

SUPPORTING INFORMATION

**Copper-catalyzed direct cross-coupling of 1,3,4-oxadiazoles with
N-tosylhydrazones: Efficient synthesis of benzylated 1,3,4-oxadiazoles**

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Copies of ¹H NMR and ¹³C NMR Spectra of Compounds

General information:

Melting points were measured on a Buchi 510 apparatus and are uncorrected. The spectra were recorded with the following instruments; IR: Perkin-Elmer RX FT-IR spectrophotometer; ESIMS: VG-Autospec micromass spectrometer. ¹H NMR and ¹³C NMR spectra were recorded on a 200 MHz and 50 MHz spectrometers using the solvent peak as internal reference (CDCl₃, δ H: 7.26; δ C: 77.0). Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constants (*J*) are in Hz. All reactions were monitored by thin-layer chromatography (TLC) using silica gel F₂₅₄ pre-coated plates. Visualization was accomplished with UV-light or I₂ stain. Solvents for the catalytic reactions were technical grade. Solvents for chromatography (EtOAc, hexane) were technical grade and distilled prior to use.

Experimental Details:

A. Typical procedure for synthesis of 1, 3, 4-oxadiazoles (1)¹:

Benzhydrazide (2 g, 14.6 mmol) and triethyl orthoformate (10 mL) were placed in a 50 mL round bottom flask, and the mixture was vigorously stirred at 120°C over night. The excess triethyl orthoformate was removed by evaporation under reduced pressure. The resulting oil was purified by column chromatography (hexane: ethyl acetate = 70:30) to afford 2-phenyl-1, 3, 4-oxadiazole (**1a**, 2 g, 10 mmol) in 96% yield.

B. Typical procedure for synthesis *N*-tosylhydrazones(2)²:

A solution of pure TsNHNH₂ (5 mmol) in methanol (5 mL) was stirred and heated to 60 °C until the TsNHNH₂ was completely dissolved. Then carbonyl compounds were slowly added to the reaction mixture. After approximately 5-30 min the crude products was obtained as precipitates. The precipitates were washed by hexane, then dried in vacuo to afford the pure *N*-tosylhydrazones (**2a-g**).

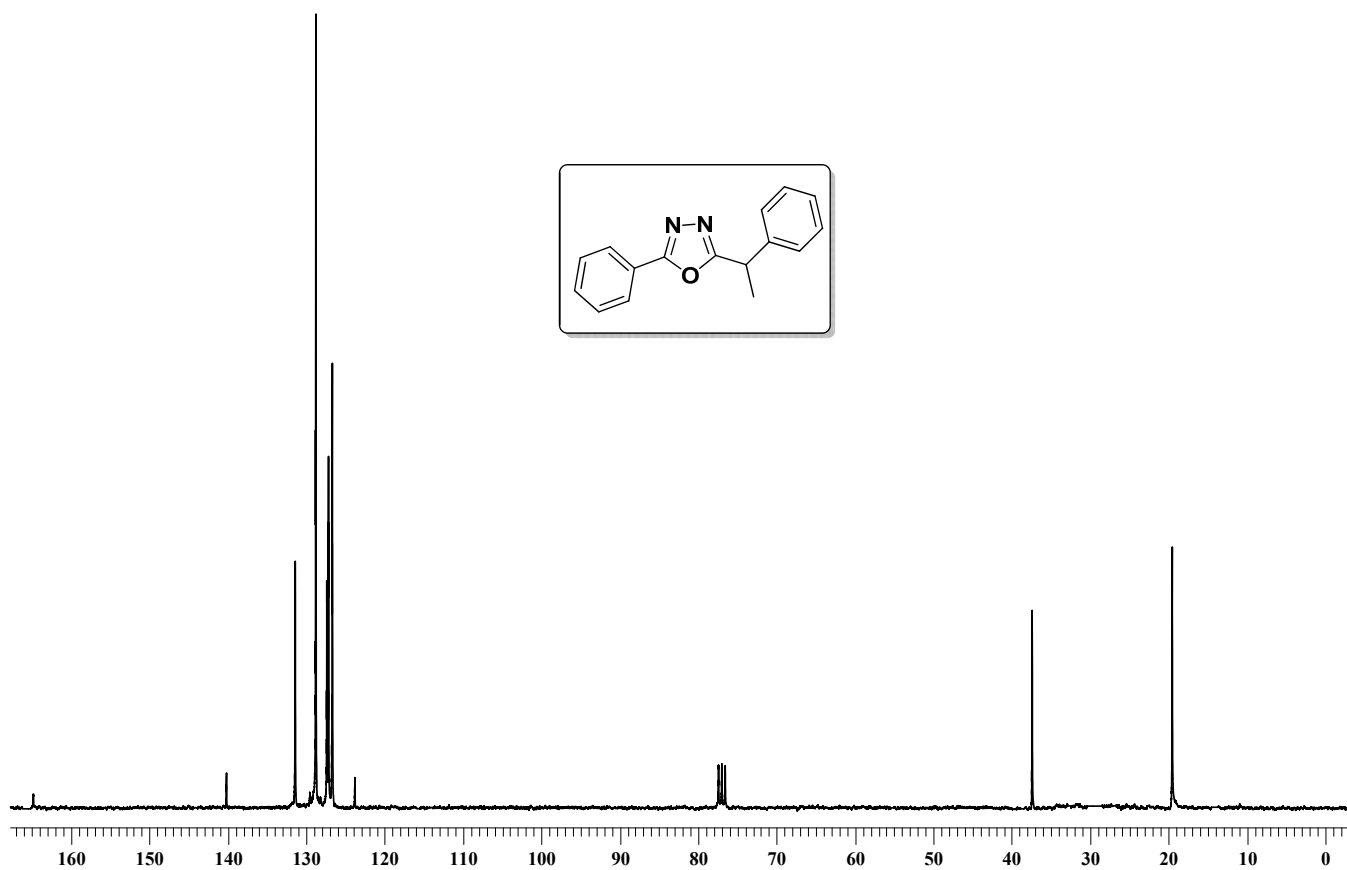
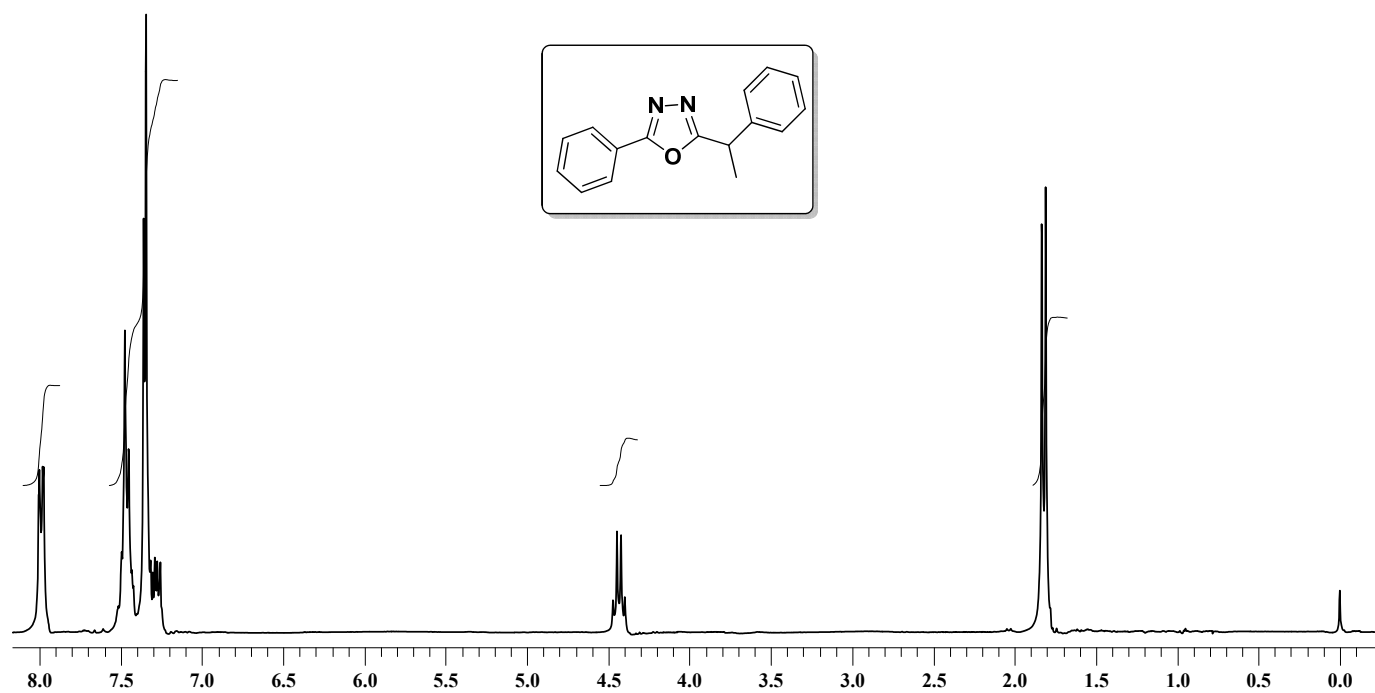
C. General experimental procedure for benzylation of 1,3,4-oxadiazoles with *N*-tosylhydrazones :

In a 10 mL round bottom flask CuI (9 mg, 0.05 equiv.), Cs₂CO₃ (812 mg, 2.5 equiv.), *N*-tosylhydrazone **2** (1.3 mmol) and 2-aryl 1,3,4-oxadiazole **1** (1.0 mmol) in toluene (3.0 mL) were taken. The reaction mixture was stirred at 110 °C for 3h. The progress of the reaction was monitored by TLC. After the consumption of the starting materials, the reaction mixture was allowed to cool, and subsequently extracted with EtOAc (2x10 mL). The combined organic extracts were dried over anhydrous Na₂SO₄. Concentration of the material in vacuo followed by flash chromatography on silica gel column afforded benzylated oxadiazole derivatives in good yield.

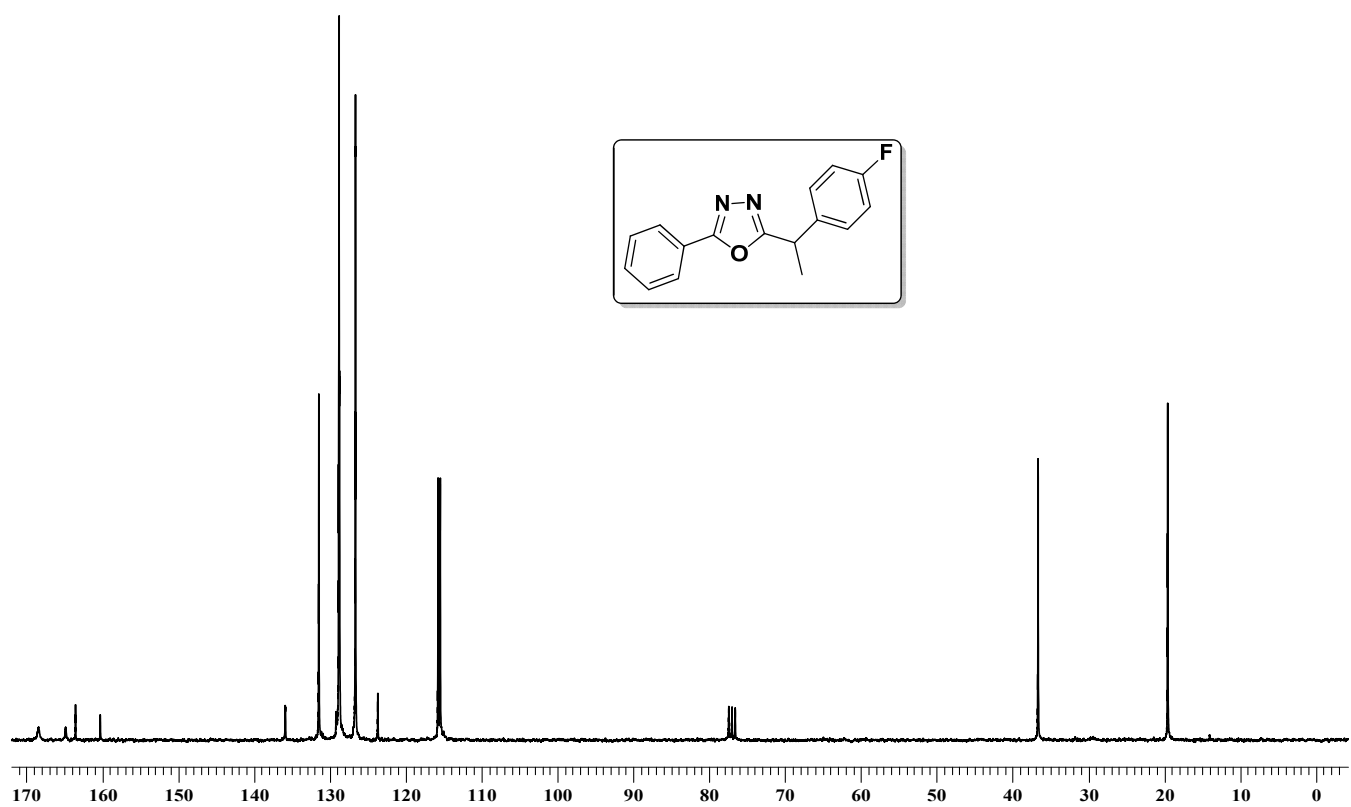
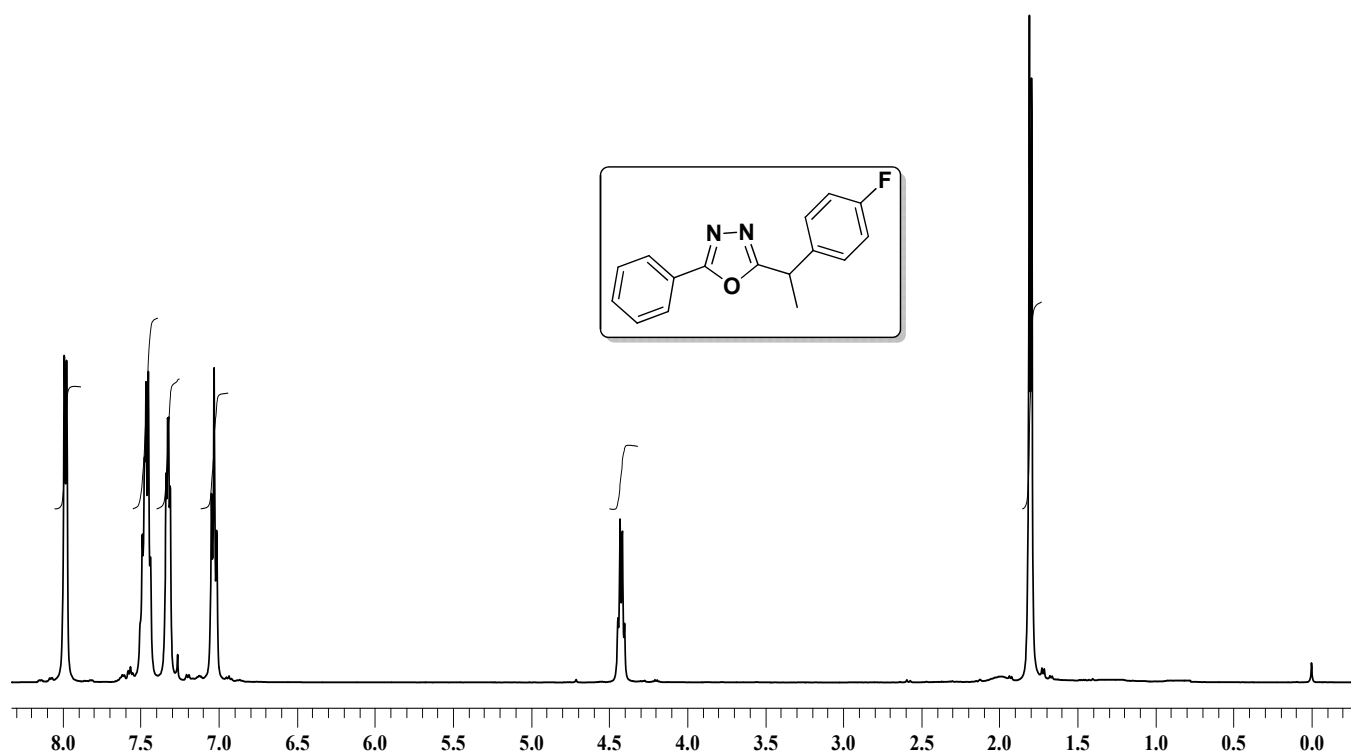
References:

- (1) C. Ainsworth, *J. Am. Chem. Soc.* **1955**, *77*, 1148.
- (2) X. Zhao; G. Wu, Y. Zang, J. Wang, *J. Am. Chem. Soc.* **2011**, *133*,

