

HETEROCYCLES, Vol. 68, No. 6, 2006, pp. 1209 - 1215. © The Japan Institute of Heterocyclic Chemistry  
Received, 14th February, 2006, Accepted, 14th April, 2006, Published online, 18th April, 2006. COM-06-10701

## MICROWAVE-PROMOTED AROMATIZATION OF 1,3,5-TRISUBSTITUTED 4,5-DIHYDRO-1H-PYRAZOLES BY CALCIUM HYPOCHLORITE UNDER SOLVENT-FREE CONDITIONS

Davood Azarifar\* and Azadeh Gharshasbi

Department of Chemistry, School of Science, Bu-Ali-Sina University, Hamadan,  
Postal code 65174, Iran

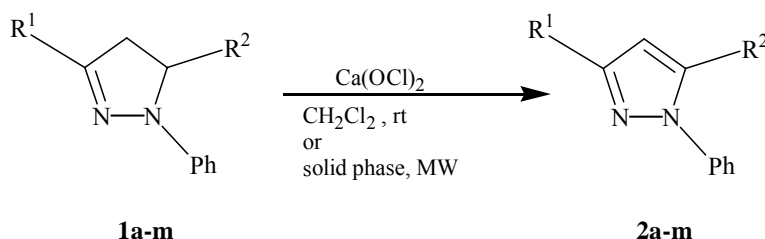
\*Corresponding author; Fax: +98-811-8272404, e-mail: [azarifar@basu.ac.ir](mailto:azarifar@basu.ac.ir)

**Abstract** - An efficient microwave-promoted aromatization of 1,3,5-trisubstituted 4,5-dihydro-1H-pyrazoles using calcium hypochlorite [Ca(OCl)<sub>2</sub>] has been reported. The reaction proceeds very fast to give pyrazoles in good yields on irradiation of a mixture of the dihydropyrazole and Ca(OCl)<sub>2</sub> on alumina without using solvent.

Application of microwave irradiation technique has received much attention in organic synthesis because it requires short reaction times and provides simplicity in handling, enhanced reaction yields, and high-purity products.<sup>1</sup> This is evidenced by a considerable research publications and reviews appeared during the last few decades.<sup>2</sup> Five- and six-membered heterocyclic compounds are important constituents that often exist in biologically active natural products and synthetic compounds of medicinal interest.<sup>3</sup> Among them, 1,3,5-trisubstituted 2-pyrazolines and the corresponding pyrazoles have attracted attention in recent years because of their various biological activities.<sup>4-9</sup> In this regard, the oxidative aromatization of pyrazolines to the corresponding pyrazoles is, therefore, of considerable importance in medicinal chemistry.<sup>10</sup> However, the aromatization of pyrazolines has not been extensively studied so far. For this oxidative conversion of pyrazolines, a limited number of reports existed in the literature which include use of cobalt soap of fatty acids,<sup>11</sup> lead tetraacetate,<sup>12</sup> manganese dioxide,<sup>13</sup> mercury oxide,<sup>14</sup> potassium permanganate,<sup>15,16</sup> silver nitrate,<sup>17</sup> iodobenzene diacetate,<sup>18</sup> and zirconium nitrate.<sup>19</sup> Most of these suffer from the use of excess reagent, longer reaction time, higher temperature, acidity of the reaction media, formation of by-products and toxicity of transition metal cations required like Co(II), Pb(IV), Hg(II), Mn(IV and VII), Ag(I), Zr(IV). To avoid these problems, we have previously reported the oxidative aromatization of several 2-pyrazolines into the corresponding pyrazoles by using readily accessible oxidants, such as trichloroisocyanuric acid,<sup>20,21</sup> 1,3-dibromo-5,5-dimethylhydantoin (DBH),<sup>22,23</sup> *N*-bromo-sulphonamides,<sup>24,25</sup> silica-supported *N*-bromosuccinimide,<sup>26</sup> and 4-(4-chlorophenyl)-1,2,4-triazole-3,5-

dione.<sup>27</sup>

In continuation of our search for other convenient oxidizing reagents, herein, we report a simple and efficient procedure for the preparation of pyrazoles (**2a-m**) by oxidative aromatization of 1,3,5-trisubstituted 4,5-dihydro-1*H*-pyrazoles (**1a-m**) on alumina without solvent using calcium hypochlorite [Ca(OCl)<sub>2</sub>] under microwave irradiated conditions (Scheme 1).



