Supplementary Information

DBU: AN EFFICIENT BASE CATALYST FOR SYNTHESIS OF THE NEW OXAZOLO[5,4-D]PYRIMIDINE DERIVATIVES

Ahmad Nikseresht,^{*a} Mehdi Bakavoli,^b Samad Shoghpour Bayraq^b

^aDepartment of Chemistry, Payame Noor University, 19395-4697 Tehran, Iran.

^bDepartment of Chemistry, School of Sciences, Ferdowsi University of Mashhad, Mashhad, 91775-1436, Iran.

E-mail: a_nik55@yahoo.com, mbakavoli@yahoo.com

S. No	CONTENTS	Page No(s)
1	General Information	2
2	Typical procedure for synthesis of compound 4	2
3	Characterization data and Copies of ¹ H NMR, ¹³ C NMR and HRMS For compound 4	2-5
4	Typical procedure for synthesis of compound 5	5
5	Characterization data and Copies of HRMS, ¹ H NMR and ¹³ C NMR For compound 5	6-8
6	General procedure for the Synthesis of oxazolo[5, 4-d]pyrimidine-5(4H)-thiones (6 and 7).	9
7	Typical procedure for synthesis of compound 6	9
8	Characterization data and Copies of ¹ H NMR, ¹³ C NMR and HRMS For compound 6.	9-12
9	Typical procedure for synthesis of compound 7.	12
10	Characterization data and Copies of HRMS, ¹ H NMR and ¹³ C NMR For Compound 7.	13-15
11	Reference	15

1. General Information

Reactions were monitored by TLC using precoated silica gel aluminum plates. Detection were done by UV (254 nm) followed by dipping in either sulfuric acid in EtOH (10%) or 0.5% phosphomolybdic acid in 95% EtOH solutions and subsequent charring at 200 °C or dipping in a 1% aqueous potassium permanganate solution and air drying. Anhydrous MgSO₄ was used to dry organic solutions during work up and the removal of solvents was carried out under vacuum with a rotary evaporator. Melting points were determined on a Buchi510 and are uncorrected. IR spectra were obtained on a Bruker Alpha-P FTIR Diamond ATR spectrophotometer. ¹H NMR and ¹³C NMR spectra were recorded with a Bruker 400 spectrometer, using tetramethylsilane as internal standard. All the assignments for proton and carbon were made *via* 2D COSY, HSQC and HMBC experiments. High Resolution mass spectra were obtained by a Thermo Scientific Exactive High Resolution MS (ESI probe).

2. Typical procedure for synthesis of compounds 4

According to our investigation of synthesis oxazole derivatives,¹ to a stirred solution of aminomalononitrile tosylate (AMNT), (2.71 g, 8.60 mmol) in 1-methyl-2-pyrrolidinone (20 mL), were added 1.0–1.1 equiv of the diphenylacetyl chloride in one portion. The reaction mixture was stirred at room temperature until the reaction was complete. Then, the mixture was diluted with a mixture of EtOAc and Et₂O (1:1), and washed with water, 10 % aqueous NaHCO₃, and water. The organic layer was dried, the solvent was evaporated *in vacuo*, and the crude product was purified by flash silica gel chromatography (1:1, PE/EtOAc).

3. Characterization data and Copies of ¹H NMR, ¹³C NMR and HRMS for compound 4

5-Amino-2-benzhydryl-4-cyano-1, 3-oxazole (4).

92% yield. White crystals; mp 163-166 °C.

IR ν_{max} 3341, 3310, 3139, 2923, 2852, 2220, 1660, 1591, 1158, 696, 744 cm⁻¹.

¹H NMR (DMSO-*d*₆, 400 MHz) δ 7.70 (br s, NH₂, 2 H), 7.2-7.4 (m, 10H_{arom.}), 5.59 (s, CH, 1 H).

¹³C NMR (DMSO-*d*₆, 100 MHz) δ 162.34 (C5), 152.65 (C2), 139.49 (2 C, 2C1'), 128.55 (4 C, 2C3', 2C5'), 128.44 (4 C, 2C2', 2 C6'), 127.13 (2 C, 2 C4'), 115.44 (CN), 82.52 (C4), 49.23 (CH).