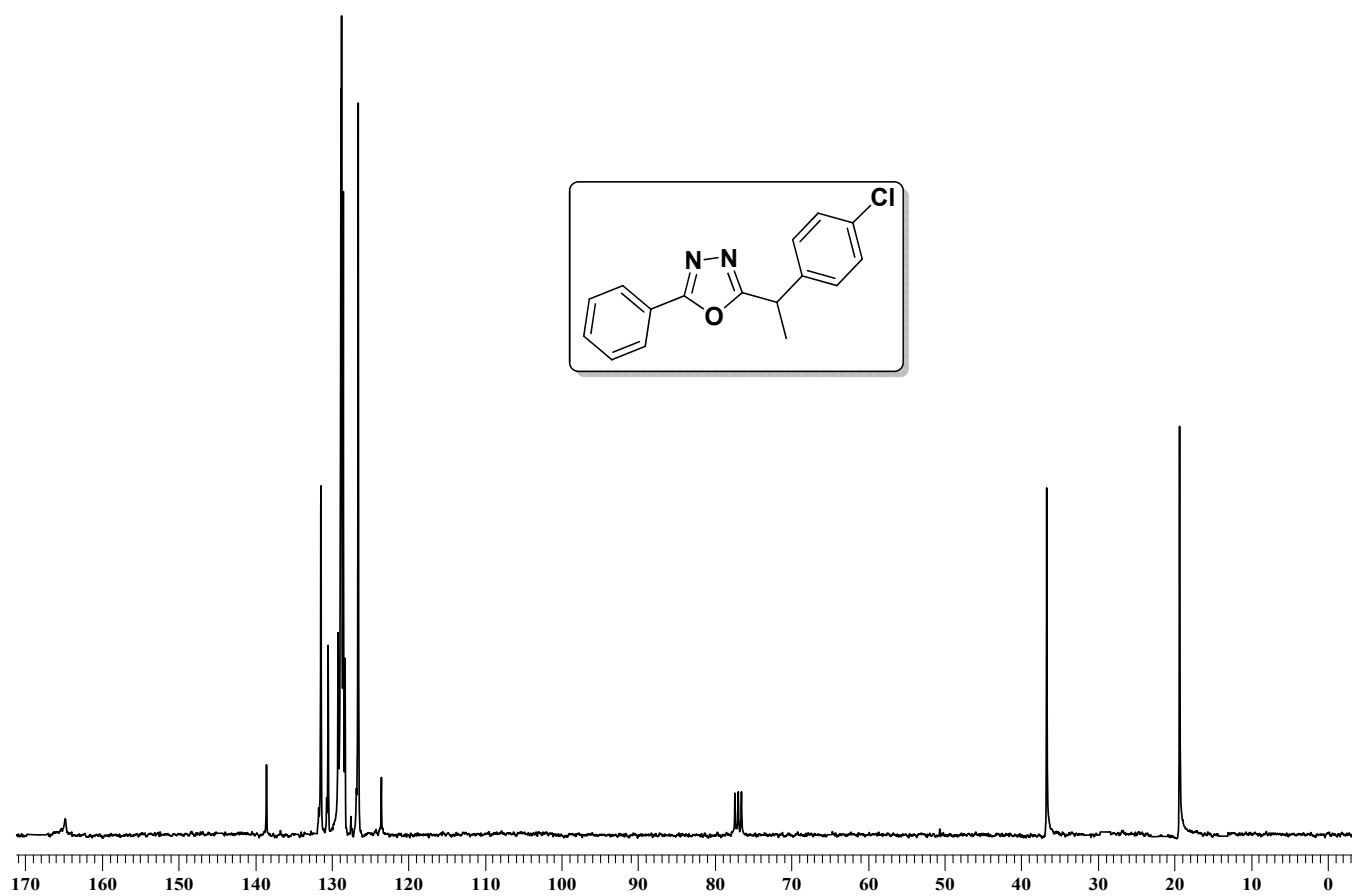
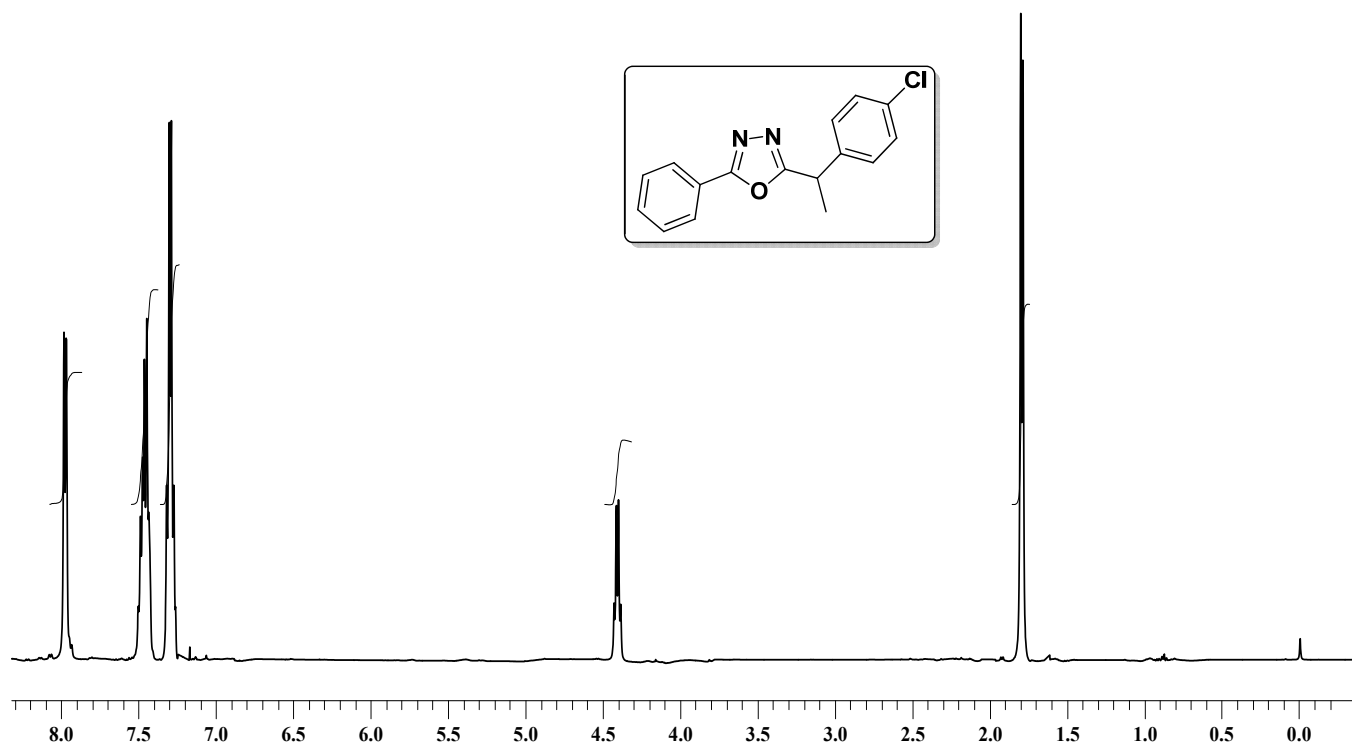
2-phenyl-5-(1-phenylethyl)-1,3,4-oxadiazole (3aa) (Table 2, entry 1)



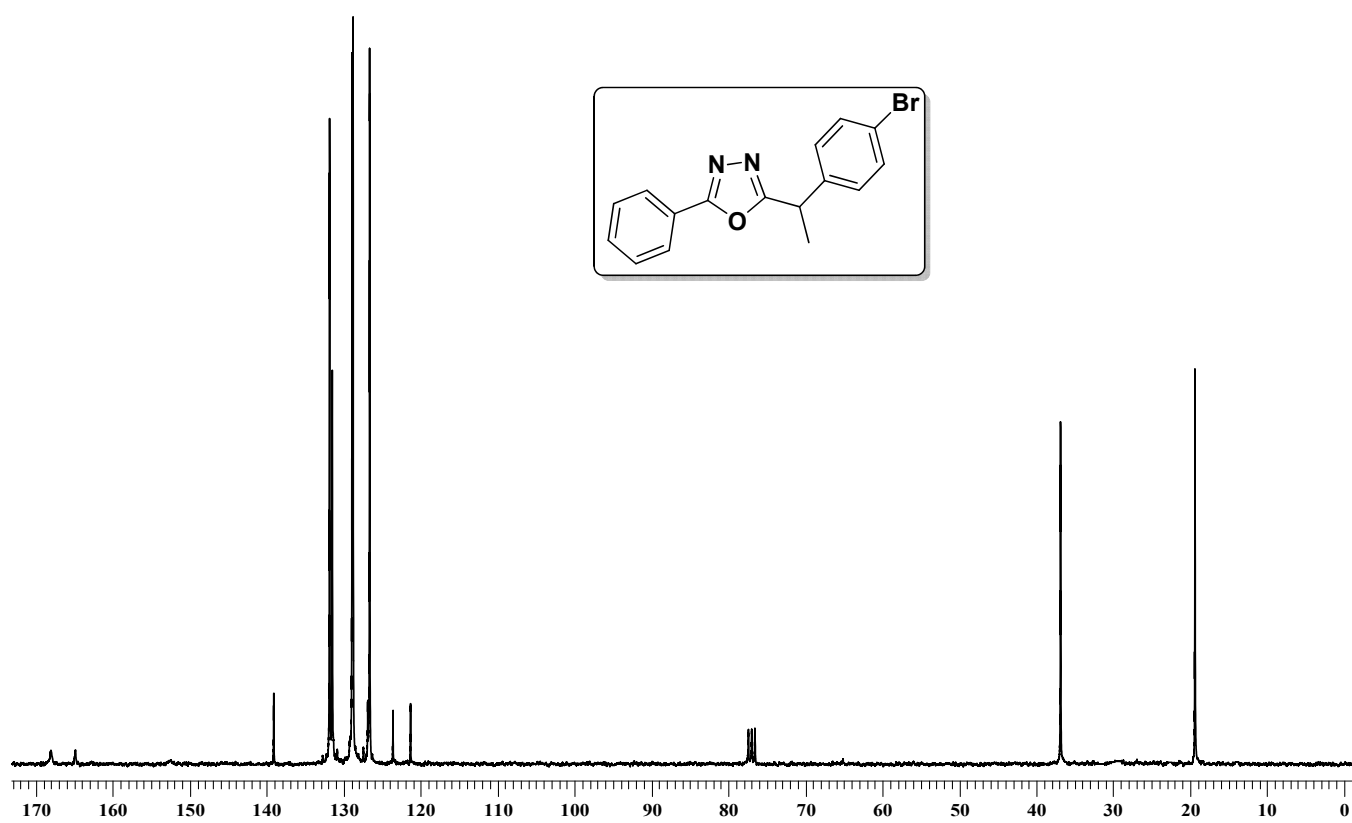
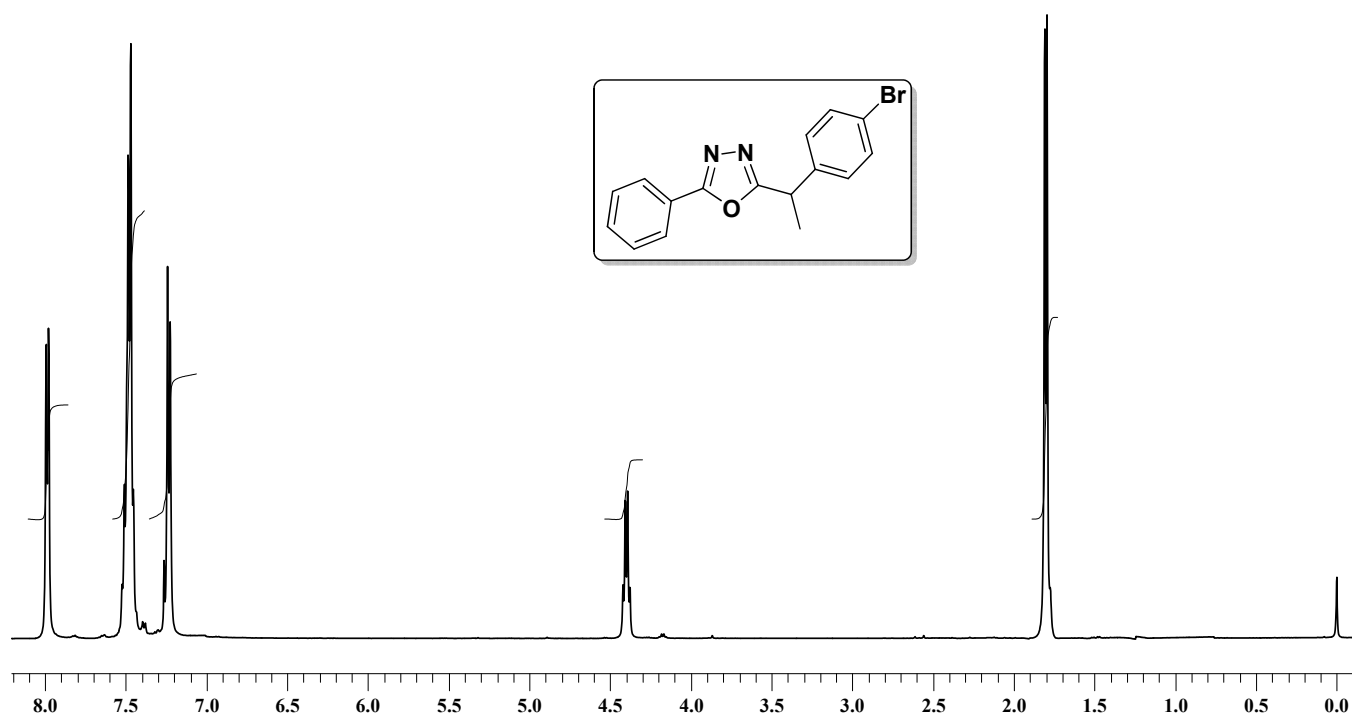
2-(1-(4-fluorophenyl)ethyl)-5-phenyl-1,3,4-oxadiazole (3ab) (Table 2, entry 2)



