EGE UNIVERSITY GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES

(MASTER OF SCIENCE THESIS)

BRIDGED BIBENZIMIDAZOLYUM BROMIDES AND THEIR APPLICATIONS TO COUPLING REACTIONS

Serpil DENİZALTI

Chemistry Department

Department Code: 405.02.01

Presentation Date: 02.08.2006

Supervisor: Prof. Dr. Engin ÇETİNKAYA

Bornova-İZMİR

Sayın **Serpil Denizaltı tarafından** yüksek lisans tezi olarak sunulan **"Bridged Bibenzimidazolium Salts and Their Applications to Coupling Reactions"** başlıklı bu çalışma E.Ü. Lisansüstü Eğitim ve Öğretim Yönetmeliği ile E.Ü. Fen Bilimleri Enstitüsü Eğitim ve Öğretim Yönergesi'nin ilgili hükümleri uyarınca tarafımızdan değerlendirilerek savunmaya değer bulunmuş ve 02.08.2006 tarihinde yapılan tez savunma sınavında aday oybirliği/oyçokluğu ile başarılı bulunmuştur.

Jüri Üyeleri: **İmza**

Jüri Başkanı : ....

Raportör Üye: ....

Üye : ....

ÖZET

KÖPRÜLÜ BİBENZİMİDAZOLYUM BROMÜRLER VE EŞLEŞME REAKSİYONLARINDAKİ UYGULAMALARI

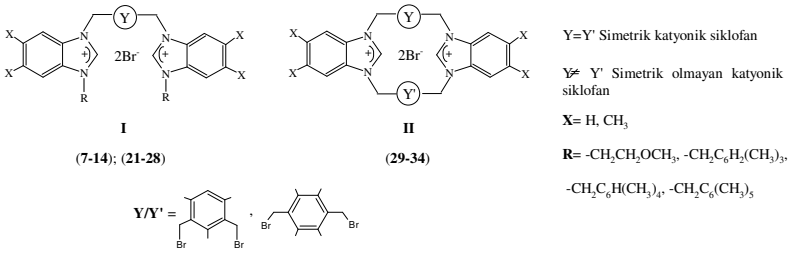
DENİZALTI, Serpil

Yüksek Lisans Tezi, Kimya Bölümü

Tez Yöneticisi: Prof. Dr. Engin Çetinkaya

Ağustos 2006, 69 sayfa

Bu tez köprülü bibenzimidazolyum bromürlerle (**I** ve **II**) ilgilidir ve üç kısımdan oluşmaktadır. İlk kısım 1,3-diazollere ait temel bilgiler, önemi ve kullanılımları hakkında kısa bir derlemedir. İkinci kısımda deneysel veriler ayrıntılı bir biçimde açıklanmıştır. Üçüncü kısım köprülü bibenzimidazolyum tuzlarının sentezi, yapı aydınlatılması ve eşleşme (Suzuki ve Heck) tepkimelerindeki katalitik aktivitelerinin incelenmesini kapsamaktadır. Bu çalışmada seri halinde mono- ve di- köprülü bibenzimdazolyum tuzları (**I** ve **II**) sentezlenmiştir.



I (**7-14**); (**21-28**) **II** (**29-34**)

I ve **II**' nin yapı aydınlatılmasından sonra (IR, ^{1}H NMR ve ^{13}C NMR) tüm tuzların $Pd(OAc)_2$ varlığında (Suzuki ve Heck) eşleşme tepkimelerindeki katalitik aktiviteleri araştırılmıştır. En iyi katalitik aktivite **I**' de (R=-$CH_2CH_2OCH_3$) gözlenmiştir.

Anahtar sözcükler:1,3-Diazoller, benzimidazolium salts, catalytic activities.

ABSTRACT

BRIDGED BIBENZIMIDAZOLYUM BROMIDES AND THEIR APPLICATIONS TO COUPLING REACTIONS

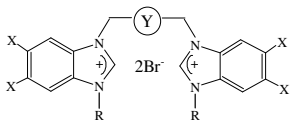
DENİZALTI, Serpil

Master of Science Thesis, Chemistry Department

Supervisor: Prof. Dr. Engin Çetinkaya

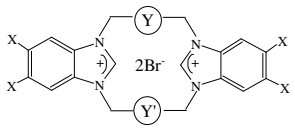
August 2006, 69 pages

This thesis is related with bridged bibenzimidazolium bromides (**I** ve **II**) and consist of three parts. The first part is a concise review about 1,3-diazoles and their importance and use. In part two the experimental details were explained. Part three covers the synthesis, characterisation, and catalytic activities of bridged bibenzimidazolium salts. In this study, series of mono- and di-bridged bibenzimidazolium bromides (**I** and **II**) were prepared.



I

(**7-14**); (**21-28**)



II

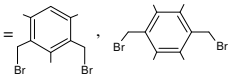
(**29-34**)

Y=Y' Symmetric cationic cyclophane

Y ≠ Y' Unsymmetric cationic cyclophane

X= H, CH_3

R= $-CH_2CH_2OCH_3$, $-CH_2C_6H_2(CH_3)_3$, $-CH_2C_6H(CH_3)_4$, $-CH_2C_6(CH_3)_5$

Y/Y' = 

After characterisation of **I** and **II** by spectroscopic methods (IR, ^1H NMR and ^{13}C NMR), catalytic activities of all the related salts in the presence of $Pd(OAc)_2$ for Suzuki and Heck reactions were examined. The best catalytic activity was observed for **I** (R=$-CH_2CH_2OCH_3$)

Keywords: 1,3-Diazoles, benzimidazolium salts, catalytic activities.

ACKNOWLEDGEMENT

I gratefully acknowledge Prof. Dr. Engin ÇETİNKAYA for her considerable contributions, precious suggestion, supports and supervision.

I'm also grateful to Prof. Dr. Bekir ÇETİNKAYA for his valuable suggestions, criticism and supports.

I thank to Research Assistant Hayati TÜRKMEN for his supportive behaviours and collaborations during this study.

I also thank to my friends Bahar BARIŞIK for their supports during my study.

I would like to thank and present my gratitude to my family who have encouraged and supported me during my studies.

Finally, I thank Ege University research fund (project number: 2005/ Fen /009) for supportting this work.

Serpil DENİZALTI

CONTENTS

Page

CONTENTS (Continue)

Page

CONTENTS (Continue)

Page

LIST OF SCHEMES AND FIGURES

Scheme **Page**

Figure

LIST OF SCHEMES AND FIGURES (Continue)

Figure **Page**

LIST OF TABLES

LIST OF TABLES (Continue)

ABBREVIATIONS

Abbreviation	Explanation
BuOH	Buthanol
$CDCl_3$	Deuteriochloroform
CD_3OD	Deuteriomethanol
CH_2Cl_2	Dichloromethane
DMA	N,N-Dimethylacetamide
DMSO	Dimethylsulfoxide
Et	Ethyl
Et_2O	Diethyl ether
EtOH	Ethanol
EtOAc	Ethyl acetate
Eq.	Equation
ero	Electron Rich Olefins
FTIR	Fourier Transform Infrared Spectrometer
GC	Gas chromatography
Hz	Hertz
IPA	Isopropyl alcohol
IR	Infrared Spectroscopy
KOH	Potassium hydroxide
KO^tBu	Potassium tert butoxide
NaH	Sodium hydride
NaOH	Sodium hydroxide
NHC	N-Heterocyclic Carbene
N.M.R	Nuclear Magnetic Resonance

ABBREVIATIONS (Continue)

Me	Methyl
MeOH	Methanol
m.p.	Melting point
THF	Tetrahydrofuran

1.INTRODUCTION

1.1 Imidazoles and Benzimidazoles

Imidazole and benzimidazole are incorporated into many important biological molecules. However imidazole and benzimidazole have become an important part of many pharmaceuticals. Synthetic imidazoles and benzimidazoles are present in many fungicides and antifungal, antiprotozoal, and antihypertensive medications.

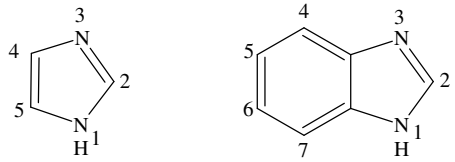


Figure 1.1 Imidazole, benzimidazole and their numbering scheme

A number of naturally occurring substances, such as histidine and the purines, have been found to contain the imidazole nucleus, while 5,6-dimethyl-1-(α-D-ribofuranosyl)benzimidazole is an integral part of the structure of vitamin B_{12}. Histidine is present in many proteins and enzymes and plays a vital part in the sructure and binding functions of hemoglobin (Mathews; Holde; Ahern, 2000).

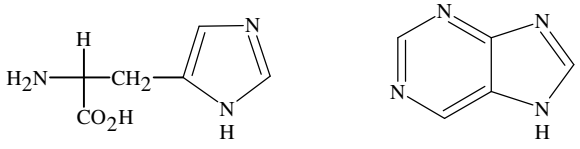


Figure 1.2 Histidine and purine

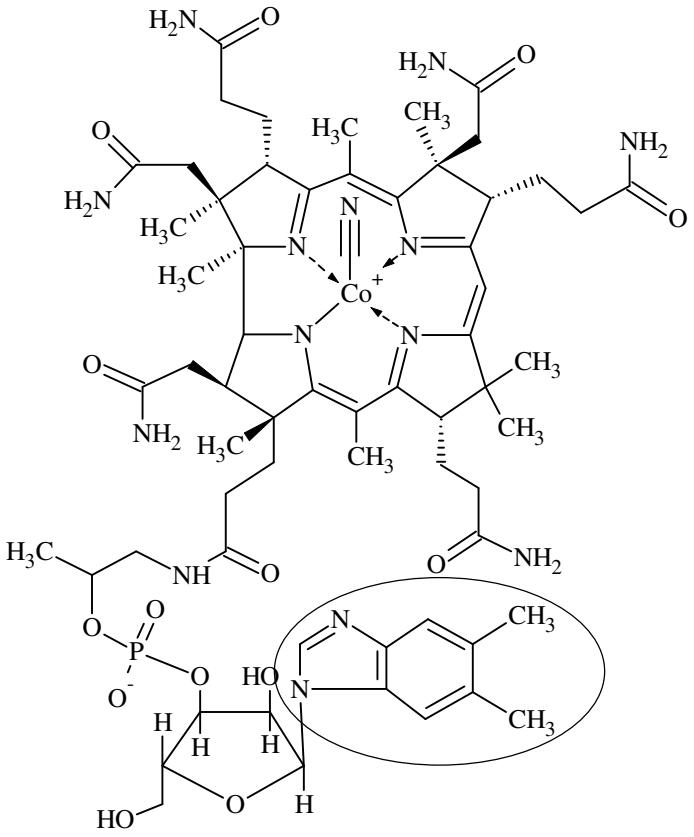
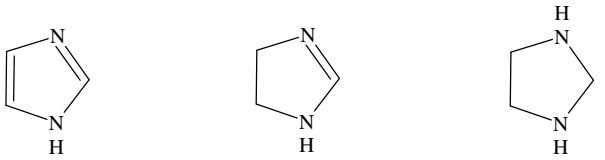


Figure 1.3 B_{12} vitamin

B_{12} vitamin (cynocobalamin) can be degradated to 5,6-dimethylbenzimidazole, and afforded important evidence of the structure.

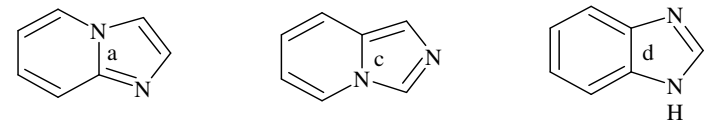
Dihydro and tetrahydro derivatives of imidazole (or 1,3-diazole) are called as imidazole-2-in and imidazolidine, respectively (Figure 1.4).



imidazole imidazole-2-in imidazolidine

Figure 1.4 Reduced form of imidazole

Three isomers of the benzimidazole molecules are known (Figure 1.5) The isomer called benzo[d]imidazole or shortly benzimidazole is the important one. Because a massive research effort has been expended upon the chemistry of benzo[d]imidazoles with particular emphasis on the synthesis of new compounds for pharmacological importance (Kutlu, 1976).



benzo[a]imidazole benzo[c]imidazole benzo[d]imidazole

Figure 1.5 Benzimidazole isomers

1.2. Properties of imidazoles and benzimidazoles

1.2.1 Physical properties

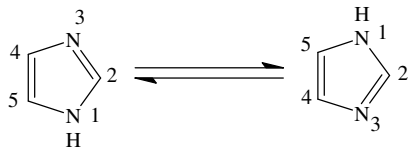
Imidazole, which is a five membered planar ring, is soluble in water and polar solvents. Imidazole and 1-methylimidazole are odourless, however they have very much higher boiling points, 256°C and 199°C, respectively. 2-Imidazolines unsubstituted at the nitrogen of the 1-position show a greater solubility in polar solvents than the 1-alkyl- or 1-aryl-substituted derivatives. 2-Imidazolines which are unsubstituted in the 1-

position are solids or heavy viscous oils, while compounds substituted in this position are most frequently liquids.

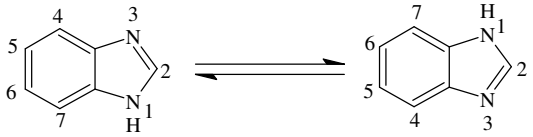
Benzimidazoles are generally crystalline solids which have high melting and boiling points. They are soluble in polar solvents but slightly soluble in nonpolar solvents. The melting and boiling points of N-substituted benzimidazoles are lower than benzimidazole itself due to lack of imino hydrogen.

1.2.2 Tautomeric character

Imino hydrogens show tautomerism in both heterocyclic system [Eq.(1.3; 1.4)].

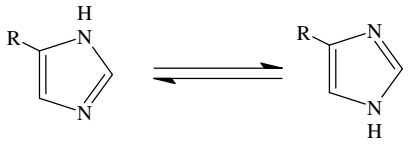


(1.3)



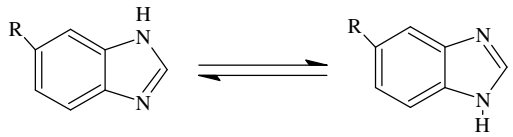
(1.4)

Consequently, in the substituted imidazoles and benzimidazoles the two isomeric structures are at equilibrium. Therefore, for naming the position of the substituent (R) is shown as 4(5) or 5(6) respectively [Eq.(1.5; 1.6)].



(1.5)

5-alkylimidazole 4-alkylimidazole

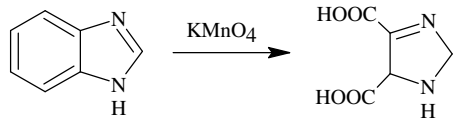


6-alkilbenzimidazole 5-alkilbenzimidazole (1.6)

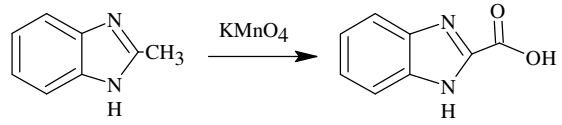
Of course, tautomerism of this kind is not possible for N-substituted imidazoles and benzimidazoles. The tautomerism in these heterocycles were discovered by Kaiser for the first time (Kaiser,1885).

1.2.3 Chemical properties

Chemical inertness is one of the most prominent properties of benzimidazoles. Imidazole ring is resistant to most of the oxidizing agents. When benzimidazole is reacted with potassium permanganate benzene ring opens by oxidation and 4,5-imidazole dicarboxylic acid forms [Eq.(1.7)]. By oxidation of 2-methyl benzimidazole with potassium permanganate 2-benzimidazole carboxylic acid forms [Eq.(1.8)].

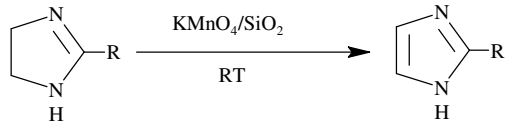


4,5 imidazoledicarboxylic acid (1.7)



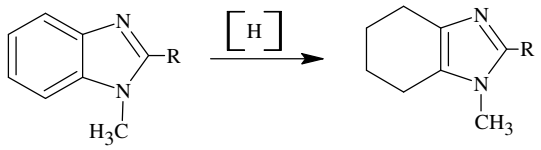
2-benzimidazolecarboxylic acid (1.8)

On the other hand, oxidation of 2-substituted imidazolines with potassium permanganate supported on silica gel yields imidazoles [Eq.(1.9)] (Baltork, 2004).



(1.9)

Benzimidazoles can not be reduced with Ni and hydrogen. But 1-methyl-2-ethyl and 1,2-dimethyl benzimidazole can be converted to their tetrahydro derivatives when they are hydrogenated in glacial acetic acid on platinium oxide [Eq.(1.10)] (Güven, 2000).



(1.10)

R= Me, Et

Imidazole is the most resistant to reduction, thus it is unaffected by sodium-liquid ammonia, concentrated hydriodic acid and red phosphorus, zinc and acid, or H_2 and a catalyst. Therefore hydrogenated derivatives cannot be obtained by reduction of imidazole but can be prepared via reaction of ethylenediamine and aldehyde derivatives.

1.3 Pharmaceutical importance of imidazoles and benzimidazoles

Substituted imidazoles are a class of pharmaceutically important heterocylic compounds, several of which have been incorporated in marketed drugs such as cimetidine and losartan. Losartan, a nonpeptide angiotensin II receptor antagonist for the treatment of hypertension, contains 2,4,5-trisubstituted imidazole (Carini,1991; Xi, 2005; Zhong, 2003).

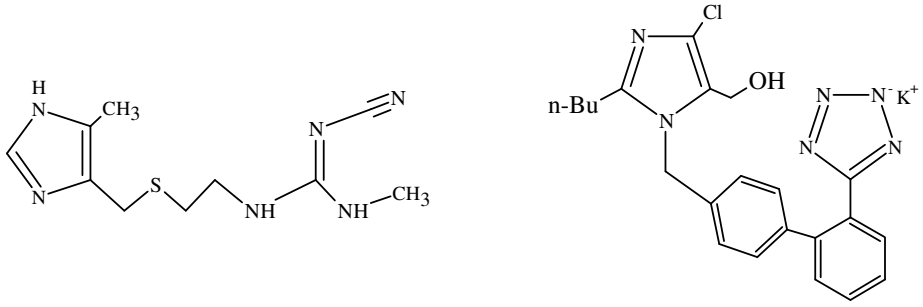


Figure 1.6 Cimetidine and Losartan

Many 2-imidazolines subtituted in the 2-position by either alkyl or aryl groups show a definite effect on the circulatory system (Ferm and Riebsomer, 1954).

Benzimidazoles posses different pharmacological activites as well. A range of benzimidazoles is now important as clinically useful drugs such as human and veterinary antihelmintics, fungicides, antineoplastics, bactericides, antihistaminics, vasodilators, hypotensives, local anesthetics and spasmolytic agents (Lednicer and Mitscer, 1977; 1980).

