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# Synthesis and Characterization of Macrocyclic Compounds Derived from Carbohydrazide

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**Abstract:** Macrocyclic compounds have attracted increasing interest owing to their role in understanding of molecular processes occurring in biochemistry, material science, and catalysis. It is well known that N atoms play a key role in the coordination of metal at the active sides of numerous metallobiomolecules. Macrocycles can selectively bind different cations in agreement with the size of the cycle, as well as the nature and number of the heteroatoms belonging to the cycle. Hydrazone Schiff bases of acyl, aroyl and hetero aroyl compounds have additional donor sites like C=O. The additional donor sites make them more flexible and versatile.

Nitrogen-containing macrocycles were synthesized in quantitative yield by reacting carbohydrazide and dialdehydes which were derived from salicylaldehyde by cyclocondensation. All the newly synthesized compounds were characterized by elemental analysis, IR, NMR and Mass spectroscopy.

**Keywords**: Macrocycles, Hydrazones, bis-Schiff bases, Carbohydrazide Derivatives.

## I. INTRODUCTION

Carbohydrazide can be prepared by the standard method of hydrazinolysis of appropriate ester and condensation reaction of hydrazine carboxylic acid and hydrazine. Carbohydrazide derivatives were widely used to remove oxygen in boiler system [1,2], Hydrazones and their derivatives represents the well-known class of compounds in organic chemistry containing N-N linkage of different nature and a C-N double bond which shows extended conjugation with lone pair on terminal nitrogen [3-6]. Both nitrogen atoms of the hydrazone group are nucleophilic, although the amino type nitrogen is more reactive. Hydrazones are mainly obtained by the condensation reaction of hydrazines/ carbohydrazide with aldehydes or ketones The carbon atom of hydrazone group has both electrophilic and nucleophilic character [7-8]. Carbohydrazide, hydrazones and similar compounds constitute a class of useful building blocks for the synthesis of a variety of heterocycles and macrocycles [9-12]. These compounds have interesting biological properties such as anti-inflammatory, antidepressant, analgesic, anticonvulsant, antitumor and anti-microbial activity, a anti-platelet, vasodilator, antiviral, anticancer, antitubercular and anti-HIV [13-15].

In recent years the chemistry of macrocyclic compounds attracts the attention of both inorganic and organic chemistry. The field of macrocyclic compounds is fast developing because of their resemblance with naturally occurring compounds and variety of applications [16-17]. All these applications prompted us to synthesize the macrocycles from carbohydrazide and dialdehydes.

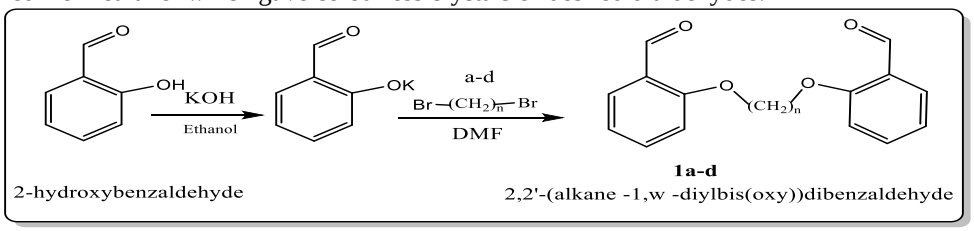
## II. MATERIALS AND METHODS

All the chemicals used were of Anal. R. grade, purchased from SD Fine Chemicals, Qualigen, Himedia. Solvents were used after purification.

**General procedure:**

**i) Synthesis of Dialdehydes: [2,2'-(alkane-1,ω-diylbis(oxy))dibenzaldehyde](1a-d):** Scheme 1.

The Ethanolic solution of Salicylaldehyde (1.22g, 10 mmol) and KOH solution (0 .56 g, 10 mmol) was stirred for 10 min, the solvent was then removed under vacuum. To the residue DMF (10 mL) and the appropriate 1,ω-dibromoalkane (5 mmol) was added. The reaction mixture was heated for 10-15 min, during which KBr separated out. Reaction mixture was then poured into cold water and the solid obtained was collected by filtration, washed with water and recrystallized from ethanol which gave colourless crystals of desired dialdehydes.



