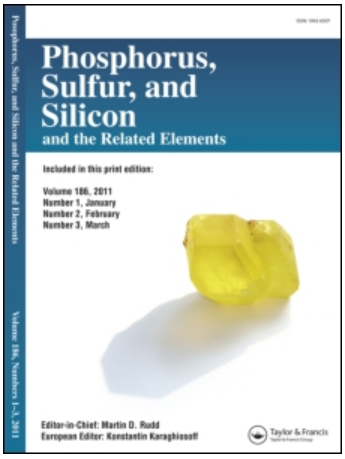



**Phosphorus, Sulfur, and Silicon and the Related Elements**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

# Mild and Ecofriendly Tandem Synthesis, and Spectral and Antimicrobial Studies of N¹-Acetyl-5-aryl-3-(substituted styryl)pyrazolines

Vijai N. Pathak[a]; Rahul Joshi[a]; Jaimala Sharma[a]; Neetu Gupta[a]; Vijay Mohan Rao[b]
[a] Centre of Advanced Studies, Department of Chemistry, University of Rajasthan, Jaipur, India [b] Department of Botany, University of Rajasthan, Jaipur, India

**To cite this Article** Pathak, Vijai N. , Joshi, Rahul , Sharma, Jaimala , Gupta, Neetu and Rao, Vijay Mohan(2009) 'Mild and Ecofriendly Tandem Synthesis, and Spectral and Antimicrobial Studies of N¹-Acetyl-5-aryl-3-(substituted styryl)pyrazolines', Phosphorus, Sulfur, and Silicon and the Related Elements, 184: 7, 1854 — 1865
**To link to this Article: DOI:** 10.1080/10426500802388318
**URL:** http://dx.doi.org/10.1080/10426500802388318

*Phosphorus, Sulfur, and Silicon*, 184:1854–1865, 2009

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500802388318

Taylor & Francis
Taylor & Francis Group

# Mild and Ecofriendly Tandem Synthesis, and Spectral and Antimicrobial Studies of $N^1$-Acetyl-5-aryl-3-(substituted styryl)pyrazolines

**Vijai N. Pathak,[1] Rahul Joshi,[1] Jaimala Sharma,[1] Neetu Gupta,[1] and Vijay Mohan Rao[2]**
[1]Centre of Advanced Studies, Department of Chemistry, University of Rajasthan, Jaipur, India
[2]Department of Botany, University of Rajasthan, Jaipur, India

*$N^1$-acetyl-5-aryl-3-(substituted styryl)pyrazolines were synthesized by the cyclocondensation of 1,5-substituted diphenyl-1,4-pentadien-3-ones with hydrazine hydrate and a cyclizing agent such as acetic acid in ethanol. The title compounds were synthesized using conventional and solvent-free approaches, which involves mechanochemical mixing, microwave-irradiation, and ultrasound-irradiation methods in the presence of a solid support. The synthesized compounds have been characterized by elemental analyses and spectral data (IR, PMR, and FAB-mass). All the synthesized compounds have been evaluated for their antibacterial and antifungal activities. Some compounds have shown promising biological activity.*

**Keywords** Bischalcones; microwave-irradiation; pyrazolines; ultrasound-irradiation



## INTRODUCTION

Pyrazoles[1] and allied derivatives are well-known, biologically important, nitrogen-containing heterocyclic compounds associated with various pharmacological activities such as COX-2 inhibiting,[2] antimicrobial,[3] antidepressant,[4] antinociceptive,[5] insecticidal,[6] antimycotic,[7] anti-inflammatory,[8] antibacterial,[9] antiandrogenic,[10] and antiamoebic.[11] A few nitrogen-containing five-membered heterocyclic

Received 13 February 2008; accepted 1 August 2008.
We express our sincere gratitude to Dr. K. P. Madhusunan, Deputy Director and Head, SAIF, Central Drug Research Institute (CDRI), Lucknow, India, for elemental analyses and spectral (IR, NMR, and FAB Mass) data. The authors are thankful to the coordinator of the Centre of Advanced Studies, Department of Chemistry, for providing chemicals. One of the authors (R. J.) is thankful to UGC, New Delhi, for financial support.

Address correspondence to Rahul Joshi, Centre of Advanced Studies, Department of Chemistry, University of Rajasthan, Jaipur 302004, India. E-mail: pathakvijain@yahoo.com

compounds are reported to have been used in the treatment of Parkinson's and Alzheimer's diseases and cerebral edema.[12,13]

Pyrazoles and their derivatives are known to act as antitubercular[14] and antitumor agents.[15] They also have a vasoconstrictor and vasodilator effect on hypoxia[15] and play the role of PR-antagonist.[17]

$\alpha$, $\beta$-Unsaturated carbonyl compounds (chalcones) have been used as synthons in the preparation of various biologically active compounds. Keeping these observations in view, we synthesized a number of bischalcones, and then these were condensed with hydrazine hydrate and phenyl hydrazine to give pyrazolines as biologically active molecules. In this method, hydrazone is formed as an intermediate, which is than cyclized to the corresponding pyrazolines in the presence of a suitable cyclizing agent such as glacial acetic acid.[18,19]

The title compounds have been synthesized using various techniques involving conventional and green chemistry routes, namely grindstone chemistry,[20] ultrasound,[21–26] and microwave chemistry.[27–29]

In the light of the above facts, we report in this article the synthesis of $N^1$-acetyl-5-aryl-3-(substituted styryl)pyrazolines from 1,5-substituted diphenyl-1,4-pentadien-3-ones. These compounds have been synthesized using all the above-mentioned procedures, and a comparative study has been done. Among the four methods used, the microwave irradiation procedure was found to be the best one due to higher yields, shorter reaction time, and enhanced selectivity.

