

## Supporting Information

### 2,5-Diaryl-1,3,4-oxadiazoles as selective COX-2 inhibitors and anti-inflammatory agents

Jagdeep Grover<sup>1</sup>, Nirav Bhatt<sup>1</sup>, Vivek Kumar<sup>2</sup>, Neeraj K. Patel<sup>1</sup>, Bhagirath J. Gondaliya<sup>1</sup>,  
Masilamani E. Sobhia<sup>2</sup>, Kamlesh K. Bhutani<sup>1</sup>, Sanjay M. Jachak<sup>1</sup> \*

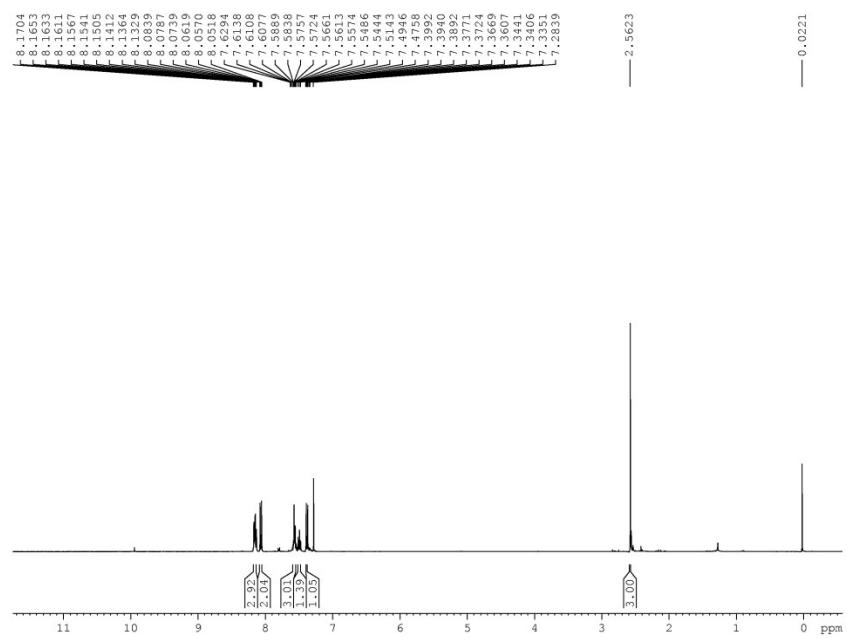
<sup>1</sup>Department of Natural Products, <sup>2</sup>Department of Pharmacoinformatics,  
National Institute of Pharmaceutical Education and Research, Sector-67, S.A.S. Nagar-160062,  
Punjab, India

*E-mail:* sanjayjachak@niper.ac.in, [sjachak11@gmail.com](mailto:sjachak11@gmail.com)

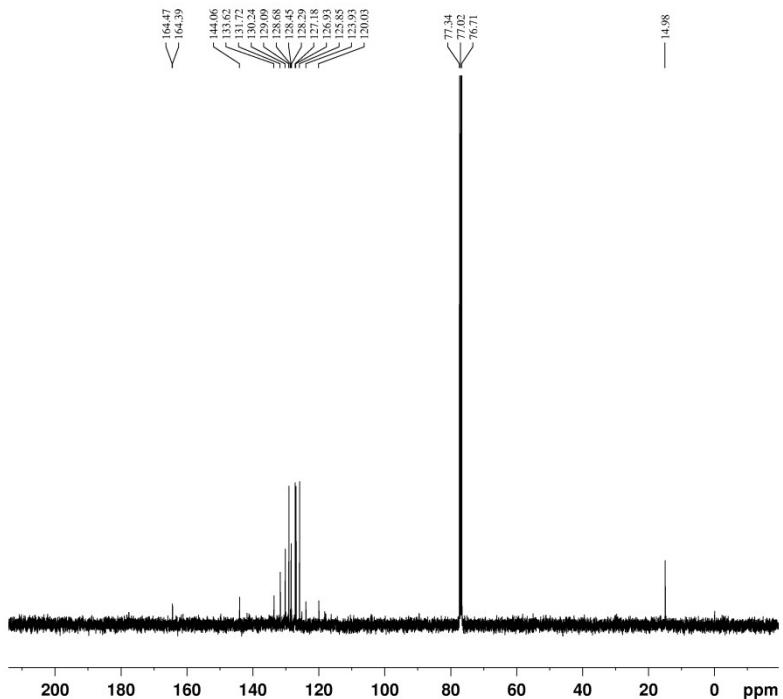
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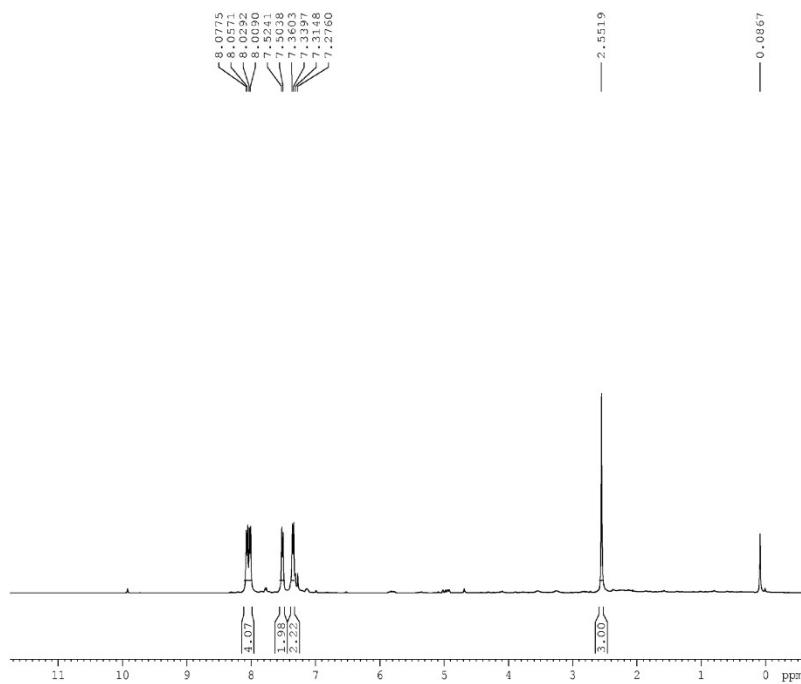
## Scanned Spectra



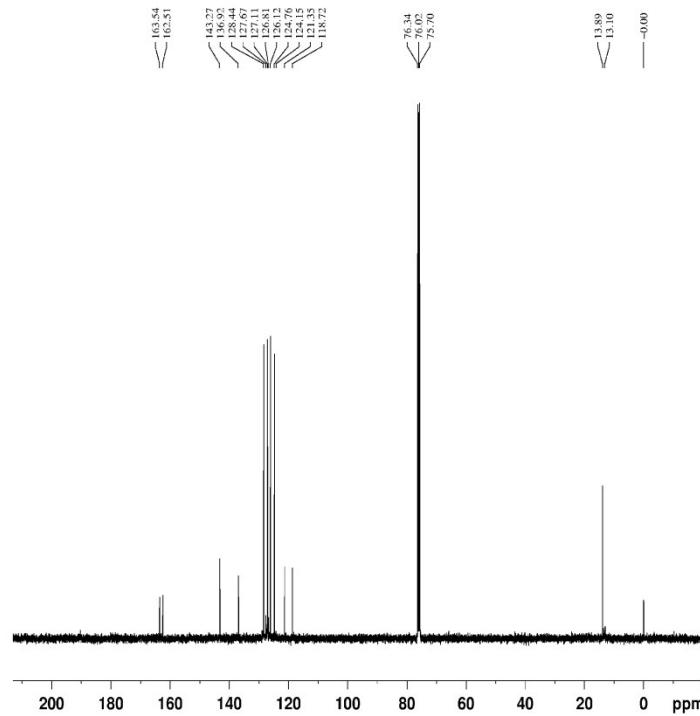
**Fig. S1:** <sup>1</sup>H NMR of 2-(4-(methylthio)phenyl)-5-phenyl-1,3,4-oxadiazole **4a**



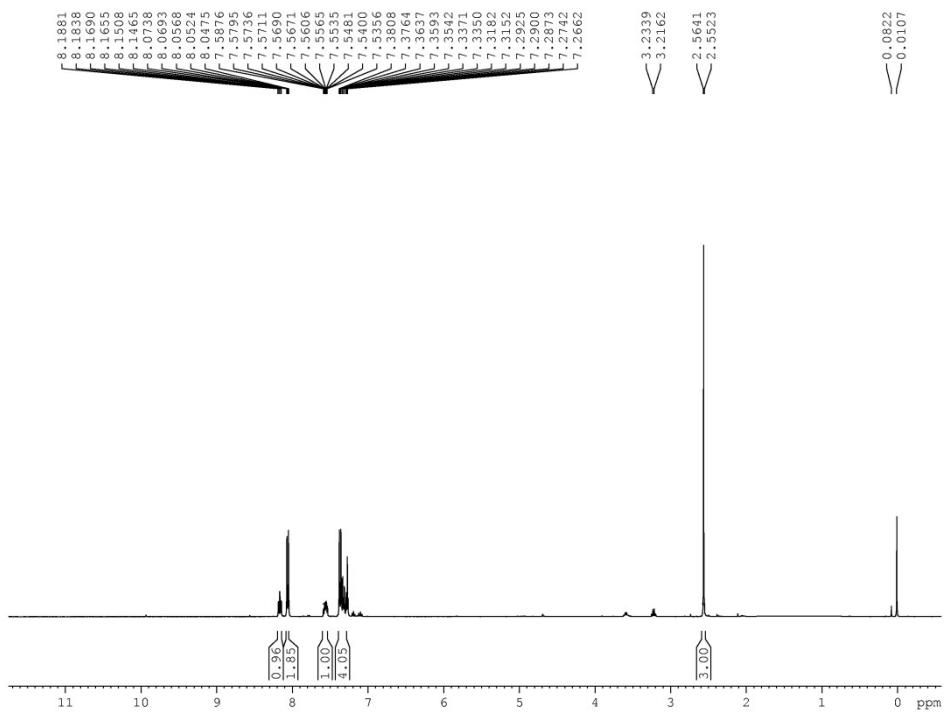
**Fig. S2:** <sup>13</sup>C NMR of 2-(4-(methylthio)phenyl)-5-phenyl-1,3,4-oxadiazole **4a**



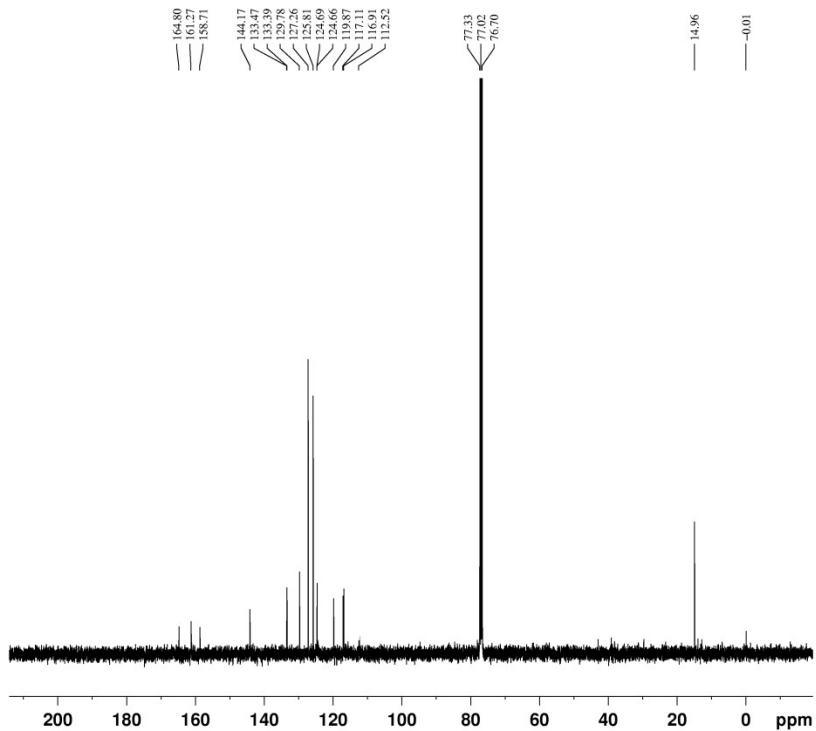
**Fig. S3:**  $^1\text{H}$  NMR of 2-(4-chlorophenyl)-5-(4-(methylthio)phenyl)-1,3,4-oxadiazole **4b**



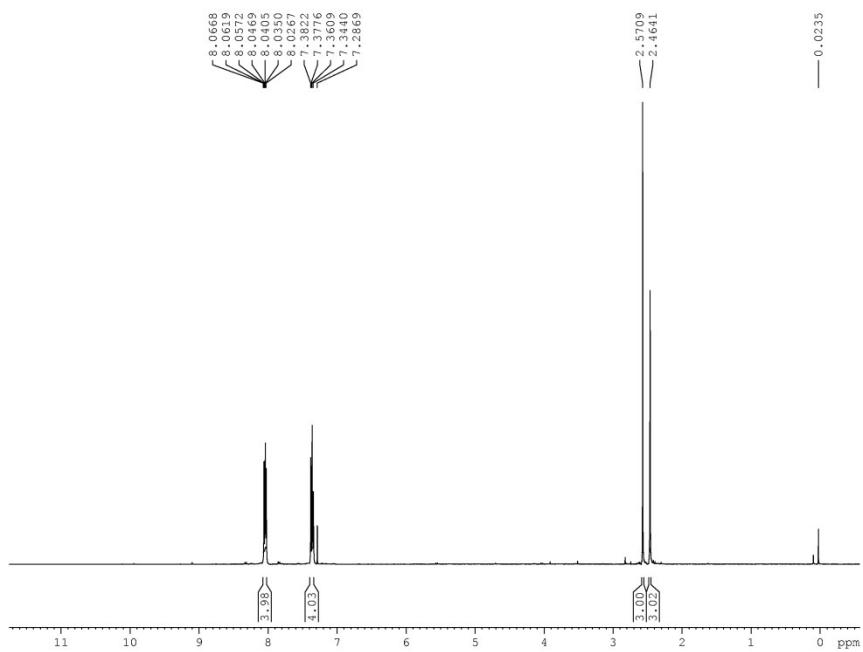
**Fig. S4:**  $^{13}\text{C}$  NMR of 2-(4-chlorophenyl)-5-(4-(methylthio)phenyl)-1,3,4-oxadiazole **4b**



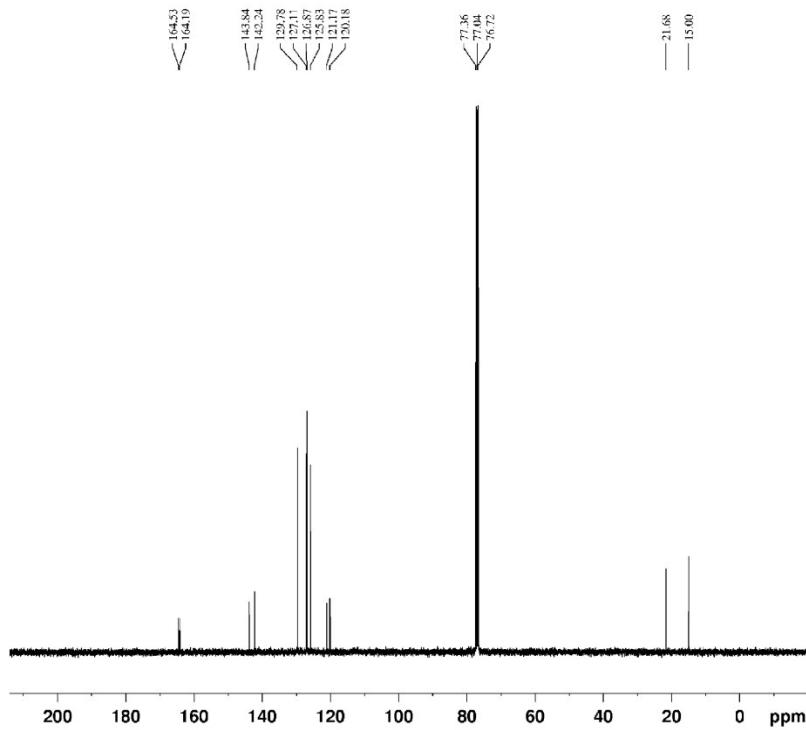
**Fig. S5:**  $^1\text{H}$  NMR of 2-(2-fluorophenyl)-5-(4-(methylthio)phenyl)-1,3,4-oxadiazole **4c**



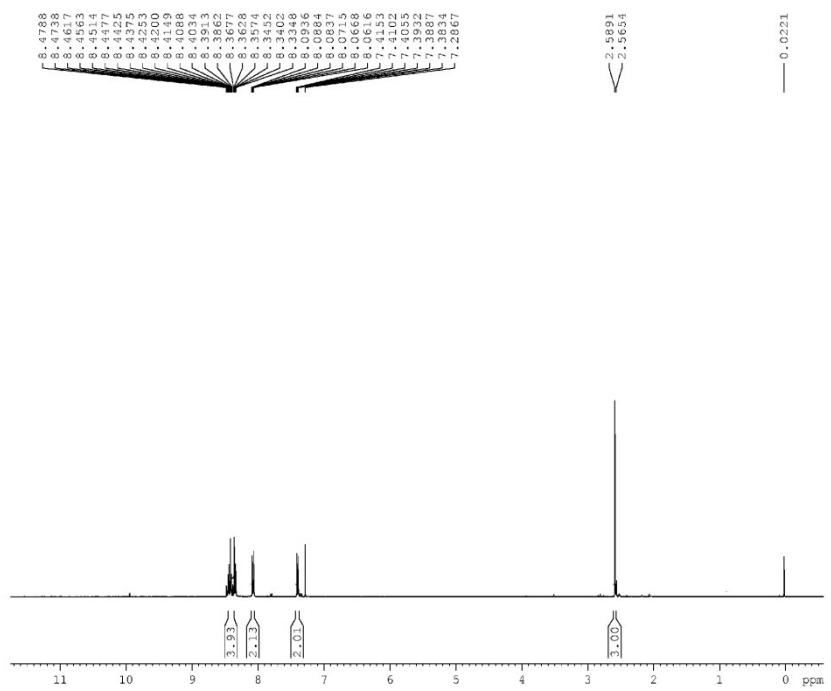
**Fig. S6:**  $^{13}\text{C}$ NMR of 2-(2-fluorophenyl)-5-(4-(methylthio)phenyl)-1,3,4-oxadiazole **4c**



