EGE ÜNİVERSİTESİ FEN BİLİMLERİ ENSTİTÜSÜ
(YÜKSEK LİSANS TEZİ)

AN INVESTIGATION OF THE METAL-HALOGEN EXCHANGE REACTION OF o-IODO SUBSTITUTED AROMATIC COMPOUNDS

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Bornova-İZMİR

Sayın Fatma ÇETİN tarafından **Yüksak Lisans Tezi** olarak sunulan '' o-İodo aril bileşiklerinin metal-halogen yerdeğiştirme reaksiyonlarının incelenmesi''adlı bu çalışma ''Lisans üstü eğitim ve Öğretim yönetmeliği'nin'' ve Enstitü yönergesinin ilgili hükümleri dikkate alınarak

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tarafından değerlendirilmiş olup,yapılan Tez Savunma Sınavında aday oy birliği/oy çokluğu ile başarılı bulunmuştur.

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o-İODO SÜBSTİTÜE ARİL BİLEŞİKLERİNİN METAL-HALOGEN YERDEĞİŞTİRME REAKSİYONLARININ İNCELENMESİ

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Oksazoline orto pozisyonunda iodo sübstitüe grubu olan aril bileşiğinin diarilbakırlityum [$(Ar)_2CuLi$], arilbakır (ArCu) organometallik reaktifleri ile metal-halojen yerdeğiştirme reaksiyonları incelendi. Ayrıca N,N-dietil-2-iodobenzamid bileşiğinin [$(Ar)_2CuLi$] organometalik reaktifle metal-halojen yerdeğiştirme reaksiyonları farklı elektrofiller kullanılarak incelendi. Ürünlerin IR ve NMR spektrumları ile karakterize edildi.

ABSTRACT

AN INVESTIGATION OF THE METAL-HALOGEN EXCHANGE REACTION OF o-IODO SUBSTITUTED ATOMATIC COMPOUND

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The metal-halogen exchange reaction of diarylcopperlithium [$(Ar)_2CuLi$] and arylcopper (ArCu) reagents with aryl oxazoline containing an iodo substituent on the ortho position was investigated.Furthermore, the reaction of [$(Ar)_2CuLi$] reagent with N,N-diethyl-2-iodobenzamide was studied.The products were characterised by spectroscopic methods.

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Fatma ÇETİN

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ABBREVIATIONS

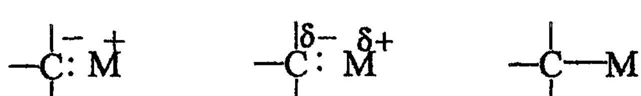
Abbreviations	Explations
THF	Tetrahydrofuran
TMEDA	Tetrametil Etilendiamin
Bu	Butyl
$CaCl_2$	Calciumchloride
$SOCl_2$	Thionylchloride
CH_2Cl_2	Methylenechloride
Na_2SO_4	Sodiumsulfate
NaOH	Sodiumhydroxide
CuCN	Copper (I) cyanide
NH_4Cl	Ammoniumchloride
Me	Methyl
Ph	Phenyl
X	Halide
R	Alkyl
RT	Room Temperature
min	minutes
TLC	Thin Layer Chromatography
IR	Infrared
NMR	Nuclear Magnetic Resonans
ppm	parts per million
HMPT	hexamethylphosphorous triamide

1. INTRODUCTION

1.1 General Information About Organometallic Compounds

The use of organometallic reagents in organic synthesis had its begining around 1900 with the work of Victor Grignard, who discovered that alkyl and aryl halides reacted with magenesium metal to give homogenous solutions.The " Grignard reagents" have proved to be versatile reagents since that time. Organolithium reagents come into synthetic use somewhat later.

Compounds that contain carbon-metal bonds are called organometallic compounds.The nature of the carbon-metal bonds vary widely , ranging from bonds that are essentially ionic to those that are primarily covalent. While the structure of the organometallic compound has some effect on the nature of the carbon-metal bond, the identity of the metal itself is of far greater importance . Carbon-sodium and carbon-potassium bonds are largely ionic in character ; carbon-lead, carbon-tin, carbon-thallium(III) and carbon-mercury bonds are essentially covalent. Carbon-lithium and carbon-magnesium bonds fall in between these extremes.



Primarily ionic (M = Na^+or K^+)   (M= Mg or Li)   Primarily covalent (M= Pb, Sn, Hg, Tl)

Organometallic compounds of lithium and magnesium are great importance in organic synthesis. They are relatively stable in ether solutions but their carbon-metal bonds have considerable ionic character. Because of this, the carbon atom of an organolithium or organo-magnesium compound that is bonded to the metal is a strong base and a powerful nucleophile.

Many solvents can be used for organometallic reagents. The solvent should be easily purified and freed from water and peroxides. It should have an appropriate boiling point or usually more important, a low enough freezing point. And it should not itsef react with organolithium compounds.

The phsical properties of the most useful solvents for organolithium compounds are listed in Table 1 and comments on the individual solvents follow.

Ethers are the most commonly used solvents for organolithium reactions. Diethyl ether is a good general-purpose choice. Most organolithium compounds are soluble in it, and it is not in most cases too rapidly cleaved by them ; it may be used at low temperatures; and it is a convenient solvent for conventional work-up procedures.

In may cases it is adequately dried by sodium wire, and its high vapour pressure at room temperature creates a " blanket " over the surface of the solution, which sometimes makes provision of a nitrogen or an argon atmosphere unnecessary.

Table 1. Solvents for Organolithium Reactions

Solvent	b.p (°C)	m.p (°C)
Pentane	36	-129
Hexane	69	-94
Benzene	80	5,5
Diethyl ether	34,5	-116
THF	64-5	-65
DME	82-3	-58
Triethylamine	89	-115
TMEDA	122	-55
Hexametapol	232	7

1.2 The Reaction of RX with Metal

1.2.1 Preparation of Organolithium and Organomagnesium Compounds

Organolithium and organomagnesium compounds are usually prepared by the reaction of an organic halide with lithium or magnesium metal. Their reactions are usually carried out in ether solvent and since organolithium and organomagnesium compounds are strong bases , care must be taken to exclude moisture. Exclution of oxygen is also important. The ethers most commonly used as solvents are diethyl ether and tetrahydrofuran.

Organolithium compounds such as methyllithium, ethyllithium and phenyllithium can be prepared in the same general way.

Scheme : 1

$$\underset{(\text{or Ar-X})}{\text{R-X}} + 2\,\text{Li} \xrightarrow{\text{ether}} \underset{(\text{or ArLi})}{\text{RLi}} + \text{LiX}$$

The order reactivity of halides RI > RBr > RCl (Alkyl and ayl fluorides are seldom used in the preparation of organolithium compounds)

Because of its insolubility in hydrocarbon solvents, methyllithium is produce normally in diethyl ether or diethoxymethane as solvent. The preparation in aromatic hydrocarbon-tetrahydrofuran (THF) mixtures containing some magnesium has been described. *(Gmelin Hanbuch ,1977 ; M.Bottrill, P.D. Gavens , J.W. Kelland, J. McMeeking, 1982 ; K.H. Thiele , 1972).* Phenyllithium, can be prepared in a mixture of 70 % cyclohexane and 30 % diethyl ether.

Organolithium compounds are usually prepared as solutions in hydrocarbon solvents. The reaction is highly exothermic, and therefore the temperature has to be controlled carefully. The rate of reaction determined by the rate of addition of the halide is limited by the capacity of the reflux condenser.

Vinyllithium can be prepared by treating vinyl chloride with a lithium-sodium mixture.

Scheme : 2

$$CH_2=CHCl + \underset{(2\,\%\ \text{Na})}{2\,\text{Li}} \xrightarrow{Et_2O} \underset{(60\,\%)}{CH_2=CHLi} + LiCl$$

Most organolithium compounds slowly attack ethers by bringing about an elimination reaction.

Scheme : 3

$$R{:}\,Li + H-CH_2-CH_2-OCH_2CH_3 \longrightarrow RH + CH_2{=}CH_2 + Li^{+-}OCH_2CH_3$$

For this reason ether solutions of organolithium reagents are not usually stored but are used directly in some other reaction. Organolithium compounds are much more stable in hydrocarbon solvents, their stability in these solvents is of special interest.It is reported that the thermal decomposition of buttyllithium in hydrocarbon solution is a first-order reaction catalysed by the corresponding lithium alkoxide which may be formed in the presence of traces of oxygen. *(J.C. Stowell, 1979 ; G. Boche, 1989 ;L. Brandsma, 1987,1990)*. The decomposition of sec- butyllithium *(M.S. Kharasch, 1945)*and ter-butyllithium *(M.T. Reetz, J.Westermann, R. Steinbach, B. Wendeeeroth, R.Peter,R. Ostarek, S. Maus, 1985)* is best described by a 0,5-order kinetic law. Nevertheless, in a closed system, e.g a transport container, there is no appreciable pressure build up as the olefin formed in the decomposition process dissolves well in the applied solvent, which is a hydrocarbon.

Table 2 Decomposition of butyllithium in ethers

Ether	**Temperature(°C)**	$t_{½}$
Diethyl ether	25	6 d
	35	31 h
Diisopropyl ether	25	28 d
Glycol dimethyl ether	25	10 min
	0	23,5 h
THF	-30	5 d

Grignard reagents are usually prepared by the reaction of an organic halide and magnesium metal (turnings) in an ether solvent.

Scheme : 4

$$R\text{-}X \;+\; Mg \longrightarrow RMgX$$

$$Ar\text{-}X \;+\; Mg \longrightarrow ArMgX$$

The order of reactivity of halides with magnesium is also RI > RBr > RCl . Very few organomagnesium fluorides have been successfully prepared. Aryl Grignard reagents are more easily prepared from aryl bromides and aryl iodides. Aryl chlorides react sluggishly.

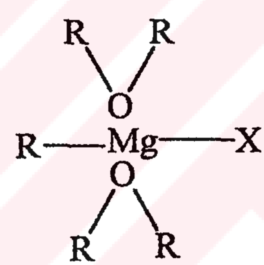
The actual structures of Grignard reagents are more complex than the general formula RMgX indicates. Experiments done with radioactive magnesium have estabilished that, for most Grignard reagents, there is an equilibrium between an alkylmagnesium halide and a dialkylmagnesium.

Scheme : 5

$$\underset{\text{Alkylmagnesium halide}}{2RMgX} \rightleftharpoons \underset{\text{Dialkylmagnesium}}{R_2Mg} + MgX_2$$

The position of the equilibrium depends upon the solvent and the identity of the specific organic group but lies far to the left in ether for simple aryl- , alkyl-,and alkenylmagnesium halides. *(Prris and Ashby, 1971)*

Grignard reagents also form complexes with their ether solvents like the one shown below.



Complex formation with molecules of ether is an important factor in the formation and stability of Grignard reagents. Organomagesium compounds can be prepared in nonethereal solvents but the preparations are more diffucult.

The mechanism by which Grignard reagents are formed is still not fully understood. The most likely path, however, appears to be the two-step radical mechanism shown below.

Scheme : 6

$$R{-}X \;+\; :Mg \longrightarrow R\,. \;+\; .\,MgX$$

$$R\,. \;+\; .MgX \longrightarrow RMgX$$

Grignard reagents and organolithium compounds abstract protons that are much less acidic than those of water and alcohols. They react with the terminal hydrogens of 1-alkynes, for example, and this is a useful method for the preparation of alkynylmagnesium halides and alkynllithiums. These reactions are also acid-base reactions.

Scheme : 7

$$RC \equiv CH \;+\; \overset{\delta-}{R'}\!:\overset{\delta+}{MgX} \longrightarrow RC \equiv \overset{\delta-}{C}\!:\overset{\delta+}{MgX} \;+\; R'\!:\!H$$

Alkynylmagnesium halide (stronger acid)	Alkane (stronger base)	Terminal alkyne (weaker base)	Grinard reagent halide (weaker acid)

$$R{-}C{\equiv}CH \;+\; \overset{\delta-}{R'}\!:\overset{\delta+}{Li} \longrightarrow R{-}C{\equiv}\overset{\delta-}{C}\!:\overset{\delta+}{Li} \;+\; R'\!:\!H$$

Alkynyllithium (stronger acid)	Alkane (stronger base)	Terminal alkyne (weaker base)	Alkyllithium (weaker acid)

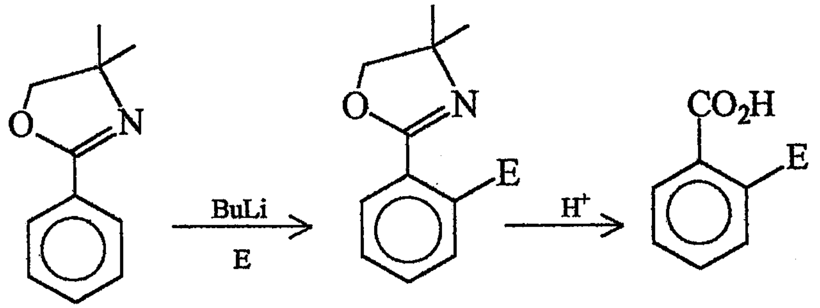
Although of limited utility in the synthesis of other types of Grignard regents, metalation is an important means of preparing lithium reagents. The exlent of lithiation is determined by the relative acidities of the available hydrogens and the directing effect of substituent groups.

Benzylic and allylic hydrogens are relatively reactive toward lithiation because of the resonance stabilization of the resulting anions.Substituents that can coordinate to the lithium ion, such as alkoxy, amido, and sulfonyl, have a powerful influence on the position and rate of lithiation of aromatic compounds. In heterocyclic compounds, the preferred site for lithiation is usually adjacent to the heteroatom.

