이학석사학위논문

Ru-Catalyzed Reconstitutive Cycloisomerization of *N*-Sulfonyl-*N*-Hydroxyamino -alkynes to Lactams

루테늄 촉매를 이용한 *엔*-설포닐-*엔*-하이드록시 아미노알카인의 분자 재배치를 통한 락탐으로의 환이성화 반응

2014년 8월

서울대학교 대학원
화학부 유기화학 전공
김 성 미

Ru-Catalyzed Reconstitutive Cycloisomerization of *N*-Sulfonyl-*N*-Hydroxyamino -alkynes to Lactams

루테늄 촉매를 이용한 *엔*-설포닐-*엔*-하이드록시 아미노알카인의 락탐으로의 분자 재배치를 통한 환이성화 반응

지도교수 이철범

이 논문을 이학석사학위논문으로 제출함
2014년 7월

서울대학교 대학원
화학부 유기화학 전공
김 성 미

김성미의 석사학위논문을 인준함
2014년 7월

위 원 장 홍 순 혁

부위원장 이 철 범

위 원 최 태 림

CONTENTS

ABSTRACT

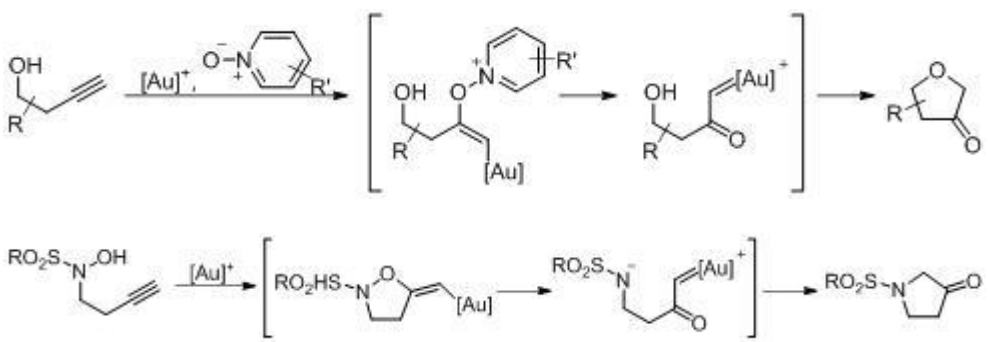
A ruthenium-catalyzed reconstitutive cycloisomerization reaction has been developed using *N*-sulfonyl-*N*-hydroxyamino-alkynes as substrates. In contrast to the gold catalysis that forms 3-pyrrolidinones from the *N*-sulfonyl-*N*-hydroxyamino-alkynes, the ruthenium catalysis gives lactams as the product. The scope and limitations as well as the mechanism of this catalytic 1,1-*gem*-difunctionalization are detailed in this dissertation.

Keywords: Ruthenium catalysis, metal vinylidene, reconstitutive cycloisomerization, lactam, terminal alkyne

Student ID: 2012-20266

INTRODUCTION

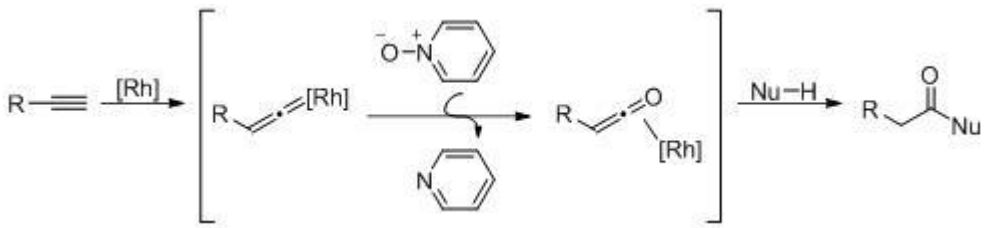
Atom-transfer reactions have received intense attention due to their aspect of increasing the molecular complexity of simple organic molecule atom- and redox-economically.[1] Weak N-O bonds are used to produce various atom- and redox-economical transformation through oxygen atom transfer to π bonds.[2][3] Recently, many transition metal-catalyzed oxygen transfer redox reactions have been published, and nitrones[4], amine-*N*-oxides [5], oximes[3b][6], hydroxamates[3d], and hydroxylamine derivatives[7] are used as a oxygen source. Scheme 1 shows some examples of gold-catalyzed oxygen transfer redox reactions.[5c], [7]



Scheme 1. Au-catalyzed oxygen-transfer redox reactions

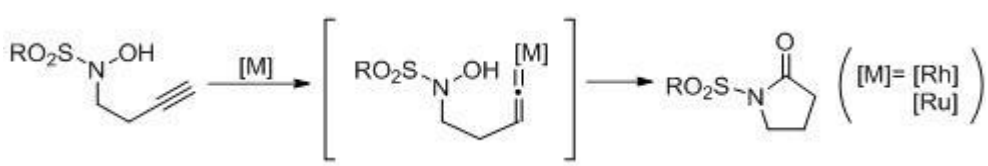
In previous studies carried out in the Lee laboratory, a transition metal-catalyzed 1,1-addition reaction through metal

vinylidene intermediates was developed using rhodium catalyst, pyridine-*N*-oxides, and terminal alkynes (Scheme 2).[8]



Scheme 2. Rh-catalyzed oxygenative addition reactions

With this background, we planned to develop the transition metal-catalyzed reconstitutive cycloisomerization reaction using *N*-sulfonyl-*N*-hydroxyaminoalkynes through metal vinylidene intermediates (Scheme 3). This unexplored reaction could offer a highly atom- and redox-econimic transformation that forms two carbon-heteroatom bonds in a single step. As a result of the reaction, highly useful lactam products[9] can be prepared by a new way.[10]



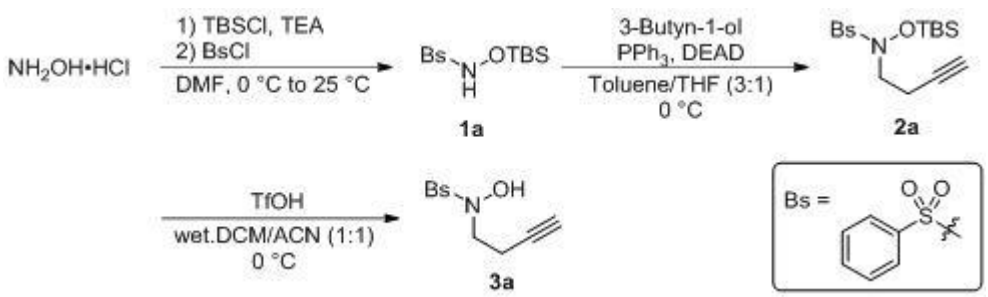
Scheme 3. Proposed reactions

RESULT AND DISCUSSION

1. Reaction Discovery and Optimization

1.1 Preparation of substrates

In order to prepare the suitable model system having an internal oxidant, substrate **3a** with nucleophile and terminal alkyne groups within the same molecule, was synthesized following the report of Shin (Scheme 4).[7]



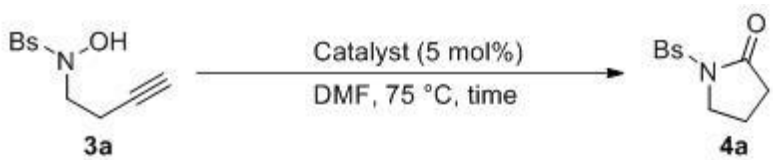
Scheme 4. Synthesis of *N*-sulfonyl-*N*-hydroxyaminoalkyne

Firstly, hydroxylamine hydrochloride was protected with *tert*-butyldimethylchlorosilane and then reacted with benzenesulfonyl chloride to provide **1a**. Then, sulfonamide **1a** was coupled with 3-butyn-1-ol using the Mitsunobu reaction. Subsequently, deprotection of the *tert*-butyldimethylsilyl group under acidic conditions gave the desired product **3a**.

1.2 Catalysts

Our initial effort was focused on screening the metal catalyst known to make metal vinylidene species (Table 1).

