# MICROWAVE INDUCED SYNTHESIS AND ANTI MICROBIAL ACTIVITIES OF SOME [3-(2-HYDROXYPHENYL)-5-ARYL-2-PYRAZOLINYL]-4-THIAZOLIDENONES

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**Abstract:** A series of new [3-(2-hydroxyphenyl)-5-aryl-2-pyrazolinyl]-4-thiazolidenones (4a-g.) has been prepared by microwave irradiation technique. O-hydroxy chalcones (1) were treated with hydrazine hydrate to afford corresponding pyrazolines (2) which were treated with chloro-acetyl chloride and ammonium thiocynate to afford the title compounds. All the transformations were carried out under MWI. The synthesized compounds were screened for their antimicrobial activity in vitro.

**Key words**: Microwave, chalcone, 3, 5-diaryl pyrazolines, pyrazoline thiazolidenones.

## Introduction

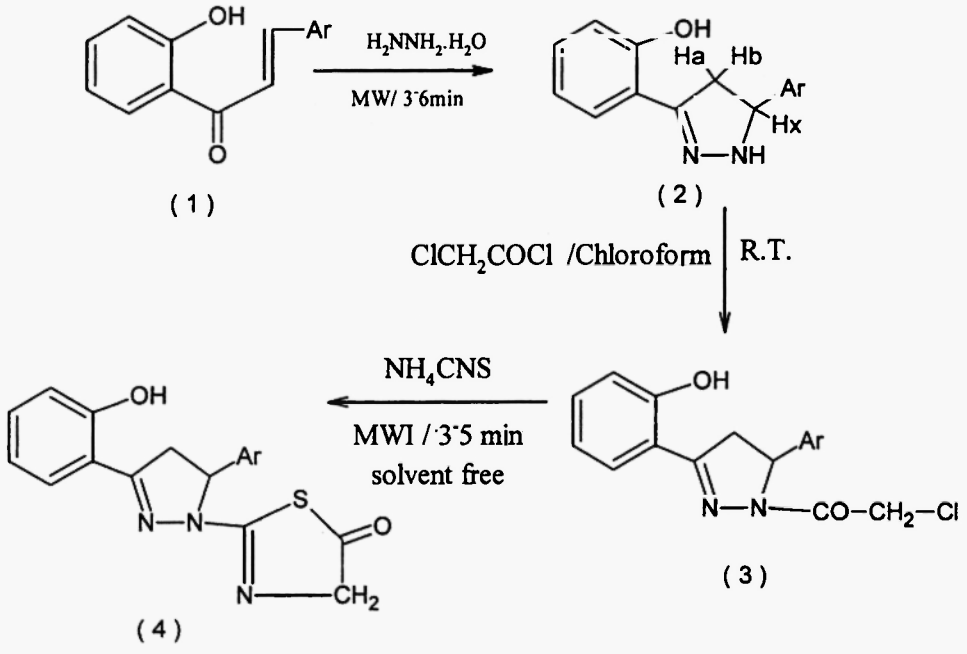
The literature survey reveals the importance of chalcones [1-3] as a valuable starting material for the synthesis of heterocycles like pyrazolines, pyrazoles, pyrimidines, isoxazolines etc. Pyrazolines are known to possess bactericidal[4], fungicidal[5], and insecticidal[6] properties. Thiazolidenone derivatives are also reported to possess various pharmacological activities such as antibacterial[7-8] antifungal[9], anticonvulsant[10-11] and anticancer[12] activity.

Microwave assisted transformations have gained momentum in recent years. Organic synthesis under microwave irradiation has significant advantages over conventional heating methods [13-15]. Instantaneous "in core" heating of the material in a highly effective and selective manner, lesser reaction time and cleaner products are the major advantages of microwave heating in contrast to conventional methods[16]. It can be termed as e-chemistry because it is easy, economic, effective, eco-friendly and is believed to be a step ahead towards green chemistry.

Keeping in view the above facts and continuation of our work on application of microwave irradiation for synthesis of heterocycles, it was thought worth while to

synthesize some new thiazolidenone derivatives incorporating pyrazoline moiety using microwave irradiation.

