

Synthesis and Characterization of Schiff bases

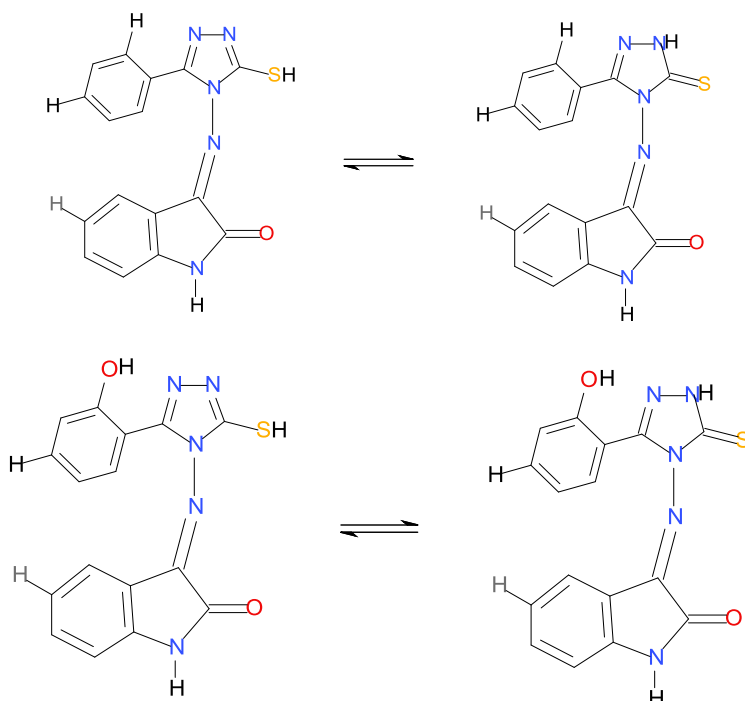
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ABSTRACT: The synthetic flexibility, diverse stereochemistry as well as the unusual coordination number of 3d transition metals in the complexes with nitrogen oxygen and sulfur donor ligands have created considerable interest in coordination chemistry of transition elements. A careful survey of literature revealed that there is a considerable scope for systematic studies including the biochemical applications of the complexes of Mn, Co and Ti with a variety of Schiff bases.

I.INTRODUCTION

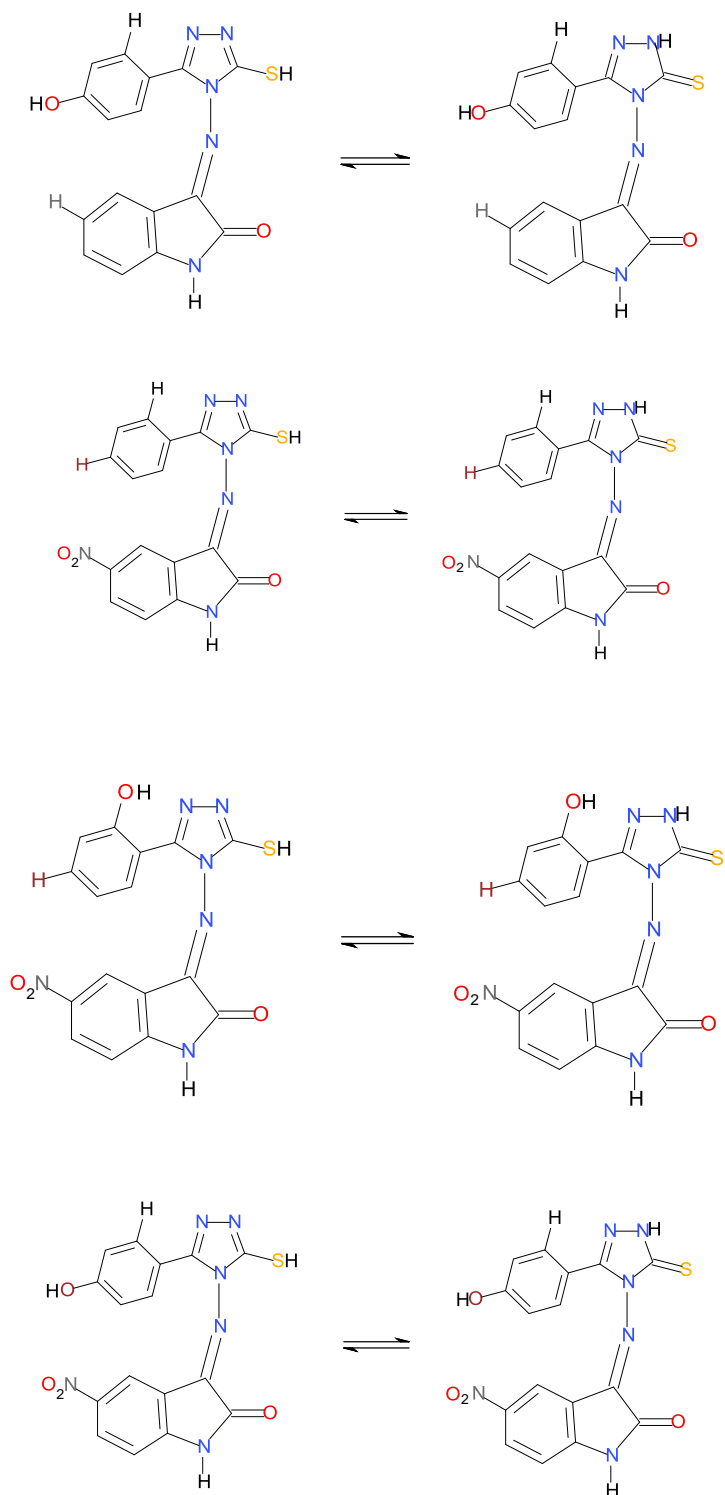
On the basis of the coordination sites available, the Schiff bases used during the course of the present investigations may be classified as follows: **1.Bifunctional Tridentate Schiff Bases Having ONS Donor Systems:** The Schiff bases belonging to this group have the functional groups, CO and SH besides the charecterstic azomethine group and offer three coordination sites:

