7.3429
7.3303
7.2967
7.2972
6.9576
6.9495
6.9282
6.9201
4.5189
1.000
1.180
1.175
1.222
7.169
1.168
2.371
0.807
PPM
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2

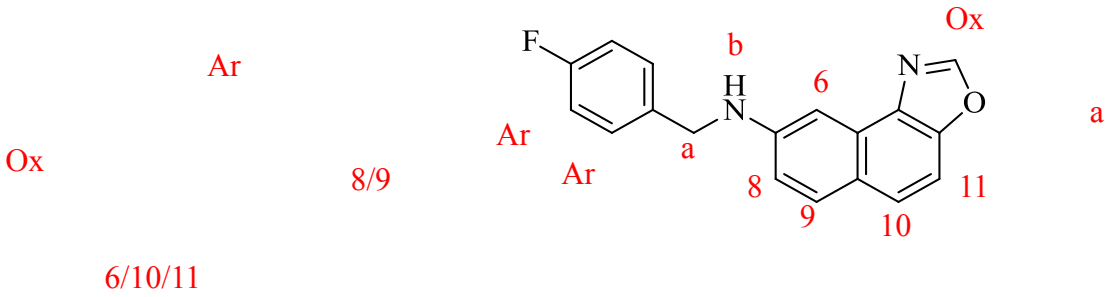

PPM 140 130 120 110 100 90 80 70 60 50

C (a)

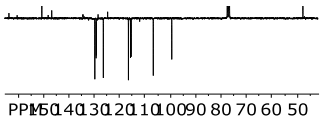
C (Ox_2)

C (Ox_4)

Figure S18. ^{1}H and ^{13}C NMR spectra of *N*-(4-fluorobenzyl)naphtho[1,2-*d*]oxazol-8-amine **(20)**



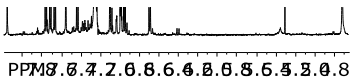
b

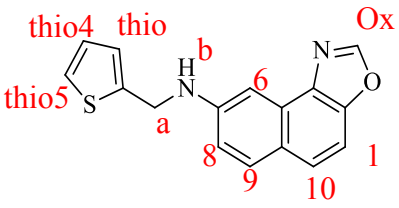


C (a)

C (Ox_2)

Figure S19. ^{1}H NMR spectrum of *N*-(thiophen-2-ylmethyl)naphtho[1,2-*d*]oxazol-8-amine **(21)**





Ox

thio5

6/10/11 a

thio3/thio4

8/9

Figure S20. Acetylcholinesterase inhibition by *trans*-amino-5-arylethenyl-oxazole derivatives. Due to the inhibition of AChE by the solvent, DMSO, maximal tested concentration of the compounds was 100 μM and, substrate (acetylthiocholine) concentration was 0.2 mM.