J. Mountain Res. P-ISSN: 0974-3030, E-ISSN: 2582-5011
Vol. 19(2), (2024), 213-219

DOI: https://doi.org/10.51220/jmr.v19-i2.22

Synthesis of *(E)*-3-(substituted phenyl)-N-(pyridin-2-yl) Acrylamide Derivatives and Their Antioxidant Activity

Arun[1*] • Kamal Singh koranga[2] • Moenuddin[2] • Priyanka parmar[1] • Veena joshi[1] • Shishir Tandon[2]

[1]*Department of Chemistry, Hemvati Nandan Bahuguna Garhwal University, SRT Campus, Tehri Garhwal 249199, Uttarakhand, India.*
[2]*Department of Chemistry, GBPUAT, Udham Singh Nagar, Uttarakhand*

*Corresponding author Email id: arunn9133@gmail.com

Received: 14.09.2024 Revised: 30.10.2024 Accepted: 18.11.2024

Abstract: The synthesis of *(E)*-3-(substituted phenyl)-N-(pyridin-2-yl) acrylamides was achieved using green chemistry techniques. This involved the utilization of triethylamine, 2-aminopyridine, and substituted cinnamic acids. The cinnamic acids were produced by mixing powdered malonic acid, a small quantity of piperidine, and pyridine with substituted benzaldehydes in a Doebner reaction. Structures of all the synthesized compounds were validated by Infrared spectroscopy (IR) and nuclear magnetic resonance (NMR) instruments. Antioxidant activity of all synthesized compounds was assessed using DPPH antioxidant activity. The present study indicates that derivatives of *(E)*-3-(substituted phenyl)-N-(pyridin-2-yl) acrylamides have the potential to be employed as herbicides and antioxidants for safeguarding agricultural crops and food products.

Keywords: DPPH • 2-aminopyridine • triethylamine • cinnamic acid

Introduction

Substituted cinnamic acid amides is an important class of compound. Acid moiety of these amides are made up of substituted cinnamic acids. Different cinnamic acid analogues have been found to occur in different plants such as *Piper caninum* (Setzer *et al*, 1999) and *Cymbopogon citratus* (Cheel *et al*, 2005a). Cinnamic acid analogues are known to have properties like, antioxidative (Chen and Ho, 1997; Ley and Bertram, 2001), anti-inflammatory (Sud'ina *et al*, 1993), antiviral (King *et al*, 1999) and antibacterial (Setzer *et al*, 1999). Cinnamic acid amides are also found in fruits, vegetables, coffee beans, propolis and olives. Substituted cinnamic acid amides are also usually found as simple derivatives including esters, glycosides, sugar esters and amides (Kavitha *et al*, 2000). Amides have recently received a lot of attention in synthetic organic chemistry due to their therapeutic and pharmacological effects. Cephalosporins and penicillins are antibiotics with an amide group. The conversion of ketones into amides results in the formation of novel bioactive natural chemicals (Jain *et al.*, 2018). These factors make an integrated synthetic method essential for amide synthesis (Gopalkrishnan *et al*, 2005). So, there is need for development of environmentally benign green procedures for the synthesis of amide derivatives.

Substituted *(E)*-3-phenyl acrylamides are cinnamic acids amides containing pyridine in their amine moiety. These compounds are not found generally in nature but because of having similar structural pattern of cinnamic acid amides having benzene ring in their amine moiety exhibit biological activities comparable to these compounds. The acrylamide moiety is a significant component that is frequently linked to several biochemical processes and displays a range of pharmacological effects. Numerous compounds with an acrylamide moiety exhibit diverse biological activities in the literature, including antiviral, antidiabetic (Elgiushy *et al*, 2018), antibacterial (Fu *et al*, 2010), antitumor (Hu *et al*, 2021), and antiproliferative (Tanis *et al*, 2019) properties. Many authorized medications, including Entacapone, Panobinostat, Belinostat, and Rifampicin, possess this moiety in their structures (Cakmak *et al*, 2023). Numerous cinnamic acid

