Electronic Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Inverse electron-demand 1,3-dipolar cycloaddition of nitrile oxide with common nitriles leading to 3-functionalized 1,2,4-oxadiazoles

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Contents

Preparation of Nitroisoxazolone 2

Nitroisoxazolone **2** was easily prepared from commercially available ethyl nitroacetate by three steps with simple experimental manipulations; 1) condensation of nitroacetate with orthoformate, 2) condensation with hydroxylamine, and 3) *N*-methylation with dimethyl sulfate.

1) Condensation of nitroacetate with orthoformate[1]

To a solution of ethyl nitroacetate (40 mL, 0.36 mol) in acetic anhydride (80 mL), trimethyl orthoformate (58 mL, 0.53 mol) was added, and the resultant mixture was heated at 100 °C for 2 d. The mixture was concentrated under reduced pressure, and the residue was used for next step without further purification.

2) Condensation with hydroxylamine[2]

To a solution of ethyl 3-methoxy-2-nitropropenoate (17.5 g, 100 mmol) in ethanol (175 mL), were added hydroxylamine hydrochloride (7.73 g, 120 mmol) and pyridine (20.2 mL, 250 mmol). The mixture was heated at 60 °C for 3 h. After cooling, pale yellow precipitates were formed and were collected to give pyridinium salt of nitroisoxazolone (14.8 g, 71 mmol, 71% yield).

3) *N*-Methylation with dimethyl sufate[3]

Pyridinium salt of nitroisoxazolone (4.18 g, 20 mmol) was heated with freshly distilled dimethyl sufate (2.3 mL, 24 mmol) without solvent at 65 °C for 3 h. The reaction mixture was cooled to room temperature, and water (100 mL) was added. Generated white precipitates were collected, and recrystallized from acetonitrile to afford isoxazolone **2** (2.26 g, 15.7 mmol, 79%).

References

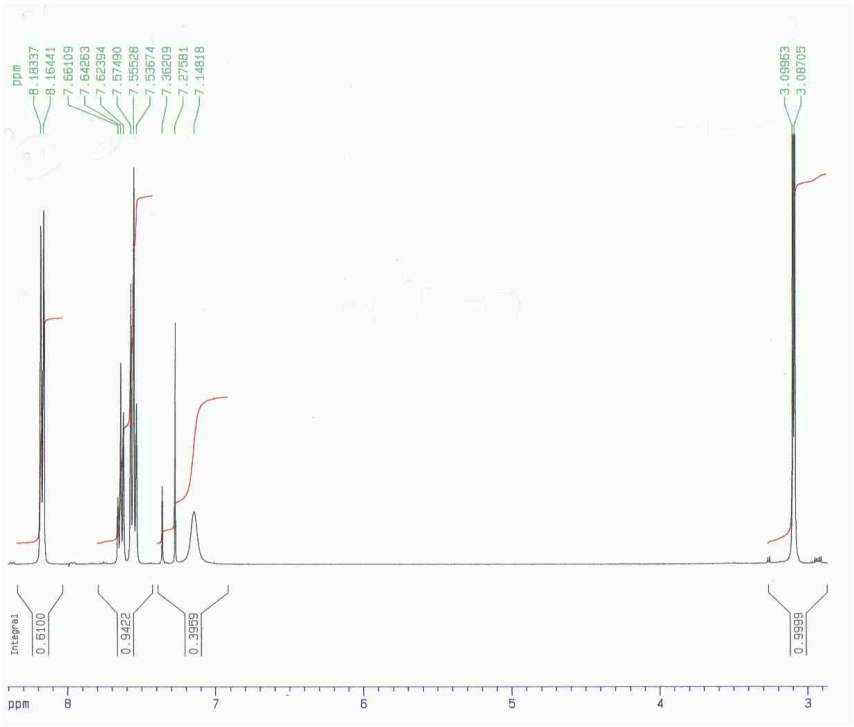
1 M. J. Kamlet, *J. Org. Chem.* **1959**, *24*, 714-715.