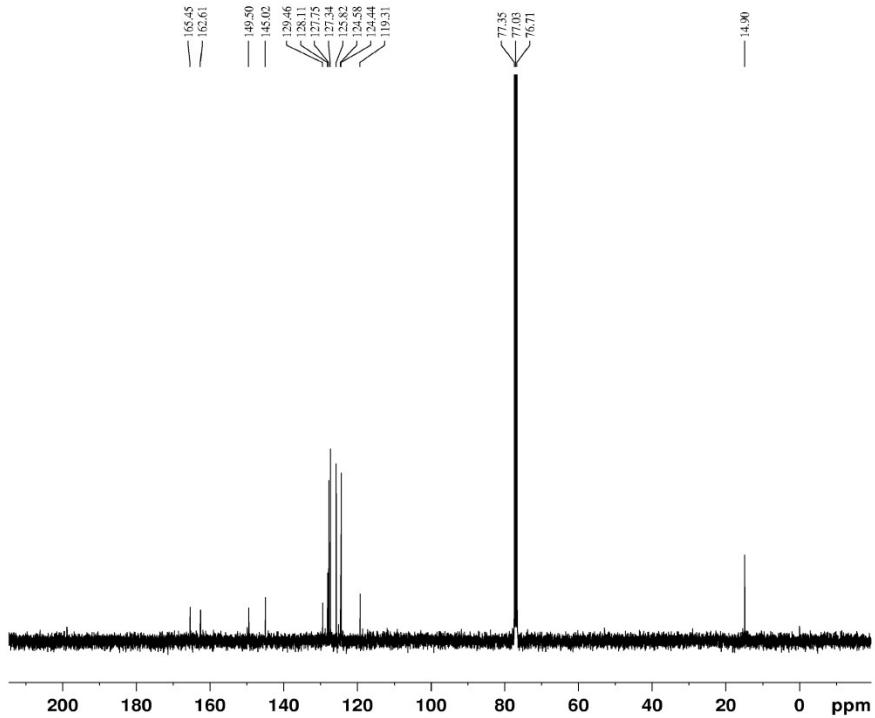
**Fig. S7:**  $^1\text{H}$  NMR of 2-(4-(methylthio)phenyl)-5-(p-tolyl)-1,3,4-oxadiazole **4d**



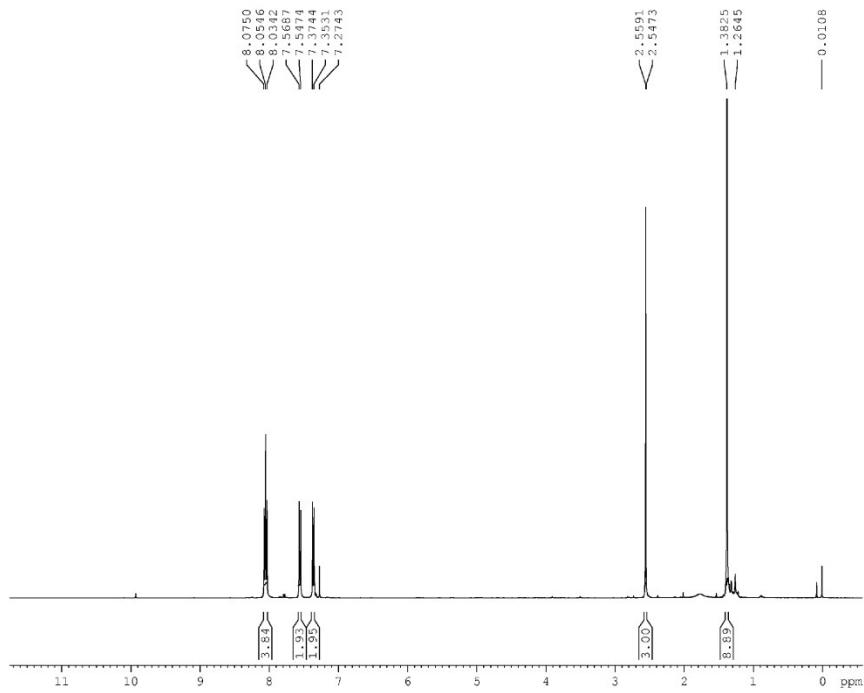
**Fig. S8:**  $^{13}\text{C}$  NMR of 2-(4-(methylthio)phenyl)-5-(p-tolyl)-1,3,4-oxadiazole **4d**



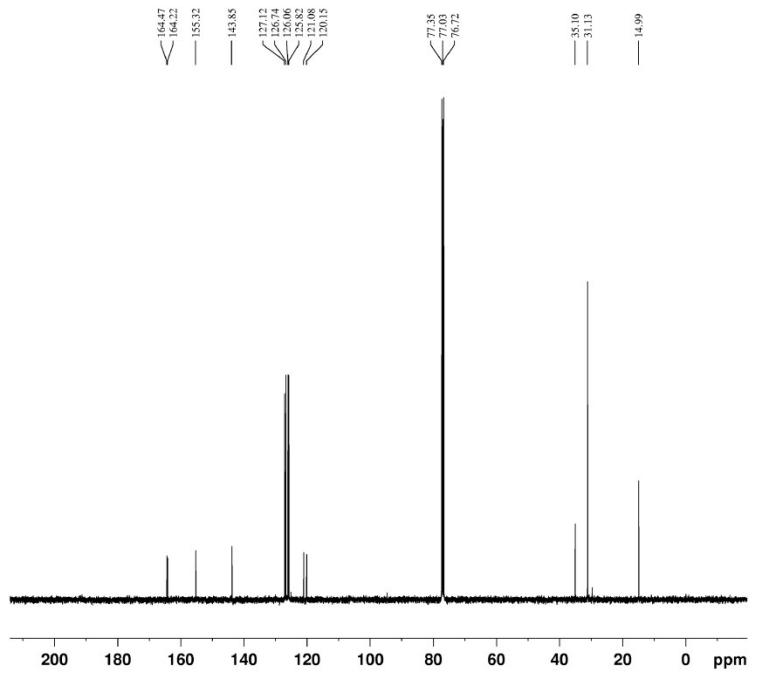
**Fig. S9:**  $^1\text{H}$  NMR of 2-(4-(methylthio)phenyl)-5-(4-nitrophenyl)-1,3,4-oxadiazole **4e**



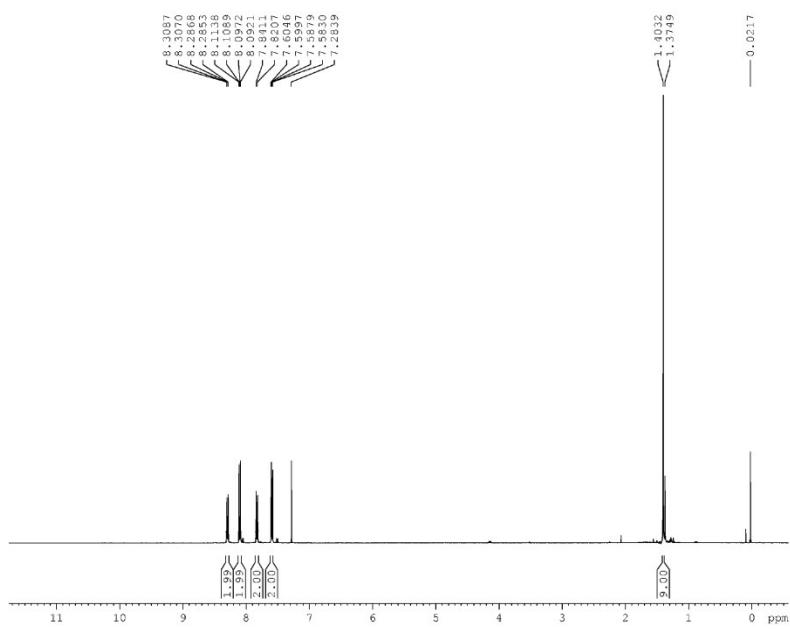
**Fig. S10:**  $^{13}\text{C}$  NMR of 2-(4-(methylthio)phenyl)-5-(4-nitrophenyl)-1,3,4-oxadiazole **4e**



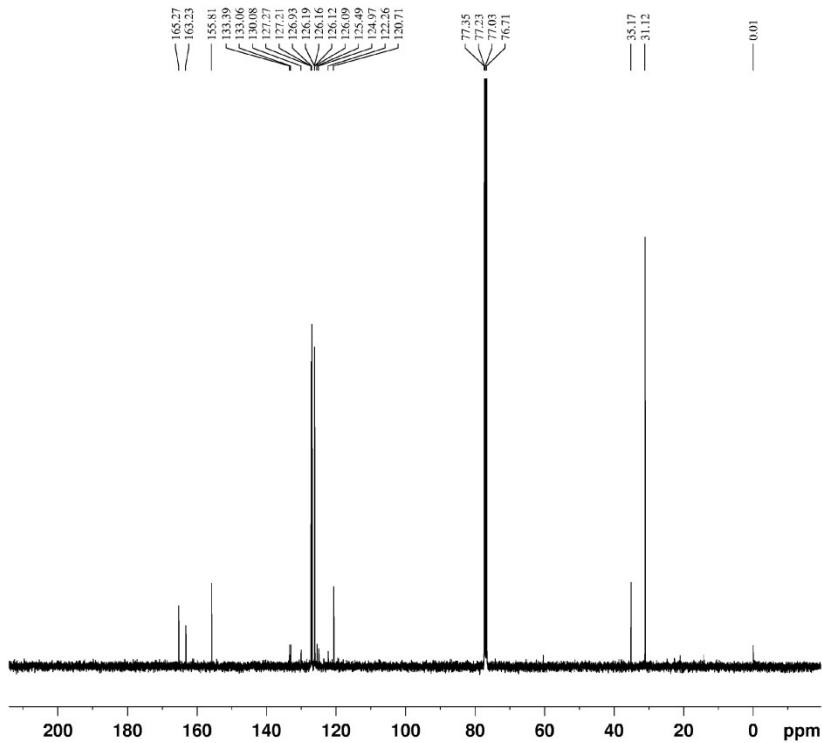
**Fig. S11:**  $^1\text{H}$  NMR of 2-(4-(tert-butyl)phenyl)-5-(4-(methylthio)phenyl)-1,3,4-oxadiazole **4f**



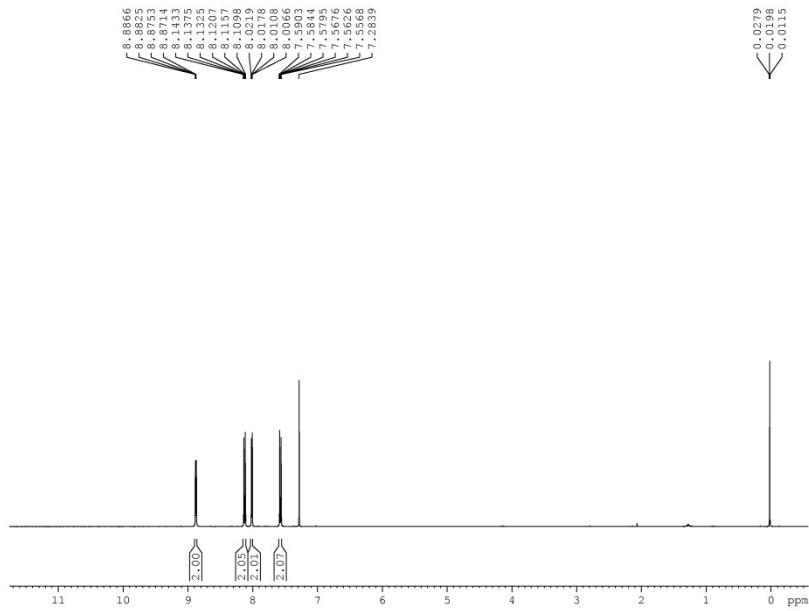
**Fig. S12:**  $^{13}\text{C}$  NMR of 2-(4-(tert-butyl)phenyl)-5-(4-(methylthio)phenyl)-1,3,4-oxadiazole **4f**



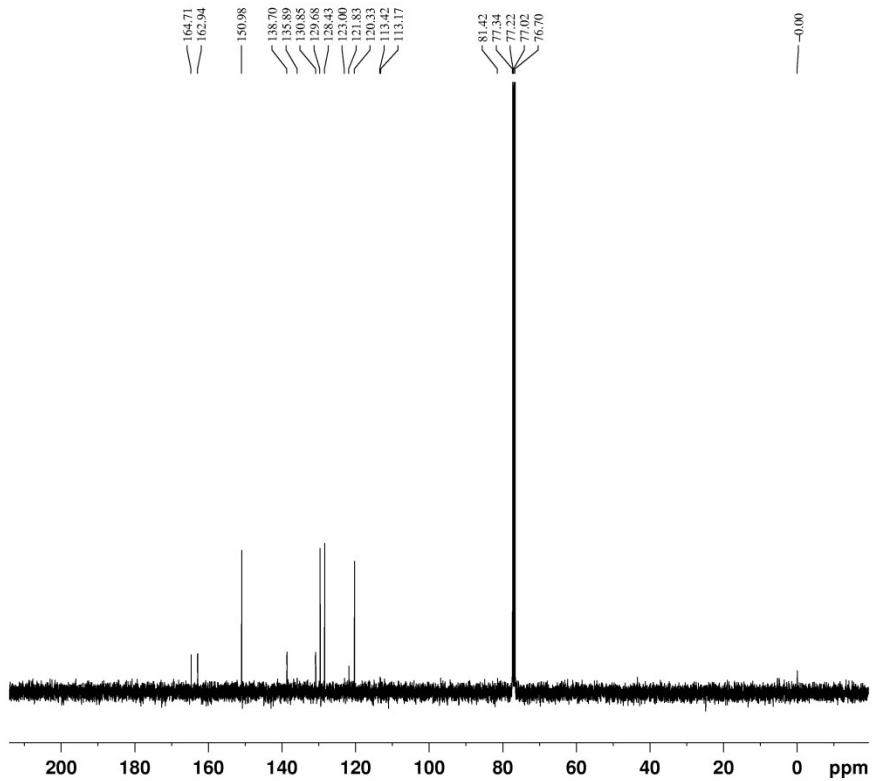
**Fig. S13:**  $^1\text{H}$  NMR of 2-(4-(tert-butyl)phenyl)-5-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazole **4g**



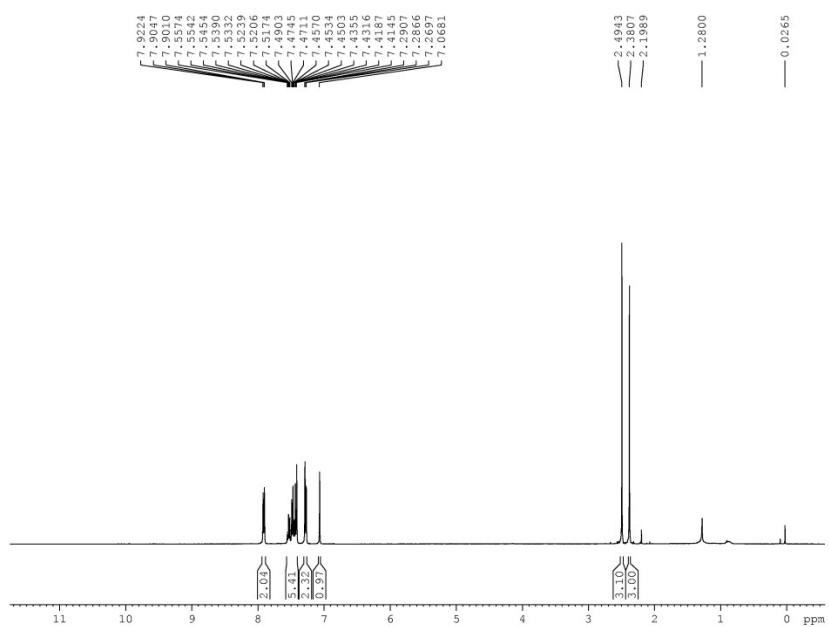
**Fig. S14:**  $^{13}\text{C}$  NMR of 2-(4-(tert-butyl)phenyl)-5-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazole **4g**



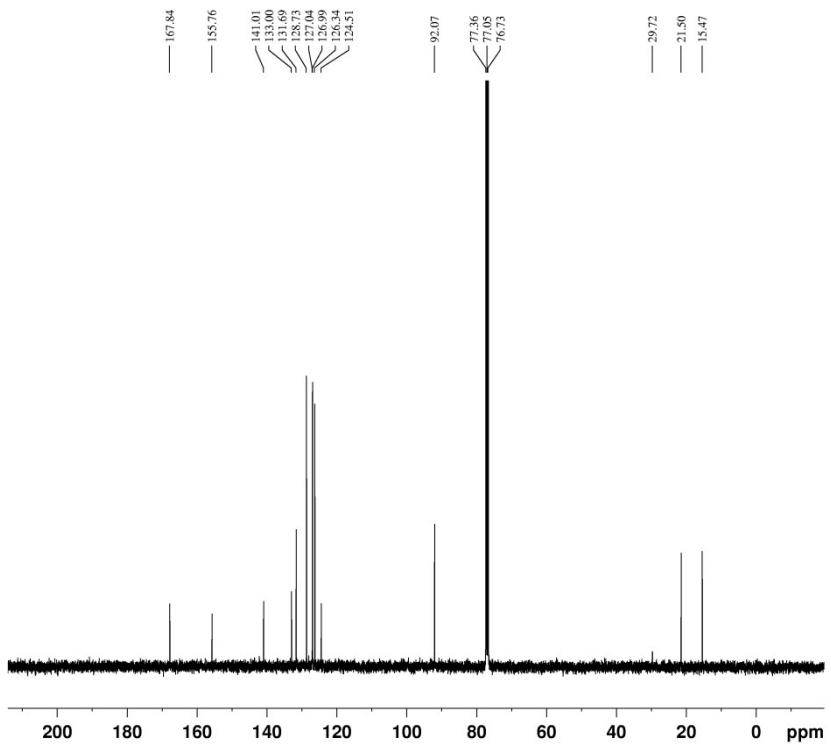
**Fig. S15:**  $^1\text{H}$  NMR of 2-(4-chlorophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazole **4h**