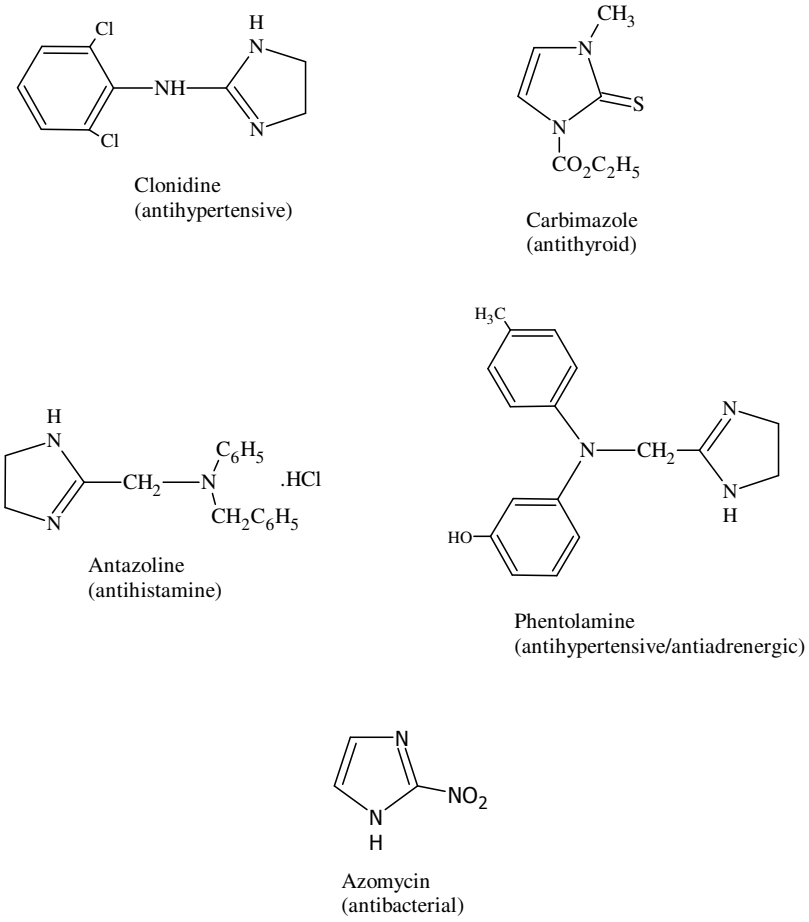
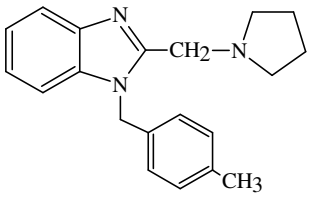
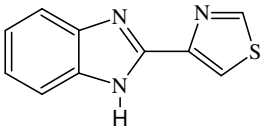


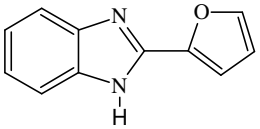
Figure 1.7 Some drugs including imidazole and imidazoline rings



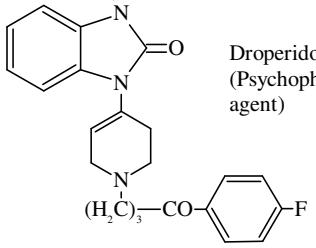
Clemizole
(Bactericide)



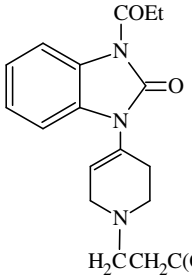
Thiabendazole
(anthelmintic)



Fuberidazole
(fungicide)



Droperidol
(Psychopharmacological
agent)



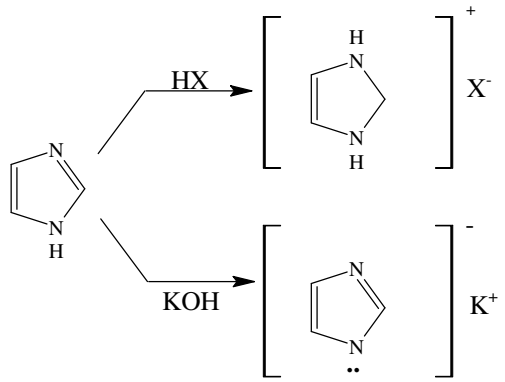
Bezitramide
(analgesic)

Figure 1.8 Some drugs including benzimidazole ring

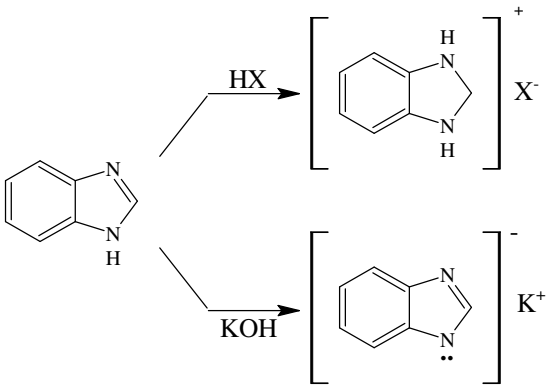
1.4 Acidic and basic properties

Unsubstituted imidazoles and benzimidazoles are amphoteric heterocycles.They can form salts with mineral acids. Their basic character is due to the presence of tertiary nitrogen which can bind a proton. Benzimidazole is less basic than imidazole. This difference arises from the conjugation between the imidazole and benzene rings. These heterocycles

are also acidic, so easily react with bases (KOH, NaOH, NaH) [Eq.(1.11; 1.12)].

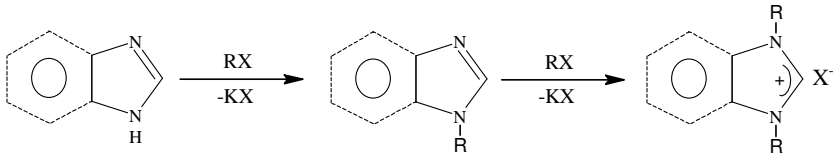


(1.11)



(1.12)

The anionic forms are excellent nucleophiles. Therefore they can easily be converted to 1-substituted 1,3-diazoles by alkylating or acylating reagents. Imidazole/benzimidazole carrying a substituent on nitrogen are also converted into quarternary salt [Eq.(1.13)].



(1.13)

1.5 The properties and use of azolium salts

1,3-Diazol(in)um salts are very versatile compounds because of their broad range of use in chemistry. They posses antielectrostatic effects. Especially, some derivatives of 1,3-disubstituted benzimidazolium salts showed this effect (Pernak, 1998).

Biological studies have indicated that azolium salts exhibit antibacterial and antifungal activities (Küçükbay, 1995; Çetinkaya, 2002; Barışık, 2005).

In recent years, ionic liquids have emerged as a set of green solvents with unique properties such as tunable polarity, high termal stability, and immiscibility with a number of organic solvents, negligible vapor pressure and recyclability (Welton, 1999; Wasserscheid, 2000). Morover, ionic liquids are simple and inexpensive to prepare and easy to recycle and their properties can be fine-tuned by changing the anion or alkyl group attached to cation. Thus, ionic liquids have been described as ‘designer solvents’.

A cyclophane is a hydrocarbon consisting of an aromatic unit (typically a benzene ring) and an aliphatic chain that forms a bridge between two non-adjacent positions of the aromatic ring. More complex derivatives with multiple aromatic units and bridges forming cagelike structures are also known. Cyclophanes are well studied in organic chemistry because they adopt unusual chemical conformations due to build-up of strain. The chemistry of cyclophanes has been interest for decades. Due to their structural versatility and opportunities for synthetic modifications, cyclophanes have received much attention in the areas of host-guest

complexation, molecular self-assembly and specific receptor activity (Rajakumar et al., 2005).

In recent years, much interest has focused on cationic azolium-linked cyclophanes systems the linking units are placed orho, meta, or para on the aromatic units; imidazolium, benzimidazolium, and benzotriazolium linking units; and aromatic units based on benzene, pyridine, and naphtalene. A number of different aspects of these azolium-linked cyclophanes have been studied, including synthesis, conformational behavior, anion binding properties, and mass spectral properties. Imidazolium and benzimidazolium units of the cyclophanes are precursors to (benz)imidazolylidenes, which are of much current interest in metal coordination chemistry. (Baker et al., 2001, 2002; Barnard et al, 2004; Simos et al., 2002; Garrison et al., 2001a,2001b; Alcalde et al., 1999; Bitter et al., 2001; Cabildol et al., 1999; Magill et al., 2001; Yuan et al., 2002; Rajakumar et al., 2000, 2002; Ramos et al., 2002).

Baker and co-workers (2004) reported a broad examination of a well-defined series of azolium-linked cyclophanes. Their study includes a 1,3,5-cyclophane and ortho-, meta-, para-, and mixed ortho/meta-substituted azolium-linked cyclophanes containing a variety of azolium units and aromatic units (Figure1.9).

1,3-Diazaol(in)um salts are used as precursor for the preparation of N-heterocyclic carbenes (NHCs) (Özdemir et. al, 2004).

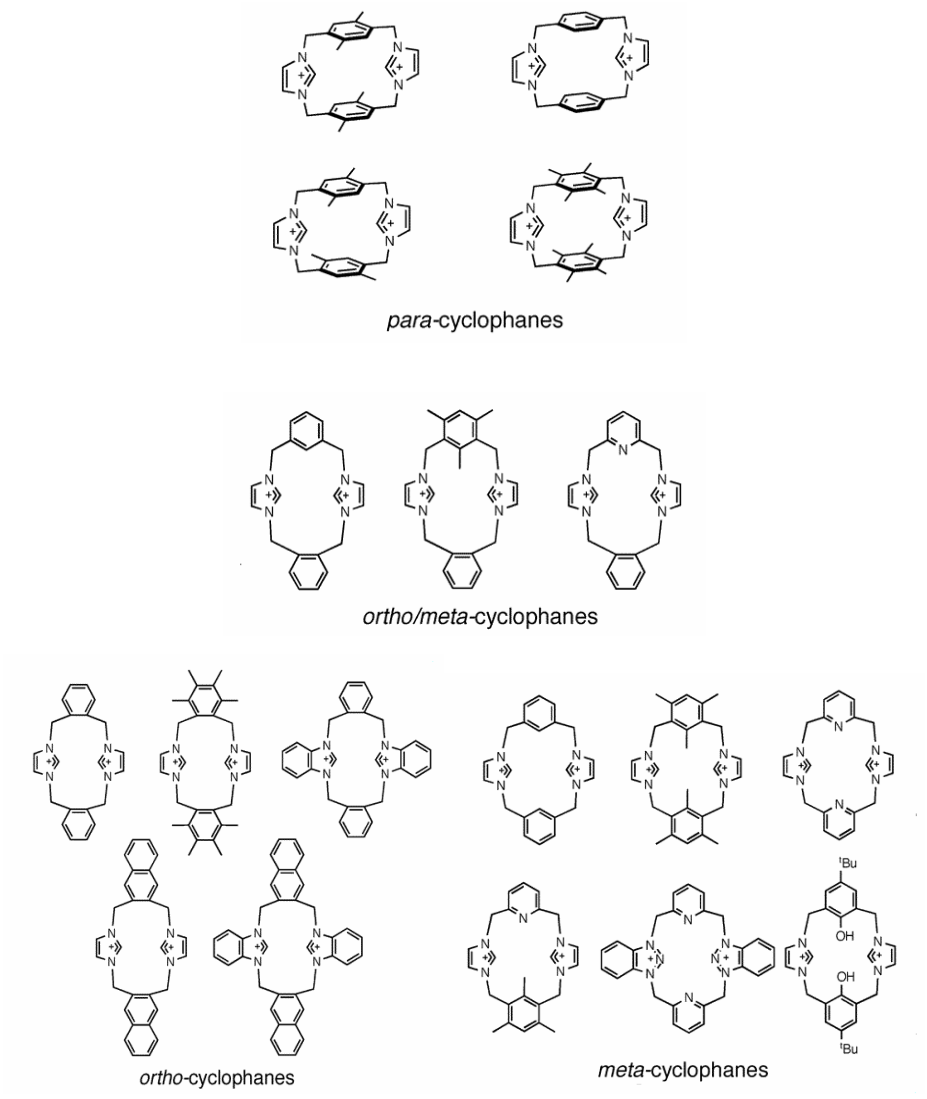
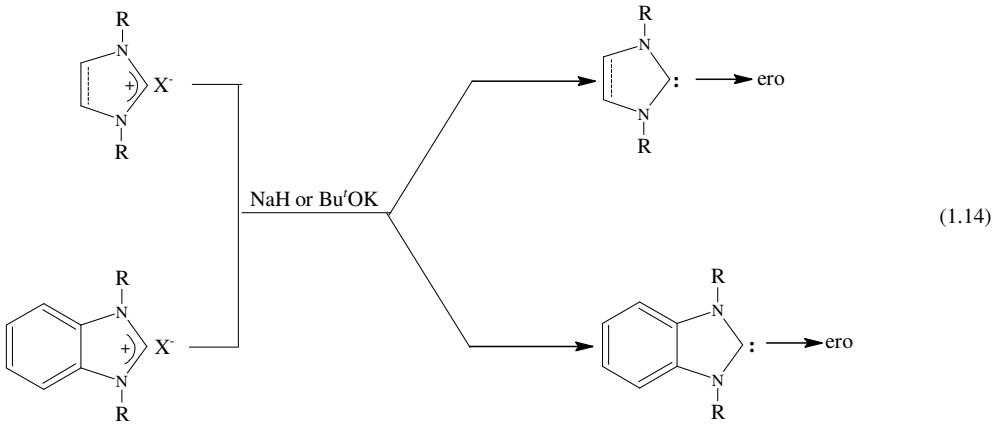


Figure 1.9 Azolium-linked cyclophanes

1.6 The conversion of 1,3-diazol(in)um salts into carbenes

Carbenes are known divalent carbon species. They are so reactive that some carbenes, such as :CH_2, :CCl_2, insert themselves into normally inert alkane C-H bonds or react with alkene to form cyclopropanes (March, 1992).

1,3-Diazol(in)um salts are converted into N-heterocyclic carbenes (NHCs). The procedure used most often is deprotonation of the corresponding azolium salts to give the free carbene [Eq.(1.14)].



(1.14)

Direct deprotonation of 1,3-disubstituted imidazolinium or disubstituted benzimidazolium salts with a less sterically demanding substituent yield dimers or electron rich olefine (ero) or enetetramines instead of free carbene (Çetinkaya et al.,1994; Shi et al., 1995).

Similar to imidazolium salts, a combination of benzimidazolium salts with metal precursors would finally lead to the corresponding NHC-metal complexes under proper conditions (Huang et al., 2005).

1.6.1 Synthesis of transition metal-NHC complexes

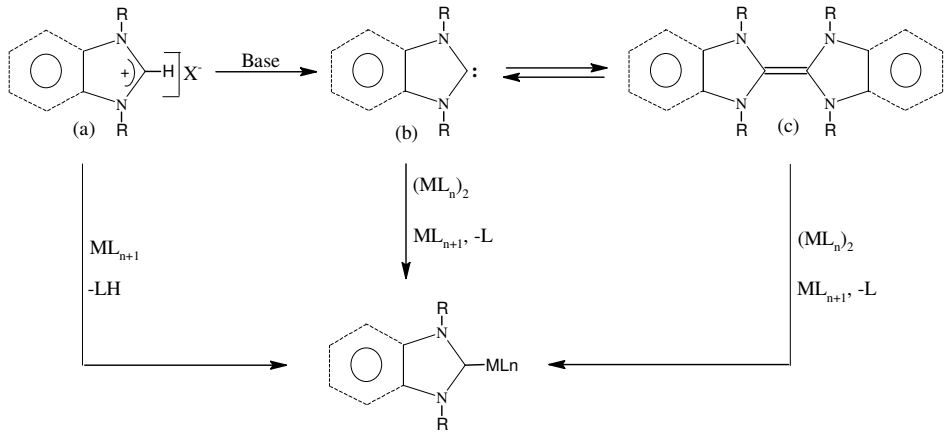
N-heterocyclic carbenes and their transition metal complexes have been focus of intense research in organometallic chemistry and homogeneous catalysis since the past decade.

Generally, three major routes are applied for the synthesis of NHC complexes

(a) the *in situ* deprotonation of ligand precursors

(b) complexation of free N-heterocyclic carbenes,

(c) the cleavage of electron-rich olefins (ero) (Scheme 1.1)

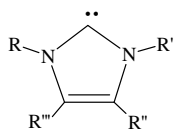


Scheme 1.1 Major synthetic pathways for the generation of transition metal NHC complexes.

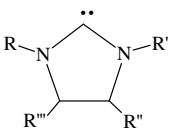
1.6.2 The importance and use of NHCs-transition metal complexes in catalysis

N-heterocyclic carbenes and their transition metal complexes have been focus of intense research in organometallic chemistry and homogeneous catalysis since the past decade.

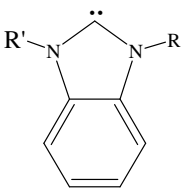
Imidazolylidenes **A**, imidazolinylidenes **B**, benzimidazolylidenes **C**, triazolinylidines **D**, and related carbenes readily complex with transition metals (Hitchcock et al., 1980; Herrmann, 2002) These ligands are excellent σ-donors and form rather strong metal-carbon bonds; therefore, catalysts containing these ligands often have better air and thermal stability than complexes containing phosphines (Peris et al.,2001; Briot et al., 2000). The use of such ligands in catalysis has lead to major advances particularly in the area of Ru-catalyzed alkene C-C bond forming reactions (Jafarpouret al., 2001; Hillier et al., 2002).



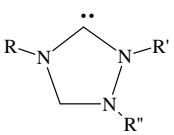
imidazolylidene
A



imidazolinylidene
B



benzimidazolylidene
C



triazolinylidene
D

In particular, palladium complexes of NHC derived from imidazolium and imidazolinium salts are highly active catalysts for a wide range of C-C coupling reactions. For example, complexes derived from

benzimidazolium precursors have been investigated for their catalytic activities for Heck reaction (Huynh et al., 2005).

The palladium-imidazolium salt systems have proved to be one of the most successful catalyst for the Suzuki coupling. Substituent on the nitrogen atoms of imidazolium significantly influence the catalytic activities. Recently, in order to find more efficient palladium catalysts, for coupling of aryl chloride for Suzuki reaction *in situ* prepared three-component system $Pd(OAc)_2$-1,3-dialkylbenzimidazolium salt-Cs_2CO_3 have been employed (Özdemir et al., 2004; Gök et al., 2005). However, despite the numerous efforts to prepare chiral carbene complexes, there have been few reports on highly enantioselective catalytic transformations using these systems. Therefore, novel strategies for the introduction of chirality into these systems are required (Perry et al., 2003).

1.7 The Aim of this study

NHCs are versatile and easy-to-make ligands with great potential in homogenous catalysis. In contrast to phosphine complexes, they have shown remarkable stability toward heat, oxygen and moisture, and represent a remarkable improvement with respect to the catalytic activity. The number, nature and position of the substituents on the nitrogen atoms and / or NHC ring have been found to play a crucial role in driving the catalytic activity.

