

SYNTHESIS OF 1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione

Submitted in partial fulfillment of the requirements for the award
of

Master of Science in Chemistry

by

A. ARUL BLESSON

(REGISTER NO.: 41910003)



**DEPARTMENT OF CHEMISTRY SCHOOL OF
SCIENCE AND HUMANITIES**

SATHYABAMA

INSTITUTE OF SCIENCE AND TECHNOLOGY

(DEEMED TO BE UNIVERSITY)

Accredited with Grade "A" by NAAC | 12B Status by UGC | Approved by AICTE

JEPPIAAR NAGAR, RAJIV GANDHI SALAI, CHENNAI - 600 119

APRIL - 2023



SATHYABAMA

INSTITUTE OF SCIENCE AND TECHNOLOGY

(DEEMED TO BE UNIVERSITY)

Accredited "A" Grade by NAAC | 12B Status by UGC | Approved by AICTE

www.sathyabama.ac.in

DEPARTMENT OF CHEMISTRY

BONAFIDE CERTIFICATE

This is to certify that this Project Report is the bonafide work of A. ARUL BLESSON (41910003) who carried out the project entitled "SYNTHESIS, CHARACTERIZATION OF 1,6-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione" under our supervision from November 2022 to May 2023.

J. Karthikeyan

08/05/2023

Internal Guide

Dr. J. KARTHIKEYAN, M.Sc., Ph.D.,

Head of the Department

Department of chemistry

HEAD OF THE DEPARTMENT

DEPARTMENT OF CHEMISTRY

J. Karthikeyan

08/05/2023

Head of the Department

(DEEMED TO BE UNIVERSITY)

Jeppiaar Nagar, Rajiv Gandhi Salai

Dr. J. KARTHIKEYAN, M.Sc., Ph.D.,

Department of chemistry

Submitted for Viva voce Examination held on 8-5-2023

Ramish

Internal Examiner

V. Subramanian

External Examiner

DECLARATION

I **A. ARUL BLESSON (41910003)**, hereby declare that the Project Report entitled "**SYNTHESIS, CHARACTERIZATION OF 1,6-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione**" done by me under the guidance of **Dr. J. KARTHIKEYAN, M.Sc., Ph.D.**, Head of the Department, Department of Chemistry at **Sathyabama Institute of Science and Technology**, Jeppiaar Nagar, Rajiv Gandhi Salai, Chennai – 600119 is submitted in partial fulfillment of the requirements for the award of Master of Science degree in Chemistry.

DATE: 08/05/2023

PLACE: CHENNAI.



A. ARUL BLESSON

SIGNATURE OF THE CANDIDATE

ACKNOWLEDGEMENT

I am pleased to acknowledge my sincere thanks to Board of Management of **SATHYABAMA** for their kind encouragement in doing this project and for completing it successfully. I am grateful to them.

I convey my thanks to **Dr. J KARTHIKEYAN, Head of the Department, Dept. of Chemistry** for providing me necessary support and details at the right time during the progressive reviews.

I would like to express my sincere and deep sense of gratitude to my Project Guide **Dr. J. KARTHIKEYAN**, Department of Chemistry for their valuable guidance, suggestions and constant encouragement paved way for the successful completion of my project work.

I wish to express my thanks to all Teaching and Non-teaching staff members of the Department of Chemistry who were helpful in many ways for the completion of the project.

A. ARUL BLESSON

ABSTRACT

1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione have been Synthesized by condensation method. The material is the curcumin related compound which is synthesis by the method of synthesis of curcumin at room temperature in ethyl acetate. This technique is alternating the initial starting material and follow the work up of synthesis of curcumin. The synthesized material has been characterized by NMR spectroscopy, Liquid Chromatography and Mass Spectroscopy (LCMS). NMR spectroscopy studies show that proton present in the compound and LCMS studies shows that the molecular weight of the compound. The functional groups present in the product and its structure was confirmed by other spectral studies.

TABLE OF CONTENTS

Chapter No	Title	Pages No
	ABSTRACT	i
	LIST OF TABELS	iv
	LIST OF FIGURES	v
	LIST OF ABBRIVIATIONS	vi
1	INTRODUCTION	7
2	LITERATURE SURVEY	9
3	AIM AND SCOPE	
	3.1 AIM	11
	3.2 SCOPE	11
4	MATERIALS AND METHODS	
	4.1 MATERIALS	12
	4.2 CHARACTERIZATION TECHNIQUES	
	4.2.1 Nuclear Magnetic Resonance NMR	12
	4.2.2 Liquid chromatography	14
	4.2.3 Mass Spectroscopy	15
	4.3 METHADODOLOGY	
	4.3.1 Synthesis of 4-(bis(2-chloro)amino)benzaldehyde	16
	4.3.2 Synthesis of 1,7-bis(2-chloroethyl)amino)phenyl) hepta-1,6-diene-3,5-dione	17
	4.3.3 Removal of Impurities	18

5	RESULT AND DISCUSSION	
5.1	CHARACTERISATION OF 1,7-bis(4-bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione	19
5.1.1	NMR Spectrum for 1,7-bis(4-bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione	19
5.1.2	LCMS Spectrum for 1,7-bis(4-bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione	21
6	CONCLUSION	22
	REFERENCE	23

LIST OF TABLES

Table No.	Title	Page No.
5.1.1	Chem NMR C^{13} Estimation graph	19
5.1.2	NMR Graph	20
5.1.3	LCMS Graph	21

LIST OF FIGURES

Figure No.	Title	Page No.
1.1	Structure of curcumin	7
1.2	Preparation of curcumin	7
4.1	Spinning momentum	12
4.2	Nuclear magnetic resonance	13
4.3	Liquid chromatography	14
4.4	Synthesis of 1,7-bis(4-bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione	17
4.5	Column chromatography	18
5.1	Chem NMR C^{13} estimation	19
5.2	Chem NMR C^{13} estimation graph	20
5.3	NMR graph	20
5.4	LCMS graph	21

