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## OLD REAGENT, NEW RESULTS: AROMATIZATION OF HANTZSCH 1,4-DIHYDROPYRIDINES WITH SUPPORTED BISMUTH NITRATE UNDER MICROWAVE IRRADIATION IN SOLVENTLESS SYSTEM

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*Hantzsch 1,4-dihydropyridines were rapidly and efficiently oxidized using bismuth nitrate supported onto silica gel under microwave irradiation.*

**Keywords:** Aromatization; bismuth nitrate; Hantzsch; microwave irradiation; solventless system

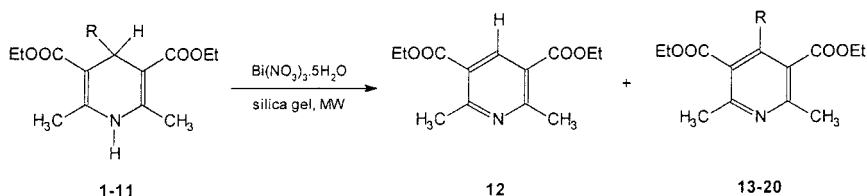
One of the most widely used synthesis of pyridines is that discovered by Hantzsch in 1882.<sup>1</sup> In this reaction, an aldehyde, ammonia, and  $\alpha,\beta$ -keto ester are condensed to afford 1,4-dihydropyridine, which is consequently oxidized to the pyridine. Since then, aromatization of Hantzsch 1,4-dihydropyridines (1,4-DHP) has attracted considerable attention, and several oxidizing agents and variety of methods have been reported in the literature.<sup>2</sup>

Recently, bismuth compounds have become attractive candidates for use as reagents in organic synthesis because most bismuth compounds are relatively nontoxic, readily available, inexpensive, and fairly insensitive to small amounts of water.<sup>3</sup> The biochemistry,<sup>4</sup> toxicology,<sup>5</sup> and environmental effects of bismuth compounds have been well documented and show that they are attractive candidates for use in green chemistry.

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Bismuth nitrate pentahydrate has been used recently as a convenient reagent for the oxidation of Hantzsch 1,4-dihydropyridines.<sup>7</sup> In spite of all advantages of the bismuth compound, this method suffers from one or the other disadvantages like long reaction time, that is 14 h in cases of taking **1a** (R=H), use of acetic acid as a solvent, moderate yields, and difficulties in isolation of products.

The reagent impregnated on solid supports, especially that are efficient in dry media<sup>8</sup> have gained popularity in organic synthesis because of their selectivity and ease of manipulation. During the course of the study of organic reactions in solvent free condition,<sup>9</sup> we have observed the usefulness of microwave irradiation in enhancing of the reaction.<sup>10</sup> In connection with these observations, we became interested in developing a rapid and environmentally friendly condition to effect 1,4-dihydropyridine to pyridine conversion under microwave irradiation in solventless system. Our initial attempts to induce oxidation of the simple Hantzsch 1,4-dihydropyridine as a test case with **1** (R=H) and bismuth nitrate without solvent under microwave irradiation was not very promising as considerable amounts of (R=H) was recovered unchanged even after relatively long reaction period, that is 10 min. However, when the reagent was supported onto an equal amount of silica gel and mixed with **1** (R=H), the oxidation was performed rapidly (in 2 min) and efficiently under microwave irradiation to afford **12** (Scheme 1). To establish the generality of the method a variety of 1,4-dihydropyridines **1–11** were oxidized under similar reaction conditions (Table I). It is noteworthy that the oxidation of 1,4-dihydropyridine with secondary alkyl and benzylic groups (entries **3**, **4**) at 4 position was accompanied by expulsion of these groups to afford **12** while in other case the substituted groups at 4 position were retained in the pyridine ring to give **13–20** (Table I).



**SCHEME 1**

In conclusion, a new expeditious, rapid, mild, and eco-friendly method for oxidation of 1,4-dihydropyridines has been developed that may find wide application in organic synthesis.

**TABLE I** Oxidation of 1,4-Dihydropyridines (**1–11**) with Bismuth Nitrate Supported onto Silica Gel Under Microwave Irradiation

Entry	R	Reaction time (sec)	Product	m.p. (°C)	m.p. <sup>(Lit)</sup> (°C)	Yield (%)
<b>1</b>	H	120	<b>12</b>	68–69	69–70 <sup>11</sup>	88
<b>2</b>	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub>	120	<b>13</b>	oil	oil <sup>11</sup>	55
<b>3</b>	(CH <sub>3</sub> ) <sub>2</sub> CH	120	<b>12</b>	68–69	69–70 <sup>11</sup>	89
<b>4</b>	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	120	<b>12</b>	68–69	69–70 <sup>11</sup>	92
<b>5</b>	C <sub>6</sub> H <sub>5</sub>	120	<b>14</b>	61–62	62–63 <sup>11</sup>	93
<b>6</b>	4-Cl-C <sub>6</sub> H <sub>4</sub>	120	<b>15</b>	66–67	66–67 <sup>11</sup>	91
<b>7</b>	2-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	120	<b>16</b>	74–75	75 <sup>12</sup>	85
<b>8</b>	3-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	120	<b>17</b>	62–63	61–63 <sup>11</sup>	88
<b>9</b>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	120	<b>18</b>	114–115	114–116 <sup>11</sup>	89
<b>10</b>	4-CH <sub>3</sub> O-C <sub>6</sub> H <sub>4</sub>	120	<b>19</b>	49–50	50 <sup>13</sup>	92
<b>11</b>	2-furyl	120	<b>20</b>	oil	oil <sup>12</sup>	88

<sup>a</sup>Yields refer to isolated products.

## EXPERIMENTAL SECTION

All of the dihydropyridines were prepared in the same manner, using the appropriate aldehyde, ammonia, and ethyl acetoacetate. All products were known and identified by comparison of their physical and spectroscopic data with those of authentic samples. All of the oxidations were carried out in the same manner. Silica gel 60 for column chromatography purchased from Merck was used as a solid support.

### Oxidation of Dihydropyridines

#### General Procedure

Bismuth nitrate pentahydrate (0.5 g, 1 mmol) was mixed with silica gel (0.5 g). The appropriate Hantzsch 1,2-dihydropyridine was added to the above supported reagent and mixed thoroughly. This mixture was put in a beaker and placed in microwave oven and irradiated for 2 min. After completion of the reaction (monitored by TLC), chloroform (5 mL) was added, and the solid filtered. From the filtrate chloroform was evaporated and the residue was crystallized from aq. EtOH to afford the corresponding pyridine (Table I).

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