

Supplementary Materials: Synthesis and p38 Inhibitory Activity of Some Novel Substituted *N,N'*-Diaryleurea Derivatives

Dianxi Zhu, Qifeng Xing, Ruiyuan Cao, Dongmei Zhao and Wu Zhong

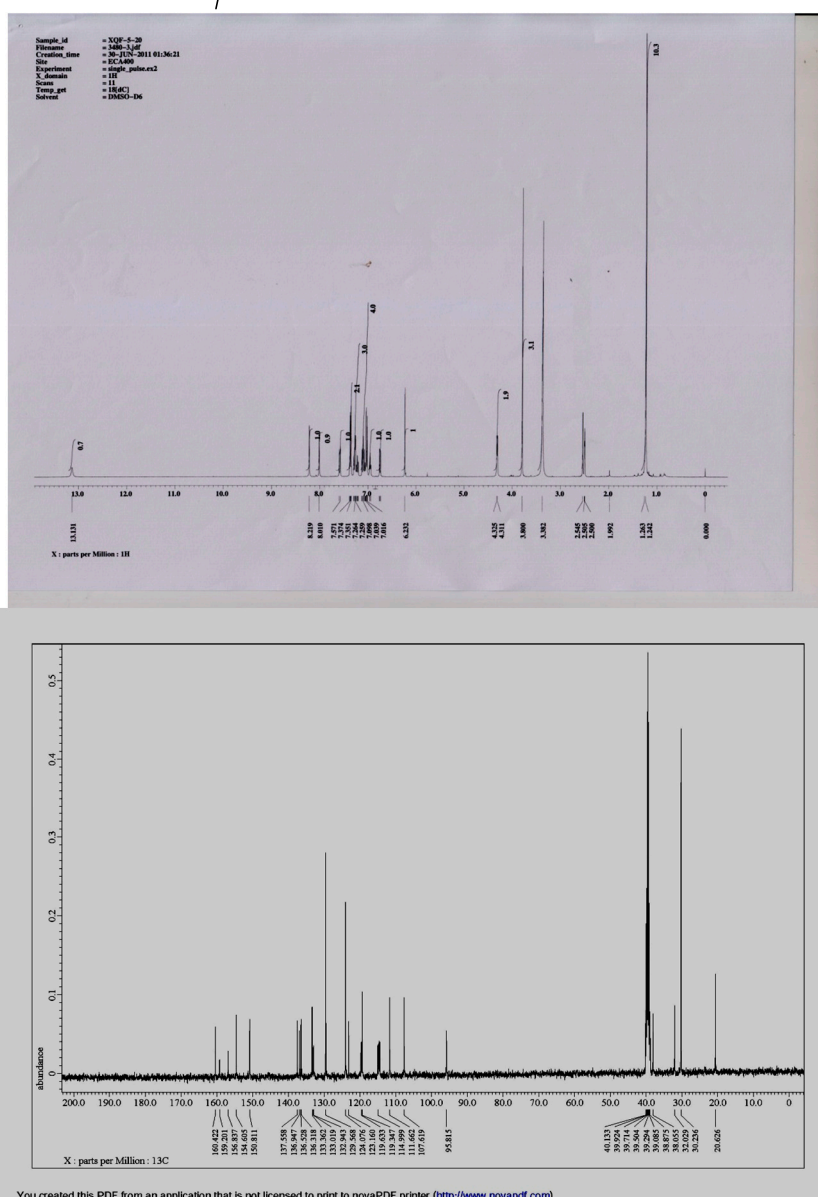
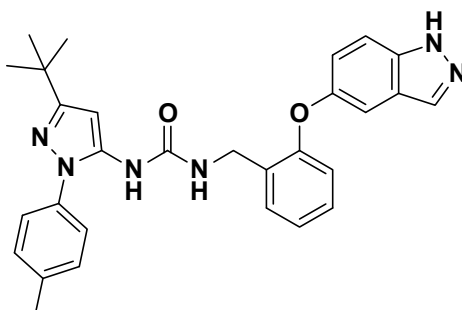


Figure S1. 1-(2-((1*H*-indazol-5-yl)oxy)benzyl)-3-(3-(tert-butyl)-1-(*p*-tolyl)-1*H*-pyrazol-5-yl)urea (**25a**).

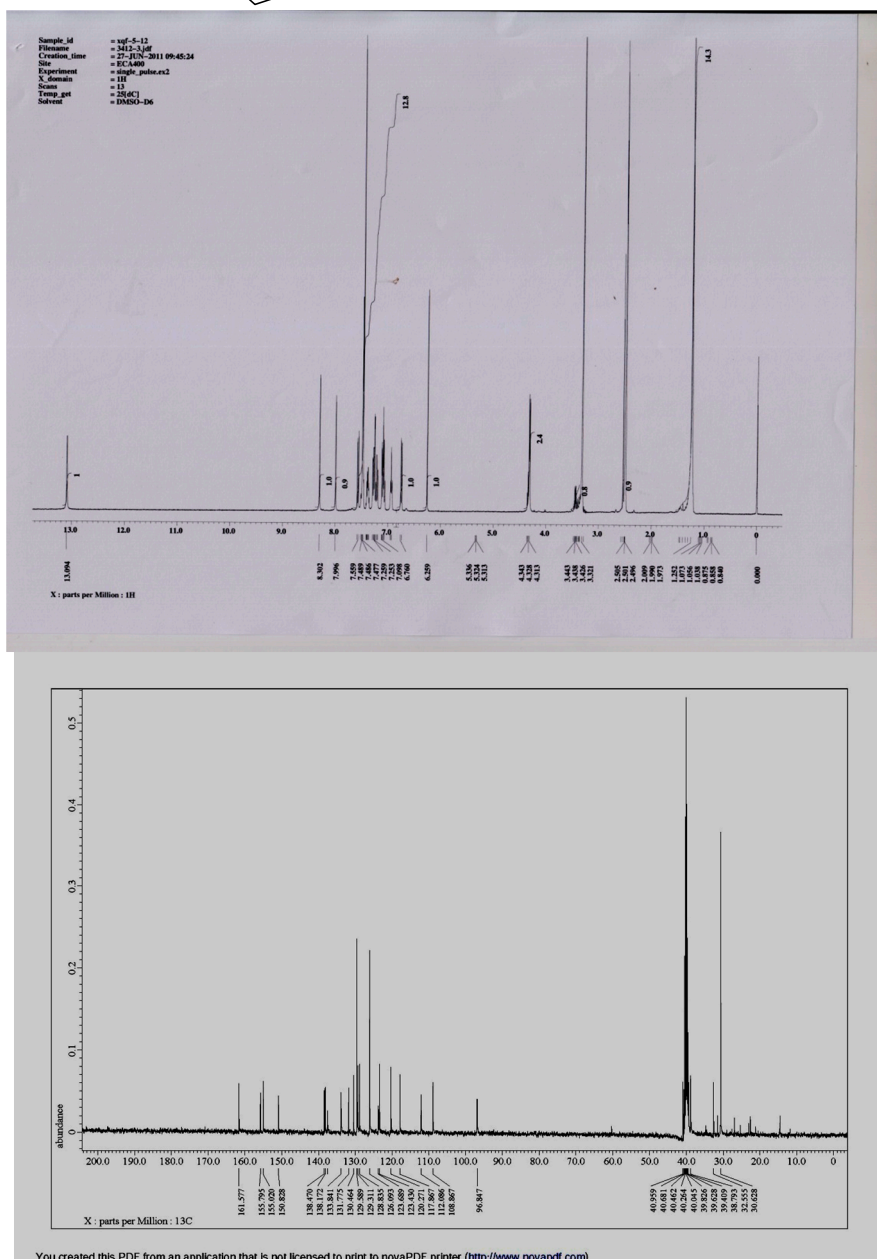
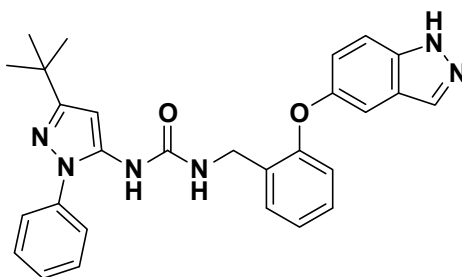


Figure S2. 1-(2-((1H-indazol-5-yl)oxy)benzyl)-3-(3-(tert-butyl)-1-phenyl-1H-pyrazol-5-yl)urea (**25b**).

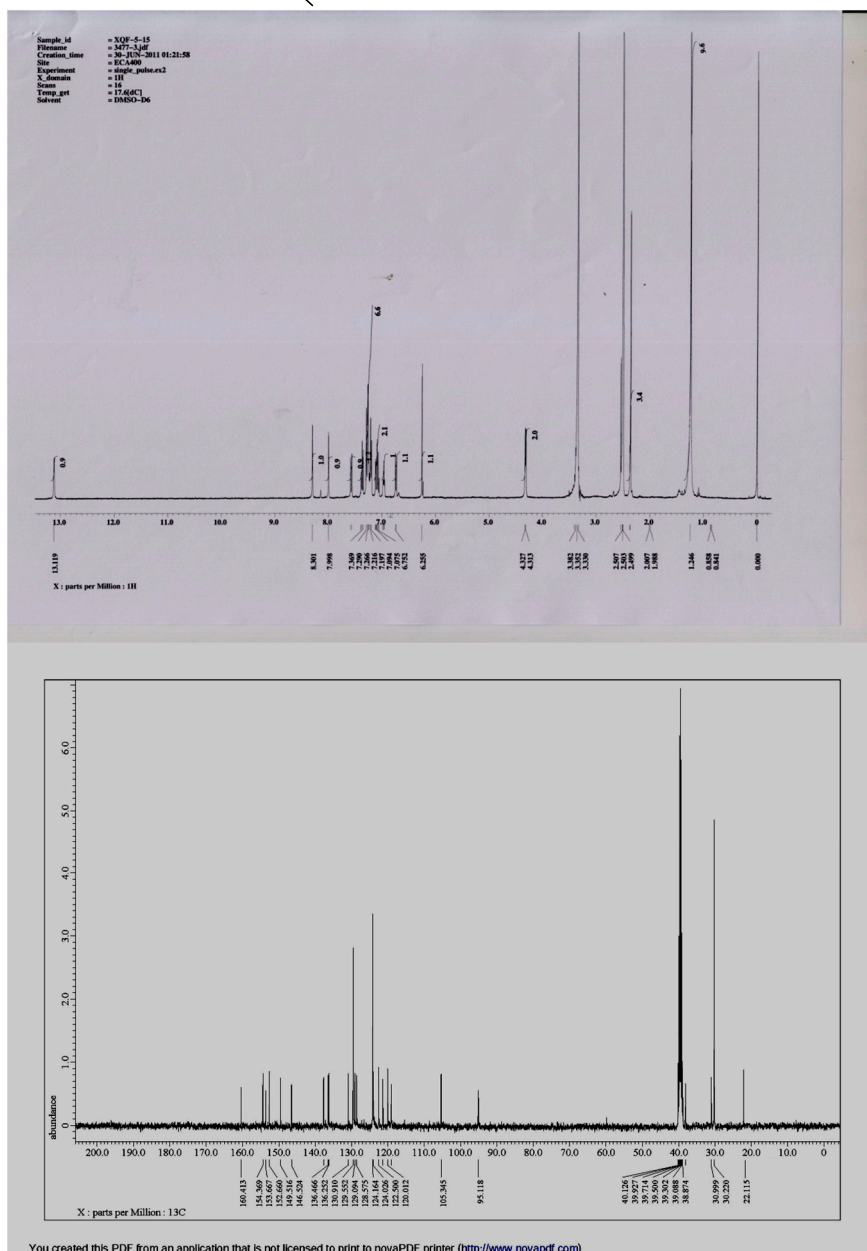
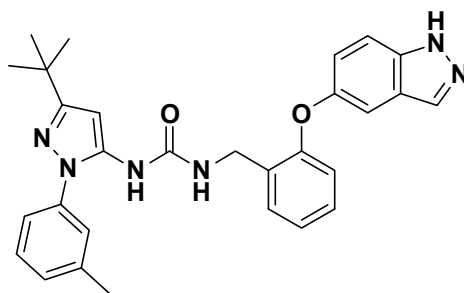


Figure S3. 1-(2-((1H-indazol-5-yl)oxy)benzyl)-3-(3-(tert-butyl)-1-(m-tolyl)-1H-pyrazol-5-yl)urea (**25c**).

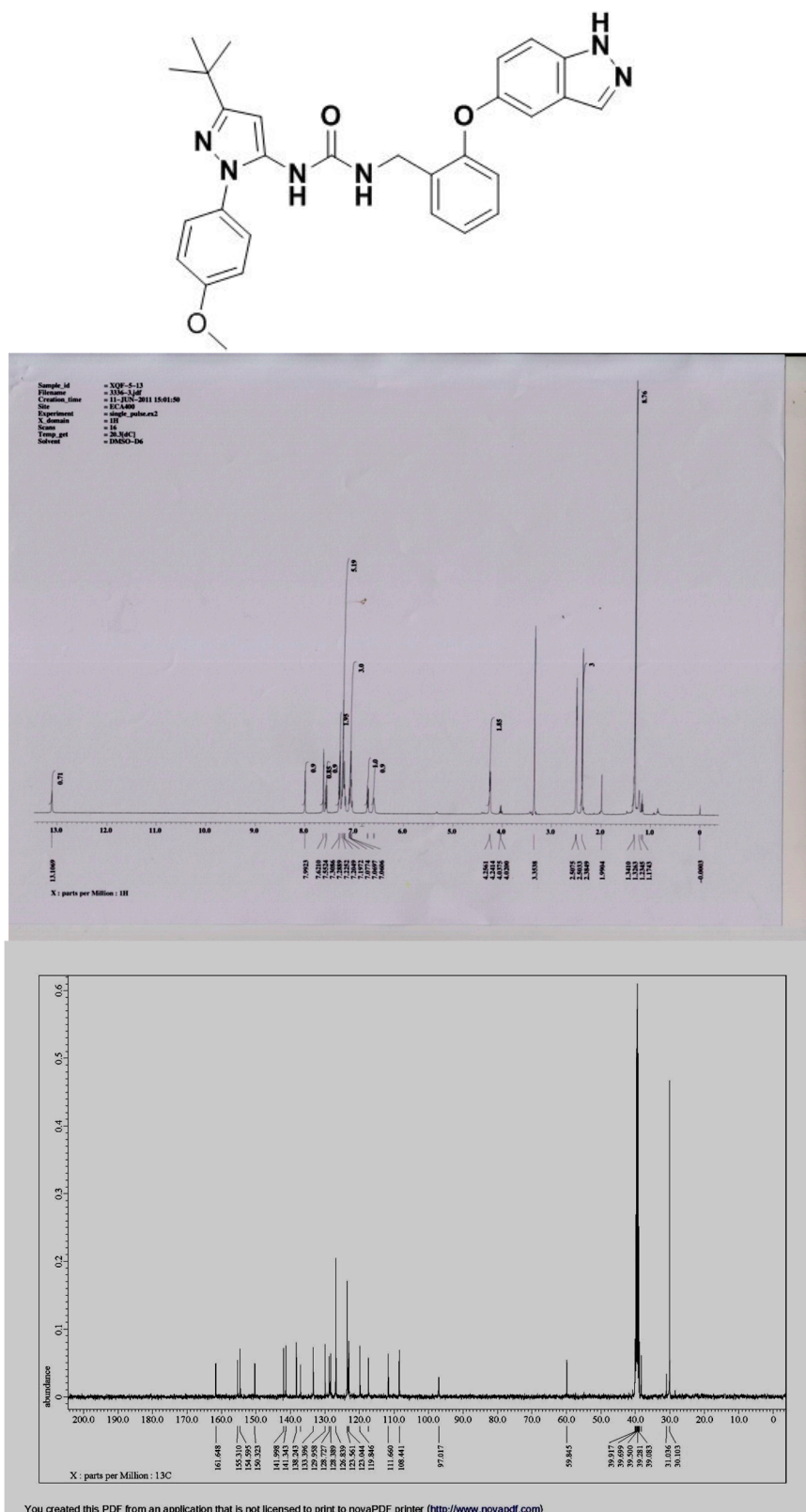


Figure S4. 1-(2-((1H-indazol-5-yl)oxy)benzyl)-3-(3-(tert-butyl)-1-(4-methoxyphenyl)-1H-pyrazol-5-yl)urea (25d).

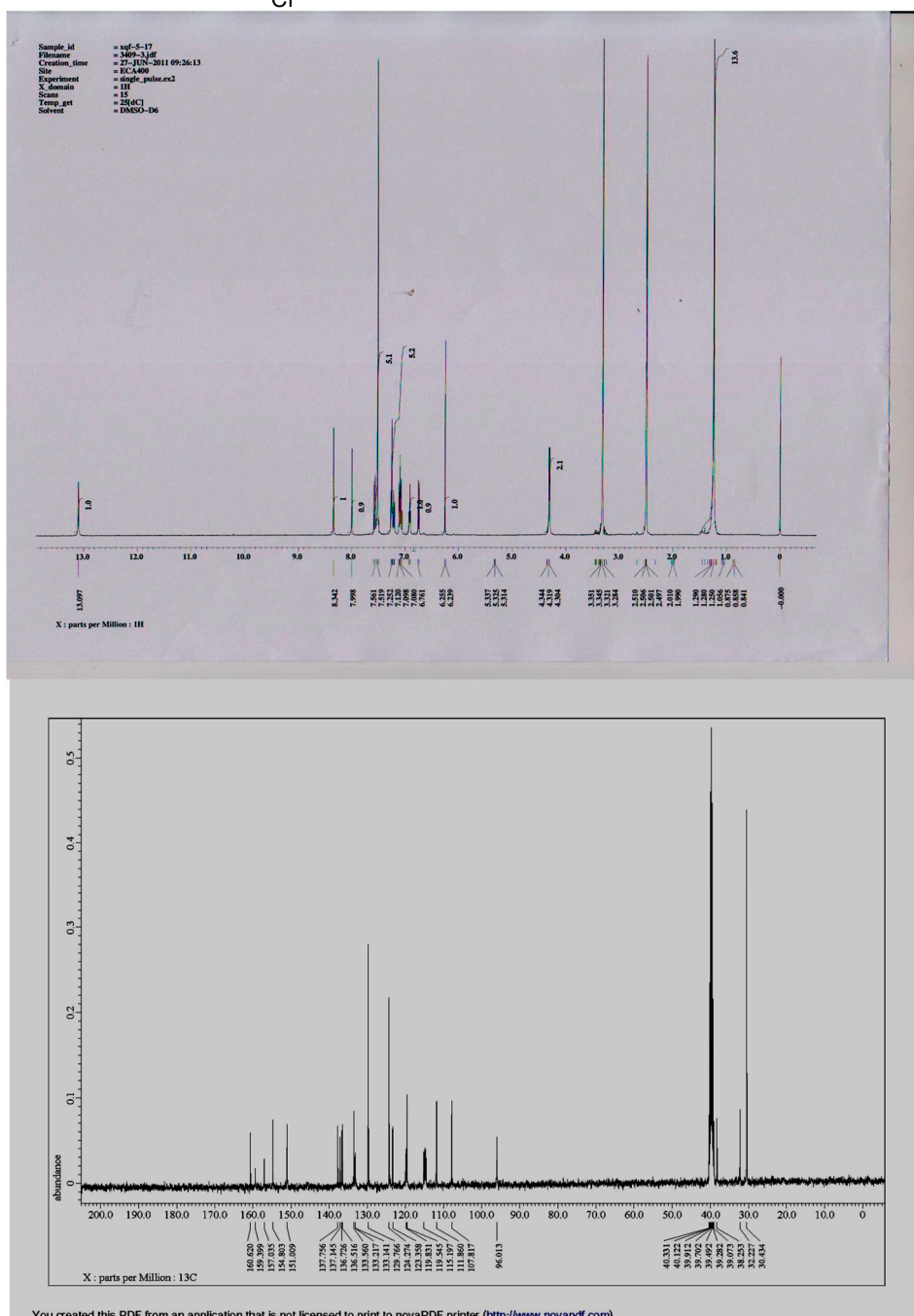
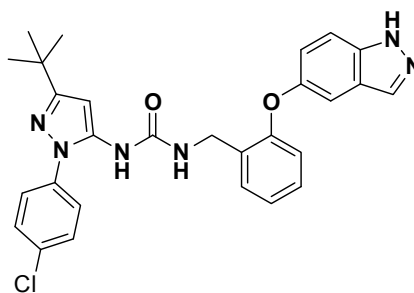


Figure S5. 1-(2-((1H-indazol-5-yl)oxy)benzyl)-3-(3-(tert-butyl)-1-(4-chlorophenyl)-1H-pyrazol-5-yl)urea (25e).

