

## Electronic Supporting Information

**Title:**

### **Synthesis and evaluation of HFIP bearing triazolo-amides as amyloid- $\beta$ aggregation inhibitor and suppressor of aggregation induced neuroinflammation**

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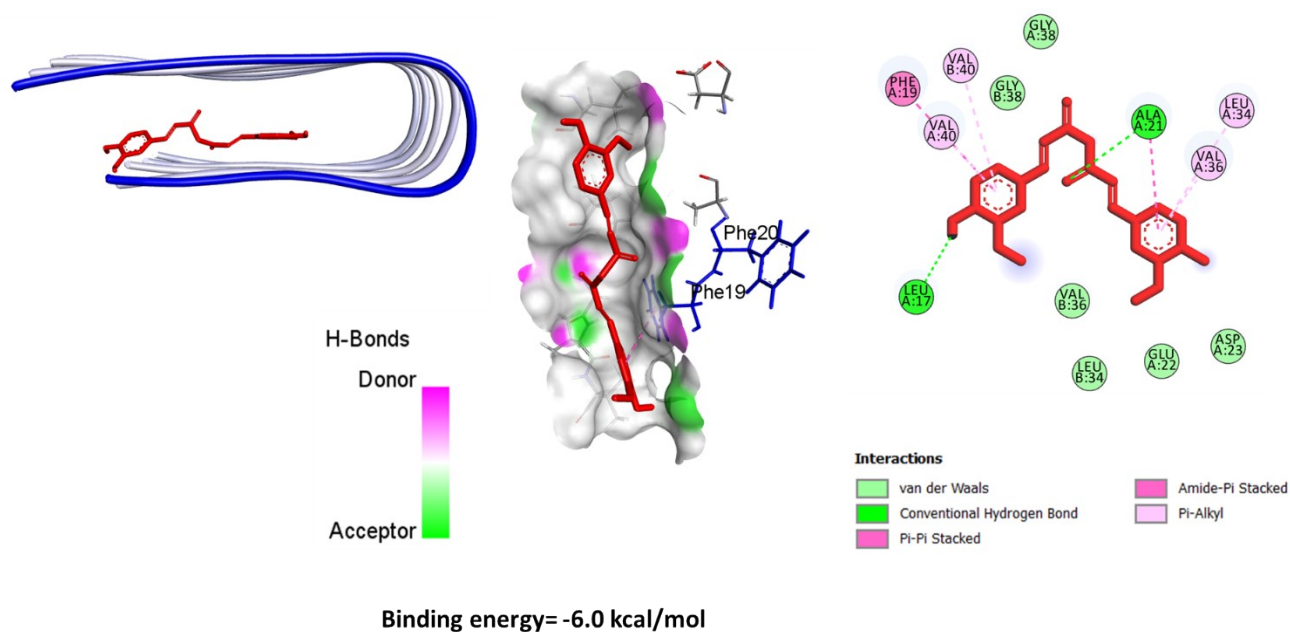
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| <b>Figure S90:</b> HRMS of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-                                                                         | S51 |

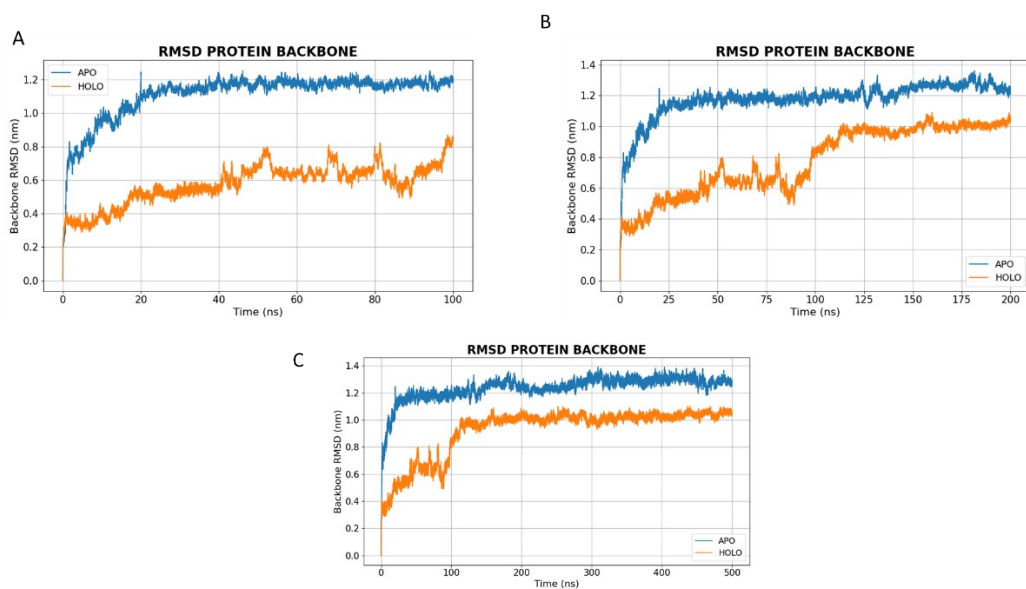
|                                                                                                                                                                |     |
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| 2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide (2b)                                                                                                     |     |
| <b>Figure S91:</b> HRMS of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [2c] | S52 |
| <b>Figure S92:</b> HRMS of 1-(3,4-dimethoxyphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [2d] | S52 |
| <b>Figure S93:</b> HRMS of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide [2e]      | S53 |
| <b>Figure S94:</b> HRMS of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2f]              | S53 |
| <b>Figure S95:</b> HRMS of 1-(3,4-dimethoxyphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2g]               | S54 |
| <b>Figure S96:</b> HRMS of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2h]       | S54 |
| <b>Figure S97:</b> HRMS of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [2i]      | S55 |
| <b>Figure S98:</b> HRMS of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [2j]      | S55 |
| <b>Figure S99:</b> HRMS of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [2k]  | S56 |
| <b>Figure S100:</b> HRMS of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methoxyphenyl)-1H-1,2,3-triazole-4-carboxamide [2m]    | S56 |
| <b>Figure S101:</b> HRMS of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methoxyphenyl)-1H-1,2,3-triazole-4-carboxamide [2m]    | S57 |
| <b>Figure S102:</b> HRMS of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide [2n]      | S57 |
| <b>Figure S103:</b> HRMS of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide (2o)              | S58 |
| <b>Figure S104:</b> HRMS of 1-(3,4-dimethylphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2p]               | S58 |
| <b>Figure S105:</b> HRMS of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2q]       | S59 |
| <b>Figure S106:</b> HRMS of 2-(4-(1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamido)phenyl)-1,1,1,3,3,3-hexafluoropropan-2-yl-methanesulfonate [2r]       | S59 |
| <b>Figure S107:</b> HRMS of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-morpholino)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2s]          | S60 |
| <b>Figure S108:</b> HRMS of N-(4-(2-chloro-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [2t]               | S60 |
| <b>Figure S109:</b> HRMS of 2-(5-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3a]         | S61 |
| <b>Figure S110:</b> HRMS of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2,5-dimethylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3b]     | S61 |
| <b>Figure S111:</b> HRMS of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-3-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3c]         | S62 |
| <b>Figure S112:</b> HRMS of 2-(5-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-5-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenol [3d]     | S62 |
| <b>Figure S113:</b> HPLC of N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenyl)-3-phenylisoxazole-5-carboxamide [1a]                                     | S63 |
| <b>Figure S114:</b> HPLC of N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenyl)-3-(p-tolyl)isoxazole-5-carboxamide (1b)                                  | S63 |
| <b>Figure S115:</b> HPLC of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [2a]    | S64 |

|                                                                                                                                                                 |     |
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| <b>Figure S116:</b> HPLC of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide (2b)     | S64 |
| <b>Figure S117:</b> HPLC of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [2c] | S65 |
| <b>Figure S118:</b> HPLC of 1-(3,4-dimethoxyphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [2d] | S65 |
| <b>Figure S119:</b> HPLC of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide [2e]      | S66 |
| <b>Figure S120:</b> HPLC of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2f]              | S66 |
| <b>Figure S121:</b> HPLC of 1-(3,4-dimethoxyphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2g]               | S67 |
| <b>Figure S122:</b> HPLC of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyl oxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2h]      | S67 |
| <b>Figure S123:</b> HPLC of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [2i]      | S68 |
| <b>Figure S124:</b> HPLC of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [2j]      | S68 |
| <b>Figure S125:</b> HPLC of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [2k]  | S69 |
| <b>Figure S126:</b> HPLC of 1-(3,4-dimethylphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [2l]  | S69 |
| <b>Figure S127:</b> HPLC of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methoxyphenyl)-1H-1,2,3-triazole-4-carboxamide [2m]     | S70 |
| <b>Figure S128:</b> HPLC of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide [2n]       | S70 |
| <b>Figure S129:</b> HPLC of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide (2o)               | S71 |
| <b>Figure S130:</b> HPLC of 1-(3,4-dimethylphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2p]                | S71 |
| <b>Figure S131:</b> HPLC of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2q]        | S72 |
| <b>Figure S132:</b> HPLC of 2-(4-(1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamido)phenyl)-1,1,1,3,3,3-hexafluoropropan-2-yl-methanesulfonate [2r]        | S72 |
| <b>Figure S133:</b> HPLC of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-morpholino propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2s]           | S73 |
| <b>Figure S134:</b> HPLC of N-(4-(2-chloro-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [2t]                | S73 |
| <b>Figure S135:</b> HPLC of 2-(5-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3a]          | S74 |
| <b>Figure S136:</b> HPLC of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2,5-dimethylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3b]      | S74 |
| <b>Figure S137:</b> HPLC of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-3-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3c]          | S75 |
| <b>Figure S138:</b> HPLC of 2-(5-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-5-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenol [3d]      | S75 |
| <b>Figure S139:</b> IC <sub>50</sub> graph of 2f compound                                                                                                       | S76 |
| <b>Table S1:</b> <i>In silico</i> ADMET property of 2f                                                                                                          | S77 |

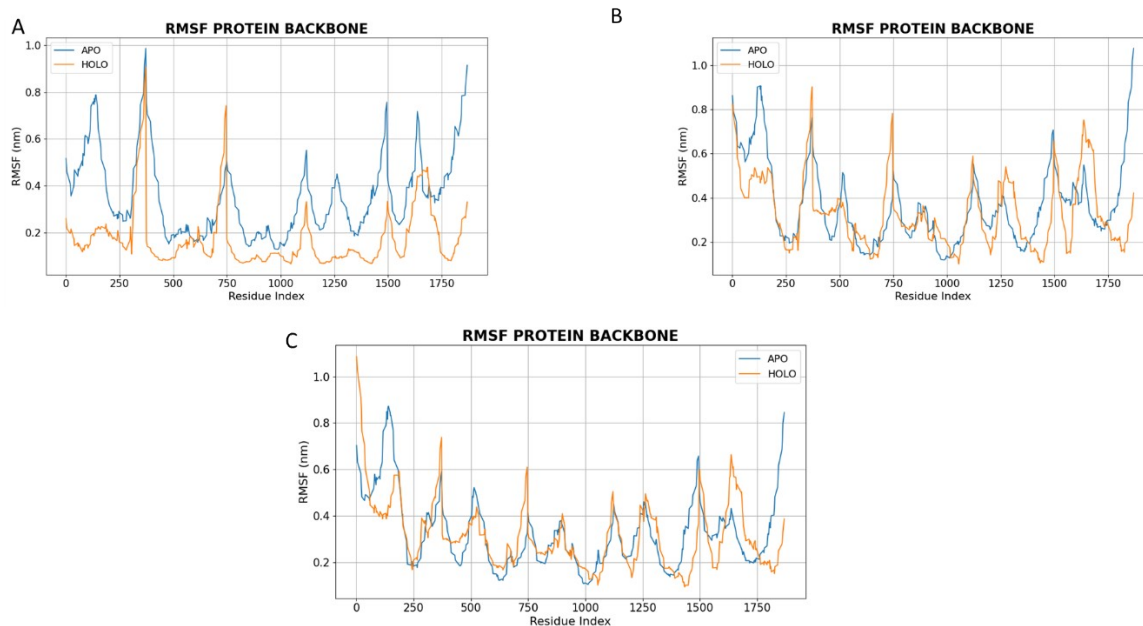
**Figure S1:** Molecular docking of Curcumin with 2BEG



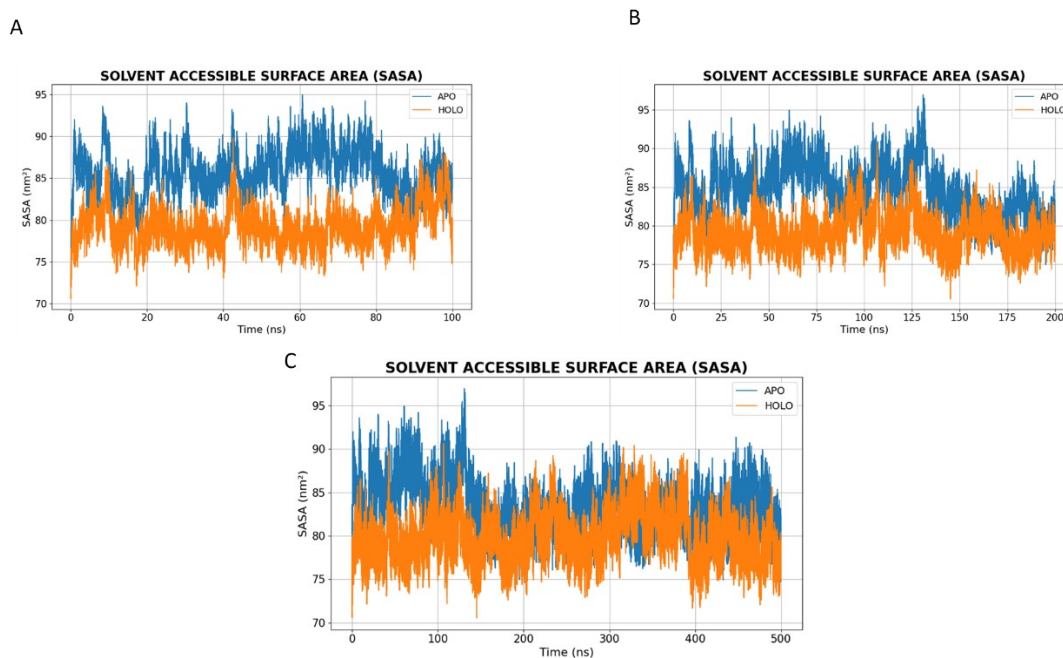
**Figure S2:** RMSD of Apo and Holo state of 2f-2BEG complex at 100, 200 and 300 ns respectively



**Figure S3:** RMSF of Apo and Holo state of 2f-2BEG complex at 100, 200 and 300 ns respectively

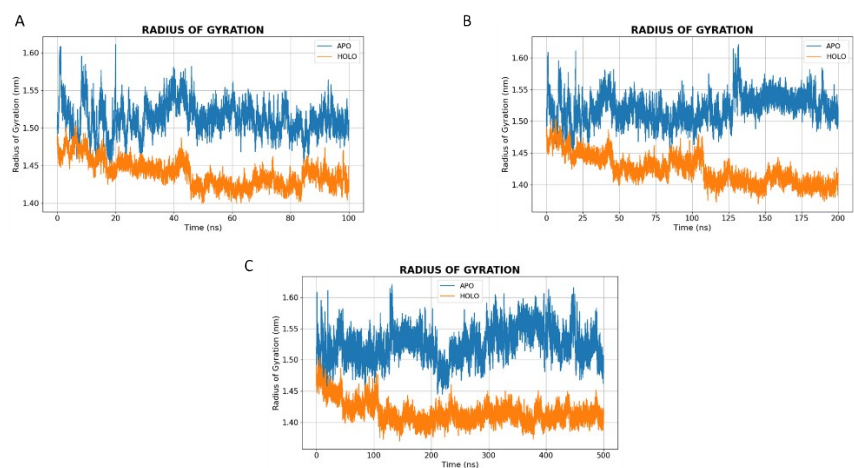


**Figure S4:** SASA of Apo and Holo state of 2f-2BEG complex at 100, 200 and 300 ns respectively

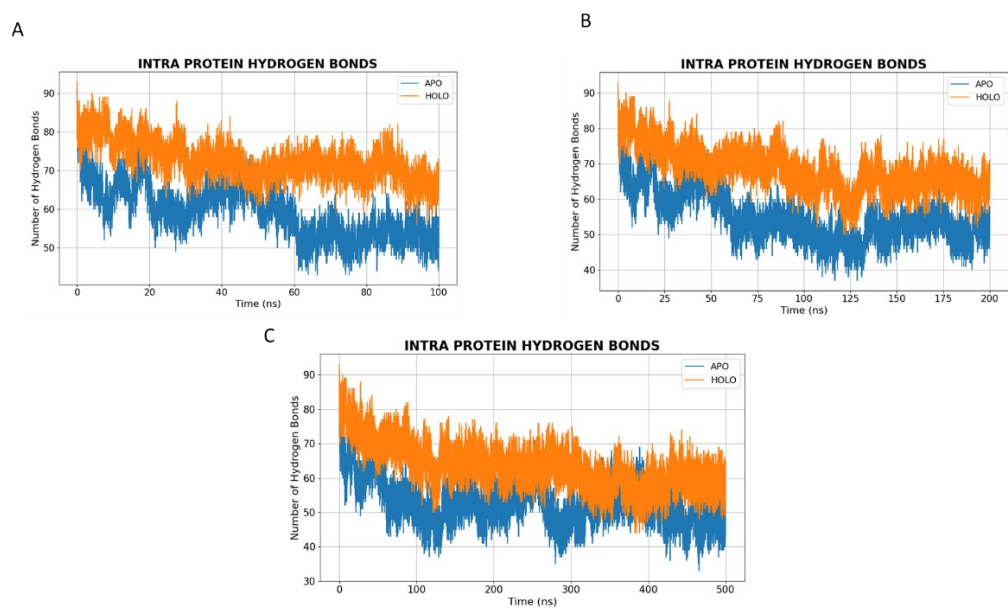




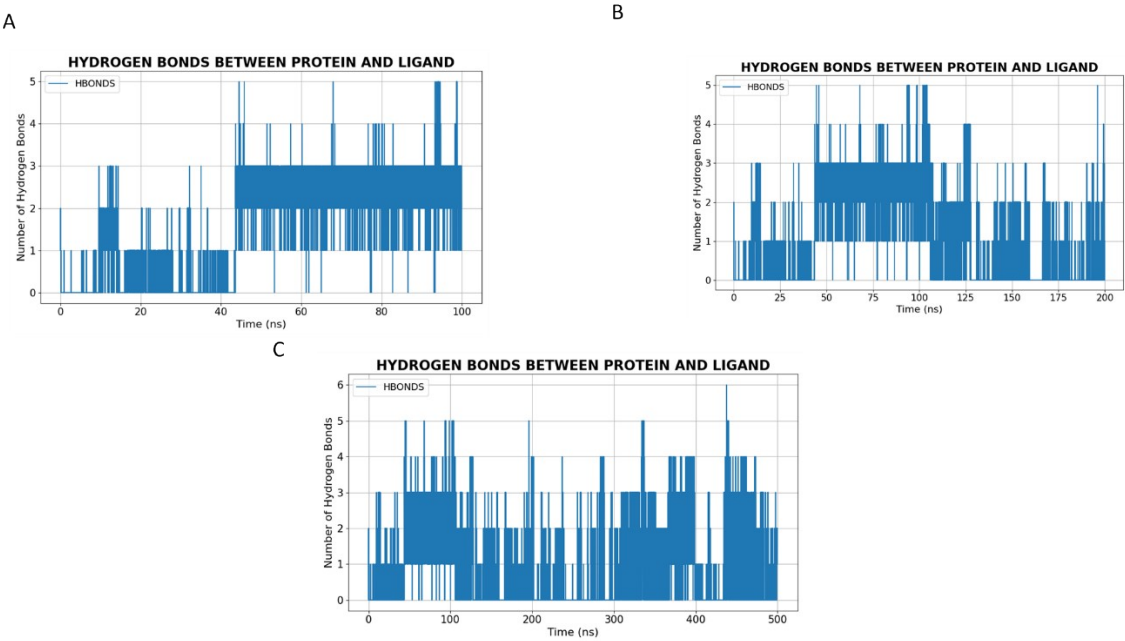
**Figure S5:** Radius of Gyration of Apo and Holo state of 2f-2BEG complex at 100, 200 and 300 ns respectively



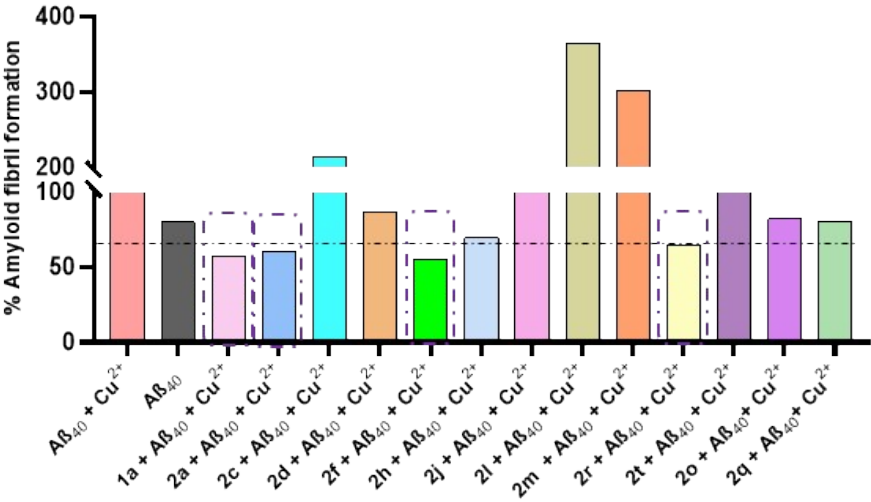
**Figure S6:** Intra-protein hydrogen bond of 2f-2BEG complex at 100, 200 and 300 ns respectively



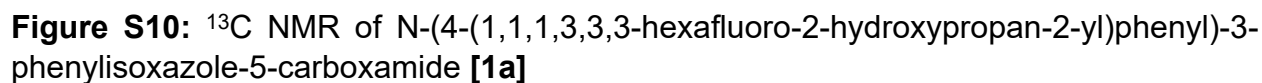
**Figure S7:** Hydrogen bond of 2f-2BEG complex at 100, 200 and 300 ns respectively



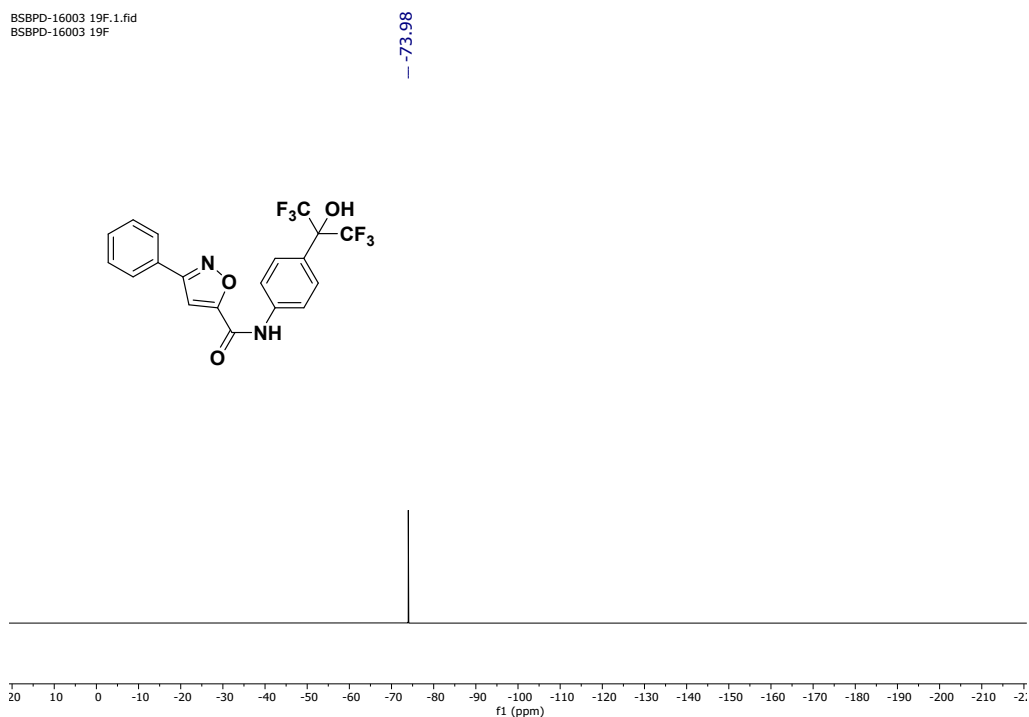
**Figure S8:** Thioflavin T assay: preliminary screening of 13 compounds in a single concentration of 50  $\mu$ M



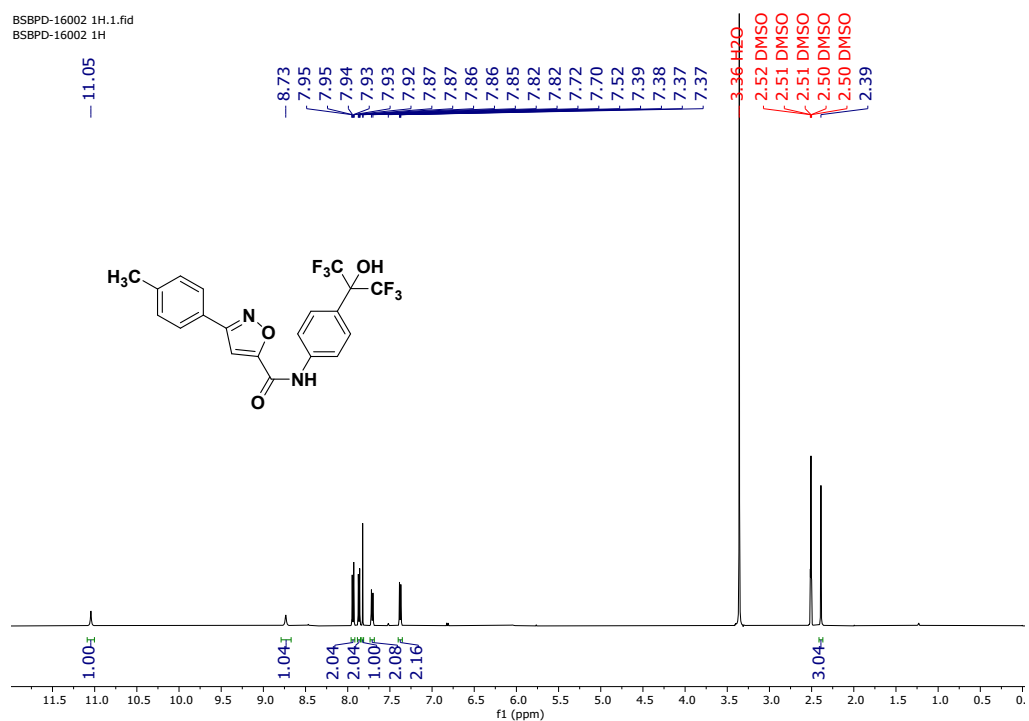
**Figure S9:**  $^1\text{H}$  NMR of N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenyl)-3-phenylisoxazole-5-carboxamide [**1a**]



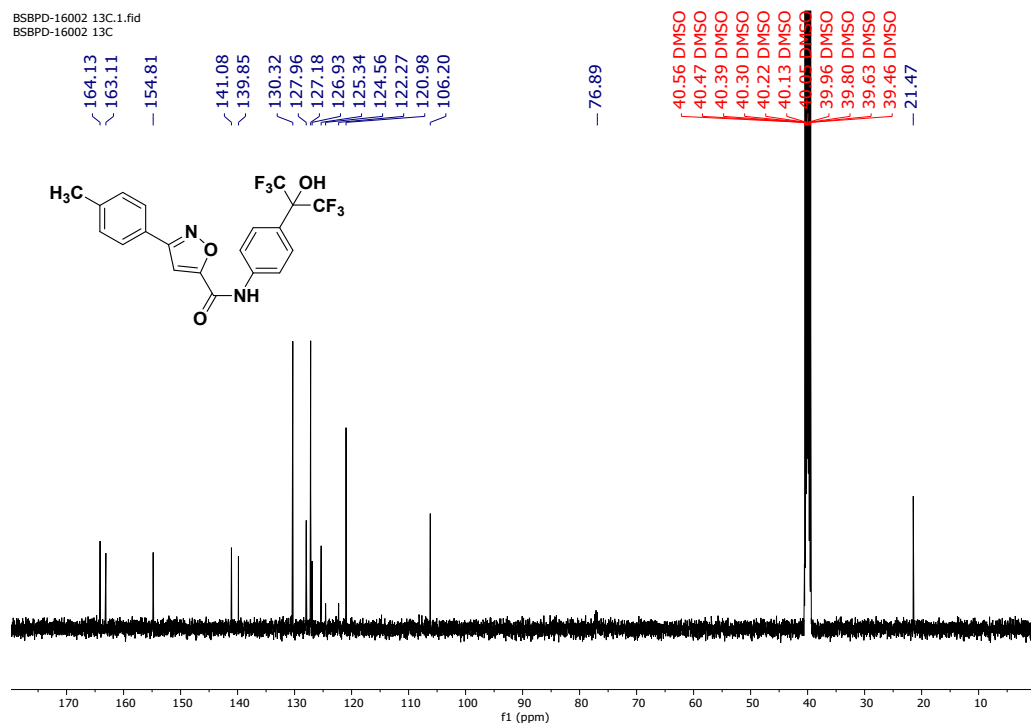
**Figure S11:**  $^{19}\text{F}$  NMR of N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenyl)-3-phenylisoxazole-5-carboxamide [**1a**]



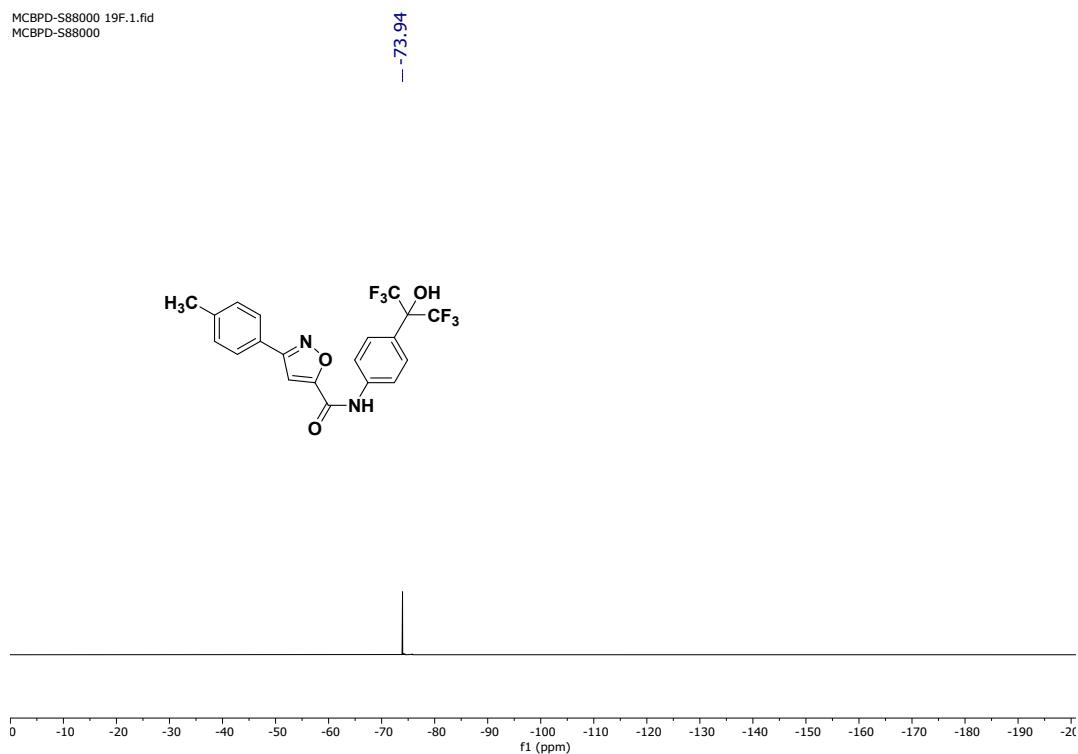
**Figure S12:**  $^1\text{H}$  NMR of N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenyl)-3-(p-tolyl)isoxazole-5-carboxamide [**1b**]



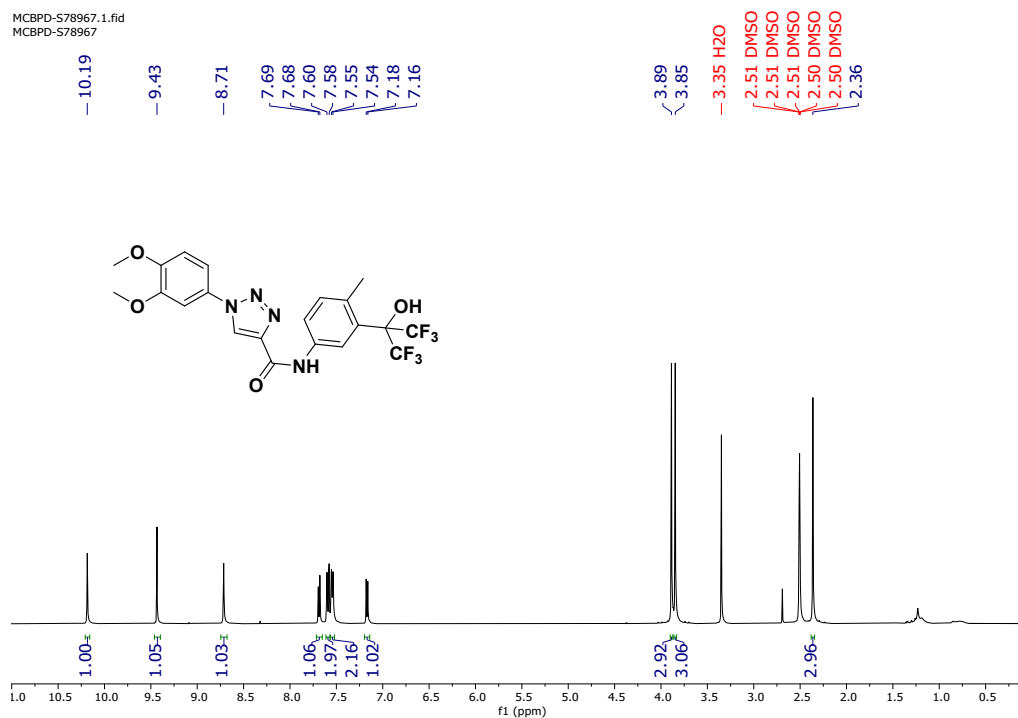
**Figure S13:**  $^{13}\text{C}$  NMR of N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenyl)-3-(p-tolyl)isoxazole-5-carboxamide [**1b**]



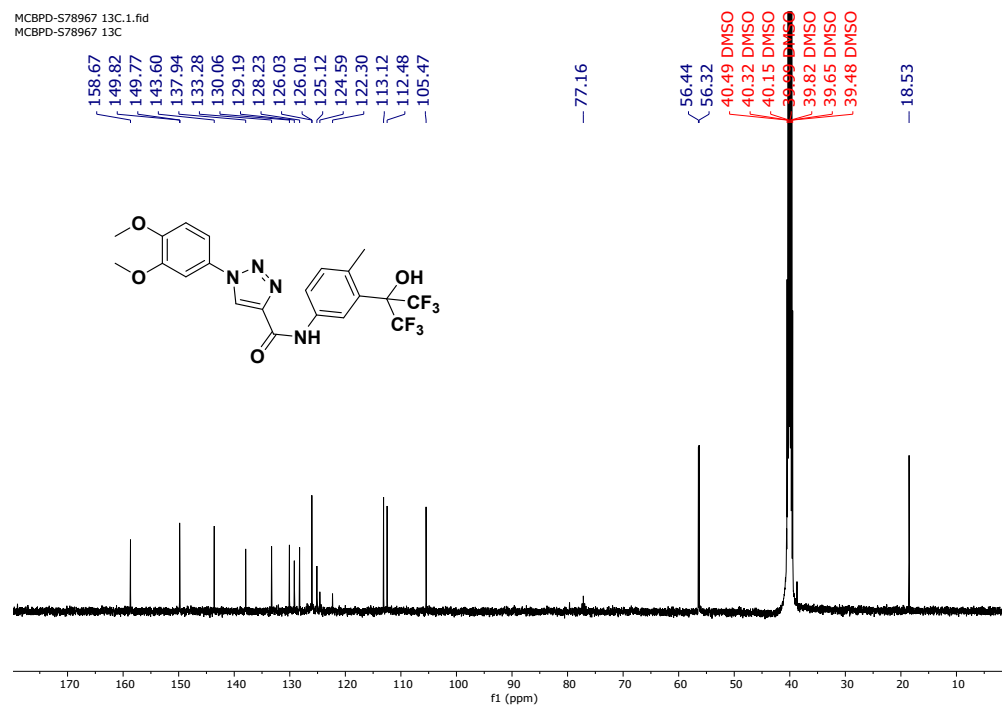
**Figure S14:**  $^{19}\text{F}$  NMR of N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenyl)-3-(p-tolyl)isoxazole-5-carboxamide [**1b**]



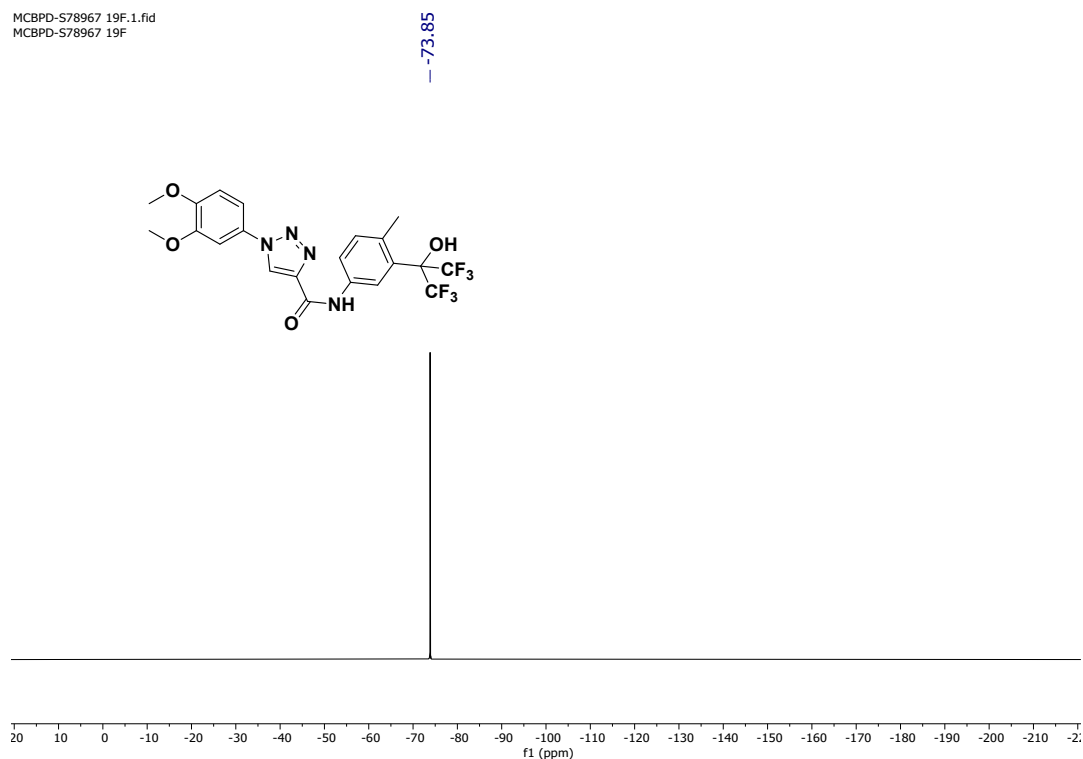
**Figure S15:**  $^1\text{H}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2a**]



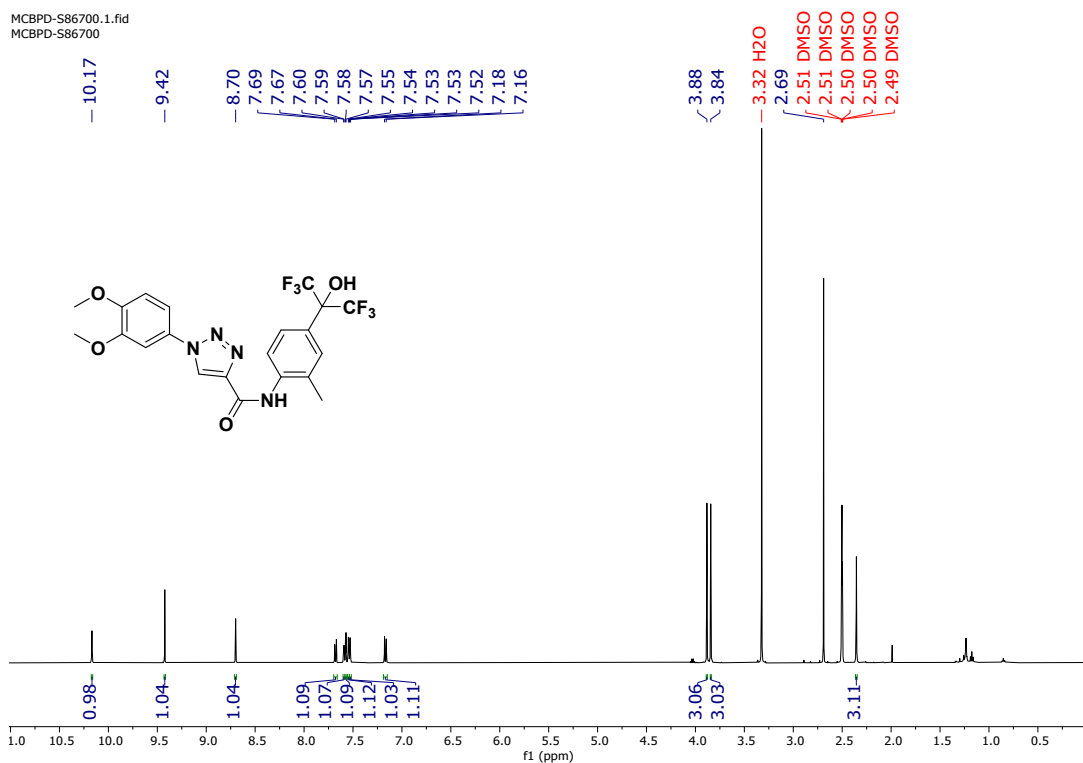
**Figure S16:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2a**]