Table 1. Screening of catalysts[a)]



3a 4a

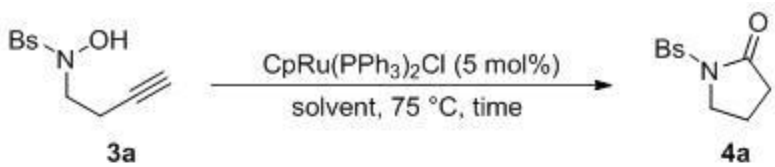
entry	catalyst	time	yield[b)]
1	$CpRu(PPh_3)_2Cl$	5 h	90%
2	$Cp^*Ru(PPh_3)_2Cl$	3 d	78%[c)]
3	$CpRu(CH_3CN)_3PF_6$	3 d	18%[c)]
4	$CpRu(CH_3CN)_3PF_6 + PPh_3$[d)]	5 h	88%
5	$TpRu(PPh_3)_2Cl$	3 d	20%[c)]
6	$TpRu(PPh_3)(CH_3CN)_2Cl$	3 d	25%[c)]
7	$[RuCl_2(p\text{-cymene})]_2$[e)]	3 d	38%
8	$RhCl(PPh_3)_3$	3 d	0%
9	$RhCl_3$	3 d	0%
10	$[RhCl(COD)]_2 + P(4\text{-}F\text{-}C_6H_4)_3$[f)]	3 d	0%

a) All reactions were performed with 0.1 mmol of alkyne and 5 mol% catalyst in 0.5 mL of DMF at 75 °C. b) Yield was determined by NMR use 1,3,5-tri-*tert*-butylbenzene as an internal standard. c) starting material remained. d) Use 5 mol% catalyst and 10 mol% ligand. e) Use 2.5 mol% catalyst. f) Use 3 mol% catalyst and 12 mol% ligand.

A series of ruthenium and rhodium catalysts were tested. The reaction was performed with alkyne **3a,** and 5 mol% of catalyst in *N,N*–dimethylformamide (DMF) at 75 °C. Only in the presence of ruthenium complex produced the desired product **4a**. Especially, $CpRu(PPh_3)_2Cl$ gave the product with the highest yield. With this result, we could assume that ruthenium catalyst, Cp ligand and PPh_3 were essential to the reaction.

1.3 Solvents

Table 2. Screening of solvents[a)]

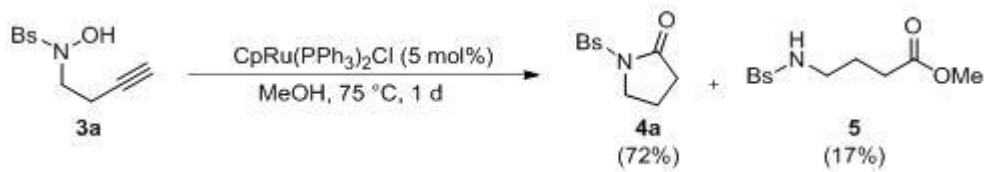


3a **4a**

entry	solvent	time	yield[b)]
1	DMF	3 h	90%
2	DCE	6 h	88%
3	ACN	1 d	84%
4	THF	1 d	83%
5	Toluene	1 d	84%
6	MeOH	1 d	72%

a) All reactions were performed with 0.1 mmol of alkyne, 5 mol% catalyst in 0.5 mL of solvent at 75 °C. b) Yield was determined by NMR use 1,3,5-tri-*tert*-butylbenzene as an internal standard.

Solvent screening studies showed that DMF was the best solvent for reconstitutive cycloisomerization reaction (Table 2). In the case of DMF, it gave the highest yield of the product within 3 hours. When methanol (MeOH) was used as a solvent (Table 2, entry 6), a 17% of side product **5** was produced by MeOH addition (Scheme 5).

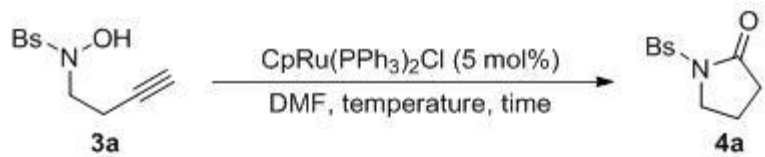


Scheme 5. Reaction in methanol

1.4 Temperature and Concentration

The reconstitutive cycloisomerization reaction was performed at various temperatures and concentrations (Table 3). Firstly, the reaction temperature was checked at the same concetraion, 0.1 M (Table 3, entry 1-6). A series of experiments showed that high temperatures provided better results in terms of the reaction rate and yield. Through the concentration screening experiments, it was found that dilute conditions gave better results (Table 3, entry 5-9). It seemed that this reconstitutive cycloisomerization is an intramolecular reaction.

Table 3. Screening of temperature and concentration[a)]



3a 4a

entry	temperature	concentration	time	yield[b)]
1	r.t.	0.1	2 d	69%[c)]
2	50 °C	0.1	5 h	64%[c)]
3	60 °C	0.1	5 h	73%[c)]
4	75 °C	0.1	3 h	90%
5	100 °C	0.1	1 h	92%
6	100 °C	0.2	5 h	86%
7	100 °C	0.4	5 h	86%
8	100 °C	0.6	5 h	80%
9	100 °C	1.0	5 h	45%[c)]

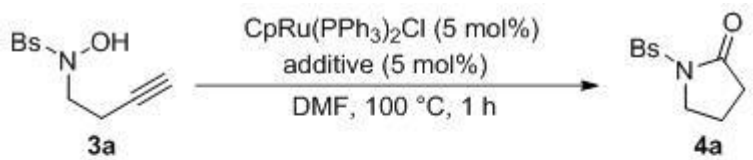
a) All reactions were performed with 0.1 mmol of alkyne and 5 mol% catalyst. b) Yield was determined by NMR use 1,3,5-tri-*tert*-butylbenzene as an internal standard. c) Starting material remained.

1.5 Additives

Experiments for finding out counteranion effects in the transition metal-catalyzed reconstitutive cycloisomerization was performed by adding various silver salts in the same amount as the ruthenium catalyst (Table 4). Before adding substrate **3a**, the reaction mixture with $CpRu(PPh_3)_2Cl$ and a silver salt in DMF

was stirred for 5 minutes for anion exchange. There was no significant difference displayed by the counteranion (Table 4, entry 1−7). When more chloride anion was added, the yield of the desired product was slightly decreased (Table 4, entry 8).

Table 4. Screening of additives[a)]



3a 4a

entry	silver salt	yield[b)]
1	no additive	90%
2	$AgNO_3$	90%
3	AgOTf	84%
4	$AgClO_4$	85%
5	$AgSbF_6$	86%
6	$AgBF_4$	87%
7	$AgPF_6$	90%
8	Bu_4N^+Cl	86%

a) All reactions were performed with 0.1 mmol of alkyne, 5 mol% catalyst and 5 mol% additive in 1.0 mL of solvent at 100 °C.
b) Yield was determined by NMR use 1,3,5-tri-*tert*-butylbenzene as an internal standard.

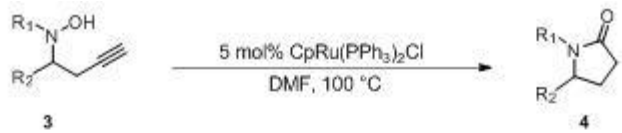
2. Substrate Scope

2.1 Substituents modification

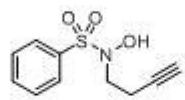
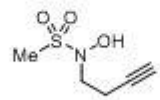
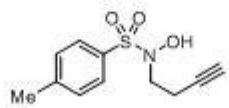
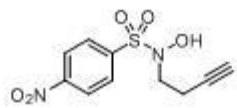
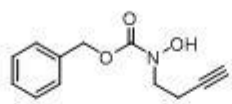
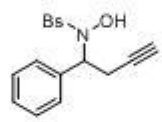
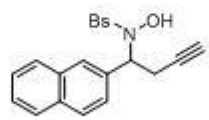
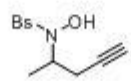
With the optimized reaction conditions, we proceeded to perform a series of experiments to investigate the scope of the ruthenium catalyzed reconstitutive cycloisomerization reaction. The desired product was formed well with sulfonamide substrates (Table 5, entry 1-4). It was also found that substrates with a stronger electron-withdrawing group gave better yields. In an effort to confirm this tendency, we also tested other substrate with weaker electron-withdrawing groups than sulfonyl group (Table 5, entry 5). With carbobenzyloxy (cbz) substituted substrates, the yield of the product was decreased to a considerable degree.