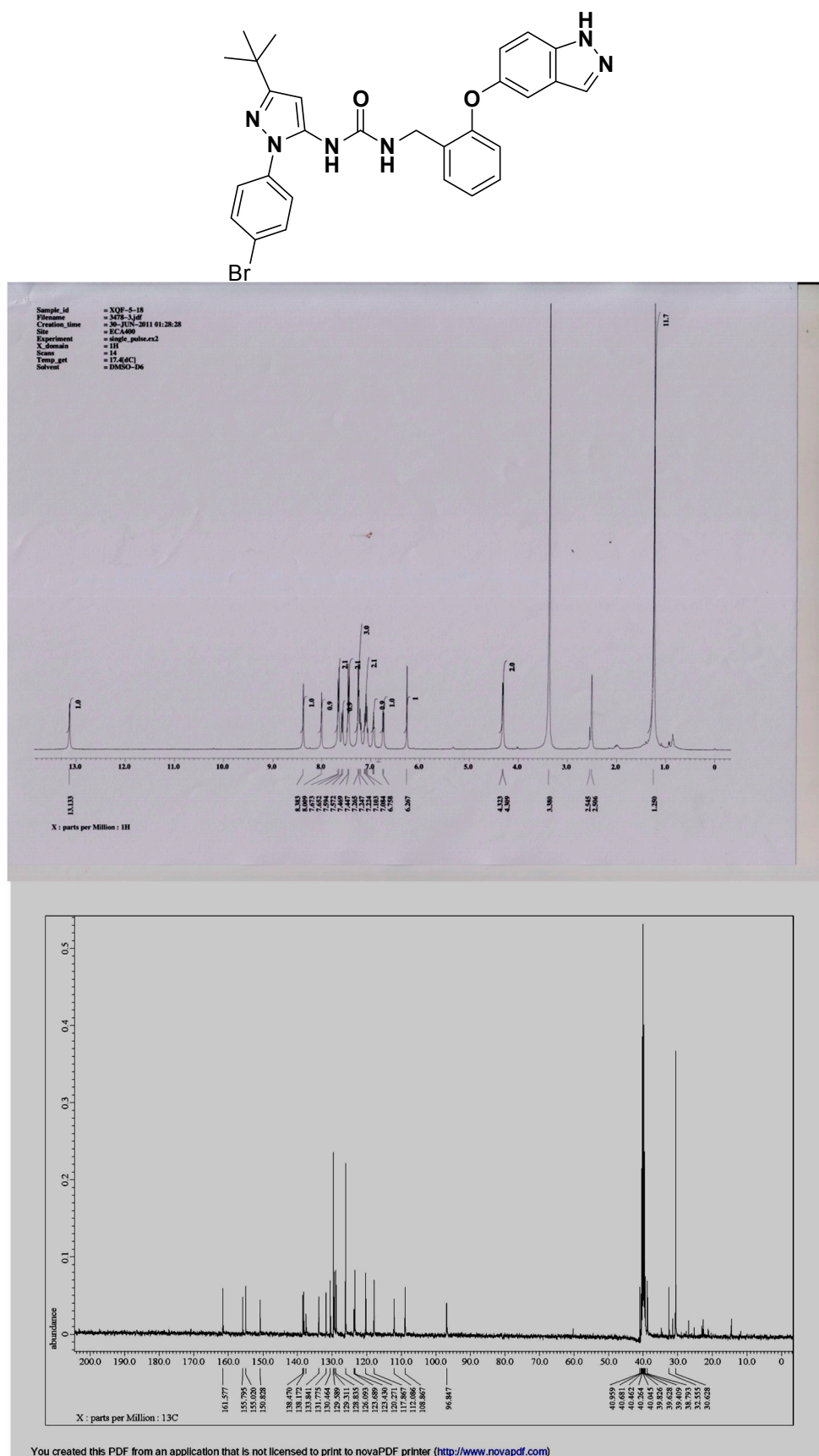


Figure S6. 1-(2-((1H-indazol-5-yl)oxy)benzyl)-3-(1-(4-bromophenyl)-3-(tert-butyl)-1H-pyrazol-5-yl)urea (25f).

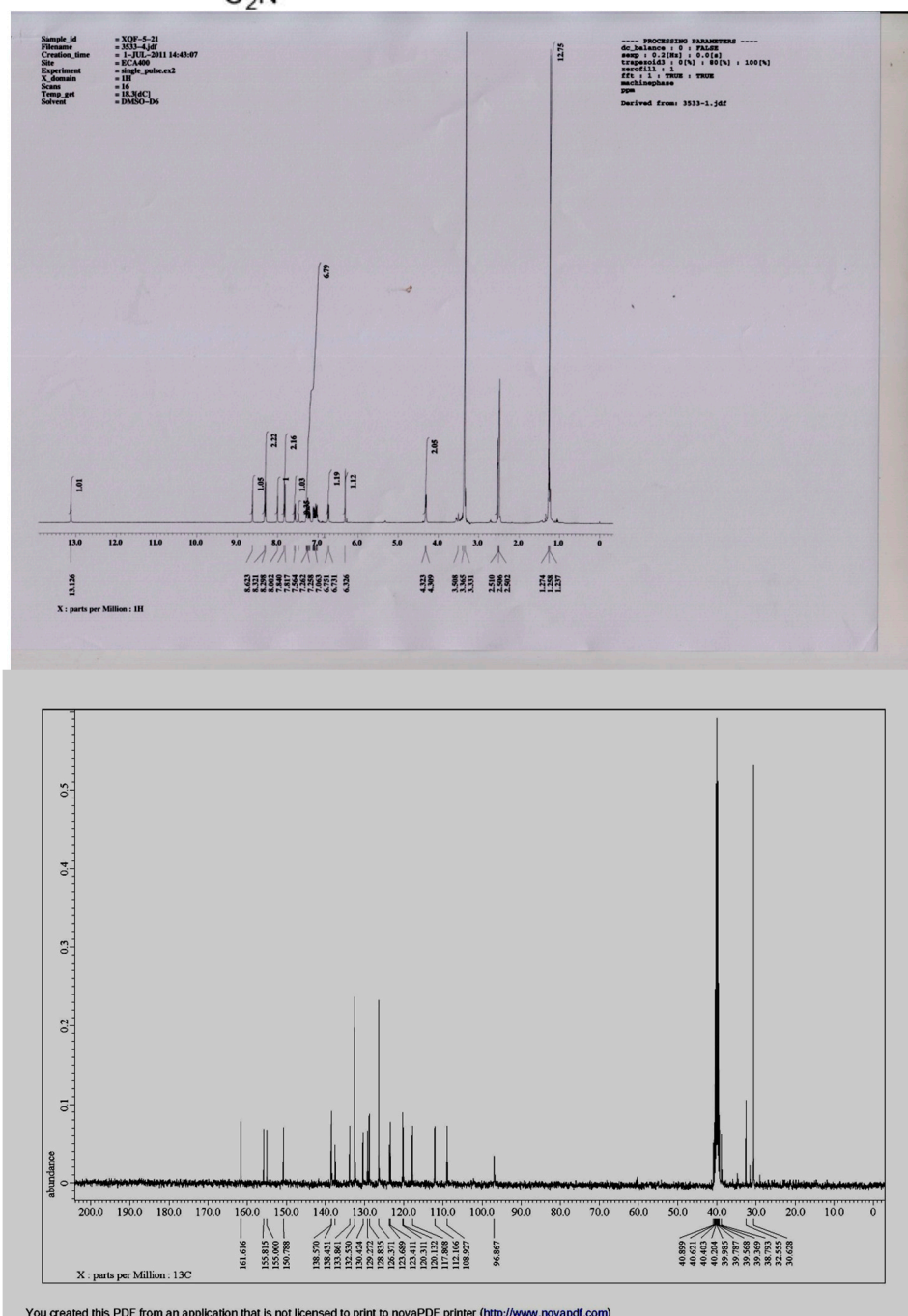
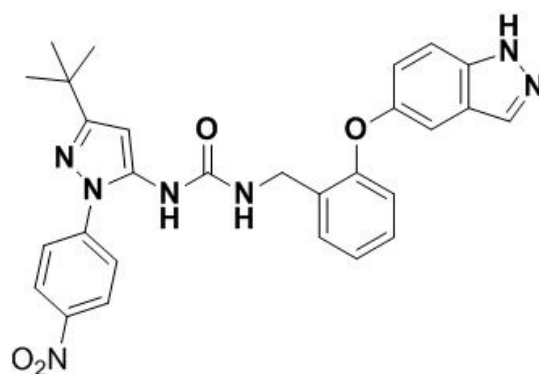


Figure S8. 1-(2-((1H-indazol-5-yl)oxy)benzyl)-3-(3-(tert-butyl)-1-(4-nitrophenyl)-1H-pyrazol-5-yl)urea (**25h**).

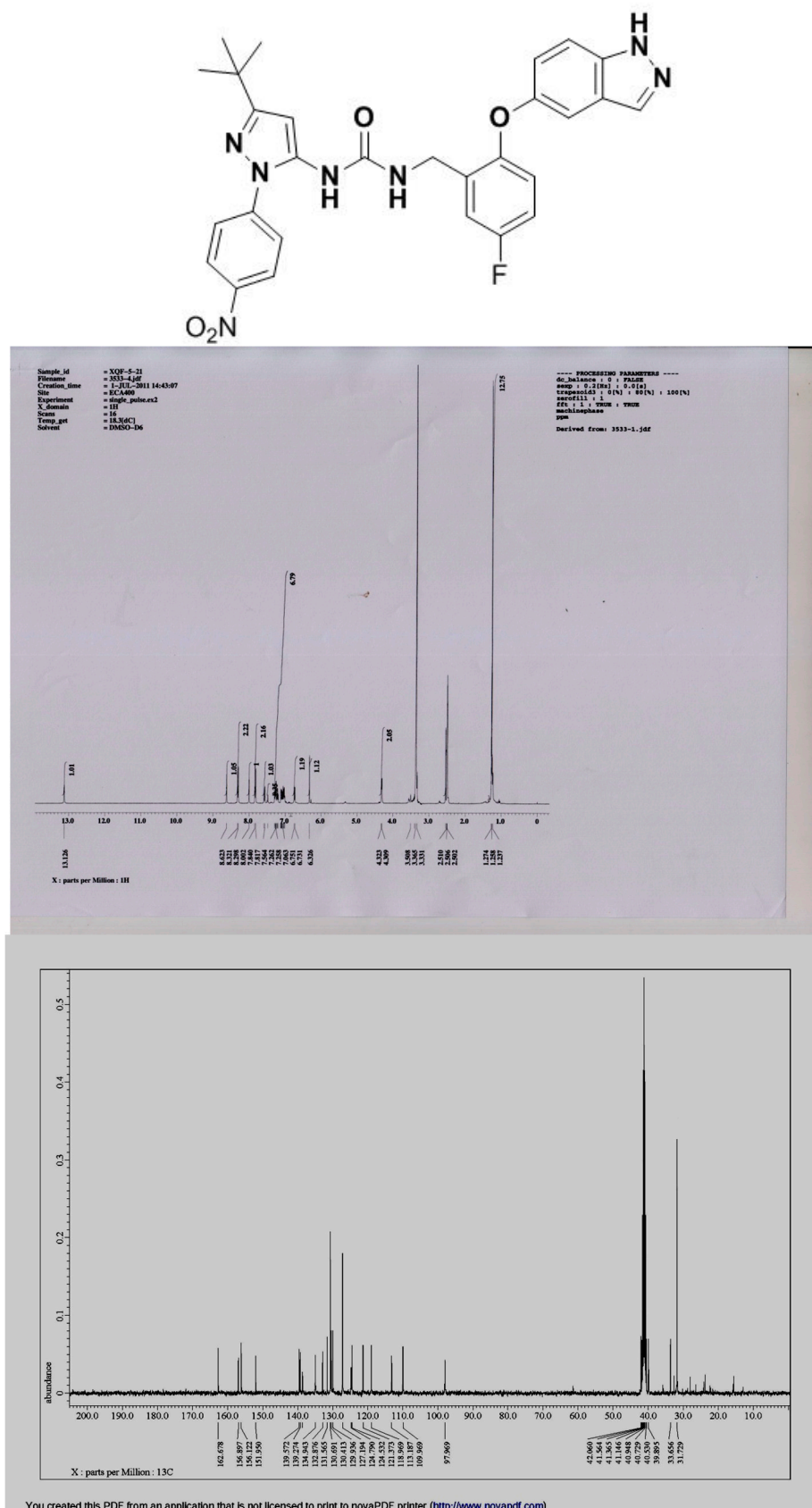


Figure S9. 1-(2-((1H-indazol-5-yl)oxy)-5-fluorobenzyl)-3-(3-(tert-butyl)-1-(4-nitrophenyl)-1H-pyrazol-5-yl)urea (25i).

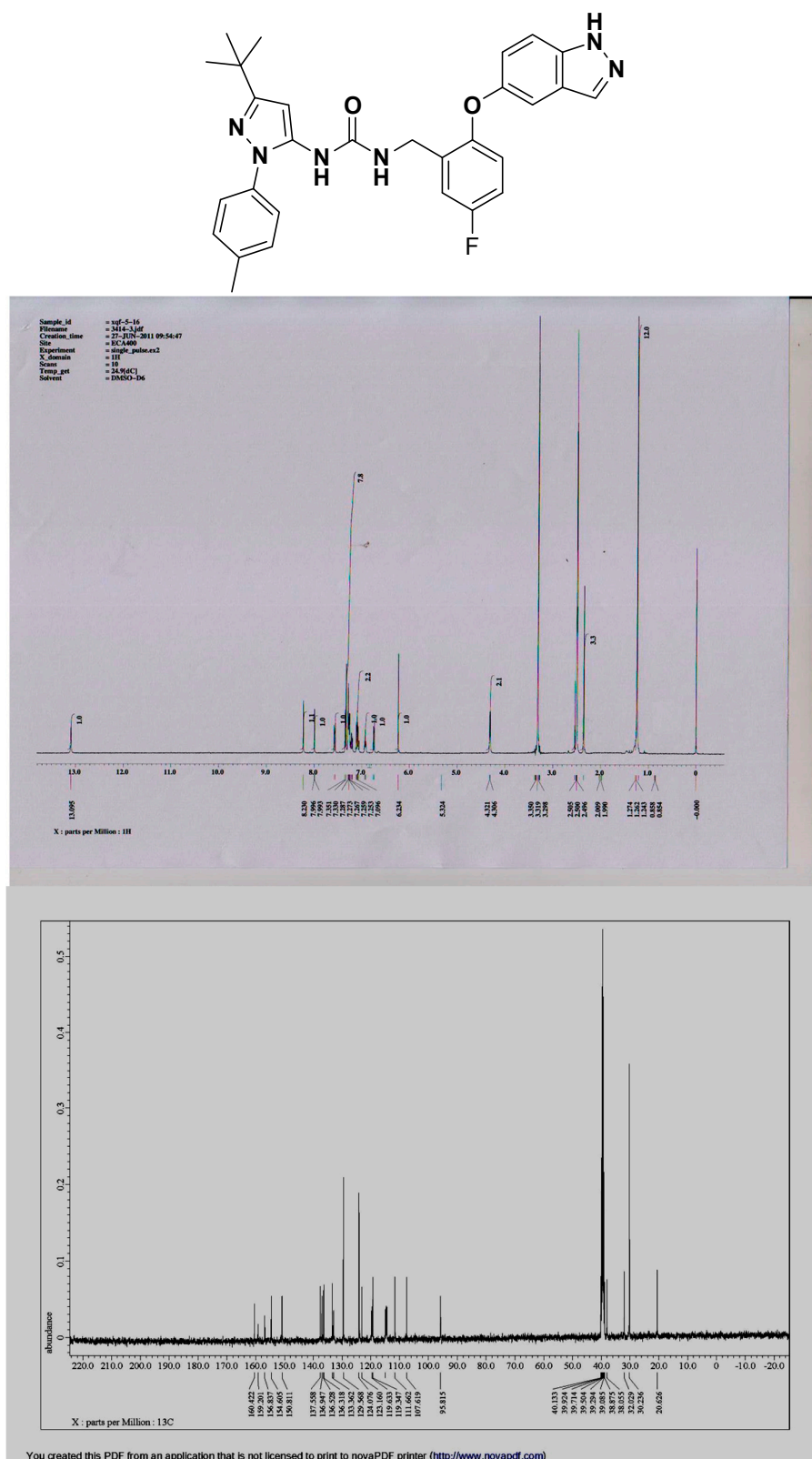


Figure S10. 1-(2-((1H-indazol-5-yl)oxy)-5-fluorobenzyl)-3-(3-(tert-butyl)-1-(p-tolyl)-1H-pyrazol-5-yl)urea (25j).

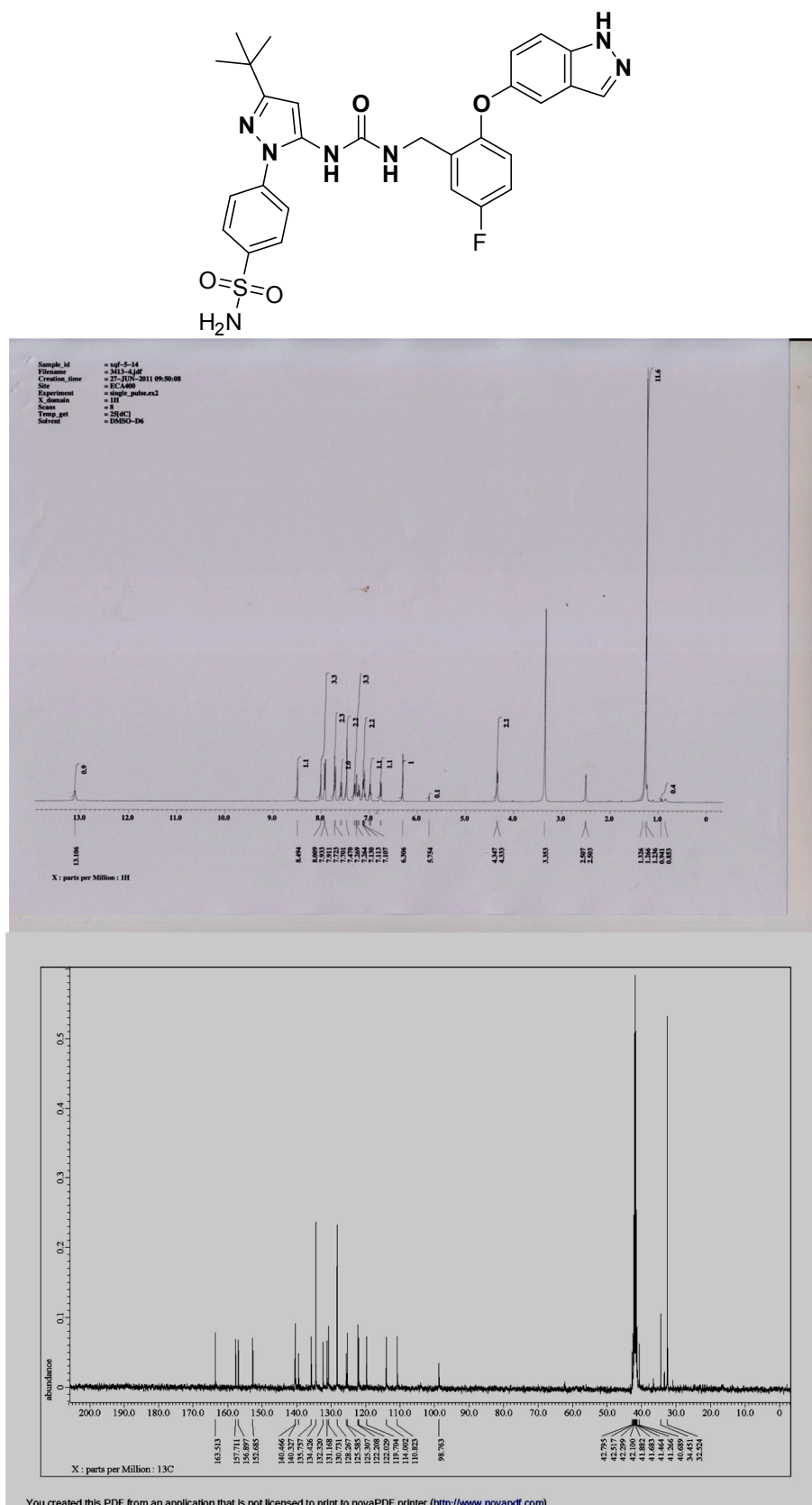


Figure S11. 4-(5-(3-(2-((1H-indazol-5-yl)oxy)benzyl)ureido)-3-(tert-butyl)-1H-pyrazol-1-yl)benzenesulfonamide (25k).