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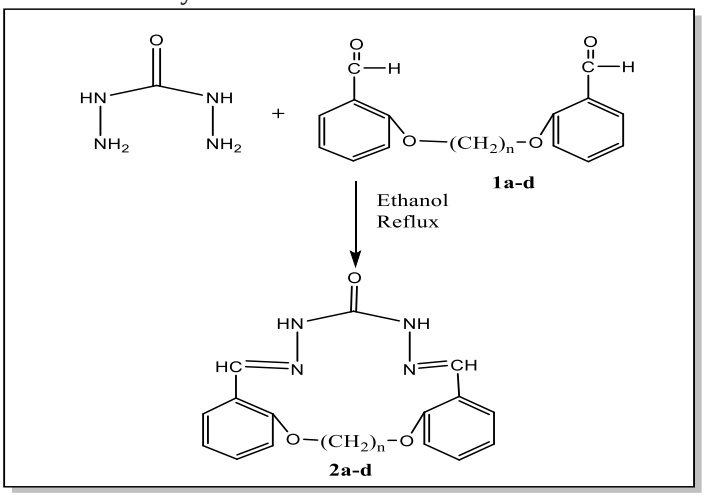
**Scheme 1.:** Synthesis of 2,2'-(alkane -1,ω-diylbis(oxy))dibenzaldehyde

**ii) Synthesis of Macrocycles: Dihydro-nH-dibenzo[dioxatetraazacyclopenta-octadecin-8(9H)-one (2a-d):** Scheme 2.

Macrocyclic Compounds 2a-d were prepared by refluxing a stirred mixture of appropriate dialdehyde 1a-d (10 mmol) and carbohydrazide (10 mmol) in ethanol (20 mL) containing few drops of conc. $H_2SO_4$. After completion of reaction the product formed was collected by filtration and washed with water.




**Scheme 2.:** Synthesis of Macrocycles(2a-d)

| **Product code** | **a** | **b** | **c** | **d** |
|---|---|---|---|---|
| **n** | 2 | 3 | 4 | 5 |

## III. RESULTS AND DISCUSSION

All the synthesised compounds were characterised on the basis of their melting point, TLC, IR, $^1$H-NMR, C$^{13}$-NMR & Mass spectral data. The percentages of element C, H and N were determined by using automated CHN analyser, results shown in table 1. IR spectra of Macrocyclic compounds show N-H stretching in the range 3195-3209 cm$^{-1}$, C=O stretch 1680-1688 cm$^{-1}$. C=N Stretch in the range 1600-1610 cm$^{-1}$. In $^1$H-NMR spectra CH=N proton observed in the range 8.49-8.52 ppm, NH proton shows peak in the range 10.49-10-60 ppm. C$^{13}$-NMR spectra contain peak because of carbon; doubly bonded to nitrogen, which confirms macrocyclization.

**Table I:** Elemental analysis and physical data of synthesized new Macrocycles.

| **S. No.** | **Code (Abbrv.)** | **Name** | **Molecular Formula** | **Elemental Anal. (calcd.) Found** | **Yield %** |
|---|---|---|---|---|---|
| 1 | 2a | (5E/Z,10E/Z)-17,18-dihydro-7H-dibenzo[e,n][1,4]dioxa[8,9,11,12]tetraazacyclopentadecin-8(9H)-one | $C17H_{16}N_4O_3$ | (C, 62.95; H, 4.97; N,17.27) C, 62.83; H, 4.62; N, 17.74 | 78 |
| 2 | 2b | (14E/Z,19E/Z)-7,8-dihydro-6H,16H-dibenzo[f,o][1,5]dioxa [9,10,12,13]tetraazacyclohexadecin-17(18H)-one | $C_{18}H_{18}N_4O_3$ | (C, 63.89; H, 5.36; N,16.56) C, 63.69; H, 5.33; N, 17.49 | 83 |
| 3 | 2c | (15E/Z,20E/Z)-6,7,8,9-tetrahydro-17H-dibenzo[b,k][1,13]dioxa [5,6,8,9]tetraazacycloheptadecin-18(19H)-one | $C_{19}H_{20}N_4O_3$ | (C, 64.76; H, 5.72; N, 15.90) C, 64.79; H, 5.70; N, 15.89 | 82 |
| 4 | 2d | (16E/Z,21E/Z)-7,8,9,10-tetrahydro-6H,18Hdibenzo[b,k][1,13]dioxa[5,6,8,9]tetraazacyclooctadecin19(20H) -one | $C_{20}H_{22}N_4O_3$ | (C, 65.56; H, 6.05; N, 15.29) C, 65.22; H, 6.40; N, 15.42 | 80 |

