



## Microwave Assisted Synthesis and Characterization of Semicarbazones

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An efficient and simple microwave assisted procedure has been developed for conversion of substituted aryl aldehyde to corresponding semicarbazone by reaction with semicarbazide hydrochloride in presence of sodium acetate. The synthesized semicarbazones have been characterized by physico-chemical and spectral data.

**Key Words:** Microwave assisted synthesis, Semicarbazones, Spectral analysis.

### INTRODUCTION

Semicarbazones are used not only for isolation, purification and characterization of aldehyde and ketone but also for protection of carbonyl groups<sup>1,2</sup>. They possess wide range of bioactivities and pharmacological applications<sup>3</sup>. A variety of semicarbazones have also been reported to possess antifungal, antibacterial<sup>4</sup> and antitubercular activities<sup>5,6</sup>. Beside these they also possess anticonvulsant activity<sup>7</sup>.

In recent year application of microwave irradiation<sup>8-10</sup> in enhancement of chemical reactions have received growing interest for variety of application including organic synthesis. Microwave assisted synthesis not only enhance reaction rate but also provide cleaner products. The present work describes a simple microwave assisted synthesis of semicarbazones from the corresponding aldehydes which are characterized by IR, <sup>1</sup>H NMR, Mass and electronic absorption spectra.

### EXPERIMENTAL

IR spectra were recorded on Perkin-Elmer Fourier-transform infrared spectrometer (model 1430) in KBr pellets in the range 4000-200 cm<sup>-1</sup> at the Micro-Analytical unit of Tanta University. <sup>1</sup>H NMR were recorded in DMSO-*d*<sub>6</sub> as a solvent on a Bruker DMX 750 (500 MHz) using tetramethylsilane as internal standard. Chemical shifts of <sup>1</sup>H NMR was expressed in parts per million (ppm, δ units) and coupling constant was expressed in units of hertz (Hz). UV-VIS spectral measurements were carried out at room temperature within the wavelength range 190-700 nm using a Cary-400 double beam recording spectrophotometer. Electron spray ionization (ESI)

mass spectra were measured using a Shimadzu LCMS-2010 eV mass spectrometer at the Gakushuin University (Japan). Melting points were measured using a Tempo melting point apparatus in open capillary tube and are uncorrected.

**Conventional method for preparation of semicarbazones:** A solution of (0.1 mol) of semicarbazide hydrochloride and (0.1 mol) of anhydrous sodium acetate in 20 mL water was added to a solution of (0.1 mol) substituted aryl aldehyde in 50 mL ethanol. The reaction mixture was then boiled under reflux for *ca.* 3-4 h. After cooling the solution to room temperature, the precipitated semicarbazone was filtered and washed repeatedly with ice cold water, dried and re-crystallized from ethanol.

**Microwave assisted synthesis of semicarbazones:** Substituted aryl aldehyde (0.01 mol) in 50 mL ethanol was added to a solution of (0.01 mol) of semicarbazide hydrochloride and (0.01 mol) of anhydrous sodium acetate in 10 mL of water, taken in a conical flask fitted with calcium chloride guard tube to absorb solvent vapours. The reaction mixture was subjected to microwave irradiation (MWI) at 480 watt. The heating was continued for 50 to 80 s. An aliquot of the reaction mixture was taken out after every 30 s to study the completion of reaction by using TLC. On completion, the reaction mixture was cooled at room temperature. When a precipitate of semicarbazone was obtained, it was filtered, washed with cold water, dried and recrystallized from ethanol. The physical parameters of all the synthesized compounds (S<sub>1</sub>-S<sub>6</sub>) are given in Table-1.