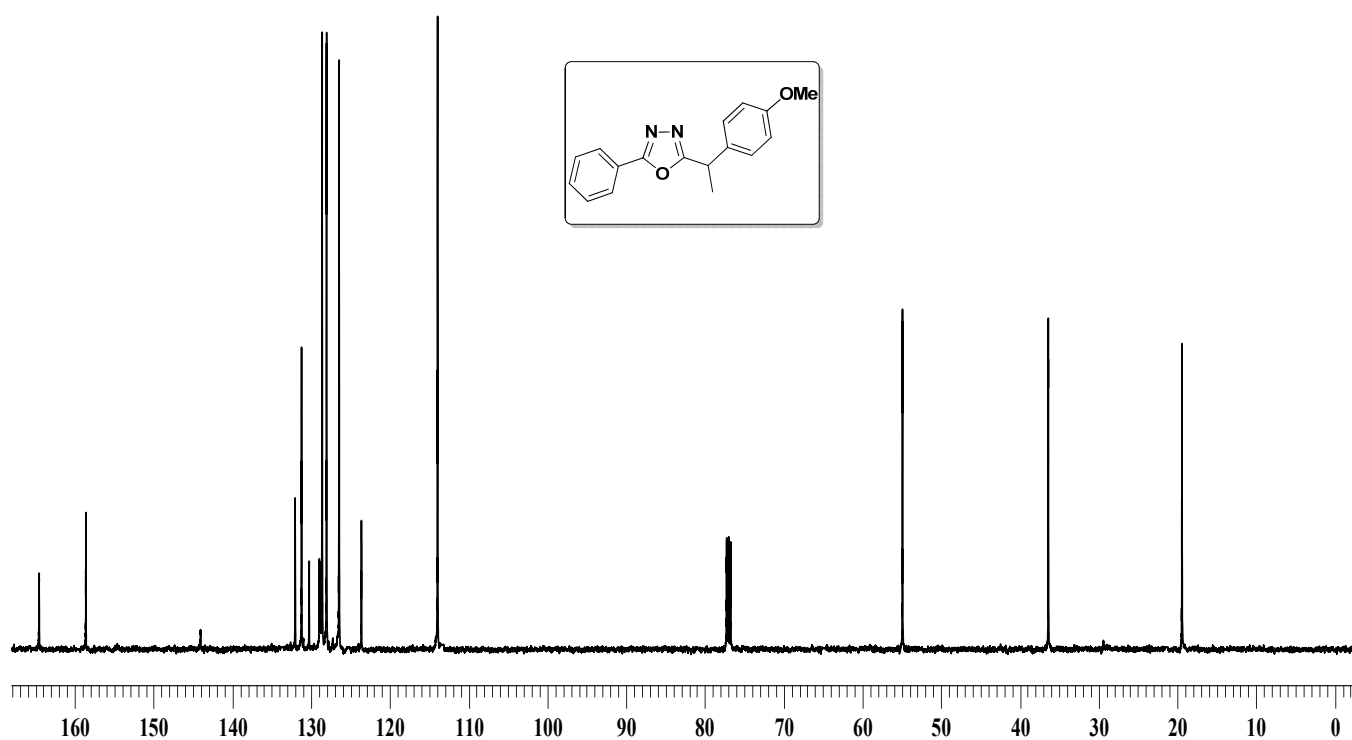
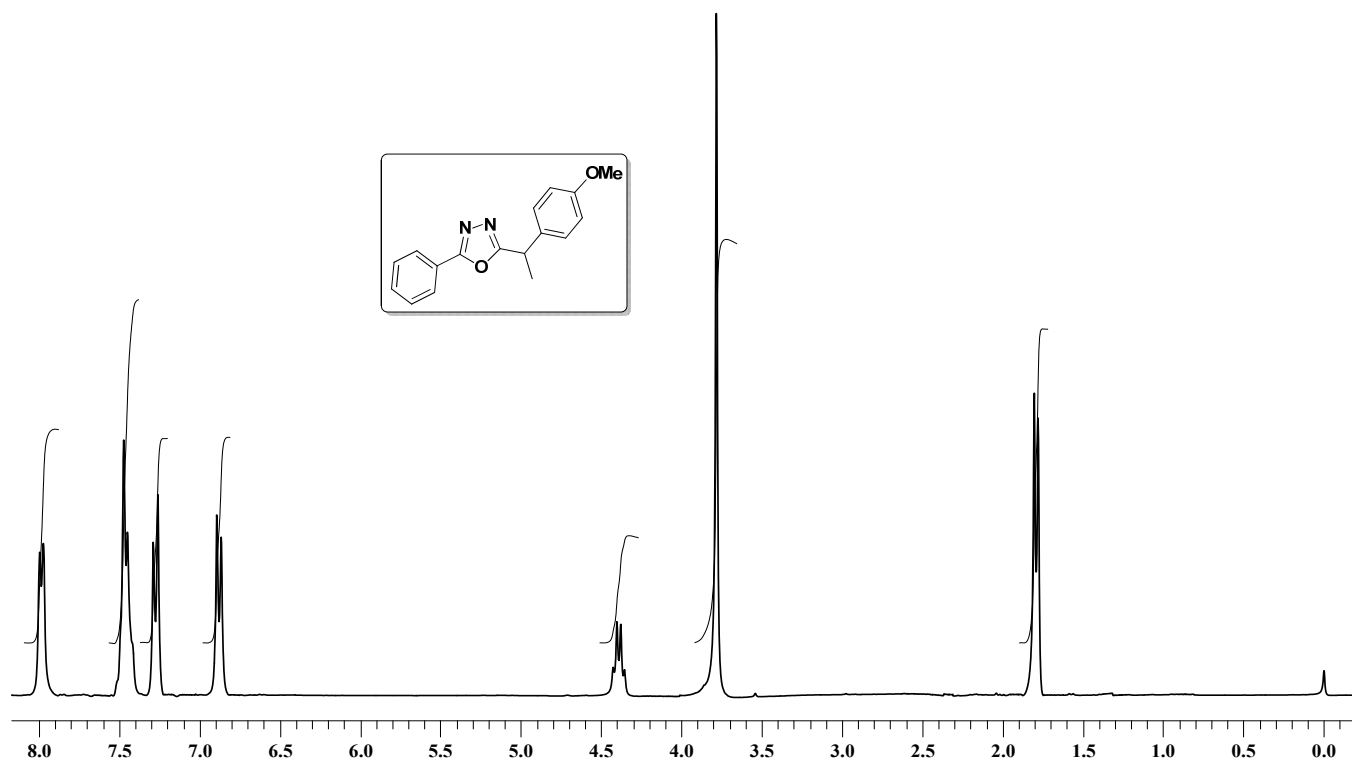
2-(1-(4-chlorophenyl)ethyl)-5-phenyl-1,3,4-oxadiazole (3ac) (Table 2, entry 3)



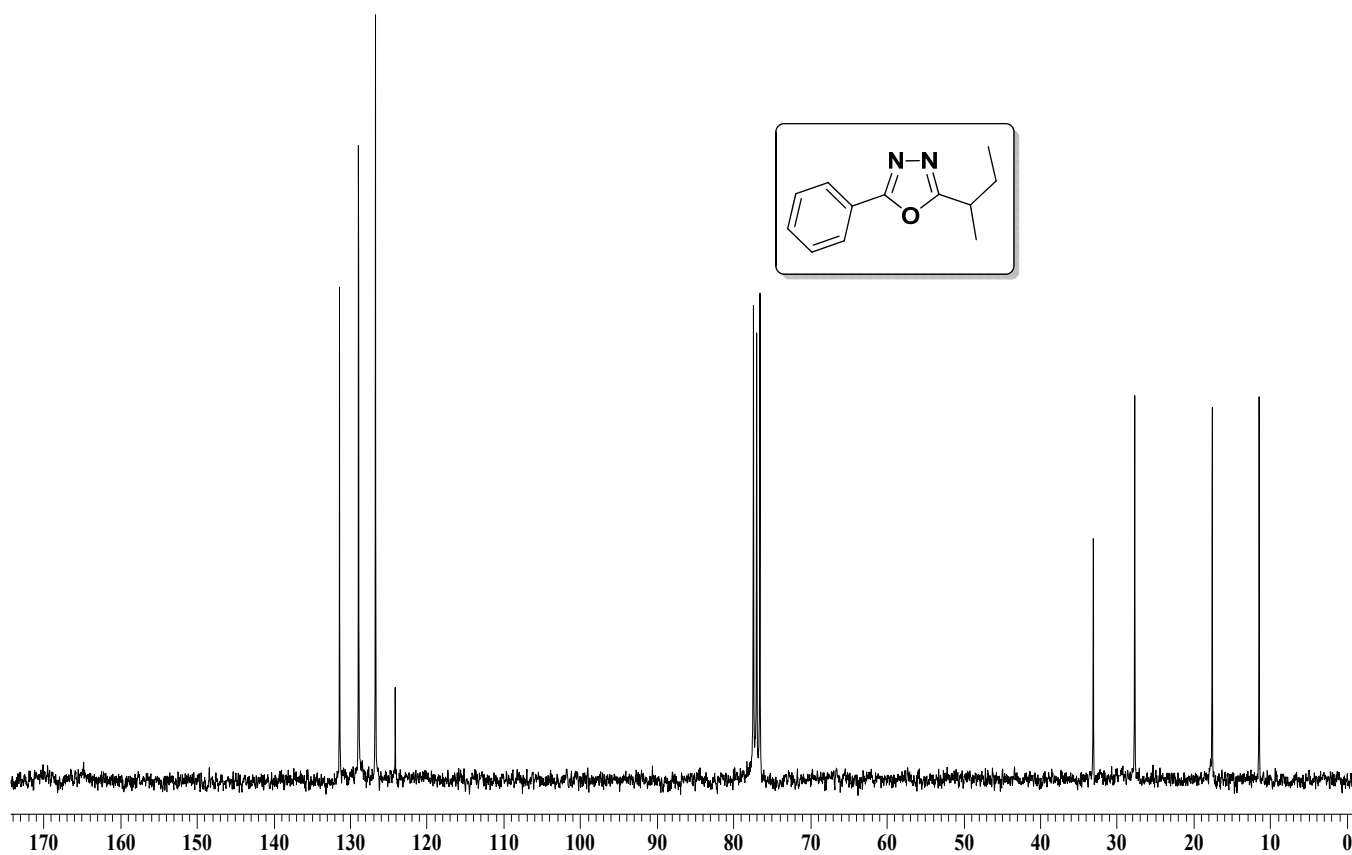
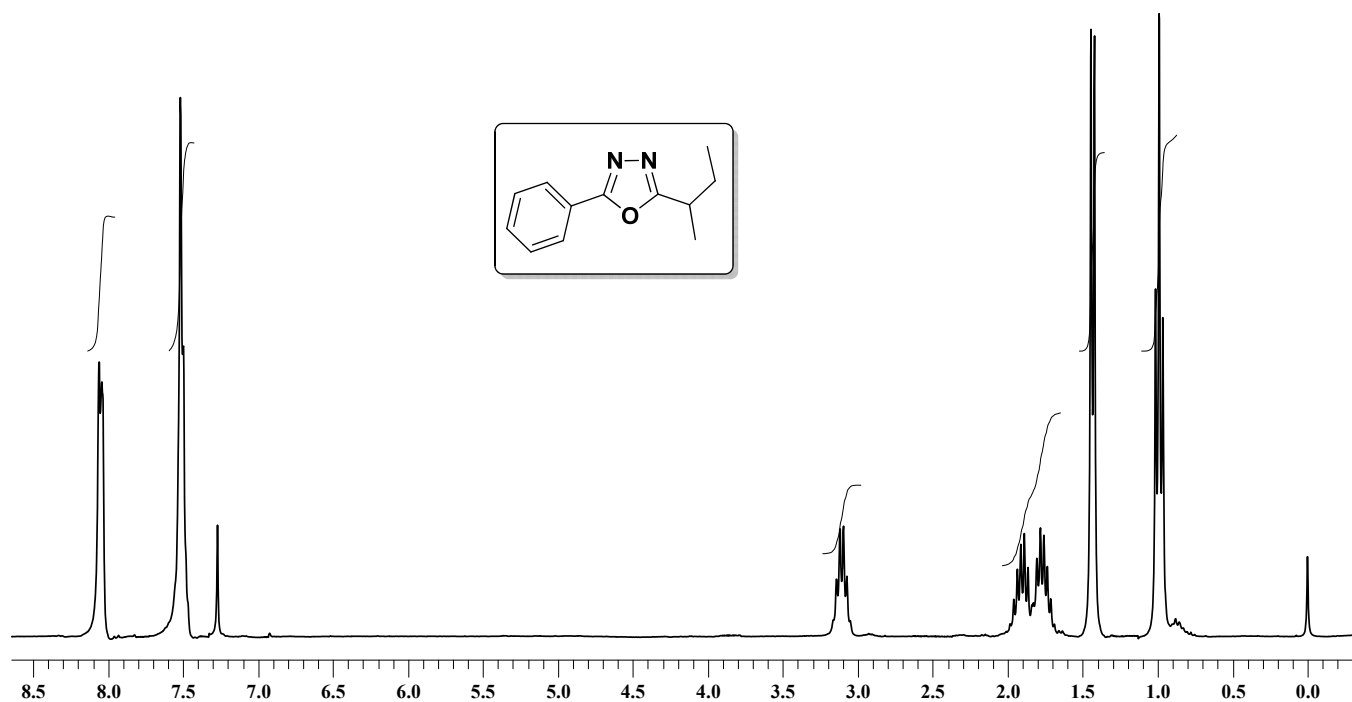
2-(1-(4-bromophenyl)ethyl)-5-phenyl-1,3,4-oxadiazole (3ad) (Table 2, entry 4)



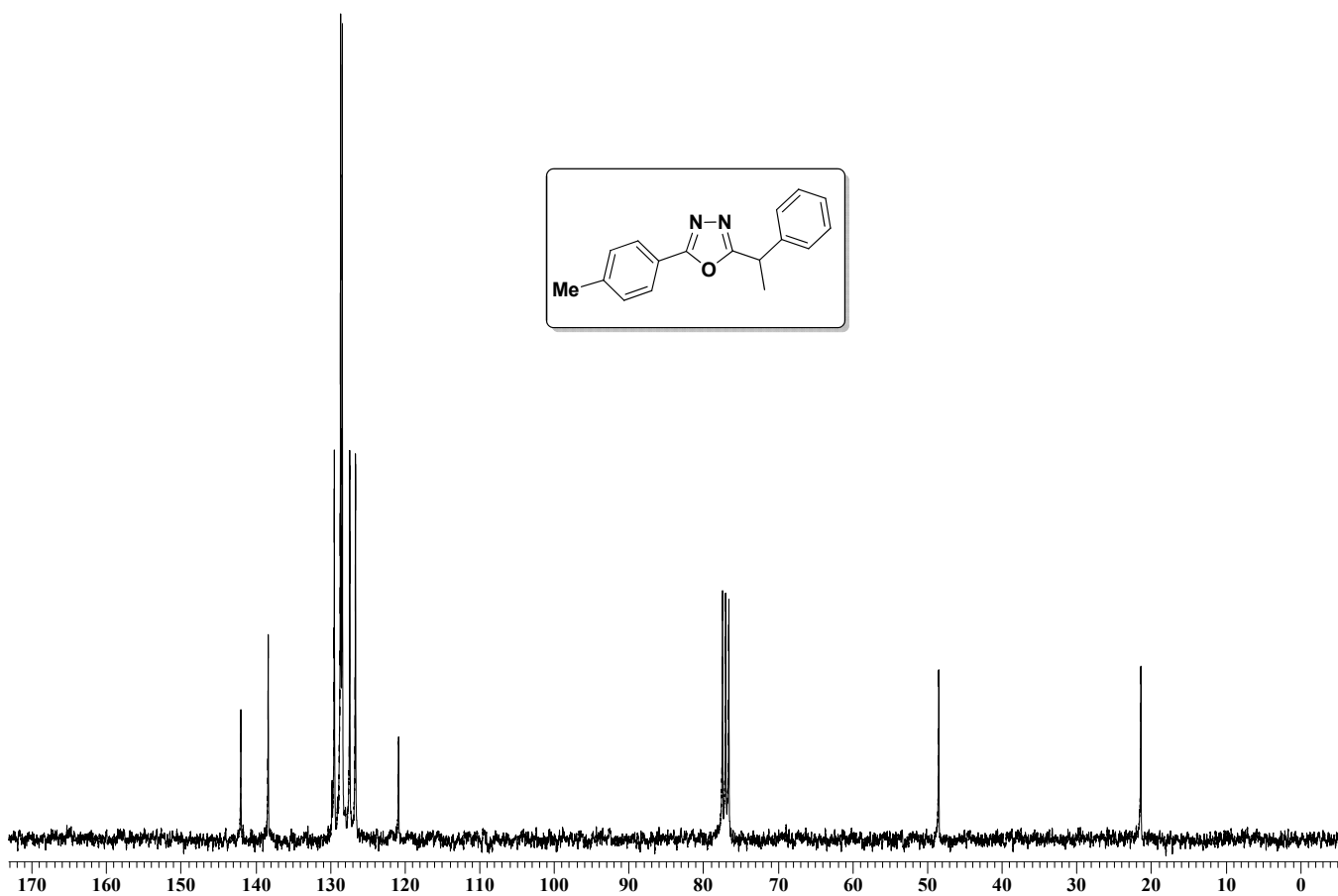
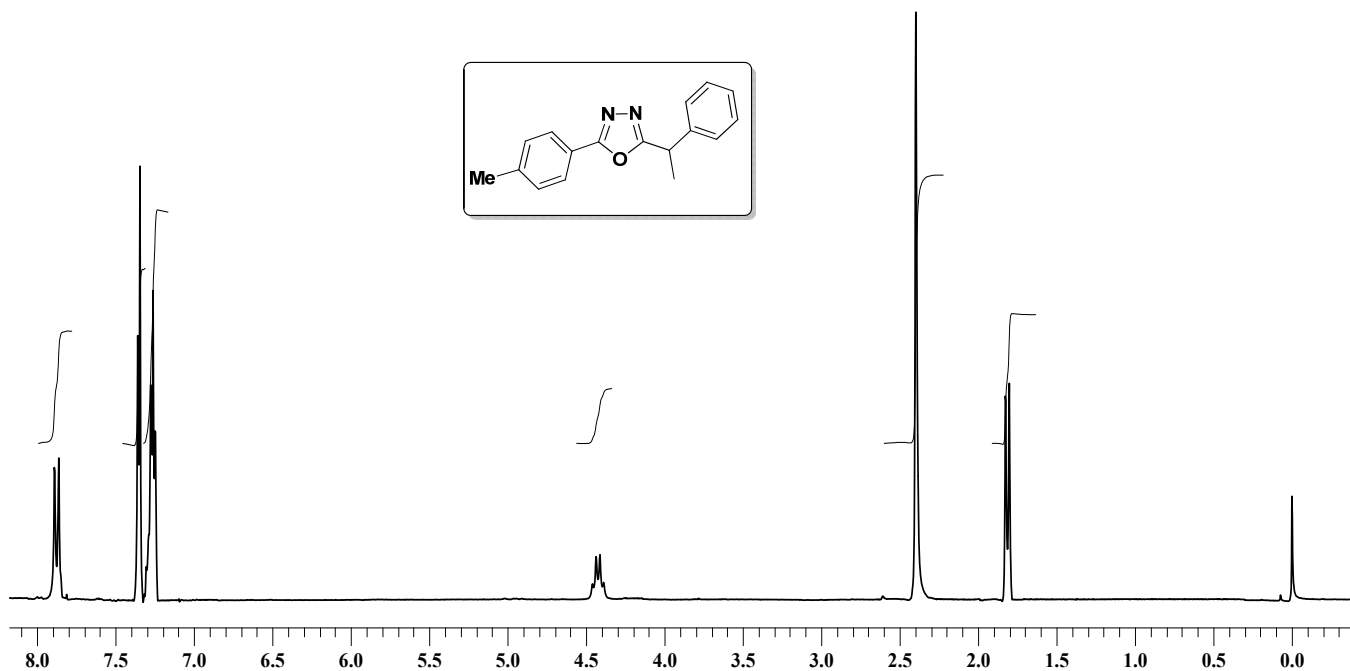
2-(1-(4-methoxyphenyl)ethyl)-5-phenyl-1,3,4-oxadiazole (3ae) (Table 2, entry 5)



