**SUPPORTING INFORMATION**

# Design, Synthesis, and Structure–Activity Relationships of Thiazole Analogs as Anticholinesterase Agents for Alzheimer's Disease

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**Table S1.** $IC_{50}$ values of compounds **2a**, **2b**, **2d**, **2e**, **2g**, **2i**, **2j** and donepezil against AChE.

| Compounds | AChE % Inhibition | | | | | | | $IC_{50}$ |
|---|---|---|---|---|---|---|---|---|
| | $10^{-3}$ M | $10^{-4}$ M | $10^{-5}$ M | $10^{-6}$ M | $10^{-7}$ M | $10^{-8}$ M | $10^{-9}$ M | (μM) |
| **2a** | 93.425 ±1.652 | 90.465 ±1.322 | 81.239 ±1.421 | 74.155 ±1.518 | 60.975 ±1.182 | 41.275 ±0.954 | 20.388 ±0.711 | 0.063 ±0.003 |
| **2b** | 90.285 ±1.451 | 82.151 ±1.478 | 74.565 ±1.279 | 63.758 ±1.230 | 57.965 ±1.023 | 43.948 ±0.963 | 21.208 ±0.839 | 0.056 ±0.002 |
| **2d** | 89.462 ±2.041 | 82.445 ±1.695 | 78.103 ±1.766 | 67.321 ±1.159 | 55.922 ±1.004 | 38.162 ±0.847 | 29.751 ±0.855 | 0.147 ±0.006 |
| **2e** | 90.611 ±1.815 | 85.387 ±1.730 | 81.828 ±1.311 | 74.797 ±1.488 | 62.356 ±1.103 | 44.275 ±0.904 | 21.599 ±0.631 | 0.040 ±0.001 |
| **2g** | 93.461 ±1.632 | 88.347 ±1.604 | 81.465 ±1.752 | 76.911 ±1.326 | 69.188 ±1.055 | 43.104 ±0.952 | 24.903 ±0.789 | 0.031 ±0.001 |
| **2i** | 95.207 ±1.502 | 92.130 ±1.798 | 86.602 ±1.214 | 80.964 ±1.124 | 71.840 ±1.270 | 42.651 ±0.866 | 22.155 ±0.830 | 0.028 ±0.001 |
| **2j** | 91.326 ±2.107 | 84.945 ±1.369 | 76.841 ±1.830 | 62.108 ±1.411 | 57.365 ±1.036 | 40.715 ±0.949 | 25.575 ±0.899 | 0.138 ±0.005 |
| **Donepezil** | 99.254 ±2.104 | 97.426 ±1.890 | 92.258 ±1.510 | 90.318 ±1.104 | 81.365 ±1.104 | 43.875 ±0.601 | 21.418 ±0.548 | 0.021 ±0.001 |