We also checked the reactivity of various aryl and alkyl substituted substrates in the tether, and it gave reasonable yields of corresponding lactams (Table 5, entry 6-8).

Table 5. Substrate scope of reconstitutive cycloisomerization[a)]



3 4

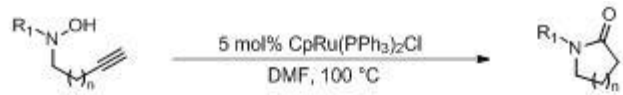
entry		substrate	product	yield[b)]
1	**3a**		**4a**	90%
2	**3b**		**4b**	84%
3	**3c**		**4c**	86%
4	**3d**		**4d**	94%
5[c)]	**3e**		**4e**	11%
6	**3f**		**4f**	47%[c)]
7	**3g**		**4g**	50%[c)]
8	**3h**		**4h**	48%

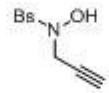
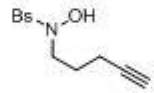
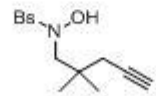
a) All reactions were performed with 1.0 mmol of alkyne, 5 mol% catalyst in 10.0 mL of DMF at 100 °C. b) Isolated yield. c) Reaction performed for 1 d. S.M remained. c) 2-step yield.

2.2 Chain length modification

After a set of experiments we carried out first to find the scope of Ru-catalyzed reconstitutive cycloisomerization reaction was focused on the synthesis of γ-lactams, we investigated the scope of the ring size of the product. Substrates were prepared using the same method for **3a** (Scheme 4). The first experiment with **3i** was performed at 100 °C which provided β-lactam product **4i** in 20% yield. But the reaction also produced many side products that were hard to identify. Because we thought this result was caused by the high reactivity of **3i**, we tested it again at lower temperature, 60 °C (Table 6, entry 1). The reaction took 24 h to give the product but only the desired product was formed with moderate yield. And we also tested **3j** to get a δ-lactam product (Table 6, entry 2). It stirred for one day at 100 °C, but conversion was very low. Due to the entropy effect, it seemed to hard to meet activated alkyne and hydroxyl group. So we designed *gem*-dimethyl group introduced substrate **3k** at homopropargylic position. Result of experiment with substrate **3k** gave better yield than one with **3j** (Table 6, entry 3). Using Ru-catalyzed reconstitutive cycloisomerization reaction, we could get β-, and δ-lactam as well as γ-lactam.

Table 6. Substrate scope of reconstitutive cycloisomerization[a)]

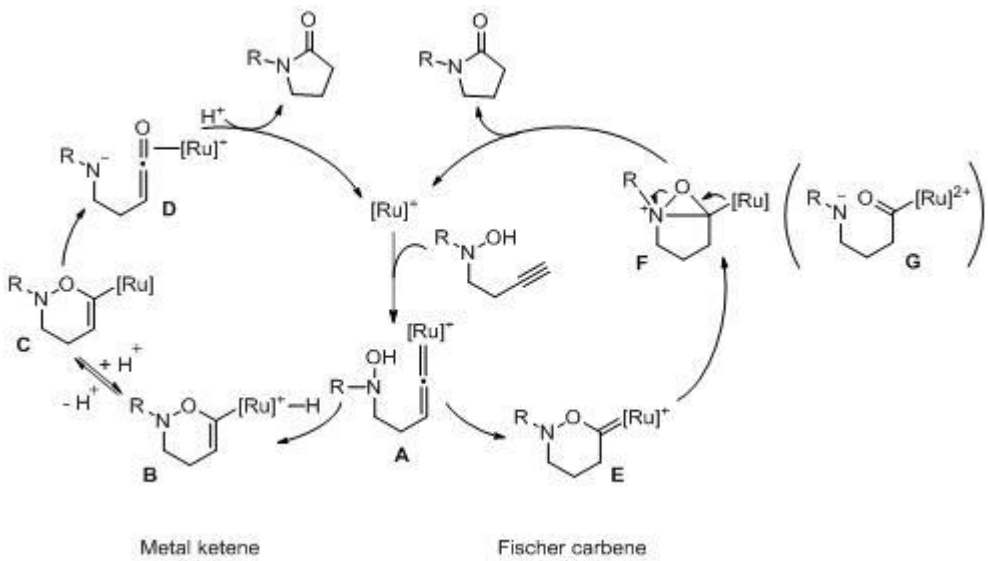


entry		substrate	product	yield[b)]
1[c)]	**3i**		**4i**	72%
2[d)]	**3j**		**4j**	10%
3[e)]	**3k**		**4k**	71%

a) All reactions were performed with 1.0 mmol of alkyne, 5 mol% catalyst in 10.0 mL of DMF at 100 °C. b) Isolated yield. c) Reaction performed for 1 d at 60 °C. S.M remained. d) Reaction run for 1 d. S.M remained. e) Reaction run for 5 h.

3. Proposed Reaction Mechanism

A plausible mechanism for the reconstitutive cycloisomerization is presented in Scheme 6. There are two possible mechanisms, the metal ketene pathway (Scheme 6, left cycle)[8][11] and Fischer carbene pathway (Scheme 6, right cycle).[12]



Scheme 6. Proposed mechanism

In the metal ketene mechanism, firstly metal vinylidene species A is formed by the reaction of the metal with a terminal alkyne. Then, the hydroxyl group adds to the Ru-carbene to form B, which is deprotonated to intermediate C. At this stage,

the ruthenium center may cause the cleavage of weak N–O bond to form metal ketene intermediate **D**. The nucleophilic addition of the nitrogen to the ketene followed by protonation forms the desired product and generates the catalyst.

In Fischer carbene mechanism, as the metal ketene mechanism, metal vinylidene **A** formed first. Then, Fischer carbene intermediate **E** is generated by the addition of hydroxyl group to the carbon–carbon double bond. At the second step, there are two possible pathways. The one involves the attack of the electon–rich nitrogen atom to the carbene carbon to form a center ring fused intermediate **F**. In the other pathway, the ruthenium donates two electrons, which induces N–O bond cleavage to generate acyl ruthenium intermediate **G**. **F** turns to the product by the N–O bond cleavage, and **G** is transformed to the lactam by nitrogen atom attack to the carbonyl carbon.

Regardless of the mechanism, several features were notable. First, substrates with a stronger electron–withdrawing group on nitrogen atom gave better results (Table 5, entry 1–5). The N–O bond cleavage step in the mechanism (Scheme 6) is believed to be the rate–determining step, since the more electron–withdrawing group, the faster the product formation. The second observation is that the reaction with substrate **3i** is too fast to control at 100 °C while reaction with **3j** was very

slow (Table 6). According to proposed mechanism, substrates should pass intermediate **B** or **E** which is cycle containing N–O bond. **3i** can form intermediate **B** or **E** much easier than **3j** because of entropy effect. So substrate **3k**, which is improved than **3j** to form 7–membered ring intermediate **B** or **E**, gave better result than **3j**.

CONCLUSION

In summary, we have developed the ruthenium-catalyzed reconstitutive cycloisomerization reaction of *N*-sulfonyl-*N*-hydroxyaminoalkynes through the ruthenium vinylidene intermediates. This method is highly useful for the synthesis of lactams atom- and redox-economically.