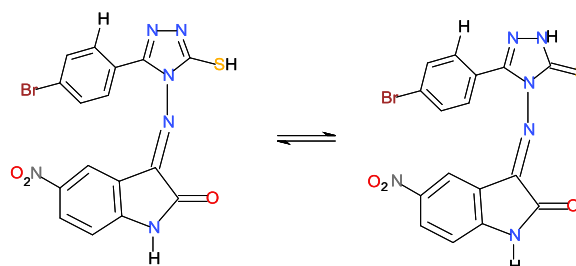


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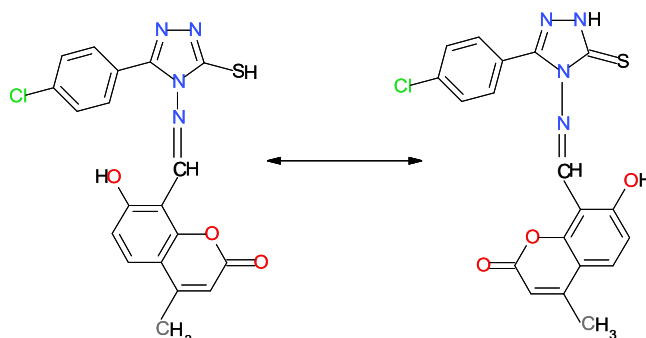
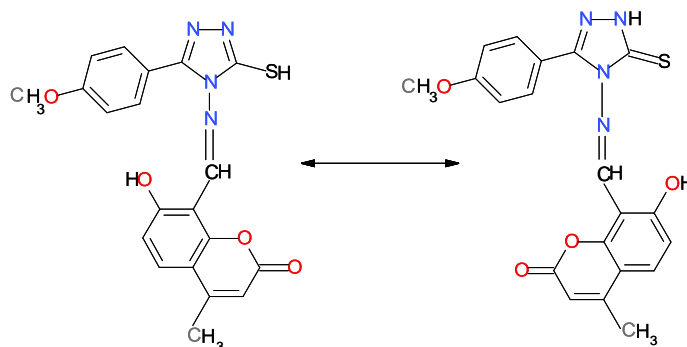
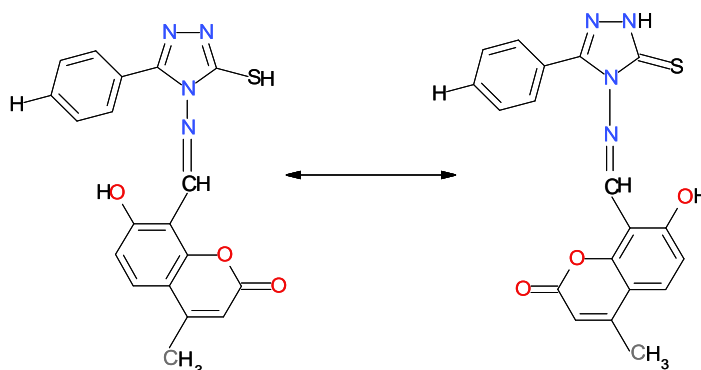
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2. Trifunctional Tetradentate Schiff Bases Having ONS Donor Systems:

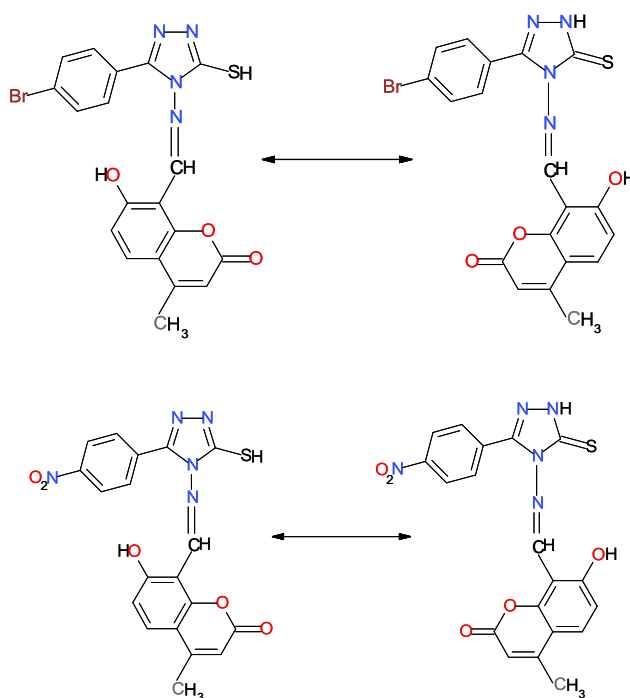
Schiff bases of this group have the functional groups, OH, CO and SH besides azomethine groups for the coordination with metal ions:



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Synthesis of the Schiff bases used during the present investigation can be discussed under the following heads:

II. EXPERIMENTAL

The melting point of synthesized compounds were determined on open aluminum block and are not corrected. Purity was checked by TLC (thin layer of silica gel) using Merck Silica gel G-60. Infrared spectra of the ligands were recorded in the region, 4000-700 cm^{-1} on Shimadzu FTIR Affinity-1 spectrophotometer in KBr pellets. ^1H NMR spectra were recorded with the help of a Varian Gemini 400 spectrometer (300 MHz) in DMSO-d_6 or CDCl_3 using TMS as internal standard. Elemental data obtained from all the synthesized compounds were found satisfactory.

All Schiff bases and their precursor were synthesized through both conventional and microwave assisted methods. The latter method provided reproducible results and analytical data related to the products obtained from both methods were found coherent.

1. Synthesis of 1,2,4-Triazole Derivatives

Selected 1,2,4-triazole derivatives were synthesized by conventional method²²⁸ and microwave assisted method²²⁹ in three steps:

(1.) Synthesis of Arylhydrazides (1)

(a) Conventional Method

To the esters of substituted aromatic acids (10mmol), hydrazine hydrate (10 mmol) was added and refluxed the solution for 30 minutes. To the refluxing mixture, 20 ml of ethanol was added as a solvent in order to homogenize

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the contents. The resulting mixture was further allowed to reflux for 6 h. Excess ethanol was distilled out and the contents were allowed to cool. The crystals formed were filtered, washed thoroughly with water and dried.

