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MICROWAVE ASSISTED SYNTHESIS OF 3-AMINO-5-METHYL ISOXAZOLE SCHIFF BASES

K. SATHISH KUMAR, VIJAY KUMAR CHITYALA, N. J. P. SUBHASHINI[a] and SHIVARAJ[*]

Department of Chemistry, Osmania University, HYDERABAD – 500007 (A.P.) INDIA
[a]Department of Chemistry, University College of Technology, Osmania University, HYDERABAD – 500007 (A.P.) INDIA

ABSTRACT

Isoxazole Schiff bases derived from 3-amino-5-methyl isoxazole with various substituted salicylaldehydes were non-conventionally synthesized by microwave assisted method. Conventional methods for synthesis of Schiff bases require refluxing at 60-80^{o}C of the reactants in different solvents for at least 3 h or more, where as the microwave-assisted synthesis has brought down the reaction time from 3 h to 30 sec. The procedure reported is simple as it requires very lesser amount of organic solvents and the time has been reduced to only 30 sec. Comparative yields of all compounds by different methods revealed that the yield is low in conventional method (70-81%) as compared to microwave assisted synthesis (90-95%). The compounds were characterized by FT-IR, ^{1}H NMR and ^{13}C NMR spectroscopic data.

Key words: Isoxazole amine, Schiff base, Microwave assisted synthesis.

INTRODUCTION

Microwave assisted synthesis has become an important technique for the rapid organic synthesis. The major advantage of this method includes decreasing in reaction time and increasing in yield[1-6]. The synthesis and characterization of Schiff bases were very important due to their potential biological applications[7-11]. It is well known that several Schiff bases have anti-inflammatory, anti-fungal, antibacterial and anti-HIV activity[12-16]. Studies on Schiff bases derived from 3-amino-5-methyl isoxazole and substituted salicyaldehyde have been reported earlier by conventional method[17-19]. In the present investigation, We report here the microwave assisted rapid organic synthesis of isoxazole Schiff bases derived from of 3-amino-5-methyl isoxazole with various substituted salicylaldehydes.

[*]Author for correspondence; E-mail: Shivaraj_sunny@yahoo.co.in, sathishdavan@gmail.com

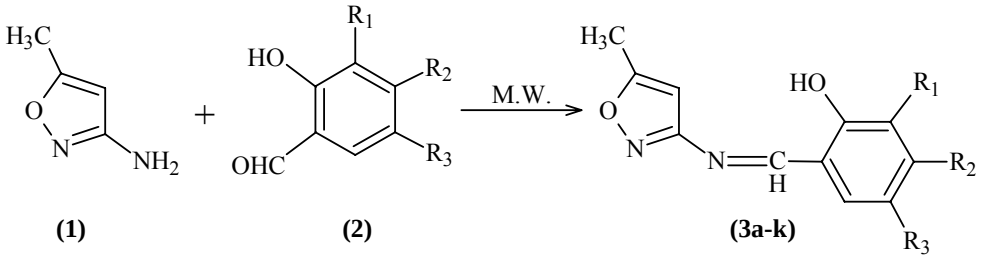
EXPERIMENTAL

Physical measurements

^{1}H NMR spectra of the compounds were recorded on Bruker-400 MHz instrument using TMS as internal standard. ^{13}C NMR spectra were recorded on Bruker-400 MHz instrument. The EI mass spectra were recorded on a VG micro mass 7070-H instrument, ESIMS spectra were recorded on VG AUTOSPEC mass spectrometer. IR spectra of the compounds were recorded using KBr pellets in the range (4000-400 cm^{-1}) on Perkin-Elmer Infrared model 337. The percentage composition of C, H and N of the compounds were determined by using micro analytical techniques on Perkin-Elmer 240C (USA) elemental analyzer. Melting points of the compounds were determined on Polomon instrument (Model. No. MP-96). All the chemicals used were of analytical reagent grade.

General procedure for the synthesis of isoxazole Schiff bases

The microwave assisted condensation of 3-amino-5-methyl isoxazole (0.01M) and substituted salicyladehydes (0.01M) were carried out in a domestic oven (LG, 1300W, 28L capacity). The reaction mixture was subjected to microwave irradiation for the period of time specified in Table 1. The purity of the compounds was checked by TLC. The obtained products were recrystallized from suitable solvent.