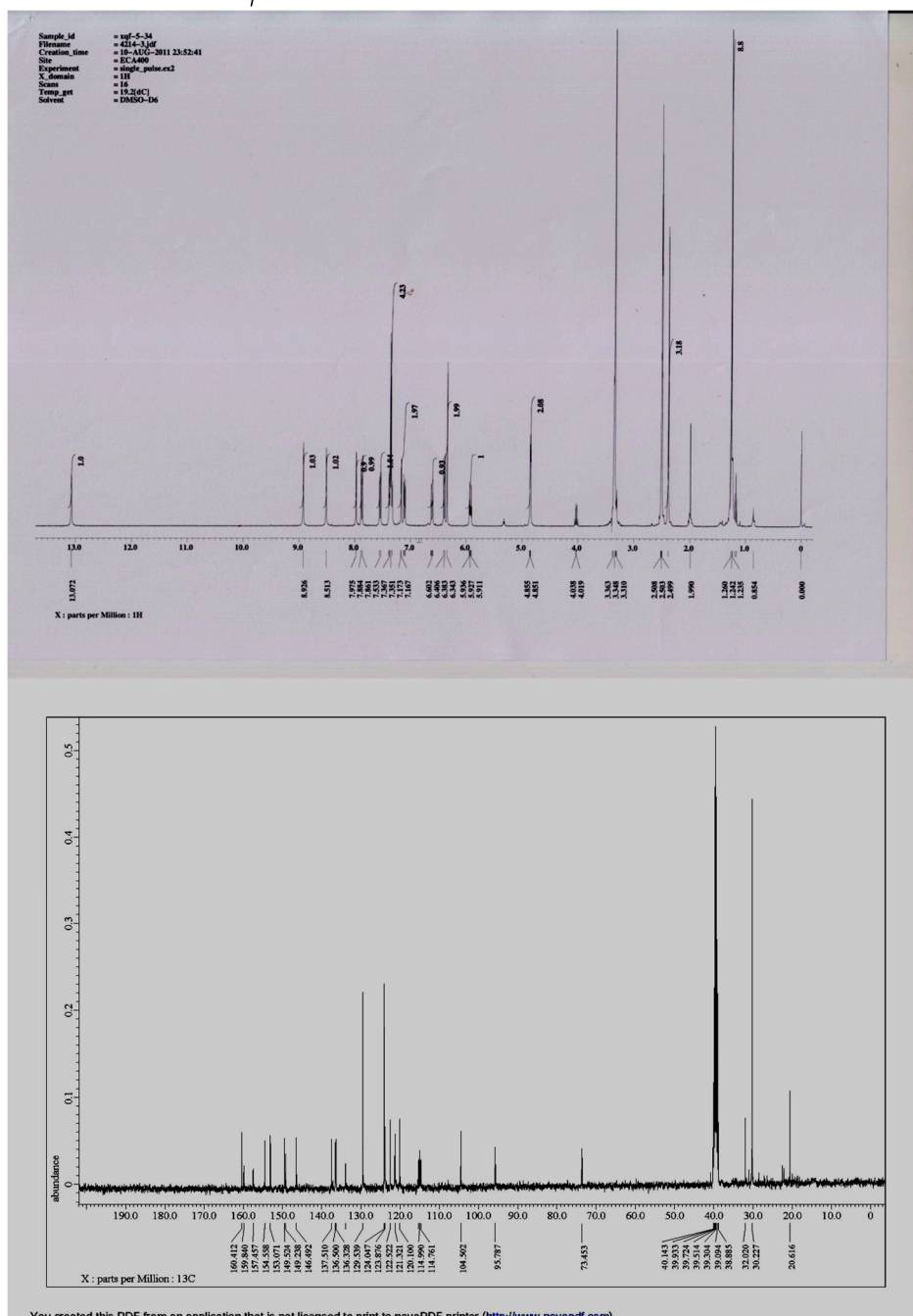
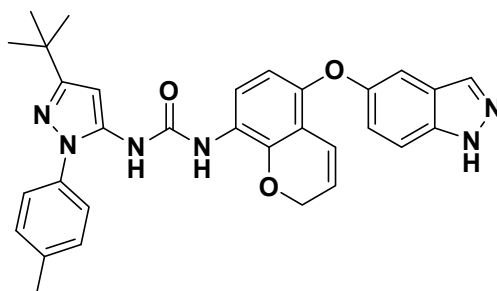


Figure S12. 1-(5-((1H-indazol-5-yl)oxy)-2H-chromen-8-yl)-3-(3-(tert-butyl)-1-(p-tolyl)-1H-pyrazol-5-yl)urea (26a).

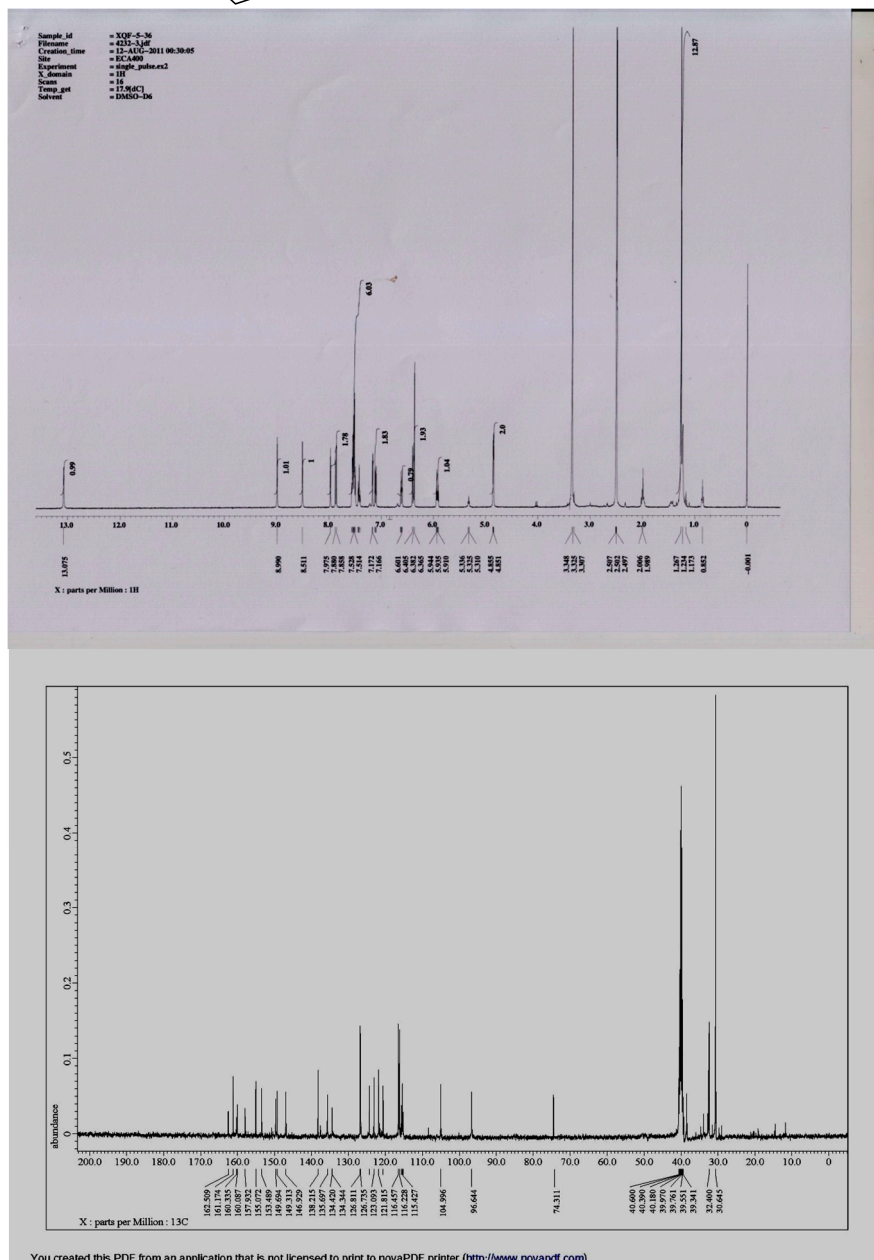
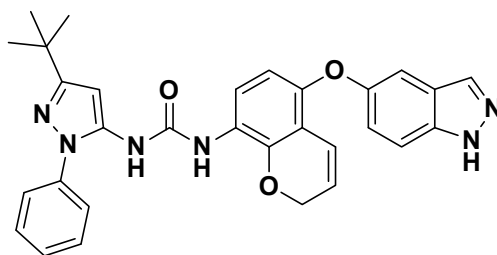


Figure S13. 1-(5-((1H-indazol-5-yl)oxy)-2H-chromen-8-yl)-3-(3-(tert-butyl)-1-phenyl-1H-pyrazol-5-yl)urea (**26b**).

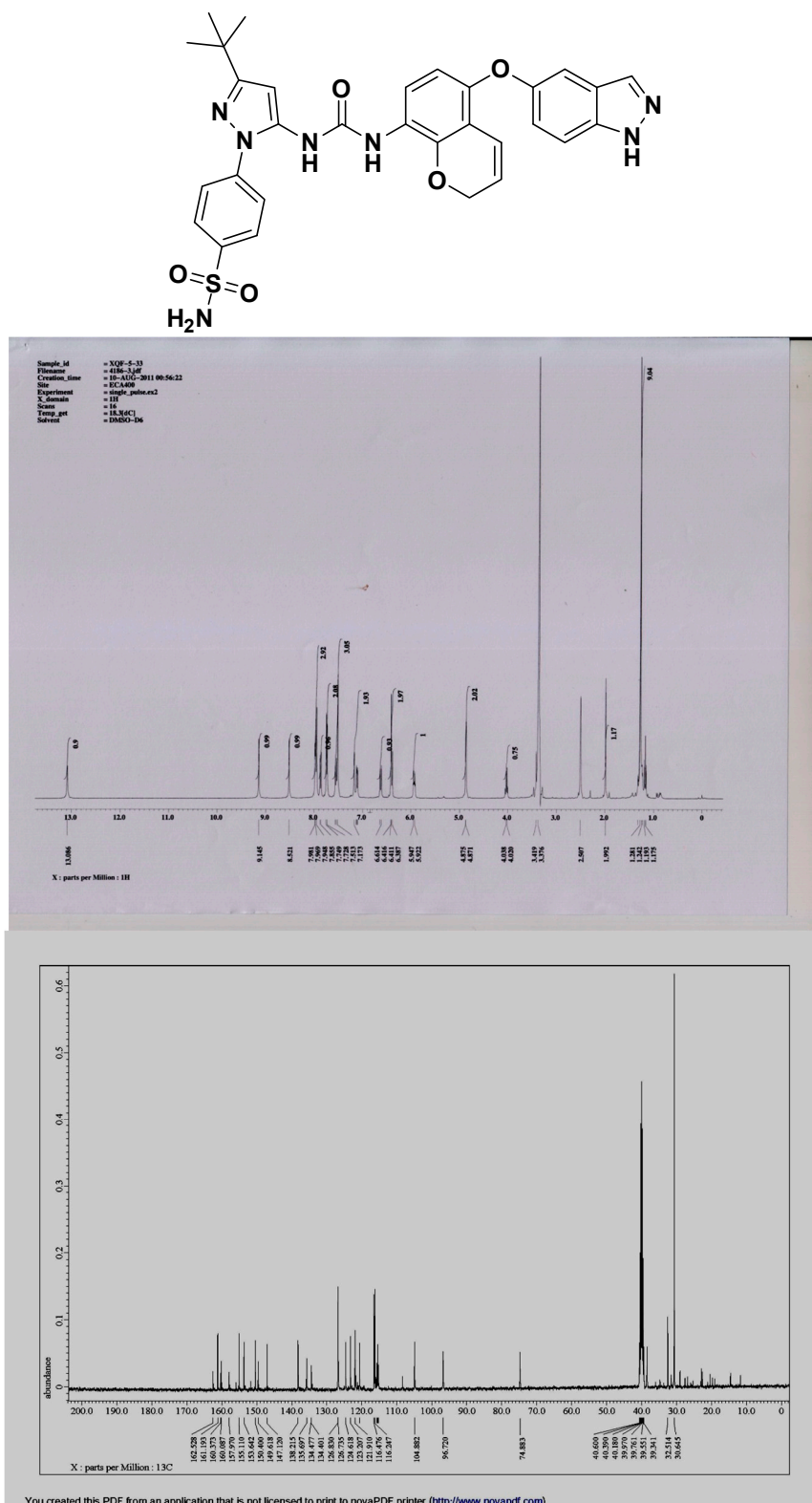


Figure S14. 4-(5-(3-(5-((1*H*-indazol-5-yl)oxy)-2*H*-chromen-8-yl)ureido)-3-(tert-butyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (**26c**).

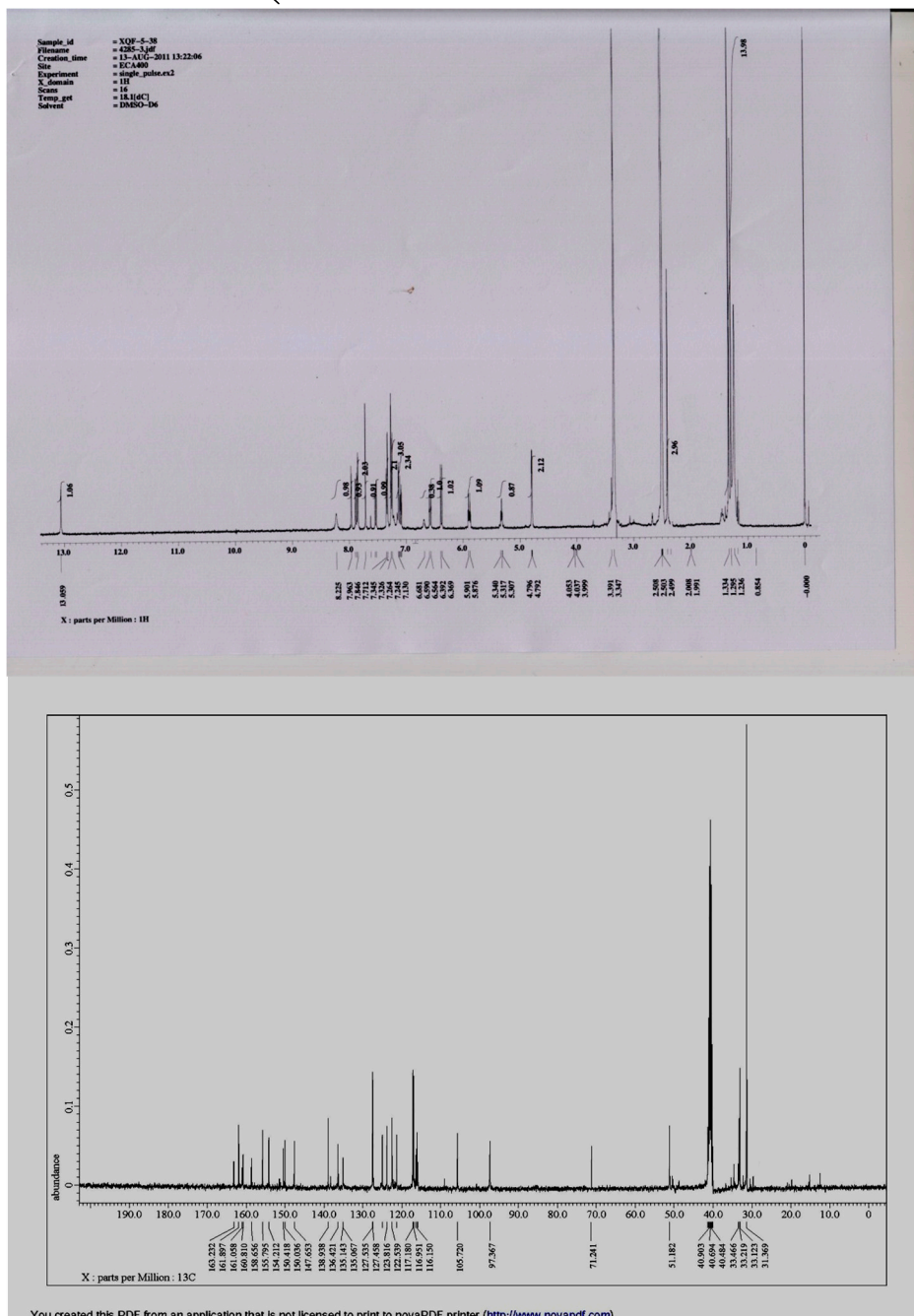
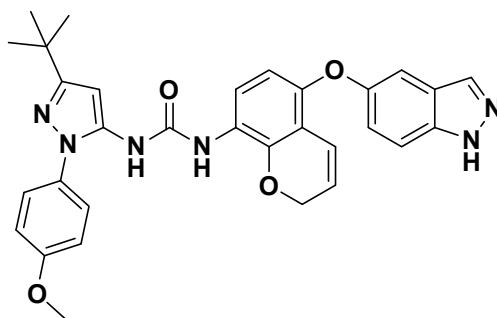


Figure S15. 1-(5-((1H-indazol-5-yl)oxy)-2H-chromen-8-yl)-3-(3-(tert-butyl)-1-(4-methoxyphenyl)-1H-pyrazol-5-yl)urea (**26d**).

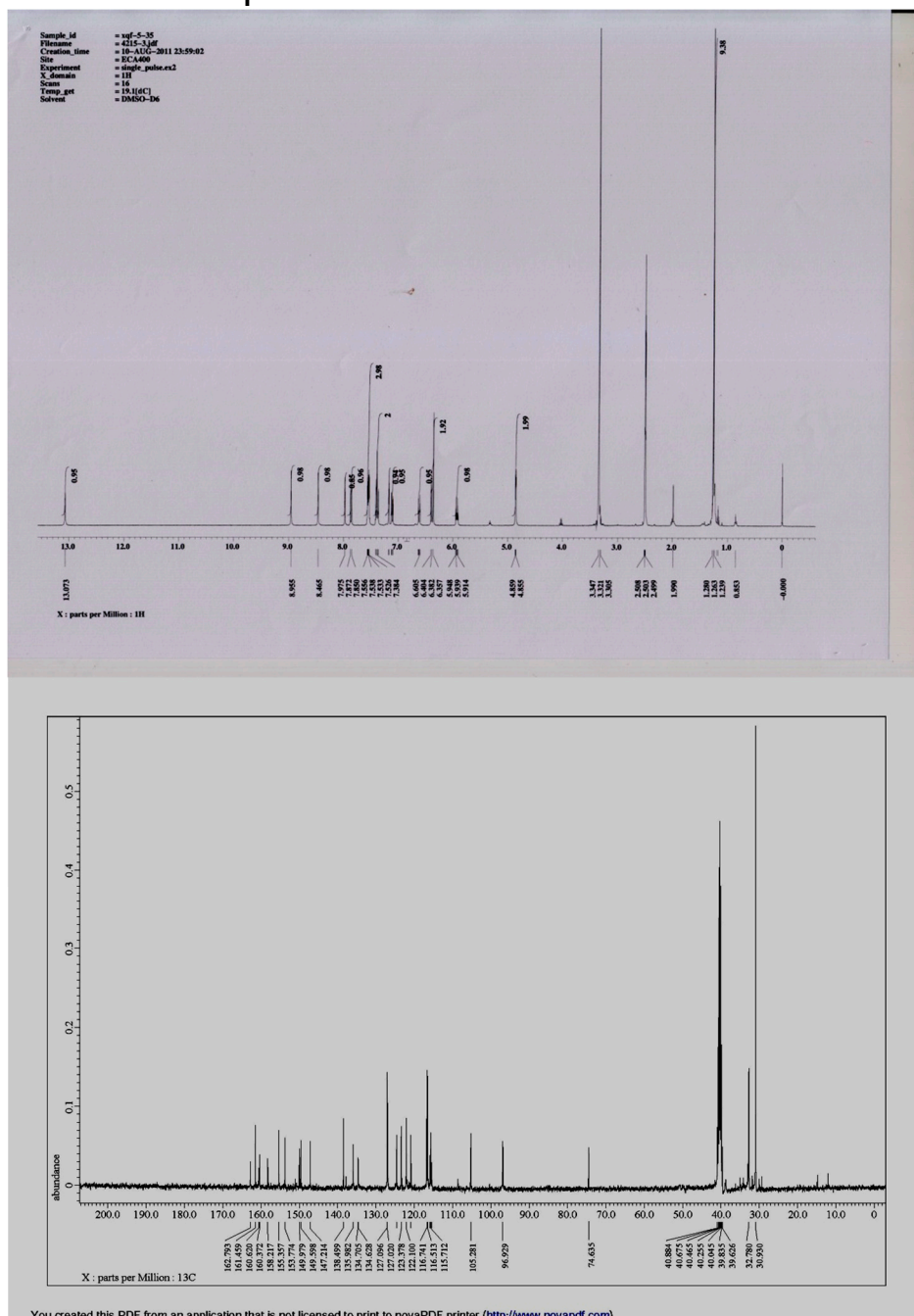
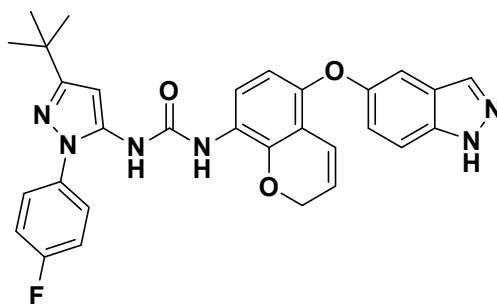


Figure S16. 1-(5-((1H-indazol-5-yl)oxy)-2H-chromen-8-yl)-3-(3-(tert-butyl)-1-(4-fluorophenyl)-1H-pyrazol-5-yl)urea (**26e**).

