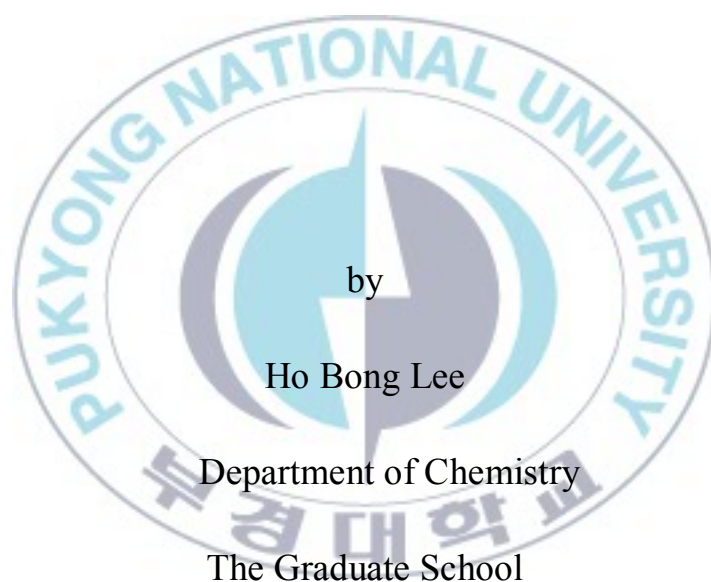


Thesis for the Degree of Master of Science

**Transition-Metal-Catalyzed Tandem C-C
Bond Formations : Synthesis of the Cyclic
Compounds**



by

Ho Bong Lee

Department of Chemistry

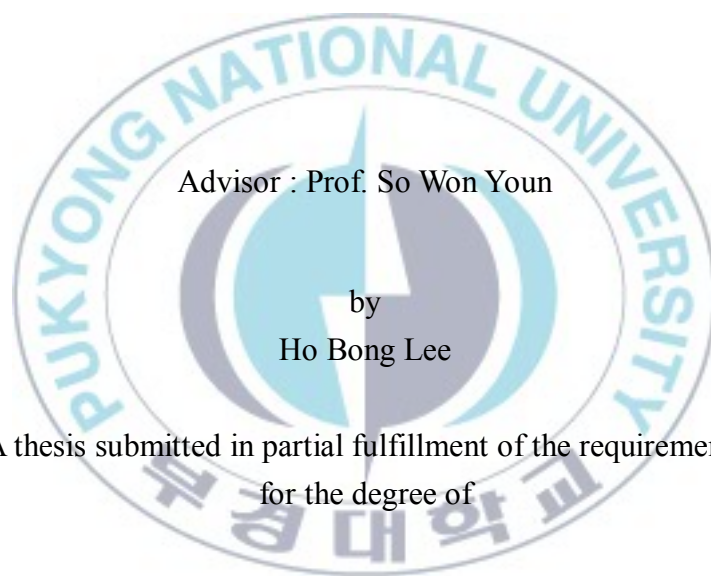
The Graduate School

Pukyong National University

February, 2009

Transition-Metal-Catalyzed Tandem C-C Bond Formations : Synthesis of the Cyclic Compounds

전이금속 촉매에 의한 연속적인 C-C 결합
형성 반응 : 고리화합물의 합성



Advisor : Prof. So Won Youn

by

Ho Bong Lee

A thesis submitted in partial fulfillment of the requirements
for the degree of

Master of Science

in Department of Chemistry, The Graduate School,
Pukyong National University

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Formation : Synthesis of the Cyclic Compounds**

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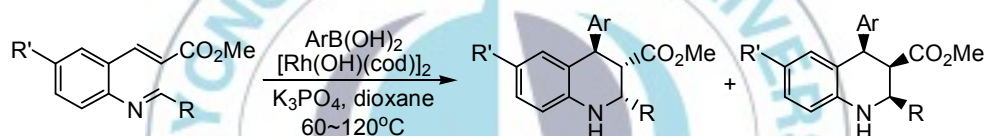
February 29, 2009

Transition Metal-Catalyzed Tandem C-C Bond Formation : Synthesis of the Cyclic Compounds

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Abstract



Transition-metal-catalyzed tandem C-C bond formations are powerful methods for the synthesis of structurally complex molecules from relatively simple starting materials in a convergent way. Treatment of imine-substituted electron-deficient alkenes with arylboronic acids in the presence of [Rh(OH)(cod)]₂ afforded the fully substituted tetrahydroquinolines via tandem conjugate addition and Mannich cyclization reaction. These reactions were performed with a variety of arylboronic acids and imine-substituted α,β -unsaturated esters to provide the corresponding tetrahydroquinoline derivatives. This process represents the first example in which an imine group can serve as a secondary electrophile that accepts the (oxa- π -allyl)rhodium(I) intermediate in an intramolecular way.

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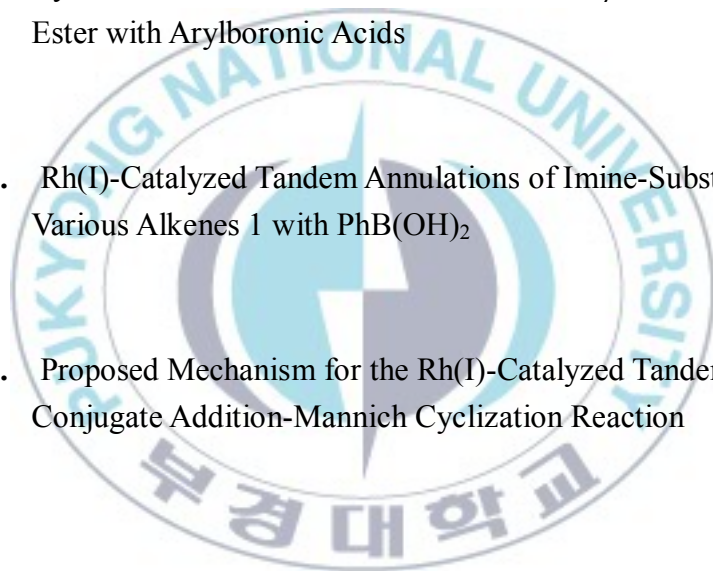
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1. Introduction

Transition-metal-catalyzed transformations are of increasing importance in synthetic organic chemistry, since a transition-metal-catalyzed reaction can directly construct complicated molecules from readily accessible starting materials under mild conditions. Therefore, the use of this type of transformation as part of a tandem reaction will be increasingly interesting. Tandem reactions are particularly appealing, as they can enhance the efficiency of reaching the target molecules. They also avoid the separation of intermediates, as it saves the number of steps, and in principle reducing the amount of waste. The versatility of the catalyst can also be exploited, through a number of different reactions occurring in the same flask.

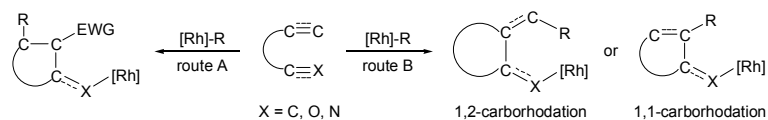
Transition-metal-catalyzed tandem transformation is a very appealing strategy as it involves a multistep transformation that enables a rapid increase in molecular complexity from readily available starting compounds.¹ Molecules that have two or more different unsaturated bonds are particularly interesting substrates for the tandem annulations involving multiple C-C bond formations with a single catalyst in one operation, allowing the construction of a variety of cyclic compounds. The more reactive functional group provides the entry point for the addition of a carbon nucleophile by way of initial intermolecular carbometalation, which triggers the second carbometalation on the less reactive functionality in an intramolecular way to construct a cyclic skeleton.

Recently, several examples of transition-metal-catalyzed tandem annulations with organoboron reagents have been demonstrated in which the tandem cyclization was triggered by conjugate addition to α,β -unsaturated carbonyl compounds or 1,2-addition across the alkynes.^{1e,3-5} Organoboronic acids and esters are relatively non-toxic, easily accessible, mostly stable

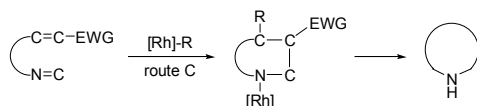
toward air and water, and hence, are often used as the organometallic compound of convenience in transition-metal-catalyzed C-C bond forming reactions. In particular, the palladium-catalyzed cross-coupling reaction of organoboronic acids has found wide applications in industrial processes as well as in laboratory syntheses.² The rhodium-catalyzed addition reaction of organoboron reagents to unsaturated organic compounds has gained much attention in organic synthesis. An organorhodium(I) intermediate generated via carborhodation onto the alkene or alkyne moiety added to the intramolecular carbonyl,^{3a-c} cyano,^{3d,e} alkyne,^{3g} and alkene^{3g-m} groups, providing five- or six-membered carbocycles via a sequential second carborhodation (Scheme 1, routes A and B). Although several Rh(I)-catalyzed tandem reactions have been described, the process involving an imine group as a second electrophile has not yet been explored.⁶ Since both α,β -unsaturated carbonyl compounds^{1e,7} and imines^{7c,8} are good acceptors of organorhodium(I) species, we envisioned that electron-deficient alkenes bearing imine moiety placed at an appropriate position are interesting bifunctional substrates with regard to the possibility of a tandem cyclization reaction, which could afford *N*-heterocycles such as tetrahydroquinolines (Scheme 1, route C). Tetrahydroquinoline derivatives constitute an important class possessing a wide range of biological activities and multiple applications and are found in a variety of natural products and pharmaceuticals that exhibit potent and varied biological activities.⁹

Scheme 1. Rhodium(I)-Catalyzed Tandem Annulation

(a) Synthesis of Carbocycles



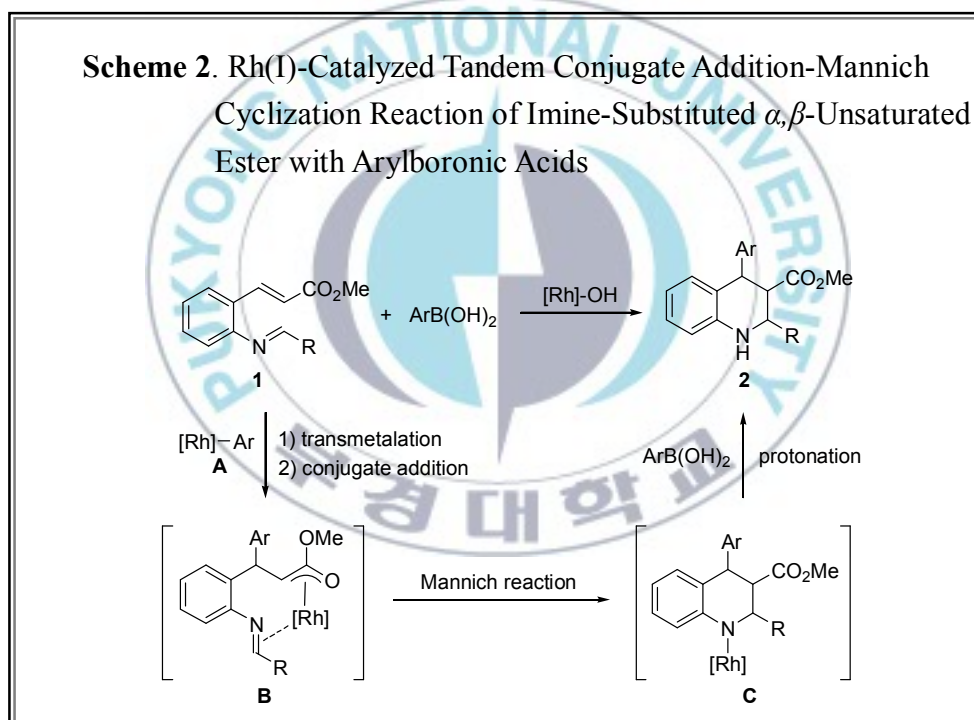
(b) Synthesis of *N*-Heterocycles



Rhodium-catalyzed tandem annulation reactions triggered by the addition of organoboron can result in a dramatic increase in molecular complexity in an atom-economical manner. The reactions included in this paper demonstrate that organorhodium(I) species can undergo multiple carboration reactions successively in preference to potentially competing processes including protonolysis. To date, Rh(I)-catalyzed tandem cyclization reactions using organoboron reagents have been reported in the context of synthesis of carbocyclic compounds.¹⁰ In parallel with our efforts to develop a catalytic system for heterocyclic synthesis,¹¹ we were interested in developing a one-pot synthesis of *N*-heterocycles, tetrahydroquinolines, whereby a single catalytic system would invoke sequential C-C bond formations in an efficient manner. Herein we report a new Rh(I)-catalyzed tandem conjugate addition-Mannich cyclization reaction of imine substituted electron-deficient alkenes with arylboronic acids. This is the first example involving imine moiety as a secondary electrophile in Rh(I)-catalyzed tandem reactions.

2. Results and Discussion

2.1. Rhodium-Catalyzed Tandem Conjugate Addition-Mannich Cyclization Reaction: Straightforward Access to Fully Substituted Tetrahydroquinolines



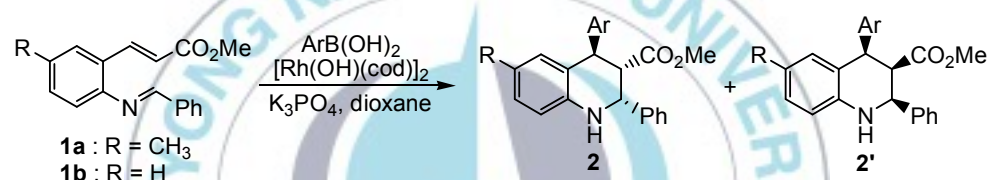
The success of a tandem cyclization triggered by the conjugate addition of an organorhodium(I) species (**A**) to an electron deficient alkene could be

achieved by choosing the adequate secondary functionality placed at an appropriate position in the molecule. The secondary functional group should not react faster than the electron-deficient alkene with the organorhodium(I) species in an intermolecular way but should be reactive enough to trap intramolecularly the (oxa- π -allyl)rhodium(I) intermediate (**B**) generated in the conjugate addition step (Scheme 2). In this regard, the combination of α,β -unsaturated ester and imine seems plausible. On the other hand, the Rh(I)-catalyzed conjugate addition reactions of organoboronic acids to α,β -unsaturated carbonyl compounds are usually carried out in water-containing solvents. However, anhydrous solvents might be required both to minimize imine hydrolysis and to prevent Rh(I)-enolate (**B**) from protonation in this tandem process.¹² The low reactivity and instability of imine moiety relative to other functional groups that were used in the related Rh(I)-catalyzed tandem reactions could present significant challenges in this process.

We focused our initial efforts on establishing optimal conditions for the Rh(I)-catalyzed tandem conjugate addition-Mannich cyclization reaction of **1a**, which was selected as the first substrate for screening of several solvents and bases. Gratifyingly, it was found that reaction between **1a** and phenylboronic acid in 1,4-dioxane for 1 h at 80 °C in the presence of [Rh(OH)(cod)]₂ (4 mol % Rh) and K₃PO₄ gave the desired 1,2,3,4-tetrahydroquinoline **2a** in 74% yield as an inseparable mixture of two diastereomers in a ratio of 77:23 favoring the *cis-trans* isomer, of which substituents on C-2 and C-3 and those on C-3 and C-4 are located in *cis* and *trans* configuration, respectively (Table 1, entry 1). The structure of the compound **2a** was determined by examination of ¹H NMR spectrum and NOE experiment. It should be noted that direct 1,2-addition of PhB(OH)₂ to the imine moiety was not observed. With the establishment of these optimized conditions, we set out to explore the scope of this tandem process. As shown in Table 1, reaction of **1** with organoboronic acids took place smoothly with good yield to provide 2,3,4-trisubstituted 1,2,3,4-

tetrahydroquinoline **2**. A wide range of arylboronic acids with electron-donating or -withdrawing substituents at various positions were found to be good nucleophiles in the reaction (Table 1, entries 1-13). Generally, electron-rich arylboronic acids required shorter reaction time and gave higher yields than their electron-deficient counterparts, which required higher catalyst loadings. 2-Naphthylboronic acid also reacted with **1a** to give the corresponding tetrahydroquinoline **2h** (Table 1, entry 8). In contrast, these cyclization reactions failed with sterically hindered aryl- (*o*-MeOC₆H₄), heteroaryl- (2-thienyl, 2-furanyl), and alkenyl- (β -styryl, (*E*)-1-octenyl) boronic acids to give the corresponding products in 15-30% yields, probably due to steric and electronic reasons, respectively.

Table 1. Rh(I)-Catalyzed Tandem Conjugate Addition-Mannich Cyclization Reactions of **1** with Various Arylboronic Acids^a



Entry	Substrate	Ar	Product	Time (h)	Yield (%) ^b	2:2' ^c
1	1a	Ph	2a	1	74	77:23
2 ^d	1b	Ph	2b	12	86	63:37
3	1a	3-MeOC ₆ H ₄	2c	1	73	77:23
4	1a	4-MeOC ₆ H ₄	2d	1	72	71:29
5	1b	4-MeOC ₆ H ₄	2e	1	75	83:17
6	1a	4-MeC ₆ H ₄	2f	1	74	71:29
7	1a	4-HOC ₆ H ₄	2g	1	74	77:23
8	1a	2-naphthyl	2h	1	70	83:17
9 ^d	1a	4-FC ₆ H ₄	2i	24	80	77:23
10	1a	4-ClC ₆ H ₄	2j	1	67	91:9

11 ^e	1a	4-BrC ₆ H ₄	2k	48	51	63:37
12 ^e	1a	3-O ₂ NC ₆ H ₄	2l	48	55	83:17
13 ^e	1a	4-CH ₃ COC ₆ H ₄	2m	48	50	67:33

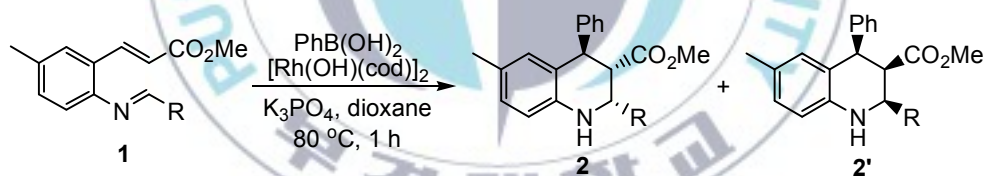
^aThe reaction was carried out with **1**, ArB(OH)₂ (2.5 equiv), [Rh(OH)(cod)]₂ (2 mol %, 4 mol % Rh), and K₃PO₄ (2 equiv) in 1,4-dioxane (0.1 M) at 80°C, unless otherwise noted.

^bIsolated yields. ^cThe ratio of two isomers was determined by ¹H NMR. ^dPerformed at 60°C.

^ePerformed with 5 mol % [Rh(OH)(cod)]₂ (10 mol % Rh).

We proceeded to examine the reaction with various imines (Table 2). Both electron-deficient and electron-rich aromatic imines as well as sterically hindered aromatic imine underwent tandem cyclization reaction to form the corresponding tetrahydroquinolines (Table 2, entries 1-3). Heteroaromatic imines (Table 2, entries 4 and 5), α,β -unsaturated imine (Table 2, entry 6), and glyoxylate imine (Table 2, entry 7) also proved to be suitable substrates, whereas aliphatic imines led to a complicated mixture and no reaction occurred with ketimine substrates.

Table 2. Rh(I)-Catalyzed Tandem Annulations of Various Imine-Substituted Unsaturated Esters **1** with PhB(OH)₂^a



Entry	Substrate	R	Product	Yield (%) ^b	2:2' ^c
1	1c	4-MeOC ₆ H ₄	2n	83	83:17
2	1d	4-O ₂ NC ₆ H ₄	2o	71	59:41
3	1e	2-BrC ₆ H ₄	2p	45	50:50
4	1f	2-(6-methylpyridinyl)	2q	55	59:41
5	1g	2-(5-methylfuranyl)	2r	55	83:17

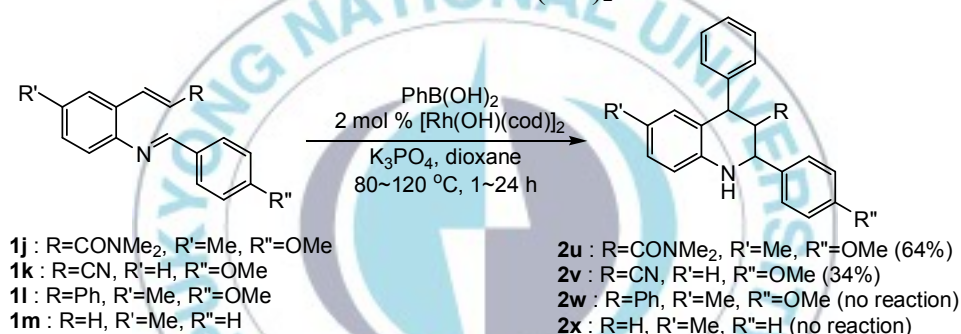
6	1h	cinnamyl	2s	45	100:0
7	1i	CO ₂ Et	2t	33	n.d. ^d

^a The reaction was carried out with **1**, PhB(OH)₂ (2.5 equiv), [Rh(OH)(cod)]₂ (2 mol %, 4 mol % Rh), and K₃PO₄ (2 equiv) in 1,4-dioxane (0.1 M) at 80°C for 1h. ^bIsolated yields.

^cThe ratio of two isomers was determined by ¹H NMR. ^dNot determined.

Last, we explored the effects of substituents at the alkene moiety. Whereas the tandem annulations of α,β -unsaturated amide (**1j**) and nitrile (**1k**) afforded the corresponding cyclized products in moderate to good yields, phenyl-substituted (**1l**) and terminal alkenes (**1m**) were unsuccessful (Scheme 3).

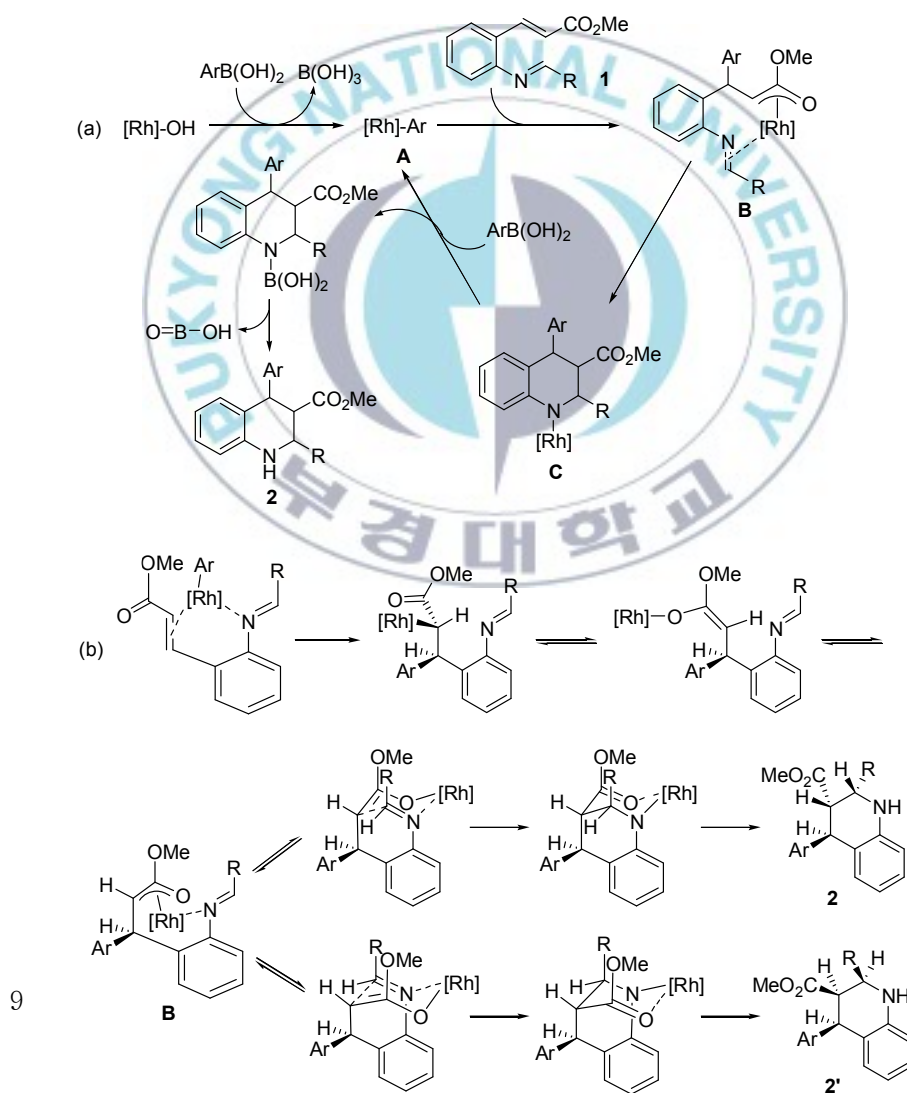
Scheme 3. Rh(I)-Catalyzed Tandem Annulations of Imine-Substituted Various Alkenes **1** with PhB(OH)₂



A plausible mechanism for Rh-catalyzed tandem cyclization presented herein is outlined in Scheme 4 and is based on the related mechanisms established for the Rh-catalyzed tandem cyclizations triggered by conjugate addition with organoboronic acids.^{3,13} Initially, an organorhodium(I) species (**A**) is generated by transmetalation of hydroxorhodium(I) with arylboronic acid. Then, conjugate addition of the arylrhodium(I) species (**A**) to substrate **1** occurs to afford the (oxa- π -allyl)rhodium(I) intermediate (**B**), which undergoes intramolecular nucleophilic addition to the pendant imine group, forming *N*-rhodium(I) species (**C**). The reaction was complete in the

absence of proton source such as H₂O, which suggests that a proton source for this reaction could be the organoboronic acid.^{3f,5c,14} Protonation of **C** with arylboronic acid releases the product **2** along with metaboric acid and **A** to promote the next catalytic cycle. Even though the dependence of stereochemical bias on the substrate structures is unclear and difficult to explain at this stage, the observed relative stereochemistry may be understood on the basis of a *Z*-enolate and a Zimmerman-Traxler-type transition state model (Scheme 4b).^{3a,f,m,4a}

Scheme 4. Proposed Mechanism for the Rh(I)-Catalyzed Tandem Conjugate Addition-Mannich Cyclization Reaction



2.2. Related Catalytic Tandem Annulation Reactions

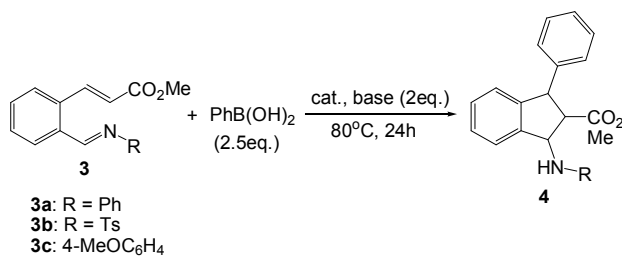
Having these promising results in hand, we next decided to extend related catalytic tandem annulations. As noted earlier, alkene or alkyne moieties generate an organometallic intermediate via carbometallation using Rh(I)^3 , $\text{Ir(I)}^{5\text{d,e}}$, $\text{Pd(0)}^{5\text{g}}$ and $\text{Ni(0)}^{5\text{a,b}}$ which is added to the intramolecular cyano- or imine groups to produce five- or six- membered rings.

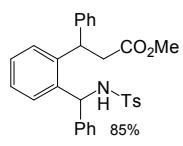
Substrates for these reactions were prepared easily via Heck and Sonogashira reactions and an imine group was prepared in reflux with the aid of a Dean-Stark apparatus to remove the water produced, sequentially.

However, some substrates were not produced via Dean-Stark system at imine preparation step. And most reactions have generated unexpected compounds or unidentified complex compounds.

At the beginning of the research, we focused our initial efforts on applying the optimized reaction conditions for **1** to similar imine substrates **3**. Reactions of **3** with PhB(OH)_2 and various bases were examined, but reactions did not occur. In the case of *p*-toluenesulfonyl substituted imine (**3b**), unexpected product in which phenyl substituents were added to α,β -unsaturated ester and imine separately, was obtained (Table 3, entry 2). And in other cases, we obtained the unidentified compounds.

Table 3. Screening Table for the Transition-Metal-Catalyzed Tandem Annulation of Various Imine-Substituted α,β -Unsaturated Esters **3** with PhB(OH)_2

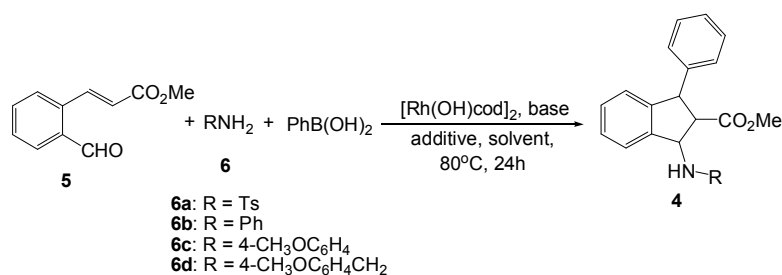


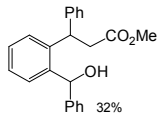
Entry	Substrate	Catalyst ^b	Base	Solvent	Product
1 ^a	3a	-	-	-	-
2	3b	[Rh(OH)cod] ₂	K ₃ PO ₄	dioxane	
3	3b	Pd(PPh ₃) ₄	-	dioxane	- ^c
4	3c	[Rh(OH)cod] ₂	K ₃ PO ₄	dioxane	- ^d
5	3c	[Rh(OH)cod] ₂	Na ₂ CO ₃	dioxane	- ^d
6	3c	[Rh(OH)cod] ₂	KOH	dioxane	- ^d
7	3c	[Rh(OH)cod] ₂	Cs ₂ CO ₃	dioxane	- ^d
8	3c	[Rh(OH)cod] ₂	K ₂ CO ₃	dioxane	- ^d
9	3c	[Rh(OH)cod] ₂	Et ₃ N	dioxane	- ^d

^aThe reaction was failed to introduce an imine substrates. ^bThe reaction was carried out with [Rh(OH)cod]₂ (2 mol %, 4 mol % Rh) and Pd(PPh₃)₄ (4 mol %), respectively. ^cStarting materials was remained > 99%. ^dThe product was not identified.