The synthetic utility of aryloxazolines has been simply demonstrated as a route to o-substitution of benzoic acid equivalents by either electrophiilic or nucleophilic substitution (eq.1, 2).*(A.I.Meyers and William Rieker;1982)*

Scheme : 8

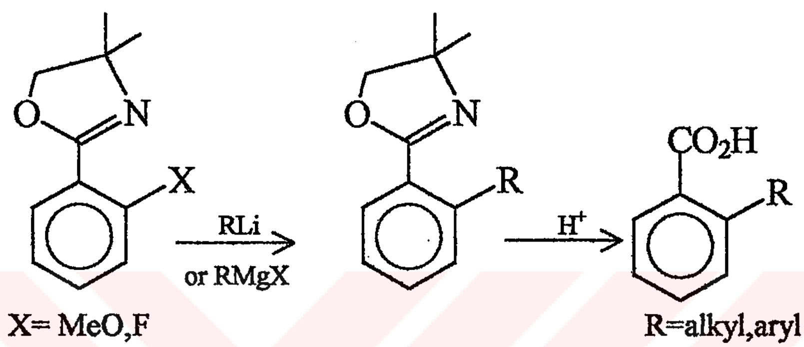
Electrophilic ortho-substitution



(e.g.1)

Scheme ; 9

Nucleophilic ortho-substitution



(e.g.2)

1.3 Organocopper Complexes Derived From Organolithium Reagents

1.3.1 Lower Order, Gilman Cuprates R_2CuLi

Historically, Gilman's original recipe for combining two equivalents of an organolithium with either CuI or CuSCN was envisioned to arrive at cuprate R_2CuLi, proceeding via an intermediate (presumed polymeric) organocopper $(RCu)_n$ *(H. Gilman, R.G. Jones, L.A.Woods, 1952).*

Scheme : 10

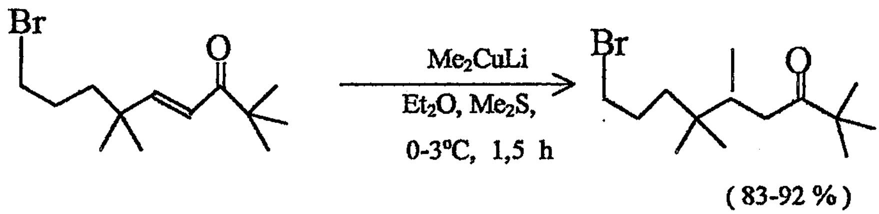
$$2RLi + CuX \longrightarrow [\,(RCu)_n + RLi\ +\ LiX\,] \longrightarrow R_2CuLi +\ \ LiX$$

X= I,Br and Cl

Generation of a homocuprate (i.e Where both R groups are the same) is a very straightforward operation, as long as good-quality CuI, CuBr or CuBr.SMe_2 is used.All reactions involving organocopper complexes should be run under either an argon or nitrogen atmosphere with a slightly positive pressure applied, being vented to a bubler. Since essentially every organocopper reaction is sensitive to moisture to some extent, the adduct to be added to the reagent must be dry.

To prepare a lower order cuprate (R_2CuLi), then, the copper salts slurried in an ethereal solvent and cooled to -78 °C, where two equivalents of the RLi are added.Warming to dissolution completes the process. Depending on the type of reaction to be perforend and the specific R_2CuLi being utilized, the cuprate may be recooled to -78 °C prior to addition of the substrate. The cornerstone of modern cuprate chemistry,Gilman's Me_2CuLi, is prepared in this manner, the subsequent chemoselective 1,4-addition of which to, e.g. a bromo enone,is described below.*(H.O. House,T.V.Lee,1978)*

Scheme : 11



1.4 Cross-Coupling Reactions

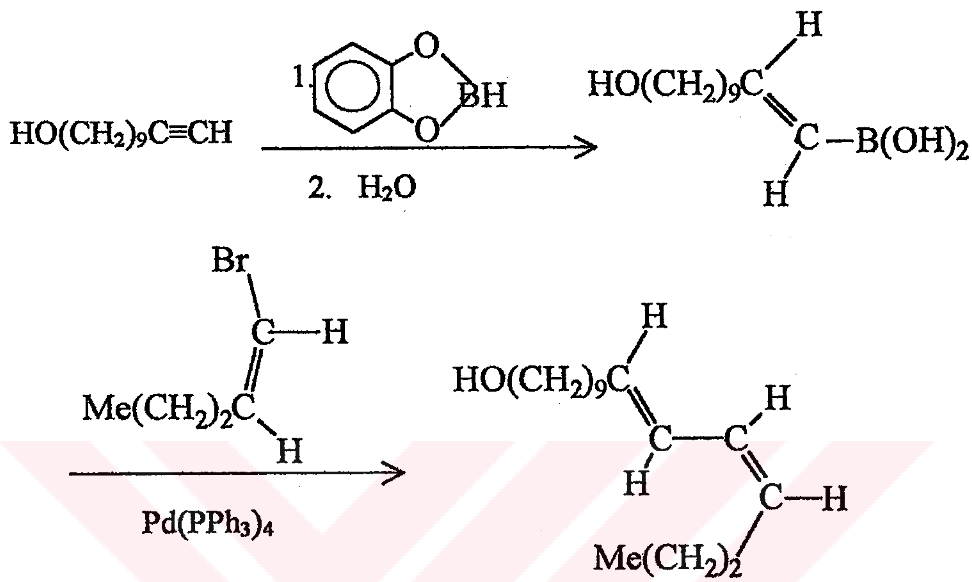
The cross-coupling between an organic halide and organoboron compound catalysed by palladium compounds has become a widely used and versatile method for the generation of carbon-carbon bonds. *(N.miyaura, T.Ishiyama, H.Sasaki, M.Satoh, A.Suzuki;1989)*

Scheme : 12

$$R^1{-}X \; + \; R^2{-}BY_2 \longrightarrow R^1{-}R^2$$

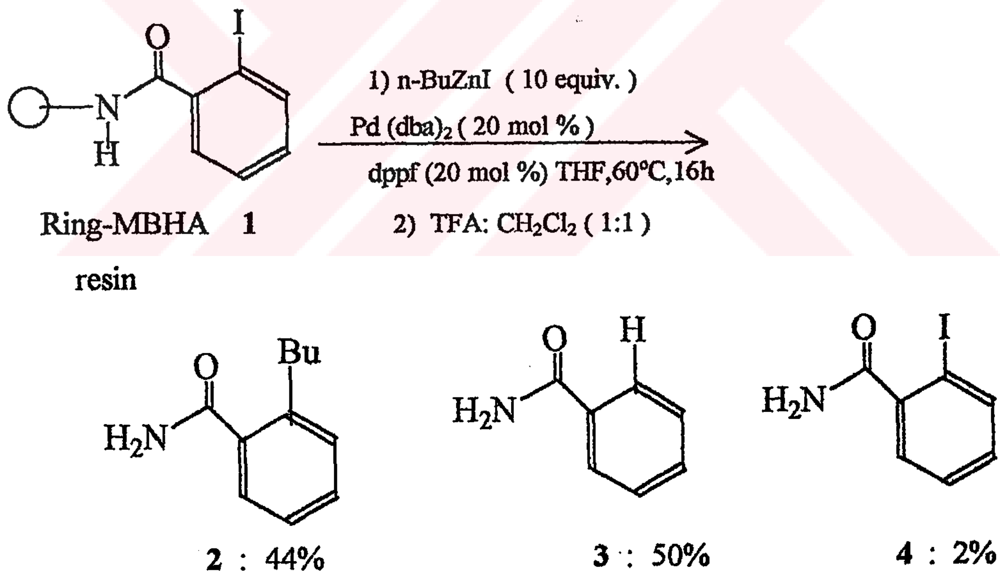
The reaction is at its most efficient when the reacting partners are an alkenyl bromide and an alkenylboron compound, such as an alkenyldihydroxyborane(alkenylboronic acid) *(N.Miyaura, H.Suginome, A.Suzuki ; 1983)*. The reaction will tolerate many fuctional groups and the stereochemistry is retained in both portions of the diene.

Scheme : 13

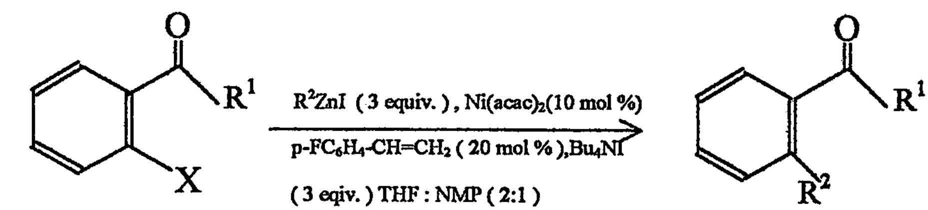


The palladium or nickel-catalyzed cross-coupling reaction between organometallic reagents and organic halides is an important method for preparing polyfunctional molecules. Especially useful is the cross-coupling reaction between aryl halides and alkyl organometallics. In this respect, the Negihi-cross-coupling reaction using alkylzinc halides has given excellent results.Unfortunately, this palladium-catalyzed cross-coupling leads to poor reactions in the solid-phase when ortho-substituted functionalized aryl iodides are used. These substrates are important for the elabration of broad-range libraries of compounds using combinatorial chemistry techniques. Thus, the reaction of the resin-bound ortho-iodobenzamide(1) with buthylzinc iodide (10 equiv.) in the presence of $Pd(dba)_2$ (20 mol %), dppf (20 mol %) in THF (60 °C,16 h) furnishes, after cleavage from the resin using TFA in CH_2Cl_2, the desired cross-coupling product (**2**) in 40% HPLC purity accompanied by the reduced starting material (**3**)in over 50 % HPLC purity as well as 2 % of unchanged 2-iodobenzamide (**4**). These reaction conditions also proved advantatgeous for the cross-coupling reaction between benzyllic zinc halides and alkyl iodides. *(Anne Eeg Jensen, Wolfgang Dohle and Paul Knochel ;2000)*

Scheme : 14



Scheme : 15



R^1= OEt, NMe_2 -5 °C to 10 °C, 16 h %70-84 yield

X= I, ONf

Alkynes are one of the most important structural building blocks in organic synthesis and material science and numerous methods are now available for the preparation of alkyne derivatives; among those, the Pd-catalyzed acetylenic coupling reaction (Sonogashira protocol) is most notable. Despite recent progress, new synthetic routes for the formation of substituted alkynes are still necessary to achieve milder reaction conditions and wider substrate scope. Since the pioneering works initiated by Hiyama and Denmark the Pd-catalyzed coupling reactions between alkynylsilanols or arylsilanols and aryl- or alkenylhalides (or their equivalents) have been emerging as a powerful new procedure for the formation of C-C bonds. These coupling reactions are especially notable because the silicon substrates are non-toxic and reaction conditions are usually mild. *(Sukbok Chang, Soon Ha Yang and Phil Ho Lee ; 2001)*

Scheme : 16

$$\text{Ph—I} + \text{Ph—}\equiv\text{—SiMe}_2\text{OH} + \text{Pd(PPh}_3)_4 + \text{additive} \xrightarrow{\text{solvent}} \text{Ph—}\equiv\text{—Ph}$$

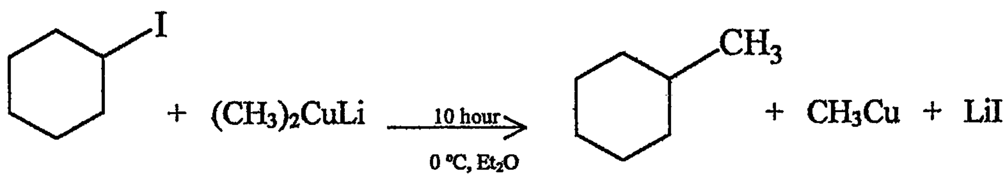
(1,0 equiv) (5 mol %)

Table 3 Effects of various additives on the Pd-catalyzed coupling between dimethyl(phenylethynyl) silanol and iodobenzene.

Additive	Solvent	T (°C)	Time (h)	Conversion(%)
None	THF	60	12	<5
K_2CO_3 (1,0)	THF	60	12	<5
CsF (1,0)	THF	60	12	<5
Ag_2O (1,0)	THF	60	2	78
TBAF (1,0)	THF	60	2	90
TBAF (2,0)	THF	60	2	90
TBAF (1,0)	Benzene	60	2	62
TBAF (1,0)	THF	40	2	45

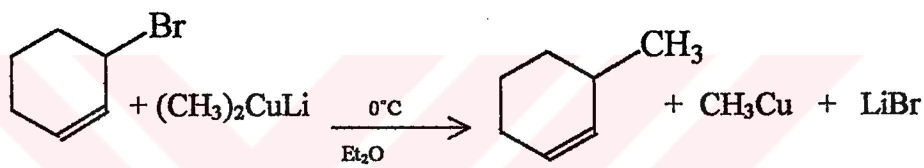
Coupling reactions of lithium dimethylcuprate with an alkyl and an allylic halide are shown below.

Scheme : 17



Methylcyclohexane (%75)

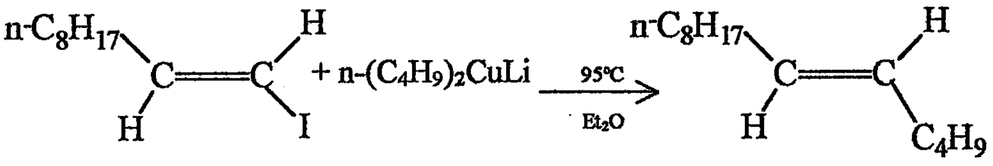
Scheme : 18



3-Methylcyclohexene
(%75)

Vinylic halides also couple with lithium dialkylcuprates. They do so in stereospecific way as the following example illustrates.

Scheme : 19

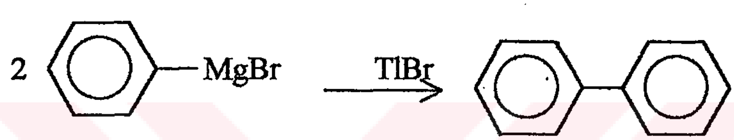


E-1-Iodo-1-decene

E-5-Tetradecene(%74)

Aryl grignard reagents undergo coupling reactions in very high yield when they are treated with thallium(I) bromide. Two examples are shown below.

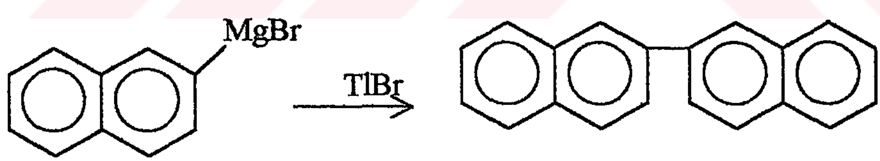
Scheme : 20



Phenylmagnesium bromide

Biphenyl(92 %)

Scheme : 21



2- Naphthylmagnesium bromide

2,2′-Binaphthyl (84%)

1.5 The Metal Halogen Exchange Reaction

Scheme : 22

$$RX + R'M \longrightarrow RM + R'X$$

The exchange reaction between alkyl halides and organometallic compounds is almost entirely limited to the cases where M is lithium and X is bromide or iodide, though it has been shown to occur with magnesium.R′ is usually ,though not always,alkyl,and often butyl;R is usually aromatic.Alkyl halides are generally not reactive enough,while allylic and benzylic halides usually give Wurtz coupling.Of course,the R which becomes bonded to the halogen is the one for which RH is the weaker acid.Vinylic halides react with retention of configuration.The mechanism when both R and R′ are aryl has been formulated.