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**2a**

IR: 3207, 3070, 2943, 2867, 1688, 1606, 1573,1506, 1469, 1422, $cm^{-1}$.

$^{1}H$ NMR (400 MHz, DMSO-$d_6$): δ 10.60 (s, 2H, NH), 6.90-8.0 (m, 8H Ar-H), 8.53 (s,2H, CH=N), 4.43 (s, 4H, O-CH2-).

$^{13}C$ NMR (126 MHz, DMSO-$d_6$): δ 160, 157,152, 134, 128, 124, 121, 111, 66. MS (m/z):324$[M]^+$.

**2b**

IR: 3217,3077, 2951, 2862, 1688, 1606, 1574,1506, 1468, 1422. $cm^{-1}$

$^{1}H$ NMR (400 MHz, DMSO-$d_6$): δ 10.56 (s, 2H, NH), 6.90-8.33 (m, 8H Ar-H), 8.53 (s,2H, CH=N), 4.49 (t, 4H, O-CH2-), 2.40 (quintet, 2H, -$CH_2$-). Fig. 1

$^{3}C$ NMR (126 MHz, $CDCl_3$): δ 160, 156, 152, 135, 130, 124, 120, 112, 64, 28. Fig.2

MS (m/z):338$[M]^+$. Fig. 3.

**2c**

IR: 3198,3069, 2944, 2867, 1680, 1604, 1577,1508, 1469, 1423. $cm^{-1}$

$^{1}H$ NMR (400 MHz, DMSO-$d_6$): δ 10.55 (s, 2H, NH), 6.90-8.10 (m, 8H Ar-H), 8.52 (s,2H, CH=N), 4.42 (t, 4H, O-$CH_2$-), 2.11 (t, 4H, -$CH_2$-$CH_2$). $^{13}C$ NMR (126 MHz, DMSO-$d_6$): δ 160, 156, 152, 134, 127,123, 120, 112, 63, 27. MS (m/z):352$[M]^+$.

**2d**

IR: 3208, 3071, 2941, 2870, 1681, 1603, 1570,1504, 1466, 1420. $cm^{-1}$

$^{1}H$ NMR (400 MHz, DMSO-$d_6$): δ 10.49 (s, 2H, NH), 6.89-7.90 (m, 8H Ar-H), 8.49 (s, 2H, CH=N), 4.12 (s, 4H, O-CH2-), 2.04 (m, 4H, -$CH_2$-$CH_2$), 1.28 (quintet, 2H, -$CH_2$-). $^{13}C$ NMR (126 MHz, DMSO-$d_6$): δ 161, 156, 153, 134, 128, 124, 119, 111, 62, 25, 11. MS (m/z):366$[M]^+$.

