

# Synthesis and Antibacterial Studies of Some Semicarbazones of Some Carbonyl Compounds

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**Abstract:** A number of semicarbazone derivatives were synthesized by the condensation reaction of appropriate ketones with semicarbazide and all the compounds were characterized by analytical and spectral studies. The compounds were evaluated for their antibacterial activity against pathogenic bacteria by using agar well diffusion method. Most of the compounds were found to have better antibacterial action than the reference standard drugs.

**Keywords:** Synthesis, condensation reaction, semicarbazones, antibacterial activity, agar well diffusion method

## 1. Introduction

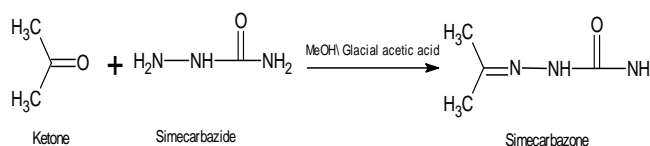
Semicarbazones [general structure : RC=NNHC(=O)NH<sub>2</sub>] are formed by the condensation of aldehydes or ketones with semicarbazide [NH<sub>2</sub>NHC(=O)NH<sub>2</sub>] [1] and have been evaluated for various biological activities including anticonvulsant [2] [3], analgesic and anti-inflammatory [4], antitubercular [5], antifungal and antibacterial [6][7], anticancer [8][9] etc. These medicinal properties of semicarbazones developed an interest among medicinal chemists and biologists to undertake their preparation and evaluate their biological properties to investigate better therapeutic agents against diseases in human beings and animals. In the present investigation we report the synthesis of some semicarbazones of some carbonyl compounds and their evaluation of antibacterial activity in view to investigate better antibacterial agents than the available antibacterial drugs.

## 2. Methodology

### 2.1. Chemistry

The melting points determined with Thomas Hoover Apparatus in open capillary method were uncorrected. The progress of reaction and purity of the compounds were monitored by thin layer chromatography and spots were visualized by exposure to iodine vapours or under UV light and separation were carried out by column chromatography by using silica gel (60-120 mesh). Elemental analysis was performed on Perkin Elmer Model 240 CAnalyser (USA) and was within 0.4% limit of the calculated values. IR spectra were recorded on JASCO FTIR- 5300 Spectrometer using KBr pellets and <sup>1</sup>H NMR spectra were determined at MHz 90 300-40 MHz on JEOL FX 90 QFT-NMR Spectrometer using tetramethyl silane as internal standard

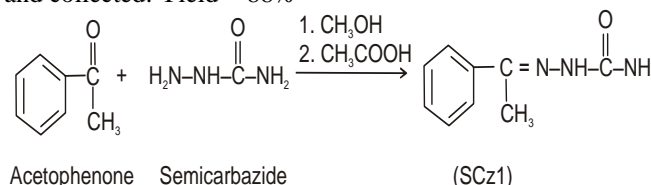
Synthesis of various semicarbazones (compounds SCz1-SCz10) was carried out according to the Scheme-1 by the condensation reaction of equimolar quantities of appropriate semicarbazide with the corresponding ketone.



Scheme-1

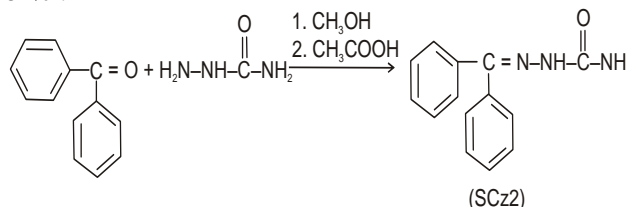
### Synthesis of acetophenone semicarbazone (SCz 1) :

Acetophenone (10 ml, 0.056 mol) was taken in a round bottom flask and 10 ml semicarbazide was added and 10 ml methanol solution with 10 ml glacial acetic acid and heated in a distillation unit, then synthesized compound was dried and collected. Yield = 88%



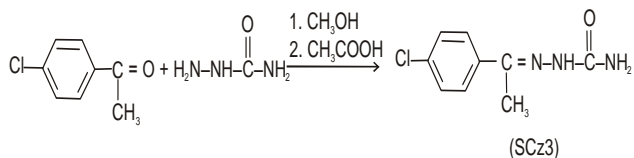
### Synthesis of benzophenone semicarbazone (SCz2)

The (0.041 mol) of benzophenone and 10 ml hydrazine hydrate in a round bottom flask of 500 ml and make alkali the solution by adding 10 ml methanol and then neutralized by adding 10 ml glacial acetic acid and heated in a distillation unit upto 1.5-2.5 h and synthesized compound was dried and collected. Yield = 82% .