Scheme 1

Thus, various substituted 2-pyrazolines were prepared according to our previously reported procedure.<sup>8</sup> We first examined the oxidation of these 2-pyrazolines (**1a-m**) with Ca(OCl)<sub>2</sub> in CH<sub>2</sub>Cl<sub>2</sub>. The reaction proceeded facilely at rt within 4.5 h to give the corresponding yields in high yields (Table 1, CH<sub>2</sub>Cl<sub>2</sub>). We found that the same reaction also took place under solvent-free conditions in much shorter reaction time in better yields by microwave irradiation (Table 1, Microwave). As shown, all the reactions proceeded in shorter reaction times (10-20 min) and high yields (85-98%) when the mixture of the pyrazolines and Ca(OCl)<sub>2</sub> on alumina was irradiated under solvent-free conditions. Most of the products were obtained in high purity (> 95% by <sup>1</sup>H NMR) after usual work-up and were further purified using silica gel column chromatography or by recrystallization for analysis. All the products were characterized on the basis of their <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR, and mass spectra and elemental analysis.

**Table 1.** Oxidative Aromatization of 1,3,5-Trisubstituted 2-Pyrazolines (**1a-m**) in CH<sub>2</sub>Cl<sub>2</sub> and under Solvent-Free Microwave-Irradiated Conditions.

| Substrate <sup>a</sup> | Product | R <sup>1</sup>                                   | R <sup>2</sup>   | CH <sub>2</sub> Cl <sub>2</sub> |             |                           | Microwave                       |             |                           |
|------------------------|---------|--|--|---------------------------------|-------------|---------------------------|---------------------------------|-------------|---------------------------|
|                        |         |  |  | Ca(OCl) <sub>2</sub><br>(equiv) | Time<br>(h) | Yield <sup>b</sup><br>(%) | Ca(OCl) <sub>2</sub><br>(equiv) | Time<br>(h) | Yield <sup>b</sup><br>(%) |
| 1a                     | 2a      | 3-Thienyl  | 4-ClC <sub>6</sub> H <sub>4</sub>                                | 3                               | 1           | 83                        | 1                               | 0.17        | 98                        |
| 1b                     | 2b      | 3-Thienyl  | Ph   | 5                               | 4           | 75                        | 3.5                             | 0.17        | 90                        |
| 1c                     | 2c      | 3-Thienyl  | 4-(CH <sub>3</sub> ) <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> | 8                               | 2.25        | 88                        | 2                               | 0.33        | 95                        |
| 1d                     | 2d      | 2-Thienyl  | 4-ClC <sub>6</sub> H <sub>4</sub>                                | 3                               | 1           | 80                        | 1                               | 0.17        | 97                        |
| 1e                     | 2e      | 2-Thienyl  | Ph   | 5                               | 4.5         | 78                        | 3.5                             | 0.17        | 92                        |
| 1f                     | 2f      | 2-Thienyl  | 4-(CH <sub>3</sub> ) <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> | 8                               | 2.25        | 85                        | 2                               | 0.33        | 88                        |
| 1g                     | 2g      | 2-Thienyl  | 1-Naphthyl   | 3                               | 2           | 85                        | 1                               | 0.2         | 98                        |
| 1h                     | 2h      | 2-Naphthyl                                       | 3-Thienyl  | 3                               | 2           | 73                        | 1                               | 0.2         | 94                        |
| 1i                     | 2i      | Ph   | 4-(CH <sub>3</sub> ) <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> | 3                               | 4           | 78                        | 1                               | 0.2         | 85                        |
| 1j                     | 2j      | 2-Naphthyl                                       | 2-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>                  | 5                               | 3           | 75                        | 2.75                            | 0.17        | 96                        |
| 1k                     | 2k      | 2-Naphthyl                                       | 4-ClC <sub>6</sub> H <sub>4</sub>                                | 3                               | 1           | 82                        | 1                               | 0.17        | 94                        |
| 1l                     | 2l      | 4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> | Ph   | 5                               | 2.5         | 75                        | 2.5                             | 0.17        | 87                        |
| 1m                     | 2m      | 4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>  | 4-(CH <sub>3</sub> ) <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> | 4                               | 3.5         | 80                        | 2.5                             | 0.17        | 98                        |

