Asian Journal of Chemistry; Vol. 36, No. 4 (2024), 859-864

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2024.31196

Magnesium Powder-Catalyzed, Highly Efficient, Solvent-Free Synthesis of Amides through *N*-Acetylation of Amines and their Antibacterial Activity

NAJMA BAJRACHARYA[1], SUNITA SHRESTHA[1,2] and GAN B. BAJRACHARYA[1,*]

[1]Laboratory of Catalysis and Frontier Molecules, Faculty of Science, Nepal Academy of Science and Technology (NAST), Khumaltar, Lalitpur, Nepal
[2]Department of Chemistry, Tri-Chandra Multiple Campus, Tribhuvan University, Ghantaghar, Kathmandu, Nepal

*Corresponding author: E-mail: ganbajracharya@yahoo.com; gan.bajracharya@nast.gov.np

Received: 10 January 2024; *Accepted*: 23 February 2024; *Published online*: 30 March 2024; AJC-21583

Magnesium powder was found to be an efficient catalyst for the acetylation of amines (**1**) with Ac_2O affording corresponding amides (**2**) in excellent yields (> 99%). This green synthetic protocol has utilized 2.5 mol% of magnesium powder and a stoichiometric amount of Ac_2O (1.2 equiv.). Amides **2a-k** were synthesized within a short reaction time (2-3 min) at an ambient temperature under solvent free condition. The products were screened against *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Staphylococcus epidermidis* bacterial strains. *N*-(2-Hydroxyphenyl)acetamide (**2f**) was found most active against Gram-positive *S. aureus* and *S. epidermidis* indicating its efficacy in treating skin diseases.

Keywords: Acylation, Antibacterial assay, Green chemistry, Skin disease, Solvent-free, Organic synthesis.

INTRODUCTION

Acetamide derivatives are reported to possess several bioactivities such as antimicrobial [1-5], antitubercular [6,7], antimalarial [8], antiparasitic [9], antidiabetic [10,11], antipsychotic [12], antioxidant activities [13], *etc.* Acetamides are used also as chemotherapeutic agents for inflammation and inflammation-associated cancers [14,15]. More than 25% of the worldwide used pharmaceutical drugs possess an amidal motif [16,17]. Because of the presence of amide linkage in the chemical structures, the compounds may display specific enhanced bioactivity [18,19]. Some examples include paracetamol (antipyretic), penicillin (antibacterial), pyrazinamide (antitubercular), *etc*.

Acylation is one of the most fundamental reactions in the organic synthesis. This reaction is extensively used to protect various functional groups such as phenols, alcohols, amines, thiols and others in order to achieve synthesis of target molecules [20]. Besides using of classical acids and bases, several Lewis acid catalysts, solid acid and heteropolyacid catalysts, organocatalysts, ionic liquids and others have been used for the acylation reactions [21]. Amides are commonly produced by *N*-acylation of amines [22-24].

Recently, we reported magnesium powder as an efficient catalyst for the acetylation of phenols with acetic anhydride under neat condition and a free radical mechanism was proposed for the transformation [21]. More recently, Anbu *et al.* [25] also reported that the acetylation of alcohols, amines, phenols and thiols is achievable under catalyst- and solvent-free conditions involving an ionic mechanism. Significantly, amine acetylation was acheived at 60 ºC in 30 min using 1.5 equiv. of acetic anhydride. Herein, the acetylation of amines (**1**) was accomplished at room temperature by using a stoichiometric amount of acetic anhydride, in the presence of a trace amount of magnesium powder, under air atmosphere. The reactions were completed within 2-3 min affording the corresponding amides (**2**) in excellent to quantitative yields just after simple work up. Moreover, obtained amides **2a-k** were further evaluated for the antibacterial activity.

EXPERIMENTAL

Chemicals and reagents were purchased from different reputed commercial supplers like Fischer, Qualigens, Aldrich, Burgoyne Burbidges and Merck. Magnesium powder and media were purchased from Himedia. Thin layer chromatography

(TLC) was performed using pre-coated Kieselgel 60 F_{254} plates of 0.2 mm thickness (E. Merck). For product identification, GC-MS spectra were recorded using Agilent 7890A GC system coupled with an Agilent 5975 C mass selective detector and IR spectra were recorded in KBr disc using an IR Tracer-100 (Shimadzu). The measured melting points are uncorrected.

General procedure for *N*-acetylation of amines: Amine (**1**, 5 mmol), powder Mg (2.5 mol%, 3 mg, 0.125 mmol) and acetic anhydride (0.57 mL, 6 mmol) were charged in a reaction tube equipped with a stirring bar. The content was stirred at 25 ºC and the reaction was monitored by TLC. After completion, the reaction mixture was diluted with EtOAc (40 mL), washed with brine, dried over Na_2SO_4, filtered, concentrated and finally vacuum dried. Corresponding amide **2** was obtained in chromatographically pure form. No further purification was required, except in the synthesis of compound **2i**.