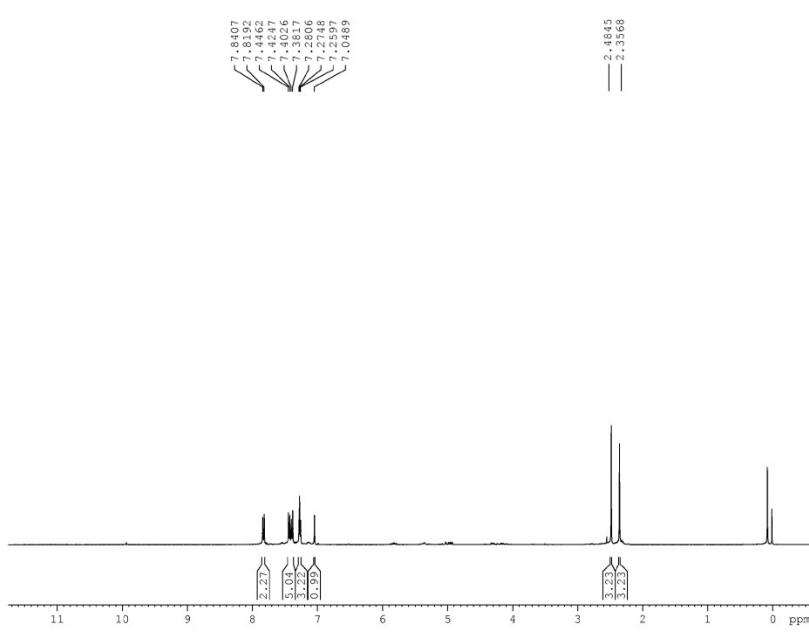
**Fig. S16:**  $^{13}\text{C}$  NMR of 2-(4-chlorophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazole **4h**



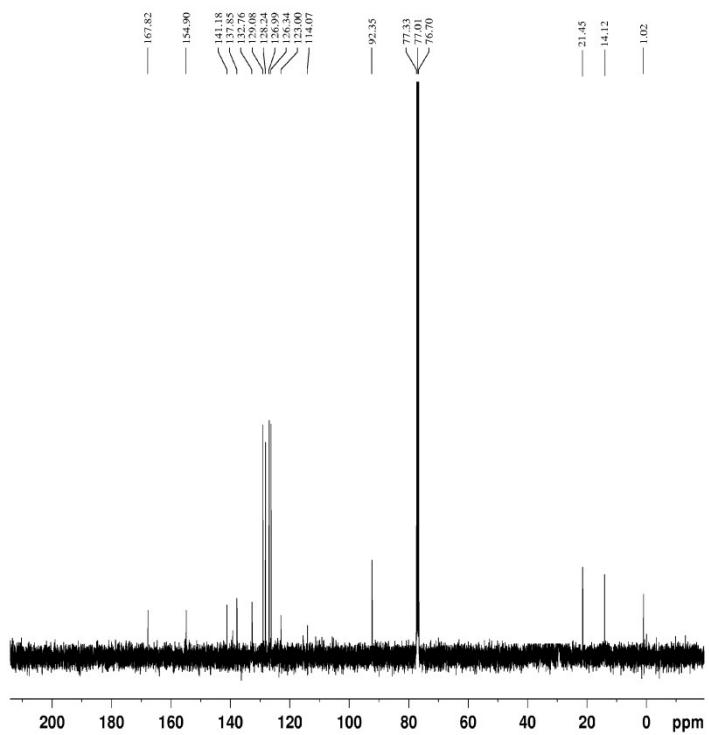
**Fig. S17:**  $^1\text{H}$  NMR of 1-(2-(4-(methylthio)phenyl)-5-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone **5a**



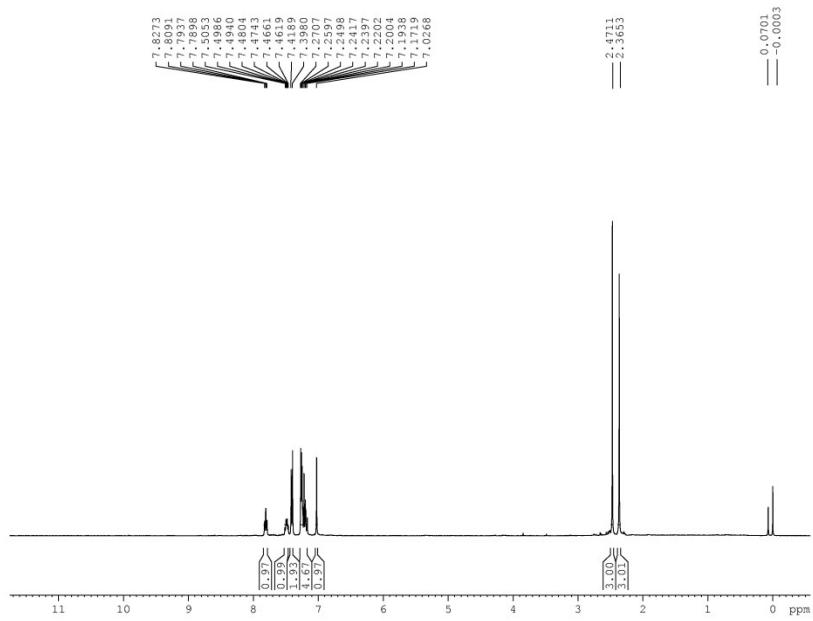
**Fig. S18:**  $^{13}\text{C}$  NMR of 1-(2-(4-(methylthio)phenyl)-5-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone **5a**



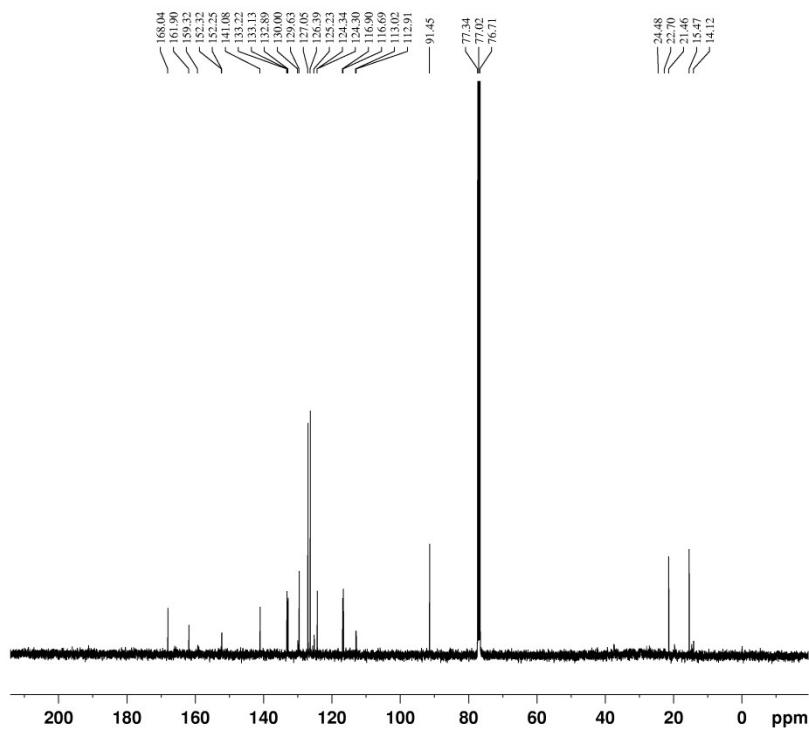
**Fig. S19:**  $^1\text{H}$  NMR of 1-(5-(4-chlorophenyl)-2-(4-(methylthio)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **5b**



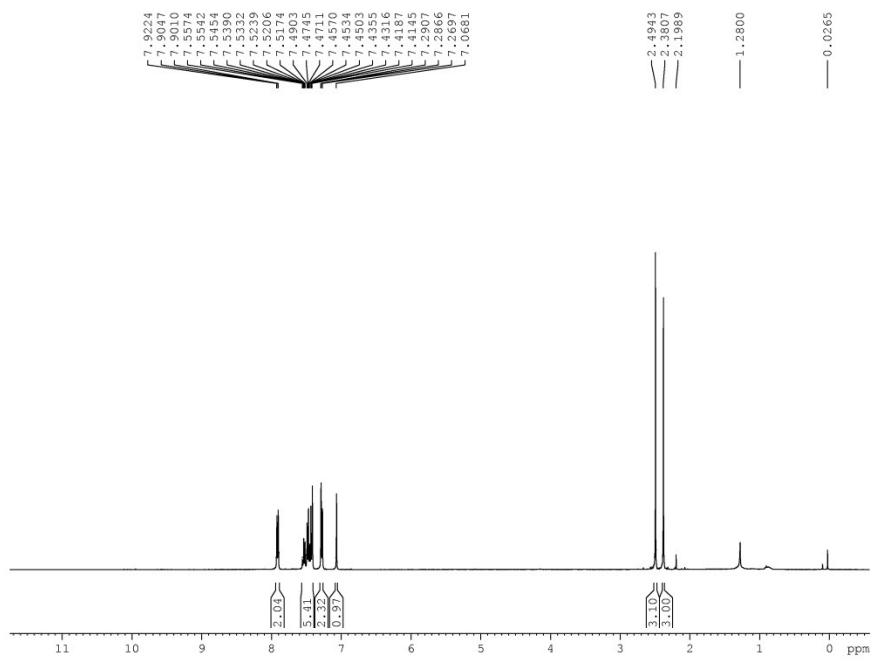
**Fig. S20:**  $^{13}\text{C}$  NMR of 1-(5-(4-chlorophenyl)-2-(4-(methylthio)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **5b**



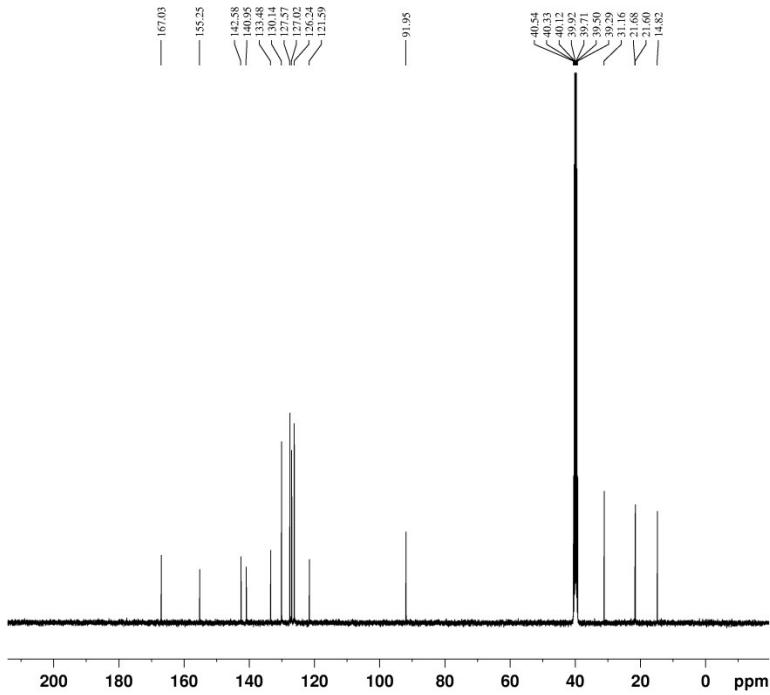
**Fig. S21:**  $^1\text{H}$  NMR of 1-(5-(2-fluorophenyl)-2-(4-(methylthio)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **5c**



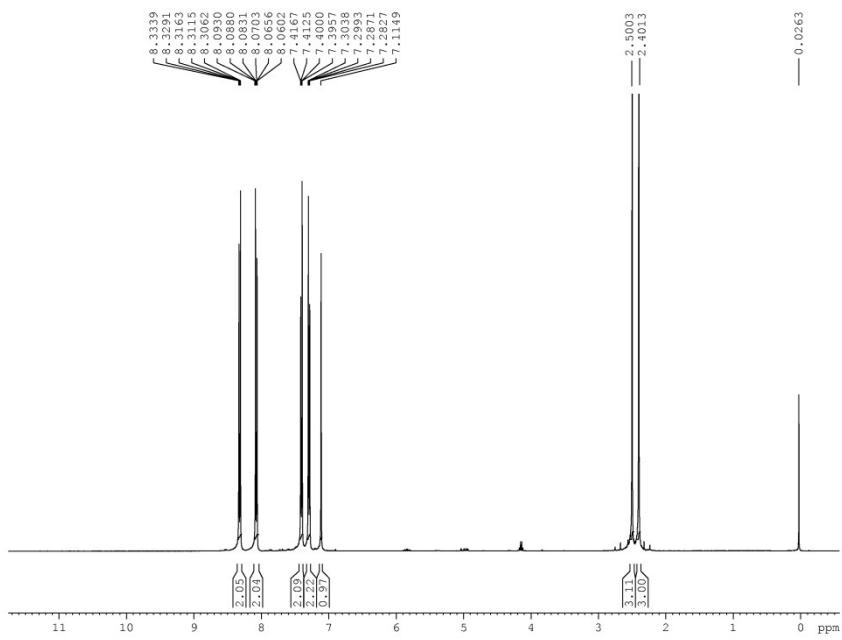
**Fig. S22**  $^{13}\text{C}$  NMR of 1-(5-(2-fluorophenyl)-2-(4-(methylthio)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **5c**



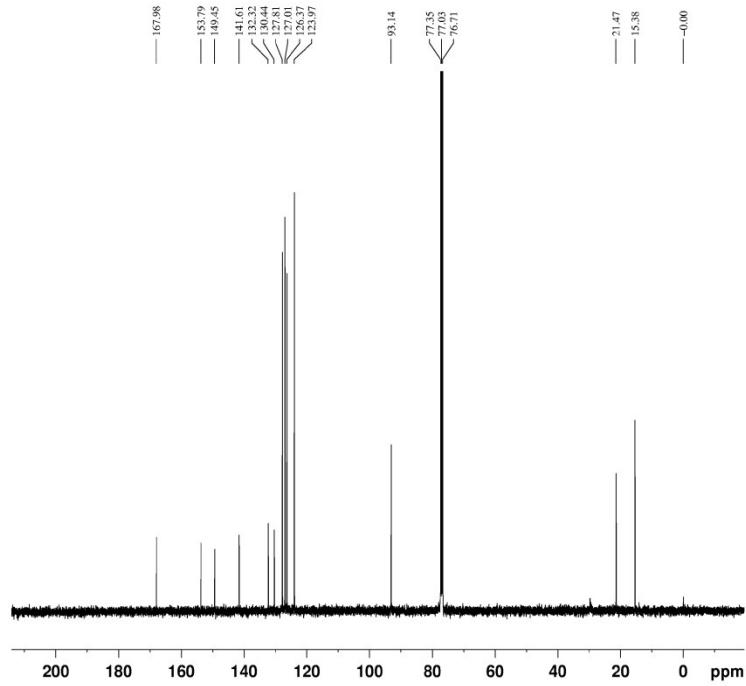
**Fig. S23:**  $^1\text{H}$  NMR of 1-(2-(4-(methylthio)phenyl)-5-(p-tolyl)-1,3,4-oxadiazol-3(2H)yl)ethanone **5d**



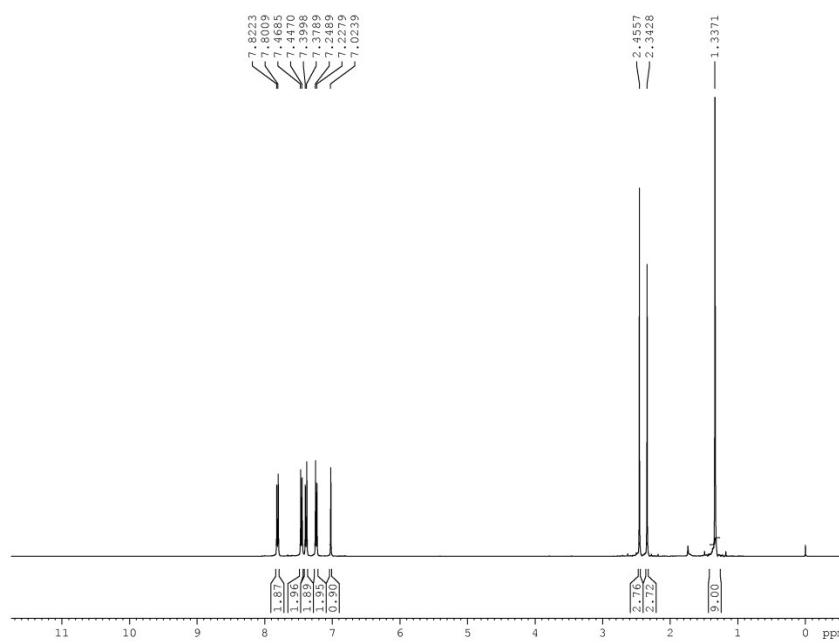
**Fig. S24:**  $^{13}\text{C}$  NMR of 1-(2-(4-(methylthio)phenyl)-5-(p-tolyl)-1,3,4-oxadiazol-3(2H)yl)ethanone **5d**