(1) **(2)** **(3a-k)**

Scheme

Table 1: Comparison of conventional and microwave assisted synthesis of the compounds (3a-k)

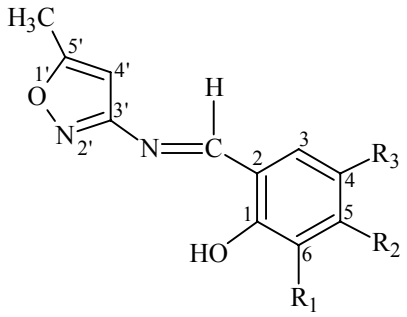
S. No.	R_1	R_2	R_3	M.P (^0C)	Conventional		Microwave	
					Time	Yield (%)	Time	Yield (%)
3a	H	H	H	128	3 hrs	79	30 sec	90

Cont…

S. No.	R_1	R_2	R_3	M.P (^oC)	Conventional		Microwave	
					Time	Yield (%)	Time	Yield (%)
3b	OCH_3	H	H	162	4 hrs	75	5 min	91
3c	OC_2H_5	H	H	147	5 hrs	81	8 min	95
3d	H	OH	H	281	4 hrs	70	6 min	92
3e	H	Cl	H	110	3 hrs	80	3 min	94
3f	H	OCH_3	H	232	3.30 hrs	72	5 min	93
3g	H	OC_2H_5	H	95	4 hrs	76	6 min	95
3h	H	H	Cl	200	2.30 hrs	70	1 min	90
3i	H	H	Br	281	2.30 hrs	70	2 min	92
3j	H	H	CH_3	216	4 hrs	73	5 min	90
3k	H	H	NO_2	210	3 hrs	70	4 min	95

RESULTS AND DISCUSSION

Spectral data of the compounds (3a-k)



2-{[(5'-Methyl-3'-isoxazolyl) imino] methyl} phenol (3a)

IR (KBr, cm^{-1}): 3383 (OH); 1624 (C=N), 1243 (C-O).

^{1}H NMR (DMSO, ppm): δ 12.29 (s, -OH), 8.92 (CH=N), 6.90-7.48 (m, H-3,4,5,6), 6.08 (s, H-4'), 2.47 (s, 5'-CH_3).

^{13}C NMR (DMSO, ppm): 169.3 (C-5'), 161.7 (C-1), 160.1 (CH=N), 153.4 (C-3'), 132.5 (C-5), 130.9 (C-3), 122.5 (C-4), 118.7 (C-2), 116.2 (C-6), 96.2 (C-4'), 12.9 (C-5'-CH_3).

3-Methoxy-2-{[(5'-methyl-3'-isoxazolyl) imino] methyl} phenol (3b)

IR (KBr, cm^{-1}): 3348 (OH); 1602 (C=N); 1256 (C-O).

^{1}H NMR ($CDCl_3$, ppm): δ 12.03 (s, -OH); 8.21 (s, CH=N); 6.04-7.56 (m, H-3,4,5), (s, 5'-CH_3), 5.18 δ (6-OCH_3)

2-Ethoxy-6-{[(5'-methyl-3'-isoxazolyl) imino] methyl} phenol (3c)

IR (KBr, cm^{-1}): 3376 (OH); 1620 (C=N). 1249 (C-O),

^{1}H NMR (DMSO, ppm): δ 12.58 (s, -OH); 8.93 (s, CH=N); 6.85-7.04 (m, H-3,4,5); 6.07 (s, H-4'); 4.15 (q, -OCH_2CH_3); 2.48 (s, 5'-CH_3); 1.51 (t, -OCH_2CH_3).

^{13}C NMR (DMSO, ppm): 171.1 (C-3'); 167.5 (CH=N); 167.1 (C-5'); 152.0 (C-1); 147.6 (C-2); 124.6 (C-3); 118.8 (C-5); 118.5 (C-6); 117.7 (C-4); 96.8 (C-4'); 64.7 (-OCH_2CH_3); 14.7 (-OCH_2CH_3); 12.6 (C-5'-CH_3).

4-{[(5'-Methyl-3'-isoxazolyl) imino]}-1, 3-benzenediol (3d)

IR (KBr, cm^{-1}): 3369 (OH); 1603 (C=N); 1230 (C-O).

^{1}H NMR (DMSO, ppm): δ 10.61 (s, -OH), 8.94 (CH=N), 6.42-7.55 (m, H-3,4,6), 12.57 (s, OH-5), 6.30 (s, H-4'), 2.31 (s, 5'- CH_3).

^{13}C NMR (DMSO, ppm): 165.3 (C-5'), 165.7 (CH=N), 166.3 (C-1), 171.0 (C-3'), 168.2 (C-5), 133.7 (C-3), 109.8 (C-4), 114.8 (C-2), 109.3 (C-6), 96.2 (C-4') 12.4 (C-5'-CH_3).

5-Chloro-2-{[(5'-methyl-3'-isoxazolyl) imino] methyl} phenol (3e)

IR (KBr, cm^{-1}): 3443 (OH); 1633 (C=N); 1257 (C-O).

^{1}H NMR ($CDCl_3$, ppm): δ 12.21 (s, -OH); 8.72 (s, CH=N); 7.21-9.16 (m, H-3,4,6), 2.73 (s, 5'-CH_3).