Because of the difficulty of preparation of imine derivatives, next, we attempted the one-pot multicomponent synthesis to avoid imine preparation step. The reactions were carried out with 2-alkenylbenzaldehyde, amines, phenylboronic acid and [Rh(OH)cod]₂ with a variety of solvents, bases, and additives. But no reaction occurred in all cases.

Table 4. Rh(I)-Catalyzed Multicomponent Tandem Annulations



Entry	RNH ₂	Base	Additive	Solvent	Product
1	6a	K ₃ PO ₄	-	MeOH	- ^b
2	6a	K ₃ PO ₄	-	Dioxane	- ^b
3	6a	K ₃ PO ₄	-	Dioxane:H ₂ O(6:1)	 32%
4	6a	K ₃ PO ₄	Sc(OTf) ₃	MeOH	- ^b
5	6b	K ₃ PO ₄	-	MeOH	- ^c
6	6b	K ₃ PO ₄	Sc(OTf) ₃	MeOH	- ^b
7	6c	-	-	<i>i</i> -PrOH	- ^b
8	6c	-	Sc(OTf) ₃	<i>i</i> -PrOH	- ^b
9	6c	-	AgOTf	<i>i</i> -PrOH	- ^b
10	6c	K ₃ PO ₄	-	<i>i</i> -PrOH	- ^b
11	6c	Cs ₂ CO ₃	-	Dioxane	- ^b
12	6c	K ₃ PO ₄	Sc(OTf) ₃	<i>i</i> -PrOH	- ^b
13	6c	K ₃ PO ₄	AgOTf	<i>i</i> -PrOH	- ^b
14	6d	K ₃ PO ₄	-	MeOH	- ^b
15	6d	K ₃ PO ₄	Sc(OTf) ₃	MeOH	- ^b

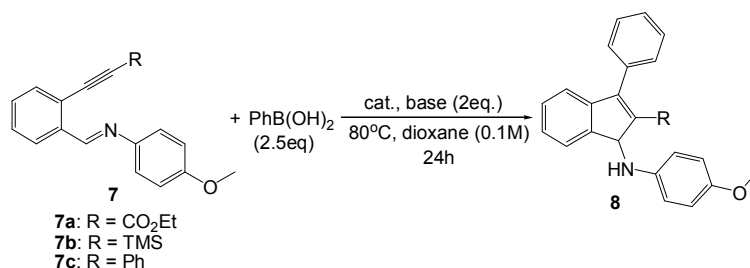
^aThe reaction was carried out with amine (1 equiv), PhB(OH)₂ (2 equiv), base (2 equiv) and [Rh(OH)(cod)]₂ (2 mol %, 4 mol % Rh) in solvent(0.1M) at 80°C.

^bStarting materials was remained > 99%. ^cThe product was not identified.

With these results, we next carried out other type transition-metal-catalyzed tandem annulations. The rhodium- and palladium-catalyzed addition reaction of organoboron reagents to unsaturated organic compounds has attention in organic synthesis. The reaction generally proceeds via rhodium and palladium/boron transmetalation generating an organometallic intermediates followed by a subsequent carbometallation step. Particularly, alkynes are good acceptors of organorhodium(I) and

organopalladium(0) species. 2-alkynylphenyl imines **7** were treated with phenylboronic acid in the presence of $[\text{Rh}(\text{OH})\text{cod}]_2$ or $\text{Pd}(\text{PPh}_3)_4$ in dioxane for 12-24 h. However, undesired products were obtained in all cases.

Table 5. The Transition-Metal-Catalyzed Tandem Annulations of Imine-Substituted Various Alkynes with $\text{PhB}(\text{OH})_2$



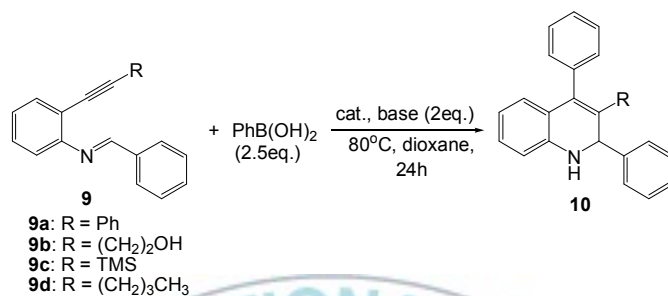
Entry	Substrate	Catalyst ^b	Base	Product
1 ^a	7a	-	-	-
2	7b	$[\text{Rh}(\text{OH})\text{cod}]_2$	K_3PO_4	 12 ~ 20%
3	7b	$[\text{Rh}(\text{OH})\text{cod}]_2$	Na_2CO_3	
4	7b	$[\text{Rh}(\text{OH})\text{cod}]_2$	KOH	
5	7b	$[\text{Rh}(\text{OH})\text{cod}]_2$	Cs_2CO_3	
6	7b	$[\text{Rh}(\text{OH})\text{cod}]_2$	K_2CO_3	
7	7b	$[\text{Rh}(\text{OH})\text{cod}]_2$	Et_3N	
8	7c	$[\text{Rh}(\text{OH})\text{cod}]_2$	K_3PO_4	
9	7c	$\text{Pd}(\text{PPh}_3)_4$	-	- ^c

^aThe reaction was failed to introduce an imine substrates. ^bThe reaction was carried out with $[\text{Rh}(\text{OH})\text{cod}]_2$ (2 mol %, 4 mol % Rh) and $\text{Pd}(\text{PPh}_3)_4$ (4 mol %), respectively. ^cStarting materials was remained > 99%.

Other 2-alkynylimine structures are tested for these tandem annulations. When we mixed iminoalkyne derivative **5d** under this reaction conditions,

formation of dimeric compounds of the starting substrates was observed in low yields as represented in Table 6 (entry 6~9). In spite of addition of AcCl as an additive, unexpected product was obtained.

Table 6. Transition-Metal-Catalyzed Tandem Annulation of Imine-Substituted Various Alkynes with PhB(OH)₂



Entry	Substrate	Catalyst ^b	Base	Additive ^c	Product
1 ^a	5a	-	-	-	-
2	5b	[Rh(OH)cod] ₂	K ₃ PO ₄	-	- ^d
3	5b	Pd(PPh ₃) ₄	-	-	- ^d
4	5c	[Rh(OH)cod] ₂	K ₃ PO ₄	-	
5	5c	Pd(PPh ₃) ₄	-	-	- ^d
6	5d	[Rh(OH)cod] ₂	K ₃ PO ₄	-	
7	5d	[Rh(OH)cod] ₂	Et ₃ N	-	
8	5d	[Rh(OH)cod] ₂	KOH	-	
9	5d	Pd(PPh ₃) ₄	-	-	
10	5d	[Rh(OH)cod] ₂	K ₃ PO ₄	AcCl	

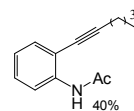
11

5d

Pd(PPh₃)₄

-

AcCl



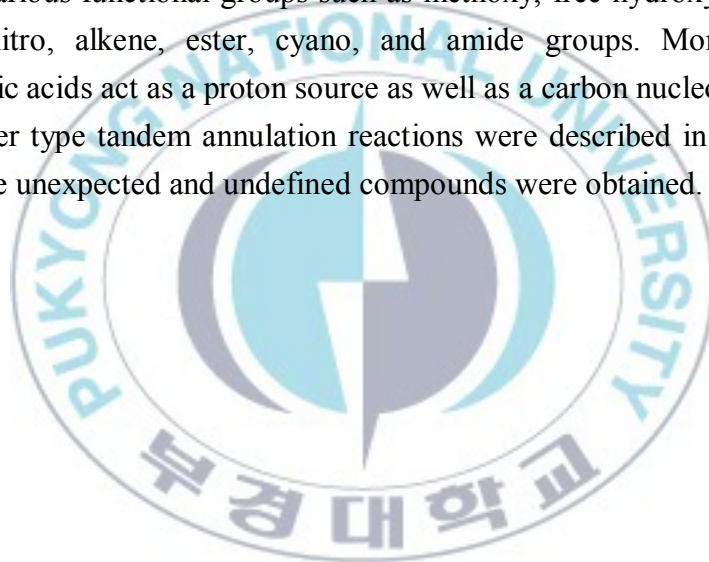
^aThe reaction was failed to introduce an imine substrates. ^bThe reaction was carried out with [Rh(OH)cod]₂ (2 mol %, 4 mol % Rh) and Pd(PPh₃)₄ (4 mol %), respectively. ^cPerformed with 2 equiv AcCl. ^dStarting materials was remained > 99%.



3. Conclusion

Transition-metal-catalyzed tandem C-C bond formations are powerful methods for the synthesis of structurally complex molecules from relatively simple starting materials in a convergent way. We have developed a new Rh(I)-catalyzed tandem conjugate addition-Mannich cyclization reaction to afford 2,3,4-trisubstituted 1,2,3,4-tetrahydroquinolines. It is interesting that sequential C-C bond formations, conjugate addition and Mannich reaction, are catalyzed by a Rh complex in a single catalytic cycle. This process represents the first example in which an imine group can serve as a secondary electrophile that accepts the (oxa- π -allyl)rhodium(I) intermediate in an intramolecular way. Noteworthy is the fact that this process can tolerate various functional groups such as methoxy, free hydroxyl, halogen, ketone, nitro, alkene, ester, cyano, and amide groups. Moreover, the arylboronic acids act as a proton source as well as a carbon nucleophile.

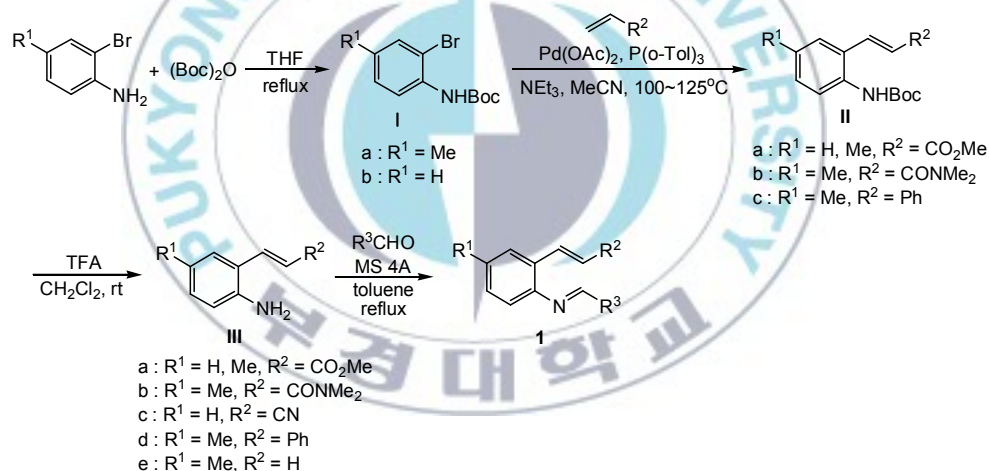
And other type tandem annulation reactions were described in this paper, though the unexpected and undefined compounds were obtained.



4. Experiment Section

4.1. General Information

Nuclear Magnetic Resonance spectra were recorded on 400 MHz instrument. Spectra were recorded in CDCl₃ solutions referenced to TMS or solvent residual peak. High Resolution Mass Spectra were measured using EI at 70 eV. IR spectra were taken as neat for liquids on NaCl plates using FT-IR Spectrophotometer. Flash chromatography was performed on silica gel 230-400 mesh. All catalysts were purchased in the higher quality and used as received. Unless otherwise noted, all commercially obtained reagents were used as received. 1,4-Dioxane and THF were all distilled from sodium benzophenone ketyl immediately prior to use. Toluene was distilled from CaH₂ immediately prior to use. Thin layer chromatograms (TLC) was visualized via UV and Cerium Molybdate (Hanessian's Stain).



4.2. General procedure for the preparation of N-Boc aniline I

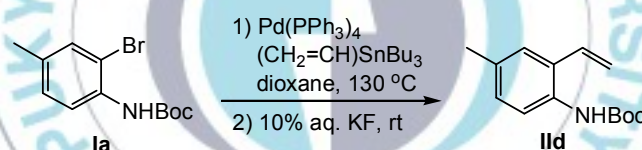
To a solution of 2-bromo-4-methylaniline or 2-bromoaniline in THF (0.4 M) was added (Boc)₂O (1equiv). The reaction mixture was stirred at reflux for 24 hours, and then the solvent was evaporated. The residue was purified

by column chromatography on silica gel (EtOAc : *n*-Hexane = 1 : 50) to give the corresponding product. (**Ia** : 92%, **Ib** : 93%)

4.3. General procedure for Heck reaction for the synthesis of **IIa-c**^{14a}

To a solution of **I** in MeCN (0.4 M) in a pressure tube were added Pd(OAc)₂ (**a-b**: 10 mol %, **c** : 1 mol %), P(*o*-Tol)₃ (**a-b**: 20 mol %, **c** : 8 mol %), NEt₃ (**a-b**: 5 equiv, **c** : 0.5 mL/1 mmol), and the corresponding olefin (**a-b**: 3 equiv, **c** : 1.25 equiv). The pressure tube was tightly capped, heated at 100 °C (**c**) or 125 °C (**a-b**) for 12 hours. After the reaction was completed, the reaction mixture was filtered through Celite, quenched with distilled water, extracted with CH₂Cl₂ (three times), washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc:*n*-Hexane = 1:10~1:20) to give the corresponding product. (**IIa** : 63~65%, **IIb** : 49%, **IIc** : 78%)

4.4. Synthesis of *N*-Boc-4-methyl-2-vinylaniline (**IIId**)^{14b}



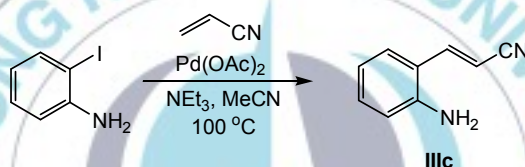
To a solution of **Ia** and tetrakis(triphenylphosphine)palladium (2 mol %) in dioxane (7.5 mL/1 mmol) in a pressure tube was added tributyl(vinyl)tin (1.2 equiv). The pressure tube was tightly capped, heated at 130 °C for 5 hours, and then cooled to rt. After 10% aqueous KF solution (12.5 mL/1 mmol) was added to the mixture, the reaction mixture was allowed to stand for 2 hours and then filtered through Celite, washed with water and EtOAc. The filtrate was transferred to separatory funnel and extracted with EtOAc (three times), washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel

(EtOAc : *n*-Hexane = 1 : 20) to give the **IIId** (48%) as a colorless oil.

4.5. General procedure for the *N*-Boc deprotection

To a solution of **II** in CH₂Cl₂ (0.3 M) was added TFA (CH₂Cl₂/TFA = 5/1). The reaction mixture was stirred at rt for 0.5-2 hours. After the reaction was completed, the residue was diluted with CH₂Cl₂, basified with sat. NaHCO₃ solution, extracted with CH₂Cl₂ (three times), washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc : *n*-Hexane = 1 : 10 ~ EtOAc only) to give the corresponding product. (**IIIa** : 90~92%, **IIIb** : 88%, **IIIc** : 91%, **IIId** : 91%, **IIIe** : 89%)

4.6. Synthesis of 3-(2-aminophenyl)acrylonitrile (**IIIc**)^{14a}



To a solution of 2-iodoaniline in MeCN (0.5 M) in a pressure tube were added Pd(OAc)₂ (1 mol %), NEt₃ (1 mL/1 mmol), and acrylonitrile (1.25 equiv). The pressure tube was tightly capped, heated at 100 °C for 40 hours. After the reaction was completed, the reaction mixture was filtered through Celite, quenched with distilled water, extracted with CH₂Cl₂ (three times), washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc : *n*-Hexane = 1 : 5) to give the **IIIc** (54%) as a yellow solid.

4.7. General procedure for the preparation of imine substrates 1

To a solution of amine in toluene (0.2 M) was added aldehyde (1.05 equiv).

The reaction mixture was stirred over molecular sieves 4Å (480 mg/1.00 mmol substrate) for 18 hours at 100 °C, after which it was filtered through Celite and concentrated *in vacuo*. The resulting imines were clean by ¹H NMR and were used in the cyclization reactions without purification.

3-[2-(Benzylideneamino)-5-methylphenyl]acrylic acid methyl ester (1a)

δ_{H} (CDCl₃, 400 MHz) 2.38 (s, 3H), 3.78 (s, 3H), 6.47 (d, $J = 16.1$ Hz, 1H), 6.94 (d, $J = 7.8$ Hz, 1H), 7.21 (dd, $J = 1.4, 8.2$ Hz, 1H), 7.44 (s, 1H), 7.49 (d, $J = 2.0$ Hz, 1H), 7.50 (d, $J = 2.0$ Hz, 2H), 7.93 (d, $J = 3.1$ Hz, 1H), 7.95 (t, $J = 2.7$ Hz, 1H), 8.22 (d, $J = 16.4$ Hz, 1H), 8.39 (s, 1H). δ_{C} (CDCl₃, 100 MHz) 20.9, 51.5, 118.4, 127.8, 128.1, 128.7, 128.9, 131.4, 131.9, 135.6, 136.0, 141.6, 148.8, 160.0, 167.5.

3-[2-(Benzylideneamino)phenyl]acrylic acid methyl ester (1b)

δ_{H} (CDCl₃, 400 MHz) 3.78 (s, 3H), 6.49 (d, $J = 16.1$ Hz, 1H), 7.00 (d, $J = 7.5$ Hz, 1H), 7.24 (t, $J = 7.2$ Hz, 1H), 7.39 (ddd, $J = 1.4, 7.5, 15.0$ Hz, 1H), 7.46-7.51 (m, 3H), 7.62 (dd, $J = 0.7, 7.8$ Hz, 1H), 7.94-7.96 (m, 2H), 8.23 (d, $J = 16.1$ Hz, 1H), 8.37 (s, 1H). δ_{C} (CDCl₃, 100 MHz) 51.4, 118.7, 125.9, 127.3, 128.2, 128.7, 128.9, 131.1, 131.6, 135.9, 141.5, 151.2, 160.7, 167.5.

3-[2-(4-Methoxybenzylideneamino)-5-methylphenyl]acrylic acid methyl ester (1c)

δ_{H} (CDCl₃, 400 MHz) 2.37 (s, 3H), 3.78 (s, 3H), 3.88 (s, 3H), 6.46 (d, $J = 16.4$ Hz, 1H), 6.92 (d, $J = 8.2$ Hz, 1H), 6.99 (d, $J = 8.6$ Hz, 2H), 7.20 (d, $J = 7.8$ Hz, 1H), 7.42 (s, 1H), 7.88 (d, $J = 8.9$ Hz, 2H), 8.20 (d, $J = 16.4$ Hz, 1H), 8.31 (s, 1H). δ_{C} (CDCl₃, 100 MHz) 20.9, 51.5, 55.4, 114.1, 118.3, 118.6, 127.8, 128.0, 129.1, 130.6, 131.9, 135.2, 141.8, 149.2, 159.3, 162.3, 167.6.

3-[5-Methyl-2-(4-nitrobenzylideneamino)phenyl]acrylic acid methyl ester (1d)

δ_{H} (CDCl₃, 400 MHz) 2.40 (s, 3H), 3.79 (s, 3H), 6.46 (d, $J = 16.4$ Hz, 1H), 6.99 (d, $J = 8.2$ Hz, 1H), 7.23-7.26 (m, 1H), 7.47 (s, 1H), 8.11 (d, $J = 8.9$ Hz, 2H), 8.23 (d, $J = 16.1$ Hz, 1H), 8.34 (d, $J = 8.6$ Hz, 2H), 8.50 (s, 1H).

δ_{C} (CDCl₃, 100 MHz) 21.0, 51.6, 117.9, 118.9, 124.0, 127.9, 128.8, 129.5, 131.9, 137.1, 141.1, 141.3, 147.5, 149.3, 157.1, 167.4.

3-[2-(2-Bromobenzylideneamino)-5-methylphenyl]acrylic acid methyl ester (1e)

δ_{H} (CDCl₃, 400 MHz) 2.39 (s, 3H), 3.79 (s, 3H), 6.46 (d, $J = 16.1$ Hz, 1H), 6.98 (d, $J = 7.9$ Hz, 1H), 7.23 (dd, $J = 1.4, 7.8$ Hz, 1H), 7.33 (ddd, $J = 1.7, 7.9, 15.4$ Hz, 1H), 7.42 (d, $J = 7.8$ Hz, 1H), 7.45 (s, 1H), 7.62 (d, $J = 7.8$ Hz, 1H), 8.23 (d, $J = 16.4$ Hz, 1H), 8.30 (dd, $J = 1.7, 7.8$ Hz, 1H), 8.79 (s, 1H).

δ_{C} (CDCl₃, 100 MHz) 20.9, 51.5, 118.5, 118.6, 126.1, 127.7, 127.7, 128.5, 129.2, 131.9, 132.5, 133.1, 134.3, 136.2, 141.5, 148.4, 158.9, 167.5.

3-[5-Methyl-2-(6-methylpyridin-2-ylmethyleneamino)phenyl]acrylic acid methyl ester (1f)

δ_{H} (CDCl₃, 400 MHz) 2.37 (s, 3H), 2.62 (s, 3H), 3.78 (s, 3H), 6.45 (d, $J = 16.4$ Hz, 1H), 7.03 (d, $J = 7.9$ Hz, 1H), 7.21 (dd, $J = 1.4, 8.2$ Hz, 1H), 7.24 (d, $J = 8.2$ Hz, 1H), 7.44 (s, 1H), 7.71 (t, $J = 7.7$ Hz, 1H), 8.11 (d, $J = 7.8$ Hz, 1H), 8.26 (d, $J = 16.1$ Hz, 1H), 8.52 (s, 1H). δ_{C} (CDCl₃, 100 MHz) 20.9, 24.2, 51.5, 118.2, 118.5, 118.9, 124.9, 127.7, 128.6, 131.9, 136.4, 136.8, 141.5, 147.7, 153.8, 158.2, 160.7, 167.5.

3-[5-Methyl-2-(5-methylfuran-2-ylmethyleneamino)phenyl]acrylic acid methyl ester (1g)

δ_{H} (CDCl₃, 400 MHz) 2.36 (s, 3H), 2.44 (s, 3H), 3.77 (s, 3H), 6.17 (dd, $J = 0.7, 3.4$ Hz, 1H), 6.45 (d, $J = 16.1$ Hz, 1H), 6.87-6.89 (m, 2H), 7.17 (dd, $J = 1.7, 7.9$ Hz, 1H), 7.41 (s, 1H), 8.05 (s, 1H), 8.17 (d, $J = 16.0$ Hz, 1H). δ_{C} (CDCl₃, 100 MHz) 13.9, 20.8, 51.4, 108.7, 118.3, 118.5, 118.7, 127.7, 127.9, 131.8, 135.3, 141.7, 147.8, 149.2, 150.7, 156.8, 167.5.

3-[5-Methyl-2-(3-phenylallylideneamino)phenyl]acrylic acid methyl ester (1h)

δ_{H} (CDCl₃, 400 MHz) 2.37 (s, 3H), 3.79 (s, 3H), 6.45 (d, $J = 16.1$ Hz, 1H), 6.88 (d, $J = 7.9$ Hz, 1H), 7.15-8.19 (m, 11H). δ_{C} (CDCl₃, 100 MHz) 20.8, 51.4, 118.3, 118.4, 127.4, 127.6, 128.1, 128.6, 128.8, 129.5, 131.8, 135.4,

135.8, 141.5, 144.1, 148.8, 161.6, 167.4.

3-[2-(Ethoxycarbonylmethyleneamino)-5-methylphenyl]acrylic acid methyl ester (1i)

δ_{H} (CDCl₃, 400 MHz) 1.42 (t, $J = 7.2$ Hz, 3H), 2.38 (s, 3H), 3.78 (s, 3H), 4.42 (q, $J = 7.2$ Hz, 2H), 6.46 (d, $J = 16.1$ Hz, 1H), 6.89 (d, $J = 8.2$ Hz, 1H), 7.20 (d, $J = 8.2$ Hz, 1H), 7.44 (s, 1H), 7.81 (s, 1H), 8.07 (d, $J = 16.1$ Hz, 1H). δ_{C} (CDCl₃, 100 MHz) 14.1, 21.0, 51.6, 62.0, 118.0, 119.8, 128.2, 128.9, 131.7, 138.4, 140.5, 145.9, 151.3, 162.9, 167.2.

3-[2-(4-Methoxybenzylideneamino)-5-methylphenyl]-*N,N*-dimethylacrylamide (1j)

δ_{H} (CDCl₃, 400 MHz) 2.36 (s, 3H), 3.02 (s, 3H), 3.09 (s, 3H), 3.85 (s, 3H), 6.87 (d, $J = 8.2$ Hz, 1H), 6.94-6.99 (m, 3H), 7.14 (dd, $J = 1.5, 7.8$ Hz, 1H), 7.36 (d, $J = 1.4$ Hz, 1H), 7.87 (d, $J = 8.9$ Hz, 2H), 8.02 (d, $J = 15.7$ Hz, 1H), 8.28 (s, 1H). δ_{C} (CDCl₃, 100 MHz) 20.8, 35.7, 37.3, 55.3, 114.0, 118.6, 119.3, 128.7, 128.9, 129.2, 130.5, 130.8, 135.0, 139.5, 149.1, 158.9, 162.2, 167.1.

3-[2-(4-Methoxybenzylideneamino)phenyl]acrylonitrile (1k)

δ_{H} (CDCl₃, 400 MHz) 3.90 (s, 3H), 6.00 (d, $J = 16.8$ Hz, 1H), 7.01-7.03 (m, 3H), 7.23 (t, $J = 8.6$ Hz, 1H), 7.43 (ddd, $J = 1.2, 7.8, 15.2$ Hz, 1H), 7.49 (d, $J = 7.0$ Hz, 1H), 7.86-7.92 (m, 3H), 8.31 (s, 1H). δ_{C} (CDCl₃, 100 MHz) 55.4, 97.0, 114.3, 118.8, 118.9, 125.7, 127.1, 127.3, 128.6, 130.8, 131.9, 147.8, 151.2, 160.3, 162.7.

***N*-(4-Methoxybenzylidene)-(4-methyl-2-styrylphenyl)amine (1l)**

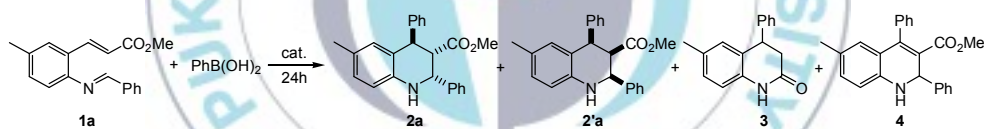
δ_{H} (CDCl₃, 400 MHz) 2.43 (s, 3H), 3.89 (s, 3H), 6.94 (d, $J = 7.8$ Hz, 1H), 7.03 (d, $J = 8.6$ Hz, 2H), 7.11-7.17 (m, 2H), 7.26-7.28 (m, 1H), 7.35-7.39 (m, 2H), 7.54-7.56 (m, 3H), 7.69 (dd, $J = 3.1, 16.4$ Hz, 1H), 7.92-7.94 (m, 2H), 8.36 (s, 1H). δ_{C} (CDCl₃, 100 MHz) 21.0, 55.3, 114.1, 118.3, 125.4, 126.1, 127.2, 128.5, 129.0, 129.2, 129.5, 130.4, 130.8, 135.1, 137.9, 147.8, 158.6, 162.1.

***N*-Benzylidene-(4-methyl-2-vinylphenyl)amine (1m)**

δ_{H} (CDCl₃, 400 MHz) 2.39 (s, 3H), 5.29 (dd, $J = 1.4, 11.0$ Hz, 1H), 5.76 (dd, $J = 1.4, 17.8$ Hz, 1H), 6.91 (d, $J = 8.2$ Hz, 1H), 7.12 (dd, $J = 1.7, 7.8$ Hz, 1H), 7.26 (dd, $J = 10.9, 17.8$ Hz, 1H), 7.42 (d, $J = 0.7$ Hz, 1H), 7.48-7.50 (m, 3H), 7.93-7.95 (m, 2H), 8.39 (s, 1H). δ_{C} (CDCl₃, 100 MHz) 21.0, 114.4, 118.1, 126.1, 128.7, 128.8, 129.3, 131.1, 133.3, 135.4, 136.4, 147.3, 159.4.

4.8. Systematic screen

Reactions were conducted at 0.1 M concentration in sealed vials under argon. To a solution of **1a** in solvent were added catalyst (5 mol %, 10 mol % Rh), base (2 equiv), additive, and phenylboronic acid (2.5 equiv). The resulting mixture was heated with stirring for 24 hours at the reported temperature. After the reaction was completed (by TLC), the mixture was cooled, quenched with distilled water, extracted with CH₂Cl₂ (three times), dried over MgSO₄, and concentrated *in vacuo*. Yields and the ratio of two isomers were determined by ¹H NMR using trichloroethylene as an internal standard. Trace amount of compound **4** was observed in most of the reactions.