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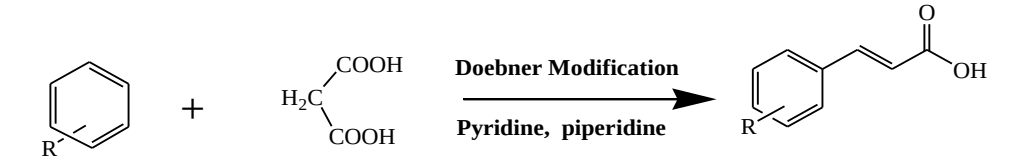
amides, both natural and artificial, were discovered to have additional biological characteristics, including the ability to prevent β-amyloid protein aggregation and to inhibit tyrosinase, α-glucosidase, cholinesterase, and MAO (Takao *et al*, 2017). Research on structure-activity correlations has shown that substituted cinnamic acid amides with catechol rest at amino acid or benzene moieties effectively scavenged DPPH radical and inhibited LPO (Chochkova *et al*, 2024). The LPO statistics proved without a reasonable doubt that the indole group increases activity. In addition, according to Georgiev et al, (2013), tyrosinase inhibition is further improved when a p-hydroxy substituted cinnamic acid moiety is present.

Substituted acrylamides have diverse biological activities but *(E)*-3-(Substituted phenyl)-N-(pyridin-2-yl) acrylamides have not been studied much for their biological activities. Only few reports are available in literature showing the studies carried out on biological activities of these compounds. The presence of a similar molecular structural pattern in two classes of compounds, namely substituted acrylamides and *(E)*-3-(substituted phenyl)-N-(pyridin-2-yl) acrylamides, prompted us to investigate the biological activities of acrylamides. It is evident that due to their similar molecular structural pattern, the potential activities found in cinnamanilids can provide insight into the biological activity potential of *(E)*-3-(substituted phenyl)-N-(pyridin-2-yl) acrylamides. This review focuses on the antioxidant properties of acrylamides. The synthesized compounds were assessed at concentrations of 50, 100, and 200 ppm for their capacity to hinder the germination of radish seeds *(Raphanus sativus L.var*. Japanese White). These compounds were compared to metribuzin (sencor), a widely used herbicide. All medications demonstrated significant effectiveness. It was observed that the activity exhibited a positive correlation with the concentration of the test solution.. All of the compounds suppressed the activity more than 70% at 100 ppm, with the exception of 4-hydroxy acrylamide (Vishnoi *et al*, 2009).

Material and Methods

Synthesis of Substituted Cinnamic acid

The method for the preparation of substituted cinnamic acid was applied was given by (Kavitha *et al*, 2000) with some modification. In a round bottom flask pulverized malonic acid (50mmol) and substituted benzaldehyde (30mmol) were taken. Then 10mL of pyridine was added. A clear solution was obtained. Then trace amount of piperidine (0.4mL) was also added. The guard tube filled with dry calcium chloride was used as a stoppered in the round bottom flask and kept on the magnetic stirrer. The reaction mixture was monitored through a silica gel TLC plate. After 24 hours, a dry glass rod was deeped in reaction mixture and it was dipped in the test tube containing 10% HCl. The formation of precipitates in sufficient amount indicates the completion of the reaction. The reaction completed within 24-36 hours. After completion of the reaction the reaction mixture was streamed in excess of dil. Hydrochloric acid. Precipitates acquired were filtered then frequently washed with cold water and dried in oven for 24 hours



Substituted Benzaldehyde **Malonic acid** **Substituted cinnamic acid**

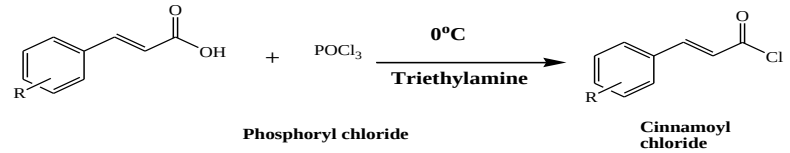
Substituents- a. 4-chloro
b. 3-chloro
c. 2-chloro
d. 4-nitro
e. 4-fluoro
f. 3-nitro
g. 4-methoxy
h. 4-hydroxy
i. 2,4-dichloro
j. 4-dimethylamino