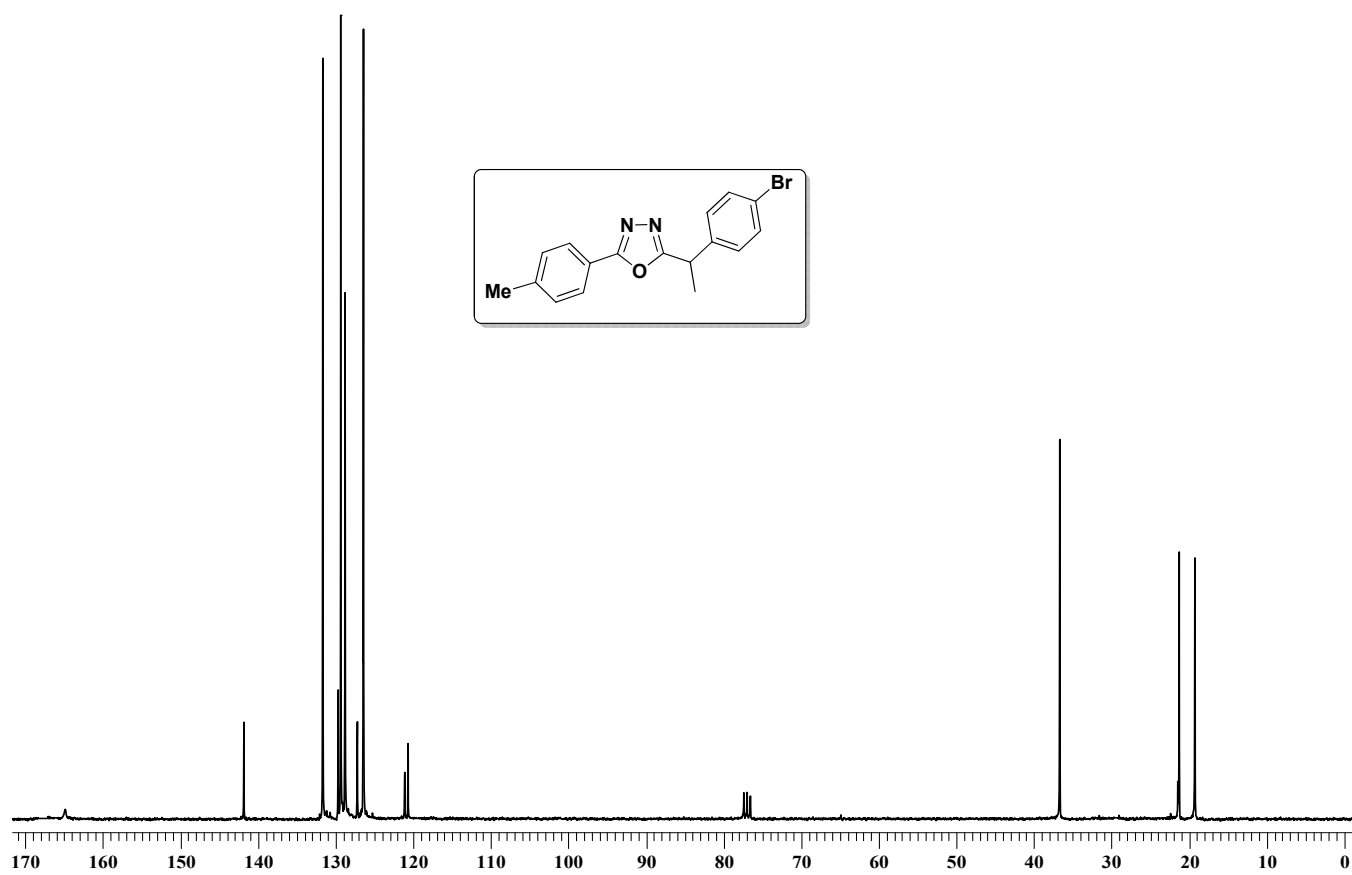
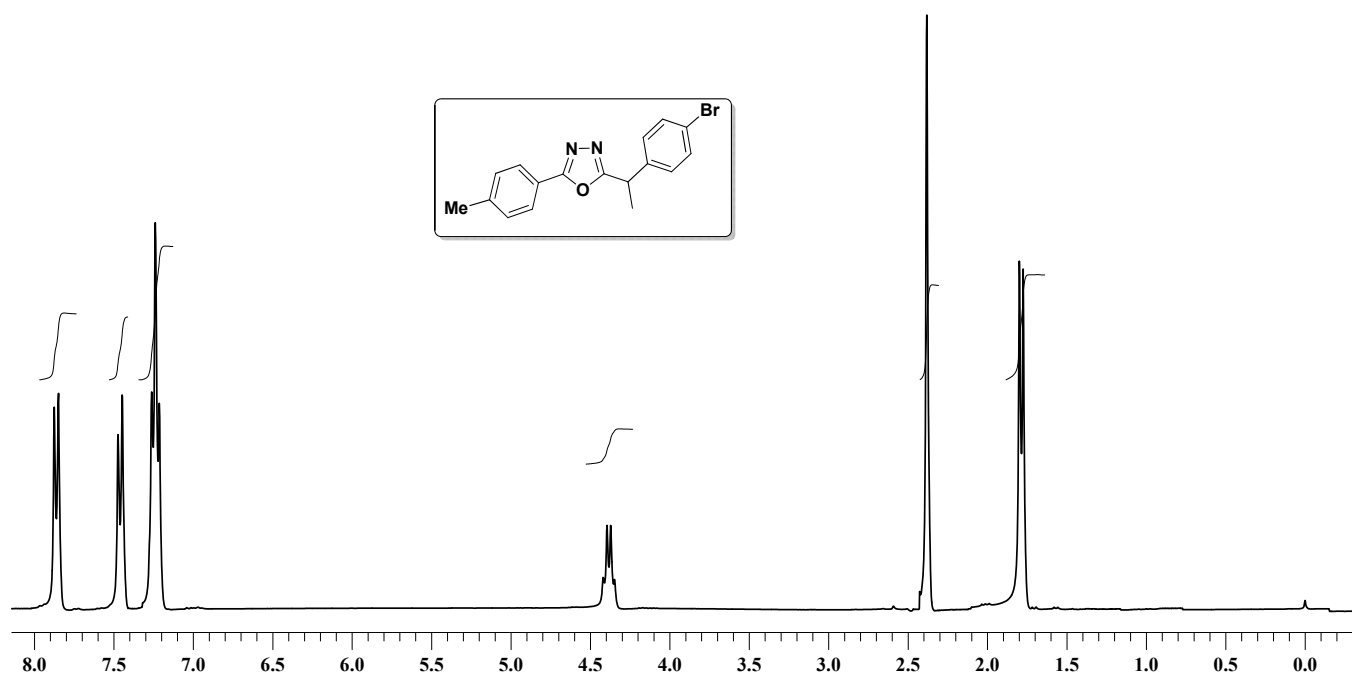
2-(*sec*-butyl)-5-phenyl-1,3,4-oxadiazole (3af) (Table 2, entry 6)



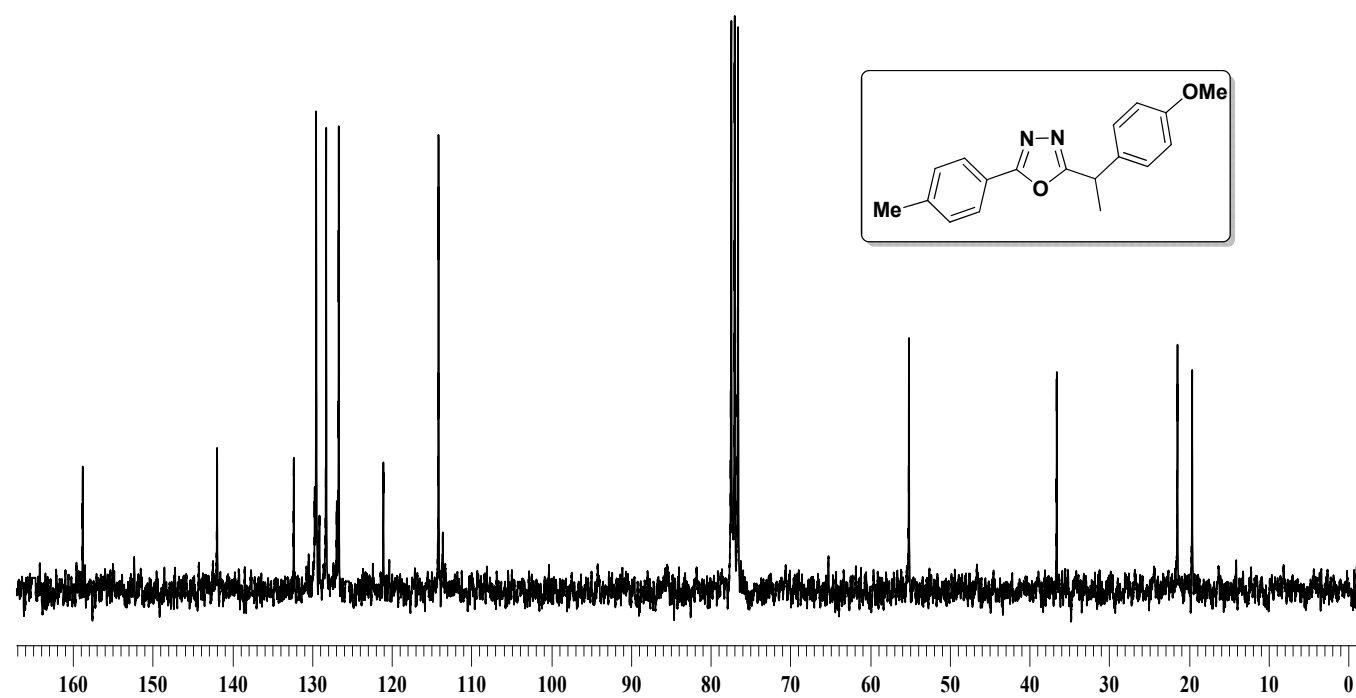
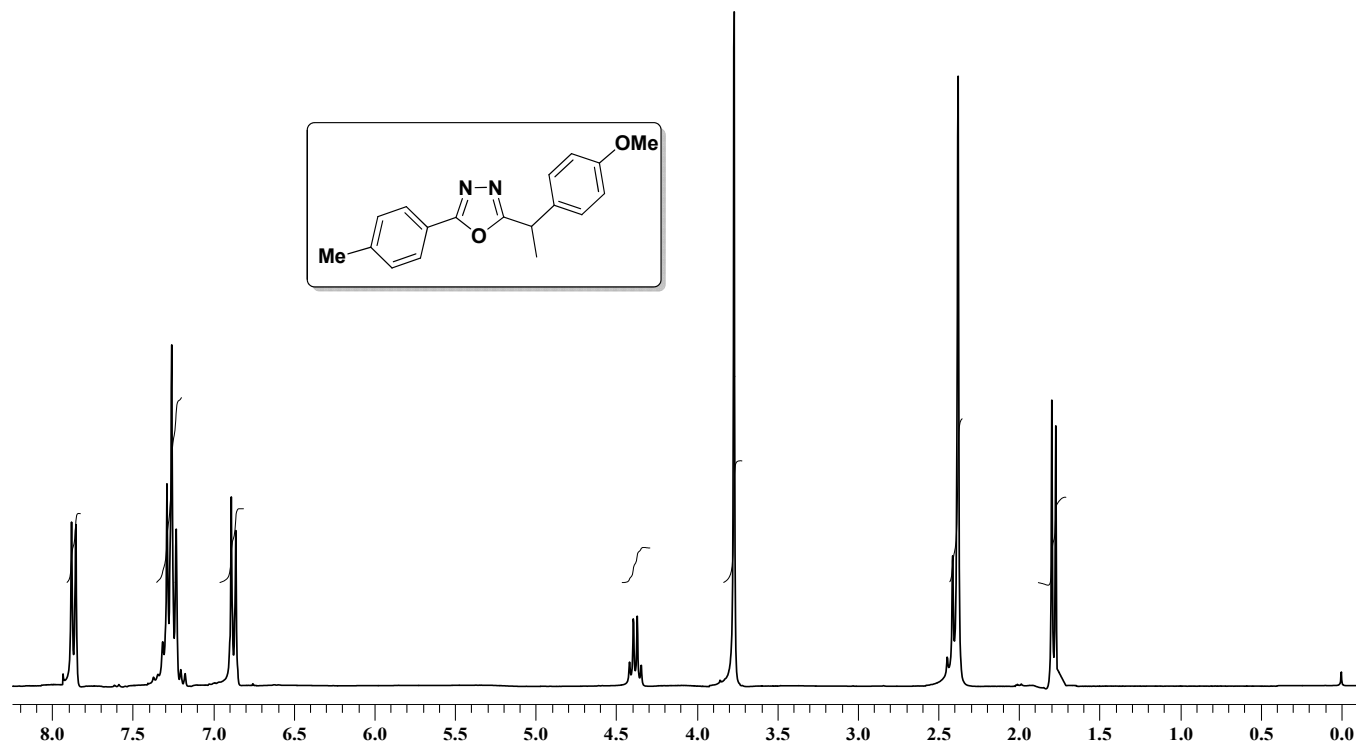
2-(1-phenylethyl)-5-(*p*-tolyl)-1,3,4-oxadiazole (3ba) (Table 3, entry 1)



