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## Research Article

### SYNTHESIS OF (2E)-1-(4-METHYLPIPERAZIN-1-YL)-3-SUBSTITUTED PHENYLPROP-2-EN-1-ONE CINNAMAMIDES

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### ABSTRACT

Cinnamamides and its derivatives possessing various vital medicinal, pharmaceuticals, agricultural, biological and many other activities. In medicinal field several Cinnamamides and their derivatives are reported to show central nervous system depressant, anticonvulsant, muscle relaxant, antiallergic, antineoplastic, antitumor, anesthetic, analgesic and anti-infective activities, etc. In the agrochemical field, insecticidal, their avian repellent, herbicidal activities, and several excellent cinnamamide fungicides, for example dimethomorph, fluormorph and pyrimorph, have been successfully developed. Inspire of wide range of their applications and very less attention is paid towards the synthesis of cinnamamides derivatives containing heterocyclic moiety. Literature survey and biological activities' of cinnamamides have motivated to undertake the synthesized novel cinnamamides entitled "(2E)-1-(4-methylpeperazin-1-yl)-3-subsituted phenylprop-2-en-1-one Cinnamamides. The present study is related to the synthesis of some novel cinnamamides containing heterocyclic moiety.

Keywords: N-methyl piperazine, aromatic aldehydes, Cinnamamides.

### INTRODUCTION

Cinnamamides constitute an important class of compounds with a variety of biological properties[1] such as nervous central system depressant, anticonvulsant, muscle relaxant, antiallergic, antioxidant[2], antineoplastic, anti-infective activities, antimicrobial activity, medicinal, pharmaceuticals[3-4], agricultural, *etc.* In agrochemical field, their avian repellent, Antifungicidal, insecticidal [5] and herbicidal activities. The Wittig reaction is an important method for the synthesis of alkenes. The double bond forms specifically at the location of the original aldehyde or ketone. The synthesized compounds are neutral molecules but positive and negative centers on adjacent atoms connected by a sigma bond.



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The nucleophilic Carbon of the witting reagent adds to the electrophilic carbon in the polar carbonyl group of aromatic aldehyde the C=O pi bond are used to form a sigma bond to the positive P atom to form intermediate known as Oxaphosphetane, which on decomposition by breaking the C-P bond and C-O bonds leads to the formation of the C=C pi bond of cinnamamides. In the present study, the attempts were made to synthesize the series of (2E)-1-(4-methylpiperazin-1-yl)-3-substituted phenylprop-2-en-1-one Cinnamamides from Wittig reagent. Synthesized compounds were characterized by elemental analysis and spectral studies.