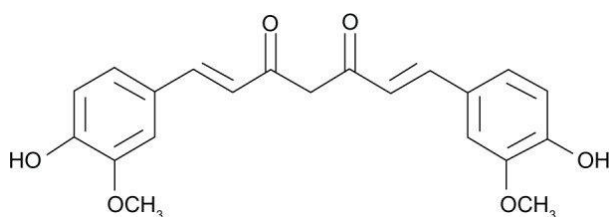
LIST OF ABBREVIATIONS

NMR	- Nuclear Magnetic resonance Spectroscopy
LCMS	- Liquid Chromatography and Mass Spectroscopy

CHAPTER 1

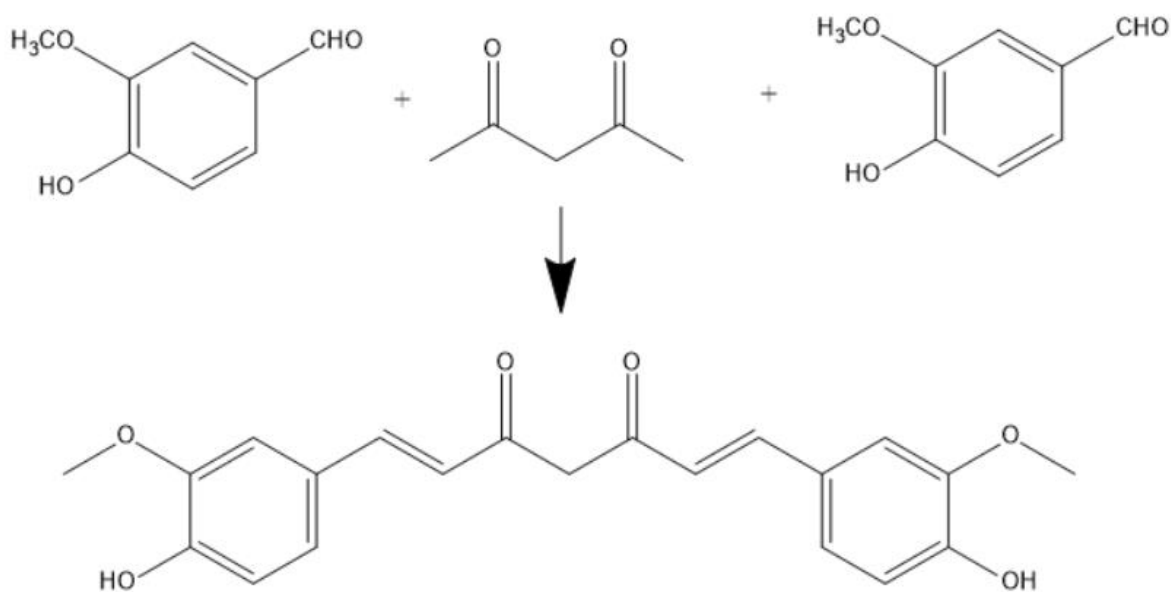
INTRODUCTION

For many centuries the dried and ground roots of *Curcuma Longa* Kunir, known as curcuma or turmeric, have been used as a dye for foods and spices (curry) in the far East. The colouring substance (1.5-2 % of the dried root) curcumin, an orange-red compound, was isolated in 1870, but it was not until 1910 that Lampe et al. elucidated the structure as shown:



which was later confirmed by synthesis. This synthesis 3, starting from vanillin builds up curcumin in eight steps and has little practical value.

It is prepared by heating vanillin, acetylacetone and boric anhydride (2 : 1 : 2) over a free flame for 30 minutes and claimed a yield of 10% in this one step procedure:



This method proved to be unsatisfactory in our hands and gave us yields of about 1.5 % only. We observed, however, that condensation of vanillin and acetylacetone in the

presence of boric anhydride took place at 150°, if minor amounts of butanol and piperidine were also present (yield = 10%). This led us to the idea that boric esters and bases like piperidine might be used with success for this type of condensation. An experiment with tributyl borate, piperidine and the reaction product of acetylacetone and boric anhydride (yield 25 %). prompted us to study all factors involved more systematically.

CHAPTER 2

LITERATURE SURVEY

H.J.J. Pabon demonstrate the preparation of curcumin with vanillin at elevated temperature and preparation of curcumin related compounds at room temperature.

Helen-Lisette Alvarado, David Limón, Ana-Cristina Calpena-Campmany, Mireia Mallandrich, Laura Rodríguez-Cid, Núria Aliaga-Alcalde, Arántzazu González-Campo, Lluïsa Pérez-García, Intrinsic Permeation and Anti-Inflammatory Evaluation of Curcumin, Bisdemethoxycurcumin and Bisdemethylcurcumin by a Validated HPLC-UV Method, International Journal of Molecular Sciences.

Florian Traxler, Johann Schinnerl and Lothar Brecker, Spectroscopic studies on the molecular interaction of curcumin and piperine shows that how to other molecule interact with the curcumin by replacing the aldehyde part on that.

Michael Flanders, William M. Gramlich, Water-Soluble and Degradation-Resistant Curcumin demonstrate that the fragmentation occurs in the curcumin and how the curcumin is reacted with the other aldehydes.

Emese Gál, Levente Csaba Nagy, demonstrated the photophysical property of curcumin and electronic structure of curcumin analogous and symmetry of curcumin derivative.

Poul Erik Hansen, Structural Studies of β -Diketones and Their Implications on Biological Effects, demonstrate the structure of curcumin and keto group arrangements in curcumin

Sherin Geevarghese Thomas, Kallikat Narayanan Rajasekharan, demonstrate the extraction of curcumin from the plant extract and the spectral studies of the plant extract.

Tian Jiang, Raja Ghosh, Catherine Charcosset, demonstrate the applications of curcumin in various fields and comprehensive review in food science and technolog

CHAPTER 3

AIM AND SCOPE

3.1 AIM

The main aim of this project is to synthesis 1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione. The compound were synthesized with well defined structure at room temperature by condensation method using boric anhydride, acetyl acetone, tri butyl borate and butylamine. The impurities were removed by column chromatography technique. The compound was characterized with the help of NMR and LCMS spectroscopy techniques.