The reaction of o-hydroxy chalcones (1) with hydrazine hydrate under solvent free microwave irradiation condition was carried out to afford corresponding 3-(2-hydroxy phenyl)-5-aryl-2- pyrazoline (2). Compounds (2) were treated with chloroacetyl chloride at room temperature to get intermediate $N^1$-chloro acetyl-3, 5- diaryl-2- pyrazolines (3). Compound (3) were treated with ammonium thiocynate under solvent free conditions using microwave irradiation to afford the thiazolidenones (4) in 80-85 % yield (Scheme-1)




**Scheme-1**

The structure of the synthesized compounds was confirmed on the basis of their elemental and spectral analysis. The IR spectra of compounds (4) gave absorption bands at 3420 $cm^{-1}$ (-OH), 1650 $cm^{-1}$ (>C=O) and 1594-1460 $cm^{-1}$ (combined vibration of C=N and N-N of pyrazoline and thiazolidenone rings). 1H-NMR spectra of compounds (4) showed the presence of ABX pattern of pyrazolines ring Double doublet were observed at δ 3.29, 3.82 and 5.45 for $H_A$, $H_B$ and Hx proton respectively. A singlet at δ-3.60 was observed for methylene protons of -CO-$CH_2$

group of thiazolidenone ring. The aromatic proton gave multiplate at δ-6.45-7.44 and a singlet for O-H proton was observed at δ 6.44. The mass spectra of these compounds gave the base peak corresponding to their molecular masses.

**Anti bacterial activity**

The newly synthesized thiazolidenones were screened for their antibacterial activity in vitro against *E.coli, S.aureus, S, albus, K.pneumonae* and *P. vulgaris* using amicacin as standard drugs. The zone of inhibition was measured in mm. Moderate to good antibacterial activity was observed for these compounds. (Table-2)

**Experimental**

All the reaction were carried out in domestic microwave oven (Samsung M 1630, frequency 2450 MHz, output 1200watts) using borosil glassware. All the melting points reported are uncorrected and were taken in open capillaries. The progress of reaction and purity of the products was checked by TLC using silica gel-G plates using Chloroform-ethyl acetate (9:1) as eluent. The IR spectra (KBr √ max $cm^{-1}$) were taken on a Perkin-Elmer spectrometer. The $^1H$ NMR spectra were recorded on Brucker –DRX 300 MHz spectrometer using $CDCl_3$ as solvent (chemical shift in δ ppm). Mass spectra (FAB) were taken on Jeol-SX-102 mass spectrometer using m-nitro benzyl alcohol as matrix. The matrix peaks were observed at m/z 107,136,154 289 and 307.

The required O-hydroxy chalcone (1a-g) and 3, 5 diaryl-2-pyrazolines (2a-g) were prepared under microwave irradiation by the reported methods[17].

**General Procedure for the Synthesis of $N^1$-chloro acetyl-3-(2-hydroxy phenyl)-5-aryl-2-pyrazolines (3a-g.)**

To a solution of 3-(2-hydroxy phenyl)-5-aryl-2-pyrazolines (0.01mole) in chloroform (20 ml) was added freshly prepared chloro acetyl chloride (0.01mole) with stirring. After complete addition the reaction mixture was further stirred at room temperature for 30 minutes. The separated solid was filtered and crystallized from ethanol to get (3a-g) in 85-90% yield. (Table-1)