HR MS: m/z calcd. for C₁₇H₁₂ON₃ (M-H⁺) 274.099, found 274.098 and m/z calcd. for C₁₇H₁₄ON₃ (MH⁺) 276.113, found 276.113.^[1]

4. Typical procedure for synthesis of compounds 5

According to our investigation of synthesis oxazole derivatives,¹ to a stirred solution of aminomalononitrile tosylate (AMNT), (2.71 g, 8.60 mmol), in pyridine (40 mL), was added the 4-nitrobenzoic acid (1.39 g, 8.15 mmol) and 1, 3-dicyclohexylcarbodiimide (DCC), (1.77 g, 8.6 mmol) and the reaction mixture was stirred at room temperature until the reaction was complete. The white precipitate (dicyclohexylurea) was removed by filtration and the filtrate was concentrated *in vacuo* to give a residue, which was purified by flash silica gel chromatography (1:1, PE/EtOAc) to give product.

5. Characterization data and Copies of HRMS, ^1H NMR and ^{13}C NMR for compound 5.

5-Amino-4-cyano-2-(4-nitrophenyl)-1,3-oxazole (5).

Yield (78%) as yellow crystals: mp 274-277 °C.

IR ν_{max} 3285, 3227, 2221, 1668, 1597, 1514, 1319, 1057, 852 cm^{-1} .

^1H NMR (DMSO- d_6 , 400 MHz) δ 8.26 (br s, NH_2 , 2 H), 8.33 (dd, $^3J = 8.8$ Hz, H2', H6', 2 H), 7.95 (dd, $^3J = 8.8$ Hz, H3', H5', 2 H).

^{13}C NMR (DMSO- d_6 , 100 MHz) δ 162.8 (C5), 147.47 (2C, C2, C4'), 131.27 (C1'), 125.74 (2C, C2', C6'), 124.50 (2C, C3', C5'), 114.87 (CN), 85.54 (C4).

HR MS: m/z calcd. for $\text{C}_{10}\text{H}_5\text{O}_3\text{N}_4$ ($\text{M}-\text{H}^+$) 229.037, found 229.036.^[1]

p-nitro-phenyl-oxazole

8.334
8.336
8.338
8.340
8.342
8.344
8.265
8.222
8.1974
7.970
7.957
7.952

4.040
4.022
3.322
3.300
2.679
2.675
2.671
2.528
2.510
2.506
2.502
2.337
2.333
2.328
1.989

1.177

NAME ARMAD11H
EXPNO 2
PROCNO 1
Date_ 20110401
Time_ 15.30
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 32
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 181
DM 60.800 usec
DE 6.50 usec
TE 298.2 K
D1 1.0000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 7.00 usec
PL1 -0.75 dB
PL1W 15.10603619 W
SF01 400.1724712 MHz
SI 32768
SF 400.1699930 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

6. General procedure for the Synthesis of oxazolo[5, 4-d]pyrimidine-5(4H)-thiones **6** and **7**.

To a solution of 1, 8-diazabicyclo[5, 4, 0]undec-7-ene (DBU) (1.0-1.1 equiv) in dry DMF, (5 mL) under argon, the corresponding aryl and alkylisothiocyanates (0.8-0.95 equiv.) and the oxazoles **4** and **5**, (1.0 equiv.) were added. The mixture was reacted at 120 °C until the reaction was complete. Thus, water and a solution of HCl (1 M) were added until PH 9. Then, the precipitate was filtered off and purified to give compound **6** and **7**.

7. Typical procedure for synthesis of compound **6**.

DBU (351 μ L, 2.3 mmol) in DMF dry (5 mL) was reacted with p-methoxyphenylisothiocyanate (270 μ L, 1.9 mmol) and oxazole **4**, (551 mg, 2 mmol). The mixture was reacted at 120 °C for overnight. Then, particulate was filtered and was purified by flash chromatography (3:1, PE: EtOAc) to give compound **6**.

8. Characterization data and Copies of ^1H NMR, ^{13}C NMR and HRMS For compound **6**.

7-Amino-2-benzhydryl-6-(4-methoxyphenyl)-oxazolo[5,4-d]pyrimidine-5(4H)-thione (**6**).

90% yield: White crystals; mp 273-276 °C.

IR ν_{max} 3392, 3330, 2954, 2852, 1692, 1509, 1257, 693, 738 cm^{-1} .