Scheme : 23

$$(ArLi)_2 + Ar'Br \rightleftharpoons (ArLiLiAr') + ArBr$$

$$(ArLiLiAr') + Ar'Br \rightleftharpoons (Ar'Li)_2 + ArBr$$

The reaction can be used to prepare α-halo organolithium and α-halo organomagnesium compounds,

Scheme : 24

$$CCl_4 + BuLi \xrightarrow[-105\,^{\circ}C]{THF} CCl_3\text{-}Li + BuCl$$

Such compounds can also be prepared by hydrogen metal exchange,e.g.,

Scheme : 25

$$Br_3CH + iso\text{-}PrMgCl \xrightarrow[-95^{\circ}C]{THF\text{-}HMPT} Br_3C\text{-}MgCl + C_3H_8$$

However,these α-halo organometallic compounds are stable at only low temperatures (~ -100°C) and only in tetrahydrofuran or mixtures of tetrahydrofuran and other solvents (e.g.,HMPT)

At ordinary temperatures they lose MX (α-elimination) to give carbenes (which then react further) or carbenoid reactions.The α-chloro-α-magnesio sulfones $ArSO_2CH(Cl)MgBr$ are exceptions,being stable in solution at room temperature and even under reflux.

When the substrate has a halogen and a hydrogen on the some carbon, halogen-metal exchange is usually more rapid than hydrogen-metal exchange (the reaction of bromoform under the conditions shown above is an exception).α-halo sodium and
α-halo potassium compounds have also been prepared by a hydrogen –metal exchange reaction.

The mechanism of the reaction of alkyllithium compounds with alkyl and aryl iodides has been shown to involve free radicals.

Scheme : 26

$$RX + R'M \rightleftarrows \underset{\text{solvent cage}}{[R^{\cdot}, X, M, R'^{\cdot}]} \rightleftarrows RM + R'X$$

2. MATERIAL AND METHOD

2.1 General Techniques and Materials

All experiments were carried out under an atmosphere of dry N_2. Ether was dried and distelled under an atmosphere of dry N_2 prior to use. The IR spectra were recorded on a Mattson 1000 FTIR spectrometer. Melting points were recorded with an electrothermal digital melting point apparatus.The ^1H NMR spectra were carried out at the TUBİTAK Research Center,Ankara, Turkey.

Bromobenzene (Sigma) and 2-Iodobenzoic acid (Aldrich) were purchased and used as received.All solvents were distilled before use. Lithium reagents were prepared as solutions in ether from the aryl bromide by standard procedures.The concentration of the reagent was determined by titration against 0.1 M HCl prior to use.

2.2 Experiments

2.2.1 Preparation of 4,4- dimethyl – 2-(2-iodophenyl)-2-oxazoline

2-iodobenzoic acid (1g , 4mmol) was added to 1,43g (12mmol) of thionyl chloride and the mixture was stirred at 25° C for 24 hr. Then 1.03g (3,8 mmol) of acid chloride was dissolved in 1,8 ml of methylene chloride and added in a dropwise manner to a magmetically stirred solution of 0,713g (8mmol) of 2-amino-2-methyl-1-propanol in 1,8 ml methylene chloride at 0° C. The mixture was stirred at 25° C for 2 hr.The white precipitate was filtered and washed with water and then combined with the methylene chloride solution to give a total yield of 1,25g (% 98) of N- (2,2 dimethyl-3-hydroxypropyl) –o- iodobenzamide. (m.p :172,2 – 175,7 ° C)

To cyclize the amide, thionyl chloride (1,48g , 0,0124 mol) was added dropwise with stirring to 1,25 g (3,8 mmol) of the benzamide. When the vigorous reaction had subsided, the yellow solution was poured into 10 ml dry ether. The hydrochloride salt was neutralized with cold 20 % NaOH and extracted with ether. The ether was dried with sodium sulphate and evaporated to yield a pale yellow oil which solidified on cooling , giving 0,96 (84 % yield) of oxazoline.

2.2.1.1 Preparation of 4,4-dimethyl-2-phenyl-2-oxazoline

Lithium (56mmol = 0,40 g) was added to phenyl bromide (9,49 mmol = 1 ml) in anhydrous ether (5 ml). The temperature was observed to rise indicating the initiation of the reaction. The solution was heated at 35° C to reflux for a further fifteen minutes,after which the phenyllithium concentration was calculated by titration.

Determination of Phenyllithium Concentration :

Phenyllithium (0,5 ml) was placed in an erlenmeyer flash by syringe.Petroleum ether (5 ml) and water (5 ml) were added. The concentration of phenyllithium was determined by titration against 0,1 M HCl . The concentration of phenyllithium was found to be 1,85 M. Phenyllithium (1,6 mmol = 1,84 ml) was taken and added to coppercyanide (0, mmol = 72 mg) in dry ether (5 ml).

The reaction was cooled by an ice bath and was mixed for 30 minutes.After that 4,4-dimethyl-2-iodophenyl-2-oxazoline (60 mg , 0,2 mmol) was added, and the reaction was mixed at 0° C for 30 minutes.The reaction was quenched by adding dilute NH_4Cl (6 ml) and water (5 ml). All of these reactions were done under a nitrogen atmosphere. The mixture was extracted into methylene chloride and washed with water. The organic phase was collected and dried with sodium sulphate. The solvent was evaporated to afford the crude product (125 mg).

Attempts at crystallisation were unsuccessful and so column chromatography was carried out. Silicagel (6g) and hexane were used to prepare the column. Afterwards, hexane-ethylacetate (20 : 1) was used as the eluent. TLC was carried out using hexane-ethylacetate (5 : 1) as eluent.

The main product eluted off the column between the 14th and 28th fractions.These fractions were united in a flask. The solvent was evaporated to afford the main product (17 mg , 50 % yield).

The product was taken and a few drops of ether and hexane were added. Then the product was left in the refrigarator. Unfortunately the product failed to crystallise. The IR and the UV spectra are given in Chapter 3.

2.2.1.2 Preparation of 4,4-dimethyl-2-(2-biphenyl)-2-oxazoline

The rection was carried out as described in section 2.2.1.1. Lithium(56mmol= 0,4g) and phenyl bromide (1ml, 9,49 mmol) were used to by prepare the lithium reagent. In dry ether (5 ml), phenyllithium (0,8 mmol , 1,45 ml) and CuCN (72 mg , 0,8 mmol) were combined at 0° C under nitrogen atmosphere to prepare the copper-lithium reagent.The reaction was cooled by an ice bath , and was mixed for 30 minutes. After that 4,4-dimethyl-2-iodophenyl-2-oxazoline (60 mg, 0,2 mmol) was added and after 1 hour stirring at room temperature , work up was carried out in the normal fashion to afford the crude product (66,5 mg).

Column chromatography was carried out using Silicagel (6gr) and hexane to prepare the column. Afterwards, hexane-methylene chloride (1 : 1) was used as the eluent. TLC was carried out using hexane-methylene chloride (1 : 2) as eluent. The main product eluted off the column between the 32nd and 71st fractions. These fractions were collected in a flask. The solvent was evaporated to afford the pure product (30 mg, 60 % yield) . This product didn't crystallise. The IR and UV spectra are given in Chapter 3.

2.2.2 Preparation of N,N-diethyl-2-iodobenzamide

2-iodobenzoic acid (1g , 4 mmol) was added to 1,43 g (12 mmol) of thionyl chloride and the mixture was stirred at 25 °C for 24 hr. Then 1,03g (3,8 mmol) of acid chloride was dissolved in 1,8 ml methylene chloride and added in a dropwise manner to a magnetically stirred solution of 0,585 g (8 mmol) of N,N –diethylamine in1,8 ml methylene chloride at 0° C. The mixture was stirred at 25° C for 2 hr.Then some water washed and the mixture was extracted with ether. The ether was dried with sodium sulphate and evaporated to yield a yellow solution, giving 1,00 g (86 % yield) amide.

2.2.2.1 Preparation of N,N-diethyl benzamide

The reaction was carried out as described in section 2.2.1.1. Lithium (56mmol = 0,4g) and phenyl bromide (1 ml , 9,49 mmol) were used to prepare the lithium reagent.In dry ether (10 ml) phenyllithium (3,2 mmol, 2,3 ml) and CuCN (144 mg , 1,6 mmol) were combined at 0° C under nitrogen atmosphere to prepare the copper-lithium reagent. The reaction was cooled by an ice bath, and was mixed for 30 minutes. After that N,N-diethyl-2-iodobenzamide (120 mg , 0,4 mmol) was added at 0° C.The solution was heated at 35° C to reflux for 1 hr, work up was carried out in the normal fashion, to afford the crude product (120 mg).

Column chromatography was carried out using Silicagel (4 gr) and hexane to prepare the column. Afterwards, hexane-ethylacetate (10 : 1) was used as eluent. The main product eluted off the column between the

29^{th} and 33^{rd} fractions. These fractions were collected in a flask. The solvent was evaporated to afford the pure product (60 mg , 86 % yield). The product didn't crystallise.The IR and UV spectra are given Chapter 3.

2.2.2.2 Preparation of N,N-diethyl-2-phenylmethyl-benzamide

This was carried out as described in section 2.2.1.1.Lithium (56 mmol =0,4 g) and phenyl bromide (1 ml , 9,49 mmol) were used to prepare the lihium reagent in dry ether (5 ml).Then phenyllithium (3,2 mmol , 3,4 ml) and CuCN (144mg , 1,6 mmol) were combined at 0 °C in dry ether (10 ml) under a nitrogen atmosphere to prepare the copper-lithium reagent. The reaction was cooled by an ice bath and mixed for 30 minutes.After that N,N-diethyl-2-iodo-benzamide (120 mg , 0,4 mmol) was added at 0 °C. The solution was heated at 35° C to reflux for 1 hour. Then benzyl chloride (1,6 mmol,0,18 ml) or benzyl bromide (1,6 mmol ,0,19 ml) was added in this reaction mixture and stirred at room temperature for 15 minutes.Work up was carried out in the normal fashion. The same product was given by the two different electrophiles.

i) Benzyl chloride was used as electrophile, to afford the crude product (185 mg).

ii) Benzyl bromide was used as electrophile, to afford the crude product (187 mg).

Column chromatography was carried out using Silicagel (20 gr) and hexane to prepare the column for the two methods. Afterwards, hexaneethyl-acetate (2 :1) was used as the eluent. TLC was carried out using hexane-ethylacetate (1:1) as eluent.

i) The main product eluted off the column between the 61st and 72nd fractions. These fractions were collected in a flask. The solvent was evaporated to afford the pure product (10 mg , 10 % yield).

ii) The main product eluted off the column between the 52nd and 71st fractions.These fractions were collected in a flask. The solvent was evaporated to afford the pure product (25 mg , 23 % yield).

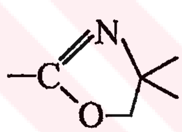
The main product didn't crystallise. The IR and UV spectra are given in Chapter 3.

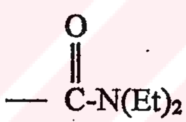
3. RESULTS AND DISCUSSION

3.1 Results

In this study we prepared o-substituted aryl derivatives.There are a lot of methods for this synthesis.One of the most common method is the metal halogen exchange reaction.

As a functional groups,we were particularly interested in the ''oxazoline'' and ''amide'' groups.

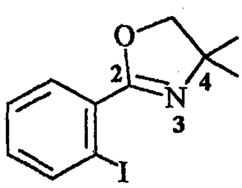




We were strongly interested in these groups because,they are useful functional groups which can be converted into other functional groups. Thus,acidic hydrolysis of these groups afford a hydroxylic acid functionality.

In our method phenylbromide was reacted with excess lithium and the resultant phenyllithium reagent was reacted with copper cyanide to afford a biphenylcopper lithium reagent.The biphenylcopper lithium reagent was reacted with 4,4-dimethyl-2-(2-iodophenyl)-2-oxazoline or N,N-diethyl-2-iodobenzamide. In another method phenyllithium reagent was reacted with 4,4-dimethyl-2-(2-iodophenyl)-2-oxazoline to give 4,4-dimethyl-2-(2-biphenyl)-2-oxazoline (Compound-II). Thus, the following reactions shown below were used to synthesise all the products.(See Table-4a and Table-4b)

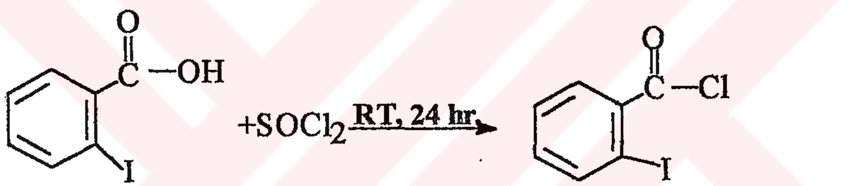
In this project, it was first necessary to prepare :



2-(2-iodophenyl)4,4-dimethyl2-oxazoline

SM-I

1st step :

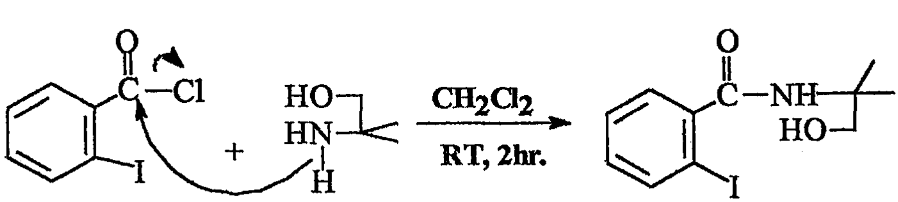


2-iodobenzoic acid

2-iodo benzoyl chloride

(100%)

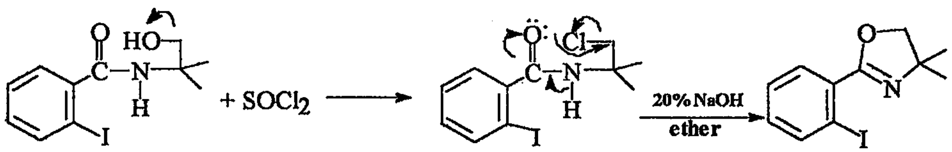
2nd step :



2-amino 2-methyl
1-propanol

(98%)

3rd step



SM-I

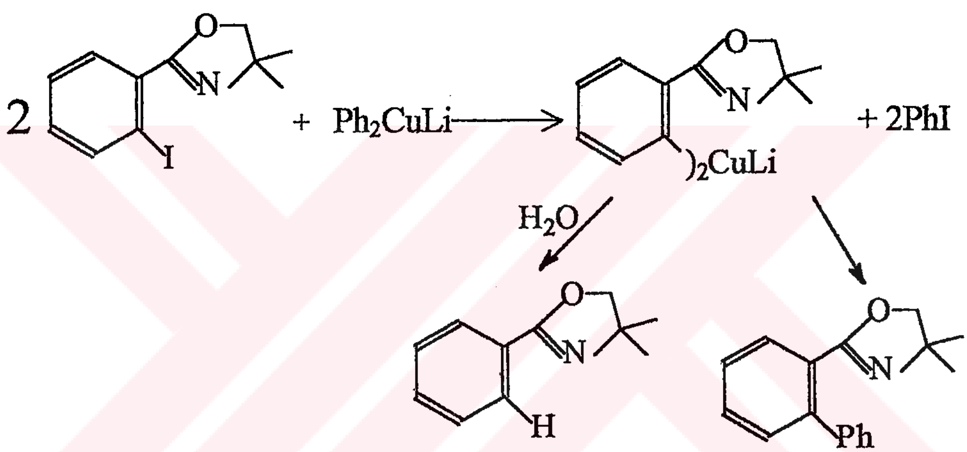
(84 %)