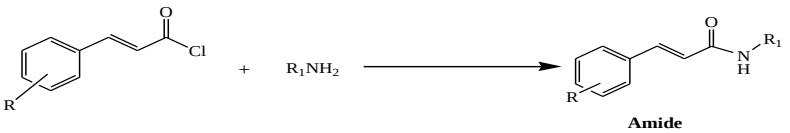
Synthesis of Substituted Cinnamic acid

DOI: https://doi.org/10.51220/jmr.v19-i2.22

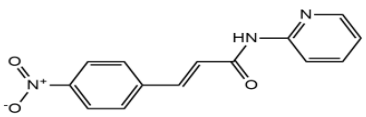
Synthesis of *(E)*-3-(substituted Phenyl)-N-(pyridin-2-yl) acrylamides

The method of preparation was done (Vishnoi *et al*, 2009) with some modification. 2- Amino pyridine (2mmol) was taken in round bottom flask and was dissolved in chloroform. It was mixed with 2.0 mmol of substituted cinnamic acid. A distinct solution was achieved. After adding 0.2 mL of triethylamine and placing the flask in an ice bath, the reaction mixture was cooled to 5°C. Subsequently, 4 mmol of $POCl_3$ was added dropwise while stirring continuously. Next, 0.4 mL of triethylamine was poured to one section. At a low temperature, the reaction mixture was further agitated. The development of the reaction was tracked on a silica gel TLC plate. Usually, the reaction was finished in 30 minutes. The reaction liquid was transferred into a beaker with crushed ice once the reaction was finished. The organic phase separated out. Then DCM is added to the reaction mixture. Two layers are formed. Organic phase is separated funnel. Aqueous layer is extracted with DCM and added to the organic phase. Anhydrous sodium sulphate was added to the DCM extract. The extract was distilled to evaporate the solvent. Thus, crude product was obtained. The crude product was recrystallized from suitable solvent.





Structure of compounds synthesized: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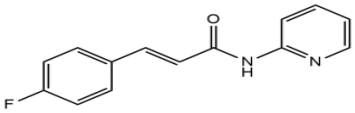
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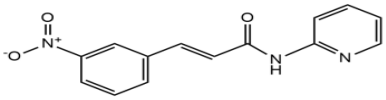
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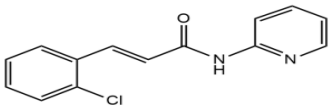
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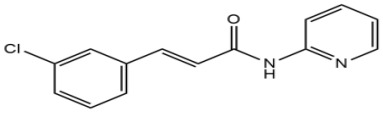
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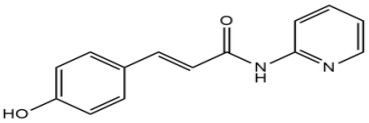
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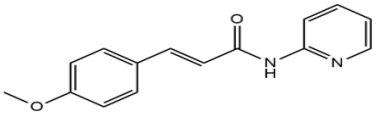
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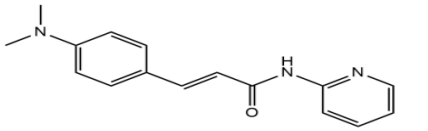
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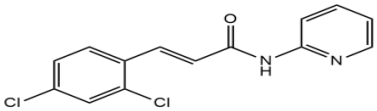
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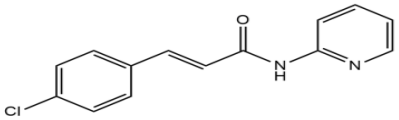
(E)-3-(4-chlorophenyl)-N-(pyridin-2-yl) acrylamide

Antioxidant Activity

DOI: https://doi.org/10.51220/jmr.v19-i2.22

Free Radical Scavenging Activity

In vitro antioxidant activity is measured using the DPPH technique, which is commonly used. This radical scavenging method is employed in the antioxidant capacity assay to measure the antioxidant's ability to quench the DPPH radical. When antioxidants reduce DPPH free radicals, they are converted to their non-radical state, which is a stable free radical with a dark purple colour. Antioxidants can easily provide electrons or hydrogen to free radicals, resulting in the formation of a simple stable molecule.