<sup>a</sup> 2-Pyrazolines were prepared according to the literature<sup>8</sup> and characterized by IR, 1H-NMR and by direct comparison with authentic materials. <sup>b</sup> Isolated yields.

The advantages of the present protocol compared to our previously reported methods<sup>20-27</sup> are safe, inexpensive, mild, short reaction time, high reaction yield and environmentally benign.

In conclusion, a practical and efficient microwave-assisted aromatization of 1,3,5-trisubstituted 2-pyrazolines has been developed using  $\text{Ca}(\text{OCl})_2$  under solvent-free condition which afforded the corresponding pyrazoles in shorter reaction times in good yields.

## EXPERIMENTAL

IR spectra were recorded using a Shimadzu 435-U-04 spectrophotometer (KBr pellets) and NMR spectra were obtained using 90 MHz JEOL FT NMR spectrometer. The microanalyses was carried out in Iranian Petroleum Research Center (Ray city, Tehran, Iran). All 2-pyrazolines were prepared according to our previously reported procedure.<sup>6</sup> Microwave-assisted reactions were conducted in a commercial Panasonic model NNS59BH microwave oven.

### Oxidation of 1,3,5-Trisubstituted 2-Pyrazolines with $\text{Ca}(\text{OCl})_2$

*General Procedure in  $\text{CH}_2\text{Cl}_2$  at rt:* A suspension of calcium hypochlorite, pyrazoline (**1a-m**) (2 mmol) (the molar ratios of  $\text{Ca}(\text{OCl})_2$  to the substrate (**1a-m**) are given in Table 2), and  $\text{CH}_2\text{Cl}_2$  (10 mL) were stirred vigorously at rt. The progress of the reactions was monitored by TLC. The reactions completed in 1.0 - 4.5 h (Table 2). After the reactions have completed, dry silica gel (1g) was added to the reaction mixture, the solid materials were removed by filtration and washed with  $\text{CH}_2\text{Cl}_2$  (10 mL). The solvent was then evaporated to leave the solid product which was further purified by flash chromatography on silica gel using acetone / petroleum ether (1:5) as an eluent to give high purity pyrazoles (**2a-m**) in 73-88% yields.

*General Procedure for solvent-free and microwave irradiation condition:* Calcium hypochlorite (the molar ratios of  $\text{Ca}(\text{OCl})_2$  to the substrate (**1a-m**) are given in Table 2) was thoroughly mixed with pyrazoline (**1a-m**) (2 mmol), and the mixture was placed in an alumina bath inside a MW oven and irradiated (900 W) for 0.17-0.33 h in the solid state. After complete conversion of the substrate (TLC), the resulting mixture was dissolved in  $\text{CH}_2\text{Cl}_2$  (20 mL), filtered off and the filtrate was then evaporated under reduced pressure to yield pyrazolines (**2a-m**) in 85-98% yields (Table 2). Where necessary, flash chromatography on silica gel using acetone/petroleum ether (1:5) as an eluent was employed to obtain high purity product. All the 2-pyrazoles were characterized on the basis of their IR,  $^1\text{H}$  NMR, and  $^{13}\text{C}$  NMR spectral and micro-analytical data as indicated bellow.