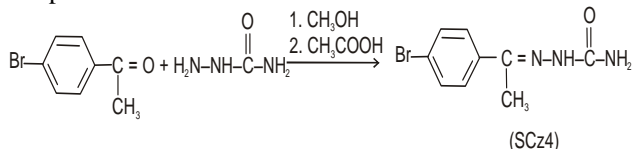
### Synthesis of p-chloroacetophenone semicarbazone (SCz3) :

The 10 ml (0.047 mol) p-chloroacetophenone solution and 10 ml of hydrazine hydrate were taken in a RBF of 500 ml and make solution alkali by adding 10 ml of methanol and the neutralizing of glacial acetic acid and heating in a distillation unit. Synthesized compound were dried and collected. Yield = 90%



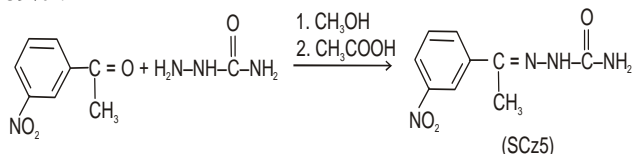
#### Synthesis of p-bromoacetophenone semicarbazone (SCz4) :

The 10 ml (0.039 mol) of p-bromoacetophenone solution and 10 ml of hydrazine hydrate solution was taken in a RBF (500 ml) and 10 ml methanol was then added 40 ml glacial acetic acid and heating in a distillation unit. Synthesized compound were dried and collected. Yield = 92% .



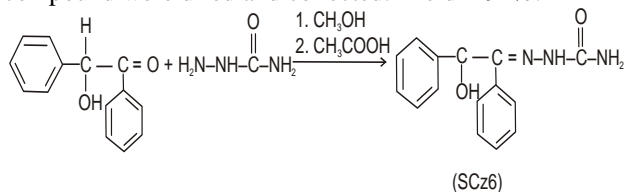
#### Synthesis of m-nitroacetophenone semicarbazone (SCz5) :

The 10 ml (0.45 mol) of m-nitroacetophenone solution and have been taken in a RBF (500 ml) and add 10 ml methanol then 10 ml glacial acetic acid and heating in distillation unit. Synthesized compound were dried and collected. Yield = 89% .



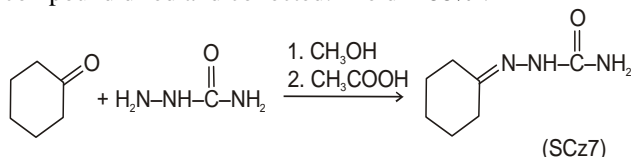
#### Synthesis of benzoin semicarbazone (SCz6) :

The 10 ml (0.037 ml) of benzoin and 10 ml hydrazine hydrate solution was taken in a RBF (500 ml) and 10 ml methanol and 10 ml glacial acetic acid were added in it. The mixture distillation in a distillation unit and synthesized compound were dried and collected. Yield = 91% .

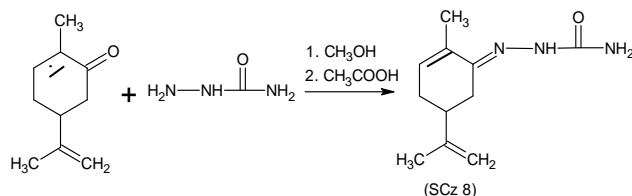


#### Synthesis of cyclohexanone semicarbazone (SCz7) :

1 gm cyclohexanone and 10 ml (0.73 mol) of hydrazine hydrate solution was taken in a RBF (500 ml) and 10 ml methanol and 10 ml of glacial acetic acid was added and mixture was distilled in distillation unit and synthesized compound dried and collected. Yield = 88% .

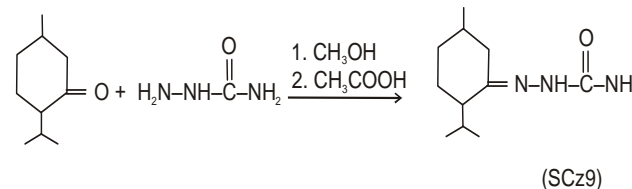


**Synthesis of carvone semicarbazone (SCz8) :** 1 gm carvone and 10 ml (0.049 mol) of hydrazine hydrate were taken in a RBF (500 ml) and 10 ml methanol and 10 ml of glacial acetic acid were added and mixture was heated in a distillation unit and synthesized compound dried and collected. Yield = 88% .