3.2 Scope

- Synthesizing of 1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione
- Characterization of 1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione by NMR and LCMS spectroscopy.
- Removal of impurities from the compound.
- Conformation of product formed by characterization by Mass spectroscopy.

CHAPTER 4

MATERIAL AND METHODOLOGY

4.1 MATERIALS:

Materials used in this reaction are 4-(bis(2-chloroethyl)amino)benaldehyde, acetyl acetone, boric anhydride, tributyl borate and butyl amine, which were purchased as purified and it can be used without further purification.

4.2. CHARACTERIZATION TECHNIQUES:

4.2.1 Nuclear Magnetic Resonance (NMR)

When a nucleus that possesses a magnetic moment (Such as a hydrogen nucleus ^1H , or carbon nucleus ^{13}C) is placed in a strong magnetic field, it begins to spin like a spinning top.

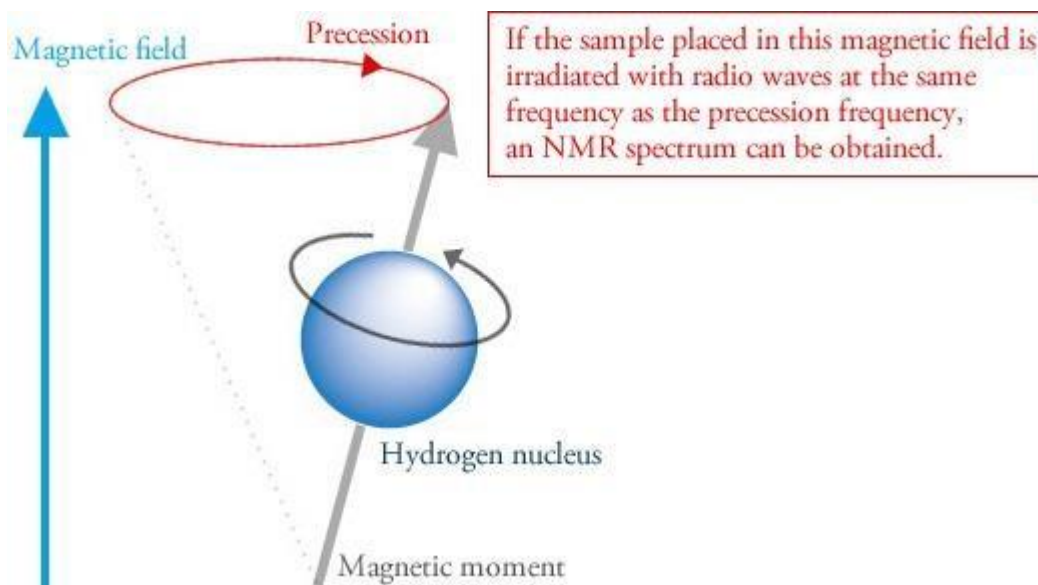


Fig 4.1 spinning momentum

Nuclear magnetic resonance is a technique that exploits the magnetic properties of certain atomic nuclei and can be used to determine the physical and chemical properties of atoms or the molecules. They can provide detailed information about the structure, dynamics, reaction state, and chemical environment of molecules. The electronic structure of a molecule and its individual functional group can be found by the intermolecular magnetic field around an atom in a molecule changes the resonance frequency. They are usually performed on the diamagnetic compounds. The nuclear magnetic resonance spectra of inorganic compounds are more complicated than organic because other nuclei also have nuclear magnetic moments. Solid-state nuclear magnetic resonance spectroscopy and even single-crystal nuclear magnetic resonance spectroscopy can be used on material that simply do not dissolve in any solvent. The theory and application of the NMR response in porous rocks are described, and the sample preparation methods, test equipment, measurement parameters, test procedure, data interpretation techniques and data reporting requirements for the principal NMR tests on core are details.

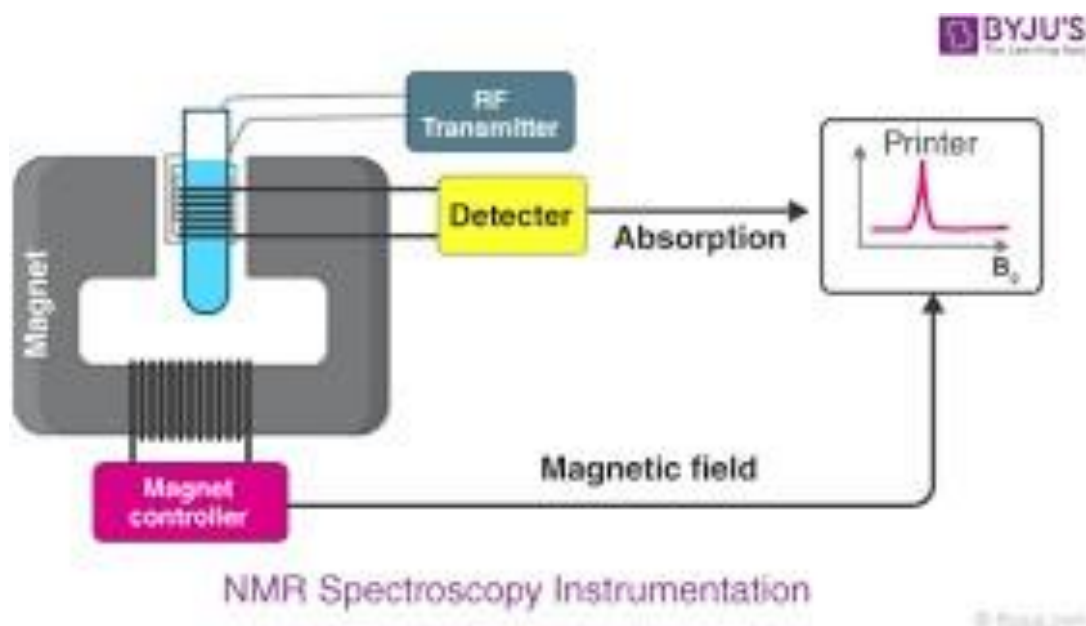


Fig 4.2 Nuclear Magnetic Resonance

4.2.2 Liquid chromatography

Liquid chromatography is a technique used to separate a sample into its individual parts. This separation occurs based on the interactions of the sample with the mobile and stationary phases. Because there are many stationary/mobile phase combinations that can be employed when separating a mixture, there are several different types of chromatography that are classified based on the physical states of those phases. Liquid-solid column chromatography, the most popular chromatography technique and the one discussed here, features a liquid mobile phase which slowly filters down through the solid stationary phase, bringing the separated components with it.