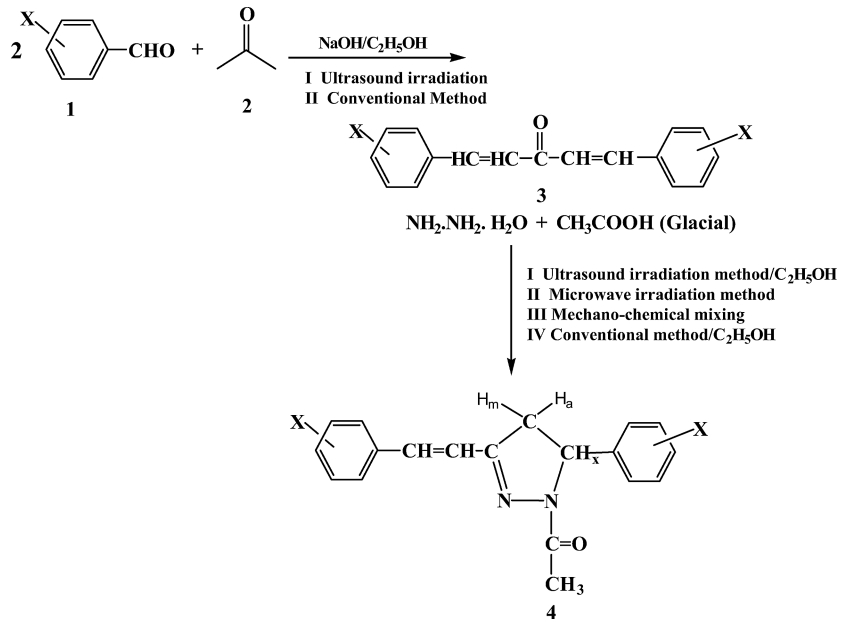
A few representative compounds were screened for their antibacterial and antifungal activity, and some of the compounds exhibited promising activity.



## RESULTS AND DISCUSSION

### Synthesis

1,5-Substituted diphenyl-1,4-pentadien-3-ones were synthesized by an aldol condensation with substituted benzaldehydes and acetone in a 2:1 ratio in the presence of ethanolic NaOH solution. This bischalcone **3** was subjected to hydrazone formation via cyclization reaction with hydrazine hydrate to give $N^1$-acetyl-5-aryl-3-(substituted styryl)pyrazolines **4**. This reaction takes place through the mediation of an appropriate $\alpha,\beta$ -unsaturated hydrazone, which immediately cyclizes to give a pyrazoline ring in the presence of a suitable cyclizing agent such as glacial acetic acid under refluxing or irradiation conditions (Scheme 1). $N^1$-acetyl-5-aryl-3-(substituted styryl) pyrazolines were synthesized by employing various reaction conditions. In




**SCHEME 1** X = H; 4–Cl; 4–$OCH_3$; 2–$OCH_3$; 3,4,5–$(OCH_3)_3$; 4F; 2–Cl; 3–F; 2F; 2,4–$(Cl)_2$.

the conventional process, the bischalcone **3**, hydrazine hydrate, and glacial acetic acid used as a cyclizing agent were dissolved in ethanol and refluxed for 10–30 h.

In contrast, under solvent-free conditions, the same reactants were ground together using a mortar and pestle to afford target compounds **4**, in higher yields and shorter reaction time. Under ultrasound-irradiation conditions, the same reactants were dissolved in a small quantity of ethanol, and the reaction mixture was sonochemically irradiated for 10–25 min. by using an ultrasonic bath. In the microwave-irradiation conditions, the reactant **3**, hydrazine hydrate, and a calculated amount of glacial acetic acid over $K_2CO_3$ were irradiated in a domestic microwave oven for 0.5–5 min. The results obtained are tabulated in Table I.

The physical, spectral, and analytical data of compounds (**4a–j**) are given in Tables II and III.