In this connection as a NHC precursor bridged bibenzimidazolium salts bearing different substituents (**7-14**; **21-28**) have been synthesized to investigate the effects of substituents on the N-atoms. Furthermore, we envisioned that benzimidazolium-linked cyclophanes would be excellent

precursors toward bis N-heterocyclic carbene. For this reason, we also synthesized symmetrical or unsymmetrical cyclophanes (**29**-**34**) and their catalytic activities were tested. In addition, synthesis of functional and chiral imidazolinium and benzimidazolium salts were attempted at the beginning of this study. But no success was obtained (see experimental part: 2.2 and 2.4).

2. EXPERIMENTAL

Starting compounds and reagents were obtained from Merck, Fluka, Alfa Aesar and Acros Organics; and solvents like dichloromethane, ethanol, diethyl ether, toluene, ethylacetate, 1-butanol were obtained from Merck and J.T. Baker.

Benzimidazole was synthesized according to the literature (Furniss et al., 1978). 2,4,6-trimethylbenzyl bromide, 2,3,5,6-tetramethylbenzyl bromide, 2,3,4,5,6-pentamethylbenzyl bromide, 1,3-bis(bromomethyl)-2,4,6-trimethylbenzene, 1,4-bis(bromethyl)-2,3,5,6-tetramethylbenzene were prepared according to literature (van der Made, 1993).

Representative protocol was given for the same class of compounds bearing different substituents and the data were presented in Tables.

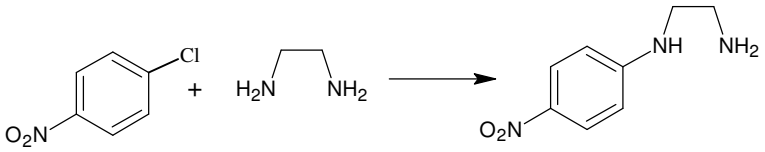
Anhydrous sodium sulphate was used for drying especially after extraction with water.

Melting points were recorded with Gallenkamp electrothermal melting point apparatus.

^{1}H NMR and ^{13}C NMR spectra were taken with Varian AS 400 Mercury instrument. As solvents $CDCl_3$, CD_3OD and d_6-DMSO were employed.

FTIR Spectra were recorded on a Perkin Elmer Spectrum 100 series. The measurements for catalytic experiments performed by GC (Thermo-Finnigan on a HP-5 capillary column and with a FID detector) in Ege University, Faculty of Science.

2.1 Synthesis of N-(4-nitrophenyl)ethylenediamine

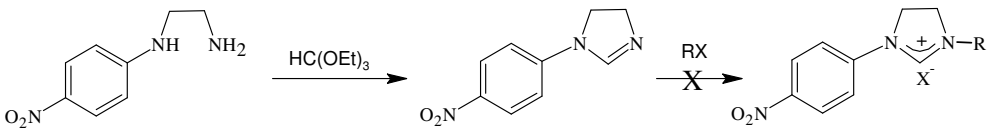


4-Nitro-chlorobenzene (5.0g; 32 mmol) and ethylenediamine (22 mL; 335 mmol) were stirred 2 h under reflux. After distillation of the excess of ethylenediamine, the crude product was taken in hot distillated water (75 mL) and filtrated. After cooling, the product was collected as an orange solide. Yield: 4.85 g; 85%; m.p: 142°C (Allali et al., 2003).

^{1}H NMR ($CDCl_3$): δ(ppm): 1.26 (s, 2H, NH_2); 3.01 (m, 2H, CH_2); 3.25 (m, 2H, CH_2); 5.07 (s, 1H, N*H*); 6.55 (d, 2H,*J* = 2.4 Hz, *H*-2; *H*-6); 8.08 (d, 2H, *J* = 2.4 Hz, *H*-3; *H*-5).

^{13}C NMR ($CDCl_3$): δ(ppm): 40.78; 45.53 (*C*H_2); 111.39 (*C*-2; *C*-6); 126.67 (C-3; *C*-5); 138.28 (*C*-4); 153.73 (*C*-1).

2.2 Synthesis of 1-(4-nitrophenyl)-4,5-dihydro-1*H*-imidazole; attempt to synthesis imidazolinium salts



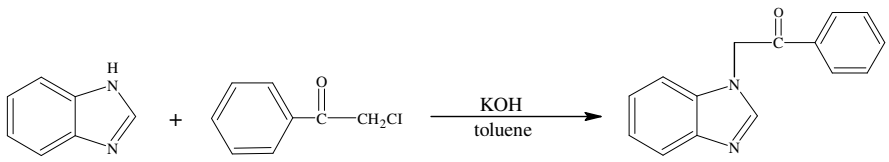
N-(4-nitrophenyl)ethylenediamine (3.0 g; 16.57 mmol) and triethyl orthoformate (15 mL) were heated for 24 h until removal of ethanol. After volatiles were removed in vacuo, the residue was washed with ether and then was filtered

off. The solid was recrystallized from ethanol. Yield: 1.6 g; 62%; m.p: 167-169 °C. Attempt to alkylation failed under various conditions.

^{1}H NMR (CD_3OD): δ(ppm): 3.35 (t, 2H, *J* = 1.4 Hz, C*H*2); 3.45 (t, 2H, *J* = 1.4 Hz, C*H*2); 6.66 (d, 2H, *J* = 2.4 Hz, *H*-2; *H*-6); 8.03 (d, 2H, *J* = 2.4 Hz, *H*-3; *H*-5); 8.08 (s, 1H, -NC*H*N).

^{13}C NMR (CD_3OD): δ(ppm): 36.99; 42.07 (*C*H_2); 110.76 (*C*-2; *C*-6); 126.08 (C-3; *C*-5); 137.24 (*C*-4); 154.58 (*C*-1); 163.144 (-N*C*HN).

2.3 Synthesis of 2-(1H-benzimidazol-1-yl)-1-phenylethanone

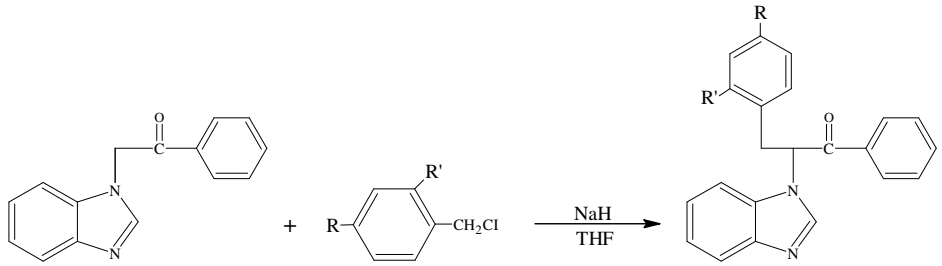


Benzimidazole (1.0 g; 8.47 mmol) and KOH (0.5 g; 8.92 mmol) were stirred in toluene for 24 h. 2-Chloroacetophenone was added to the mixture and then refluxed overnight. Then solvent was removed, the residue was treated with a mixture of dichorometane and water. Dichloromethane phase was concentrated and the solid was precipitated by addition of diethyl ether. Yield: 0.8 g; 40 %; m.p.:150-152 °C.

^{1}H NMR ($CDCl_3$): δ(ppm): 5.54 (s, 2H, -NCH_2COC_6H_5); 7.23- 7.29 (m, 3H); 7.54 (t, 2H, *J* = 1.9 Hz); 7.67 (t, 1H, *J* = 1.9 Hz); 7.71 (m, 1H); 8.00 (t, 2H, *J* = 1.9 Hz) (Ar-*H*); 7.91 (s, 1H, NC*H*N).

^{13}C NMR (CH_3OD): δ(ppm): 50.59 (-N*C*H_2COC_6H_5); 109.50; 120.76; 122.56; 123.49; 128.27; 129.39; 134.49; 134.66; 143.81 (C_{a}romatic); 144.01 (N*C*HN); 191.53 (*C*O).

2.4 Synthesis of 2-(1H-benzimidazol-1-yl)-3-aryl-1-phenylpropan-1-one(Ia, b)



Ia, b

Table 2.1 Compounds Ia and Ib; and their yields

Compound No	R	R'	Yield (%)
Ia	CI	CI	41
Ib	CI	H	53

A solution of 2-(1H-benzimidazol-1-yl)-1-phenylethanone (2.0 g; 8.47 mmol) in anhydrous THF (30 mL) was added to a suspension of NaH (0.24 g; 10.16 mmol) in the same solvent. The mixture was stirred for 1 h and the appropriate benzyl chloride (1.66 g; 8.47 mmol) was added dropwise. After 3 hours of stirring at 50 °C, the reaction mixture was quenched by the addition of methanol and evaporated. The residue was partitioned between water and diethyl ether. The organic extract was washed with a saturated sodium chloride solution, dried over Na_2SO_4 and evaporated. The crude product was purified by silica gel column chromatography using CH_2CI_2/EtOAc as eluent.

^{1}H NMR data of 2-(1H-benzimidazol-1-yl)-3-aryl-1-phenylpropan-1-one are given in Table 2.2. ^{13}C NMR data of 2-(1H-benzimidazol-1-yl)-3-aryl-1-phenylpropan-1-one are given in Table 2.3.

Table 2.2 ^{1}H NMR data for 2-(1H-benzimidazol-1-yl)-3-aryl-1-phenylpropan-1-one

Compound No	2-CH	Aromatics	Alkyl
Ia	7.89 (s)	6.58 (d, *J* 2); 6.77-7.81 (m)	3.35;3.67 (m, CH_2); 6.14 (m, C*H*)
Ib	8.18 (s)	6.89-7.91 (m)	3.43; 3.61 (m, CH_2); 6.10 (m, C*H*)

Table 2.3 ^{13} C NMR data for 2-(1H-benzimidazol-1-yl)-3-aryl-1-phenylpropan-1-one

Compound No	2-CH	C=O	Aromatics	Alkyl
Ia	143.78	194.23	109.85; 120.89; 122.85; 123.79; 127.65; 128.65; 129.26; 129.61; 132.38; 132.72; 133.21; 134.27; 134.56; 134.59; 134.73; 142.25	35.81 (*C*H_2); 53.71 (*C*H)
Ib	144.01	194.27	109.89; 121.05; 121.87; 122.86; 123.74; 128.61; 129.19; 129.30; 130.48; 133.51; 134.50; 134.81; 142.35	37.21 (*C*H_2); 60.88(*C*H)

$CDCl_3$ was used as a solvent. Chemical shift values are given in ppm and *J* values are given in Hz. Abbreviations: s: singlet; t: triplet; q: quartet; m: multiplet

2.5 Synthesis of 1-substitutedbenzimidazoles and bibenzimidazoles (1-6)

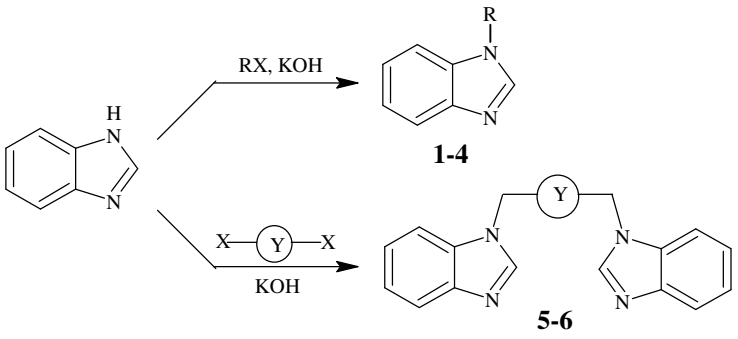


Table 2.4 Melting points and yields of the compounds **1-6**

Compound No	R	Y	m.p (°C)	Yield (%)
1	$-CH_2CH_2OCH_3$	-	-	70
2	$-CH_2C_6H_2(CH_3)_3$	-	103-104	60
3	$-CH_2C_6H(CH_3)_4$	-	168-172	77
4	$-CH_2C_6(CH_3)_5$	-	104-107	73
5	-	$-CH_2C_6H(CH_3)_3CH_2-$	233-235	56
6	-	$-CH_2C_6(CH_3)_4CH_2-$	237-238	67

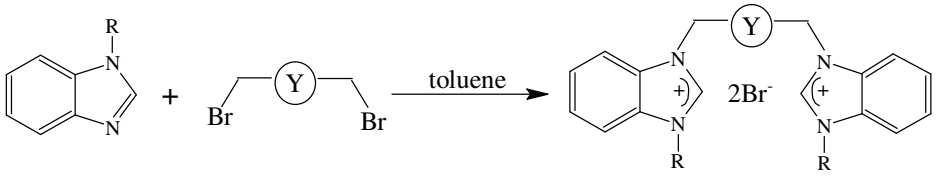
Benzimidazole (3.0 g; 25.42 mmol) and KOH (1.5 g; 26.8 mmol) were dissolved in ethanol (20 mL) and stirred for 1 hour at room temperature. 2-Chloroethyl methyl ether was added and the mixture was refluxed for 24 h. Following the completion of the process ethanol was removed. The residue was treated with a mixture of dichloromethane and water. The dried dichloromethane phase was concentrated. The oily product was distilled under vacuum (b.p: 105-106 °C/0.1mmHg).

The compounds **3**, **4** and **6** were synthesized using the same procedure but in toluene instead of ethanol. Compound **2** was recrystallized

from CH_2CI_2/hexane.The other compounds (**3, 4, 5, 6**) were recrystallized from CH_2Cl_2/Et_2O.

^{1}H NMR data of 1-substitutedbenzimidazoles and bibenzimidazoles are given in Table 3.1. ^{13}C NMR data of 1-alkylbenzimidazoles are given in Table 3.2.

2.6 The reactions of 1-substituted benzimidazoles with 1,3-bis(bromomethyl)-2,4,6-trimethylbenzene and 1,4-bis(bromomethyl)-2,3,5,6-tetramethylbenzene



7-14

Table 2.5 Melting points and yields of the compounds **7-14**

Compound No	Y	R	m.p(°C)	Yield
7	$-CH_2C_6H(CH_3)_3CH_2-$	$-CH_2CH_2OCH_3$	171-174	90
8	$-CH_2C_6H(CH_3)_3CH_2-$	$-CH_2C_6H_2(CH_3)_3$	199-201	80
9	$-CH_2C_6H(CH_3)_3CH_2-$	$-CH_2C_6H(CH_3)_4$	200-202	60
10	$-CH_2C_6H(CH_3)_3CH_2-$	$-CH_2C_6(CH_3)_5$	217-221	65
11	$-CH_2C_6(CH_3)_4CH_2-$	$-CH_2CH_2OCH_3$	265-267	82
12	$-CH_2C_6(CH_3)_4CH_2-$	$-CH_2C_6H_2(CH_3)_3$	308-310	80
13	$-CH_2C_6(CH_3)_4CH_2-$	$-CH_2C_6H(CH_3)_4$	250-251(dec.)	89
14	$-CH_2C_6(CH_3)_4CH_2-$	$-CH_2C_6(CH_3)_5$	220-221(dec.)	77

1-methoxyethylbenzimidazole (1,0 g; 5,7 mmol) was dissolved in toluene and then bis(bromomethyl)mesitylene (0,87 g; 2,85 mmol) was added. The mixture was refluxed for 4 h. The solid that separated out after cooling was filtered off and washed with diethyl ether (5 mL). The product was recrystallized from CH_2Cl_2/Et_2O.

The compounds (**8**-**14**) were synthesized in the same manner as described for **7**.

^{1}H NMR data of **7-14** are given in Table 3.3. ^{13}C NMR data of **7-14** are given in Table 3.4.

2.7 Synthesis of 1-substituted-5,6-dimethylbenzimidazole and bibenzimidazoles (15-20)

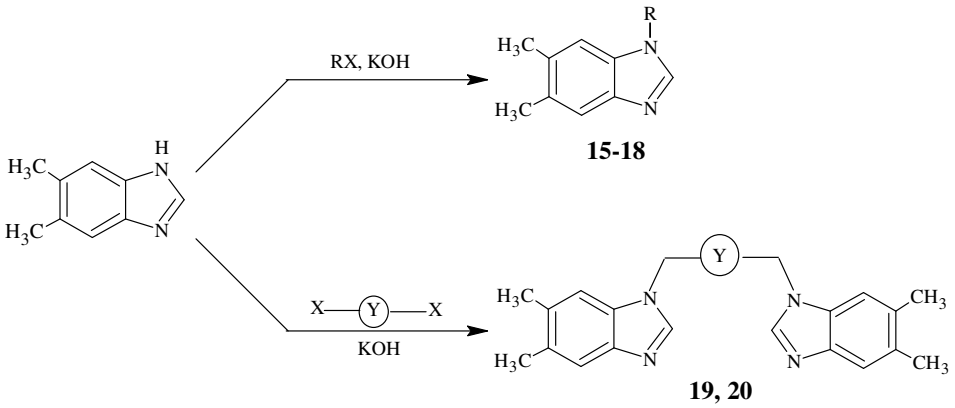


Table 2.6 Melting points and yields of the compounds **15-20**

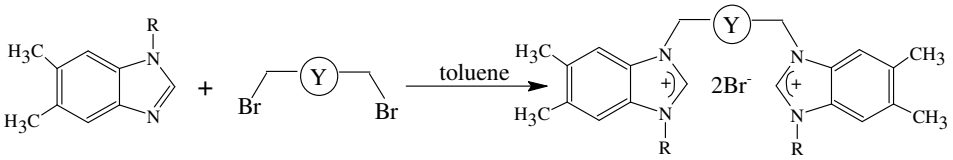
Compound No	R	Y	m.p(°C)	Yield (%)
15	$-CH_2CH_2OCH_3$	-	-	79
16	$-CH_2C_6H_2(CH_3)_3$	-	99-102	52
17	$-CH_2C_6H(CH_3)_4$	-	127-130	51
18	$-CH_2C_6(CH_3)_5$	-	154-157	50
19	-	$-CH_2C_6H(CH_3)_3CH_2-$	224-226	53
20	-	$-CH_2C_6(CH_3)_4CH_2-$	281-282	50

5,6-dimethylbenzimidazole (3.0 g; 20.52mol) and KOH (1.8 g; 21.0 mmol) were dissolved in BuOH (25 ml) and stirred for 2 h at room temperature. 2-Chloroethyl methyl ether was added and the mixture was refluxed for 24 h. Volatiles were evaporated. The residue was extracted with dichloromethane and the dichloromethane phase was washed with water. After the dichloromethane phase was dried over Na_2SO_4, it was removed . The residue was distilled under vacuum to obtain the product (b.p: 102-103 °C/0.1mmHg).

Compound **16** was recrystallized from CH_2CI_2/hexane.The other compounds (**17, 18, 19, 20**) were recrystallized from CH_2Cl_2/Et_2O.

^{1}H NMR data of **15-20** are given in Table 3.5. ^{13}C NMR data of **15-20** are given in Table 3.6.