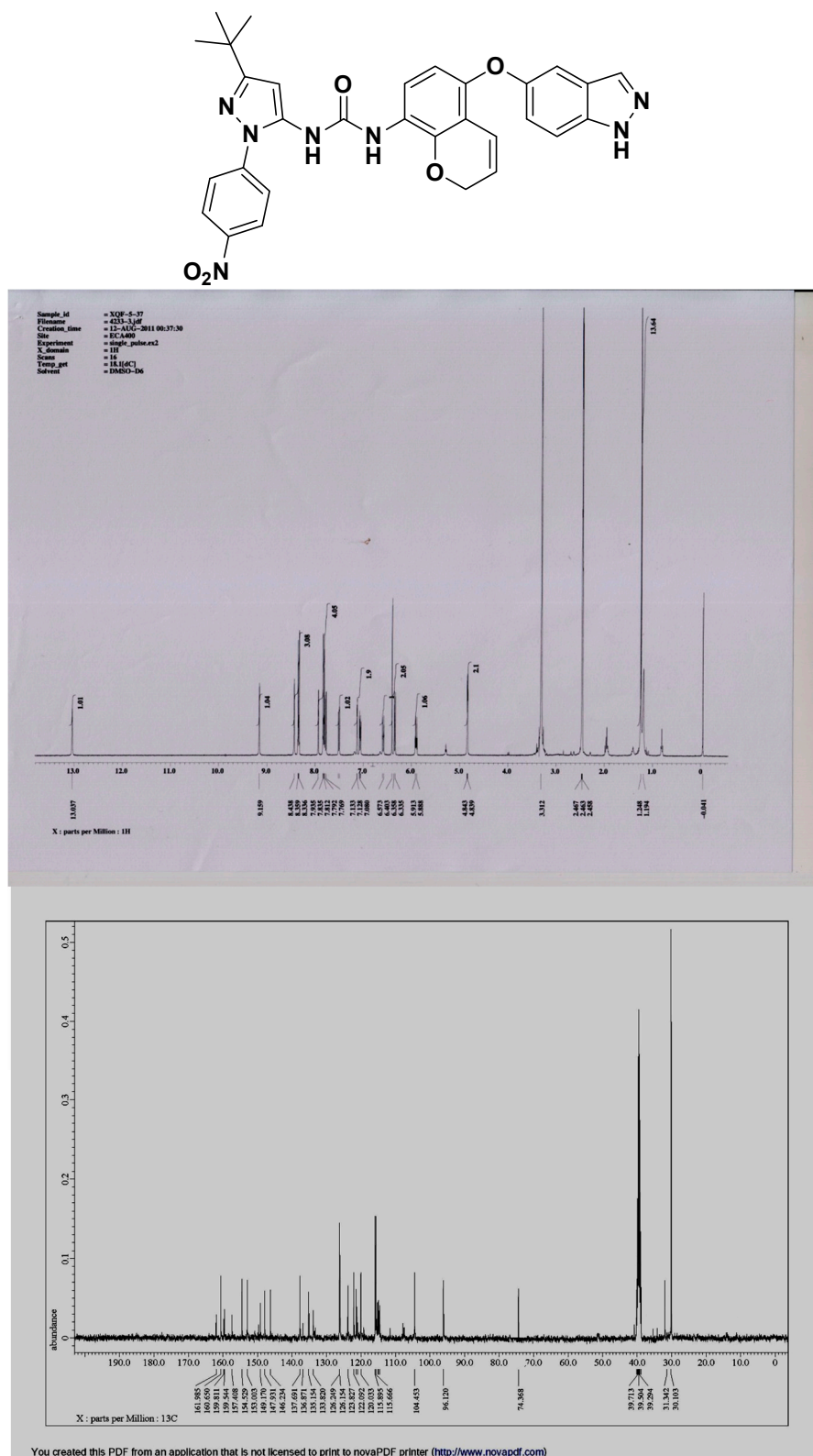


Figure S17. 1-(5-((1H-indazol-5-yl)oxy)-2H-chromen-8-yl)-3-(3-(tert-butyl)-1-(4-nitrophenyl)-1H-pyrazol-5-yl)urea (**26f**).

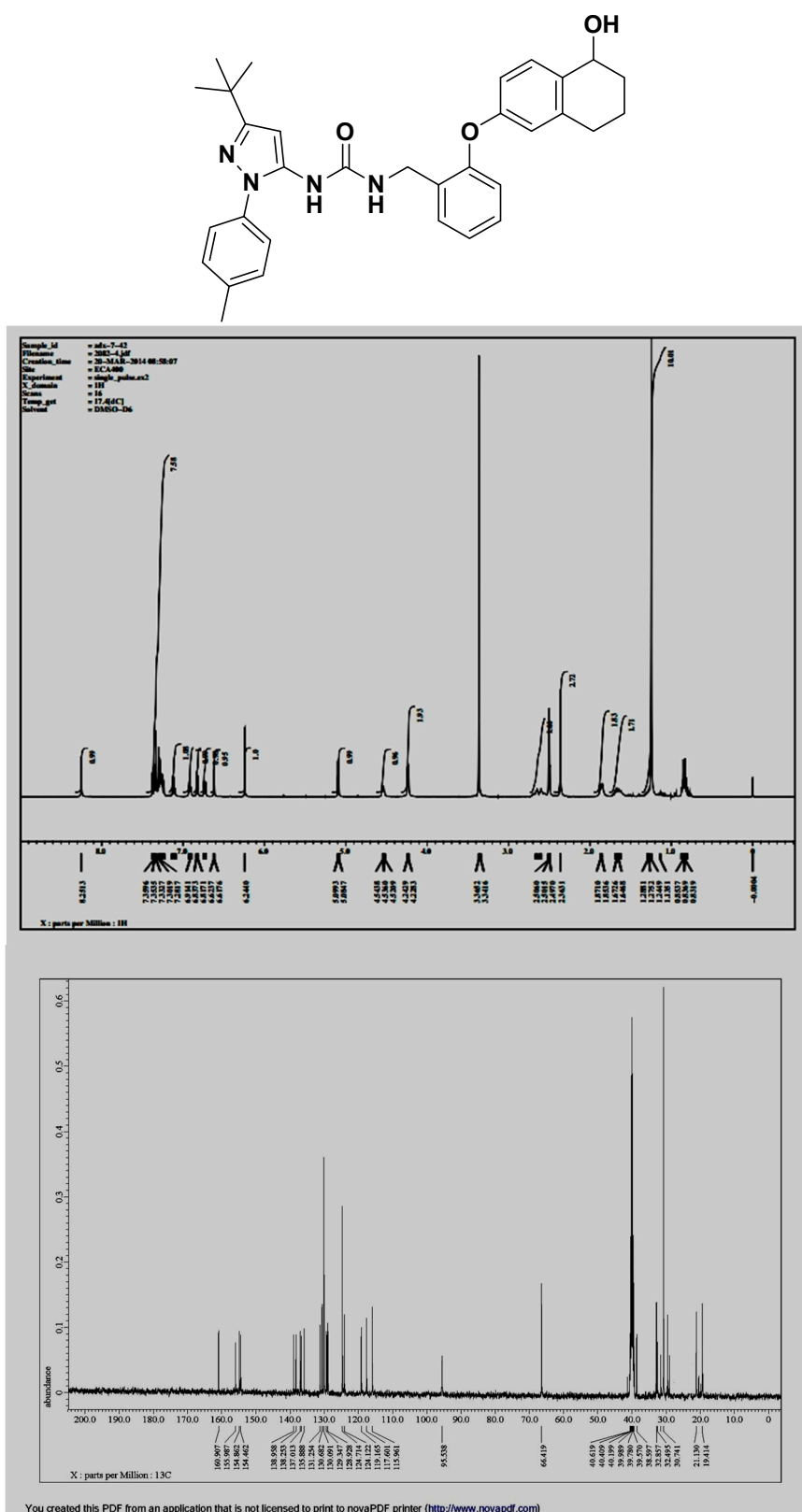


Figure S18. 1-(3-(tert-butyl)-1-(p-tolyl)-1H-pyrazol-5-yl)-3-(2-((5-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)oxy)benzyl)urea (27a).

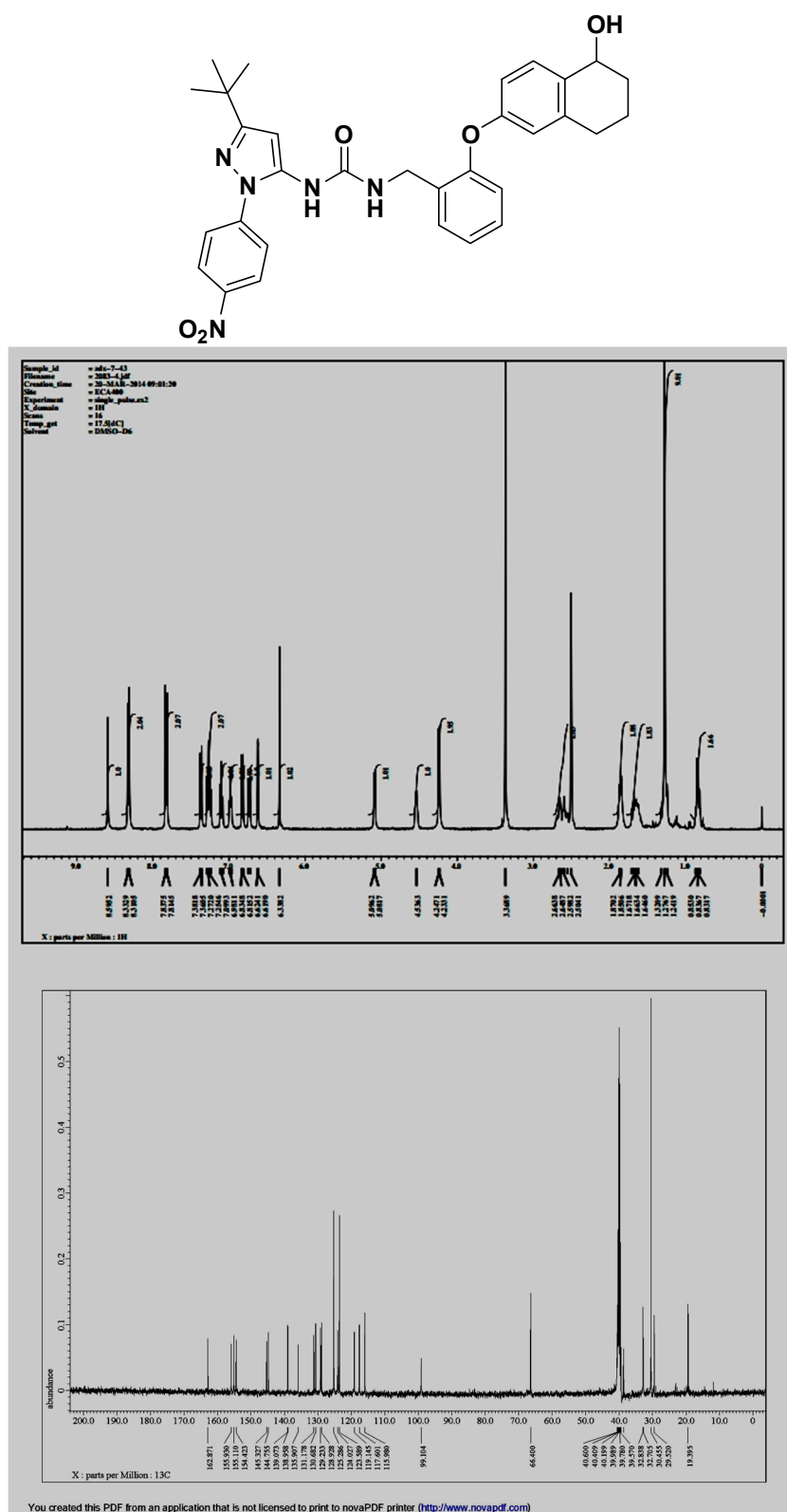


Figure S19. 1-(3-(tert-butyl)-1-(4-nitrophenyl)-1H-pyrazol-5-yl)-3-(2-((5-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)oxy)benzyl)urea (**27b**).

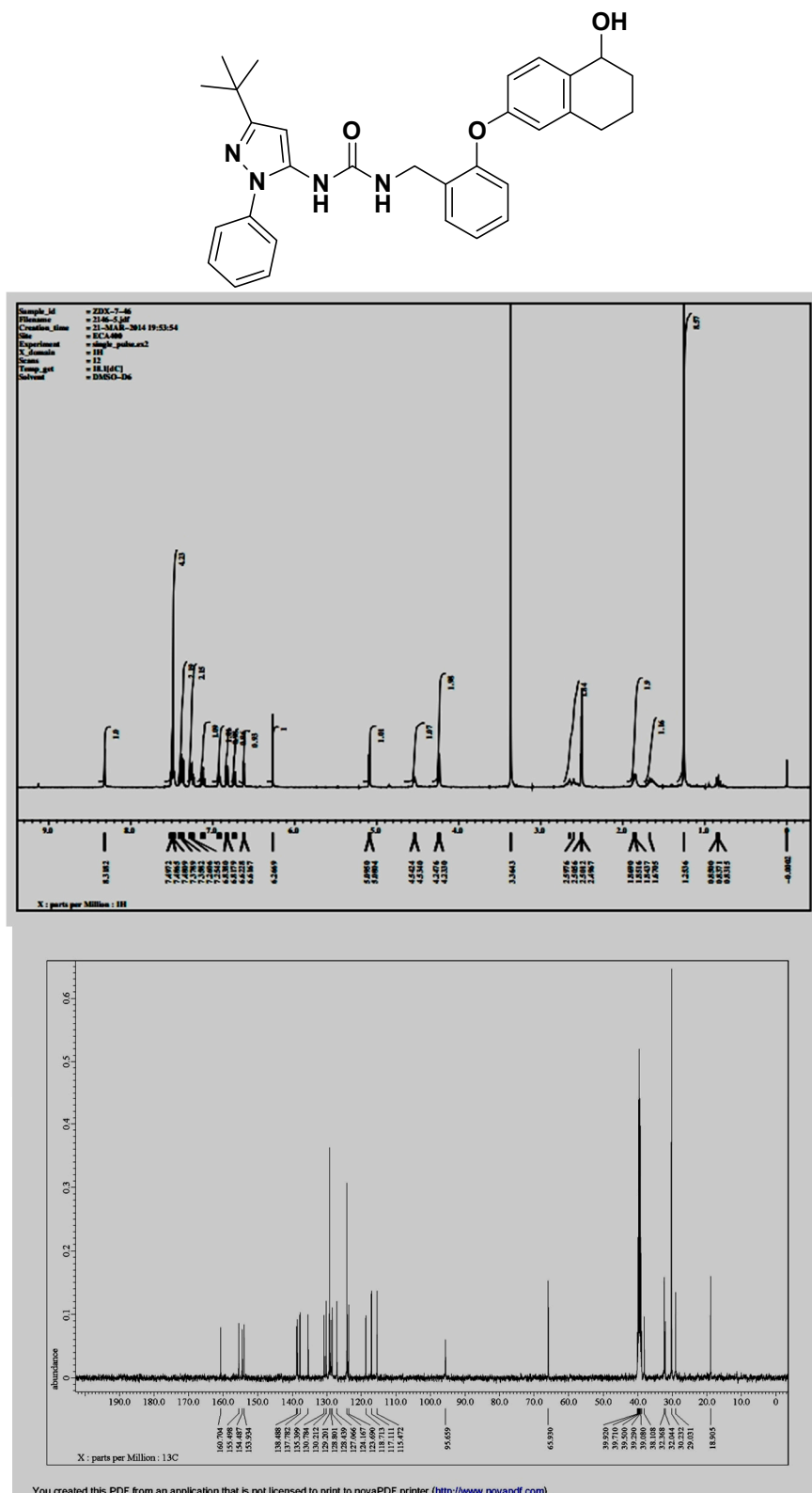


Figure S20. 1-(3-(tert-butyl)-1-phenyl-1H-pyrazol-5-yl)-3-(2-((5-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)oxy)benzyl)urea (**27c**).

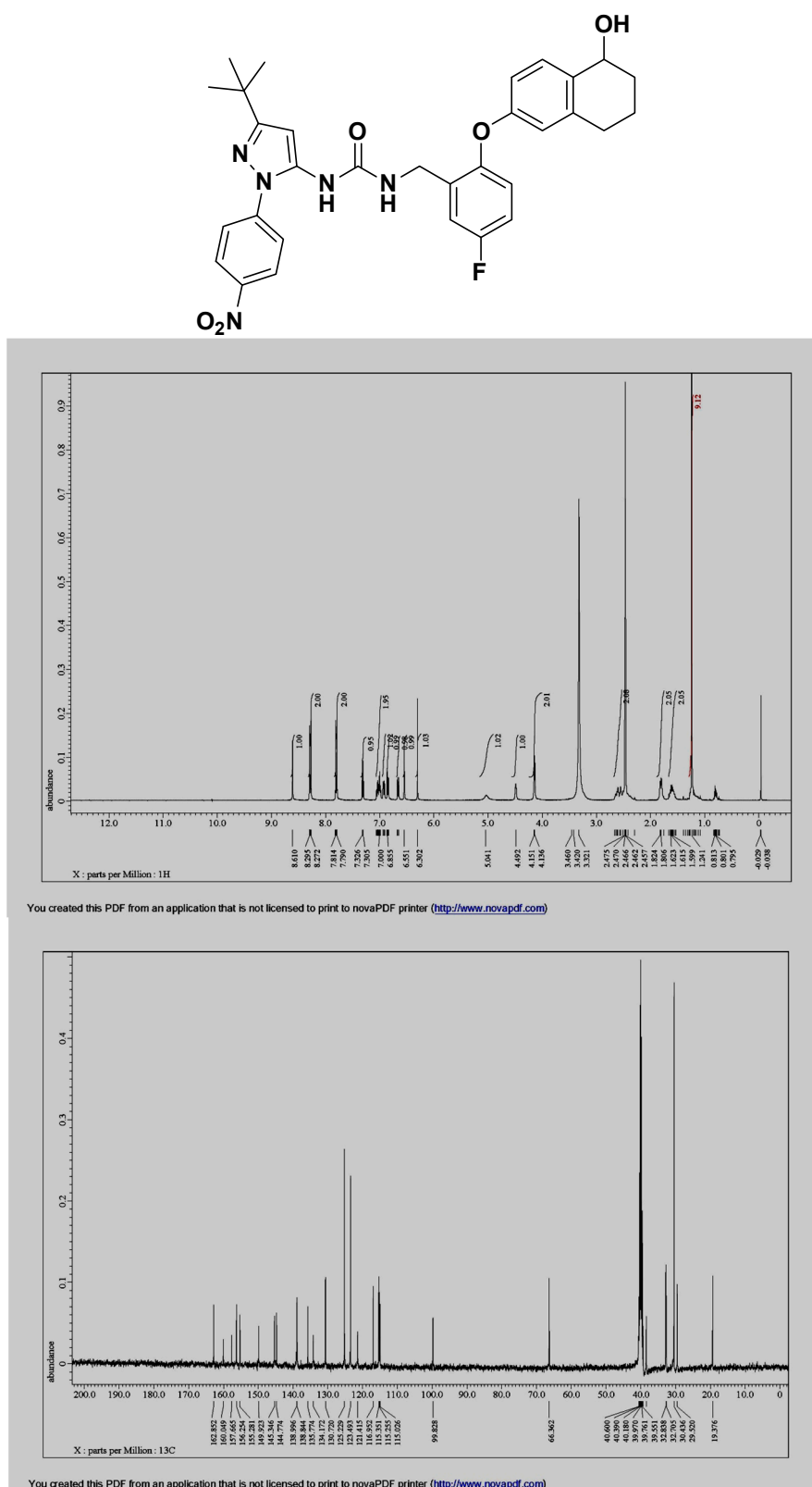


Figure S21. 1-(3-(tert-butyl)-1-(4-nitrophenyl)-1H-pyrazol-5-yl)-3-(5-fluoro-2-((5-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)oxy)benzyl)urea (27d).