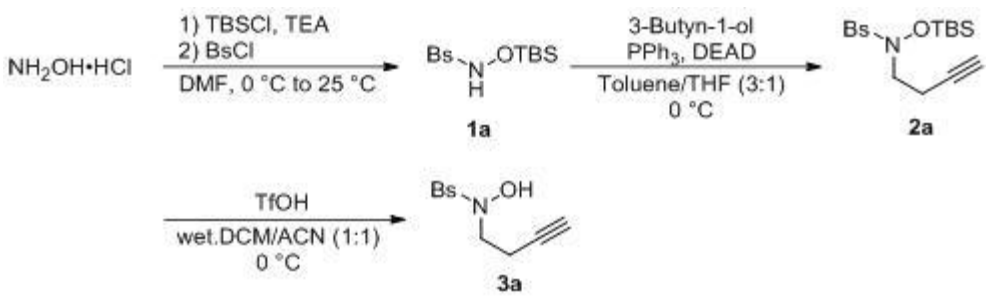
EXPERIMENTAL SECTION

General information. Unless otherwise noted, all reactions of substrates preparation were conducted in flame-dried glassware under an argon atmosphere using anhydrous solvent (obtained by passing through activated alumina columns of solvent purification systems from Glass Contour). Commercially abailable reagents were used without further purification. The progress of reaction was checked on thin layer chromatography (TLC) plates (Merck 5554 Kiesel gel 60 F254), and the spots were visualized under 254 nm UV light and/or charring after dipping it into a vanillin solution, a $KMnO_4$ solution, or a phosphomolybdic acid solution. Flash column chromatography was performed on silica gel (Merck 9385 Kiesel gel 60) using hexanes-ethyl acetate (v/v). ^1H and ^{13}C NMR spectra were obtained in $CDCl_3$, on an Agilent 400-MR DD2 Magnetic Resonance System (400 MHz) and a Varian/Oxford As-500 (500 MHz) spectrophotometer. ^1H NMR spectra were reported in parts per million (ppm) on the δ scale from an internal standard of residual chloroform (7.26 ppm). Data for ^1H NMR were reported as follows chemical shift, multiplicity (s = siglet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant in Herts (Hz) and integration. Data for ^{13}C NMR spectra

were reported in terms of chemical shift in ppm from the central peak of $CDCl_3$ (77.23 ppm). And gas chromatography data were obtained on a Hewlett Packard HP 6890 Series GC systems.

Preparation of substrates

N-sulfonyl-*N*-hydroxyaminoalkynes



N-sulfonyl-*N*-hydroxylamine derivatives **3** were prepared according to the procedure described in the reference literature[7] : A flame-dried round-bottomed flask with a magnetic stirbar was filled with hydroxylamine hydrochloride (2.085 g, 30 mmol) and *tert*-butyldimethylsilyl chloride (4.522 g, 30 mmol) in anhydrous DMF (75 mL). To the reaction mixture triethylamine (18.8 mL, 120 mmol) was added dropwise at 0 °C and warmed to room temperature. After 1 h, the solution was cooled to 0 °C and benzenesulfonyl chloride (3.45 mL, 27 mmol) was added in

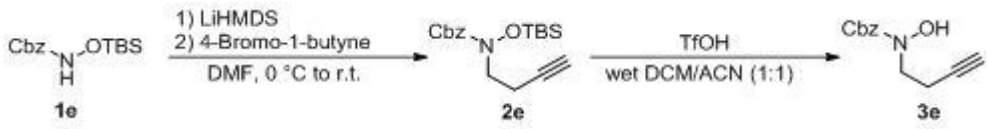
one portion, and stirred for another 1 h at room temperature. The reaction mixture was extracted with *n*-hexane for three times and the combined organic layers was washed with H_2O, 2N HCl solution, dried over $MgSO_4$, filtered and concentrated under reduced pressure. *N*-benzenesulfonyl-*O*-silylhydroxylamine **1a** (6.054 g, 21.1 mmol, 78% yield).

To a mixture of *N*-benzenesulfonyl-*O*-silylhydroxylamine **1a** (1.5 g, 5.22 mmol), 3-butyn-1-ol (0.43 mL, 5.74 mmol) and PPh3 (2.738 g, 10.4 mmol) in toluene/THF (21 mL, 3:1), DEAD (1.23 mL, 7.83 mmol) was added slowly at 0 °C. After stirring 1 h at this temperature, the reaction mixture was washed with water and extracted with EtOAc. The combined organic layer was washed with water, dried over $MgSO_4$ and concentrated. Purification by flash column chromatography on a silica gel gave the product **2a** (1.666 g, 4.91 mmol, 94% yield) as a viscous oil.

Substrate **2a** (1.5 g, 4.42 mmol) was dissolved in water saturated CH_2Cl_2 and CH_3CN (24 mL, 1:1) and TfOH (0.78 mL, 8.84 mmol) was added dropwise at 0 °C. The reaction mixture was stirred for 1 h at this temperature and sat. $NaHCO_3$ (aq. 12 mL) was added. After separation of layers, the aqueous layer was extracted with CH_2Cl_2. The combine organic phase was dried over $MgSO_4$ and solvent was removed by evaporator. Purification was performed with silica gel chromatography to give

desired product **3a** (965.8 mg, 4.29 mmol, 97% yield) as white crystal.

Benzyl but−3−yn−1−yl(hydroxy)carbamate



Benzyl but−3−yn−1−yl(hydroxy)carbamate **3e** was prepared according to the modified procedure described in the reference literature[7][13] : To Benzyl ((*tert*−butyldimethylsilyl)oxy) carbamate **1e** (1.652 g, 5.87 mmol) solution in DMF (11.7 mL), LiHMDS (1.0M in THF 5.87mL, 5.87 mmol) was added slowly at 0 ° C. After 30 min 4−bromo−1−butyne (0.55 mL, 5.87 mmol) was added at 0 ° C and warmed to room temperature. After another 2 h, reaction mixture was extracted with EtOAc, dried over $MgSO_4$, filtered, and concentrated. Purification was performed with silica gel chromatography to give product **2e** (1.057 g, 3.17 mmol, 56% yield) as pale yellow liquid.

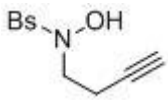
Substrate **2e** (580 mg, 1.74 mmol) was dissolved in water saturated CH_2Cl_2 and CH_3CN (9.3 mL, 1:1) and TfOH (0.78 mL, 3.48 mmol) was added dropwise at 0 °C. The reaction mixture was stirred for 1 h at this temperature and sat. $NaHCO_3$

(aq. 4.6 mL) was added. After separation of layers, the aqueous layer was extracted with CH_2Cl_2. The combine organic phase was dried over $MgSO_4$ and solvent was removed by evaporator. Purification was performed with silica gel chromatography to give desired product **3e** (358.59 mg, 1.64 mmol, 94% yield) as white solid.

Procedure for the reconstitutive cycloisomerization reaction (Table 5, Table 6)

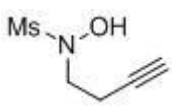
A flame-dried reaction tube equipped with a screw cap was charged with *N*-sulfonyl-*N*-hydroxyamonialkyne (1.0 mmol), $CpRu(PPh_3)_2Cl$ (36.3 mg, 0.05 mmol, 5 mol%) and DMF (10 mL). After sealing the tube with a screw cap, the resulting orange solution was heated at 100 °C. The reaction was monitored by TLC analysis. Upon complete consumption of the starting alkyne (1 to 24 h), the reaction mixture was cooled to ambient temperature. The crude is extracted with diethyl ehter, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography on silica gel afforded the desired product lactam **4** in an analytically pure form.

Characterization of substrates



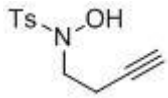
N-(But-3-yn-1-yl)-*N*-hydroxybenzenesulfonamide (3a)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 7.6 Hz, 2H), 7.70 (t, J = 7.9 Hz, 1H), 7.59 (t, J = 7.8 Hz, 2H), 6.39 (s, 1H), 3.12 (t, J = 7.2 Hz, 2H), 2.54 (td, J = 7.2, 2.6 Hz, 2H), 2.00 (t, J = 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.31, 132.51, 129.89, 129.22, 80.64, 70.38, 51.51, 17.50.



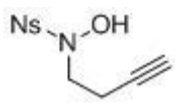
N-(But-3-yn-1-yl)-*N*-hydroxymethanesulfonamide (3b)

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (br s, 1H), 3.38 (t, J = 7.2 Hz, 2H), 2.95 (s, 3H), 2.61 (td, J = 7.0, 2.3 Hz, 2H), 2.04 (t, J = 2.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 80.58, 70.53, 51.40, 31.52, 17.71.