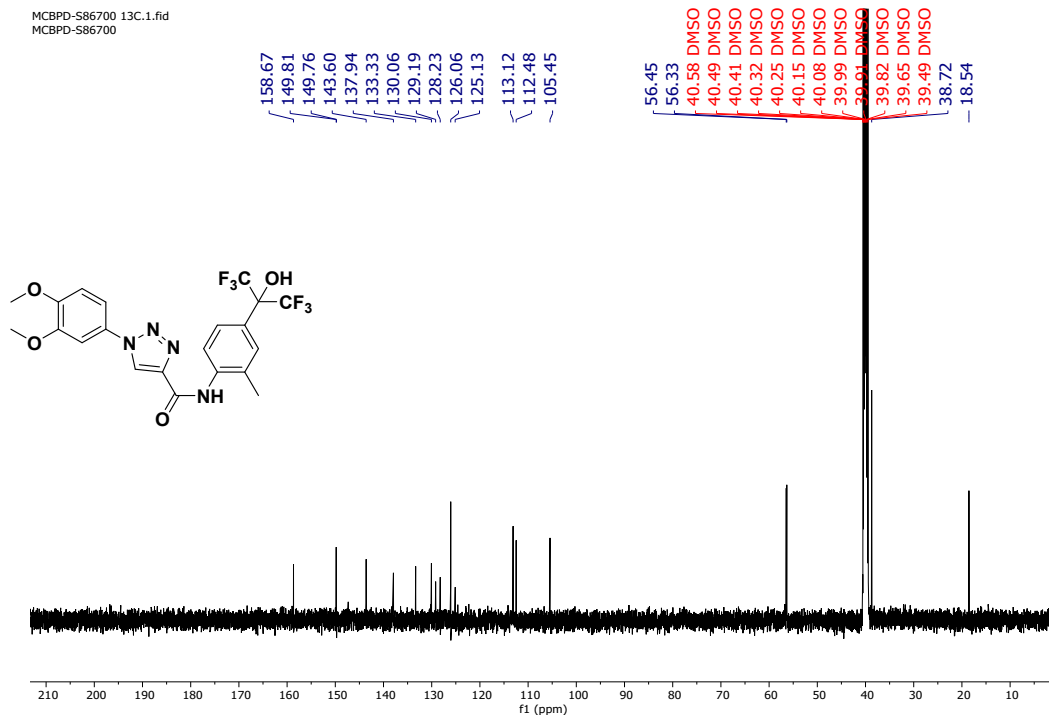
**Figure S17:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2a]**



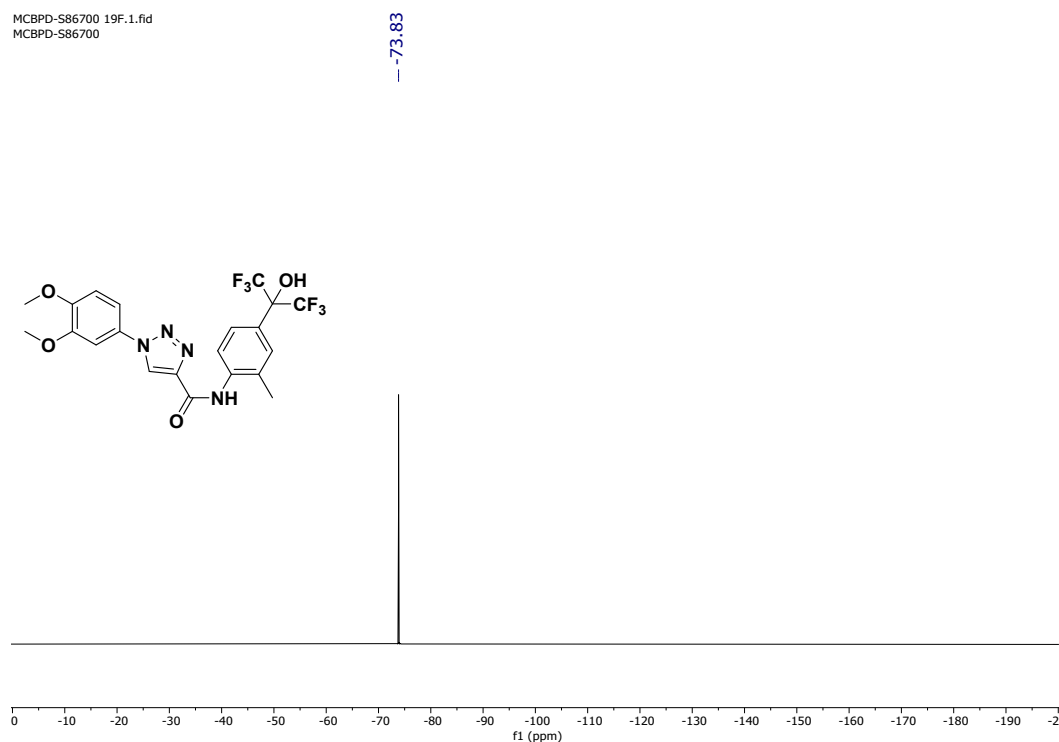
**Figure S18:**  $^1\text{H}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2b]**



**Figure S19:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2b**]

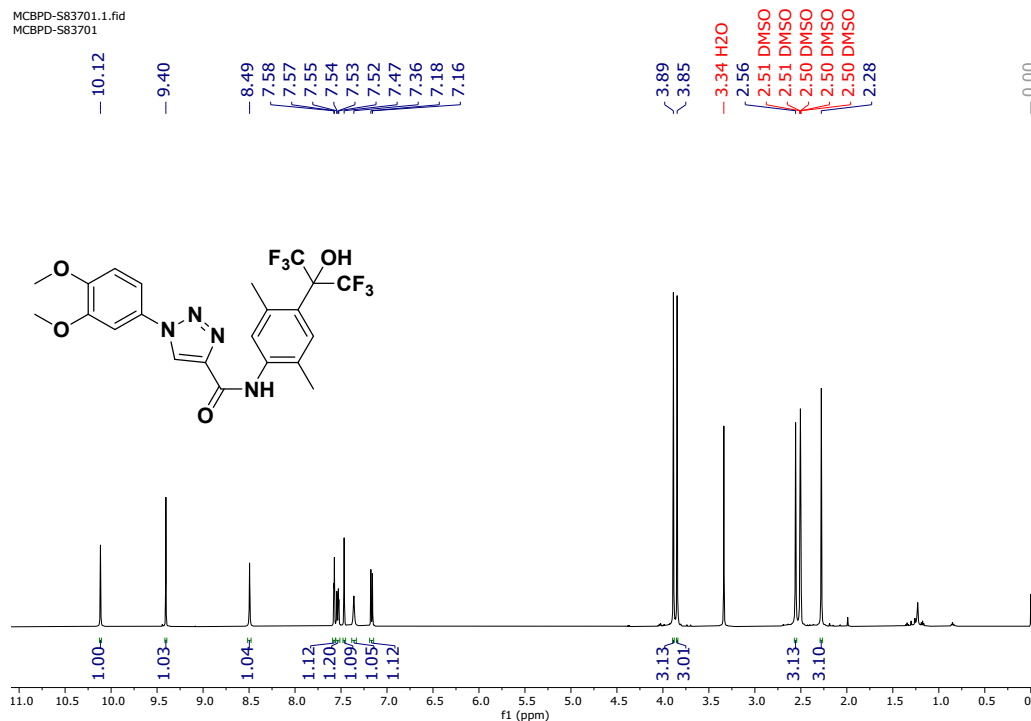


**Figure S20:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2b**]

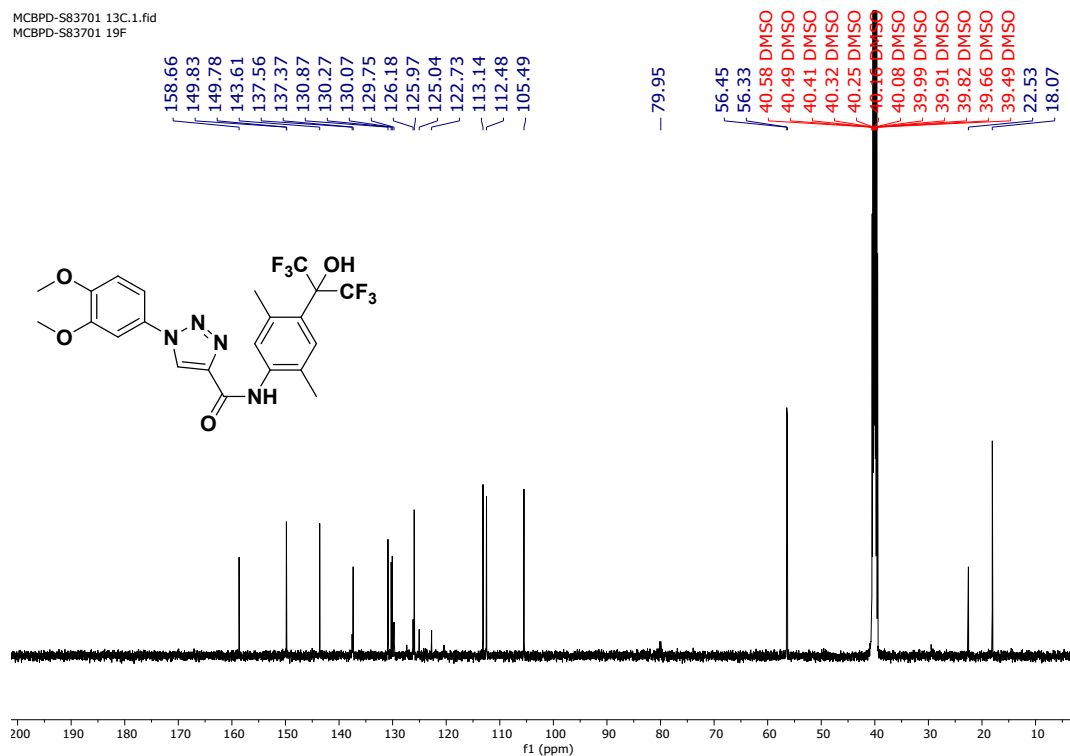




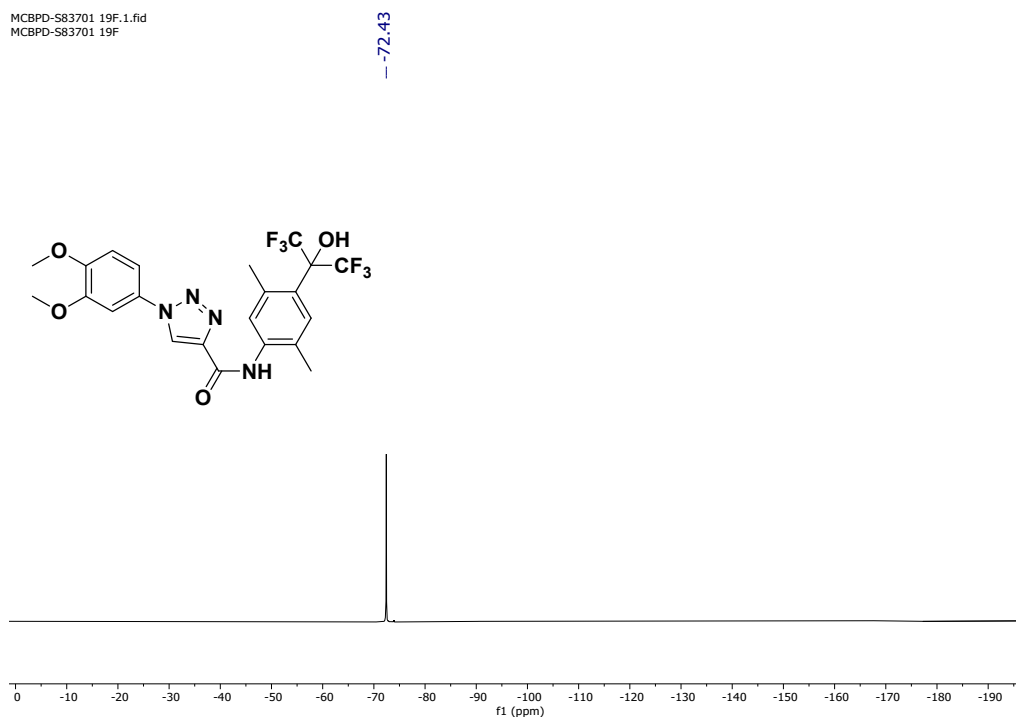
**Figure S21:**  $^1\text{H}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2c**]



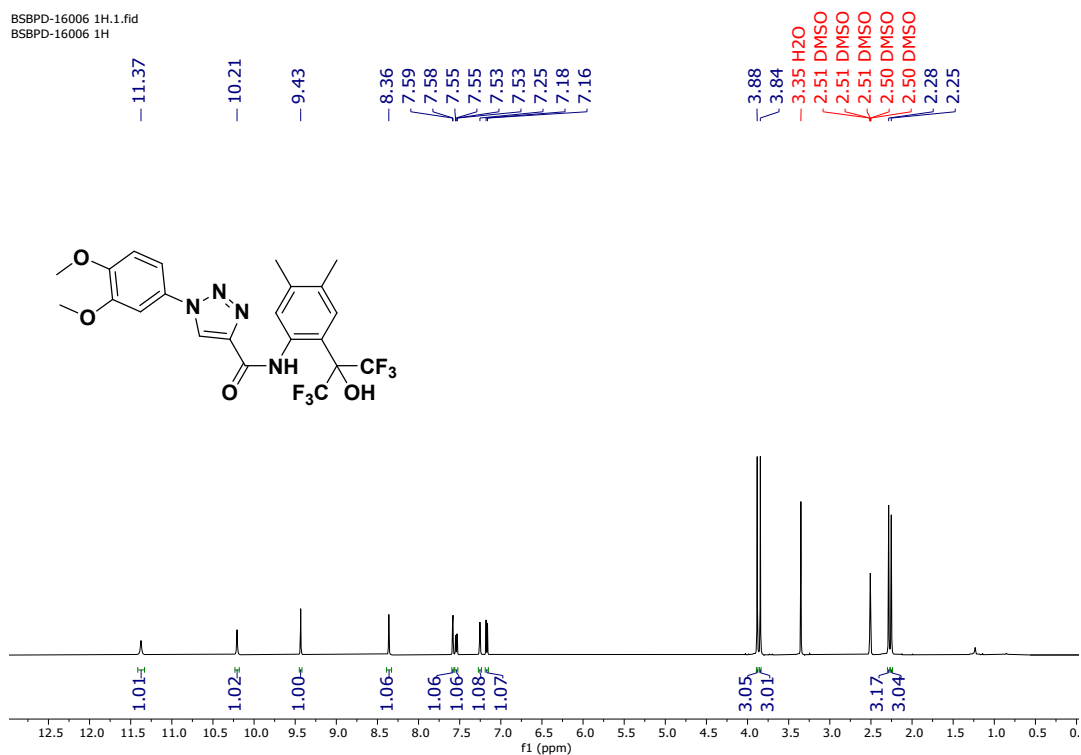
**Figure S22:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2c**]



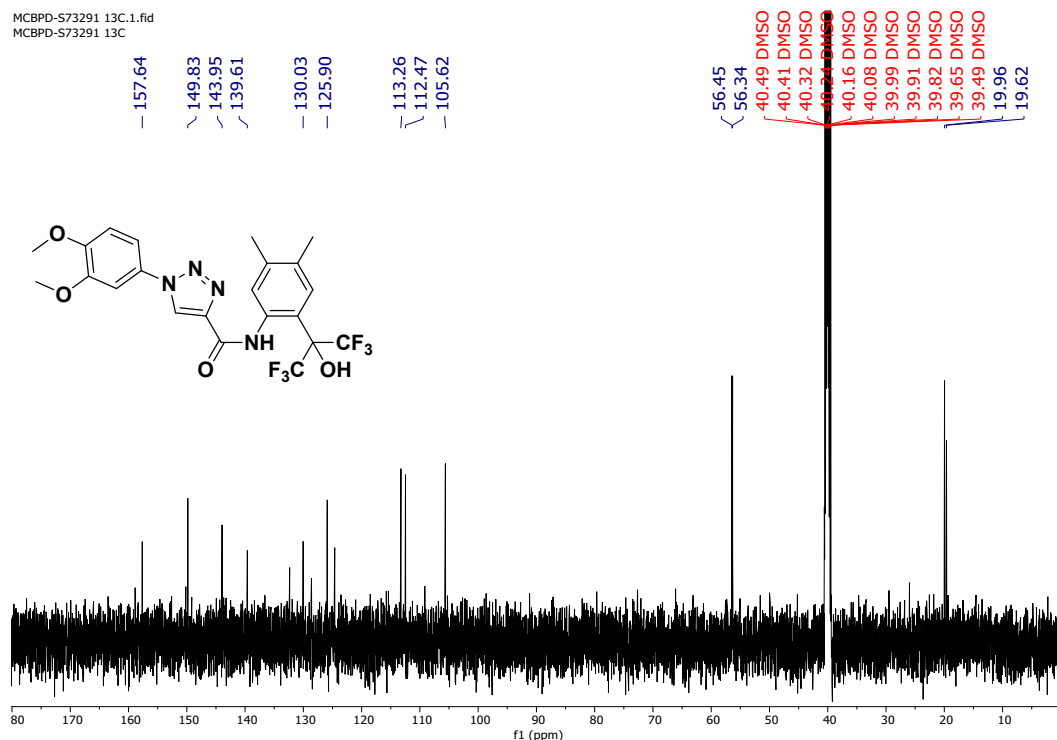
**Figure S23:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2c**]



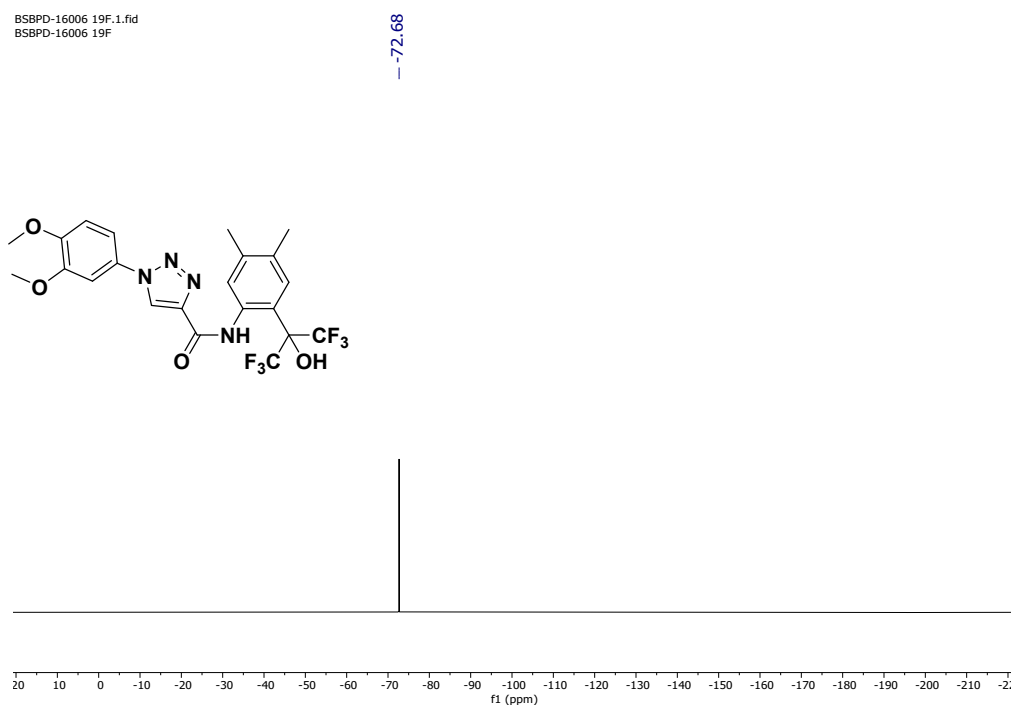
**Figure S24:**  $^1\text{H}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2d**]



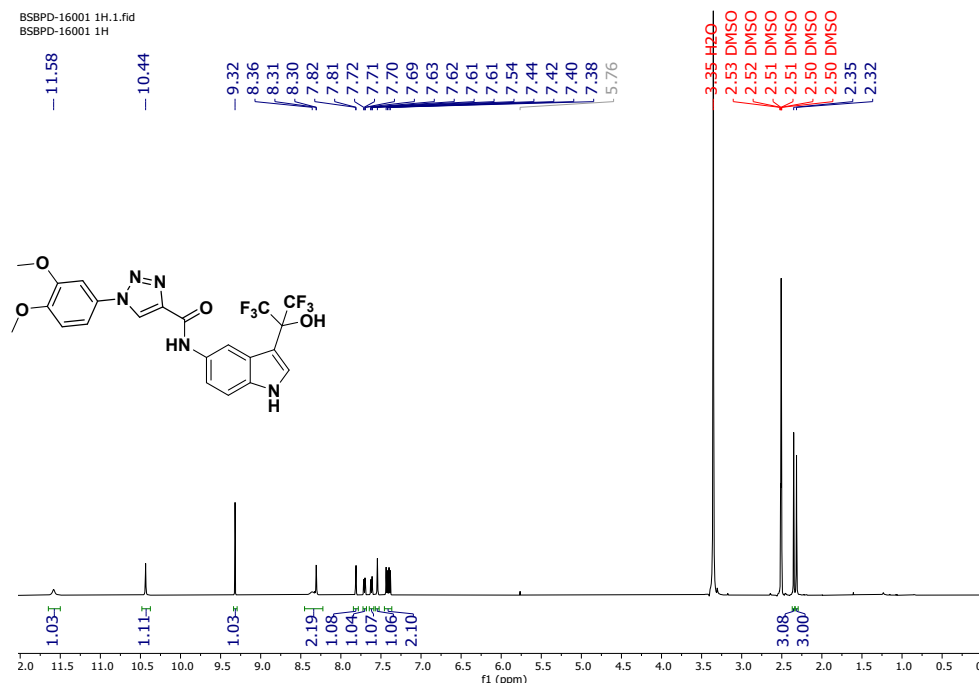
**Figure S25:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2d**]



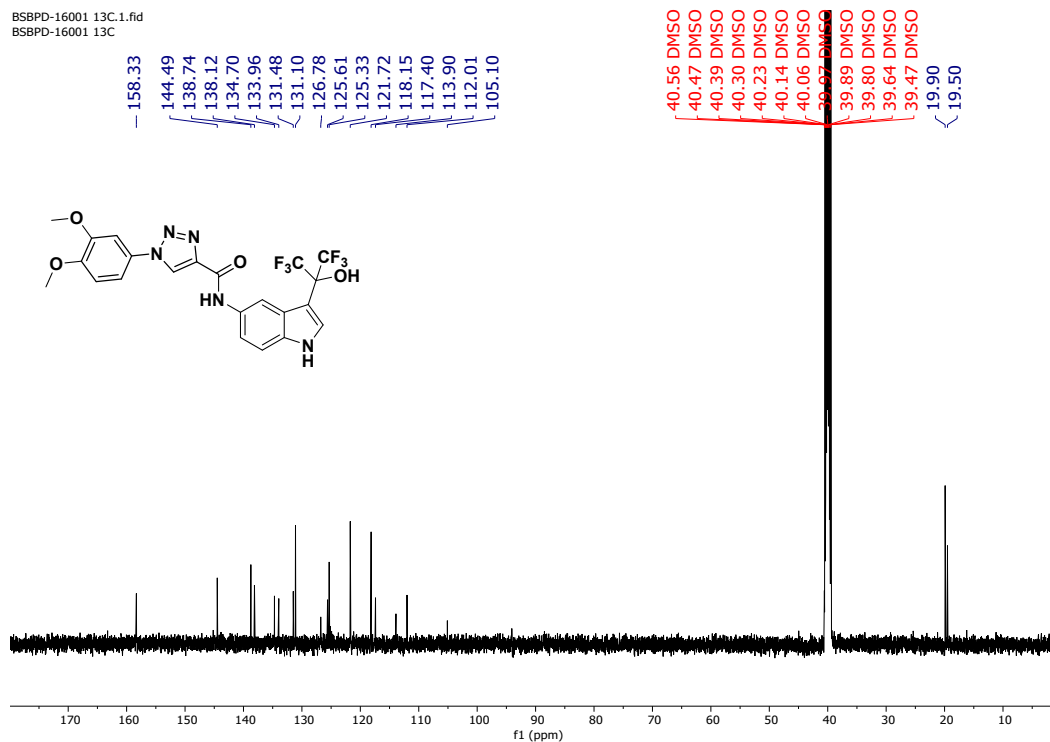
**Figure S26:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2d**]



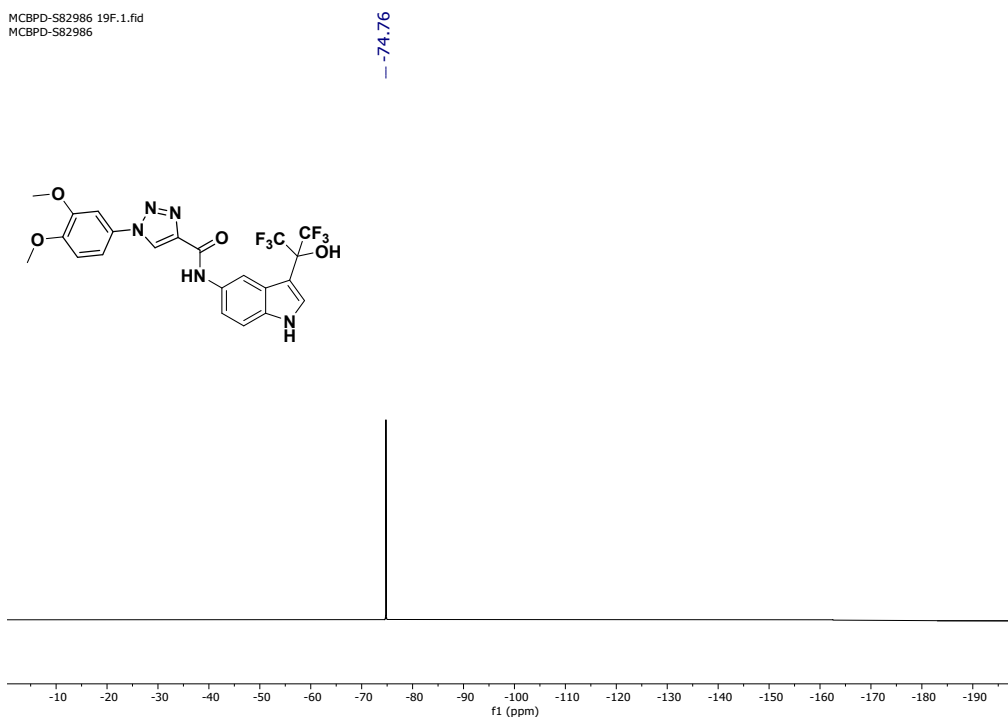
**Figure S27:**  $^1\text{H}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide [**2e**]



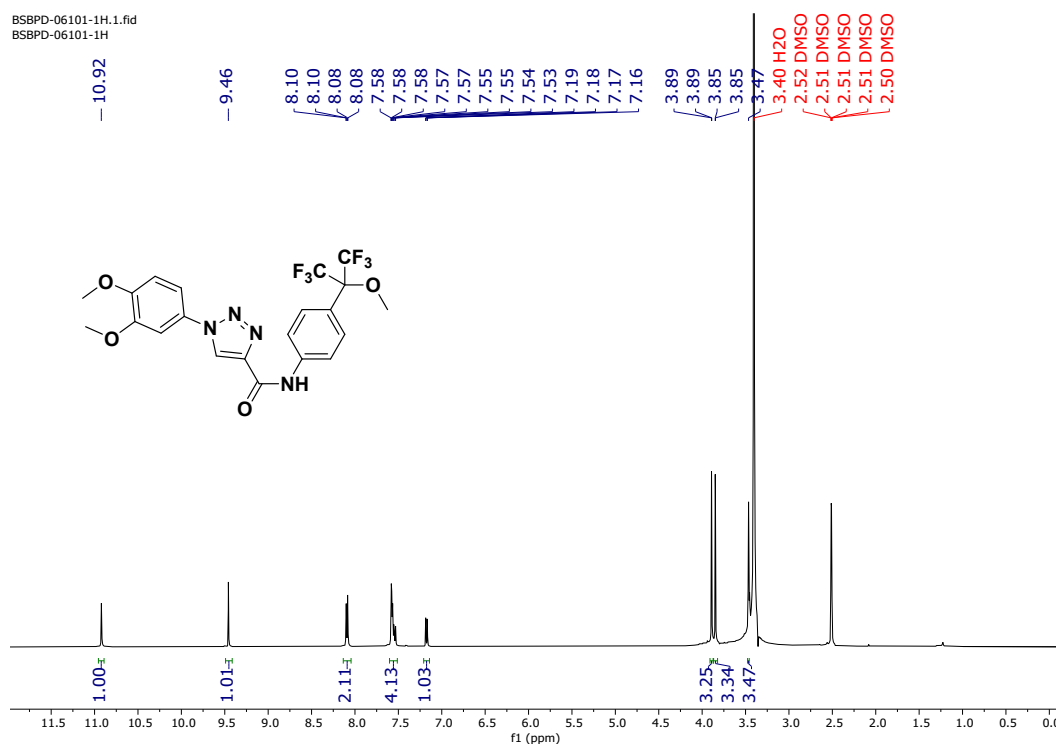
**Figure S28:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide [**2e**]



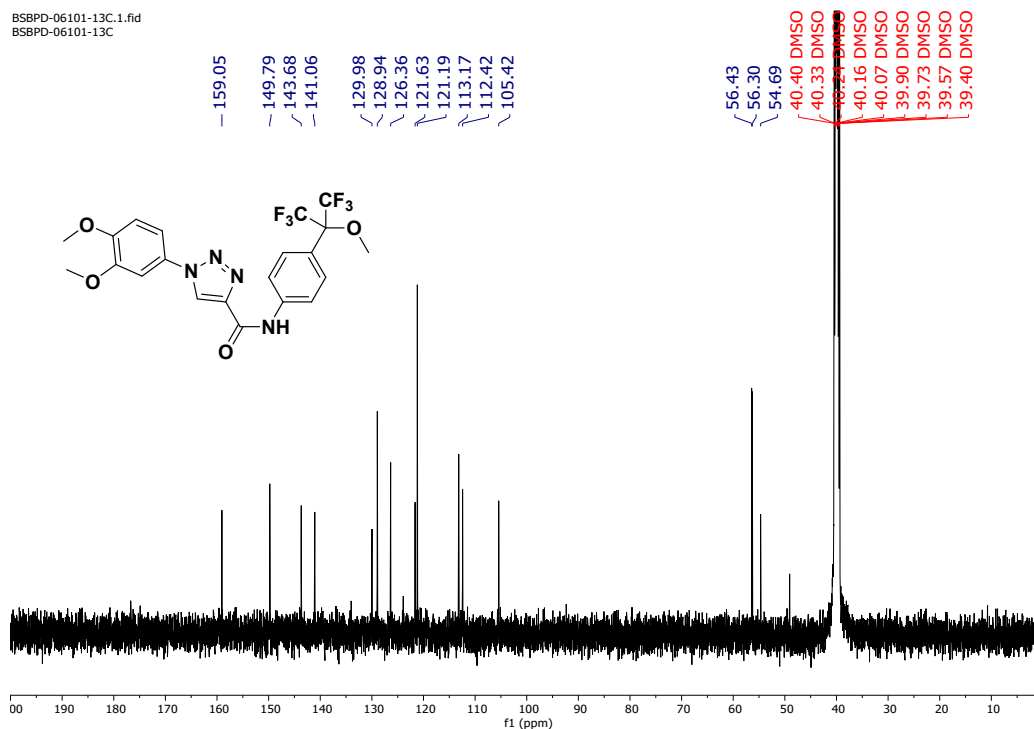
**Figure S29:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide [**2e**]



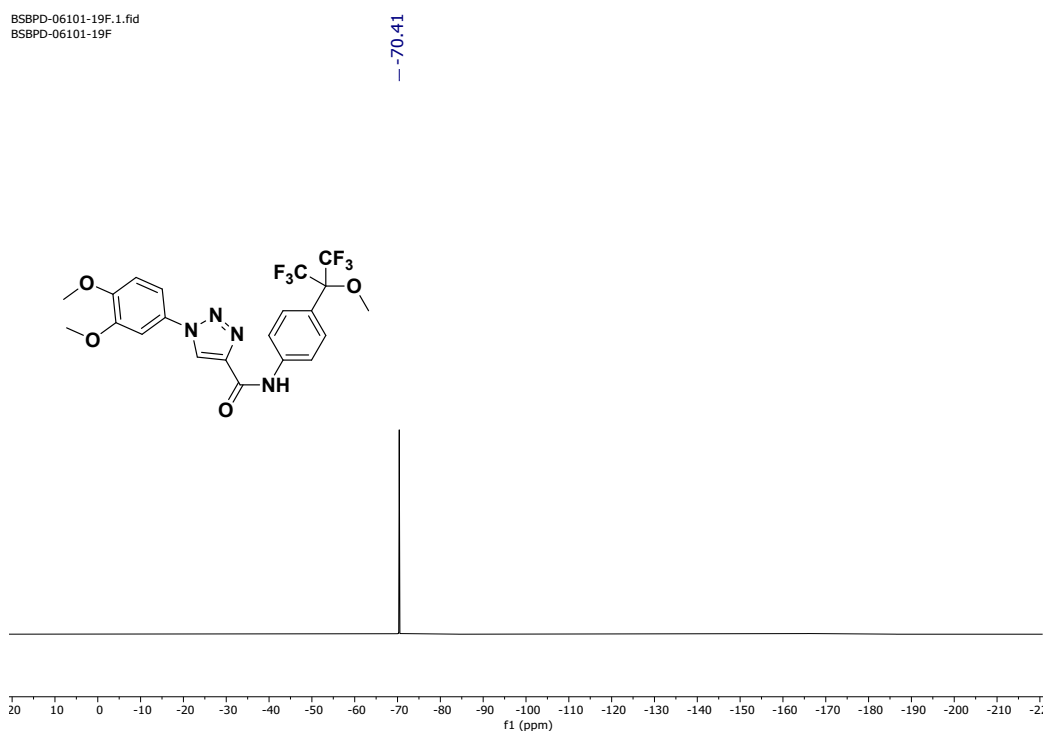
**Figure S30:**  $^1\text{H}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [**2f**]



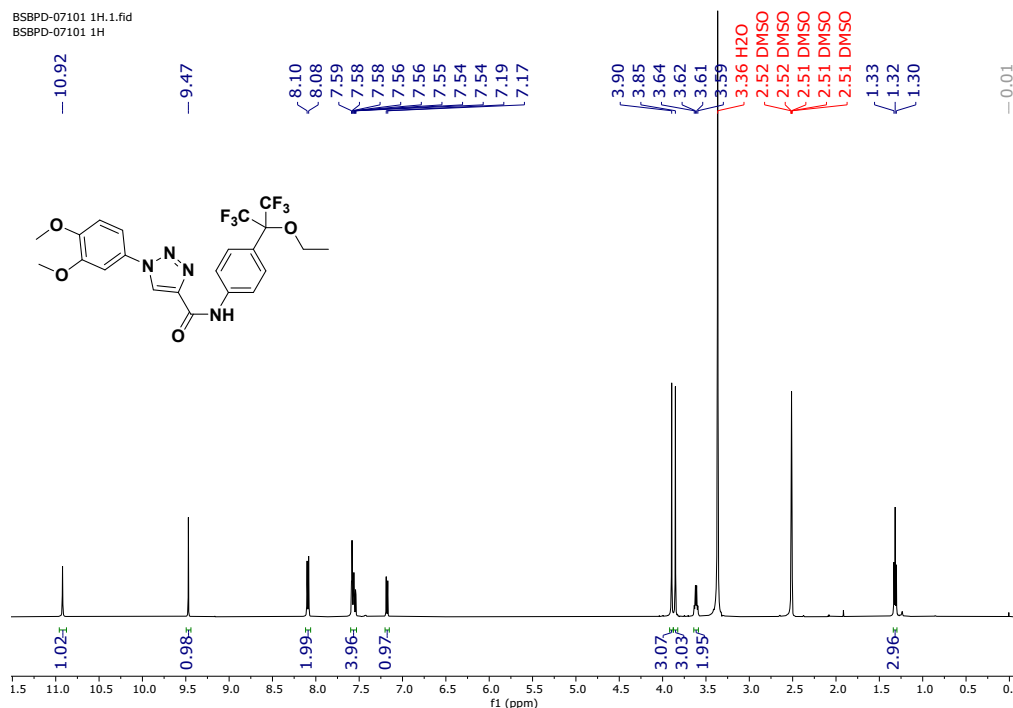
**Figure S31:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2f]**



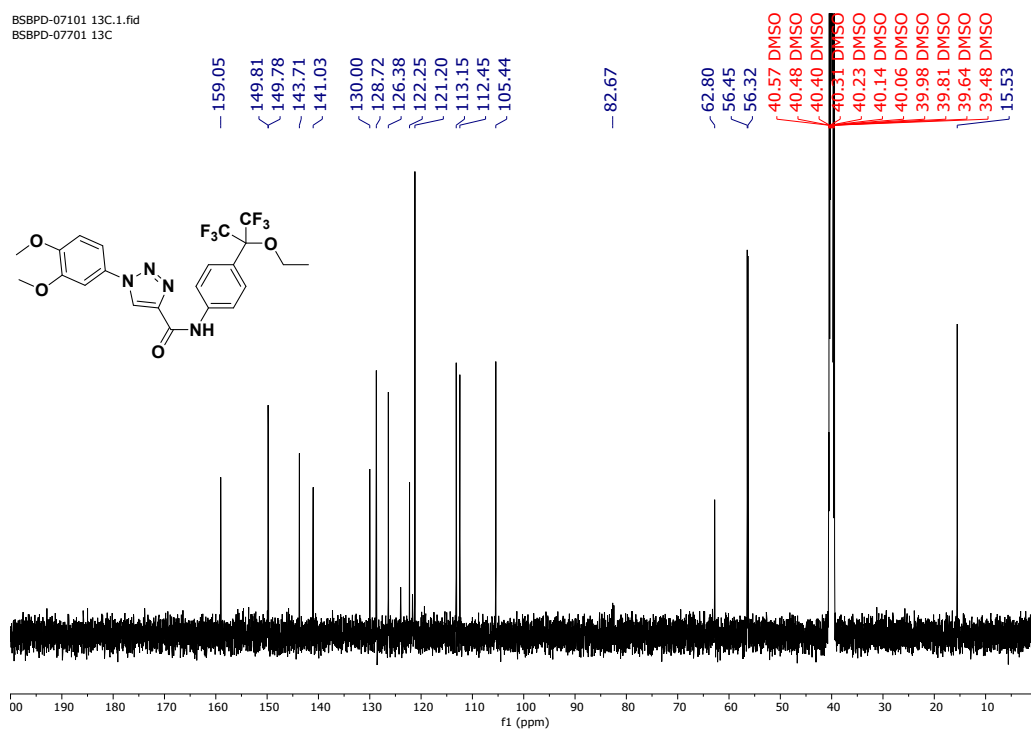
**Figure S32:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2f]**



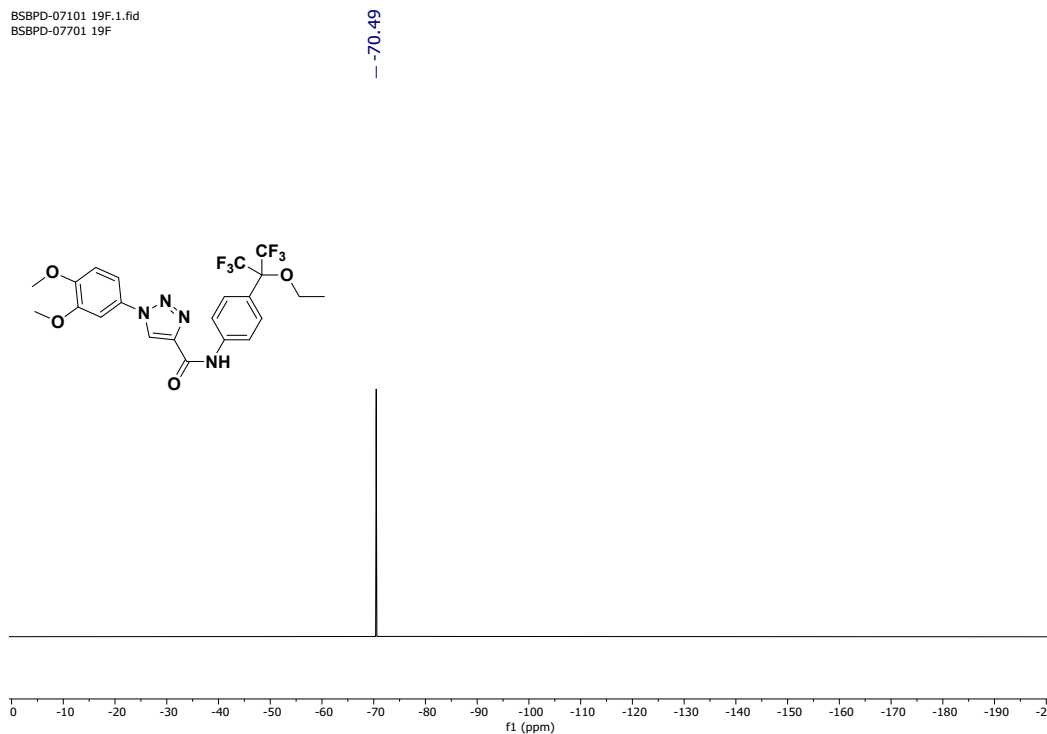
**Figure S33:**  $^1\text{H}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [**2g**]