2 N. Nishiwaki, Y. Takada, Y. Inoue, Y. Tohda and M. Ariga, *J. Heterocycl. Chem.* **1995**, *32*, 473-475.

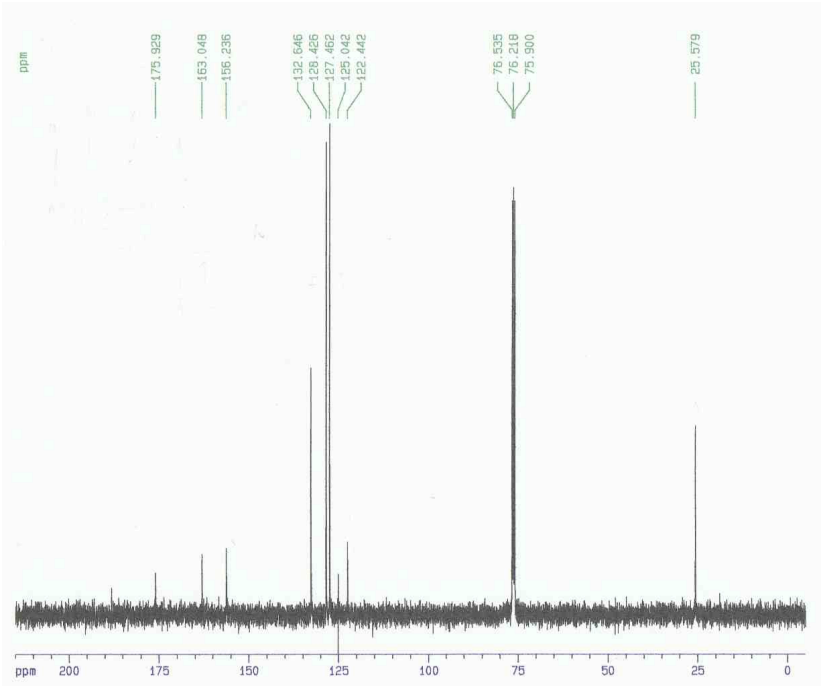
3 N. Nishiwaki M. Nakanishi, T. Hida, Y. Miwa, M. Tamura, K. Hori, Y. Tohda and M. Ariga, *J. Org. Chem.* **2001**, *66*, 7535-7538.

3-(*N*-Methylcarbamoyl)-5-phenyl-1,2,4-oxadiazole (3e)

^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)



5-(4-Methoxyphenyl)-3-(*N*-methylcarbamoyl)-1,2,4-oxadiazole (3g)

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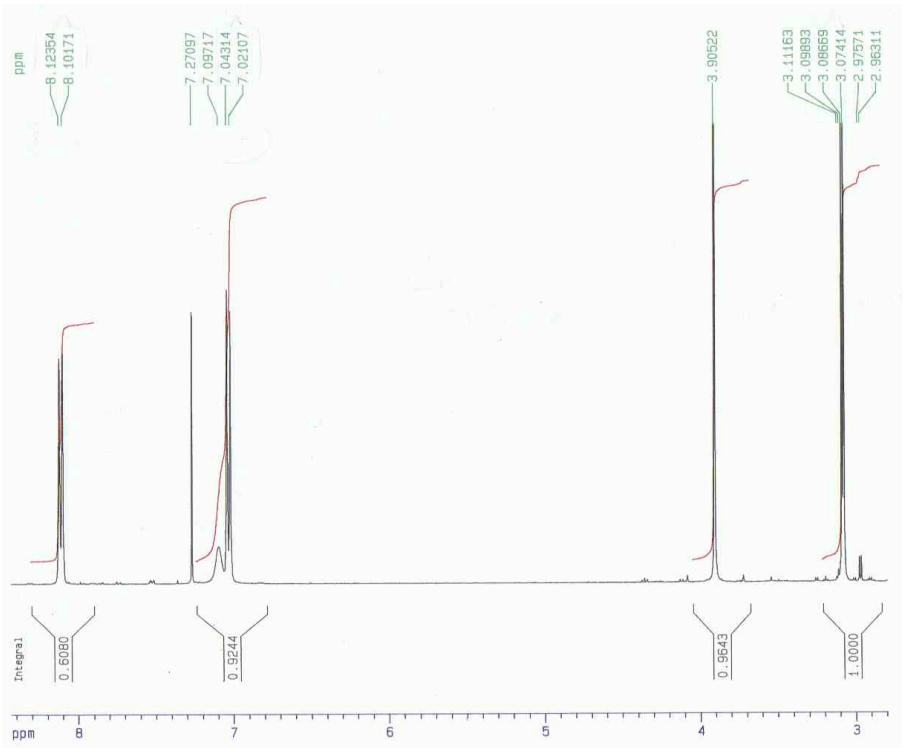