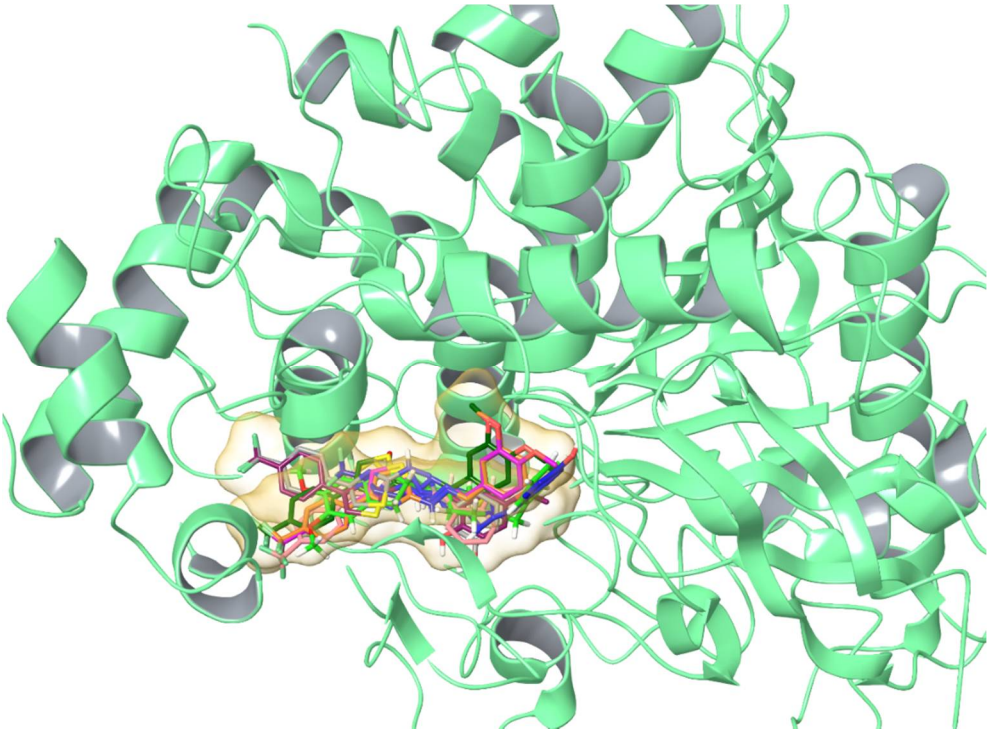
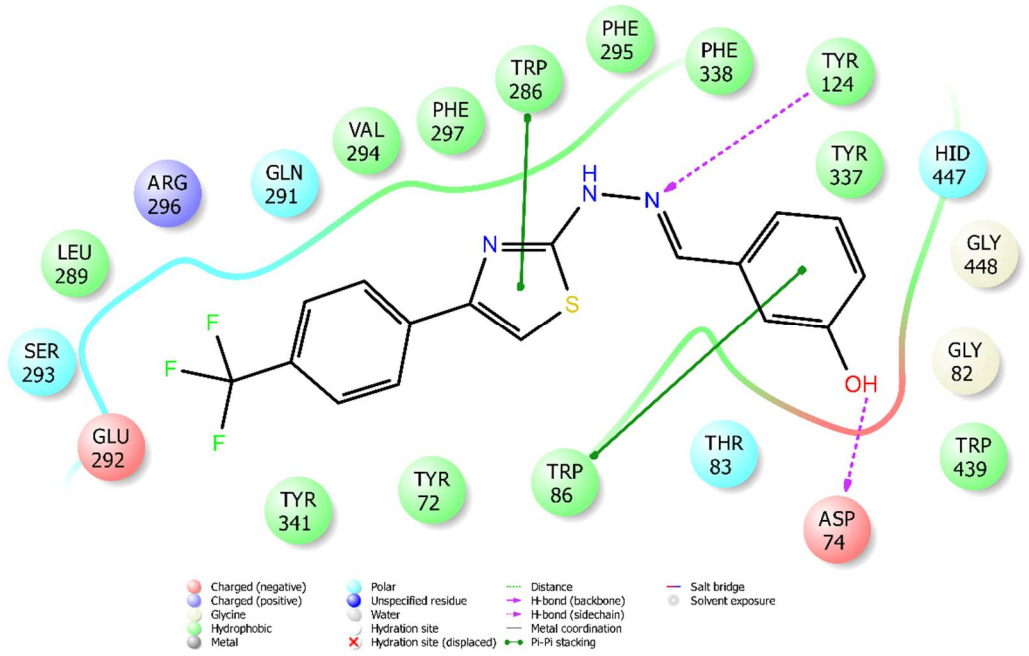
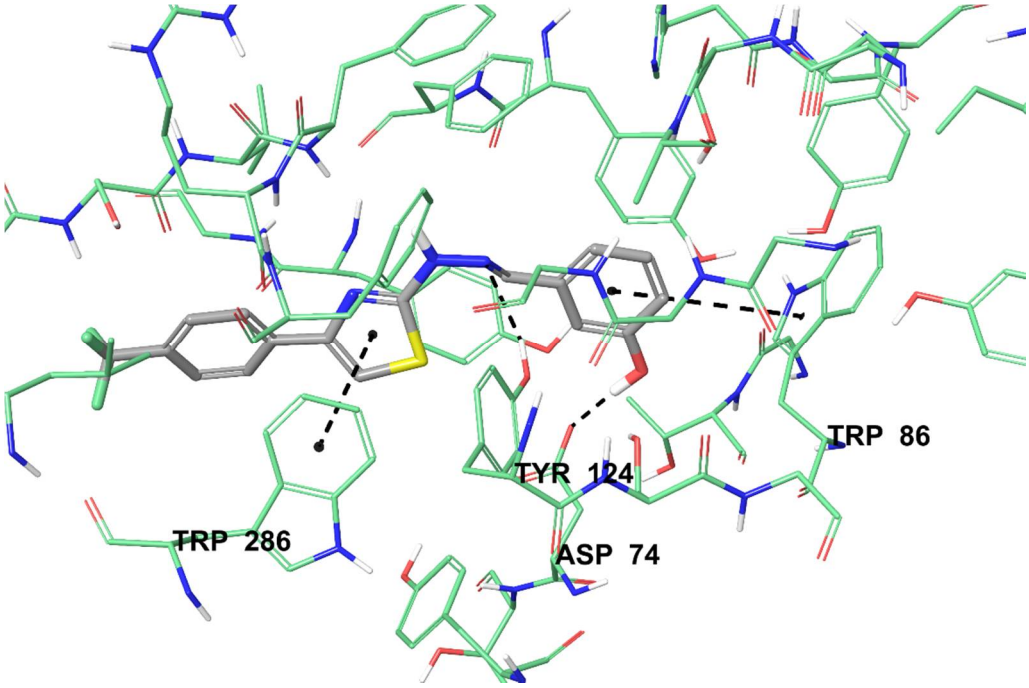