***N*-Phenylacetamide (2a):** The general procedure was followed by using aniline (**1a**, 466 mg, 5 mmol) to obtain **2a** as a colourless solid. Yield: 628 mg, 93%. m.p.: 114 ºC (reported 112-114 ºC) [26,27]. R_f = 0.43 (silica gel, hexane:EtOAc, 1:1). GC-MS: calcd. for C_8H_9NO (M^+) 135.0684, found 135.1. IR (KBr, cm^{-1}): 3294 (νNH); 3194, 3138, 3064 (νCH arom.), 1666 (νCO), 1494 (δHNC), 1438 (δHCH), 1321 (δHCC + νCC) [28].

***N*-(4-Methoxyphenyl)acetamide (2b):** The general procedure was followed by using 4-methoxyaniline (**1b**, 616 mg, 5 mmol) to obtain **2b** as a purple solid. Yield: 719 mg, 87%. m.p.: 127-129 ºC (reported 126-129 ºC) [26,29]. R_f = 0.23 (silica gel, hexane:EtOAc, 1:1). GC-MS: calcd. for $C_9H_{11}NO_2$ (M^+) 165.0790, found: 165.1. IR (KBr, cm^{-1}): 3244 (νNH), 3190, 3130, 3070 (νCH arom.), 1654 (νCO),1512 (δHNC), 1409 (δHCH), 1321 (δHCC + νCC).

***N*-(*m*-Tolyl)acetamide (2c):** The general procedure was followed by using *m*-toluidine (**1c**, 536 mg, 5 mmol) to obtain **2c** as a colourless solid. Yield: 710 mg, 95%. m.p.: 65-66 ºC (reported 65–69 ºC) [26,27]. R_f = 0.43 (silica gel, hexane: EtOAc, 1:1). GC-MS: calcd. for $C_9H_{11}NO$ (M^+) 149.0841, found: 149.1. IR (KBr, cm^{-1}): 3300 (νNH); 3145, 3049 (νCH arom.); 1674 (νCO); 1404 (δHCH); 1317 (δHCC + νCC).

***N*-(*o*-Tolyl)acetamide (2d):** The general procedure was followed by using *o*-toluidine (**1d**, 536 mg, 5 mmol) to obtain **2d** as a colourless solid. Yield: 706 mg, 95%. m.p.: 108-111 ºC (reported 108-110 ºC) [26,27]. R_f = 0.35 (silica gel, hexane: EtOAc, 1:1). GC-MS: calcd. for $C_9H_{11}NO$ (M^+) 149.0841, found: 149.1. IR (KBr, cm^{-1}): 3292 (νNH); 3194, 3034, 2980 (νCH arom.); 1651 (νCO); 1529 (δHNC); 1456 (δHCH); 1371 (δHCC + νCC).

***N*-(4-Hydroxyphenyl)acetamide (2e):** The general procedure was followed by using 4-aminophenol (**1e**, 545 mg, 5 mmol) to obtain **2e** as a cream white solid. Yield: 700 mg, 93%. m.p.: 170 ºC (reported 168-169 °C) [26,30]. R_f = 0.80 (silica gel, CH_3OH). GC-MS: calcd. for $C_8H_9NO_2$ (M^+) 151.0633, found: 151.1. IR (KBr, cm^{-1}): 3327 (νOH); 3165 (νNH); 2929, 2881 (νCH arom.); 1656 (νCO); 1510 (δHNC); 1440 (δHCH); 1325 (δHCC + νCC).

***N*-(2-Hydroxyphenyl)acetamide (2f):** The general procedure was followed by using 2-aminophenol (**1f**, 545 mg, 5 mmol) to obtain **2f** as a colourless solid. Yield: 666 mg, 88%. m.p.: 206 ºC (reported 207-209 ºC) [26]. R_f = 0.52 (silica gel, hexane:EtOAc, 1:1). GC-MS: calcd. for $C_8H_9NO_2$ (M^+) 151.0633, found: 151.1. IR (KBr, cm^{-1}): 3404 (νOH); 3080 (νNH); 2976, 2881 (νCH arom.); 1660 (νCO); 1456 (δHNC); 1382 (δHCH); 1330 (δHCC + νCC).

***N*-(4-Bromophenyl)acetamide (2g):** The general procedure was followed by using 4-bromoaniline (**1g**, 860 mg, 5 mmol) to obtain **2g** as a colourless solid. Yield: 999 mg, 94%. m.p.: 164-166 ºC (reported 166-170 ºC) [26,27,31,32]. R_f = 0.40 (silica gel, hexane:EtOAc, 1:1). GC-MS: calcd. for C_8H_8BrNO (M^+) 212.9789, found: 213.0. IR (KBr, cm^{-1}): 3294 (νNH); 3186, 3115, 3053 (νCH arom.); 1672 (νCO); 1485 (δHNC); 1388 (δHCH); 1305 (δHCC + νCC).

