



# Synthesis and Characterization of Macrocycles Derived from Bis-Triazole

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## Abstract

The new macrocyclic Schiff bases were obtained by condensing the 5,5'-(butane-1,4-diyl)bis(4-amino-4H-1,2,4-triazole-3-thiol) with the corresponding dialdehyde. The dialdehydes needed for the macrocycles were synthesized by using substituted hydroxyl aldehyde, which was converted into its potassium salt and treated with appropriate dibromoalkane to afford the corresponding dialdehyde. All the synthesized compounds were characterized by IR, <sup>1</sup>H-NMR, mass and some of the representative by <sup>13</sup>C-NMR spectra.

**Keywords:** Synthesis, Characterization, Macrocycles, Derived, Bis-Triazole.

## Introduction

Macrocycles are an important class of useful compounds for selective complexation of different anions, cations or neutral molecules. These compounds have wide applications varied from complex formation to the development of new sensors. These materials emerged with improved properties and antimicrobial activity. Macrocycles containing heteroatom like nitrogen or sulphur display a high affinity for the d block transition metal cations than oxygen atom in the cycle. Macrocyclic compounds can selectively bind different cations in agreement with the nature and number of the heteroatoms belonging to the cycle as well as the size of the cycle<sup>1</sup>. Their complex structures attract the attention towards the development of novel cyclization technologies with improved efficiency.

The macrocyclic Schiff base compounds and their transition metal complexes are the important component of coordination chemistry. They are extensively studied for their capacity to bind and transport metal ions, for the possibility to act as model for metalloproteinase<sup>2</sup>.

The wide interest in the designing of macrocyclic compound containing five and six member heterocyclic rings as subunits has led to the preparation of a range of such compounds, which have been shown multiple applications in variety of fields<sup>3</sup>.

The triazole ring is chemically stable to oxidative and reductive conditions, also to acidic and basic hydrolysis, as well as it is relatively resistant to metabolic degradation<sup>4,5</sup>. Triazole derivatives have possessed extensive biological properties such as antitumor<sup>6</sup>, anti-tubercular<sup>7</sup> and analgesic activities<sup>8</sup>. The inclusion ofazole fragments in the ring of macrocycles can be enhanced the range of the application of these compounds<sup>9</sup>, for example as ligands and biologically active substances. So we

have planned to synthesize some macrocycles having triazole moiety.

## Material and Methods

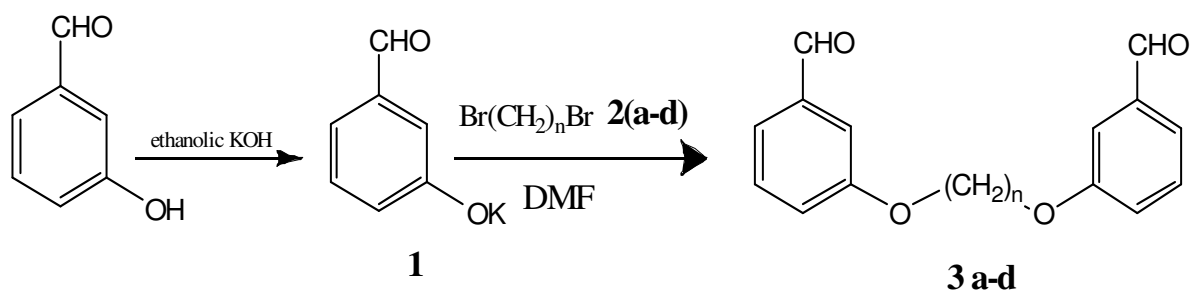
The IR spectra were recorded on FTIR spectrometer in the range 4000 to 400 cm<sup>-1</sup> at SAIF Punjab University Chandigarh and Bruker optics alpha – T FTIR spectrometer at Department of Chemistry, Sant Gadge Baba Amravati University, Amravati. The <sup>1</sup>H NMR spectra were recorded on a Bruker advance II 400 NMR spectrometer at SAIF Punjab University Chandigarh using TMS as an internal standard and DMSO as a solvent. MS-EI spectral data from at SAIF IIT Madras, Chennai. C, H, N analysis of representative compound was carried out on Eager Xperience instrument and nitrogen estimation by Kjeldhal's method.