Entry	Catalyst	Base	Additive	Solvent	$T(^{\circ}\text{C})$	1a (%)	2a+2'a	2a:2'a	3 (%)
1	[Rh(OH)(cod)] ₂	-	-	dioxane	60	46	35	50:50	10
2	[Rh(OH)(cod)] ₂	KOH ^a	-	dioxane	60	74	15	50:50	-
3	[Rh(OH)(cod)] ₂	-	MS 4Å ^b	dioxane	60	32	51	50:50	10
4	[Rh(OH)(cod)] ₂	KOH ^a	MS 4Å ^b	dioxane	60	85	13	48:52	-
5	[Rh(OH)(cod)] ₂	NEt ₃	-	dioxane	60	10	90	67:33	-
6	[Ir(cod)Cl] ₂	NEt ₃	-	toluene	60	100	-	-	-
7	[Rh(OH)(cod)] ₂	NEt ₃	-	dioxane	80	-	100	71:29	-

8	[Rh(OH)(cod)] ₂	NEt ₃	-	toluene	80	33	66	75:25	-
9	[Rh(OH)(cod)] ₂	NEt ₃	-	THF	80	4	95	33:67	-
10	[Rh(OH)(cod)] ₂	NEt ₃	-	acetone	80	29	71	29:71	-
11	[Rh(OH)(cod)] ₂	KOH ^a	-	dioxane	80	-	79	78:22	17
12	[Rh(OH)(cod)] ₂	KOH	-	dioxane	80	6	75	67:33	15
13	[Rh(OH)(cod)] ₂	NaOH ^a	-	dioxane	80	9	65	71:29	13
14	[Rh(OH)(cod)] ₂	NaOH	-	dioxane	80	-	87	70:30	13
15	[Rh(OH)(cod)] ₂	Na ₂ CO ₃	-	dioxane	80	8	66	62:38	13
16	[Rh(OH)(cod)] ₂	K ₂ CO ₃	-	dioxane	80	-	81	70:30	16
17	[Rh(OH)(cod)] ₂	Cs ₂ CO ₃	-	dioxane	80	-	100	42:58	-
18	[Rh(OH)(cod)] ₂	K ₃ PO ₄	-	dioxane	80	-	100	72:28	-
19	[Rh(OH)(cod)] ₂	-	-	dioxane	80	7	70	67:33	16
20	[Rh(OH)(cod)] ₂	-	H ₃ BO ₃ ^c	dioxane	80	-	52	75:25	32
21	[Rh(OH)(cod)] ₂	K ₃ PO ₄	H ₂ O ^d	dioxane	80	-	40	72:28	-
22	[Rh(OH)(cod)] ₂	K ₃ PO ₄	MS 4Å ^b	dioxane	80	-	100	75:25	-
23	[Rh(OH)(cod)] ₂	K ₃ PO ₄	-	dioxane	60	-	100	71:29	-
24	[Rh(OH)(cod)] ₂	K ₃ PO ₄	-	dioxane	40	60	40	71:29	-
25	[Rh(OH)(cod)] ₂	K ₃ PO ₄	-	dioxane	RT	100	-	-	-
26 ^e	[Rh(OH)(cod)] ₂	K ₃ PO ₄	-	dioxane	60	-	100	75:25	-
27 ^f	[Rh(OH)(cod)] ₂	K ₃ PO ₄	-	dioxane	60	4	93	71:29	3

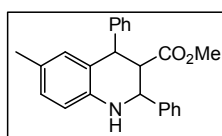
^a Performed with 0.3 equiv of base. ^b Performed with Molecular Sieves 4Å (480 mg/1 mmol substrate). ^c Performed with 1.2 equiv of H₃BO₃. ^d Performed in dioxane/H₂O (10/1). ^e Performed with 2 mol% [Rh(OH)(cod)]₂ (4mol % Rh). ^f Performed with 1 mol % [Rh(OH)(cod)]₂ (2mol % Rh).

4.9. General procedure for rhodium(I)-catalyzed tandem conjugate addition-Mannich cyclization reaction of imine-substituted electron-deficient alkenes **1** with arylboronic acids

To a solution of the substrate **1** (0.15 mmol) in 1,4-dioxane (0.1 M) were added [Rh(OH)(cod)]₂, K₃PO₄ (2 equiv, 0.3 mmol), and boronic acid (2.5

equiv, 0.375 mmol). The resulting mixture was stirred at the reported temperature for 1-48 hours. After the reaction was completed, the reaction mixture was quenched with distilled water, extracted with CH₂Cl₂ (three times), washed with brine, dried over MgSO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc : *n*-Hexane = 1:2~1:10) to give the corresponding product **2**.

6-Methyl-2,4-diphenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2a)

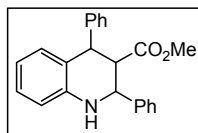


2 mol % [Rh(OH)(cod)]₂ at 80 °C for 1 h

a pale yellow solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 77:23 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 3.35 (dd, J = 4.1, 7.2 Hz, 1H), 3.42 (s, 3H), 4.30 (d, J = 7.2 Hz, 1H), 4.71 (d, J = 4.1 Hz, 1H), 6.55 (s, 1H), 6.60 (d, J = 7.9 Hz, 1H), 6.90 (d, J = 7.8 Hz, 1H), 7.16-7.42 (m, 10H). δ_{C} (CDCl₃, 100 MHz) 20.5, 42.6, 51.2, 52.0, 54.6, 114.1, 121.8, 126.3, 126.5, 126.6, 126.9, 127.7, 127.9, 128.2, 128.3, 128.6, 129.3, 130.8, 141.4, 141.7, 144.9, 171.7. Representative signals corresponding to the minor isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 3.13 (s, 3H), 3.24 (dd, J = 3.2, 6.0 Hz, 1H), 4.66 (d, J = 5.8 Hz, 1H), 4.87 (d, J = 3.1 Hz, 1H), 6.63 (d, J = 8.2 Hz, 1H), 6.66 (s, 1H), 6.90 (d, J = 7.8 Hz, 1H), 7.16-7.42 (m, 10H). δ_{C} (CDCl₃, 100 MHz) 20.5, 47.4, 50.6, 53.0, 58.6, 114.5, 114.8, 121.8, 125.2, 126.1, 127.0, 127.1, 128.1, 128.4, 128.5, 128.9, 129.5, 129.8, 140.8, 141.2, 142.5, 169.8. ν_{max} (NaCl)/cm⁻¹ 3384, 3025, 2921, 2852, 2351, 1735, 1617, 1508, 1454, 1360, 1264, 1219, 1165, 1088, 1029, 811, 752, 701. HREIMS m/z 357.1728 (M)⁺, calcd for C₂₄H₂₃NO₂ 357.1729.

2,4-Diphenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2b)

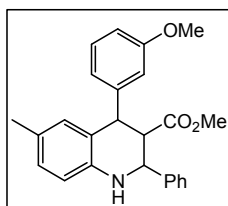


2 mol % [Rh(OH)(cod)]₂ at 60 °C for 12 h

a yellow oil (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 63:37 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 3.41 (dd, $J = 4.4, 7.9$ Hz, 1H), 3.43 (s, 3H), 4.32 (d, $J = 7.9$ Hz, 1H), 4.76 (d, $J = 4.4$ Hz, 1H), 6.62-7.44 (m, 14H). δ_{C} (CDCl₃, 100 MHz) 42.2, 51.2, 51.7, 54.7, 113.8, 117.7, 122.0, 126.3, 126.6, 127.4, 127.8, 128.3, 128.6, 129.3, 130.5, 141.5, 143.6, 144.5, 171.5. Representative signals corresponding to the minor isomer: δ_{H} (CDCl₃, 400 MHz) 3.14 (s, 3H), 3.26 (dd, $J = 3.3, 5.9$ Hz, 1H), 4.69 (d, $J = 6.1$ Hz, 1H), 4.92 (d, $J = 3.5$ Hz, 1H), 6.62-7.44 (m, 14H). δ_{C} (CDCl₃, 100 MHz) 47.3, 50.6, 52.8, 58.4, 114.5, 117.6, 121.6, 126.4, 126.5, 127.0, 127.2, 128.1, 128.4, 128.9, 129.5, 140.6, 141.0, 144.9, 169.8. ν_{max} (NaCl)/cm⁻¹ 3392, 3028, 2951, 2855, 2356, 1735, 1605, 1490, 1454, 1434, 1366, 1267, 1162, 1117, 1077, 1029, 802, 750, 701. HREIMS m/z 343.1570 (M)⁺, calcd for C₂₃H₂₁NO₂ 343.1572.

4-(3-Methoxyphenyl)-6-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2c)

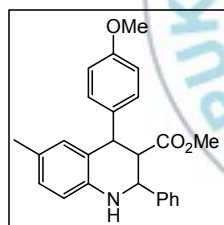


2 mol % [Rh(OH)(cod)]₂ at 80 °C for 1 h

a pale yellow solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 77:23 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 3.34 (dd, $J = 4.1, 6.8$ Hz, 1H), 3.42 (s, 3H), 3.77 (s, 3H), 4.27 (d, $J = 6.8$ Hz, 1H), 4.71 (d, $J = 4.1$ Hz, 1H), 6.58-7.41 (m, 12H). δ_{C} (CDCl₃, 100 MHz) 20.5, 42.7, 51.2, 51.9, 54.6, 55.1, 114.1, 121.6, 121.7, 126.3, 126.6, 127.0, 127.7, 127.9, 128.2, 128.3, 128.6, 129.2, 130.7, 141.3, 141.6, 146.6, 159.4, 171.6. Representative signals corresponding to the minor isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 3.16 (s, 3H), 3.23 (dd, $J = 3.3, 6.0$ Hz, 1H), 3.75 (s, 3H), 4.62 (d, $J = 5.8$ Hz, 1H), 4.86 (d, $J = 3.1$ Hz, 1H), 6.58-7.41 (m, 12H). δ_{C} (CDCl₃, 100 MHz) 20.5, 47.5, 50.6, 52.9, 55.0, 58.6, 111.0, 112.7, 113.3, 114.5, 114.7, 119.6, 121.9, 128.1, 128.9, 129.3, 129.3, 129.7, 140.8, 142.4, 142.8, 159.4, 169.8. ν_{max} (NaCl)/cm⁻¹ 3382, 3031, 2922, 2855, 2362, 1734, 1599, 1508, 1489, 1455, 1436, 1357, 1264, 1216, 1158, 1048, 811, 738, 701. HREIMS m/z 387.1832 (M)⁺, calcd for C₂₅H₂₅NO₃ 387.1834.

4-(4-Methoxyphenyl)-6-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2d)



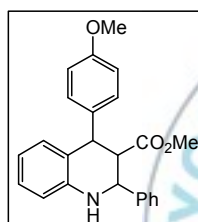
2 mol % [Rh(OH)(cod)]₂ at 80 °C for 1 h

a white solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 71:29 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 3.30 (dd, $J = 4.1, 7.2$ Hz, 1H), 3.42 (s, 3H), 3.79 (s, 3H), 4.24 (d, $J = 7.2$ Hz, 1H), 4.69 (d, $J = 4.1$ Hz, 1H), 6.55 (s, 1H), 6.58 (d, $J = 8.2$ Hz, 1H), 6.81-7.41 (m, 10H). δ_{C} (CDCl₃, 100 MHz) 20.5, 41.7, 51.2, 52.1, 54.7, 55.1, 113.6, 114.1, 122.2,

126.3, 126.6, 127.7, 128.1, 128.2, 128.6, 130.2, 130.7, 136.9, 141.3, 141.7, 158.1, 171.7. Representative signals corresponding to the minor isomer: $\delta_{\text{H}}(\text{CDCl}_3, 400 \text{ MHz})$ 2.14 (s, 3H), 3.15 (s, 3H), 3.20 (dd, $J = 3.4, 5.8 \text{ Hz}$, 1H), 3.80 (s, 3H), 4.60 (d, $J = 5.8 \text{ Hz}$, 1H), 4.86 (d, $J = 3.1 \text{ Hz}$, 1H), 6.61 (d, $J = 8.2 \text{ Hz}$, 1H), 6.65 (s, 1H), 6.81-7.41 (m, 10H). $\delta_{\text{C}}(\text{CDCl}_3, 100 \text{ MHz})$ 20.6, 46.5, 50.6, 53.1, 55.1, 58.6, 114.8, 126.9, 127.8, 128.0, 129.2, 130.5, 133.1, 140.8, 141.7, 158.5, 169.9 (8 carbons are missing due to overlapping). $\nu_{\text{max}} (\text{NaCl})/\text{cm}^{-1}$ 3393, 3025, 2920, 2849, 2362, 1735, 1615, 1508, 1456, 1363, 1249, 1175, 1105, 1032, 812, 743, 701. HREIMS m/z 387.1833 (M^+), calcd for $\text{C}_{25}\text{H}_{25}\text{NO}_3$ 387.1834.

4-(4-Methoxyphenyl)-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2e)

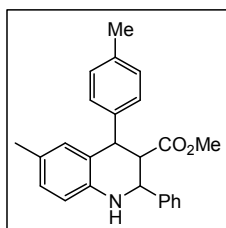


2 mol % $[\text{Rh}(\text{OH})(\text{cod})]_2$ at $80 \text{ }^\circ\text{C}$ for 1 h
a white solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 83:17 mixture of isomers. Signals corresponding to the major isomer: $\delta_{\text{H}}(\text{CDCl}_3, 400 \text{ MHz})$ 3.35 (dd, $J = 4.1, 7.9 \text{ Hz}$, 1H), 3.42 (s, 3H), 3.78 (s, 3H), 4.25 (d, $J = 7.8 \text{ Hz}$, 1H), 4.74 (d, $J = 4.4 \text{ Hz}$, 1H), 6.63-7.43 (m, 13H). $\delta_{\text{C}}(\text{CDCl}_3, 100 \text{ MHz})$ 41.4, 51.2, 51.8, 54.8, 55.1, 113.6, 113.8, 117.7, 122.3, 126.6, 127.4, 127.8, 128.3, 130.2, 130.4, 136.6, 141.6, 143.6, 158.1, 171.6. Representative signals corresponding to the minor isomer: $\delta_{\text{H}}(\text{CDCl}_3, 400 \text{ MHz})$ 3.15 (s, 3H), 3.22 (dd, $J = 3.3, 6.0 \text{ Hz}$, 1H), 3.79 (s, 3H), 4.62 (d, $J = 6.2 \text{ Hz}$, 1H), 4.90 (d, $J = 3.1 \text{ Hz}$, 1H), 6.61- 7.43 (m, 13H). $\delta_{\text{C}}(\text{CDCl}_3, 100 \text{ MHz})$ 46.5, 50.6, 53.0, 53.4, 58.4, 113.7, 114.4, 114.5, 122.1, 126.3, 126.9, 127.2, 127.9, 128.1, 128.1, 128.6, 128.9, 129.4,

130.5, 133.0, 140.7, 144.8, 158.5, 169.9. ν_{\max} (NaCl)/ cm^{-1} 3382, 3018, 2922, 2852, 2360, 1736, 1650, 1606, 1541, 1509, 1456, 1366, 1249, 1163, 1111, 1032, 831, 751, 701. HREIMS m/z 373.1680 (M)⁺, calcd for C₂₄H₂₃NO₃ 373.1678.

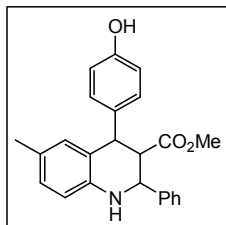
6-Methyl-2-phenyl-4-*p*-tolyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2f)



2 mol % [Rh(OH)(cod)]₂ at 80 °C for 1 h
a pale yellow solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 71:29 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 2.33 (s, 3H), 3.32 (dd, J = 4.1, 7.2 Hz, 1H), 3.42 (s, 3H), 4.27 (d, J = 6.8 Hz, 1H), 4.70 (d, J = 4.1 Hz, 1H), 6.57 (s, 1H), 6.60 (d, J = 8.2 Hz, 1H), 6.89 (dd, J = 1.9, 7.7 Hz, 1H), 7.04-7.42 (m, 9H). δ_{C} (CDCl₃, 100 MHz) 20.5, 21.0, 42.2, 51.2, 52.1, 54.6, 114.1, 122.1, 126.3, 126.6, 127.7, 128.1, 128.2, 128.6, 129.0, 129.1, 130.8, 135.9, 141.7, 141.9, 171.7. Representative signals corresponding to the minor isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 2.34 (s, 3H), 3.16 (s, 3H), 3.22 (dd, J = 3.2, 6.0 Hz, 1H), 4.62 (d, J = 5.8 Hz, 1H), 4.87 (d, J = 3.4 Hz, 1H), 6.64 (d, J = 8.2 Hz, 1H), 6.66 (s, 1H), 6.89 (dd, J = 1.9, 7.7 Hz, 1H), 7.04-7.42 (m, 9H). δ_{C} (CDCl₃, 100 MHz) 20.5, 21.1, 47.0, 50.6, 53.0, 58.6, 114.8, 122.1, 127.0, 127.8, 128.0, 129.3, 129.3, 136.5, 138.0, 140.8, 141.4, 142.3, 169.9 (2 carbons are missing due to overlapping). ν_{\max} (NaCl)/ cm^{-1} 3376, 3019, 2921, 2849, 2362, 1734, 1615, 1508, 1451, 1431, 1363, 1267, 1218, 1165, 1085, 1026, 812, 743, 700. HREIMS m/z 371.1887 (M)⁺, calcd for C₂₅H₂₅NO₂ 371.1885.

4-(4-Hydroxyphenyl)-6-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2g)

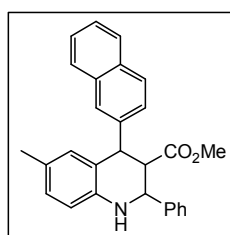


2 mol % [Rh(OH)(cod)]₂ at 80 °C for 1 h

a pale yellow solid (EtOAc : *n*-Hexane = 1 : 3)

The compound exists as a 77:23 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 3.32 (dd, $J = 4.3, 7.4$ Hz, 1H), 3.43 (s, 3H), 4.22 (d, $J = 7.5$ Hz, 1H), 4.70 (d, $J = 4.1$ Hz, 1H), 5.45 (br s, 1H), 6.56 (s, 1H), 6.59 (d, $J = 8.2$ Hz, 1H), 6.67-7.41 (m, 10H). δ_{C} (CDCl₃, 100 MHz) 20.5, 41.6, 51.3, 52.1, 54.8, 114.1, 115.2, 122.3, 126.3, 126.5, 127.7, 128.3, 128.6, 130.4, 130.7, 136.6, 141.2, 141.6, 154.2, 172.1. Representative signals corresponding to the minor isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 3.17 (s, 3H), 3.23 (dd, $J = 3.2, 6.0$ Hz, 1H), 4.59 (d, $J = 5.8$ Hz, 1H), 4.85 (d, $J = 3.1$ Hz, 1H), 6.62-7.41 (m, 12H). δ_{C} (CDCl₃, 100 MHz) 20.5, 46.4, 50.9, 53.3, 58.5, 115.0, 115.2, 122.2, 127.0, 127.9, 128.1, 128.2, 128.9, 129.3, 130.6, 132.8, 140.6, 142.2, 154.7, 170.5. ν_{max} (NaCl)/cm⁻¹ 3365, 3025, 2923, 2849, 2362, 1733, 1717, 1651, 1615, 1508, 1456, 1436, 1363, 1261, 1218, 1168, 1097, 1026, 834, 808, 735, 701. HREIMS m/z 373.1680 (M)⁺, calcd for C₂₄H₂₃NO₃ 373.1678.

6-Methyl-4-naphthalen-2-yl-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2h)

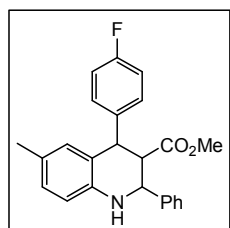


2 mol % $[\text{Rh}(\text{OH})(\text{cod})]_2$ at 80 °C for 1 h

a pale yellow solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 83:17 mixture of isomers. Signals corresponding to the major isomer: $\delta_{\text{H}}(\text{CDCl}_3, 400 \text{ MHz})$ 2.10 (s, 3H), 3.41 (s, 3H), 3.49 (dd, $J = 4.1, 7.9 \text{ Hz}$, 1H), 4.45 (d, $J = 7.9 \text{ Hz}$, 1H), 4.77 (d, $J = 4.5 \text{ Hz}$, 1H), 6.55 (s, 1H), 6.63 (d, $J = 8.2 \text{ Hz}$, 1H), 6.90-7.83 (m, 13H). $\delta_{\text{C}}(\text{CDCl}_3, 100 \text{ MHz})$ 20.4, 42.4, 51.2, 51.7, 55.0, 114.1, 121.8, 125.5, 125.9, 126.4, 126.6, 127.0, 127.2, 127.5, 127.8, 128.1, 128.3, 128.6, 129.4, 130.9, 132.3, 133.2, 141.4, 141.7, 142.0, 171.6. Representative signals corresponding to the minor isomer: $\delta_{\text{H}}(\text{CDCl}_3, 400 \text{ MHz})$ 2.11 (s, 3H), 3.09 (s, 3H), 3.32 (dd, $J = 3.1, 6.1 \text{ Hz}$, 1H), 4.83 (d, $J = 5.8 \text{ Hz}$, 1H), 4.93 (d, $J = 3.1 \text{ Hz}$, 1H), 6.67 (d, $J = 7.8 \text{ Hz}$, 1H), 6.70 (s, 1H), 6.90-7.83 (m, 13H). $\delta_{\text{C}}(\text{CDCl}_3, 100 \text{ MHz})$ 20.5, 47.6, 50.6, 52.9, 58.7, 114.5, 114.8, 121.8, 125.2, 125.6, 125.7, 125.8, 126.2, 126.3, 127.4, 128.0, 128.1, 128.9, 129.9, 132.6, 133.4, 133.6, 138.8, 140.7, 142.5, 169.8. $\nu_{\text{max}}(\text{NaCl})/\text{cm}^{-1}$ 3376, 3031, 2921, 2855, 2362, 1734, 1717, 1649, 1620, 1508, 1456, 1357, 1261, 1216, 1165, 1026, 814, 748, 698. HREIMS m/z 407.1885 (M^+), calcd for $\text{C}_{28}\text{H}_{25}\text{NO}_2$ 407.1885.

4-(4-Fluorophenyl)-6-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2i)

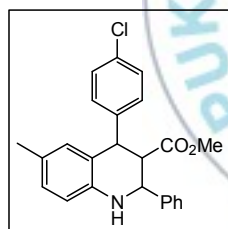


2 mol % [Rh(OH)(cod)]₂ at 60 °C for 24 h

a white solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 77:23 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 3.33 (dd, $J = 4.3$, 8.0 Hz, 1H), 3.43 (s, 3H), 4.26 (d, $J = 8.2$ Hz, 1H), 4.72 (d, $J = 4.1$ Hz, 1H), 6.49 (s, 1H), 6.59 (d, $J = 8.2$ Hz, 1H), 6.88-7.43 (m, 10H). δ_{C} (CDCl₃, 100 MHz) 20.4, 41.4, 51.2, 52.0, 54.9, 114.0, 115.0, 115.2, 121.8, 126.5, 127.8, 128.4, 130.8, 140.3, 140.4, 141.2, 141.6, 160.2, 162.7, 171.5. Representative signals corresponding to the minor isomer: δ_{H} (CDCl₃, 400 MHz) 2.15 (s, 3H), 3.14 (s, 3H), 3.21 (dd, $J = 3.3$, 6.0 Hz, 1H), 4.65 (d, $J = 5.8$ Hz, 1H), 4.86 (d, $J = 3.1$ Hz, 1H), 6.62-7.41 (m, 12H). δ_{C} (CDCl₃, 100 MHz) 20.5, 46.5, 50.6, 53.1, 58.5, 114.6, 121.6, 126.3, 126.9, 127.9, 129.1, 131.1, 133.1, 136.9, 137.9, 140.6, 142.5, 160.7, 163.1, 169.7. ν_{max} (NaCl)/cm⁻¹ 3383, 3028, 2917, 2850, 1738, 1603, 1507, 1454, 1220, 1158, 1094, 1015, 841, 812, 737, 701. HREIMS m/z 375.1634 (M)⁺, calcd for C₂₄H₂₂FNO₂ 375.1635.

4-(4-Chlorophenyl)-6-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2j)



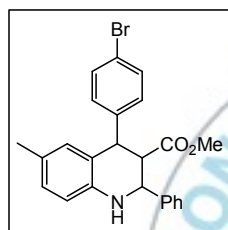
2 mol % [Rh(OH)(cod)]₂ at 80 °C for 1 h

a pale yellow solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 91:9 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 2.13 (s, 3H), 3.33 (dd, $J = 4.3$, 8.0 Hz, 1H), 3.44 (s, 3H), 4.24 (d, $J = 8.2$ Hz, 1H), 4.72 (d, $J = 4.5$ Hz, 1H), 6.47 (s, 1H), 6.58 (d, $J = 7.9$ Hz, 1H), 6.88-7.43 (m, 10H). δ_{C} (CDCl₃, 100 MHz) 20.4, 41.6, 51.3, 51.8, 55.0, 114.1, 121.5, 126.5, 127.0, 127.8, 128.3,

128.4, 130.6, 130.7, 132.2, 141.2, 141.5, 143.2, 171.4. Representative signals corresponding to the minor isomer: $\delta_{\text{H}}(\text{CDCl}_3, 400 \text{ MHz})$ 2.14 (s, 3H), 3.15 (s, 3H), 3.20 (dd, $J = 3.4, 6.1 \text{ Hz}$, 1H), 4.63 (d, $J = 5.8 \text{ Hz}$, 1H), 4.85 (d, $J = 3.1 \text{ Hz}$, 1H), 6.61-7.43 (m, 12H). $\delta_{\text{C}}(\text{CDCl}_3, 100 \text{ MHz})$ 20.8, 43.3, 50.6, 53.4, 55.0, 114.6, 124.7, 127.9, 128.2, 128.5, 128.6, 128.7, 129.0, 129.7, 133.3, 133.5, 137.9, 146.8, 148.8, 167.5. $\nu_{\text{max}}(\text{NaCl})/\text{cm}^{-1}$ 3365, 3021, 2922, 2849, 2356, 1735, 1615, 1508, 1489, 1455, 1241, 1218, 1165, 1089, 1014, 813, 740, 700. HREIMS m/z 391.1341 (M^+), calcd for $\text{C}_{24}\text{H}_{22}\text{ClNO}_2$ 391.1339.

4-(4-Bromophenyl)-6-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2k)

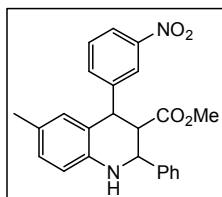


5 mol % $[\text{Rh}(\text{OH})(\text{cod})]_2$ at $80 \text{ }^\circ\text{C}$ for 48 h
a white solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 63:37 mixture of isomers. Signals corresponding to the major isomer: $\delta_{\text{H}}(\text{CDCl}_3, 400 \text{ MHz})$ 2.13 (s, 3H), 3.33 (dd, $J = 4.3, 8.0 \text{ Hz}$, 1H), 3.44 (s, 3H), 4.23 (d, $J = 8.2 \text{ Hz}$, 1H), 4.32 (br s, 1H), 4.72 (d, $J = 4.1 \text{ Hz}$, 1H), 6.47 (s, 1H), 6.57-7.43 (m, 11H). $\delta_{\text{C}}(\text{CDCl}_3, 100 \text{ MHz})$ 20.4, 41.6, 51.3, 51.8, 55.0, 114.1, 120.4, 121.4, 126.3, 126.5, 127.8, 128.3, 128.4, 128.6, 131.1, 131.4, 141.2, 141.5, 143.7, 171.4. Representative signals corresponding to the minor isomer: $\delta_{\text{H}}(\text{CDCl}_3, 400 \text{ MHz})$ 2.14 (s, 3H), 3.15 (s, 3H), 3.20 (dd, $J = 3.2, 6.0 \text{ Hz}$, 1H), 4.06 (br s, 1H), 4.62 (d, $J = 6.2 \text{ Hz}$, 1H), 4.85 (d, $J = 3.1 \text{ Hz}$, 1H), 6.59-7.43 (m, 12H). $\delta_{\text{C}}(\text{CDCl}_3, 100 \text{ MHz})$ 20.5, 46.7, 50.7, 52.9, 58.6, 114.9, 120.9, 121.2, 127.0, 127.1, 128.1, 128.2, 128.3, 129.1, 130.6, 131.3, 140.3, 140.6, 142.5, 169.5. $\nu_{\text{max}}(\text{NaCl})/\text{cm}^{-1}$

3382, 3019, 2922, 2849, 2351, 1734, 1717, 1615, 1508, 1487, 1456, 1363, 1258, 1216, 1167, 1068, 1012, 808, 743, 698. HREIMS m/z 435.0830 (M)⁺, calcd for C₂₄H₂₂BrNO₂ 435.0834.