Evaluation of antioxidant activity of synthesized compound are studied by the DPPH assay**.** Antioxidant activity of the compounds increases with increase in the concentration of the compound the observed IC_{50} values and free radical scavenging activity in terms of % inhibition. Standard antioxidants like BHT and gallic acid for free radical scavenging activity of all the compounds was compared. The value of IC50 decreases as the antioxidant activity of the substances increases.

Amongst all the *(E)*-3-(substituted phenyl)-N-(pyridin-2-yl acrylamides, *(E)*-3-(4-methoxypheyl) -N-(pyridin-2-yl) acrylamide [A-7] exhibited the highest free radical scavenging activity (IC50=213.6µg/ml) which is comparable to standard Gallic acid. *(E)*-3-(4-dimethylamino phenyl)-N-(pyridin-2-yl) acrylamide, [A-10] (IC50=272.3µg/ml) also showed a good activity followed by *(E)*-3-(4-hydroxyphenyl)-N-(pyridin-2-yl)acrylamide [A-8] (IC50=372.9µg/ml), *(E)*-3-(3-nitrophenyl)-N-(pyridin-2-yl) acrylamides [A-6] (IC50=764.6µg/ml). *(E)*-3-(2,4-dichlorophenyl)-N-(pyridin-2-yl) acrylamide [A-9] (IC50=436.0µg/ml) and *(E)*-3-(3-chlorophenyl)-N-(pyridin-2-yl) acrylamide [A-2] (IC50=438.8µg/ml) exhibited the activity at par. *(E)*-3-(4-flourophenyl)-N-(pyridin-2-yl) acrylamide [A-5] (IC_{50}= 548µg/ml) and *(E)*-3-(2-chlorophenyl)-N-(pyridin-2-yl) acrylamide [A-3] (IC_{50}=530.8µg/ml) also exhibited the activity at par. *(E)*-3-(4-nitrophenylphenyl)-N-(pyridin-2-yl) acrylamide [A-4] (IC_{50}=883.3µg/ml) exhibited the lowest free radical scavenging activity followed by *(E)*-3-(4-chlorophenyl)-N-(pyridin-2-yl) acrylamide [A-1] (IC_{50}=873.8µg/ml) also exhibited the low free radical scavenging activity. All the synthesized compound showed the less activity the standard BHT (IC_{50}=123.8µg/ml) and Gallic acid (IC_{50}=157.8).

The synthesized compound was similar in structural pattern to the acrylamides the compounds clear indication from the observed results was that the presence of electron donating group (pyridine) at the amide nitrogen play an important role in scavenging the free radicals attributing to moderate to good antioxidant activity of synthesized Acrylamide derivatives. Compounds A-7 and A-10 containing good electron donating groups (-OCH_3 and -2,4-dimethyl) at phenyl ring respectively, showed much better antioxidant activity with IC_{50} values at 213.4 ±0.17µg/ml and 272.7 ±0.35 µg/ml, respectively. However, Due to the presence of the electron withdrawing group such as 4-nitro, 3-nitro and 4-chloro on phenyl ring compounds respectively [A-4], [A-6] and [A-1] significantly decreases the activity **(Nimse *et al,* 2015).**

Hence following are the increasing order of the free radical scavenging activity-
BHT > Gallic acid>[A-7]>[A-10]>[A-8]>[A-9]>[A-2]>[A-3]>[A-5]>[A-6]> [A-1]>[A-4]

Table 1:% DPPH radical Scavenging activity at 100, 200 and 300ppm concentration of *(E)*-3-(substituted phenyl)-N-(pyridin-2-yl) acrylamides.