**Figure S1.** The superimposition pose of selected compounds in the enzyme active site (AChE PDB Code: 4EY7).

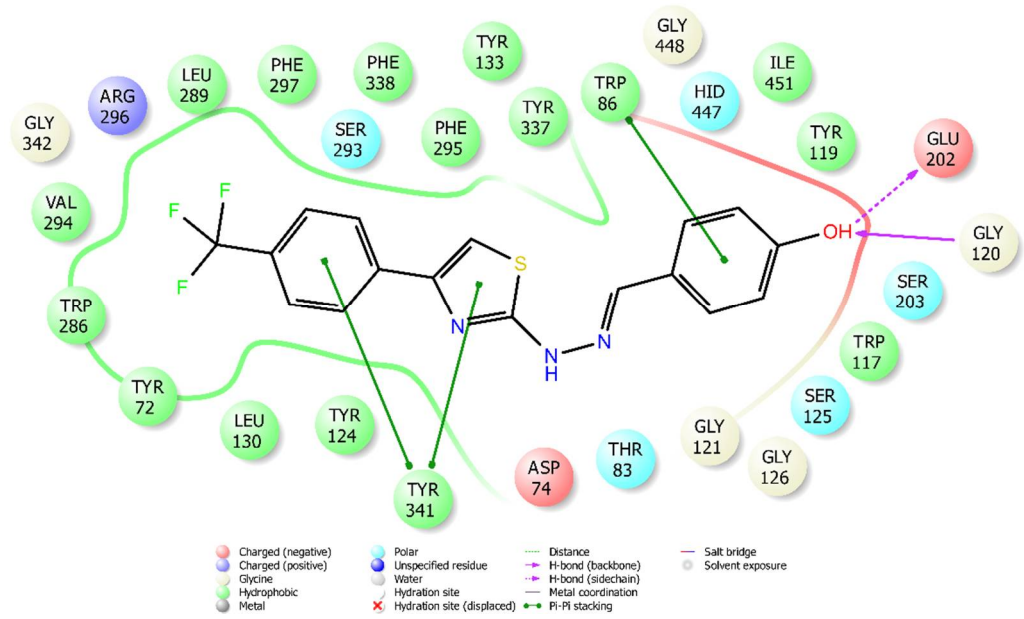



**A**

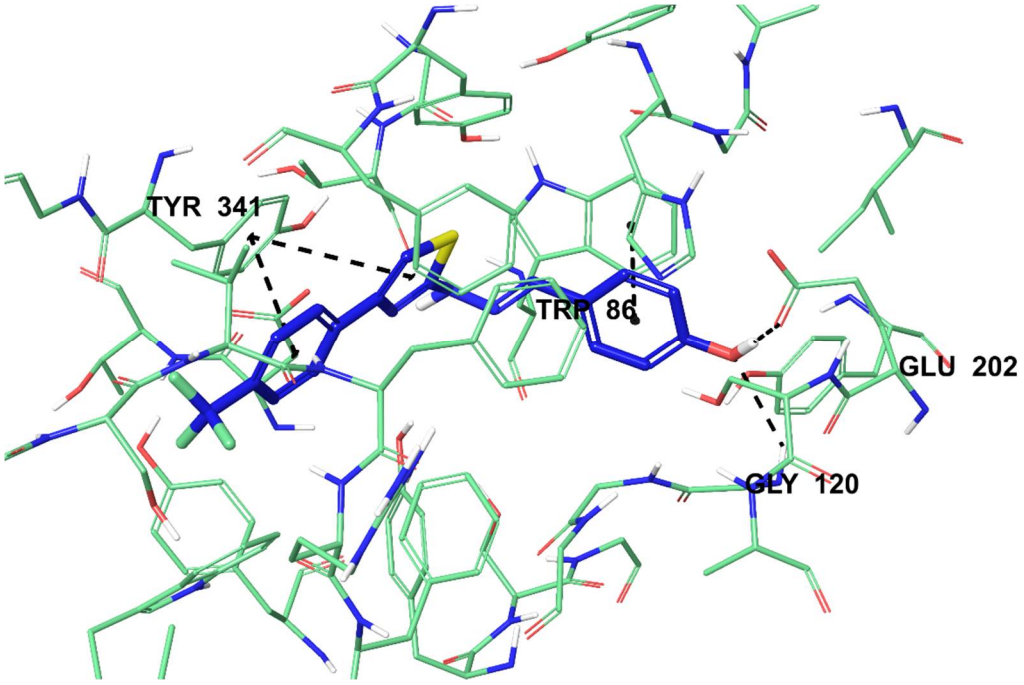



**B**

**Figure S2.** The two- (**A**) and three-dimensional (**B**) interacting mode of compound **2a** in the active region of AChE. The inhibitor and important residues in the active site of enzyme are presented by tube model and colored with grey and aquamarine, respectively (AChE PDB Code: 4EY7).