6-Methyl-4-(3-nitrophenyl)-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2l)

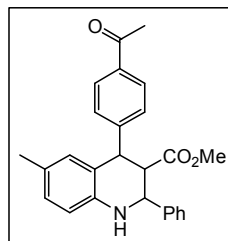


5 mol % [Rh(OH)(cod)]₂ at 80 °C for 48 h

a yellow solid (EtOAc : *n*-Hexane = 1 : 5)

The compound exists as a 83:17 mixture of isomers. Signals corresponding to the major isomer: δ_H (CDCl₃, 400 MHz) 2.11 (s, 3H), 3.44 (dd, J = 4.4, 9.2 Hz, 1H), 3.46 (s, 3H), 4.37 (d, J = 9.2 Hz, 1H), 4.41 (br s, 1H), 4.80 (d, J = 4.4 Hz, 1H), 6.36 (s, 1H), 6.60 (d, J = 8.1 Hz, 1H), 6.90-8.18 (m, 10H). δ_C (CDCl₃, 100 MHz) 20.4, 41.5, 51.5, 51.6, 55.3, 114.2, 120.7, 121.8, 124.3, 126.5, 127.1, 128.0, 128.4, 128.8, 129.2, 130.3, 135.8, 146.7, 148.3, 171.0 (2 carbons are missing due to overlapping). Representative signals corresponding to the minor isomer: δ_H (CDCl₃, 400 MHz) 2.14 (s, 3H), 3.15 (s, 3H), 3.27 (dd, J = 3.3, 6.2 Hz, 1H), 3.46 (s, 3H), 4.80 (m, 1H), 4.88 (d, J = 3.0 Hz, 1H), 6.52 (s, 1H), 6.65 (d, J = 8.1 Hz, 1H), 6.90-8.18 (m, 10H). δ_C (CDCl₃, 100 MHz) 20.5, 46.8, 50.8, 53.0, 58.4, 115.1, 120.3, 122.3, 124.7, 126.3, 127.3, 128.3, 128.7, 135.7, 140.3, 142.6, 143.6, 144.9, 169.3 (3 carbons are missing due to overlapping). ν_{max} (NaCl)/cm⁻¹ 3393, 3019, 2922, 2853, 2362, 1737, 1617, 1527, 1508, 1451, 1349, 1266, 1167, 1117, 1080, 1023, 812, 736, 699. HREIMS m/z 402.1581 (M)⁺, calcd for C₂₄H₂₂N₂O₄ 402.1580.

4-(4-Acetylphenyl)-6-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2m)

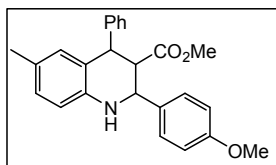


5 mol % [Rh(OH)(cod)]₂ at 80 °C for 48 h

a pale yellow solid (EtOAc : *n*-Hexane = 1 : 3)

The compound exists as a 67:33 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 2.12 (s, 3H), 2.59 (s, 3H), 3.42 (dd, $J = 4.1, 8.6$ Hz, 1H), 3.44 (s, 3H), 4.33 (d, $J = 8.6$ Hz, 1H), 4.76 (d, $J = 4.1$ Hz, 1H), 6.43 (s, 1H), 6.60 (d, $J = 8.2$ Hz, 1H), 6.89-7.91 (m, 10H). δ_{C} (CDCl₃, 100 MHz) 20.4, 26.5, 42.0, 51.3, 51.5, 55.1, 114.1, 121.2, 126.5, 127.0, 128.2, 128.3, 128.4, 129.7, 130.5, 135.6, 141.2, 141.5, 150.2, 171.3, 197.8 (1 carbon is missing due to overlapping). Representative signals corresponding to the minor isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 2.60 (s, 3H), 3.13 (s, 3H), 3.24 (dd, $J = 3.2, 6.0$ Hz, 1H), 4.73 (d, $J = 5.8$ Hz, 1H), 4.87 (d, $J = 3.1$ Hz, 1H), 6.57 (s, 1H), 6.64 (d, $J = 8.2$ Hz, 1H), 6.89-7.91 (m, 10H). δ_{C} (CDCl₃, 100 MHz) 20.5, 26.5, 47.2, 50.7, 52.8, 58.6, 115.0, 120.9, 126.3, 127.1, 127.9, 128.5, 128.6, 129.1, 129.8, 136.0, 140.5, 142.5, 147.1, 169.4, 199.6 (1 carbon is missing due to overlapping). ν_{max} (NaCl)/cm⁻¹ 3375, 3025, 2920, 2849, 2356, 1734, 1683, 1605, 1508, 1456, 1435, 1417, 1361, 1268, 1168, 1119, 1016, 958, 842, 813, 736, 701. HREIMS m/z 399.1837 (M)⁺, calcd for C₂₆H₂₅NO₃ 399.1834.

2-(4-Methoxyphenyl)-6-methyl-4-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2n)

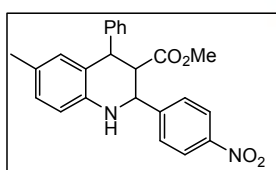


2 mol % [Rh(OH)(cod)]₂ at 80 °C for 1 h

a pale yellow solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 83:17 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 2.13 (s, 3H), 3.32 (dd, $J = 4.1, 7.2$ Hz, 1H), 3.44 (s, 3H), 3.78 (s, 3H), 4.28 (d, $J = 7.2$ Hz, 1H), 4.67 (d, $J = 4.1$ Hz, 1H), 6.54 (s, 1H), 6.59 (d, $J = 8.2$ Hz, 1H), 6.78-7.34 (m, 10H). δ_{C} (CDCl₃, 100 MHz) 20.4, 42.5, 51.2, 52.0, 54.2, 55.1, 113.6, 114.1, 121.9, 126.4, 126.8, 127.7, 128.2, 128.3, 129.3, 130.7, 133.7, 141.4, 144.9, 159.0, 171.7. Representative signals corresponding to the minor isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 3.16 (s, 3H), 3.20 (dd, $J = 3.3, 6.0$ Hz, 1H), 3.80 (s, 3H), 4.64 (d, $J = 6.2$ Hz, 1H), 4.82 (d, $J = 3.4$ Hz, 1H), 6.65-7.34 (m, 12H). δ_{C} (CDCl₃, 100 MHz) 20.5, 47.3, 50.6, 53.1, 55.2, 58.0, 113.8, 114.8, 121.8, 127.0, 127.5, 127.9, 129.5, 132.8, 141.2, 142.5, 159.2, 169.9 (3 carbons are missing due to overlapping). ν_{max} (NaCl)/cm⁻¹ 3384, 3025, 2917, 2850, 2360, 1739, 1611, 1508, 1456, 1362, 1248, 1174, 1110, 1032, 833, 810, 737, 702. HREIMS m/z 387.1832 (M)⁺, calcd for C₂₅H₂₅NO₃ 387.1834.

6-Methyl-2-(4-nitrophenyl)-4-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2o)



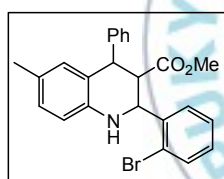
2 mol % [Rh(OH)(cod)]₂ at 80 °C for 1 h

a yellow solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 59:41 mixture of isomers. Signals corresponding

to the major isomer: $\delta_{\text{H}}(\text{CDCl}_3, 400 \text{ MHz})$ 2.15 (s, 3H), 3.37 (dd, $J = 4.3, 7.0 \text{ Hz}$, 1H), 3.43 (s, 3H), 4.29 (d, $J = 6.8 \text{ Hz}$, 1H), 4.81 (d, $J = 4.1 \text{ Hz}$, 1H), 6.58 (s, 1H), 6.64 (d, $J = 8.2 \text{ Hz}$, 1H), 6.92 (dd, $J = 1.5, 8.0 \text{ Hz}$, 1H), 7.14-7.36 (m, 7H), 8.13 (d, $J = 8.9 \text{ Hz}$, 2H). $\delta_{\text{C}}(\text{CDCl}_3, 100 \text{ MHz})$ 20.5, 42.6, 51.4, 51.9, 54.2, 114.4, 121.7, 123.5, 126.8, 127.6, 127.8, 128.4, 128.5, 129.2, 130.9, 140.5, 144.3, 147.4, 149.2, 171.1. Signals corresponding to the minor isomer: $\delta_{\text{H}}(\text{CDCl}_3, 400 \text{ MHz})$ 2.15 (s, 3H), 3.12 (s, 3H), 3.27 (dd, $J = 3.1, 5.8 \text{ Hz}$, 1H), 4.68 (d, $J = 5.8 \text{ Hz}$, 1H), 4.99 (d, $J = 2.8 \text{ Hz}$, 1H), 6.67-8.26 (m, 12H). $\delta_{\text{C}}(\text{CDCl}_3, 100 \text{ MHz})$ 20.8, 43.6, 50.9, 114.7, 123.6, 124.9, 126.4, 127.2, 127.9, 128.5, 129.2, 129.9, 133.1, 133.8, 144.6, 146.3, 147.9, 167.0 (2 carbons are missing due to overlapping). $\nu_{\text{max}} (\text{NaCl})/\text{cm}^{-1}$ 3385, 3018, 2918, 2851, 2360, 1734, 1600, 1527, 1508, 1456, 1345, 1266, 1220, 1165, 1110, 1030, 856, 813, 739, 701. HREIMS m/z 402.1581 (M)⁺, calcd for C₂₄H₂₂N₂O₄ 402.1580.

2-(2-Bromophenyl)-6-methyl-4-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2p)



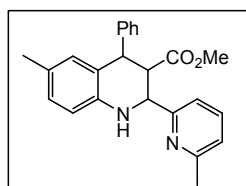
2 mol % [Rh(OH)(cod)]₂ at 80 °C for 1 h

a pale yellow solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 50:50 mixture of isomers. $\delta_{\text{H}}(\text{CDCl}_3, 400 \text{ MHz})$ 2.15 (s, 3H), 2.18 (s, 3H), 3.09 (s, 3H), 3.35 (t, $J = 3.4 \text{ Hz}$, 1H), 3.39 (s, 3H), 3.47 (dd, $J = 3.3, 6.0 \text{ Hz}$, 1H), 4.45 (d, $J = 3.4 \text{ Hz}$, 1H), 4.67 (d, $J = 5.8 \text{ Hz}$, 1H), 4.93 (d, $J = 3.4 \text{ Hz}$, 1H), 5.25 (d, $J = 3.1 \text{ Hz}$, 1H), 6.65 (t, $J = 7.4 \text{ Hz}$, 2H), 6.69 (s, 1H), 6.75 (s, 1H), 6.90-7.58 (m, 20H). $\delta_{\text{C}}(\text{CDCl}_3, 100 \text{ MHz})$ 20.5, 20.6, 44.3, 47.0, 49.5, 49.8, 50.5, 51.2, 52.3, 57.2, 114.8, 115.1, 121.5, 122.3, 122.9, 123.1, 126.1, 126.5, 127.0, 127.1, 127.2, 127.3, 127.5, 127.6,

127.8, 127.9, 128.0, 128.2, 128.4, 129.0, 129.2, 129.4, 129.7, 130.9, 132.8, 133.0, 139.2, 140.0, 141.0, 141.8, 142.3, 145.1, 169.5, 171.6. ν_{\max} (NaCl)/ cm^{-1} 3364, 3019, 2918, 2849, 2362, 1735, 1617, 1508, 1470, 1435, 1265, 1170, 1024, 813, 736, 702. HREIMS m/z 435.0834 (M)⁺, calcd for $C_{24}H_{22}BrNO_2$ 435.0834.

6-Methyl-2-(6-methylpyridin-2-yl)-4-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2q)



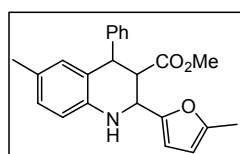
2 mol % $[\text{Rh}(\text{OH})(\text{cod})]_2$ at 80 °C for 1 h

a pale yellow solid (EtOAc : *n*-Hexane = 1 : 5)

The compound exists as a 59:41 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl_3 , 400 MHz) 2.16 (s, 3H), 2.51 (s, 3H), 3.40 (s, 3H), 3.58 (dd, $J = 5.5, 10.9$ Hz, 1H), 4.18 (br s, 1H), 4.52 (d, $J = 5.5$ Hz, 1H), 4.69 (d, $J = 10.9$ Hz, 1H), 6.60 (d, $J = 8.2$ Hz, 1H), 6.77 (d, $J = 1.4$ Hz, 1H), 6.89 (dd, $J = 1.7, 8.2$ Hz, 1H), 7.03 (d, $J = 7.5$ Hz, 1H), 7.09-7.28 (m, 6H), 7.49 (t, $J = 7.7$ Hz, 1H). δ_{C} (CDCl_3 , 100 MHz) 20.3, 24.4, 45.8, 48.3, 51.0, 53.7, 114.7, 119.7, 122.1, 122.3, 126.8, 128.1, 128.5, 129.1, 130.2, 136.7, 141.2, 142.6, 158.1, 159.7, 171.9 (1 carbon is missing due to overlapping). Signals corresponding to the minor isomer: δ_{H} (CDCl_3 , 400 MHz) 2.14 (s, 3H), 2.51 (s, 3H), 3.40 (dd, $J = 3.9, 5.6$ Hz, 1H), 3.44 (s, 3H), 4.35 (d, $J = 5.5$ Hz, 1H), 4.71 (d, $J = 2.7$ Hz, 1H), 5.04 (br s, 1H), 6.62 (s, 1H), 6.72 (d, $J = 7.9$ Hz, 1H), 6.92 (d, $J = 7.7$ Hz, 1H), 7.00 (d, $J = 7.5$ Hz, 1H), 7.18-7.31 (m, 5H), 7.48 (t, $J = 7.7$ Hz, 1H). δ_{C} (CDCl_3 , 100 MHz) 20.5, 24.2, 43.6, 50.0, 51.4, 54.2, 115.0, 117.8, 121.6, 126.4, 127.0, 128.3, 129.2, 130.8, 136.6, 141.1, 145.1, 157.1, 158.8, 171.6 (2 carbons are missing due

to overlapping). ν_{\max} (NaCl)/ cm^{-1} 3399, 3025, 2922, 2851, 2345, 1740, 1617, 1593, 1558, 1541, 1508, 1456, 1363, 1315, 1264, 1233, 1168, 1074, 1030, 806, 737, 702. HREIMS m/z 372.1836 (M)⁺, calcd for C₂₄H₂₄N₂O₂ 372.1838.

6-Methyl-2-(5-methylfuran-2-yl)-4-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester (2r)



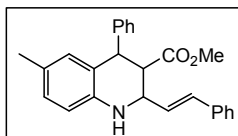
2 mol % [Rh(OH)(cod)]₂ at 80 °C for 1 h

a yellow solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 83:17 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 2.10 (s, 3H), 2.21 (s, 3H), 3.39 (dd, J = 3.8, 8.2 Hz, 1H), 3.57 (s, 3H), 4.21 (br s, 1H), 4.37 (d, J = 8.2 Hz, 1H), 4.75 (d, J = 4.1 Hz, 1H), 5.84 (d, J = 2.0 Hz, 1H), 5.99 (d, J = 2.8 Hz, 1H), 6.50 (s, 1H), 6.58 (d, J = 8.2 Hz, 1H), 6.84 (d, J = 7.9 Hz, 1H), 7.19-7.31 (m, 5H). δ_{C} (CDCl₃, 100 MHz) 13.4, 20.5, 42.5, 49.8, 49.9, 51.5, 106.1, 107.3, 114.8, 122.8, 126.4, 127.5, 128.0, 128.2, 129.4, 130.8, 140.6, 144.9, 151.1, 152.2, 171.6. Representative signals corresponding to the minor isomer: δ_{H} (CDCl₃, 400 MHz) 2.13 (s, 3H), 2.26 (s, 3H), 3.28 (s, 3H), 3.36 (m, 1H), 4.57 (d, J = 5.8 Hz, 1H), 4.83 (d, J = 2.7 Hz, 1H), 5.89 (d, J = 2.1 Hz, 1H), 6.17 (d, J = 3.1 Hz, 1H), 6.65 (s, 1H), 6.68 (d, J = 8.2 Hz, 1H), 6.90 (d, J = 8.2 Hz, 1H), 7.19-7.31 (m, 5H). ν_{\max} (NaCl)/ cm^{-1} 3385, 3019, 2923, 2849, 2356, 1740, 1617, 1559, 1508, 1454, 1435, 1373, 1265, 1220, 1168, 1121, 1025, 812, 789, 737, 702. HREIMS m/z 361.1679 (M)⁺, calcd for C₂₃H₂₃NO₃ 361.1678.

6-Methyl-4-phenyl-2-styryl-1,2,3,4-tetrahydroquinoline-3-carboxylic

acid methyl ester (2s)

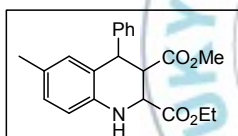


2 mol % [Rh(OH)(cod)]₂ at 80 °C for 1 h

a pale brown oil (EtOAc : *n*-Hexane = 1 : 10)

δ_{H} (CDCl₃, 400 MHz) 2.11 (s, 3H), 3.30 (dd, $J = 3.8, 8.5$ Hz, 1H), 3.58 (s, 3H), 4.13 (br s, 1H), 4.26 (dd, $J = 3.8, 7.2$ Hz, 1H), 4.45 (d, $J = 8.6$ Hz, 1H), 6.34-7.34 (m, 15H). δ_{C} (CDCl₃, 100 MHz) 20.5, 42.6, 51.2, 51.6, 53.8, 114.8, 122.6, 126.5, 127.7, 127.8, 128.1, 128.3, 128.5, 129.3, 130.8, 132.0, 136.5, 140.3, 144.8, 172.0 (2 carbons are missing due to overlapping). ν_{max} (NaCl)/cm⁻¹ 3384, 3025, 2923, 2849, 2351, 1734, 1717, 1694, 1649, 1541, 1507, 1456, 1363, 1263, 1162, 1074, 1023, 967, 811, 746, 700. HREIMS m/z 383.1886 (M)⁺, calcd for C₂₆H₂₅NO₂ 383.1885.

6-Methyl-4-phenyl-1,2,3,4-tetrahydroquinoline-2,3-dicarboxylic acid 2-ethyl ester 3-methyl ester (2t)



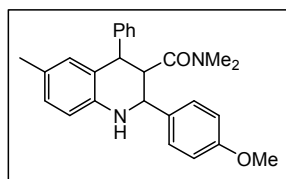
2 mol % [Rh(OH)(cod)]₂ at 80 °C for 1 h

a yellow solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a mixture of isomers and the ratio of isomers could not be determined. δ_{H} (CDCl₃, 400 MHz) 1.24 (t, $J = 7.2$ Hz, 3H), 2.18 (s, 3H), 3.28 (s, 3H), 3.93 (d, $J = 18.1$ Hz, 1H), 4.15 (q, $J = 7.1$ Hz, 1H), 4.22 (d, $J = 18.4$ Hz, 1H), 4.76 (d, $J = 9.9$ Hz, 1H), 5.05 (d, $J = 9.9$ Hz, 1H), 6.43 (d, $J = 7.9$ Hz, 1H), 6.76 (s, 1H), 6.93 (d, $J = 7.9$ Hz, 1H), 7.08-7.23 (m, 5H). δ_{C} (CDCl₃, 100 MHz) 14.1, 14.2, 20.7, 21.3, 46.7, 47.5, 50.6, 51.4, 60.8, 61.4, 70.6, 106.8, 109.2, 121.1, 123.6, 125.4, 125.9, 126.9, 127.2, 127.7, 127.9, 128.1, 128.5, 128.7, 130.4, 130.7, 130.9, 134.4, 136.9, 140.0, 148.3,

163.0, 169.1, 170.1, 170.7 (3 carbons are missing due to overlapping). ν_{\max} (NaCl)/ cm^{-1} 3210, 3025, 2950, 2849, 2351, 1748, 1701, 1617, 1497, 1456, 1373, 1279, 1199, 1165, 1104, 1026, 803, 737, 700. HREIMS m/z 353.1628 (M)⁺, calcd for C₂₁H₂₃NO₄ 353.1627.

2-(4-Methoxyphenyl)-6-methyl-4-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid *N,N*-dimethylamide (2u)



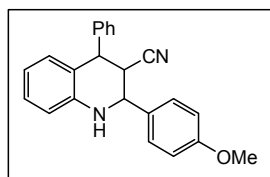
2 mol % [Rh(OH)(cod)]₂ at 120 °C for 1 h

a white solid (EtOAc : *n*-Hexane = 1 : 2)

The compound exists as a 71:29 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 1.96 (s, 3H), 2.12 (s, 3H), 2.51 (s, 3H), 3.45 (dd, $J = 3.2, 5.6$ Hz, 1H), 3.79 (s, 3H), 4.61 (d, $J = 4.5$ Hz, 1H), 4.81 (d, $J = 2.7$ Hz, 1H), 6.59 (s, 1H), 6.64 (d, $J = 7.5$ Hz, 1H), 6.84-7.37 (m, 10H). δ_{C} (CDCl₃, 100 MHz) 20.6, 35.1, 36.7, 45.8, 48.2, 55.2, 59.0, 113.7, 115.8, 126.9, 127.1, 127.4, 127.6, 128.1, 128.7, 129.8, 134.1, 134.7, 135.5, 141.4, 159.3, 169.4. Signals corresponding to the minor isomer: δ_{H} (CDCl₃, 400 MHz) 2.14 (s, 3H), 2.47 (s, 3H), 2.77 (s, 3H), 3.67 (t, $J = 4.1$ Hz, 1H), 3.77 (s, 3H), 4.31 (d, $J = 4.4$ Hz, 1H), 4.52 (d, $J = 3.8$ Hz, 1H), 6.61-7.31 (m, 12H). δ_{C} (CDCl₃, 100 MHz) 20.5, 35.4, 36.8, 44.3, 47.8, 53.5, 55.2, 113.5, 114.4, 122.9, 126.2, 127.7, 128.3, 129.2, 130.8, 133.2, 141.8, 146.7, 159.2, 170.8 (2 carbons are missing due to overlapping). ν_{\max} (NaCl)/ cm^{-1} 3218, 3059, 2923, 2849, 2362, 1733, 1714, 1636, 1603, 1555, 1542, 1508, 1457, 1397, 1340, 1252, 1178, 1094, 1031, 831, 754, 702. HREIMS m/z 400.2153 (M)⁺, calcd for C₂₆H₂₈N₂O₂ 400.2151.

2-(4-Methoxyphenyl)-4-phenyl-1,2,3,4-tetrahydroquinoline-3-

carbonitrile (2v)

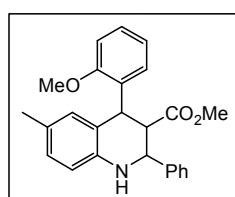


2 mol % [Rh(OH)(cod)]₂ at 80 °C for 3 h

a yellow solid (EtOAc : *n*-Hexane = 1 : 10)

The compound exists as a 53:47 mixture of isomers. Signals corresponding to the major isomer: δ_{H} (CDCl₃, 400 MHz) 3.17 (t, J = 3.1 Hz, 1H), 3.80 (s, 3H), 4.22 (br s, 1H), 4.39 (d, J = 2.7 Hz, 1H), 4.51 (d, J = 3.1 Hz, 1H), 6.72-7.36 (m, 13H). δ_{C} (CDCl₃, 100 MHz) 41.0, 45.9, 51.4, 55.3, 114.1, 114.2, 114.8, 117.8, 118.5, 127.3, 128.1, 128.4, 128.7, 128.8, 131.0, 131.1, 143.6, 143.7, 159.8. Representative signals corresponding to the minor isomer: δ_{H} (CDCl₃, 400 MHz) 3.25 (dd, J = 2.2, 5.3 Hz, 1H), 3.82 (s, 3H), 4.13 (br s, 1H), 4.72 (d, J = 5.5 Hz, 1H), 4.82 (d, J = 2.4 Hz, 1H), 6.61-7.56 (m, 13H), δ_{C} (CDCl₃, 100 MHz) 43.3, 47.7, 55.3, 57.9, 114.2, 115.1, 118.4, 118.5, 120.2, 127.9, 128.0, 128.1, 128.2, 128.6, 129.6, 131.0, 139.7, 144.4, 159.9. ν_{max} (NaCl)/cm⁻¹ 3384, 3008, 2922, 2852, 2362, 2237, 1734, 1606, 1511, 1486, 1453, 1340, 1298, 1250, 1180, 1110, 1027, 829, 751, 704. HREIMS m/z 340.1574 (M)⁺, calcd for C₂₃H₂₀N₂O 340.1576.

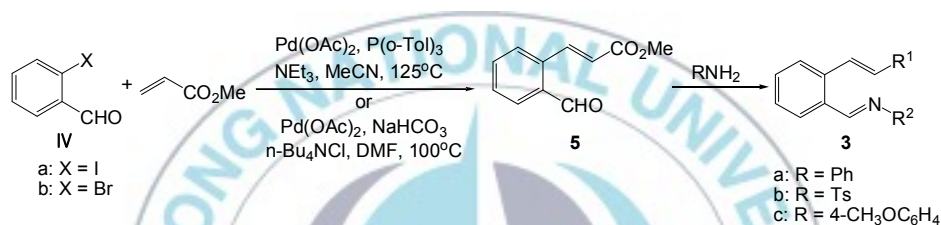
4-(2-Methoxyphenyl)-6-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester



10 mol % [Rh(OH)(cod)]₂ at 120 °C for 4 h

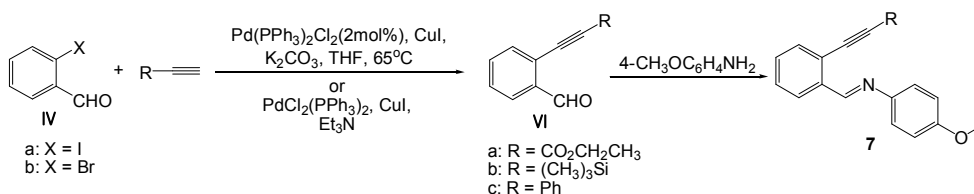
a pale yellow solid (EtOAc : *n*-Hexane = 1 : 10)

δ_{H} (CDCl₃, 400 MHz) 2.16 (s, 3H), 3.08 (s, 3H), 3.36 (dd, $J = 3.1, 6.2$ Hz, 1H), 3.88 (s, 3H), 4.05 (br s, 1H), 4.83 (d, $J = 3.1$ Hz, 1H), 5.18 (d, $J = 6.2$ Hz, 1H), 6.64 (d, $J = 7.8$ Hz, 1H), 6.73 (s, 1H), 6.84 (t, $J = 7.5$ Hz, 1H), 6.89 (d, $J = 7.8$ Hz, 2H), 7.12 (dd, $J = 1.4, 7.6$ Hz, 1H), 7.20 (ddd, $J = 1.2, 8.6, 15.7$ Hz, 1H), 7.29 (d, $J = 6.8$ Hz, 1H), 7.34 (t, $J = 7.2$ Hz, 2H), 7.43 (d, $J = 7.2$ Hz, 2H). δ_{C} (CDCl₃, 100 MHz) 20.6, 38.3, 50.2, 50.5, 55.5, 58.3, 109.9, 115.2, 120.0, 122.1, 126.4, 126.9, 127.4, 127.7, 127.9, 128.5, 128.9, 129.4, 130.0, 141.1, 143.1, 157.8, 170.1. ν_{max} (NaCl)/cm⁻¹ 3374, 3026, 2917, 2856, 2368, 1733, 1616, 1508, 1493, 1454, 1435, 1349, 1266, 1218, 1171, 1089, 1030, 812, 753, 701.



4.10. General procedure for Heck reaction for the synthesis of 5

To a solution of 2-bromobenzaldehyde(IVb) in DMF (0.4 M) were added Pd(OAc)₂ (5 mol %), NaHCO₃ (5 equiv), *n*-Bu₄NCl (1.1 equiv), and the methyl acrylate (3 equiv). The reaction mixture was stirred at 100°C for 12 hours. After the reaction was completed, the reaction mixture was filtered through Celite and then the solvent was evaporated. The residue was purified by column chromatography on silica gel (EtOAc:*n*-Hexane = 1:8) to give the 5(64%) as a yellow solid.

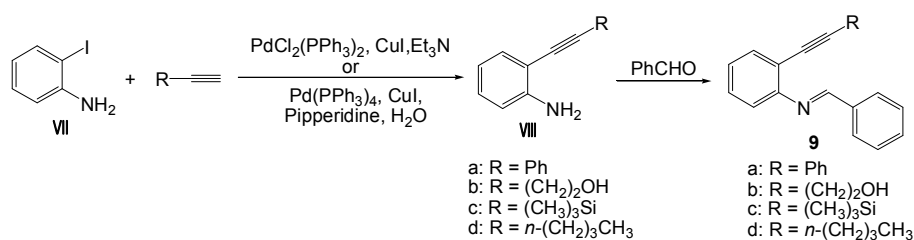


4.11. General procedure for Sonogashira reaction for the synthesis of VIa

To a solution of 2-iodobenzaldehyde(IVa) in THF (0.3 M) were added PdCl₂(PPh₃)₂ (2 mol %), CuI (4 mol %), and the ethyl propiolate (4 equiv). The reaction mixture was stirred at 65°C for 12 hours. After the reaction was completed, quenched with distilled water, extracted with CH₂Cl₂ (three times), washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc : *n*-Hexane = 1:10) to give the VIa(85%) as a yellow solid.