This schematic is of the basic instrumentation of a liquid-solid chromatograph. The solvent inlet brings in the mobile phase which is then pumped through the inline solvent filter and passed through the injection valve. This is where the mobile phase will mix with the injected sample. It then gets passed through another filter and then passed through the column where the sample will be separated into its components. The detector detects the separation of the analytes and the recorder, or usually a computer will record this information. The sample then goes through a backpressure filter and into waste.

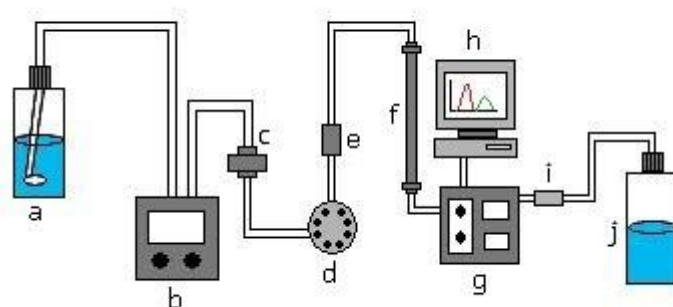


Fig 4.3 Liquid chromatography

A basic LC system consists of (a) a solvent inlet filter, (b) pump, (c) inline solvent filter, (d) injection valve, (e) precolumn filter, (f) column, (g) detector, (h) recorder, (i) backpressure regulator, and a (j) waste reservoir.

4.2.3 Mass spectroscopy

Mass spectrometry is an analytical tool useful for measuring the **mass-to-charge ratio** (m/z) of one or more molecules present in a sample. These measurements can often be used to calculate the **exact molecular weight** of the sample components as well. Typically, mass spectrometers can be used to identify unknown compounds via molecular weight determination, to quantify known compounds, and to determine structure and chemical properties of molecules.

How does a mass spectrometer perform such a feat? Every mass spectrometer consists of at least these three components:

- Ionization Source
- Mass Analyzer
- Ion Detection System

1. The Ionization Source

Molecules are converted to **gas-phase ions** so that they can be moved about and manipulated by external electric and magnetic fields. In our laboratory we use a technique called nanoelectrospray ionization, which is somewhat similar to how cars are industrially painted. This method allows for creating positively or negatively charged ions, depending on the experimental requirements. Nanoelectrospray ionization can directly couple the outlet of a small-scale chromatography column directly to the inlet of a mass spectrometer. The flow from the column is passed through a needle that is 10-15 μm at its tip.

2. The Mass Analyzer

Once ionized, the ions are sorted and separated according to **mass-to-charge** (m/z) ratios. There are a number of mass analyzers currently available, each of which has trade-offs relating to speed of operation, resolution of separation, and other operational requirements. The specific types in use at the Broad Institute are discussed in the next section. The mass analyzer often works in concert with the ion detection system.

3. Ion Detection System

The separated ions are then measured and sent to a data system where the m/z ratios are stored together along with their relative abundance. A **mass spectrum** is simply the m/z ratios of the ions present in a sample plotted against their intensities. Each peak in a mass spectrum shows a component of unique m/z in the sample, and heights of the peaks connote the relative abundance of the various components in the sample.

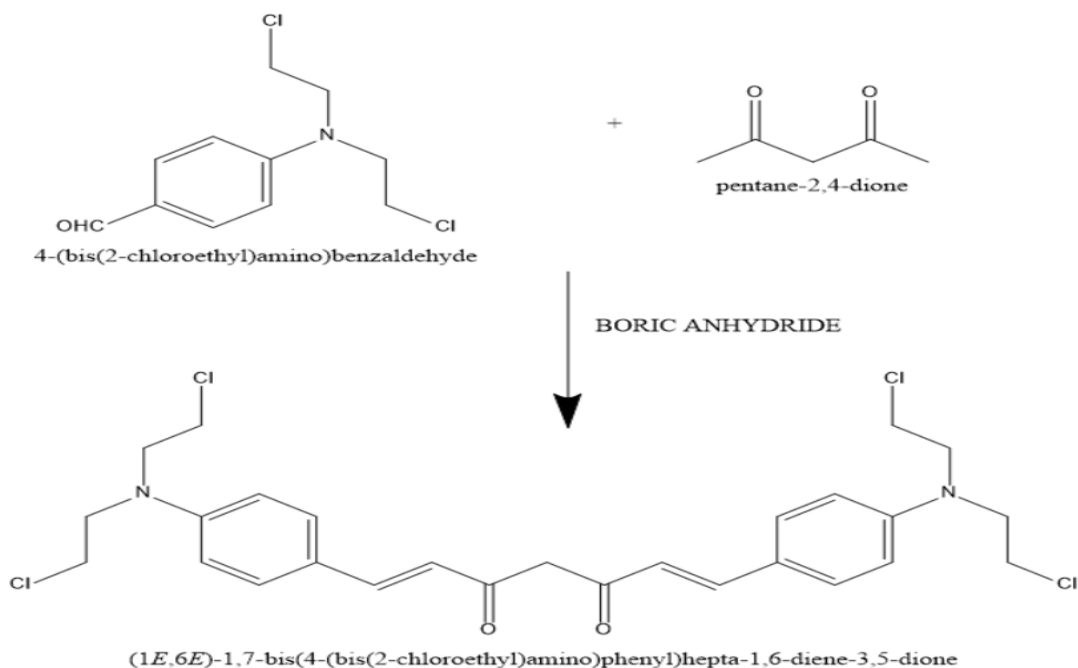
4.3 METHODOLOGY:

4.3.1 Synthesis of 4-(bis(2-chloro)amino)benzaldehyde:

N,N-bis(2-chloroethylaniline (II). The procedure was a modification of that of Ross. To 170 g. (102 ml., 1.1 mole) phosphorus oxychloride chilled in an ice bath 100 g (0.55 mole) of N-phenyldiethanolamine was slowly added. After the addition was completed, the mixture was warmed on the steam bath for one hour and then taken up in 500ml of benzene. The benzene solution was poured onto 500g of ice and the layers were separated. The aqueous layer was washed with three 50ml portion of benzene and the combined benzene solutions were dried over anhydrous magnesium sulphate. Removal of the benzene left an oil which was taken up in the minimum amount of hot absolute methanol. On chilling with stirring 98g (82%) of product, m.p.41-45°. By use of this inverse quenching of the reaction mixture no difficulty in inducing the crude material to crystallize was encountered, even when the alumina chromatography step included in the procedure of Ross was omitted.

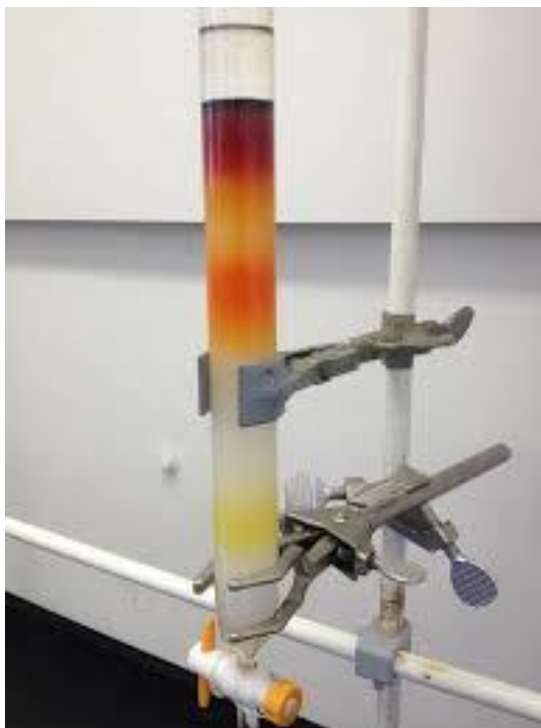
4.3.2 Synthesis of 1,7-bis(4-bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione: -

4-(bis(2-chloroethyl)amino)benzaldehyde (60 g, 0.4 mole) and 210 ml (184 g) of tributyl borate (0.8 mole) were dissolved in 200 ml of dry ethyl acetate. The compound formed from 20 g of acetylacetone (0.2 mole) and 10 g of boric anhydride (0.14 mole) was added and the mixture stirred for 5 min. While stirring, 1 ml of butylamine was added drop by drop every 10 min (total 4 ml). Stirring was continued for 4 h, after which the mixture was allowed to stand overnight. The next day 300 ml of 0.4 N hydrochloric acid (60") were added and the mixture was stirred for 60 min. The layers were separated, and the aqueous layer was extracted three times with 100 ml of ethyl acetate. The combined ethyl acetate layers were washed acidfree and evaporated to about 150 ml. Then 100 ml of methanol were added and, after 3 h in the refrigerator, curcumin was filtered off, washed with cold methanol until the wash liquid was yellow and dried. Yield 50 g of pale blue or colourless product is obtained.



4.3.3 Removal of impurities

The impurities are removed by the column chromatography. The compound is occur at the aqueous phase so the compound is separated at the initial percentage of the chromatograph, so the compound is easily separated out.



4.5 column chromatography

CHAPTER 5

RESULT AND DISCUSSION

5.1 CHARACTERIZATION OF 1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione

5.1.1 NMR SPECTRAM FOR 1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione

The NMR spectrum of 1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione are shown in Fig.5.2, the estimated NMR spectral peak is obtained at 200ppm, 150ppm, 130ppm, 110ppm and 70ppm correspond to C=O stretching of ketone group, C-N stretching, C=C stretching, C-C stretching and C-X stretching respectively. The peak at 150ppm is the characteristic peak for 1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione compound.