## EXPERIMENTAL

All melting points were determined in open glass capillary tubes and are uncorrected. The IR spectra ($\upsilon_{max}$ in $cm^{-1}$) were recorded

**TABLE I Results and Conditions for the Synthesis of $N^1$-Acetyl-5-aryl-3-(substituted styryl)pyrazolines (4)**

| | Yield (%) | | | | Time required | | | | Temp. (°C) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | i | ii | iii | iv | | |
| Compound | i | ii | iii | iv | min. | min. | min. | hrs. | i | ii |
| **4a** | 90 | 86 | 80 | 73 | 0.5 | 10 | 25 | 12 | 70 | 30 |
| **4b** | 91 | 87 | 78 | 70 | 2.5 | 12 | 25 | 14 | 50 | 30 |
| **4c** | 89 | 85 | 80 | 75 | 1.0 | 15 | 20 | 24 | 65 | 30 |
| **4d** | 84 | 80 | 73 | 68 | 0.8 | 20 | 35 | 24 | 60 | 30 |
| **4e** | 92 | 87 | 82 | 76 | 2.7 | 12 | 28 | 18 | 62 | 30 |
| **4f** | 94 | 91 | 80 | 75 | 2.9 | 22 | 30 | 25 | 70 | 30 |
| **4g** | 88 | 84 | 76 | 69 | 3.2 | 25 | 38 | 28 | 75 | 30 |
| **4h** | 90 | 78 | 70 | 64 | 3.0 | 22 | 36 | 24 | 68 | 30 |
| **4i** | 87 | 82 | 78 | 65 | 2.5 | 15 | 25 | 18 | 70 | 30 |
| **4j** | 79 | 76 | 70 | 63 | 3.0 | 25 | 35 | 15 | 55 | 30 |

i. By Microwave irradiation with $K_2CO_3$; reactions were carried out in a LG MS-194A domestic microwave oven with maximum 800W power.

ii. By ultrasound irradiation with ethanol; reactions were carried out in an ultrasonic bath Toshniwal SW-4,150W with ± 37 KHz output frequency.

iii. By mechano-chemical mixing with $Mg(HSO_4)_2$.

iv. By conventional method.



on a Shimadzu IR 435U-04 infrared spectrophotometer using potassium bromide pellets. PMR spectra were recorded on JEOL FX-90 Q (89.55Hz) spectrometer using $CDCl_3$ as a solvent. TMS was used as an internal standard (chemical shift in $\delta$ ppm). Mass spectra were recorded on Jeol SX-102 (FAB) mass spectrometer. The purity of compounds was

**TABLE II Physical Data of $N^1$-Acetyl-5-aryl-3-(substituted styryl)pyrazolines (4)**

| Compounds No. | X | Molecular Formula | Molecular Weight | Melting Point(°C) |
|---|---|---|---|---|
| **4a** | H | $C_{19}H_{18}N_2O$ | 290 | 76 |
| **4b** | 4-Cl | $C_{19}H_{16}Cl_2N_2O$ | 359 | 216 |
| **4c** | 4-$OCH_3$ | $C_{21}H_{22}N_2O_3$ | 350 | 167 |
| **4d** | 4-F | $C_{19}H_{16}F_2N_2O$ | 326 | 135 |
| **4e** | 2-Cl | $C_{19}H_{16}Cl_2N_2O$ | 359 | 192 |
| **4f** | 2,4-($Cl_2$) | $C_{19}H_{14}Cl_4N_2O$ | 428 | 231 |
| **4g** | 3-F | $C_{19}H_{16}F_2N_2O$ | 326 | 119 |
| **4h** | 2-$OCH_3$ | $C_{21}H_{22}N_2O_3$ | 350 | 147 |
| **4i** | 3,4,5-$(OCH_3)_3$ | $C_{25}H_{30}N_2O_7$ | 470 | 180 |
| **4j** | 2-F | $C_{19}H_{16}F_2N_2O$ | 326 | 95 |