***N*-(4-Nitrophenyl)acetamide (2h):** The general procedure was followed by using 4-nitroaniline (**1h**, 690 mg, 5 mmol) to obtain **2h** as a pale yellow solid. Due to poor solubility of the product, an excess of EtOAc was needed to use for its extraction during work up process. Yield: 893 mg, 99%. m.p.: 214 ºC (reported 210-214 ºC) [26,31]. R_f = 0.25 (silica gel, hexane: EtOAc, 1:1). GC-MS: calcd. for $C_8H_8N_2O_3$ (M^+) 180.0535, found: 180.1. IR (KBr, cm^{-1}): 3275 (νNH); 3217, 3157, 3091 (νCH arom.); 1679 (νCO); 1564 (νNO); 1498 (δHNC); 1404 (δHCH); 1348 (δHCC + νCC).

***N*-(2-Nitrophenyl)acetamide (2i):** Following the general procedure, the reactions of 2-nitroaniline (**1i**, 691 mg, 5 mmol) were performed at two different temperatures (25 and 100 ºC) to obtain compound **2i**. The product was purified by recrystallization with 75% EtOH producing yellow crystals. Yield: 827 mg, 92% (at 25 ºC, reaction time 16 h). Yield: 890 mg, 99% (at 100 ºC, reaction time 2 h). m.p.: 91 ºC (reported 90-91 ºC) [33]. R_f = 0.64 (silica gel, hexane:EtOAc, 1:1). GC-MS: calcd. for $C_8H_8N_2O_3$ (M^+) 180.0535, found: 180.1. IR (KBr, cm^{-1}): 3373 (νNH); 3165, 3089 (νCH arom.); 1712 (νCO); 1585(νNO); 1496 (δHNC); 1431 (δHCH); 1346 (δHCC + νCC).

***N*-(Naphthalen-1-yl)acetamide (2j)**: The general procedure was followed by using 1-naphthylamine (**1j**, 716 mg, 5 mmol) to obtain **2j** (886 mg, 96%) as a colourless solid. Yield: 886 mg, 96%. m.p.: 160 ºC (reported 159-160 ºC) [26]. R_f = 0.36 (silica gel, hexane:EtOAc, 1:1). GC-MS: calcd. for $C_{12}H_{11}NO$ (M^+) 185.0841, found: 185.1. IR (KBr, cm^{-1}): 3271 (νNH); 3049 (νCH arom.); 1654 (νCO); 1500 (δHNC); 1456 (δHCH); 1342 (δHCC + νCC).

***N*-Benzylacetamide (2k):** The general procedure was followed by using benzylamine (**1k**, 536 mg, 5 mmol) to obtain **2k** as a colourless solid. Yield: 714 mg, 96%. m.p.: 60 ºC (reported 58-60 ºC) [26,34]. R_f = 0.71 (silica gel, CH_3OH). GC-MS: calcd. for $C_9H_{11}NO$ (M^+) 149.0841, found: 149.1. IR (KBr, cm^{-1}): 3292 (νNH); 3088, 3032 (νCH arom.); 1643 (νCO); 1552 (δHNC); 1446 (δHCH); 1328 (δHCC + νCC).

Antibacterial assay: The agar well diffusion method was employed to evaluate the antimicrobial activity of the synthesized amides **2a**-**k** against four bacterial strains *viz. E. coli* (ATCC 8739), *P. aeruginosa* (ATCC 9027), *S. aureus* (ATCC 6538P) and *S. epidermidis* (ATCC 12228) [35-37]. Mueller-Hinton agar (MHA) plates were uniformly swabbed with standardized bacterial suspension (equivalent to McFarland 0.5)

prepared in Mueller-Hinton broth (MHB). Sample solutions of the amides **2a**-**k** were prepared in DMSO with 50 mg/mL concentration each. Wells (6 mm in diameter) were bored on the media plates and then loaded 50 µL of each sample solution in triplicates. Antibiotic gentamycin (10 µg/disc) was used as a positive control, while DMSO was served as a negative control. After 24 h of incubation at 37 ºC, the antibacterial effect was evaluated by measuring the ZOI appeared.

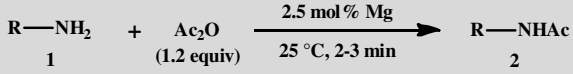
Next, the samples displaying antibacterial activity against the specific bacteria were further considered for the determination of minimum inhibition concentration (MIC) values by two-fold serial dilution technique, the Broth macrodilution method [38]. Briefly, the standardized bacterial suspension was diluted to 1:10 using normal saline (1.5×10^7 CFU/mL). A mixture of equal volumes of MHB (1 mL) and each sample solution (1 mL) was then serially diluted in another 14 sterile test tubes that contained 1 mL of MHB (total volume in each tube = 1 mL). The above bacterial suspension (50 µL) was then inoculated (5×10^5 CFU/mL). Thereafter, the tubes were incubated at 37 ºC for 24 h. The lowest concentration, at which no bacterial growth observed visually, was taken as the MIC. minimum bactericidal concentration (MBC) values were subsequently determined through sub-culture of the content from the tubes showing no bacterial growth by direct streaking on sterile MHA plates. After incubation at 37 ºC for 24 h, the plates were examined for the growth of bacteria and thus MBC values were determined.