<u>**Reactions of Organocopper Reagents with SM-I :**</u>

First of all, Ph_2CuLi (biphenylcopperlithium) (Gilmann reagents) was prepared (at 0°C and for 30 min.). In all experiments, we used SM-I (at 0°C , for 30min.).Only in experiment 3, we finished the reaction at this time(see Table-4a).In that experiment, we obtained the mixture of Compound-I (50 % yield) and Compound-II (40% yield).However, when this reaction was repeated under the same conditions but with the addition of TMEDA, we obtained only Compound-II (40 % yield).In other experiments, the reaction was stirred at RT. If the stirring was finished after 1 hour, we obtained only Compound-II (36% yield). However,if the reaction was repeated in the same contions in dry hexane, we obtained a higher yield of Compound-II (56 % yield).If the stirring was finished after 30 minutes at RT, we obtained the mixture of Compound-I (37% yield) and Compound-II (24 % yield).

$$PhBr + 2\,Li \xrightarrow[15\ mins]{35\ ^\circ C} PhLi + LiBr$$

$$2\,PhLi + CuCN \xrightarrow[30\ mins]{0\ ^\circ C} Ph_2CuLi + LiCN$$



Compound-I **Compound -II**

Table-4a Products and Yield of Oxazolines Synthesis

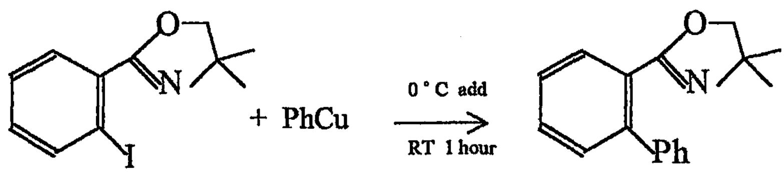
Exp.	Conditions	Compound- I (% yield)	Compound-II (% yield)
1	0 °C 30 minutes RT 1 hour	———	% 36
2	0 °C 30 minutes RT 30 minutes	% 37	% 24
3	0 °C 30 minutes	% 50	% 40
4	0 °C 30 minutes (in TMEDA)	———	% 40
5	0 °C 30 minutes RT 1 hour (in dry hexane)	———	% 56

Overall, it appears that at low temperature $(Ox\text{-}Ph)_2CuLi$ is formed and reacts with PhI and electrophile (H_2O) but at room temperature and in apolar solvents this reagent only reacts with PhI.

In a separate experiments, PhCu (phenylcopper) reagent was prepared at 0 °C for 30 minutes by mixing 1 equivalent of CuCN with 1 equlavent of PhLi.Then we added SM-I at 0 °C for 30 minutes and then the stirring was continued at RT for 1 hour. We obtained only Compound-II (60 % yield).

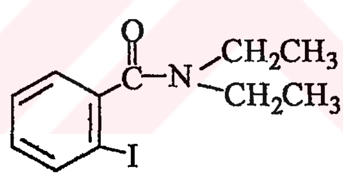
$$PhBr + 2\,Li \xrightarrow[15\ mins]{35\ ^{\circ}C} PhLi + LiBr$$

$$PhLi + CuCN \xrightarrow[30\ mins]{0\ ^{\circ}C} PhCu + LiCN$$



SM-I **Compound – II**
(% 60 yield)

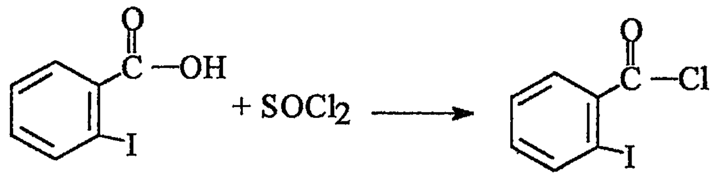
Finally we also decided to prepare



N,N-dimethyl 2-iodo benzamide
SM-II

and investigate the chemistry of this material with organometallic reagents (see table-4b)

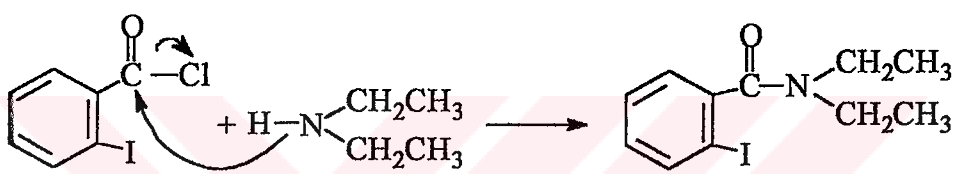
1st step :



2-iodo benzoic acid

2-iodo acid chloride

2nd step :



N,N-dimethyl 2-iodo benzamide

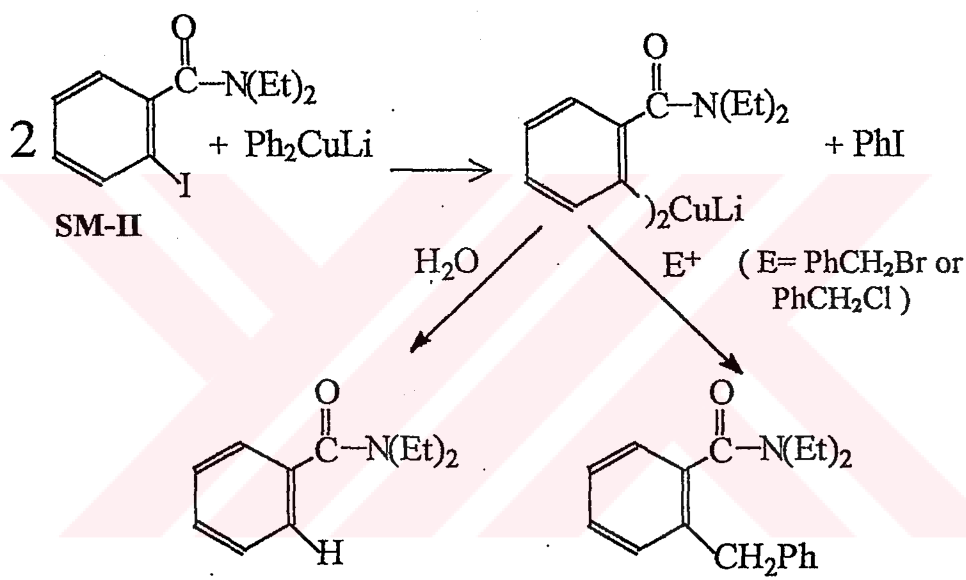
SM-II (86% yield)

<u>Reactions of Organocopper Reagents with SM-II</u> :

First of all, Ph_2CuLi (biphenylcopperlithium) (Gilmann Reagents) reagent was prepared at 0 °C for 30 minutes. Then we added SM-II at 0 °C and the mixture was stirred at 35°C for 1 hour or 30 minutes.After this time an electrophile was added to the reaction mixture. In these reactions we used different electrophiles and we obtanied only Compound-III or the mixture of Compound-III and Compound-IV. Thus, the following reactions shown below were used to synthesise all the products.(See Table-4b)

$$PhBr + 2Li \xrightarrow[15\ minutes]{35\ ^\circ C} PhLi + LiBr$$

$$2\,PhLi + CuCN \xrightarrow[30 minutes]{0\ ^\circ C} Ph_2CuLi + LiCN$$



Compound-III **Compound-IV**

From the first experiment we can conclude that metal-halogen exchange does occur as the primary process in the reaction of Ph_2CuLi with SM-II.

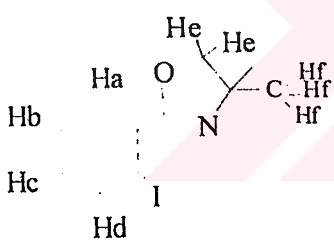
In this case, there was no evidence of reaction of $(2\text{-}Et_2N\text{-}CO\text{-}Ph)_2CuLi$ with PhI. Thus,it appears that $(2\text{-}Et_2N\text{-}CO\text{-}Ph)_2CuLi$ is less reactive than $(Ox\text{-}Ph)_2CuLi$. However when $(2\text{-}Et_2N\text{-}CO\text{-}Ph)_2CuLi$ was reacted with $PhCH_2Cl$ or $PhCH_2Br$, reaction did occur albeit in low to moderate yield.

Table-4b **Table of Amide Synthesis results**

Exp.	Conditions	Electrophile	Compounds (% yield)
1	0 °C add 35 °C 1 hour	H_2O (RT 10 mins)	**Compound- III (% 86)**
2	0 °C add 35 °C 1 hour	Ph – CH_2Cl (RT 1 hour)	**Compound –III + Compound-IV** (% 56) (% 10)
3	0 °C add 3 5 °C 1 hour	Ph – CH_2Cl (RT 15 mins)	(% 55) (% 10)
4	0 °C add 35 °C 30 mins	Ph – CH_2Br (RT 15 mins)	Compound-III + Compound-IV (% 40) (% 23)

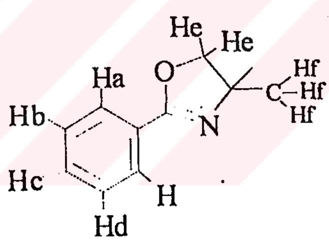
3.2 SPECTROSCOPIC DATA

3.2.1 NMR

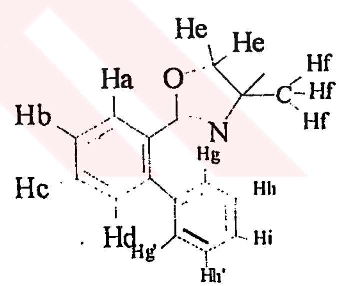


Starting Material-I

(SM-I)



Compound-I



Compound-II

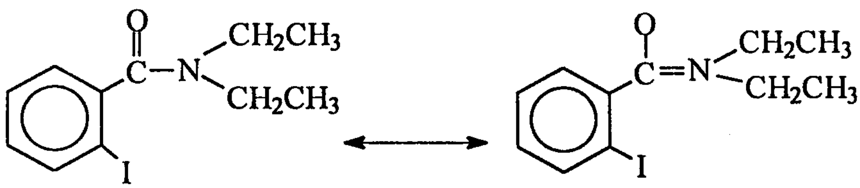
The NMR spectra for SM-I gave a very simple spectrum with all the signals well separated from each other.The oxazoline methyl and methylene signals are clearly visible at 1,3 and 4,00 ppm respectively.In the aromatic region,there are two doublets of doublets and two triplet of doublets.The double doublets are clearly due to H_a and H_d .The most deshielded of these double doublets appears at 7,8 ppm and must be H_d . This is because H_d is ortho to I and meta to the oxazoline group.Both of these situations lead to greater deshielding.In contrast H_a (7,5 ppm) is ortho to the oxazoline group which has a relatively strong deshilding effect but this effect is reduced by being meta to I which has a moderate shielding effect.The remaining signals (H_c and H_d) can be assigned based on coupling constants.

The NMR spectrum of Compound-I is given is in Figure-4.Assignment of all the hydrogens in this molecule was straightforward.As expected,the most deshielded of the aromatic signals were the ortho hydrogens H_a.These appeared at 7,85 ppm.

The NMR spectrum of Compound-II is given is in Figure-6.The aromatic regions of this spectrum is complicated by the additional phenyl group. However,in each case a double doublet at 7,67 ppm can be assigned to H_a .

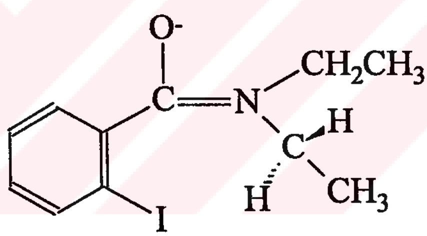
Table 5 NMR Result of Starting Material-I

H	Calculation ppm	Observed ppm	Calculating Coupling	Observed Coupling
H_a	7,67	7,50		
H_b	7,42	7,25	$J_{Ha\text{-}Hb}$=8	$J_{Ha\text{-}Hb}$=7,90
			$J_{Ha\text{-}Hc}$=1	$J_{Ha\text{-}Hc}$=1,10
H_c	7,24	6,98	$J_{Hc\text{-}Hd}$=8	$J_{Hc\text{-}Hd}$=7,65
H_d	7,86	7,80	$J_{Hb\text{-}Hd}$=2	$J_{Hb\text{-}Hd}$=1,70
H_e	3,70	4,00		
H_f	1,10	1,30		

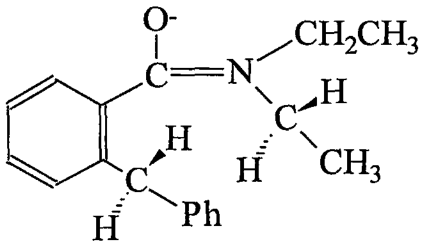


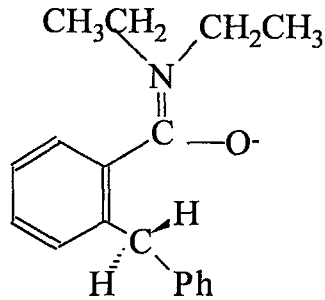
SM-II

The NMR spectrum of the SM-II is given in figure-8.In this case,there is restricted rotation about the amide C-N bond.As a result,there are two inequivalent CH_3 signals.However there is also restricted rotation about one of the N-ethyl bonds.As a result,one of the methylene CH_2 signals is split into 2 separate signals.as a second consequence,the remaining CH_2 signals are now diastereotopic which also results in them not being strictly equivalent.



The NMR specrum of t Compound-III is given in Figure-10.In this compound there is also resticted rotation about the amide C-N bond.However in this case,instead of seeing two different methyl groups,one sees a single broad peak.This is because the rate of rotation about the C-N bond is faster so we do not see 2 separate methyl triplets.However it is also not fast enough that both methyl groups are identical.Therefore a broad peak results.The methylene Signals appear as 2 broad peaks that have not quite coallesced.