**TABLE III Spectral and Analytical Data of N[1]-Acetyl-5-aryl-3-(substituted styryl)pyrazolines (4)**

| Compound | IR(KBr) $\upsilon_{max}(cm^{-1})$ | $^1$HNMR($CDCl_3$) (ppm) | Mass m/z | Found(Calcd.) (%) C | H | N |
|---|---|---|---|---|---|---|
| **4a** | 3020(aromatic C-Hstr.),2870 (aliphatic C-Hstr.), 1624(>C═Ostr.), 1610(>C═N str.), 1590(>C═C<), 985(trans C-H def.) | 2.37(s, $COCH_3$, 3H), 3.0 (dd, J = 17.37, 4.2, 1H,$CH_{2(pyraz.)}$ 3.6 (dd,J = 17.37, 11.7,1H,$CH_{2(pyraz.)}$ 5.5(dd,J = 11.7, 4.2, 1H,CH(pyraz), 6.6 (d, J = 8.1 Hz,1H,(CH═**CH**—C═N) ,7.0 (d, J = 8.1Hz , 1H ,(**CH**═CH—C═N) 6.6–7.5(m ,Ar-H, 8H) | 291 | 78.67 (78.62) | 6.15 (6.20) | 9.67 (9.65) |
| **4b** | 3050(aromatic C-Hstr.),2910 (aliphatic C-Hstr.), 1650(>C═Ostr.), 1630(>C═N str.), 1600(>C═C<), 987(trans C—H def.), 780(C—Clstr.) | 2.39(s, $COCH_3$, 3H), 2.9 (dd, J = 17.34, 4.5, 1H,$CH_{2(pyraz.)}$3.5 (dd,J = 17.34, 11.9,1H,$CH_{2(pyraz.)}$ 5.5(dd,J = 11.9, 4.5, 1H,CH(pyraz), 6.7 (d, J = 8.1 Hz,1H,(CH═CH—C═N), 7.0(d, J = 8.1Hz, 1H,(CH═CH—C═N) 6.6-7.5(m, Ar-H, 8H) | $^{358/362}$ isotopic cluster | 63.46 (63.50) | 4.47 (4.45) | 7.82 (7.79) |
| **4c** | 3030(aromatic C-Hstr.),2935 (aliphatic C-Hstr.), 1650(>C=Ostr.), 1585(>C═N str.), 1550(>C═C<), 970(trans C—H def.) 1190(C-Ostr.) | 2.34(s, $COCH_3$, 3H), 3.5 (dd, J = 17.32, 4.3, 1H,$CH_{2(pyraz.)}$ 3.8 (dd,J = 17.32, 11.7,1H,$CH_{2(pyraz.)}$ 5.5(dd,J = 11.7, 4.3, 1H,CH(pyraz) , 6.6 (d, J = 8.2 Hz,1H,(CH═CH—C═N), 6.9 (d, J = 8.2Hz, 1H,(CH═CH—C═N) 3.1( s, $(OCH_3)_2$, 6H), 6.6-7.5(m ,Ar-H, 8H)_ | — | 71.96 (72.00) | 6.30 (6.28) | 7.97 (8.00) |
| **4d** | 3025(aromatic C-Hstr.),2930 (aliphatic C-Hstr.), 1656(>C=Ostr.), 1600(>C═N str.), 1555(>C═C<), 955(trans C—H def.) 1040(C-Fstr.) | 2.35(s, $COCH_3$, 3H), 3.1 (dd, J = 11.8 , 4.5, 1H,$CH_{2(pyraz.)}$ 3.6 (dd,J = 11.8 , 8.76,1H,$CH_{2(pyraz.)}$ 5.6 (dd,J = 8.76, 4.5, 1H,CH(pyraz), 6.7–7.4 (m, Ar-H,8H & merged, 2H, ($-\overset{\beta}{C}H=\overset{\alpha}{C}H-C=N$) | — | 69.87 (69.93) | 4.85 (4.90) | 8.56 (8.58) |
| **4e** | 3045(aromatic C-Hstr.),2925 (aliphatic C-Hstr.), 1642(>C=Ostr.), 1620(>C═N str.), 1590(>C═C<), 982(trans C-H def.) 755 (C-Clstr.) | 2.41(s, $COCH_3$, 3H), 2.7 (dd, J = 17.20, 4.3, 1H,$CH_{2(pyraz.)}$ 3.8 (dd,J = 17.20, 11.6,1H,$CH_{2(pyraz.)}$ 5.4(dd,J = 11.6, 4.3, 1HCH(pyraz), 6.8-7.7 (m , Ar-H,8H & merged, 2H, ($-\overset{\beta}{C}H=\overset{\alpha}{C}H-C=N$) | — | 63.52 (63.50) | 4.49 (4.45) | 7.82 (7.79) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **4f** | 3070(aromatic C-Hstr.),2970 (aliphatic C-Hstr.), 1656(>C=Ostr.), 1665(>C=N str.), 1590(>C=C<), 950(trans C-H def.) 770(C-Clstr.) | 2.51(s, $COCH_3$, 3H), 2.9 (dd, J = 17.37, 5.1, 1H, $CH_{2(pyraz.)}$ 3.7 (dd,J = 17.37, 11.7,1H,$CH_{2(pyraz.)}$ 5.5 (dd,J = 11.7, 5.1, 1H,CH(pyraz), 6.9–7.8 (m, Ar-H,6H & merged, 2H, ($-\overset{\beta}{C}H=\overset{\alpha}{C}H-C=N$) | — | 53.20 (53.27) | 3.28 (3.27) | 6.59 (6.54) |
| **4g** | 3020(aromatic C-Hstr.),2925 (aliphatic C-Hstr.), 1650(>C=Ostr.), 1600(>C=N str.), 1550(>C=C<), 922(trans C-H def.) 1030(C-Fstr.) | 2.37(s, $COCH_3$, 3H), 2.8 (dd, J = 11.5, 4.4, 1H,$CH_{2(pyraz.)}$ 3.6 (dd,J = 11.5, 8.46,1H,$CH_{2(pyraz.)}$ 5.5 (dd,J = 8.46, 4.4, 1H,CH(pyraz), 6.6–7.4 (m , Ar-H,8H & merged, 2H, ($-\overset{\beta}{C}H=\overset{\alpha}{C}H-C=N$) | — | 69.82 (69.93) | 4.83 (4.90) | 8.52 (8.58) |
| **4h** | 3040(aromatic C-Hstr.),2915 (aliphatic C-Hstr.), 1660(>C=Ostr.), 1625(>C=N str.), 1610(>C=C<), 950(trans C—H def.),1140(C-Ostr.) | 2.42(s, $COCH_3$, 3H), 2.9 (dd, J = 17.37, 4.5, 1H,$CH_{2(pyraz.)}$ 3.5 (dd,J = 17.37, 11.5,1H,$CH_{2(pyraz.)}$ 5.7(dd,J = 11.5, 4.5, 1H,CH(pyraz), 6.8 (d, J = 8.2 Hz,1H,(CH=CH—C=N), 7.3 (d, J = 8.2Hz, 1H,(CH=CH—C=N) 3.8( s, $(OCH_3)_2$, 6H), 6.6–7.6 (m, Ar-H, 8H) | — | 71.96 (72.00) | 6.25 (6.28) | 7.94 (8.00) |
| **4i** | 3015(aromatic C-Hstr.),2930 (aliphatic C-Hstr.), 1654(>C=Ostr.), 1605(>C=N str.), 1560(>C=C<), 925(trans C-H def.),1135(C-Ostr.) | 2.39(s, $COCH_3$, 3H), 3.0 (dd, J = 17.19, 4.3, 1H,$CH_{2(pyraz.)}$ 3.6 (dd,J = 17.19, 11.9,1H,$CH_{2(pyraz.)}$ 5.5(dd,J = 11.9, 4.3, 1H,CH(pyraz), 6.3 (d, J = 8.2 Hz,1H,(CH=CH—C=N), 6.6 (d, J = 8.2Hz, 1H,(CH=CH—C=N) 3.8 (s, $(OCH3)_3$, 18H), 6.5–7.5 (m, Ar-H, 4H) | — | 63.79 (63.82) | 6.37 (6.38) | 5.93 (5.95) |
| **4j** | 3020(aromatic C-Hstr.),2920 (aliphatic C-Hstr.), 1645(>C=Ostr.), 1600(>C=N str.), 1550(>C=C<), 920(trans C-H def.) 1020(C-Fstr.) | 2.37(s, $COCH_3$, 3H), 2.6 (dd, J = 11.4, 4.4, 1H,$CH_{2(pyraz.)}$ 3.3 (dd, J = 11.4, 8.46,1H,$CH_{2(pyraz.)}$ 5.4 (dd, J = 8.46, 4.4, 1H,CH(pyraz), 6.5–7.4 (m, Ar-H,8H & merged, 2H, ($-\overset{\beta}{C}H=\overset{\alpha}{C}H-C=N$) | — | 69.90 (69.93) | 4.82 (4.90) | 8.50 (8.58) |