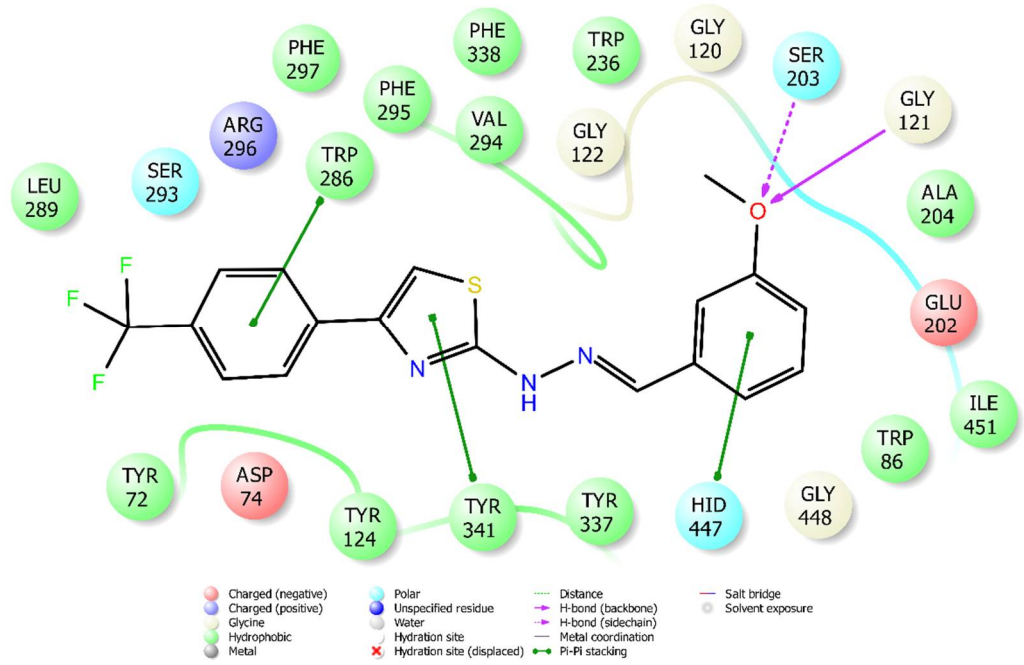



**A**

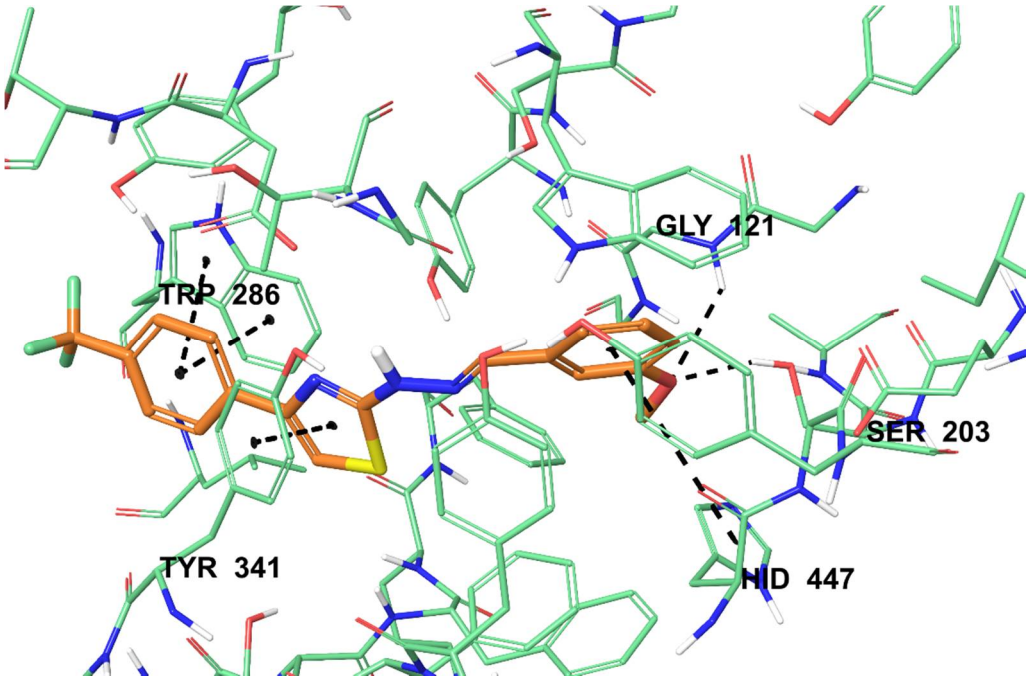



**B**

**Figure S3.** The two- (**A**) and three-dimensional (**B**) interacting mode of compound **2b** in the active region of AChE. The inhibitor and important residues in the active site of enzyme are presented by tube model and colored with blue and aquamarine, respectively (AChE PDB Code: 4EY7).

