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Synthesis and antimicrobial activity of N, N-dialkyl cinnamamides

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ABSTRACT

N- Substituted cinnamamide posses a wide range of biological activity, and thus, new derivatives of cinnamamide were synthesized by using new method which fallows the path of witting reaction. N, N-dialkyl cinnamamides were synthesized and screened for their antimicrobial activity. Against gram positive as well as gram negative microorganisms.

Key words: N,N- dialkyl cinnamamide, antimicrobial activity.

INTRODUCTION

The point of interest in the cinnamamide is the biological activity. The literature survey revels that the cinnamamide and its derivatives gain immense important in human life due to their variety of applications in medicinal[1-3], Pharmacological[4-6] and agricultural field[7-9]. Various N,N-dialkyl cinnamamide were synthesized by using the path of witting reaction, such as (2E)-N,N dimethyl-3-phenyl prop-2-enamide, (2-E)-3-(4-methoxyphenyl) N,Ndimethyl prop-2-enamide etc.same of them shows remarkable biological activity and help to find better alternative against pathogens. P-methoxy cinnamamide has great application in drug and medicinal field; it is used as precursor in the synthesis of anticancer drug taxol[10]. Trimethoxy cinnamamide is used as tranquilizer and CNS depressant in mice[11].

All the synthesized compounds were screened for their antimicrobial activity using cup-plate diffusion method[12]. Both gram-positive and gram-negative microorganisms were used for the testing.

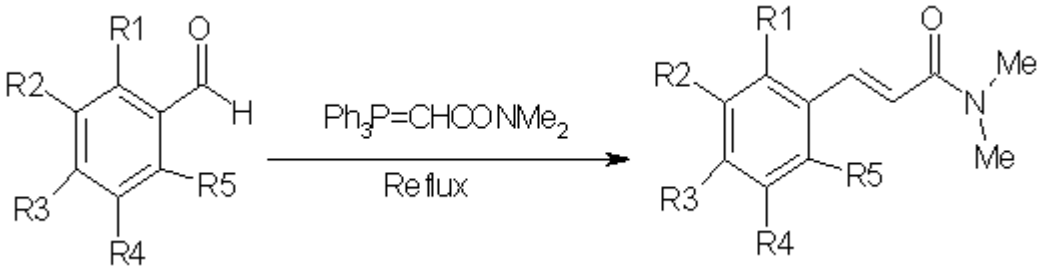
EXPERIMENTAL

Preparation of Witting reagent

N, N dimethyl chloracetamide were prepared by using equimolar solution of chloroacetychloride and dimethylamine in chloroform at 0°C.This chloracetamide is converted to its salt by adding its solution in benzene to the stirred solution of triphenylphosphine and reaction mixture was refluxed for 4-6 hrs. After that solid obtained was filter and air dried. Now, this salt is dissolved in 100 ml water and 90 ml dry benzene and add 1-2 drops of phenolphthalein indicator and add 10 N NaOH till pink colour persist, Benzene layer was separated wash with water and concentrated to 1/3 volume. Finally scratched with n-Hexane to obtain solid witting reagent ($Ph_3P=CHCONMe_2$).

Preparation of derivatives

Equimolar solution of witting reagent and different aromatic aldehydes were taken in dry benzene and reflux till the product obtain. Progress of reaction was monitor by thin layer chromatography.



Aromatic aldehyde Cinnamamide

Scheme 1

Table 1: Substituted aromatic aldehydes

Entries↓	R1	R2	R3	R4	R5
a	H	H	H	H	H
b	H	H	OMe	H	H
c	H	OMe	OMe	H	H
d	H	OMe	OMe	OMe	H
e	H	OMe	H	OMe	H
f	H	-O-CH2-O-		H	H
g	NO_2	H	H	H	H

Melting points were taken by open capillary method .IR spectra were recorded on Perkin-Elmer spectrometer in KBr pellets. ^{1}H NMR spectra were recorded with TMS as internal standard using $CDCl_{-3.}$ All synthesized compound were purified by coloum chromatography. All chemicals used were of analar grade.