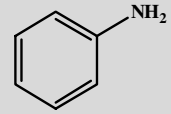
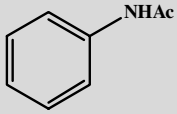
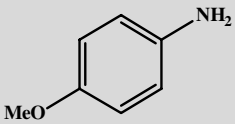
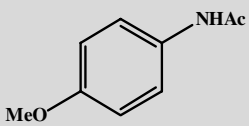
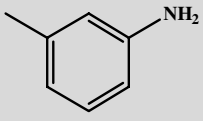
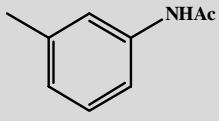
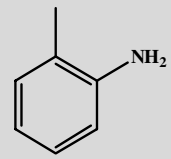
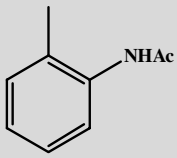
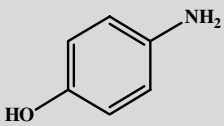
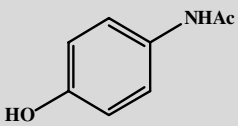
RESULTS AND DISCUSSION

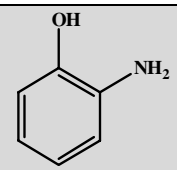
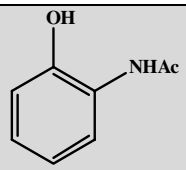
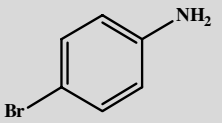
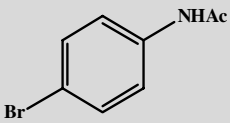
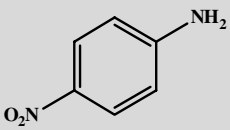
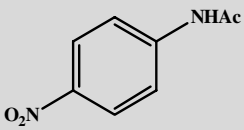
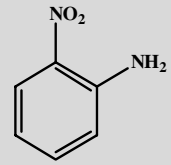
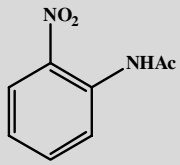
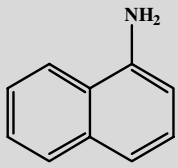
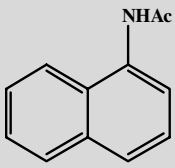
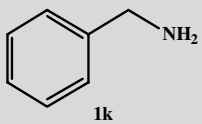
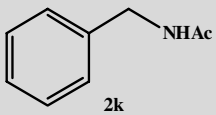
Based on the reported work [21], we developed to explore magnesium powder for the catalytic organic transformations. Now, we have investigated the *N*-acetylation of amines. At first, aniline (**1a**) was chosen as a model substrate. After a few trials, it was found that the reaction of **1a** with 1.2 equiv. of Ac_2O, in the presence 2.5 mol% Mg, at 25 ºC, was achieved to be completed within 2 min affording *N*-phenylacetamide (**2a**) in 93% yield (Table-1, entry 1). When the catalyst loading was reduced to 1 mol%, **2a** was produced with the same yield but required a prolonged reaction time (*i.e.* 14 min). The acetylation of **1a** can be achieved without expending catalyst producing **2a** in 92% yield, after 14 min [25].

After obtaining an optimized reaction condition in hand, the scope of the reaction was studied. Amines bearing an electron donating group (OMe, Me or OH) either at *ortho*-, *meta*- or *para*-position were tolerated affording corresponding amides (**2b**-**f**) within 2-3 min, with excellent yields (Table-1, entries 2-6). In case of substrates **1e** and **1f** containing both the amino and hydroxyl groups, corresponding *N*-acetylation products

TABLE-1
Mg POWDER-CATALYZED *N*-ACETYLATION OF AMINES (**1**) TO AMIDES (**2**)



Entry	Substrate used	Product	Reaction time	Isolated yield (%)	Molecular ion peak (M^+)	C=O stretching (cm^{-1})	m.p. (°C)	
							Found	Reported
1	 **1a**	 **2a**	2 min	93	135.1	1666	114	112-114 [26,27]
2	 **1b**	 **2b**	2 min	87	165.1	1654	127-129	126-129 [26,29]
3	 **1c**	 **2c**	2 min	95	149.1	1674	65-66	65-69 [26,27]
4	 **1d**	 **2d**	2 min	95	149.1	1651	108-111	108-110 [26,27]
5	 **1e**	 **2e**	3 min	93	151.1	1656	170	168-169 [26,30]

6	 1f	 2f	3 min	88	151.1	1660	206	207-209 [26]
7	 1g	 2g	3 min	94	213.0	1672	164-166	166-170 [27,31,32]
8	 1h	 2h	3 min	99	180.1	1679	214	210-214 [26,31]
9	 1i	 2i	16 h	92	180.1	1697	91	90-91 [33]
10*			2 h	99				
11	 1j	 2j	3 min	96	185.1	1654	160	159-160 [26]
12	 1k	 2k	3 min	96	149.1	1643	60	58-60 [26,34]

*Reaction temperature was 100 °C.