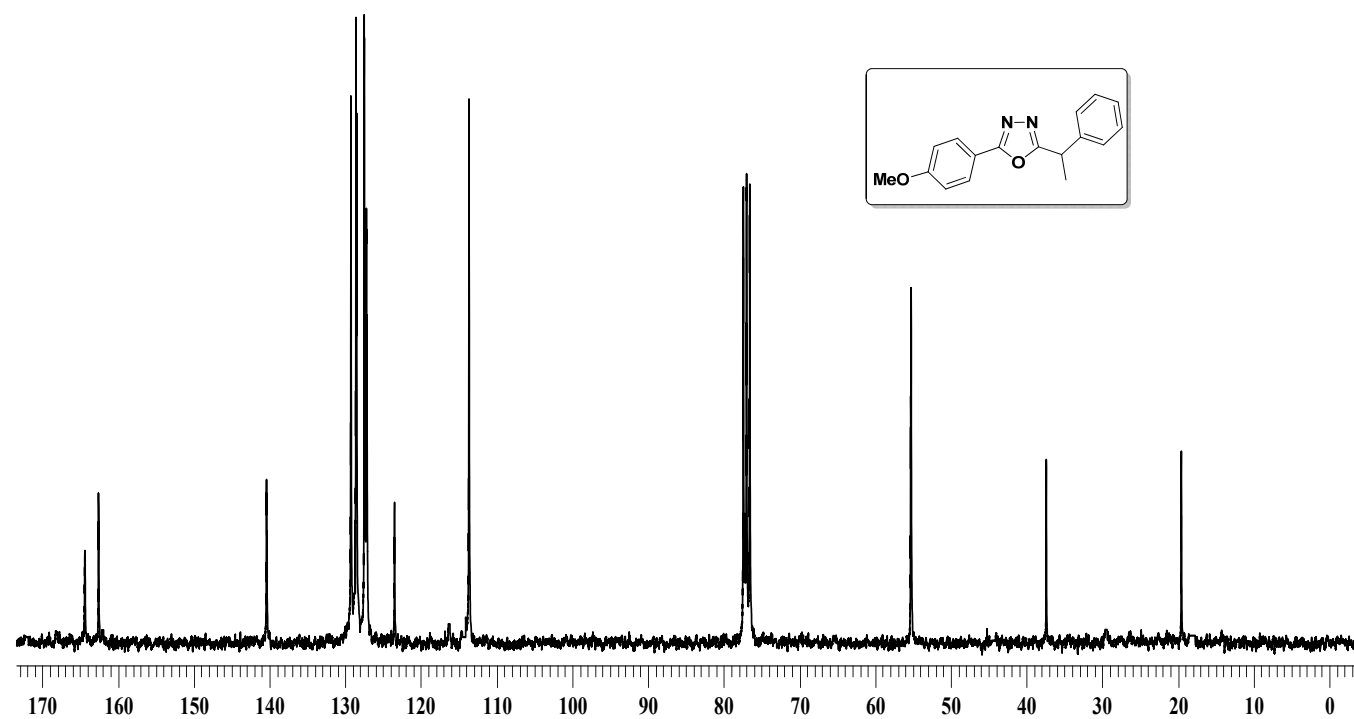
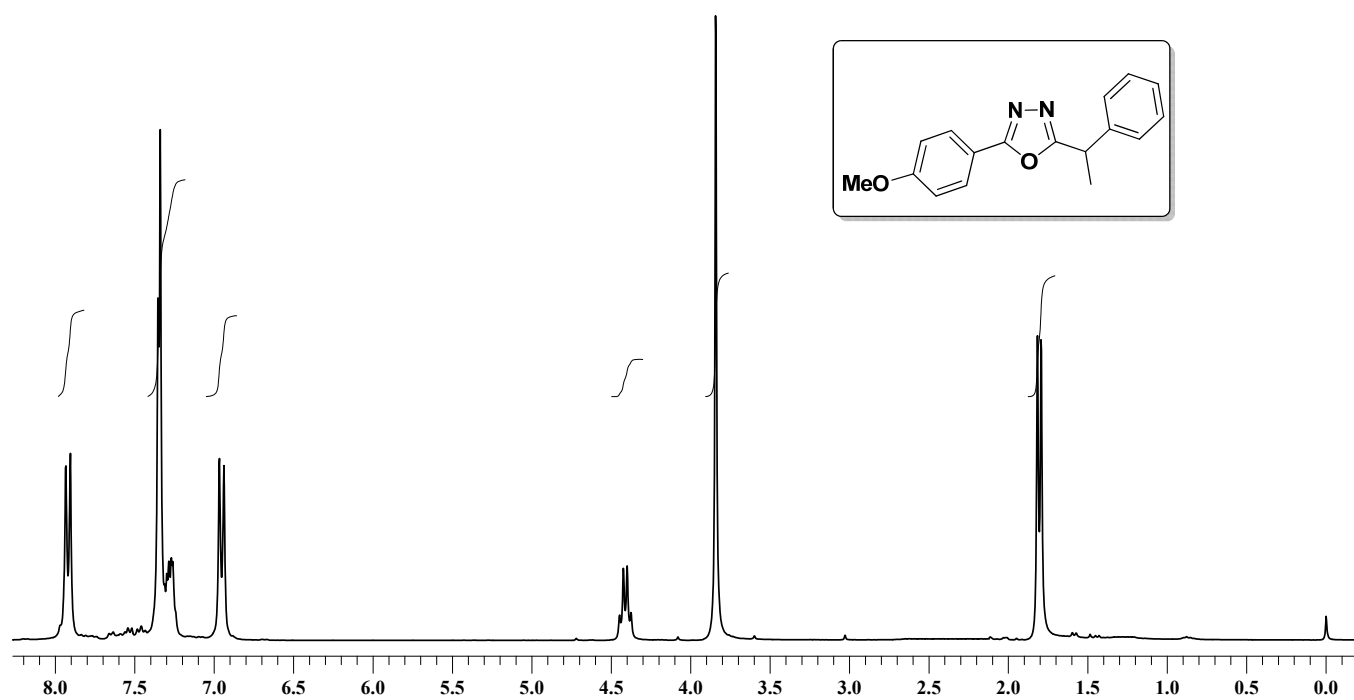
2-(1-(4-bromophenyl)ethyl)-5-(*p*-tolyl)-1,3,4-oxadiazole (3bd) (Table 3, entry 2)



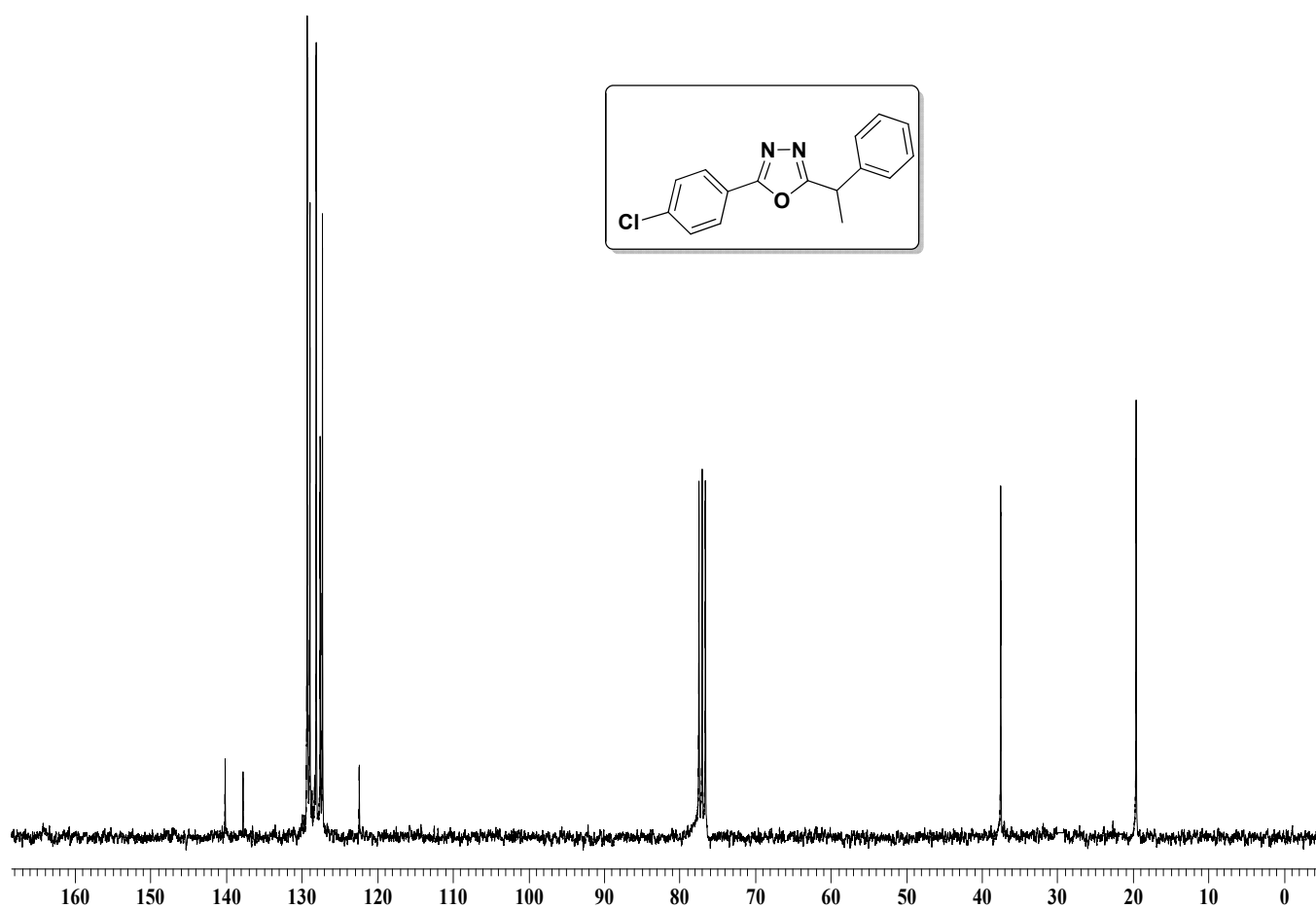
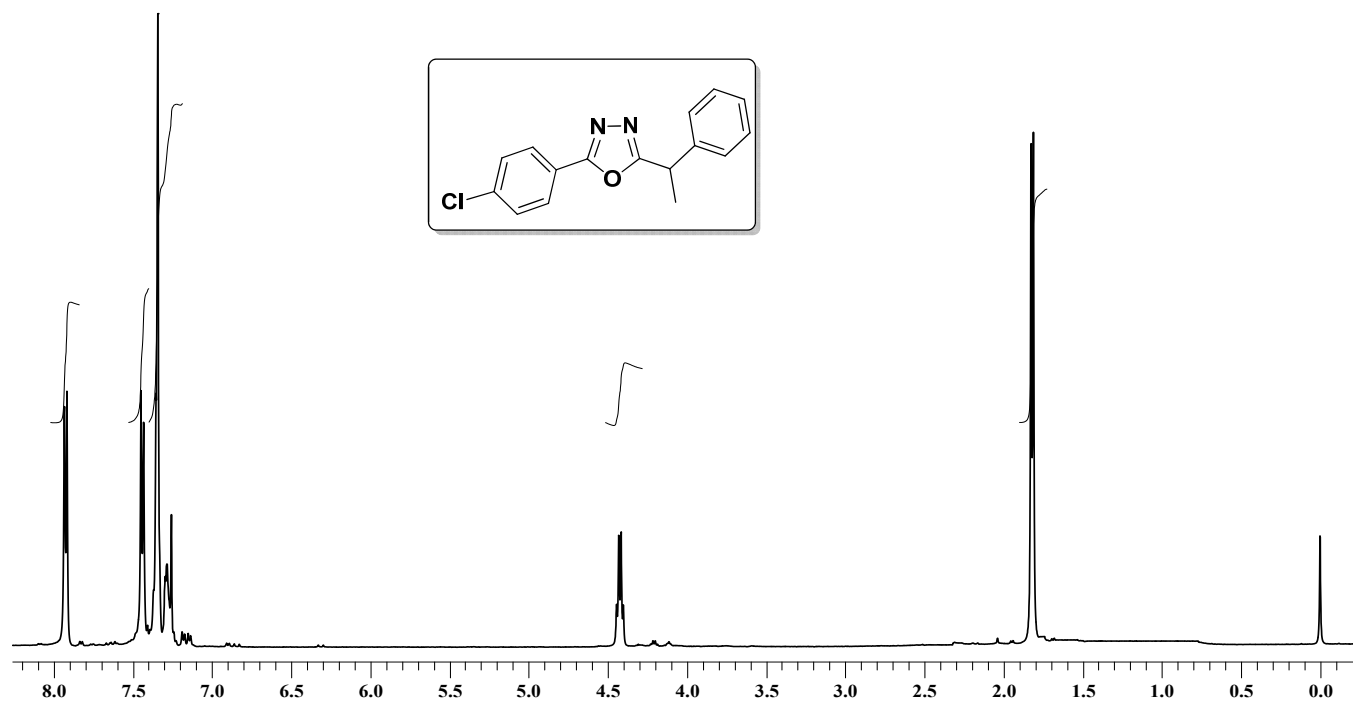
2-(1-(4-methoxyphenyl)ethyl)-5-(*p*-tolyl)-1,3,4-oxadiazole (3be) (Table 3, entry 3)



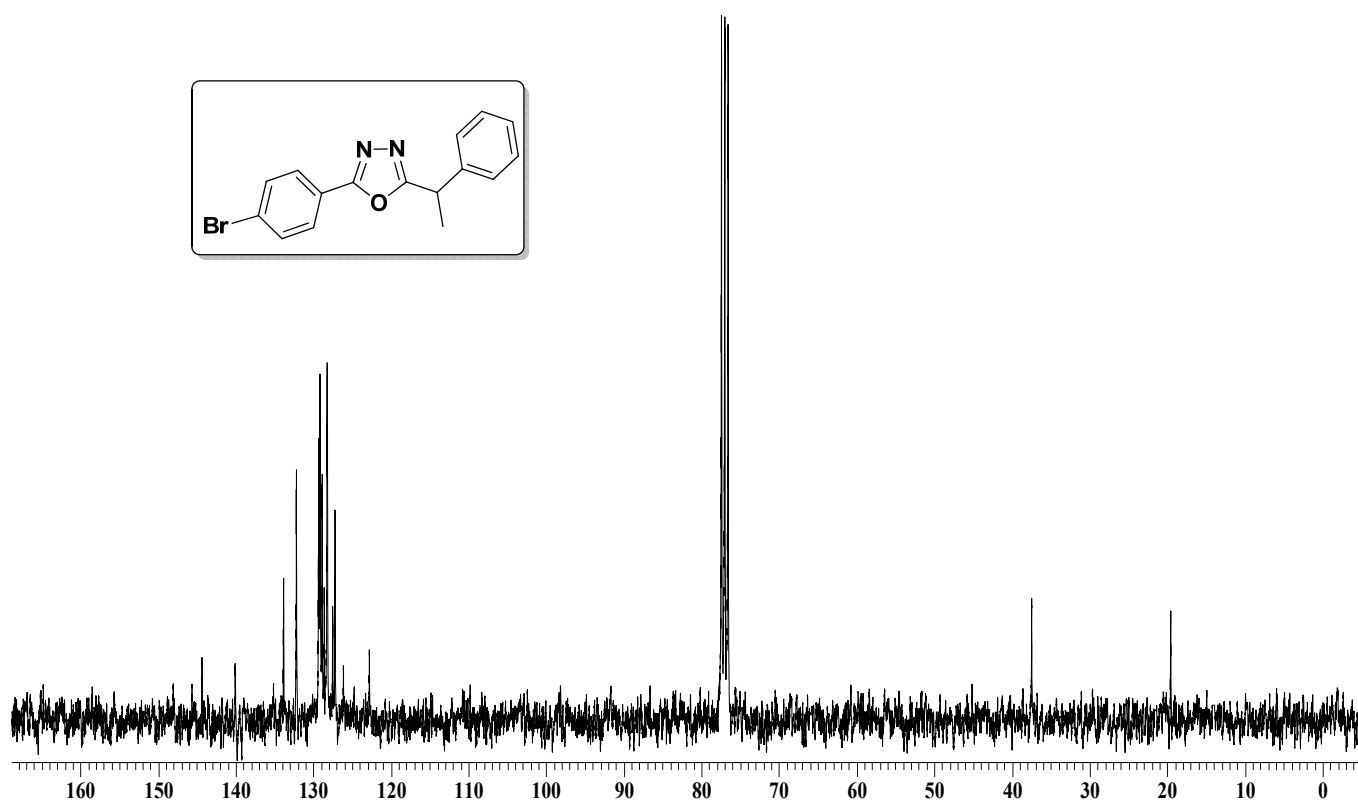
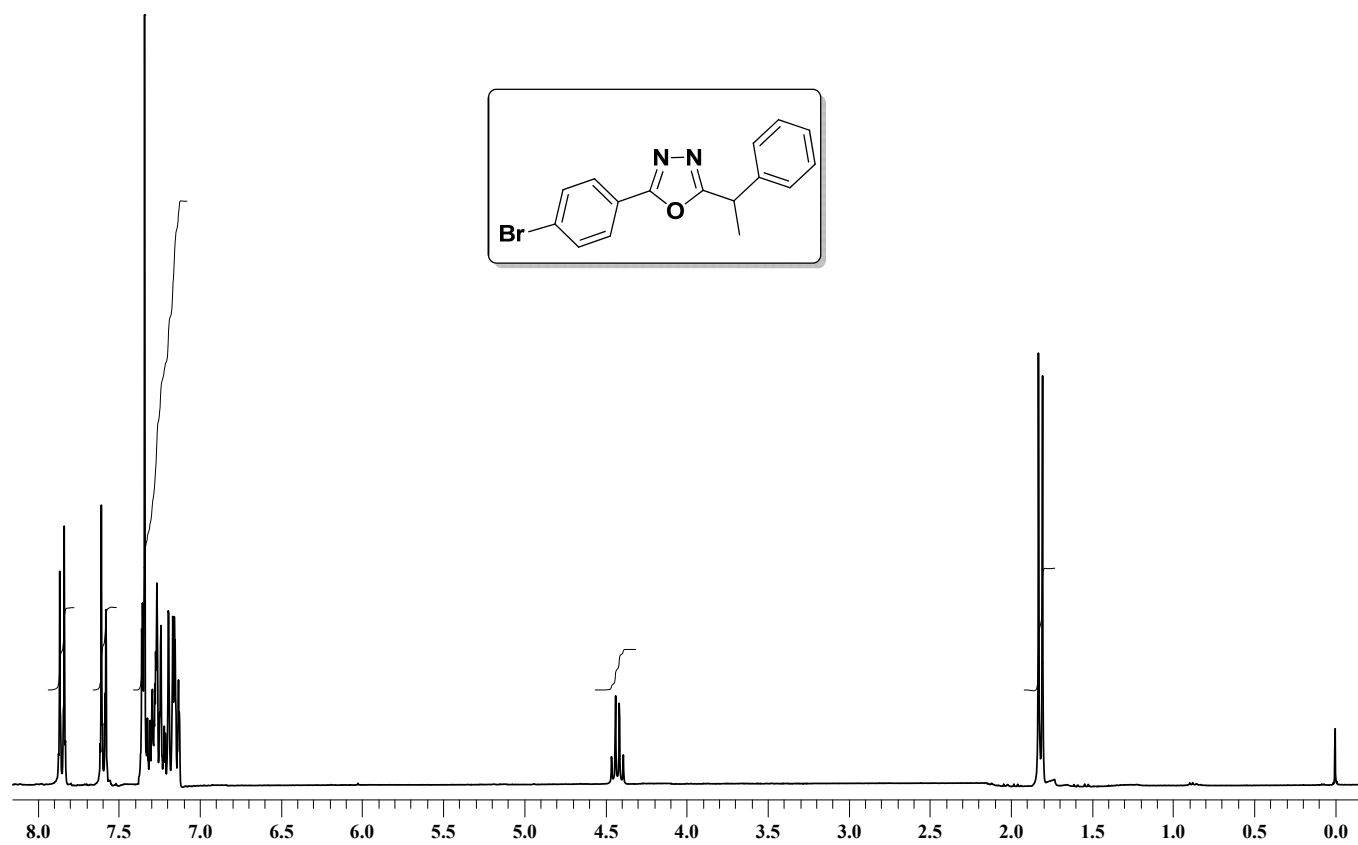
2-(4-methoxyphenyl)-5-(1-phenylethyl)-1,3,4-oxadiazole (3ca) (Table 3, entry 4)