^1H NMR (DMSO- d_6 , 400 MHz) δ 9.90 (br s, NH_2 , 2 H), 7.46 (m, 2 $\text{H}_{4'}$, 2 H), 7.31 (m, 2 $\text{H}_{3'}$, 2 $\text{H}_{5'}$, 4 H), 7.23 (m, 2 $\text{H}_{2'}$, 2 $\text{H}_{6'}$, 4H), 7.15 (m, $\text{H}_{3''}$, $\text{H}_{5''}$, 2H), 6.73 (d, $\text{H}_{2''}$, $\text{H}_{6''}$, 2H), 5.06 (s, CH, 1 H), 3.68 (s, CH_3 , 3 H).

^{13}C NMR (DMSO- d_6 , 100 MHz) δ 170.27, 158.9 (C2), 154 (C3a), 150 (2 C, C7, C4''), 114 (C7a), 140 (2 C, 2C1'), 131 (2 C, C2'', C6''), 129 (4 C, 2C3', 2C5'), 128.4 (4 C, 2 C2', 2 C6'), 128.5 (C1''), 127 (2 C, 2 C4'), 110.86 (2C, C3'', C5''), 55 (CH_3), 50 (CH).

HR MS: m/z calcd. for $\text{C}_{25}\text{H}_{21}\text{O}_2\text{N}_4\text{S}$ MH^+ 441.138, found 441.138 and m/z calcd. for $\text{C}_{25}\text{H}_{19}\text{O}_2\text{N}_4\text{S}$ M-H^+ 439.123, found 439.123.^[1]

NAME AHWAD11H
EXPNO 116
PROCNO 1
Date_ 20110913
Time_ 8.05
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT DMSO-d6
NS 32
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 90.5
DW 60.800 usec
DE 6.50 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1

===== CHANNEL f1 =====
NUC1 1H
P1 7.00 usec
PL1 -0.75 dB
PL1W 15.10603619 W
SFO1 400.1724712 MHz
SI 32768
SF 400.1700009 MHz
WDW EM
SSE 0
LB 0.30 Hz
GB 0
PC 1.00

diphenyl-oxa-py-ph-OMe (1st spot)

Diphenyl-1-oxa-ph-OMe 3rd spot fr (213-231)

9. Typical procedure for synthesis of compound 7

DBU (305 μ L, 2 mmol) in DMF dry (5 mL) was reacted with ethylisothiocyanate (156 μ L, 1.7 mmol) and oxazole **5** (460 mg, 2 mmol). The mixture was reacted at 120 $^{\circ}$ C under argon for overnight. Then, participate was filtered and was purified and recrystallized in EtOH, provided compound **7**.

10. Characterization data and Copies of ^1H NMR, ^{13}C NMR and HRMS For compound 7

7-Amino-6-ethyl-2-(4-nitrophenyl)-oxazolo[5,4-d]pyrimidine-5(4H)-thione (7).

81% yield: Yellow crystal; mp 201-203 °C.

IR ν_{max} 3438, 3413, 2975, 2930, 1625, 1549, 1313, 1339, 854 cm^{-1} .

^1H NMR (DMSO- d_6 , 400 MHz) δ 8.5 (s, NH_2 , 2 H), 8.17-8.39 (m, 4 $\text{H}_{\text{arom.}}$), 3.76 (q, CH_2 , 2 H), 1.20 (t, CH_3 , 3 H).

^{13}C NMR (DMSO- d_6 , 100 MHz) δ 162.8 (C2), 147 (2C, C3a, C4'), 131 (C7), 127 (C1'), 125.6 (2C, C2', C6'), 124 (2C, C3', C5'), 117 (C7a), 40 (CH_2), 15 (CH_3).

HR MS: m/z calcd. for $\text{C}_{13}\text{H}_{12}\text{O}_3\text{N}_5\text{S}$ MH^+ 318.066, found 318.066 and m/z calcd. for $\text{C}_{13}\text{H}_{10}\text{O}_3\text{N}_5\text{S}$ M-H^+ 316.051, found 316.050.

REFERENCE

[1] Bakavoli, M.; Nikseresht, A.; Lari, J.; Vahedi, H. *Asian J. Chem.* **2013**, Vol. 25, 9, 5079-5083.