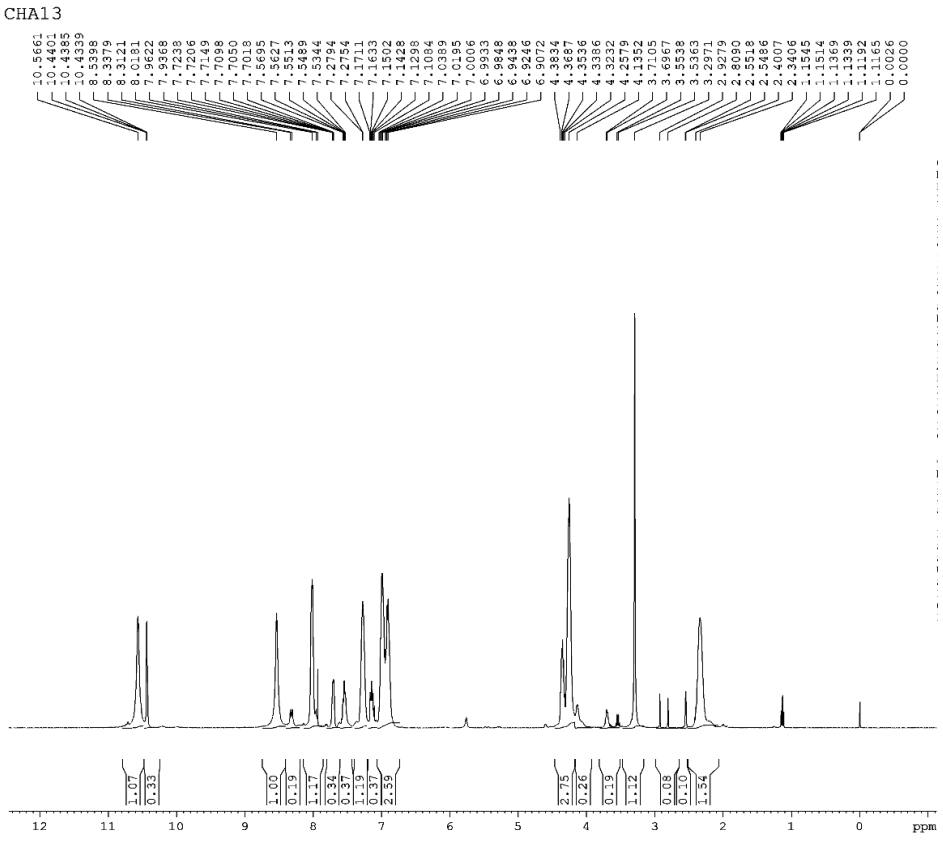


Fig. 1. $^{1}H$-NMR spectrum of 2b ($CHAl_3$)

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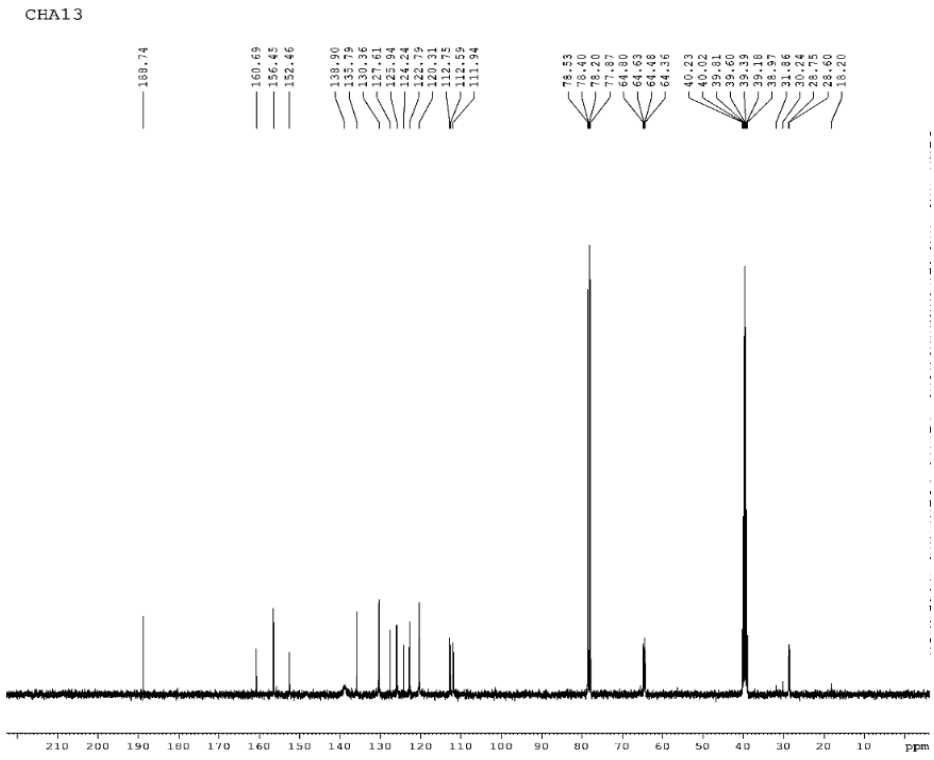