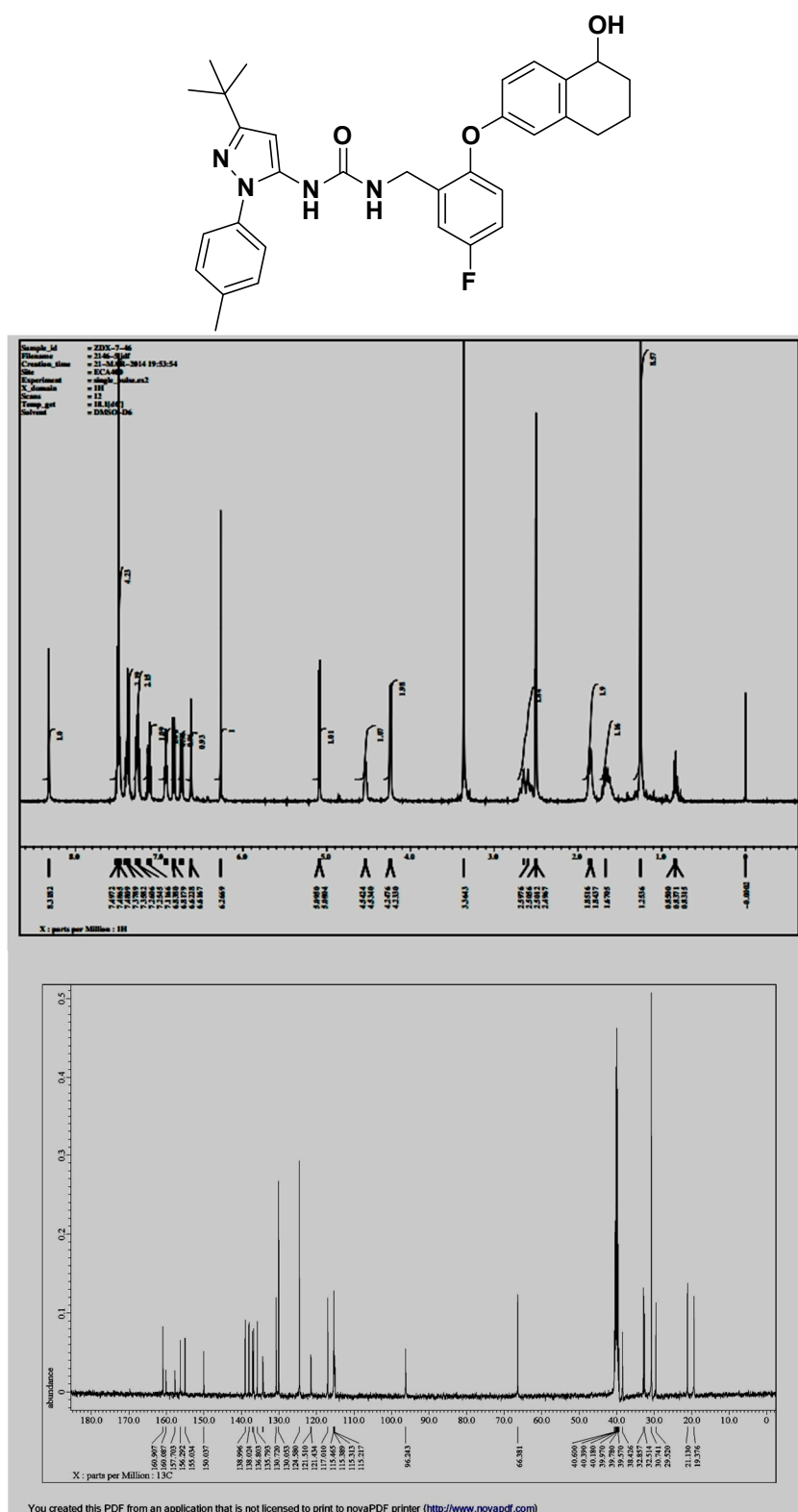


Figure S22. 1-(3-(tert-butyl)-1-(p-tolyl)-1H-pyrazol-5-yl)-3-(5-fluoro-2-((5-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)oxy)benzyl)urea (27e).

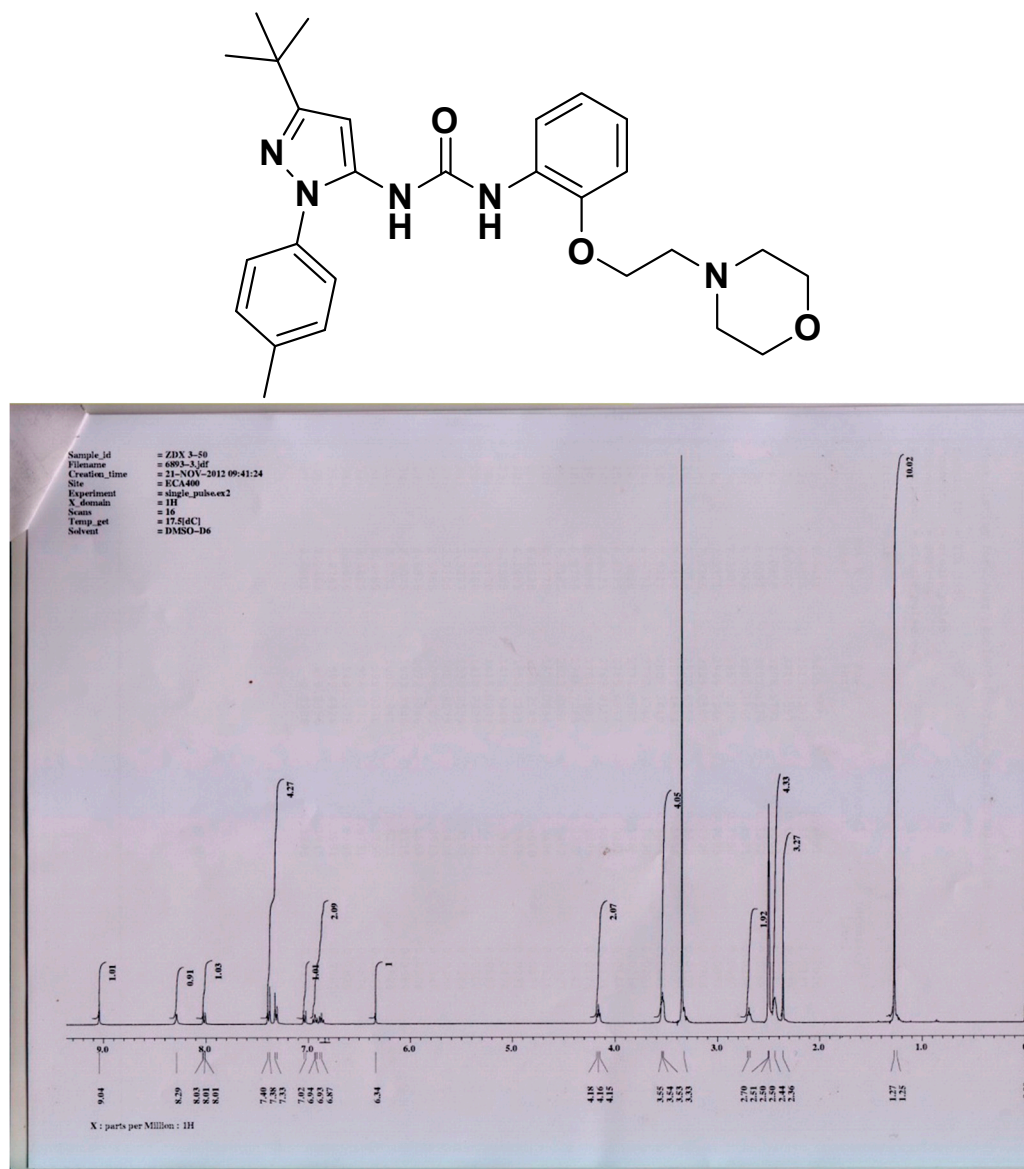


Figure S23. 1-(3-(tert-butyl)-1-(p-tolyl)-1H-pyrazol-5-yl)-3-(2-(2-morpholinoethoxy)phenyl)urea (28a).

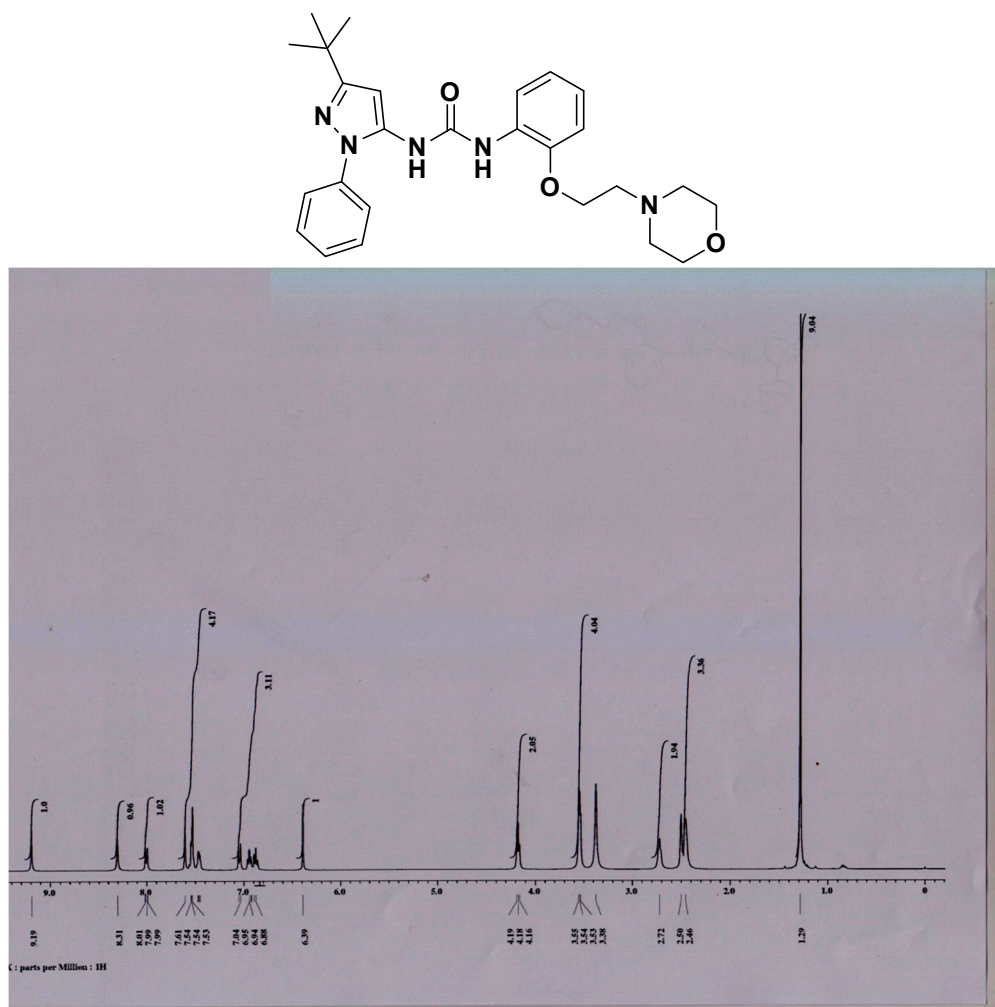


Figure S24. 1-(3-(tert-butyl)-1-phenyl-1H-pyrazol-5-yl)-3-(2-(2-morpholinoethoxy)phenyl)urea (**28b**).

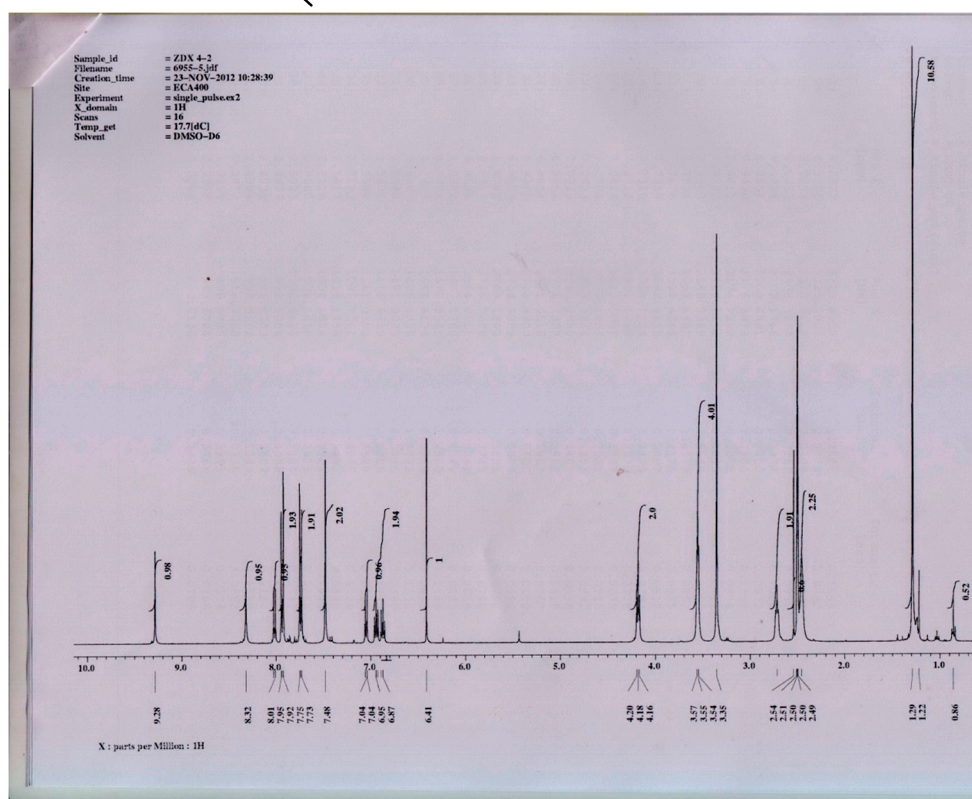
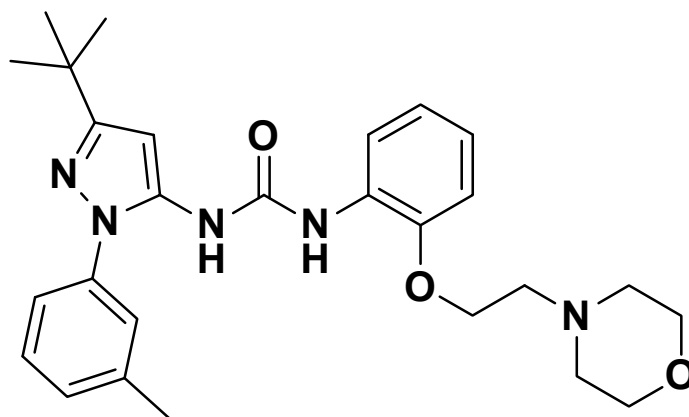


Figure S25. 1-(3-(tert-butyl)-1-(m-tolyl)-1H-pyrazol-5-yl)-3-(2-(2-morpholinoethoxy)phenyl)urea (**28c**).

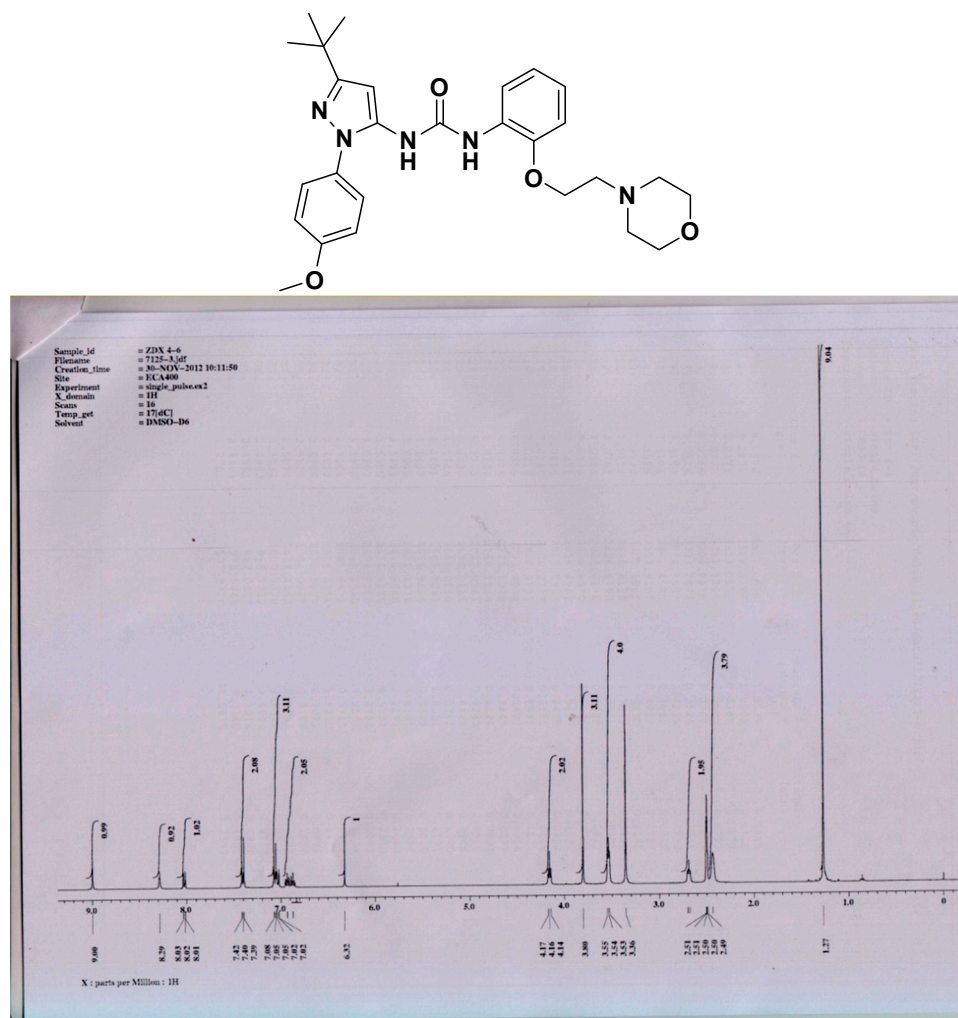


Figure S26. 1-(3-(tert-butyl)-1-(4-methoxyphenyl)-1H-pyrazol-5-yl)-3-(2-(2-morpholinoethoxy)phenyl)urea (**28d**).