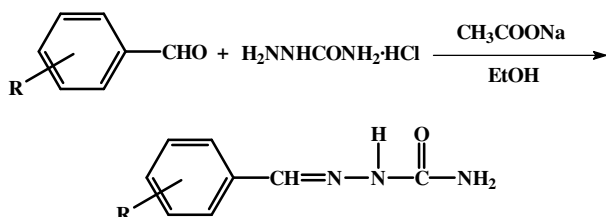
### RESULTS AND DISCUSSION

The semicarbazones (S<sub>1</sub>-S<sub>6</sub>) were synthesized according to **Scheme-I**. The general procedure is mentioned for conven-

TABLE-1  
PHYSICAL PARAMETERS OF THE SYNTHESIZED COMPOUNDS (S<sub>1</sub>-S<sub>6</sub>)

Compd. No.	m.f.	m.w.	m.p. (°C)	Conventional method		Microwave method	
				Time (h)	Yield (%)	Time (s)	Yield (%)
S <sub>1</sub>	C <sub>8</sub> H <sub>9</sub> N <sub>3</sub> O	163.1786	220	4	74.1	80	96.3
S <sub>2</sub>	C <sub>8</sub> H <sub>8</sub> N <sub>3</sub> OBr	242.0747	250	3	69.2	60	94.2
S <sub>3</sub>	C <sub>8</sub> H <sub>8</sub> N <sub>3</sub> OCl	197.6237	235	4	70.2	70	89.1
S <sub>4</sub>	C <sub>8</sub> H <sub>8</sub> N <sub>3</sub> OF	181.1691	220	4	68.8	75	90.7
S <sub>5</sub>	C <sub>8</sub> H <sub>8</sub> N <sub>3</sub> O <sub>3</sub>	208.1762	245	3	78.2	60	95.0
S <sub>6</sub>	C <sub>9</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub>	193.2048	215	4	71.6	80	85.0

tional and microwave method using different types of aldehyde which were subjected to reaction with semicarbazide hydrochloride in the presence of sodium acetate to give semicarbazones.



Scheme-I: Preparation of the synthesized semicarbazones. R = H (S<sub>1</sub>), R = 3-Br (S<sub>2</sub>), R = 3-Cl, (S<sub>3</sub>), R = 4-F (S<sub>4</sub>), R = 3-NO<sub>2</sub> (S<sub>5</sub>), R = 4-OCH<sub>3</sub> (S<sub>6</sub>)

From Table-1, it is evident that there was significant difference in time taking for the preparation of semicarbazones by conventional method which ranges from 3-4 h. While the preparation of all the semicarbazones using microwave method takes only 60-80 s for completion of reaction. Similarly there was significant difference in yield of the semicarbazone prepared by conventional and microwave assisted method. Conventional method gave poor yield of semicarbazone ranging from 68-78 %, while microwave method provide better yield ranging between 85-96 %. This clearly indicates that preparation of semicarbazones by microwave method takes much less time, provide better yield and cleaner product as compared to conventional method. Thus household microwave can be used to carry out the organic synthesis. The isolated products were characterized on the basis of IR, <sup>1</sup>H NMR, UV-VIS spectroscopy and mass spectrometry.

The IR spectra of the semicarbazones (Table-2) showed bands at 1599-1579 cm<sup>-1</sup> which may be assigned to ν(C=N) vibration of azomethine group<sup>11</sup>. The strong band at 1698-1646 cm<sup>-1</sup> can be attributed to (C=O) stretching vibration. In the 3500-3000 cm<sup>-1</sup> region, the spectra of all the compounds have strong bands at 3460-3449 cm<sup>-1</sup> which may be assigned to ν(*sec*-NH) while bands at 3282-3229 cm<sup>-1</sup> are attributed to ν(amide NH<sub>2</sub>). The bands at 2942-2924 and 888-833 cm<sup>-1</sup> are assigned to ν(Ar-CH stretch) and ν(Ar-H stretch), respectively.

The <sup>1</sup>H NMR spectra of all the semicarbazones (Table-2) showed singlet at δ values ranging from 10.07 to 10.48 ppm, which is assigned to -NH-C=O protons. Another singlet was observed at δ values ranging from 6.39 to 6.57 ppm corresponding to O=C-NH<sub>2</sub> protons. The proton attached to azomethine (Ar-CH=N) also observed as a singlet at δ value ranging from 7.76 to 8.57 ppm. The <sup>1</sup>H NMR spectra showed two to three distinct aromatic zones of triplet and multiplet at δ value 7.34 to 7.80 ppm due to the aromatic protons.