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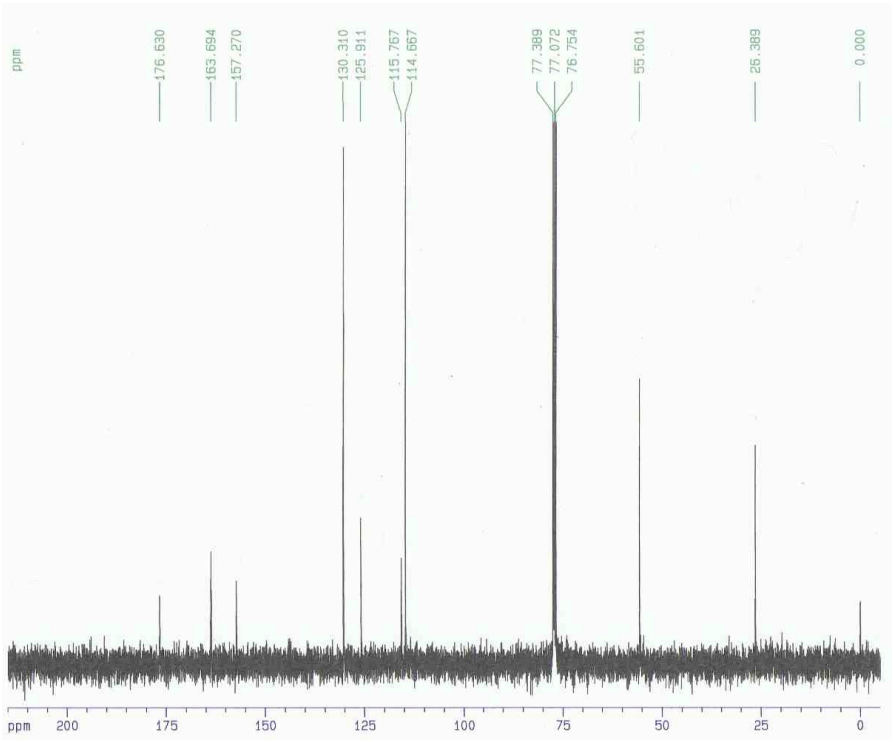

5-(4-Chlorophenyl)-3-(*N*-methylcarbamoyl)-1,2,4-oxadiazole (3i)

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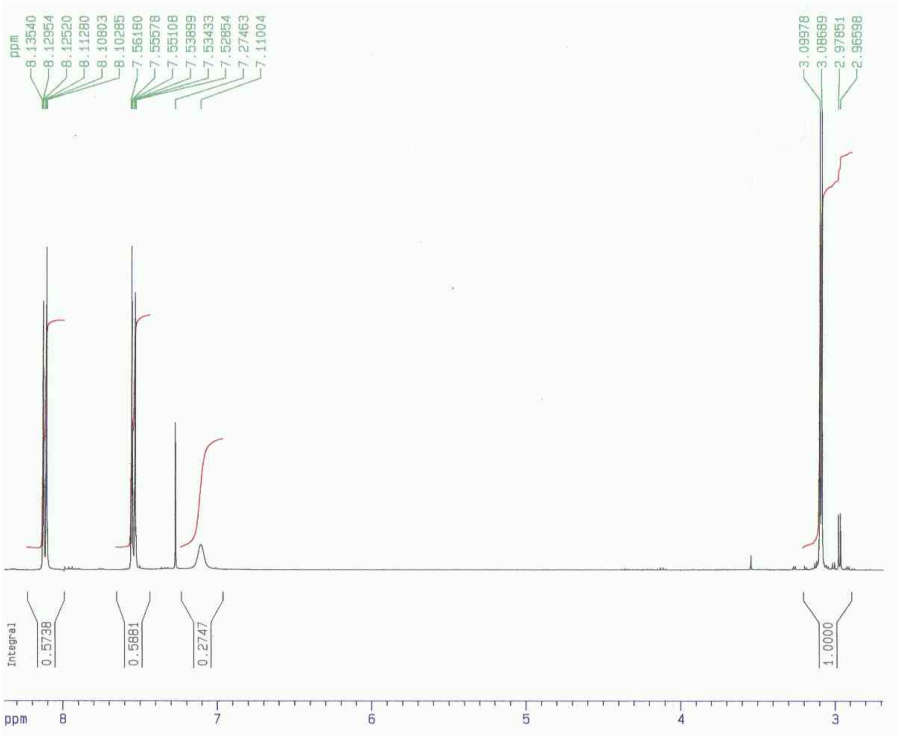