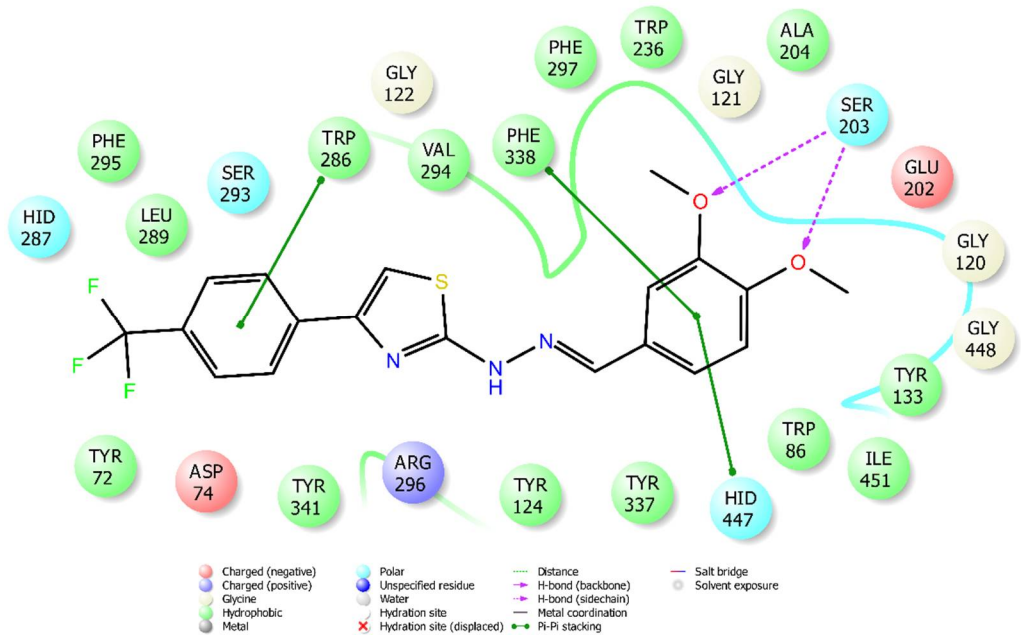



**A**

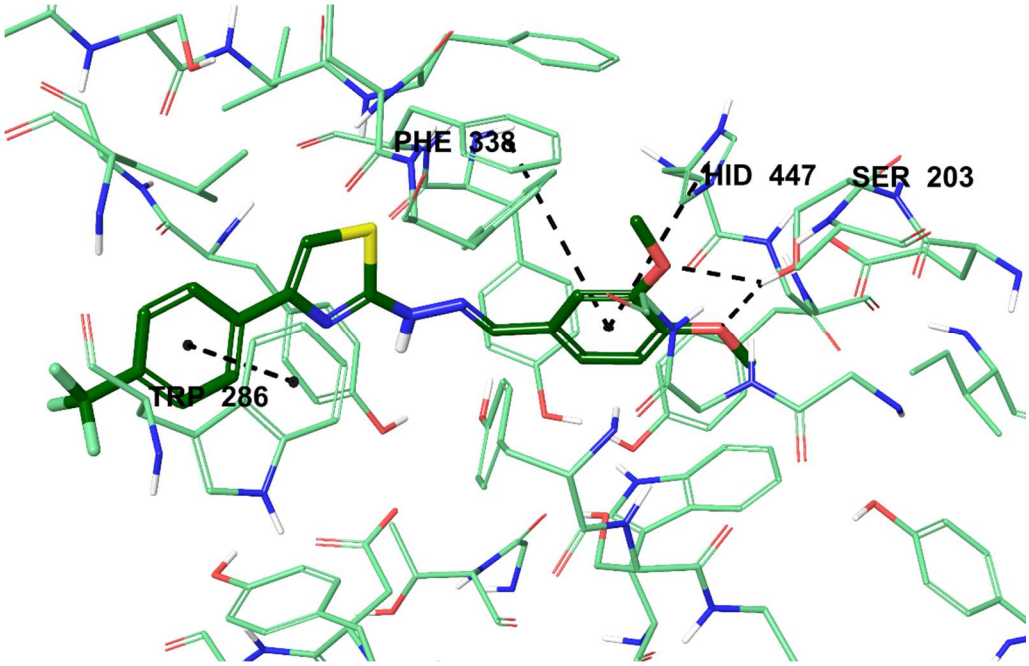



**B**

**Figure S4.** The two- (**A**) and three-dimensional (**B**) interacting mode of compound **2e** in the active region of AChE. The inhibitor and important residues in the active site of enzyme are presented by tube model and colored with orange and aquamarine, respectively (AChE PDB Code: 4EY7).

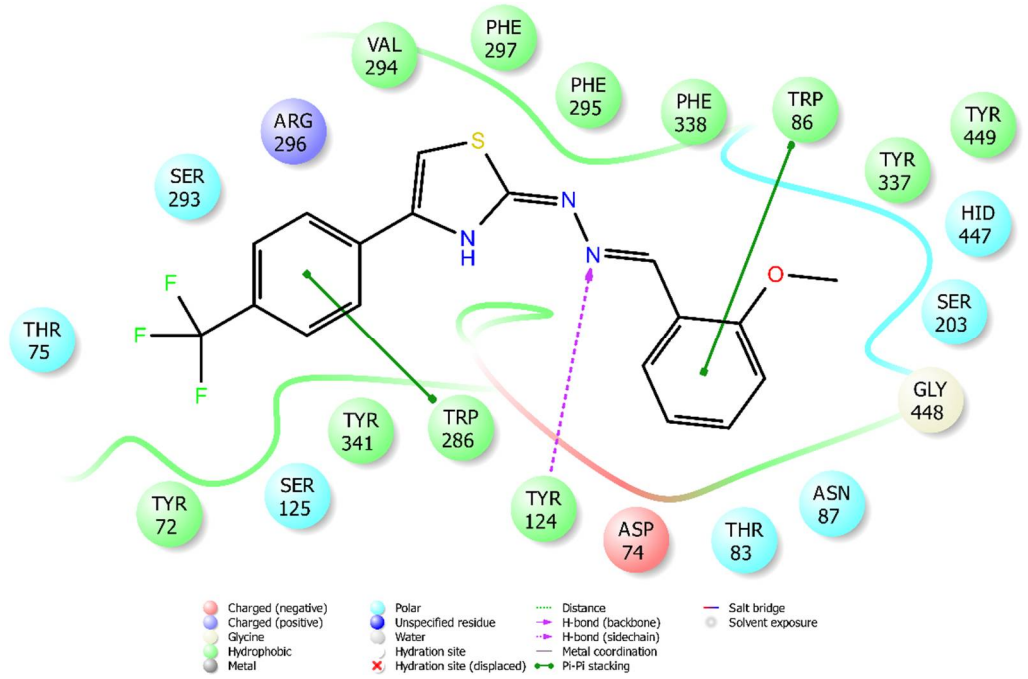



**A**

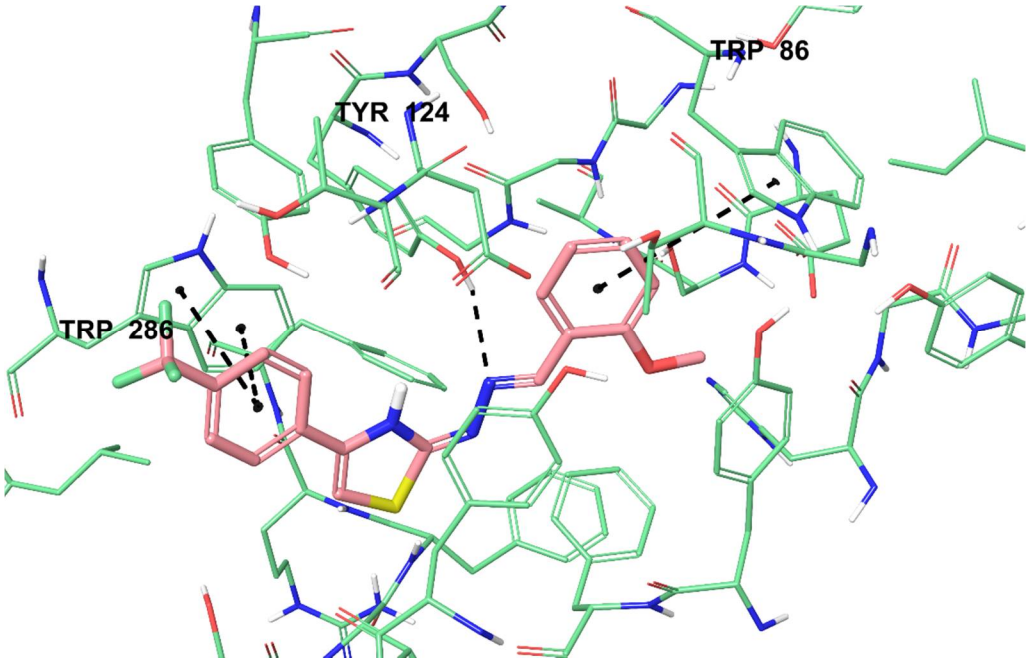



**B**

**Figure S5.** The two- (**A**) and three-dimensional (**B**) interacting mode of compound **2g** in the active region of AChE. The inhibitor and important residues in the active site of enzyme are presented by tube model and colored with dark green and aquamarine, respectively (AChE PDB Code: 4EY7).