**5-(4-Chlorophenyl)-1-phenyl-3-(3-thienyl)pyrazole (2a):** Yield: 98%; yellow solid; mp 145-148 °C (recrystallization from EtOH). IR (KBr): 1591, 1490, 1400, 1356, 968, 832  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (90 MHz,

CDCl<sub>3</sub>)  $\delta$  ppm 7.15-8.05 (m, 12H, ArH), 6.85 (s, 1H, pyrazole). <sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 149.50 (C=N), 138.83, 136.22, 133.42, 132.84 (C<sub>arom</sub>), 132.35, 131.03, 130.65, 129.21, 126.27, 124.98, 123.51, 121.32 (CH<sub>arom</sub>), 96.50 (C5 in pyrazole), 95.12 (C4 in pyrazole). Anal. Calcd for C<sub>19</sub>H<sub>13</sub>N<sub>2</sub>SCl: C 67.76; H, 3.86; N, 8.32. Found: C 67.72; H, 3.83; N, 8.28.

**1,5-Diphenyl-3-(3-thienyl)pyrazole (2b):** Yield: 90%; yellow solid; mp 138-140 °C. IR (KBr): 1587, 1488, 1402, 1357, 969, 769 cm<sup>-1</sup>. <sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 7.25-8.08 (m, 13H, ArH), 7.05 (s, 1H, pyrazole). <sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 150.12 (C=N), 137.16, 134.93, 133.87 (C<sub>arom</sub>), 132.12, 131.34, 130.70, 129.13, 128.50, 126.88, 125.48, 123.64, 121.26 (CH<sub>arom</sub>), 103.12 (C5 in pyrazole), 99.36 (C4 in pyrazole). Anal. Calcd for C<sub>19</sub>H<sub>14</sub>N<sub>2</sub>S: C 75.49; H, 4.63; N, 9.27. Found: C 75.32; H, 4.53; N, 9.18.

**5-(4-Dimethylaminophenyl)-1-phenyl-(3-thienyl)pyrazole (2c):** Yield: 95%; yellow solid; mp 120-123 °C. IR (KBr): 1604, 1504, 1402, 1325, 980, 827 cm<sup>-1</sup>. <sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 6.99-7.58 (m, 12H, ArH), 6.95 (s, 1H, pyrazole), 2.82 (s, 6H, NMe<sub>2</sub>). <sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 151.24 (C=N), 148.09, 144.23, 142.53, 139.65 (C<sub>arom</sub>), 130.14, 129.82, 128.94, 128.09, 127.12, 126.06, 125.10, 124.32 (CH<sub>arom</sub>), 111.34 (C5 in pyrazole), 106.82 (C4 in pyrazole), 42.12 (NMe<sub>2</sub>). Anal. Calcd for C<sub>21</sub>H<sub>19</sub>N<sub>3</sub>S: C 73.04; H, 5.51; N, 12.17. Found: C 72.95; H, 5.48; N, 12.04.

**5-(4-Chlorophenyl)-1-phenyl-3-(2-thienyl)pyrazole (2d):** Yield: 97%; yellow solid; mp 135-138 °C. IR (KBr): 1572, 1491, 1467, 1371, 969, 829 cm<sup>-1</sup>. <sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 6.99-7.69 (m, 12H, ArH), 6.90 (s, 1H, pyrazole). <sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 150.17 (C=N), 137.64, 136.53, 135.37, 133.20, (C<sub>arom</sub>), 132.45, 132.02, 130.65, 129.36, 125.63, 124.75, 123.27, 122.06 (CH<sub>arom</sub>), 96.98 (C5 in pyrazole), 96.01 (C4 in pyrazole). Anal. Calcd for C<sub>19</sub>H<sub>13</sub>N<sub>2</sub>SCl: C 67.76; H, 3.86; N, 8.32. Found: C 67.68; H, 3.82; N, 8.28.