## EXPERIMENTAL

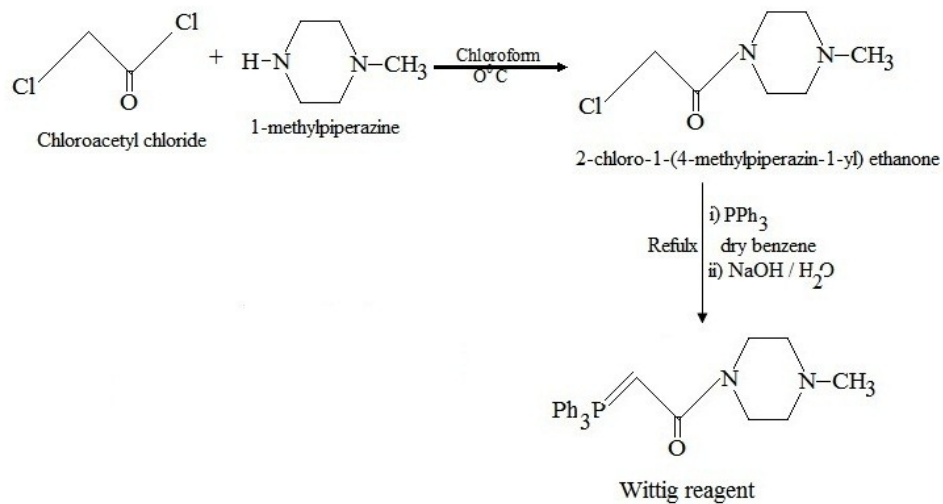
### Part-I-Synthesis of Wittig reagent

N-methyl piperazine chloracetamide were synthesized by using equimolar solution of chloroacetylchloride and N-methyl piperazine in chloroform at 0°C with continuous stirring in fuming chamber. When this reaction mixture gives the salt by adding its solution in benzene to the stirred solution of triphenylphosphine and reaction mixture was refluxed for 4-6 hrs. The solid products obtained were filtered and air dried. Thus for Purification obtained salt was dissolved in 100 ml water then 90 ml of dry benzene, add 1-2 drops of phenolphthalein indicator and add NaOH solution in it till pink colour persist this was indicates that the neutralization of present acid from reagent. Then benzene layer was separated and washed with water and concentrated to one third volume. Finally the product scratched with n-Hexane to obtain solid witting reagent.

### Part-II- Synthesis of (2E)-1-(4-methylpiperazin-1-yl)-3-Substituted phenylprop-2-en-1-one Cinnamamides

Equimolar solution of Wittig reagent and different aromatic aldehydes were taken in dry benzene and refluxed for 4 to 6 hrs. The progress of reaction was monitored by thin layer chromatography. Melting points were taken by open capillary method. The elemental analysis was calculated for carbon, hydrogen, nitrogen and chlorine. IR spectra were recorded with TMS as internal standard using CDCl<sub>3</sub>. All Synthesized compounds were purified by column chromatography. All chemicals used were of analytical grade.

## SCHEME: - I



## SCHEME: - II

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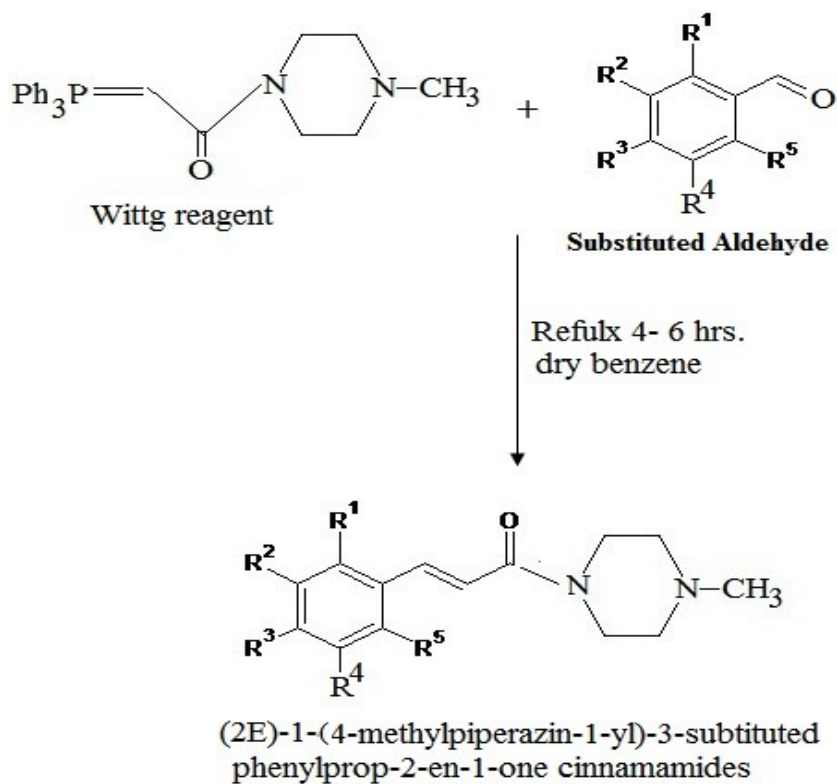