(b) Microwave Assisted Method

A mixture of esters of substituted aromatic acids (10 mmol) and hydrazine hydrate (10 mmol) exposed to microwave irradiations intermittently at 30 seconds for four minutes in microwave oven. After completion of reaction, the contents were allowed to cool at room temperature. The crystals separated out were filtered, washed thoroughly with water and dried to get aryl hydrazide(1)

(2.) Synthesis of 5-Substitutedphenyl-1,3,4-oxadiazole-2-thiols (2).

(a) Conventional Method

To a solution of aryl hydrazide1 (10 mmol) in ethanol (30 ml),potassium hydroxide (10 mmol) in absolute ethanol (50 ml) andcarbon disulfide (20mmol) were added and refluxed for about 5 h.till evolution of hydrogen sulfide was ceased. The reaction mixture was cooled at room temperature and diluted with water. On acidification with dilute hydrochloric acid, the required oxadiazolesderivative was precipitated. It was filtered, washed thoroughly with cold water and recrystallized from ethanol.

(b) Microwave Assisted Method

A mixture of aryl hydrazide 1 (10 mmol) and potassium hydroxide (10 mmol) was well grinded to make a fine homogeneous powder. To this powder carbon disulfide (20 mmol) was added and exposed to microwave irradiations intermittently at 20 seconds for two minutes. The reaction mixture was cooled and neutralized with dilute hydrochloric acid. The solid separated out on neutralization was filtered, washed with cold water and dried. There is no need to purify the product 1,3,4-oxadiazole-2-thiol derivatives (2) for further reaction (scheme-1).

(3.) Synthesis of 3-substituted-4-amino-5-mercapto-1,2,4-triazole

(a) Conventional Method

A mixture of compound2(10 mmol) and hydrazine hydrate (10 mmol) in dry pyridine (15 ml) was refluxed for about 4 h. The reaction mixture was cooled at room temperature and neutralized with dilute hydrochloric acid. The solid precipitated out was filtered, washed thoroughly with cold water andrecrystallized from ethanol.