### General procedure for the synthesis of dialdehydes 3(a-d):

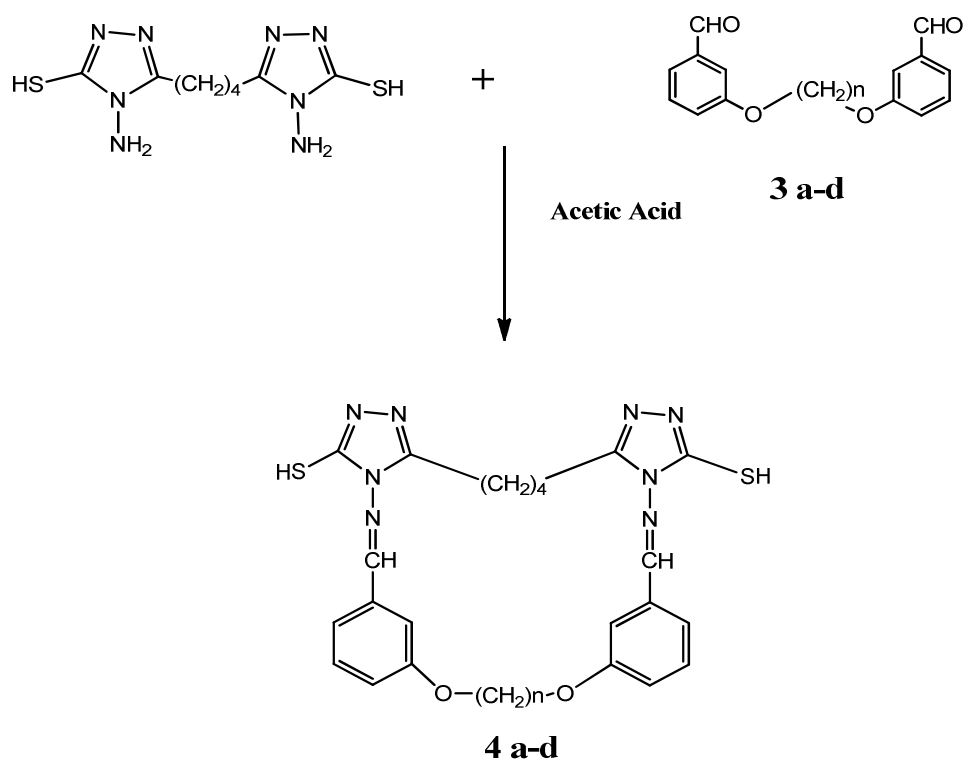
The conversion of 3-hydroxy Benzaldehyde [0.01M] into its potassium salt by reported method<sup>10</sup> and followed by its reaction with the appropriate dihalocompounds 2(a-d) [0.005M] in DMF under reflux condition to give corresponding dialdehydes. The reaction was monitored by TLC. After completion of reaction, crude solid was filtered and recrystallised from ethanol to give pure compound 3(a-d).

### General procedure for the synthesis of macrocycles 4 (a-d):

To a solution of bis triazole (5, 5'-(butane-1, 4-diyl)bis(4-amino-4H-1,2,4-triazole-3-thiol) in acetic acid, the appropriate dialdehyde was added. The reaction mixture was then heated under reflux. After completion of reaction, the solvent was removed under reduced pressure. The residue obtained was washed with water followed by acetone and the product obtained was recrystallised from appropriate solvent to give the corresponding macro cycle.