Table-1:-Substituted aromatic aldehydes used in the synthesis of Cinnamamides

Sr No.	Entries	R1	R2	R3	R4	R5
1	Ia	H	H	H	H	H
2	Ib	H	H	OMe	H	H
3	Ic	H	OMe	OMe	H	H
4	Id	H	OMe	OMe	OMe	H
5	Ie	H	-O-CH <sub>2</sub> -O-		H	H
6	If	NO <sub>2</sub>	H	H	H	H
7	Ig	H	H	Cl	H	H
8	Ih	H	H	NO <sub>2</sub>	H	H
9	Ii	H	H	N(Me) <sub>2</sub>	H	H

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10	Ij	H	H	OH	H	H
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**Table-2:- Characteristics data for synthesized Cinnamamides**

Sr. No.	Entries	Molecular Formula	Molecular weight	Yield %	M.P. °C
1	Ia	C <sub>14</sub> H <sub>18</sub> ON <sub>2</sub>	230	76	69
2	Ib	C <sub>15</sub> H <sub>20</sub> O <sub>2</sub> N <sub>2</sub>	260	62	165
3	Ic	C <sub>16</sub> H <sub>22</sub> O <sub>3</sub> N <sub>2</sub>	290	54	205
4	Id	C <sub>17</sub> H <sub>24</sub> O <sub>4</sub> N <sub>2</sub>	320	78	172
5	Ie	C <sub>15</sub> H <sub>18</sub> O <sub>3</sub> N <sub>3</sub>	288	66	62
6	If	C <sub>14</sub> H <sub>17</sub> O <sub>3</sub> N <sub>2</sub>	261	58	102
7	Ig	C <sub>14</sub> H <sub>17</sub> ON <sub>2</sub> Cl	264.5	78	79
8	Ih	C <sub>14</sub> H <sub>17</sub> O <sub>3</sub> N <sub>3</sub>	275	70	218
9	Ii	C <sub>16</sub> H <sub>23</sub> ON <sub>2</sub>	259	56	200
10	Ij	C <sub>14</sub> H <sub>18</sub> O <sub>2</sub> N <sub>2</sub>	246	64	82

**Table-3:-Elemental analysis of synthesized compounds-**

Sr. No.	Entries	Molecular Formula	% C	% H	% O	% N	% Cl
1	Ia	C <sub>14</sub> H <sub>18</sub> ON <sub>2</sub>	73.06 (73.04)	7.88 (7.83)	7.00 (6.96)	12.19 (12.17)	---
2	Ib	C <sub>15</sub> H <sub>20</sub> O <sub>2</sub> N <sub>2</sub>	69.26 (69.23)	7.72 (7.69)	12.36 (12.31)	10.82 (10.77)	---
3	Ic	C <sub>16</sub> H <sub>22</sub> O <sub>3</sub> N <sub>2</sub>	66.26 (66.21)	7.64 (7.59)	16.62 (16.55)	9.70 (9.66)	---
4	Id	C <sub>17</sub> H <sub>24</sub> O <sub>4</sub> N <sub>2</sub>	63.80	7.54	20.06	8.80	---

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			(63.75)	(7.50)	(20.00)	(8.75)	
5	<b>Ie</b>	C <sub>15</sub> H <sub>18</sub> O <sub>3</sub> N <sub>3</sub>	62.58 (62.50)	6.30 (6.25)	16.71 (16.66)	14.62 (14.58)	---
6	<b>If</b>	C <sub>14</sub> H <sub>17</sub> O <sub>3</sub> N <sub>2</sub>	64.42 (64.36)	6.53 (6.51)	18.42 (18.39)	10.75 (10.72)	---
7	<b>Ig</b>	C <sub>14</sub> H <sub>17</sub> ON <sub>2</sub> Cl	64.02 (63.51)	6.48 (6.42)	6.10 (6.05)	10.56 (10.58)	13.40 (13.42)
8	<b>Ih</b>	C <sub>14</sub> H <sub>17</sub> O <sub>3</sub> N <sub>3</sub>	62.12 (61.10)	6.21 (6.18)	17.46 (17.45)	15.28 (15.27)	---
9	<b>Ii</b>	C <sub>16</sub> H <sub>23</sub> ON <sub>2</sub>	74.16 (74.13)	8.90 (8.88)	6.20 (6.17)	10.84 (10.81)	---

In bracket calculated percentages of element.