Sr.No.	Sample Name	Free radical scavenging activity			
		100µg/ml	200µg/ml	300µg/ml	IC_{50}
1.	Gallic acid	46.3±0.13	52.4±0.08	60.2±0.08	157.8±1.2
2.	BHT	48.2±0.08	55.5±0.13	61.6±0.08	123.8±1.46

3.	A-1	12.8±0.08	12.8±0.20	26.5±0.13	873.8±11.6
4.	A-2	6.1±0.13	12.8±0.13	26.5±0.13	438.8±8.0
5.	A-3	14.4±0.13	20.0±0.13	31.4±0.13	530.8±2.28
6.	A-4	10.3±0.2	15.4±0.13	20.4±0.13	883.7±12.0
7.	A-5	22.4±0.2	29.9±0.13	34.5±0.13	548.4±3.32
8.	A-6	9.5±0.13	17.5±0.13	21.5±0.13	764.6±12.53
9.	A-7	30±0.08	46.9±0.08	65.9±0.08	213.6±0.17
10.	A-8	18.9±0.13	30.1±0.13	42.1±0.08	372.9±1.2
11.	A-9	5.5±0.13	14.8±0.08	32.9±0.08	436.0±1.57
12.	A-10	19.1±0.08	45.1±0.08	51.1±0.08	272.7±0.35
	CD at 5%	**0.218**	**0.208**	**0.178**	

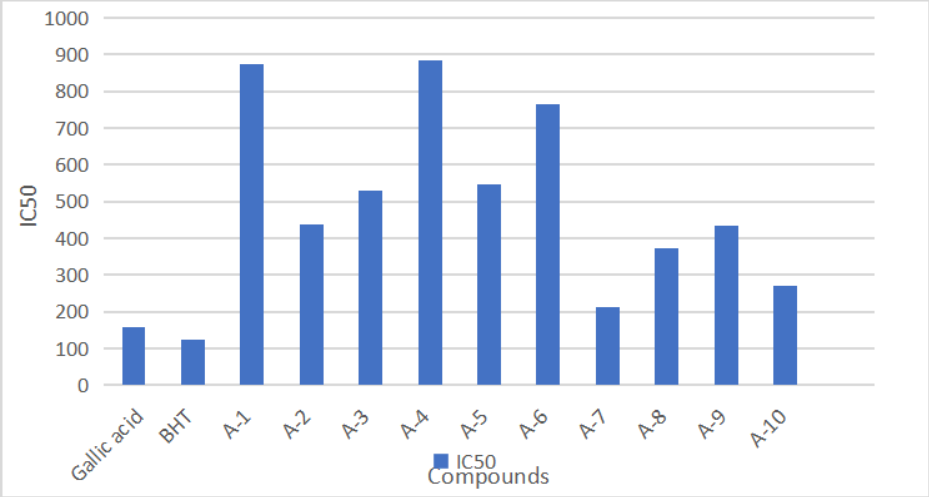

Fig 1: IC_{50} DPPH radical scavenging activity of *(E)*-3-(substituted phenyl)-N-(pyridin-2-yl) acrylamides and standards

Spectral Characterization

(a) *(E)*-3-(4-chlorophenyl)-N-(pyridin-2-yl) acrylamide[A-1]

IR:3234 (-NH), 2918(-CH), 1678(-C=O),1624 (-C=C),1552 (-C=N), 1532 (-NH bending), 1325 (-CN).

^{1}H NMR (500 MHz, DMSO) δ 6.35(1H, d, J=15.9Hz, =C-H), 7.45 (1H, d, J=15.9 Hz, =C-H), 7.52-7.58 (4H, m, Ar-H), 7.48 (d, J = 8.4Hz, 1H), 6.88 (d, J= 16.0 Hz, CH), 6.57 (d, J=16.0 Hz, CH), 7.80(s, NH).