2e and **2f** were selectively formed over the *O*-acetylation products. *N*-Acetylation of the substrates with an electron withdrawing group (Br or NO_2) at *para*-position was also proceeded smoothly (entries 7-8). However, because of intervention of hydrogen bonding, the *N*-acetylation of 2-nitroaniline (**1i**), containing a nitro group at *ortho*-position, was found to be sluggish. The reaction required 16 and 2 h for the completion to afford *N*-(2-nitrophenyl)acetamide (**2i**) at 25 and 100 ºC reaction temperature, respectively (entries 9 and 10). In optimized reaction conditions, *N*-(naphthalen-1-yl)acetamide (**2j**) was isolated in 96% yield by using 1-naphthylamine (**1j**) as substrate (entry 11). Similarly, an aliphatic amine, such as benzylamine (**1k**), was found equally facile producing **2k** in 96% isolated yield (entry 12). All the products were confirmed by recording of GC-MS spectrum, IR spectrum and melting point.

Biological activity: To determine the antibacterial activity of the synthesized amides (**2a**-**k**), wells on the bacteria inoculated MHA plates were loaded with the amide solution prepared in DMSO at 2.5 mg/well dose level. The zone of inhibition (ZOI) produced in the antibacterial assay was measured and the results are tabulated in Table-2. The growth of Gram-negative bacteria *E. coli* was inhibited by amides **2a**-**c**, **2e**, **2g** and **2i** with the ZOI ranging from 10 to 16 mm (entries 1-3, 5, 7 and 9). Among the amides used, *N*-(*m*-tolyl)acetamide (**2c**) has produced the highest ZOI (16.0 ± 0.58 mm) against *E. coli* (entry 3). *N*-(4-Methoxyphenyl)acetamide (**2b**) has substantial antibacterial activity against all the four bacteria tested (entry 2). *N*-(2-Hydroxyphenyl)acetamide (**2f**) was found effective against *P. aeruginosa*, *S. aureus* and *S. epidermidis* (entry 6). Among 11 amides tested, only compounds **2b** and **2f** were found effective against both the Gram-positive *S. aureus* and *S. epidermidis* (entries 2 and 6). A high ZOI (20.33 ± 0.33 mm) was exhibited by *N*-(2-nitrophenyl)acetamide (**2i**) against *S. aureus* (entry 9). *N*-(*o*-Tolyl)acetamide (**2d**) (entry 4), *N*-(4-nitrophenyl)acetamide (**2h**) (entry 8), *N*-(naphthalen-1-yl)acetamide (**2j**) (entry 10) and *N*-benzylacetamide (**2k**) (entry 11) were found completely ineffective against the four bacterial strains tested.

The results of MIC and MBC values are given in Table-3. *N*-(2-Hydroxyphenyl)acetamide (**2f**) was found highly antibacterial against Gram-positive *S. aureus* and *S. epidermidis* with MIC values of 1.56 and 0.78 µg/mL, respectively (entry 6). It also displayed antibacterial effect against Gram-negative *P. aeruginosa*. Amides **2b** and **2e** have displayed bactericidal effect against *E. coli* (entries 2 and 5), while amides **2a**, **2c**, **2g**

TABLE-2
ANTIBACTERIAL ACTIVITY OF THE AMIDES (**2a-k**)

Amides used	ZOI against the bacterial strains ± standard error mean (mm)			
	Gram-negative bacteria		Gram-positive bacteria	
	E. coli	*P. aeruginosa*	*S. aureus*	*S. epidermidis*
N-Phenylacetamide (**2a**)	13.33 ± 0.88	12.0 ± 1.0	–	–
N-(4-Methoxyphenyl)acetamide (**2b**)	12.67 ± 0.88	8.67 ± 0.33	16.33 ± 1.20	8.67 ± 0.33
N-(*m*-Tolyl)acetamide (**2c**)	16.00 ± 0.58	–	–	–
N-(*o*-Tolyl)acetamide (**2d**)	–	–	–	–
N-(4-Hydroxyphenyl)acetamide (**2e**)	11.67 ± 0.33	9.33 ± 0.33	–	–
N-(2-Hydroxyphenyl)acetamide (**2f**)	–	12.66 ± 0.67	12.67 ± 0.33	11.00 ± 0.58
N-(4-Bromophenyl)acetamide (**2g**)	10.00 ± 0	–	–	–
N-(4-Nitrophenyl)acetamide (**2h**)	–	–	–	–
N-(2-Nitrophenyl)acetamide (**2i**)	14.66 ± 0.33	–	20.33 ± 0.33	–
N-(Naphthalen-1-yl)acetamide (**2j**)	–	–	–	–
N-Benzylacetamide (**2k**)	–	–	–	–
Gentamycin	20	24	23	26

(–)-Sign indicates no significant ZOI was observed.