Table 2: Properties of compounds

Entries	Molecular formula	C	H	N	Yield (%)
a	$C_{11}H_{13}NO$	75.40	7.48	7.88	76
b	$C_{12}H_{15}NO_2$	70.08	7.34	6.77	68
c	$C_{13}H_{17}NO_3$	66.32	7.29	5.94	52
d	$C_{14}H_{19}NO_4$	66.34	7.27	5.96	78
e	$C_{13}H_{17}NO_3$	63.37	7.22	5.27	65
f	$C_{12}H_{13}NO_3$	65.72	5.97	6.34	78
g	$C_{11}H_{12}N_2O_3$	74.82	7.20	7.96	70

Spectral data

a. (2E)-N, N-dimethyl-3-phenylprop-2-enamide

IR (cm^{-1}) - 1656, 1595
^1H NMR (δ ppm) - 3.18 (S), (6H), NMe_2
6.44 (d) (1H), (CH=CHCO), J=15.95 Hz
7.2 &7.5 (m), (5H), (C_6H_5)
7.6 (d), (1H), (CH=CHC_6H_5), J=15.95 Hz

b. (2E) -3-(4-methoxyphenyl)-N, N-dimethylprop-2-enamide

IR (cm^{-1}) 1685, 1600
^1H NMR (δ ppm) - 3.26 (s), (6H), NMe2
3.9 (s), (3 H) OMe
7.69 (d), (1H), (CH=CHC_6H_5), J=15.59 Hz
7.47 (d), (2H), (CH=CH- Ar), J=8.80 Hz
6.84 (d), (2H) (CH=CH- Ar) J=8.80 Hz
6.42 (d), (1H), (CH=CHCO), J=15.59 Hz

c. (2E) -3-(3, 4-dimethoxyphenyl)-N, N-dimethylprop-2-enamide

IR (cm^{-1}) - 1678, 1646
^1H NMR (δ ppm) - 3.29 (s), (6H), NMe2
3.87(s), (6H), OMe
7.69 (d), (1H), (CH=CHC_6H_5), J=15.73 Hz
6.9-7.2 (m),(3H), Ar-H
6.42 (d), (1H), (CH=CHCO), J=15.73 Hz

d. (2E) -N, N-dimethyl-3-(3, 4, 5-trimethoxyphenyl) prop-2-enamide

IR (cm^{-1}) - 1688, 1636
^1H NMR (δ ppm) - 3.18 (s), (6H), NMe2
3.97 (s),(9H),OMe
7.64 (d), (1H), (CH=CHC6H5), J=15.87 Hz
6.8-7.2 (m), (2H), Ar-H
6.42 (d), (1H), (CH=CHCO), J=15.87 Hz

e. (2E) -3-(2, 4-dimethoxyphenyl)-N, N-dimethylprop-2-enamide

IR (cm^{-1}) - 1668, 1642
^1H NMR (δ ppm) - 3.22 (s), (6H), NMe2
3.82(s), (6H), OMe
7.59 (d), (1H), (CH=CHC6H5), J=1568 Hz
6.7-7.2 (m), (3H), Ar-H
6.52 (d), (1H), (CH=CHCO), J=15.68 Hz

f. (2E) -3-(1, 3-benzodioxol-5-yl)-N, N-dimethylprop-2-enamide

IR (cm^{-1}) - 1678, 1646
^1H NMR (δ ppm) - 3.15 (s),(6H), NMe_2
6.03 (s), (2H), (-OCH_2O-)
6.75-7.15 (m), (3H), (Ar-H)
6.98 (d), (1H), (Arch=CH), J=15.6Hz
7.7 (d), (1H), (CH=CHCO), J=15.6Hz