**Table-1** : Physical data of compounds (3a-g) and (4a-g)

| Compd | Ar | Molecular formula Molecular weight | M.P.°C | Reaction time min | % yield | % N | |
|---|---|---|---|---|---|---|---|
| | | | | | | Calculated | found |
| 3a | Phenyl | $C_{17}H_{15}O_2N_2Cl$ (314.5) | 164 | 4.0 | 80 | 8.90 | 8.79 |
| 3b | 4-Methoxyphenyl | $C_{18}H_{17}O_2N_3Cl$ (344.5) | 183 | 3.5 | 85 | 8.12 | 8.10 |
| 3c | 3,4-Dimethoxyphenyl | $C_{19}H_{19}O_4N_2Cl$ (374.5) | 148 | 4.0 | 86 | 7.47 | 7.5 |
| 3d | 3,4,5-Trimethoxyphenyl | $C_{20}H_{21}O_5N_2Cl$ (404.5) | 204 | 4.5 | 85 | 6.92 | 6.87 |
| 3e | 4-Chlorophenyl | $C_{17}H_{14}O_2N_2Cl_2$ (349) | 192 | 3.0 | 86 | 8.02 | 7.88 |
| 3f | 4,5 Dimethylaminophenyl | $C_{19}H_{20}O_2N_3Cl$ (357.5) | 184 | 3.5 | 83 | 11.74 | 11.61 |
| 3g | 4-hydroxyphenyl | $C_{15}H_{13}O_3N_2Cl$ (304.5) | 140 | 4.0 | 80 | 9.19 | 9.10 |
| 4a | Phenyl | $C_{18}H_{15}O_3N_2S$ (337) | 178 | 4.5 | 80 | 12.4 | 12.32 |
| 4b | 4-Methoxyphenyl | $C_{19}H_{17}O_3N_3S$ (367) | 168 | 5.0 | 83 | 11.4 | 11.3 |
| 4c | 3,4-Dimethoxyphenyl | $C_{20}H_{19}O_4N_3S$ (397) | 158 | 5.0 | 82 | 10.5 | 10.55 |
| 4d | 3,4,5-Trimethoxyphenyl | $C_{21}H_{21}O_5N_3S$ (427) | 176 | 6.0 | 85 | 9.33 | 9.61 |
| 4e | 4-Chlorophenyl | $C_{18}H_{14}O_2N_3SCl$(371.5) | 140 | 4.0 | 85 | 11.3 | 11.0 |
| 4f | 4,5Dimethylaminophenyl | $C_{20}H_{20}O_2N_3S$ (380) | 174 | 4.0 | 84 | 14.73 | 14.61 |
| 4g | 4-hydroxyphenyl | $C_{18}H_{15}O_3N_3S$ (353) | 278 | 5.0 | 80 | 11.9 | 12.01 |

**Table-2** : Antibacterial activity of synthesized compounds (4a-g)

| S.No. | Compound | Zone of inhibition in mm. | | | | |
|---|---|---|---|---|---|---|
| | | *S. aureus* | *S. albus* | *E. coli* | *K. pneumoniae* | *P. vulgaris* |
| 1 | 3a | 08 | 08 | 09 | 10 | 08 |
| 2 | 3b | 14 | 18 | 10 | 14 | 11 |
| 3 | 3c | 16 | 18 | 10 | 14 | 10 |
| 4 | 3d | 15 | 20 | 13 | 18 | 09 |
| 5 | 3e | 18 | 16 | 10 | 14 | 14 |
| 6 | 3f | 12 | 18 | 12 | 09 | 12 |
| 7 | 3g | 16 | 16 | 10 | 12 | 18 |
| Amicacin | | 22 | 24 | 14 | 20 | 22 |

**Synthesis of 3-(2-hydroxy phenyl)-5-aryl-2-pyrazolinyl -4-thiazolidenones (4a-g)**

An intimate mixture of compound (3) (0.01mole) and $NH_4CNS$ (0.02mole) was prepared in DMF (5 ml). The mixture was dried in air and dried residue was subjected to microwave irradiation for 3-5 minutes. After completion of reaction as indicated by TLC the residue was extracted with ethanol. The separated solid was

filtered, washed with water and crystallized from benzene-petroleum ether (40°-60°) to afford (4a-g) in 80-85 %yield. (Scheme-1)

**3-(2-Hydroxy phenyl)-5-phenyl-2-pyrazolinyl -4-thiazolidenone, 4a**

IR (KBr) 3429, 2945, 1661, 1596, 1455

**3-(2-Hydroxy phenyl)-5-(4-methoxy phenyl)-2-pyrazolinyl -4-thiazolidenone, 4b**

IR(KBr) 3390 2934 1696 1613 1514, 1492; $^1$H NMR ($CDCl_3$) δ-1.57 (s,$OCH_3$), 3.36 (dd, $H_A$), 3.86 (dd, $H_B$), 5.54 (dd,Hx), 3.29 ( s, $OCH_2$ ); FAB.M.S: m/z (368, 367, 341)

**3-(2-Hydroxy phenyl)-5-(3,4-dimethoxy phenyl)-2-pyrazolinyl -4-thiazolidenone, 4c**

IR(KBr) 3427, 2936, 1658, 1594, 1460.