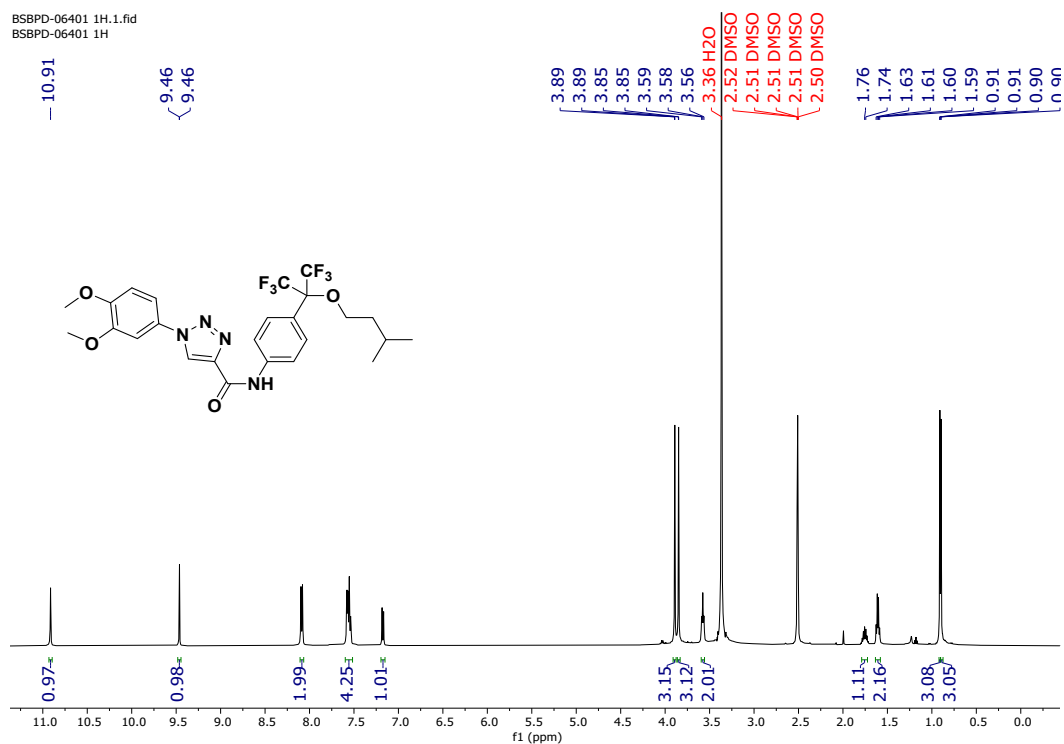
**Figure S34:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [**2g**]



**Figure S35:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [**2g**]

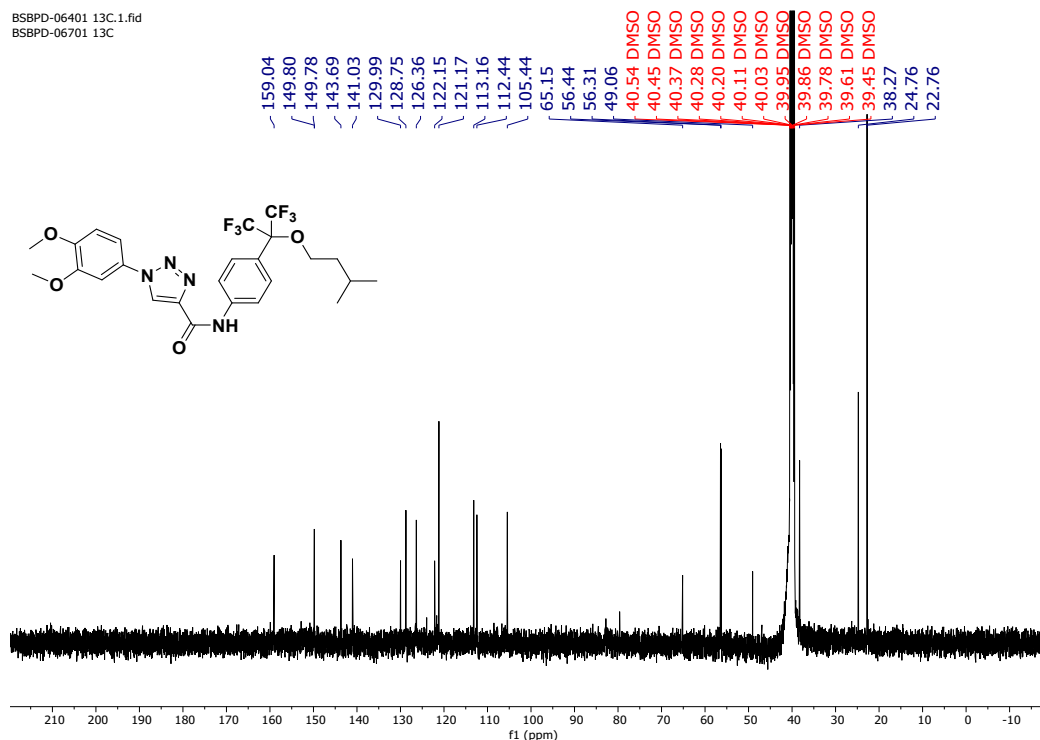


**Figure S36:**  $^1\text{H}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [**2h**]

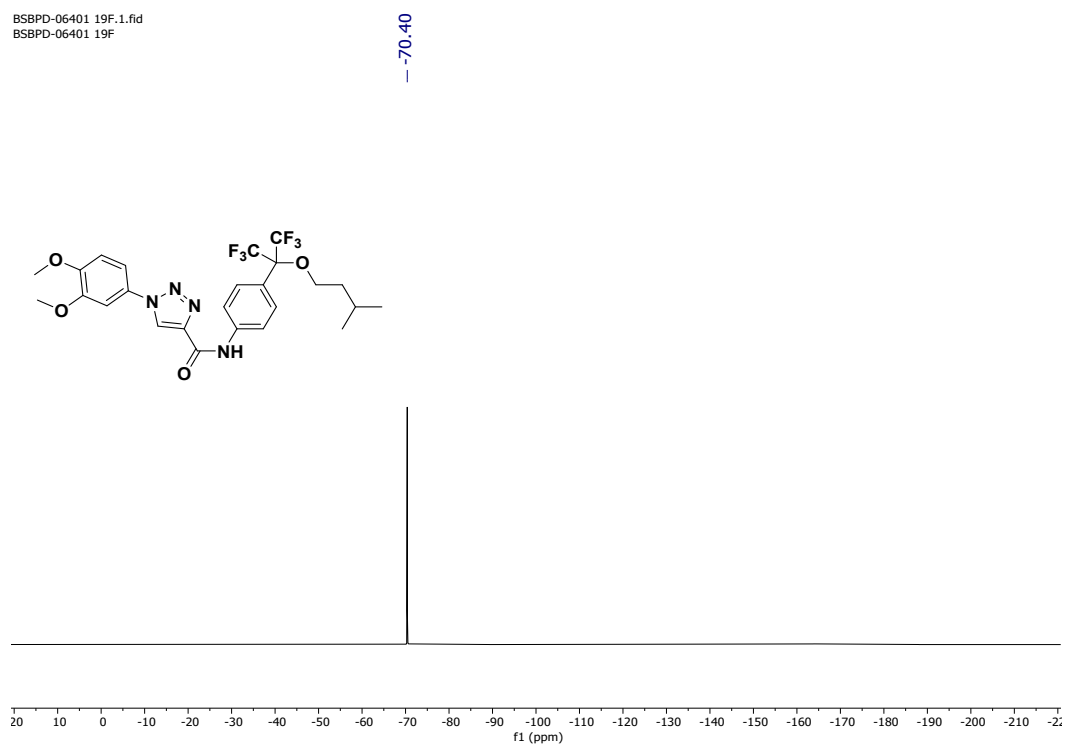




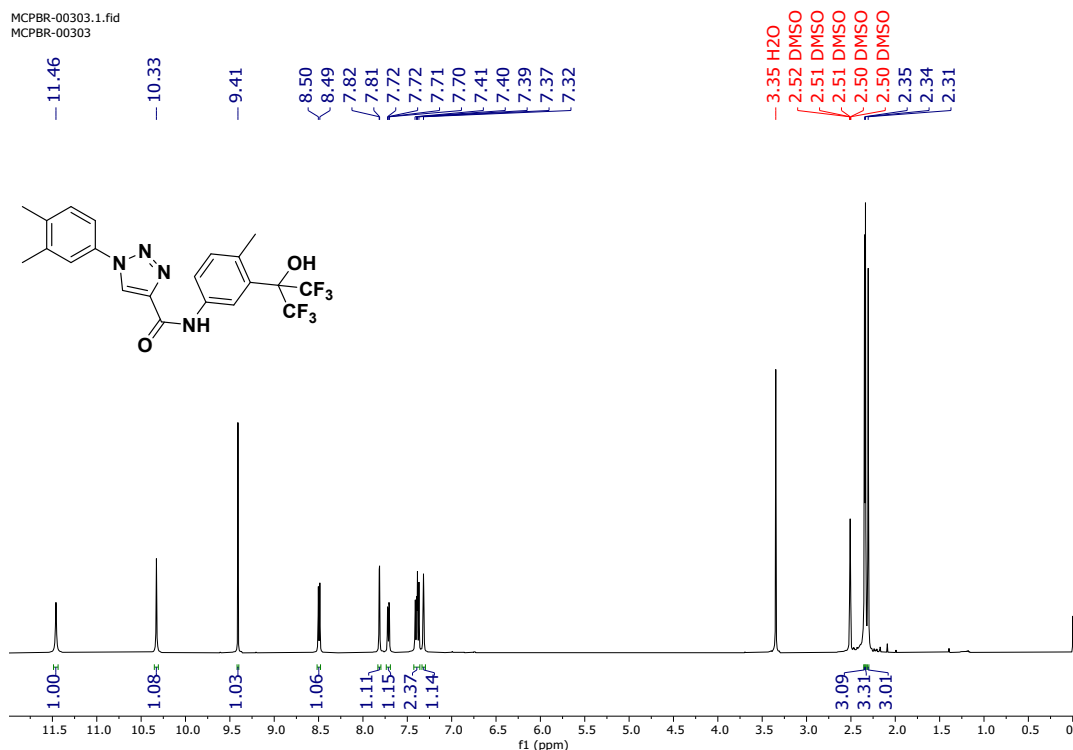
**Figure S37:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [**2h**]



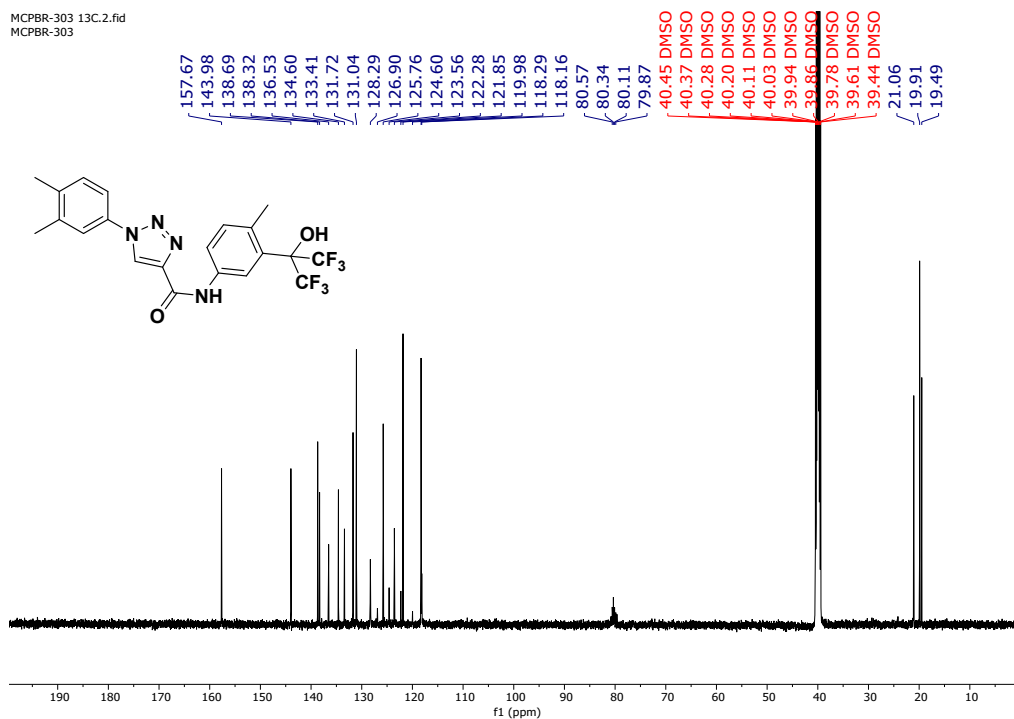
**Figure S38:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [**2h**]



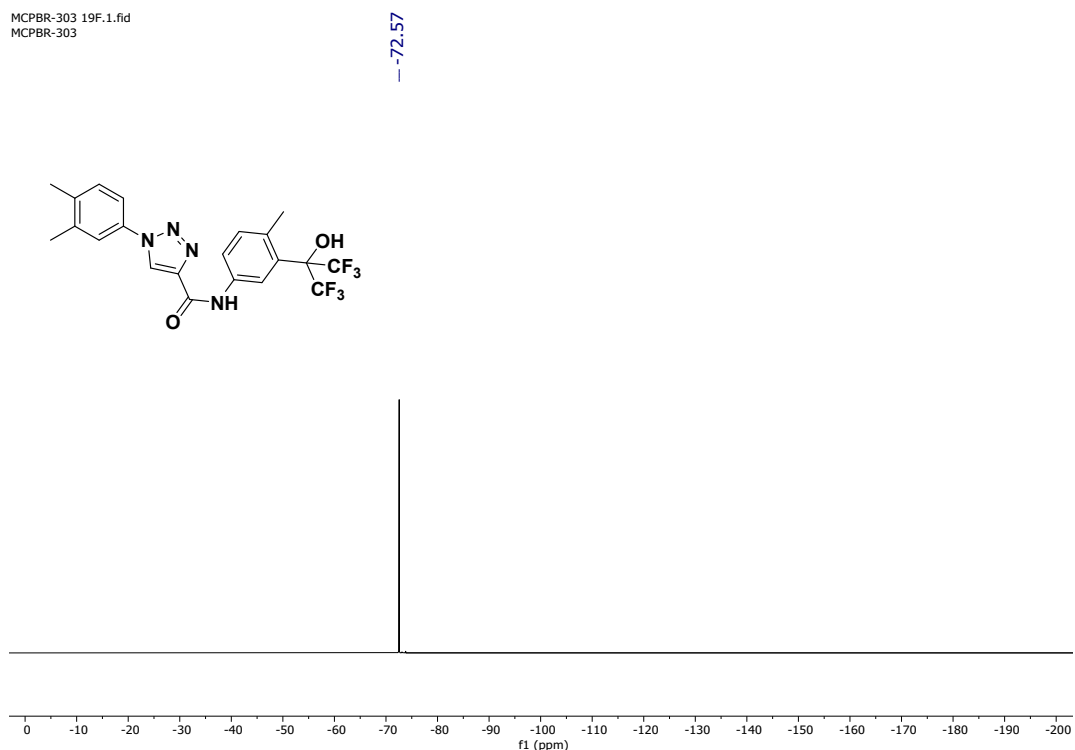
**Figure S39:**  $^1\text{H}$  NMR of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2i**]



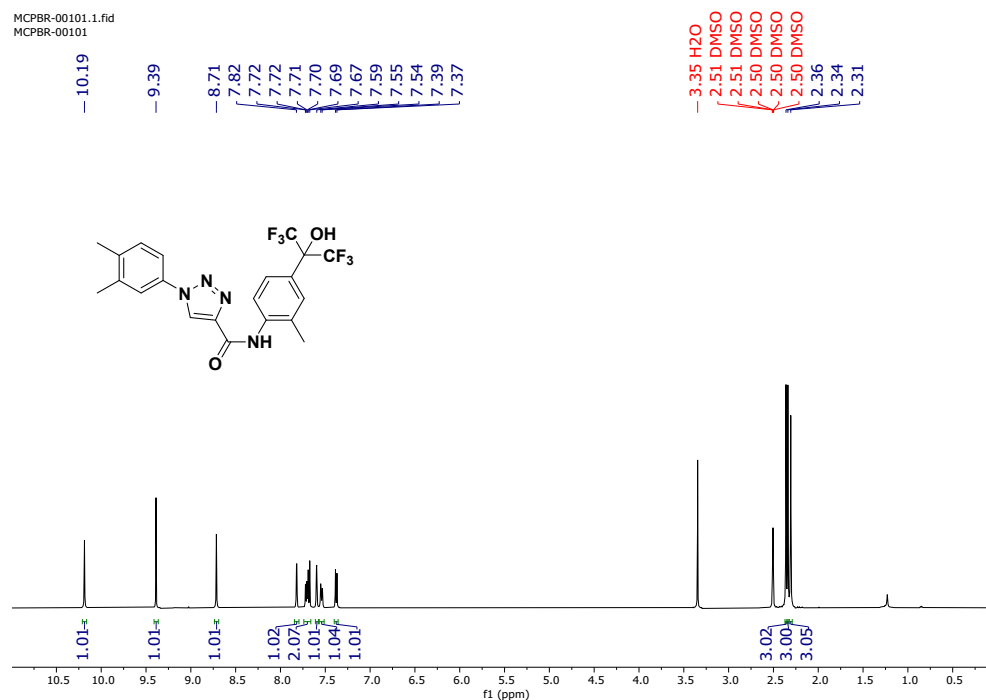
**Figure S40:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2i**]



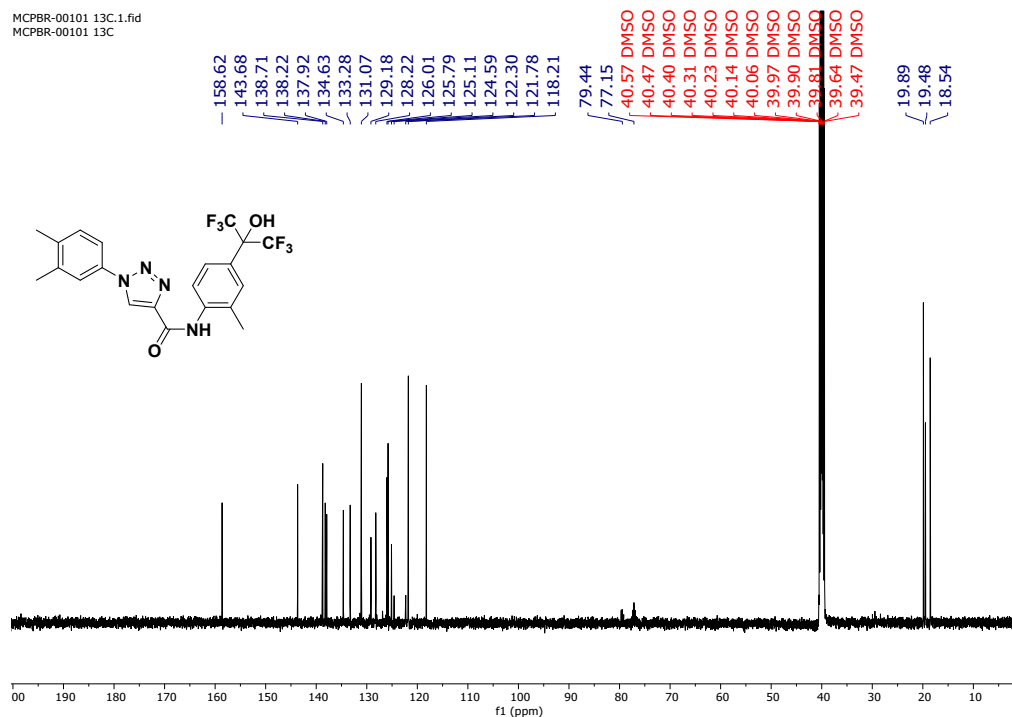
**Figure S41:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2i]**



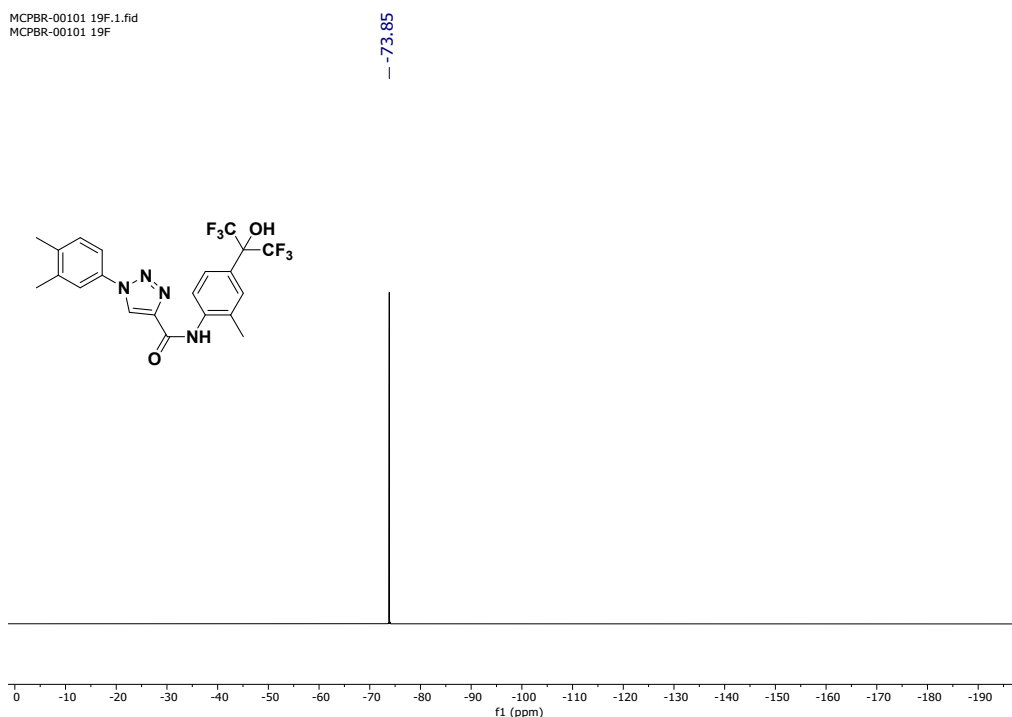
**Figure S42:**  $^1\text{H}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2j]**



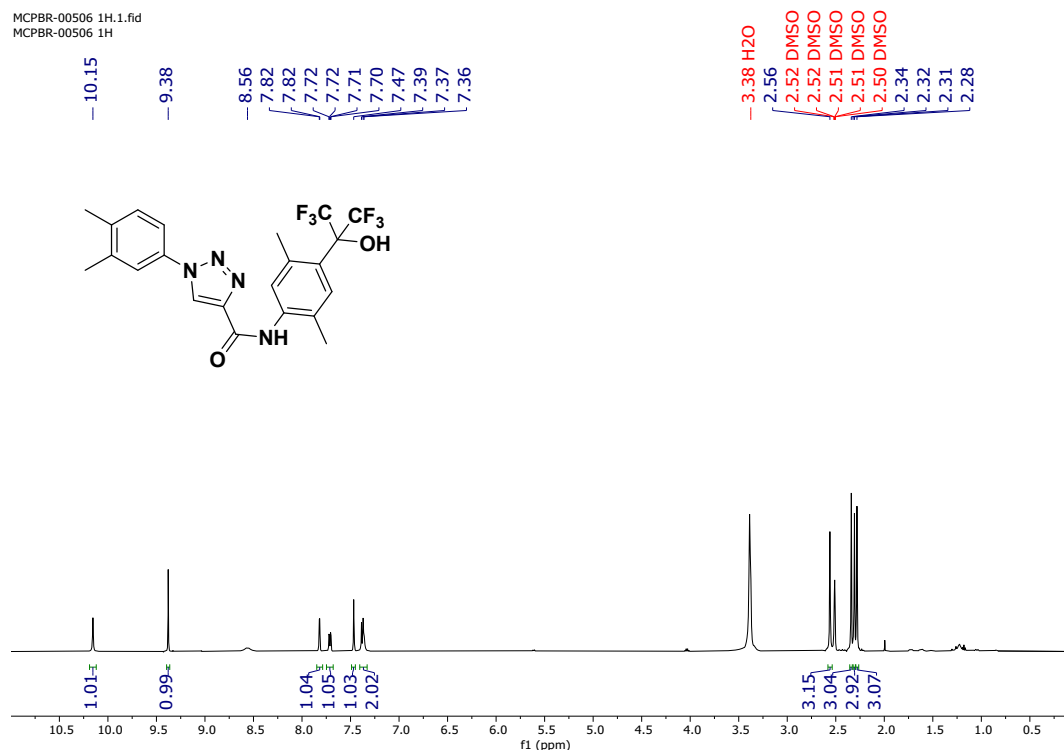
**Figure S43:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [2j]



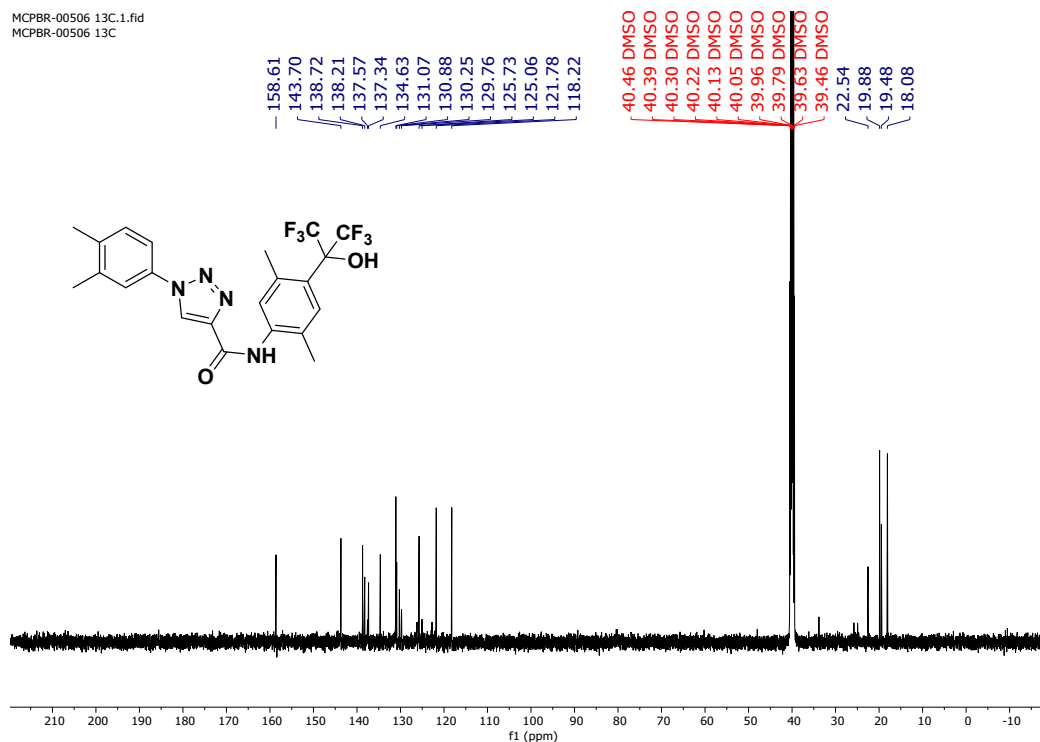
**Figure S44:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [2j]



**Figure S45:**  $^1\text{H}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2k**]

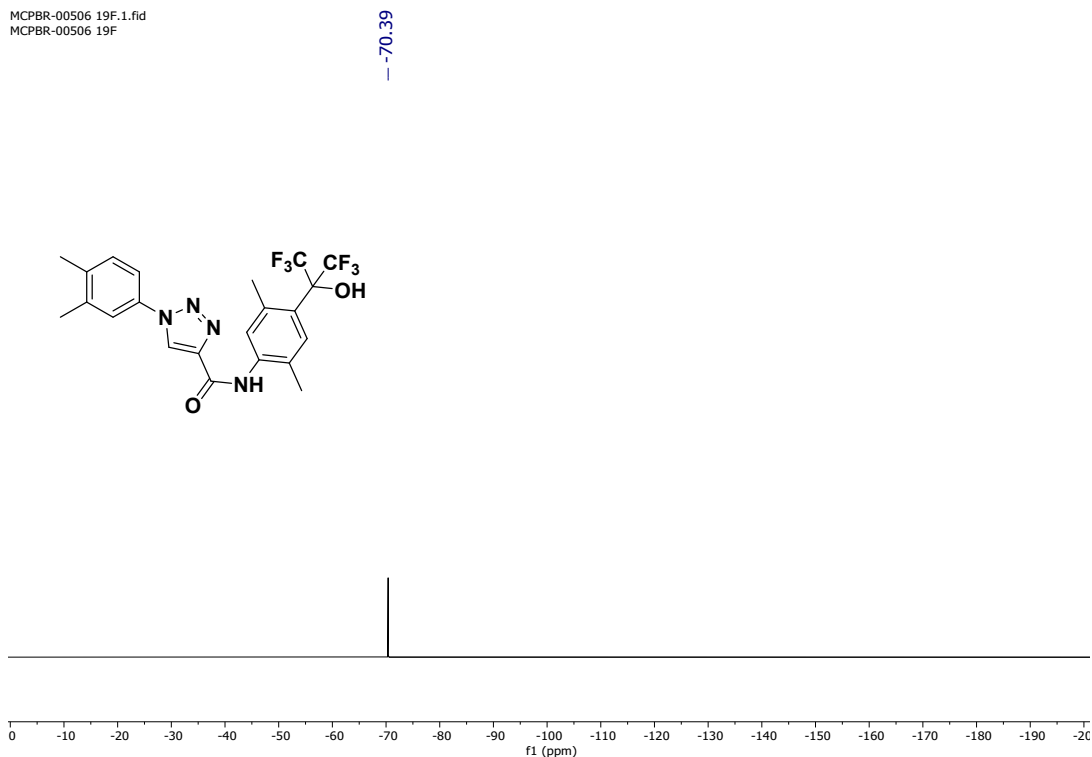


**Figure S46:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2k**]



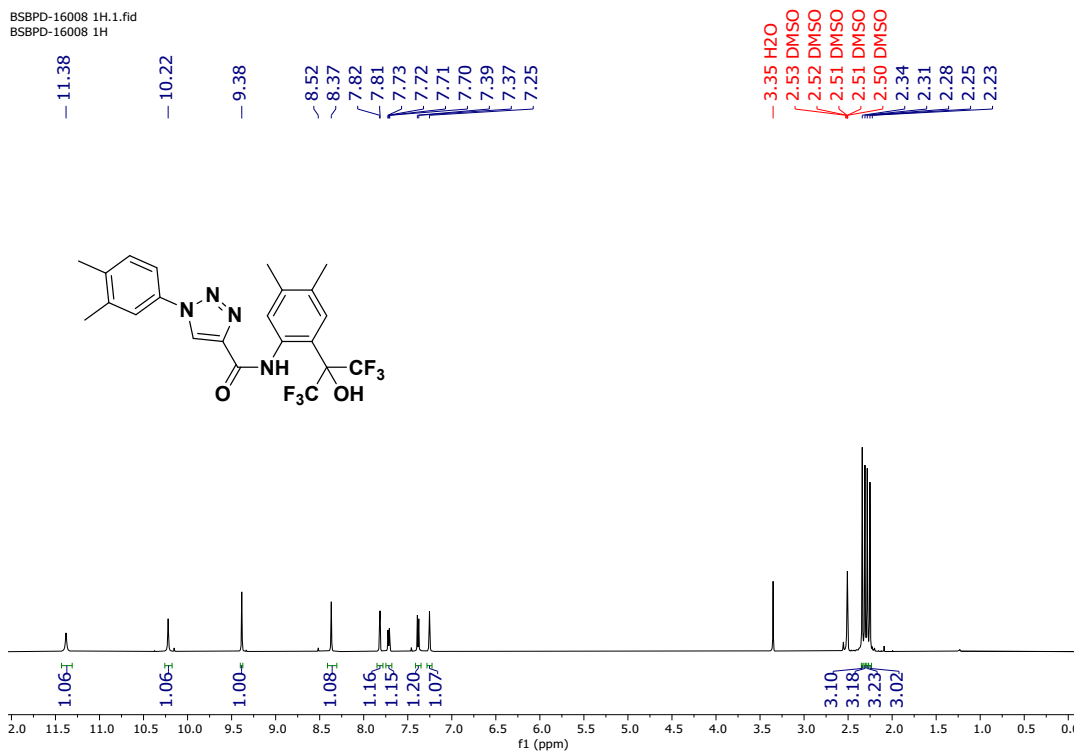
**Figure S47:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2k]**

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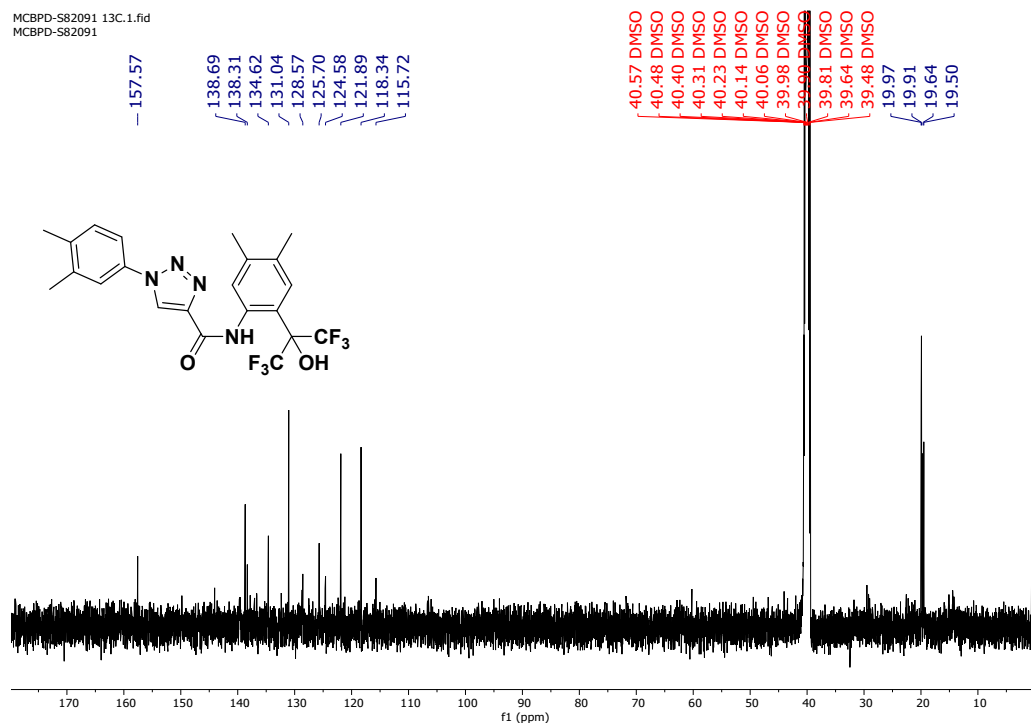


**Figure S48:**  $^1\text{H}$  NMR of 1-(3,4-dimethylphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2l]**

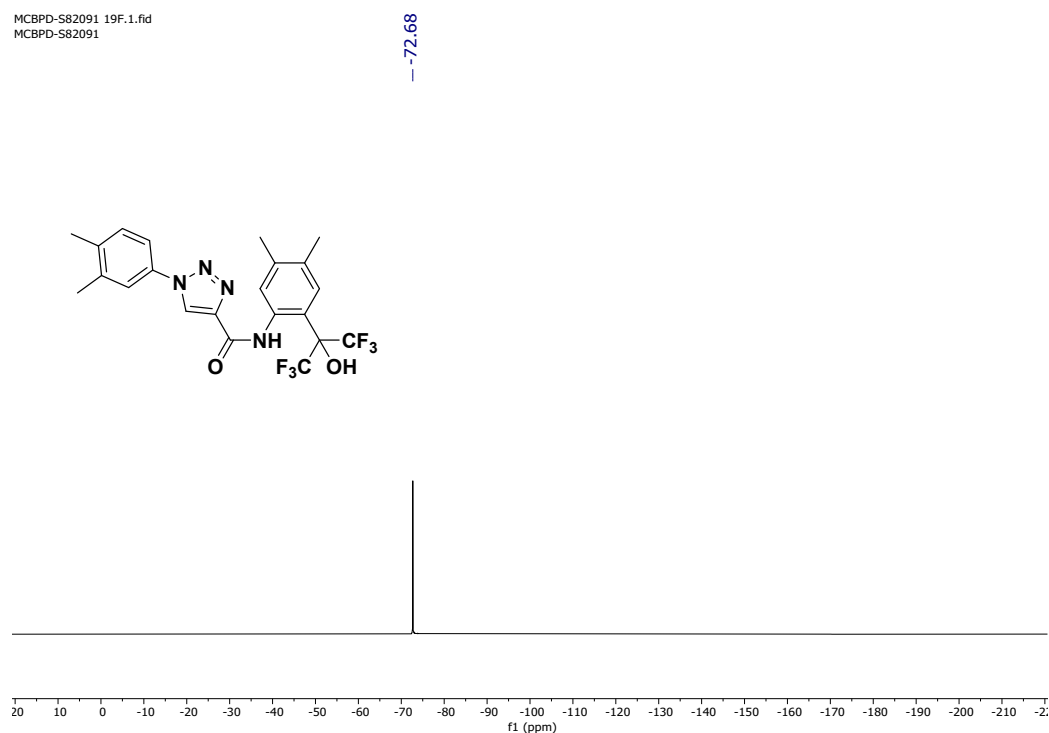
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BSBPD-16008 1H



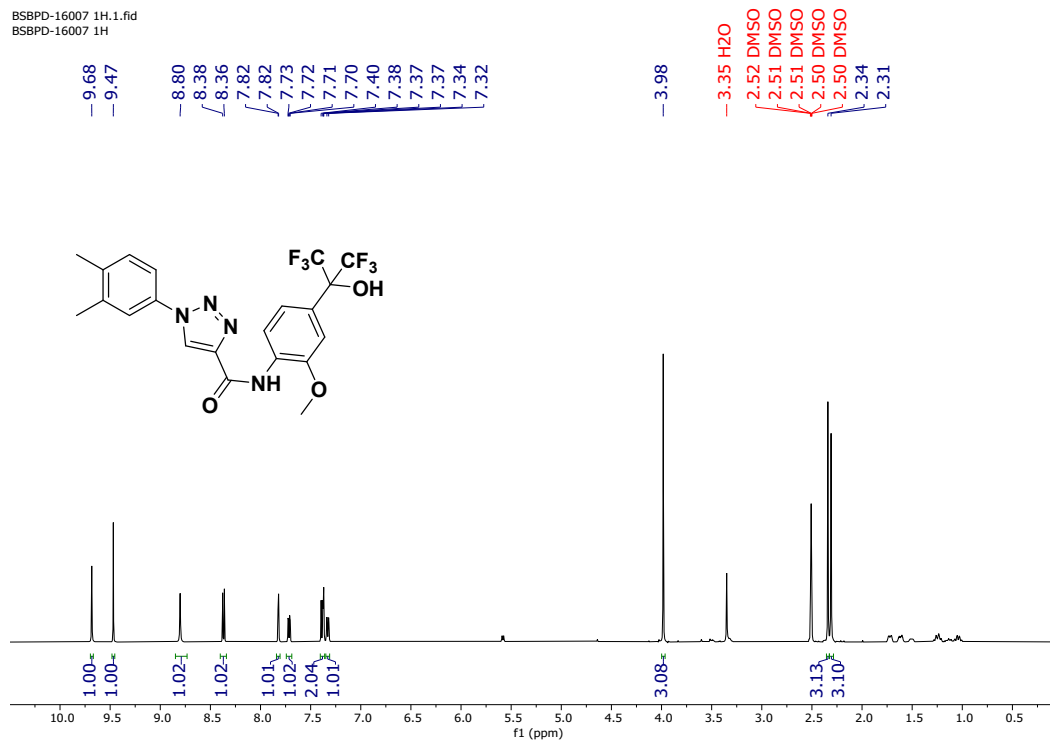
**Figure S49:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethylphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2I**]



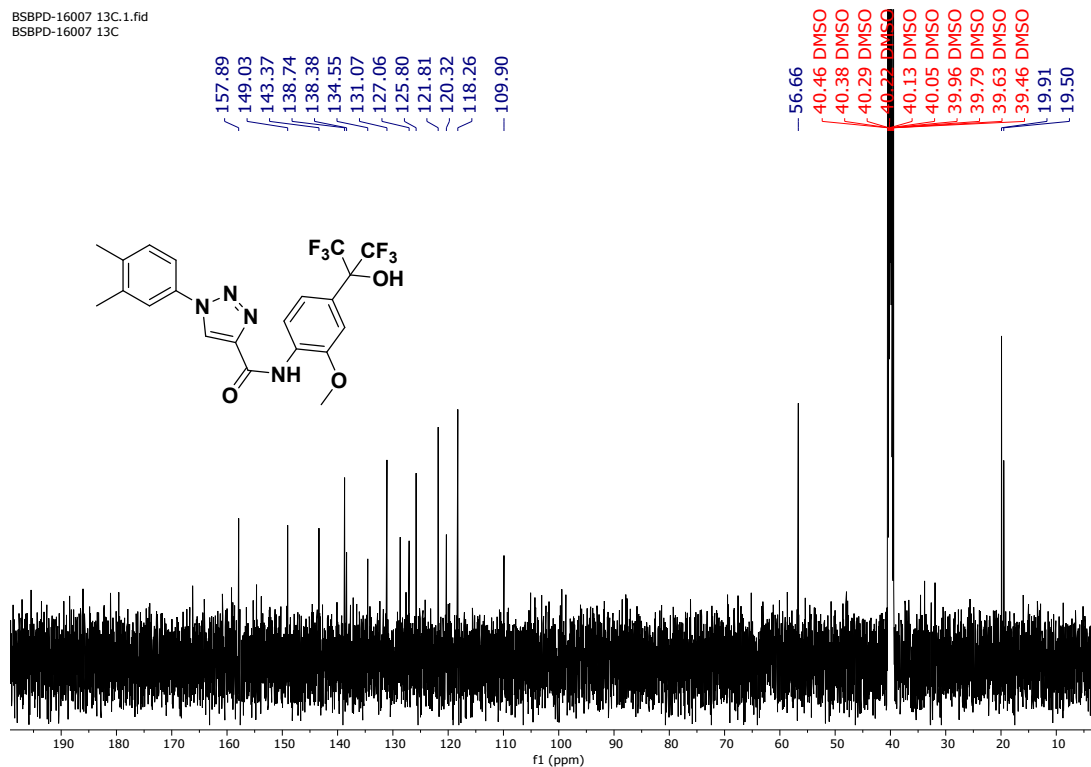
**Figure S50:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethylphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2I**]



**Figure S51:**  $^1\text{H}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methoxyphenyl)-1H-1,2,3-triazole-4-carboxamide [**2m**]



**Figure S52:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methoxyphenyl)-1H-1,2,3-triazole-4-carboxamide [**2m**]