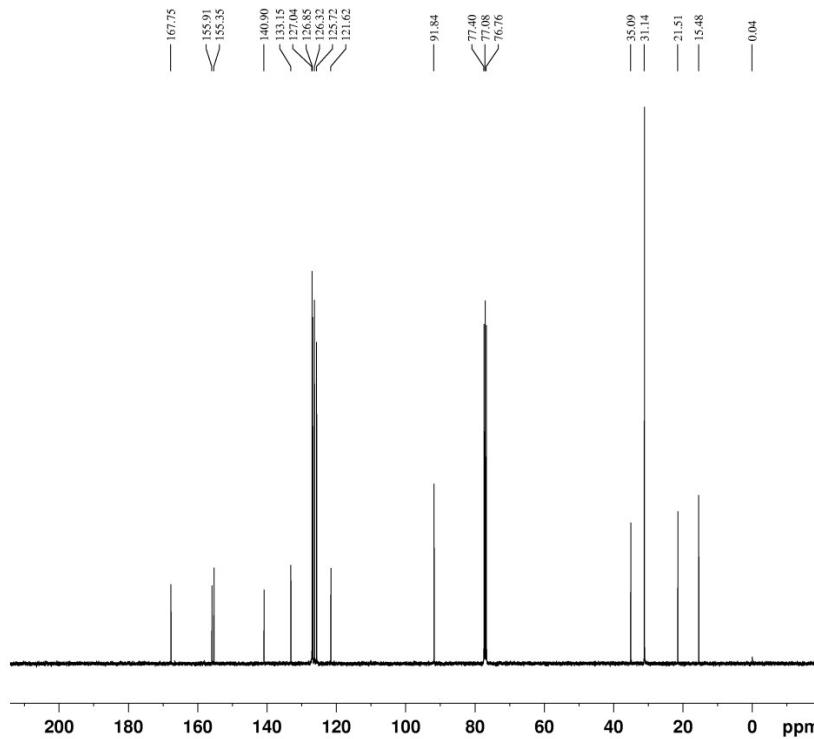
**Fig. S25:**  $^1\text{H}$  NMR of 1-(2-(4-(methylthio)phenyl)-5-(4-nitrophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **5e**



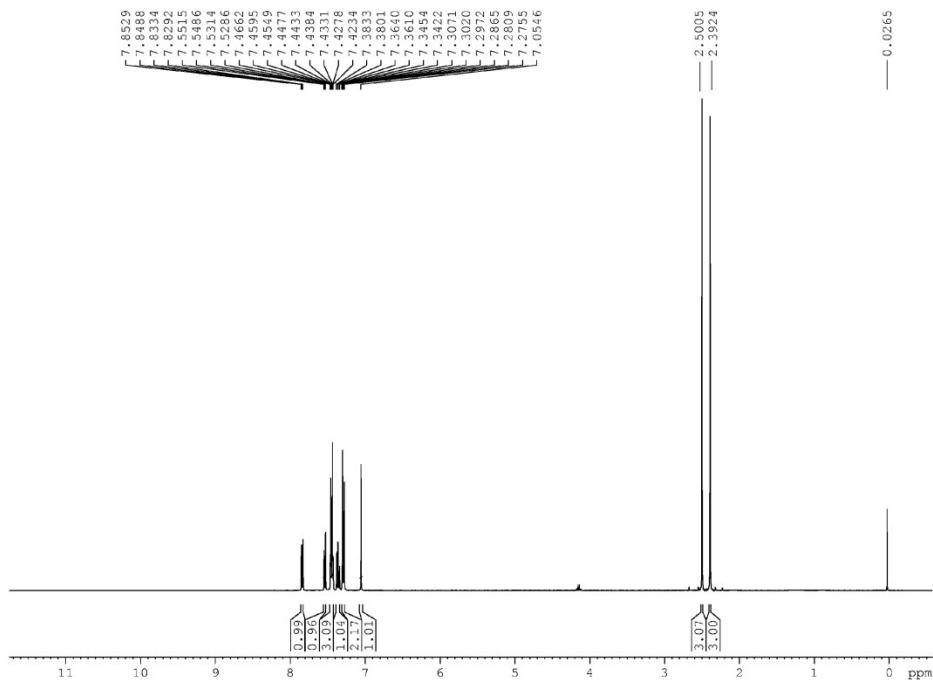
**Fig. S26:**  $^{13}\text{C}$  NMR of 1-(2-(4-(methylthio)phenyl)-5-(4-nitrophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **5e**



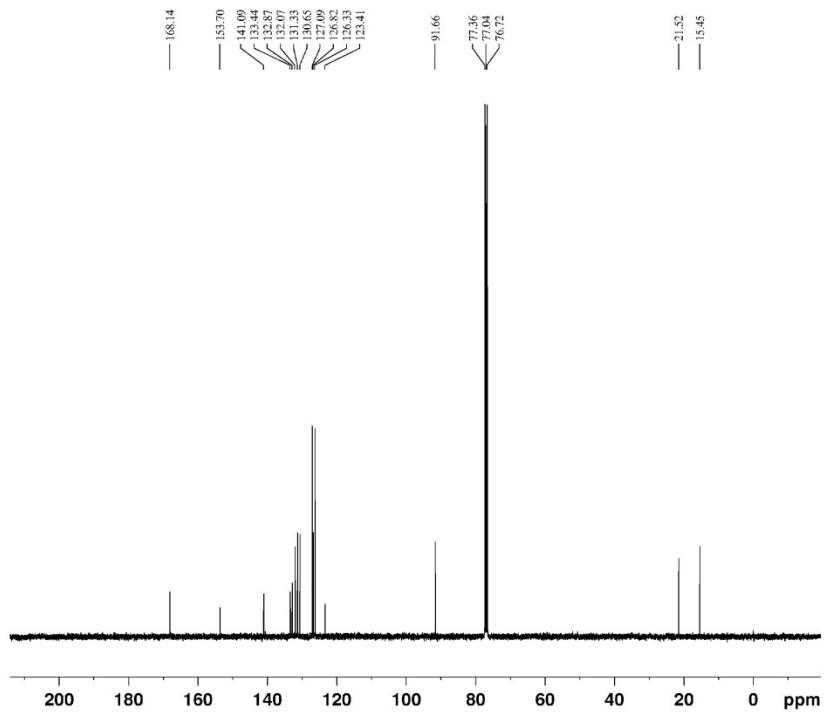
**Fig. S27:**  $^1\text{H}$  NMR of 1-(5-(4-(tert-butyl)phenyl)-2-(4-(methylthio)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **5f**



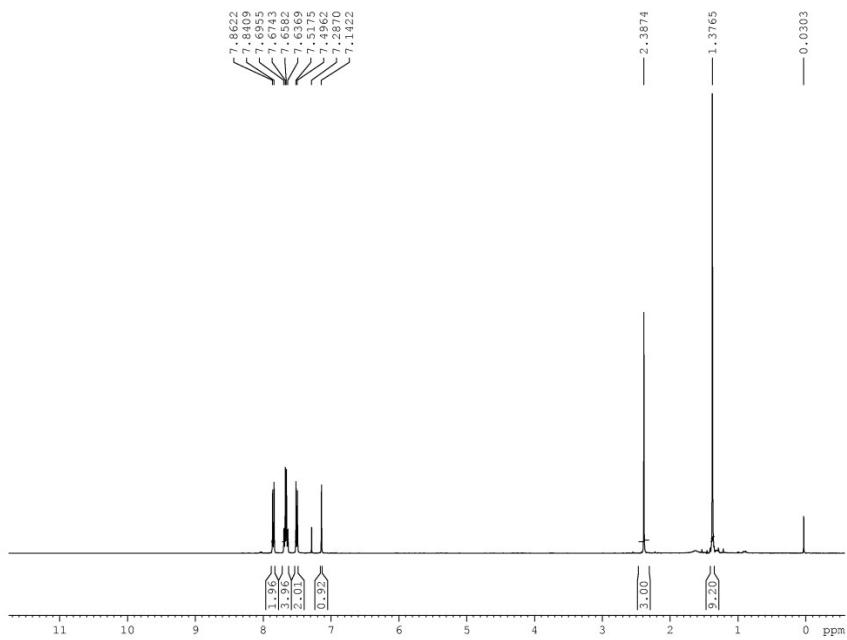
**Fig. S28:**  $^{13}\text{C}$  NMR of 1-(5-(4-(tert-butyl)phenyl)-2-(4-(methylthio)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **5f**



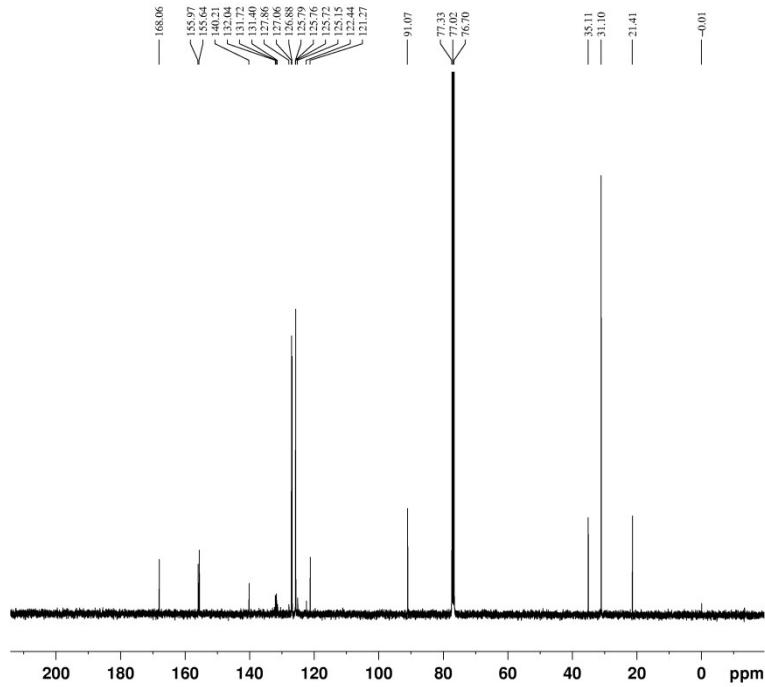
**Fig. S29:**  $^1\text{H}$  NMR of 1-(5-(2-chlorophenyl)-2-(4-(methylthio)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **5g**



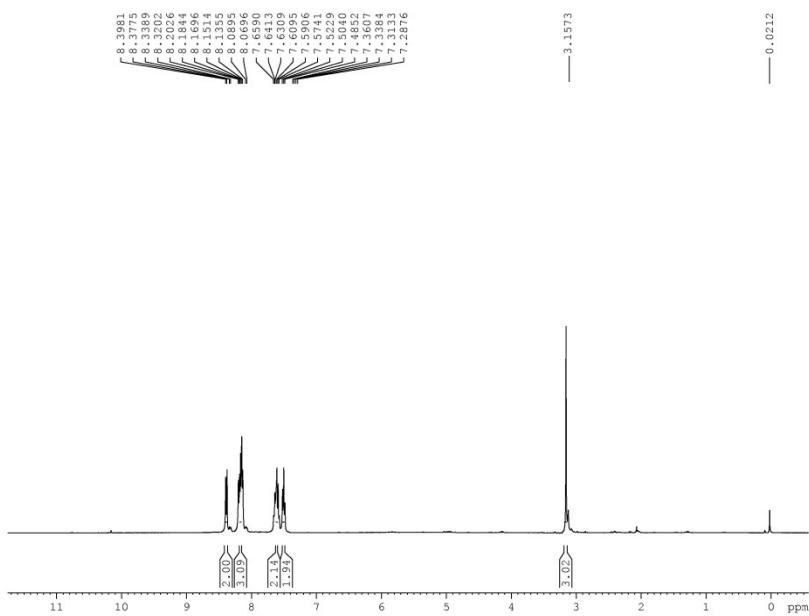
**Fig. S30:**  $^{13}\text{C}$  NMR of 1-(5-(2-chlorophenyl)-2-(4-(methylthio)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **5g**



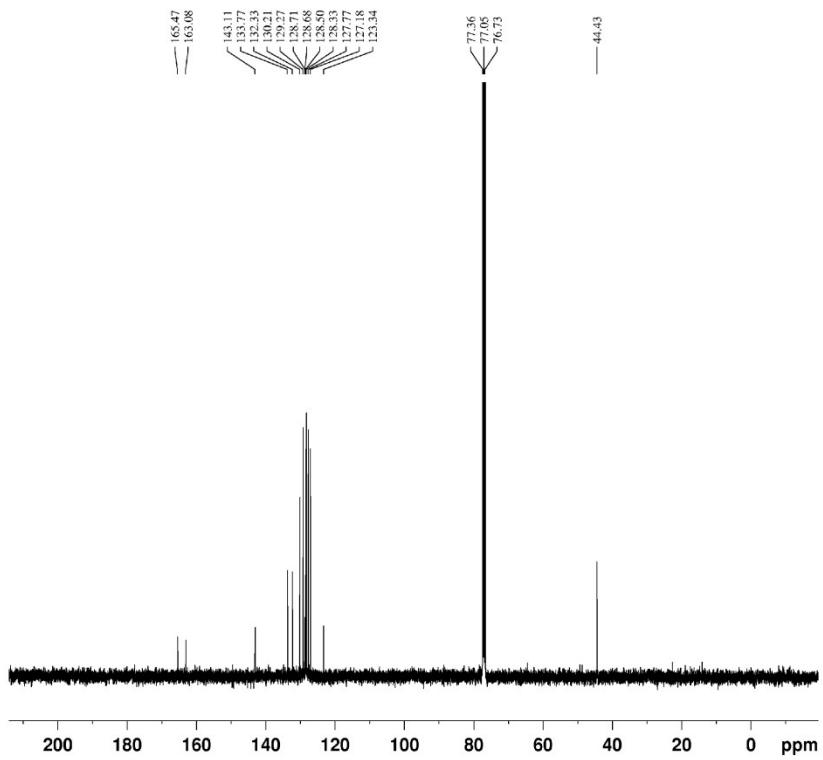
**Fig. S31:**  $^1\text{H}$  NMR of 1-(5-(4-(tert-butyl)phenyl)-2-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **5h**



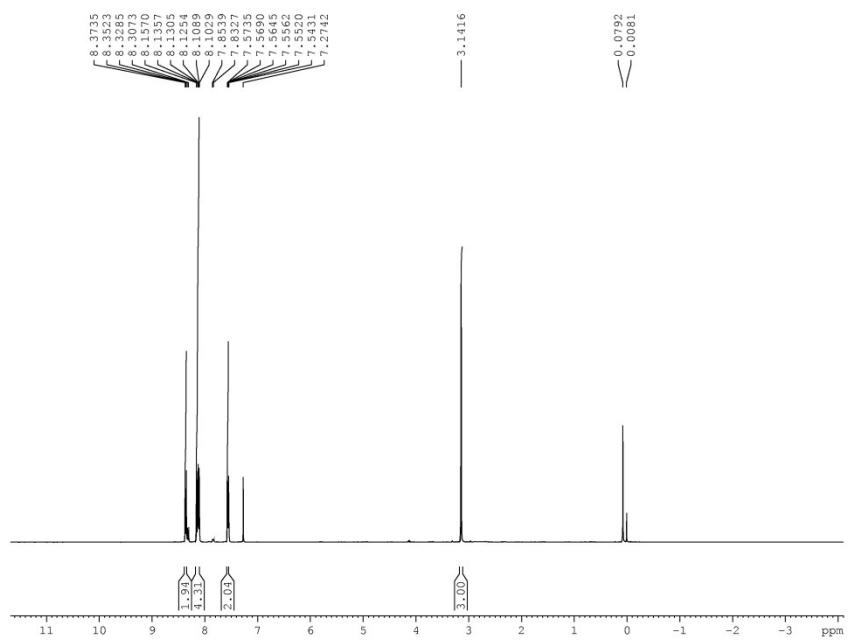
**Fig. S32:**  $^{13}\text{C}$  NMR of 1-(5-(4-(tert-butyl)phenyl)-2-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **5h**



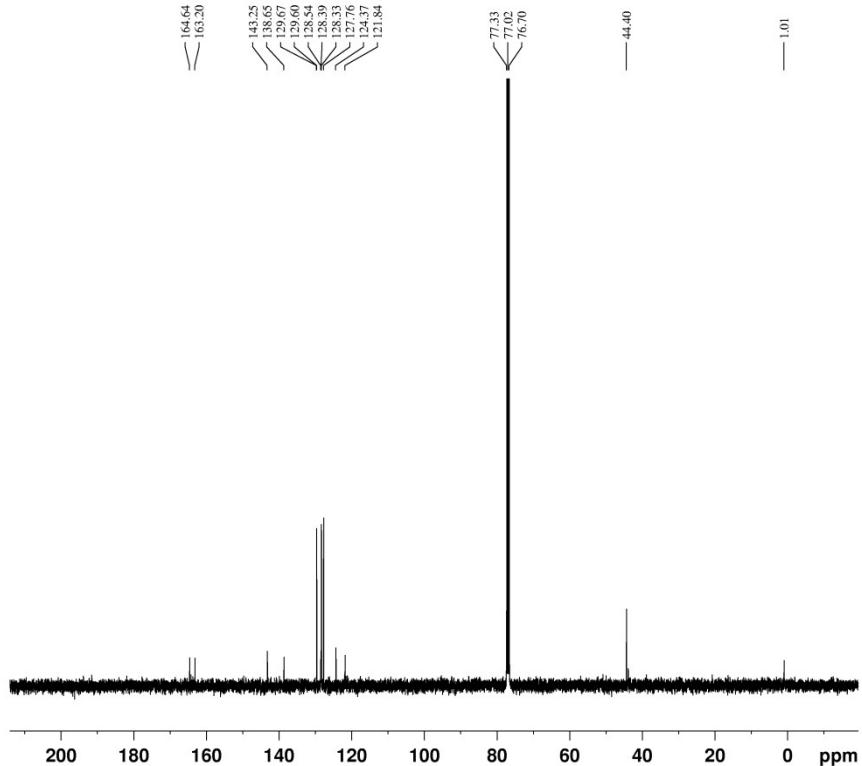
**Fig. S33:**  $^1\text{H}$  NMR of 2-(4-(methylsulfonyl)phenyl)-5-phenyl-1,3,4-oxadiazole **6a**