TABLE-3
MIC AND MBC VALUES OF THE AMIDES (**2a-k**)

Amides used	MIC (MBC) values (µg/mL)			
	Gram-negative bacteria		Gram-positive bacteria	
	E. coli	*P. aeruginosa*	*S. aureus*	*S. epidermidis*
N-Phenylacetamide (**2a**)	6.25 (12.50)	12.50 (12.50)	–	–
N-(4-Methoxyphenyl)acetamide (**2b**)	12.50 (12.50)	12.50 (12.50)	25.00 (25.00)	25.00 (25.00)
N-(*m*-Tolyl)acetamide (**2c**)	3.12 (6.25)	–	–	–
N-(*o*-Tolyl)acetamide (**2d**)	–	–	–	–
N-(4-Hydroxyphenyl)acetamide (**2e**)	6.25 (6.25)	25.00 (25.00)	–	–
N-(2-Hydroxyphenyl)acetamide (**2f**)	–	12.50 (25.00)	1.56 (1.56)	0.78 (6.25)
N-(4-Bromophenyl)acetamide (**2g**)	3.12 (6.25)	–	–	–
N-(4-Nitrophenyl)acetamide (**2h**)	–	–	–	–
N-(2-Nitrophenyl)acetamide (**2i**)	1.56 (12.50)	–	6.25 (25.00)	–
N-(Naphthalen-1-yl)acetamide (**2j**)	–	–	–	–
N-Benzylacetamide (**2k**)	–	–	–	–

(–)-Sign = Value not determined as no significant ZOI was observed in the Agar well diffusion assay.

and **2i** were bacteriostatic (entries 1, 3, 7 and 9). Among these amides, *N*-(2-nitrophenyl)acetamide (**2i**) was found more efficient exhibiting MIC value of 1.56 µg/mL against *E. coli* (entry 9). Amide **2i** has also displayed effective antibacterial activity by inhibiting *S. aureus* with the MIC value of 6.25 µg/mL.

Antibacterial activity of compounds **2a** and **2g** against *E. coli* and *S. aureus* is reported by Jagessar & Rampersaud [39]. In contrast, this work showed that the amides **2a** and **2g** were effective against *E. coli* but ineffective against *S. aureus*. Antibacterial activity of *N*-(2-hydroxyphenyl)acetamide (**2f**) against *P. aeruginosa* and *S. aureus* is recently reported by Hifnawy *et al.* [40]. In some other reports, compound **2f** is reported to be ineffective against *E. coli*, *S. aureus*, methicillin-resistant *S. aureus*, methicillin-resistant *S. epidermidis*, *B. subtilis*, *Klebsiella pneumoniae* and *Enterococcus faecalis* [40-44]. Compound **2f** has also displayed anti-inflammatory [14,45-47] and antitumor [48] activities. It also possesses strong apoptotic activity and inhibits the growth of U87 in a dose dependent manner [49]. The antibacterial activity of *N*-(4-hydroxyphenyl)-acetamide (**2e**) against *E. coli* has been reported by Jayadevappa *et al.* as well [2].

Conclusion

In conclusion, a convenient and green approach for the *N*-acetylation of amines with acetic anhydride in the presence of magnesium powder is presented . This reaction was promoted rapidly with an excellent yield at ambient temperature. Simple work up procedure could provide pure amide products and no column chromatography was needed. Nowadays, identification of new potent antibacterial agents is an immense importance task in order to combat antibacterial resistance. This study reveals that simple and readily available *N*-(2-hydroxyphenyl)acetamide (**2f**) could be an effective antibacterial agent which appeals for further investigations.