checked by TLC using silica gel-G as an adsorbent and UV light– or iodine-accomplished visualization. The microwave-assisted reactions were carried out in domestic MW oven (LG MS-194 A) with 800 W and the ultrasound-assisted reactions were carried out in an ultrasonic bath (Toshniwal SW-4) operating at 37 KHz output frequency.

1,5-substituted diphenyl-1,4-pentadien-3-ones **3** and $N^1$-acetyl-5-aryl-3-(substituted styryl)pyrazolines **4** were synthesized by the following routes.

## 1,5-Substituted diphenyl-1,4-pentadien-3-ones (3a–j)

Various 1,5-substituted diphenyl-1,4-pentadien-3-ones were prepared by a method on the literature method (conventional).[30]

### *Ultrasound-Irradiation Method*

A mixture of substituted benzaldehydes (5 mmol), acetone (2.5 mmol, 0.14 g), and ground sodium hydroxide pellets (0.5 g) was placed in a conical flask. Ethanol (5 mL) was added, and the conical flask was covered with porous parafilm. This reaction mixture was introduced under ultrasonic waves at 12°C for 10–15 min. using an ultrasonic bath to afford the substituted bischalcones. This reaction mixture was neutralized by pouring into ice cold 2N HCl. The solid was suction-filtered, washed with water, dried, and recrystallized from rectified spirit to afford the substituted bischalcones.



### *Microwave-Irradiation Method*

1,5-Substituted diphenyl-1,4-pentadien-3-one **3** could not be synthesized by using this method, due to the low boiling point of acetone (56°C).

## $N^1$-Acetyl-5-aryl-3-(substituted styryl)pyrazolines 4(a–j)

### *Ultrasound-Irradiation Method*

A mixture of ground 1,5-substituted diphenyl-1,4-pentadien-3-one **3** (2 mmol), hydrazine hydrate (16%, 1 mL), and glacial acetic acid (1 mL) was dissolved in ethanol (15 mL) in a conical flask (250 mL). The conical flask was covered with porous parafilm. This reaction mixture was introduced under ultrasonic waves at 30°C for 5–25 min. (indicated in Table I). After completion of the reaction, the alcohol was removed, and the resultant residue was neutralized by pouring into ice cold $NaHCO_3$ solution. The resultant solid was suction filtered, washed with water, dried, and recrystallized from benzene.