The NMR spectrum of Compound-V is given in Figure-12.This compound is the most sterically hindered of the amide derivatives we have prepared and this has interesting consequences on the NMR spectrum of this molecule.There are now 4 methyl resonances.This occurs because, on the NMR time scale,the molecule exists as a mixture of 2 diastereomers.There are 3 CH_2 groups in this molecule but in each diastereomer there is again a restricted rotation that results in broad peaks for all the CH_2 signals.

Table 6 NMR Results of Starting Material-II

H	Calculation ppm	Observed ppm	Calculation Coupling	Observed Coupling
H_a	7,67	7,40	$J_{Ha\text{-}Hb}$=8	$J_{Ha\text{-}Hb}$=7,80
H_b	7,45	7,20	$J_{Ha\text{-}Hc}$=2	$J_{Ha\text{-}Hc}$=1,50
H_c	7,24	7,08	$J_{Hc\text{-}Hd}$=8	$J_{Hc\text{-}Hd}$=7,55
H_d	7,86	7,82	$J_{Hb\text{-}Hd}$=2	$J_{Hb\text{-}Hd}$=1,60

3.2.2 IR

The IR spectra of compounds I, II, III, IV, V and starting materials (SM- I and SM- II) were carried out in CH_2Cl_2 solution. The main features of the spectra are recorded in Table- 4 .

All the compounds of amide had an intense aromatic C-H band at approximately 3060 and 3020 cm^{-1}. For Compounds III , IV , V and SM -II , carbonyl peaks were seen near 1660 cm^{-1} , in addition aliphatic C- H bands were seen between 2840 and 2970 cm^{-1}. For these compounds, C-N-C bands were seen between 1150 and 1100 cm^{-1} .

For Compound I and II , a band at approximately 1040 cm^{-1} could be assigned to a C-O-C stretch. In the fingerprint region bands at approximately 700 and 760 cm^{-1} could be assigned to aromatic C- H bads.

Table – 7 : Expected and observed IR data.

Compound	**Substituent**	**Expected Peaks (cm^{-1})**	**Observed Peaks (cm^{-1})**
I	Aromatic = CH	3000 - 3100	3060
	Ar – C = N	1640 - 1050	1649
	- O- CH_2	720 - 770	777
	C- O – C	1040	1060
	Aliphatic – CH	2870	2873,2877
	- C – C -	1500-1600	1517
II	Aromatic = CH	3000 - 3100	3052
	Ar – C = N	1640 - 1050	1649,1348,1305
	-CH- bending	720 - 770	744
	C- O – C	1040	1070
	Aliphatic – CH	2870	2855,2953
	- C – C -	1500 - 1600	1457
SM- I	Aromatic = CH	3000 - 3100	3058,2967
	Ar – C = N	1640 - 1050	1657,1465,1430
	-CH- bending	720 - 770	729,763
	C- O – C	1040	1081
	Aliphatic – CH	2870	2927,2890
	- C – C –	1500 – 1600	1583
	C- I	~ 500	501,451

Compound	Substituent	Expected Peaks (cm^{-1})	Observed Peaks (cm^{-1})
SM-II	$-\overset{\overset{O}{\|}}{C}-$	1715 - 1650	1637
	Aromatic =CH	3000 – 3100	3053
	CH- bending	720 - 770	770
	Aliphatic-CH_3 and CH_2	2990 - 2850	2076,2937,2875
	C- N – C	1100 - 1150	1100,1014,1160
	C-H	1475,1450,1375	1428,1377
	C- I	~ 500	572,508
III	$-\overset{\overset{O}{\|}}{C}-$	1715 - 1650	1629
	Aromatic =CH	3000 – 3100	2982
	CH- bending	720 - 770	788,709
	Aliphatic-CH_3 and CH_2	2990 - 2850	2935
	C- N – C	1100 - 1150	1221,1097
	C-H	1475-1450,1375	1427,1379
IV	$-\overset{\overset{O}{\|}}{C}-$	1715 - 1650	1634
	Aromatic =CH	3000 – 3100	3059
	CH- bending	720 - 770	748, 700,5
	Aliphatic-CH_3 and CH_2	2990 - 2850	2927, 2850
	C- N – C	1100 - 1150	1097
	C-H	1475-1450,1375	1428, 1378

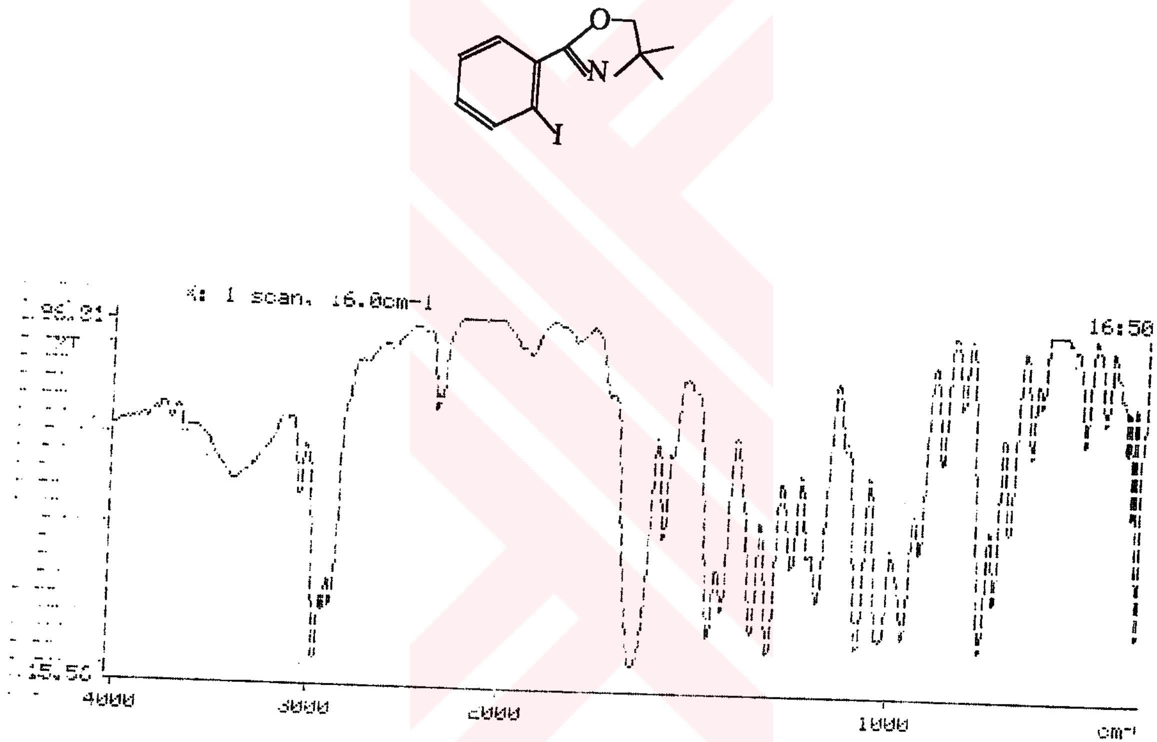


Figure-1 : The IR spectra of 4,4-dimethyl-2-(2-iodophenyl)-2-oxazoline **(SM-I)**

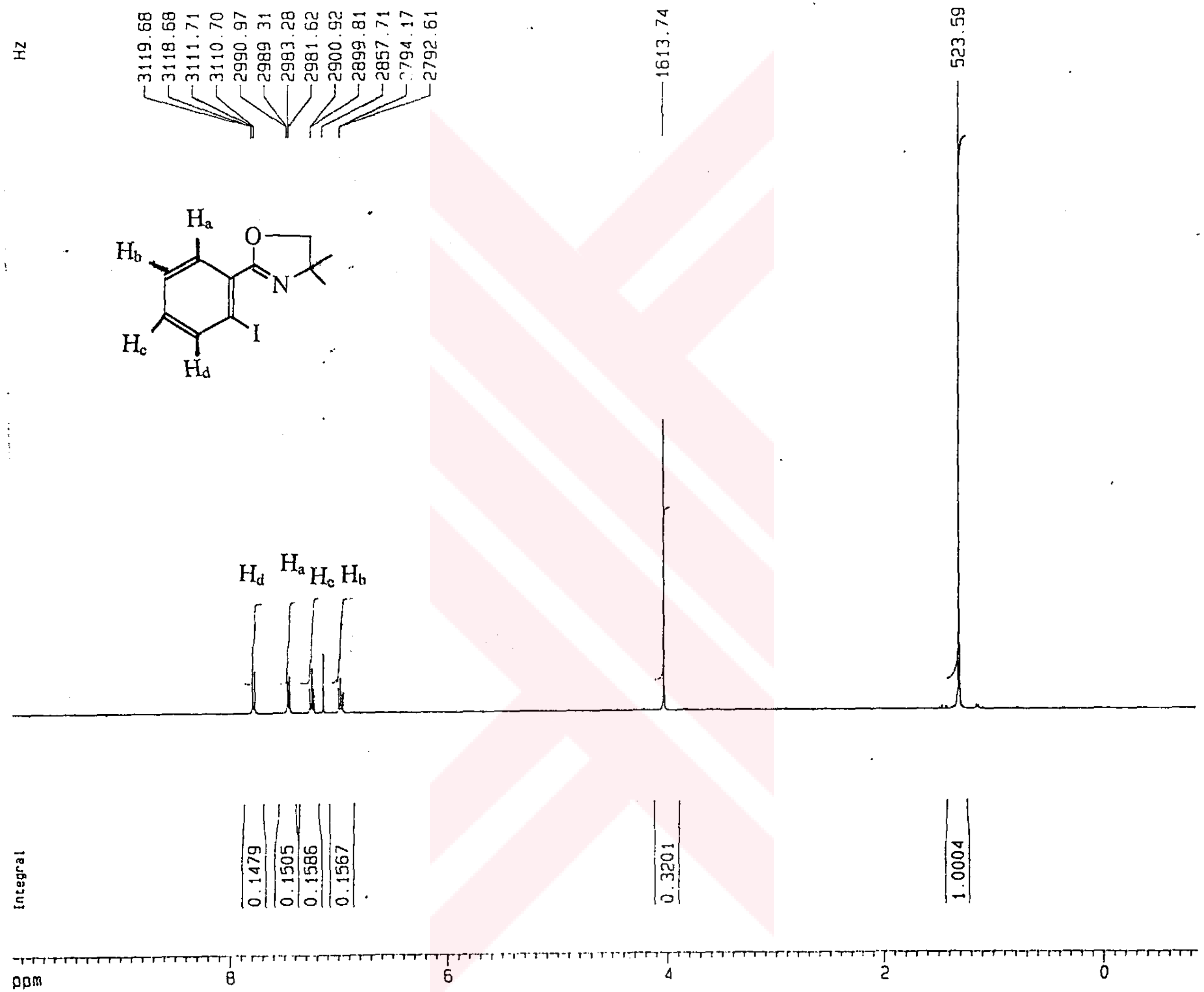


Figure-2 : The NMR spectra of 4,4-dimethyl-2-(2-iodophenyl)-2-oxazoline **(SM-I)**

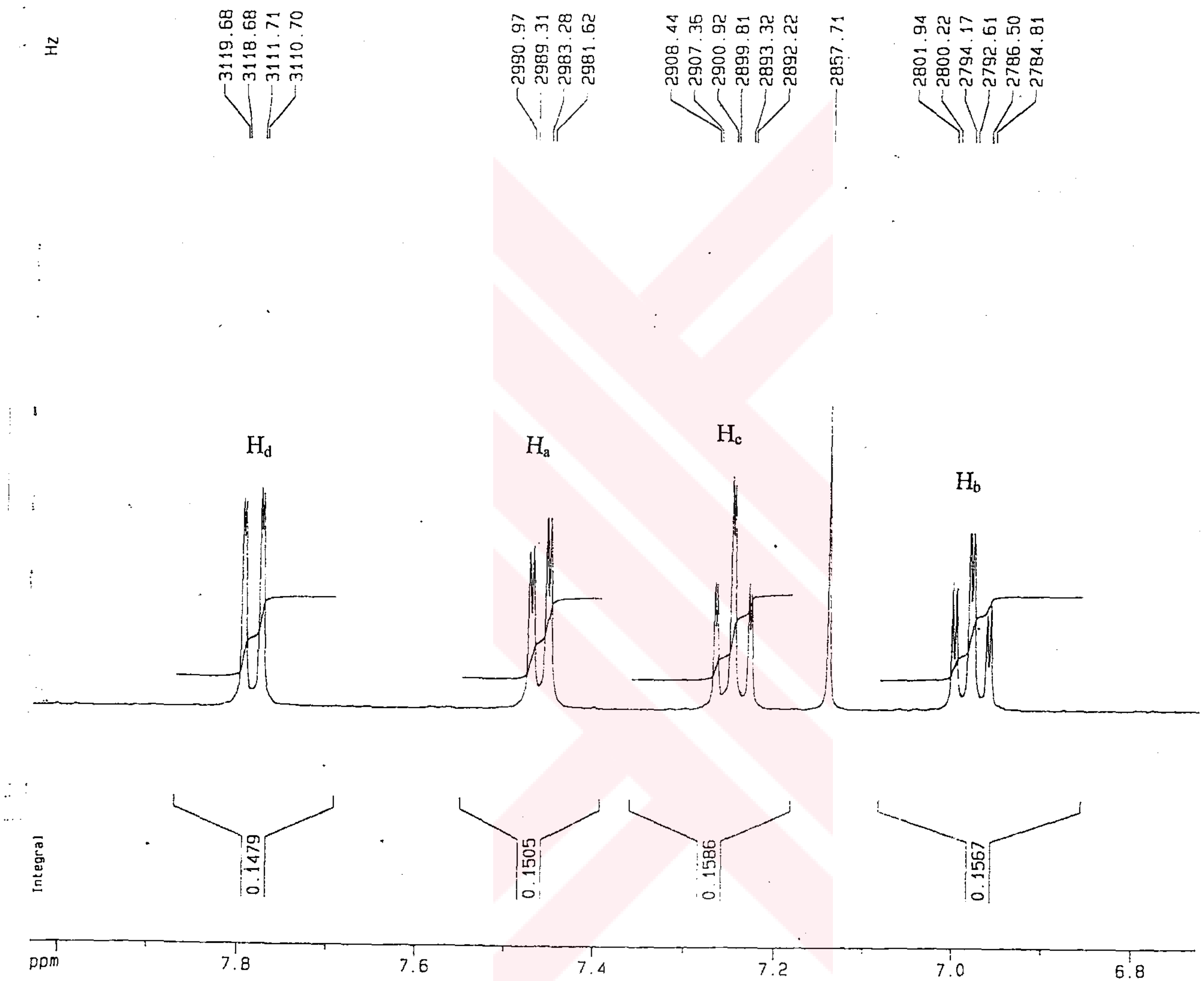


Figure-2 : The NMR spectra of 4,4-dimethyl-2-(2-iodophenyl)-2-oxazoline (**SM-I**)