Table 3: Microbial testing with different species

Entries→ Species↓	$C_{11}H_{13}NO$ (a)	$C_{12}H_{15}NO_2$ (b)	$C_{13}H_{17}NO_3$ (c)	$C_{14}H_{19}NO_4$ (d)	$C_{13}H_{17}NO_3$ (e)	$C_{12}H_{13}NO_3$ (f)	$C_{11}H_{12}N_2O_3$ (g)
Bacillus subtilis	++	+	+	+++	+	++	+
Staphylococcus aureus	++	-	+++	++	++	+	++
Proteus velgaris	+++	+	++	+	-	+	+++
E.coli	+	++	-	++	+++	++	++
Salmonella paratyphi A	++	+++	+	+++	++	-	++
Salmonella paratyphi B	+	++	+	++	++	+	++
Pseudomonas aeruginosa	+++	+	++	+	+++	++	-
E.coli MCTC	++	++	+	+++	+	++	+++

Where: + = good, ++ = fair, +++ = Better, — = Not effective

g. (2E) -3-(2-nitrophenyl)-N, N-dimethylprop-2-enamide

IR (cm^{-1}) - 1664, 1680

^1H NMR (δ ppm) - 3.20 (S), (6H), $(CH3)_2$

6.42 (d), (1H) (CH=CHCO), J=15.75 Hz

7.2-7.4 (m), (4H) (-C6H4)

7.8 (d), (1H), (CH=CHC6H5), J=15.75 Hz

Microbial evaluation

The cup plate method was performed using nutrient agar. This agar media was inoculated with culture of different microorganisms such as *Bacillus subtilis, Staphylococcus aureus, Proteus velgaris, E. coli, Salmonella paratyphi* A and B, *Pseudomonas aeruginosa*, *E. coli* MCTC etc.and plate's discs saturated with solution of each compound were placed on the agar medium. All plates were incubated for 48 hours at 37 ^{0}C. Zone of inhibition was measured in mm.

RESULTS AND DISCUSSION

In vitro antibacterial activities of the synthesized compounds were evaluated against representative gram-positive and gram-negative organisms. The study was performed to find and develop novel antibacterial agent of synthetic origin giving a broad spectrum of activity and potency. Aim of this work is to develop a new method for the synthesis of N,N-dialkyl cinnamamide and its derivatives which show antibacterial activity and has great application in the medicinal,agricultural and pharmacological fields.

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REFERENCES

1. W.A. Lott, W.G. Christiansen, *J. Am. Pharma. Assoc.* **23**: 788 (1934).
2. E.van Heyningen, C.N.Brown, F.Jose, J.K.Henderson and P.Stark, *J. Med. Chem.,* **9**: 675 (1966).
3. R.B.Moffett, *J. Med. Chem.* **7**: 319-325 (1964).
4. B.W.Horrom, U.S. Patent, **3**: 133, 963 (1964) *Chem. Abstr.* **61**: 3032 (1964).
5. M.Bayssat, L. Fontaine, M. Grand, *Chem. Abstr.* **74**: 3326 (1971).
6. Parke,Davis and Co., British Patent, 663, 903, 1951, *Chem. Abstr.* **46**: 6336 (1952).
7. N.Plotnikoff, F.Will, A.Evans and P.Meekma, *Arch. Int.Pharmacodyn. Ther.* **195**: 330 (1972).
8. H.W. Schultz and G.A.Wiese, *J. Am. Pharma. Assoc. Sci.* Ed. **48**: 750 (1959).
9. H.Schwartz, J.B.Skaptason, *British Patent,* **1**: 171, 042 (1969) *Chem.Abstr.* **72**: 66658 (1970).
10. Madhan A., Kumar A.R., Rao B.V., *Tetrahedron Lett. Symmetry,* **12**: 2009 (2001).
11. M.L. Sharma, Yoginder Paul, R.C. Sharma, *J.Indian Chem. Soc.* **66**: 3234 (1989).
12. Barry A.L.The antimicrobial suceptibility test, Principle and practices, edited by Illus Lea and Fibiger, Philadelphia, U.S.A, 180 (1976).
13. Hoffmann, Corrison, American Cyn.Co. *Chem. Abstr.* 1966
14. Hoffmann, Corrison, American Cyn.Co., *Chem. Abstr.* (1964).
15. B.Bhatia, S. Jain, A.De, I. Begchi and J.Iqbal. *Tetrahedron Lett.* **37**: 7311 (1996).