### *Microwave-Assisted Solvent-Free Synthesis*

A mixture of ground 1,5-substituted diphenyl-1,4-pentadien-3-one **3** (2 mmol), hydrazine hydrate (16%, 1 mL), and glacial acetic acid (1 mL) impregnated on potassium carbonate as a solid support were placed in a conical flask (250 mL), and this reaction mixture was irradiated inside a microwave oven at 800 W for a few minutes (indicated in Table I). After completion of the reaction, benzene was added to it. The mixture was filtered, benzene was removed, and the resultant residue was neutralized by pouring into ice cold $NaHCO_3$ solution. The product was suction-filtered, washed with water, dried, and recrystallized from benzene. The catalyst left as a residue during filtration was washed 2–3 times with hot benzene and dried in vacuum for reuse.



### *Mechano-Chemical Mixing (Solvent-Free Synthesis)*

A mixture of 1,5-substituted diphenyl-1,4-pentadien-3-one **3** (2mmol), hydrazine hydrate (16%, 1 mL), $Mg(HSO_4)_2$ (0.3g), and glacial acetic acid (1 mL) were ground together in a mortar using a pestle. An orangish-colored tacky solid was obtained in 10–30 min. (indicated in Table I). The reaction proceeds exothermically, as indicated by a rise in temperature of 12–15°C. After completion of the reaction, the reaction mixture was neutralized by pouring into $NaHCO_3$ solution. The product was collected by filtration, washed with water, dried, and recrystallized from benzene.

### *Conventional Method*

A solution of 1,5-substituted diphenyl-1,4-pentadien-3-one **3** (2 mmol), hydrazine hydrate (16%, 1 mL), and glacial acetic acid (1 mL) in ethanol was refluxed for 12–30 h. The reaction progress was monitored by TLC. The reaction mixture was kept overnight at room temperature. The reaction mixture was neutralized by pouring into ice cold $NaHCO_3$ solution. The resulting solid was suction-filtered, washed with water, dried, and recrystallized from benzene.

All the synthesized compounds along with their characteristics data are given in Table II.

The comparative yields by all the four methods *viz* ultrasound-irradiation, microwave-assisted, mechano-chemical, and conventional are given in the Table I.

The structure of the synthesized compounds **(4a–j)** was confirmed by their IR, $^1$H NMR, and FAB mass spectral analysis.

**TABLE IV Antibacterial Activity of $N^1$-Acetyl-5-aryl-3-(substituted styryl)pyrazolines (4)**

| | Mean value of Area of inhibition in mm 1000 ppm IZ(IA) | | Mean value of Area of inhibition in mm 800 ppm IZ(IA) | | Mean value of Area of inhibition in mm 400 ppm IZ(IA) | | Mean value of Area of inhibition in mm 200 ppm IZ(IA) | |
|---|---|---|---|---|---|---|---|---|
| Compounds | *E.coli* | *B.subtilis* | *E.coli* | *B.subtilis* | *E.coli* | *B.subtilis* | *E.coli* | *B.subtilis* |
| Streptomycin | 8.2 | 6.0 | 8.0 | 5.8 | 7.6 | 5.4 | 6.6 | 4.4 |
| **4a** | 14.0 | 6.6 | 12.0 | 5.5 | 9.0 | 4.7 | 5.4 | 2.2 |
| | (1.70) | (1.10) | (1.50) | (0.94) | (1.18) | (0.86) | (0.81) | (0.52) |
| **4b** | 27.6 | 6.1 | 25.0 | 5.0 | 20.0 | 4.4 | 14.0 | 2.7 |
| | (3.36) | (1.02) | (3.12) | (0.87) | (2.63) | (0.81) | (2.12) | (0.61) |
| **4c** | 13.6 | 5.2 | 12.0 | 4.6 | 9.2 | 3.7 | 7.4 | 1.8 |
| | (1.65) | (0.86) | (1.50) | (0.78) | (1.21 ) | (0.67) | (1.12) | (0.40) |
| **4d** | 10.0 | 3.1 | 8.0 | 2.5 | 7.1 | 2.0 | 5.9 | 1.10 |
| | (1.21) | (0.51) | (0.97) | (0.42) | (0.93) | (0.39) | (0.89) | (0.25) |
| **4e** | 33.3 | 6.1 | 30.0 | 5.7 | 26.0 | 5.0 | 20.0 | 2.0 |
| | (4.06) | (1.02) | (3.75) | (0.98) | (3.42) | (0.96) | (3.03) | (0.45) |
| **4f** | 27.0 | 4.3 | 24.0 | 3.9 | 20.0 | 2.7 | 15.0 | 2.7 |
| | (3.29) | (0.71) | (3.0) | (0.67) | (2.63) | (0.51) | (2.27) | (0.61) |
| **4g** | 38.0 | 7.5 | 29.4 | 6.3 | 24.4 | 6.1 | 18.0 | 3.2 |
| | (4.63) | (1.10) | (3.67) | (0.94) | (3.21) | (0.86) | (2.72) | (0.52) |
| **4h** | 9.0 | 5.9 | 7.6 | 4.3 | 7.0 | 2.9 | 5.2 | 1.8 |
| | (1.09) | (1.10) | (0.95) | (0.74) | (0.92) | (0.55) | (0.78) | (0.52) |
| **4i** | 40.0 | 6.6 | 33.0 | 5.5 | 31.0 | 4.7 | 24.0 | 2.2 |
| | (4.87) | (1.10) | (4.12) | (0.94) | (4.07) | (0.86) | (3.63) | (0.52) |
| **4j** | 9.4 | 6.1 | 8.0 | 5.0 | 7.2 | 4.4 | 6.0 | 2.7 |
| | (1.14) | (1.02) | (1.0 ) | (0.87) | (0.94) | (0.81) | (0.90) | (0.61) |

IZ = Inhibition area (zone) excluding diameter of disc.
IA = Activity Index = inhibition area of sample/inhibition area of standard.