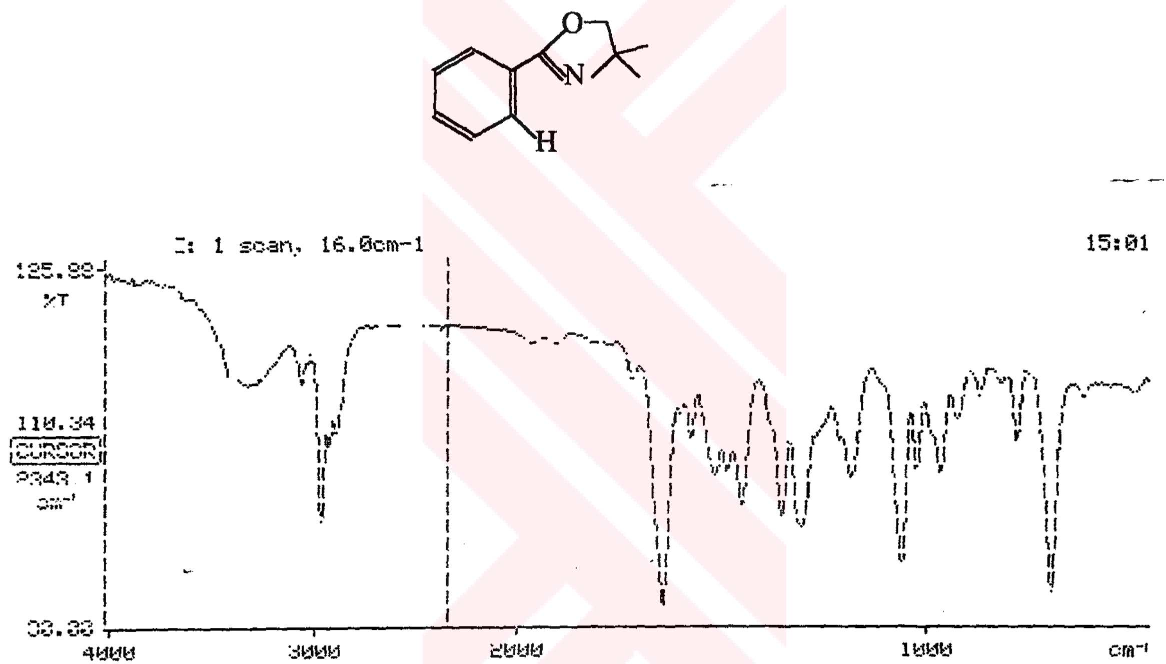


Figure-3 : The IR spectra of 4,4-dimethyl-2-phenyl-2-oxazoline **(Compound-I)**

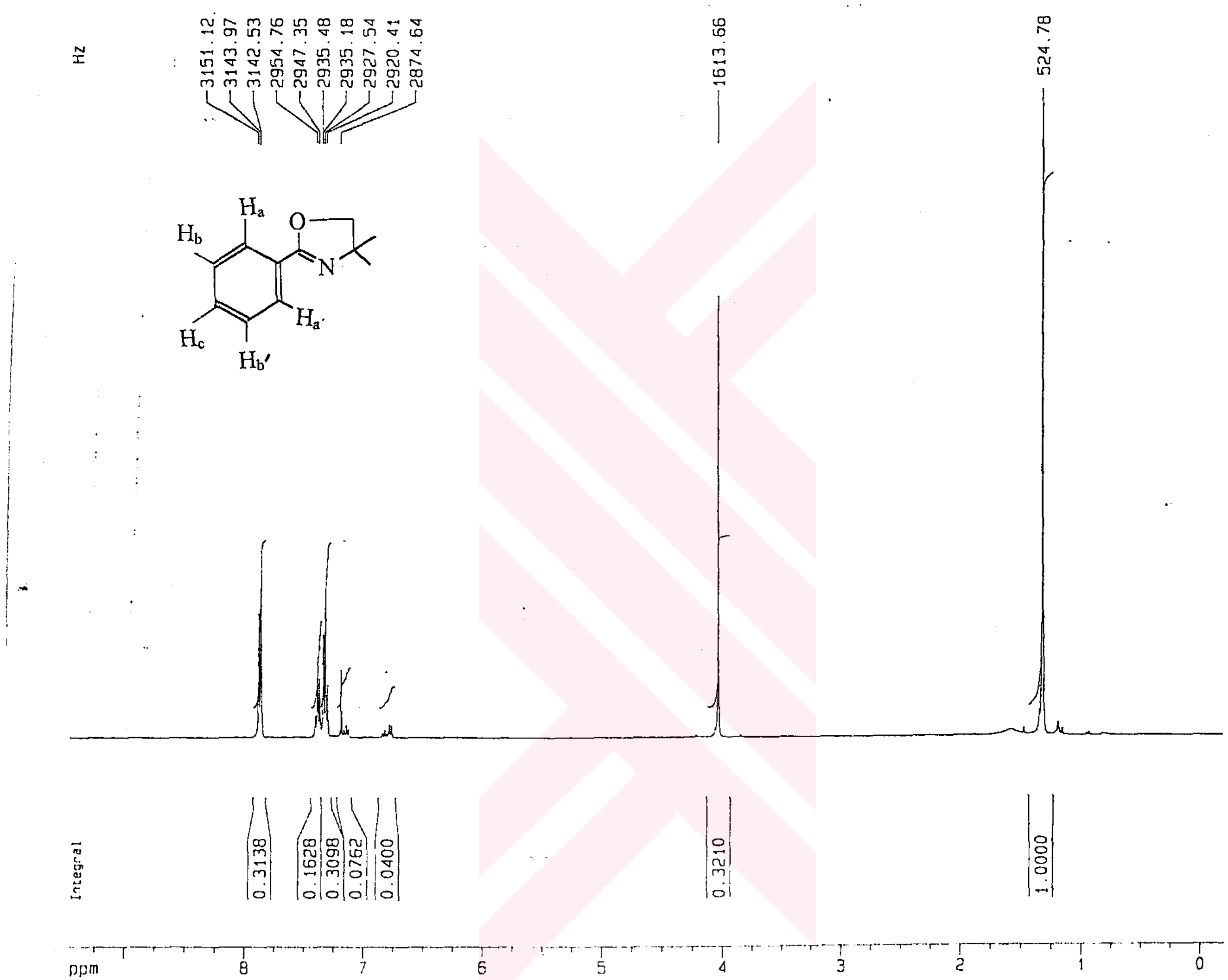


Figure-4 : The NMR spectra of 4,4-dimethyl-2-phenyl-2-oxazoline **(Compound-I)**

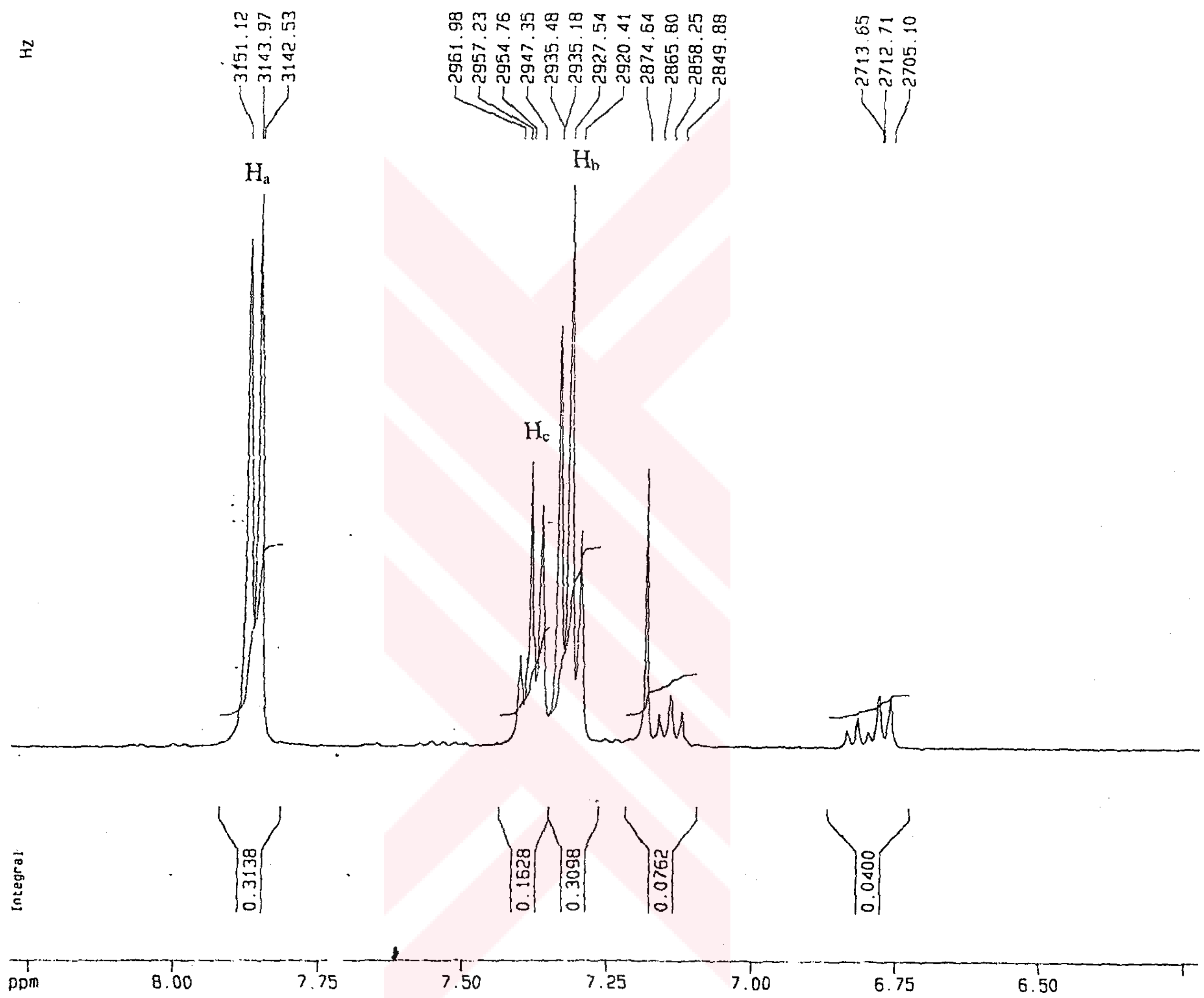


Figure-4 : The NMR spectra of 4,4-dimethyl-2-phenyl-2-oxazoline **(Compound-I)**

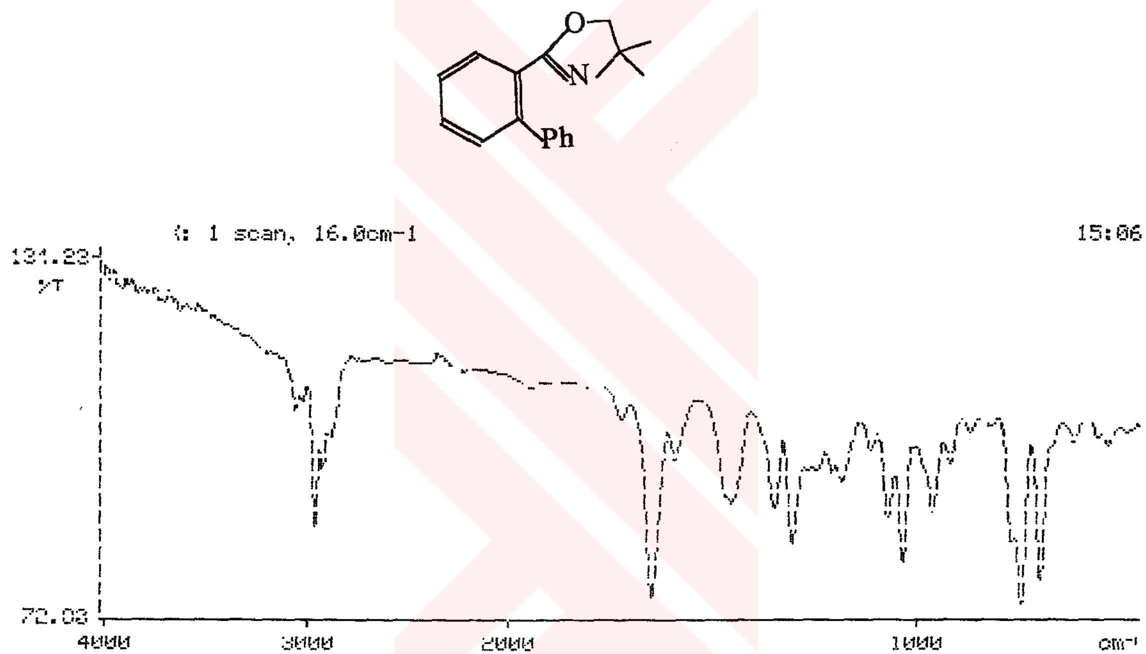


Figure-5 : The IR spectra of 4,4-dimethyl-2-(2-biphenyl)-2-oxazoline **(Compound-II)**