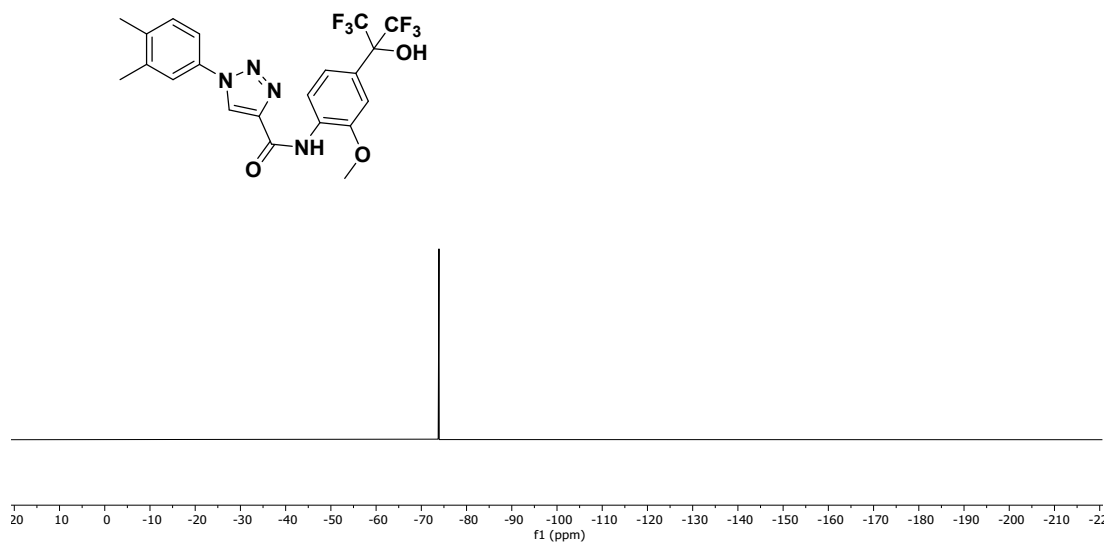




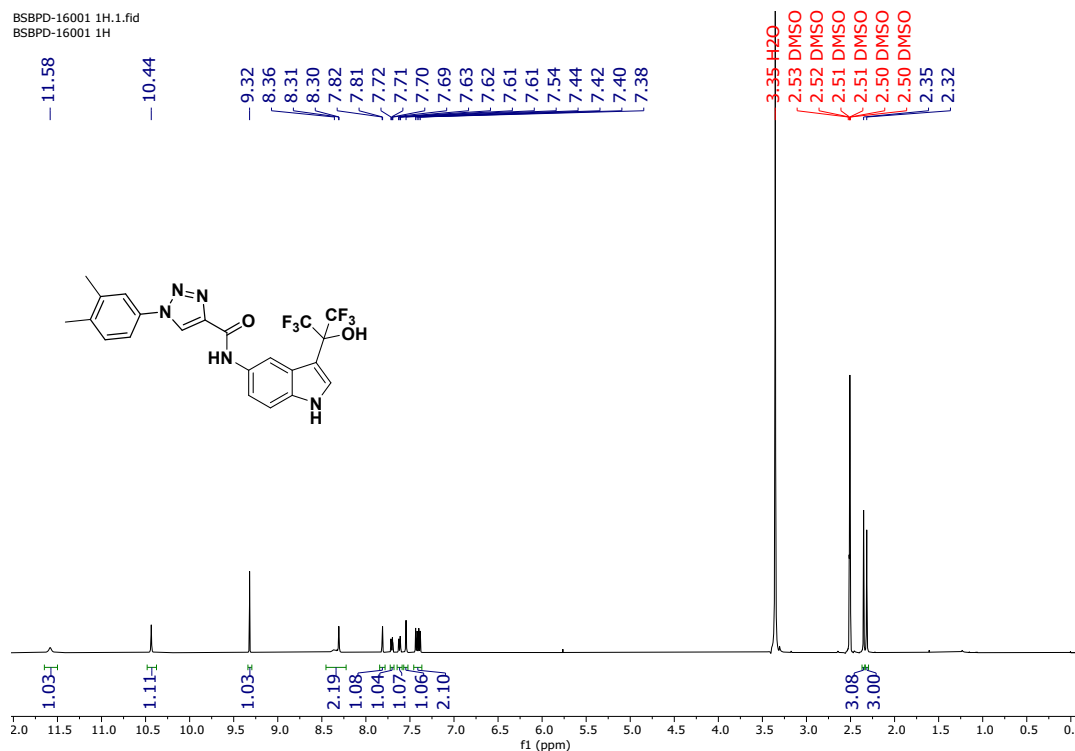
**Figure S53:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methoxyphenyl)-1H-1,2,3-triazole-4-carboxamide **[2m]**

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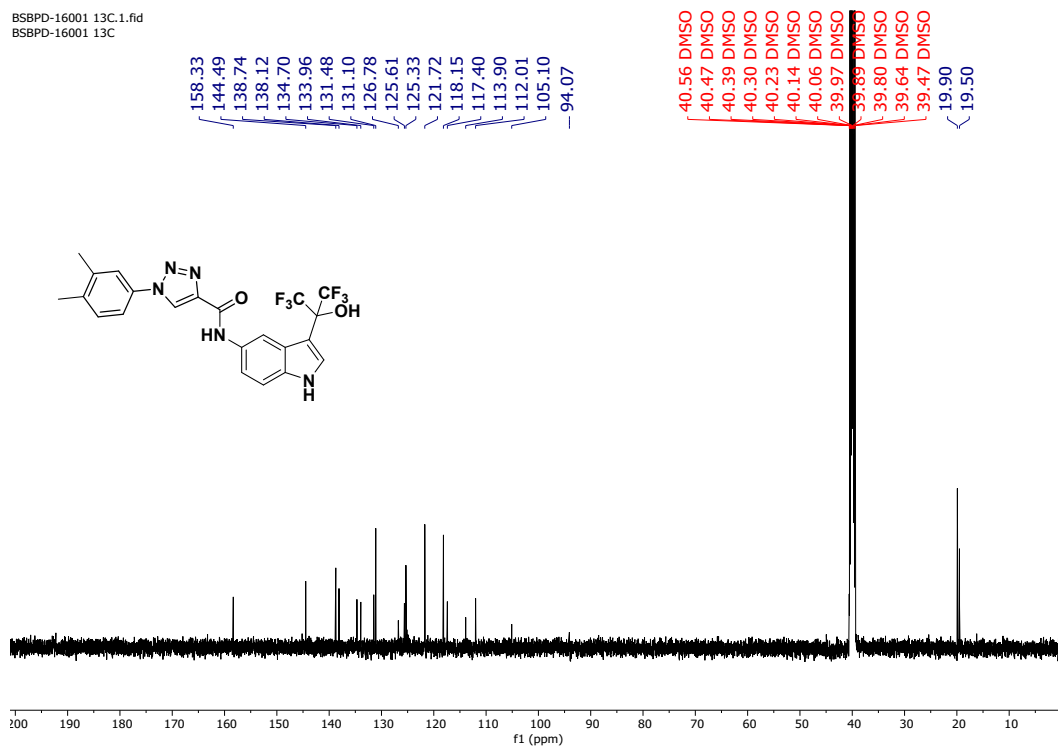
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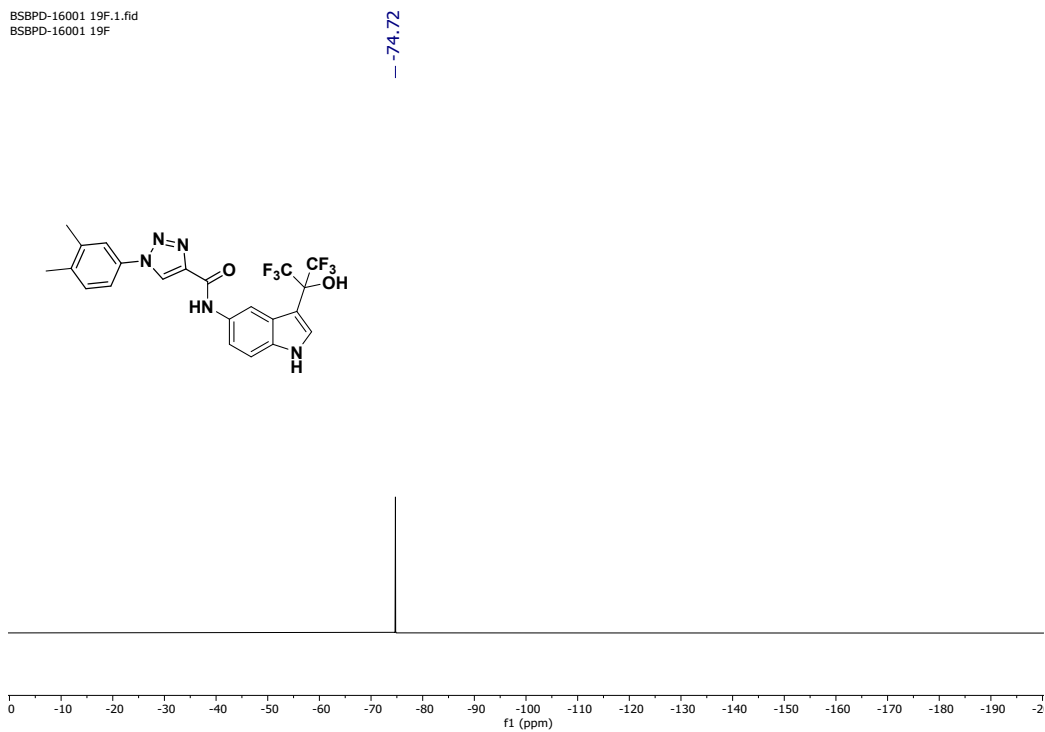
**Figure S54:**  $^1\text{H}$  NMR of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide **[2n]**



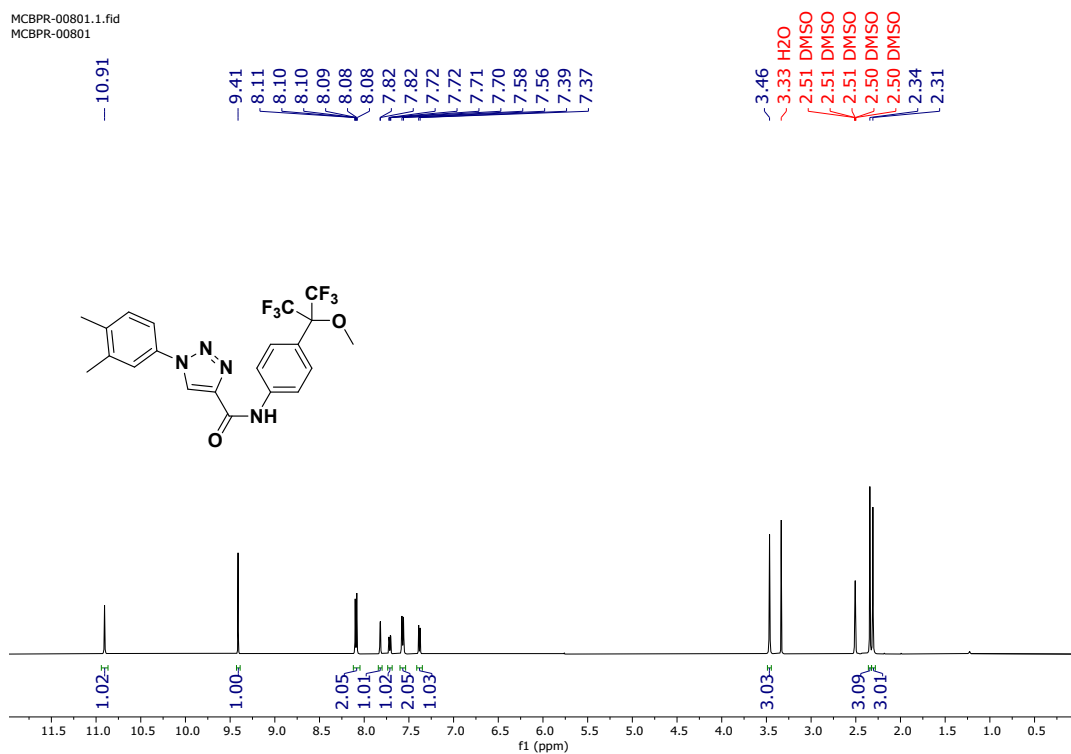
**Figure S55:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide [2n]



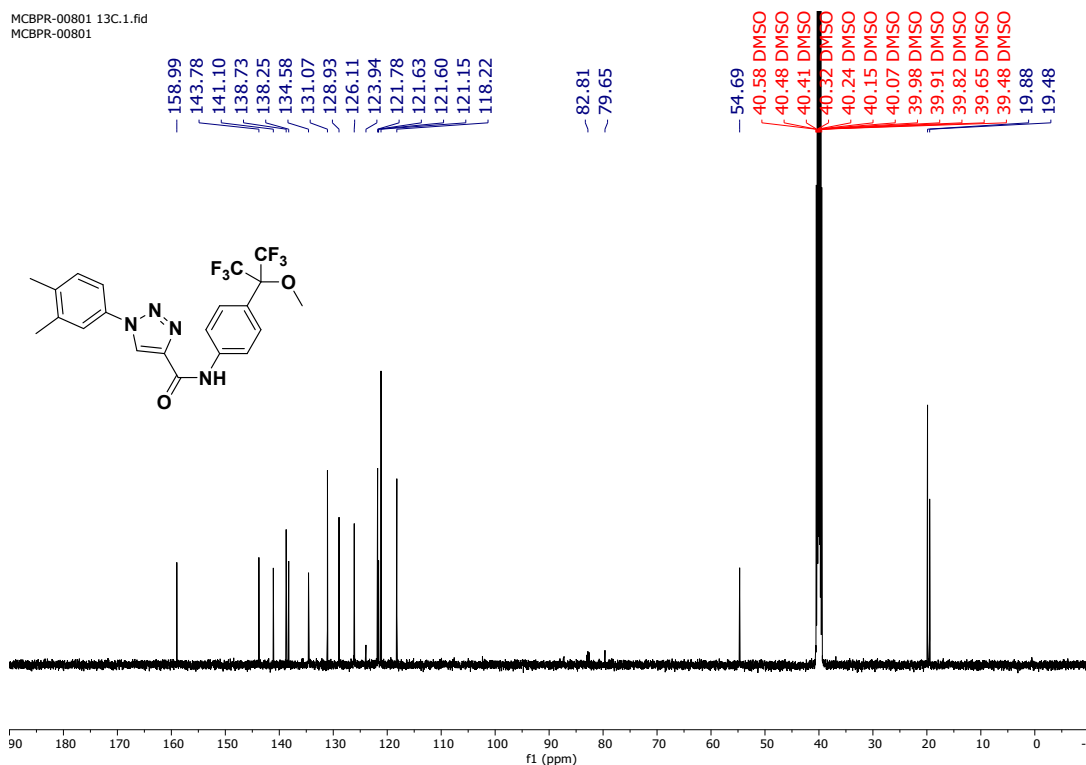
**Figure S56:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide [2n]



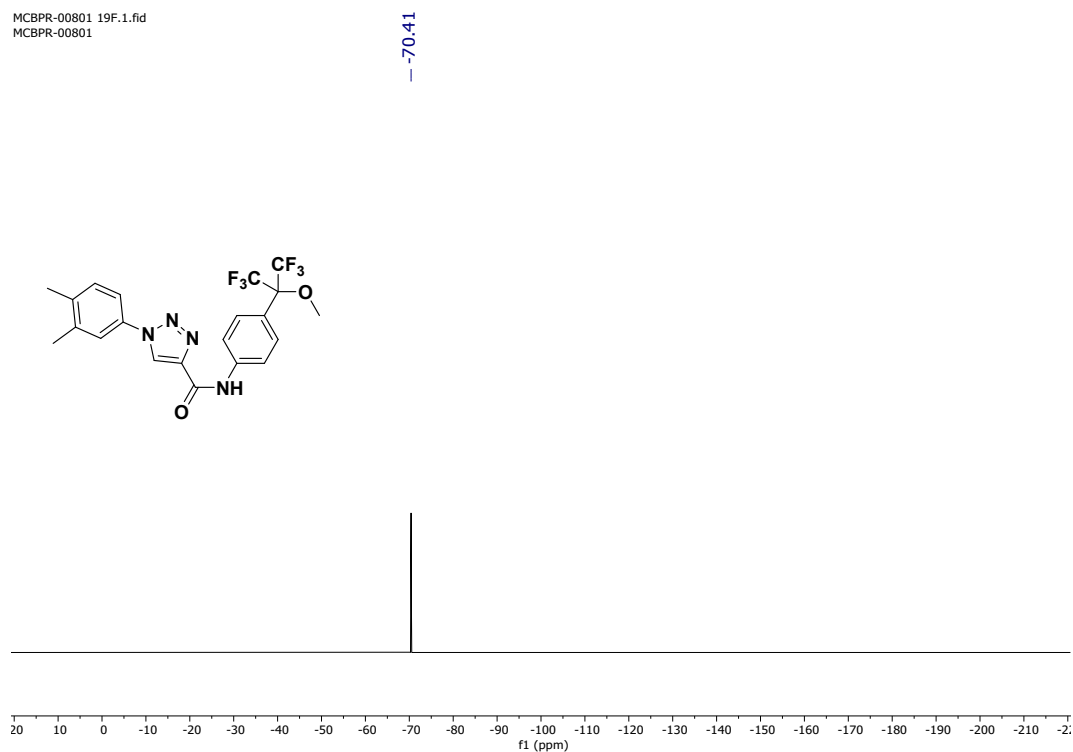
**Figure S57:**  $^1\text{H}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2o]



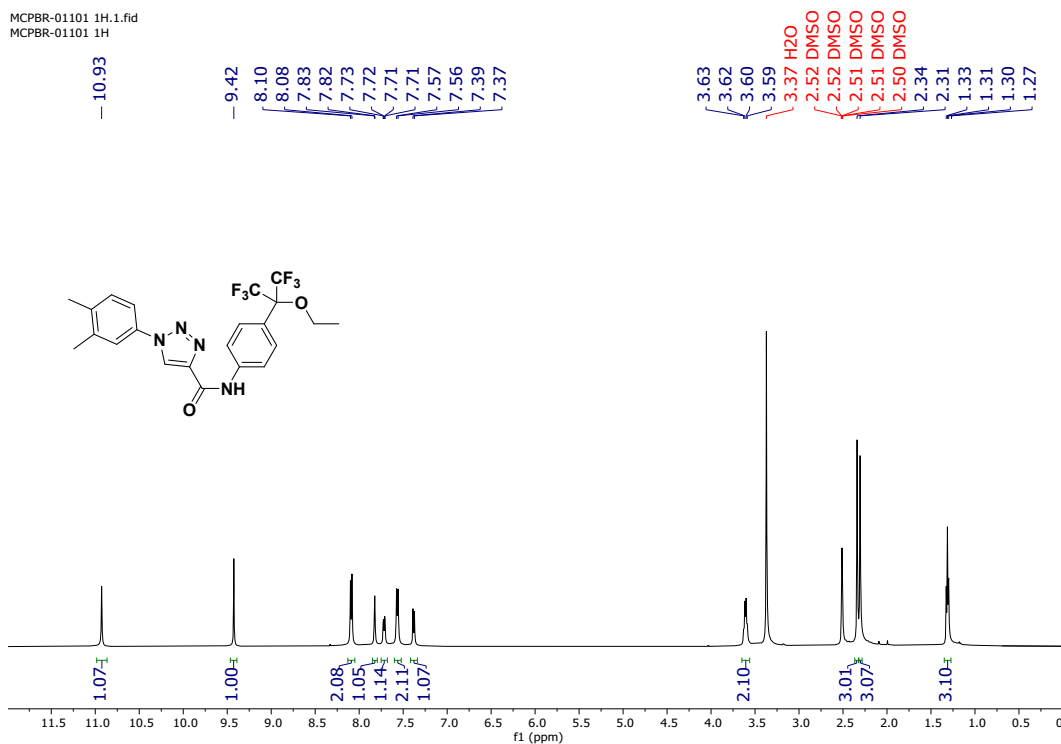
**Figure S58:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2o]



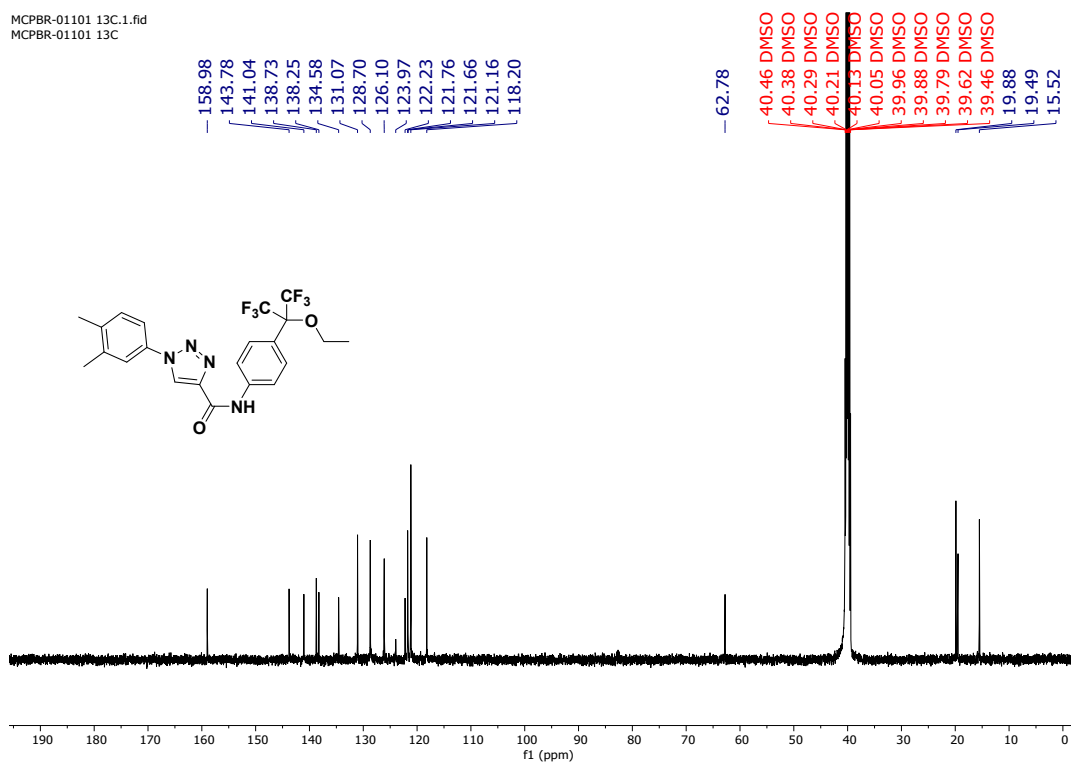
**Figure S59:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2o]



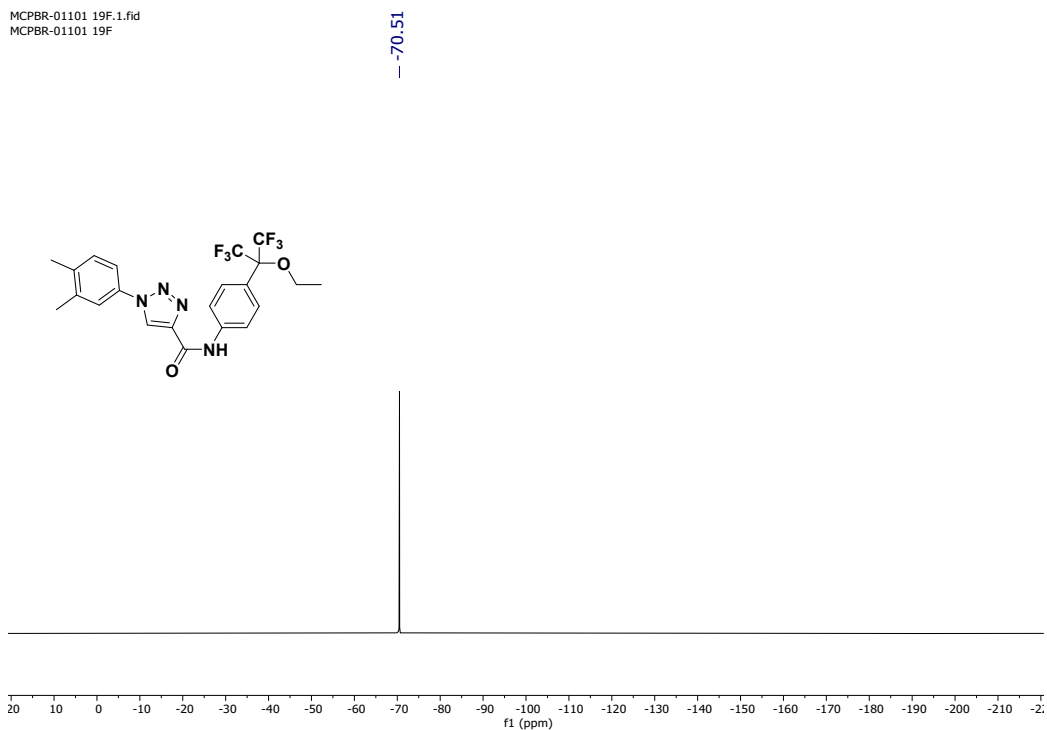
**Figure S60:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(2-ethoxy-1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2p]



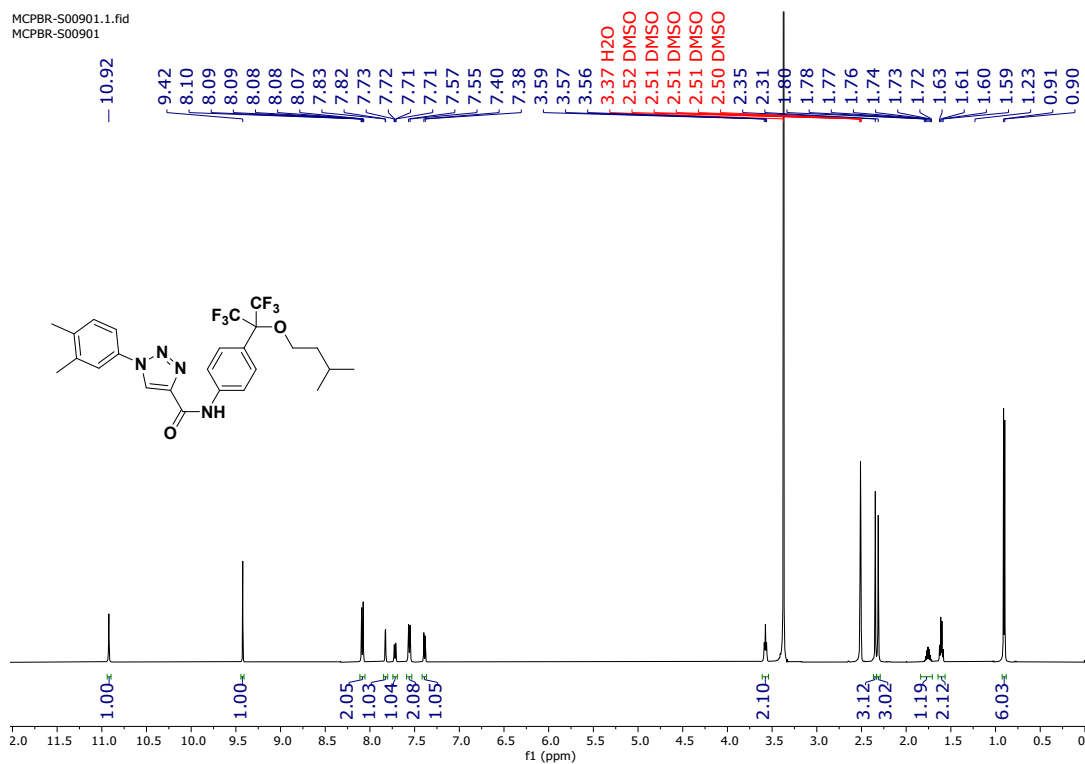
**Figure S61:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2p]



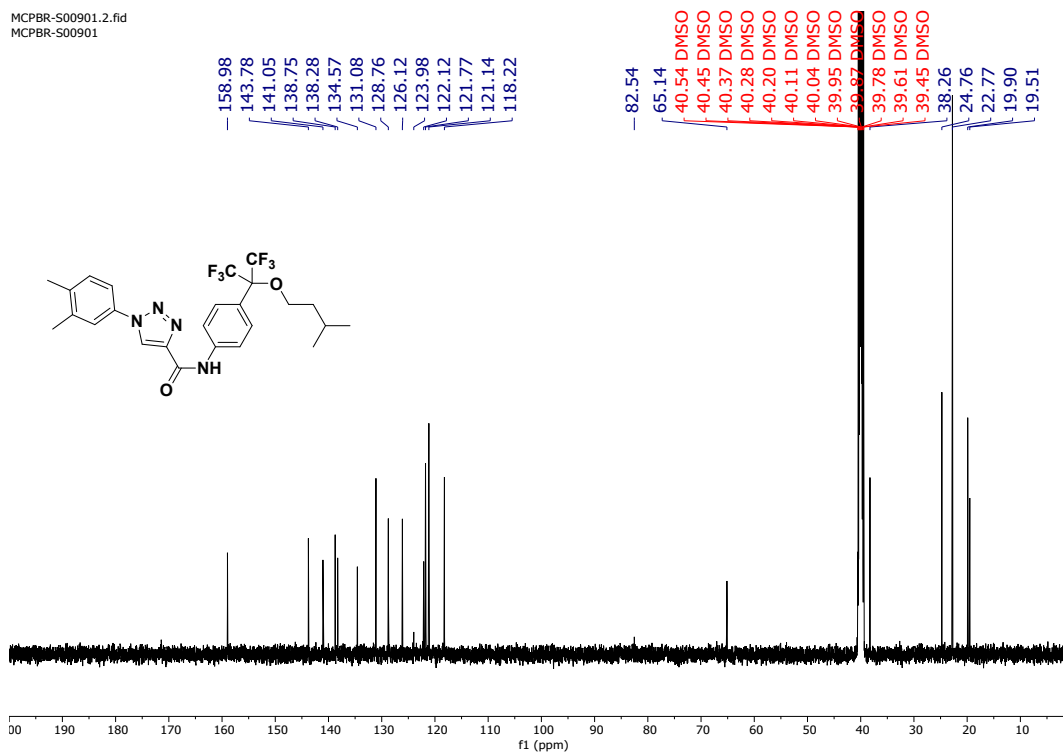
**Figure S62:**  $^{19}\text{F}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2p]



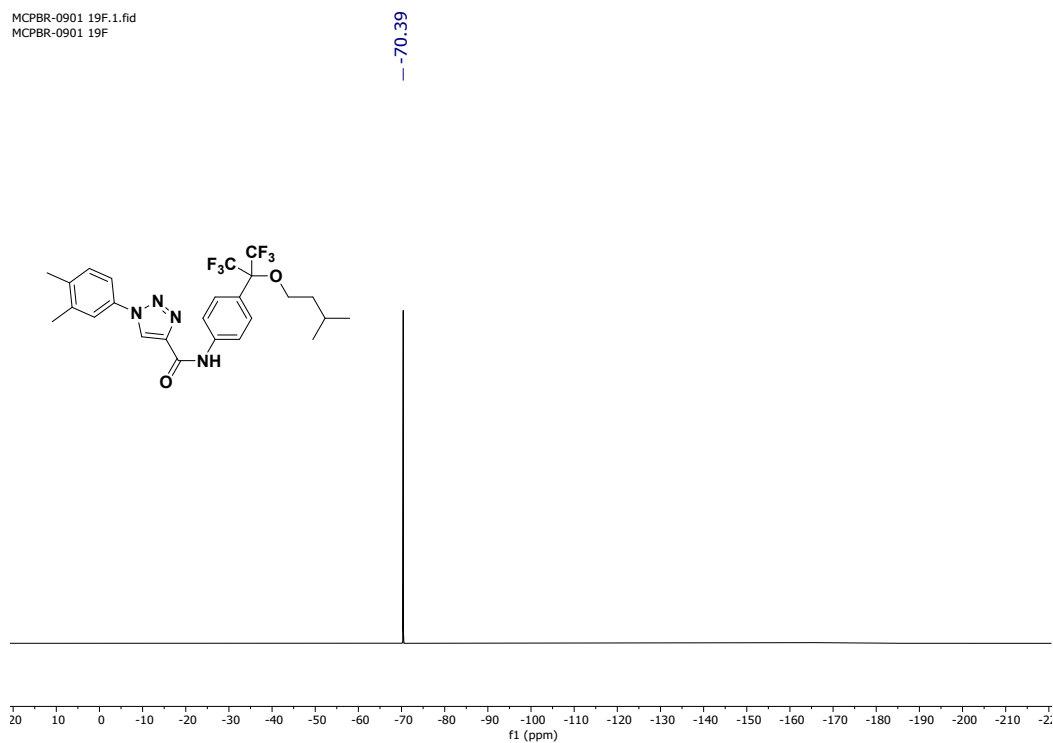
**Figure S63:**  $^1\text{H}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2q]



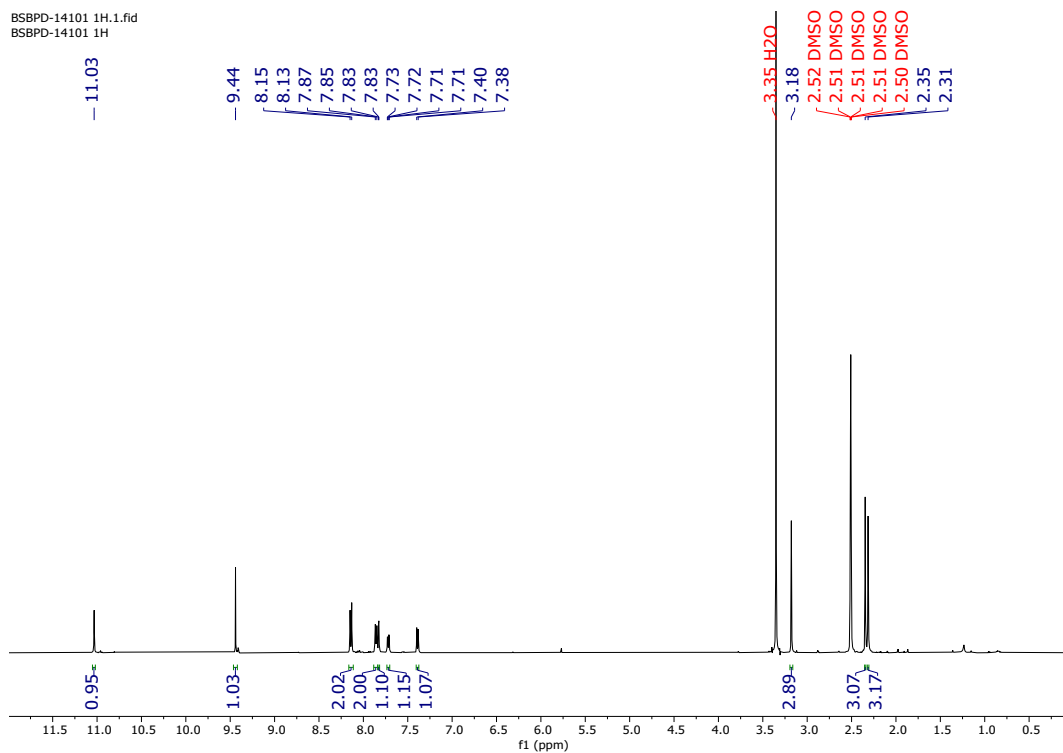
**Figure S64:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2q]



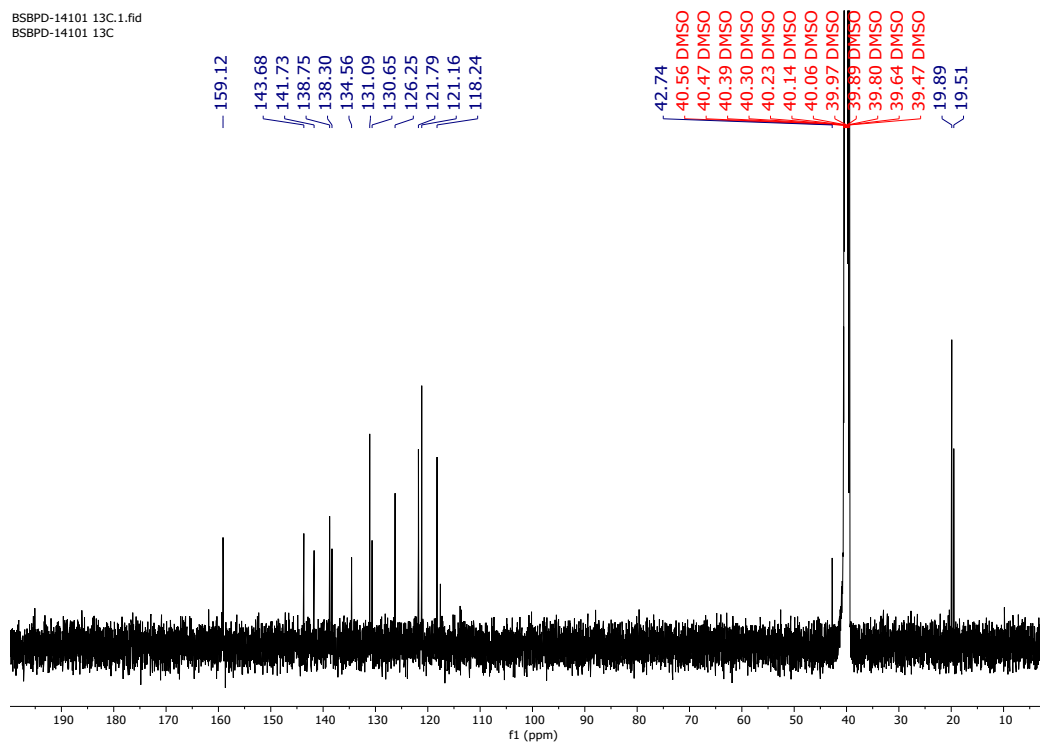
**Figure S65:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2q]



**Figure S66:**  $^{19}\text{F}$  NMR of 2-(4-(1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamido)phenyl)-1,1,1,3,3,3-hexafluoropropan-2-yl-methanesulfonate [2r]



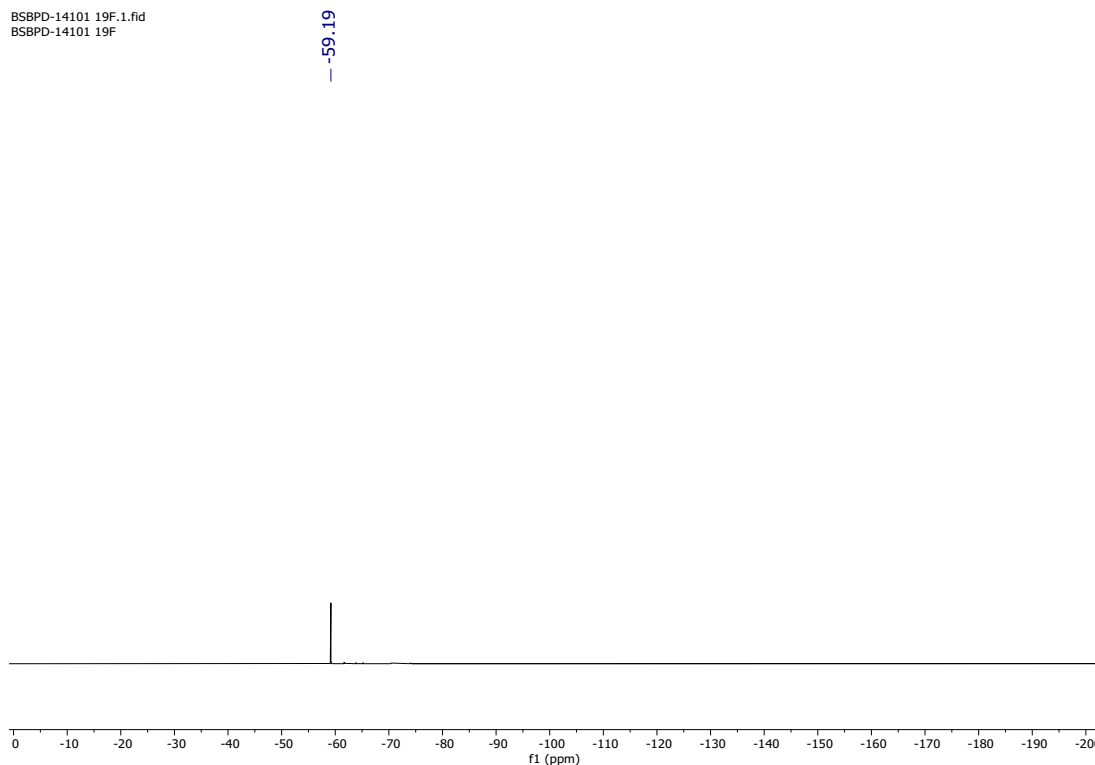
**Figure S67:**  $^{13}\text{C}$  NMR of 2-(4-(1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamido)phenyl)-1,1,1,3,3,3-hexafluoropropan-2-yl-methanesulfonate [**2r**]



**Figure S68:**  $^{19}\text{F}$  NMR of 2-(4-(1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamido)phenyl)-1,1,1,3,3,3-hexafluoropropan-2-yl-methanesulfonate [**2r**]