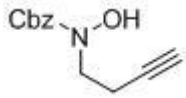
N-(But-3-yn-1-yl)-*N*-hydroxy-4-methylbenzenesulfonamide (3c)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.2 Hz, 2H), 7.37 (d, J = 7.9 Hz, 2H), 6.29 (s, 1H), 3.09(t, J = 7.3 Hz, 2H), 2.53 (td, J = 7.3, 2.6 Hz, 2H), 2.46 (s, 3H), 2.00 (t, J = 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.43, 129.90, 129.86, 129.31, 80.79, 70.26, 51.60, 21.90, 17.44.



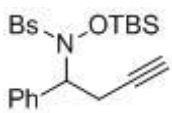
N-(But-3-yn-1-yl)-*N*-hydroxy-4-nitrobenzenesulfonamide (3d)

^{1}H NMR (400 MHz, DMSO): δ 10.70 (s, 1H), 8.46 (d, J = 8.9 Hz, 2H), 8.09 (d, J = 8.9 Hz, 2H), 2.98 (t, J = 6.7 Hz, 2H), 2.88 (t, J = 2.6 Hz, 1H), 2.40 (td, J = 6.7, 2.6, 2H); ^{13}C NMR (100 MHz, DMSO): δ 150.62, 137.91, 130.87, 124.33, 81.39, 72.62, 51.95, 16.42.



Benzyl but−3−yn−1−yl(hydroxy)carbamate (3e)

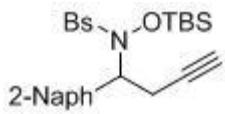
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 - 7.27 (m, 5H), 5.17 (s, 2H), 3.73 (t, J = 7.0 Hz, 2H), 2.53 (td, J = 7.0, 2.5 Hz, 2H), 1.93 (t, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.94, 128.75, 128.56, 128.37, 81.17, 70.16, 68.32, 49.21, 44.04, 17.15; IR (neat): ν_{max} 3288, 2942, 1701, 1455, 1359, 1215, 1108, 1027, 739 cm^{-1}.



N−((*tert*−Butyldimethylsilyl)oxy)−*N*−(1−phenylbut−3−yn−1−yl) benzenesulfonamide (2f)

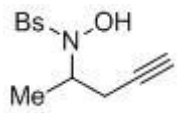
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 − 7.78 (m, 2H), 7.63 − 7.56 (m, 1H), 7.50 − 7.43 (m, 2H), 7.39 (dd, J = 7.2, 1.9 Hz, 2H), 7.27 − 7.19 (m, 3H), 5.07 (dd, J = 10.5, 3.9 Hz, 1H), 2.65 (ddd, J = 17.2, 10.5, 2.6 Hz, 1H), 2.12−2.01 (m, 1H), 1.90 (t, J = 2.7 Hz, 1H), 0.89 (s, 9H), 0.29 (s, 3H), −0.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.60, 135.69, 133.09, 129.00, 128.56, 128.41, 128.08, 80.67, 70.83, 63.62, 25.74, 22.96,

18.07, −2.85, −3.55.



N−((tert−Butyldimethylsilyl)oxy)−*N*−(1−(naphthalen−2−yl)but−3−yn−1−yl)benzenesulfonamide (2g)

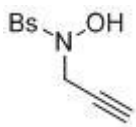
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 - 7.69 (m, 6H), 7.57 - 7.43 (m, 4H), 7.35 (t, J = 7.6 Hz, 2H), 5.22 (dd, J = 10.5, 3.9 Hz, 1H), 2.82 (ddd, J = 17.1, 10.5, 2.4 Hz, 1H), 2.21 (d, J = 17.1 Hz, 1H), 1.91 (d, J = 2.4 Hz, 1H), 0.90 (s, 9H), 0.30 (s, 3H), −0.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.81, 134.08, 133.60, 133.16, 132.88, 129.26, 128.85, 128.35, 127.92, 127.69, 127.36, 126.46, 126.25, 80.85, 71.52, 64.77, 26.37, 19.48, 18.78, −4.04, −4.37.



N−Hydroxy−*N*−(pent−4−yn−2−yl)benzenesulfonamide (3h)

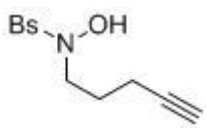
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 7.8 Hz, 2H), 7.66 (t, J = 7.3 Hz, 1H), 7.56 (t, J = 7.5 Hz, 2H), 6.35 (s, 1H), 4.17 - 4.05 (m, 1H), 2.40 - 2.25 (m, 2H), 2.01 (s, 1H), 1.02

(d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.38, 134.00, 129.29, 129.18, 81.00, 70.73, 55.80, 24.33, 15.10.



N-Hydroxy-*N*-(prop-2-yn-1-yl)benzenesulfonamide (3i)

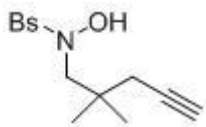
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 8.4 Hz, 2H), 7.70 (t, J = 7.5 Hz, 1H), 7.58 (t, J = 7.7 Hz, 2H), 6.96 (s, 1H), 3.94 (s, 2H), 2.15 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.49, 132.74, 130.09, 129.19, 75.84, 74.03, 43.32; IR (neat): ν_{max} 3391, 3292, 3059, 2979, 1336, 1174, 1063, 890, 753 cm^{-1}.



N-Hydroxy-*N*-(pent-4-yn-1-yl)benzenesulfonamide (3j)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, J = 7.3 Hz, 2H), 7.68 (t, J = 7.7 Hz, 1H), 7.58 (t, J = 7.8 Hz, 2H), 6.33 (s, 1H), 3.03 (t, J = 6.7 Hz, 2H), 2.30 (td, J = 7.0, 2.6 Hz, 2H), 1.97

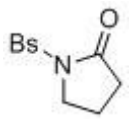
(t, J = 2.7 Hz, 1H), 1.85 (p, J = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.16, 132.43, 129.86, 129.12, 83.51, 69.29, 51.63, 25.75, 15.90; IR (neat): ν_{max} 3396, 3293, 2940, 2118, 1447, 1345, 1170, 1069, 735 cm^{-1}.



***N*-(2,2-Dimethylpent-4-yn-1-yl)-*N*-hydroxybenzenesulfonamide (3k)**

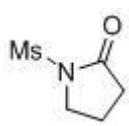
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 7.1 Hz, 2H), 7.69 (t, J = 6.8 Hz, 1H), 7.58 (t, J = 7.6 Hz, 2H), 6.91 (s, 1H), 2.88 (s, 2H), 2.22 (s, 2H), 2.00 (s, 1H), 1.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.04, 133.43, 129.65, 129.14, 81.93, 70.63, 61.86, 34.89, 30.28, 25.57; IR (neat): ν_{max} 3384, 3300, 2966, 2116, 1447, 1336, 1169, 1090, 748 cm^{-1}.

Characterization of products



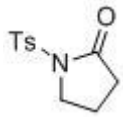
1-(Phenylsulfonyl)pyrrolidin-2-one (4a)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 7.2 Hz, 2H), 7.66 (t, J = 8.1 Hz, 1H), 7.55 (t, J = 7.7 Hz, 2H), 3.92 (t, J = 8.2 Hz, 2H), 2.45 (t, J = 8.0 Hz, 2H), 2.14 - 2.04 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.51, 138.15, 134.17, 129.18, 128.05, 47.43, 32.30, 18.28.



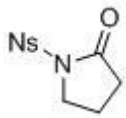
1-(Methylsulfonyl)pyrrolidin-2-one (4b)

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.87 (t, J = 7.0 Hz, 2H), 3.26 (d, J = 1.4 Hz, 3H), 2.57 (t, J = 8.1 Hz, 2H), 2.21 - 2.08 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.82, 46.75, 40.66, 32.41, 18.51.



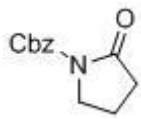
1-((4-methylphenyl)sulfonyl)pyrrolidin-2-one (4c)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 3.90 (t, J = 7.0 Hz, 2H), 2.44 (s, 3H), 2.43 (t, J = 8.1 Hz, 2H), 2.13 - 2.01 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.53, 145.37, 135.35, 129.87, 128.30, 47.47, 32.45, 21.91, 18.41.