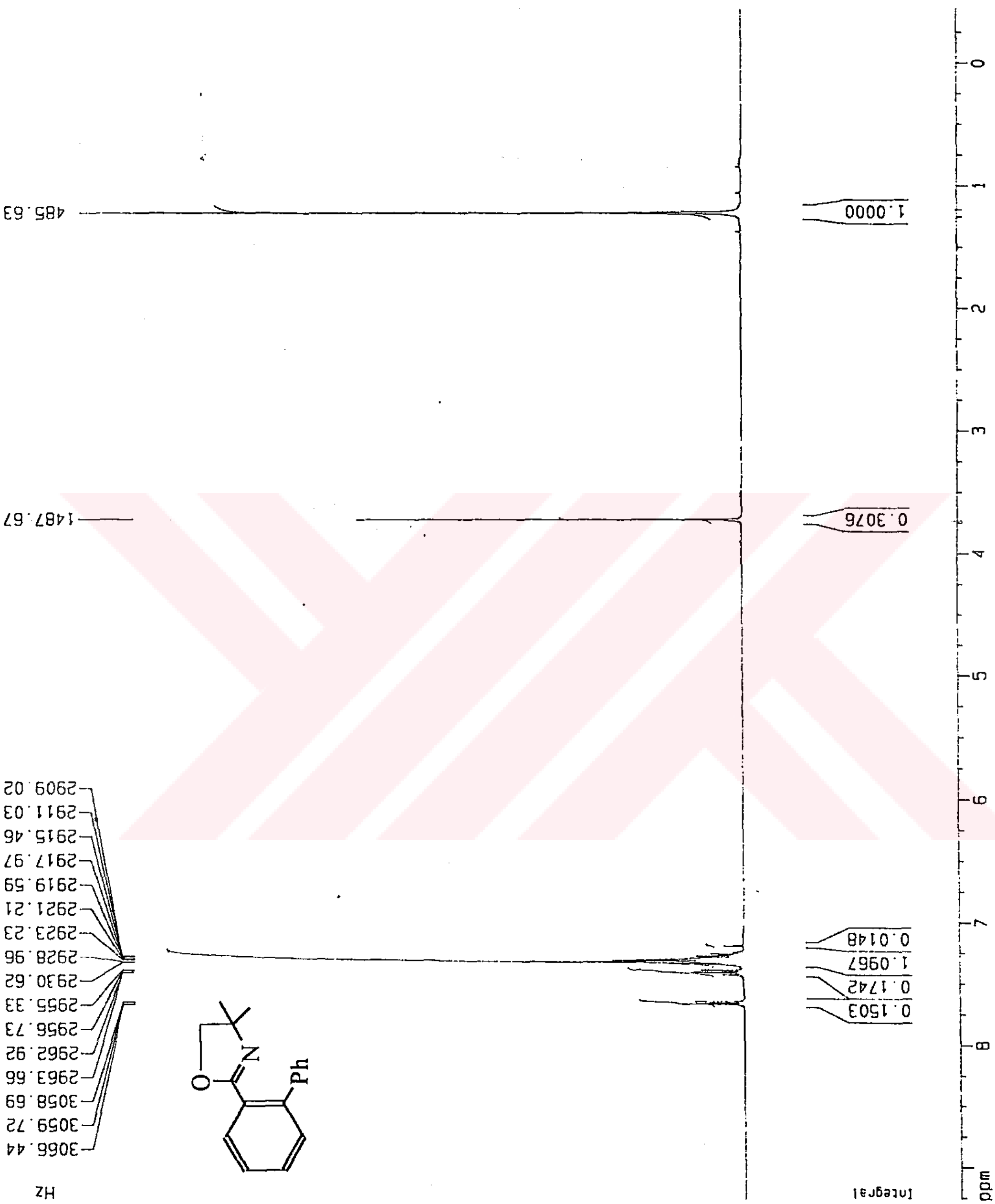


Figure-6 : The NMR spectra of 4,4-dimethyl-2-(2-biphenyl)-2-oxazoline (Compound-II)

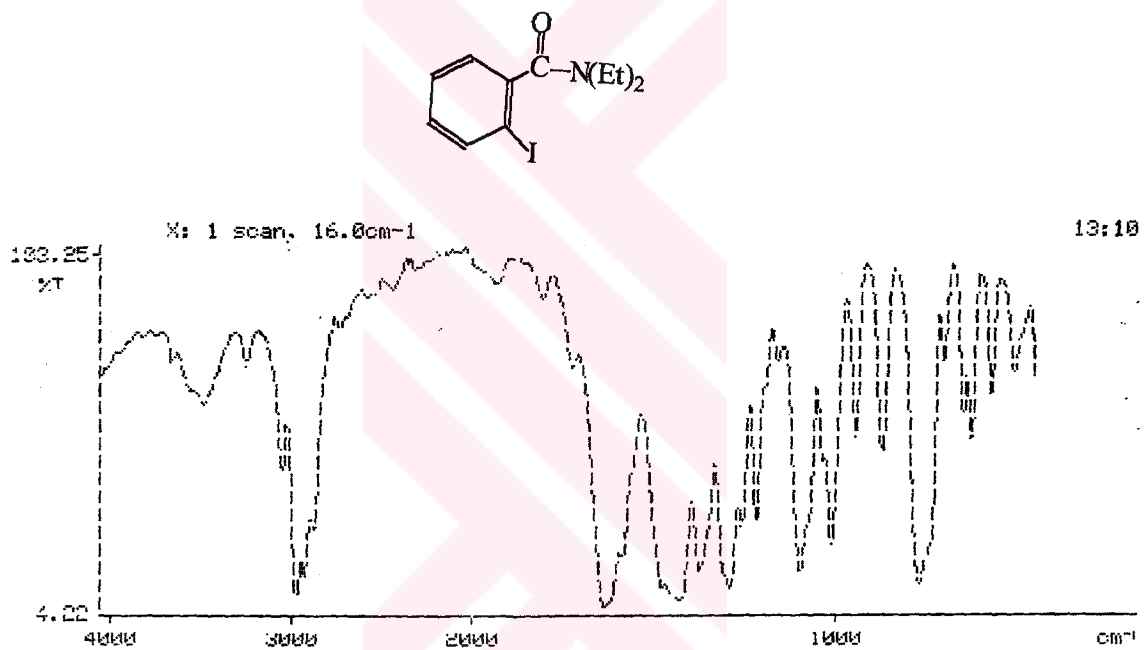


Figure-7 : The IR spectra of N,N-diethyl-2-iodobenzamide **(SM-II)**

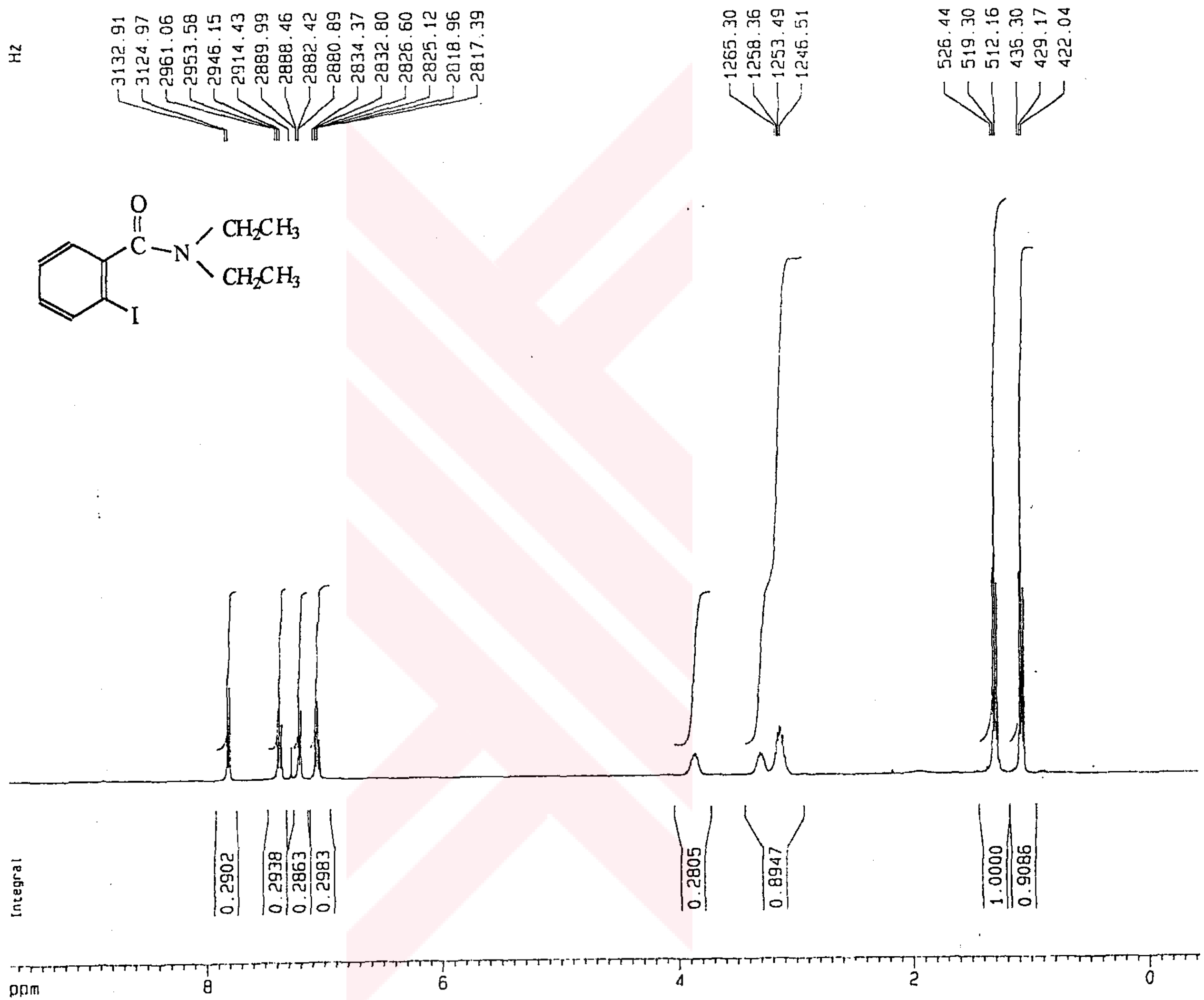


Figure-8 : The NMR spectra of N,N-diethyl-2-iodobenzamide (SM-II)

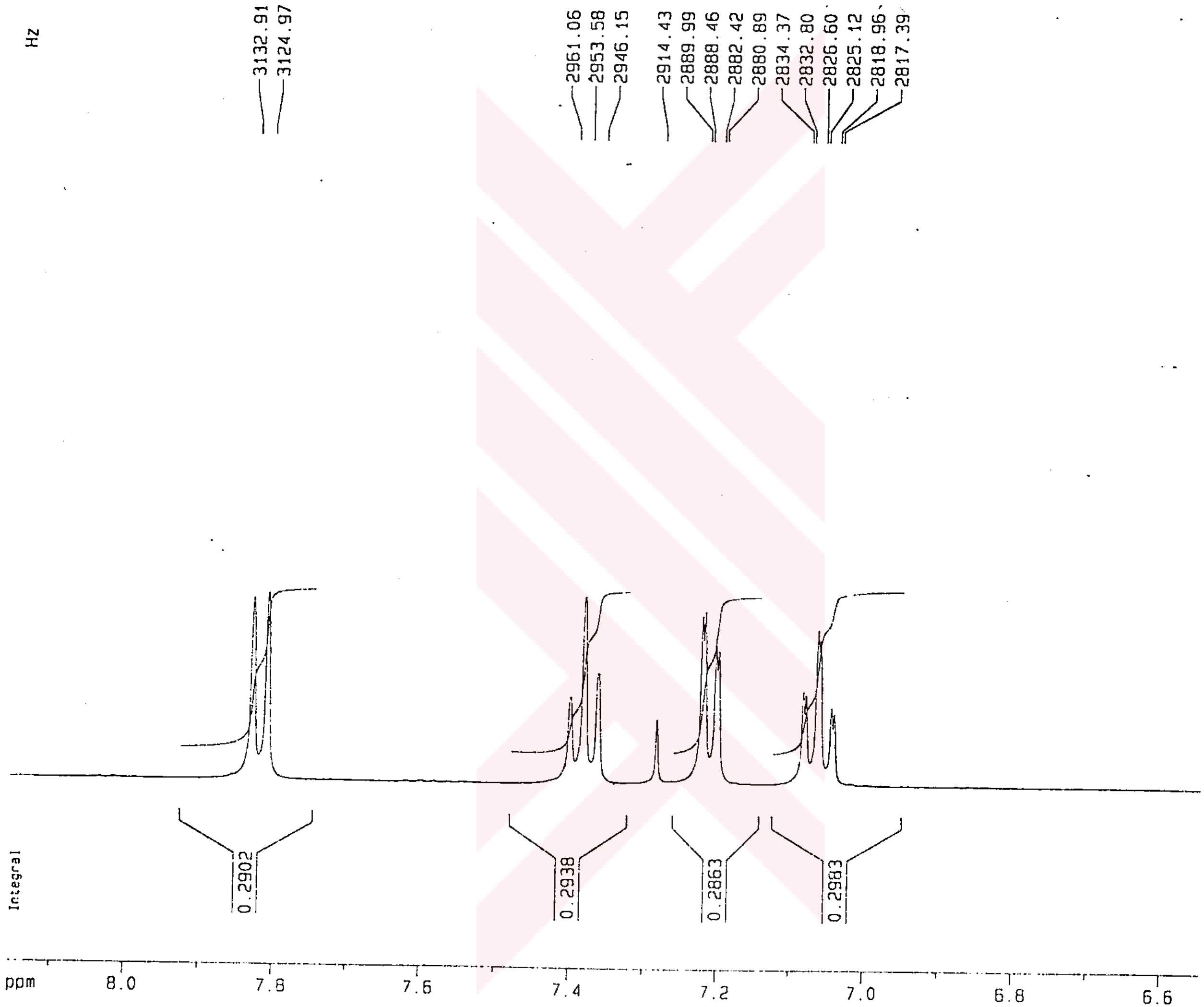


Figure-8 : The NMR spectra of **N**,N-diethyl-2-iodobenzamide **(SM-II)**

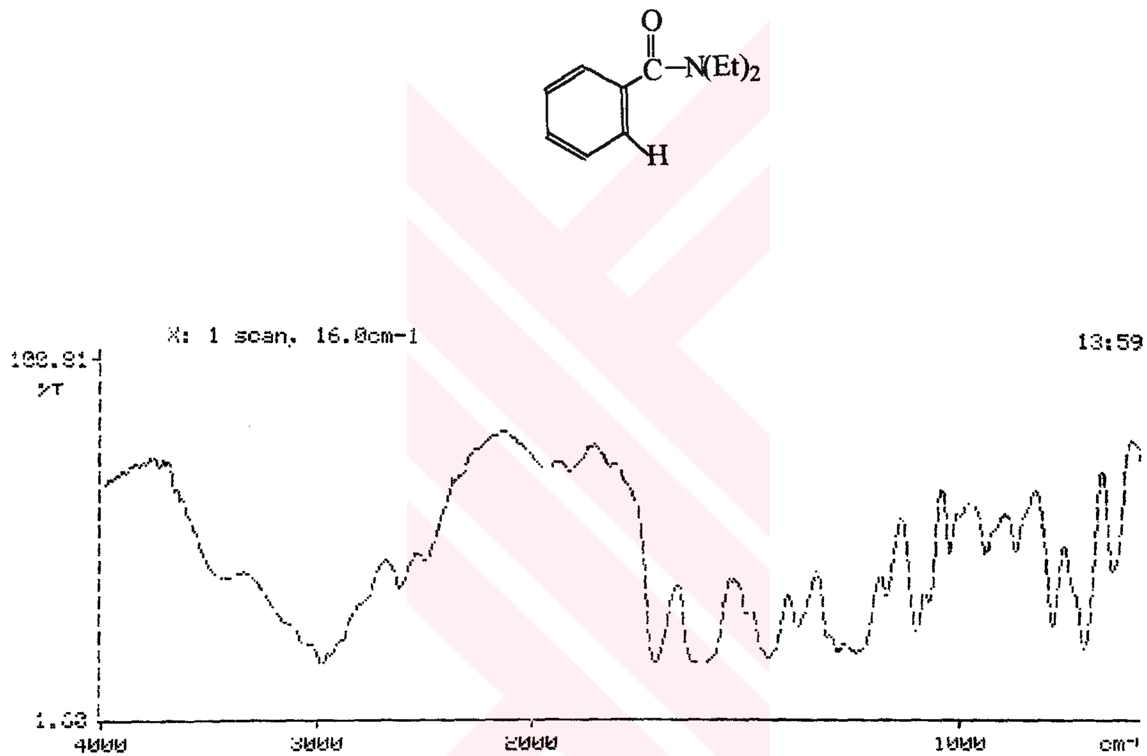


Figure-9 : The IR spectra of N,N-diethyl benzamide (Compound-III)