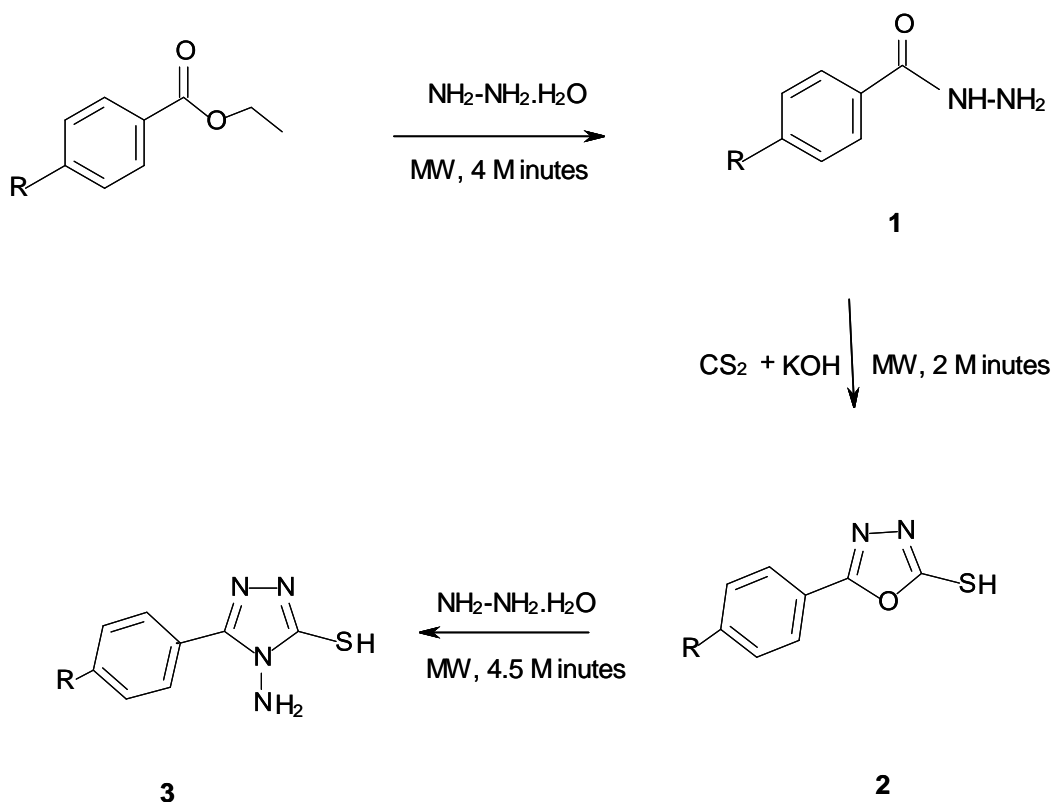
(b) Microwave Assisted Method

A mixture of compound2(10 mmol) and hydrazine hydrate (10 mmol) was exposed to microwave irradiations intermittently at 30 seconds for 4.5 minutes. After completion of reaction, the hot reaction mixture was cooled at room temperature and neutralized with dilute hydrochloric acid. The solid separated out was filtered, washed thoroughly with water and crystallized from ethanol(scheme1).

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2. Synthesis of 5-Nitroisatin²³⁰:

Isatin (3.4 mmol) dissolved in (3.2 ml) of conc. sulphuric acid was added drop wise into (3.4 mmol) solution of nitric acid prepared in (3.8 ml) of conc. sulphuric acid over a period of 1 hour whilst the temperature was maintained between 0 to 4°C. The reaction mixture was poured into 25 ml of ice water and precipitates were collected followed by its washing with water. The crude product was crystallized from alcohol. m.p: 255-258 °C.

3. Synthesis of 8-Formyl-7-hydroxyl-4-methylcoumarin²³¹⁻²³².

It was synthesized in two steps:

(1) Synthesis of 7-Hydroxy-4-methylcoumarin

Concentrated sulfuric acid (20 ml) was added to a 100 ml round bottom flask and cooled to 0-5 °C in an ice bath. A solution of resorcinol (0.001 mol) in ethylacetoacetate (0.0015 mol) was added to sulfuric acid under constant stirring at 0-5 °C. The reaction mass was stirred overnight at room temperature and then poured in to crushed ice under vigorous stirring. An off-white solid obtained was filtered and recrystallised from ethanol. m.p: 180-182 °C.

(2) Synthesis of 8-Formyl-7-hydroxy-4-methylcoumarin

Hexamethylene tetramine (0.003 mol) was added to the solution of 7-hydroxy-4-methyl-coumarin (0.001 mol) in glacial acetic acid and heated at 80-85 °C at water bath for 6.0 h. A hot mixture of 5 ml water and 30 ml hydrochloric acid was added to the reaction mixture, kept for 30 minutes and cooled to room temperature. It was extracted with diethyl ether and on evaporation of ether, a pale yellow solid was obtained. m.p. 176-178 °C.

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4. Synthesis of Bifunctional Tridendate 1,2,4-triazole Isatin Schiff Bases:

(a) Conventional Method

The equimolar quantity of 3-substituted-4-amino-5-mercapto-1,2,4-triazole (10 mmol) and isatin (10 mmol) containing 3-4 drops concentrated HCl in hot methanol (60 ml) was refluxed for 5.30-6.00 h. After completion of reaction as monitored by TLC, the reaction mixture was cooled at room temperature. The solid separated out was filtered, washed with cold methanol, dried and recrystallized from methanol.

(b) Microwave Assisted Method

A mixture of 3-substituted-4-amino-5-mercapto-1,2,4-triazole (1 m mol) and isatin (1 mmol) in methanol (10 ml) containing concentrated HCl (3-4 drops) was subjected to microwave irradiation intermittently at 30 seconds for 5.0-5.5 minutes. After completion of reaction as monitored by TLC, the reaction mixture was cooled. The solid separated out, was filtered, washed with cold methanol, dried and recrystallized from methanol.