Fig. 2. $C^{13}$-NMR spectrum of 2b ($CHAl_3$)

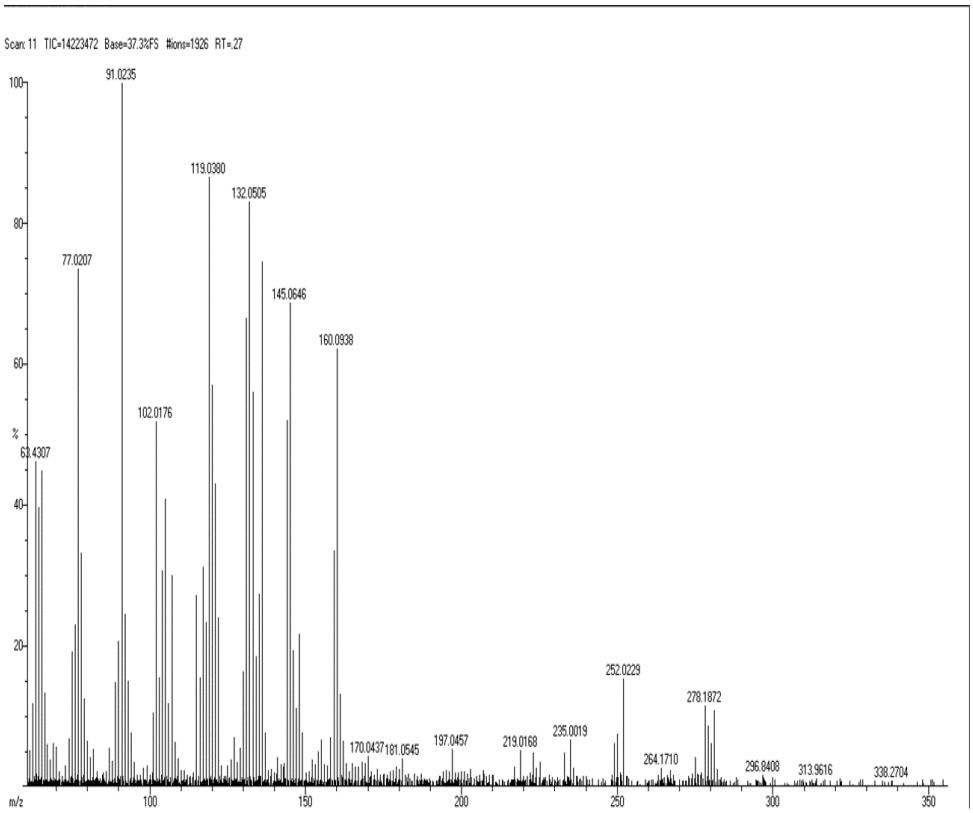


Fig. 3. Mass spectrum of 2b ($CHAl_3$)

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## IV. CONCLUSION

The importance of carbohydrazide derivatives in commercial and pharmacological fields increased our interest in carbohydrazide derivatives which led to the synthesis and characterization of macrocycles. We have successfully synthesized hydrazone-based macrocycles by macrocyclization of Carbohydrazide and Dialdehydes. The synthesised compounds were characterised by $^{1}$HNMR, C$^{13}$NMR, Mass Spectroscopy and elemental analysis.

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