**1,5-Diphenyl-3-(2-thienyl)pyrazole (2e):** Yield: 92%; yellow solid; mp 118-120 °C. IR (KBr): 1580, 1495, 1452, 1353, 960, 833 cm<sup>-1</sup>. <sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 7.00-7.90 (m, 13H, ArH), 6.85 (s, 1H, pyrazole). <sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 150.53 (C=N), 139.38, 136.31, 134.15 (C<sub>arom</sub>), 132.69, 132.02, 130.86, 129.82, 128.30, 126.29, 125.06, 123.94, 122.64 (CH<sub>arom</sub>), 110.22 (C5 in pyrazole), 100.14 (C4 in pyrazole). Anal. Calcd for C<sub>19</sub>H<sub>14</sub>N<sub>2</sub>S: C 75.49; H, 4.63; N, 9.27. Found: C 75.68; H, 4.58; N, 9.12.

**5-(4-Dimethylaminophenyl)-1-phenyl-(2-thienyl)pyrazole (2f):** Yield: 88%; yellow solid; mp 112-115 °C. IR (KBr): 1604, 1488, 1461, 1377, 921, 828 cm<sup>-1</sup>. <sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 7.06-7.59 (m, 12H, ArH), 6.90 (s, 1H, pyrazole), 2.88 (s, 6H, NMe<sub>2</sub>). <sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 150.54 (C=N), 148.98, 147.73, 145.47, 142.48 (C<sub>arom</sub>), 133.59, 131.84, 130.10, 129.17, 128.67, 127.02, 126.66, 125.73 (CH<sub>arom</sub>), 114.27 (C5 in pyrazole), 109.83 (C4 in pyrazole), 42.84 (NMe<sub>2</sub>). Anal. Calcd for C<sub>21</sub>H<sub>19</sub>N<sub>3</sub>S: C 73.04; H, 5.51; N, 12.17. Found: C 72.95; H, 5.38; N, 12.14.

**5-(1-Naphthyl)-1-phenyl-3-(2-thienyl)pyrazole (2g):** Yield: 98%; yellow solid; mp 115-118 °C. IR (KBr): 1598, 1490, 1444, 1338, 973, 812  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.00-7.89 (m, 15H, ArH), 6.77 (s, 1H, pyrazole).  $^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 150.68 (C=N), 139.56, 139.16, 138.18, 136.57, 134.91 ( $\text{C}_{\text{arom}}$ ), 133.17, 132.45, 132.24, 131.03, 130.65, 129.21, 126.27, 124.98, 124.35, 123.51, 123.96, 121.32 ( $\text{CH}_{\text{arom}}$ ), 115.31 (C5 in pyrazole), 112.77 (C4 in pyrazole). Anal. Calcd for  $\text{C}_{23}\text{H}_{16}\text{N}_2\text{S}$ : C 78.41; H, 4.54; N, 7.95. Found: C 78.45; H, 4.43; N, 7.92.

**3-(2-Naphthyl)-1-phenyl-5-(3-thienyl)pyrazole (2h):** Yield: 94%; yellow solid; mp 128-132 °C. IR (KBr): 1590, 1493, 1439, 1375, 964, 815  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.14-8.54 (m, 15H, ArH), 7.04 (s, 1H, pyrazole).  $^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 150.34 (C=N), 139.16, 138.18, 136.57, 134.91, 134.50 ( $\text{C}_{\text{arom}}$ ), 134.23, 133.98, 133.59, 131.84, 130.10, 129.17, 128.67, 127.02, 126.66, 125.73, 125.13, 124.75 ( $\text{CH}_{\text{arom}}$ ), 107.32 (C5 in pyrazole), 99.12 (C4 in pyrazole). Anal. Calcd for  $\text{C}_{23}\text{H}_{16}\text{N}_2\text{S}$ : C 78.41; H, 4.54; N, 7.95. Found: C 78.21; H, 4.24; N, 7.85.