(b) *(E)*-3-(3-chlorophenyl)-N-(pyridin-2-yl) acrylamide[A-2]

IR:3250 (-NH), 2914 (-CH), 1699 (-C=O), 1625 (-C=C), 1545 (-C=N), 1516 (-NH bending), 1320 (-CN).

^{1}H NMR (500 MHz, DMSO) δ 6.22 (1H, d, J=8.4 Hz, =C-H), 6.65 (1H, d, J=14.2Hz, =C-H), 7.18-7.28 (4H, m, Ar-H), 7.38-7.45 (3H , m, Ar-H), 7.64 (2H, d, J=8.2Hz, CH), 8.18 (s, NH)

(c) *(E)*-3-(2-chlorophenyl)-N-(pyridin-2-yl) acrylamide[A-3]

IR: 3264 (-NH), 2950(-CH), 1654 (-C=O), 1624 (-C=C), 1557 (-C=N), 1524 (-NH bending), 1315(-CN).

^{1}H NMR (500 MHz, DMSO) δ 6.54 (1H, d, J=10.8Hz, =C-H), 6.85 (1H, d, J=15.8 Hz, =C-H), 7.27-7.48 (4H, m, Ar-H), 7.50-7.58 (3H, m, Ar-H), 7.84(2H, d, J= 7.6 Hz, CH), 8.23 (s, NH).

(d) *(E)*-3-(4-nitrophenyl)-N-(pyridin-2-yl) acrylamide[A-4]

IR: 3285 (-NH), 2936 (-CH), 1663 (-C=O), 1628 (-C=C), 1534(-C=N), 1551(-NH bending), 1334 (-CN) .

^{1}H NMR (DMSO, 500MHz): δ 6.35 (1H, d, J=8.4Hz, =C-H), 7.3 (2H, d, J=7.0Hz, =C-H), 7.56-7.77 (5H, m, Ar-H), 8.1-8.12 (2H, d, J=7.6Hz, CH), 8.22-8.34 (2H, s, CH), 8.46 (s, NH).

(e) *(E)*-3-(4-fluorophenyl)-N-(pyridin-2-yl) acrylamide[A-5]

IR: 3240 (-NH), 2912 (-CH), 1681 (-C=O), 1618 (-C=C), 1586 (-C=N), 1542 (-NH bending), 1308 (-CN).

^{1}H NMR (DMSO, 500MHz): δ 6.89 (1H, d, J=8.4Hz, =C-H), 6.55 (2H, t, =C-H), 7.15 (2H, d, J=7.0Hz, CH), 7.4-7.67 (5H, m, Ar-H), 8.1-8.12 (2H, d, J=7.6Hz, CH), 8.16-8.36 (2H, s, CH), 8.45 (s, NH).

(f) *(E)*-3-(3-nitrophenyl)-N-(pyridin-2-yl) acrylamide[A-6]

IR: 3297 (-NH), 2940 (-CH), 1665 (-C=O), 1630 (-C=C), 1538(-C=N), 1556 (N-H bending), 1338 (-CN).

^{1}H NMR (DMSO, 500MHz): δ6.52(1H, d, J=16 Hz, =C-H), 6.85(2H, t, CH), 7.56(2H, d, J=7.0Hz, CH), 7.70-7.85(5H, m, Ar-H), 8.1-8.12(2H, d, J=7.6Hz, CH), 8.30-8.40(2H, S, CH), 8.51 (S, NH).

(g) *(E)*-3-(4-methoxyphenyl)-N-(pyridin-2-yl) acrylamide [A-7]

IR: 3229 (-NH), 2946(-CH), 1640 (-C=O), 1618 (-C=C), 1514 (-C=N), 1514 (N-H bending), 1390 (-CN).