ACKNOWLEDGEMENTS

One of the authors, N.B. thanks Nepal Academy of Science and Technology (NAST) for providing the research assistantship. The authors thanks Mr. Mohan Paudel for accessing Scifinder database and Analytical Service Centre, NAST for recording of the spectra.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. T. Nomura, T. Iwaki, Y. Narukawa, K. Uotani, T. Hori and H. Miwa, *Bioorg. Med. Chem.*, **14**, 3697 (2017); https://doi.org/10.1016/j.bmc.2006.01.036
2. A.S. Sheikh, H. Nadeem, M.T. Khan, A. Saeed and B. Murtaza, *ACS Omega*, **8**, 9785 (2023); https://doi.org/10.1021/acsomega.2c05782
3. M.D. Altintop, U. Abu-Mohsen, Y. Okay, R. Demirel and Z.A. Kaplancikli, *Turk. J. Pharm. Sci.*, **12**, 29 (2015).
4. H. Lu, X. Zhou, L. Wang and L. Jin, *Molecules*, **25**, 1772 (2020); https://doi.org/10.3390/molecules25081772
5. M.M. Ghorab, A.S. Alqahtani, A.M. Soliman and A.A. Askar, *Int. J. Nanomed.*, **15**, 3161 (2020); https://doi.org/10.2147/IJN.S241433
6. W. Ang, Y.N. Lin, T. Yang, J.Z. Yang, W.Y. Pi, Y.H. Yang, Y.F. Luo, Y. Deng and Y.Q. Wei, *Molecules*, **17**, 2248 (2012); https://doi.org/10.3390/molecules17022248
7. B. Tanwar, A. Kumar, P. Yogeeswari, D. Sriram and A.K. Chakraborti, *Bioorg. Med. Chem. Lett.*, **26**, 5960 (2016); https://doi.org/10.1016/j.bmcl.2016.10.082
8. R. Zogota, L. Kinena, C. Withers-Martinez, M.J. Blackman, R. Bobrovs, T. Pantelejevs, I. Kanepe-Lapsa, V. Ozola, K. Jaudzems, E. Suna and A. Jirgensons, *Eur. J. Med. Chem.*, **163**, 344 (2019); https://doi.org/10.1016/j.ejmech.2018.11.068
9. S.K. Tipparaju, S.P. Muench, E.J. Mui, S.N. Ruzheinikov, J.Z. Lu, S.L. Hutson, M.J. Kirisits, S.T. Prigge, C.W. Roberts, F.L. Henriquez, A.P. Kozikowski, D.W. Rice and R.L. McLeod, *J. Med. Chem.*, **53**, 6287 (2010); https://doi.org/10.1021/jm9017724
10. A.P.G. Nikalje, S. Choudhari and H. Une, *Eur. J. Exp. Biol.*, **2**, 1302 (2012).
11. Md..J Naim, Md.J. Alam, F. Nawaz, V.G.M. Naidu, S. Aaghaz, M. Sahu, N. Siddiqui and O. Alam, *Bioorg. Chem.*, **73**, 24 (2017); https://doi.org/10.1016/j.bioorg.2017.05.007
12. S. Kumar, A.K. Wahi and R. Singh, *Trop. J. Pharm. Res.*, **10**, 265 (2011); http://dx.doi.org/10.4314/tjpr.v10i3.6
13. S. Ölgen, F. Bakar, S. Aydin, D. Nebioglu and S. Nebioglu, *J. Enzyme Inhib. Med. Chem.*, **28**, 58 (2013); https://doi.org/10.3109/14756366.2011.631183
14. H. Jawed, S.U.A. Shah, S. Jamall and S.U. Simjee, *Int. Immunopharmacol.*, **10**, 900 (2010); https://doi.org/10.1016/j.intimp.2010.04.028
15. P. Rani, D. Pal, R.R. Hegde and S.R. Hashim, *J. Chemother.*, **28**, 255 (2016); https://doi.org/10.1179/1973947815Y.0000000060
16. A.K. Ghose, V.N. Viswanadhan and J.J. Wendoloski, *J. Comb. Chem.*, **1**, 55 (1999); https://doi.org/10.1021/cc9800071
17. J.S. Carey, D. Laffan, C. Thomson and M.T. Williams, *Org. Biomol. Chem.*, **4**, 2337 (2006); https://doi.org/10.1039/B602413K
18. R. Wolf and S. Brenner, *Dermatology*, **189**, 1 (1994); https://doi.org/10.1159/000246749
19. P. Rajput and A. Sharma, *J. Pharmacol. Med. Chem.*, **2**, 22 (2018).
20. A. Kokel, C. Schäfer and B. Török, *Curr. Org. Synth.*, **16**, 615 (2019); https://doi.org/10.2174/1570179416666190206141028
21. G.B. Bajracharya and S.S. Shrestha, *Synth. Commun.*, **48**, 1688 (2018); https://doi.org/10.1080/00397911.2018.1459721
22. D.H. Kim, *J. Heterocycl. Chem.*, **13**, 179 (1976); https://doi.org/10.1002/jhet.5570130201
23. T.S. Ibrahim, I.A. Seliem, S.S. Panda, A.M.M. Al-Mahmoudy, Z.K.M. Abdel-Samii, N.A. Alhakamy, H.Z. Asfour and M. Elagawany, *Molecules*, **25**, 2501 (2020); https://doi.org/10.3390/molecules25112501