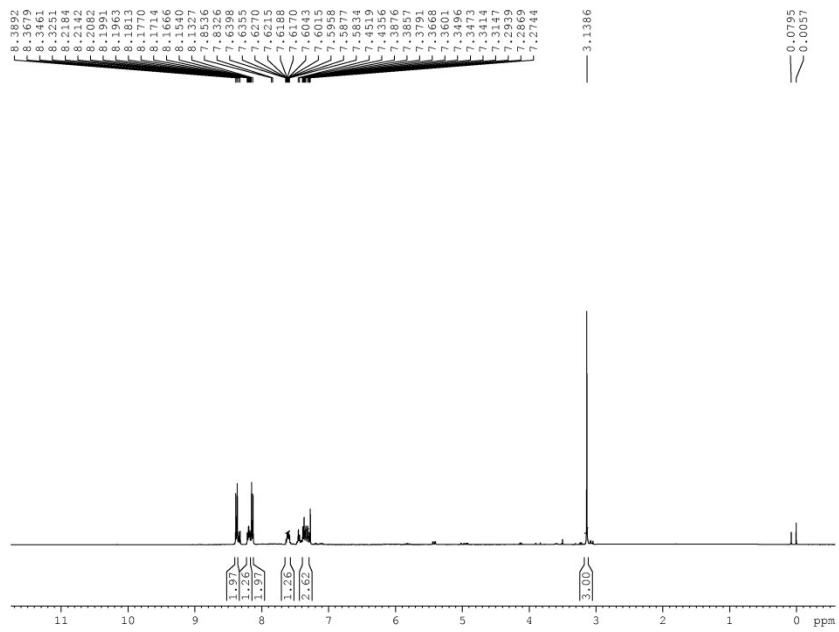
**Fig. S34:**  $^{13}\text{C}$  NMR of 2-(4-(methylsulfonyl)phenyl)-5-phenyl-1,3,4-oxadiazole **6a**



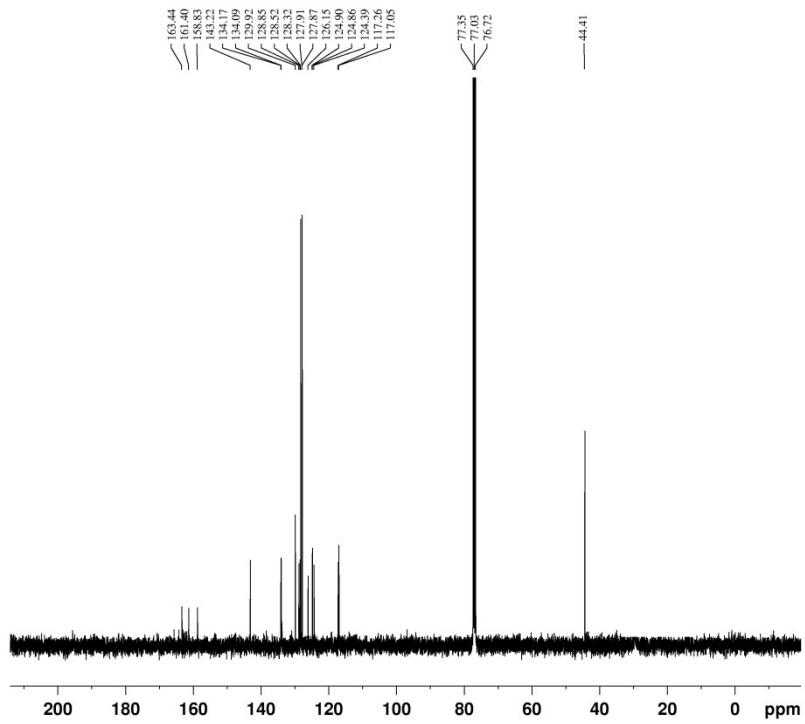
**Fig. S35:**  $^1\text{H}$  NMR of 2-(4-chlorophenyl)-5-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazole **6b**



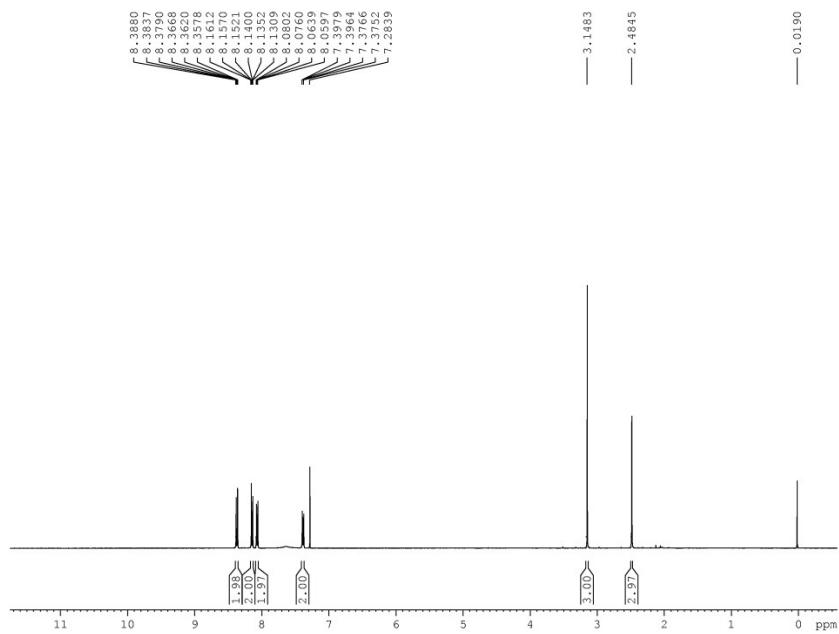
**Fig. S36:**  $^{13}\text{C}$  NMR of 2-(4-chlorophenyl)-5-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazole **6b**



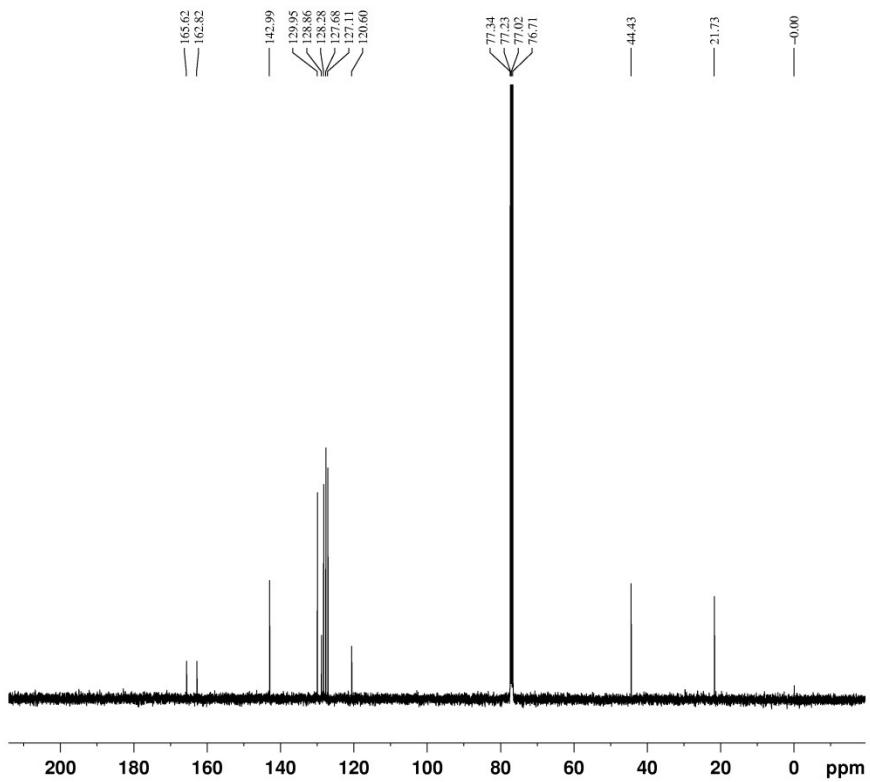
**Fig. S37:**  $^1\text{H}$  NMR of 2-(2-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazole **6c**



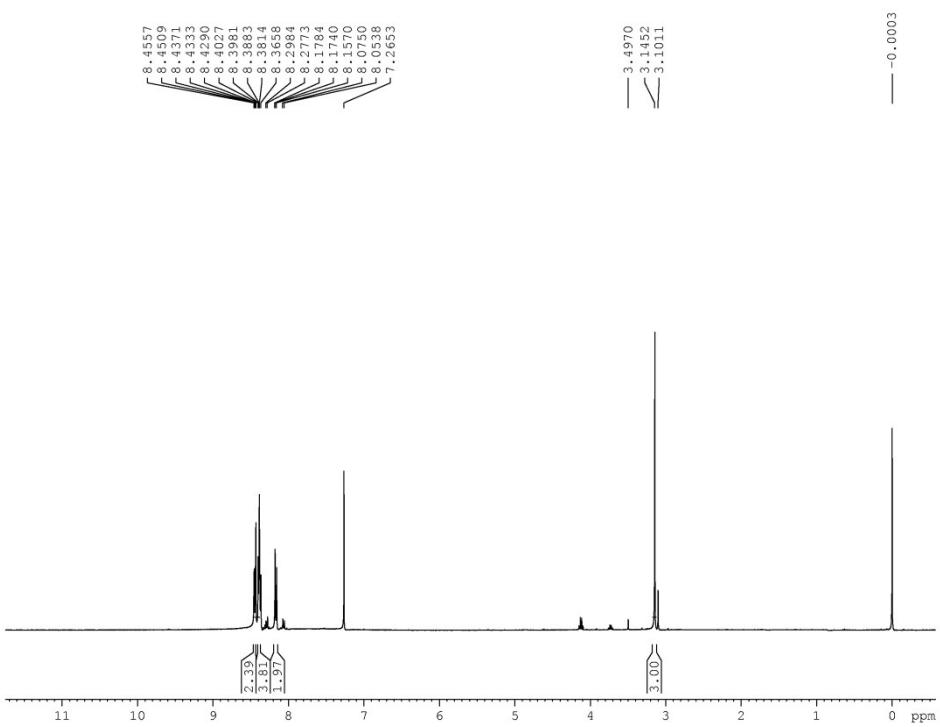
**Fig. S38:**  $^{13}\text{C}$  NMR of 2-(2-fluorophenyl)-5-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazole **6c**



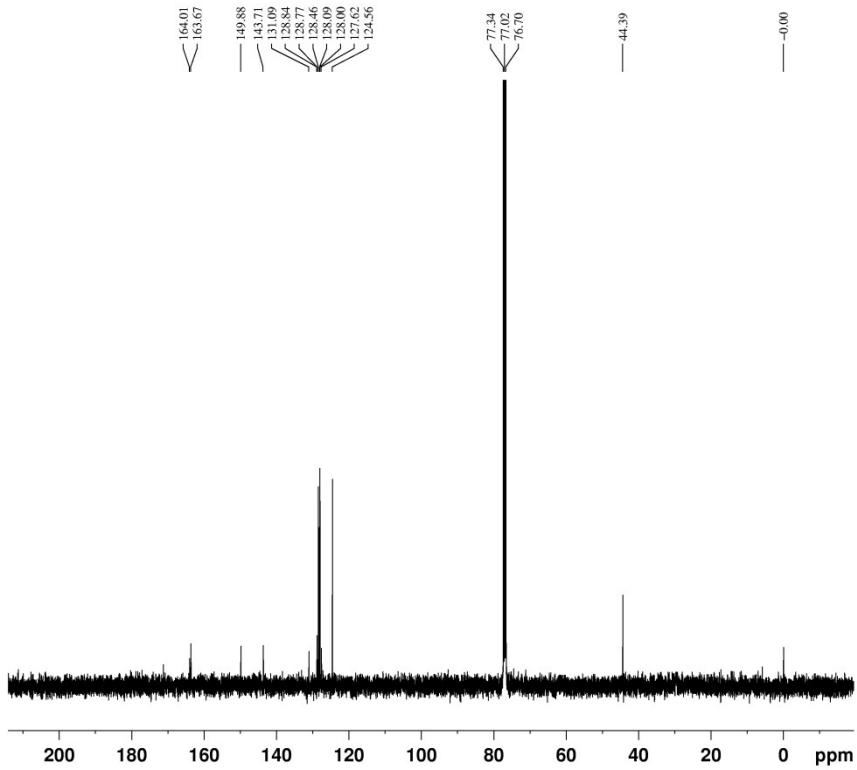
**Fig. S39:**  $^1\text{H}$  NMR of 2-(4-(methylsulfonyl)phenyl)-5-(p-tolyl)-1,3,4-oxadiazole **6d**



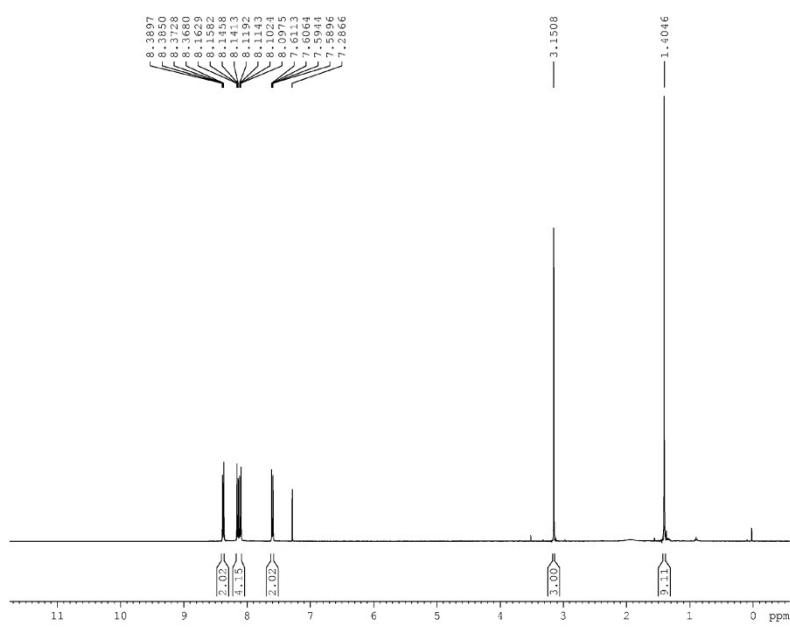
**Fig. S40:**  $^{13}\text{C}$  NMR of 2-(4-(methylsulfonyl)phenyl)-5-(p-tolyl)-1,3,4-oxadiazole **6d**



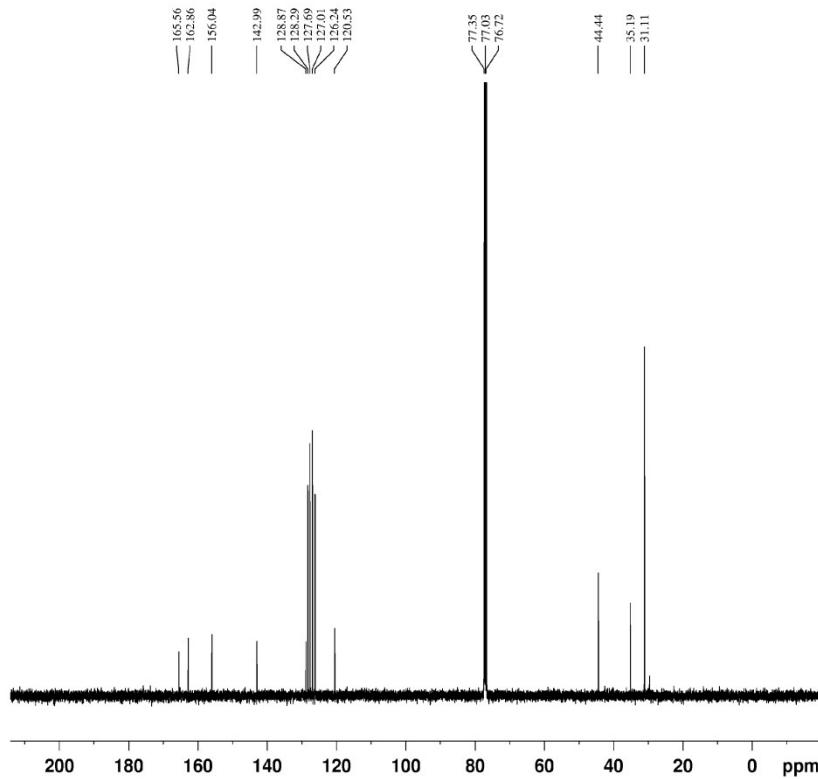
**Fig. S41:**  $^1\text{H}$  NMR of 2-(4-(methylsulfonyl)phenyl)-5-(4-nitrophenyl)-1,3,4-oxadiazole **6e**



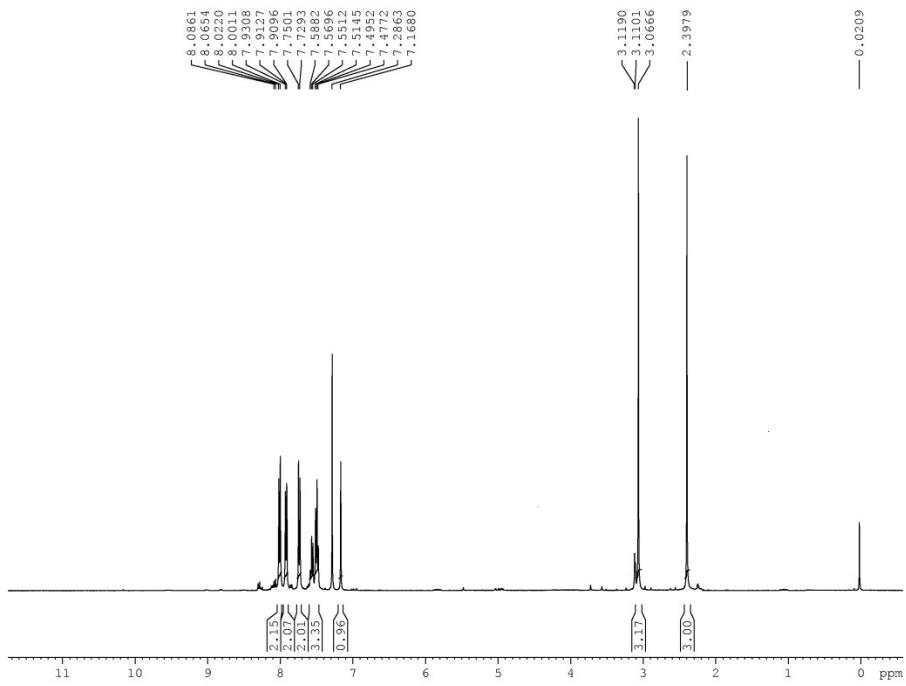
**Fig. S42:**  $^{13}\text{C}$  NMR of 2-(4-(methylsulfonyl)phenyl)-5-(4-nitrophenyl)-1,3,4-oxadiazole **6e**