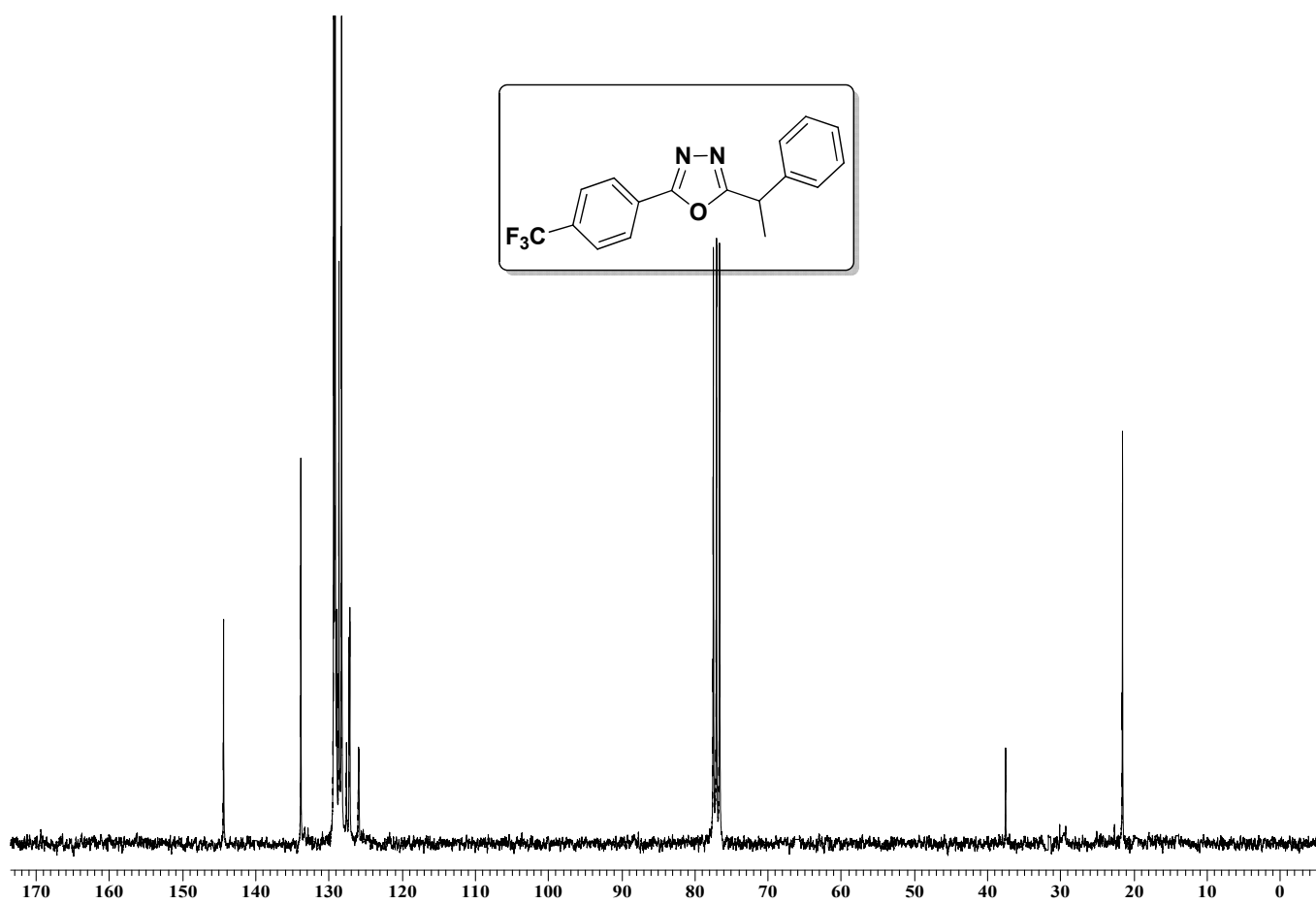
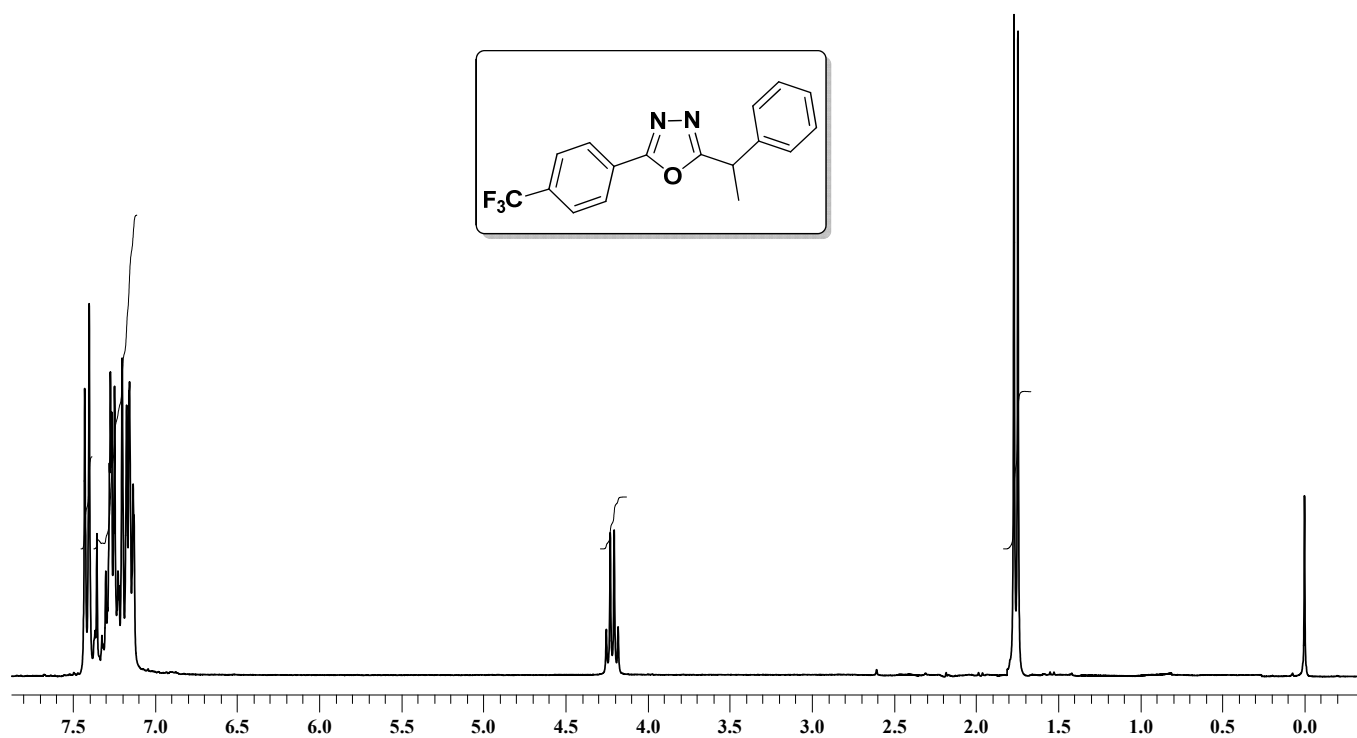
2-(4-chlorophenyl)-5-(1-phenylethyl)-1,3,4-oxadiazole (3da) (Table 3, entry 5)



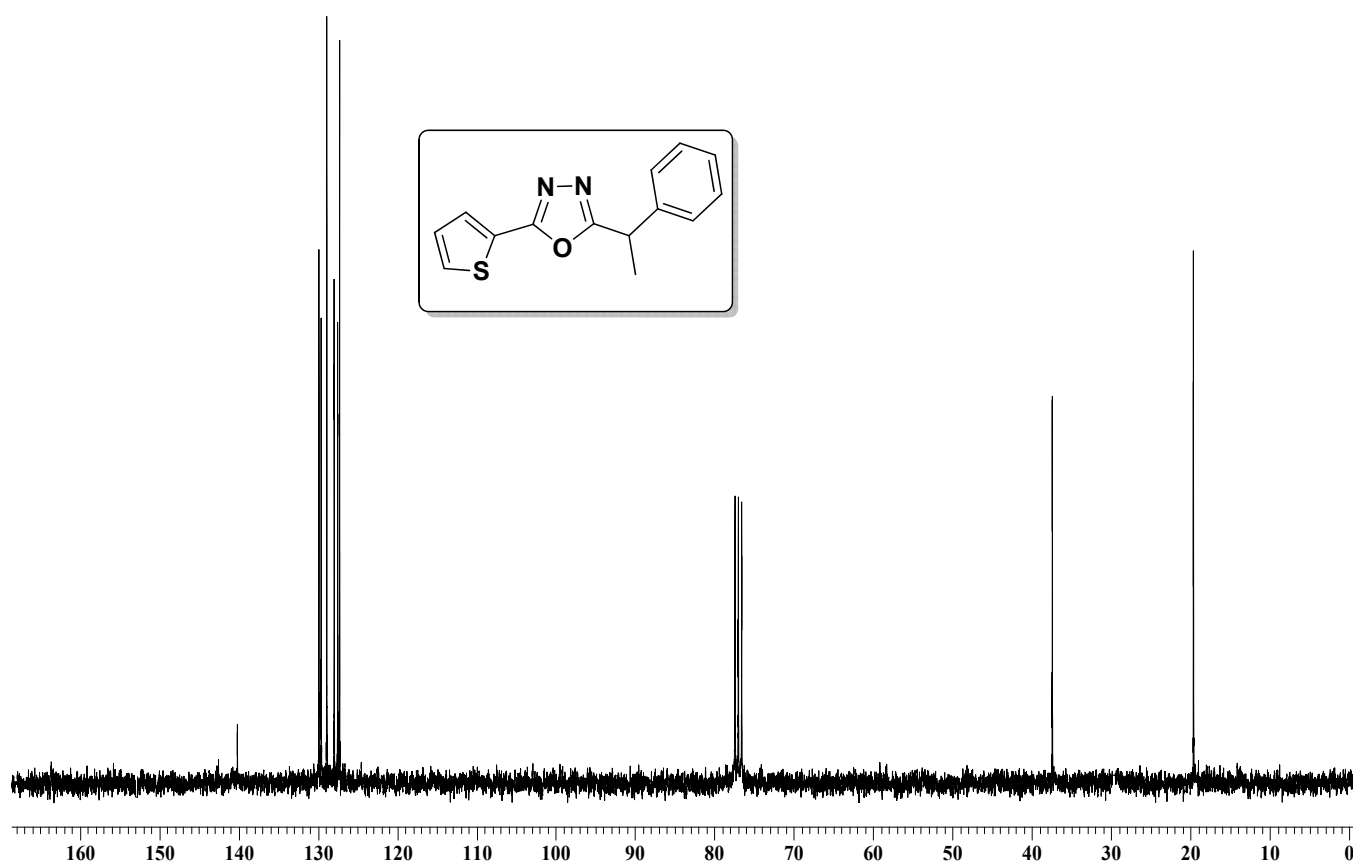
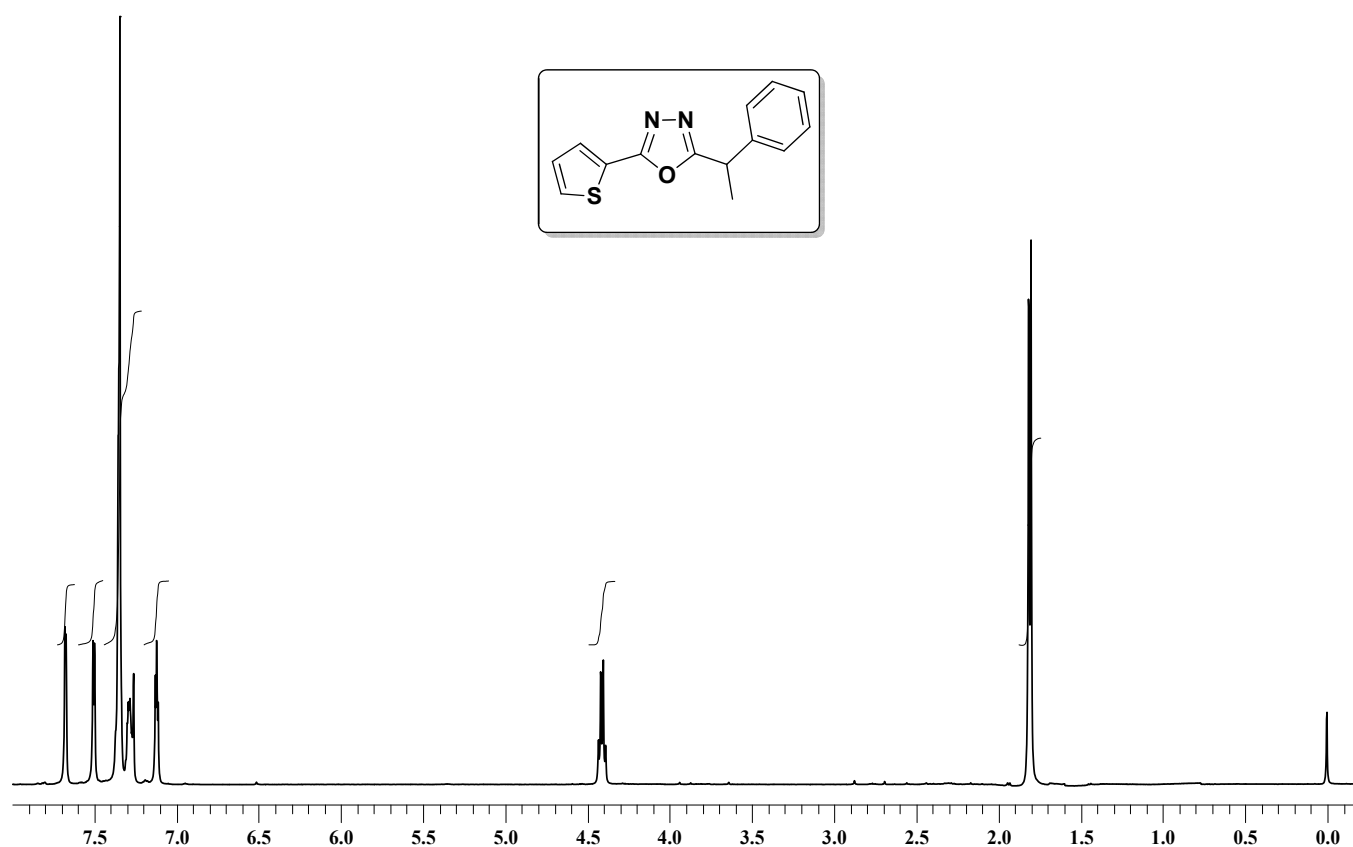
2-(4-bromophenyl)-5-(1-phenylethyl)-1,3,4-oxadiazole (3ea) (Table 3, entry 6)