4.12. General procedure for Sonogashira reaction for the synthesis of VIb,c

To a solution of 2-bromobenzaldehyde(IVb) in Et₃N (0.25 M) were added PdCl₂(PPh₃)₂ (2 mol %), CuI (1 mol %), and the corresponding terminal acetylene (1.2 equiv). The reaction mixture was stirred at 50°C for 12 hours. After the reaction was completed, the reaction mixture was filtered through Celite and then the solvent was evaporated. The residue was purified by column chromatography on silica gel (EtOAc : *n*-Hexane = 1:10~20) to give the corresponding product. (VIb : 97%, VIc : 98%)



4.13. General procedure for Sonogashira reaction for the synthesis of VIIIa,c,d

To a solution of 2-iodoaniline(VII) in Et₃N (0.25 M) were added PdCl₂(PPh₃)₂ (2 mol %), CuI (1 mol %), and the corresponding terminal acetylene (1.2 equiv). The reaction mixture was stirred at 50°C for 12 hours. After the reaction was completed, the reaction mixture was filtered through Celite and then the solvent was evaporated. The residue was purified by column chromatography on silica gel (EtOAc : *n*-Hexane = 1:20~50) to give the corresponding product. (VIIIa : 99%, VIIIc : 89%, VIII d : 96%)

4.14. General procedure for Sonogashira reaction for the synthesis of VIIIb

To a solution of 2-iodoaniline(VII) in H₂O (0.2 M) were added Pd(PPh₃)₄ (0.5 mol %), CuI (1 mol %), piperidine (1.5 equiv), and the 3-butyn-1-ol (2 equiv). The reaction mixture was stirred at 70°C for 12 hours. After the reaction was completed, quenched with distilled water, extracted with CH₂Cl₂ (three times), washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc : *n*-Hexane = 1:3) to give the VIIIb(98%) as a colorless oil.

4.15. General procedure for the preparation of imine substrates 3, 7, 9

To a solution of V, VI, VII in toluene (0.2 M) was added the corresponding amine or aldehyde (1.05 equiv). The reaction mixture was refluxed with the aid of a Dean-Stark apparatus to remove the water produced. The reaction was monitored by TLC to establish completion. The reaction mixture was then cooled to room temperature, and the solvent was removed under reduced pressure. The resulting imines were clean by ^1H NMR and were used in the cyclization reactions without purification.



5. Reference

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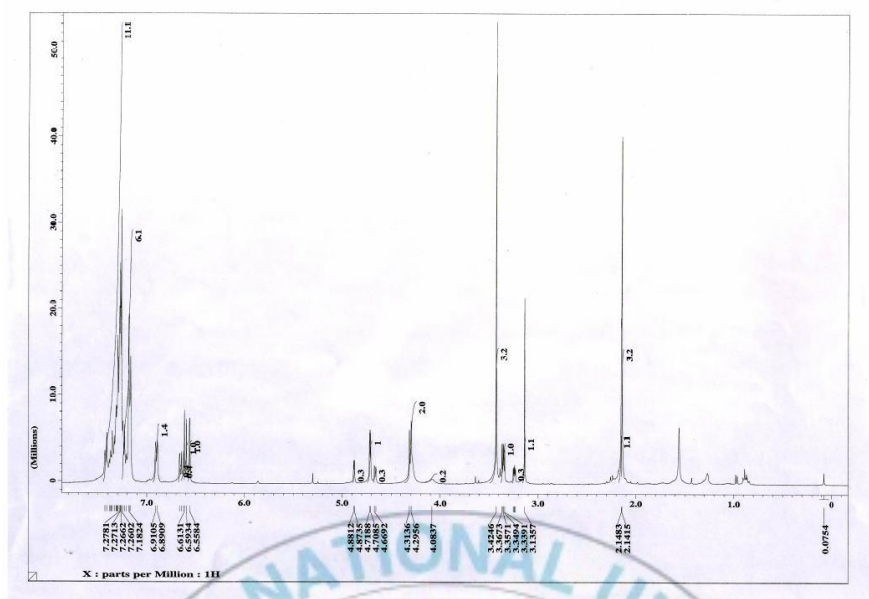
(12) It was found that both water and protic acid such as H₃BO₃ were detrimental to the reaction presented herein (see Supporting Information). It has been reported that boric acid is presumed to facilitate the release of rhodium from the iminorhodium(I) intermediate by protonolysis in the Rh-catalyzed reaction of ethyl cyanofornate with arylboronic acids; see: Shimizu, H.; Murakami, M. *Chem. Commun.* **2007**, 2855.

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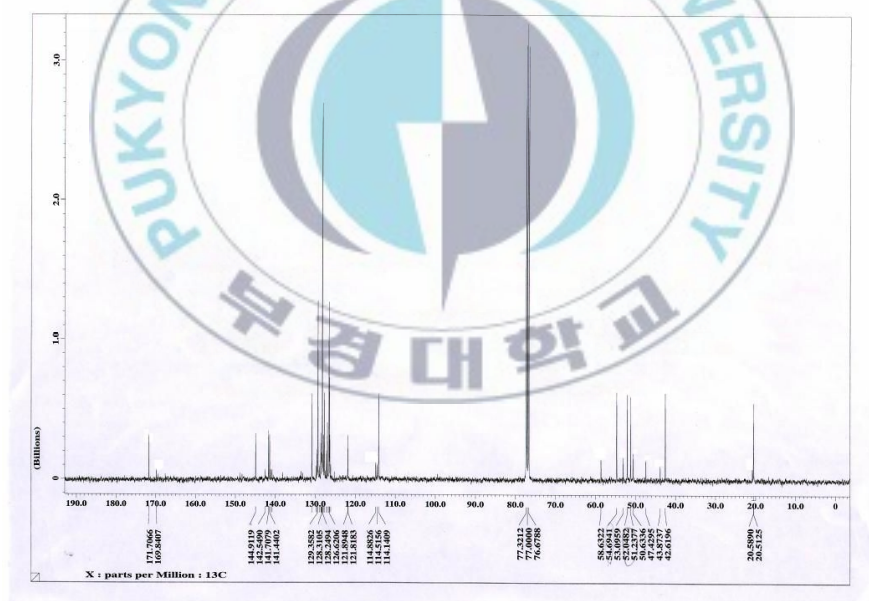
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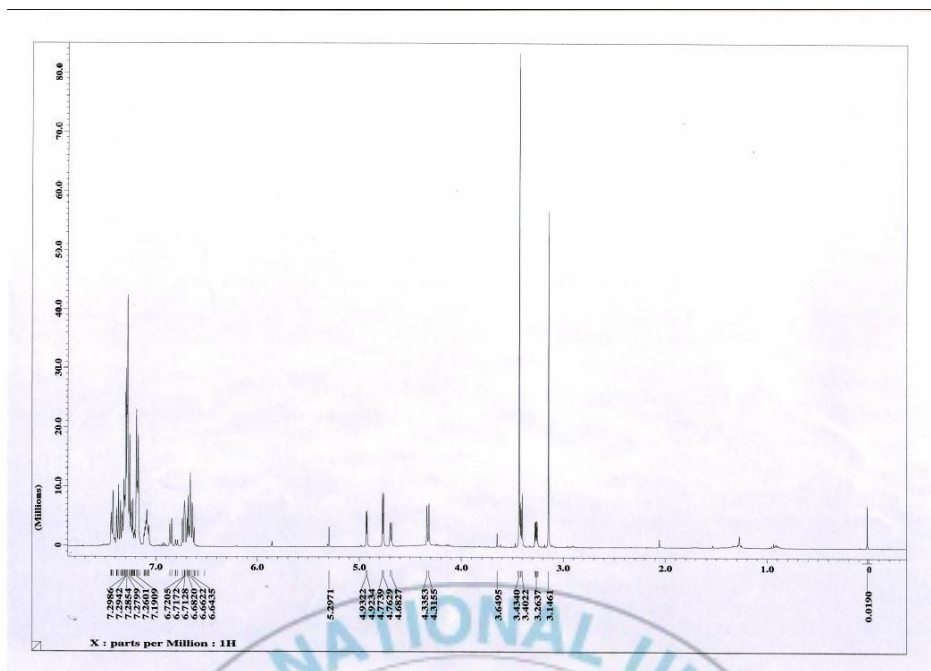
6. Spectral Data



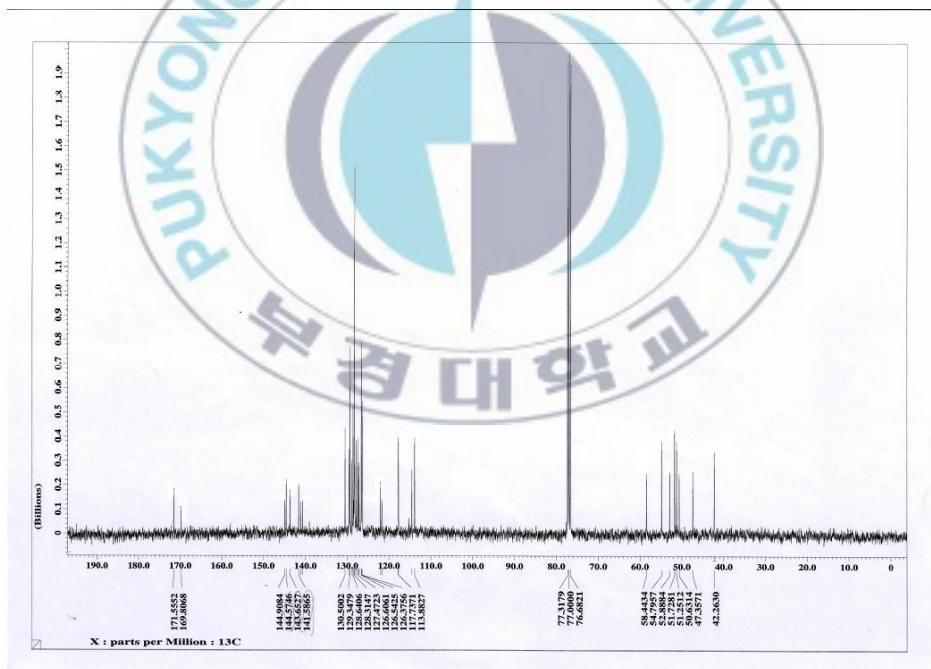
¹H NMR Spectrum of Compound **2a** (CDCl₃, 400 MHz)



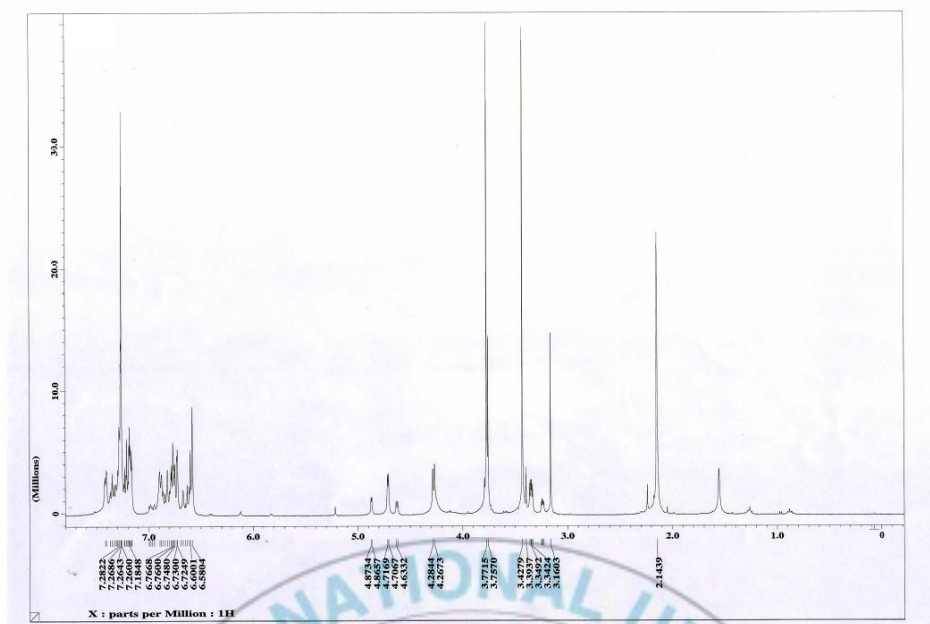
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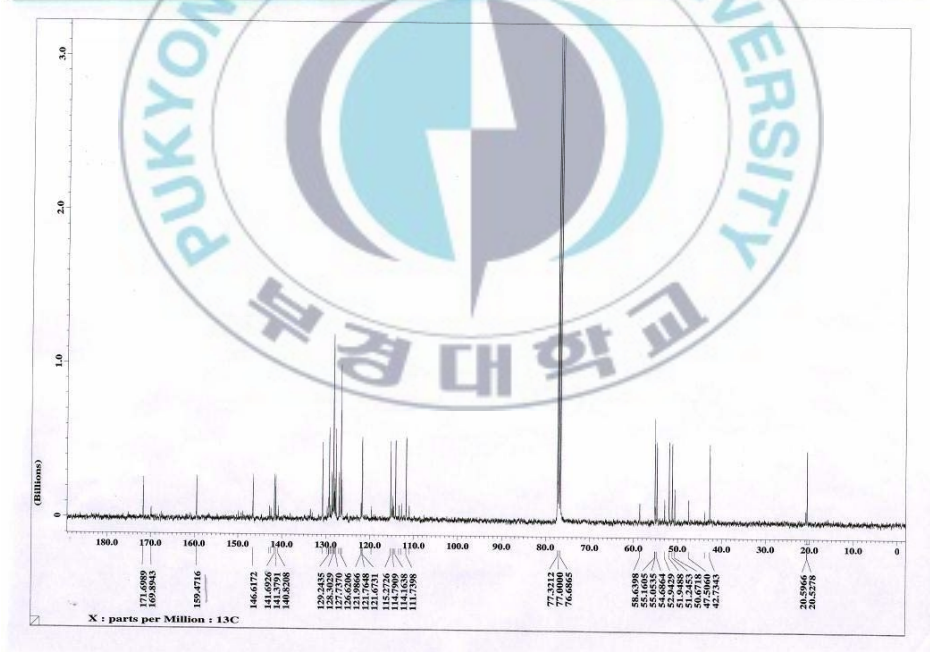
¹H NMR Spectrum of Compound **2b** (CDCl₃, 400 MHz)



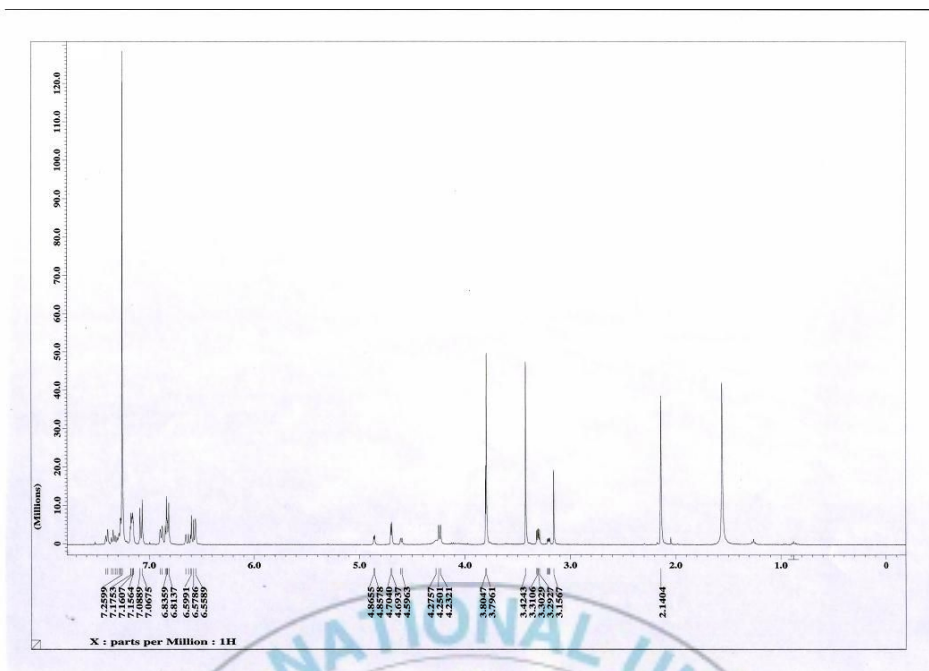
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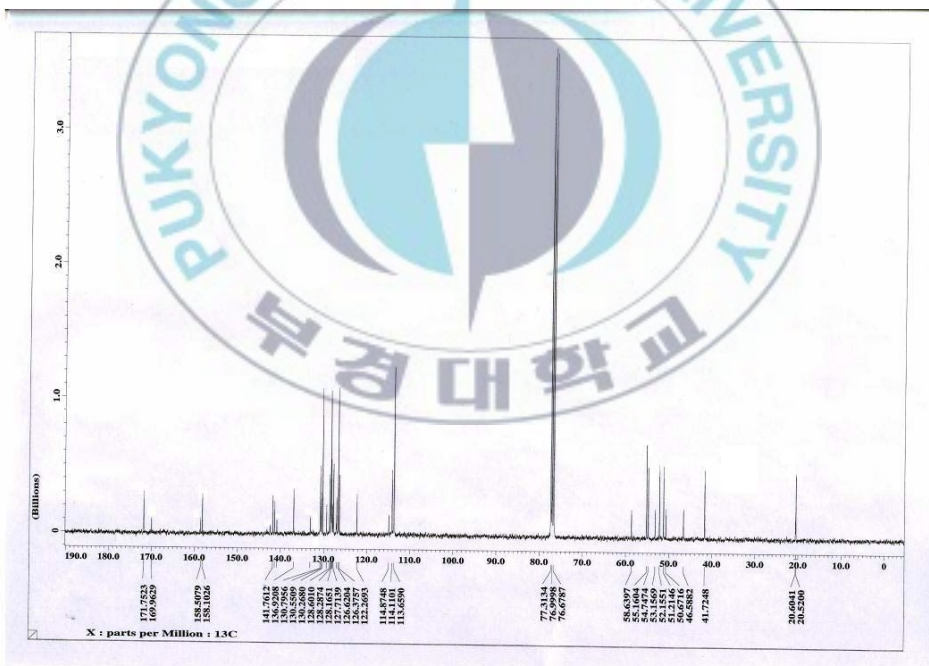
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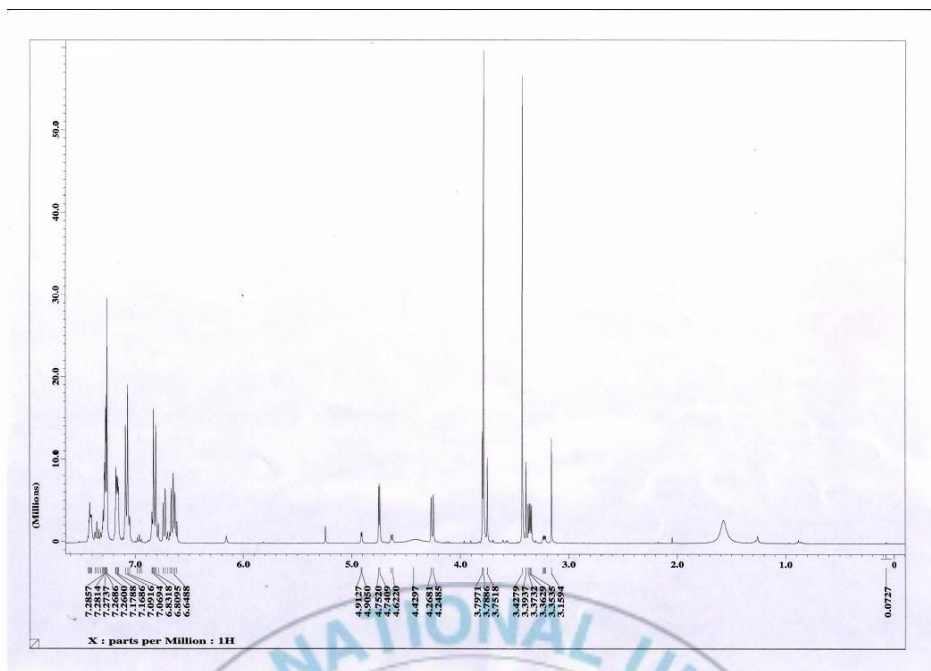
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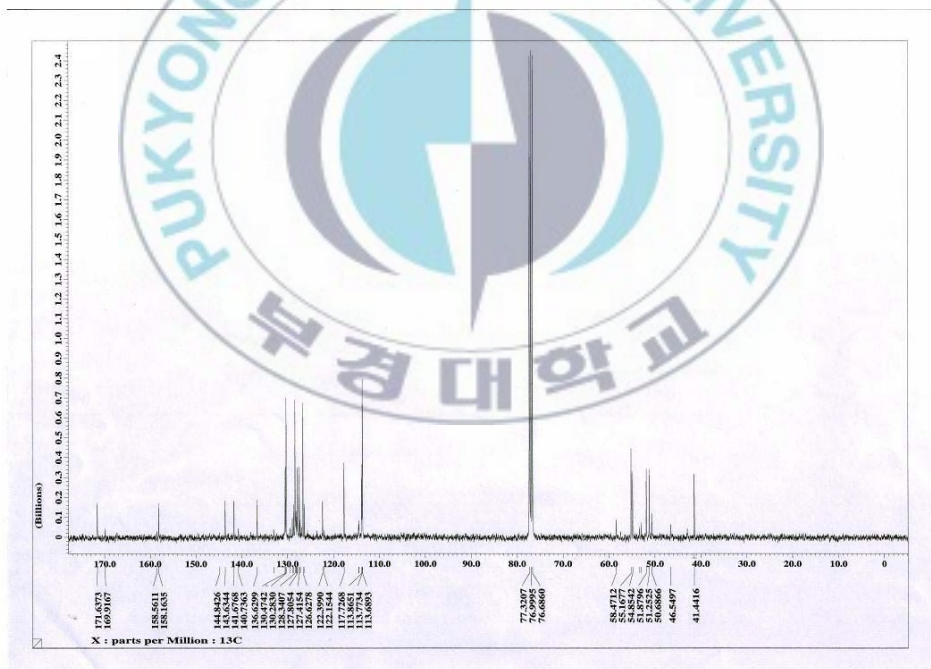
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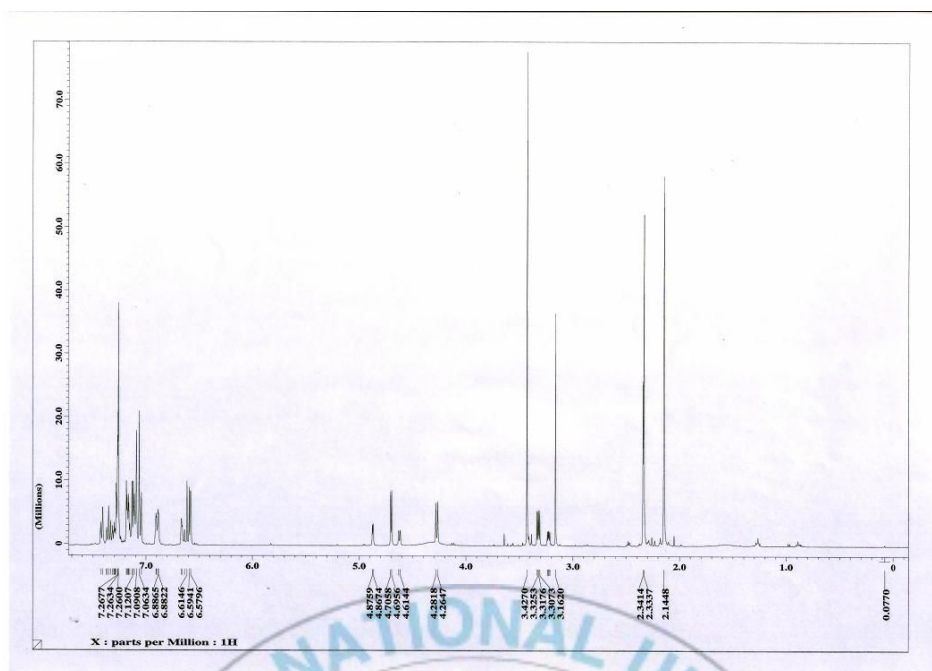
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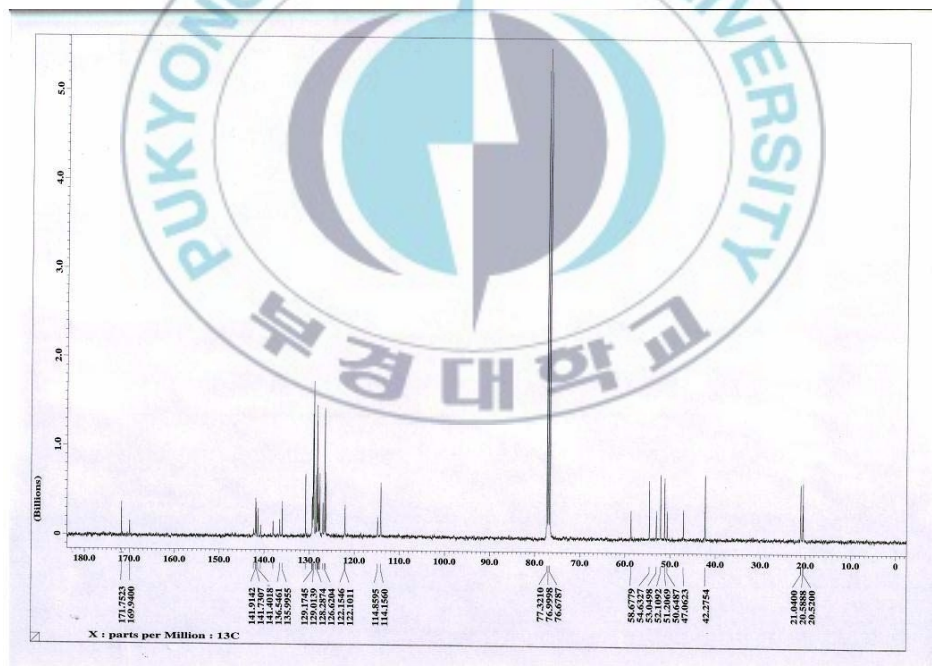
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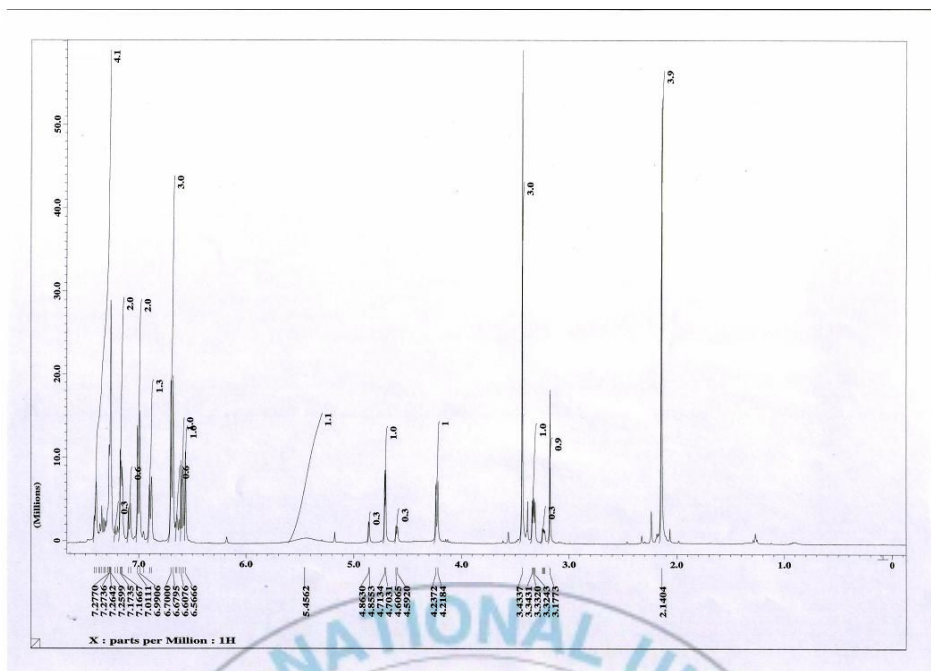
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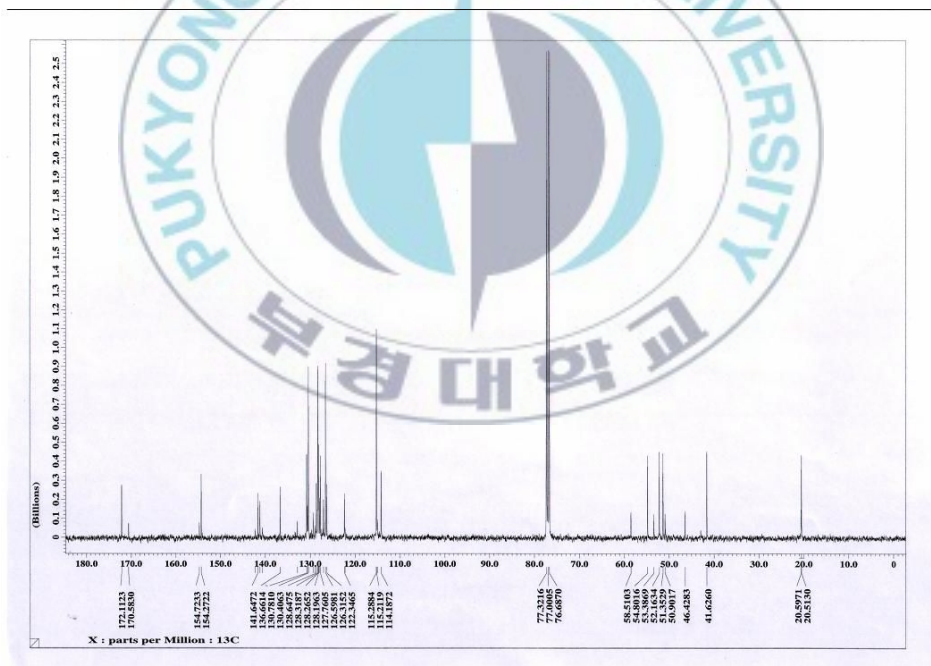
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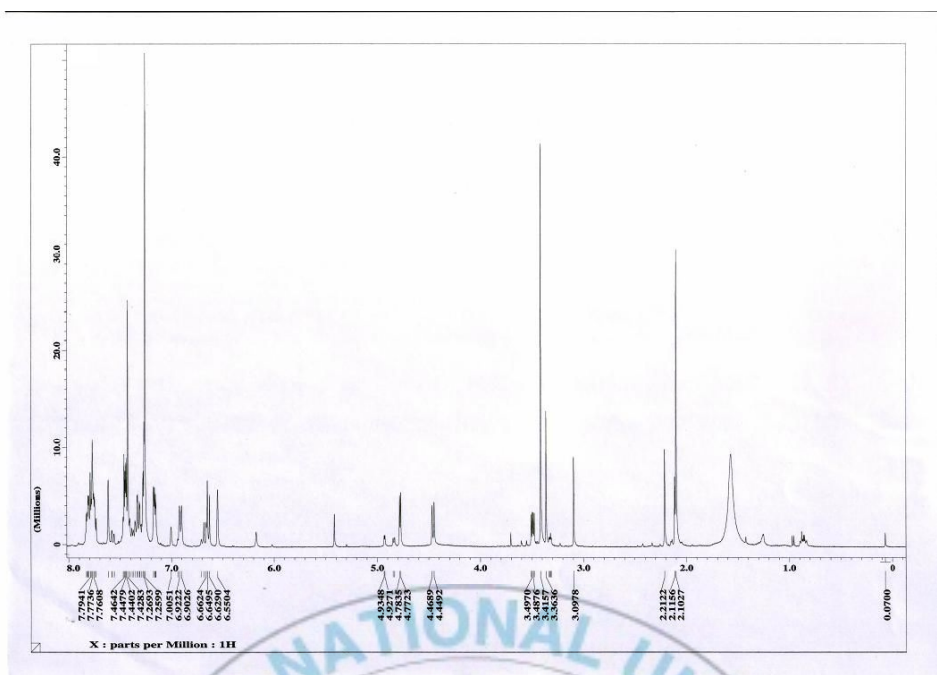
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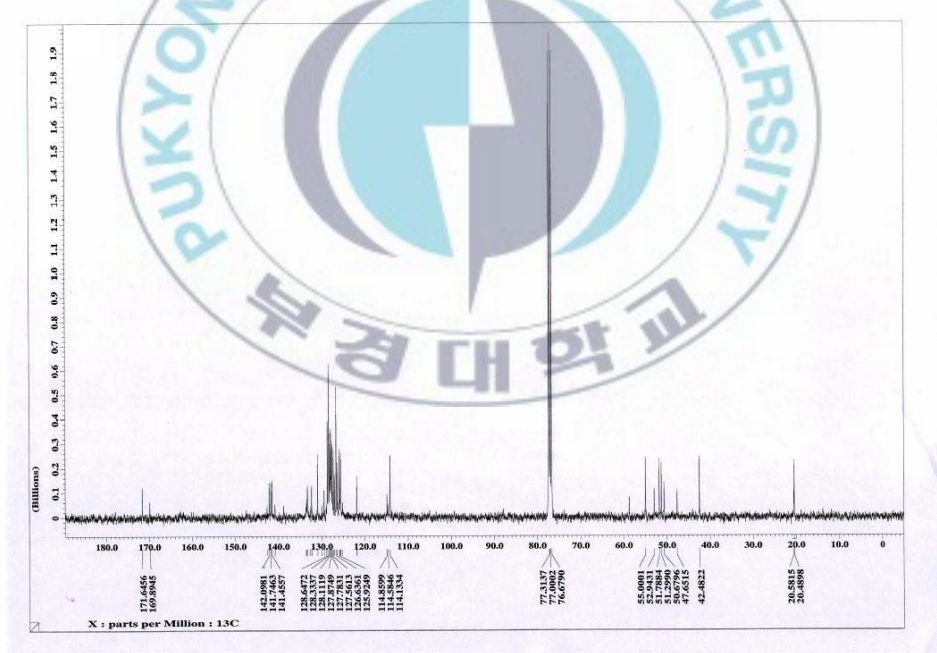
^1H NMR Spectrum of Compound **2g** (CDCl_3 , 400 MHz)