The following four 1,2,4-triazole isatin Schiff bases were synthesized during the course of present work:

- (i) 3-[3-Phenyl-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]iminoisatin: $C_{16}H_{11}N_5OS$
- (ii) 3-[3'-(2''-Hydroxyphenyl)-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]iminoisatin: $C_{16}H_{11}N_5O_2S$
- (iii) 3-[3'-(4''-Hydroxyphenyl)-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]iminoisatin: $C_{16}H_{11}N_5O_2S$
- (iv) 3-[3'-(4''-Bromophenyl)-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]iminoisatin: $C_{16}H_{10}N_5OSBr$

5. Synthesis of Bifunctional Tridendate 1,2,4-Triazole Nitroisatin Schiff Bases:

(a) Conventional Method

The equimolar quantity of 3-substituted-4-amino-5-mercapto-1,2,4-triazole (10 mmol) and 5-nitroisatin (10 mmol) containing 3-4 drops concentrated HCl in hot methanol (45 ml) was refluxed for 4-5 h. After completion of reaction the reaction as monitored by TLC, the reaction mixture was cooled at room temperature. The solid separated out was filtered, washed with cold methanol, dried and recrystallized from methanol.

(b) Microwave Assisted Method

A mixture of 3-substituted-4-amino-5-mercapto-1,2,4-triazole (1 m mol) and 5-nitroisatin (1 mmol) in methanol (8 ml) containing concentrated HCl (3-4 drops) was subjected to microwave irradiation intermittently at 30 seconds for 4-5 minutes. After completion of reaction as monitored by TLC, the reaction mixture was cooled. The solid separated out, was filtered, washed with cold methanol, dried and recrystallized from methanol.

The following four 1,2,4-triazole nitroisatin Schiff bases were synthesized during the course of present work:

- (i) 3-[3'-Phenyl-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]imino-5-nitroisatin: $C_{16}H_{10}N_6O_3S$
- (ii) 3-[3'-(2''-Hydroxyphenyl)-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]imino-5-nitroisatin: $C_{16}H_{10}N_6O_4S$
- (iii) 3-[3'-(4''-Hydroxyphenyl)-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]imino-5-nitroisatin: $C_{16}H_{10}N_6O_4S$
- (iv) 3-[3'-(4''-Bromophenyl)-2',4'-dihydro-1',2',4'-triazol-5'-mercapto-4'-yl]imino-5-nitroisatin: $C_{16}H_9N_6O_3SBr$

6. Synthesis of Trifunctional Tetrudentate 1,2,4-Triazole Coumarin Schiff Bases:

(a) Conventional Method

The equimolar quantity of 3-substituted-4-amino-5-mercapto-1,2,4-triazole (10 mmol) and 8-formyl-7-hydroxyl-4-methylcoumarin (10 mmol) containing 3-4 drops concentrated HCl in hot ethanol (50 ml) was refluxed for 5.00-5.30 h on water bath. After completion of reaction as monitored by TLC, the reaction mixture was cooled at room temperature. The solid separated out was filtered, washed with alcohol, dried and recrystallized from ethanol.

Microwave Assisted Method

A mixture of 3-substituted-4-amino-5-mercapto-1,2,4-triazole (1 m mol) and 8-formyl-7-hydroxyl-4-methylcoumarin (1 m mol) in ethanol (10 ml) containing concentrated HCl (0.5 ml) was subjected to microwave irradiation intermittently at 30 seconds for 4-5 minutes. After completion of reaction as monitored by TLC, the reaction mixture was cooled at room temperature. The solid separated out was filtered, washed with alcohol, dried and recrystallized from ethanol.

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The following five 1,2,4-triazole coumarin Schiff bases were synthesized during the course of present work:

- (i) 8-[[3-phenyl-5-mercapto-1,2,4-triazol-4-yl]iminomethyl]-7-hydroxy-4-methyl chromen-2-one: $C_{19}H_{14}N_4O_3S$
- (ii) 8-[[3-(4-methoxyphenyl)-5-mercapto-1,2,4-triazol-4-yl]iminomethyl]-7-hydroxy-4-methyl-chromen-2-one: $C_{20}H_{16}N_4O_4S$
- (iii) 8-[[3-(4-chlorophenyl)-5-mercapto-1,2,4-triazol-4-yl]iminomethyl]-7-hydroxy-4-methyl-chromen-2-one: $C_{19}H_{13}N_4O_3S$
- (iv) 8-[[3-(4-bromophenyl)-5-mercapto-1,2,4-triazol-4-yl]iminomethyl]-7-hydroxy-4-methyl-chromen-2-one: $C_{19}H_{13}N_4O_3SBr$

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