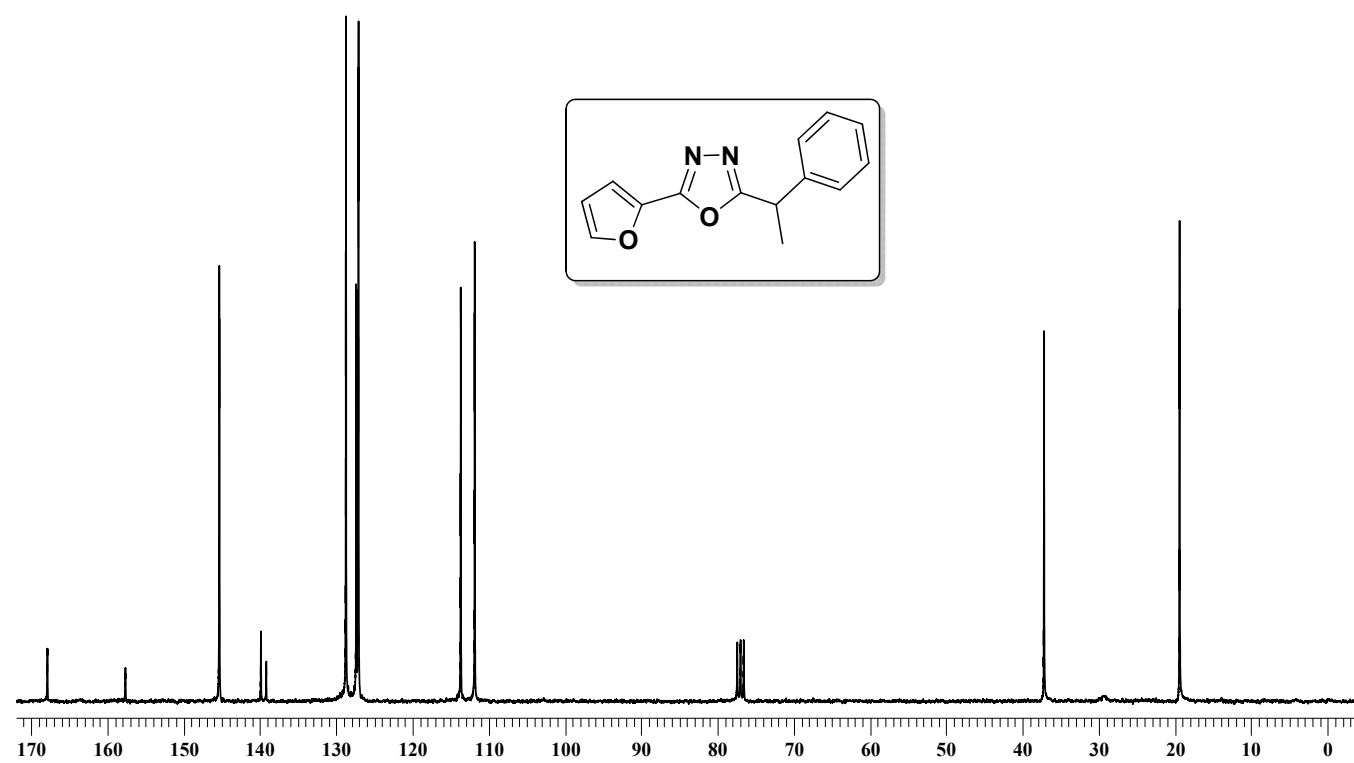
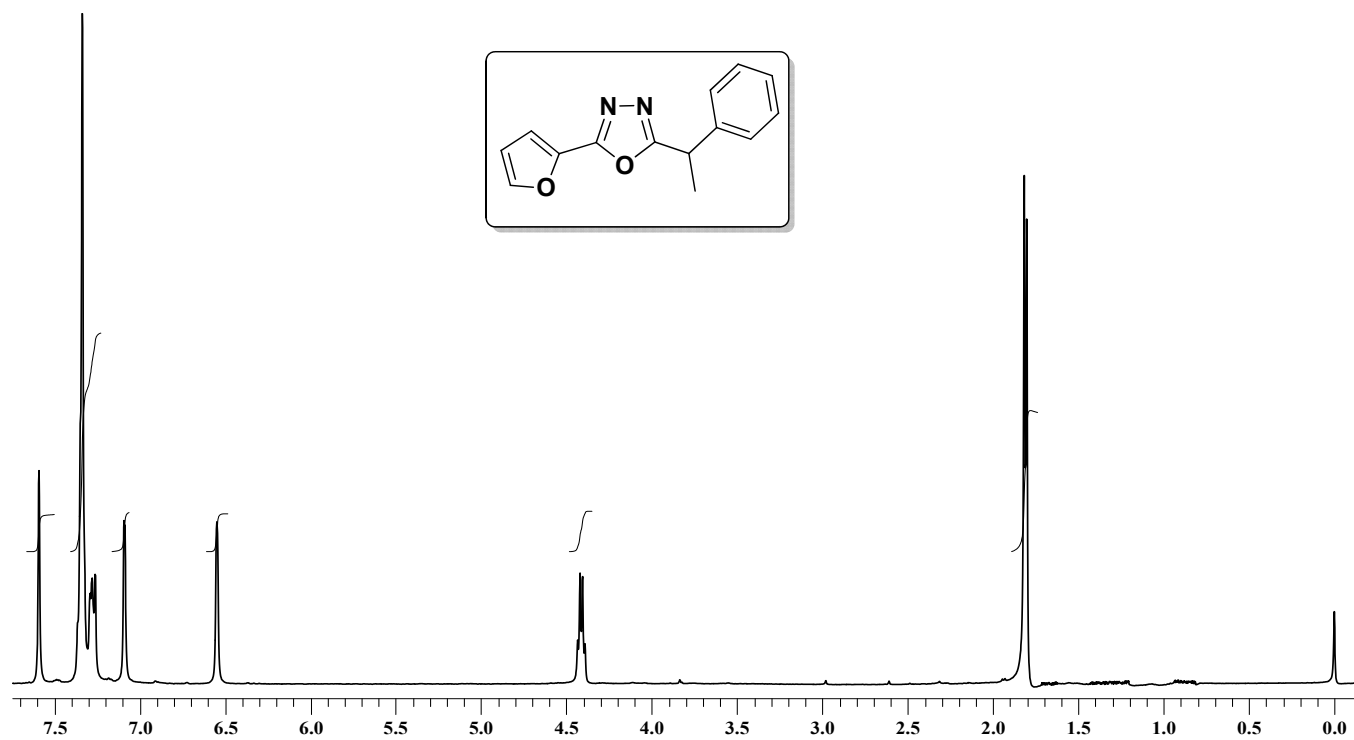
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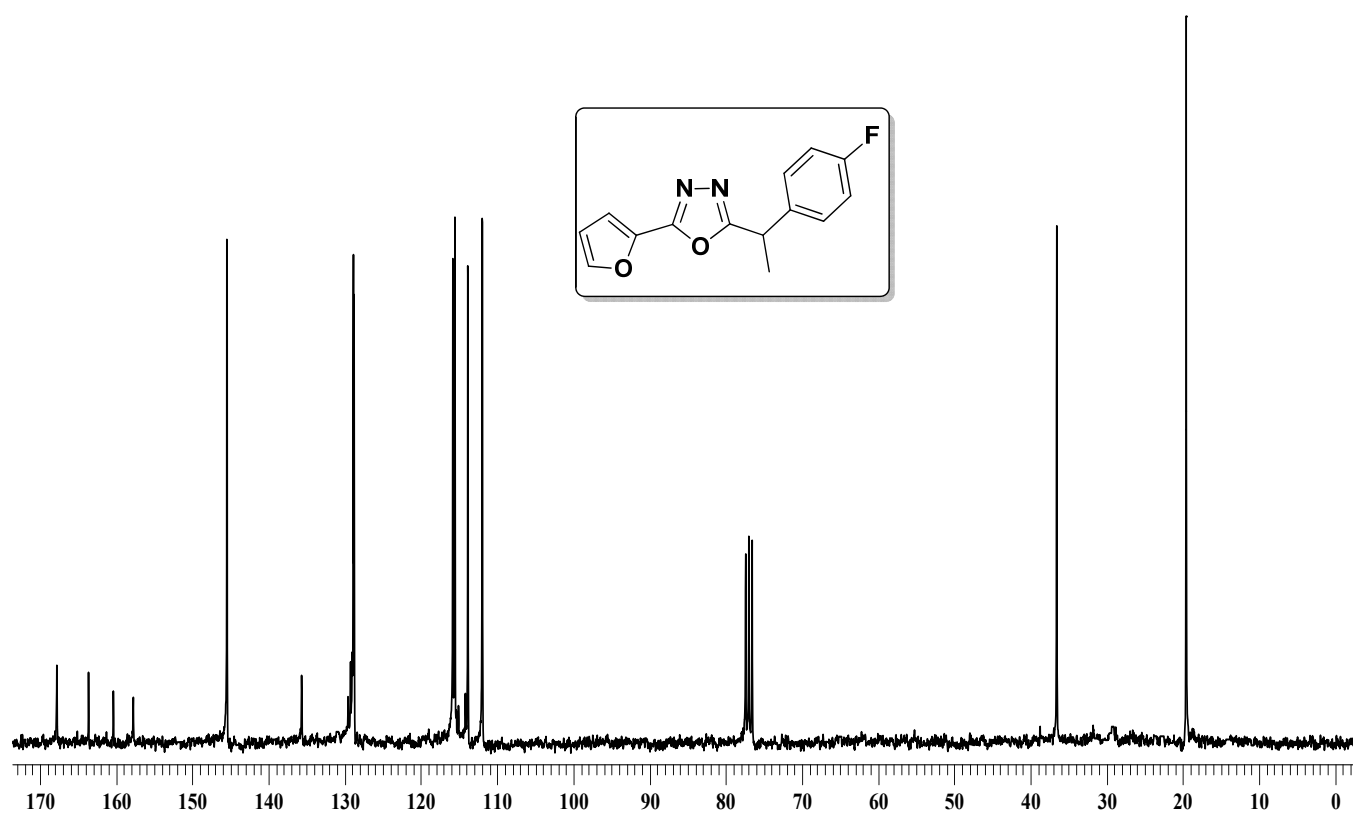
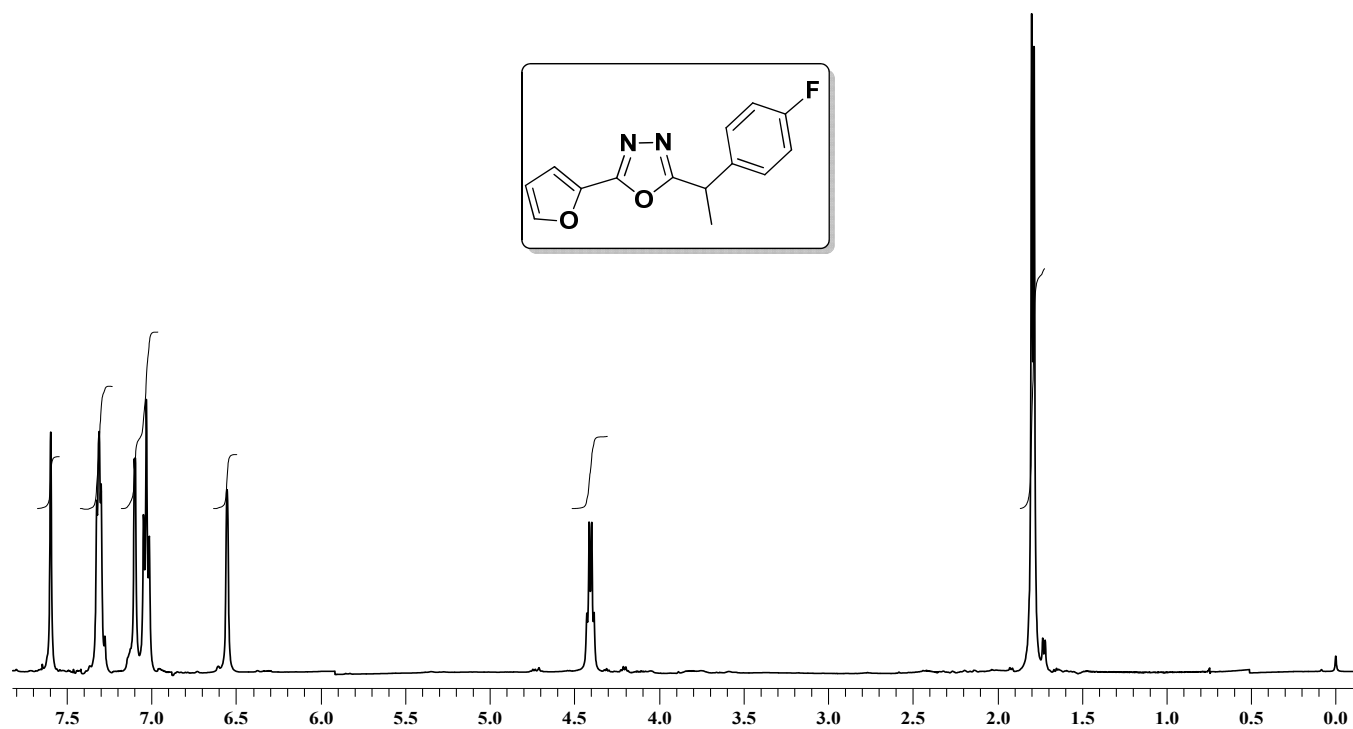
2-(1-phenylethyl)-5-(thiophene-2-yl)-1,3,4-oxadiazole (3ga) (Table 3, entry 8)



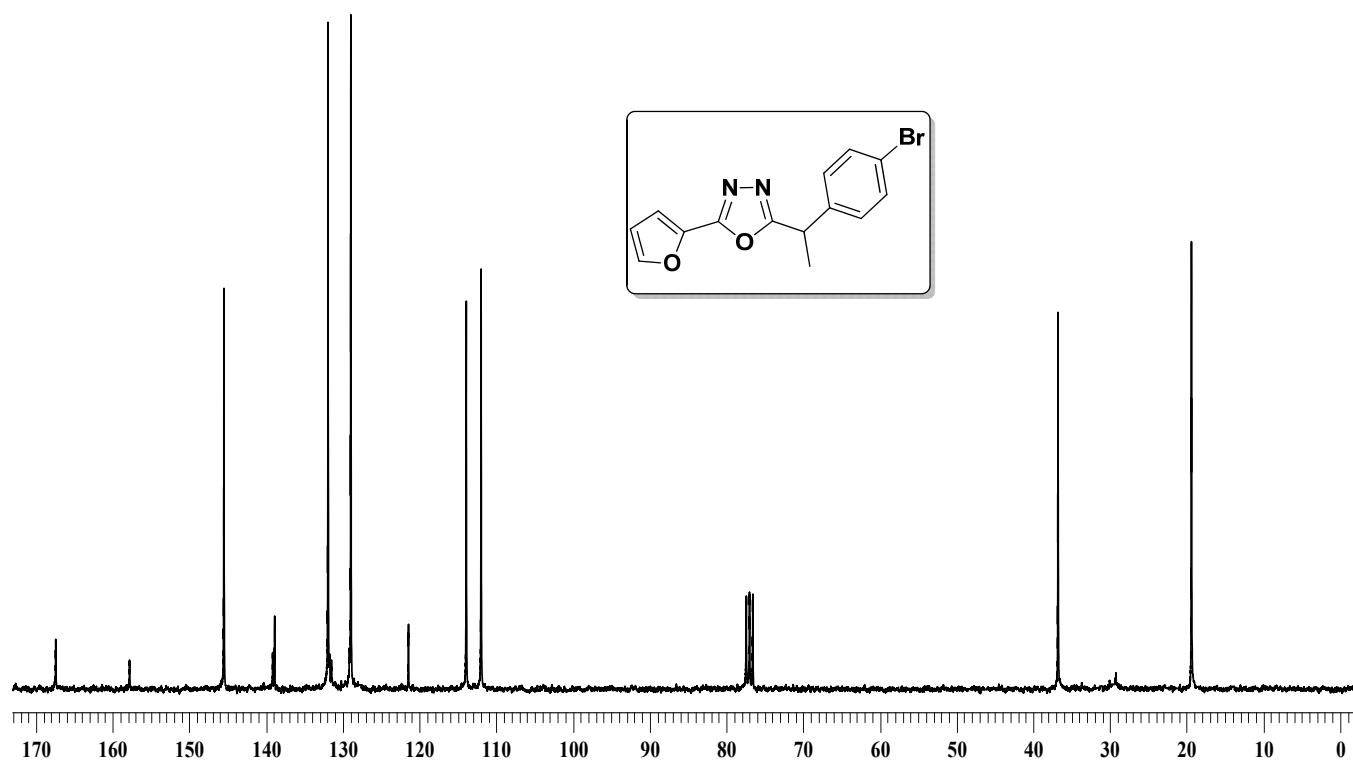
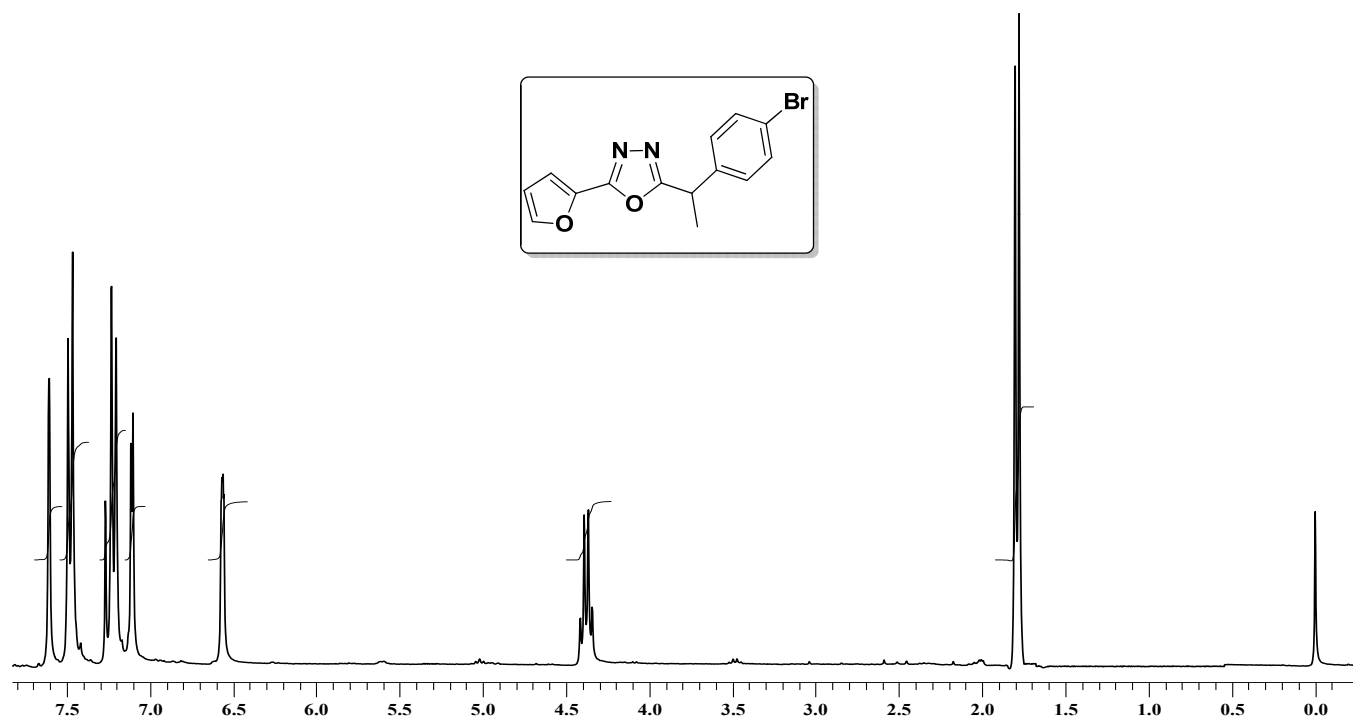
2-(furan-2-yl)-5-(1-phenylethyl)-1,3,4-oxadiazole (3ha) (Table 3, entry 9)