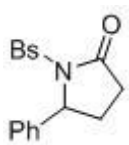
1-((4-Nitrophenyl)sulfonyl)pyrrolidin-2-one (4d)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, J = 9.0 Hz, 2H), 8.26 (d, J = 10.7 Hz, 2H), 3.95 (t, J = 7.1 Hz, 2H), 2.48 (t, J = 8.1 Hz, 2H), 2.18 - 2.08 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.63, 143.59, 129.80, 124.45, 47.60, 32.23, 18.54.



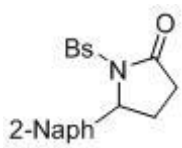
Benzyl 2-oxopyrrolidine-1-carboxylate (4e)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 - 7.40 (m, 2H), 7.40 - 7.29 (m, 3H), 5.28 (s, 2H), 3.91 - 3.73 (m, 2H), 2.54 (t, J = 8.1 Hz, 2H), 2.03 (dt, J = 15.7, 7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.20, 151.71, 135.55, 128.79, 128.60, 128.43, 68.19, 46.62, 32.99, 17.77.



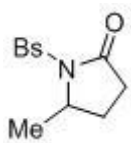
5-Phenyl-1-(phenylsulfonyl)pyrrolidin-2-one (4f)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 - 7.64 (m, 2H), 7.59 - 7.52 (m, 1H), 7.42 - 7.33 (m, 2H), 7.31 - 7.22 (m, 3H), 7.14 - 7.07 (m, 2H), 5.47 (t, J = 9.7 Hz, 1H), 2.77 - 2.46 (m, 3H), 2.02 - 1.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.68, 140.62, 138.56, 133.91, 128.96, 128.68, 128.53, 128.28, 126.24, 63.20, 30.80, 28.40; IR (neat): ν_{max} 3065, 2967, 2256, 1951, 1737, 1448, 1360, 1169, 1089, 954, 725 cm^{-1}.



5-(Naphthalen-2-yl)-1-(phenylsulfonyl)pyrrolidin-2-one (4g)

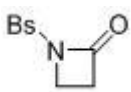
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 - 7.78 (m, 1H), 7.75 (d, J = 8.5 Hz, 1H), 7.69 (d, J = 7.9 Hz, 2H), 7.66 - 7.60 (m, 1H), 7.57 - 7.44 (m, 4H), 7.28 (dd, J = 12.8, 4.8 Hz, 2H), 7.17 (dd, J = 8.5, 1.8 Hz, 1H), 5.64 (dd, J = 8.4, 1.9 Hz, 1H), 2.81 - 2.51 (m, 3H), 2.08 - 1.99 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.85, 138.51, 137.76, 133.99, 133.13, 129.13, 128.70, 128.63, 128.14, 127.83, 126.81, 126.59, 125.26, 123.78, 63.37, 30.83, 28.44; IR (neat): ν_{max} 3059, 2971, 2256, 1952, 1737, 1448, 1360, 1169, 1089, 953, 910, 819, 726 cm^{-1}.



5-Methyl-1-(phenylsulfonyl)pyrrolidin-2-one (4h)

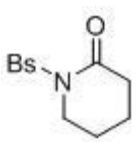
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 8.3 Hz, 2H), 7.64 (t, J = 8.1 Hz, 1H), 7.54 (t, J = 7.6 Hz, 2H), 4.61 - 4.48 (m, 1H), 2.64 - 2.50 (m, 1H), 2.43 - 2.21 (m, 2H), 1.79 - 1.67 (m,

1H), 1.47 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.45, 139.14, 133.99, 129.02, 128.30, 56.60, 30.65, 26.75, 21.61; IR (neat): ν_{max} 3068, 2978, 1902, 1732, 1448, 1355, 1168, 1120, 1089, 956, 733 cm^{-1}.



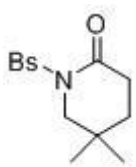
1-(Phenylsulfonyl)azetidin-2-one (4i)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 8.2 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.58 (t, J = 7.1 Hz, 2H), 3.67 (t, J = 5.1 Hz, 2H), 3.05 (t, J = 5.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.72, 138.54, 134.37, 129.70, 127.51, 40.28, 37.12.



1-(Phenylsulfonyl)piperidin-2-one (4j)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, J = 7.3 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 3.91 (t, J = 9.4 Hz, 2H), 2.41 (t, J = 6.7 Hz, 2H), 1.94 - 1.86 (m, 2H), 1.82 - 1.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.36, 139.23, 133.82, 128.83, 128.76, 47.15, 34.25, 23.47, 20.52.



5,5-Dimethyl-1-(phenylsulfonyl)piperidin-2-one (4k)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 7.2 Hz, 2H), 7.60 (t, J = 8.1 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 3.62 (s, 2H), 2.40 (td, J = 7.1, 2.3 Hz, 2H), 1.57 (td, J = 7.2, 1.8 Hz, 2H), 1.06 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.32, 139.08, 133.81, 128.79, 128.76, 57.46, 33.61, 31.27, 30.68, 25.90; IR (neat): ν_{max} 3351, 3059, 2963, 1972, 1683, 1449, 1344, 1167, 1087, 1024, 920, 876, 750 cm^{-1}.

REFERENCES

[1] a) B. M. Trost, *Science* 1991, *254*, 1471 - 1477; b) N. Z. Burns, P. S. Baran, R.W. Hoffmann, *Angew. Chem. Int. Ed.* 2009, *48*, 2854 - 2867.

[2] For thermal reactions: a) R. M. Coates, C. W. Hutchins, *J. Org. Chem.* 1979, *44*, 4742 - 4744; b) P. J. Pye, Y. L. Zhong, G. O. Jones, R. A. Reamer, K. N. Houk, D. Askin, *Angew. Chem. Int. Ed.* 2008, *47*, 4134 - 4136; c) J. E. Baldwin, R. G. Pudussery, *J. Am. Chem. Soc.* 1968, *90*, 5325 - 5326.

[3] For metal-catalyzed reactions with copper: a) M. Kinugasa, S. Hashimoto, *J. Chem. Soc. Chem. Commun.* 1972, 466 - 467; b) I. Nakamura, T. Araki, M. Terada, *J. Am. Chem. Soc.* 2009, *131*, 2804 - 2805; c) D. J. Michaelis, C. J. Shaffer, T. P. Yoon, *J. Am. Chem. Soc.* 2007, *129*, 1866 -1867; for metal-catalyzed reactions with platinum d) I. Nakamura, Y. Sato, M. Terada, *J. Am. Chem. Soc.* 2009, *131*, 4198 - 4199.

[4] a) H. S. Yeom, J. E. Lee, S. Shin, *Angew. Chem. Int. Ed.* 2008, *47*, 7040 - 7043; b) H. S. Yeom, Y. Lee, J.-E. Lee, S. Shin, *Org. Biomol. Chem.* 2009, *7*, 4744 - 4752; c) H. S. Yeom,

Y. Lee, J. Jeong, E. So, S. Hwang, J.-E. Lee, S. S. Lee, S. Shin, *Angew. Chem. Int. Ed.* 2010, *49*, 1611 - 1614.

[5] a) L. Cui, G. Zhang, Y. Peng, L. Zhang, *Org. Lett.* 2009, *11*, 1225 - 1228; b) L. Cui, Y. Peng, L. Zhang, *J. Am. Chem. Soc.* 2009, *131*, 8394 -8395; c) L. Ye, L. Cui, G. Zhang, L. Zhang, *J. Am. Chem. Soc.* 2010, *132*, 3258 - 3259.

[6] I. Nakamura, D. Zhang, M. Terada, *J. Am. Chem. Soc.* 2010, *132*, 7884 - 7886.

[7] H. Yeom, S. Shin, *Chem. Eur. J.* 2011, *17*, 1764-1767.

[8] I. Kim, C. Lee, *Angew. Chem. Int. Ed.* 2013, *52*, 10023-10026.