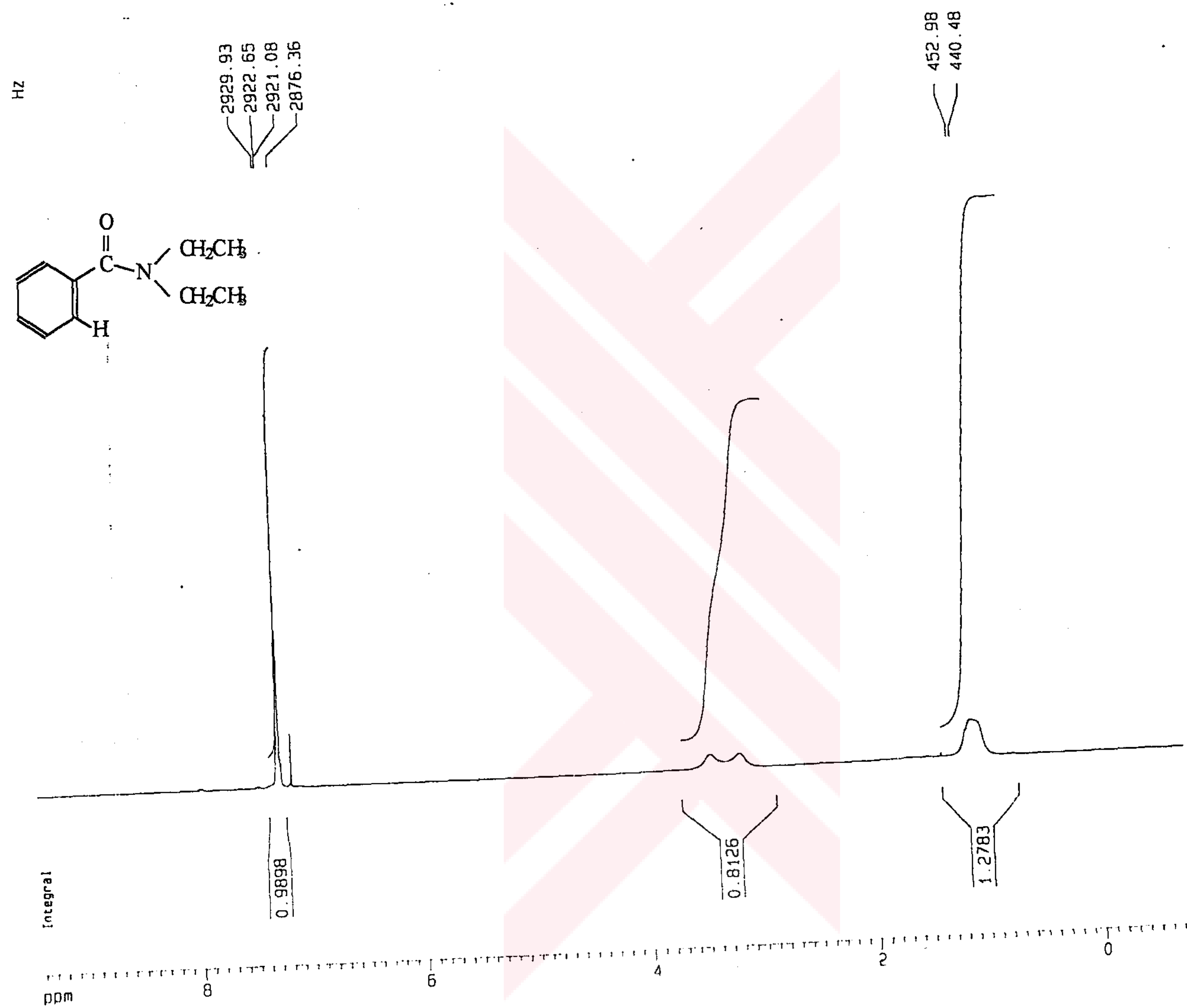


Figure-10 : The NMR spectra of N,N-diethyl benzamide (**Compound-III**)

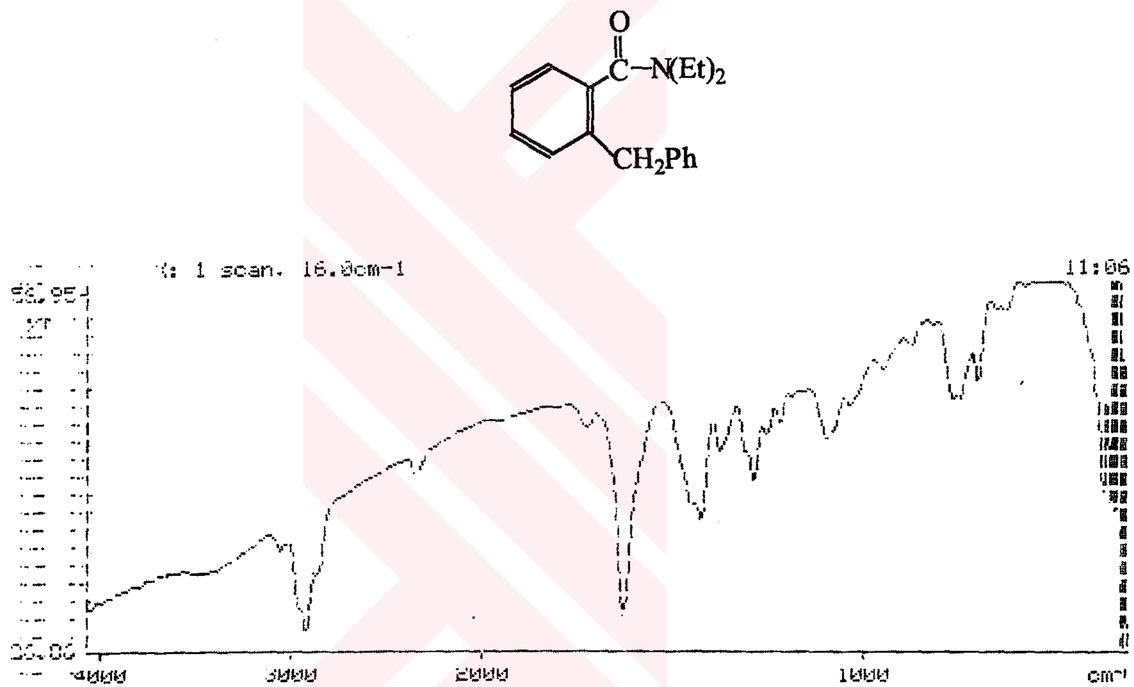


Figure-11 : The IR spectra of N,N-diethyl-2-phenylmethyl-benzamide (**Compound-IV**)

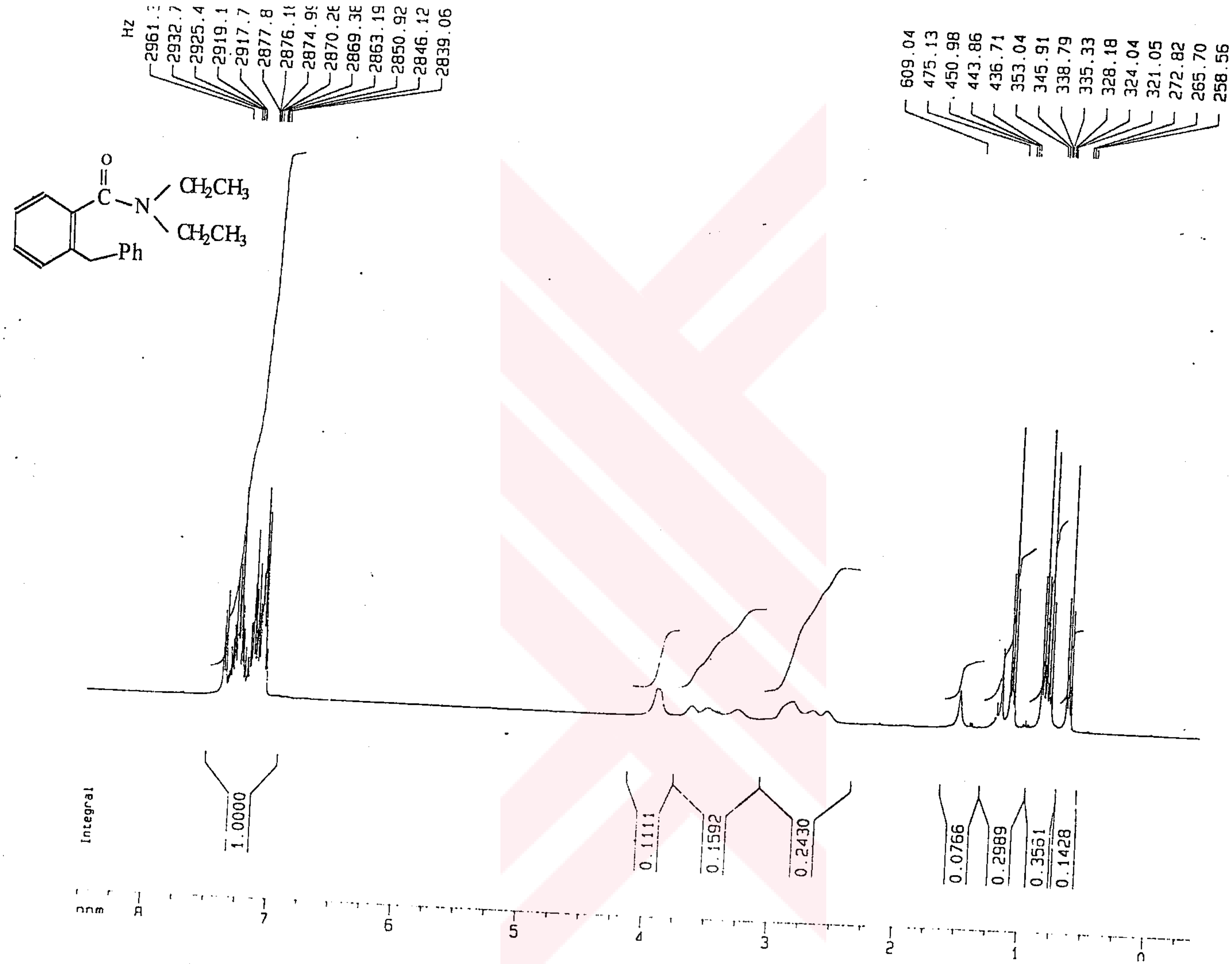


Figure-12 : The NMR spectra of N,N-diethyl-2-phenylmethyl-benzamide (**Compound-IV**)

REFRENCES

A.Maercker,1987,Angew.Chem.;26,972p.; 1987,Angew.Chem.Int.Ed.Engl. 99,1002p

Anne Eeg Jensen,Wolfgang Dohle and Paul Knochel,2000, Tetrahedron,56,4197p.

A.I.Meyers and William Rieker,1982,Tetrahedron Letters,23,2091p.

Ashby,Pham,1987,J.Org.Chem.;52,1291p.

Bailey,Patricia,Nurmi,Wang,1986,Tetrahedron Lett.;27,1861p

Bailey,Patricia,1988,J.Organomet.Chem.;352,1-46p.

Bailey,Punzalan,1990,J.Org.Chem.;55,54404p.

Beletskaya,Artamkina,Reutov,1976,Russ.Chem.Rev.;45,330-347p.

B.H.Lipsthutz,J.A.Kozlowski,R.S.Wilhelm,1983,J.Org.Chem.;48,546p.

B.H.Lipshutz,J.A.Kozlowski,R.S.Wilhelm,1983,J.Org.Chem.;48,546p.

F.Wöhler,1840,Ann.Chem.Pharm (Heildelberg),35,111p.

G.Boche, 1989 ,Angew.Chem.;101,286p.

Handlingof Butyllithium,Chemetall,Frankfurt,1993.

H.Gilman,R.O.Jones,L.A.Woods,1952,J.Org.Chem.,17,1630p.

H.O.house,C.Y.Chu,J.M.Wilkirs,1975,J.Org.Chem.;40,1460p.

H.O.House,T.V.Lee,1978,J.Org.Chem.,33,949p.

J.E.Mallet,1851,Ann. Chem.Pharm.(Heidelberg),79,223p.

J.C.Stowell,1979,Carbanions in Organic Sythesis,Wiley,New York.

J.P.Collman,L.S.Hegedus,J.r.Norton,F.G.Finke,Princples and Aplications ofn Organotransitition Chemistry,682p.

K.Ziegler,H.G.Gellert,Liebigs,1950,Ann.Chem.Soc.;567,179p.

Lebley,Landua,1969,J.Am.Chem.Soc.;91,748p.

M.T.Reetzs,J.Westermann,R.Steinbach,B.Wenderoth,R.Peter,R,Ostarek, S.Maus,1985,Chem.Ber.;118,1421p.

M.S.Kharasch,J.H:Cooper,1945,J.Org.Chem.;10,46p.

N.Miyaura,T.Ishiyama,H.Sasaki,M.Satoh,A.Suzuki,1989,J.Org.Chem.; 53,729p

Organometallics in Organic Synthesis,FMC Coporation,Lithium Division, Gastorid,Nc,1987.

P.A.Fowell,C.T.Mortimer,1961,J.Chem.Soc.,3793p.

Parham,Bradsher,1982,Acc.Chem.Res.;15,300-305p.

Pearson,Cower,Beckler,1959,J.Org.Chem.;24,504p.

R.A.Finnegar,H.W.Kutta,1965,J.Org.Chem.;30,4138p.

R.Bach,J.R.Wasson,in Krick .Otwer Encyclopedia of Chemical Techonology,1981, New York,3rd edn.;vol.14,467p.

R.L.Epply,J.A.Dixon,1968,J.Organomet.Chem.;11,147p.

Sukbok Chang,Soon Ha Yang and Phil Ho Lee ,2001,Tetrahedron Letters,,42,4833p.

Tamborski,Moore,1971,J.Organometa.Chem.;26,153p.

Ward,Lawler,Cooper,1969,J.Am.Chem.Soc.;91,746p.

W.H.Glaze,G.M.Adams,1966,J.Am.Chem.Soc.;88,4653p.

Zakharkin,Okhlobystin,Blevitch,1964,J.Organomet.Chem.;2,309p.

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