**5-(4-Dimethylaminophenyl)-1,3-diphenylpyrazole (2i):** Yield: 85%; yellow solid; mp 68-71 °C. IR (KBr): 1538, 1506, 1456, 1329, 971, 772  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.07-7.56 (m, 15H, ArH), 6.93 (s, 1H, pyrazole), 2.86 (s, 6H,  $\text{NMe}_2$ ).  $^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 151.53 (C=N), 142.33, 140.51, 138.61, 134.29 ( $\text{C}_{\text{arom}}$ ), 129.20, 127.02, 126.41, 125.72, 124.81, 122.42, 121.61, 120.35 ( $\text{CH}_{\text{arom}}$ ), 102.12 (C5 in pyrazole), 95.14 (C4 in pyrazole), 42.26 ( $\text{NMe}_2$ ). Anal. Calcd for  $\text{C}_{23}\text{H}_{21}\text{N}_3$ : C 81.42; H, 6.19; N, 12.39. Found: C 81.38; H, 6.12; N, 12.35.

**3-(2-Naphthyl)-1-phenyl-5-(2-methylphenyl)pyrazole (2j):** Yield: 96%; yellow solid; mp 149-152 °C (Lit.,<sup>20</sup> mp 151-152 °C).

**5-(4-Chlorophenyl)-3-(2-naphthyl)-1-phenylpyrazole (2k):** Yield: 94%; yellow solid; mp 128-130 °C (Lit.,<sup>20</sup> mp 130-133 °C).

**3-(4-Methoxyphenyl)-1,5-diphenylpyrazole (2l):** Yield: 87%; yellow solid; mp 74-76 °C (Lit.,<sup>20</sup> mp 75-77 °C).

**5-(Dimethylaminophenyl)-1-phenyl-3-(4-methylphenyl)pyrazole (2m):** Yield: 98%; yellow solid; mp 118-120 °C. IR (KBr): 1600, 1520, 1440, 1370, 990, 773  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.18-7.75 (m, 13H, ArH), 7.10 (s, 1H, pyrazole), 2.85 (s, 6H,  $\text{NMe}_2$ ), 2.68 (s, 3H, Me).  $^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 151.45 (C=N), 165.80, 143.92, 142.28, 136.22, 132.07 ( $\text{C}_{\text{arom}}$ ), 128.92, 128.09, 127.99, 127.12, 126.06, 125.10, 124.32 ( $\text{CH}_{\text{arom}}$ ), 111.24 (C4 in pyrazole), 107.12 (C5 in pyrazole), 41.83 ( $\text{NMe}_2$ ), 19.62 ( $\text{CH}_3$ ). Anal. Calcd for  $\text{C}_{24}\text{H}_{23}\text{N}_3$ : C 81.59; H, 6.51; N, 11.90. Found: C 81.55; H, 6.45; N, 11.78.

## ACKNOWLEDGMENT

We wish to thank the University of Bu-Ali Sina, Hamadan, Iran, for financial support to carry out this

research.