**3-(2-Hydroxy phenyl)-5-(3, 4, 5-trimethoxy phenyl)-2-pyrazolinyl -4-thiazolidenone, 4d**

**IR(KBr)** 3428, 2940, 1660, 1590, 1462; $^1$H NMR ($CDCl_3$) δ-1.60 (S,$OCH_3$), 3.31 (dd, $H_A$), 3.81 (dd, $H_B$), 5.47 (dd,Hx), 3.95 ( S, $OCH_2$ ). FAB.M.S: m/z (427, 405, 327).

**3-(2-Hydroxy phenyl)-5-(4-chloro phenyl)-2-pyrazolinyl -4-thiazolidenone, 4e**

IR (KBr) 3233, 2933, 1675, 1596, 1490; $^1$H NMR ($CDCl_3$) δ-3.25 (dd, $H_A$), 3.86 (dd, $H_B$), 5.51 (dd,Hx), 3.94 ( S, $OCH_2$ ); FAB.M.S: m/z 372, 371, 349, 345.

**3-(2-Hydroxy phenyl)-5-(4-dimethylamino-phenyl)-2-pyrazolinyl -4-thiazolidenone, 4f**

IR(KBr) 3402, 2928, 1638, 1594, 1445; $^1$H NMR ($CDCl_3$) δ-1.56 (S,2 $CH_3$), 3.38 (dd, $H_A$), 3.87 (dd, $H_B$), 5.46 (dd,Hx), 4.33( S, -$OCH_2$ -); FAB.M.S: m/z 380, 379, 354.

**3-(2-Hydroxy phenyl)-5-(4-hydroxyphenyl)-2-pyrazolinyl -4-thiazolidenone, 4g**

IR (KBr) 3430, 2940, 1668, 1616, 1598, 1568, 1517, 1490, 1423

## Conclusion

In above synthetic scheme we use microwave irradiation technique, this is a solvent free reaction condition that leads to considerable saving in the reaction time and energetically profitable. The solvent free condition contributes to saving in cost and diminishes the waste disposal problem. Some compounds have shown potential antibacterial activity

## Acknowledgment

The authors are highly thankful Dr.B.L.Verma Retd. Professor of Chemistry, M.L. Sukhadia University, Udaipur for valuable suggestion and guidance. Thanks are also due to Dr. K.P.Madhusudhan, Director SAIF, CDRI, Lucknow for spectral analysis.

## References

1. J. Russel and Clarke H, *J. Am. Chem. Soc.* 613651 (1939).
2. B. S. Dawane, Y.B. Vibhute, V. P. Chavan, A. S. Mane and M .S. Shingare, Korean, *J. Med. Chem.* **10**(2), 78 (2000).
3. S. Akila, S. Selvi and K. Balasubramanian, *Tetrahedron*, **57**, (60), 3465 (2001).
4. H. Z. Katri and S. A. Vunil, *J. Ind. Chem. Soc.* **58**,168 (1961).
5. S. N.Thore, D. B. Shinde and M. S. Shangare, *Orient J. Chem.* **11**, 2 (1995).
6. S. G. Roelofvan, C. Arnold and Wellvngak, *J. Agric. Food. Chem.* **27**, 406 (1979).
7. B. K. Garnaik and R. K. Behra, *Indian J .Chem.* **27B**, 1157 (1988).
8. E. V. Vladzimivskaya, O. T. Novikevich and O.G. Demchuk, Farm Zh. (Kiev) **6**, 67 (1991).
9. R. Lakhan, and R. L. Singh, *J. Agricl. Food. Chem.* **39 (3)**, 580 (1991).
10. S. H. El-Feky and Abd.El Samii, Z K, Arch Pharma (Weinheim) **324**, 381 (1991).
11. S. H. El-Feky, Pharmazie, **48**, 894 (1993).
12. S. Grasso A. Chimirri, P. Monforte, G. Fenech, and M. Zappala, *Farmaco.*, **41(12)**, 713 (1986).
13. R. N. Gedey, F. E. Smith and K. C. Westaway, *Can. J. Chem.* **66**, 17 (1988).
14. R. S. Verma, T. B. Lamiture and M. Verma, *Tetrahedron Lett.* **34**, 3029 (1993).
15. S. Caddick, *Tetrahedron*, **51**, 10403 (1995).
16. R. S. Verma, *Green Chemistry*, **43** (1999).
17. N. S. Rao, "Microwave assisted Synthesis of some chalcone derivatives" Ph.D. Thesis" M L Sukhadia University, Udaipur 2006.

Received April 7, 2007