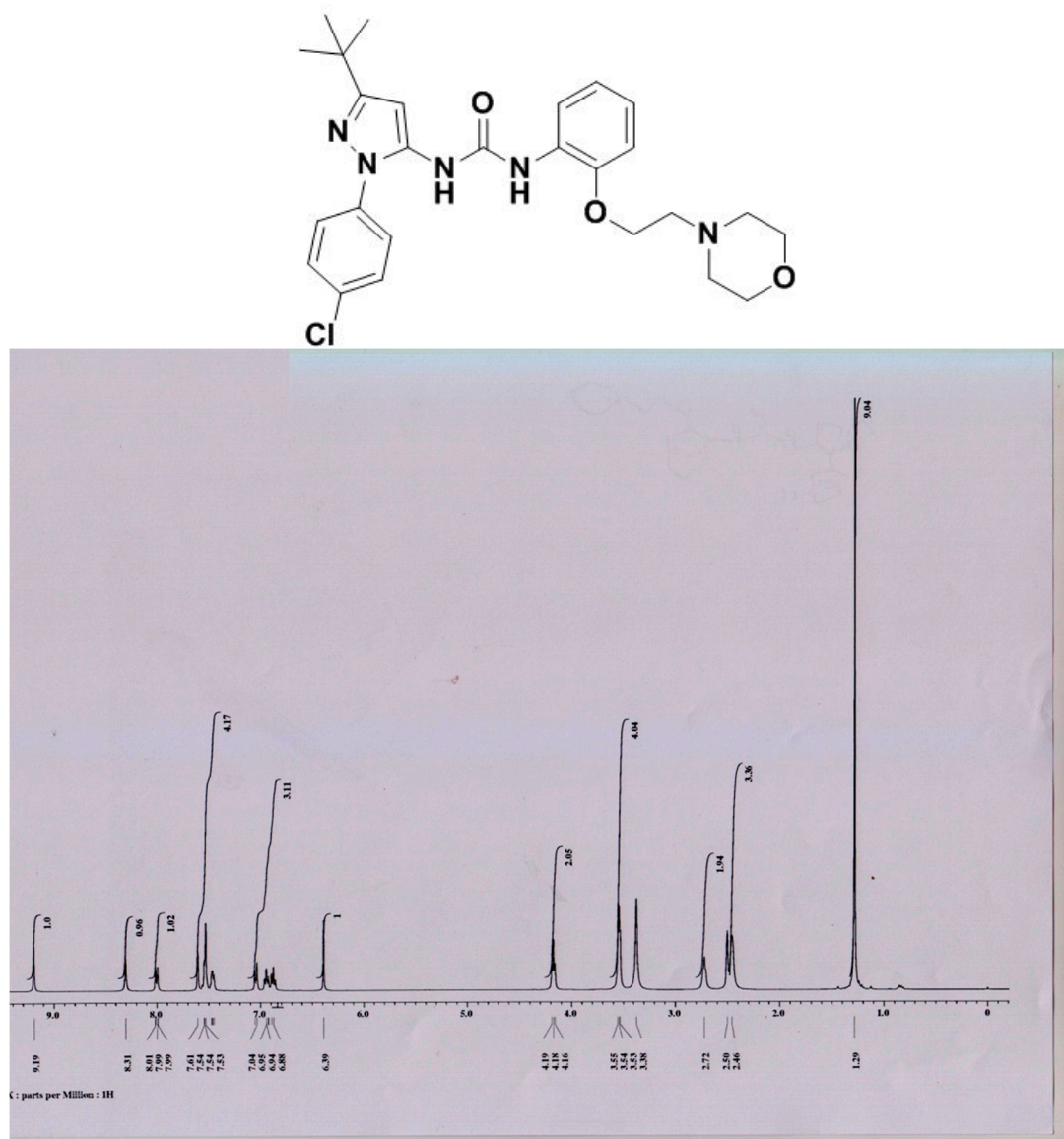


Figure S27. 1-(3-(tert-butyl)-1-(4-chlorophenyl)-1H-pyrazol-5-yl)-3-(2-(2-morpholinoethoxy)phenyl)urea (28e).

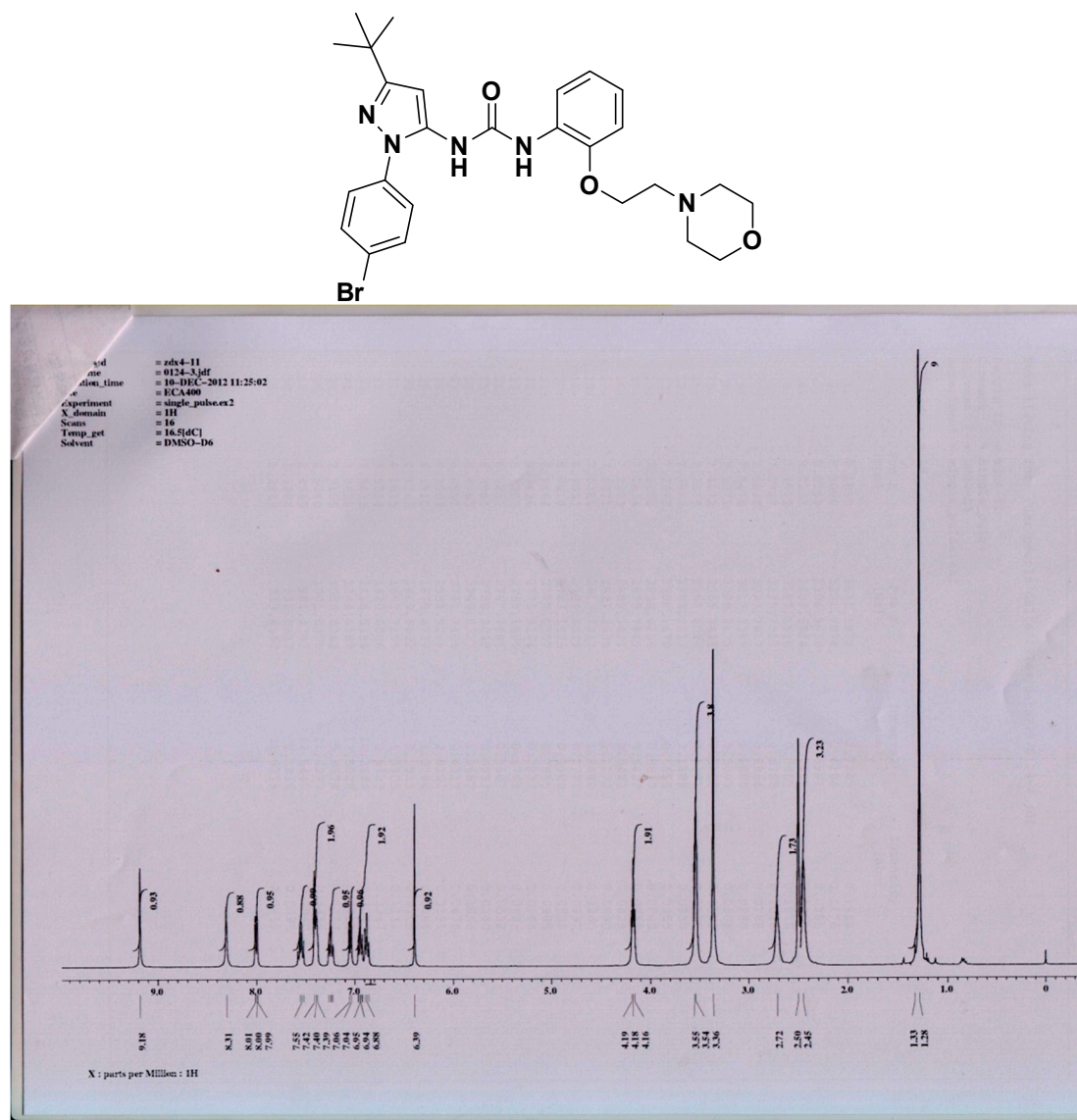


Figure S28. 1-(1-(4-bromophenyl)-3-(tert-butyl)-1H-pyrazol-5-yl)-3-(2-(2-morpholinoethoxy)phenyl)urea (**28f**).

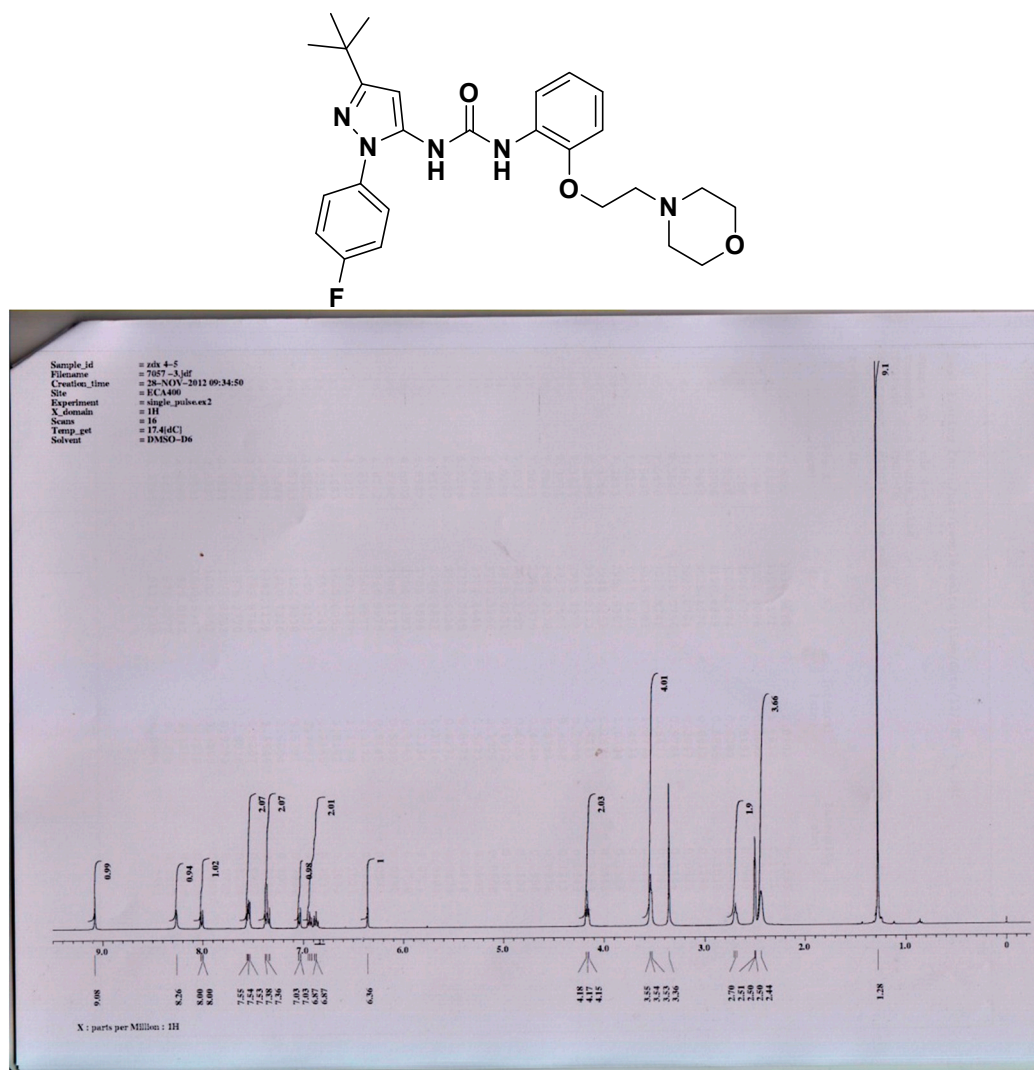


Figure S29. 1-(3-(tert-butyl)-1-(4-fluorophenyl)-1H-pyrazol-5-yl)-3-(2-(2-morpholinoethoxy)phenyl)urea (28g).

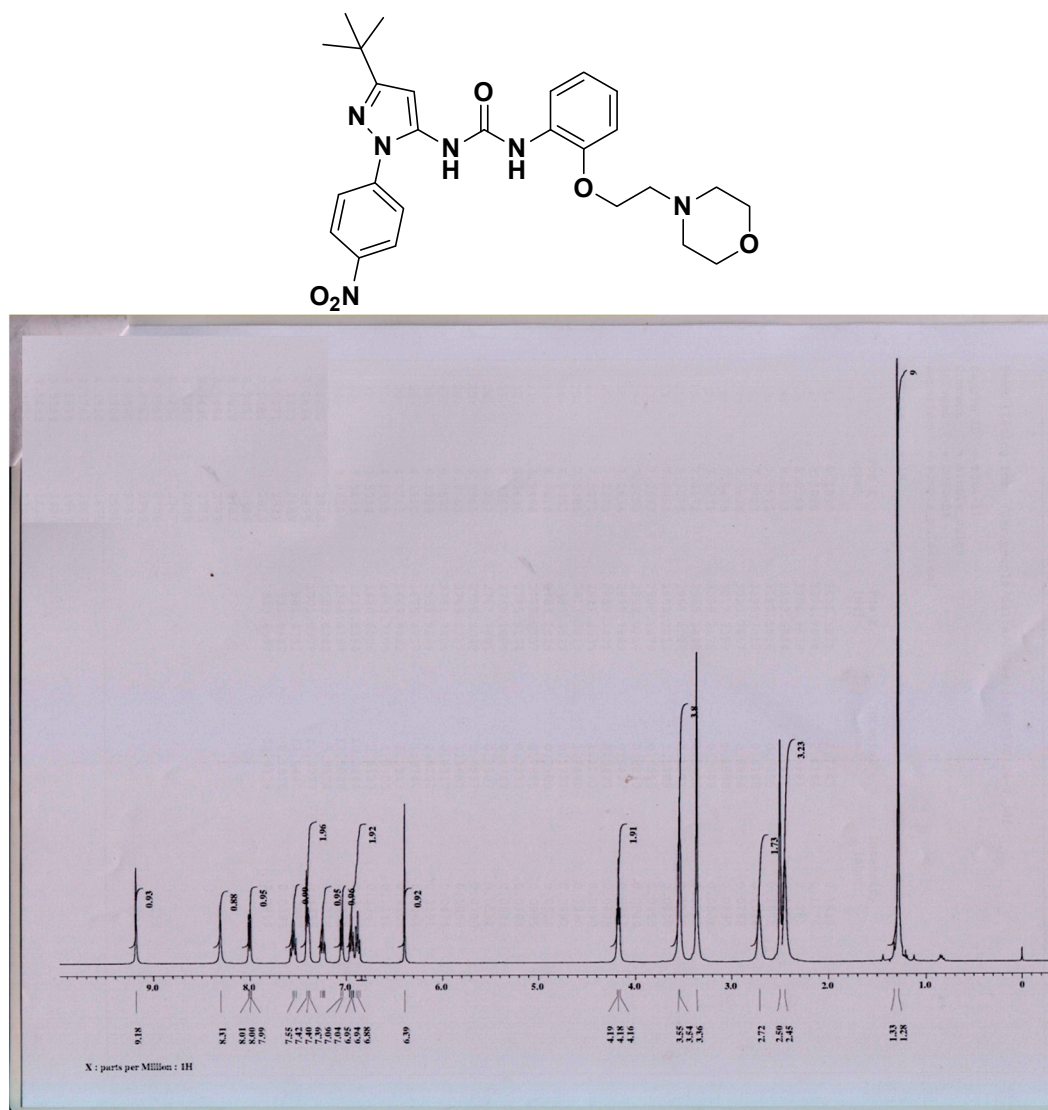


Figure S30. 1-(3-(tert-butyl)-1-(4-nitrophenyl)-1H-pyrazol-5-yl)-3-(2-(2-morpholinoethoxy)phenyl)urea (**28h**).

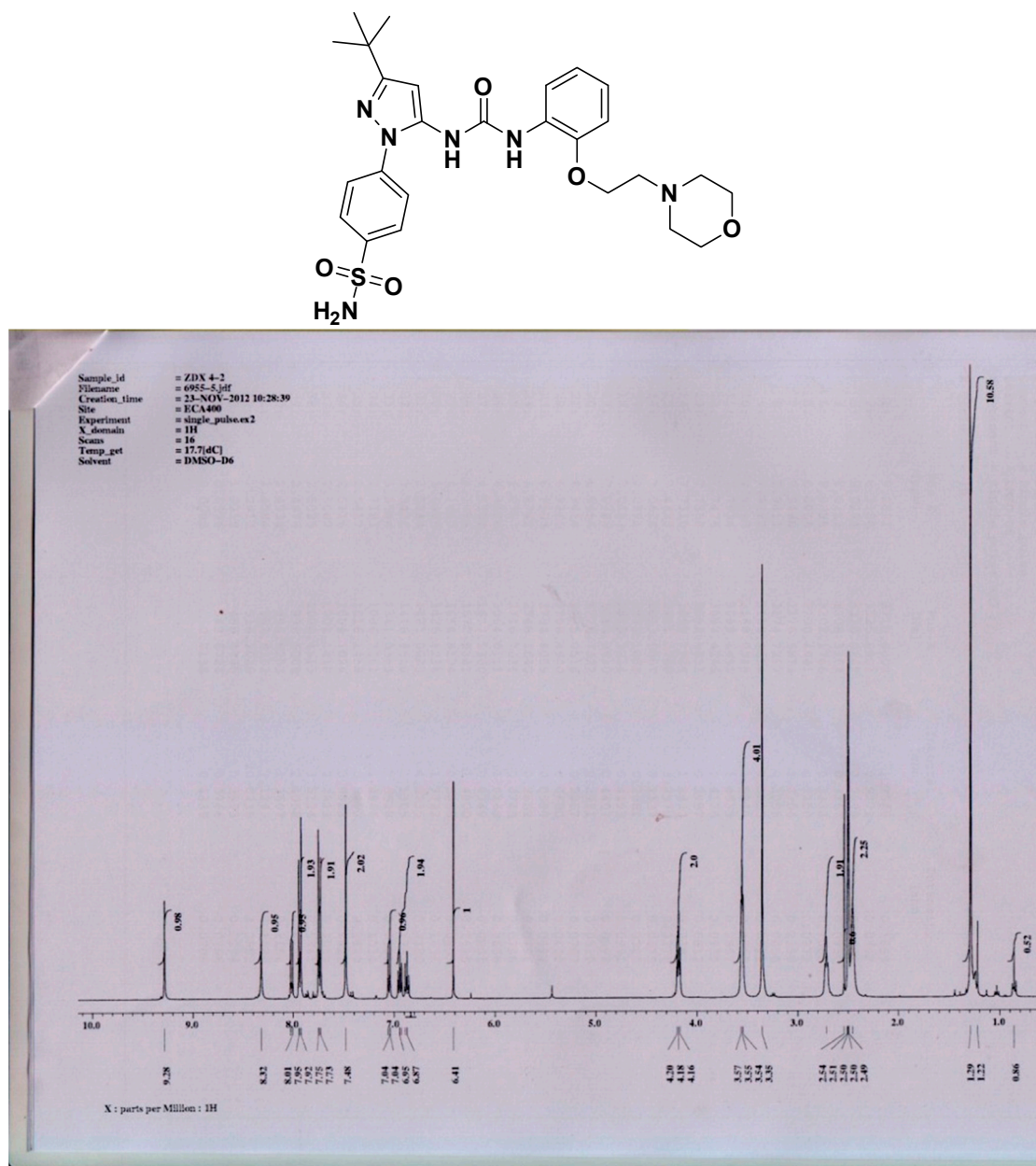
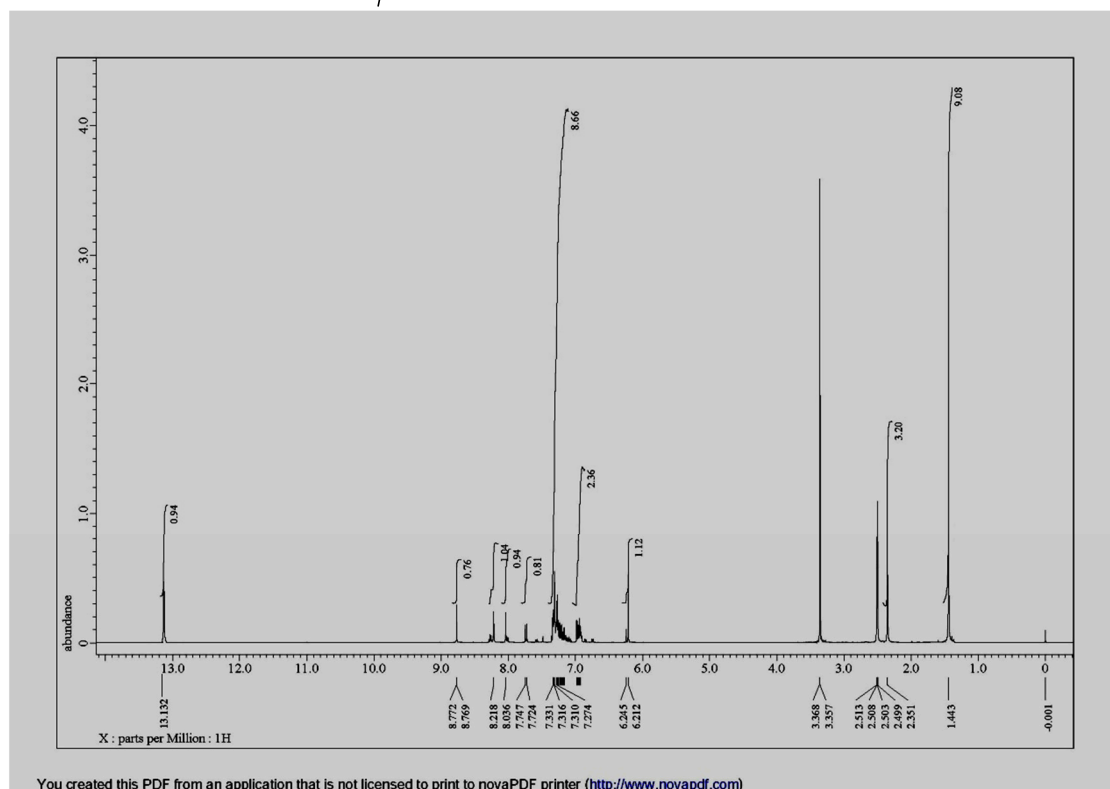
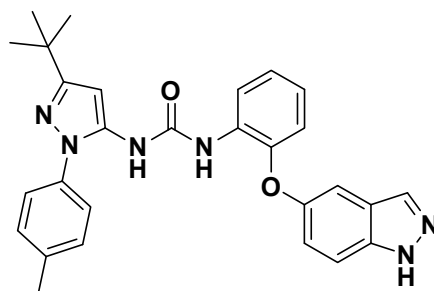


Figure S31. 4-(3-(tert-butyl)-5-(3-(2-(2-morpholinoethoxy)phenyl)ureido)-1H-pyrazol-1-yl)benzenesulfonamide (28i).