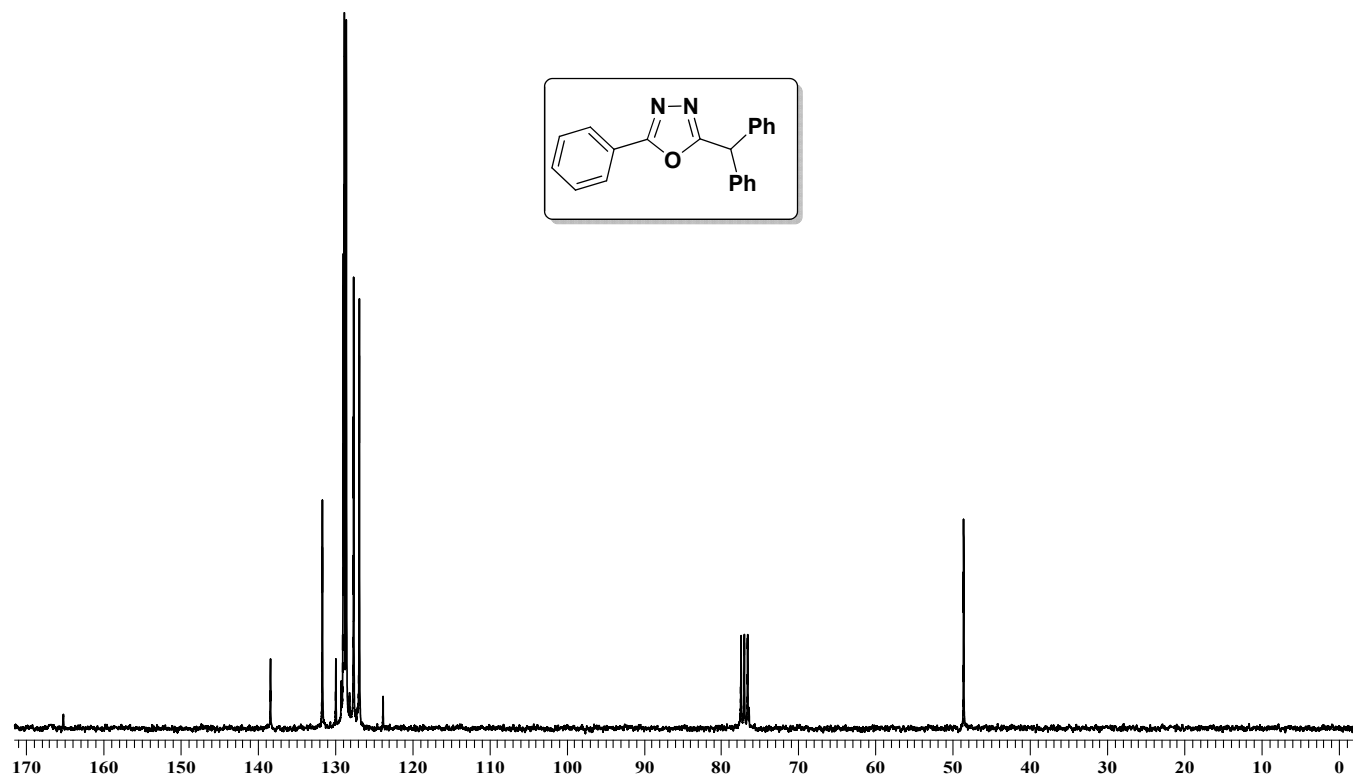
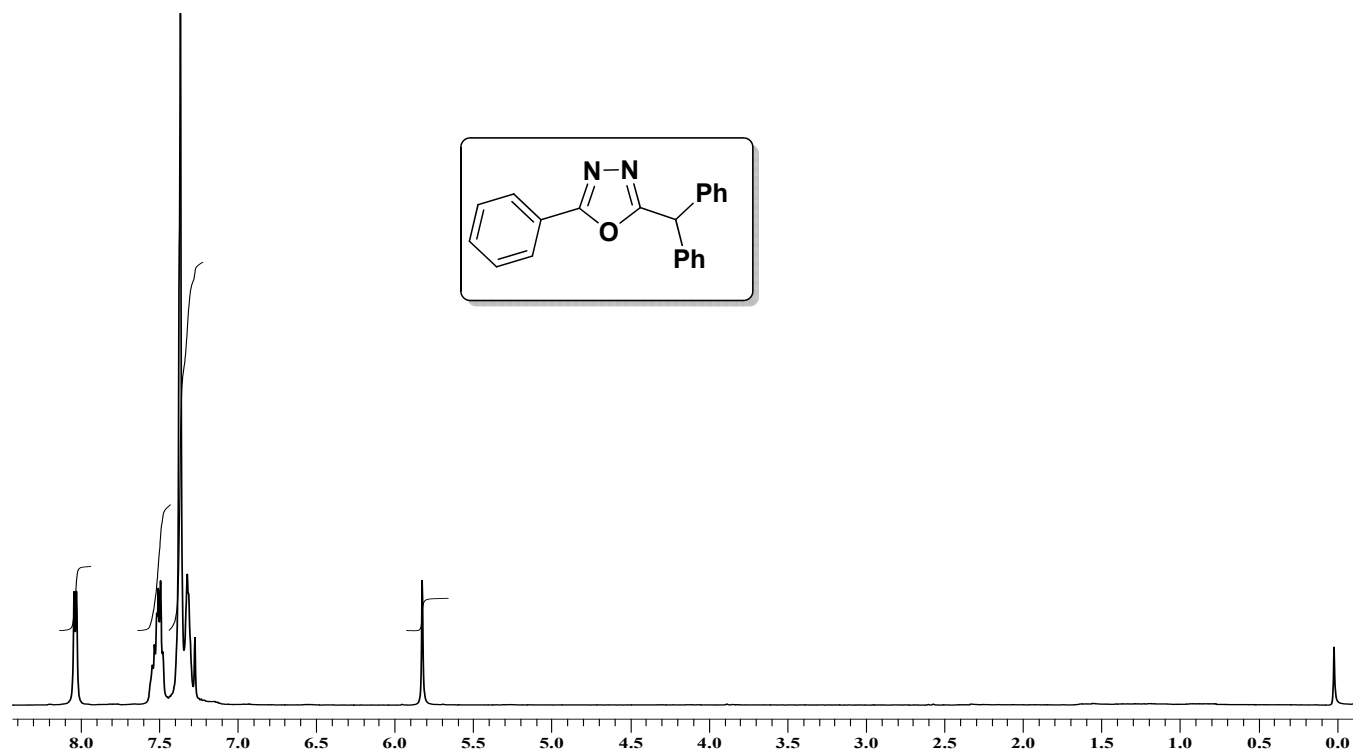
2-(1-(4-fluorophenyl)ethyl)-5-(furan-2-yl)-1,3,4-oxadiazole (3hb) (Table 3, entry 10)



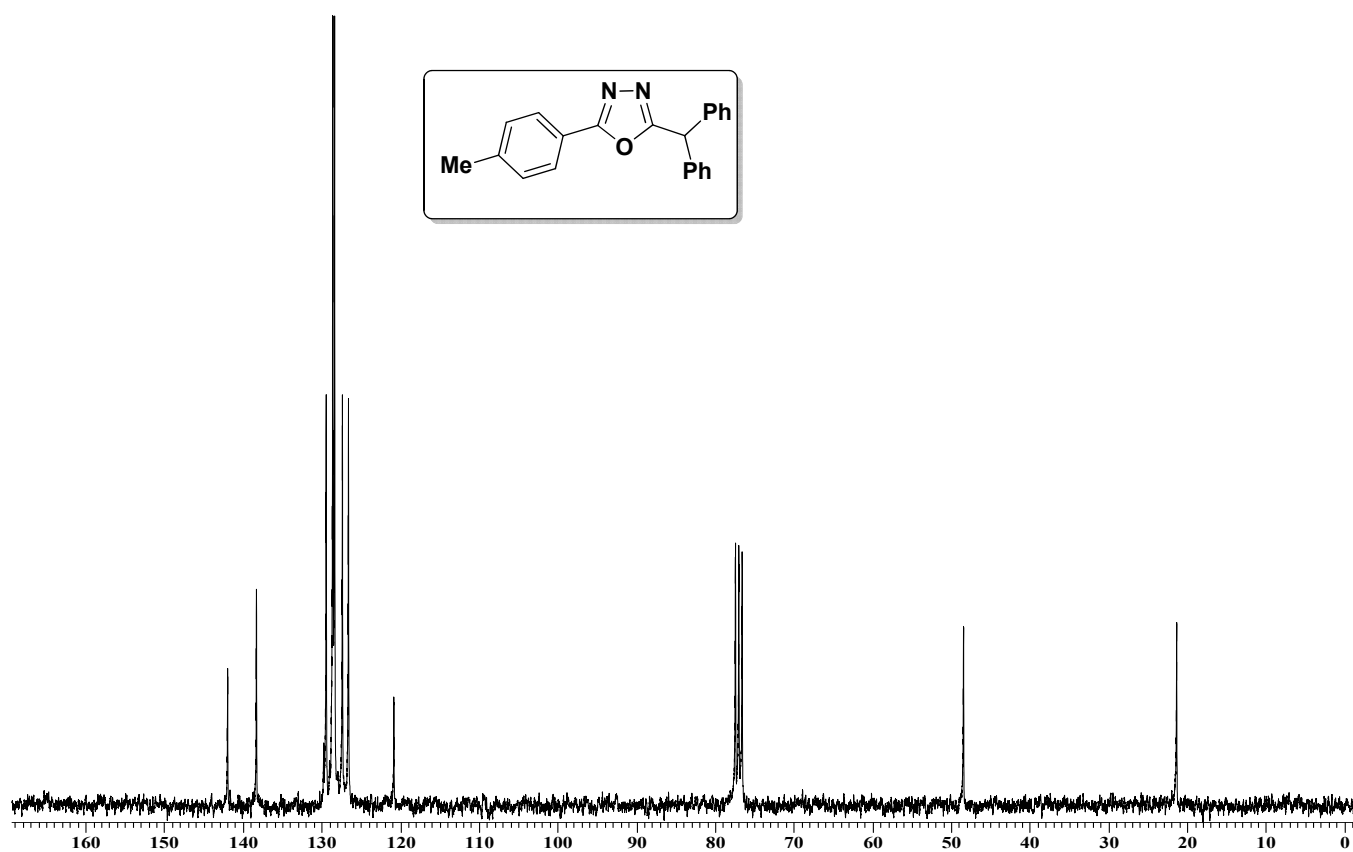
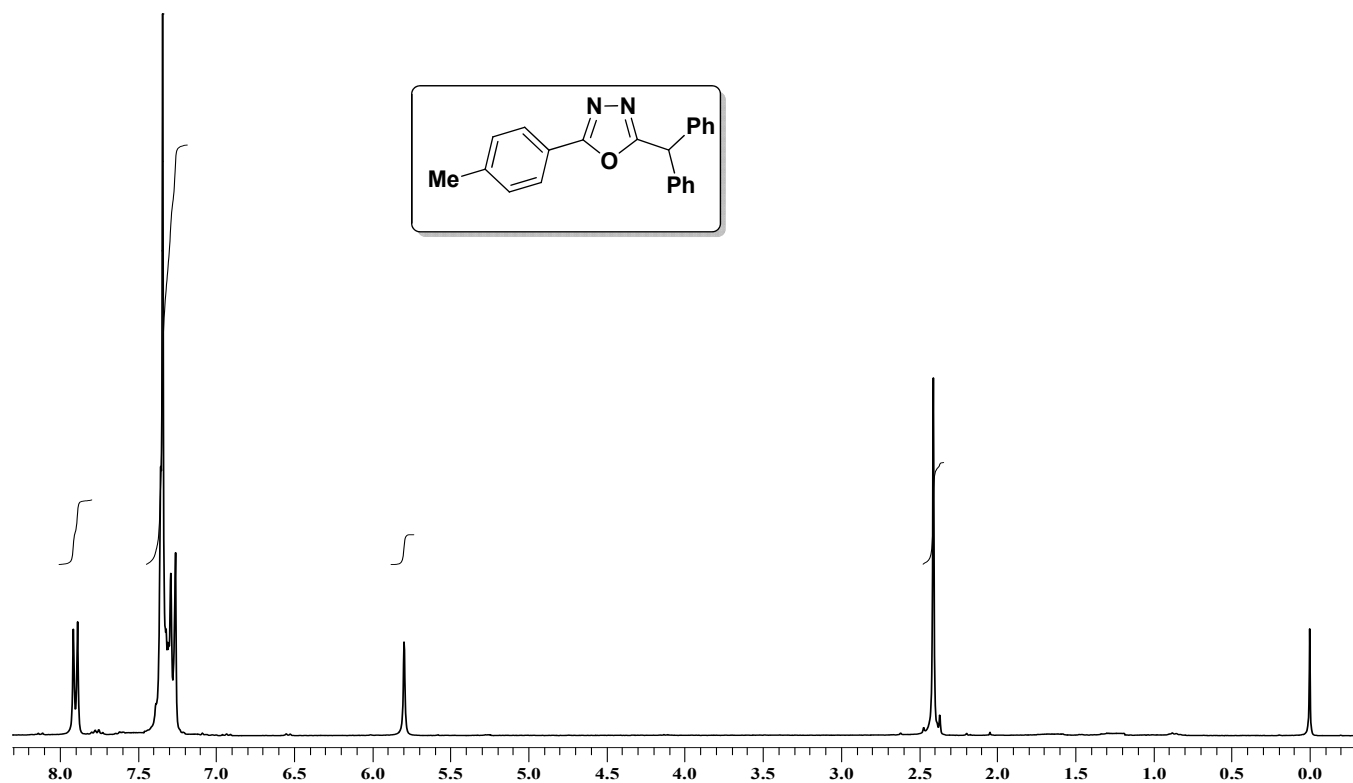
2-(1-(4-bromophenyl)ethyl)-5-(furan-2-yl)-1,3,4-oxadiazole (3hd) (Table 3, entry 11)



2- Benzhydryl-5-phenyl-1,3,4-oxadiazole (3ag)



2-benzhydryl-5-(*p*-tolyl)-1,3,4-oxadiazole (3bg)



2-benzhydryl-5-(4-bromophenyl)-1,3,4-oxadiazole (3eg)