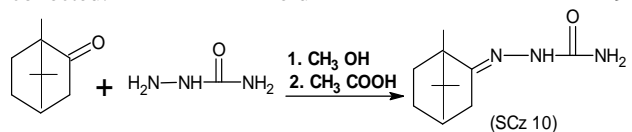
#### Synthesis of menthone semicarbazone (SCz9) :

1 gm menthone (0.047 mol) and 10 ml of hydrazine hydrate were taken in a RBF (500 ml) and 10 ml methanol and 10 ml of glacial acetic acid was added mixture was heated in a distillation unit and synthesized compound dried and collected. Yield = 88%



#### Synthesis of camphor semicarbazone (SCz10)

1 gm camphor (0.047 mol) and 10 ml of hydrazine hydrate were taken in a RBF (500 ml) and 10 ml methanol and 10 ml of glacial acetic acid was added. The mixture was heated in a distillation unit and the synthesized compound dried and collected. Yield = 92%



## 2.2 Biological Activity

### 2.2.1. Antibacterial Test

The antibacterial activity was determined by agar well diffusion method [7] against 24 hrs of old culture of pathogenic bacteria such as Gram-positive bacteria (*Staphylococcus aureus*) and Gram-negative bacteria (*Escherichia coli*) cultivated in nutrient agar on petri dishes using Sulfamethoxazole and trimethoprim as standard drugs. The zone of inhibition was compared with standard drugs after 48 hrs incubation at 37°C. The results of antibacterial activity are presented in Table 2.

## 3. Results and Discussion

In the present investigation, the procedure of synthesis of various semicarbazones (SCz-1 to SCz10; Scheme-1) is a simple, straight forward and all the compounds are easily prepared in good yields. Besides this the reagents used for the preparation are easily available and cheap.

The structures of all the synthesized compounds were characterized by physical, analytical and spectral data which are given in tables 1 and 2. In general the characterization data showed good agreement with the proposed synthesized compounds. Antibacterial activity data are summarized in Table 1. The results of the *in vitro* antibacterial activity of test compounds are shown in Table 2.

It is apparent from antibacterial screening results that compounds SCz1, SCz3, SCz4, SCz5, SCz9 and SCz10 have produced better activity than the standard drugs against both Gram positive (*S.aureas*) and Gram negative (*E.coli*)

bacteria. However, compound (SCz3) demonstrated excellent and better antibacterial action against *S. aureus* and *E. coli* at 100mg/ mL concentration in comparison to both standard drugs. Among the all compounds, compounds SCz3, SCz4 and SCz5 were found to possess very good antibacterial action against *S. aureus* and *E. coli*, however, compounds SCz1, SCz2, SCz9 and SCz10 and compounds SCz1, SCz9 and SCz10 have exhibited in some extent better antibacterial action against *S. aureus* and *E. coli* in comparison to standard drugs. The remaining compounds of

the entire series possesses only moderate to poor antibacterial activity.

Thus it is appeared from the data of antibacterial screening that most of the compounds exhibited promising results as compared to both of these standard drugs and potential compounds are further required for detailed investigation in laboratory animals in view to complete the first step of drug development programme, enable to know valuable information related to efficacy of these compounds as antibacterial agents.

**Table 1:** Physical data of semicarbazones

Comp. Code	Molecular formula	Molecular weight	M. p. °C	Elemental Analysis (%)					
				Calculated			Observed		
				C	H	N	C	H	N
SCz1	C <sub>9</sub> H <sub>11</sub> N <sub>3</sub> O	177	199	61.01	6.21	23.72	61.46	6.38	23.88
SCz2	C <sub>14</sub> H <sub>13</sub> N <sub>3</sub> O	239	186	70.29	5.43	17.57	70.49	5.64	17.72
SCz3	C <sub>9</sub> H <sub>10</sub> N <sub>3</sub> ClO	211.5	201	51.06	4.72	19.85	51.12	4.91	19.95
SCz4	C <sub>9</sub> H <sub>10</sub> N <sub>3</sub> OBr	256	208	42.18	3.90	16.40	42.30	3.99	16.52
SCz5	C <sub>9</sub> H <sub>10</sub> N <sub>4</sub> O <sub>3</sub>	222	257	48.64	4.50	25.22	48.69	4.65	25.36
SCz6	C <sub>15</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub>	269	206	66.91	5.57	15.61	66.99	5.69	15.71
SCz7	C <sub>7</sub> H <sub>13</sub> N <sub>3</sub> O	155	137	54.19	8.38	27.09	54.32	8.46	27.21
SCz8	C <sub>11</sub> H <sub>17</sub> N <sub>3</sub> O	207	163	63.76	8.21	20.29	63.90	8.31	20.32
SCz9	C <sub>11</sub> H <sub>21</sub> N <sub>3</sub> O	211	189	62.55	9.95	19.90	62.75	10.17	19.98
SCz10	C <sub>11</sub> H <sub>19</sub> N <sub>3</sub> O	209	238	63.15	9.09	20.09	63.32	9.30	20.26