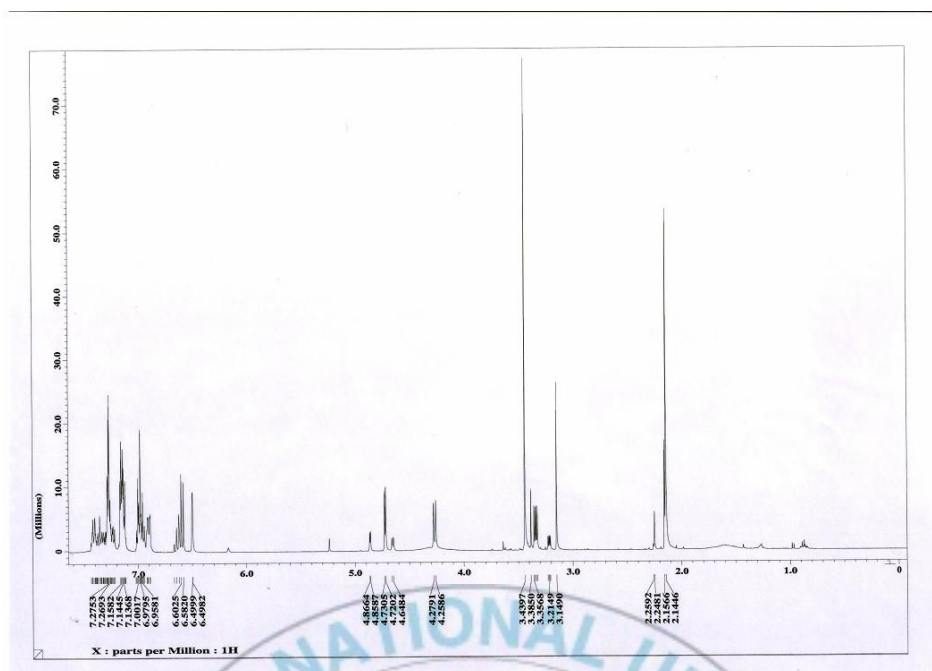
^{13}C NMR Spectrum of Compound **2g** (CDCl_3 , 100 MHz)



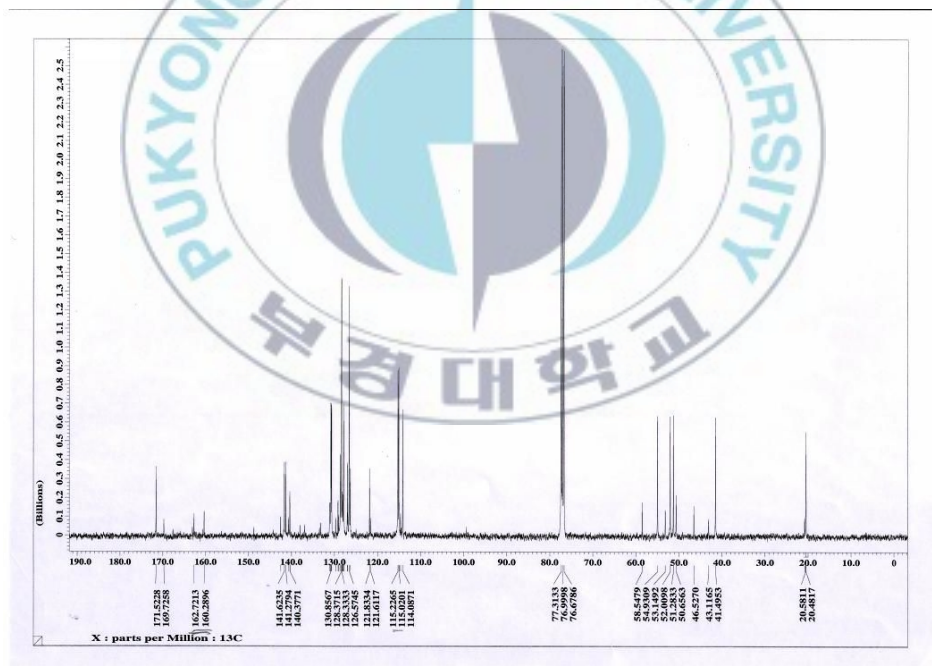
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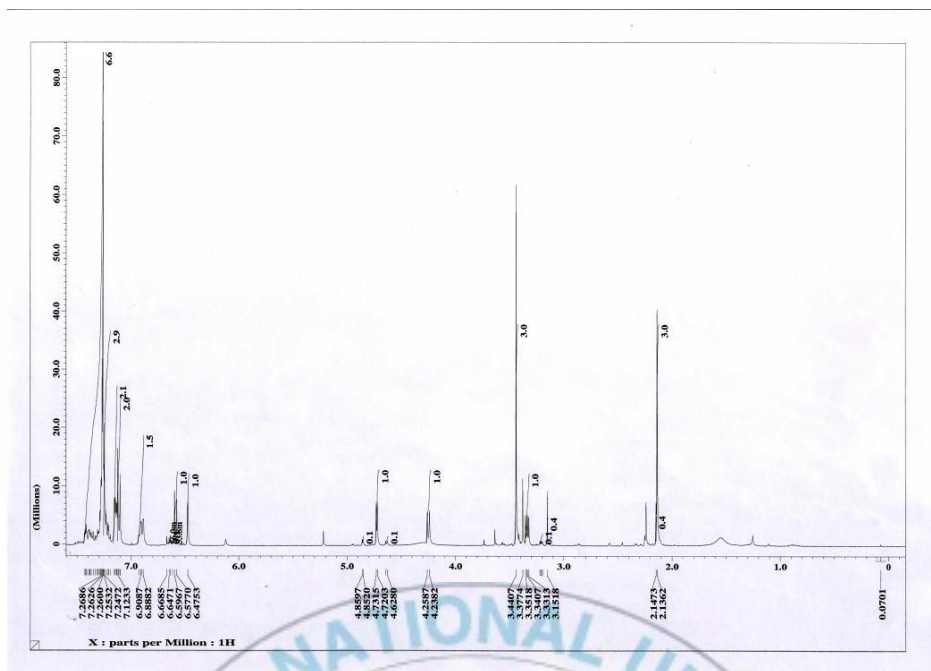
¹³C NMR Spectrum of Compound **2h** (CDCl₃, 100 MHz)



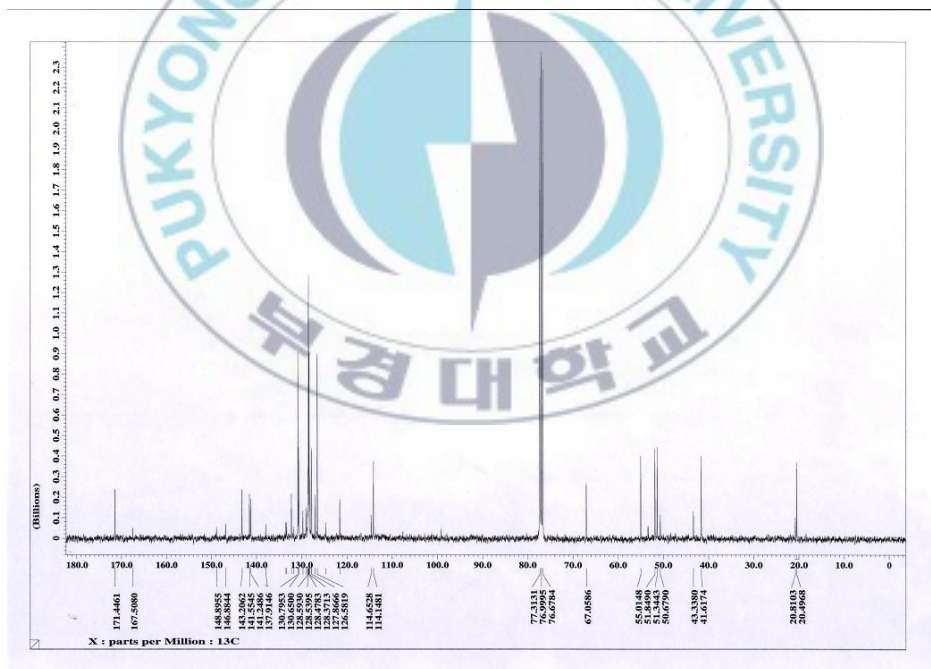
^1H NMR Spectrum of Compound **2i** (CDCl_3 , 400 MHz)



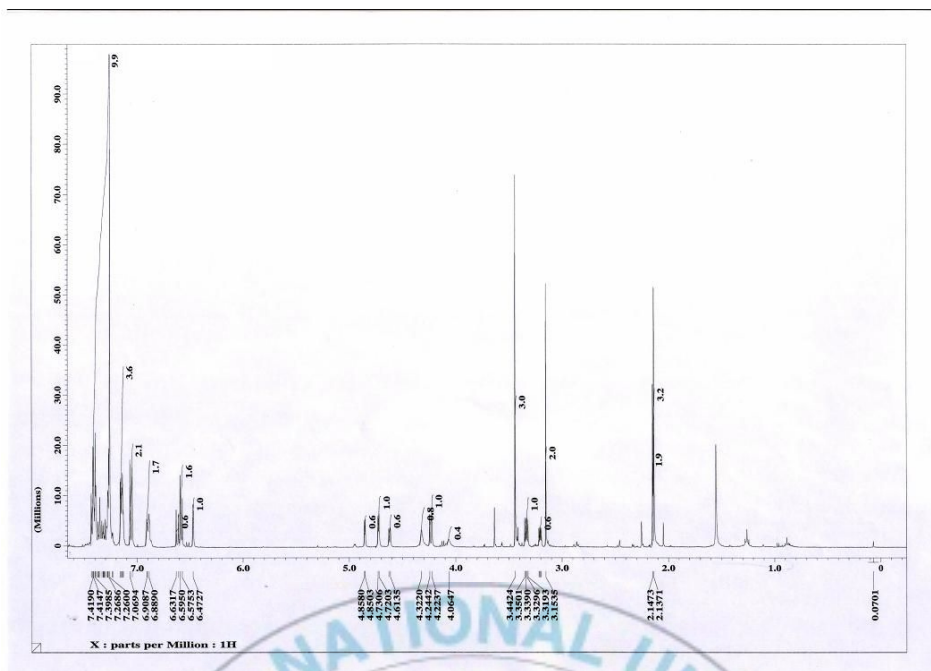
^{13}C NMR Spectrum of Compound **2i** (CDCl_3 , 100 MHz)



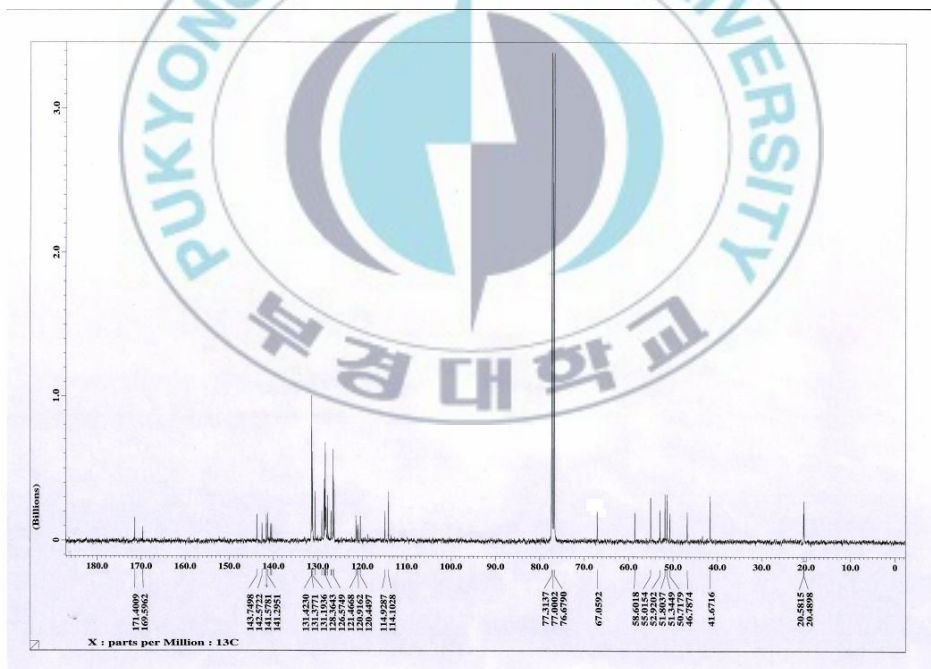
¹H NMR Spectrum of Compound **2j** (CDCl₃, 400 MHz)



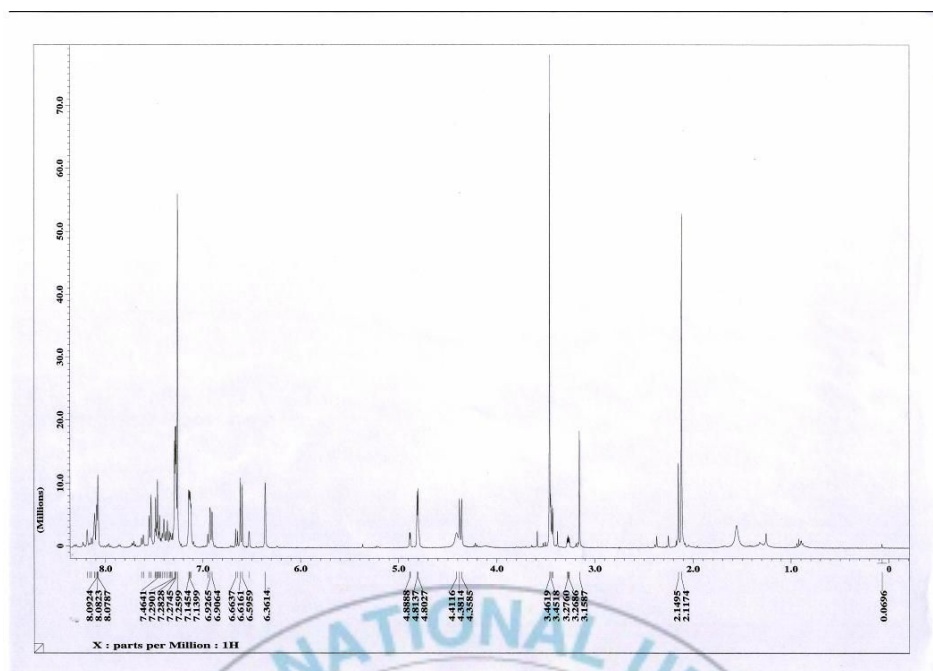
¹³C NMR Spectrum of Compound **2j** (CDCl₃, 100 MHz)



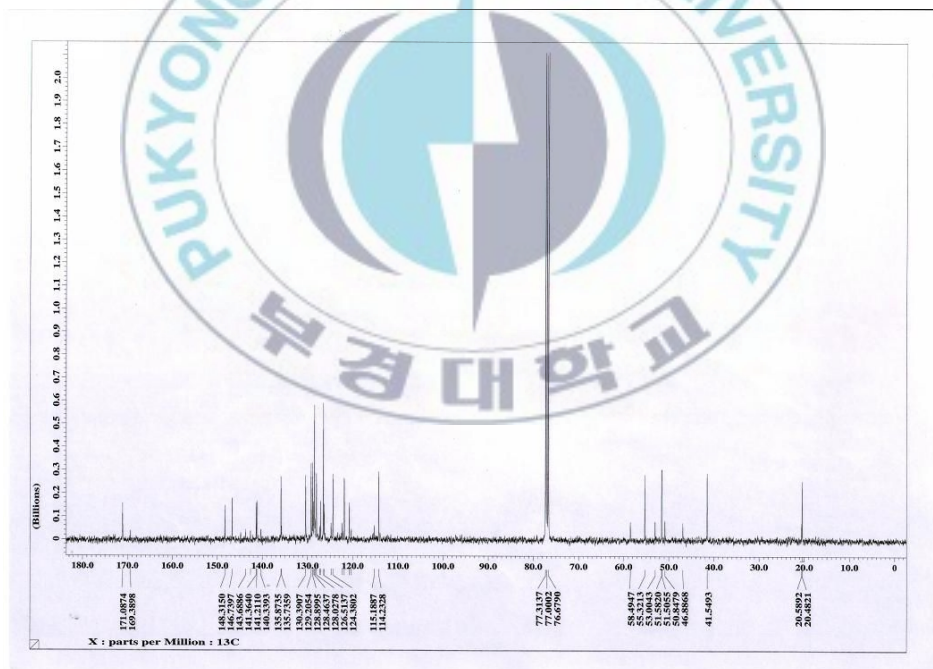
¹H NMR Spectrum of Compound **2k** (CDCl₃, 400 MHz)



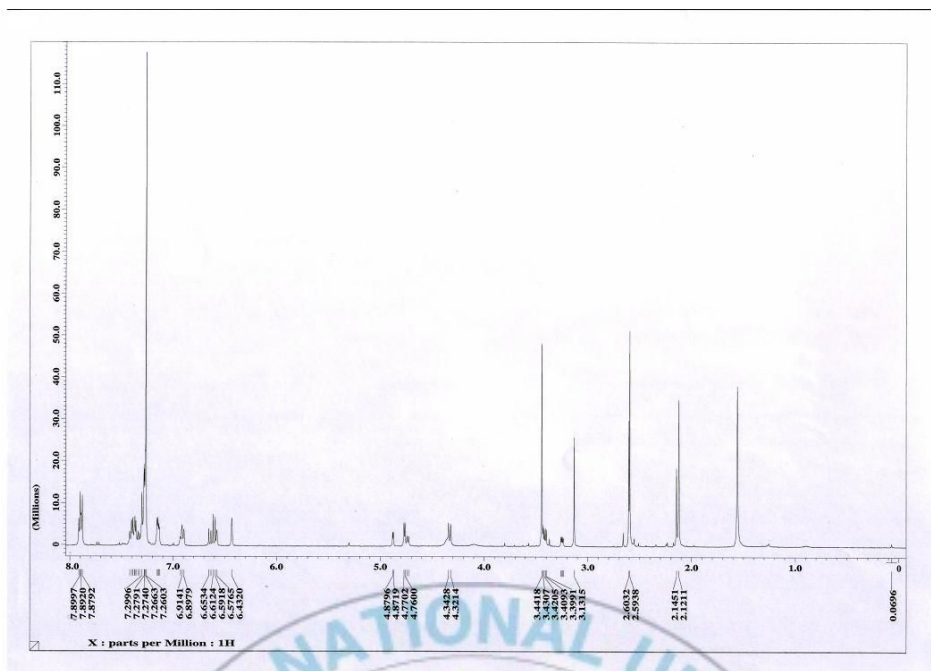
¹³C NMR Spectrum of Compound **2k** (CDCl₃, 100 MHz)



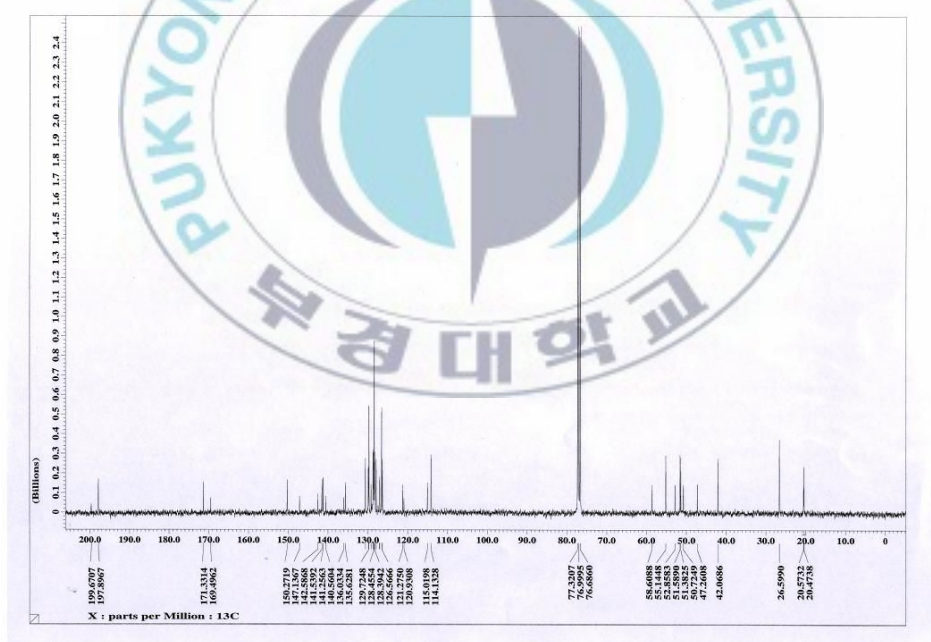
¹H NMR Spectrum of Compound 2I (CDCl₃, 400 MHz)



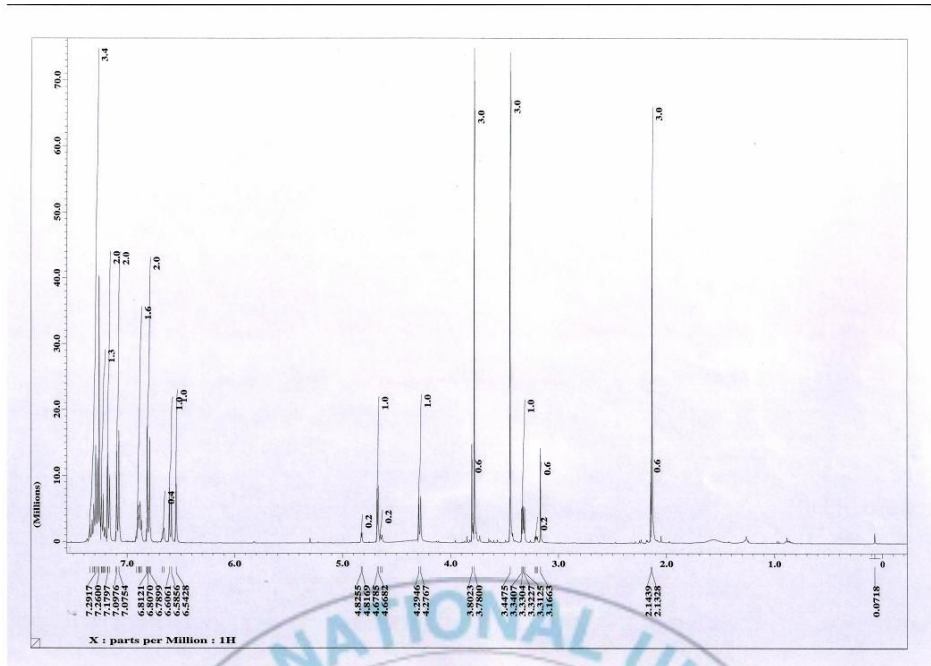
¹³C NMR Spectrum of Compound 2I (CDCl₃, 100 MHz)



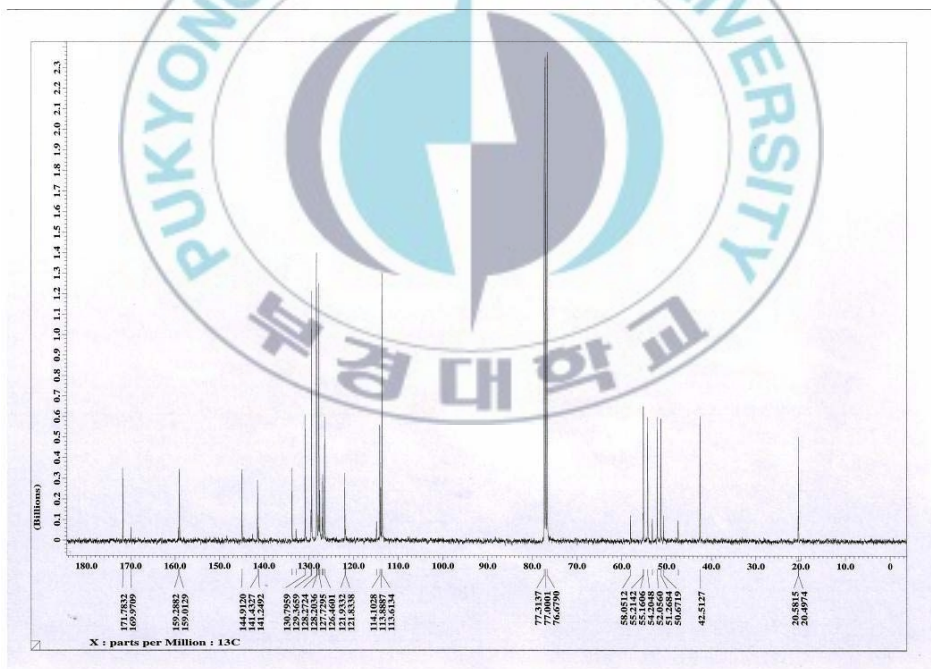
¹H NMR Spectrum of Compound 2m (CDCl₃, 400 MHz)



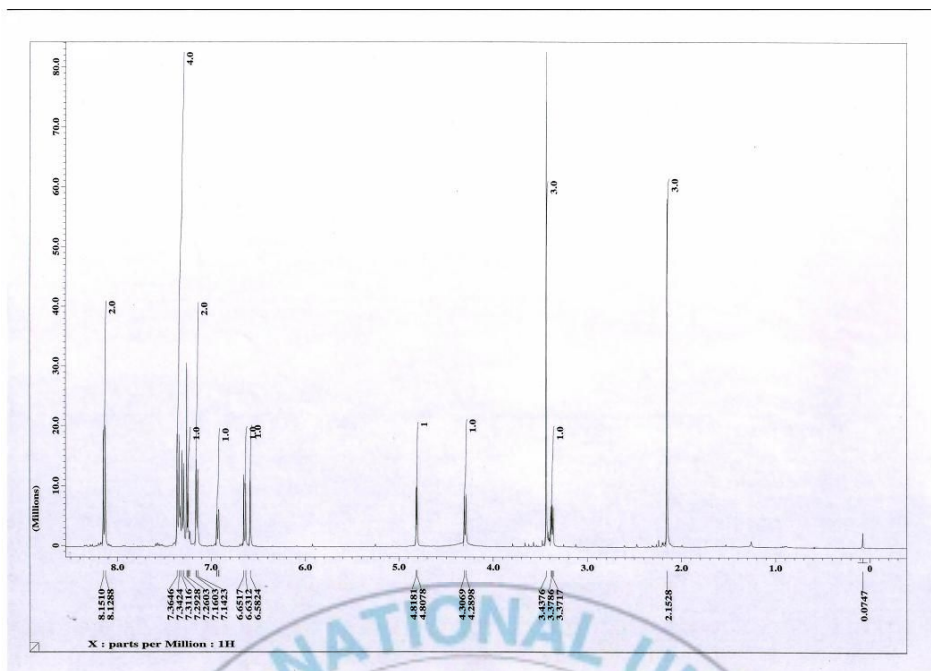
¹³C NMR Spectrum of Compound 2m (CDCl₃, 100 MHz)