2.8 Reaction of 1-substituted-5,6-dimethylbenzimidazoles with 1,3-bis(bromomethyl)-2,4,6-trimethylbenzene and 1,4-bis(bromomethyl)-2,3,5,6-tetramethylbenzene



21-28

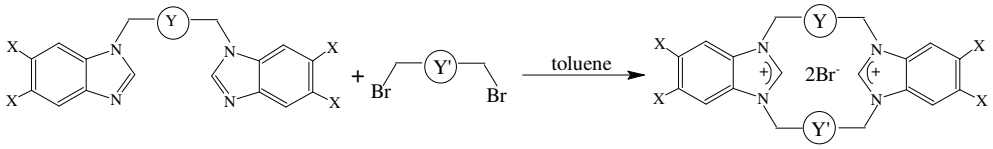
Table 2.7 Melting points and yields of the compounds **21-28**

Compound No	Y	R	m.p(°C)	Yield
21	$-CH_2C_6H(CH_3)_3CH_2-$	$-CH_2CH_2OCH_3$	250-253	59
22	$-CH_2C_6H(CH_3)_3CH_2-$	$-CH_2C_6H_2(CH_3)_3$	172-175	34
23	$-CH_2C_6H(CH_3)_3CH_2-$	$-CH_2C_6H(CH_3)_4$	192-194	46
24	$-CH_2C_6H(CH_3)_3CH_2-$	$-CH_2C_6(CH_3)_5$	197-199	40
25	$-CH_2C_6(CH_3)_4CH_2-$	$-CH_2CH_2OCH_3$	268-269	70
26	$-CH_2C_6(CH_3)_4CH_2-$	$-CH_2C_6H_2(CH_3)_3$	226-228	57
27	$-CH_2C_6(CH_3)_4CH_2-$	$-CH_2C_6H(CH_3)_4$	220-222	75
28	$-CH_2C_6(CH_3)_4CH_2-$	$-CH_2C_6H(CH_3)_5$	218-220	59

1-Methoxyethyl-5,6-dimethylbenzimidazole (1.0 g; 4.9 mmol) was dissolved in toluene and then 1,4-bis(bromomethyl)-2,3,5,6-tetramethylbenzene (0.78 g; 2.45 mmol) was added. The mixture was refluxed for 4 h. The solid that separated out after cooling was filtered off and washed with diethyl ether (5 mL). The product was recrystallized from CH_2Cl_2/Et_2O.

The rest of benzimidazolium halides (**26, 27, 28**) were synthesized with the same method as mentioned above. But synthesis of **21, 22, 23, 24** were carried out at room temperature for 24 hours. ^{1}H NMR data of **21-28** are given in Table 3.7. ^{13}C NMR data of **21-28** are given in Table 3.8.

2.9 Synthesis of cationic cyclophanes (29, 30 31, 32, 33, 34)



29-34

Table 2.8 Melting points and yields of the compounds **29-34**

Compound No	X	Y	Y'	m.p(°C)	Yield
29	H	$-CH_2C_6H(CH_3)_3CH_2-$	$-CH_2C_6H(CH_3)_3CH_2-$	294(dec.)	65
30	H	$-CH_2C_6(CH_3)_4CH_2-$	$-CH_2C_6(CH_3)_4CH_2-$	348-350(dec.)	70
31	CH_3	$-CH_2C_6H(CH_3)_3CH_2-$	$-CH_2C_6H(CH_3)_3CH_2-$	295(dec.)	60
32	CH_3	$-CH_2C_6(CH_3)_4CH_2-$	$-CH_2C_6(CH_3)_4CH_2-$	329(dec.)	66
33	H	$-CH_2C_6H(CH_3)_3CH_2-$	$-CH_2C_6(CH_3)_4CH_2-$	291(dec.)	66
34	CH_3	$-CH_2C_6H(CH_3)_3CH_2-$	$-CH_2C_6(CH_3)_4CH_2-$	327-330(dec.)	47

1,3-bis(benzimidazol-1-ylmethyl)-2,4,6-trimethylbenzene (1.0 g; 2.6 mmol) was dissolved in toluene and then bis(bromomethyl)mesitylene (0.8 g; 2.6 mmol) was added. The mixture was refluxed for overnight. The solid

that separated out after cooling was filtered off and washed with diethyl ether (5 mL). The product was recrystallized from MeOH.

The cyclophanes were synthesized with this method. ^{1}H NMR data of **29-34** are given in Table 3.9. ^{13}C NMR data of **29-34** are given in Table 3.10.

2.10 Catalytic Experiments

2.10.1 General procedure for the Suzuki coupling reactions

A two-necked 25mL flask fitted with a reflux condenser and septum was charged with 4-Choloroacetophenone (154.6 mg; 1.0 mmol), phenylboronic acid (182.9 mg; 1.5 mmol), diethyleneglycol di-n-butyl ether (internal standard), Cs_2CO_3 (488.73 mg; 1.5 mmol) and benzimidazolium salts (3 mmol %) and $Pd(OAc)_2$ (3 mmol %) in 3 mL of IPA was added. The flask was placed in a preheated oil bath (80 ^{0}C) under argon atmosphere. The conversion was monitored by gas chromatography.

2.10.2 General procedure of Heck coupling reactions

Aryl halides (1.0 mmol), Cs_2CO_3 (1.5 mmol), olefin (1.5 mmol), diethyleneglycol di-n-butyl ether (internal standard), $Pd(OAc)_2$ (3 mmol %), benzimidazolium salts (3 mmol %) were introduced into a two necked flask and then DMA (3 mL) was added. The flask was placed in a preheated oil bath (100 ^{0}C) under argon atmosphere. The conversion was monitored by gas chromatography.

3. RESULTS AND DISCUSSION

Despite the fact that derivatives of five-membered carbenes such as imidazol-2-ylidenes and imidazolin-2-ylidenes have been known for a quite a long time, the chemistry of benzimidazol-2-ylidenes is relatively poorly explored. This lack of knowledge is unexpected considering the wide range of applications that representatives of this group compounds have found in various fields, particularly as easier synthesis of precursor as the later.

It is known that benzannulated carbenes derived from benzimidazolium precursors exhibit the topology of an unsaturated NHC, but show spectroscopic and structural properties and the reactivity with a saturated N-heterocyclic ring (Hahn et al.,1999; 2000).

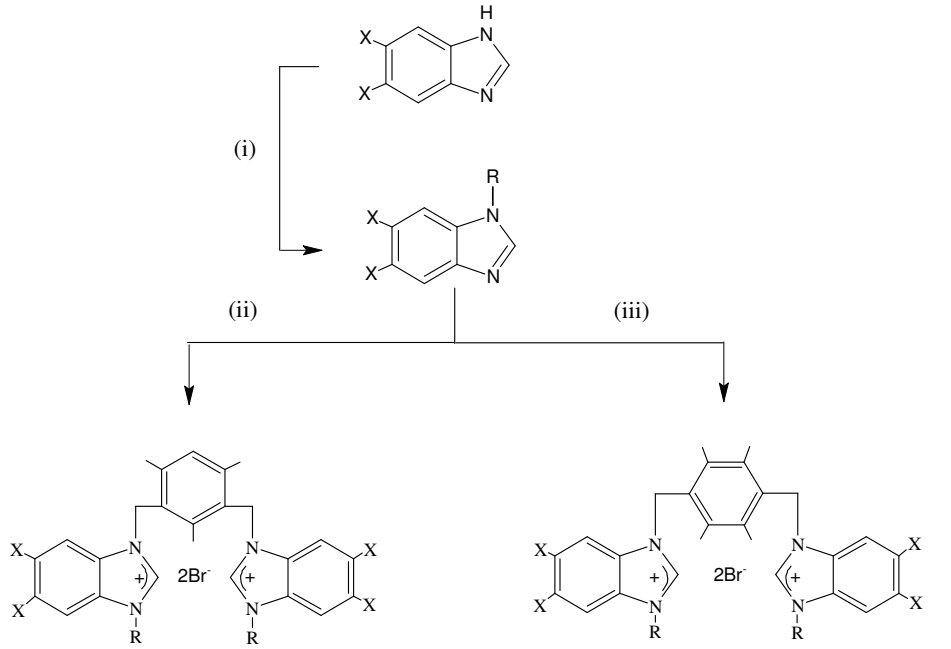
In this part of the thesis, the synthesis and characterization of benzimidazolium and cationic cylophanes as NHC precursors were described. Their catalytic properties were examined *in situ* formed complexes.

3.1 Synthesis of mono-bridged bibenzimidazolium salts, I (**7-14; 21-28**)

The benzimidazolium salts were synthesized according to the steps illustrated in Scheme 3.1. At the first step, 1-substituted benzimidazoles were prepared by treating benzimidazole and appropriate alkyl or benzylic halide under basic conditions (Step (i)). Bridged bibenzimidazolium salts (**7-14**; **21-28**) were obtained via alkylation of the latter product with 1,3-bis(bromomethyl)-2,4,6-trimethylbenzene and 1,4-bis(bromomethyl)-2,3,5,6-tetramethylbenzene, respectively in toluene at reflux or at room temperature (Step (ii, iii)).

The IR data for benzimidazolium salts (**7-14**; **21-28**) clearly indicate the presence of the –C=N- group with a υ(C=N) vibration between 1558-1561 cm^{-1} (Gök et al., 2005).

These benzimidazolium salts have been characterized by ^{1}H and ^{13}C NMR spectroscopy. ^{1}H NMR chemical shifts were consistent with the proposed structures; the resonances for C_2-hydrogenes were observed as sharp singlets between 9.51-10.86 ppm. ^{13}C NMR of these salts showed the C_2 carbon at 140.44-142.23 ppm (Tables 3.3; 3.4; 3.7; 3.8 and Figures 3.1; 3.2; 3.3; 3.4).



	X	R
7	H	$-CH_2CH_2OCH_3$
8	H	$-CH_2C_6H_2(CH_3)_3$
9	H	$-CH_2C_6H(CH_3)_4$
10	H	$-CH_2C_6(CH_3)_5$
21	CH_3	$-CH_2CH_2OCH_3$
22	CH_3	$-CH_2C_6H_2(CH_3)_3$
23	CH_3	$-CH_2C_6H(CH_3)_4$
24	CH_3	$-CH_2C_6(CH_3)_5$

	X	R
11	H	$-CH_2CH_2OCH_3$
12	H	$-CH_2C_6H_2(CH_3)_3$
13	H	$-CH_2C_6H(CH_3)_4$
14	H	$-CH_2C_6(CH_3)_5$
25	CH_3	$-CH_2CH_2OCH_3$
26	CH_3	$-CH_2C_6H_2(CH_3)_3$
27	CH_3	$-CH_2C_6H(CH_3)_4$
28	CH_3	$-CH_2C_6(CH_3)_5$

Scheme 3.1 Reagents and conditions of reactions: (i) RX, KOH, toluene, EtOH or BuOH; (ii) 1,3-bis(bromomethyl)-2,4,6-trimethylbenzene, toluene, reflux; (iii) 1,4-bis(bromomethyl)-2,3,5,6-tetramethylbenzene, toluene, reflux.

3.2 Synthesis of symmetrical cationic cyclophanes, II (29-32)

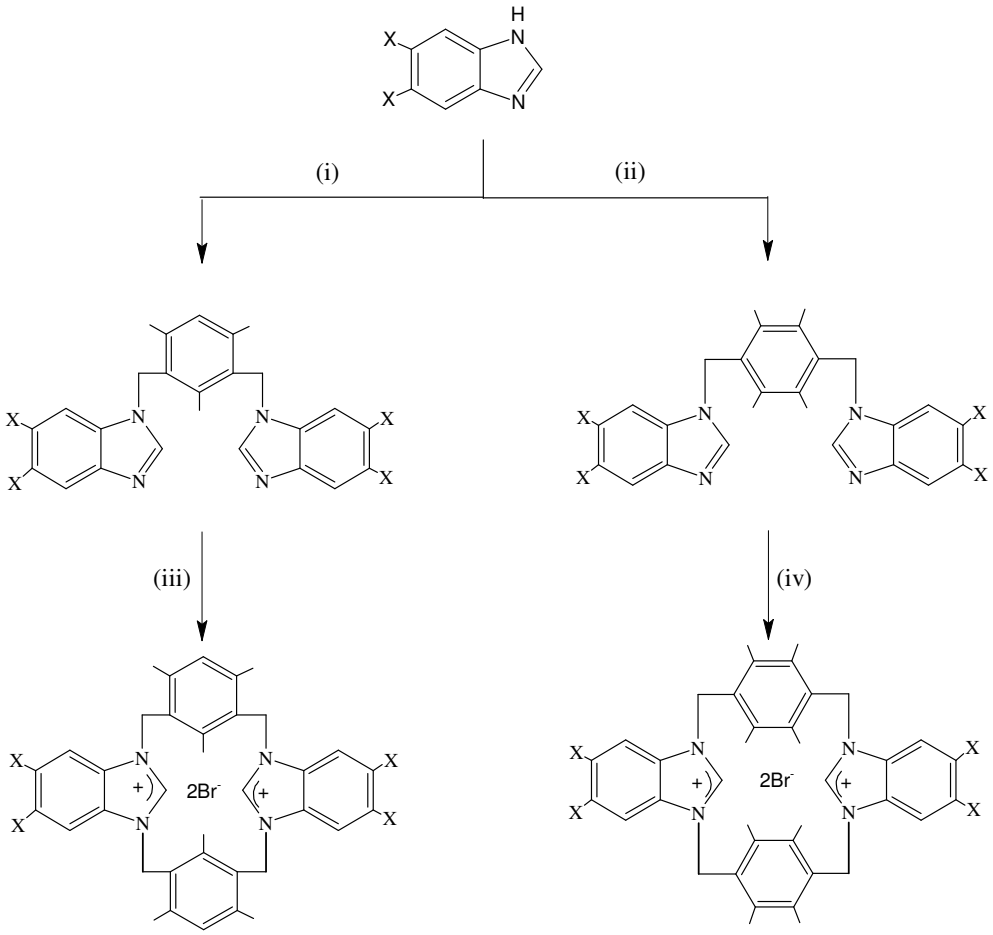
Symmetrical cyclophanes were prepared according to the procedure indicated in Scheme 3.2 and described in the experimental section. The

bridged benzimidazoles were synthesized by N-alkylation of (5,6-dimethyl)benzimidazole with the corresponding *m*- or *p*- dibromides in the presence of KOH in a suitable solvent (Step (i, ii)). Then symmetrical cyclophanes (**29**, **30**, **31**, **32**) were synthesized from reaction of the mono-bridged benzimidazoles with 1,3-bis(bromomethyl)-2,4,6-trimethylbenzene or 1,4-bis(bromomethyl)-2,3,5,6-tetramethylbenzene (Step (iii, iv)). In general cyclophanes, as their bromide salts, were insoluble in acetone, sparingly soluble in DMSO and methanol. These salts were purified by recrystallization from methanol.

The IR data for symmetrical cationic cyclophanes (**29, 30, 31, 32**) clearly indicate the presence of the –C=N- group with a υ(C=N) vibration between 1546-1573 cm^{-1}.

The ^{1}H NMR spectrum of metacyclophanes displayed the methyl protons as a 18 protons singlet about δ = 1.5; 2.4 ppm. The N-methylene protons as doublets about δ = 5.5; 5.8 ppm. C_2-H signals were observed approximate δ = 7.2 ppm. ^{13}C NMR showed the C_2 carbon at 141 ppm.

The ^{1}H NMR spectrum of paracyclophanes showed the methyl protons as a singlet at 2.1 ppm. The benzylic protons appeared as a singlet at 5.7-5.8 ppm. The resonances for C_2-hydrogenes were observed as a singlets between 6.22-7.23 ppm. ^{13}C NMR of paracyclophanes showed the C_2 carbon at 137-138 ppm (Tables 3.9; 3.10 and Figures 3.5; 3.6).



X = H; **29**

X = CH_3; **31**

X = H; **30**

X = CH_3; **32**

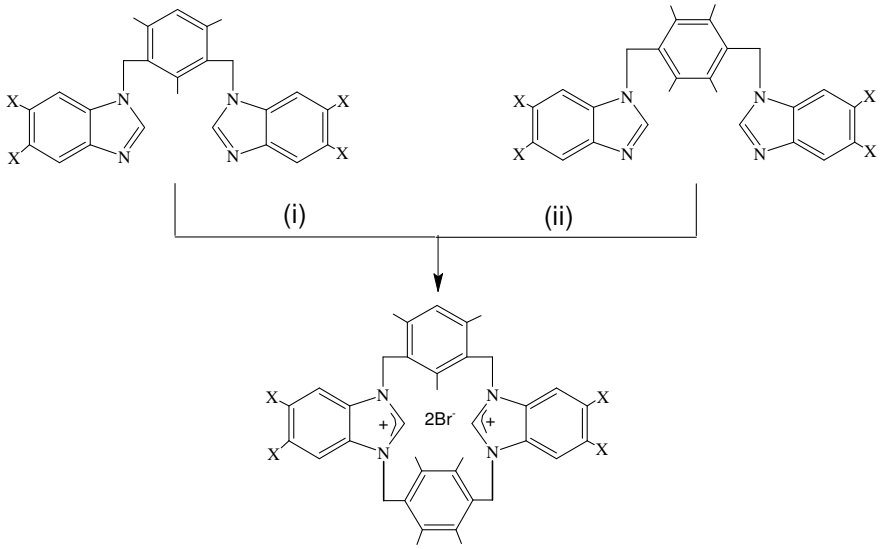
Scheme 3.2 Reagents and conditions of reactions: (i) 1,3-bis(bromomethyl)-2,4,6-trimethylbenzene, KOH, toluene, EtOH or BuOH; (ii) 1,4-bis(bromomethyl)-2,3,5,6-tetramethylbenzene, KOH, toluene, EtOH or BuOH; (iii) 1,3-bis(bromomethyl)-2,4,6-trimethylbenzene, toluene, reflux; (iv) 1,4-bis(bromomethyl)-2,3,5,6-tetramethylbenzene, tolune, reflux.

3.3 Synthesis of unsymmetrical cationic cyclophanes, II (33, 34)

The unsymmetrical cationic cyclophanes were synthesized with the same method that mentioned above for symmetrical ones. And procedure was illustrated in Scheme 3.3.

The IR data show the presence of the –C=N- group with a υ(C=N) vibration between 1563-1569 cm^{-1}.

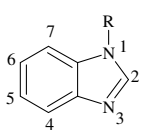
^{1}H and ^{13}C NMR spectra of these compounds were taken in CD_3OD. C_2-H signals were observed as a singlet between 6.45-6.67 ppm. The benzylic protons appeared as a multiply between 5.44-6.05 ppm. In ^{13}C NMR C_2 carbon appeared between 141-142 ppm (Tables 3.9; 3.10 and Figures 3.7; 3.8).



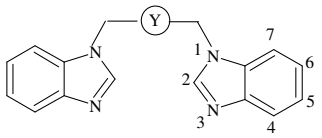
X = H; **33**

X = CH_3; **34**

Scheme 3.3 Reagents and conditions of reactions: (i) 1,4-bis(bromomethyl)-2,3,5,6-tetramethylbenzene; (ii) 1,3-bis(bromomethyl)-2,4,6-trimethylbenzene, tolune,reflux.