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Figure S32. 1-(2-((1H-indazol-5-yl)oxy)phenyl)-3-(3-(tert-butyl)-1-(p-tolyl)-1H-pyrazol-5-yl)urea(**29a**).

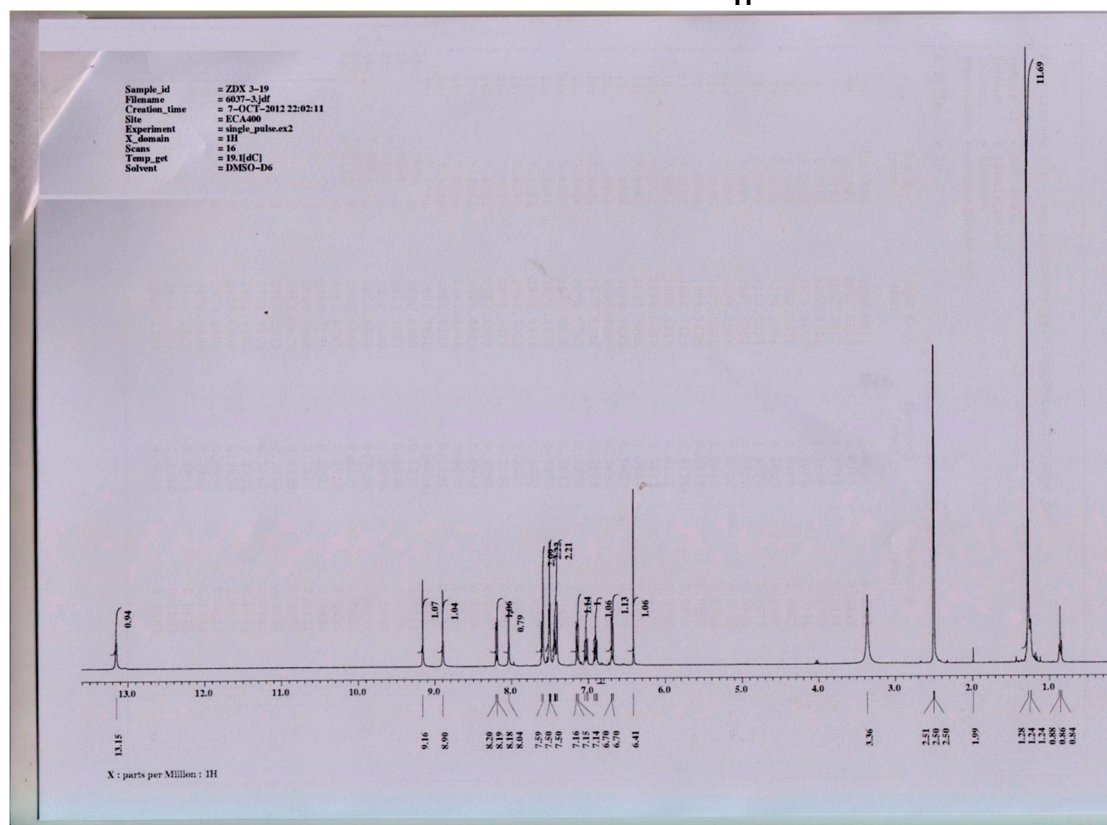
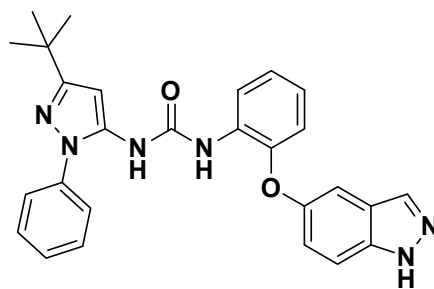
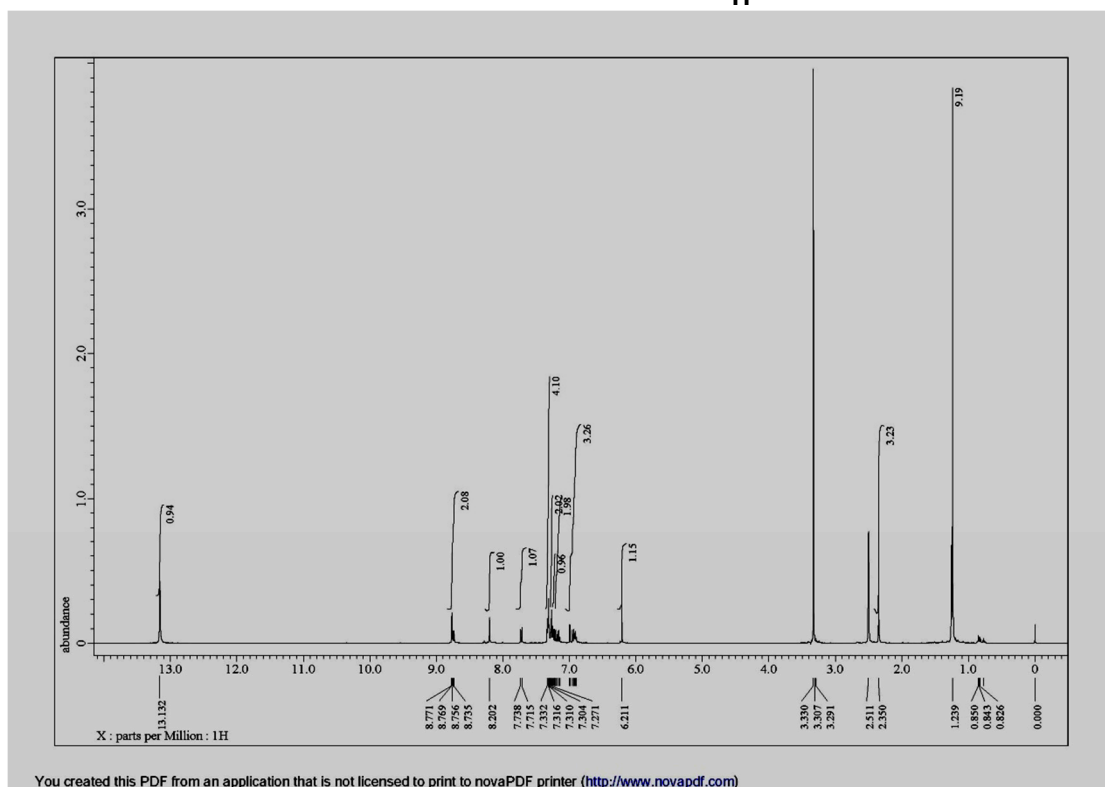
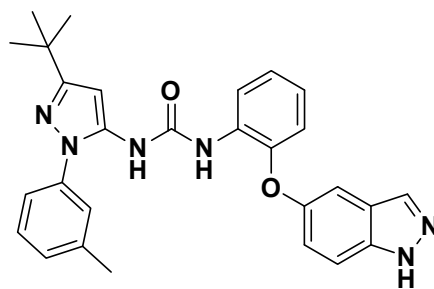


Figure S33. 1-(2-((1H-indazol-5-yl)oxy)phenyl)-3-(3-(tert-butyl)-1-phenyl-1H-pyrazol-5-yl)urea(29b).



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Figure S34. 1-(2-((1H-indazol-5-yl)oxy)phenyl)-3-(3-(tert-butyl)-1-(m-tolyl)-1H-pyrazol-5-yl)urea(29c).

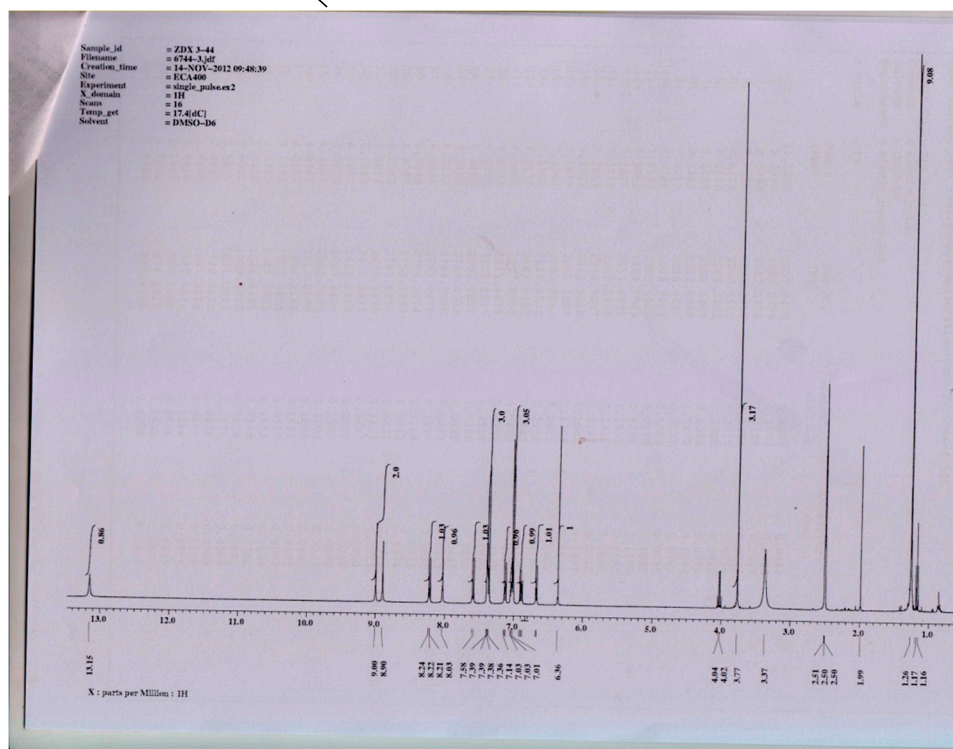
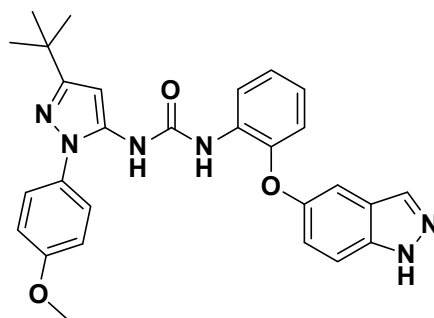


Figure S35. 1-(2-((1H-indazol-5-yl)oxy)phenyl)-3-(3-(tert-butyl)-1-(4-methoxyphenyl)-1H-pyrazol-5-yl)urea (**29d**).

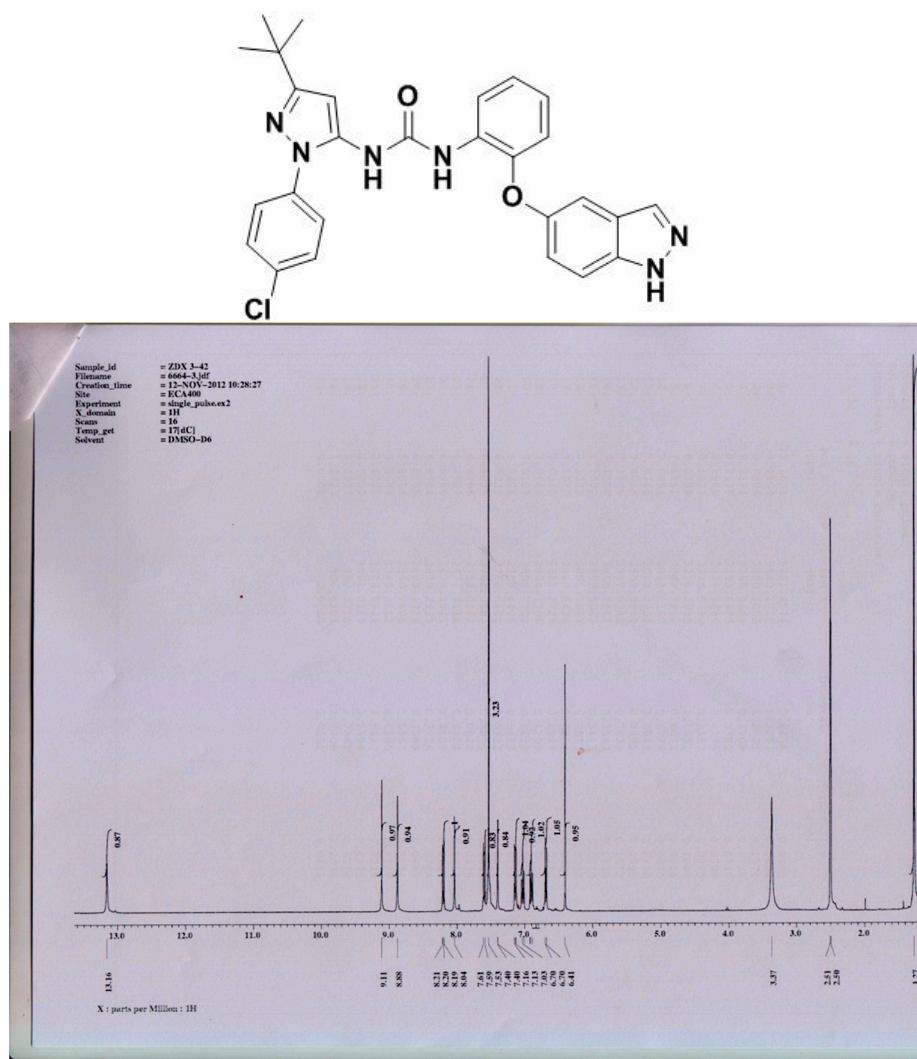


Figure S36. 1-(2-((1H-indazol-5-yl)oxy)phenyl)-3-(3-(tert-butyl)-1-(4-chlorophenyl)-1H-pyrazol-5-yl)urea (29e).

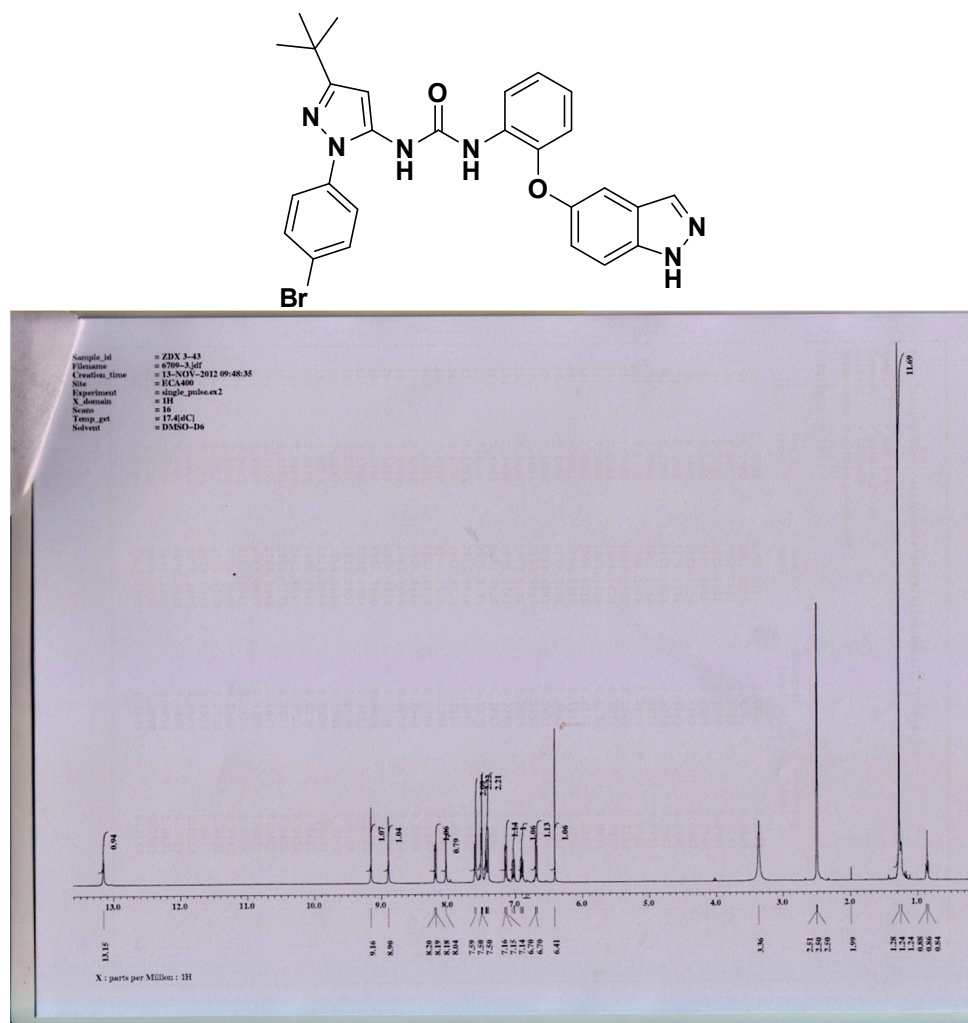


Figure S37. 1-(2-((1H-indazol-5-yl)oxy)phenyl)-3-(1-(4-bromophenyl)-3-(tert-butyl)-1H-pyrazol-5-yl)urea (**29f**).

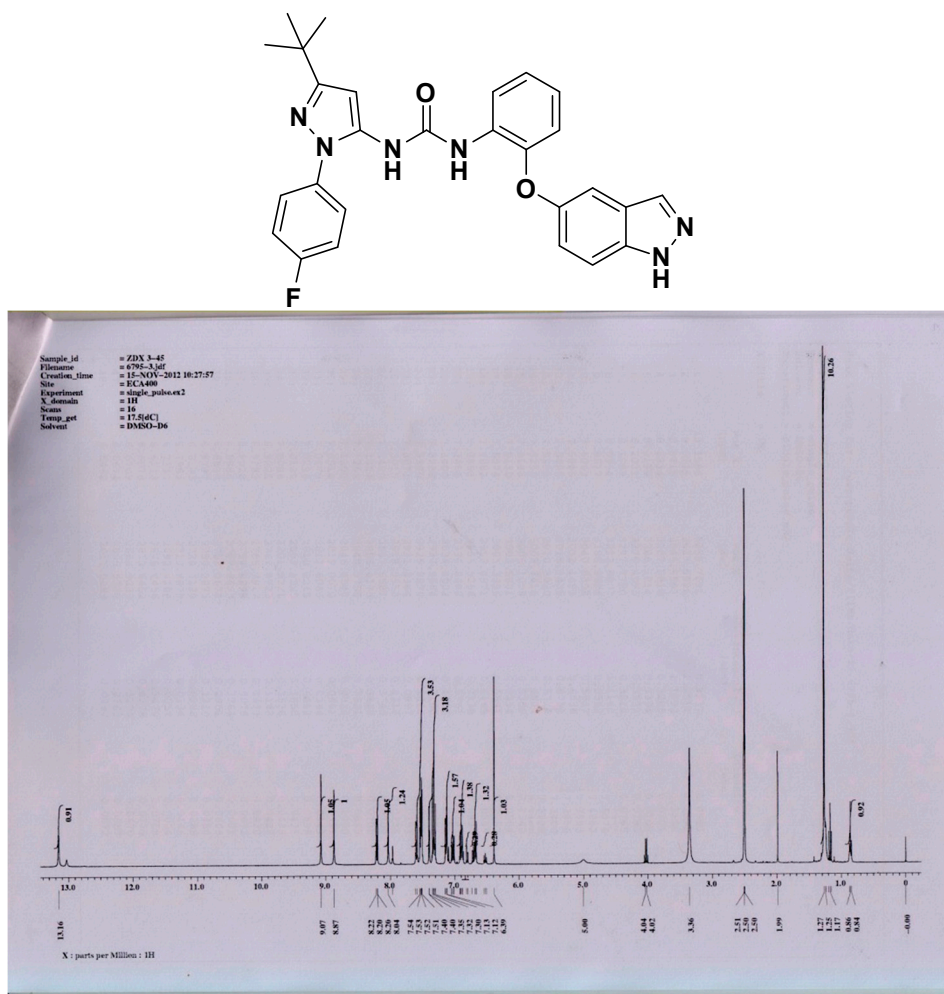


Figure S38. 1-(2-((1H-indazol-5-yl)oxy)phenyl)-3-(3-(tert-butyl)-1-(4-fluorophenyl)-1H-pyrazol-5-yl)urea (**29g**).