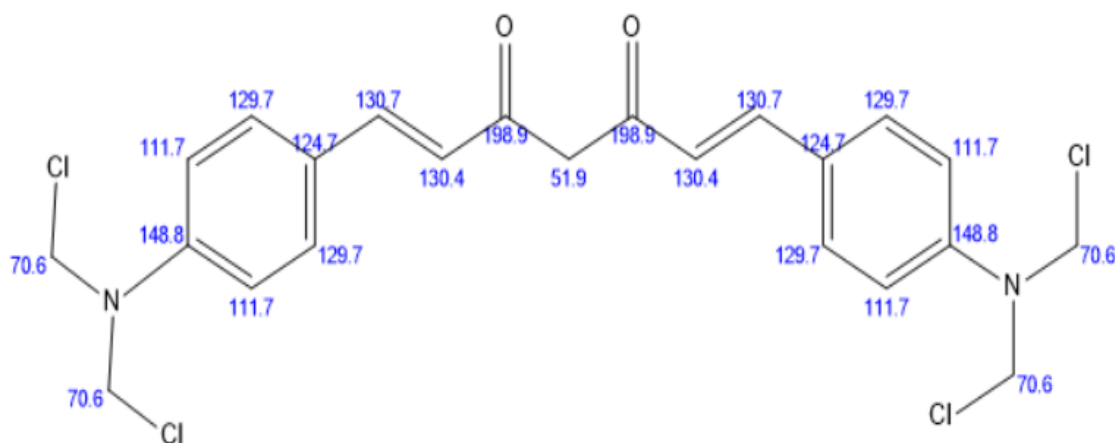


Fig 5.1 ChemNMR C^{13} Estimation

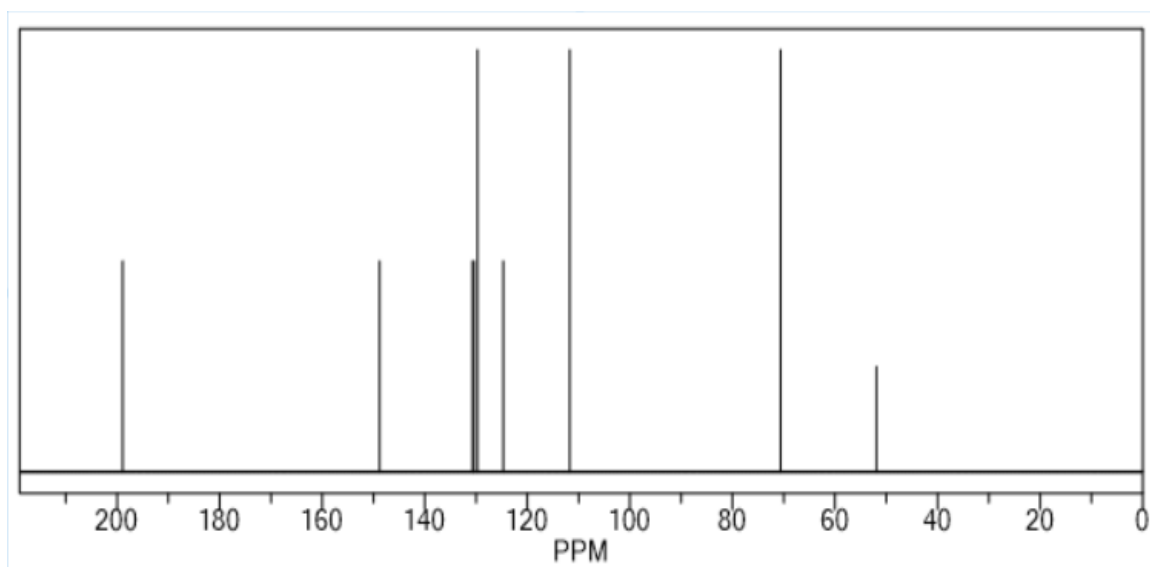


Fig 5.1.1 (5.1) ChemNMR C^{13} Estimation graph

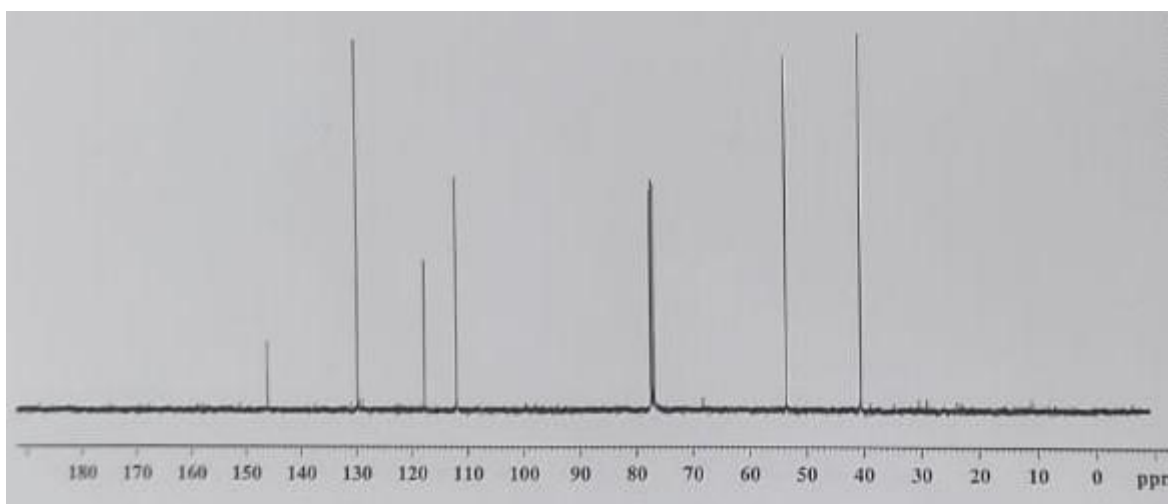


Fig 5.1.2 (5.2) NMR graph

The actual NMR spectral peak is obtained at 200ppm, 150ppm, 130ppm, 110ppm and 70ppm correspond to C=O stretching of ketone group, C-N stretching, C=C stretching, C-C= stretching and C-X stretching respectively. The peak at 150ppm is the characteristic peak for 1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione compound. So the NMR values confirms that the compound 1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione is obtained.

5.1.2 LCMS Spectrum for 1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione

The LCMS spectroscopy shows that the compound exact mass of the compound is 498.04 and molecular weight of the compound is 500.24. And the elemental analysis of percentage of elements present in the compound is,