## REFERENCES

1. A. Loupy, A. Petit, J. Hamelin, F. Texier-Boullet, P. Jacquault, and D. Mathe, *Synthesis*, 1998, 1213.
2. (a) S. Caddick, *Tetrahedron*, 1995, **52**, 1403. (b) R. S. Varma, "Microwave-Assisted Reactions under Solvent-Free 'Dry' Conditions" in *Microwaves: Theory and Application in Material Processing*, V. Cark, D. Sutton, and W. Lewis, Eds; American Ceramic Society, Ceramic Transactions 1997, pp 357-65. (c) R. S. Varma, *Green Chem.*, 1999, **1**, 43. (d) G. Majetich and R. Hicks, *J. Microwave Power Electromagn. Energy*, 1995, **30**, 27. (e) R. Gupta, A. K. Gupta, S. Paul, and P. Kachroo, *Ind. J. Chem.*, 1995, **34B**, 151.
3. T. L. Gilchrist, *Heterocyclic Chemistry*, 3<sup>rd</sup> ed.; Addison-Wesley Longman, Ltd.; England, 1998. (b) D. Lednicner, *Strategies for Organic Drugs Synthesis and Design*; Willey & Sons; New York, 1998; chapters 8 and 9.
4. S. G. Roelf Van, C. Arnold, and K. Wellnga, *J. Agric. Food Chem.*, 1979, **84**, 406.
5. G. H. Keats, *Brit. Pat.*, Oct. 21, 1970, **1**, 209, 631.
6. A. Singh, S. Rathod, B. N. Berad, S. D. Patil, and A. G. Dosh, *Orient. J. Chem.*, 2000, **16**, 315.
7. H. Z. Katri and S. A. Vunii, *J. Ind. Chem. Soc.*, 1981, **58**, 168.
8. D. Azarifar and M. Shaebanzadeh, *Moleclues*, 2002, **7**, 885.
9. D. Azarifar and H. Ghasemnejad, *Molecules*, 2003, **8**, 642.
10. (a) E. Takabata, R. Kodama, Y. Tanaka, R. Dohmori, H. Tachizawa, and T. Naita, *Chem. Pharm. Bull.*, 1979, **16**, 1900. (b) S. S. Parmar, B. R. Pandy, C. Dwivedi, and R. D. Harbison, *J. Pharm. Sci.*, 1974, **63**, 1152. (c) T. Godfrained, R. Miller, and M. Wibo, *Pharmacol. Rev.*, 1986, **38**, 321. (d) P. Mager, R. A. Coburn, A. J. Solo, D. J. Triggle, and H. Rothe, *Drug Des. Discovery*, 1992, **8**, 273.
11. J. N. Shah and C. K. Shah, *J. Org. Chem.*, 1978, **43**, 1266.
12. W. A. F. Gladstone and R. O. C. Norman, *J. Chem. Soc., Chem. Commun.*, 1966, 1536.
13. I. Bhanthnagar and M. V. George, *Tetrahedron*, 1968, **24**, 1293.
14. K. Auwers and P. Heimke, *Liebigs Ann.*, 1927, **458**, 186.
15. L. I. Smith and K. L. Howard, *J. Am. Chem. Soc.*, 1943, **65**, 159.
16. F. Strauss, C. Muffat, and W. Heitz, *Ber. Dtsch. Chem. Ges.*, 1918, **51**, 1457.
17. R. P. Dodwadmath and T. S. Wheeler, *Proc. Ind. Acad. Sci.*, 1935, **2A**, 438.
18. S. P. Singh, D. Kumar, O. Prakash, and R. P. Kapoor, *Synth. Commun.*, 1997, **27**, 2683.
19. G. Sabitha, G. S. K. Reddy, C. S. Reddy, N. Fatima, and J. S. Yadav, *Synthesis*, 2003, 1267.

20. M. A. Zolfigol, D. Azarifar, and B. Maleki, *Tetrahedron Lett.*, 2004, **45**, 2181.
21. D. Azarifar and B. Maleki, *J. Chin. Chem. Soc.*, 2004, **51**, 1373.
22. D. Azarifar, M. A. Zolfigol, and B. Maleki, *Bull. Korean Chem. Soc.*, 2004, **25**, 23.
23. D. Azarifar, M. A. Zolfigol, and B. Maleki, *Synthesis*, 2004, 1744.
24. R. Ghorbani-Vaghei, D. Azarifar, and B. Maleki, *Bull. Korean Chem. Soc.*, 2004, **25**, 953.
25. R. Ghorbani-Vaghei, D. Azarifar, A. Khazaei, and B. Maleki, *Phosphorus, Sulfur, Silicon*, 2004, **179**, 1877.
26. D. Azarifar and B. Maleki, *Heterocycles*, 2005, **65**, 865.
27. M. A. Zolfigol, D. Azarifar, S. Mallakpour, I. Mohammadpour-Baltork, A. Forghaniha, B. Maleki, and M. Abdollahi-Alibeik, *Tetrahedron Lett.*, 2006, **47**, 833.