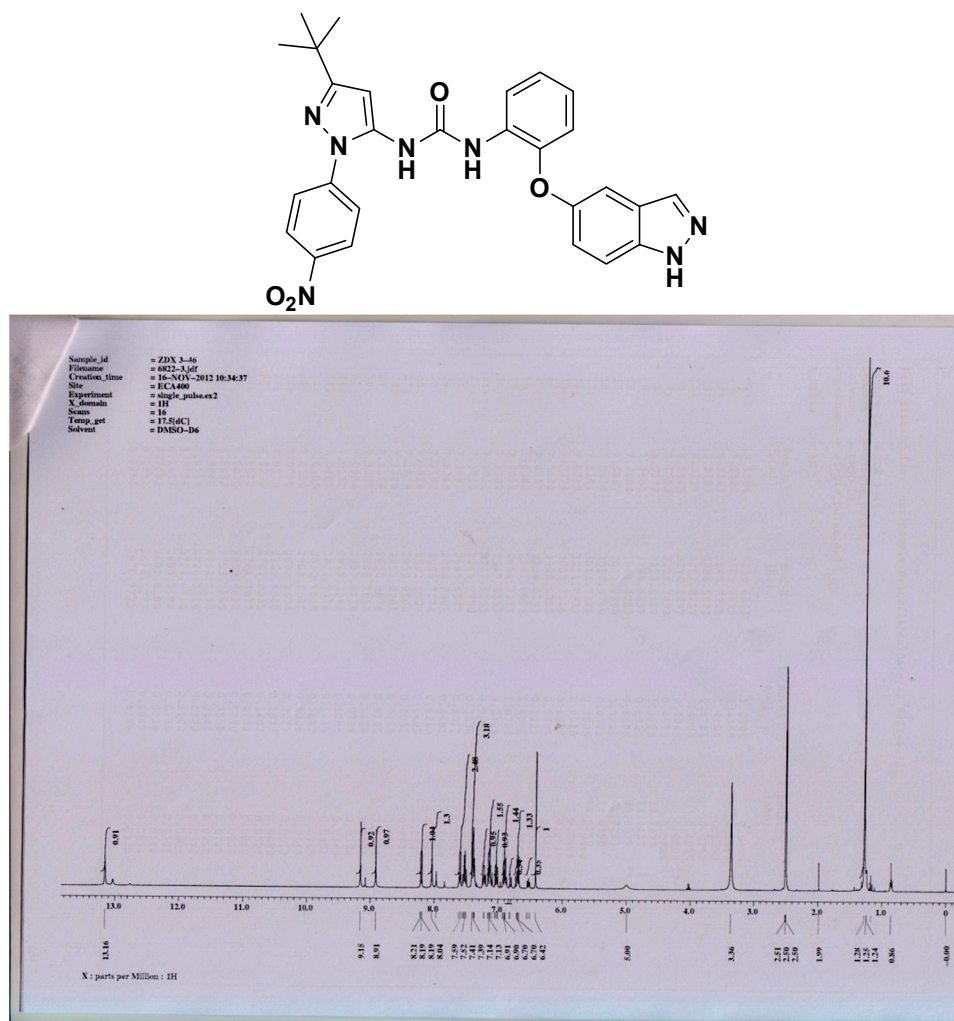


Figure S39. 1-(2-((1H-indazol-5-yl)oxy)phenyl)-3-(3-(tert-butyl)-1-(4-nitrophenyl)-1H-pyrazol-5-yl)urea (29h).

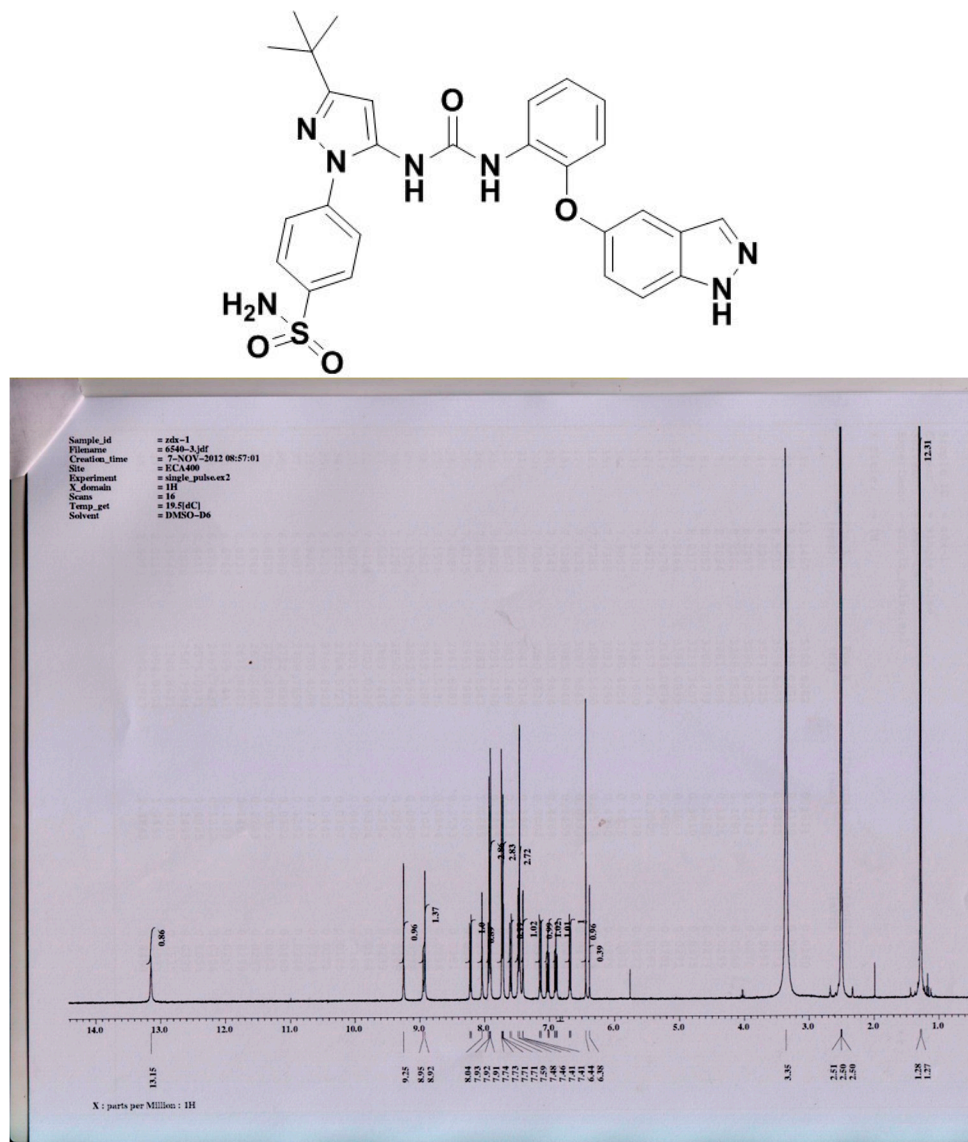


Figure S40. 4-(5-(3-(2-((1H-indazol-5-yl)oxy)phenyl)ureido)-3-(tert-butyl)-1H-pyrazol-1-yl)benzenesulfonamide (29i).

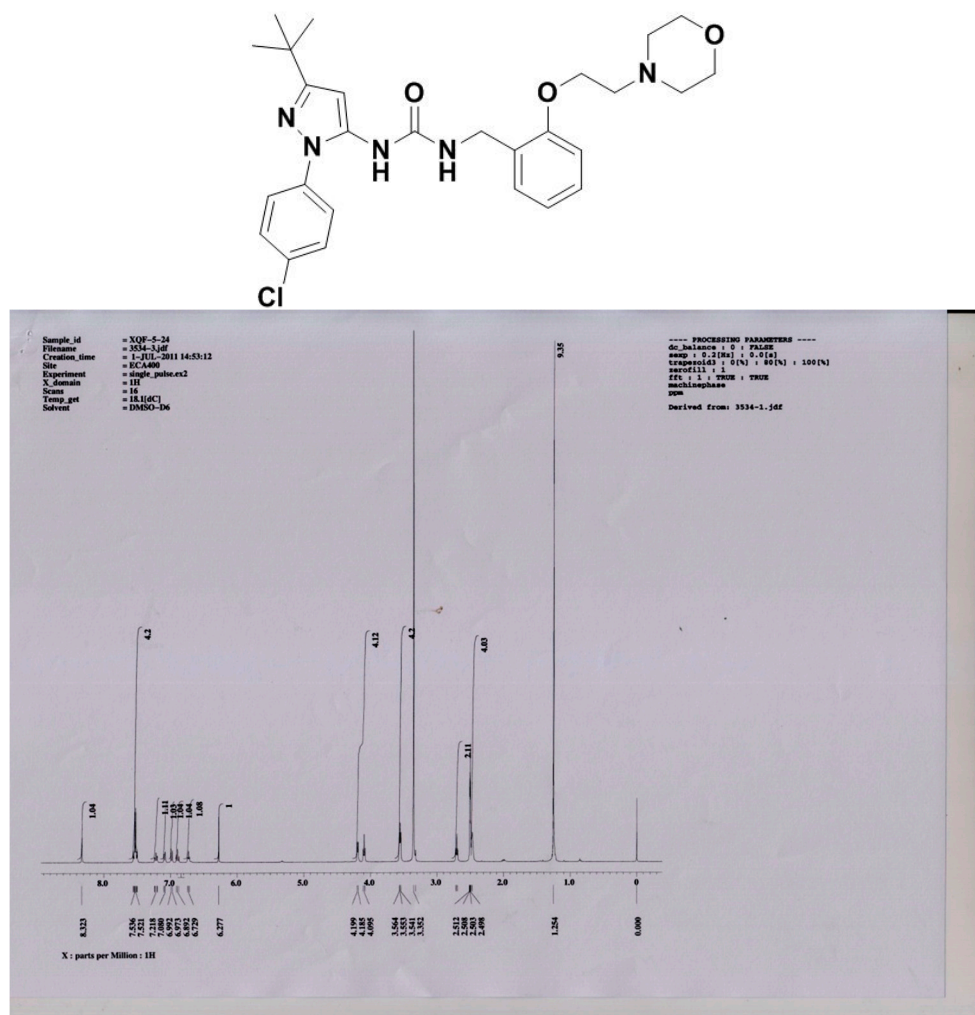


Figure S41. 1-(3-(tert-butyl)-1-(4-chlorophenyl)-1H-pyrazol-5-yl)-3-(2-(2-morpholinoethoxy)benzyl)urea (**30a**).

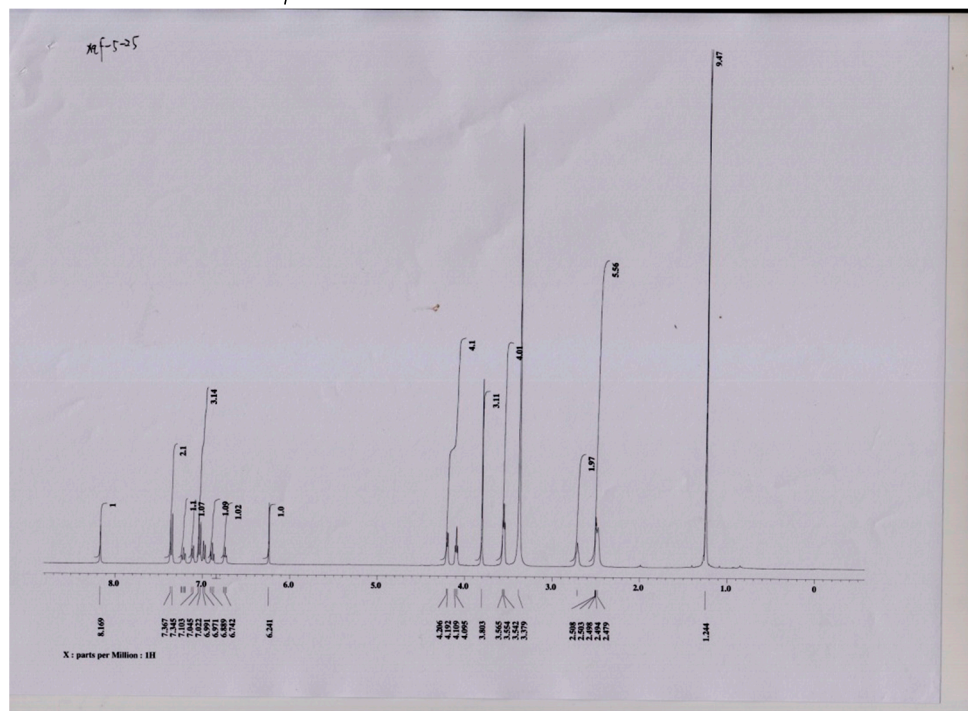
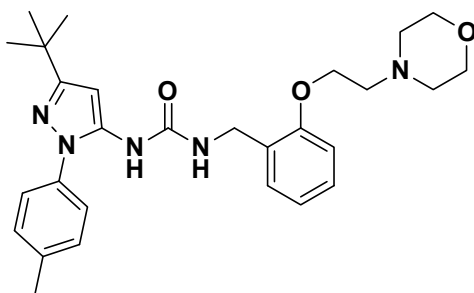


Figure S42. 1-(3-(tert-butyl)-1-(p-tolyl)-1H-pyrazol-5-yl)-3-(2-(2-morpholinoethoxy)benzyl)urea (**30b**).

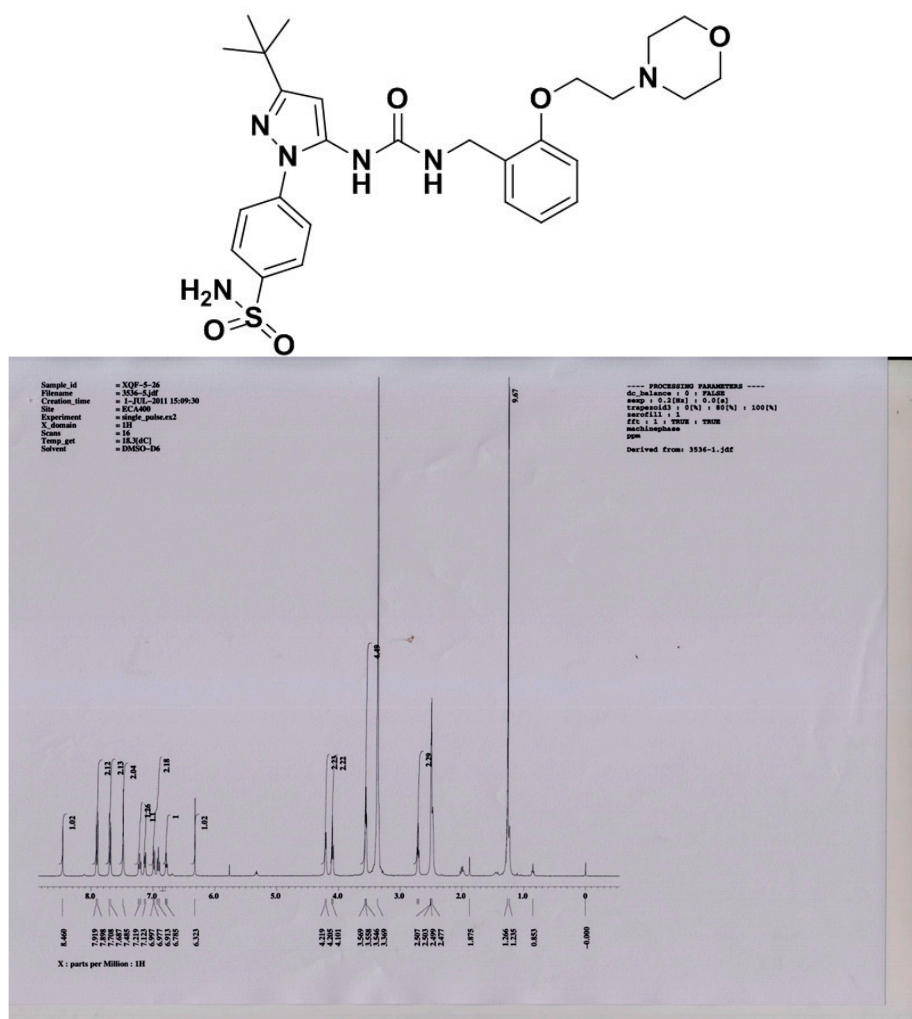


Figure S43. 4-(3-(tert-butyl)-5-(3-(2-(2-morpholinoethoxy)benzyl)ureido)-1H-pyrazol-1-yl)benzenesulfonamide (30c).

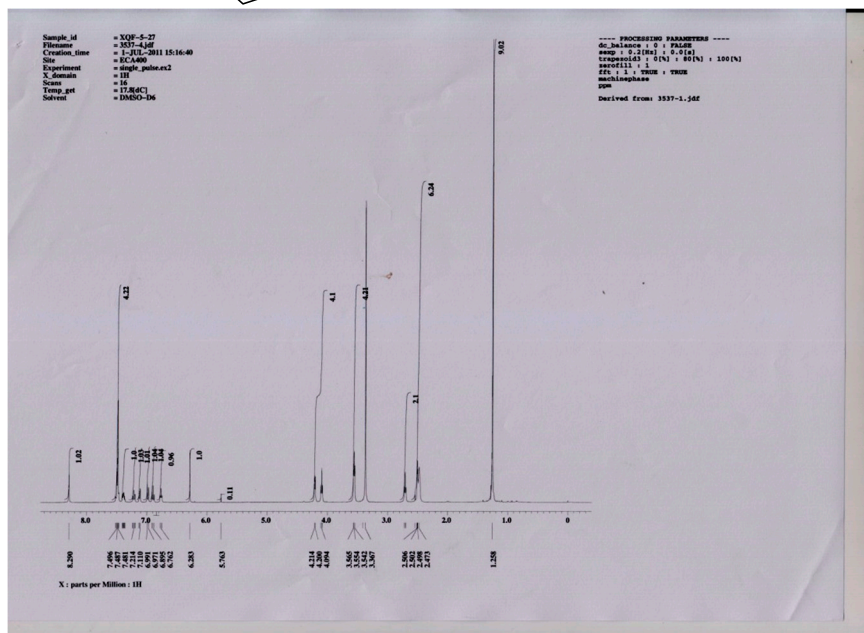
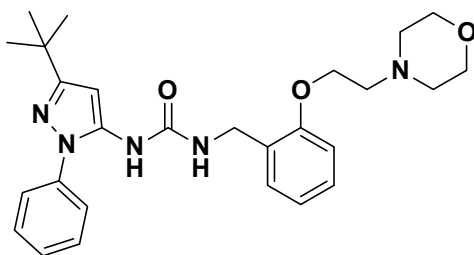


Figure S44. 1-(3-(tert-butyl)-1-phenyl-1H-pyrazol-5-yl)-3-(2-(2-morpholinoethoxy)benzyl)urea (**30d**).