24. A. Ami´c and M. Molnar, *Org. Prep. Proc. Int.*, **49**, 249 (2017); https://doi.org/10.1080/00304948.2017.1320914
25. N. Anbu, N. Nagarjun, M. Jacob, J.M.V.K. Kalaiarasi and A. Dhakshinamoorthy, *Chemistry*, **1**, 69 (2019); https://doi.org/10.3390/chemistry1010006
26. M.T. Sangole, S.M. Thorat, S.P. Deshmukh, M. Muthukrishnan, S. Shirsath and M. Mujahid, *Indian J. Chem.*, **58B**, 1125 (2019).
27. S.A. Trujillo, D. Peña-Solórzano, O.R. Bejarano and C. Ochoa-Puentes, *RSC Adv.*, **10**, 40552 (2020); https://doi.org/10.1039/D0RA06871C
28. Y. Umar, A. Abu-Thabit, P. Jerabek and P. Ramasami, *J. Theor. Comput. Chem.*, **18**, 1950009 (2019); https://doi.org/10.1142/S0219633619500093
29. J. Yin, J. Zhang, C. Cai, G.J. Deng and H. Gong, *Org. Lett.*, **21**, 387 (2019); https://doi.org/10.1021/acs.orglett.8b03542
30. G.R. Lloyd, D.Q.M. Craig and A. Smith, *J. Pharm. Sci.*, **86**, 991 (1997); https://doi.org/10.1021/js970137w
31. J.L. Jat, P. Kumar, S. Verma, D. Chandra, V. Singh and B. Tiwari, *New J. Chem.*, **46**, 14782 (2022); https://doi.org/10.1039/D2NJ02755K
32. P. Lian, R. Li, X. Wan, Z. Xiang, H. Liu, Z. Cao and X. Wan, *Org. Chem. Front.*, **9**, 311 (2022); https://doi.org/10.1039/D1QO01613J
33. E. Kianmehr and S.B. Nasab, *Eur. J. Org. Chem.*, 6447 (2018); https://doi.org/10.1002/ejoc.201800779
34. A.K. Chakraborti and R. Gulhane, *Chem. Commun.*, 1896 (2003); https://doi.org/10.1039/B304178F
35. C. Perez, M. Pauli and P. Bazerque, *Acta Biol. Med. Exp.*, **15**, 113 (1990).
36. R.K. Gupta, G.M.S. Thakuri, G.B. Bajracharya and R.N. Jha, *Bibechana*, **18**, 143 (2021); https://doi.org/10.3126/bibechana.v18i2.31234
37. C.M. Nemkul, G.B. Bajracharya and I. Shrestha, *J. Plant Resour.*, **19**, 151 (2021).
38. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically, Approved Standard, 9th Edn, CLSI Document M07-A9, vol. 32, No. 2, Clinical and Laboratory Standards Institute, Wayne, PA (2012).
39. R. Jagessar and D. Rampersaud, *New York Sci. J.*, **1**, 22 (2008).
40. M.S. Hifnaway, H.M. Hassan, R. Mohammed, M.M. Fouda, A.M. Sayed, A.A. Hamed, S.F. AbouZid, M.E. Rateb, H.A. Alhadrami and U.R. Abdelmohsen, *Mar. Drugs*, **18**, 243 (2020); https://doi.org/10.3390/md18050243
41. Z. Shang, X. Li, L. Meng, C. Li, S. Gao, C. Huang and B. Wang, *Chin. J. Ocean Limnol.*, **30**, 305 (2012); https://doi.org/10.1007/s00343-012-1075-1
42. Y. Dashti, T. Grkovic, U.R. Abdelmohsen, U. Hentschel and R.J. Quinn, *Mar. Drugs*, **12**, 3046 (2014); https://doi.org/10.3390/md12053046
43. J. Wang, W. He, X. Qin, X. Wei, X. Tian, L. Liao, S. Liao, B. Yang, Z. Tu, B. Chen, F. Wang, X. Zhou and Y. Liu, *RSC Adv.*, **5**, 68736 (2015); https://doi.org/10.1039/C5RA10828D
44. B. Peng, Q. Peng, J. She, B. Yang and X. Zhou, *Rec. Nat. Prod.*, **16**, 639 (2022); http://doi.org/10.25135/rnp.312.22.01.2314
45. K. Perveen, F. Hanif, H. Jawed and S.U. Simjee, *BioMed Res. Int.*, 635143 (2013); https://doi.org/10.1155/2013/635143
46. A. Gul, B. Kunwar, M. Mazhar, K. Perveen, S.U. Simjee, *Inflammation*, **40**, 1177 (2017); https://doi.org/10.1007/s10753-017-0561-1
47. A. Arif, S. Majeed, S.U. Simjee, M. Sarfaraz, S.S. Kashif, M. Lodhi, N. Khatian, A. Aziz and H.K. Majeed, *Pak-Euro J. Med. Life Sci.*, **5**, 309 (2022); https://doi.org/10.31580/pjmLs.v5i2.2528
48. A. Aziz, F. Hanif, S. Majeed, K. Iftikhar and S.U. Simjee, *Toxicol. in Vitro*, **60**, 296 (2019); https://doi.org/10.1016/j.tiv.2019.06.011
49. F. Hanif, K. Perveen, H. Jawed, A. Ahmed, S.M. Malhi, S. Jamall and S.U. Simjee, *Cancer Cell Int.*, **14**, 133 (2014); https://doi.org/10.1186/s12935-014-0133-5