**A**




**B**

**Figure S6.** The two- (**A**) and three-dimensional (**B**) interacting mode of compound **2d** in the active region of AChE. The inhibitor and important residues in the active site of enzyme are presented by tube model and colored with pink and aquamarine, respectively (AChE PDB Code: 4EY7).

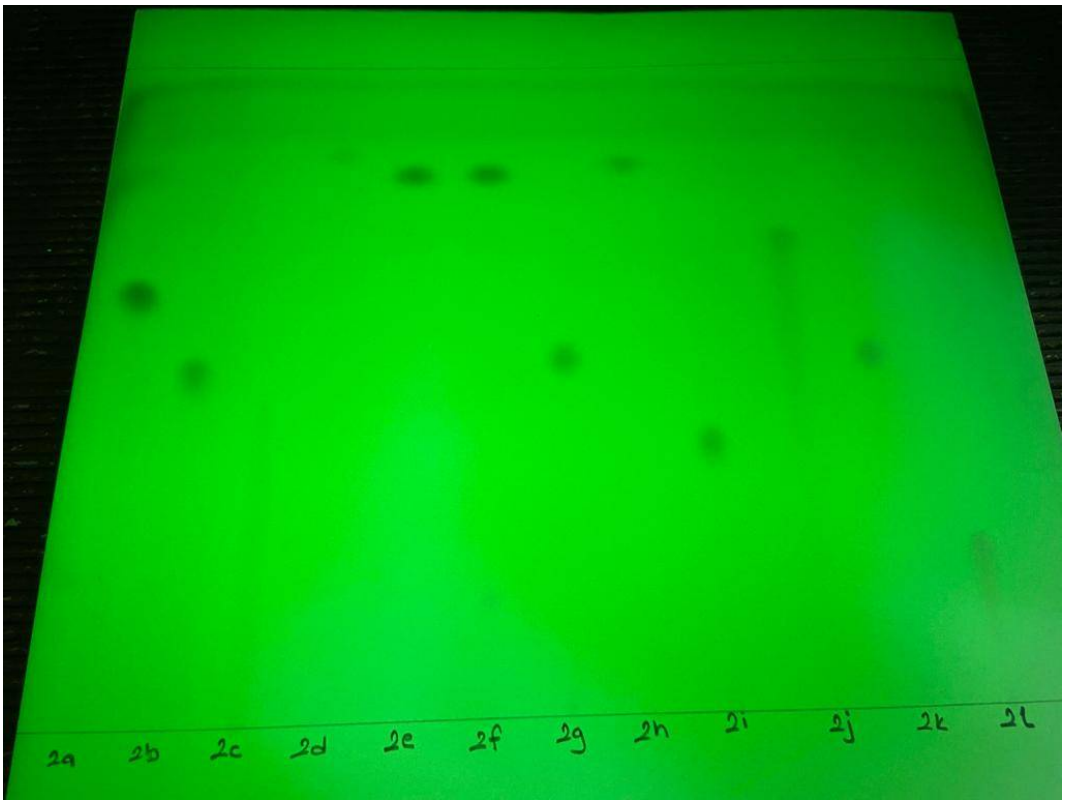
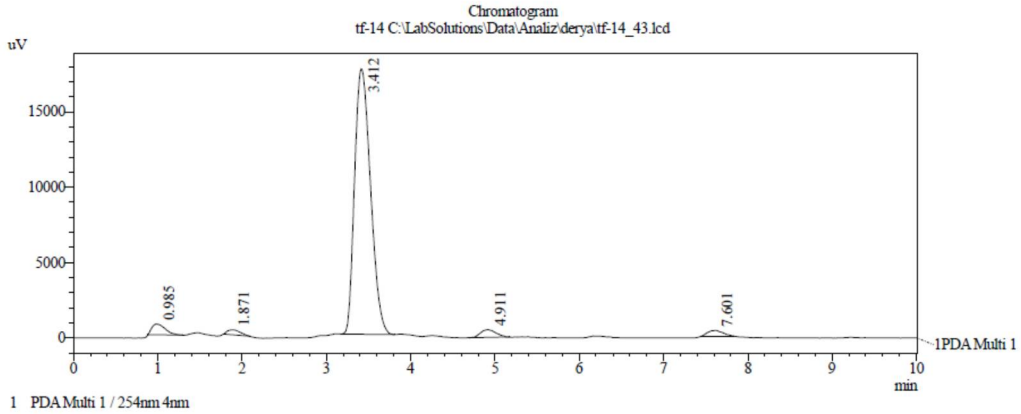



**Figure S7.** The thin-layer chromatography of the synthesized compounds.

# ==== Shimadzu LCMSsolution Analysis Report ====

| | |
|---|---|
| Acquired by | : Admin |
| Sample Name | : tf-14 |
| Sample ID | : |
| Vail # | : 32 |
| Injection Volume | : 0.3 uL |
| Data File Name | : tf-14_43.lcd |
| Method File Name | : isocratic.lcm |
| Batch File Name | : batch.lcb |
| Report File Name | : DefaultLCMS.lcr |
| Data Acquired | : 12.03.2020 01:13:26 |
| Data Processed | : 12.03.2020 01:23:28 |