**TABLE V Antifungal Activity of $N^1$-Acetyl-5-aryl-3-(substituted styryl)pyrazolines (4)**

| | Mean value of Area of inhibition in mm 1000 ppm IZ(IA) | | Mean value of Area of inhibition in mm 800 ppm IZ(IA) | | Mean value of Area of inhibition in mm 400 ppm IZ(IA) | | Mean value of Area of inhibition in mm 200 ppm IZ(IA) | |
|---|---|---|---|---|---|---|---|---|
| Compounds | *C.albicans* | *T.rubrum* | *C.albicans* | *T.rubrum* | *C.albicans* | *T.rubrum* | *C.albicans* | *T.rubrum* |
| Griseofulvin | 1.0 | 23.0 | 0.8 | 22.5 | 0.76 | 21.6 | 0.66 | 18.7 |
| **4a** | 0.94 | 26.4 | 0.67 | 20.0 | 0.59 | 15.5 | 0.54 | 11.4 |
| | (0.94) | (1.14) | (0.83) | (0.88) | (0.77) | (0.72) | (0.81) | (0.61) |
| **4b** | 1.0 | 38.4 | 0.74 | 23.6 | 0.68 | 17.9 | 0.51 | 15.0 |
| | ( 1.0 ) | (1.65) | (0.92) | (1.04) | (0.89) | (0.83) | (0.77) | (0.80) |
| **4c** | 1.44 | 17.6 | 1.08 | 15.9 | 0.98 | 12.5 | 0.69 | 8.2 |
| | (1.44) | (0.76) | (1.35) | (0.71) | (1.28) | (0.58) | (1.06) | (0.44) |
| **4d** | 1.40 | 23.4 | 1.0 | 22.0 | 0.92 | 21.8 | 0.46 | 13.9 |
| | (1.40) | (1.01) | (1.25) | (0.98) | (1.20) | (1.0 ) | (0.71 ) | (0.74) |
| **4e** | 0.78 | 26.0 | 0.56 | 24.2 | 0.49 | 18.5 | 0.36 | 14.6 |
| | (0.78) | (1.13) | (0.70) | (1.07) | (0.64) | (0.86) | (0.54) | (0.78) |
| **4f** | 1.30 | 29.6 | 0.96 | 26.4 | 0.80 | 23.2 | 0.56 | 17.2 |
| | ( 1.3 ) | (1.28) | (1.20) | (1.17) | (1.05) | (0.83) | (0.84) | (0.92) |
| **4g** | 0.70 | 16.5 | 0.50 | 15.4 | 0.41 | 11.4 | 0.28 | 9.0 |
| | (0.70) | (0.71) | (0.62) | (0.68) | (0.53) | (0.52) | (0.42) | (0.48) |
| **4h** | 2.30 | 41.6 | 1.70 | 38.4 | 1.54 | 22.7 | 0.94 | 17.9 |
| | (2.30) | (1.80) | (2.12) | (1.70) | (2.02) | (1.05) | (1.42) | (0.95) |
| **4i** | 0.80 | 17.4 | 0.70 | 14.3 | 0.55 | 12.3 | 0.40 | 9.0 |
| | (0.80) | (0.75) | (0.87) | (0.63) | (0.72) | (0.57) | (0.60) | (0.48) |
| **4j** | 0.70 | 35.3 | 0.55 | 28.1 | 0.43 | 20.3 | 0.30 | 11.9 |
| | (0.70) | (1.53) | (0.68) | (1.25) | (0.56) | (0.94) | (0.45) | (0.64) |

IZ = Inhibition area (zone) excluding diameter of disc.
IA = Activity Index = inhibition area of sample/inhibition area of standard.

## Antimicrobial Activity

All the representative compounds were screened for their antimicrobial activity against the gram-negative bacteria *Escherichia coli*; gram-positive bacteria *Bacillus subtilis*; fungi *Candida albicans*, a diploid sexual fungus[31]; and *Trichophyton rubrum*, a causative agent of dermatophytosis,[32] which may cause infection in immunocomprised hosts[33] at different concentrations by disc diffusion method.[34] Streptomycin and Griseofulvin were used as standard drugs for evaluating antibacterial and antifungal activities, respectively. Compounds **4b**, **4f**, and **4i** showed enhanced antibacterial and antifungal activity at 200 ppm, 400 ppm, 800 ppm, and 1000 ppm due to the presence of chlorine and methoxy moieties attached with the pyrazole ring. Compounds **4f** and **4i** showed very effective antibacterial compared to the other compounds. The results obtained are presented in Tables IV and V.