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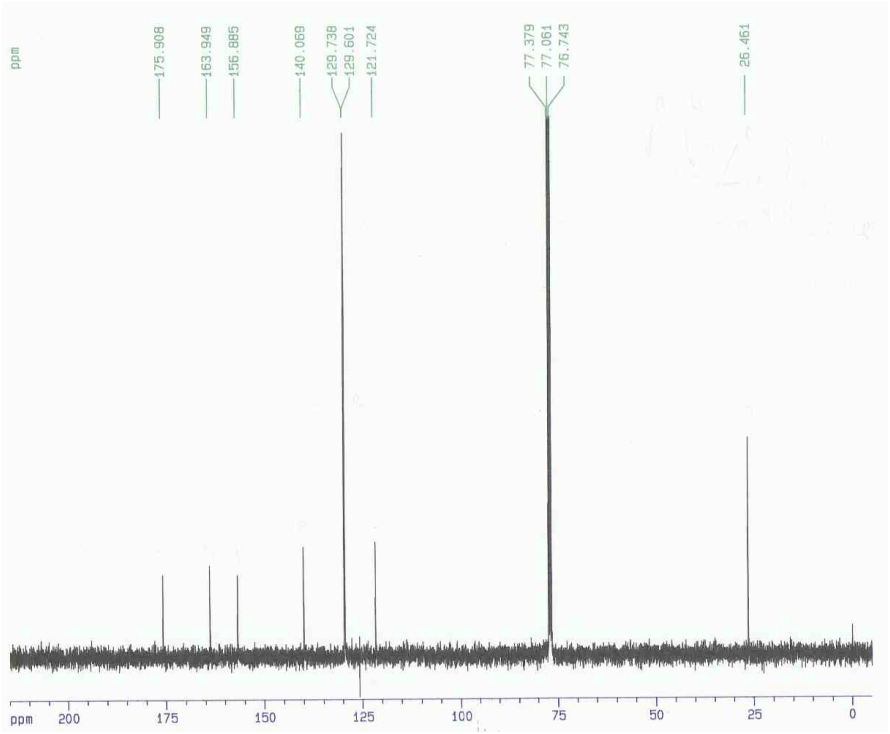

3-(*N*-Methylcarbamoyl)-5-(3-pyridyl)-1,2,4-oxadiazole (**3j**)

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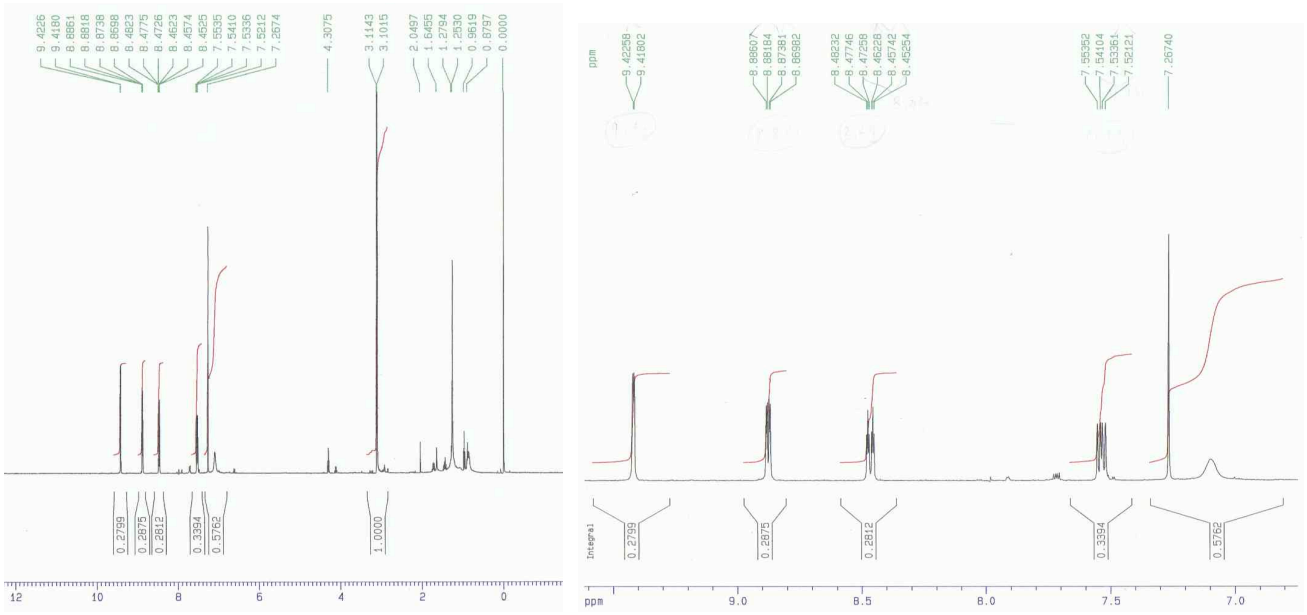