[9] a) E. Chain, *Nobel Lecture*, *March 20*, 1946; b) P. Sammes, *Chem. Rev.* 1976, *76*, 113-155; c) D. Sole, J. Bonjoch, *Chem. Rev.* 2000, *100*, 3455-3482; d) B. Alcaide, P. Almendros, C. Aragoncillo, *Chem. Rev.* 2007, *107*, 4437-4492.

[10] a) P. Hrnciar, F. Stappenbeck, J. White, *J. Org. Chem.* 1999, *64*, 7871-7884; b) R. Bossio, C. Marcos, S. Marcaccini, R.

Pepino, *Tetrahedron Lett.* 1997, *38*, 2519-2520; c) K. Emelen, T. Wit, G. Hoornaert, F. Compernolle, *Tetrahedron*, 2002, 58, 4225-4236; d) H. Staudinger, J. Meyer, *Helv. Chim. Acta* 1919, *2*, 635-646.

[11] a) H. C. Lo, D. B. Grotjahn, *J. Am. Chem. Soc.* 1997, *119*, 2958-2959; b) D. B. Grotjahn, L. S. B. Collins, M. Wolpert, G. A. Bikzhanova, H. C. Lo, D. Combs, J. L. Hubbard, *J. Am. Chem. Soc.* 2001, *123*, 8260 - 8270; c) I. Kim, S. Roh, D. Lee, C. Lee, *Org. Lett.* 2014, *16*, 2482-2485.

[12] Y. Rhee, B. Trost, *J. Am. Chem. Soc.* 1999, *121*, 11680-11683.

[13] To synthesize 1e: L. Qin, Z. Zhou, J. Wei, T. Yan, H. Wen, *Synth. Commun.* 2010, *40*, 642-646.

국문 초록

루테늄 촉매를 이용하여 엔-설포닐-엔-하이드록시아미노알카인이 분자 재배치를 통한 환이성화 반응을 통해 락탐을 형성하는 반응을 개발하였다. 이 반응에서 말단 알카인이 루테늄에 의해 루테늄 vinylidene을 형성한 후, 산소 원자의 anti-Markovnikov 첨가 반응이 진행되어 metallacycle이 형성된다. 그 후 약한 결합인 N-O 결합이 끊어지고 질소 원자가 전자가 부족한 탄소에 첨가하며 락탐 고리를 형성한다. 이 반응을 통해 다양한 크기의 락탐 고리를 효율적으로 합성할 수 있다.

주요어: 루테늄 촉매반응, metal vinylidene, 환이성화 반응, 아미드 결합, 락탐, 말단 알카인

학번: 2012-20266

감사의 글

긴장되고 설레는 마음으로 대학원에 들어와 실험실 생활을 시작한 지 어느덧 2년 반이라는 시간이 훌쩍 지났습니다. 많은 분들의 도움이 있었기에 석사학위 과정을 알차게 보낼 수 있었기에 이 자리를 빌어 감사의 인사를 드리려합니다.

우선 학위 과정 동안 열정으로 지도해 주신 이철범 교수님께 감사드립니다. 언제나 학생들에게 최고의 연구 환경을 제공해 주신 점, 그리고 학자로서의 모범을 보여주실 뿐만 아니라, 인생을 살아가는 자세에 대해서도 스스로를 돌아볼 수 있게 해 주신 점 진심으로 감사드립니다.

또한 유기화학을 공부할 수 있는 소중한 첫 기회를 제공해 주셨던 성균관대학교의 윤재숙 교수님께도 이 자리를 빌려 감사를 드립니다.

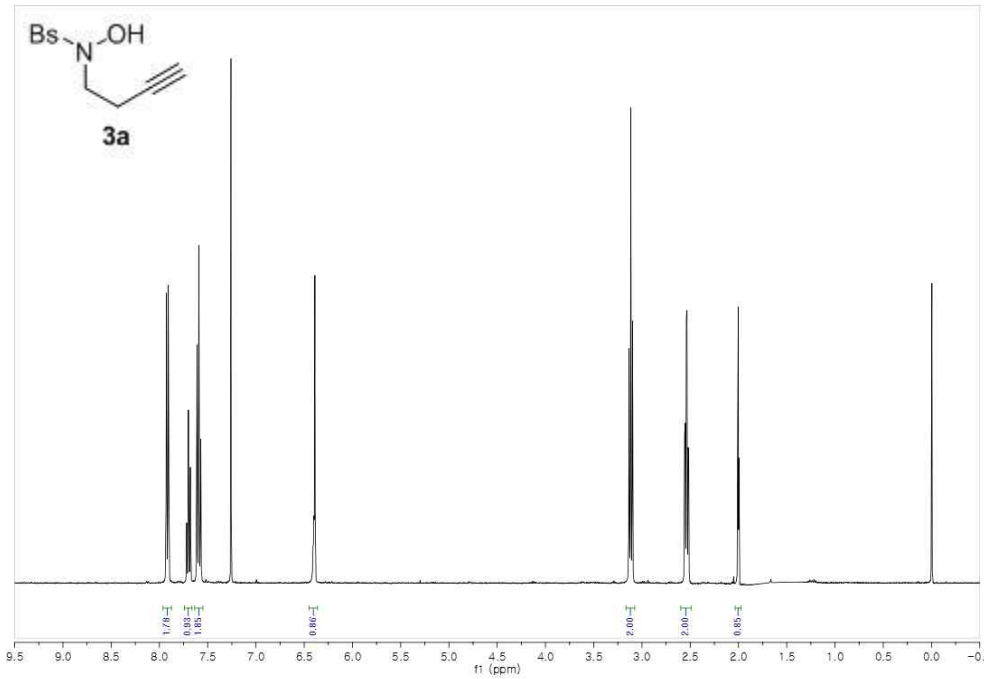
고된 대학원 생활이었지만 다정하게 도움을 주던 실험실 동료들 덕분에 하루하루를 즐겁게 지낼 수 있었습니다. 먼저 사수인 인수오빠. 많이 부족한 저를 항상 이끌어주셔서 정말 감사합니다. 그리고 동기인 저를 언제나 이것저것 챙겨주던 상원오빠, 이런 저런 생각을 제공해 주시던 동길오빠, 실험실에 들어와 가장 처음 실험실에 적응하는데 많은 도움 주신 3번 라인의 은혜언니, 호윤오빠, 맛있는 먹거리를 제공해주시던 승주언니, 친절한 진이 오빠, 유쾌한 동석오빠, 쓴 소리도 마다 않는 선우오빠, 박사 과정을 마친 혜진언니, 지금은 졸업하고 없는 재우오빠, 그리고 희경이, 태훈이, 경민이, 보란이 모두 감사드립니다.

그리고 누구보다도 실험실 생활을 해 나가는 데에 가장 큰 도움을 준 성현오빠에게 감사 인사를 드립니다.

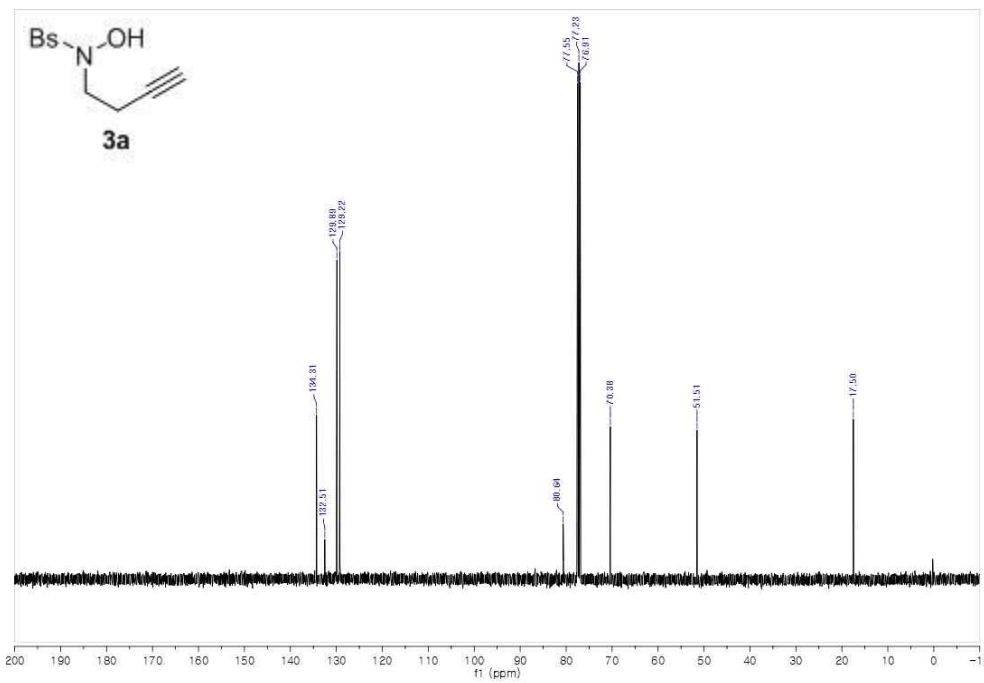
실험실 동료 분들 모두 지금 진행하고 계신 연구에 좋은 결실이 있기를 진심으로 기원하며, 원하시는 목표 모두 빠른 시일 내로 이루실 수 있길 바랍니다.