5-Methoxy-2-{[(5'-methyl-3'-isoxazolyl) imino] methyl} phenol (3f)

IR (KBr, cm^{-1}): 3430 (OH); 1601 (C=N); 1224 (C-O).

^{1}H NMR ($CDCl_3$, ppm): δ 12.90 (s, -OH); 8.79 (s, CH=N); 7.27 (d, H-3); 6.52 (m, H-4,6); 3.37 (s, 5-OCH_3); 6.07 (s, H-4'); 2.73 (s,5'-CH_3).

^{13}C NMR ($CDCl_3$, ppm): 166.2 (CH=N); 165.0 (C-1); 167.4 (C-3'); 164.1 (C-5'); 107.3 (C-4); 170.8 (C-5); 134.5 (C-3); 112.4 (C-2); 101.0 (C-6); 96.4 (C-4'); 12.7 (C-5'-CH_3) 55.50 (C-5- OCH_3).

4-Allyl-2-{[(5'-methyl-3'-isoxazolyl) imino] methyl} phenol (3g)

IR (KBr, cm^{-1}): 3410 (OH); 1637 (C=N); 1277 (C-O).

^{1}H NMR ($CDCl_3$, ppm): δ 12.89 (s, -OH); δ 9.2 (s, CH=N); 6.10-7.43, (m, H-3,4,6), 2.43 (s, 5'-CH_3), allyl=CH, 5.4 δ; $=CH_2$ 4.6 δ.

4-Chloro-2-{[(5'-methyl-3'-isoxazolyl)imino]methyl}phenol (3h)

IR (KBr, cm^{-1}): 3331 (OH); 1628 (C=N); 1248 (C-O).

^{1}H NMR (DMSO, ppm): δ 12.52 (s, -OH); 8.75 (CH=N); 7.51 (s, H-3); 7.35 (d, H-5); 6.68 (d, H-6); 6.05 (s, H-4'); 2.40 (s, 5'- CH_3).

^{13}C NMR (DMSO, ppm): 169.6 (C-5'); 163.2 (CH=N); 159.5 (C-1); 151.4 (C-3'); 133.8 (C-5); 131.3 (C-3); 128.9 (C-4); 120.5 (C-2); 118.1 (C-6); 96.5 (C-4') 12.6 (C-5'-CH_3).

4-Bromo-2-{[(5'-methyl-3'-isoxazolyl)imino]methyl}phenol (3i)

IR (KBr, cm^{-1}): 3446 (OH); 1616 (C=N); 1187 (C-O).

^{1}H NMR (DMSO, ppm): δ 12.11 (s, -OH); 8.93 (s, CH=N); 7.25 (m, H-3,5); 6.93 (d, H-6); 6.12 (s, H-4'); 2.50 (s, 5'-CH_3); 2.35 (s, 4-CH_3) .

^{13}C NMR (DMSO, ppm): 163.2 (C-5'); 159.1 (C-1); 165.2 (CH=N); 171.2 (C-3'); 136.7 (C-5); 132.7 (C-3); 110.4 (C-4); 119.2 (C-2); 119.2 (C-6); 95.1 (C-4'); 12.3 (C-5'-CH_3).

4-Methyl-2-{[(5'-methyl-3'-isoxazolyl)imino]methyl}phenol (3j)

IR (KBr, cm^{-1}): 3421 (OH); 1615 (C=N); 1254 (C-O).

^{1}H NMR ($CDCl_3$, ppm): δ 12.11 (s, -OH); 8.93 (s, CH=N); 7.25 (m, H-3,5); 6.93 (d, H-6); 6.12 (s, H-4'); 2.50 (s, 5'-CH_3); 2.35 (s, 4-CH_3) .

^{13}C NMR ($CDCl_3$, ppm): 171.1 (C-3'); 167.8 (CH=N); 159.7 (C-5'); 118.1 (C-2); 133.3 (C-3); 136.2 (C-5); 117.5 (C-6); 128.7 (C-4); 96.4 (C-4'); 21 (C-4-CH_3); 12.6 (C-5'-CH_3).

2-{[(5'-Methyl-3'-isoxazolyl)imino]methyl}-4-nitrophenol (3k)

IR (KBr, cm^{-1}): 3440 (OH); 1636 (C=N). 1247 (C-O);

^{1}H NMR (DMSO, ppm): δ 13.20 (s, -OH); 9.01 (s, CH=N); 7.11- 8.42 (m, H-3,5,6); 6.12 (s, H-4'); 2.52 (s, 5'-CH_3).

^{13}C NMR (DMSO, ppm): 165.5 (CH=N); 163.0 (C-1); 159.8 (C-3'); 157.5 (C-5'); 141.0 (C-4); 128.4 (C-5); 123.5 (C-3); 119.6 (C-2); 117.8 (C-6); 94.6 (C-4'); 12.0 (C-5'-CH_3).

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