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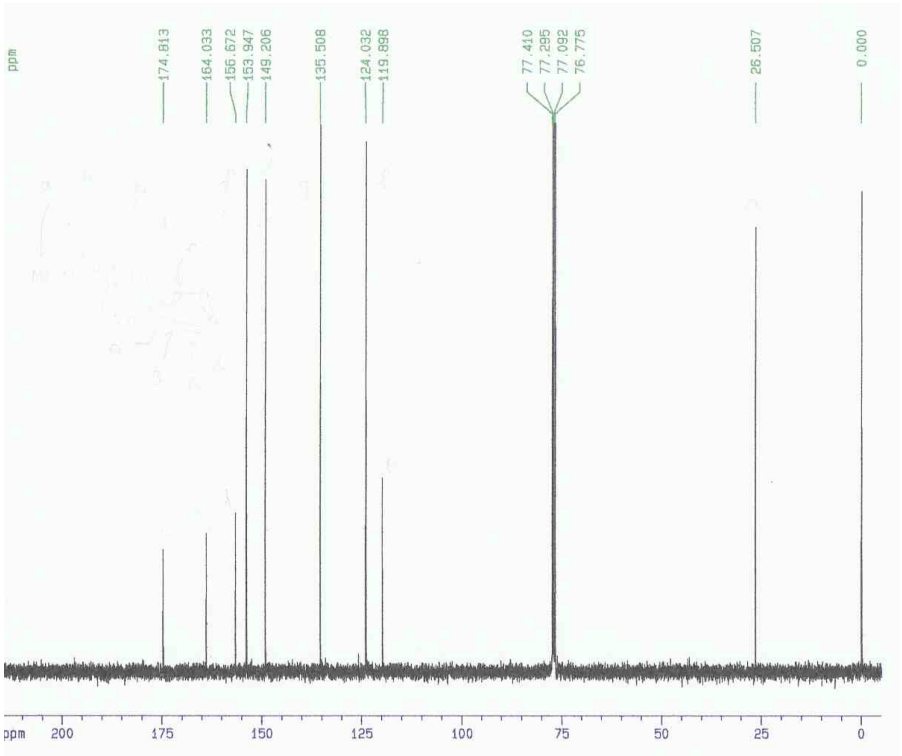

3-(*N*-Methylcarbamoyl)-5-(4-pyridyl)-1,2,4-oxadiazole (3k)

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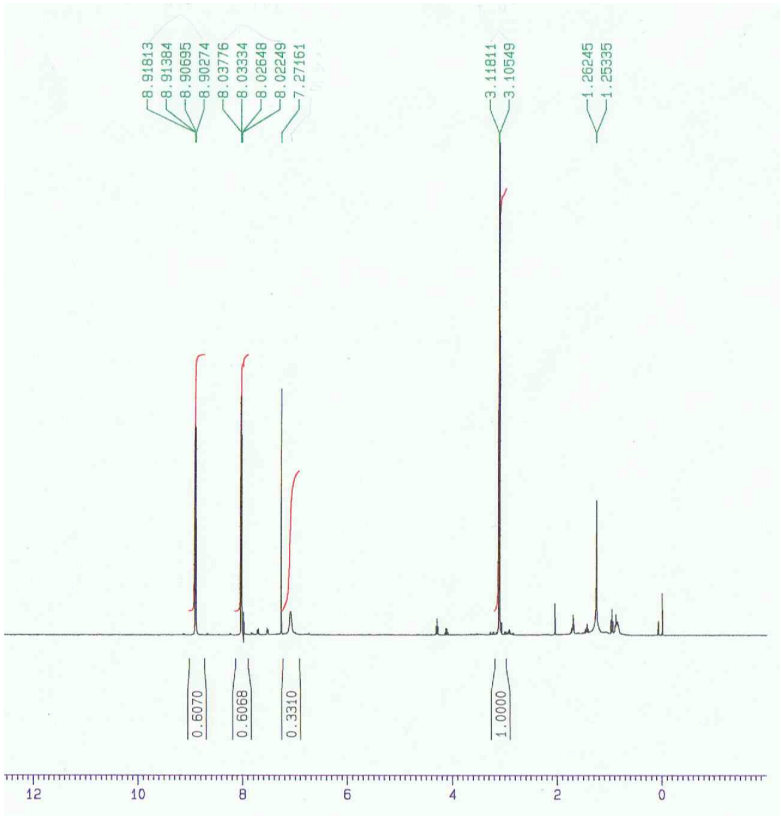

^{13}C NMR ($CDCl_3$)