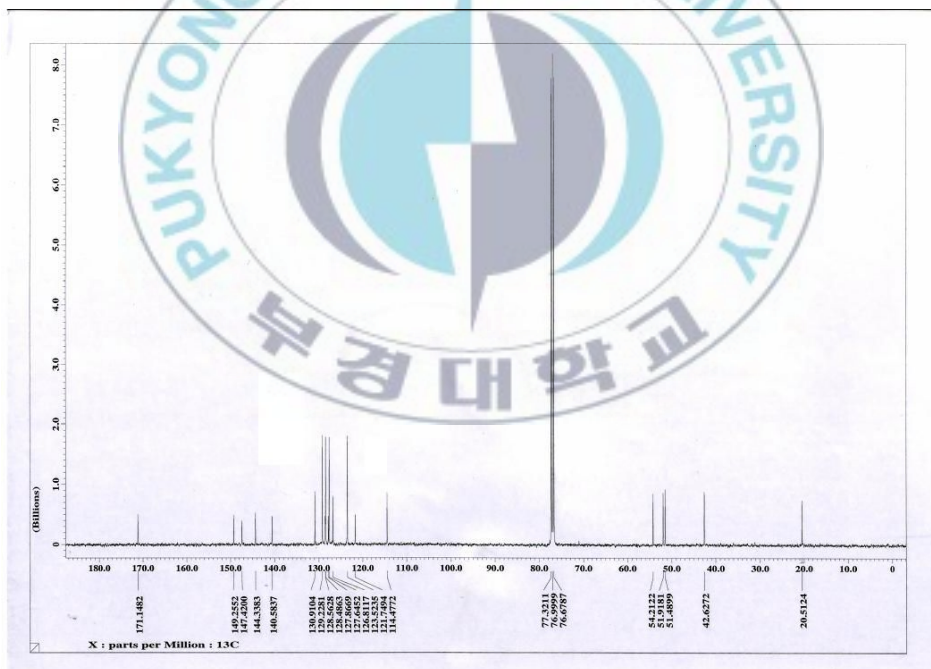
¹H NMR Spectrum of Compound **2n** (CDCl₃, 400 MHz)



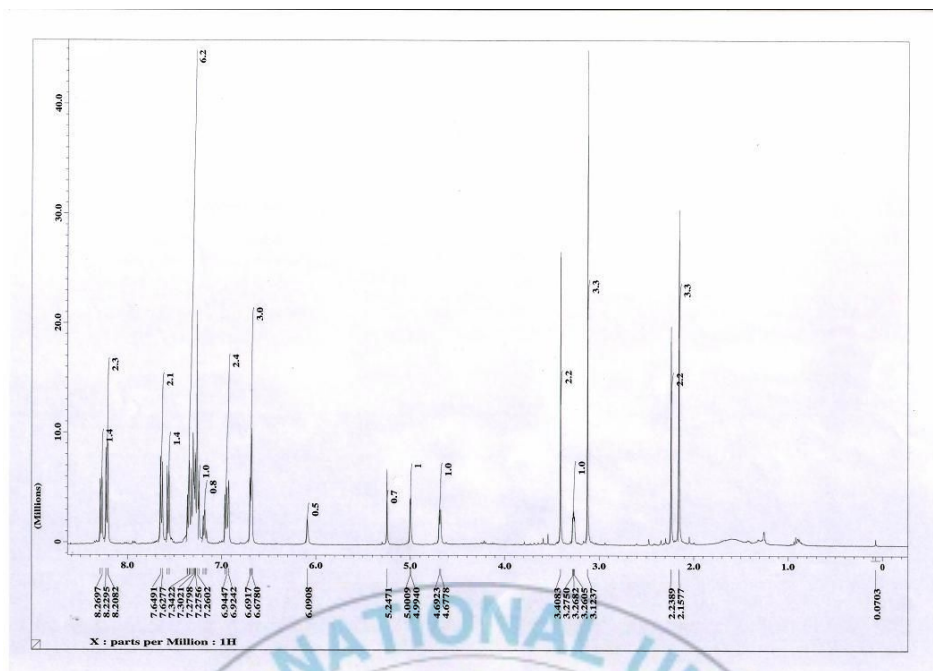
¹³C NMR Spectrum of Compound **2n** (CDCl₃, 100 MHz)



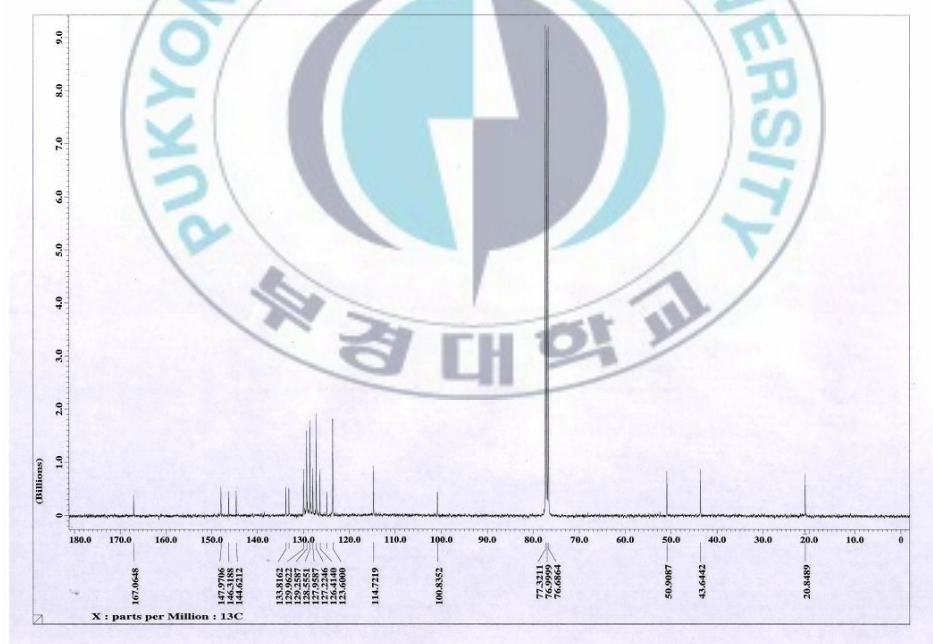
¹H NMR Spectrum of Compound **2o** (CDCl₃, 400 MHz)



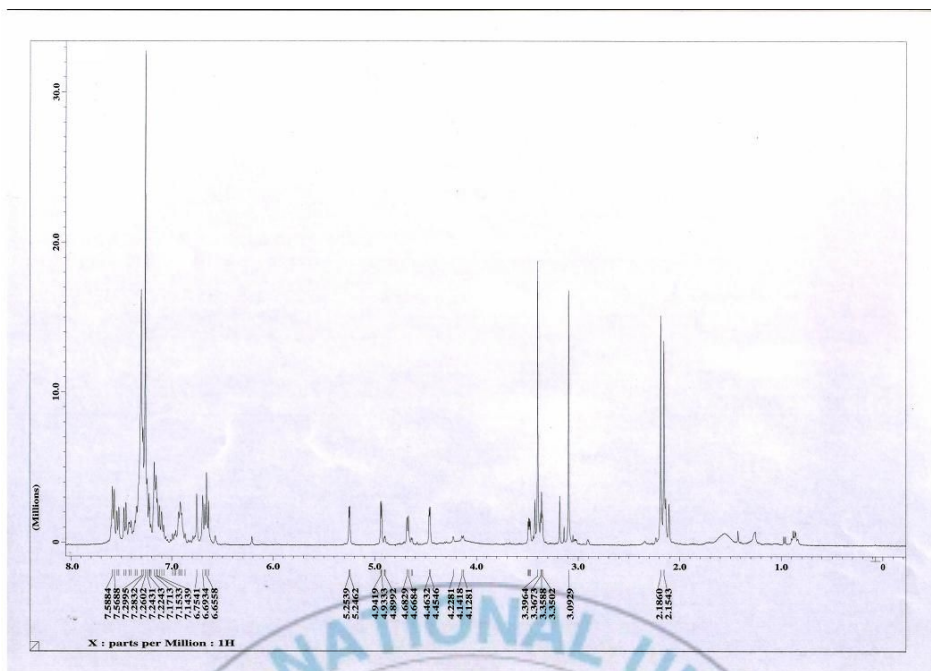
¹³C NMR Spectrum of Compound **2o** (CDCl₃, 100 MHz)



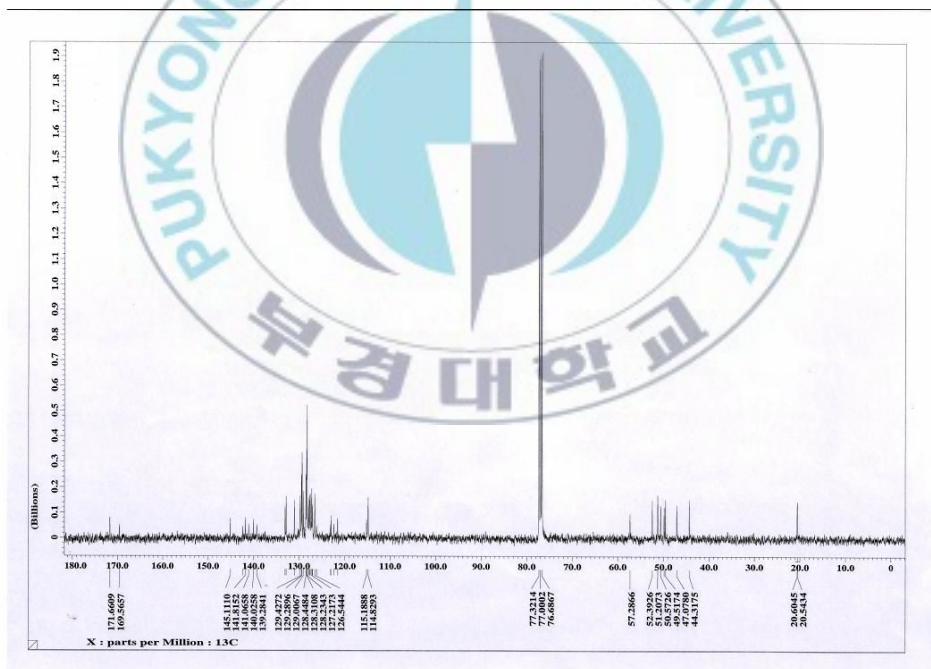
¹H NMR Spectrum of Compound 2'o (CDCl₃, 400 MHz)



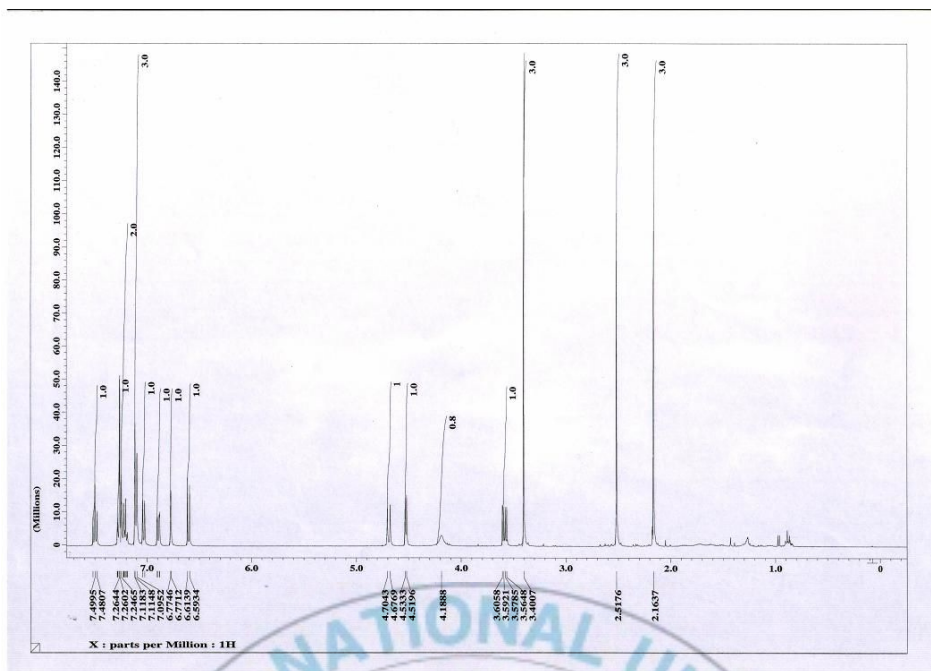
¹³C NMR Spectrum of Compound 2'o (CDCl₃, 100 MHz)



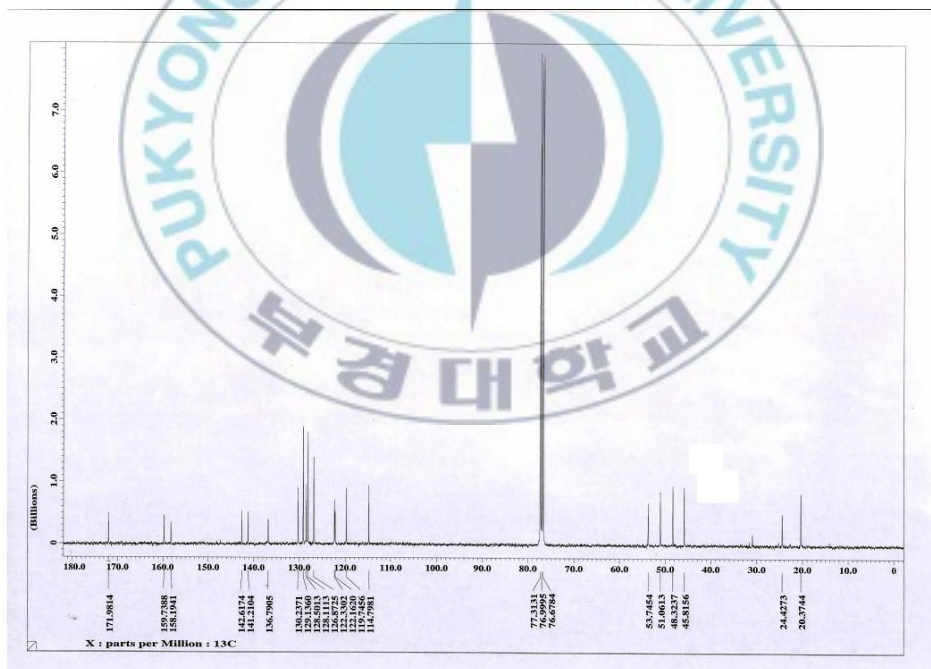
^1H NMR Spectrum of Compound **2p** (CDCl_3 , 400 MHz)



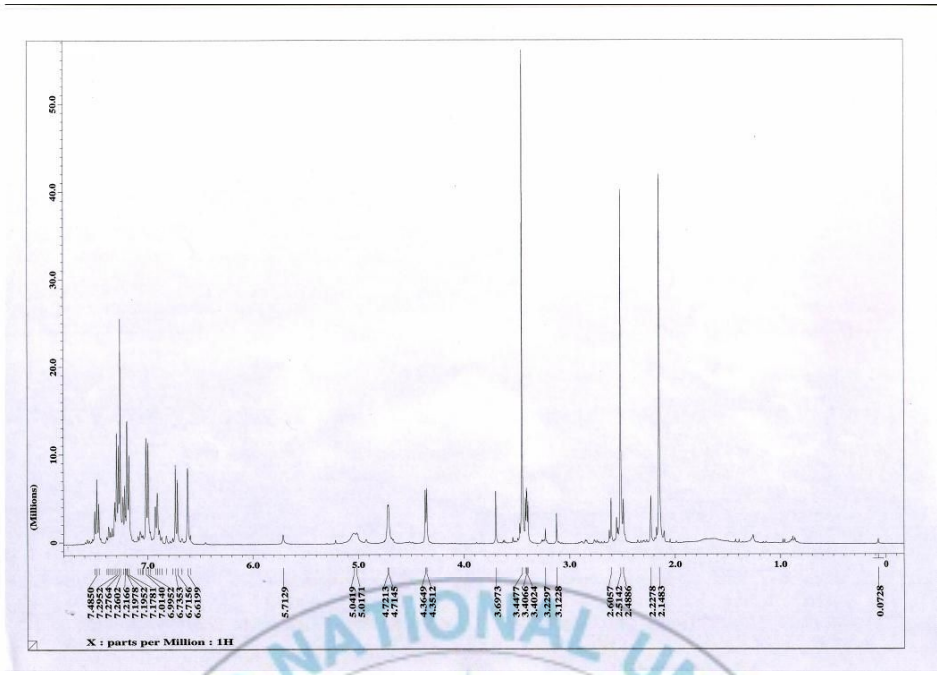
^{13}C NMR Spectrum of Compound **2p** (CDCl_3 , 100 MHz)



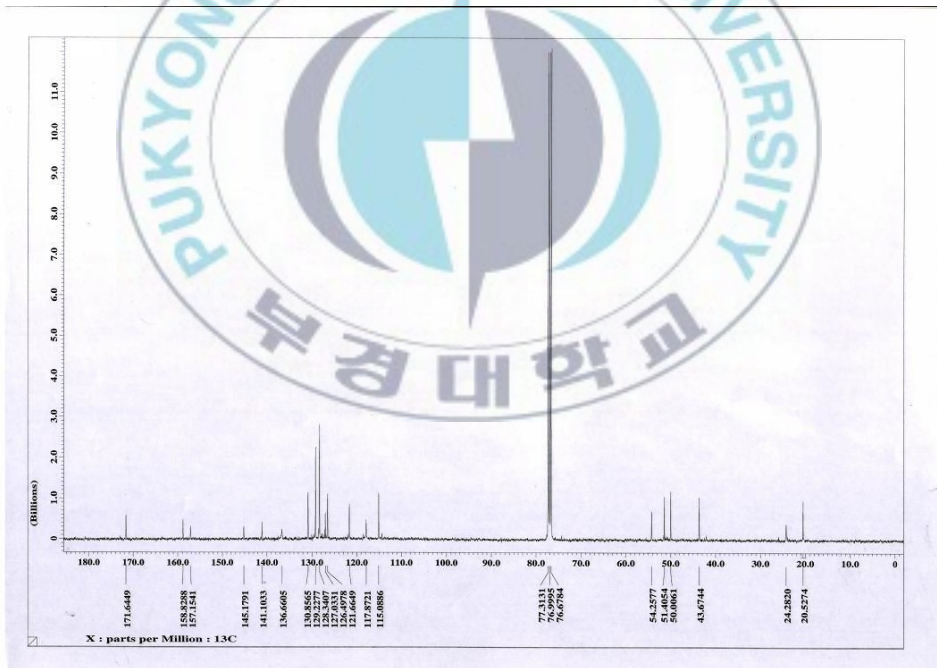
¹H NMR Spectrum of Compound **2q** (CDCl₃, 400 MHz)



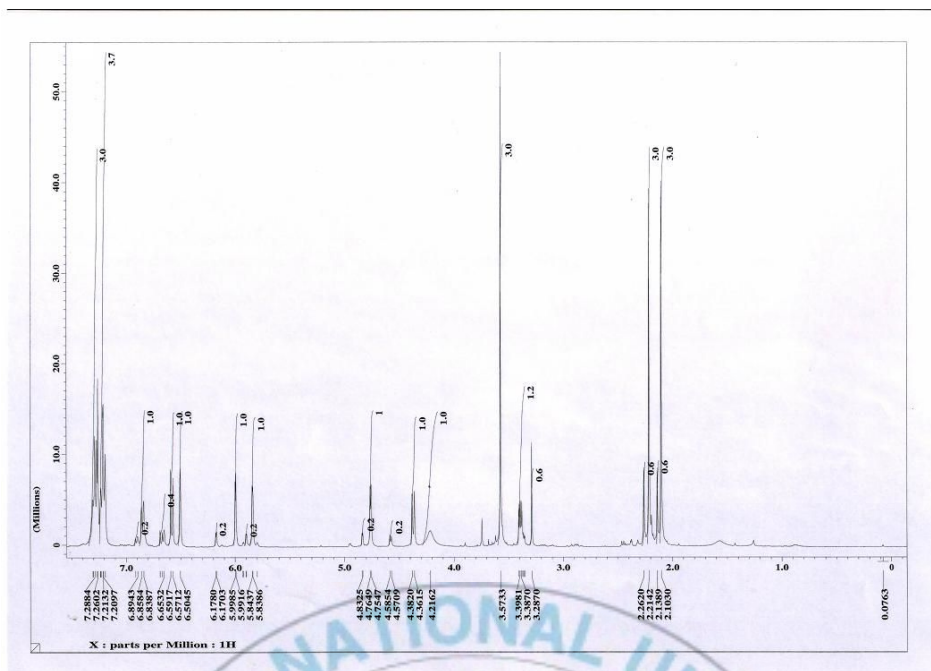
¹³C NMR Spectrum of Compound **2q** (CDCl₃, 100 MHz)



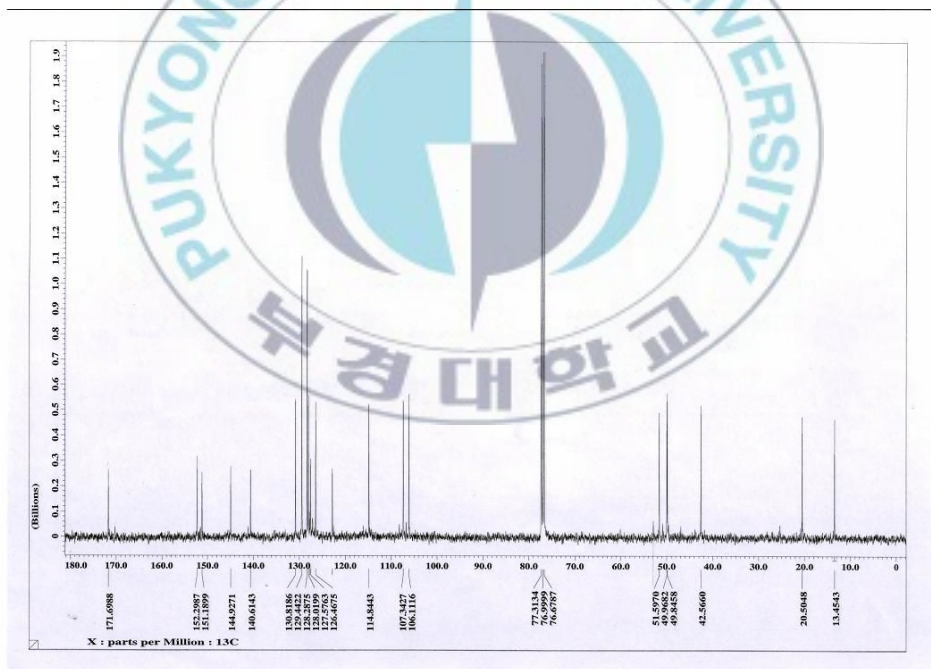
¹H NMR Spectrum of Compound 2'q (CDCl₃, 400 MHz)



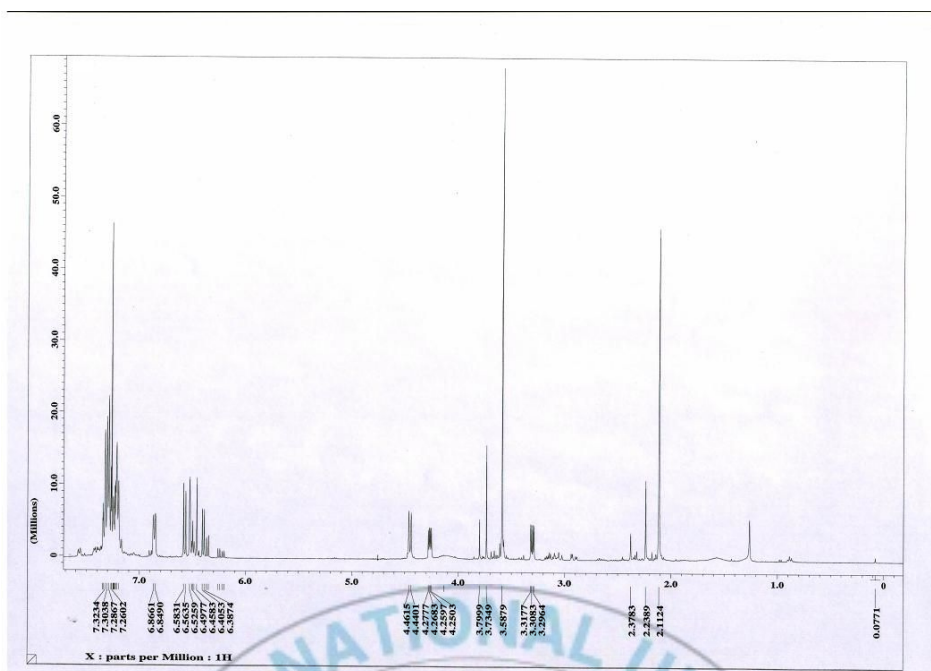
¹³C NMR Spectrum of Compound 2'q (CDCl₃, 100 MHz)



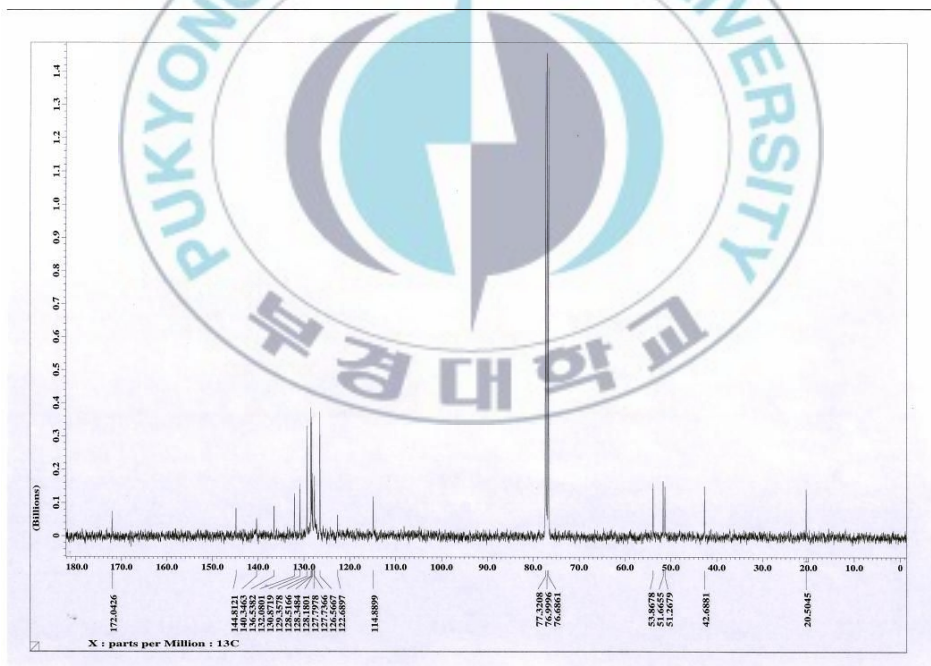
^1H NMR Spectrum of Compound **2r** (CDCl_3 , 400 MHz)



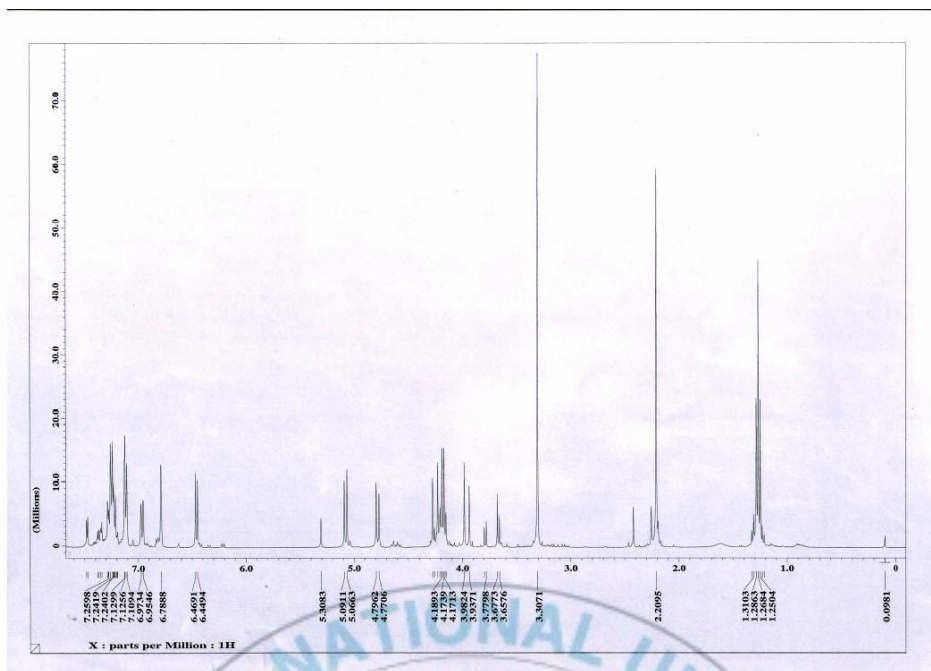
^{13}C NMR Spectrum of Compound **2r** (CDCl_3 , 100 MHz)