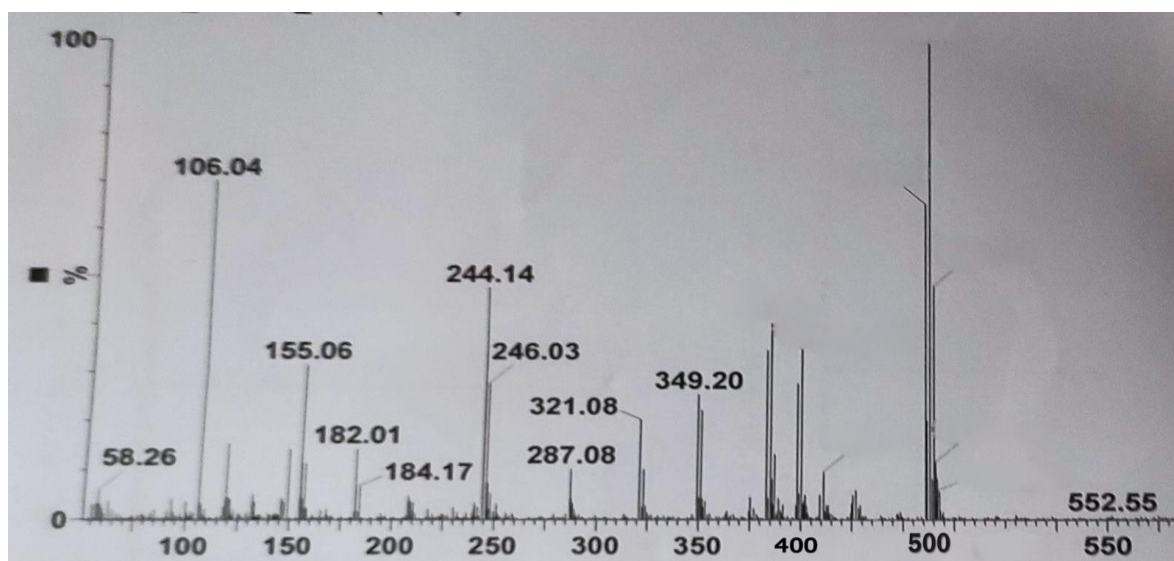
CARBON – 55.22

HYDROGEN – 4.43

CHLORINE – 28.35

NITROGEN – 5.60

OXYGEN – 6.40



5.1.3 (5.3) LCMS graph

The graph shows that the actual molecular peak is attained at 500, which shows that the compound is slightly formed and the peak value shows the actual molecular weight of the compound.

CHAPTER 6

CONCLUSION

In summary, 1,7-bis(4-(bis(2-chloroethyl)amino)phenyl)hepta-1,6-diene-3,5-dione was synthesized using 4-(bis(2-chloro)amino)benzaldehyde, acetyl acetone, boric anhydride, tributylamine and ethyl acetate at room temperature. The NMR values shows the bonding and stretching on the compound, and the LCMS shows the actual molecular weight of the compound.

REFERENCE

1. Helen-Lisette Alvarado, David Limón, Ana-Cristina Calpena-Campmany, Mireia Mallandrich, Laura Rodríguez-Cid, Núria Aliaga-Alcalde, Arántzazu González-Campo, Lluïsa Pérez-García, Intrinsic Permeation and Anti-Inflammatory Evaluation of Curcumin, Bisdemethoxycurcumin and Bisdemethylcurcumin by a Validated HPLC-UV Method, *International Journal of Molecular Sciences*, 10.3390/ijms24076640, **24**, 7, (6640), (2023).
2. Dawid Lazewski, Malgorzata Kucinska, Edward Potapskiy, Joanna Kuzminska, Lukasz Popenda, Artur Tezyk, Tomasz Goslinski, Marcin Wierzchowski, Marek Murias, Enhanced Cytotoxic Activity of PEGylated Curcumin Derivatives: Synthesis, Structure–Activity Evaluation, and Biological Activity, *International Journal of Molecular Sciences*, 10.3390/ijms24021467, **24**, 2, (1467), (2023).
3. Matteo Perini, Silvia Pianezze, Luca Ziller, Roberto Larcher, Roberto Pace, Stable Isotope Ratio Analysis for the Authentication of Natural Antioxidant Curcuminoids from *Curcuma longa* (Turmeric), *Antioxidants*, 10.3390/antiox12020498, **12**, 2, (498), (2023).
4. Joana R. M. Ferreira, Mariana Alves, Bárbara Sousa, Sandra I. Vieira, Artur M. S. Silva, Samuel Guieu, Ângela Cunha, Raquel Nunes da Silva, Curcumin-based molecular probes for fluorescence imaging of fungi, *Organic & Biomolecular Chemistry*, 10.1039/D2OB01872A, **21**, 7, (1531-1536), (2023).
5. Nikolay S. Zimnitskiy, Vladislav Yu. Korotaev, Alexey Yu. Barkov, Ivan A. Kochnev, Vyacheslav Ya. Sosnovskikh, Hemicurcuminoids (1-styryl-1,3-diketones) – valuable multi-faceted building blocks for organic synthesis, *New Journal of Chemistry*, 10.1039/D2NJ04338F, **47**, 11, (5110-5149), (2023).
6. Hae Un Kim, Taehyun Kim, Chanhyeok Kim, Taiho Park, Sunyoung Sohn, Efficient organic deep-red to near-infrared light emitters based on boron difluoride curcuminoid derivatives, *Dyes and Pigments*, 10.1016/j.dyepig.2022.111064, **211**, (111064), (2023).
7. Roopa Venkataraj, Madanan Kailasnath, Curcumin: Nature's Gold for Photonic Applications, *Encyclopedia of Materials: Electronics*, 10.1016/B978-

0-12-819728-8.00064-4, (529-575), (2023).