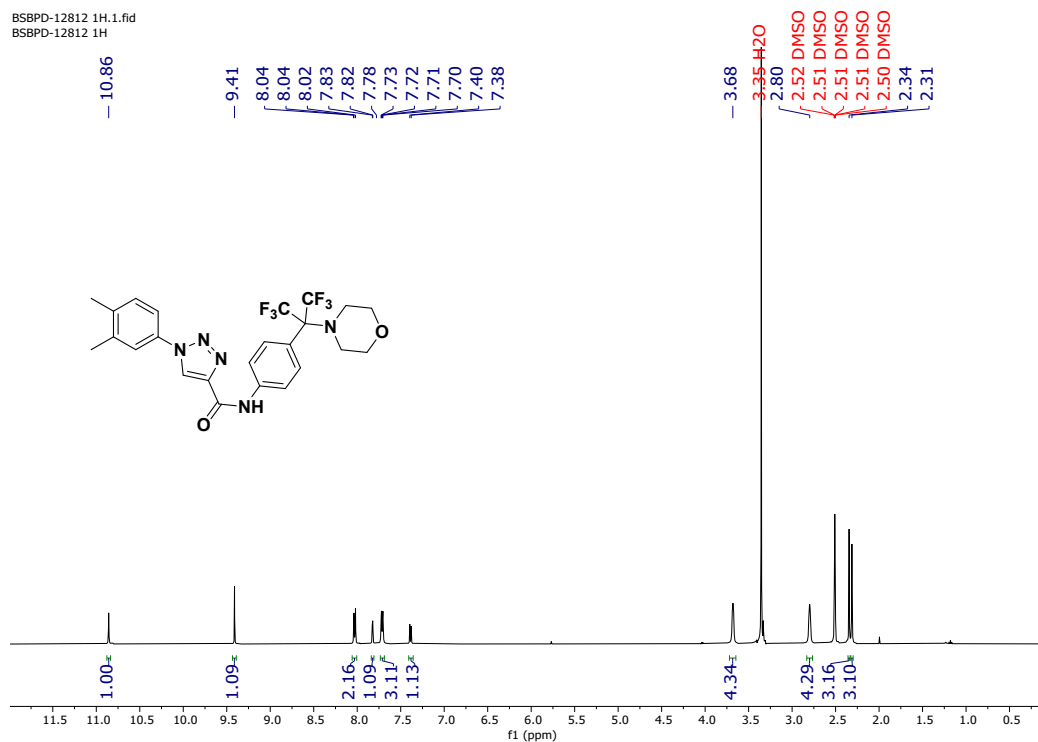


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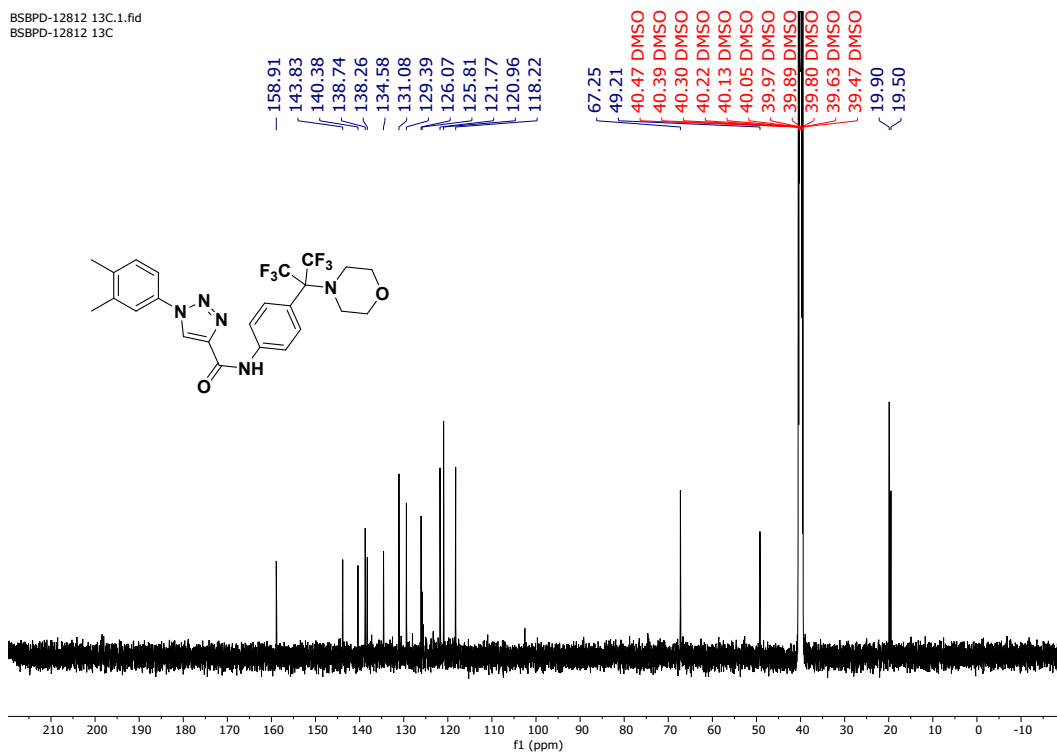


**Figure S69:** <sup>1</sup>H NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-morpholinopropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [**2s**]

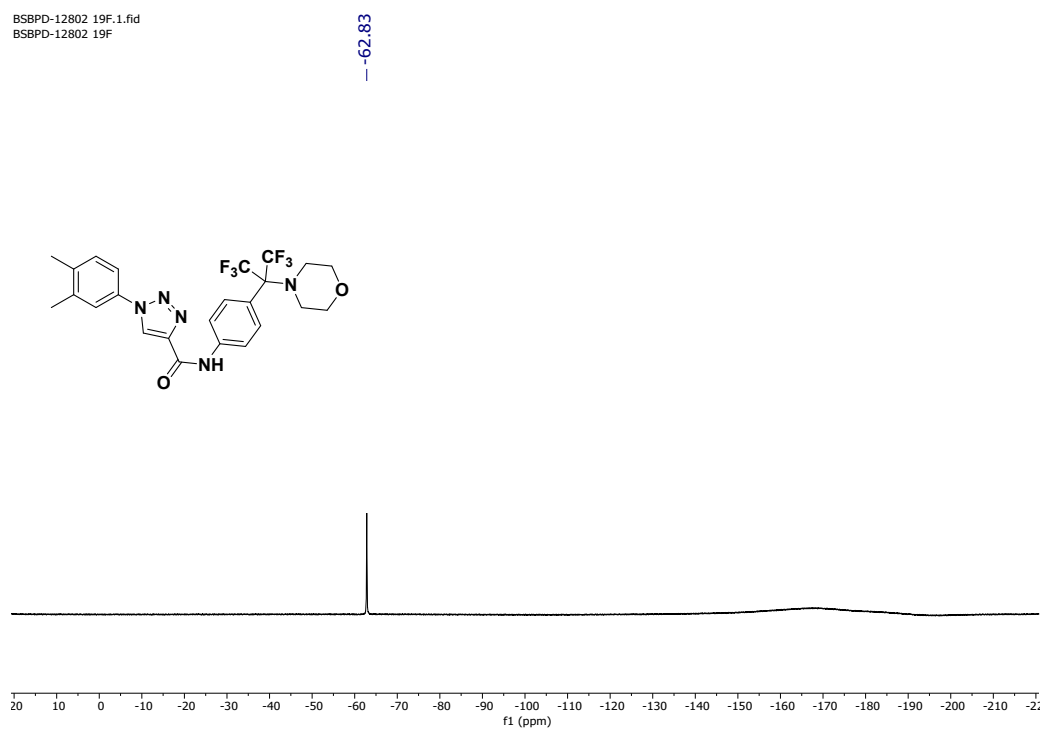
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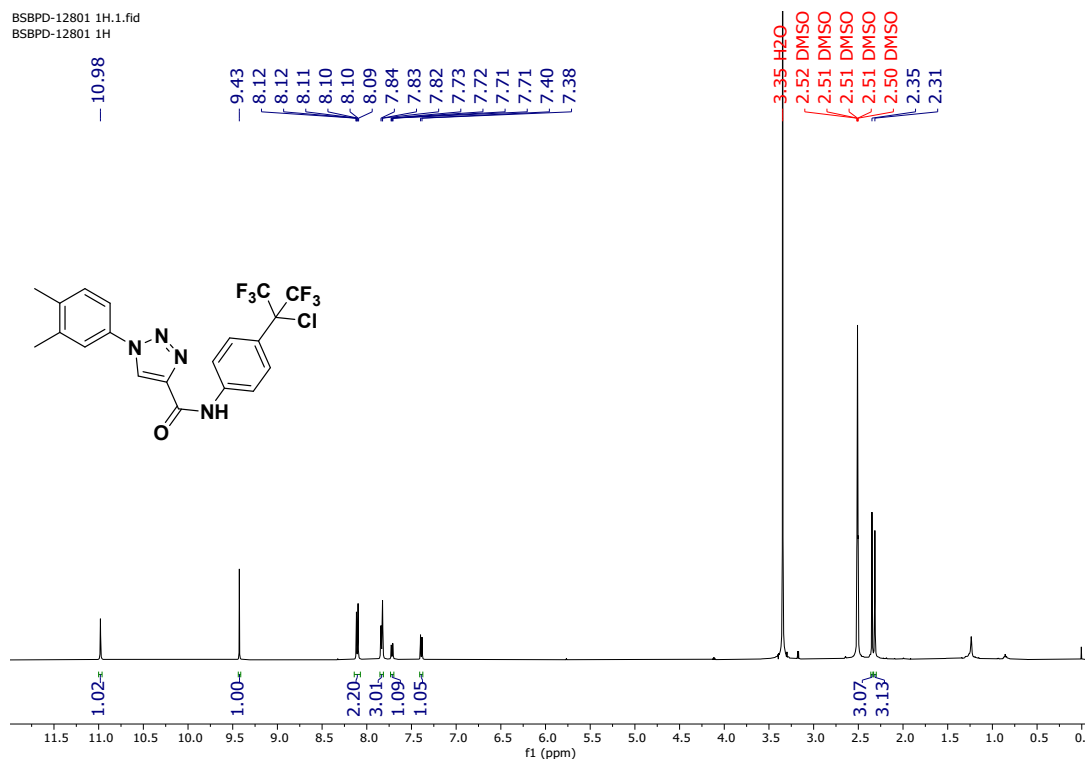
**Figure S70:** <sup>13</sup>C NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-morpholinopropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [**2s**]



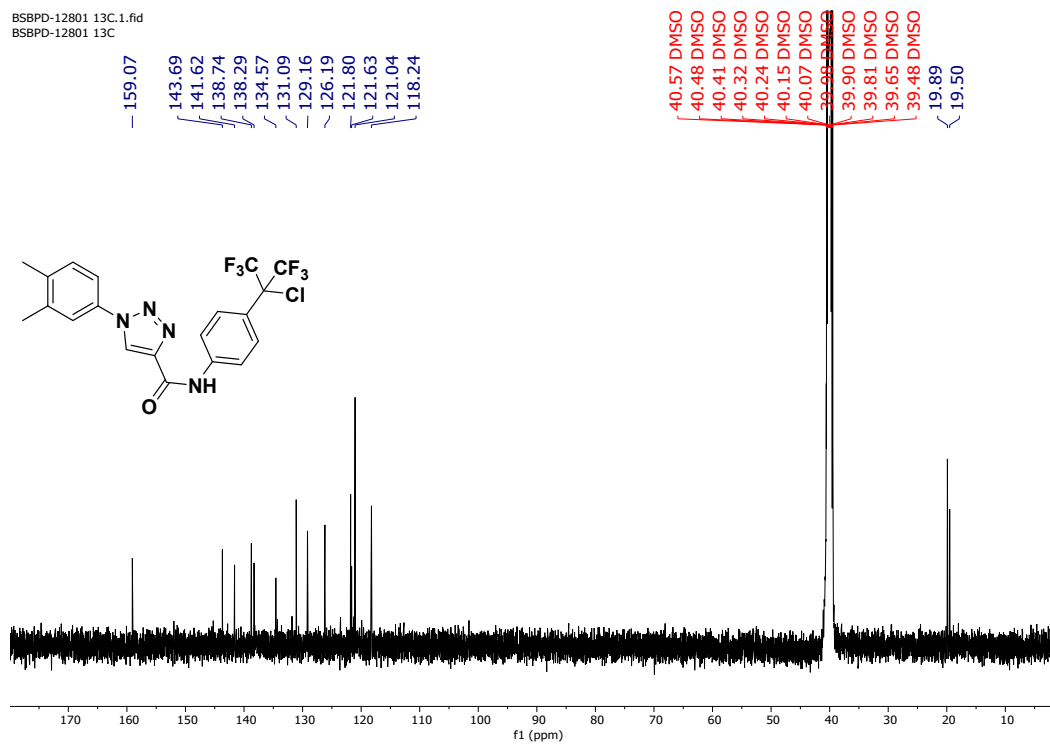
**Figure S71:**  $^{13}\text{C}$  NMR of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-morpholinopropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [2s]



**Figure S72:**  $^{19}\text{F}$  NMR of N-(4-(2-chloro-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [2t]

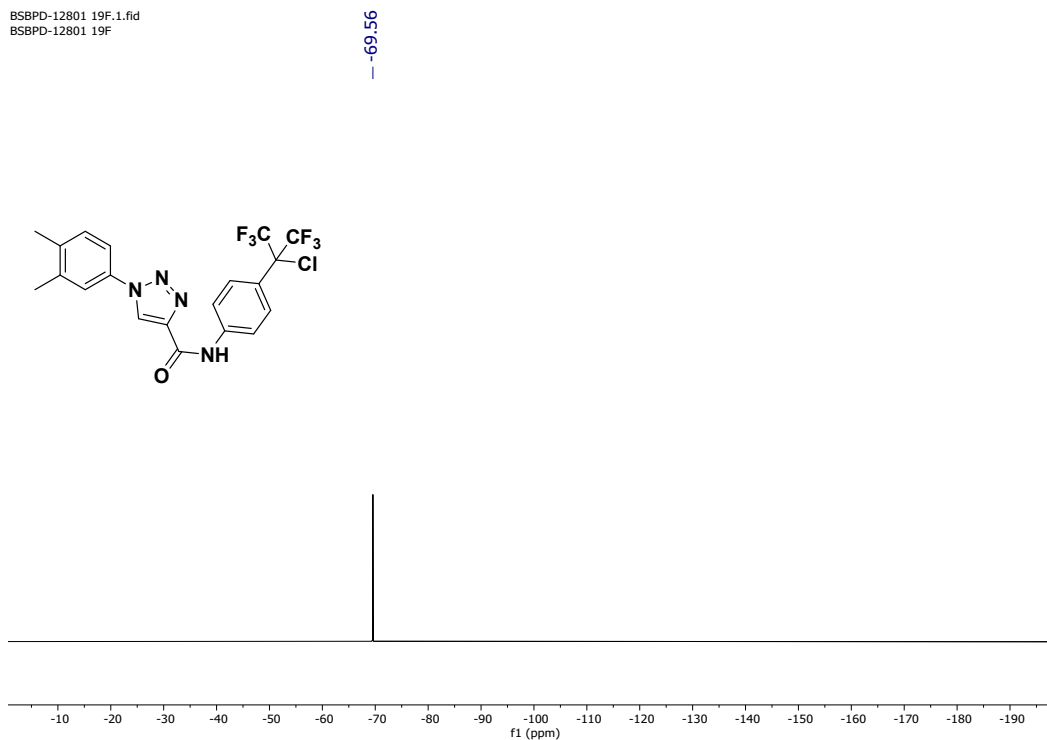


**Figure S73:** <sup>13</sup>C NMR of N-(4-(2-chloro-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2t**]

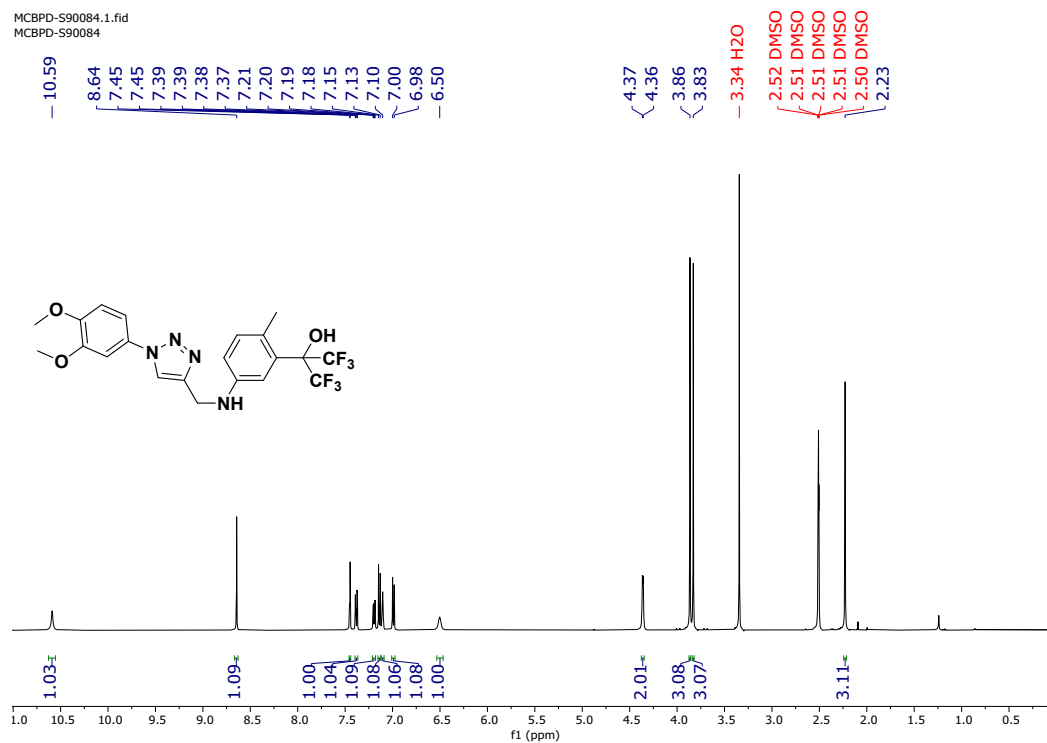


**Figure S74:** <sup>19</sup>F NMR of N-(4-(2-chloro-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2t**]

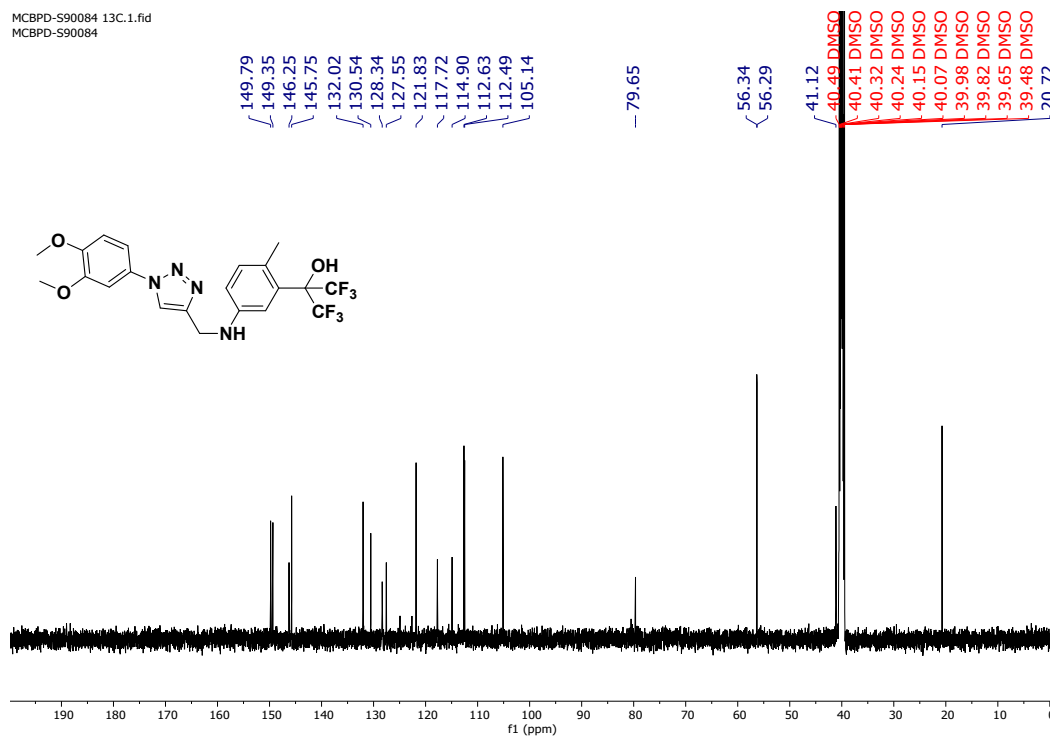
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BSBPD-12801 19F



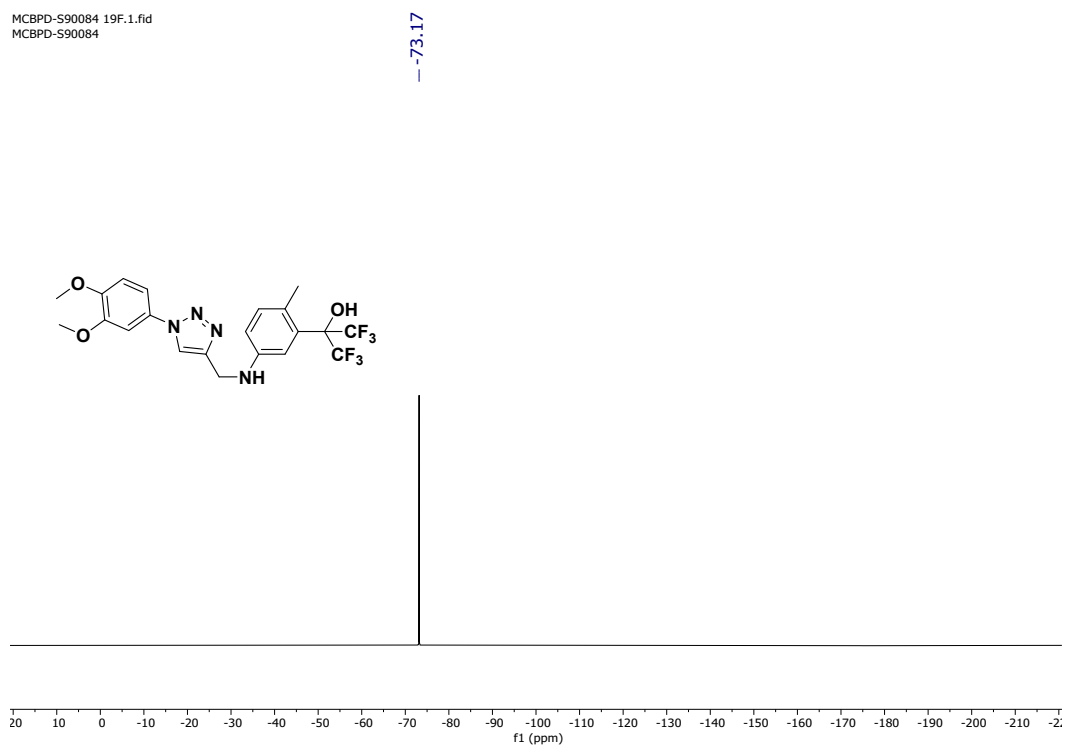
**Figure S75:** <sup>1</sup>H NMR of 2-(5-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3a]



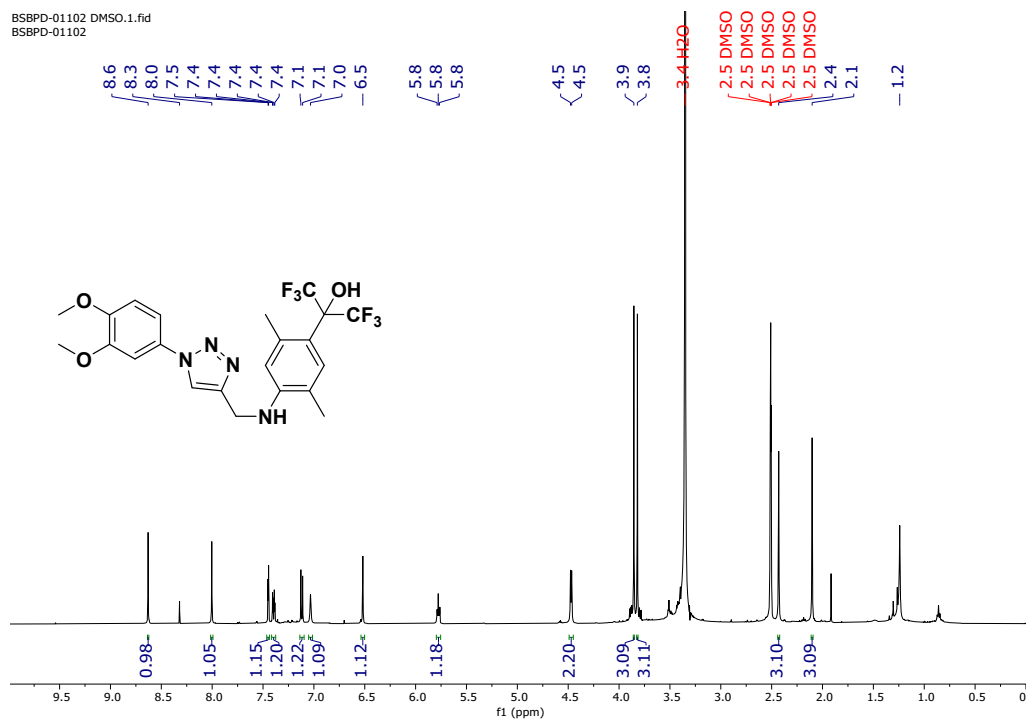
**Figure S76:** <sup>13</sup>C NMR of 2-(5-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3a]



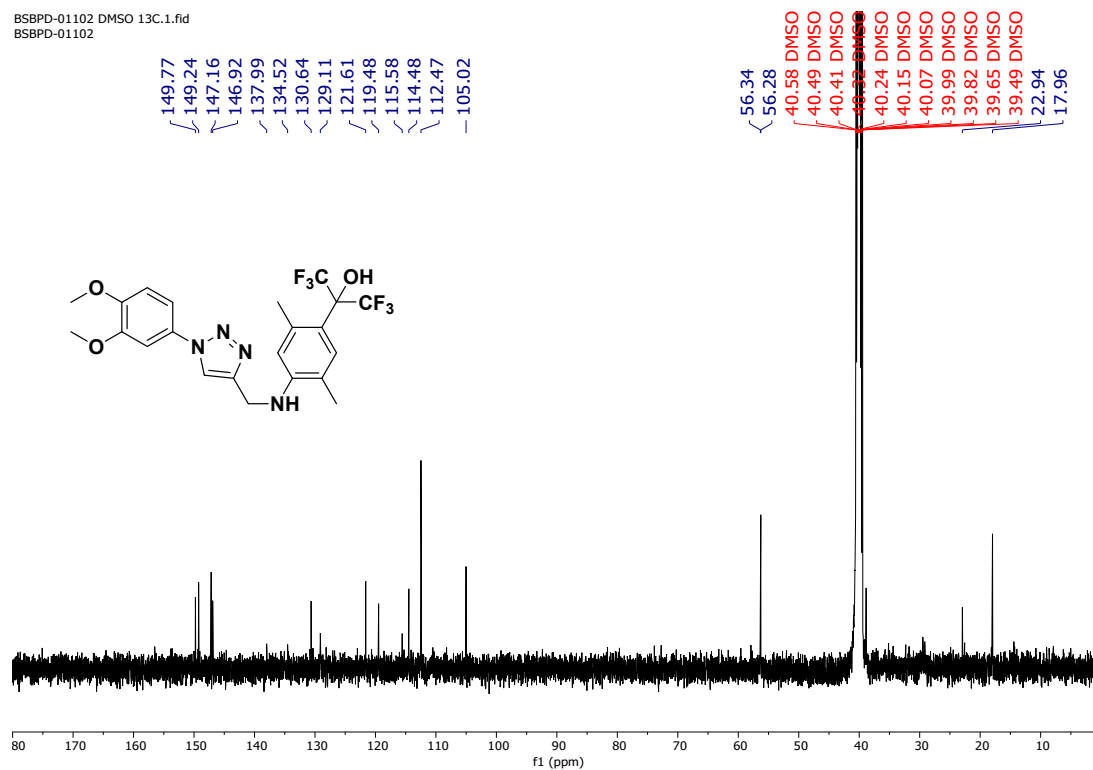
**Figure S77:**  $^{13}\text{C}$  NMR of 2-(5-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3a]



**Figure S78:**  $^{19}\text{F}$  NMR of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2,5-dimethylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3b]

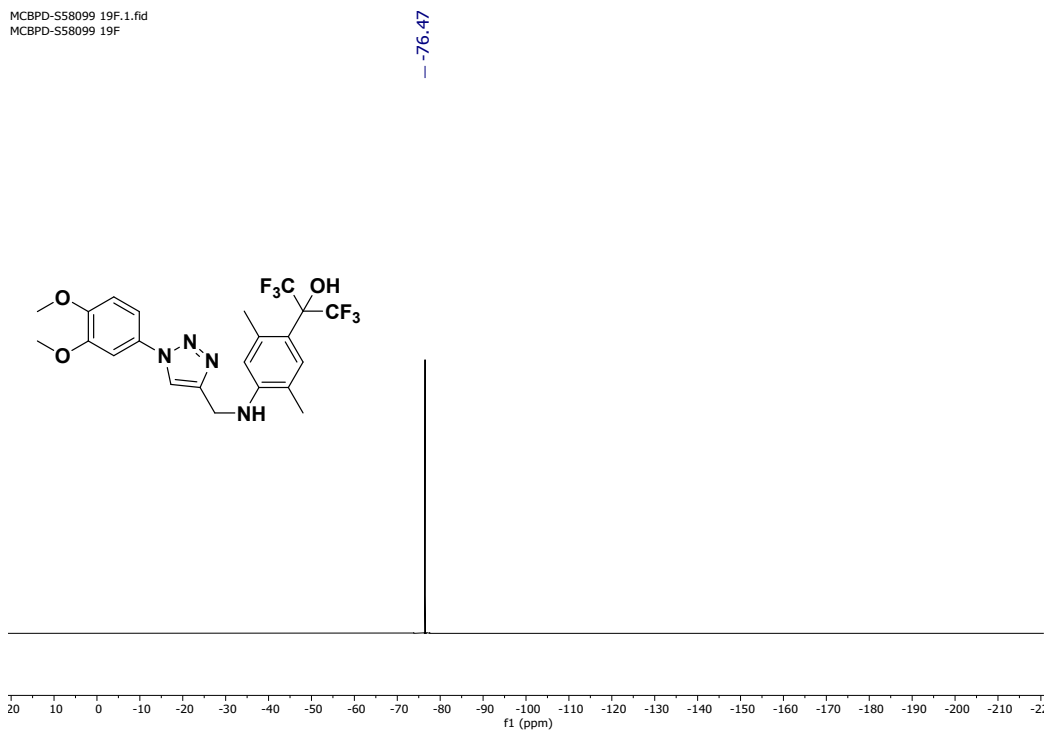


**Figure S79:** <sup>13</sup>C NMR of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2,5-dimethylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [**3b**]



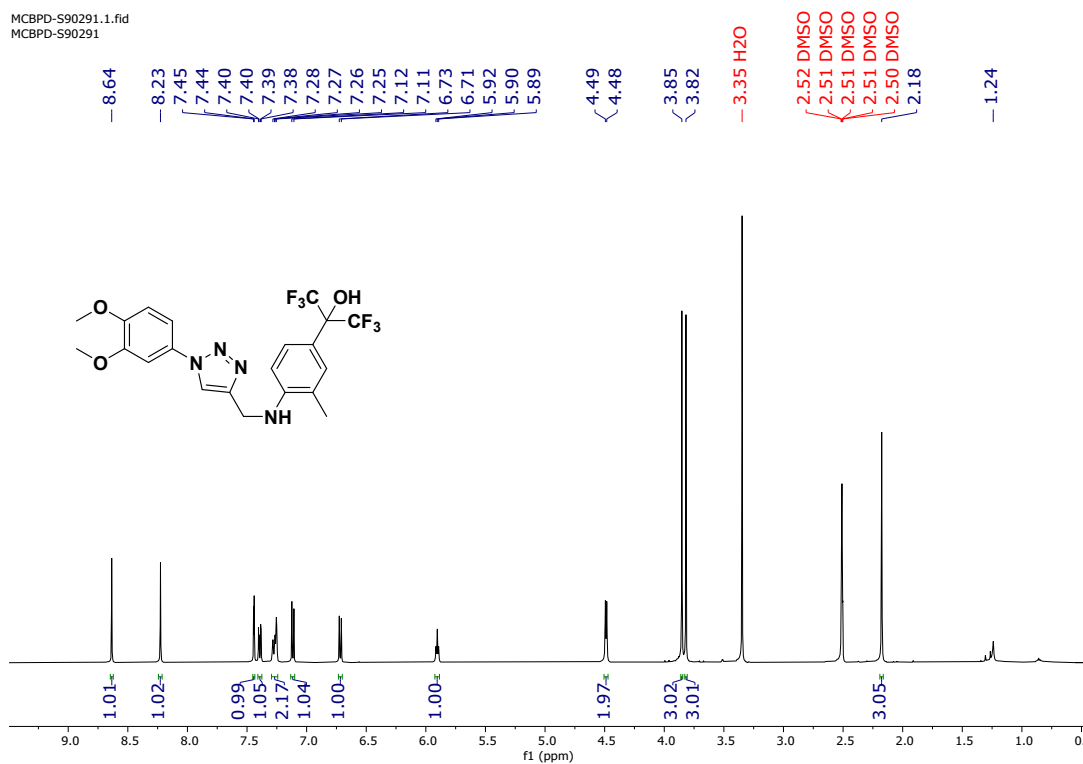
**Figure S80:** <sup>19</sup>F NMR of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2,5-dimethylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [**3b**]

MCBPD-S58099 19F.1.fid  
MCBPD-S58099 19F

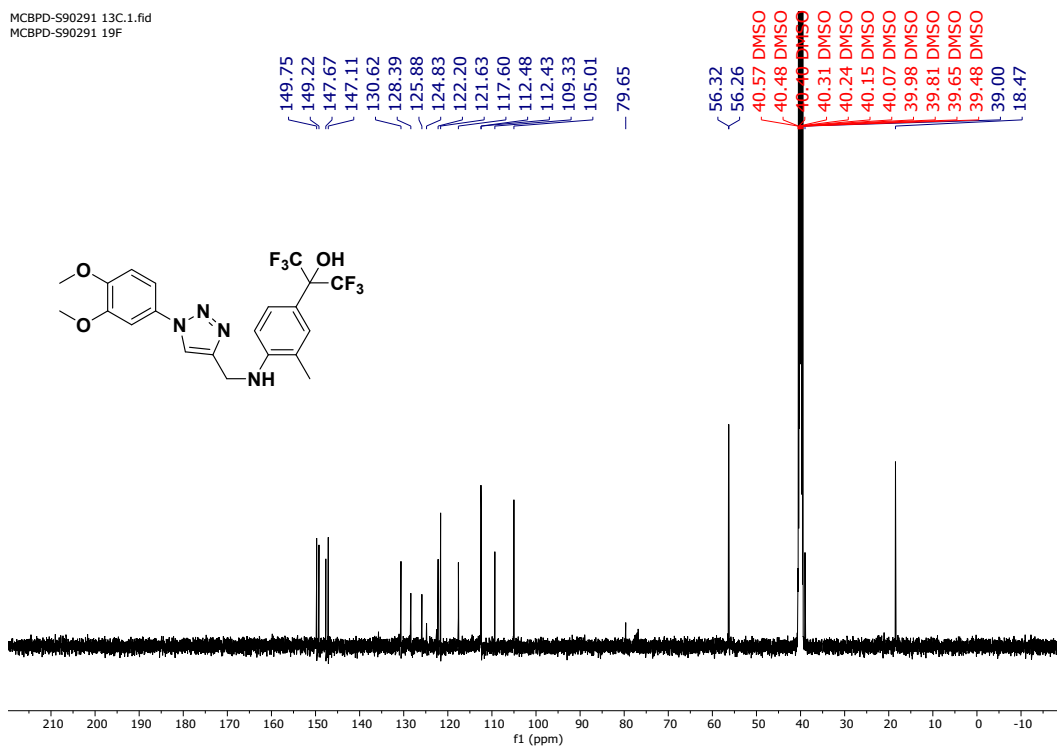


**Figure S81:** <sup>1</sup>H NMR of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-3-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3c]

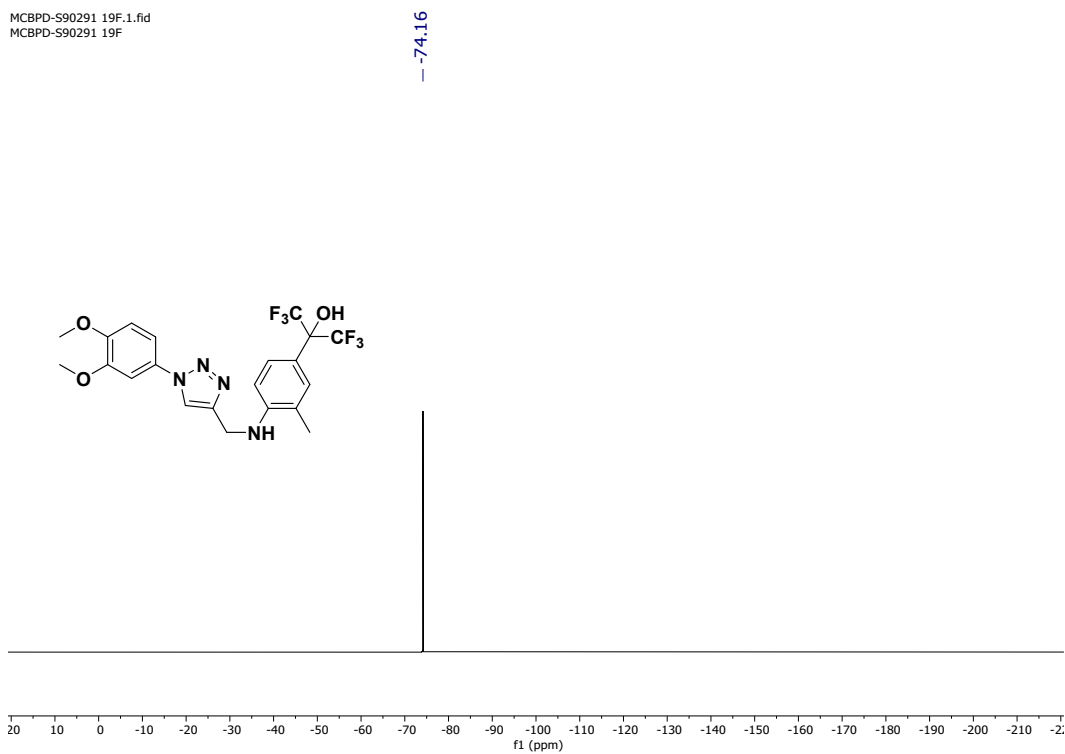
MCBPD-S90291.1.fid  
MCBPD-S90291



**Figure S82:** <sup>13</sup>C NMR of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-3-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3c]

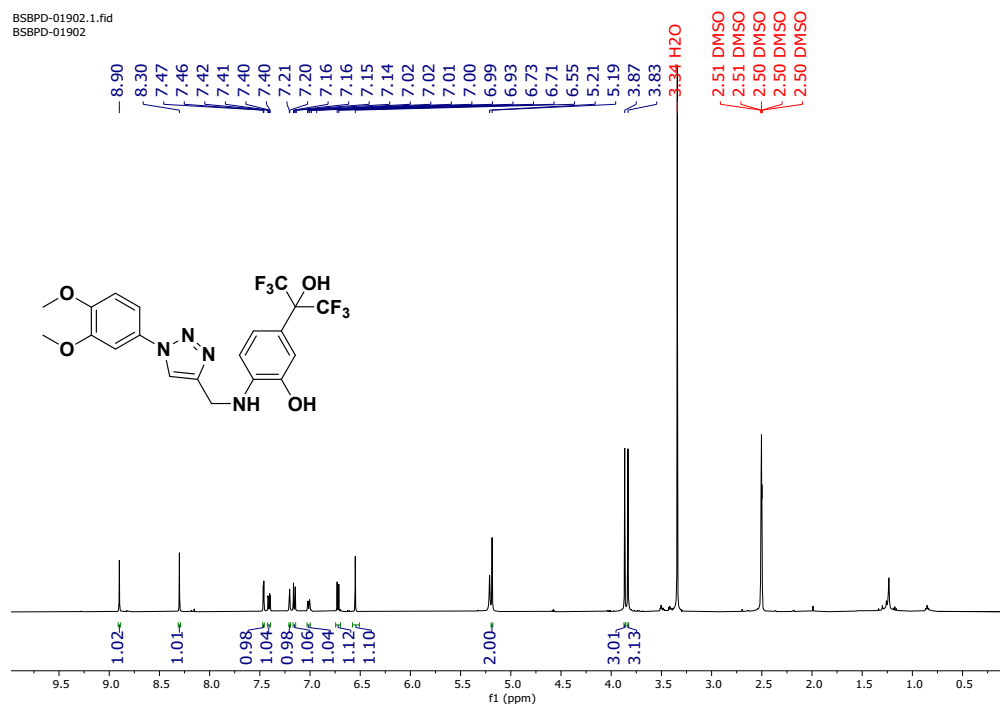


**Figure S83:**  $^{19}\text{F}$  NMR of 2-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-3-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [3c]

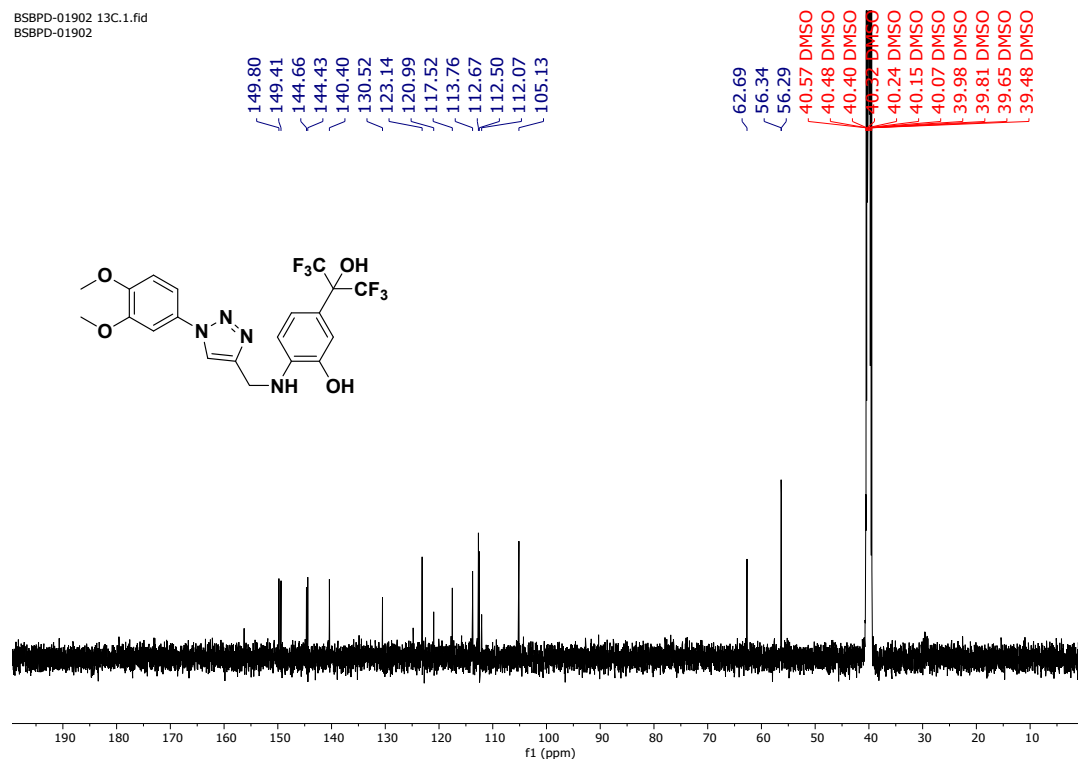


**Figure S84:**  $^1\text{H}$  NMR of 2-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-5-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenol [3d]