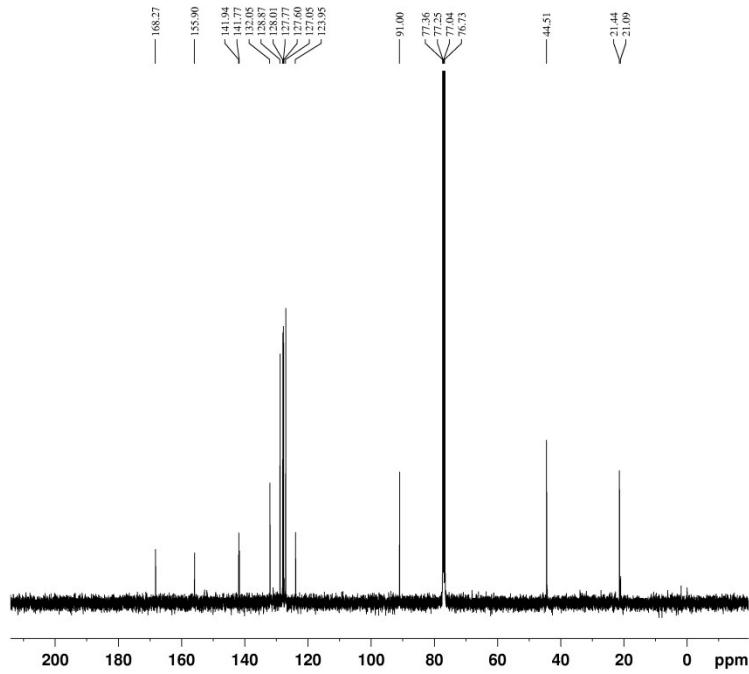
**Fig. S43:**  $^1\text{H}$  NMR of 2-(4-(tert-butyl)phenyl)-5-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazole **6f**



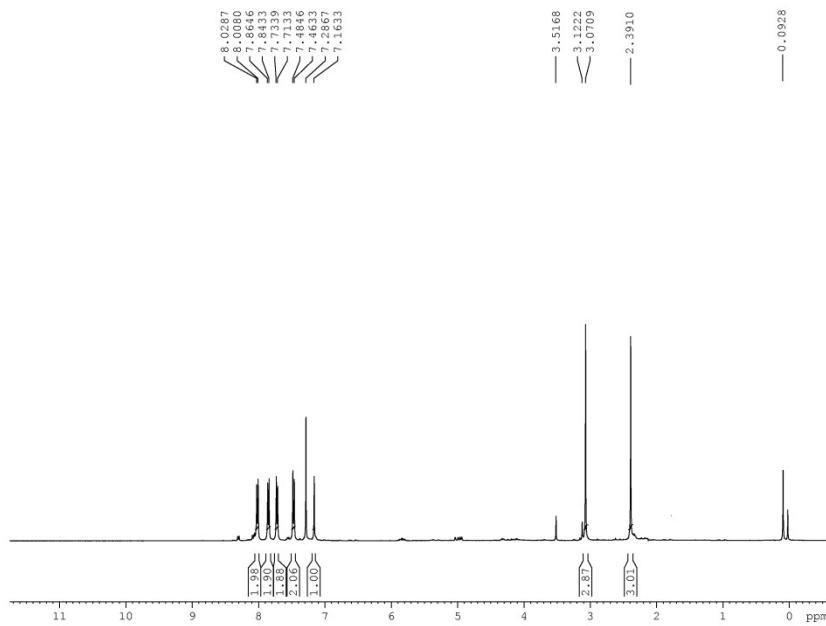
**Fig. S44:**  $^{13}\text{C}$  NMR of 2-(4-(tert-butyl)phenyl)-5-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazole **6f**



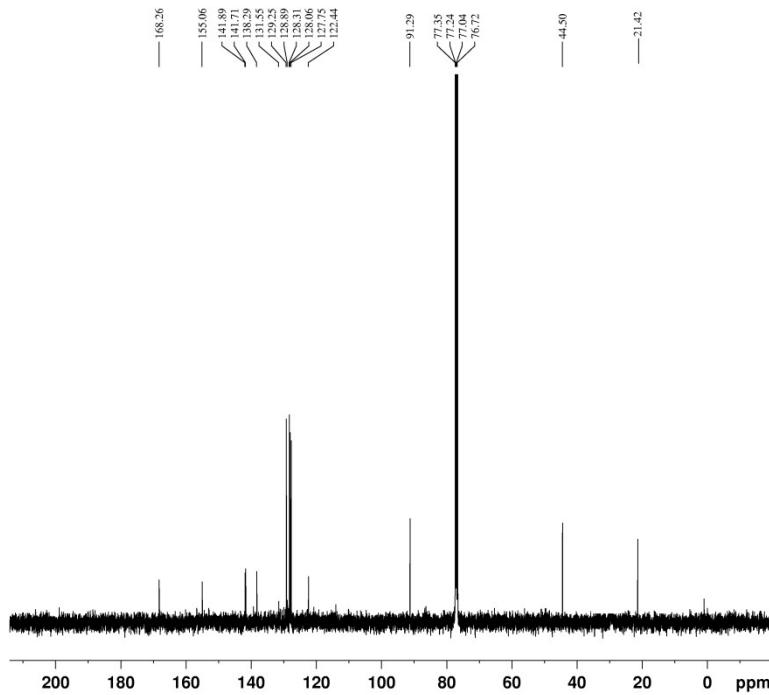
**Fig. S45:**  $^1\text{H}$  NMR of 1-(2-(4-(methylsulfonyl)phenyl)-5-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone **7a**



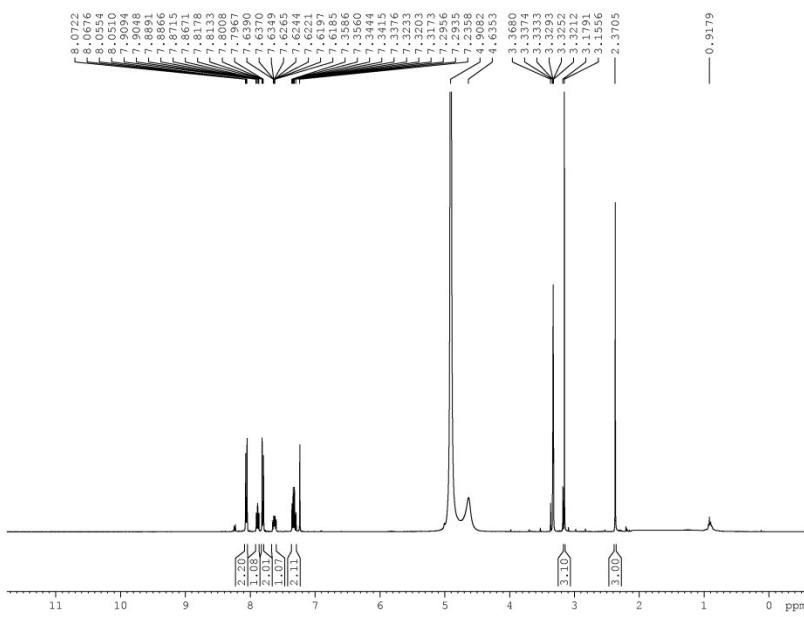
**Fig. S46:**  $^{13}\text{C}$  NMR of 1-(2-(4-(methylsulfonyl)phenyl)-5-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone **7a**



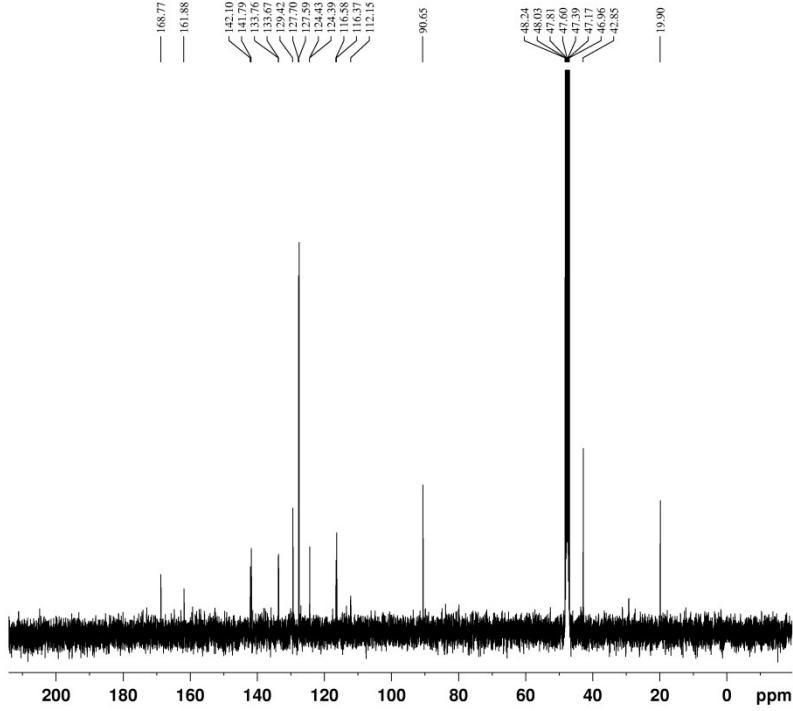
**Fig. S47:**  $^1\text{H}$  NMR of 1-(5-(4-chlorophenyl)-2-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **7b**



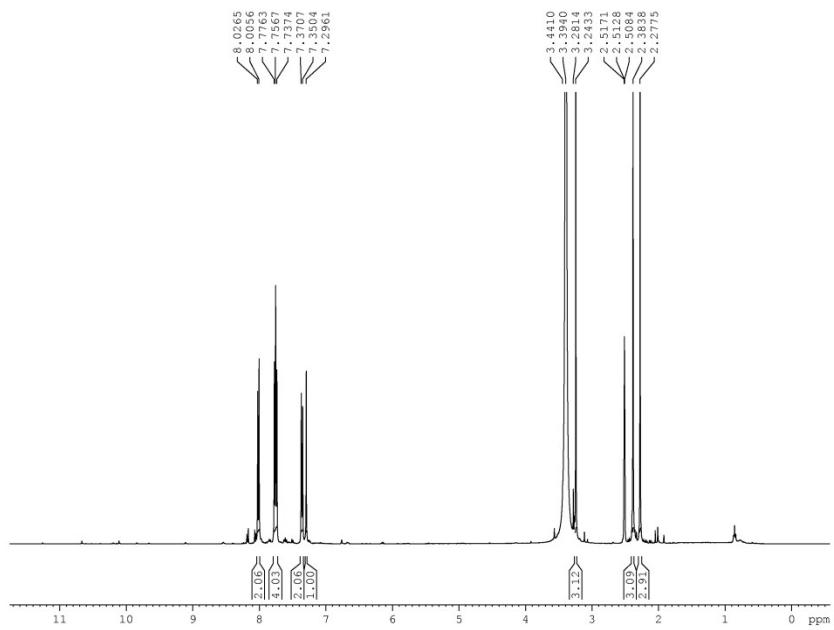
**Fig. S48:**  $^{13}\text{C}$  NMR of 1-(5-(4-chlorophenyl)-2-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **7b**



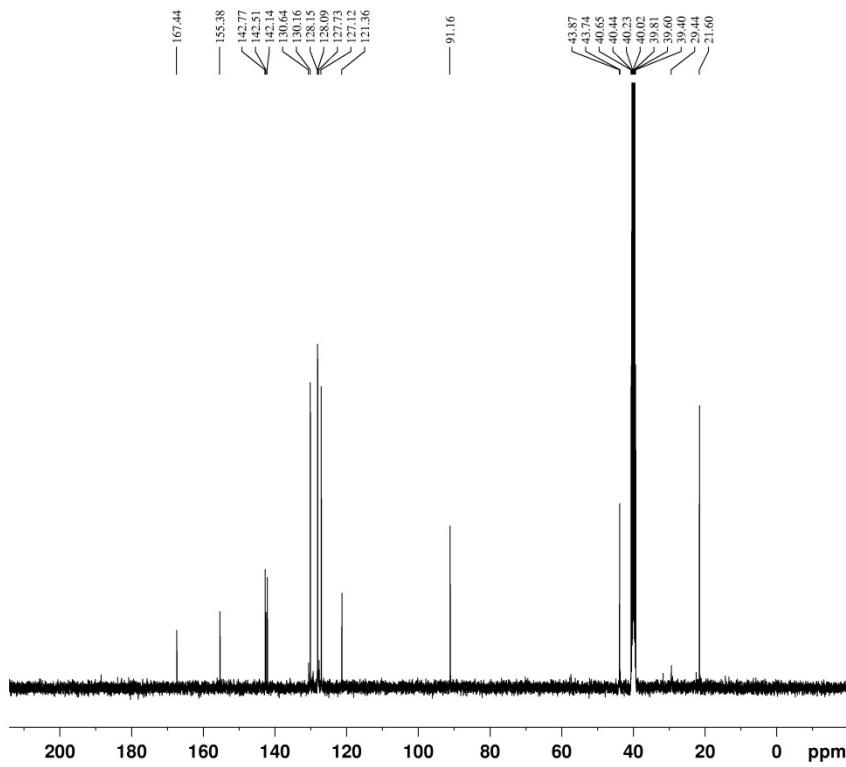
**Fig. S49:**  $^1\text{H}$  NMR of 1-(5-(2-fluorophenyl)-2-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **7c**



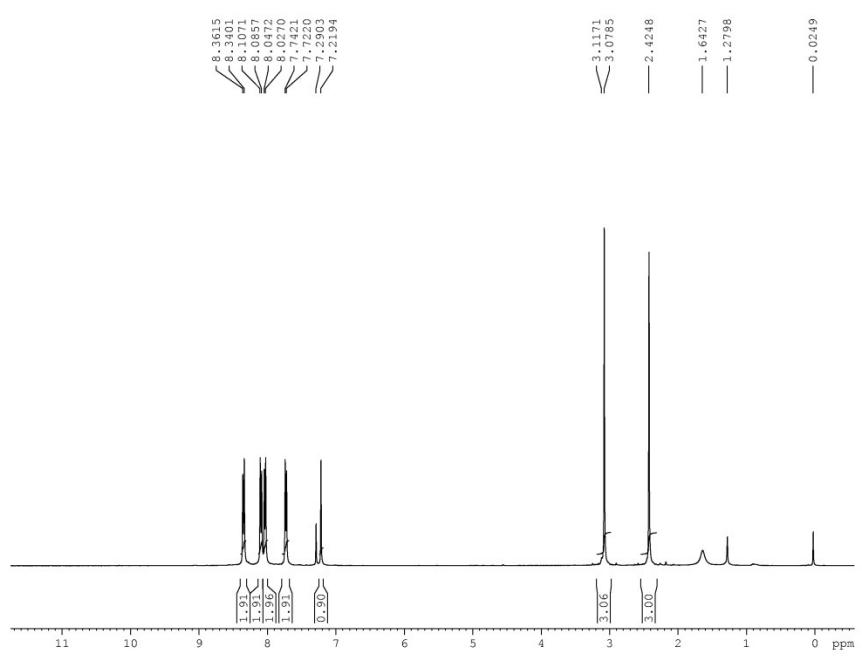
**Fig. S50:**  $^{13}\text{C}$  NMR of 1-(5-(2-fluorophenyl)-2-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **7c**



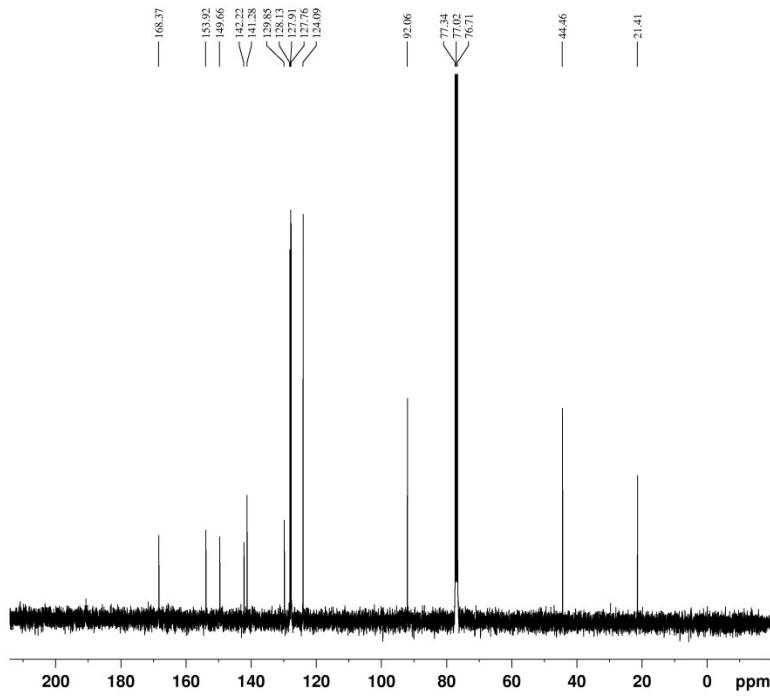
**Fig. S51:**  $^1\text{H}$  NMR of 1-(2-(4-(methylsulfonyl)phenyl)-5-(p-tolyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **7d**