^{1}H NMR (500 MHz, DMSO) δ 3.73 (3H, s, CH_3), 6.22 (1H, d, J=15.7 Hz, =C-H), 6.38(1H, d, J=15.7 Hz, =C-H), 6.88-6.93(2H, m, Ar-H), 7.20-7.26 (1H, m, CH), 7.44(2H, d, J=8.4Hz, CH), 8.35 (s, NH).

(h) *(E)*-3-(4-hydroxyphenyl)-N-(pyridin-2-yl) acrylamide [A-8]

IR: 3260 (-NH), 2935 (-CH), 1687 (-C=O), 1615(-C=C), 1510 (-C=N), 1508 (-NH bending), 1388 (-CN).

^{1}H NMR (500 MHz, DMSO) δ 6.07(1H, d, J=15.7 Hz, =C-H), 6.38(1H, d, J=15.7 Hz, =C-H), 6.88-6.93(2H, m, Ar-H), 7.15-7.55 (1H, m, CH), 7.2 (2H, d, J=7.2 Hz, CH), 8.35 (s, NH).

(i) *(E)*-3-(2,4-dichlorophenyl)-N-(pyridin-2-yl) acrylamide [A-9]

IR: 3211 (-NH), 2920 (-CH), 1667 (-C=O), 1605 (-C=C), 1505 (-C=N), 1504 (-N-H bending), 1382 (-CN),

^{1}H NMR (500 MHz, DMSO) δ 6.54 (1H, d, J=10.8Hz, =C-H), 7.45 (1H, d, J=15.9Hz, =C-H), 7.52 - 7.58(4H, m, Ar-H), 7.48 (d, J = 8.4Hz, 1H), 6.88 (d, J= 16.0 Hz, 8.35 (s, NH).

(j) *(E)*-3-(2,4-dimethylaminophenyl)-N-(pyridin-2-yl) acrylamide [A-10]

IR:3254 (-NH), 2940 (-CH),1745 (-C=O), 1687 (-C=C), 1524 (-C=N)
1512 (-NH bending), 1385 (-CN).

^{1}H NMR (500 MHz, DMSO) δ 7.69 (d, *J* = 8.6 Hz, 2H), 6.78 (d, *J* = 8.5 Hz, 2H), 2.77 (d, *J* = 265.2 Hz, 8H), 2.51 (s, 1H), 2.51 (s, 1H).

Acknowledgements

The authors are thankful For providing the NMR data carried out by the IIT Roorkee Uttarakhand and GBPUAT, Department of Chemistry for all the biological Activity.

References

Çakmak Ş and Erdoğan T (2023). Some bis (3-(4-nitrophenyl) acrylamide derivatives: Synthesis, characterization, DFT, antioxidant, antimicrobial properties, molecular docking and molecular dynamics simulation studies. *Indian Journal of Biochemistry and Biophysics (IJBB)*, 60(3), 209-223.

Cheel J, Theoduloz C, Rodriguez J and Schmeda-Hirschmann G (2005.a). Free radical scavengers and antioxidants from lemongrass *(Cymbopogon citratus (DC.) Stapf.)*. *J. Agric. Food Chem,* 53, 8512-8518.

Chen J H and Ho C T (1997). Antioxidant activities of caffeic acid and its related hydroxycinnamic acid compounds. *J. Agric. Food Chem,* 45(7),2374-2378.

Chochkova M, Stoykova B, Petrova P, Štícha M and Ivanova G (2024). Synthesis of novel boldine amides and their in vitro inhibitory effects on a mushroom tyrosinase. *Journal of Chemical Technology and Metallurgy*, 59(4), 855-862.

Elgiushy H, Hammad S, Hassan A and Aboutaleb N (2018). Acrylamide moiety, a valuable fragment in medicinal chemistry: insight into synthetic methodologies, chemical reactivity and spectrum of biological activities of acrylamide derivatives. *Journal of Advanced Pharmacy Research*, 2(4), 221-237.