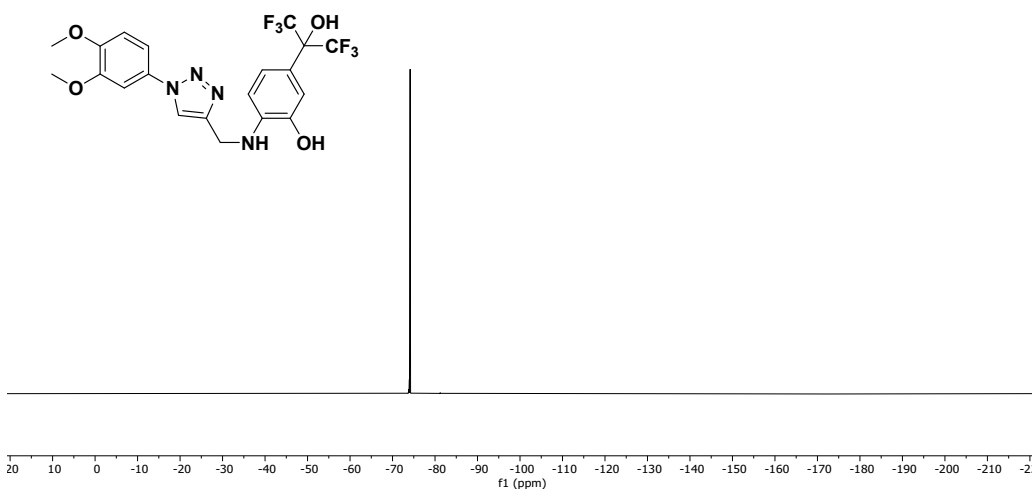
**Figure S85:** <sup>13</sup>C NMR of 2-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-5-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenol [3d]



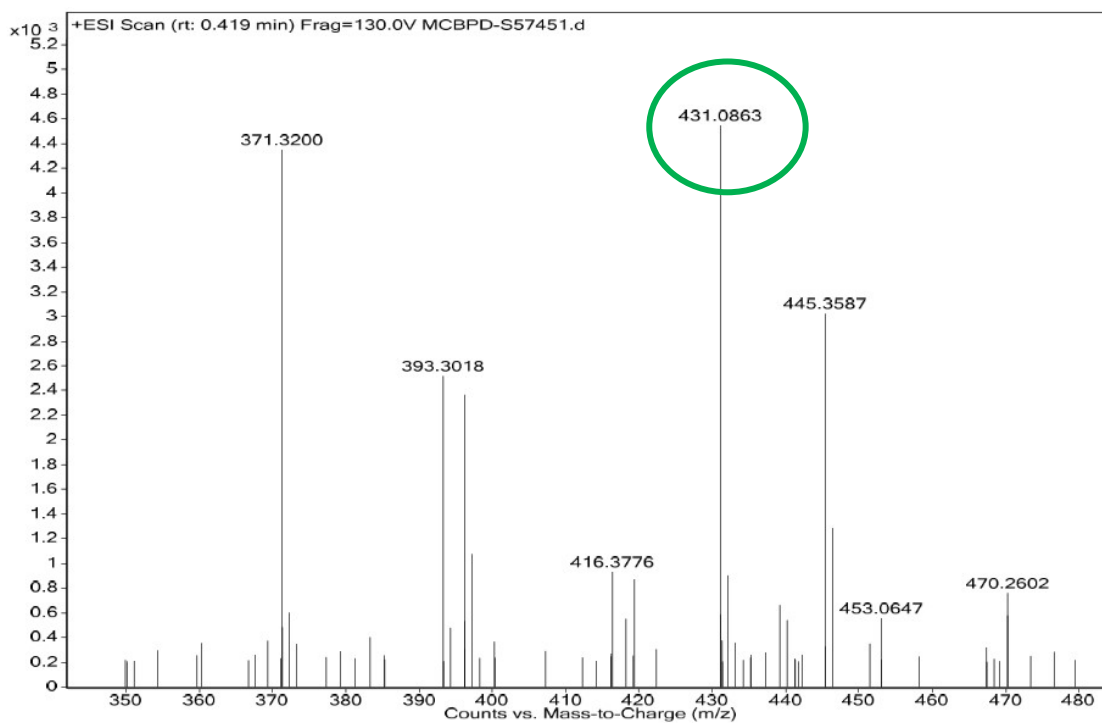
**Figure S86:** <sup>19</sup>F NMR of 2-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-5-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenol [3d]

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BSBPD-01902

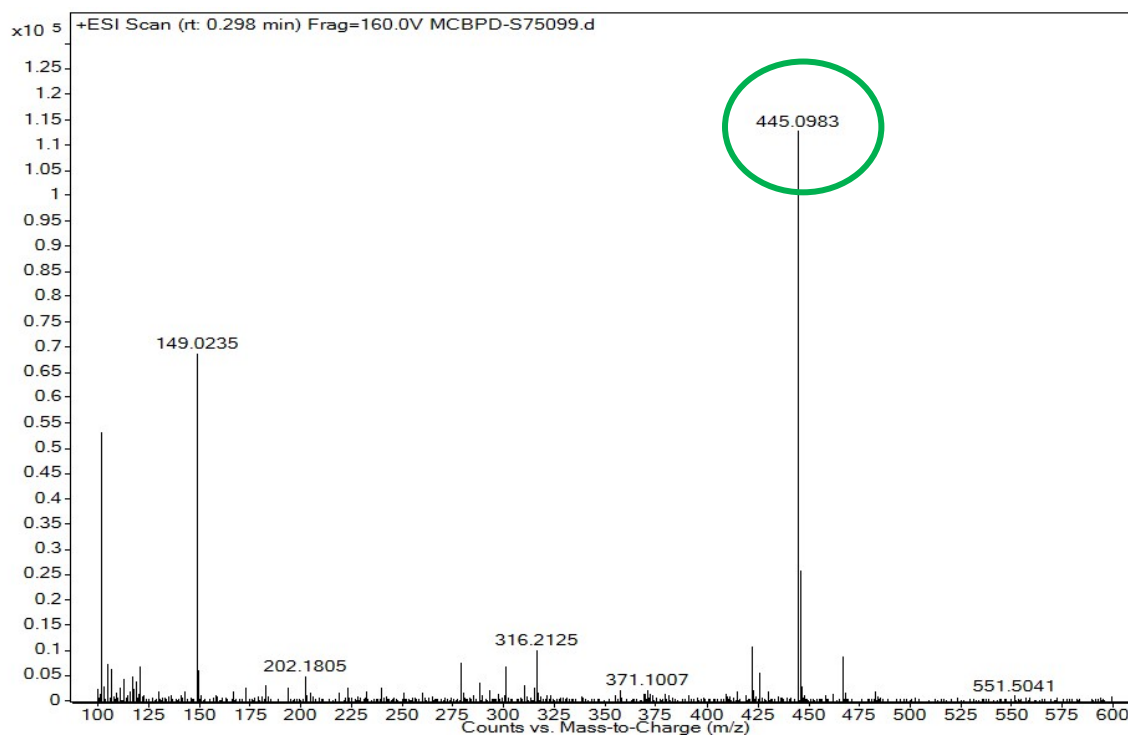
-74.15



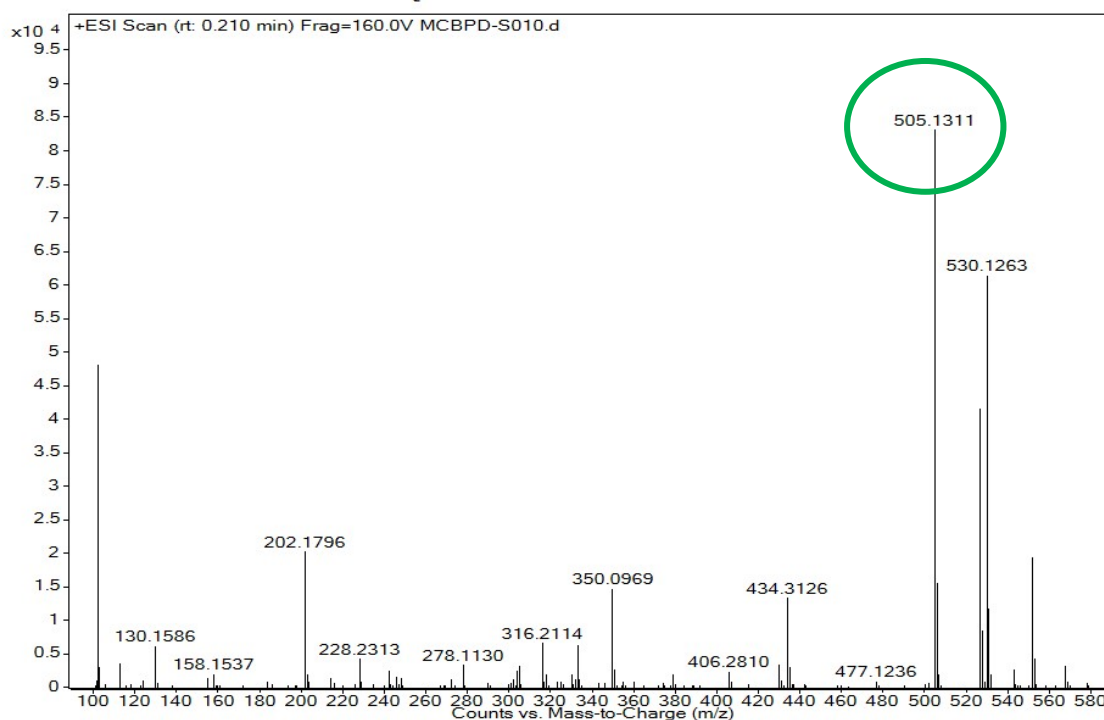
**Figure S87:** HRMS of N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenyl)-3-phenylisoxazole-5-carboxamide [1a]



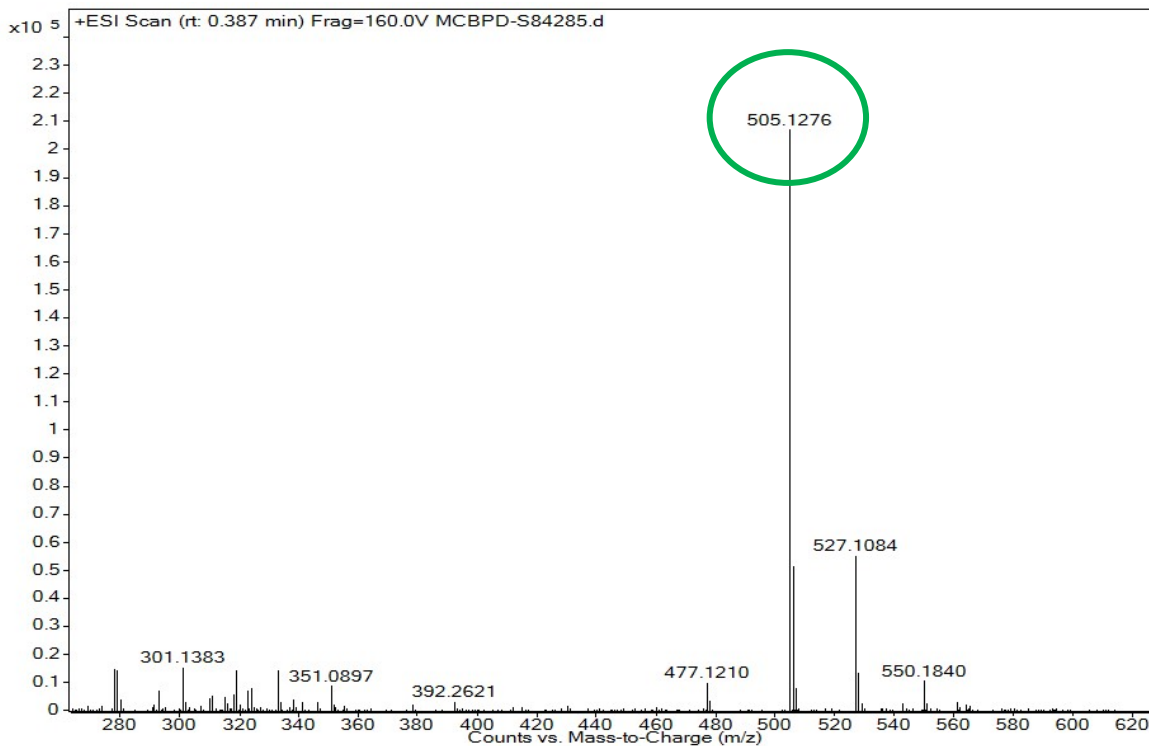
**Figure S88:** HRMS of N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenyl)-3-(p-tolyl)isoxazole-5-carboxamide [1b]



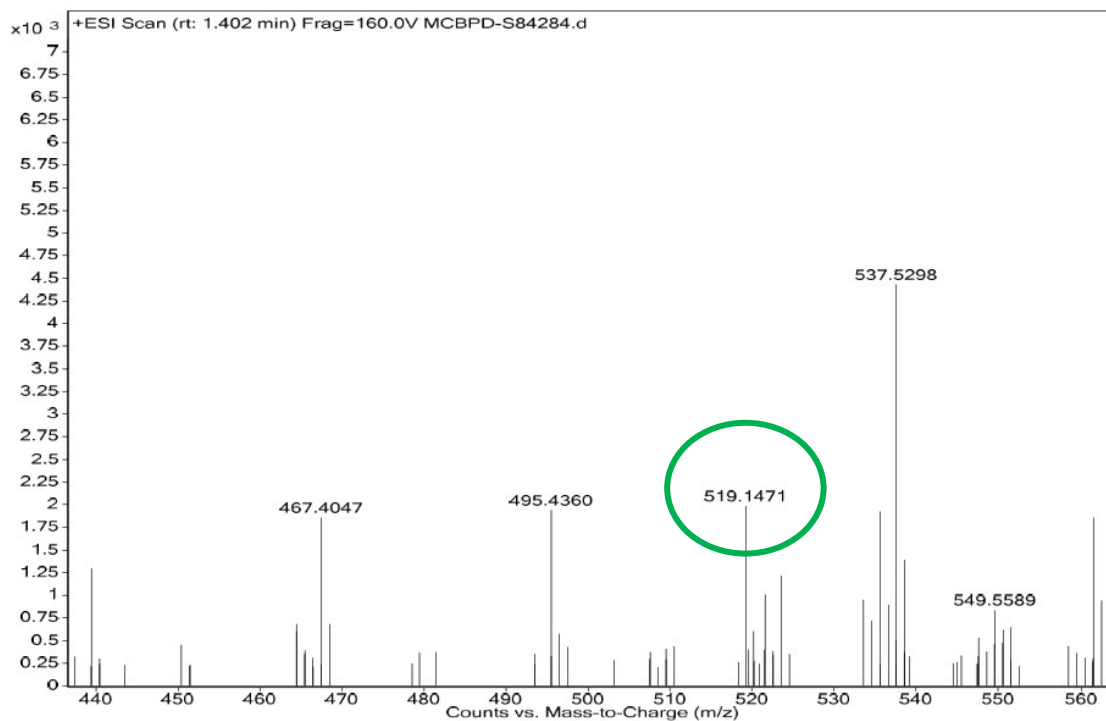
**Figure S89:** HRMS of of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2a**]



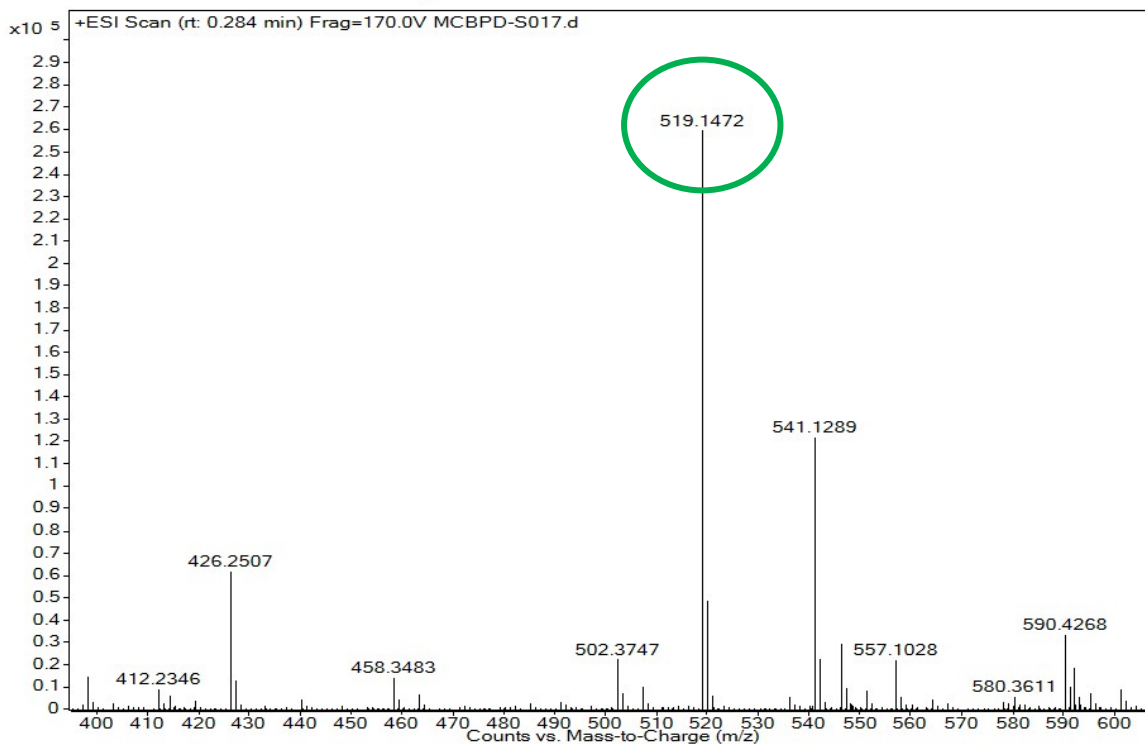
**Figure S90:** HRMS of of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2b**]



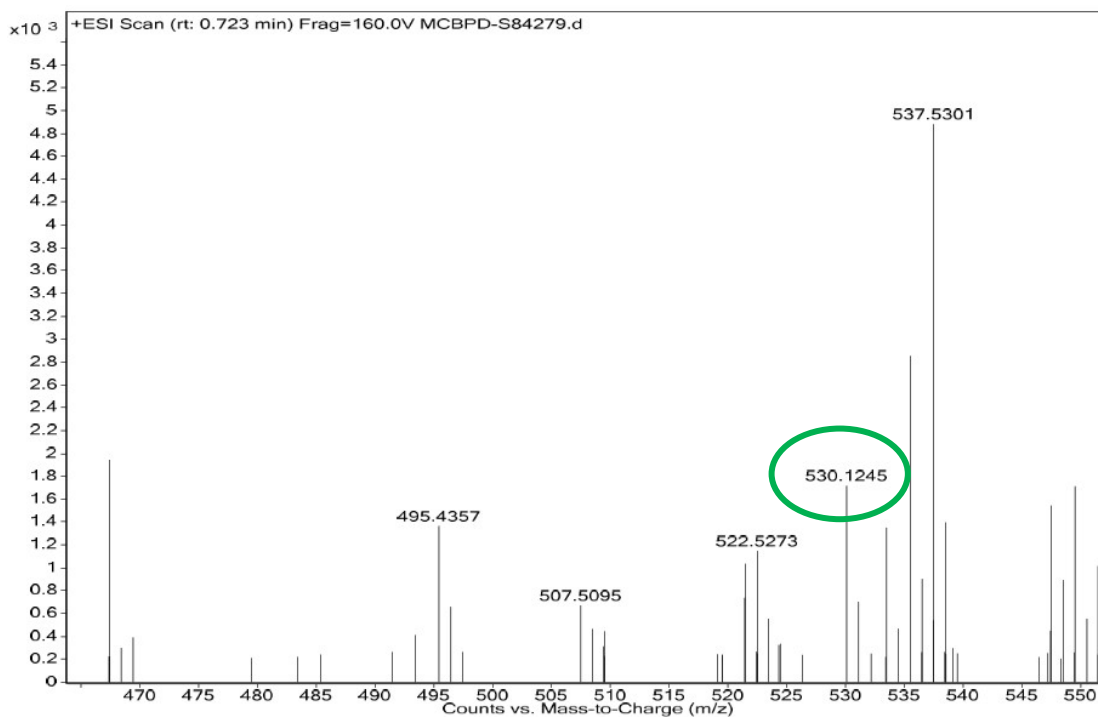
**Figure S91:** HRMS of of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2c**]



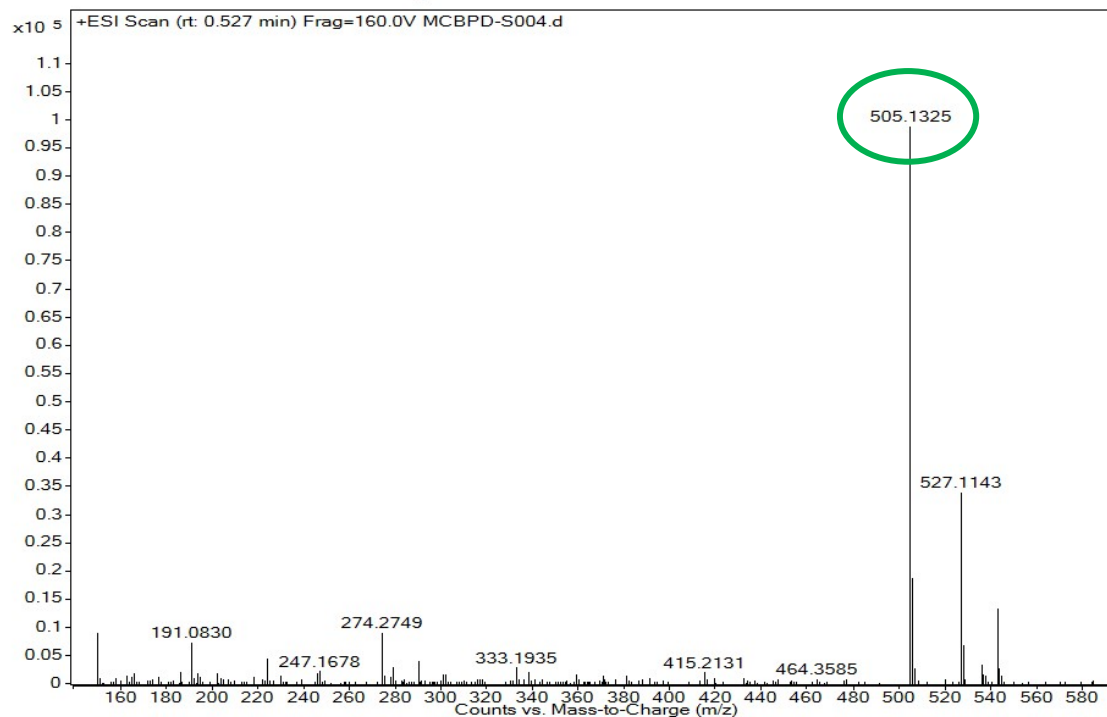
**Figure S92:** HRMS of of 1-(3,4-dimethoxyphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2d**]



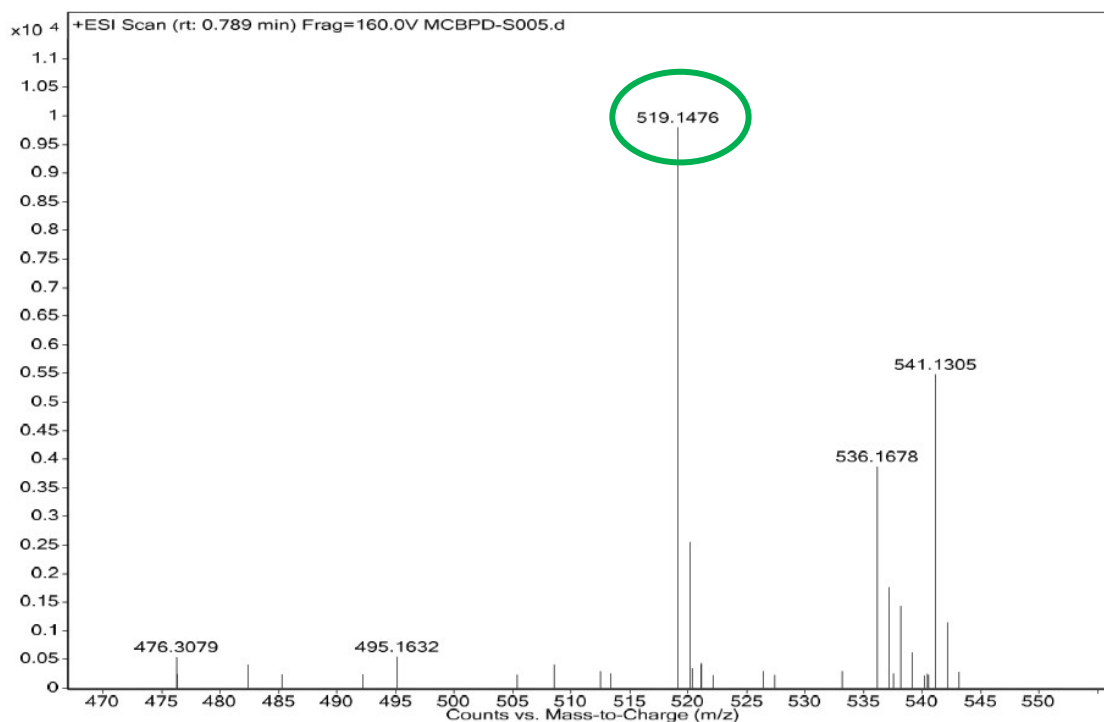
**Figure S93:** HRMS of of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide [**2e**]



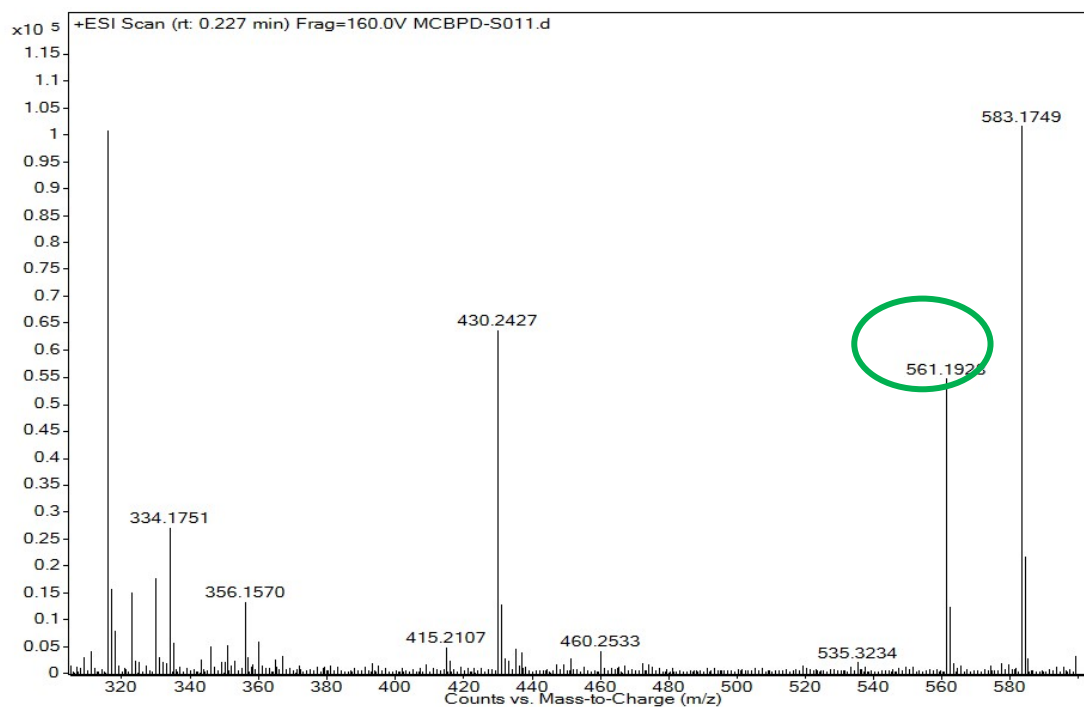
**Figure S94:** HRMS of of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [**2f**]



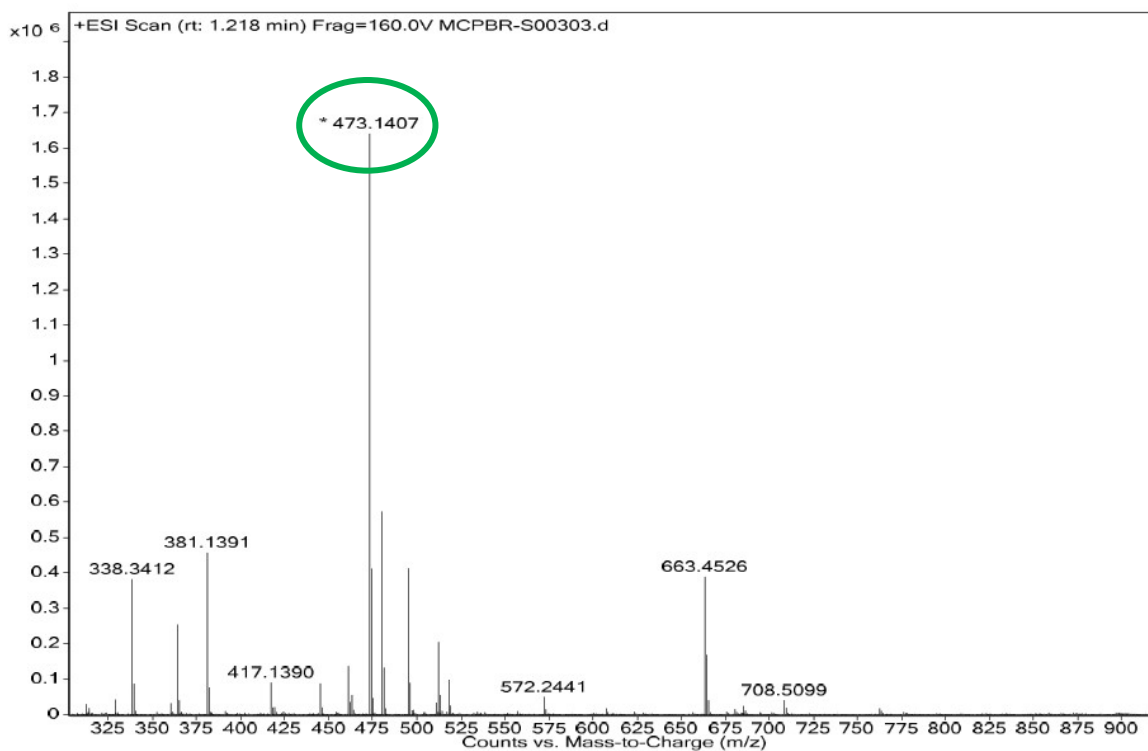
**Figure S95:** HRMS of of 1-(3,4-dimethoxyphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2g]**



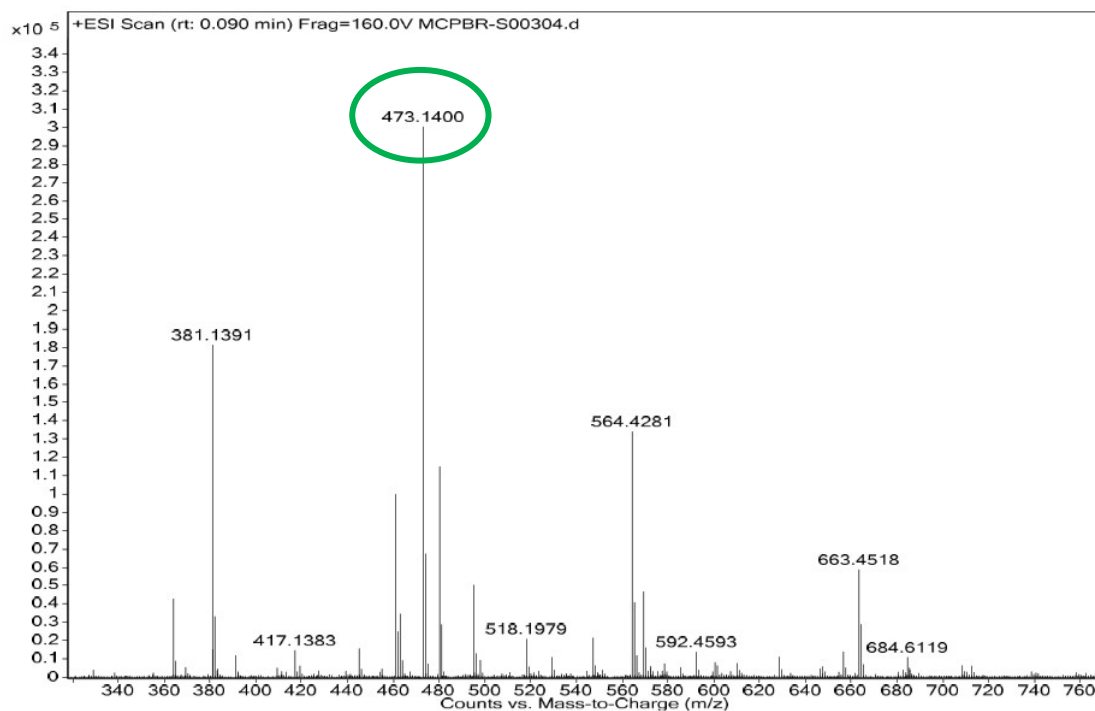
**Figure S96:** HRMS of of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2h]**



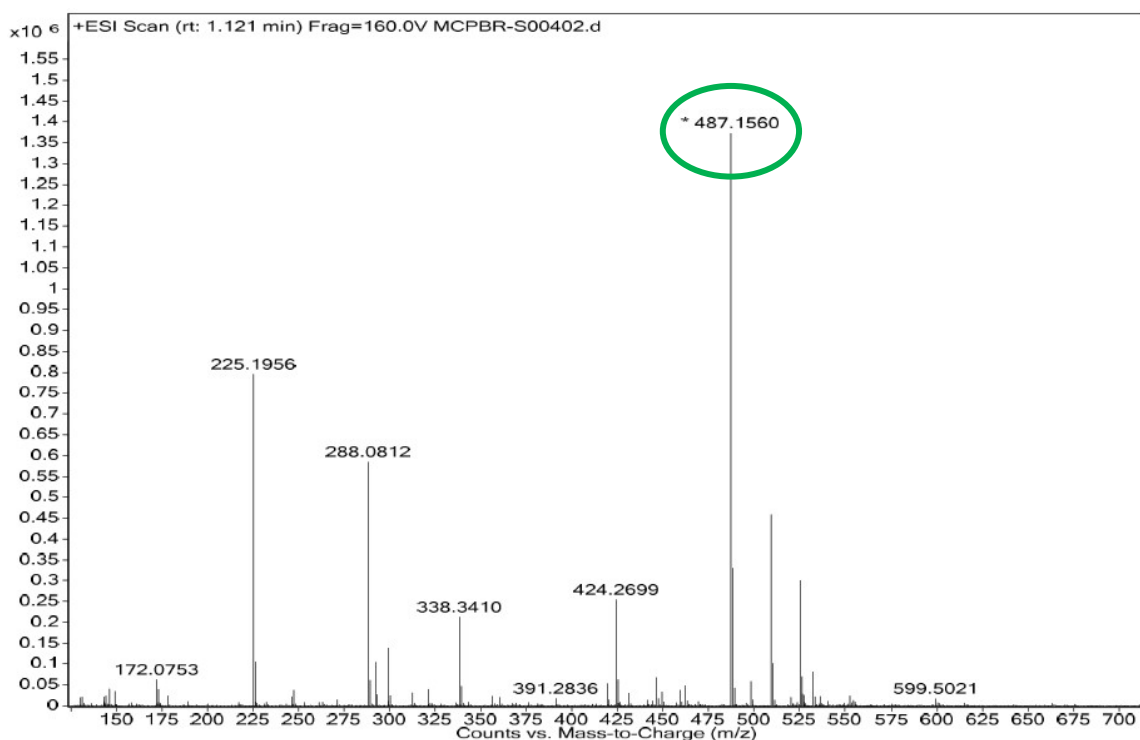
**Figure S97:** HRMS of of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2i]**



**Figure S98:** HRMS of of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2j]**



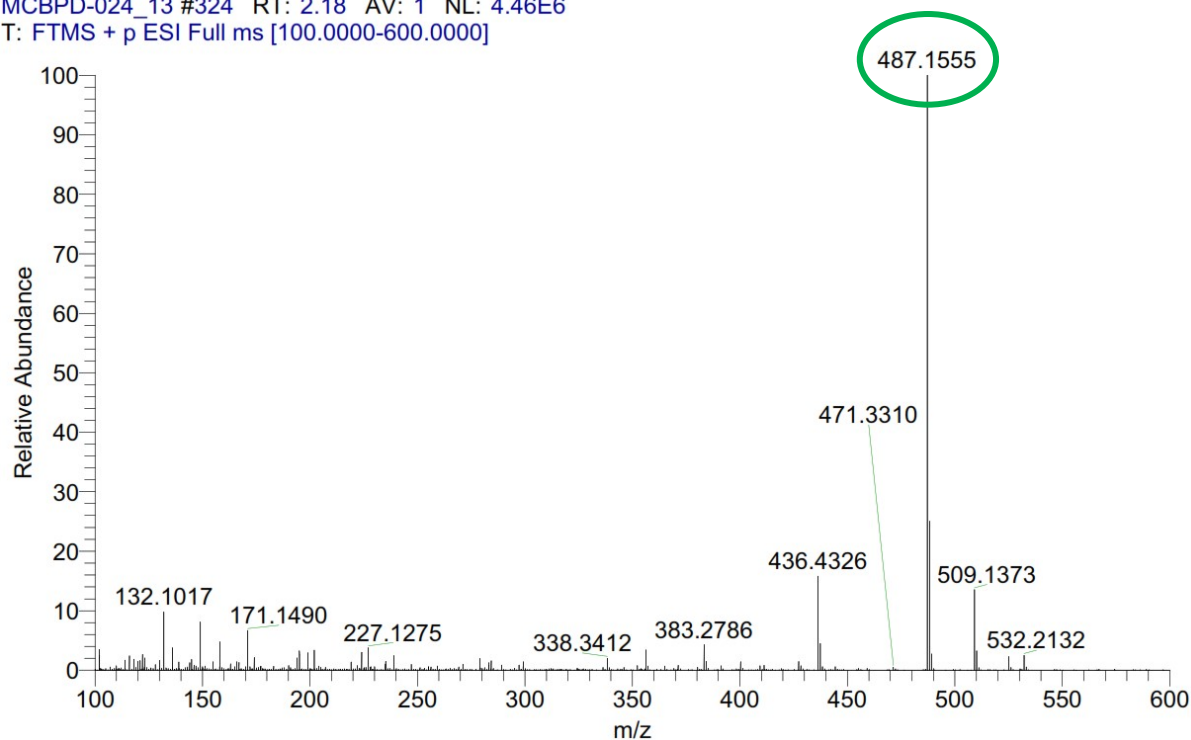
**Figure S99:** HRMS of of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2k]**



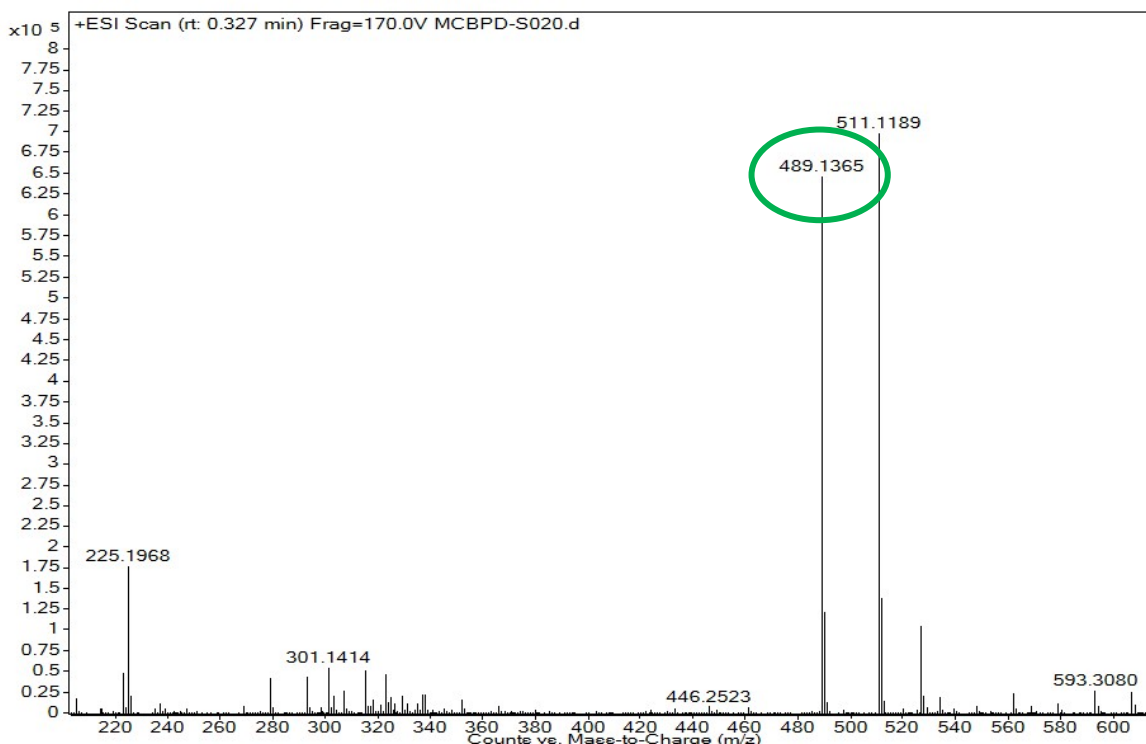
**Figure S100:** HRMS of of 1-(3,4-dimethylphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2l]**