## REFERENCES

[1] S.M. Landge, A. Schmidt, V. Outerbridge, and B. Török, *Synlett*, 1600 (2007).
[2] R. Garg , A. Kurup , S. B. Mekapati, and C. Hansch, *Chem. Rev.*, **103,** 703 (2003).
[3] S. S. Kargaokar, P. H. Patel, M. J. Shah, and H. H. Parekh, *Indian J. Pharmacol.*, **58**(6), 222 (1996).
[4] E. Palaska , M. Aytemin , T. Uzbay, and D. Erol , *Eur. J. Med. Chem.*, **36,** 539 (2001).
[5] A. Shafiee, M. Bagheri, M. Shekarchi, and M. Abdollahi, *J. Pharmaceut Sci.*, **6**(3), 360 (2003).
[6] S. Kristopher, *M. Pesticides Biochem. Physiology*, **81**(2), 136 (2005).
[7] J. Matysiak and A. Niewiadomy, *Bioorg. Med. Chem.*, **11**(10), 2285 (2003).
[8] F. Flora, M. Hanna, and S. Adel, *Bioorg. Med. Chem.*, **14**(11), 3927 (2006).
[9] S. Shinde, W. Jadhav, R. Pawar, and S. Bhusare, *J. Chinese Chem.Soc.*, **51,** 775 (2004).
[10] G. Amr Ael, N. A. Abdel-Latif, and M.M. Abdalla, *Bioorg. Med.Chem.*, **14**(2), 373 (2006).
[11] M. Abid and A. Azam, *Eur. J. Med. Chem.*, **40**(9), 935 (2005).
[12] G. Ucar, N. Gokhan, A. Yesilada, and A.A. Bilgin, *Neurosci. Lett.*, **382**(3), 327 (2005).
[13] H. Yamashita, K. Okumaura, H. Luzika, and N. Ohto, *Eur. Pat.*, 22691 (1989).
[14] P. T. Chovatia, J. D. Akabari, P. K. Kachhadia, P. D. Zalavadia, and H. S. Joshi, *J. Serb. Chem. Soc.*, **71**(7), 713 (2007).
[15] V. Zsoldos Mady, A. Csampai, R. Szabo, E. Meszaros Alapi, J. Pasztor, F. Hudecz, and P. Sohar, *Chem. Med. Chem.*, **1**(10), 1119 (2006).
[16] R. M. Wadsworth, *Trends in Pharmacol. Sci.*, **15**(2), 47 (1994).
[17] D. G. Jones, X. Liang, E. L. Stewart, R. A. Noe, L. S. Kallander, K. P. Madauss, S. P. Williams, S. K. Thompson, D. W. Gray, and W. J. Hoekstra, *Bioorg. Med. Chem. Lett.*, **15**(13), 3203 (2005).
[18] K. Vounauwers, *Ber. Dt. Chem. Ges.*, **41,** 4230 (1908).
[19] A. Baker and V.S. Butt, *J. Chem. Soc.*, 2142 (1949).
[20] F. Toda, Ed., *Topics in Current Chemistry, Vol. 254: Organic Solid State Reactions*, (Springer, Berlin, 2005), and references cited therein.

[21] S. Kenneth and J. Gareth, *Annu. Rev. Mater. Sci*., **29,** 295 (1999).
[22] P. Mingos and D. R. Baghurst, *Chem. Soc. Rev*., **20,** 1 (1991).
[23] C. Einhorn, J. Einhorn, M. J. Dickens, and J. L. Luche, *Tetrahedron Lett*., **31,** 4129 (1990).
[24] J. L. Luche, Ed., *Synthetic Organic Sonochemistry* (Wiley-VCH, Weinheim, Germany, 2005).
[25] T. J. Mason, *Sonochemistry* (Oxford University Press, Oxford, UK, 2000).
[26] B. Török, K. Balázsik, K. Felföldi, and M. Bartók, *Ultrasonics Sonochem.*, **8,** 191 (2001).
[27] S. Varma, *Green Chemistry*, **1,** 43 (1999).
[28] A. Loupy, *Microwave in Organic Synthesis* (Wiley-VCH, Weinheim, Germany, 2005).
[29] C.O. Kappe and A. Stadler, *Microwave in Organic and Medicinal Chemistry* (Wiley-VCH, Weinheim, Germany (2005).
[30] P. N. Rao, *Indian J. Pharma. Sci.*, **51**(5), 207 (1989).
[31] K. J. Ryan, C. G. Ray, Eds., *Sherris Medical Microbiology*, 4th ed. (McGraw, New York, 2004).
[32] R. Arenas, J. Dominguez-Cherrit, and L. M. Fernandez, *Int. J. Dern.*, **34**(2), 138 (1995).
[33] R. F. Squeo, R. Beer, D. Silver, I. Weitzman, and M. Grossman, *Am. Acad. Dermatol.*, **39,** 379 (1998).
[34] R. Cruickshank, *Medicinal Microbiology II*, 12th ed. (Churchill Livingstone, Edinburgh, UK, 1975).