**Scheme-1**  
 Synthesis of dialdehydes



**Scheme-2**  
 Synthesis of Macrocycles

**Table-1**  
 Macrocycles 4a-d with its yield

Product (4)	n	Yield
a	2	80%
b	3	78%
c	4	87%
d	5	60%

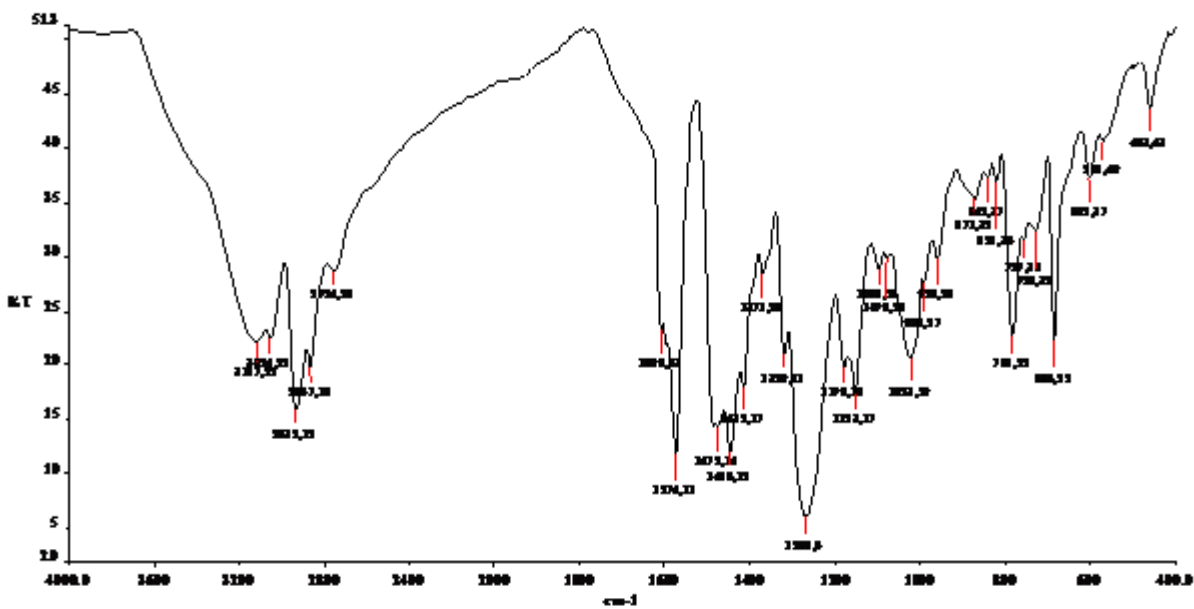


Figure-1  
 IR spectrum of 4d

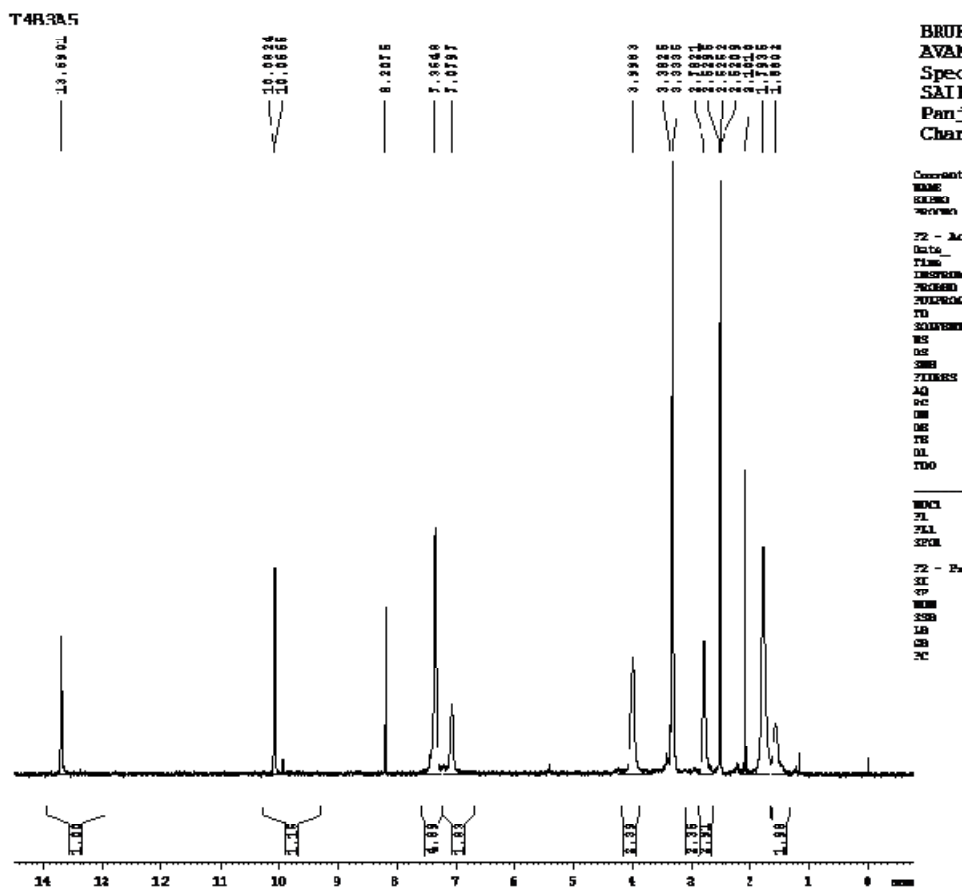


Figure-2  
<sup>1</sup>H-NMR spectrum of 4d

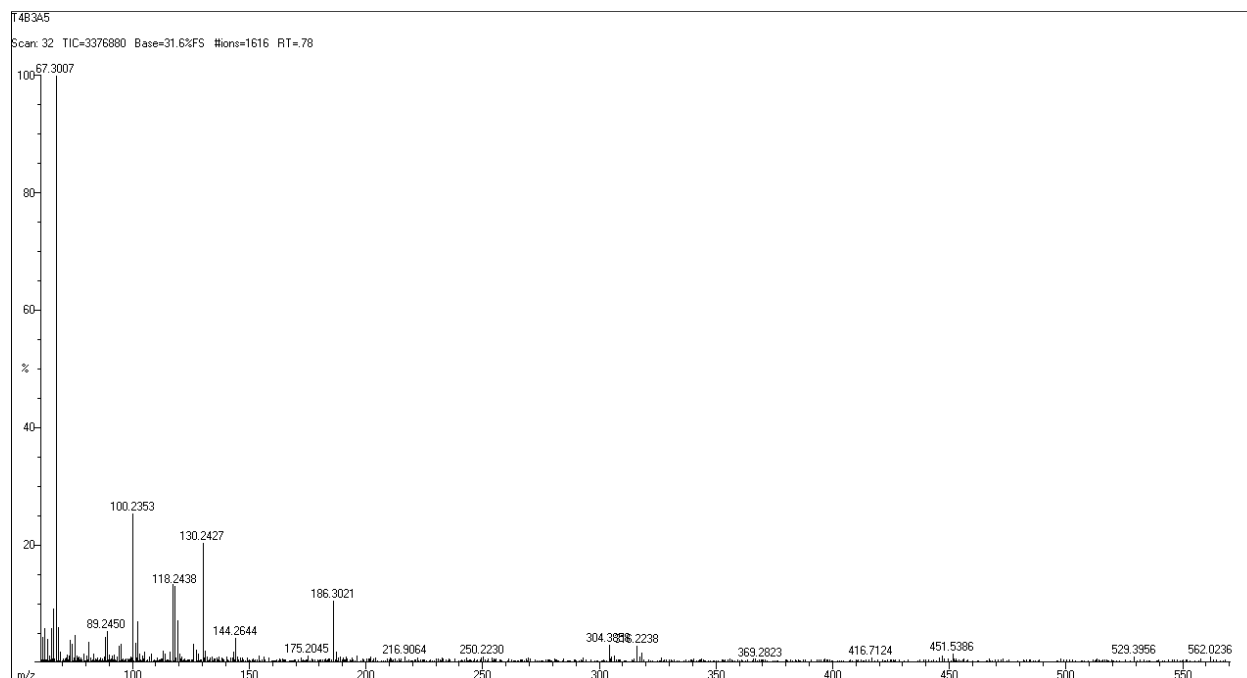


Figure-3  
 Mass spectrum of 4d

## Results and Discussion

In search of expedient pathway to prepare the target macrocycles, our attentions focus on di-aldehyde and bis-triazole. Bis-triazole {5,5'-(butane-1,4-diyl)bis(4-amino-4H-1,2,4-triazole-3-thiol)} synthesized from thiocarbohydrazide by the reported method<sup>11</sup>. Various synthetic techniques have been developed for the synthesis of macrocyclic compounds, among these, the high dilution method is a versatile procedure and most of the favorite<sup>12,13</sup>. This paper described the synthesis of macrocycles having triazole moiety, the compounds 4 a-d via condensation of appropriate dialdehyde (3 a-d) derived from 3-hydroxy aldehyde; with bis triazole in refluxing acetic acid.

The IR spectra of 5,5'-(butane-1,4-diyl)bis(4-amino-4H-1,2,4-triazole-3-thiol) showed the absorption bands at 3161 and 3286  $\text{cm}^{-1}$  due to the  $\text{NH}_2$  group, which were not present in the IR spectra of macrocyclic compounds 4(a-d). Similarly, the  $^1\text{H NMR}$  spectrum of bis triazole showed a broad signal at  $\delta$  5.56 ppm attributed to  $\text{NH}_2$  group protons, which was absent in  $^1\text{H NMR}$  spectra of compounds 4 (a-d). The absence of the IR absorption and  $^1\text{H NMR}$  signals due to the  $\text{NH}_2$  group of compounds 4 (a-d) confirmed the formation of the azomethine linkage. The presence of IR absorption band at 2754  $\text{cm}^{-1}$  and  $^1\text{H NMR}$  signal at  $\delta$  13.6 confirms that -SH group present in compounds 4 (a-d).