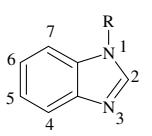
1-4



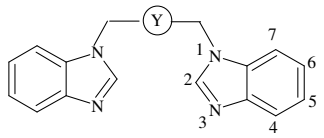
5, 6

Table 3.1 ^{1}H NMR data for 1-substitutedbenzimidazoles and bibenzimidazoles

Compound No	H^{2}(s)	H^{4-7}	Others
1	7,94	7.23-7.80 (m)	3.28 (s, -OCH_3); 3.67; 4.27 (t, *J*1.4 Hz; -CH_2CH_2OCH$_3$)
2	7,44	7.29-7.83 (m)	2.23; 2.33 (s, 2,4,6-CH$_2$C$_6$H$_2$(CH_3)$_3$); 5.23 (s, 2,4,6-CH_2C$_6$H$_2$(CH$_3$)$_3$); 6.96 (s, 2,4,6-CH$_2$C$_6$$H_2$(CH$_3$)$_3$)
3	7,36	7.80 (dd, *J* 1.8 Hz); 7.47 (dd, *J* 1.5 Hz); 7.27-7.34 (m)	5.29 (s, 2,3,5,6-CH_2C$_6$H(CH$_3$)$_4$); 2.29; 2.16 (2,3,5,6-CH$_2$C$_6$H(CH_3)$_4$); 7.05 (s, 2,3,5,6-CH$_2$C$_6$$H$(CH$_3$)$_4$)
4	7,24	7.12-7.75 (m)	2.13; 2.14; 2.19 (s, 2,3,4,5,6-CH$_2$C$_6$(CH_3)$_5$); 5.22 (s, 2,3,4,5,6-CH_2C$_6$(CH$_3$)$_5$)
5	7,44	7.30-7.83 (m)	2.14; 2.36 (s, -NCH$_2$C$_6$H(CH_3)$_3$CH$_2$N-); 5.31 (s, -NCH_2C$_6$H(CH$_3$)$_3$CH_2N-); 7.15 (s, - NCH$_2$C$_6$$H$(CH$_3$)$_3CH_2$N-)
6	7,42	7.32-7.85 (m)	2.26 (s, -NCH$_2$C$_6$(CH_3)$_4$CH$_2$-); 5.38 (s, - NCH_2C$_6$(CH$_3$)$_4$CH_2N-)



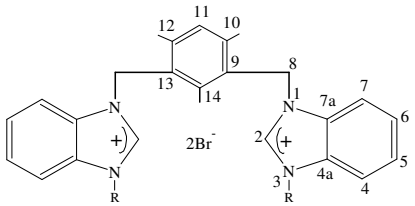
1-4



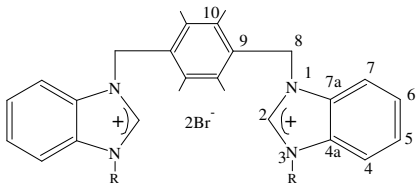
5, 6

Table 3.2 ^{13}C NMR data for 1-substitutedbenzimidazoles and bibenzimidazoles

Compound No	2-CH	Aromatics	Alkyl
1	143.86	109.76; 120.48; 122.29; 123.07; 134.08; 143.81	45.17; 59.22 (-*C*H2*C*H2OCH3); 77.92 (-O*C*H3)
2	144.19	109.83; 120.57; 122.53; 123.13;127.39; 129.92; 134.43; 138.16; 139.03; 141.98	19.80; 21.26 (2,4,6-CH2C6H2(*C*H3)3); 43.37 (2,4,6-*C*H2C6H2(CH3)3)
3	143.93	109.83; 120.48; 122.68; 123.20; 130.04; 132.89; 134.14; 134.33; 134.88; 141.91	44.13 (2,3,5,6-*C*H2C6H(CH3)4); 20.66; 15.72 (2,3,5,6-CH2C6H(*C*H3)4)
4	144.08	109.80; 120.48; 122.62; 123.11; 127.34; 133.67; 133.73; 134.31; 136.48; 142.04	16.74; 17.08; 17.37 (2,3,4,5,6-NCH2C6(*C*H3)5); 44.62 (2,3,4,5,6-N*C*H2C6(CH3)5)
5	143.99	109.73; 120.67; 122.81; 123.41; 129.53; 131.91; 134.23;138.48; 139.40; 141.61	15.81; 20.22 (-NCH2C6H(*C*H3)3CH2N-); 43.89 (-N*C*H2C6H(CH3)3*C*H2N-)
6	144.38	109.67; 120.77; 122.70; 123.25; 131.54; 134.33; 135.41; 141.83	16.83 (-NCH2C6(*C*H3)4CH2N-); 44.53 (-N*C*H2C6(CH3)4*C*H2N-)



7-10



11-14

R = -$CH_2CH_2OCH_3$; **7,11**

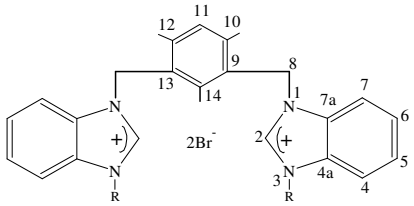
R = -$CH_2C_6H_2(CH_3)_3$; **8, 12**

R = -$CH_2C_6H(CH_3)_4$; **9, 13**

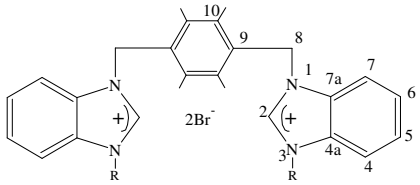
R = -$CH_2C_6(CH_3)_5$; **10, 14**

Table 3.3 ^{1}H NMR data for **7-14**

Compound No	H^2(s)	H^{4-7}	H^{11}(s)	H^8(s)	Others
7	10,27	7.62;7.67 (t, *J* 2 Hz); 7.83; 8.24 (d, *J* 2.1 Hz)	7,15	5,80	2.30; 2.48 (s, -$NCH_2C_6H(CH_3)_3CH_2N$); 3.22 (s, -OCH_3); 3.80 (t, *J* 1.2 Hz, -$NCH_2CH_2OCH_3$); 4.97 (t, *J* 1.2 Hz, -$NCH_2CH_2OCH_3$)
8	10,86	6.89; 8.27 (d, *J* 2.1 Hz);7.39; 7.62 (t, *J* 2.0 Hz)	6,84	5,84	2.23; 2.25; 2.32; 2.57 (s, -$NCH_2C_6H(CH_3)_3CH_2N$; 2,4,6-$CH_2C_6H_2(CH_3)_3$); 6.09 (s, 2,4,6-$CH_2C_6H_2(CH_3)_3$); 7.26 (s, 2,4,6-$CH_2C_6H_2(CH_3)_3$)
9	10,83	6.82; 8.22 (d, *J* 2.2 Hz); 7.34; 7.60 (m)	7,00	5,86	2.17; 2.20 (s, 2,3,5,6-$CH_2C_6H(CH_3)_4$); 2.33; 2.58 (s, -$NCH_2C_6H(CH_3)_3CH_2N$); 6.15 (s, 2,3,5,6-$CH_2C_6H(CH_3)_4$); 7.32 (s, 2,3,5,6-$CH_2C_6H(CH_3)_4$)
10	10,75	6.84; 8.18 (d, *J* 2.1 Hz); 7.33; 7.58 (t, *J* 2.1 Hz)	7,23	6,10	2.05-2.54 (m, -$NCH_2C_6H(CH_3)_3CH_2N$; 2,3,4,5,6-$CH_2C_6(CH_3)_5$); 6.11 (s, 2,3,4,5,6-$CH_2C_6(CH_3)_5$)
11	9,51	7.72-8.21 (m)	-	5,84	2.24 (s, -$NCH_2C_6(CH_3)_4CH_2N$); 3.18 (s, -OCH_3); 3.72; (t, *J* 1.3 Hz, -$NCH_2CH_2OCH_3$);4.77 (t, *J* 1.3 Hz, -$NCH_2CH_2OCH_3$)
12	10,77	6.87; 8.53 (d, *J* 2.2 Hz); 7.37; 7.66 (t, *J* 2.0 Hz)	-	5,93	1.95; 2.22; 2.34 (s,-$NCH_2C_6(CH_3)_4CH_2N$; 2,4,6-$CH_2C_6H_2(CH_3)_3$); 6.07 (s, 2,4,6-$CH_2C_6H_2(CH_3)_3$); 6.83 (s, 2,4,6-$CH_2C_6H_2(CH_3)_3$)
13	10,78	6.77; 8.49 (d, *J* 2.2 Hz); 7.34; 7.65 (t, *J* 2.1 Hz)	-	5,93	2.16; 2.19; 2.32 (s,-$NCH_2C_6(CH_3)_4CH_2N$; 2,3,5,6-$CH_2C_6H(CH_3)_4$); 6.14 (s, 2,3,5,6-$CH_2C_6H(CH_3)_4$)
14	10,78	6.77; 8.47 (d, *J* 2.1 Hz); 7.32; 7.63 (t, *J* 1.9 Hz)	-	5,91	2.16-2.33 (m, -$NCH_2C_6(CH_3)_4CH_2N$; 2,3,4,5,6-$CH_2C_6(CH_3)_5$); 6.13 (s, 2,3,4,5,6-$CH_2C_6(CH_3)_5$)



7-10



11-14

R = $-CH_2CH_2OCH_3$; **7,11**

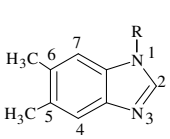
R = $-CH_2C_6H_2(CH_3)_3$; **8, 12**

R = $-CH_2C_6H(CH_3)_4$; **9, 13**

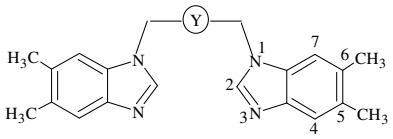
R = $-CH_2C_6(CH_3)_5$; **10, 14**

Table 3.4 ^{13}C NMR data for **7-14**

Compound No	2-CH	Aromatics	Alkyl
7	141.69	113.97; 114.39; 126.88; 127.56; 127.65; 131.59; 132.75; 132.81; 140.49;140.98	17.66;20.25 (-$NCH_2C_6H(CH_3)_3CH_2N$); 46.97 (-$NCH_2C_6H_1(CH_3)_3CH_2N$); 48.05; 59.20 (-$NCH_2CH_2OCH_3$); 71.17 (-$NCH_2CH_2OCH_3$)
8	141.87	114.32; 114.38; 126.14; 126.98; 127.48; 127.60; 132.05; 132.09; 132.86; 133.57; 133.82; 136.99; 140.50; 140.94;	17.13; 17.27; 17.49; 17.68; 20.28 (2,4,6-$CH_2C_6H_2(CH_3)_3$; -$NCH_2C_6H(CH_3)_3CH_2N$-); 47.32; 49.77 (2,4,6-$CH_2C_6H_2(CH_3)_3$; -$NCH_2C_6H(CH_3)_3CH_2N$-)
9	141.92	126.90; 127.52; 127.66; 128.84; 132.05; 132.90; 133.37; 134.10; 134.98; 140.47; 141.00	16.29; 20.70 (2,3,5,6-$CH_2C_6H(CH_3)_4$); 17.66; 20.26 (-$NCH_2C_6H(CH_3)_3CH_2N$-); 47.30; 49.26 (-$NCH_2C_6H(CH_3)_3CH_2N$; 2,3,5,6-$CH_2C_6H(CH_3)_4$)
10	141.97	114.15; 114.49; 125.96; 126.81; 127.59; 127.72; 130.29; 131.94; 132.06; 132.94; 137.90; 139.44; 140.50; 141.05	17.64; 20.19; 20.49; 21.20 (-$NCH_2C_6H(CH_3)_3CH_2N$-; 2,3,4,5,6-$CH_2C_6(CH_3)_5$); 47.25; 48.50 (-$NCH_2C_6H(CH_3)_3CH_2N$-; 2,3,4,5,6-$CH_2C_6(CH_3)_5$)
11	142.23	127.36; 127.54; 130.64; 132.00; 132.32; 136.45	17.21 (-$NCH_2C_6(CH_3)_4CH_2N$-); 40.89; 58.84 (-$NCH_2CH_2OCH_3$); 56.70 (-$NCH_2C_6(CH_3)_4CH_2N$-); 70.06 (-$NCH_2CH_2OCH_3$)
12	142.09	113.97; 115.06; 125.94; 127.72; 127.75; 129.46; 130.29; 131.88; 132.10; 136.69; 137.81; 139.38	17.40; 20.44; 21.19 (-$NCH_2C_6(CH_3)_4CH_2N$-; 2,4,6-$CH_2C_6H_2(CH_3)_3$); 47.09; 48.26 (-$NCH_2C_6(CH_3)_4CH_2N$-; 2,4,6-$CH_2C_6H_2(CH_3)_3$)
13	142.09	114.07; 114.96; 127.62; 128.90; 129.23; 129.44; 132.00; 132.07; 133.31; 134.92; 136.68	16.22; 17.40; 20.69 (-$NCH_2C_6(CH_3)_4CH_2N$-; 2,3,5,6-$CH_2C_6H(CH_3)_4$); 47.89; 49.07 (-$NCH_2C_6(CH_3)_4CH_2N$-; 2,3,5,6-$CH_2C_6H(CH_3)_4$)
14	141.94	114.23; 114.88; 126.26; 127.57; 127.66; 129.47; 132.03; 132.05; 133.49; 133.72; 136.65; 136.86	17.20; 17.41; 17.48, 20.69 (-$NCH_2C_6(CH_3)_4CH_2N$-; 2,3,4,5,6-$CH_2C_6(CH_3)_5$); 47.87; 49.62 (-$NCH_2C_6(CH_3)_4CH_2N$-; 2,3,4,5,6-$CH_2C_6(CH_3)_5$)



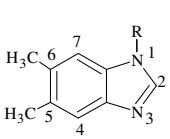
15-18



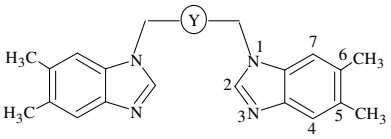
19, 20

Table 3.5 ^{1}H NMR data for **15-20**

Compound No	H^{2}(s)	H^{4-7}(s)	Others
15	7,85	7.16; 7.55	2.36;2.38 (s, Ar-CH_3); 3.30 (s, -NCH_2CH_2OCH_3); 3.68 (t, *J* 1.3 Hz, -NCH_2CH_2OCH_3); 4.25 (t, *J* 1.3 Hz, -NCH_2CH_2OCH_3)
16	7,57	7.30; 7.24	2.24; 2.32; 2.39; 2.43 (s, Ar-CH_3; 2,4,6-CH_2C$_6$H$_2$(CH_3)$_3$); 5.19 (s, 2,4,6-CH_2C$_6$H$_2$(CH$_3$)$_3$); 6.99 (s, 2,4,6-CH$_2$C$_6$$H_2$(CH$_3$)$_3$)
17	7,59	7.31; 7.29	2.15; 2.28 (s, 2,3,5,6-CH$_2$C$_6$H(CH_3)$_4$); 2.40; 2.45 (s, Ar-CH_3); 5.25 (s, 2,3,5,6-CH_2C$_6$H(CH$_3$)$_4$); 7.07 (s, 2,3,5,6-CH$_2$C$_6$$H$(CH$_3$)$_4$)
18	7,58	7.32; 7.30	2.20; 2.27; 2.31; 2.41; 2.45 (s, Ar-CH_3; 2,3,4,5,6-CH$_2$C$_6$(CH_3)$_5$); 5.25 (s, 2,3,4,5,6-CH_2C$_6$(CH$_3$)$_5$)
19	7,57	7.31; 7.24	2.14; 2.34 (s, -NCH$_2$C$_6$H(CH_3)$_3$CH$_2$N-); 2.38; 2.41 (s, Ar-CH_3); 5.24(s, -NCH_2C$_6$H(CH$_3$)$_3$CH_2N-); 7.12(s, -NCH$_2$C$_6$$H$(CH$_3$)$_3CH_2$N-)
20	7,60	7.30; 7.31	2.24 (s, -NCH$_2$C$_6$(CH_3)$_4$CH$_2$N-); 2.41; 2.45 (s, Ar-CH_3); 5.31 (s, -NCH_2C$_6$(CH$_3$)$_4$CH_2N-)



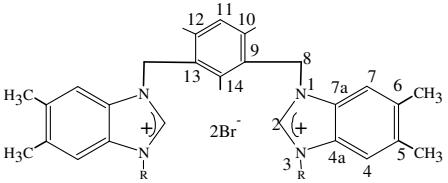
15-18



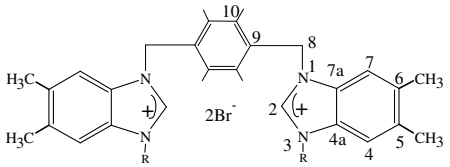
19, 20

Table 3.6 [13] C NMR data for **15-20**

Compound No	2-CH	Aromatics	Alkyl
15	143.04	109.89; 120.50; 131.17; 132.22; 132.58; 142.46	20.41; 20.79 (Ar-*C*H_3); 45.14; 59.26 (-*C*H_2*C*H_2O*C*H_3); 70.99 (-$CH_2CH_2OCH_3$)
16	142.45	110.00; 120.41; 127.47; 129.86; 131.57; 132.37; 132.95; 138.07; 138.99; 141.00	19.75; 20.48; 20.85; 21.24 (Ar-*C*H_3; 2,4,6-$CH_2C_6H_2$(*C*H_3)$_3$); 43.28 (2,4,6-*C*$H_2C_6H_2(CH_3)_3$)
17	140.86	110.03; 120.25; 130.05; 131.89; 132.57; 132.76; 132.86; 134.14; 134.87	15.66; 20.50; 20.63; 20.85 (2,3,5,6-CH_2C_6H(*C*H_3)$_4$; Ar-*C*H_3)
18	142.83	109.95; 120.52; 127.62; 131.39; 132.15; 132.95; 133.59; 133.75; 136.32; 141.30	16.70; 17.06; 17.35; 20.50; 20.84 (Ar-*C*H_3; 2,3,4,5,6-CH_2C_6(*C*H_3)$_5$); 44.48 (2,3,4,5,6-*C*$H_2C_6(CH_3)_5$)
19	142.60	109.89; 120.59; 129.66; 131.67; 131.75; 132.54; 132.86; 138.46; 139.25; 140.79	15.738; 20.15 (-NCH_2C_6H(*C*H_3)$_3CH_2$N-); 20.48; 20.86 (Ar-*C*H_3); 43.76 (-N*C*H_2C_6H(C*H*$_3$)$_3$*C*H_2N-)
20	142.45	109.92; 120.54; 131.55; 131.81; 132.59; 132.80; 135.36; 140.85	16.78 (-NCH_2C_6(*C*H_3)$_4CH_2$N-); 20.51; 20.88 (Ar-*C*H_3); 44.45 (-N*C*$H_2C_6(CH_3)_4$*C*H_2N-)