### Spectral Data Studies:-

**Ia**=(2E)-1-(4-methylpiperazin-1-yl)-3- phenylprop-2-en-1-one Cinnamamides-

IR (cm<sup>-1</sup>)1656, 1595

<sup>1</sup>H NMR-(δ)-2.2(s), (3H), NMe; 2.9(t), (4H); 3.5(t), (4H); 6.7(d), (1H), (CH=CHCO), J=15.94 HZ; 6.8(d), (1H), (CH=CHC<sub>6</sub>H<sub>5</sub>) J=15.94 HZ; 7.2-7.5(m), (5H), (C<sub>6</sub>H<sub>5</sub>).

**Ib**- IR (cm<sup>-1</sup>)1685, 1600

<sup>1</sup>H NMR-(δ)-2.2(s), (3H), NMe; 2.9(t), (4H); 3.5(t), (4H); 6.9(d), (1H), (CH=CHCO), J=15.60 HZ; 7.0(d), (1H), (CH=CHC<sub>6</sub>H<sub>5</sub>) J=15.60HZ; 3.2(s), (3H), (OMe); 7.2(d), (2H); 7.4(d), (2H).

**Ic**- IR (cm<sup>-1</sup>)1678, 1644



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<sup>1</sup>H NMR-( $\delta$ )-2.2(s), (3H), NMe; 2.9(t), (4H); 3.5(t), (4H); 6.9(d), (1H), (CH=CHCO), J=15.70 HZ; 7.2(d), (1H), (CH=CHC<sub>6</sub>H<sub>5</sub>) J=15.70HZ; 3.2(s), (6H), (OMe); 6.9-7.1(m), (3H), Ar-H.

**Id-** IR (cm<sup>-1</sup>)1688, 1636

<sup>1</sup>H NMR-( $\delta$ )-2.2(s), (3H), NMe; 2.9(t), (4H); 3.5(t), (4H); 6.9(d), (1H), (CH=CHCO), J=15.84 HZ; 7.4(d), (1H), (CH=CHC<sub>6</sub>H<sub>5</sub>) J=15.84HZ; 3.2(s), (9H), (OMe); 6.6(s), (2H), Ar-H.

**Ie-**IR(cm<sup>-1</sup>) 1670, 1650

<sup>1</sup>H NMR-( $\delta$ )-2.2(s), (3H), NMe; 2.9(t), (4H); 3.5(t), (4H); 6.9(d), (1H), (CH=CHCO), J=15.84 HZ; 7.4(d), (1H), (CH=CHC<sub>6</sub>H<sub>5</sub>) J=15.84HZ; 4.8(s), (4H), (H<sub>2</sub>COCH<sub>2</sub>); 7.4-7.6(s), (3H), Ar-H.

**If-** IR (cm<sup>-1</sup>)1664, 1680

<sup>1</sup>H NMR-( $\delta$ )-2.2(s), (3H), NMe; 2.9(t), (4H); 3.5(t), (4H); 6.8(d), (1H), (CH=CHCO), J=15.72 HZ; 7.3(d), (1H), (CH=CHC<sub>6</sub>H<sub>5</sub>) J=15.72HZ; 7.4-7.5(m), (4H), Ar-H. 1H

**Ig-** IR (cm<sup>-1</sup>)1656, 1580

<sup>1</sup>H NMR-( $\delta$ )-2.2(s), (3H), NMe; 2.9(t), (4H); 3.5(t), (4H); 6.6(d), (1H), (CH=CHCO), J=15.70 HZ; 6.8(d), (1H), (CH=CHC<sub>6</sub>H<sub>5</sub>) J=15.70HZ; 7.3-7.5(m), (4H).