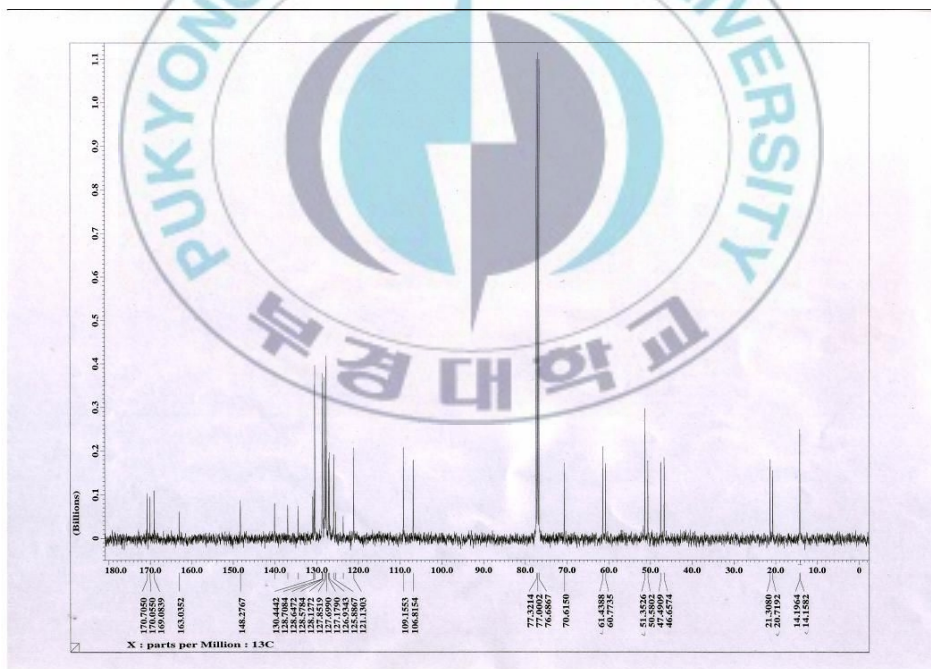
^1H NMR Spectrum of Compound 2s (CDCl_3 , 400 MHz)



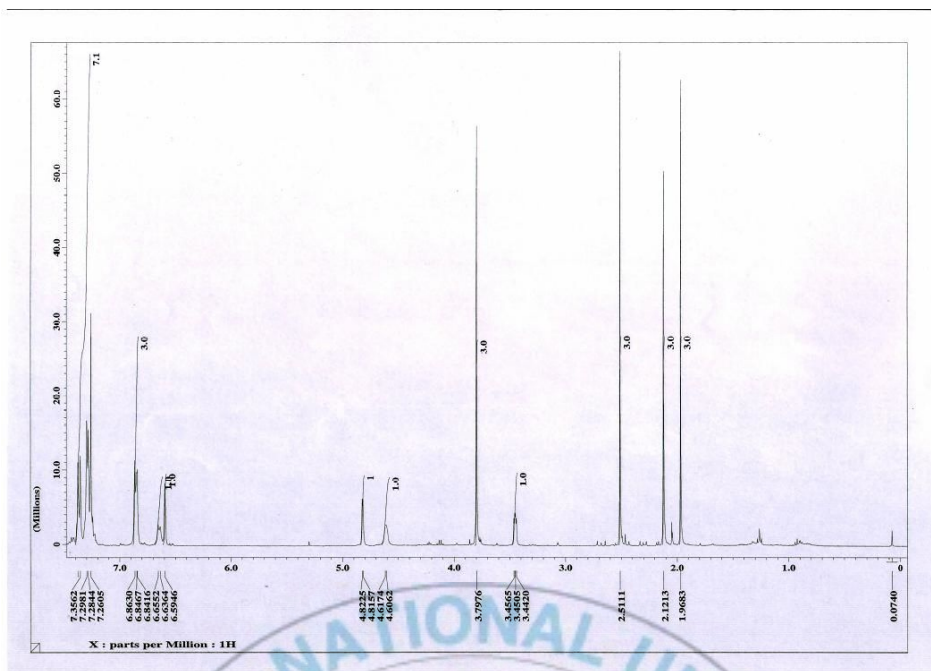
^{13}C NMR Spectrum of Compound 2s (CDCl_3 , 100 MHz)



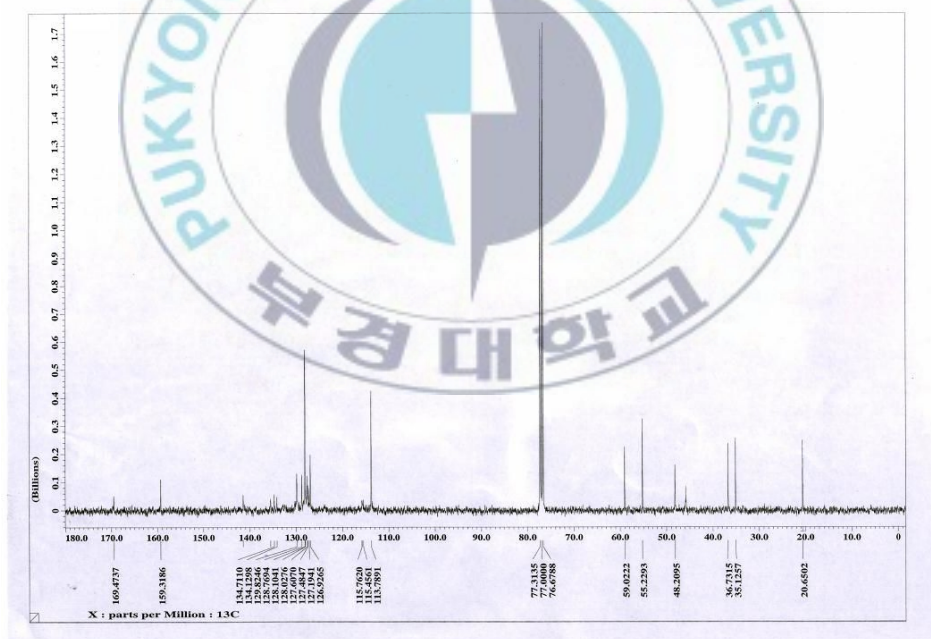
¹H NMR Spectrum of Compound 2t (CDCl₃, 400 MHz)



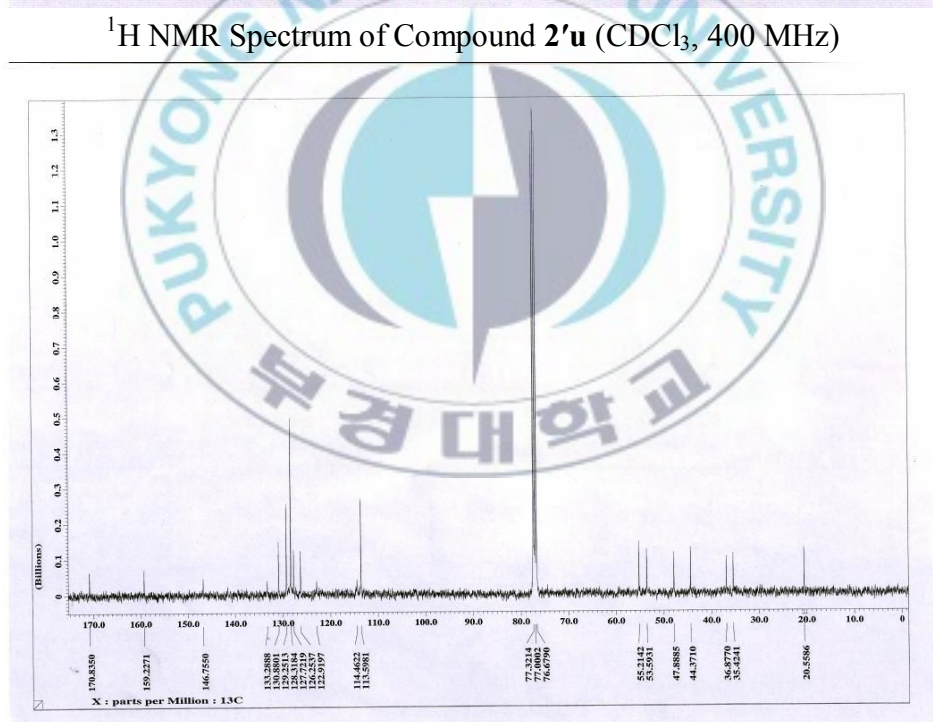
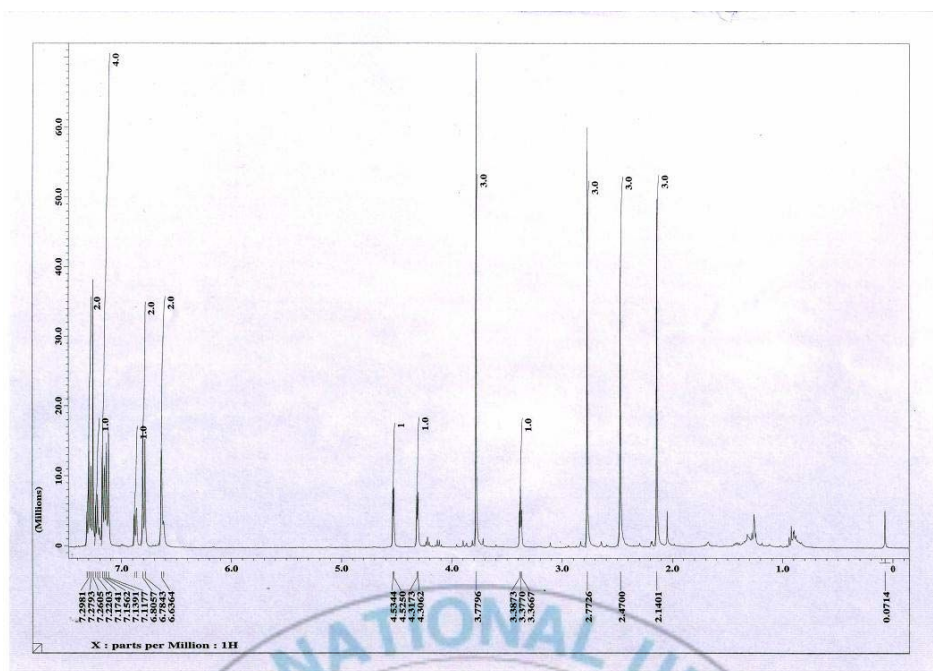
¹³C NMR Spectrum of Compound 2t (CDCl₃, 100 MHz)

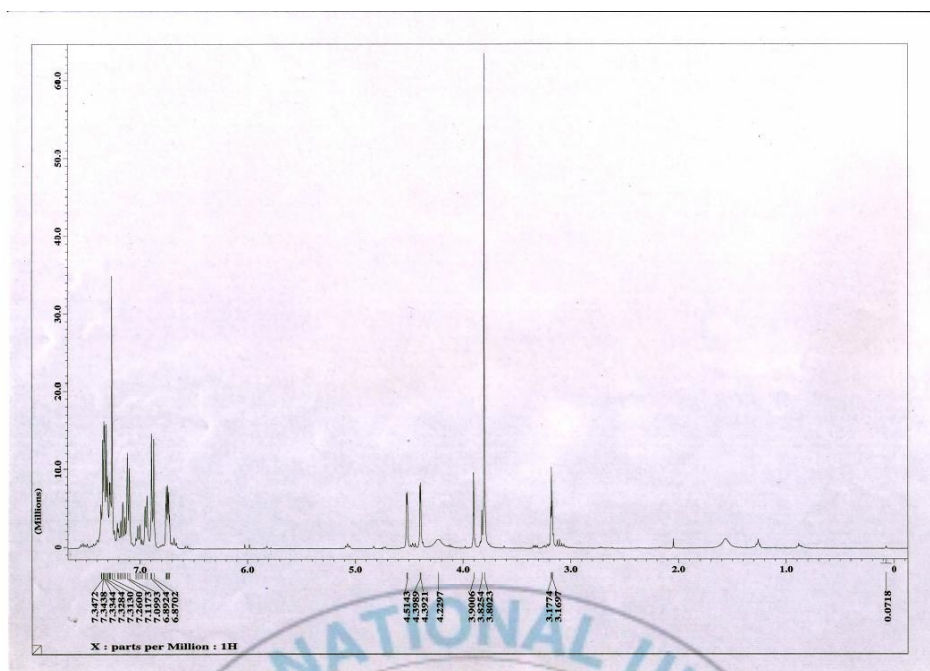


¹H NMR Spectrum of Compound **2u** (CDCl₃, 400 MHz)

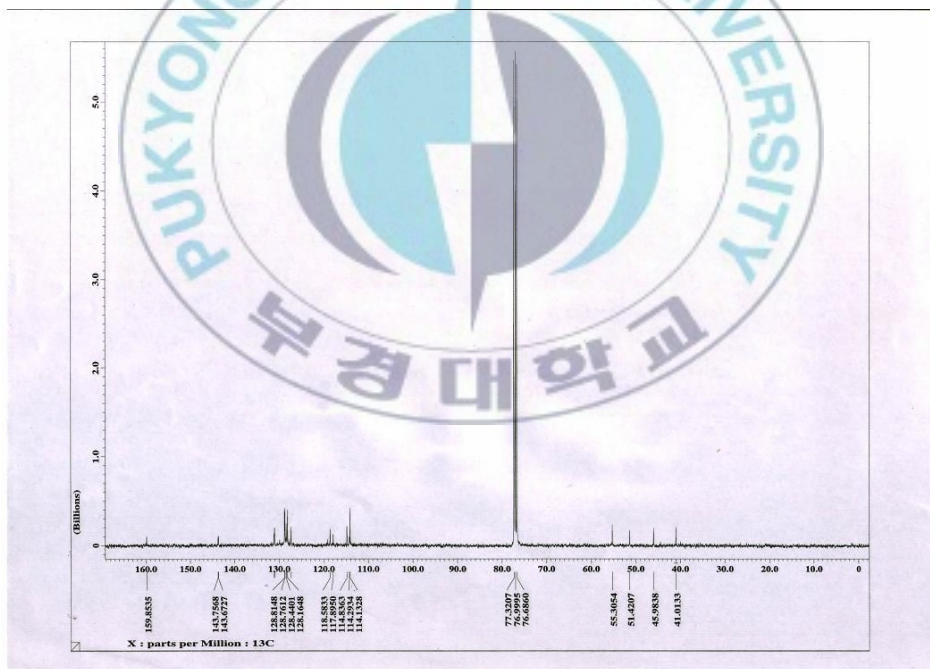


¹³C NMR Spectrum of Compound **2u** (CDCl₃, 100 MHz)

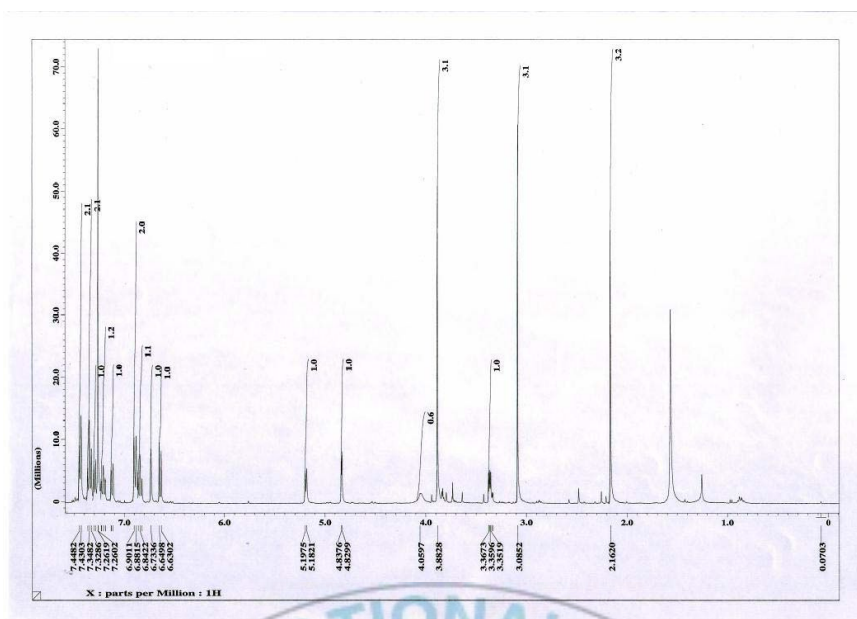




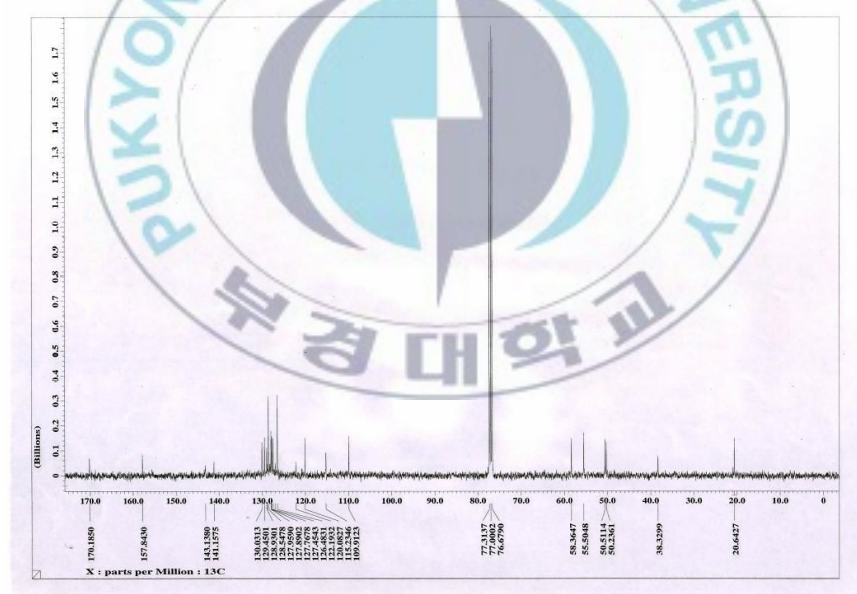
^1H NMR Spectrum of Compound **2v** (CDCl_3 , 400 MHz)

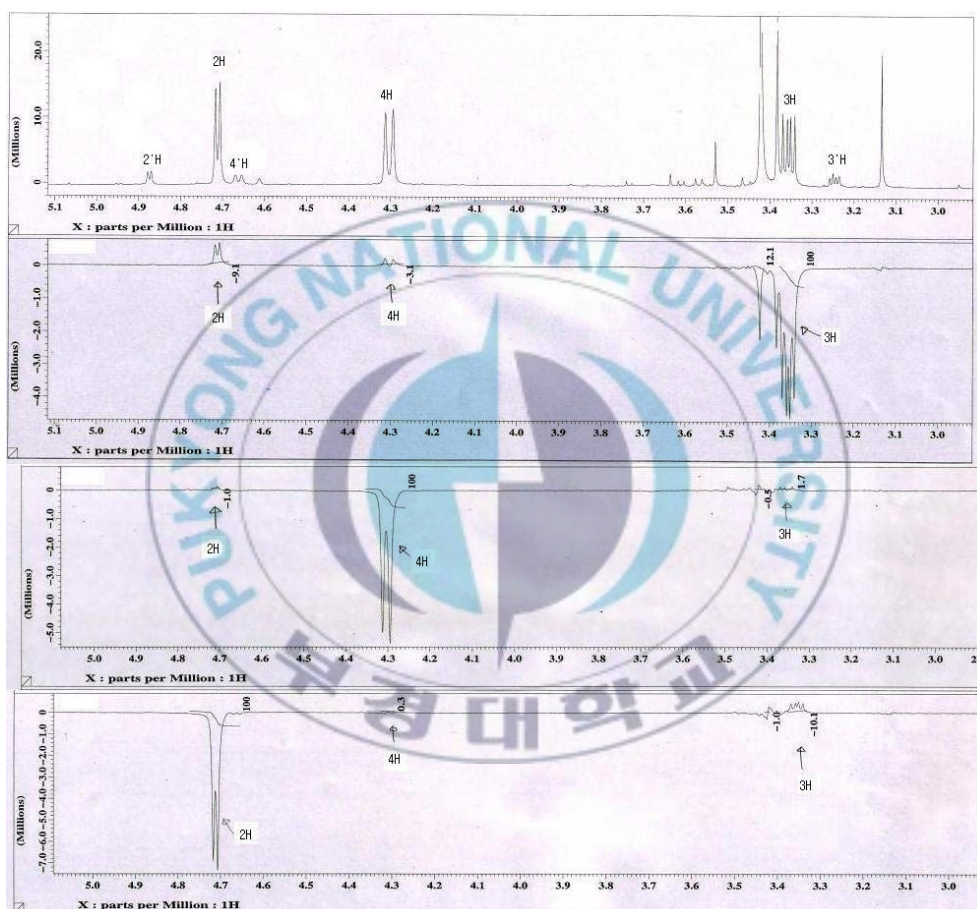
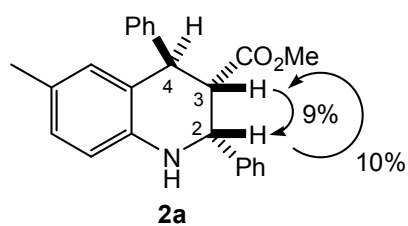


^{13}C NMR Spectrum of Compound **2v** (CDCl_3 , 100 MHz)

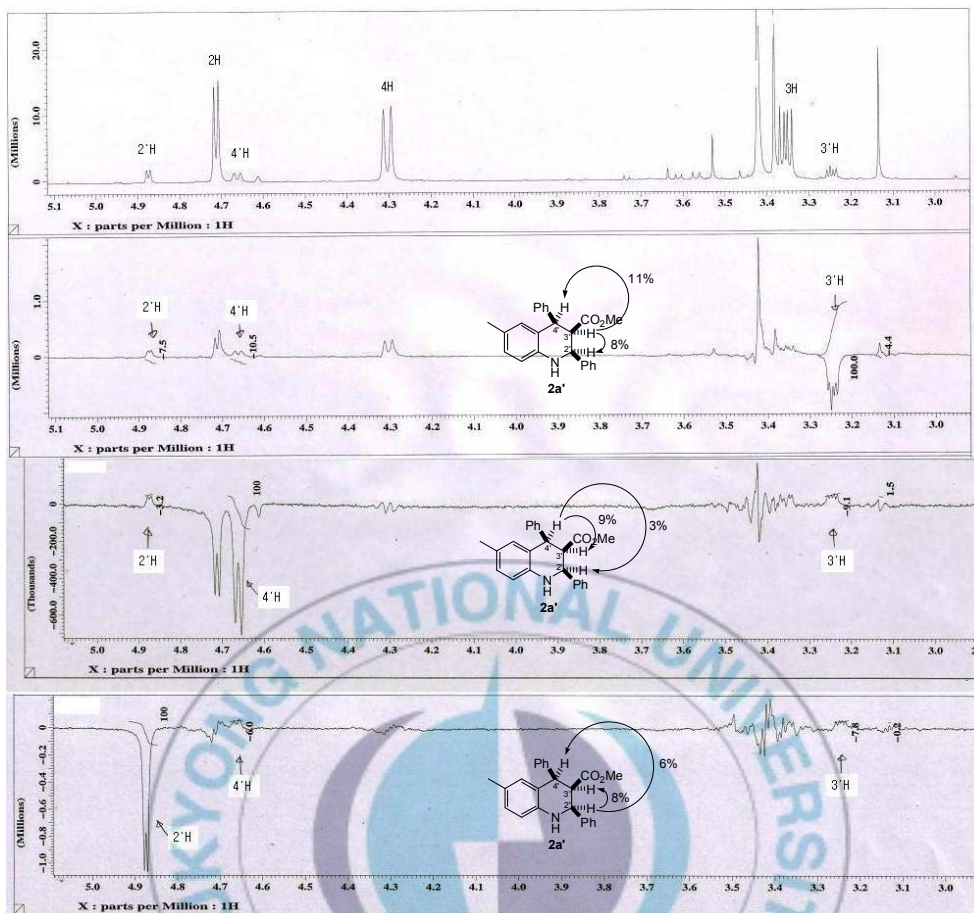


¹H NMR Spectrum of 4-(2-Methoxyphenyl)-6-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid methyl ester

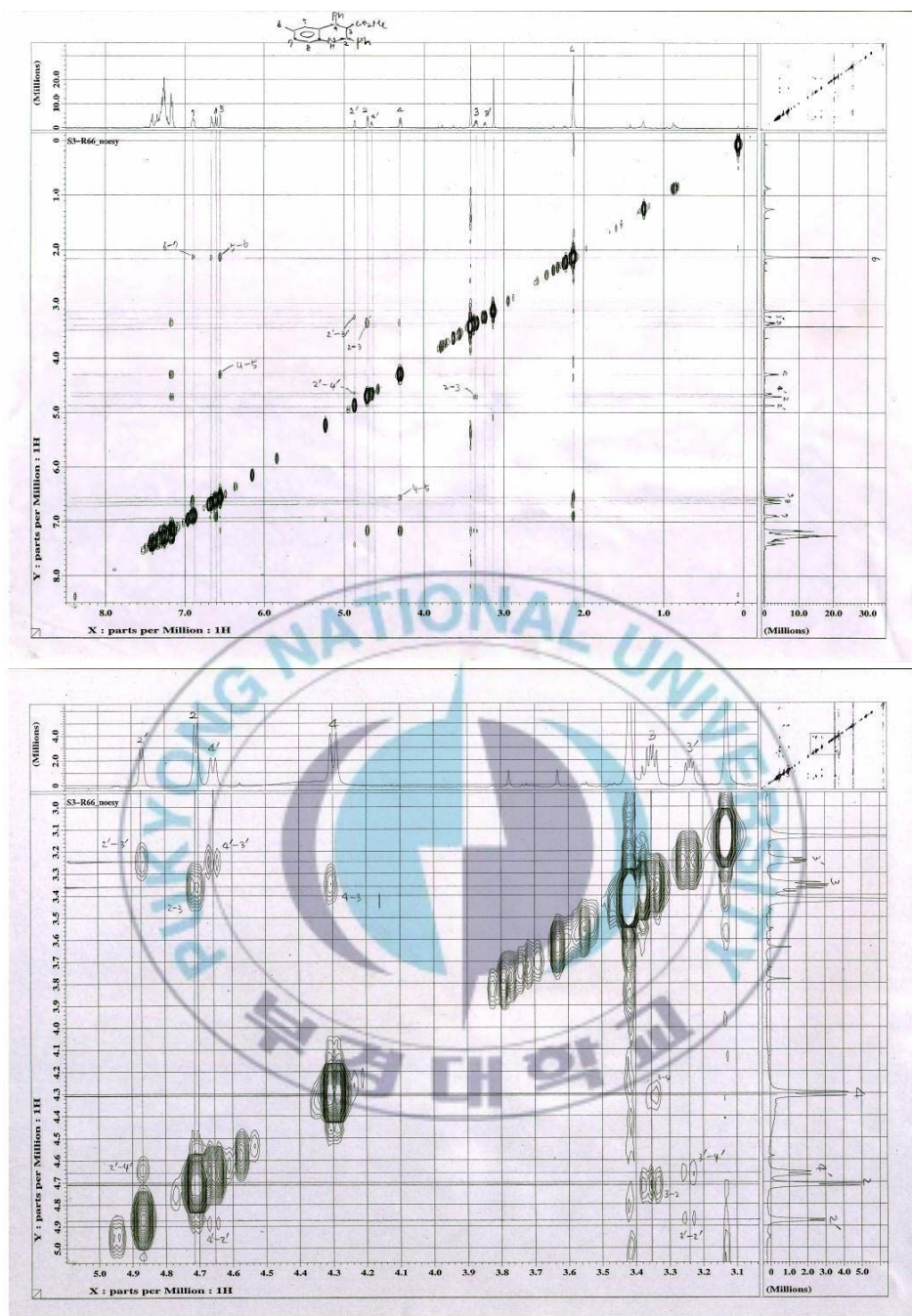




NOE Spectrum of Compound **2a**

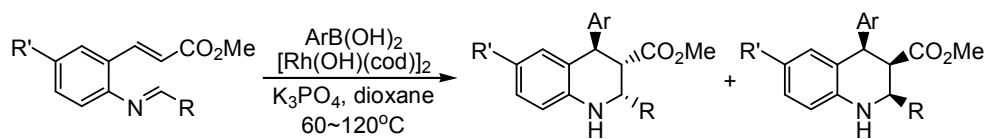


NOE Spectrum of Compound 2'a



NOESY Spectrum of Compound 2a

7. Korean Abstract



전이금속 촉매를 이용한 연속적인 C-C 결합 형성 반응은 간단한 물질로부터 복잡한 화합물을 만드는데 아주 효율적인 반응이고, 특히 고리 화합물을 만드는데 다양한 연속적인 결합 방법들이 적용되고 있다. 이 연구에서는 로듐(I) 촉매를 이용한 연속적인 콘쥬게이트 첨가반응과 Mannich 고리형성반응을 이용해 테트라하이드로퀴놀린을 만들 수 있었고, 다양한 치환기의 도입이 가능하였다.

이 반응은 연속적인 C-C 결합 형성 반응에서, 이민이 두번째 친전자체로서 작용하여 (oxa- π -allyl)rhodium(I) 중간체와 분자내 반응을 통해 고리가 형성되는 첫번째 예이다.