21-24



25-28

R = -$CH_2CH_2OCH_3$; **21, 25**

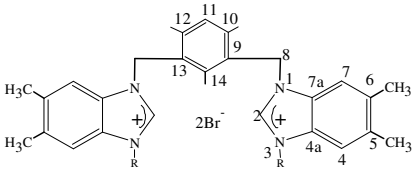
R = -$CH_2C_6H_2(CH_3)_3$; **22, 26**

R = -$CH_2C_6H(CH_3)_4$; **23, 27**

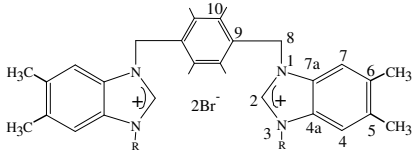
R = -$CH_2C_6(CH_3)5$; **24, 28**

Table 3.7 ^{1}H NMR data for **21-28**

Compound No	H^2(s)	H^{4-7}	H^{11}	H^8(s)	Others
21	10.09	7.52; 7.94	7.16	5.68	2.26; 2.45; 2.49; 2.50 (s, $NCH_2C_6H(CH_3)_3CH_2N$, Ar-CH_3); 3.24 (s, -OCH_3); 3.79; 4.88 (t, *J*1.2 Hz; -$NCH_2CH_2OCH_3$)
22	10.58	6.56; 8.00	7.21	5.69	2.15; 2.16; 2.20; 2.21; 2.38; 2.44 (s, 2,4,6-$CH_2C_6H_2(CH_3)_3$; Ar-CH_3; $NCH_2C_6H(CH_3)_3CH_2N$); 5.94 (s, , 2,4,6-$CH_2C_6H_2(CH_3)$; 6.78 (s, 2,4,6-$CH_2C_6H_2(CH_3)_3$)
23	10.52	7.00;7.82	7.23	5.74	2.17; 2.22 (s ,2,3,5,6-$CH_2C_6H(CH_3)_4$); 2.20; 2.31(s, Ar-CH_3); 2.41; 2.53 (s, -$NCH_2C_6H(CH_3)_3CH_2N$); 6.05 (s, 2,3,5,6-$CH_2C_6H(CH_3)_4$); 6.56 (s, 2,3,5,6-$CH_2C_6H(CH_3)_4$)
24	9.56	6.93; 7.21	7.09	5.69	2.19; 2.22; 2.26; 2.29; 2.31; 2.35; 2.39;(s, Ar-CH_3, ,2,3,4,5,6-CH_2C_6 (CH_3)$_5$), $NCH_2C_6H(CH_3)_3CH_2N$); 5.84 (s, 2,3,4,5,6-CH_2C_6 (CH_3)$_5$)
25	10,02	7.56; 8.05	-	5,71	2.28 (s, -$NCH_2C_6(CH_3)_4CH_2N$); 2.43; 2.50 (s, Ar-CH_3); 3.26 (s, -OCH_3); 3.79; 4.84 (t, *J*1.2 Hz, -$CH_2CH_2OCH_3$)
26	10,60	6.61; 8.16	-	5,79	2.21; 2.22 (s, 2,4,6-$CH_2C_6H_2(CH_3)_3$); 2.25; 2.50 (s, Ar-CH_3); 2.33 (s, -$NCH_2C_6(CH_3)_4CH_2N$); 6.84 (s, 2,4,6-$CH_2C_6H_2(CH_3)_3$)
27	10,63	6.99; 8.13	-	5,78	2.15; 2.17; 2.20; 2.33; 2.45 (s, 2,3,5,6-$CH_2C_6H(CH_3)_4$; -$NCH_2C_6(CH_3)_4CH_2N$-; Ar-CH_3); 6.07 (s, 2,3,5,6-$CH_2C_6H(CH_3)_4$); 6.51 (s, 2,3,5,6-$CH_2C_6H(CH_3)_4$)
28	10,57	6.53; 8.06	-	5,76	2.17; 2.18; 2.22; 2.23; 2.33; 2.44 (s, -$NCH_2C_6(CH_3)_4CH_2N$; Ar-CH_3; 2,3,4,5,6-$CH_2C_6(CH_3)_5$); 6.53 (s, 2,3,4,5,6-$CH_2C_6(CH_3)_5$)



21-24



25-28

R = -$CH_2CH_2OCH_3$; **21, 25**

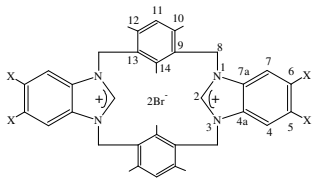
R = -$CH_2C_6H_2(CH_3)_3$; **22, 26**

R = -$CH_2C_6H(CH_3)_4$; **23, 27**

R = -$CH_2C_6(CH_3)_5$; **24, 28**

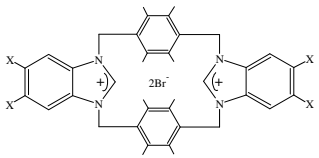
Table 3.8 ^{13}C NMR data for **21-28**

Compound No	2-CH	Aromatics	Alkyl
21	140.70	113.49; 113.78; 127.04; 130.13; 131.23; 132.63; 137.76; 137.89; 140.41	17.58; 20.18; 20.84; 20.94 (-$NCH_2C_6H(CH_3)_3CH_2N$; Ar-CH_3); 46.71; (-$NCH_2C_6H(CH_3)_3CH_2N$); 47.71; 59.21 (-$NCH_2CH_2OCH_3$); 71.19 (, -OCH_3)
22	140.89	113.78; 113.95; 126.14; 126.93; 130.19; 130.35; 130.65; 132.71; 137.75; 137.84; 137.91; 139.33; 140.05; 140.69	17.39; 20.12; 20.44; 20.76; 21.07; 21.19 (-$NCH_2C_6H(CH_3)_3CH_2N$; Ar-CH_3; 2,4,6-$CH_2C_6H_2(CH_3)_3$); 46.94; 48.17 (-$NCH_2C_6H(CH_3)_3CH_2N$-; 2,4,6-$CH_2C_6H_2(CH_3)_3$)
23	140.70	113.70; 113.97; 127.11; 129.02; 130.54; 130.63; 132.70; 133.24; 134.12; 134.89; 137.52; 137.70; 140.47	16.26; 17.59; 20.18; 20.69; 20.76; 21.08 (-$NCH_2C_6H(CH_3)_3CH_2N$; Ar-CH_3; 2,3,5,6-$CH_2C_6H(CH_3)_4$); 46.97; 48.92 (-$NCH_2C_6H(CH_3)_3CH_2N$-; 2,3,5,6-$CH_2C_6H(CH_3)_4$)
24	140.57	113.31; 113.19; 125.15; 127.24; 130.52; 131.68; 133.64; 133.94; 134.19; 137.47; 137.68; 138.03; 138.94; 139.34	15.98; 17.19; 17.30; 19.72; 20.64; 20.88 (-$NCH_2C_6H(CH_3)_3CH_2N$; Ar-CH_3; 2,3,4,5,6-$CH_2C_6(CH_3)_5$); 47.84; 48.03 (-$NCH_2C_6H(CH_3)_3CH_2N$-; 2,3,4,5,6-$CH_2C_6(CH_3)_5$)
25	140.44	113.62; 113.89; 129.41; 130.11; 131.32; 136.46; 137.85; 138.03	17.34 (-$NCH_2C_6(CH_3)_4CH_2N$-); 20.86; 20.96 (Ar-CH_3); 47.21 (-$NCH_2C_6(CH_3)_4CH_2N$-); 47.68; 59.26 (-$CH_2CH_2OCH_3$); 71.83 (-OCH_3)
26	141.00	113.72; 114.09; 126.13; 129.48; 130.19; 130.36; 130.61; 136.54; 137.76; 137.79; 137.96; 139.26	17.32; 20.41; 20.77 (2,4,6-$CH_2C_6H_2(CH_3)_3$; -$NCH_2C_6(CH_3)_4CH_2N$-); 21.08; 21.18 (Ar-CH_3); 47.43; 47.99 (2,4,6-$CH_2C_6H_2(CH_3)_3$; -$NCH_2C_6(CH_3)_4CH_2N$)
27	140.95	113.98; 129.10; 129.47; 130.50; 130.61; 133.18; 134.05; 134.82; 136.55; 137.57; 137.81	16.20; 17.32 (2,3,5,6-$CH_2C_6H(CH_3)_4$); 20.69 (-$NCH_2C_6(CH_3)_4CH_2N$-); 20.74; 21.12 (Ar-CH_3); 47.40; 48.80 (2,3,5,6-$CH_2C_6H(CH_3)_4$; -$NCH_2C_6(CH_3)_4CH_2N$-)
28	140.91	113.87; 114.09; 126.50; 129.48; 130.54; 130.61; 133.53; 133.63; 136.52; 136.70; 137.45; 137.72	17.07; 17.21; 17.33; 17.50 (2,3,4,5,6-$CH_2C_6(CH_3)_5$; -$NCH_2C_6(CH_3)_4CH_2N$-); 20.75; 21.14 (Ar-CH_3); 47.36; 49.31 (2,3,4,5,6-$CH_2C_6(CH_3)_5$; -$NCH_2C_6H_0(CH_3)_4CH_2N$-)



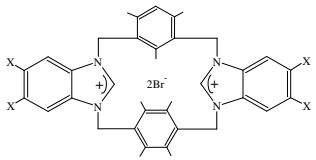
X=H, **29**

X=CH_3, **31**



X=H, **30**

X=CH_3, **32**

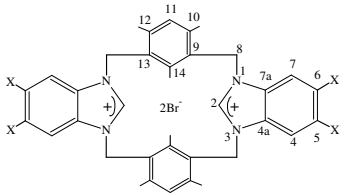


X=H, **33**

X=CH_3, **34**

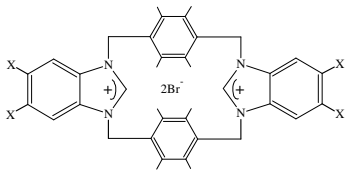
Table 3.9 ^{1}H NMR data for **29-34**

Compoud No	H^2(s)	H^{4-7}	H^{11}(s)	H^8/ H^{15}	Others
29	7,22	7.80-8.30 (m)	7.78 (s)	5.56; 5.80 (d, *J* 3.7 Hz)	1.59; 2.43 (s, -$NCH_2C_6H(CH_3)_3CH_2N$-)
30	7,23	7.90-8.37 (m)	-	5.81 (s)	2.10 (s, -$NCH_2C_6(CH_3)_4CH_2N$-)
31	7,20	8.08 (s)	7.62 (s)	5.49; 5.72 (d, *J* 3.7 Hz)	1.54; 2.41 (s, -$NCH_2C_6H(CH_3)_3CH_2N$-); 3.31 (s, Ar-CH_3)
32	6,22	8.14 (s)	-	5.73 (s)	2.07 (s, -$NCH_2C_6(CH_3)_4CH_2N$-); 2.53 (s, Ar-CH_3)
33	6,67	7.89-8.35 (m)	7.29 (s)	5.61-6.05 (m)	2.15; 2.23 (s, -$NCH_2C_6H(CH_3)_3CH_2N$-); 2.31 (s, -$NCH_2C_6(CH_3)_4CH_2N$-)
34	6,45	8.07; 8.10 (s)	7.27 (s)	5.44-5.97 (m)	2.57 (s, Ar-CH_3); 2.29(s, -$NCH_2C_6(CH_3)_4CH_2N$-); 2.17; 2.22 (s,-$NCH_2C_6H(CH_3)_3CH_2N$-)



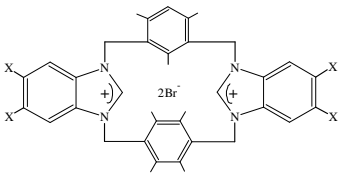
X=H, **29**

X=CH_3, **31**



X=H, **30**

X=CH_3, **32**



X=H, **33**

X=CH_3, **34**

Table 3.10 ^{13}C NMR data for **29-34**

Compound No	2-CH	Aromatics	Alkyl
29	140.99	114.71; 127.91; 128.06; 132.54; 133.01; 138.50; 138.73	15.62; 20.66 (-$NCH_2C_6H(CH_3)_3CH_2N$-); 46.31 (-$NCH_2C_6H(CH_3)_3CH_2N$-)
30	136.72	114.97; 128.16; 130.87; 132.89; 136.40	16.79 (-$NCH_2C_6(CH_3)_4CH_2N$-); 46.82 (-$NCH_2C_6(CH_3)_4CH_2N$-)
31	140.86	114.26; 128.33; 131.04; 137.65; 138.43	15.93; 20.73 (-$NCH_2C_6H(CH_3)_3CH_2N$-); 20.92 (Ar-CH_3); 46.17 (-$NCH_2C_6H(CH_3)_3CH_2N$)
32	137.96	114.38; 131.02; 131.31; 136.25	16.74 (-$NCH_2C_6H(CH_3)_4CH_2N$-); 20.92 (Ar-CH_3); 46.60 (-$NCH_2C_6(CH_3)_4CH_2N$-)
33	141.98	113.79; 113.85; 127.58; 128.08; 128.12; 131.20; 132.50; 132.67; 132.82	14.61;15.60; 18.60 (-$NCH_2C_6H(CH_3)_3CH_2N$-; -$NCH_2C_6(CH_3)_4CH_2N$-); 45.72; 46.35 (-$NCH_2C_6H(CH_3)_3CH_2N$-; -$CH_2C_6(CH_3)_4CH_2$-)
34	141.78	113.28; 127.73; 131.18; 131.32; 131.36; 132.40; 135.23; 135.85; 136.50; 138.70; 138.73; 138.89	14.56; 15.52; 18.59; 19.56 (-$NCH_2C_6H(CH_3)_3CH_2N$-; -$NCH_2C_6(CH_3)_4CH_2N$-; Ar-CH_3); 45.56; 46.19 (-$NCH_2C_6H(CH_3)_3CH_2N$-; -$NCH_2C_6(CH_3)_4CH_2N$-