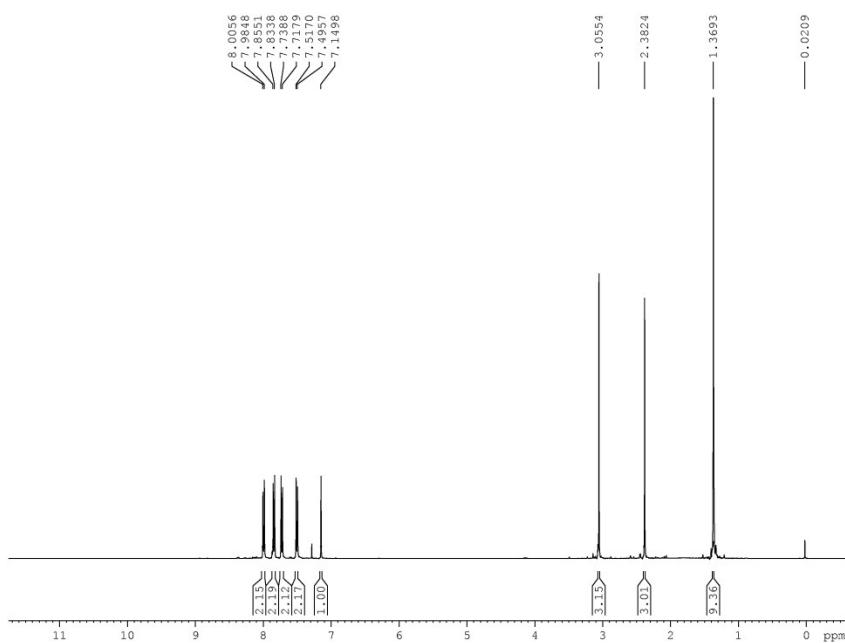
**Fig. S52:**  $^{13}\text{C}$  NMR of 1-(2-(4-(methylsulfonyl)phenyl)-5-(p-tolyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **7d**



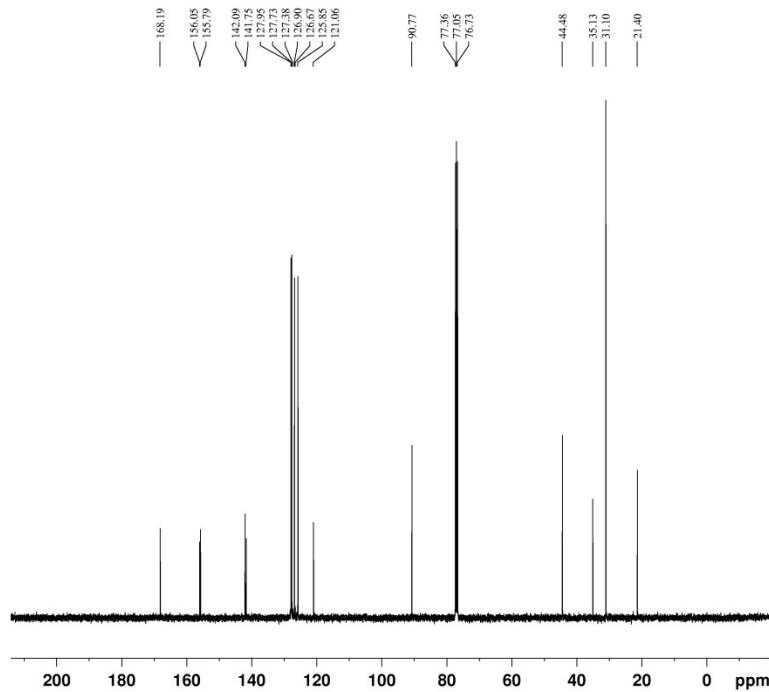
**Fig. S53:**  $^1\text{H}$  NMR of 1-(2-(4-(methylsulfonyl)phenyl)-5-(4-nitrophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **7e**



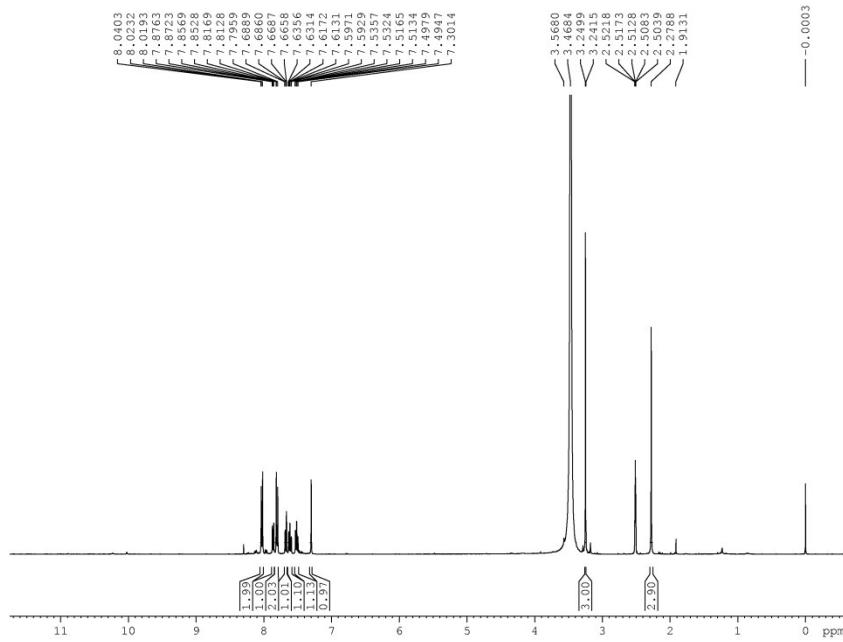
**Fig. S54:**  $^{13}\text{C}$  NMR of 1-(2-(4-(methylsulfonyl)phenyl)-5-(4-nitrophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **7e**



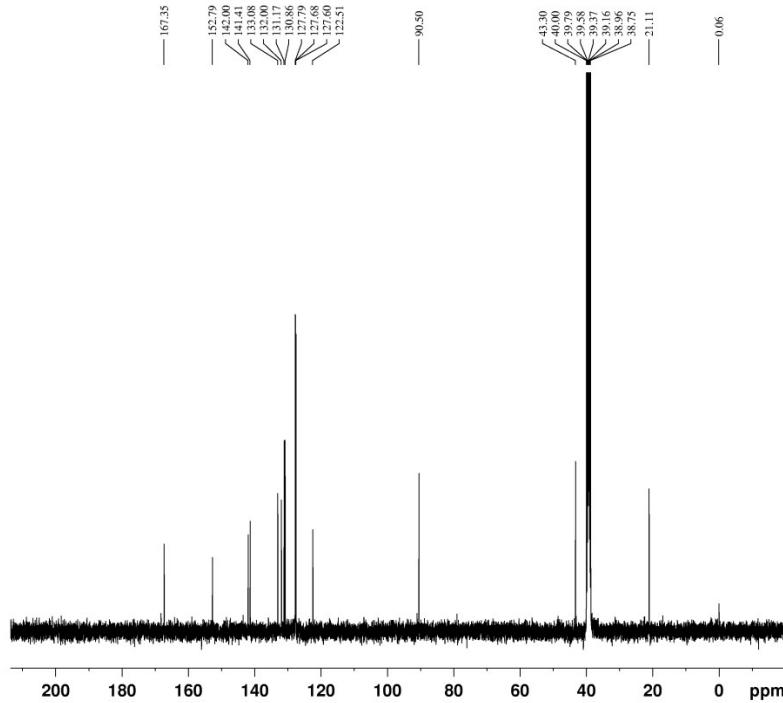
**Fig. S55:**  $^1\text{H}$  NMR of 1-(5-(4-(tert-butyl)phenyl)-2-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **7f**



**Fig. S56:**  $^{13}\text{C}$  NMR of 1-(5-(4-(tert-butyl)phenyl)-2-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **7f**



**Fig. S57:**  $^1\text{H}$  NMR of 1-(5-(2-chlorophenyl)-2-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **7g**

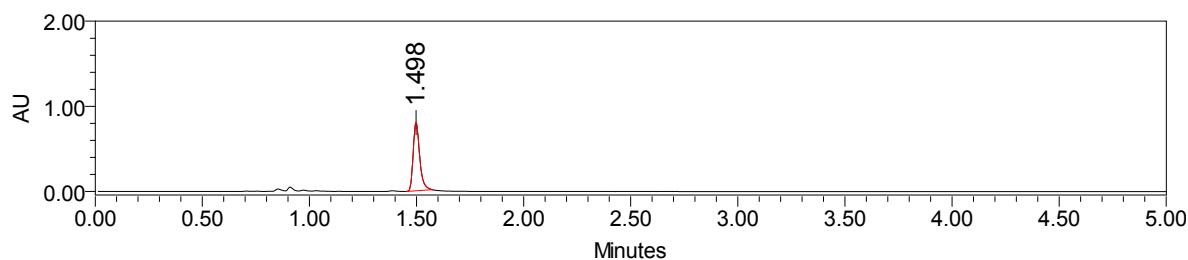


**Fig S58:**  $^{13}\text{C}$  NMR of 1-(5-(2-chlorophenyl)-2-(4-(methylsulfonyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone **7g**

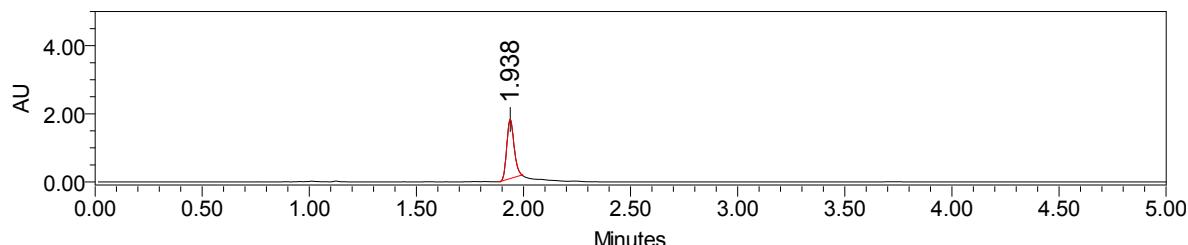
## Purity Determination

Purity of compounds (**4a-h**, **5a-h**, **6a-f** and **7a-g**) was determined on UPLC. The analysis was performed on Waters ACQUITY UPLC H-Class system, equipped with a binary pump, auto sampler, photodiode array detector (PDA) and Empower<sup>TM</sup> 3 software (Waters, Milford, MA, USA), on Column BEH Shield RP-18 column (2.1 × 100 mm, 1.7 µm, Waters, Milford, MA, USA). Mobile Phase consisted of Isocratic Water:ACN (30:70), flow rate was set to 0.3 mL/min, injection volume was 2 µL, column temperature was maintained at 30°C and detection was carried out using a PDA detector at  $\lambda_{\text{max}}$  254 nm.