**Table 2:** Spectral data of the semicarbazone derivatives

S. No.	Compound Name	Compd Code	IR KBr V cm <sup>-1</sup>	<sup>1</sup> HNMR (d <sub>6</sub> -DMSO) δ ppm
1.	Acetophenone semicarbazone	SCz1	3470 (NH), 2998 (CH) 1610 (C=N) 1725 (CO)	6.1 (S, 2H, NH <sub>2</sub> ), 0.9 (S, 3H, CH <sub>3</sub> ), 7.0 (S, 1H, NH)
2.	Benzophenone semicarbazone	SCz2	3480 (NH), 3010(CH) 1725 (CO) 1640 (C=N)	6.0 (S, 2H, NH <sub>2</sub> ), 6.8 (S, 1H, NH), 7.4-7.7 (m, 10H, Ar-H)
3.	p-Chloroacetophenone semicarbazone	SCz3	3472 (NH) 3020 (CH) 1630 (C=N) 1728 (CO)	6.3 (S, 2H, NH <sub>2</sub> ), 0.9 (S, 3H, CH <sub>3</sub> ) 7.1(S, 1H, NH), 4.3 (S, 8H, CH <sub>3</sub> )
4.	p-Bromoacetophenone semicarbazone	SCz4	3470 (NH) 3010 (CH) 1624 (C=N) 1740 (CO)	6.2 (S, 2H, NH <sub>2</sub> ), 0.8 (S, 3H, CH <sub>3</sub> ) 7.0(S, 1H, NH), 4.0 (S, 8H, CH <sub>2</sub> )
5.	m-nitroacetophenone semicarbazone	SCz5	3458 (NH) 2990 (CH) 1626 (C=N) 1732 (CO)	6.0 (S, 2H, NH <sub>2</sub> ), 0.9 (S, 3H, CH <sub>3</sub> ) 7.1(S, 14H, NH), 6.9(S, 2H, CH <sub>3</sub> ), 5.8 (S, 4H, CH <sub>2</sub> )
6.	Benzoin semicarbazone	SCz6	3460 (NH) 3300 (OH) 2992 (CH) 1728 (CO) 1628 (C=N)	4.0 (S, 1H, OH), 6.1 (S, 2H, NH <sub>2</sub> ) 7.0(S, 1H, NH) 7.3-7.8 (m, 10H, Ar-H)
7.	Cyclohexanone semicarbazone	SCz7	3475 (NH) 2980 (CH) 1730 (CO) 1630 (C=N)	1.3 (m, 10H, 5CH <sub>2</sub> ), 5.8 (S, 2H, NH <sub>2</sub> ) 6.9 (S, 2H, NH)
8.	Carvone semicarbazone	SCz8	3476 (NH) 2996 (CH) 1748 (CO) 1710 (C=N)	5.9 (S, 2H, NH <sub>2</sub> ), 0.9 (S, 6H, 2CH <sub>3</sub> ), 0.9 (S, 6H, 2CH <sub>3</sub> ) 7.0(S, 1H, NH) 2.9 (m, 6H, 3CH <sub>2</sub> )
9.	Menthone semicarbazone	SCz9	3470 (NH) 3020 (CH) 1620 (CO) 1726 (C=N)	5.8 (S, 2H, NH <sub>2</sub> ), 0.8 (S, 9H, 3CH <sub>3</sub> ) 7.0(S, 1H, NH), 3.0(m, 6H, 3CH <sub>3</sub> )
10.	Camphor semicarbazone	SCz10	3480 (NH) 3033 (CH) 1645 (CO) 1720 (C=N)	6.2 (S, 2H, NH <sub>2</sub> ), 0.9 (S, 6H, 2CH <sub>3</sub> ) 6.9(S, 1H, NH), 2.8 (m, 6H, 3CH <sub>3</sub> )

**Table 3:** *In vitro* antibacterial activities of semicarbazones

Compound Code	% Inhibition			
	<i>S. aureus</i>		<i>E. coli</i>	
	50 mg/mL	100 mg/mL	50 mg/mL	100 mg/mL
SCz-1	75	70	65	60
SCz-2	60	55	40	45
SCz-3	80	90	80	95
SCz-4	75	76	79	90
SCz-5	82	85	85	90
SCz-6	30	30	35	36
SCz-7	35	38	40	45
SCz-8	40	42	45	48
SCz-9	68	65	75	74
SCz-10	65	68	68	70
Sulfamethoxazole	50	55	48	50
Trimethoprim	45	45	46	48

#### 4. Conclusion

The present study revealed the synthesis, characterization and biological evaluation of different semicarbazones. Compounds were synthesized by condensation reaction of appropriate ketone with semicarbazide and screened for antibacterial activity. All of these compounds exhibited antibacterial effect but most of these compounds showed better antibacterial action than the two standard drugs used for the comparison. The present study indicates that the most potential compounds warrant further detailed investigation in order to develop better antibacterial agents.

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#### Author Profile



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