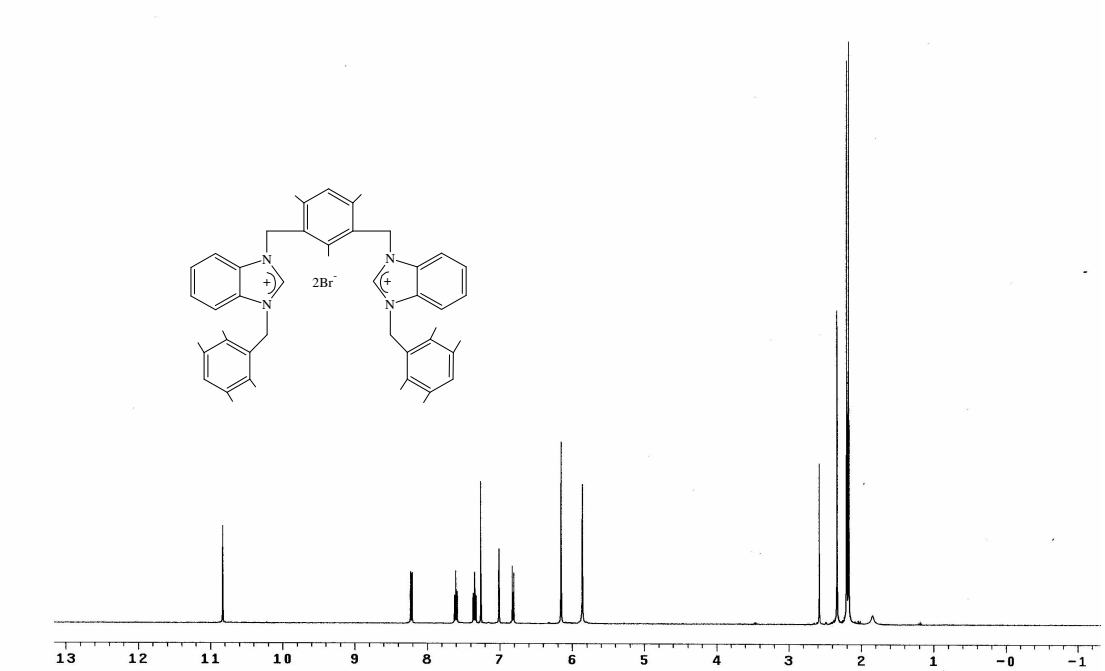


Figure 3.1 1H NMR Spectrum of compound **9**

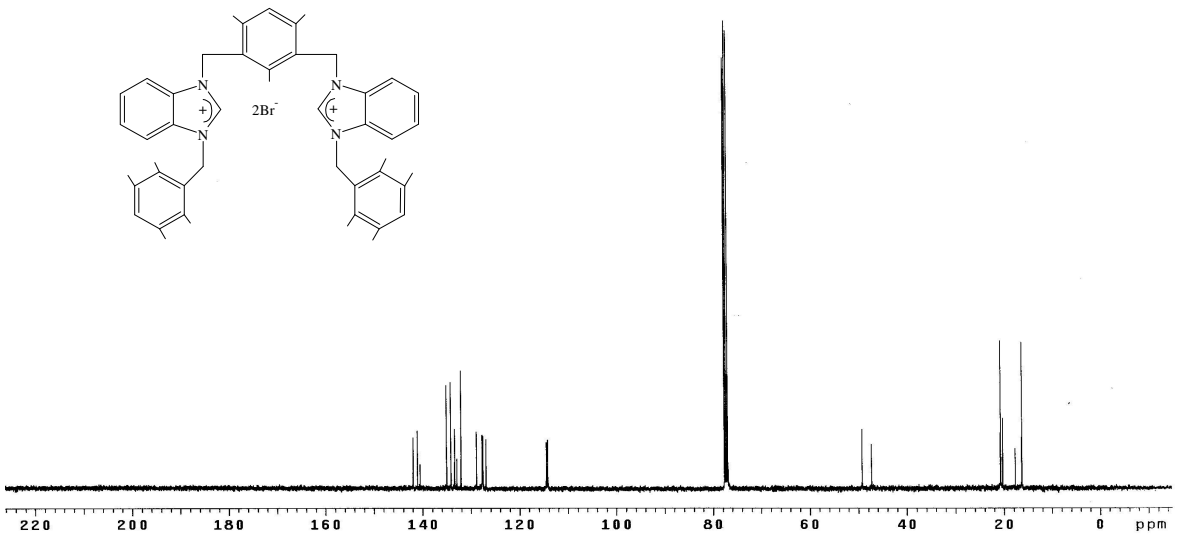


Figure 3.2 ^{13}C NMR Spectrum of compound **9**

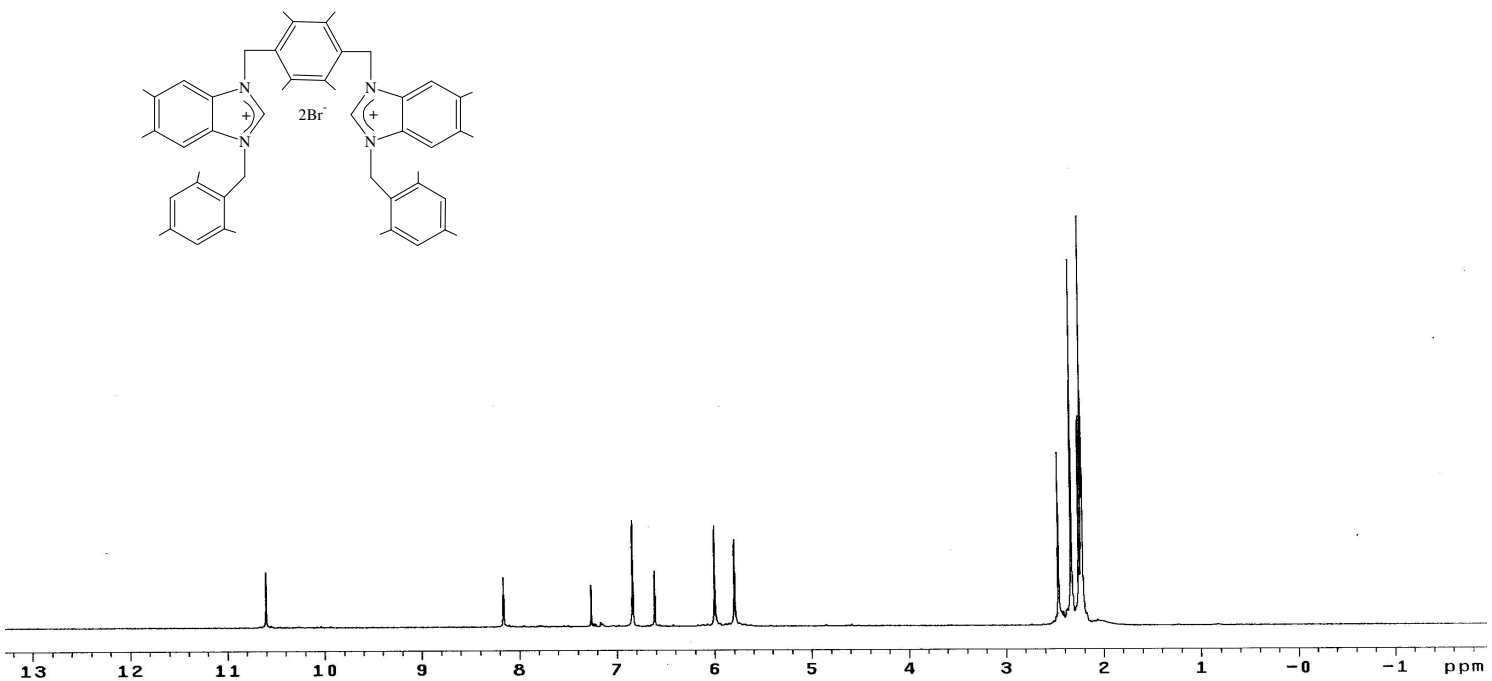


Figure 3.3 ^{1}H NMR Spectrum of compound **26**

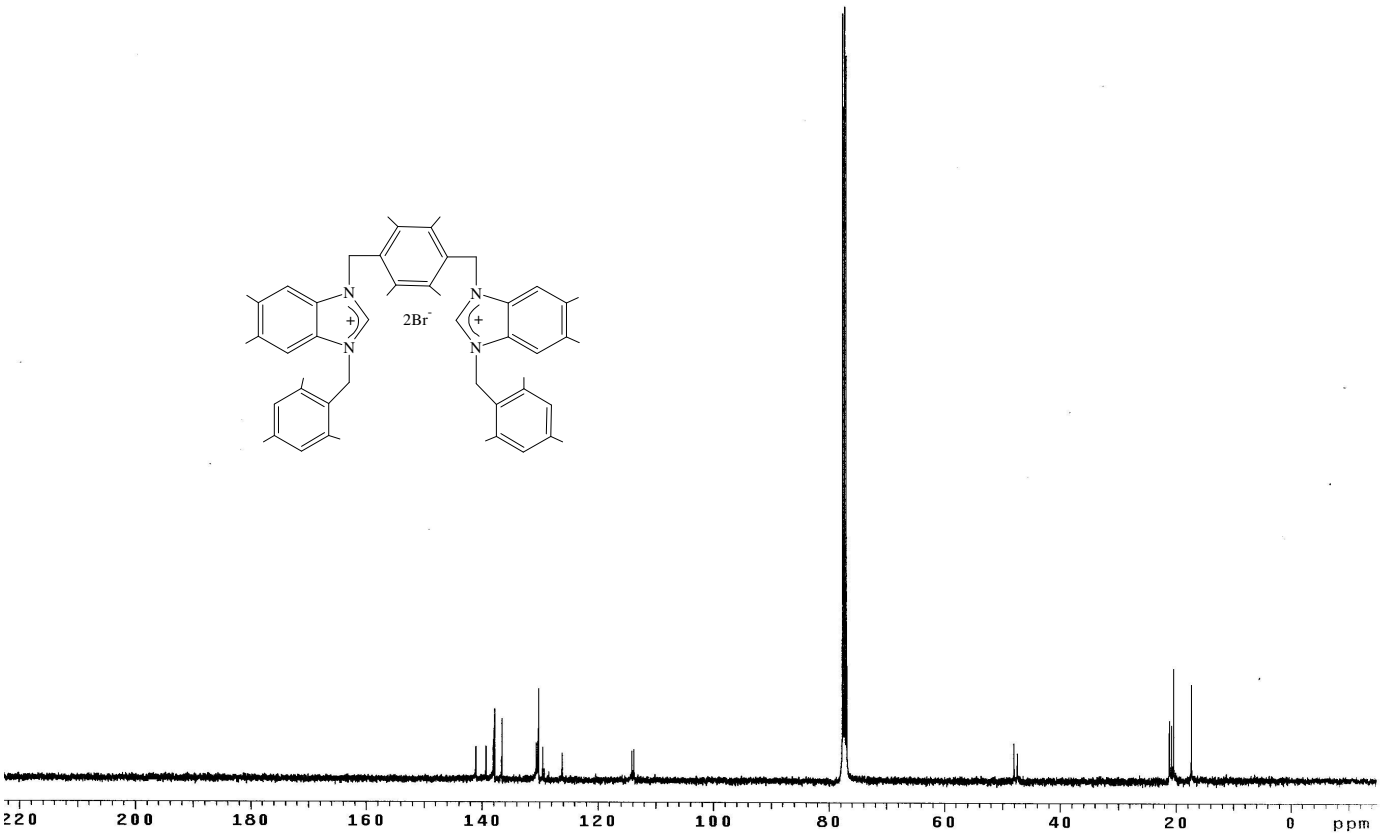


Figure 3.4 ^{13}C NMR Spectrum of compound **26**

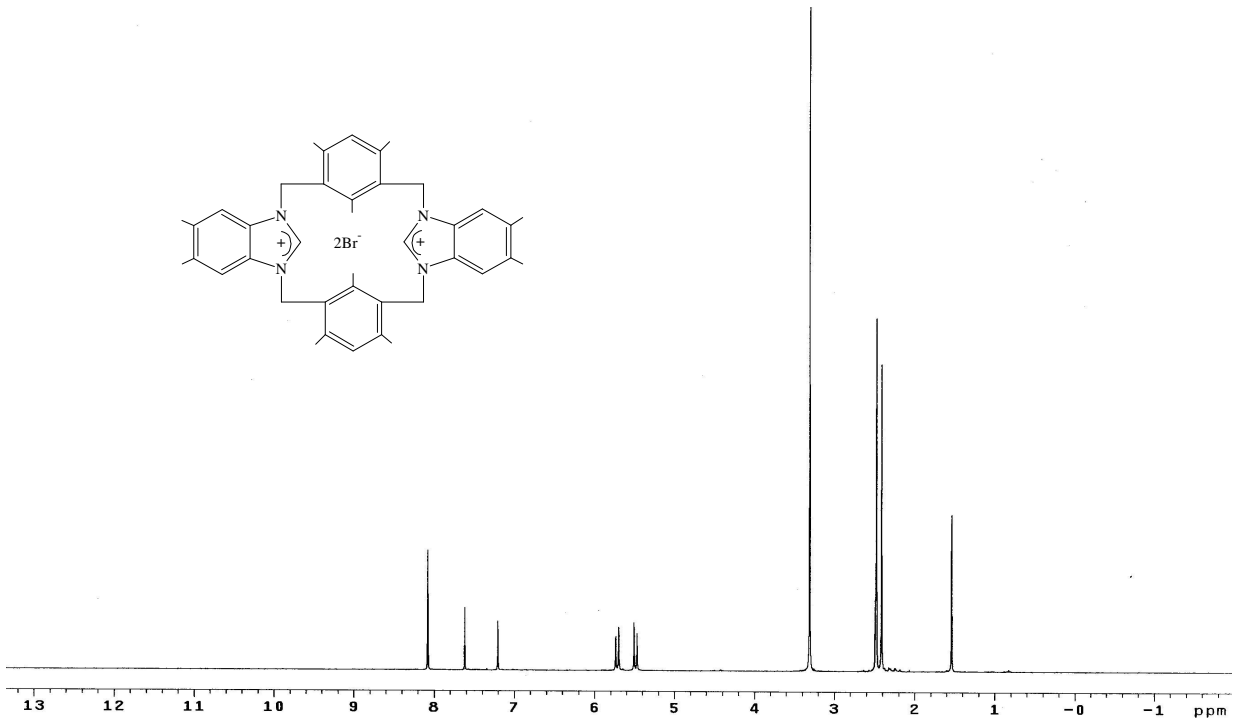


Figure 3.5 ^{1}H NMR Spectrum of compound **31**

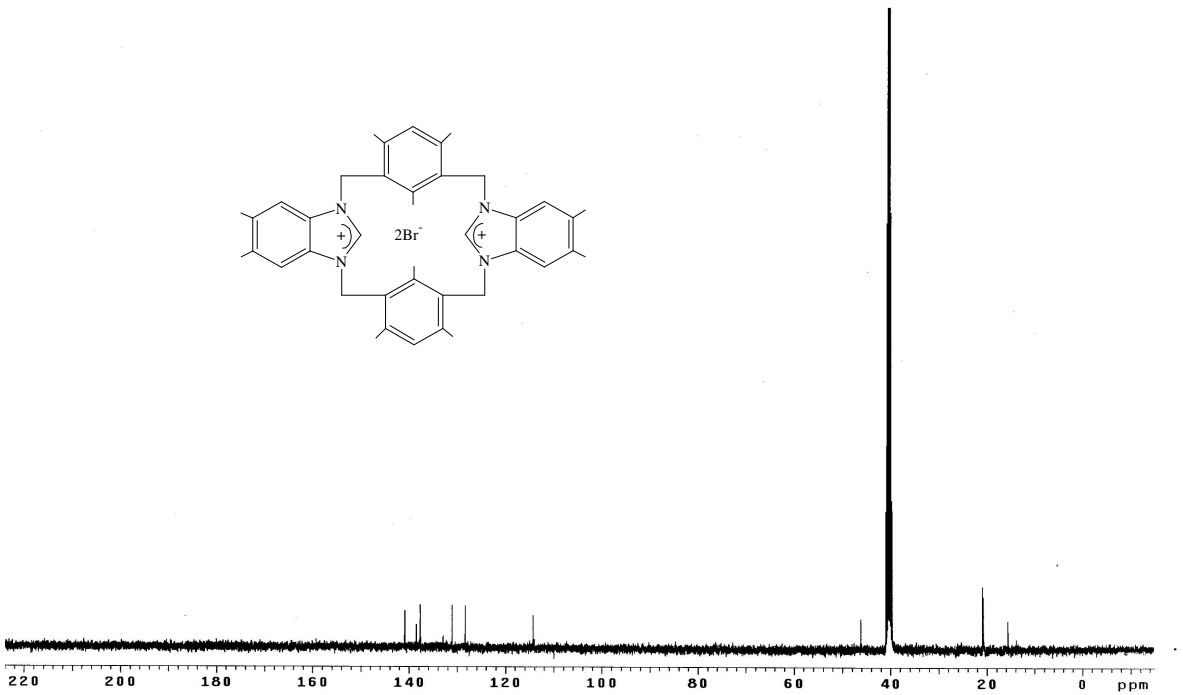


Figure 3.6 ^{13}C NMR Spectrum of compound **31**

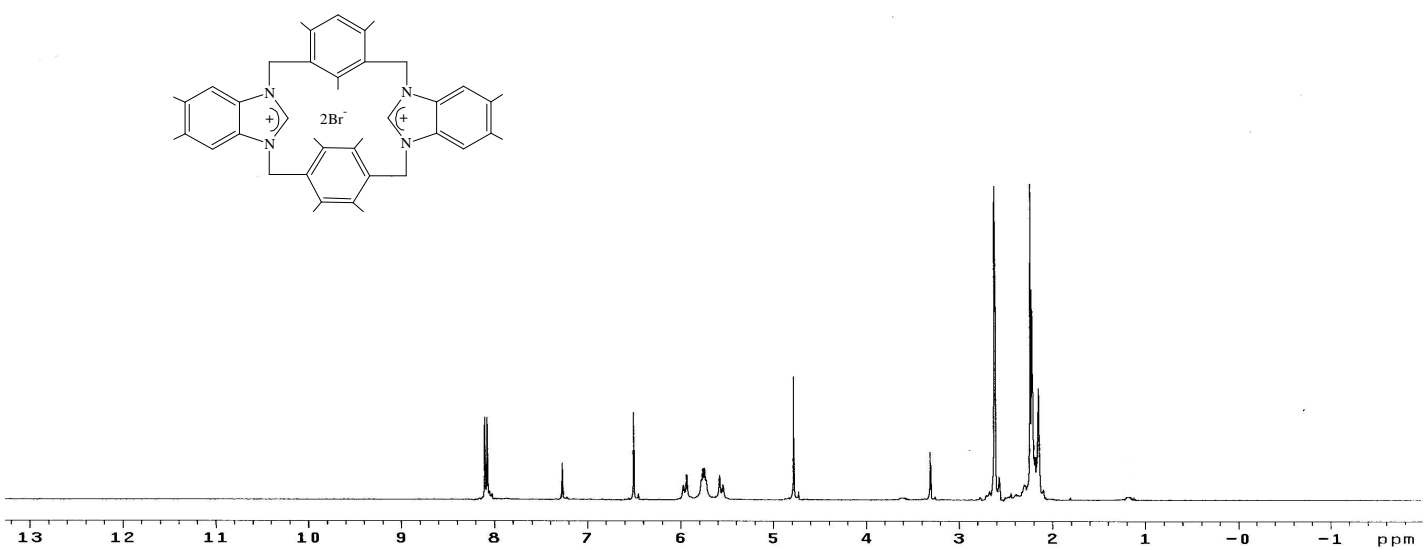


Figure 3.7 ^{1}H NMR Spectrum of compound **34**

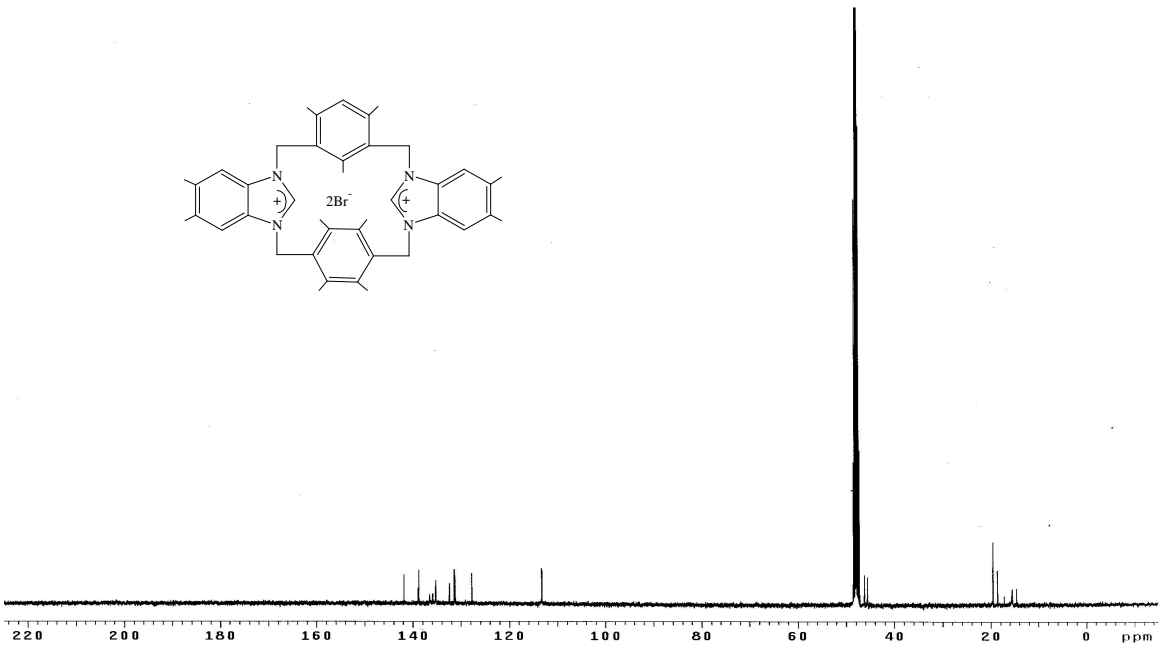


Figure 3.8 ^{13}C NMR Spectrum of compound **34**

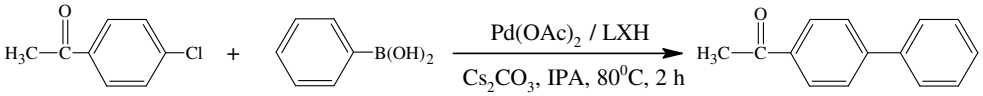
3.4 The Suzuki Coupling Reaction

The Suzuki coupling, where organoboronic acids are employed as neuclophilic partners to couple with electrophiles such as aryl halides, is one of the most important protocols in organic synthesis, permitting the construction of a wide variety of organic compounds ranging from artificial materials to natural products (Miyaura, 1995; Suzuki, 1999; Stanforth, 1998).

The reactions are usually carried out homogenously in the presence of a base under inert atmosphere. The reactivity of the aryl halide component decreases drastically in the order X = I > Br > CI and electron-withdrawing substituents R are required for the chlorides to react.

To survey the reaction parameters for the catalytic Suzuki reaction, a series of experiments has been performed with aryl halide and phenylboronic acid. We found that the reactions performed in IPA with Cs_2CO_3 as the base at 80°C appeared to be best. We started our investigation with the coupling of 4-chloroacetophenone and phenylboronic acid, in the presence of $Pd(OAc)_2$. It is evident that the NHC precursors that contain electron donating methoxyethyl substituent (**7**, **11**, **21**, **25**) are the most effective of the salts examined. Table 3.11 summarizes the results obtained in the presence of **7**-**14**; **21**-**28; 29-34**.

Table 3.11 The Suzuki coupling reaction of 4-chloroacetophenone with phenylboronic acid.