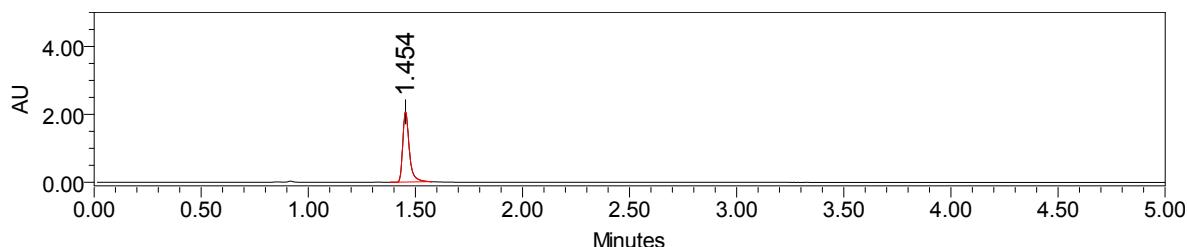
### UPLC chromatograms



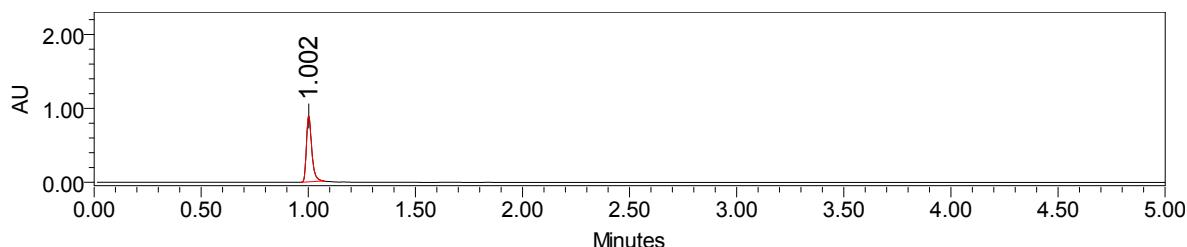
**Fig. S59:** UPLC of compound **4a**



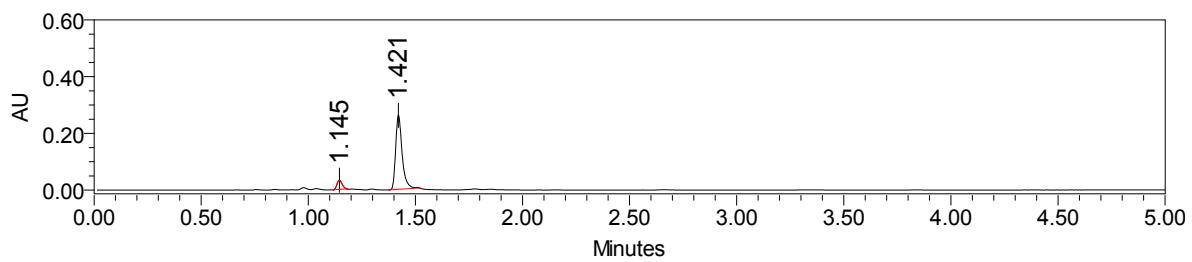
**Fig. S60:** UPLC of compound **4b**



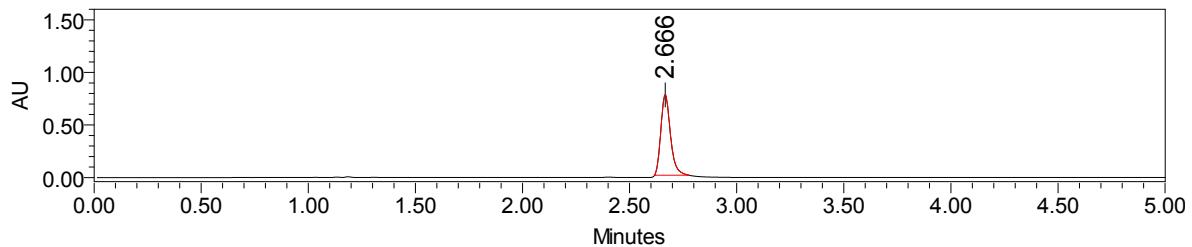
**Fig. S61:** UPLC of compound **4c**



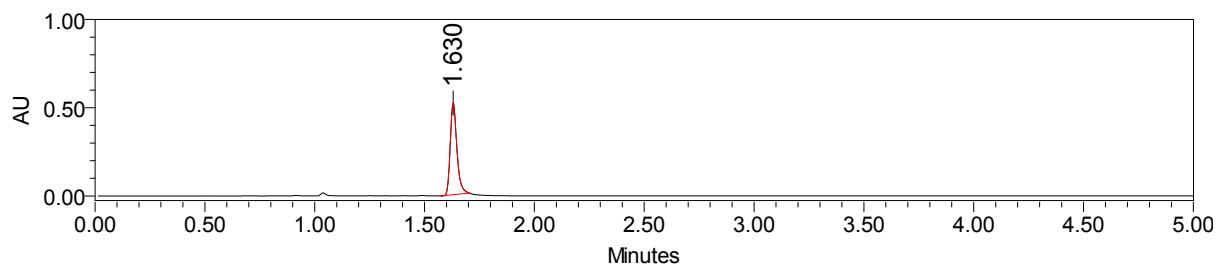
**Fig. S62:** UPLC of compound **4d**



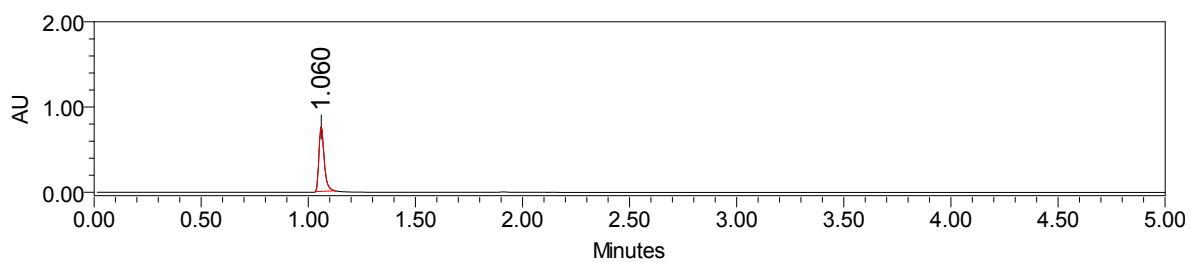
**Fig. S63:** UPLC of compound **4e**



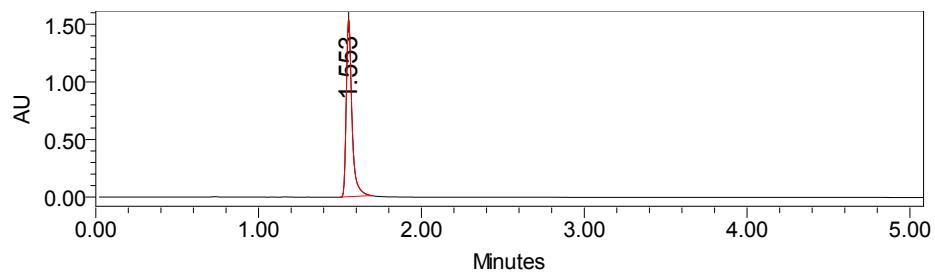
**Fig. S64:** UPLC of compound **4f**



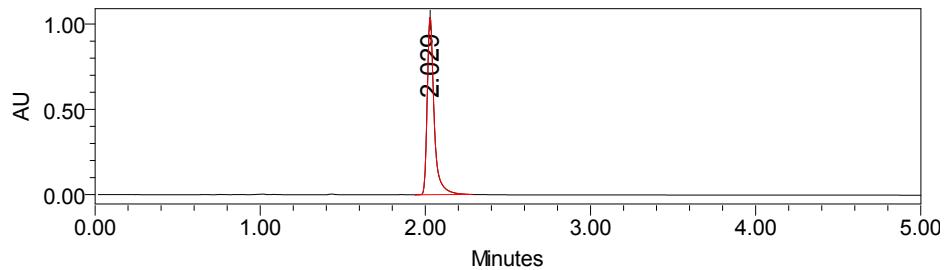
**Fig. S65:** UPLC of compound **4g**



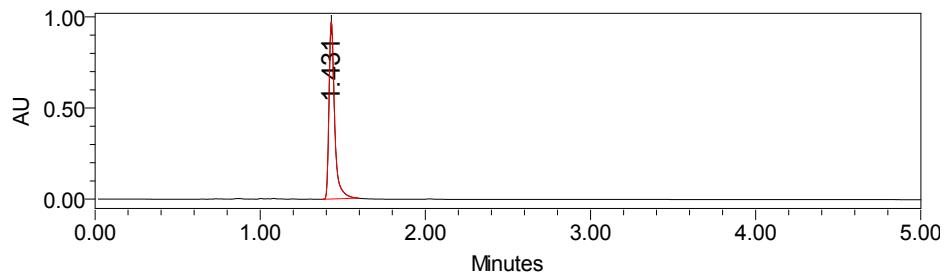
**Fig. S66:** UPLC of compound **4h**



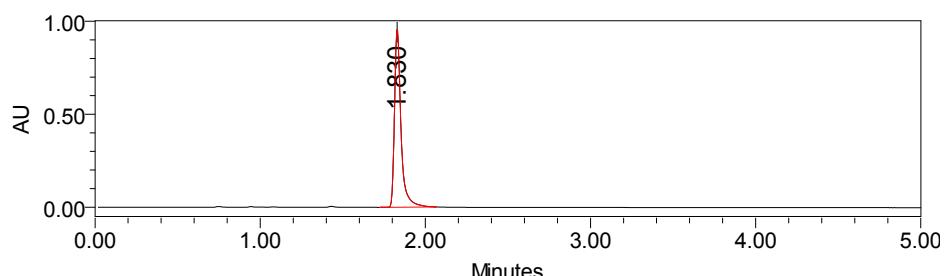
**Fig. S67:** UPLC of compound **5a**



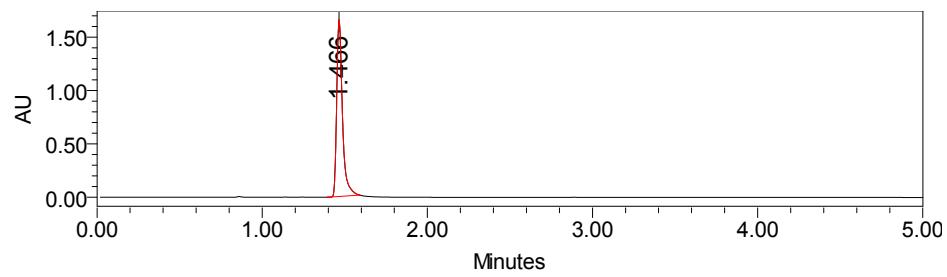
**Fig. S68:** UPLC of compound **5b**



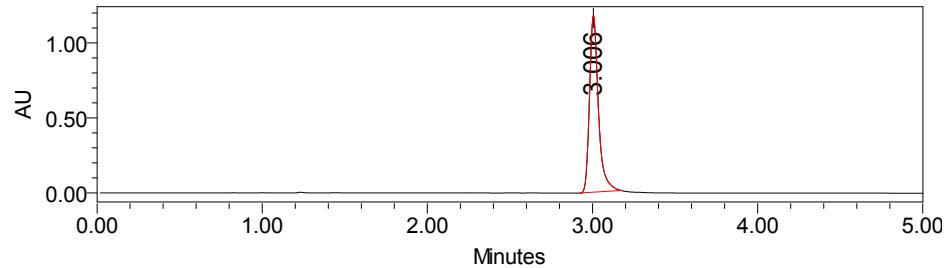
**Fig. S69:** UPLC of compound **5c**



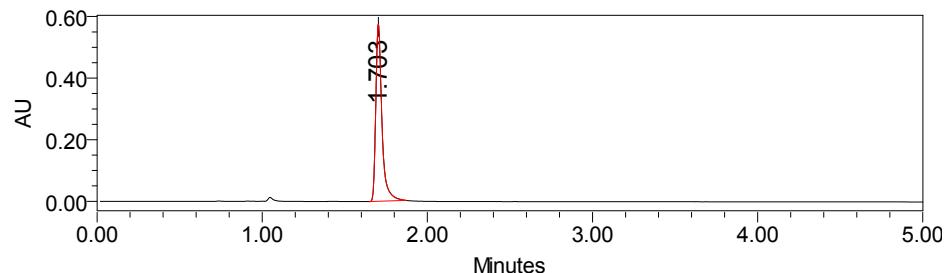
**Fig. S70:** UPLC of compound **5d**



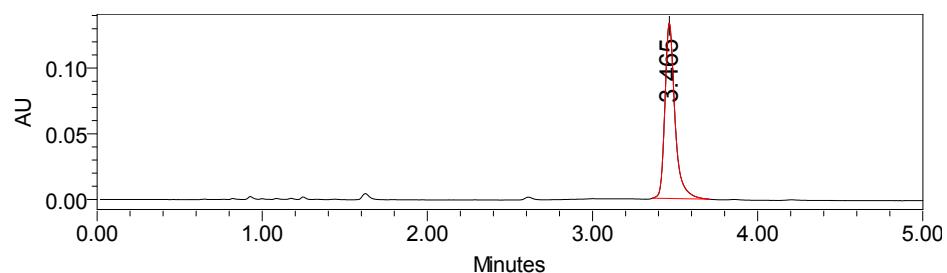
**Fig. S71:** UPLC of compound 5e



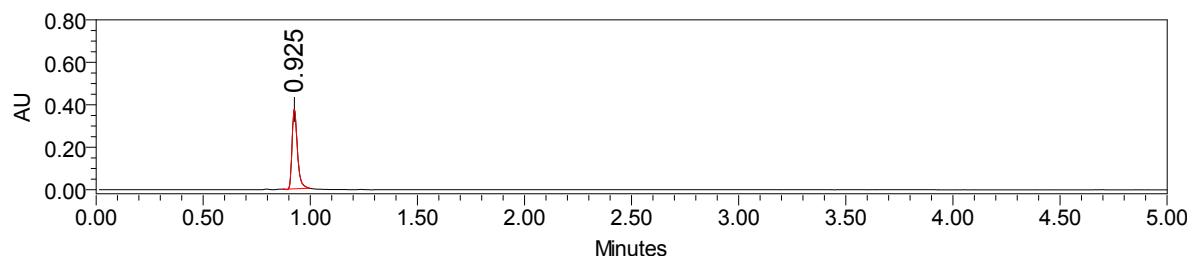
**Fig. S72:** UPLC of compound 5f



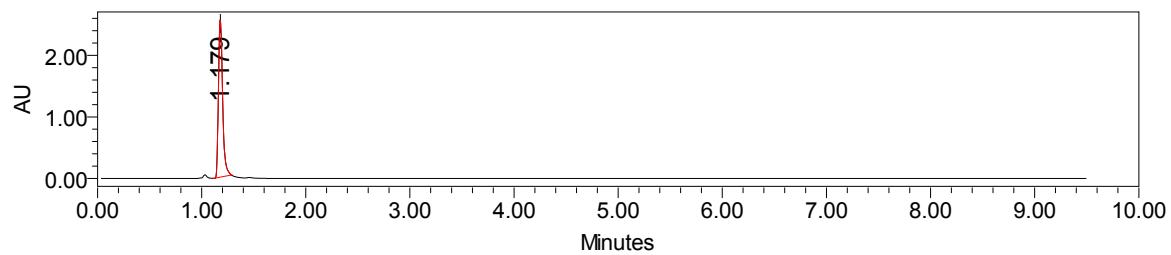
**Fig. S73:** UPLC of compound 5g



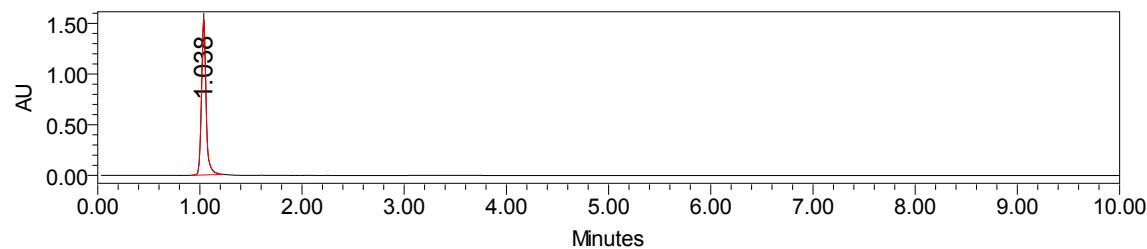
**Fig. S74:** UPLC of compound 5h



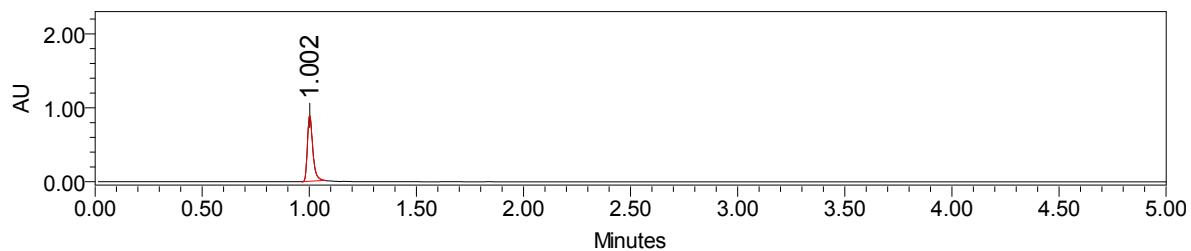
**Fig. S75:** UPLC of compound **6a**



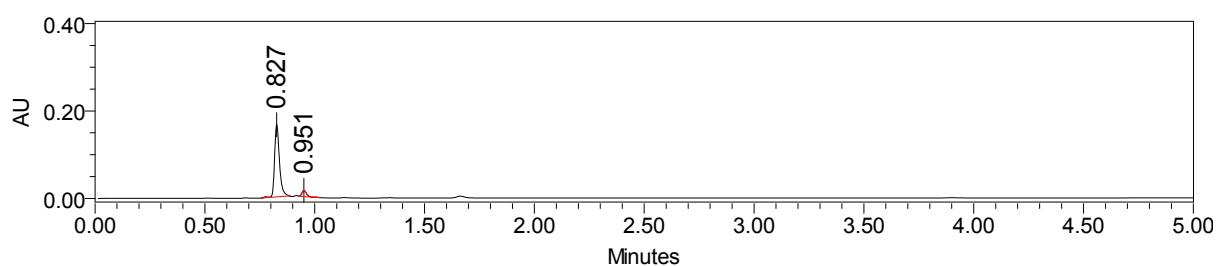
**Fig. S76:** UPLC of compound **6b**



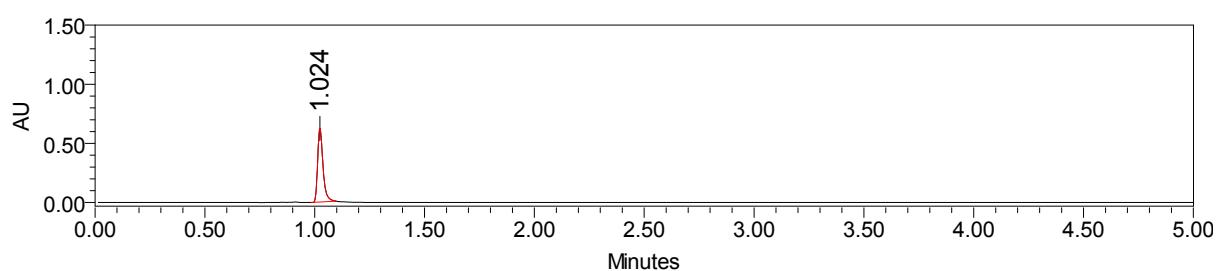
**Fig. S77:** UPLC of compound **6c**



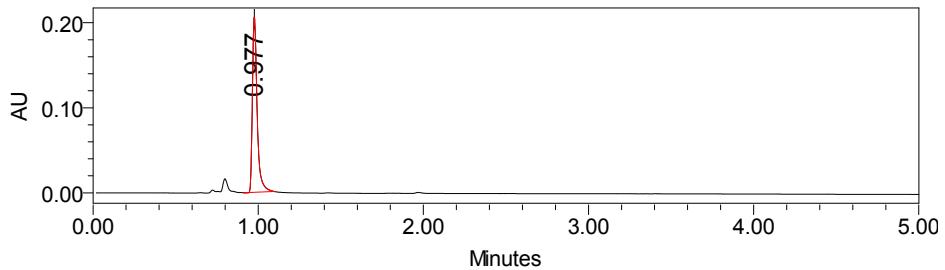
**Fig. S78:** UPLC of compound **6d**



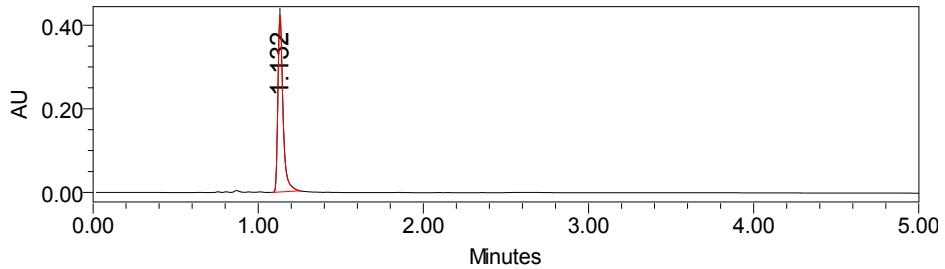
**Fig. S79:** UPLC of compound **6e**



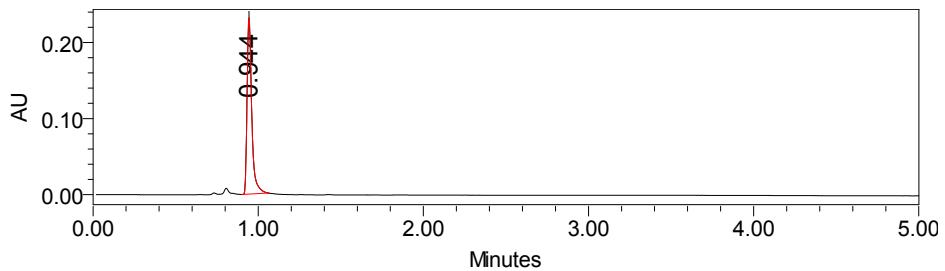
**Fig. S80:** UPLC of compound **6f**



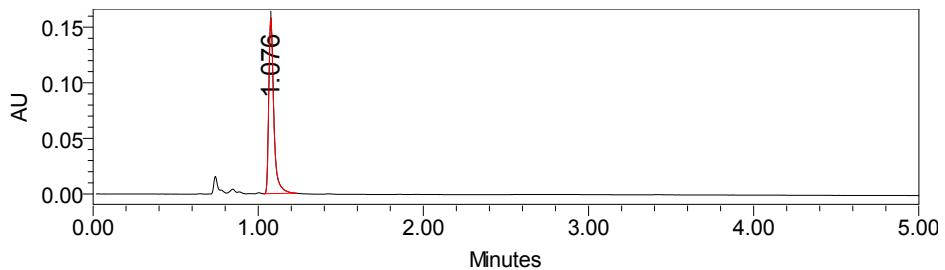
**Fig. S81:** UPLC of compound **7a**



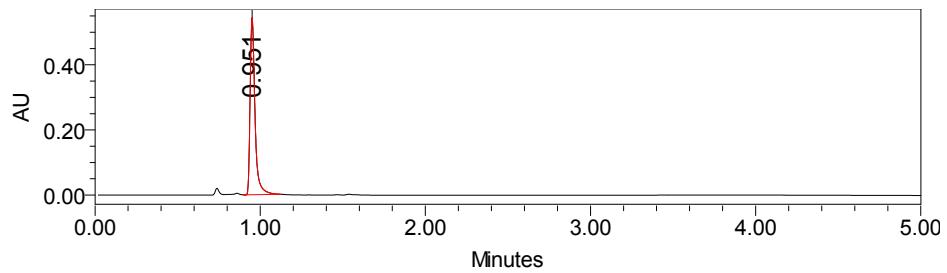
**Fig. S82:** UPLC of compound **7b**



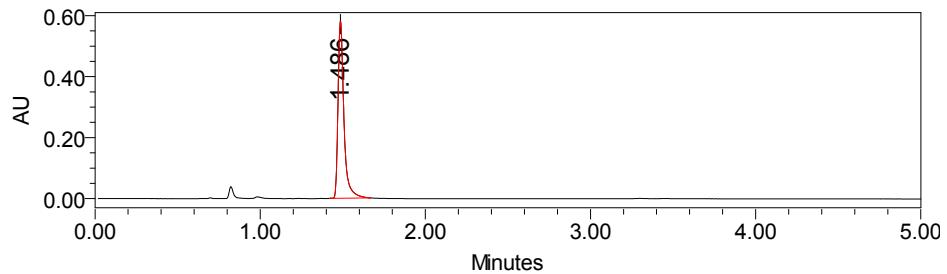
**Fig. S83:** UPLC of compound **7c**



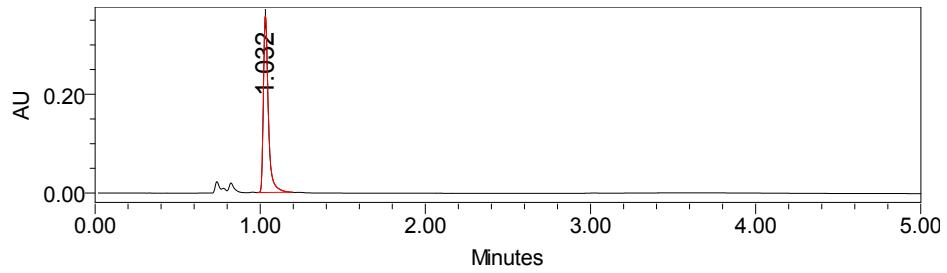
**Fig. S84:** UPLC of compound **7d**



**Fig. S85:** UPLC of compound 7e



**Fig. S86:** UPLC of compound 7f



**Fig. S87:** UPLC of compound 7g



**Fig. S88:** Photographic image of paw (circled in red): Normal control group at 3h A) Top view; B) Lateral view