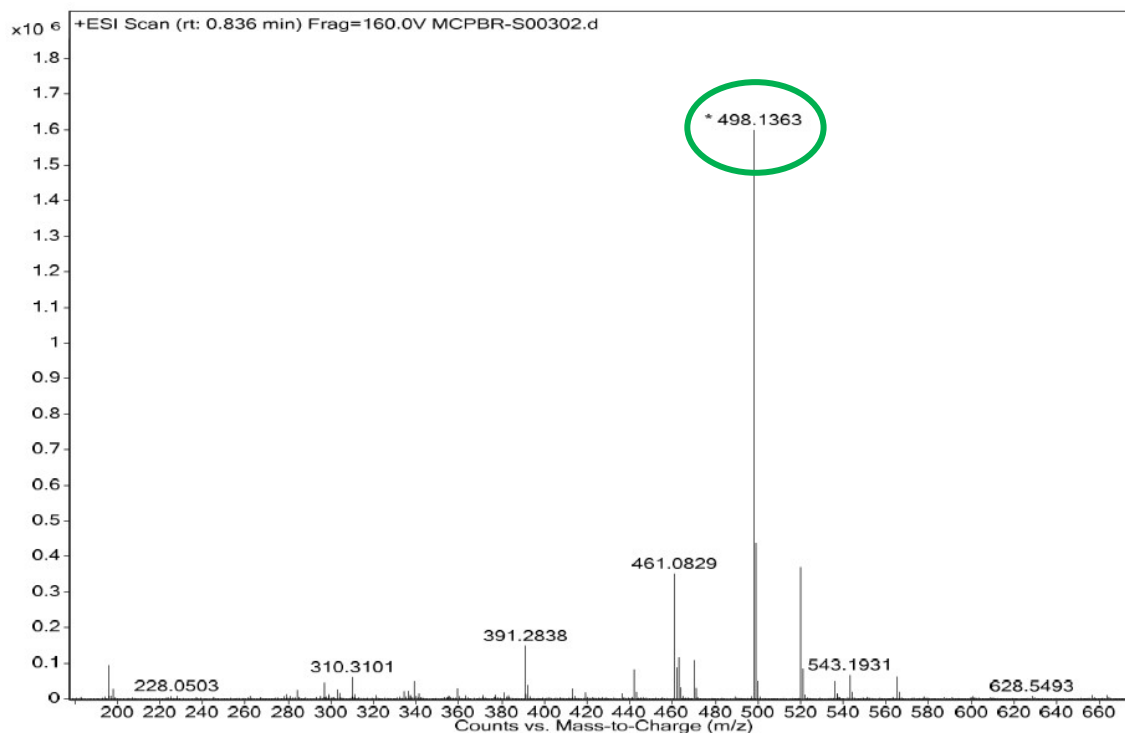
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T: FTMS + p ESI Full ms [100.0000-600.0000]



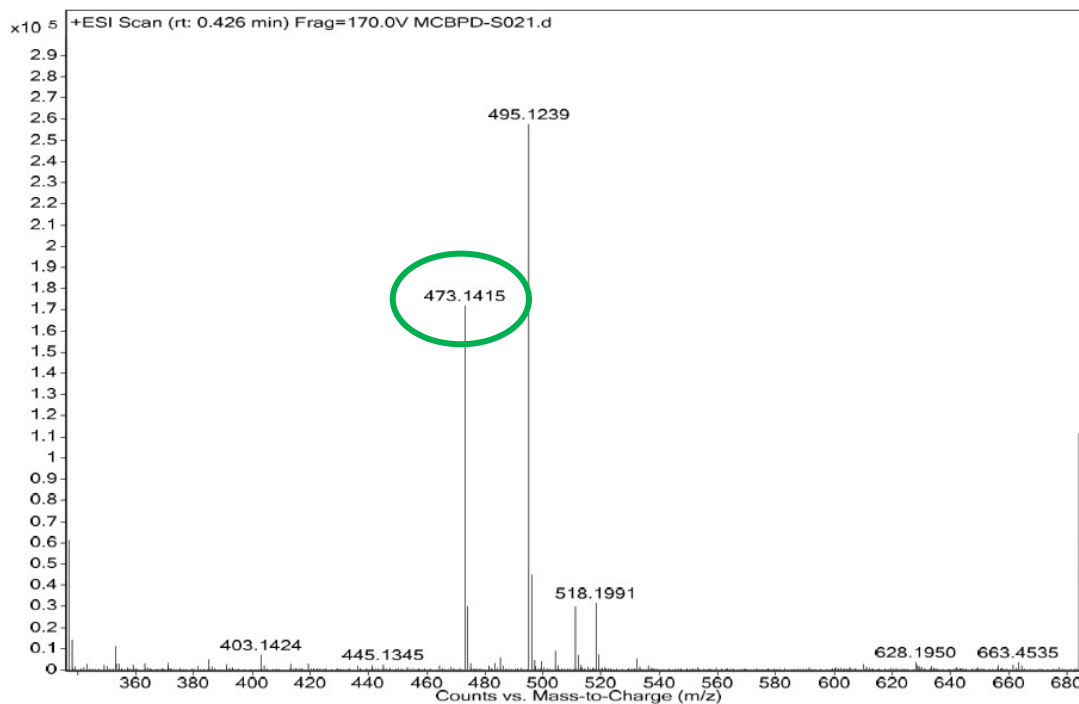
**Figure S101:** HRMS of of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methoxyphenyl)-1H-1,2,3-triazole-4-carboxamide [**2m**]



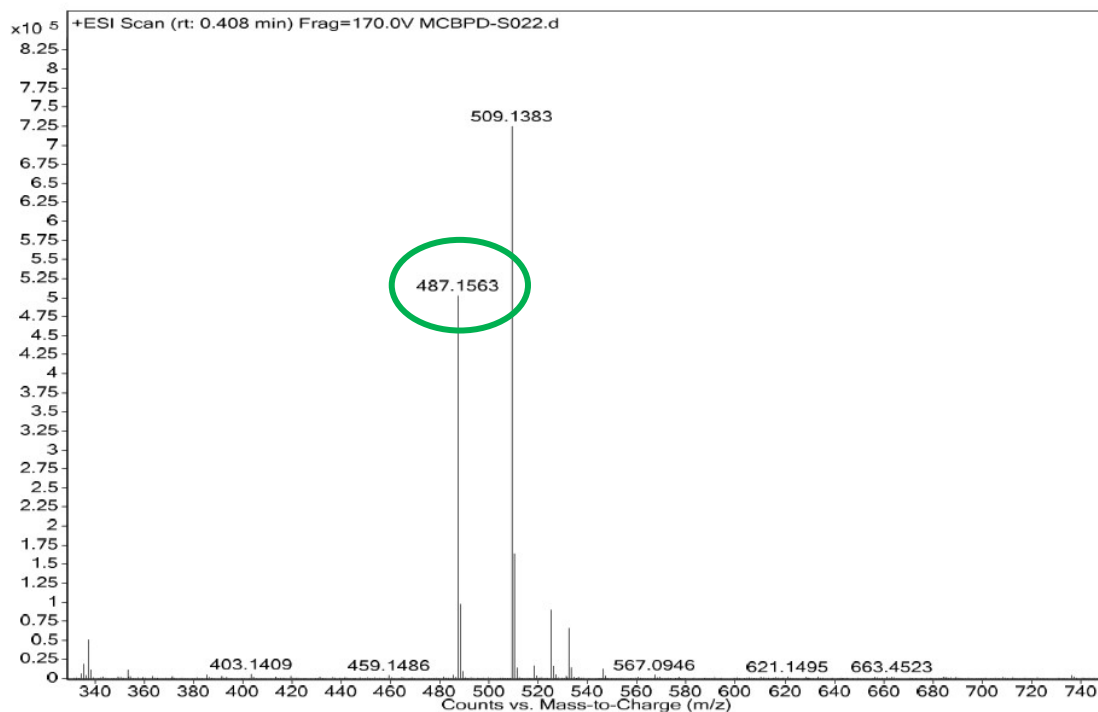
**Figure S102:** HRMS of of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide [**2n**]



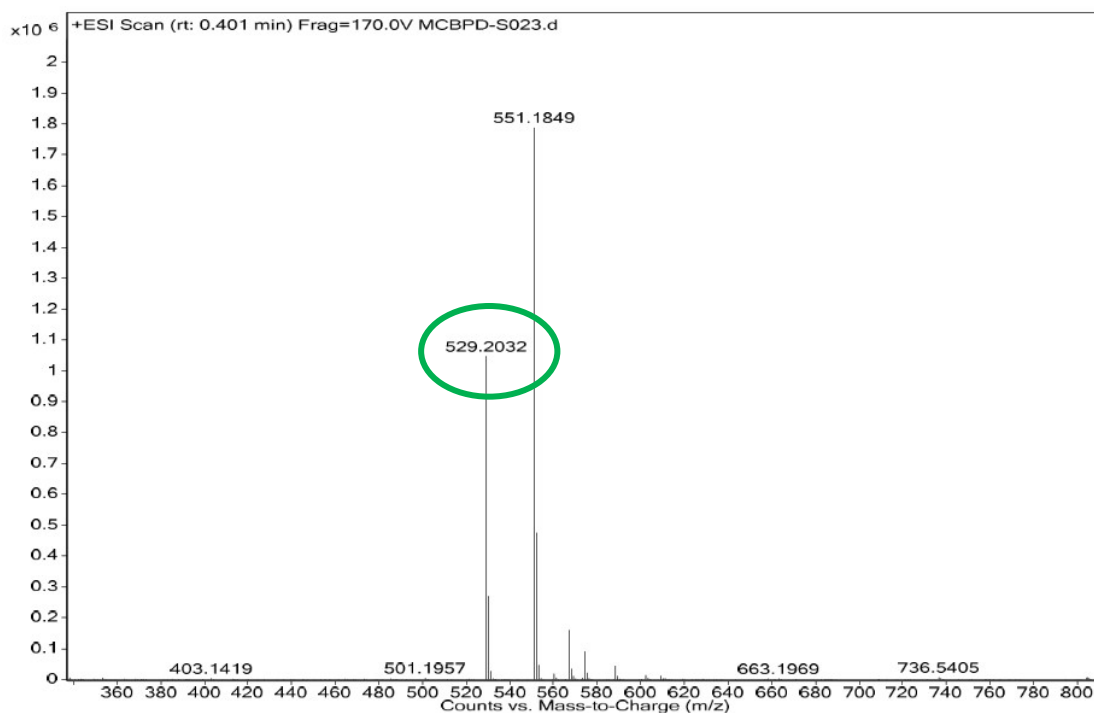
**Figure S103:** HRMS of of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2o]**



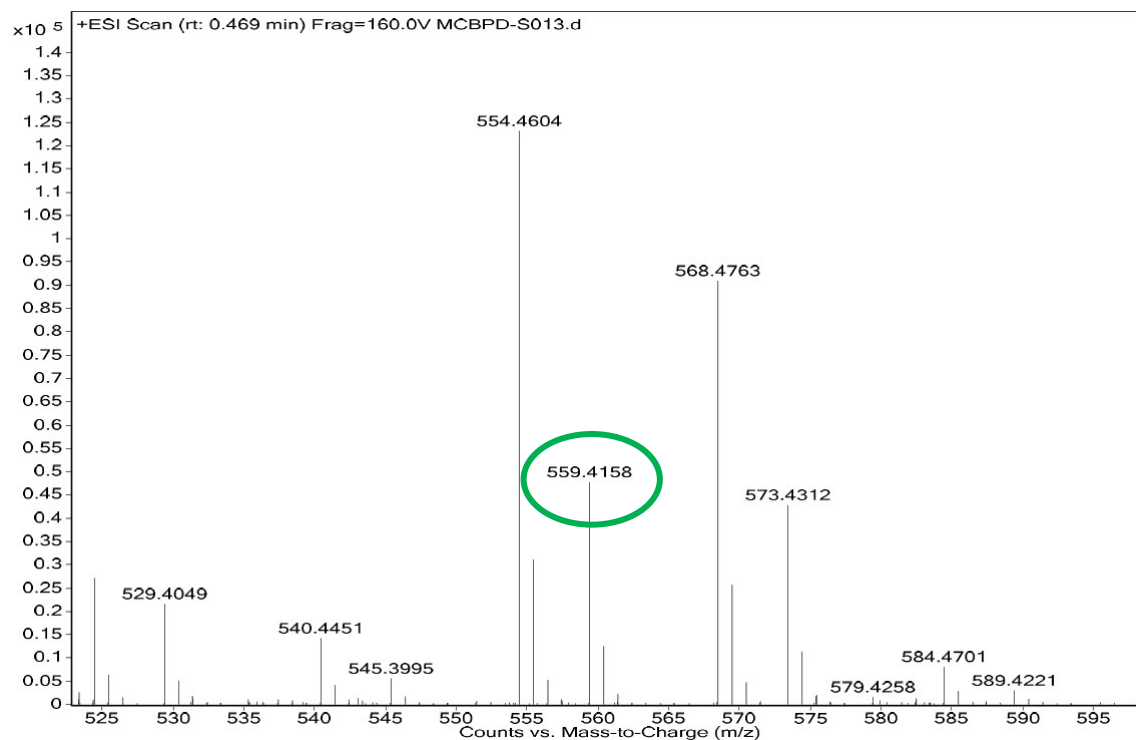
**Figure S104:** HRMS of of 1-(3,4-dimethylphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2p]**



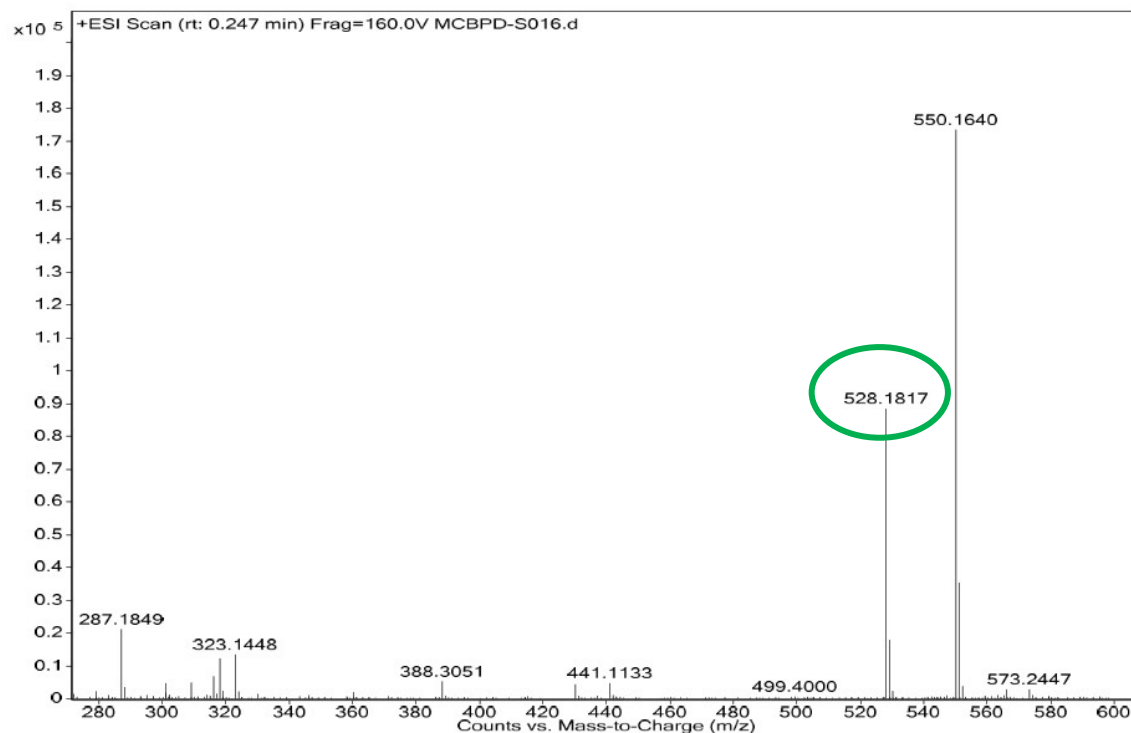
**Figure S105:** HRMS of of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2q]**



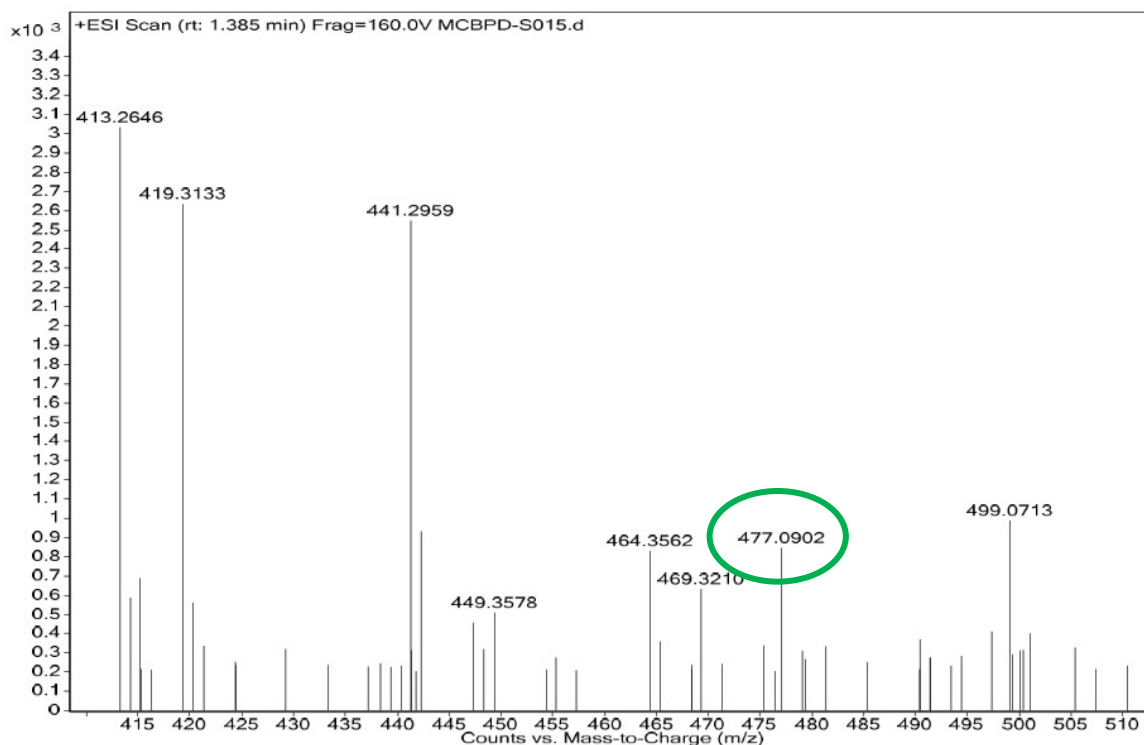
**Figure S106:** HRMS of of 2-(4-(1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamido)phenyl)-1,1,1,3,3,3-hexafluoropropan-2-yl-methanesulfonate **[2r]**



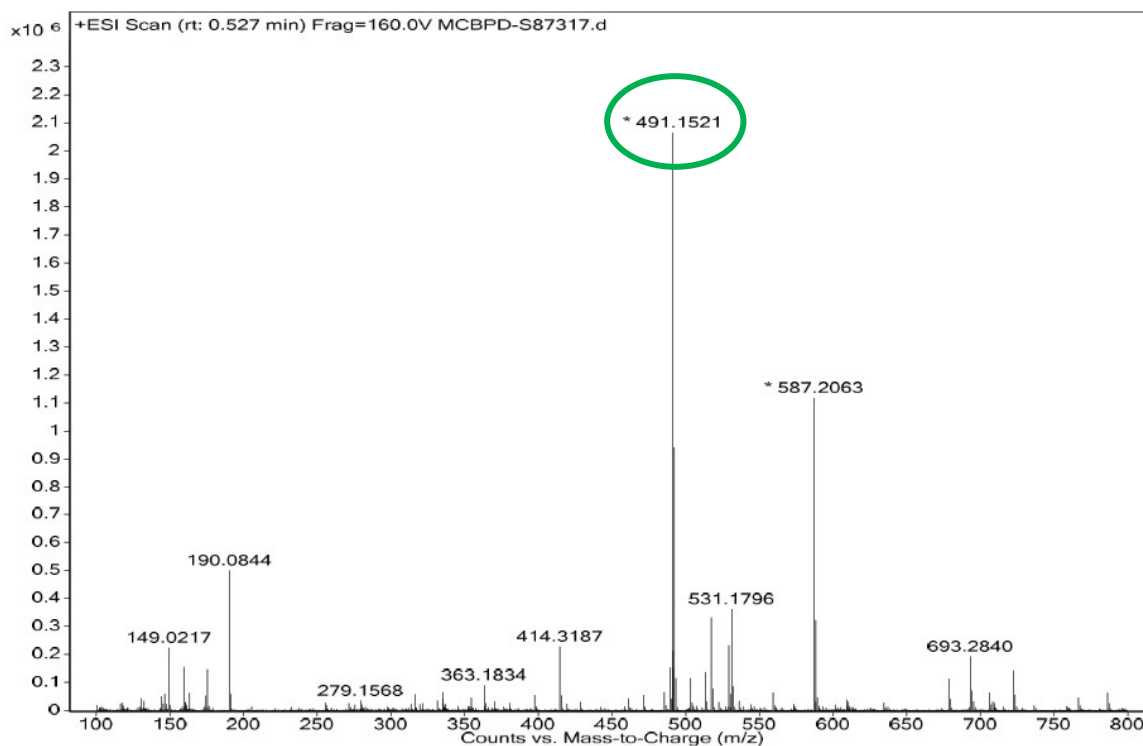
**Figure S107:** HRMS of of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-morpholinopropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [**2s**]



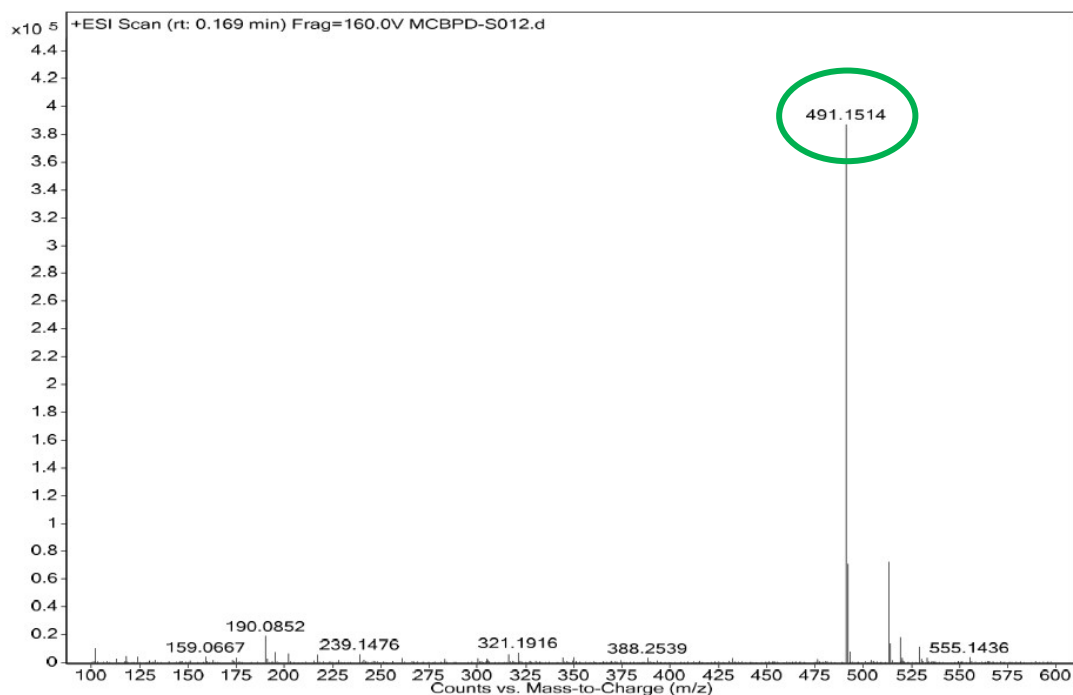
**Figure S108:** HRMS of of N-(4-(2-chloro-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide [**2t**]



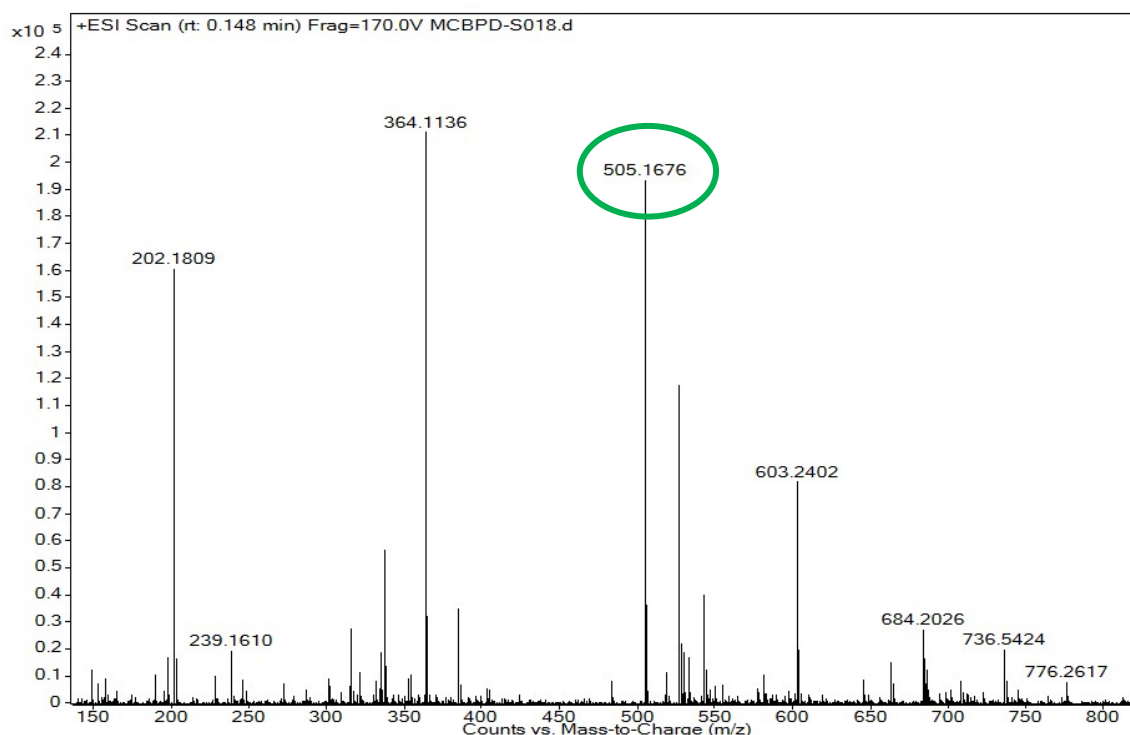
**Figure S109:** HRMS of of 2-(5-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [**3a**]



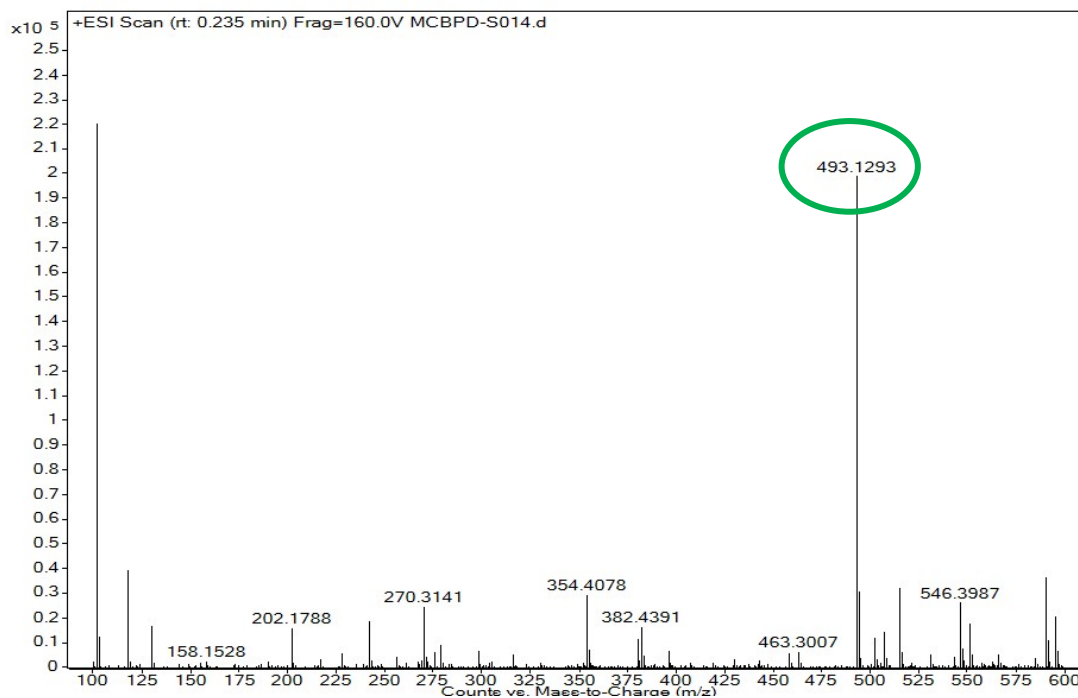
**Figure S110:** HRMS of of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2,5-dimethylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [**3b**]



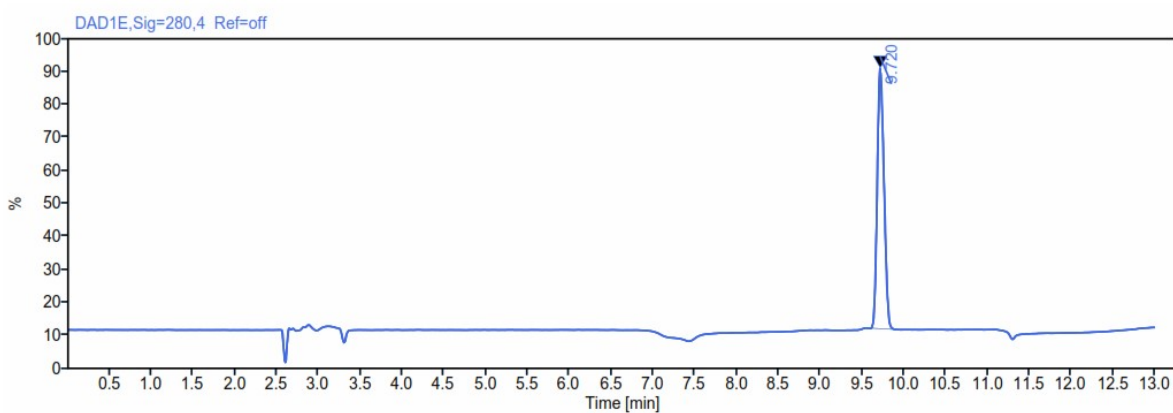
**Figure S111:** HRMS of of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-3-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol [**3c**]



**Figure S112:** HRMS of of 2-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-5-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenol [**3d**]

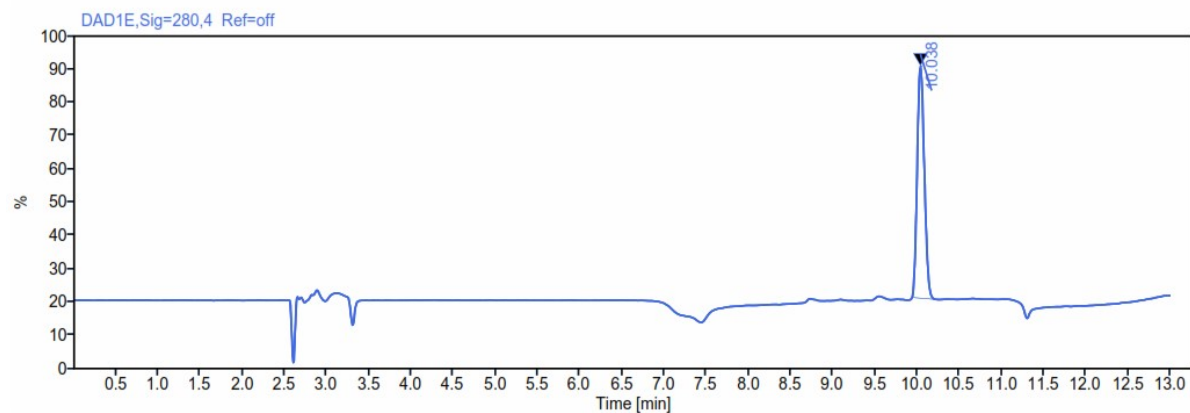


**Figure S113:** HPLC of of N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenyl)-3-phenylisoxazole-5-carboxamide [**1a**]



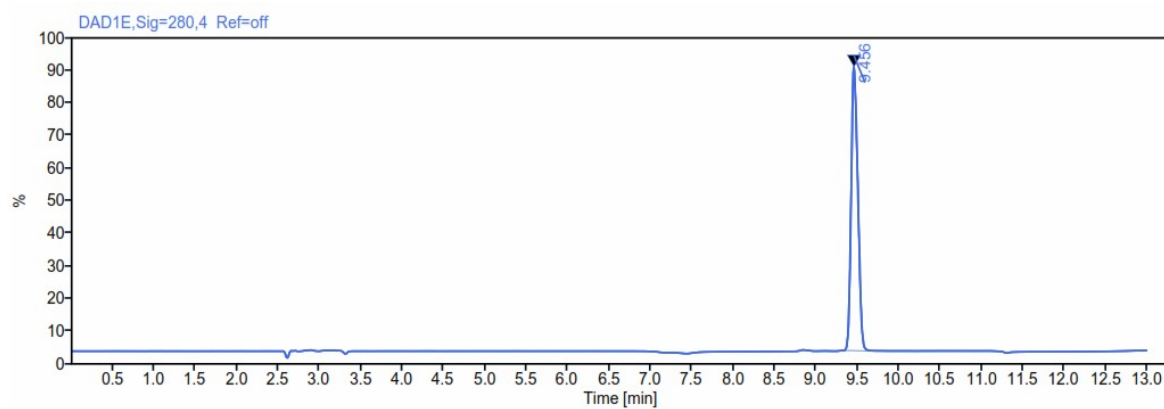
| Signal Type | DAD1   |        |        |             |             |                  |                     |                             |  |
|-------------|--------|--------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 9.720       | 84.11  | 476.84 | 100.00 | 0.32        |             | 1.14747          |                     | 63088.78667                 |  |
| Sum         |        | 476.84 |        |             |             |                  |                     |                             |  |

**Figure S114:** HPLC of of N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenyl)-3-(p-tolyl)isoxazole-5-carboxamide [**1b**]



| Signal Type | DAD1   |        |        |             |             |                  |                     |                             |  |
|-------------|--------|--------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 10.038      | 38.50  | 226.57 | 100.00 | 0.29        |             | 1.16414          |                     | 63011.58104                 |  |
| Sum         |        | 226.57 |        |             |             |                  |                     |                             |  |

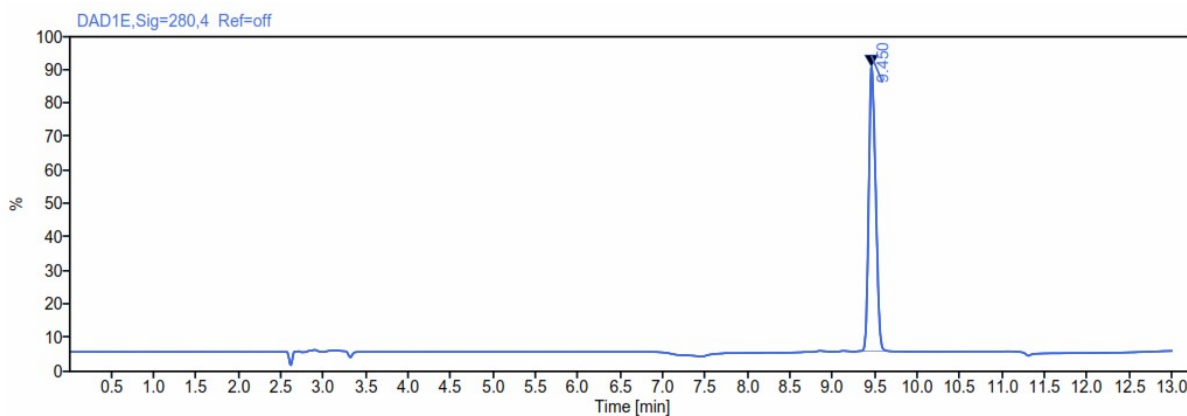
**Figure S115:** HPLC of of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2a]**



| Signal Type | DAD1   |         |        |             |             |                  |                     |                             |  |
|-------------|--------|---------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area    | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 9.456       | 427.77 | 2418.88 | 100.00 | 0.37        |             | 1.19769          |                     | 59305.96536                 |  |
| Sum         |        | 2418.88 |        |             |             |                  |                     |                             |  |

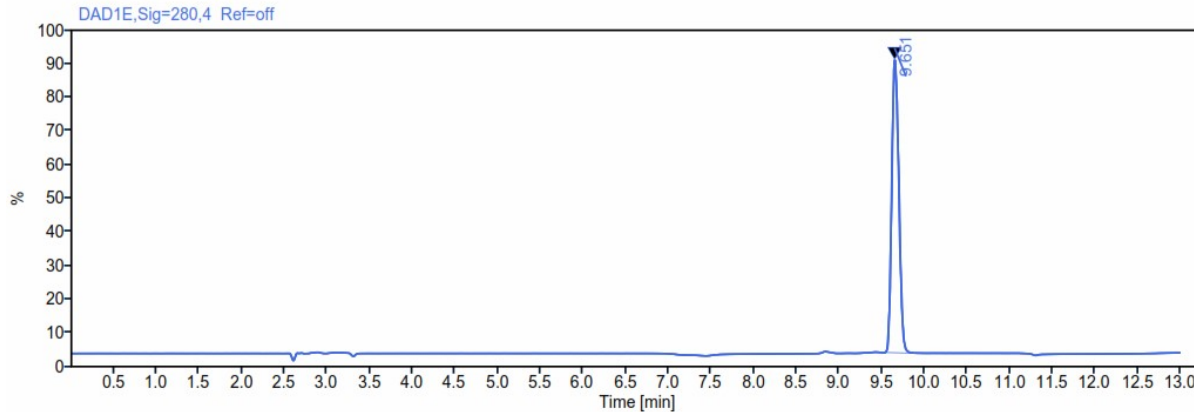
**Figure S116:** HPLC of of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2b]**





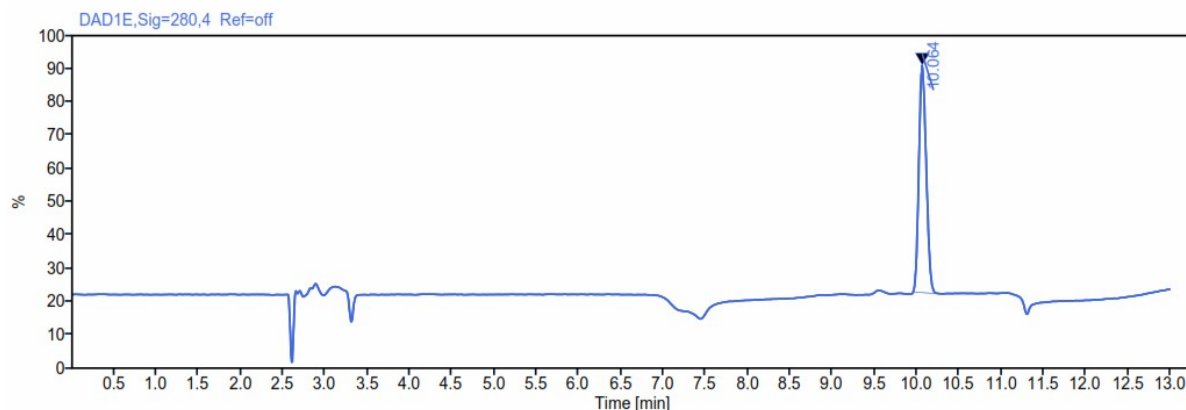
| Signal Type | DAD1   |         |        |             |             |                  |                     |                             |  |
|-------------|--------|---------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area    | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 9.450       | 219.56 | 1246.53 | 100.00 | 0.38        |             | 1.16271          |                     | 59111.38828                 |  |
| Sum         |        | 1246.53 |        |             |             |                  |                     |                             |  |

**Figure S117:** HPLC of of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2c]**



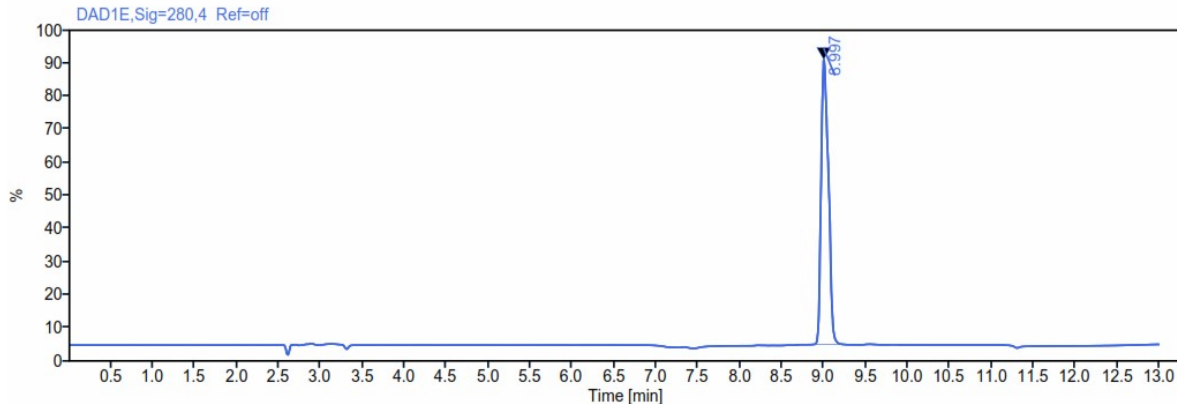
| Signal Type | DAD1   |         |        |             |             |                  |                     |                             |  |
|-------------|--------|---------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area    | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 9.651       | 424.60 | 2436.14 | 100.00 | 0.38        |             | 1.12669          |                     | 60952.67208                 |  |
| Sum         |        | 2436.14 |        |             |             |                  |                     |                             |  |