8. Dilipkumar Pal, Pooja Sahu, Antiviral Potential of Curcumins: Ethnopharmacology, Chemistry, and Clinical Studies Focusing on Mechanism of Action and Future Perspectives, Anti-Viral Metabolites from Medicinal Plants, 10.1007/978-3-030-83350-3_30-1, (1-36), (2023).
9. Marco A. Obregón-Mendoza, William Meza-Morales, Yair Alvarez-Ricardo, M. Mirian Estévez-Carmona, Raúl G. Enríquez, High Yield Synthesis of Curcumin and Symmetric Curcuminoids: A “Click” and “Unclick” Chemistry Approach, Molecules, 10.3390/molecules28010289, **28**, 1, (289), (2022).
10. Yang-Je Cheng, Cai-Wei Li, Cing-Ling Kuo, Tzenge-Lien Shih, Jih-Jung Chen, Improved Synthesis of Asymmetric Curcuminoids and Their Assessment as Antioxidants, Molecules, 10.3390/molecules27082547, **27**, 8, (2547), (2022).
11. Michael Flanders, William M. Gramlich, Water-Soluble and Degradation-Resistant Curcumin Copolymers from Reversible Addition–Fragmentation Chain (RAFT) Copolymerization, Macromolecules, 10.1021/acs.macromol.2c00123, **55**, 10, (4064-4075), (2022).
12. Michael Flanders, William M. Gramlich, Water-Soluble and Degradation-Resistant Curcumin Copolymers from Reversible Addition–Fragmentation Chain (RAFT) Copolymerization, Macromolecules, 10.1021/acs.macromol.2c00123, **55**, 10, (4064-4075), (2022).
13. Sitabja Mukherjee, Santosh K. Kar, Curcuminoids: The Novel Molecules of Nature, Herbs and Spices - New Processing Technologies, 10.5772/intechopen.99201, (2021).
14. Emese Gál, Levente Csaba Nagy, Photophysical Properties and Electronic Structure of Symmetrical Curcumin Analogues and Their BF₂ Complexes, Including a Phenothiazine Substituted Derivative, Symmetry, 10.3390/sym13122299, **13**, 12, (2299), (2021).
15. Poul Erik Hansen, Structural Studies of β -Diketones and Their Implications on Biological Effects, Pharmaceuticals, 10.3390/ph14111189, **14**, 11, (1189), (2021).
16. Abraham A. Abe, Cesare Oliviero Rossi, Paolino Caputo, Maria Penelope De Santo, Nicolas Godbert, Iolinda Aiello, Spicy Bitumen: Curcumin Effects on the Rheological and Adhesion Properties of Asphalt, Materials,

- 10.3390/ma14071622, **14**, 7, (1622), (2021).
17. Matteo Mari, Debora Carrozza, Erika Ferrari, Mattia Asti, Applications of Radiolabelled Curcumin and Its Derivatives in Medicinal Chemistry, International Journal of Molecular Sciences, 10.3390/ijms22147410, **22**, 14, (7410), (2021).
 18. Filippa Lo Cascio, Paola Marzullo, Rakez Kaye, Antonio Palumbo Piccionello, Curcumin as Scaffold for Drug Discovery against Neurodegenerative Diseases, Biomedicines, 10.3390/biomedicines9020173, **9**, 2, (173), (2021).
 19. Sherin Geevarghese Thomas, Kallikat Narayanan Rajasekharan, Extraction of Curcumin from Turmeric Powder Through Complexation, Oriental Journal Of Chemistry, 10.13005/ojc/370325, **37**, 3, (695-699), (2021).
 20. Digambara Patra, Riham El Kurdi, Curcumin as a novel reducing and stabilizing agent for the green synthesis of metallic nanoparticles, Green Chemistry Letters and Reviews, 10.1080/17518253.2021.1941306, **14**, 3, (474-487), (2021).
 21. Shoaib Taavoni, Mohammad Hadi Baghersad, Synthesis and Evaluation of Radical Scavenging Activity of (Pyrazole-3,5-Diyl)Bis(Ethene-2,1-Diyl)Bis(2-Methoxyphenol) Derivatives, Polycyclic Aromatic Compounds, 10.1080/10406638.2021.2022725, **43**, 2, (1008-1018), (2021).
 22. Pudi Manga Veni, Padma Suhasini Kilaru, Green synthesis of 1,7-bis(substituted phenyl)1,6-heptadiene-3,5-diones and their inhibition of human pathogenic bacteria, Toxicological & Environmental Chemistry, 10.1080/02772248.2021.1917576, **103**, 2, (129-136), (2021).
 23. Tian Jiang, Raja Ghosh, Catherine Charcosset, Extraction, purification and applications of curcumin from plant materials-A comprehensive review, Trends in Food Science & Technology, 10.1016/j.tifs.2021.04.015, **112**, (419-430), (2021).
 24. Fiona C. Rodrigues, NV Anil Kumar, Goutam Thakur, The potency of heterocyclic curcumin analogues: An evidence-based review, Pharmacological Research, 10.1016/j.phrs.2021.105489, **166**, (105489), 2021
 25. Vinh Tien Nguyen, Thien Minh Huynh, Thi Nhu Quynh Nguyen, Tan Hoang Le, Enhancing the stability of synthesized curcumin by spray-drying

- microencapsulation with soy lecithin and gum Arabic, *Brazilian Journal of Chemical Engineering*, 10.1007/s43153-021-00124-3, **38**, 3, (563-572), (2021).
26. Sung-Jen Hung, Yi-An Hong, Kai-Yu Lin, Yi-Wen Hua, Chia-Jou Kuo, Anren Hu, Tzenge-Lien Shih, Hao-Ping Chen, Efficient Photodynamic Killing of Gram-Positive Bacteria by Synthetic Curcuminoids, *International Journal of Molecular Sciences*, 10.3390/ijms21239024, **21**, 23, (9024), (2020).
 27. Elena Horosanskaia, Lina Yuan, Andreas Seidel-Morgenstern, Heike Lorenz, Purification of Curcumin from Ternary Extract-Similar Mixtures of Curcuminoids in a Single Crystallization Step, *Crystals*, 10.3390/cryst10030206, **10**, 3, (206), (2020).
 28. Le Thi Bich Nguyet, Vinh Tien Nguyen, Smart Starch-Gelatin Films Incorporated with Curcumin, *Oriental Journal Of Chemistry*, 10.13005/ojc/360610, **36**, 6, (1088-1095), (2020).
 29. Martina Pini, Roberto Rosa, Paolo Neri, Anna Maria Ferrari, LCA Application to Chemical Synthesis at Laboratory Scale, Life Cycle Assessment in the Chemical Product Chain, 10.1007/978-3-030-34424-5_5, (101-123), (2020).
 30. Sari Honda, Rika Ishida, Kayo Hidaka, Toshiya Masuda, Stability of Polyphenols under Alkaline Conditions and the Formation of a Xanthine Oxidase Inhibitor from Gallic Acid in a Solution at pH 7.4, *Food Science and Technology Research*, 10.3136/fstr.25.123, **25**, 1, (123-129), (2019).