UV-VIS spectra of the semicarbazones were recorded over the range 200-500 nm in methanol and displayed two main bands (Table-2). The first band located at 209-221 nm range is due to the high energy π-π\* transition corresponding to the <sup>1</sup>L<sub>a</sub>-<sup>1</sup>A state in the aromatic moiety<sup>12</sup>. The second band at 277-289 nm range is assigned to n-π\* transition within the CH=N group<sup>13</sup>.

The mass spectra of the semicarbazones, under EI condition, showed the prominent molecular ion peaks for S<sub>1</sub> and S<sub>5</sub> at m/z 164.255 and 209.217 due to M<sup>+</sup>+1. S<sub>2</sub>, S<sub>3</sub>, S<sub>4</sub> and S<sub>6</sub> showed the prominent mass peaks at m/z 242.300, 198.199, 181.152 and 193.100 corresponding to the molecular weight of the parent ion [M]<sup>+</sup>. All the above observations suggests that the synthesized semicarbazones (S<sub>1</sub>-S<sub>6</sub>) are TLC and spectroscopic pure.

TABLE-2  
SPECTRAL DATA OF THE SYNTHESIZED COMPOUNDS (S-S<sub>6</sub>)

Compd. No.	IR (KBr, ν <sub>max</sub> , cm <sup>-1</sup> )	<sup>1</sup> H NMR (DMSO-d <sub>6</sub> , δ ppm)	UV-VIS (λ <sub>max</sub> , nm)
S <sub>1</sub>	3453 ( <i>sec</i> -NH), 3282 (amide-NH <sub>2</sub> ), 1598 (C=N), 1646 (C=O), 2930 (Ar-CH), 850 (Ar-H).	10.24 (s, 1H, NH), 7.34-7.8 (m, 5H, phenyl), 6.48 (s, 1H, N=CH).	217, 282
S <sub>2</sub>	3459 ( <i>sec</i> -NH), 3274 (amide-NH <sub>2</sub> ), 1590 (C=N), 1695 (C=O), 2924 (Ar-CH), 887 (Ar-H).	10.229 (s, 1H, NH), 7.302-7.77 (m, 3H, 4, 5, 6 - phenyl), 7.814 (s, 1H, 2-phenyl), 6.583 (s, 1H, N=CH).	220, 283
S <sub>3</sub>	3460 ( <i>sec</i> -NH), 3254 (amide-NH <sub>2</sub> ), 1590 (C=N), 1698 (C=O), 2925 (Ar-CH), 888 (Ar-H).	10.347 (s, 1H, NH), 7.34-7.85 (m, 3H 4, 5, 6-phenyl), 7.921 (s, 1H, 2-phenyl), 6.591 (s, 1H, N=CH).	217, 283
S <sub>4</sub>	3457 ( <i>sec</i> -NH), 3271 (amide-NH <sub>2</sub> ), 1597 (C=N), 1666 (C=O), 2924 (Ar-CH), 867(Ar-H).	10.244 (s, 1H, NH), 7.18-7.21 (m, 2H, 3, 5-Phenyl), 7.75-7.8 (m, 2H, 2, 6, phenyl), 6.509 (s, 1H, N=CH).	216, 277
S <sub>5</sub>	3460 ( <i>sec</i> -NH), 3229 (amide-NH <sub>2</sub> ), 1579 (C=N), 1659 (C=O), 2928 (Ar-CH), 833(Ar-H).	10.482 (s, 1H, NH), 7.61-7.17 (m, 3H, phenyl), 8.25-8.41 (m, 1H phenyl), 6.57 (s, 1H, N=CH).	209, 278
S <sub>6</sub>	3449 ( <i>sec</i> -NH), 3278 (amide-NH <sub>2</sub> ), 1599 (C=N), 1644 (C=O), 2942 (Ar-CH), 865 (Ar-H).	10.07 (s, 1H, NH), 6.929 (m, 2H, 3,5, phenyl), 7.619-7.7769 (m, 2H, 2,6-phenyl), 6.39 (s, 1H, N=CH).	221, 289

## Conclusion

In this paper, it is demonstrated that microwave assisted synthesis of semicarbazone is facile in comparison to conventional method. It will provide easy and faster, methodology for preparation of semicarbazones to protect the carbonyl groups.

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