Fu J, Cheng K, Zhang Z M, Fang R Q and Zhu H L (2010). Synthesis, structure and structure–activity relationship analysis of caffeic acid amides as potential antimicrobials. *European Journal of Medicinal Chemistry*, 45(6),2638-2643.

Georgiev L, Chochkova M, Totseva I, Seizova K, Marinova E, Ivanova G, and Milkova T

DOI: https://doi.org/10.51220/jmr.v19-i2.22

(2013). Anti-tyrosinase, antioxidant and antimicrobial activities of hydroxycinnamoyl amides. *Med. Chem. Res,* 22(9), 4173-4182.

Gopalakrishnan M, Sureshkumar P, Kanagarajan V and Thanusu J (2005). Organic synthesis in solid media; Alumina supported sodium hydrogen sulphate as an effective and reusable catalyst for 'one-pot's synthesis of amides from ketones in dry media under microwave irradiation. *Lett. Org. Chem,* 2(5), 444-446.

Hu X, Tang S, Yang F, Zheng P, Xu S, Pan Q and Zhu W (2021). Design, synthesis, and antitumor activity of imatinib derivatives containing acrylamide moiety. *Molecules*, 26(10), 3041.

Jain P. U and Samant S. D (2018). A facile one-pot transformation of aromatic aldehydes /ketones to amides: Fe_2O_3@ SiO_2 as an environmentally benign core-shell catalyst. *Chemistry Select*, 3(7),1967-1975.

Kavitha J, Vanisree M, Subbaraju, G. V (2000). Synthesis of O-geranyl coniferyl alcohol, a metabolite of *Fagara rhetza*. *Indian J. Chem*, 40, 522-523

King P. I, Ma G, Miao W, Jia Q, McDougall B. R, Reinecke M. G and Robinson, W. E (1999). Analogues of the Di caffeoylquinic and dicaffeoyltartaric acids as potent inhibitors of human immunodeficiency virus type 1 integrase and replication. *J. Med. Chem,* 42, 497-509.

Ley J. P and Bertram H. J (2001). Synthesis of polyhydroxylated aromatic Mandelic acid amides and their antioxidative potential. *Tetra,* 57(7), 1277-1282.

Mahajan S, Slathia N and Kapoor K. K (2020). Beckmann rearrangement: Thiamine hydrochloride as a remarkable catalyst for one-pot synthesis of amides from ketones. *Tetrahedron Lett,* 61(20), 151859.

Setzer W. N, Vogler B, Schmidt J. M, Leahy J. G and Rives R (2004). Antimicrobial activity of Artemisia douglasiana leaf essential oil. *Fitoterapia*, 75(2), 192-200.

Sud'Ina G. F, Mirzoeva O. K, Pushkareva M. A, Korshunova G, Sumbatyan N. V and Varfolomeev S. D (1993). Caffeic acid phenethyl ester as a lipoxygenase inhibitor with antioxidant properties. *FEBS Lett,* 329(1-2), 21-24.

Takao K, Toda K, Saito T and Sugita Y (2017). Synthesis of amide and ester derivatives of cinnamic acid and its analogs: evaluation of their free radical scavenging and monoamine oxidase and cholinesterase inhibitory activities. *Chem. Pharm. Bull,* 65(11),1020-1027.

Tanış E, Cankaya N, and Yalçın S (2019). Synthesis, characterization, computation of global reactivity descriptors and antiproliferative activity of N-(4-nitrophenyl) acrylamide. *Russian Journal of Physical Chemistry B*, 13, 49-61.

Vishnoi S, Agrawal V and Kasana V K (2009). Synthesis and structure− activity relationships of substituted cinnamic acids and amide analogues: a new class of herbicides. *J. Agric. Food Chem*, 57(8), 3261-3265.

Yu L, Guo L, Hu W, Zhang Z, Bai Y, Ye J. and Li L (2019). One-pot conversion of ketones to amides via Beckmann rearrangement catalyzed by metal chloride-ionic liquids under solvent-free conditions. *Catal. Commun*, 123, 119-123.