**<Chromatogram>**




PeakTable

PDA Ch1 254nm 4nm

| Peak# | Ret. Time | Area | Height | Area % | Height % |
|---|---|---|---|---|---|
| 1 | 0.985 | 7787 | 705 | 3.059 | 3.608 |
| 2 | 1.871 | 3512 | 321 | 1.380 | 1.643 |
| 3 | 3.412 | 232017 | 17619 | 91.149 | 90.187 |
| 4 | 4.911 | 6455 | 509 | 2.536 | 2.603 |
| 5 | 7.601 | 4776 | 383 | 1.876 | 1.959 |
| Total | | 254546 | 19537 | 100.000 | 100.000 |

**Figure S8.** Purity of compound **2i**.

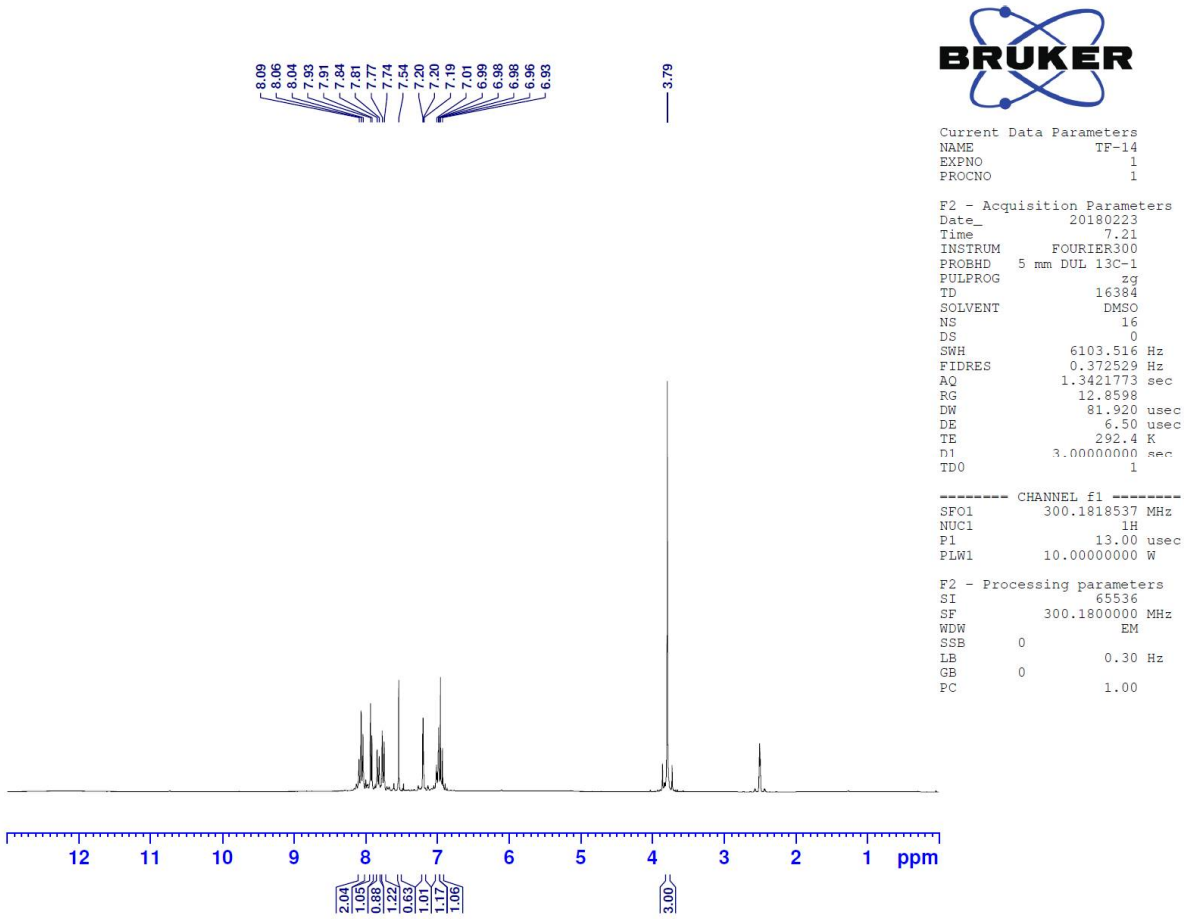



**Figure S9.** $^{1}$H NMR spectra of the compound **2i**.

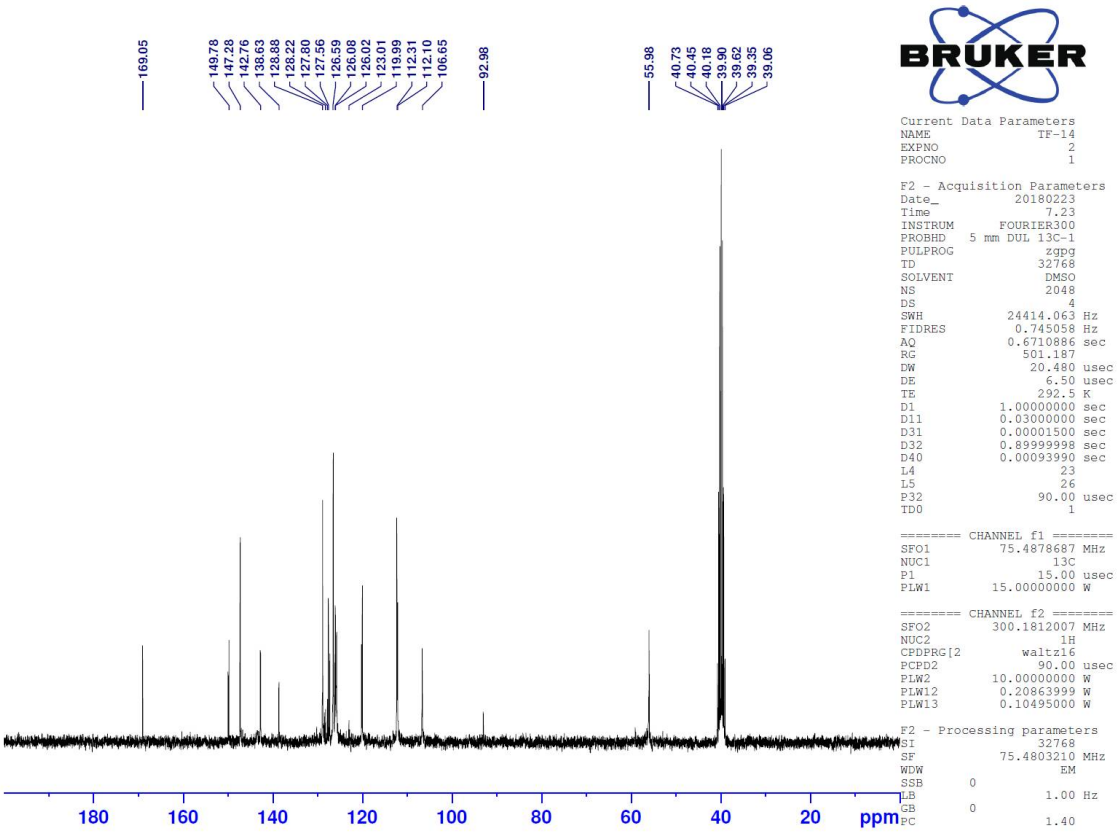



**Figure S10.** $^{13}$C NMR spectra of the compound **2i**.

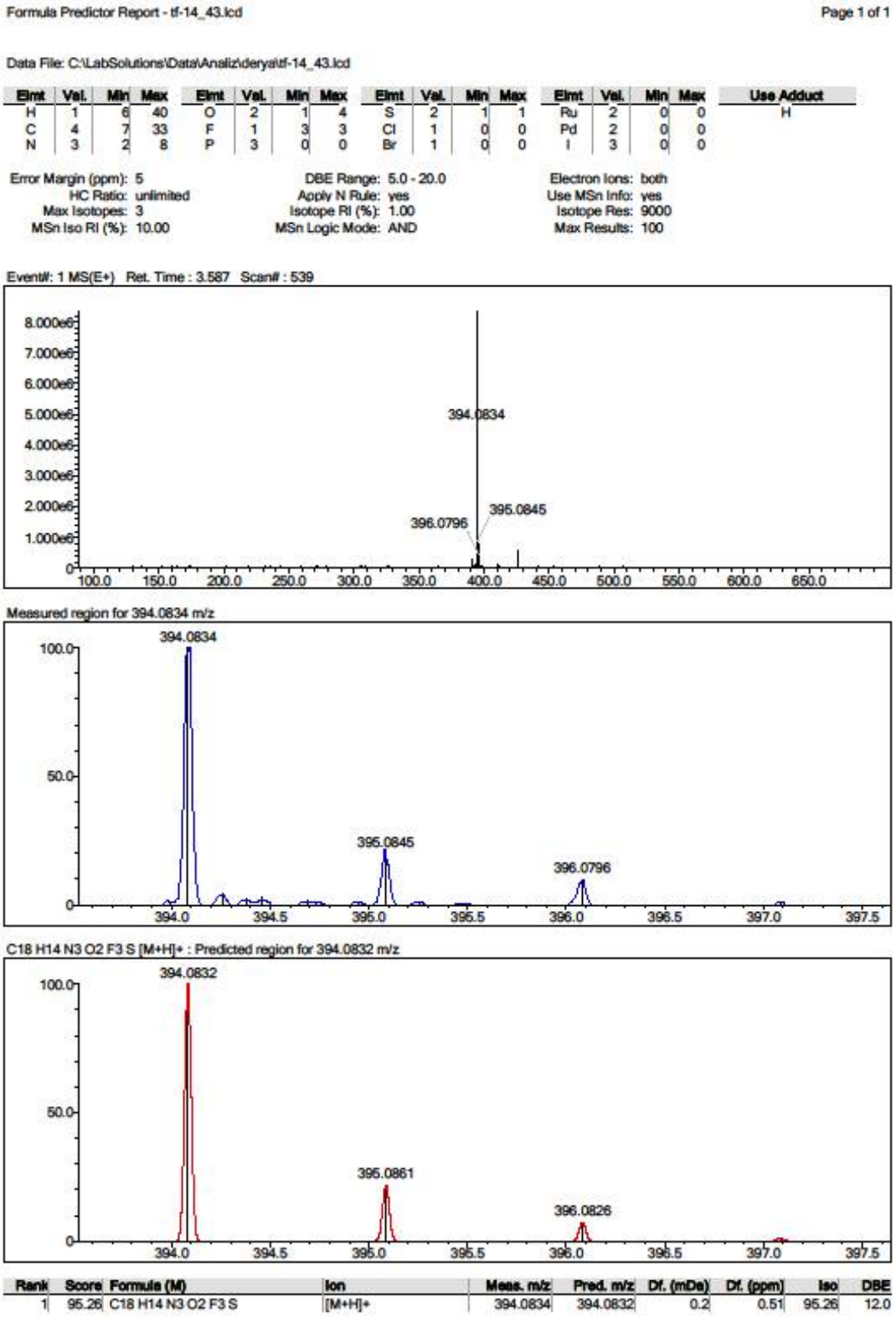



**Figure S11.** HRMS spectra of the compound **2i**.