**Figure S118:** HPLC of of 1-(3,4-dimethoxyphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2d]**



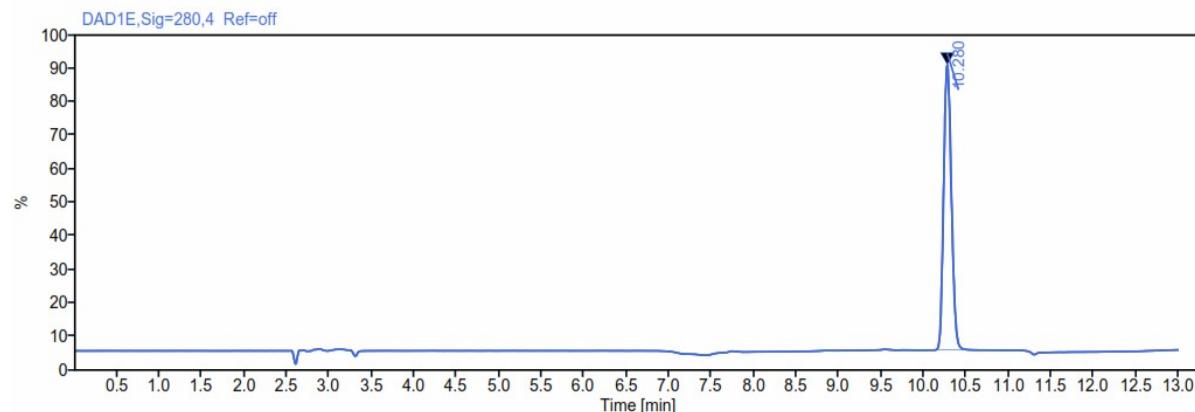
| Signal Type | DAD1   |        |        |             |             |                  |                     |                             |  |
|-------------|--------|--------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 10.064      | 34.87  | 211.82 | 100.00 | 0.33        |             | 1.14324          |                     | 59642.30588                 |  |
| Sum         |        | 211.82 |        |             |             |                  |                     |                             |  |

**Figure S119:** HPLC of of 1-(3,4-dimethoxyphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide **[2e]**



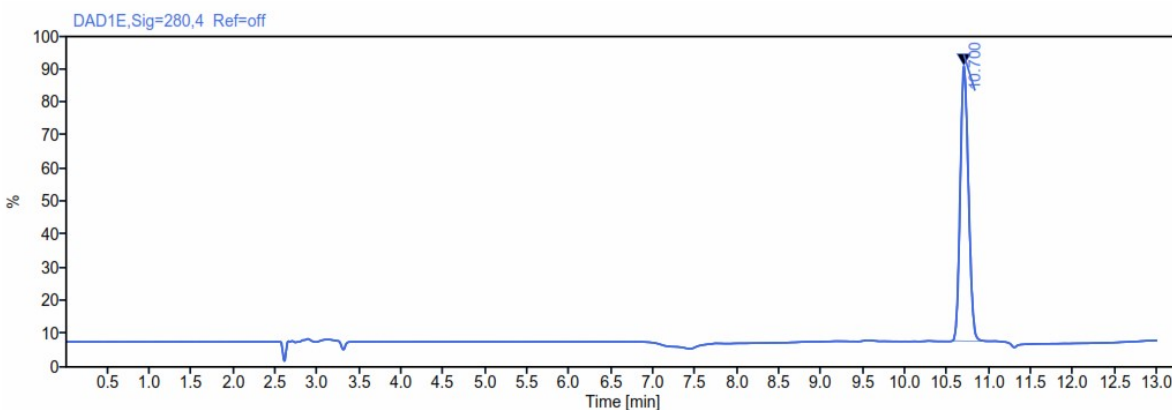
| Signal Type | DAD1   |         |        |             |             |                  |                     |                             |  |
|-------------|--------|---------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area    | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 8.997       | 299.93 | 1801.58 | 100.00 | 0.44        |             | 1.25304          |                     | 46653.58505                 |  |
| Sum         |        | 1801.58 |        |             |             |                  |                     |                             |  |

**Figure S120:** HPLC of of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2f]**



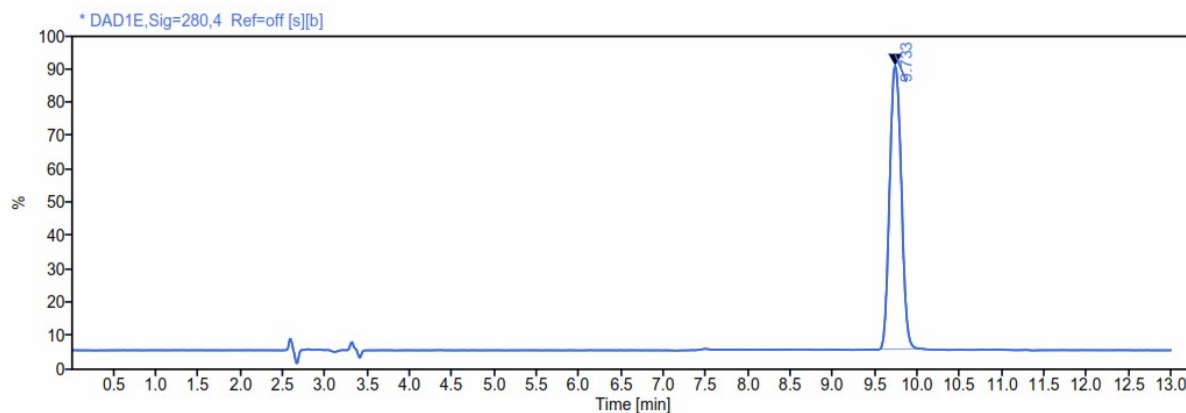
| Signal Type | DAD1   |         |        |             |             |                  |                     |                             |  |
|-------------|--------|---------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area    | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 10.280      | 224.38 | 1425.35 | 100.00 | 0.47        |             | 1.13190          |                     | 58111.19161                 |  |
| Sum         |        | 1425.35 |        |             |             |                  |                     |                             |  |

**Figure S121:** HPLC of of 1-(3,4-dimethoxyphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2g]**



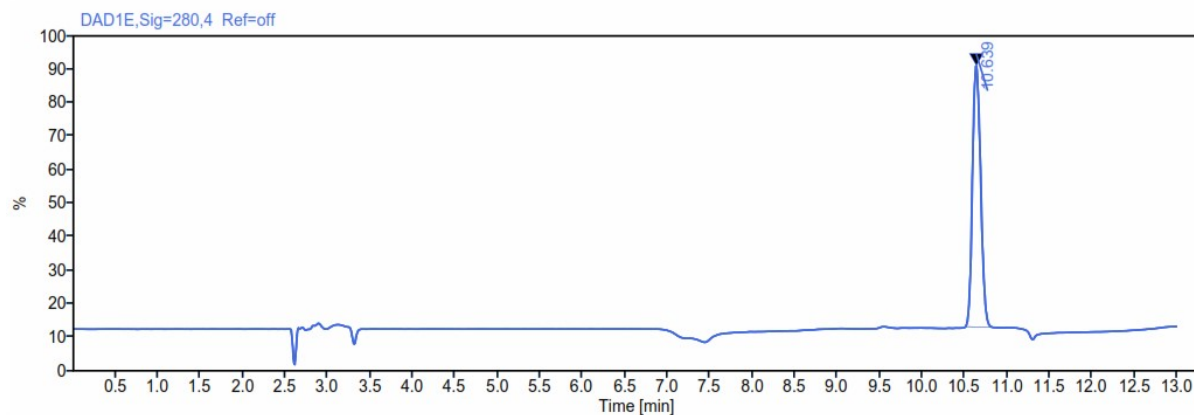
| Signal Type | DAD1   |        |        |             |             |                  |                     |                             |  |
|-------------|--------|--------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 10.700      | 145.43 | 995.67 | 100.00 | 0.42        |             | 1.16585          |                     | 54695.85710                 |  |
| Sum         |        | 995.67 |        |             |             |                  |                     |                             |  |

**Figure S122:** HPLC of of 1-(3,4-dimethoxyphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2h]**



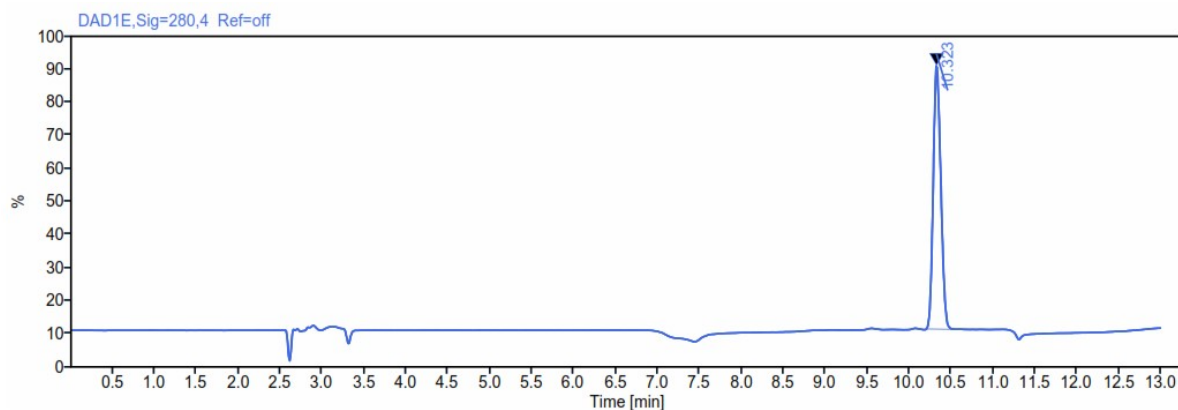
| Signal Type | DAD1   |         |        |             |             |                  |                     |                             |  |
|-------------|--------|---------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area    | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 9.733       | 379.95 | 3647.75 | 100.00 | 0.47        | 1000.0      | 1.06751          |                     | 23563.43902                 |  |
| Sum         |        | 3647.75 |        |             |             |                  |                     |                             |  |

**Figure S123:** HPLC of of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4-methylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2i]**



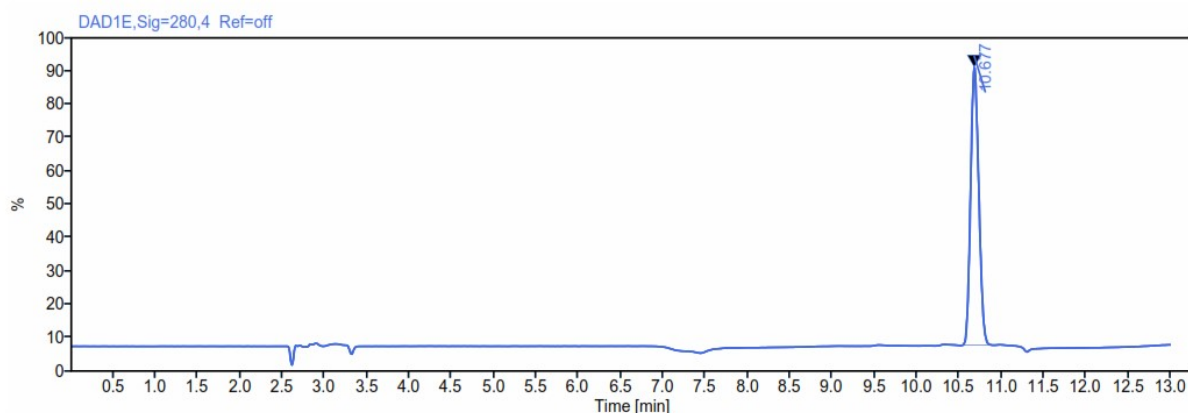
| Signal Type | DAD1   |        |        |             |             |                  |                     |                             |  |
|-------------|--------|--------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 10.639      | 72.70  | 490.15 | 100.00 | 0.41        |             | 1.11228          |                     | 55173.22083                 |  |
| Sum         |        | 490.15 |        |             |             |                  |                     |                             |  |

**Figure S124:** HPLC of of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2j]**



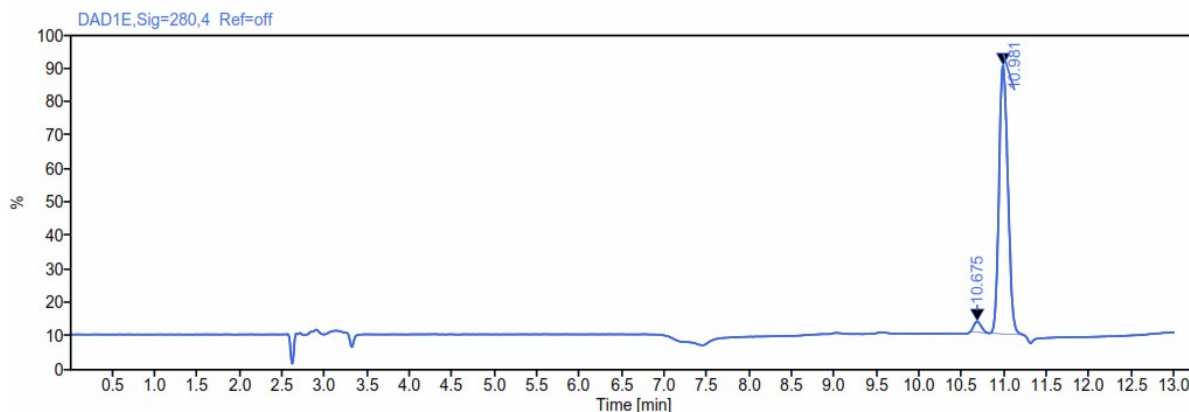
| Signal Type | DAD1   |        |        |             |             |                  |                     |                             |  |
|-------------|--------|--------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 10.323      | 85.11  | 537.76 | 100.00 | 0.36        |             | 1.17532          |                     | 58767.72497                 |  |
| Sum         |        | 537.76 |        |             |             |                  |                     |                             |  |

**Figure S125:** HPLC of of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2k]**



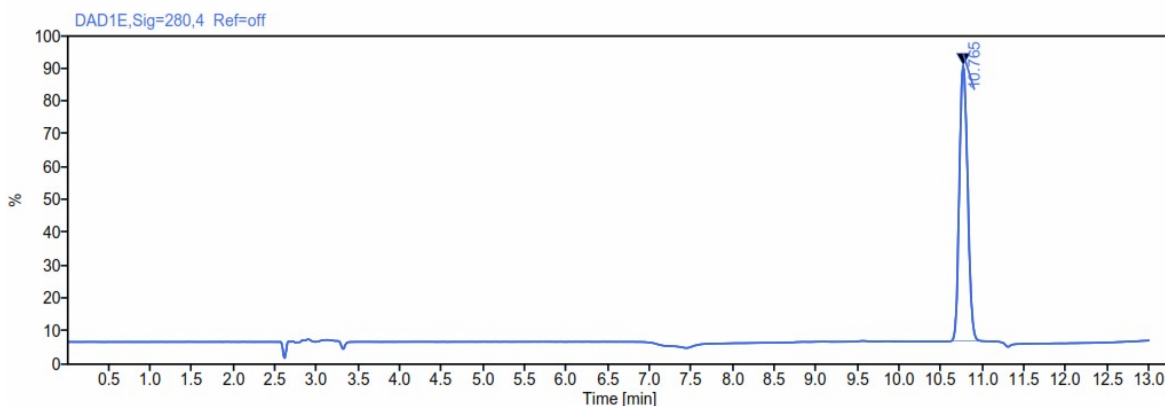
| Signal Type | DAD1   |        |        |             |             |                  |                     |                             |  |
|-------------|--------|--------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 10.677      | 147.03 | 994.31 | 100.00 | 0.37        |             | 1.16384          |                     | 55366.68219                 |  |
| Sum         |        | 994.31 |        |             |             |                  |                     |                             |  |

**Figure S126:** HPLC of of 1-(3,4-dimethylphenyl)-N-(2-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-4,5-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2l]**



| Signal Type | DAD1   |        |       |             |             |                  |                     |                             |  |
|-------------|--------|--------|-------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area% | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 10.675      | 3.64   | 22.29  | 3.28  | 0.22        |             | 1.11295          |                     | 63530.84773                 |  |
| 10.981      | 90.51  | 656.94 | 96.72 | 0.41        |             | 1.12069          | 1.69028             | 51537.66888                 |  |
| Sum         |        | 679.23 |       |             |             |                  |                     |                             |  |

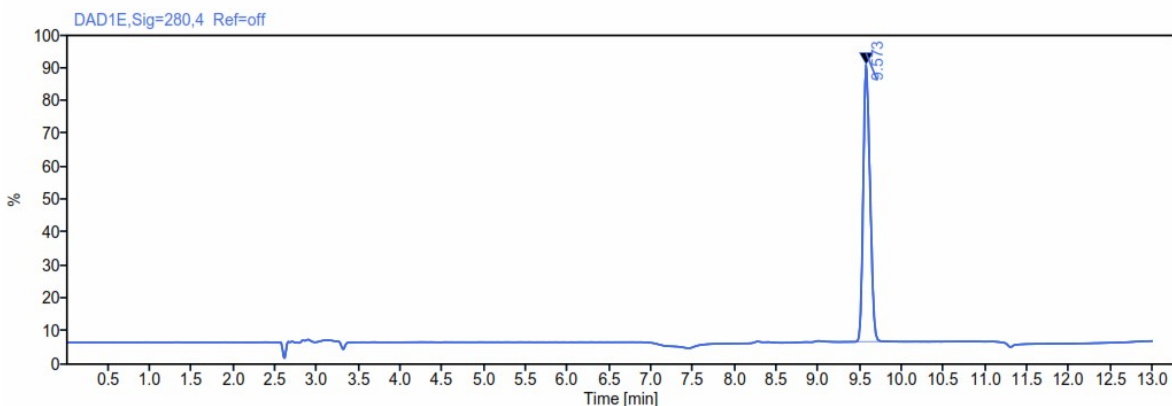
**Figure S127:** HPLC of of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-2-methoxyphenyl)-1H-1,2,3-triazole-4-carboxamide [**2m**]



| Signal Type | DAD1   |         |        |             |             |                  |                     |                             |  |
|-------------|--------|---------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area    | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 10.765      | 165.25 | 1137.73 | 100.00 | 0.46        |             | 1.11558          |                     | 54597.76959                 |  |
| Sum         |        | 1137.73 |        |             |             |                  |                     |                             |  |

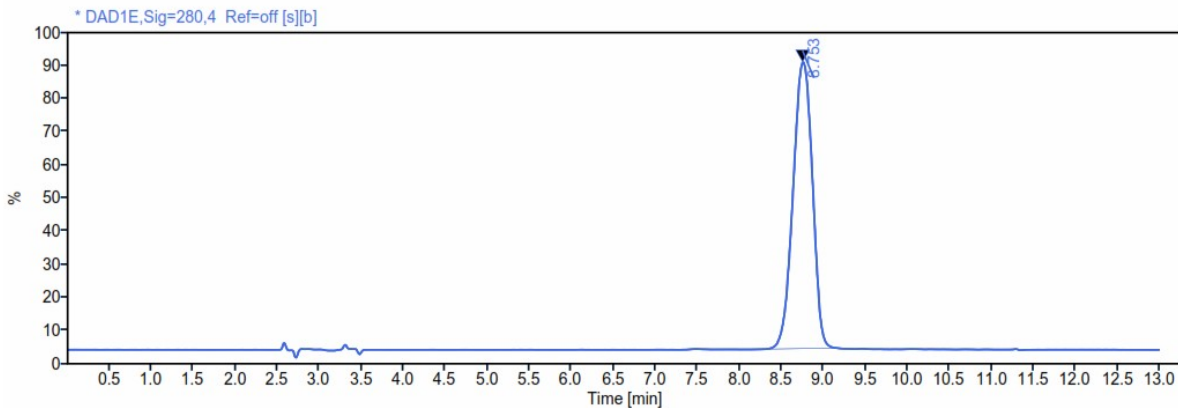
**Figure S128:** HPLC of of 1-(3,4-dimethylphenyl)-N-(3-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)-1H-indol-5-yl)-1H-1,2,3-triazole-4-carboxamide [**2n**]





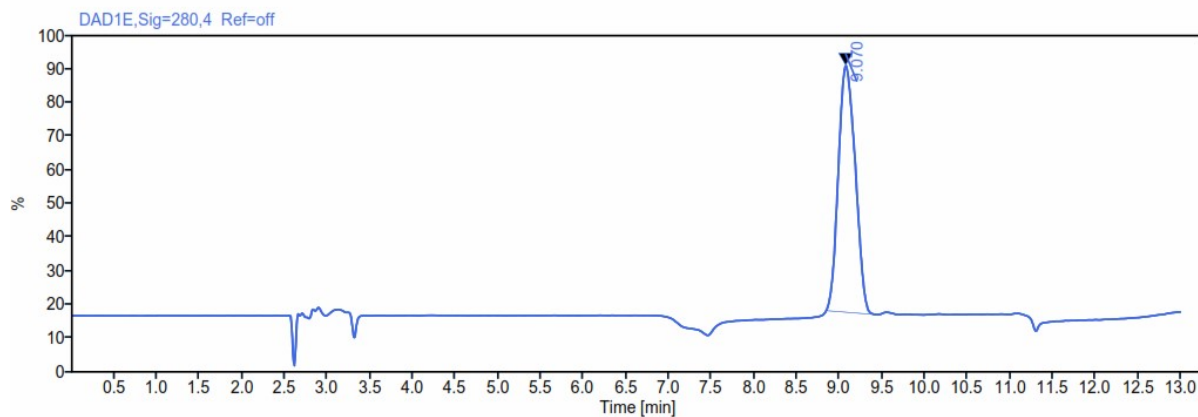
| Signal Type | DAD1   |        |        |             |             |                  |                     |                             |  |
|-------------|--------|--------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 9.573       | 167.32 | 954.39 | 100.00 | 0.39        |             | 1.19011          |                     | 59090.42021                 |  |
| Sum         |        | 954.39 |        |             |             |                  |                     |                             |  |

**Figure S129:** HPLC of of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2o]**



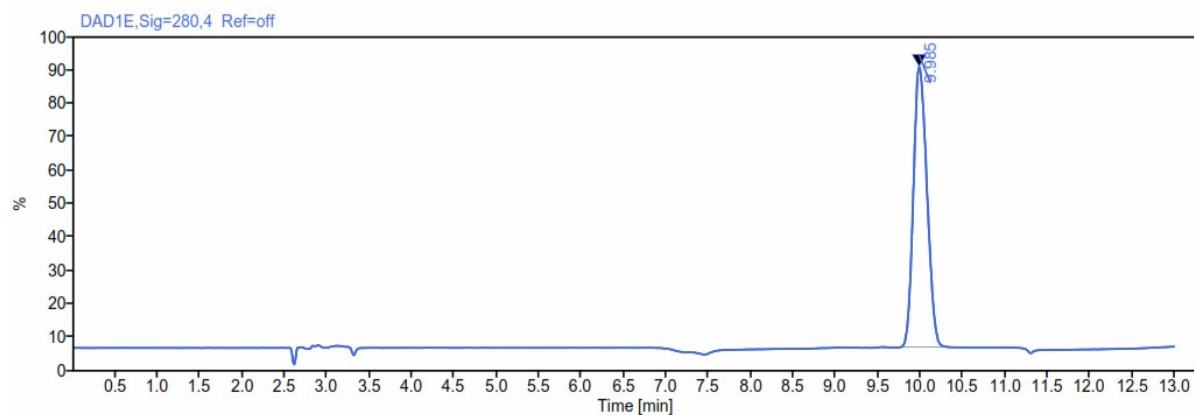
| Signal Type | DAD1   |          |        |             |             |                  |                     |                             |  |
|-------------|--------|----------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area     | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 8.753       | 659.48 | 10606.80 | 100.00 | 0.85        | 1000.0      | 0.94568          |                     | 6854.43165                  |  |
| Sum         |        | 10606.80 |        |             |             |                  |                     |                             |  |

**Figure S130:** HPLC of of 1-(3,4-dimethylphenyl)-N-(4-(2-ethoxy-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2p]**



| Signal Type | DAD1   |        |        |             |             |                  |                     |                             |  |
|-------------|--------|--------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 9.070       | 47.66  | 658.13 | 100.00 | 0.59        |             | 1.08304          |                     | 8995.99109                  |  |
| Sum         |        | 658.13 |        |             |             |                  |                     |                             |  |

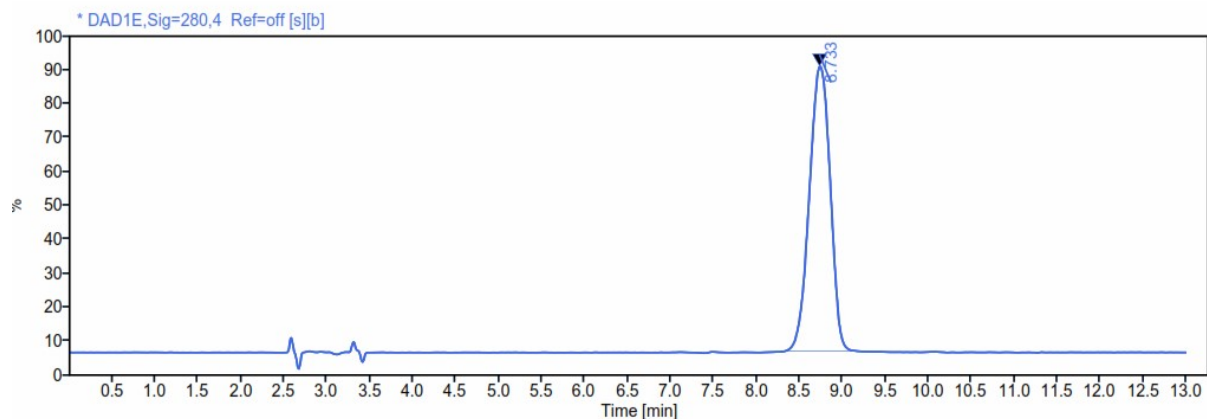
**Figure S131:** HPLC of of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-(isopentyloxy)propan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide **[2q]**



| Signal Type | DAD1   |         |        |             |             |                  |                     |                             |  |
|-------------|--------|---------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area    | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 9.985       | 162.79 | 1815.22 | 100.00 | 0.61        |             | 1.18542          |                     | 17171.88534                 |  |
| Sum         |        | 1815.22 |        |             |             |                  |                     |                             |  |

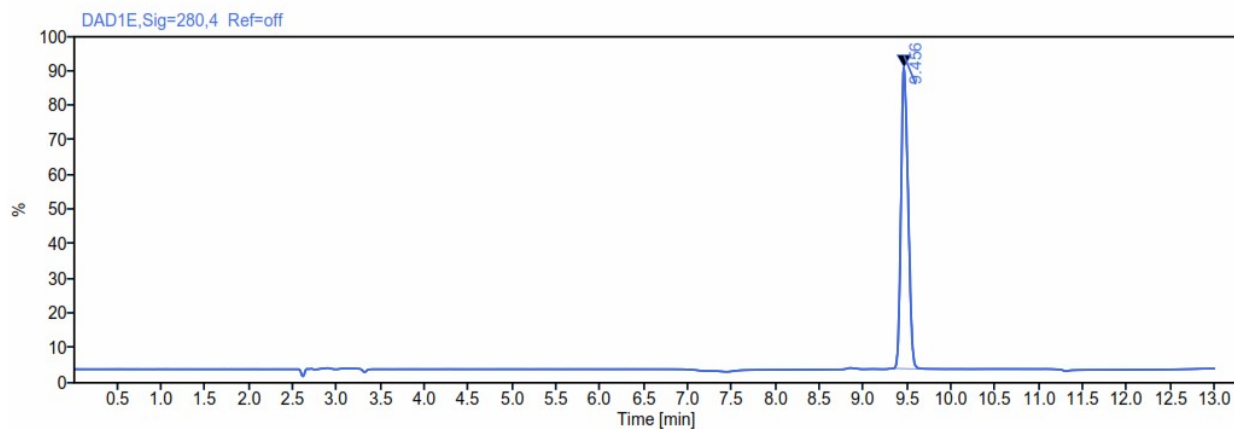
**Figure S132:** HPLC of of 2-(4-(1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamido)phenyl)-1,1,1,3,3,3-hexafluoropropan-2-yl-methanesulfonate **[2r]**





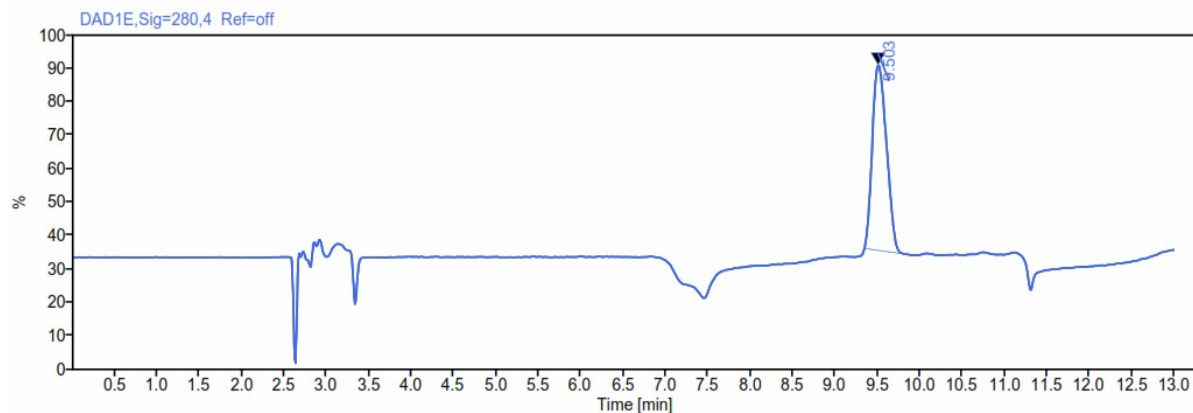
| Signal Type | DAD1   |         |        |             |             |                  |                     |                             |
|-------------|--------|---------|--------|-------------|-------------|------------------|---------------------|-----------------------------|
| RT [min]    | Height | Area    | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |
| 8.733       | 302.12 | 5112.98 | 100.00 | 0.82        | 1000.0      | 0.95383          |                     | 5999.58953                  |
| Sum         |        | 5112.98 |        |             |             |                  |                     |                             |

**Figure S133:** HPLC of of 1-(3,4-dimethylphenyl)-N-(4-(1,1,1,3,3,3-hexafluoro-2-morpholinopropan-2-yl)phenyl)-1H-1,2,3-triazole-4-carboxamide [**2s**]



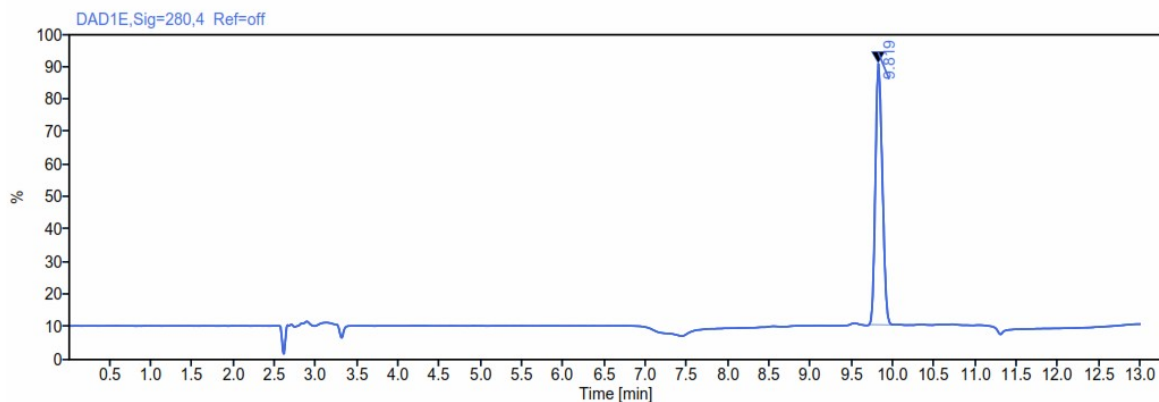
| Signal Type | DAD1   |         |        |             |             |                  |                     |                             |
|-------------|--------|---------|--------|-------------|-------------|------------------|---------------------|-----------------------------|
| RT [min]    | Height | Area    | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |
| 9.456       | 427.77 | 2418.88 | 100.00 | 0.37        |             | 1.19769          |                     | 59305.96536                 |
| Sum         |        | 2418.88 |        |             |             |                  |                     |                             |

**Figure S134:** HPLC of of N-(4-(2-chloro-1,1,1,3,3,3-hexafluoropropan-2-yl)phenyl)-1-(3,4-dimethylphenyl)-1H-1,2,3-triazole-4-carboxamide **[2t]**



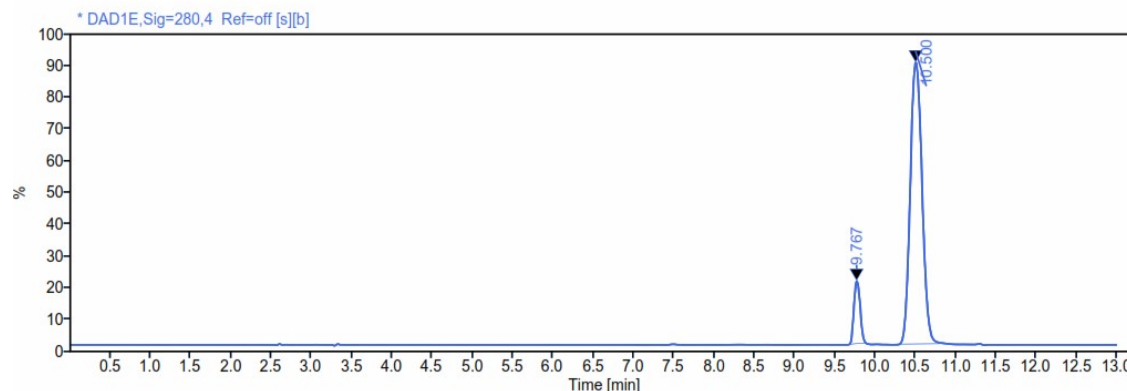
| Signal Type | DAD1   |        |        |             |             |                  |                     |                             |  |
|-------------|--------|--------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 9.503       | 16.92  | 196.95 | 100.00 | 0.48        |             | 1.16911          |                     | 13832.67638                 |  |
| Sum         |        | 196.95 |        |             |             |                  |                     |                             |  |

**Figure S135:** HPLC of of 2-(5-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol **[3a]**



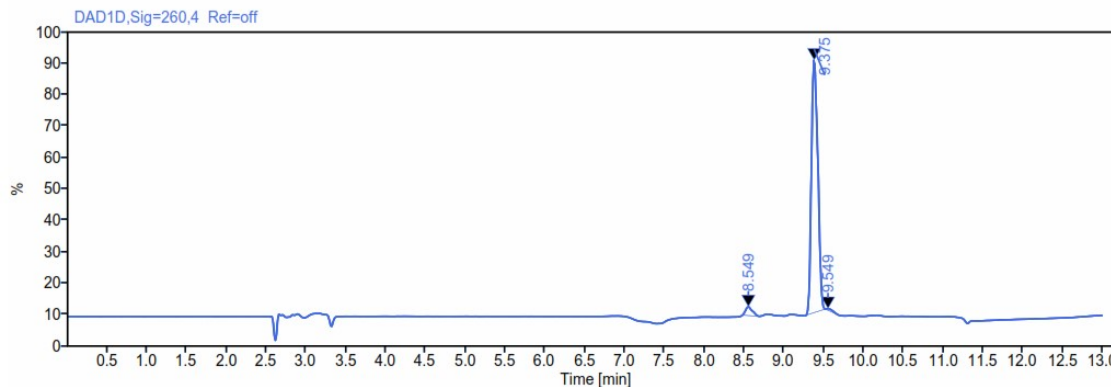
| Signal Type | DAD1   |        |        |             |             |                  |                     |                             |  |
|-------------|--------|--------|--------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 9.819       | 92.68  | 548.41 | 100.00 | 0.31        |             | 1.12223          |                     | 59114.74925                 |  |
| Sum         |        | 548.41 |        |             |             |                  |                     |                             |  |

**Figure S136:** HPLC of of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-2,5-dimethylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol **[3b]**



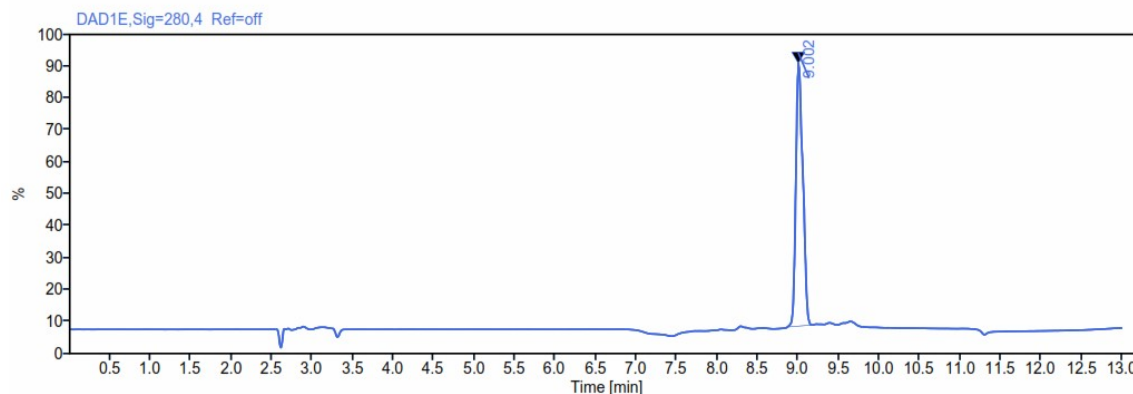
| Signal Type |        | DAD1    |       |             |             |                  |                     |                             |  |
|-------------|--------|---------|-------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area    | Area% | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 9.767       | 166.71 | 881.59  | 10.42 | 0.23        | 1000.0      | 1.15285          |                     | 74028.94743                 |  |
| 10.500      | 746.24 | 7579.72 | 89.58 | 0.82        | 1000.0      | 1.10693          | 3.54825             | 24257.87909                 |  |
| Sum         |        | 8461.31 |       |             |             |                  |                     |                             |  |

**Figure S137:** HPLC of of 2-(4-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-3-methylphenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol **[3c]**



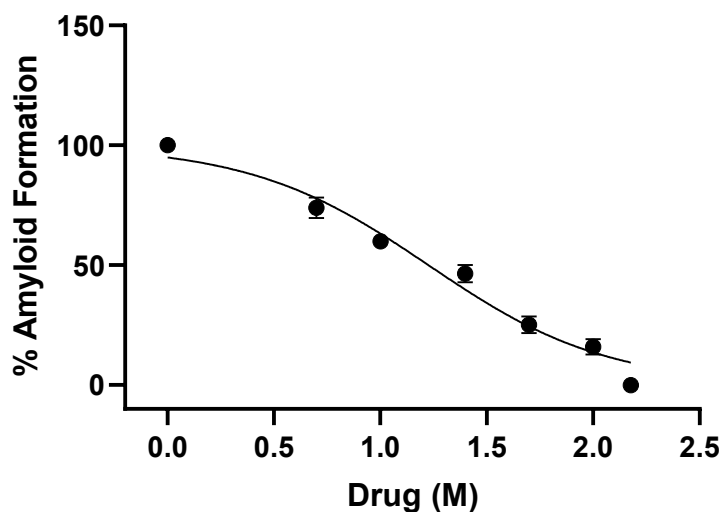
| Signal Type |        | DAD1   |       |             |             |                  |                     |                             |  |
|-------------|--------|--------|-------|-------------|-------------|------------------|---------------------|-----------------------------|--|
| RT [min]    | Height | Area   | Area% | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |  |
| 8.549       | 4.17   | 24.68  | 3.54  | 0.21        |             | 1.24256          |                     | 45986.54061                 |  |
| 9.375       | 119.59 | 668.19 | 95.72 | 0.24        |             | 1.24548          | 5.23351             | 57411.12074                 |  |
| 9.549       | 0.76   | 5.17   | 0.74  | 0.16        |             | 1.26201          | 1.16299             | 72737.66936                 |  |
| Sum         |        | 698.04 |       |             |             |                  |                     |                             |  |

**Figure S138:** HPLC of 2-(((1-(3,4-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)amino)-5-(1,1,1,3,3,3-hexafluoro-2-hydroxypropan-2-yl)phenol **[3d]**



| Signal Type | DAD1   |        |        |             |             |                  |                     |                             |
|-------------|--------|--------|--------|-------------|-------------|------------------|---------------------|-----------------------------|
| RT [min]    | Height | Area   | Area%  | Width [min] | Peak Purity | Peak Tail Factor | Peak Resolution USP | Peak Theoretical Plates USP |
| 9.002       | 142.54 | 855.05 | 100.00 | 0.31        |             | 1.25014          |                     | 45673.84413                 |
| Sum         |        | 855.05 |        |             |             |                  |                     |                             |

**Figure S139:** IC<sub>50</sub> graph of 2f against A $\beta$ <sub>42</sub> aggregation



**IC<sub>50</sub> determination:** Different concentrations of compound 2f were incubated with 5 $\mu$ M of A $\beta$ <sub>42</sub> for 24 h at 37°C and the IC<sub>50</sub> was determined by using thioflavin assay (n=3). The average of the fluorescence intensity is reported.

## ADMET properties:

**Table S1:**

| Compounds | Molecular weight ≤ 400 | Aromatic rings ≤ 4 | Heavy atoms ≤ 40 | Hydrogen bond number (donor) 0 to 6 | Hydrogen bond number (acceptor) 2 to 20 | HumanOralAbsorption <25 poor >80 High | Total polar surface area ≤ 80 Å <sup>2</sup> |
|-----------|------------------------|--------------------|------------------|-------------------------------------|-----------------------------------------|---------------------------------------|----------------------------------------------|
| <b>2f</b> | 504.388                | 3                  | 35               | 1                                   | 6                                       | 2                                     | 133.83                                       |

**Table S2:**

| Compounds | SASA 300 to 1000 | QPlogPo/w -2.5 to 6.5 | QPlogS -6.5 to 0.5 | QPlogHERG Below <5 | QPPCaco <25 poor >500 great | QPlogBB -3.0 to 1.2 | Rule of Five 0 to 5 |
|-----------|------------------|-----------------------|--------------------|--------------------|-----------------------------|---------------------|---------------------|
| <b>2f</b> | 717.859          | 5.003                 | -6.825             | -5.833             | 1040.424                    | -0.49               | 2                   |

**SASA**= Solvent accessible surface area. Recommended values 300 to 1000

**QPlogPo/w**= Predicted octanol/water partition coefficient. Recommended values -2.0 – 6.5.

**QPlogS**= Predicted aqueous solubility, log S. Recommended values -6.5 – 0.5.

**QPlogHERG**= Predicted IC50 value for blockage of HERG K<sup>+</sup> channels. Recommended values below <5

**QPPCaco**= Predicted apparent Caco-2 cell permeability in nm/sec. Recommended values <25 is poor and > 500 is great.

**QPlogBB**= Predicted brain/blood partition coefficient. Recommended values -3.0 – 1.2.

**Rule of 5**= Rule of Five, The rules are mol\_MW < 500, QPlogPo/w < 5, donorHB ≤ 5, and acceptHB ≤ 10.