**Macrocycle 4a:**  $\text{C}_{24}\text{H}_{24}\text{N}_8\text{O}_2\text{S}_2$ : Yield: 80%; N: 21.52 (20.21). IR ( $\text{cm}^{-1}$ ): 3055 (Aromatic C-H stretch), 2756 (S-H stretch), 1600, 1575 (C=N stretch).  $^1\text{H NMR}$  (400 MHz,  $\text{DMSO}-d_6$ ):

$\delta$  13.8 (s, 2H, 2-SH),  $\delta$  10.1 (s, 2H, 2-CH=N),  $\delta$  7.2-7.5 (m, 8H, H aromatic),  $\delta$  4.4 (s, 4H, 2-O-CH<sub>2</sub>),  $\delta$  2.8 (s, 4H, CH<sub>2</sub>-CH<sub>2</sub>),  $\delta$  1.8 (s, 4H, CH<sub>2</sub>-CH<sub>2</sub>). MS (EI) m/z: 520 [ $\text{M}^+$ ], 488, 264, 119, 91, 69.

**Macrocycle 4b:**  $\text{C}_{25}\text{H}_{26}\text{N}_8\text{O}_2\text{S}_2$ : Yield: 78%; N: 20.96 (20.62). IR ( $\text{cm}^{-1}$ ): 3054 (Aromatic C-H stretch), 2756 (S-H stretch), 1601, 1575 (C=N stretch).  $^1\text{H NMR}$  (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  13.76 (s, 2H, 2-SH),  $\delta$  10.3 (s, 2H, 2-CH=N),  $\delta$  7.2-7.4 (m, 8H, H aromatic),  $\delta$  4.34 (s, 4H, 2-O-CH<sub>2</sub>),  $\delta$  2.78 (s, 4H, CH<sub>2</sub>-CH<sub>2</sub>),  $\delta$  1.79 (s, 4H, 2-CH<sub>2</sub>),  $\delta$  2.5 (s, 2H, CH<sub>2</sub>). MS (EI) m/z: 534 [ $\text{M}^+$ ], 551, 277, 93.

**Macrocycle 4c:**  $\text{C}_{26}\text{H}_{28}\text{N}_8\text{O}_2\text{S}_2$ : Yield: 87%; N: 20.42 (20.11). IR ( $\text{cm}^{-1}$ ): 3054 (Aromatic C-H stretch), 2756 (S-H stretch), 1600, 1575 (C=N stretch).  $^1\text{H NMR}$  (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  13.75 (s, 2H, 2-SH),  $\delta$  10.2 (s, 2H, 2-CH=N),  $\delta$  7.4-7.46 (m, 8H, H aromatic),  $\delta$  4.13 (s, 4H, 2-O-CH<sub>2</sub>),  $\delta$  2.4 (s, 4H, 2-CH<sub>2</sub>),  $\delta$  2.7 (t, 4H, 2-CH<sub>2</sub>),  $\delta$  1.75 (t, 4H, 2-CH<sub>2</sub>-CH<sub>2</sub>). MS (EI) m/z: 548 [ $\text{M}^+$ ], 515, 291, 92.

**Macrocycle 4d:**  $\text{C}_{24}\text{H}_{30}\text{N}_8\text{O}_2\text{S}_2$ : Yield: 60%; Calcd.: C, 57.63; H, 5.37; N, 19.91. (Found: C, 56.32; H, 5.52; N, 20.51); IR ( $\text{cm}^{-1}$ ): 3054 (Aromatic C-H stretch), 2754 (S-H stretch), 1609, 1574 (C=N stretch). (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  13.69 (s, 2H, 2-SH),  $\delta$  10.06 (s, 2H, 2-CH=N),  $\delta$  7.07-7.36 (m, 8H, H aromatic),  $\delta$  3.99 (s, 4H, 2-O-CH<sub>2</sub>),  $\delta$  2.78 (s, 4H, 2-CH<sub>2</sub>),  $\delta$  2.10 (s, 4H, 2-CH<sub>2</sub>),  $\delta$  1.79 (s, 4H, 2-CH<sub>2</sub>),  $\delta$  1.58 (s, 2H, -CH<sub>2</sub>).  $^{13}\text{C NMR}$  (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  (ppm): 22.14, 22.29, 38.6, 67.61, 112.2, 119.0,

121.7, 122.5, 133.5, 139.0, 158.0, 162.8, 164.3. MS (E/I) m/z: 562[M<sup>+</sup>], 529, 416, 250, 67.

## Conclusion

Macrocycles were identified using elemental analysis, IR, <sup>1</sup>H NMR, and MS spectral data. The described synthetic procedures are fairly simple, rational from the viewpoint of yield and atom economical since all carbon, nitrogen, and sulfur atoms of the parent compounds are included into the product molecules. Naturally occurring macrocycles have been successfully used in the clinical practice; new chemo type macrocycles emerge with great potential and improved biological activity and thus represent an important class of drugs. Macrocyclization has thus developing into powerful and an extremely useful reaction in organic synthesis. We also successfully synthesized macrocycles having triazole moiety.

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