**Ih-** IR (cm<sup>-1</sup>)1664, 1680

<sup>1</sup>H NMR-( $\delta$ )-2.2(s), (3H), NMe; 2.9(t), (4H); 3.5(t), (4H); 6.7(d), (1H), (CH=CHCO), J=15.70 HZ; 6.8(d), (1H), (CH=CHC<sub>6</sub>H<sub>5</sub>) J=15.70HZ; 7.3-7.4(m), (4H).

**Ii-** IR (cm<sup>-1</sup>)1654, 1546



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$^1\text{H}$  NMR-( $\delta$ )-2.2(s), (3H), NMe; 2.9(t), (4H); 3.5(t), (4H); 6.7(d), (1H), (CH=CHCO), J=15.70 HZ; 6.8(d), (1H), (CH=CHC<sub>6</sub>H<sub>5</sub>) J=15.70HZ; 7.3-7.4(m), (4H); 2.5 (s), (6H), NMe<sub>2</sub>.

Ij- IR (cm<sup>-1</sup>)1656, 1680, 2550

$^1\text{H}$  NMR-( $\delta$ )-2.2(s), (3H), NMe; 2.9(t), (4H); 3.5(t), (4H); 6.7(d), (1H), (CH=CHCO), J=15.70 HZ; 6.8(d), (1H), (CH=CHC<sub>6</sub>H<sub>5</sub>) J=15.70HZ; 7.3-7.4(m), (4H); 5.6 (s), (1H), OH.

### RESULT AND DISCUSSION

All synthesized novel cinnamamides compounds contained heterocyclic moiety in the form of N-methyl Piperazine. The Wittig reaction is an important method for the synthesis of alkenes. By using this method novel cinnamamides containing heterocyclic moiety entitled (2E)-1-(4-methylpiperazin-1-yl)-3-substituted phenylprop-2-en-1-one Cinnamamides are synthesized from different aromatic aldehydes and Wittig reagents having good yields. The yields of synthesized compounds were ranging from 54 to 78%. All synthesized compounds were characterized on the basis of melting point, elemental analysis, R<sub>f</sub> value, IR spectra and  $^1\text{H}$ NMR spectral analysis.

### REFERENCES

- (1) Han X. B. Feng H. J. Chen G. R. Li Y. C. Chin. J. Med. Chem., 2003, 13,334, 355.
- (2)Fatima Velez-Gonzalez, David Ortegon-Reyna, Angel A Ramos, ARKIVOC (v), 2008, 55-64.
- (3) Pathan R.U.andPatil S.L., Oriental Journal of Chemistry 2008, Vol 24(2), 709-712.
- (4) Gregory N. Beatch Cindy J. Longley, Michael J. Walker Richard A. Wall, mar 30, 2010, Patent No US7, 687, 536 B2, 1-36.
- (5) Yumei Xiao Yang BoLi Huizhu Yuan Shuqing Wan Yanjun Xu and Zhaohai Qin Molecules, 2008, 16, 8945-8957.
- (6) Brackman Gilles Celen Shari Hillaert Ulrik Calenbergh Serge Van Paul Cos Maes





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Louis Nelis Hans J Coenye Tom, PlosOne, 2011, 6, 1, 16084.

(7) [Wu L, Jin C, Sun X](#), [Biomacromolecules](#), 2011, 10; 12(1), 235-41.

(8) Kakwani Manoj D Desai Palsule Lele Arundhati C Ray Mukhtikant Rajan M G, Bioorganic & Medicinal Chemistry Letters, 2011, Vol 21, 6523–6526

(9) Wu Linbo Jin Chunli and Sun Xiangying., [Biomacromolecules](#), 2011, 12 (1), 235–241

(10) Jin Chunli Sun Xiangying Wu Linbo., [Designed Monomers & Polymers](#), 2011 Volume 14, 47-55(9).