Entry	LXH	Yield (%)
1	**7**	94
2	**8**	80
3	**9**	79
4	**10**	90
5	**11**	93
6	**12**	89
7	**13**	85
8	**14**	91
9	**21**	97
10	**22**	83
11	**23**	80
12	**24**	91
13	**25**	95
14	**26**	87
15	**27**	82
16	**28**	90
17	**29**	75
18	**30**	70
19	**31**	73
20	**32**	60
21	**33**	80
22	**34**	88

Abbreviation; LXH= benzimidazolium salts; IPA= isopropylalcohol

3.5 The Heck Coupling Reaction

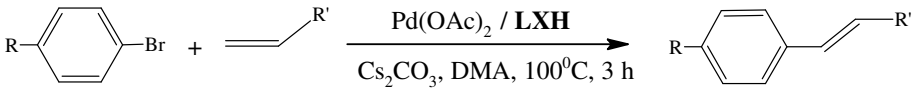
The Heck coupling reaction is one of the most important methods for C-C bond formation in general organic synthesis, synthesis of pharmaceuticals, agrochemicals and natural products.

The coupling reactions of aryl halides with olefins are called Heck coupling reactions. Palladium species have largely been used as catalyst for C-C bond forming reactions. The reactions are usually carried out homogenously in the presence of a base under inert atmosphere. It is worth noting that in situ formation of the azolium salt led to significantly better results than the use of the performed complex.

For the choice of base, we surveyed Cs_2CO_3, Na_2CO_3 and KO^tBu. Finally, we found that use of 3% $Pd(OAc)_2$, 3% ligand and 1.5 mmol Cs_2CO_3 in DMA at 100°C led to the best conversion within 3 h. Under the determined reaction conditions, we investigated reaction of aryl halides with n-butyl acrylate or styrene and observed that reactions at 100 °C gave good to excellent products (62-100%). As expected, we could observe that the NHC precursors that contain electron donating methoxyethyl group (**7**, **11**, **21**, **25**) were the most effective of the salts examined. We expected that activities of these salts would increase in the order: pentamethylbenzene substituent (**a**) (**10**, **14**, **24**, **28**)> tetramethylbenzene substituent (**b**) (**9**, **13**, **23**, **27**)> trimethylbenzene substituent (**c**) (**8**, **12**, **22**, **26**). But the catalytic activity increased in the squence **a > c > b**. This observation indicates that the effect of p-substituent was significant. Also, benzimdazolium salts bearing methyl groups on 5,6-positions of benzene ring have shown better catalytic activity than nonsubstituted counterparts. This observation is

consistent with the previous reports (Türkmen and Çetinkaya, 2006). The results obtained were summarized in Table 3.12

Table 3.12 The Heck reaction catalyzed by in situ formed (LHX + $Pd(OAc)_2$)



Entry	LXH	Aryl Halide	Olefin	Yield (%)
1	**7**	4-Bromoacetophenone	n-butyl acrylate	98
2	**8**	‘’	‘’	90
3	**9**	‘’	‘’	80
4	**10**	‘’	‘’	94
5	**11**	‘’	‘’	96
6	**12**	‘’	‘’	88
7	**13**	‘’	‘’	82
8	**14**	‘’	‘’	91
9	**21**	‘’	‘’	100
10	**22**	‘’	‘’	92
11	**23**	‘’	‘’	88
12	**24**	‘’	‘’	96
13	**25**	‘’	‘’	100
14	**26**	‘’	‘’	91
15	**27**	‘’	‘’	83
16	**28**	‘’	‘’	92
17	**29**	‘’	‘’	70
18	**30**	‘’	‘’	67
19	**31**	‘’	‘’	73
20	**32**	‘’	‘’	67
21	**33**	‘’	‘’	75
22	**34**	‘’	‘’	83
23	**7**	4-Bromoanisole	‘’	78
24	**8**	‘’	‘’	68
25	**9**	‘’	‘’	62
26	**10**	‘’	‘’	75
27	**11**	‘’	‘’	77
28	**11**	4-Bromoacetophenone	Styrene	88
29	**25**	Bromobenzene	n-butyl acrylate	80

Abbreviation; LXH= benzimidazolium salts; DMA= N,N-Dimethylacetamide

In conclusion, in this thesis, mono- and di-bridged bibenzimidazolium bromides (**I**, **II**) were synthesized and their catalytic activities were tested for Suzuki and Heck reactions. We examined Suzuki reaction of 4-chloroacetophenone and phenylboronic acid, in the presence of $Pd(OAc)_2$. The results were summarized in Table 3.11. The mono-bridged bibenzimidazolium salts containing electron donating methoxyethyl substituent (**7**, **11**, **21**, **25**) are the most effective of the salts examined. Catalytic activity increased in the sequence: pentamethyl substituent (**a**) > trimethyl substituent (**c**) > tetramethyl substituent (**b**). This observation indicates the influence of *p*- substituent was significant. Also, benzimidazolium salts bearing methyl groups on 5,6-positions have shown better activity than those not bearing methyl substituent. Besides, unsymmetrical cyclophanes gave the better results than the symmetrical ones. The Heck coupling reactions were performed between aryl halides with n-butyl acrylate or styrene in the presence of $Pd(OAc)_2$ in DMA at 100 ^{0}C. The results obtained were summarized Table 3.12. As is seen in Table, similar to Suzuki reaction, the best catalytic activity was observed at salts bearing one methoxyethyl substituent on nitrogen atom (**7**, **11**,**21**,**25**).

REFERENCES

Alcalde, E., Alvarez-Rúa, C., García-Granda, S., García-Rodriguez, E., Mesquida, N., Pérez- García, L., 1999, Hydrogen bonded driven anion binding by dicationic [1_4] imidazoliophanes, *Chem. Commun*., 295-296

Allali, M., Benoist, E., Habbadi, N., Gressier, M., Souizi, A., Dartiguenave, M., 2003, Design and synthesis of new ethylenediamine or propylenediamine diacetic acid derivatives for Re(I) organometallic chemistry, *Tetrahedron*, 60: 1167-1174

Baker, M.V., Skelton, B.W., White, A.H., Williams, C.C., 2001, Palladium carbene complexes derived from imidazolium-linked ortho-cyclophanes, *J. Chem. Soc*., *Dalton Trans*., 111-120

Baker, M.V., Skelton, B.W., White, A.H., Williams, C.C., 2002, Synthesis and characterization of a saddle-shaped nickel-carbene complex derived from an imidazolium-linked meta-cyclophane, *Organometallics*, 21: 2674-2678

Barışık, B., 2005, 1,3-Disubstituted Benzimidazolium salts, Yüksek lisans tezi, Ege Üniversitesi Fen Bilimleri Enstitüsü, 60s

Barnard, P.J., Baker, M.V., Berners-Price, S.J., Skelton, B.W., White, A.H., 2004, Dinuclear gold (I) complexes of bridging bidentate carbene ligands: synthesis, structure and spectroscopic characterisation, *Dalton Trans.*, 1038-1047

REFERENCES (continue)

Bitter, I., Török, Z., Csokai, V., Grün, A., Balázs, B., Tóth, G., Keserü, G.M., Kovári, Z., Czugler, M., 2001, Synthesis and conformational analysis of dicationic N,N'-Bridged bis(benzimidazolium) and Bis(imidazolium) macrocycles, *Eur. J. Org. Cem.*, 2861-2868

Briot, A., Bujard, M., Gouverneur, V., Nolan, S.P., Mioskowski, C., 2000, Improvement in olefin metathesis using a new generation of ruthenium catalyst bearing an imidazolylidene ligand: synthesis of heterocycles, *Org. Letters*, 2: 1517-1519

Cabildo, P., Sanz, D., Claramunt, R.M., Bourne, S.A., Alkorta, I., Elguero, J., 1999, Synthesis and structural studies of some [1_4] paraccyclo-bis-(1,2) pyrazolium- and (1,3) imidazolium-phanes, *Tetrahedron*, 58: 2327-2340

Carini, D.J., Duncia, J.V., Aldrich, P.E., Chiu, A.T., Johnson, A.L., Pierce, M.E., Price, W.A., Santella, J.B. III., Wells, G.J., Wexler, R.R., Wong, P.C., Yoo, S.-E., Timmermans, P.B.M.W.M., 1991, Nonpeptide, Angiotensin II receptor antagonists: the discovery of a series of N-(Biphenylmethyl) imidazoles as potent, orally active antihypertensives, *J. Med. Chem.*, 34: 2525-2547

REFERENCES (continue)

Çetinkaya, E., Hitchcock, P.B., Küçükbay, H., Lappert, M.F., Al-Juaid, S., 1994, Preparation and characterisation of two enetetramine-derived carbenerhodium (I) chloride complexes RhCl $(L^R)_3$ and $[RhCl(COD)L^R]$ $\{L^R=CN(Me)C(CH_4)CNMe\text{-}o\}$and the preparation and X-ray structures of the enetetramine $L^R{}_2$ and its salt $[L^R{}_2]$ $[BF_4]_2$, *J. Organomet. Chem.*, 481: 89-95

Çetinkaya, E., Denizci, A., Özdemir, İ., Öztürk, H.T., Karaboz, İ., and Çetinkaya, B., 2002, Remarkable substituent effects on antimicrobial activities of 1,3-diorganylimidazolium salts , *J. Chemotherapy,* 14: 241-245

Ferm, R., Riebsomer, J.L., 1954, The chemstry of the 2-imidazolines and imidazolidines, 593-613

Furniss, B.S., et al., 1978, Vogel's Textbook of Practical Organic Chemistry, 4. Pres

Garrison, J.C., Simons, R.S., Kofron, W.G., Tessier, C.A., Youngs, W.J., 2001, Synthesis and structural characterization of a silver complex of a mixed donor N-heterocyclic carbene linked cyclophane, *Chem. Commun.*, 1780-1781

REFERENCES (continue)

Garrison, J.C., Simons, R.S., Talley, J.M., Wesdemiotis, C., Tessier, C.A., Youngs, W.J., 2001, Synthesis and structural characterization of an imidazolium-linked cylophane and the silver complex of an N-heterocyclic carbene-linked cyclophane, *Organometallics*, 20: 1276-1278

Gök, Y., Gürbüz, N., Özdemir, İ., Çetinkaya, B., Çetinkaya, E., 2005, Benzimidazolin-2-ylidene-palladium-catalysed coupling reactions of aryl halides, *Appl. Organometal. Chem*, 19: 870-874

Güven, M., 2000, Benzimidazol Türevlerinin Sentezi ve Özelliklerinin İncelenmesi, Yüksek Lisans Tezi, İnönü Üniversitesi Fen Bilimleri Enstitüsü, 71s

Hahn, F.E., Wittenbecher, L., Boese, R., Bläser, D., 1999, N,N'-Bis(2,2-dimethylpropyl) benzimidazolin-2-ylidene: A stable nucleophilic carbene derived from benzimidazole, *Chem. Eur. J.*, 5: 1931-1935

Hahn, F.E., Wittenbecher, L., Van, D.L., Fröhlich, R., 2000, Evidence for an equilibrium between an N-heterocyclic carbene and its dimer in solution, *Angew. Chem. Int. Ed.*, 39: 541-544

Herrmann, W. A., 2002, N-heterocyclic carbenes: A new concept in organometallic catalysis, *Angew. Chem. Int. Ed.*, 41: 1290-1309

REFERENCES (continue)

Hillier, A.C., Grasa, A., Viciu, M.S., Lee, H.M., Yang, C., Nolan, S. P., 2002, Catalytic cross-coupling reactions mediated by palladium/ nucleophilic carbene systems, J. Organomet. Chem., 653: 69-82

Hitchcock, P.B., Lappert, M.F., Terreros, P., Wainwright, K.P., 1980, The synthesis and properties of the transannularly bonded electron-rich olefin derived from 1,4,8,11-tetra-azacyclotetradecane; X-ray crystal structure of the chelating cis-dicarbene rhodium (I) salt obtained therefrom*, J. Cem. Soc., Cem. Commun.*, 1180-1181

Huang, W., Guo, J., Xiao, Y., Zhu, M., Zou, G., Tang, J., 2005, Palladium-benzimidazolium salt catalyat systems for Suzuki coupling: Development of a practical and highly active palladium catalyst system for coupling araomatic halides with aryl boronic acids, *Tetrahedron*, 61: 9783-9790

Huynh, H.V., Ho, H.H.J., Neo, T.C., Koh, L.L., 2005, Solvent-controlled selective synthesis of a *trans*-configured benzimidazoline-2-ylidene palladium (II) complex and investigations of its Heck-type catalytic activity, *J. Organomet. Chem.*, 690: 3854-3860

Jafarpour, L. Nolan, S.P., 2001, Development of olefin metathesis catalyst precursors bearing nucleophilic carbene ligands, *J. Organomet. Chem.,* 617-618: 17-27

Kaiser, 1885, *Ber.*, 18: 2942

REFERENCES (continue)

Kutlu, H., 1976, Farmasötik Kimya IV (Heterosiklik Seri İlaçlar 1), İstanbul Üniversitesi Eczacılık Fak. Farmasötik Kimya Kürsüsü, 512s.

Küçükbay, H., Çetinkaya, E., and Durmaz, R., 1995, Synthesis and antimicrobial activity of substituted benzimidazole, benzothiazole and imidazole, derivatives, *Arzneim.-frosch./Drug Res.*, 45(II),12: 1331-1334

Lednicer, D., Mitscher, L.A., 1977, The Organic Chemistry of Drug Synthesis, John Wiley & Sons, Vol:1, 471s

Lednicer, D., Mitscher, L.A., 1980, The Organic Chemistry of Drug Synthesis, John Wiley & Sons, Vol:2, 526s

Magill, A.M., McGuinness, D.S., Cavell, K.J., Britovsek, G.S.P., Gibson, V.C., White, A.J.P., Williams, D.J., White, A.H., Skelton, B.W., 2001, Palladium (II) complexes containing mono-, bi-, and tridentate carbene ligands. Synthesis, characterisation and application as cataysts in C-C coupling reactions, *J. Organomet. Chem.*, 617-618: 546-560

March, J., 1992, Advanced Organic Cemistry, John Wiley & Sons, 4th edition

Mathews, C.K., van Holde, K.E., Ahern, K.G., 2000, Biochemistry, Benjamin/ Cummings, an imprint of Addison Wesley Longman, 3th edition

REFERENCES (continue)

Miyaura, N. Suzuki, A., 1995, Palladium-catalyzed cross-coupling reactions of organoboron compounds, *Chem. Rev.*, 95: 2457-2483

Mohammadpoor-Baltork, I., Zolfigol, M.A., Abdollahi-Alibeik, M., 2004, Novel and chemoselective dehydrogenation of 2-substituted imidazolines with potassium permanganate supported on silica gel, *Tetrahedron Letters*, 45: 8687-8690

Özdemir, İ., Gök, Y., Gürbüz, N., Çetinkaya, E., Çetinkaya, B., 2004, Palladium-catalyzed Suzuki reaction using 1,3-dialkylbenzimidazol-2-ylidene ligands in aqueous media, *Heteroatom Chem.*, 15: 419-423

Özdemir, İ., Gök, Y., Gürbüz, N., Yaşar, S., Çetinkaya, E., Çetinkaya, B., 2004, In-situ generated functionalized benzimidazol-2-ylidene-palladium catalyst for Suzuki reaction, *Polish J. Chem.*, 78: 2141-2147

Peris, E., Mata, J., Loch, J.A., Crabtree, R.H., 2001, A Pd complex of tridentate pincer CNC bis-carbene ligand as a robust homogenous Heck catalyst, *Chem. Commun.*, 201-202

Pernak, J., Arndt, A., Pozniak, R., 1998, The antielectrostatic effect of benzimidazolium salts, *Polymer*, Vol.39, No.3: 605-609

Perry, C.M., Burgess, K., 2003, Chiral N-heterocyclic carbene-transition metal complexs in asymmetric catalysis, *Tetrahedron: Asymmetry*, 14: 951-961

REFERENCES (continue)

Rajakumar, P., Murali, V., 2000, Benzotriazolophanes-new class of novel cyclophanes, *Tetrahedron*, 56: 7995-7999

Rajakumar, P., Dhanasekaran, M., 2002, Synthesis of intra-annularly functionalized cationic pyridinophanes, *Tetrahedron*, 58: 1355-1359

Rajakumar, P., Selvam, S., Dhanasekaran, M., 2005, Synthesis and sttructural characterization of chiral dicationic imidazolophanes, *tetrahedron Letters.*, 46: 6127-6130

Ramos, S., Alcalde, E., Doddi, G., Mencarelli, P., Péreez-García, L., 2002, Quantitative evaluation of the chloride template effect in the formation of dicationic [1_4] imidazoliophanes, *J. Org. Chem.*, 67: 8463-8468

Shi, Z., Thummel, R.P., 1995, N,N'-Bridged derivatives of 2,2'-Bibenzimidazole, *J. Org. Chem.*, 5935-5945

Simons, R.S., Garrison, J.C., Kofron, W.G., Tessier, C.A., Youngs, W.J., 2002, Synthesis and structural characterization of two bis-imidazolium-linked cyclophanes: precursors toward ´carbeneporphyrinoid` ligands, *Tetrahedron Letters*, 43: 3423-3425

Stanforth, S.P., 1998, Catalyticcross-coupling reactions in biaryl synthesis, *Tetrahedron*, 54: 263-303

REFERENCES (continue)

Suzuki, A., 1999, Recent advances in the cross-coupling reactions of organoboron derivatives with organic electrophiles, *J. Organomet. Cem.*, 576: 147-168

Türkmen, H., Çetinkaya, B., 2006, 1,3-Diarylimidazolidin-2-ylidene(NHC) complexes of Pd (II): Electronic effects on cross-coupling reactions and thermal decompositions, *J. Organomet. Cem.*, (in press)

Van der Made, A.W., van der Made, R.H., 1993, A convenient procedure for bromomethylation of aromatic compounds. Selective mono-, bis-, or trisbromomethylation, *J. Org. Cem.*, 58: 1262-1263

Wasserscheid, P., Keim, W., 2000, Ionic liquids-new ˝solutions˝ for transition metal catalysis, *Angew. Chem. Int. Ed.*, 39: 3772-3789

Welton, T., 1999, Room-temperature ionic liquids. Solvents for synthesis and catalysis, *Chem. Rev.*, 99: 2071-2083

Xi, N., Xu, S., Cheng, Y., Tasker, A.S., Hungate, R.W., Reider, P.J., 2005, Regio-controlled synthesis of N-substituted imidazoles, *Tetrahedron Letters*, 46: 7315-7319

Zhong, Y.-L., Lee, J., Reamer, R.A., Askin, D., 2004, New method fort he synthesis of diversely functionalized imidazoles from N-acylated α-aminonitriles, *Org. Lett.*, 6: 929-931

CIRRICULUM VITAE

Name:	Serpil Denizaltı
Date of Birth:	14.08.1981
Place of Birth:	İzmir
Maritial Status:	Single
Sex:	Female
Residance Address:	Fevzi Çakmak Mah. Alparslan Sok. No:4/1 Balçova/İzmir
e-mail:	sdenizalti@yahoo.com
Telephone:	0 232 277 50 34

Education:

Name of University	Degree	Period
Ege University	BSc In Chemistry	1998-2003
Ege University	MSc. In Org.Chem.	2004-2006

Poster Presentation:

Çetinkaya, E., Denizaltı, S., 2006, Köprülü Benzimidazolyum Tuzlarının Sentezi ve Katalitik Uygulamaları, XX. Uluslararası Kimya Kongresi, Kayseri