마지막으로 석사학위 과정을 마치는 동안 어려움도 많았는데 언제나 든든한 지원군이 되어주신 사랑하는 아빠, 엄마 그리고 윤미언니, 수미언니, 동환이에게 깊은 감사를 전합니다.

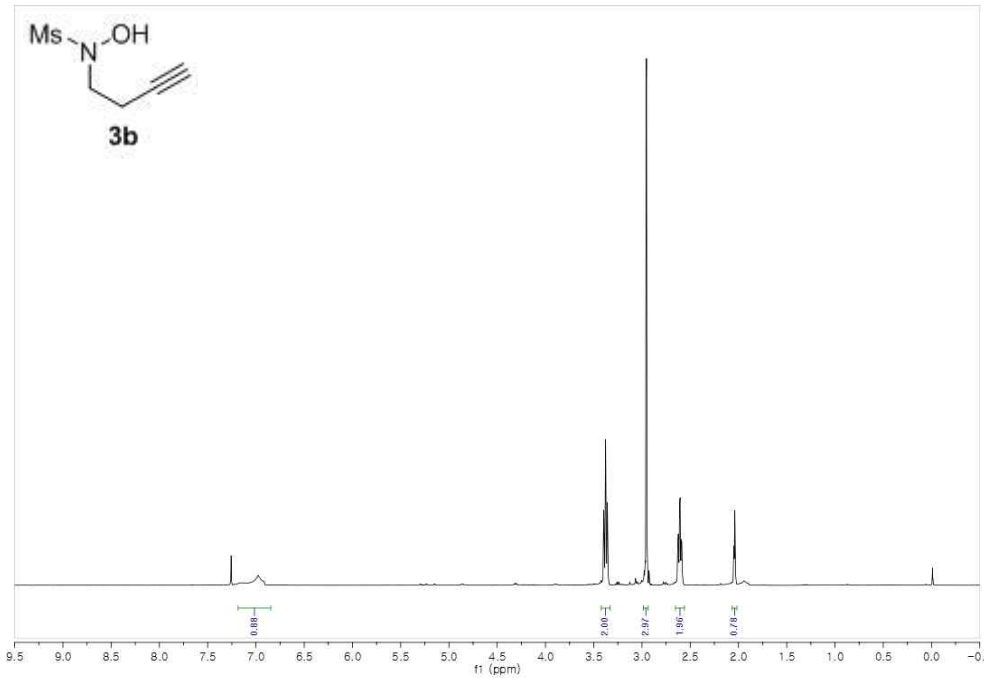
SPECTRA



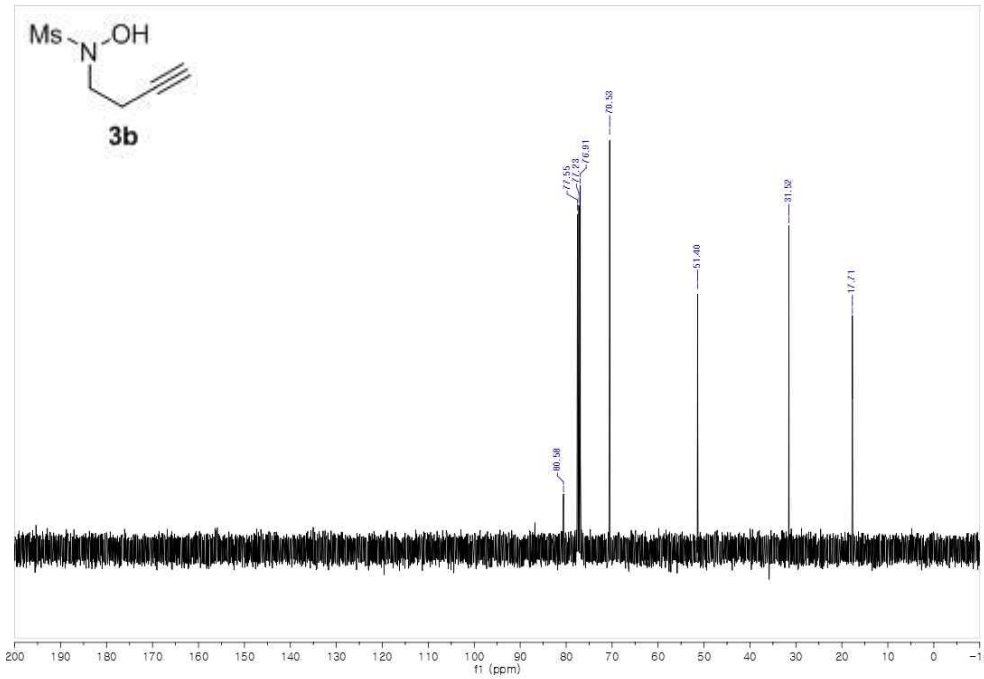
^{1}H NMR (400 MHz, $CDCl_3$) of **3a**



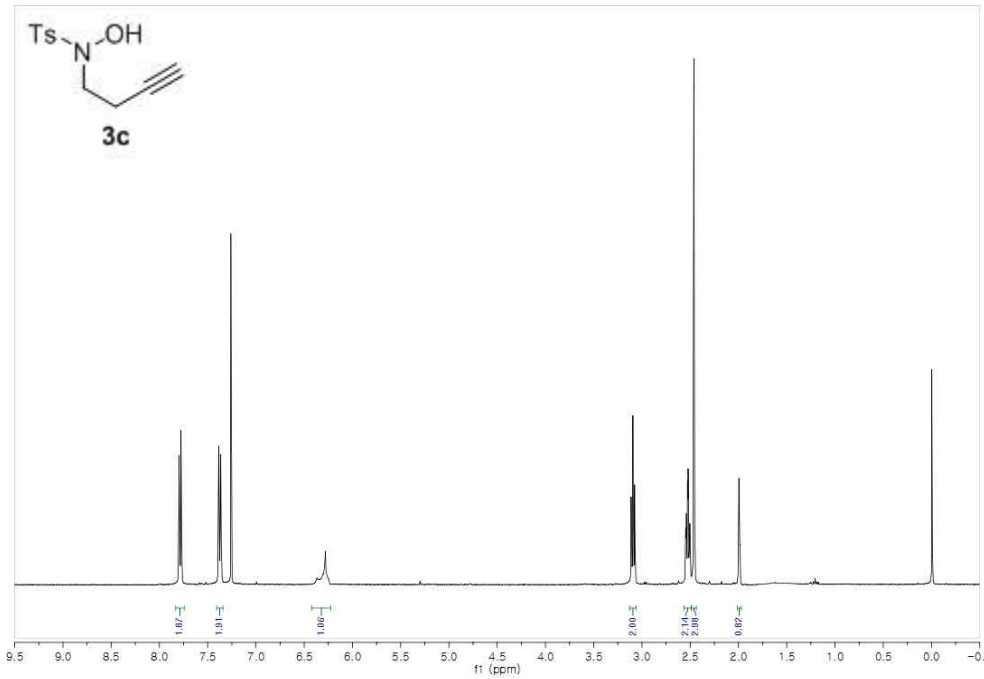
^{13}C NMR (100 MHz, $CDCl_3$) of **3a**



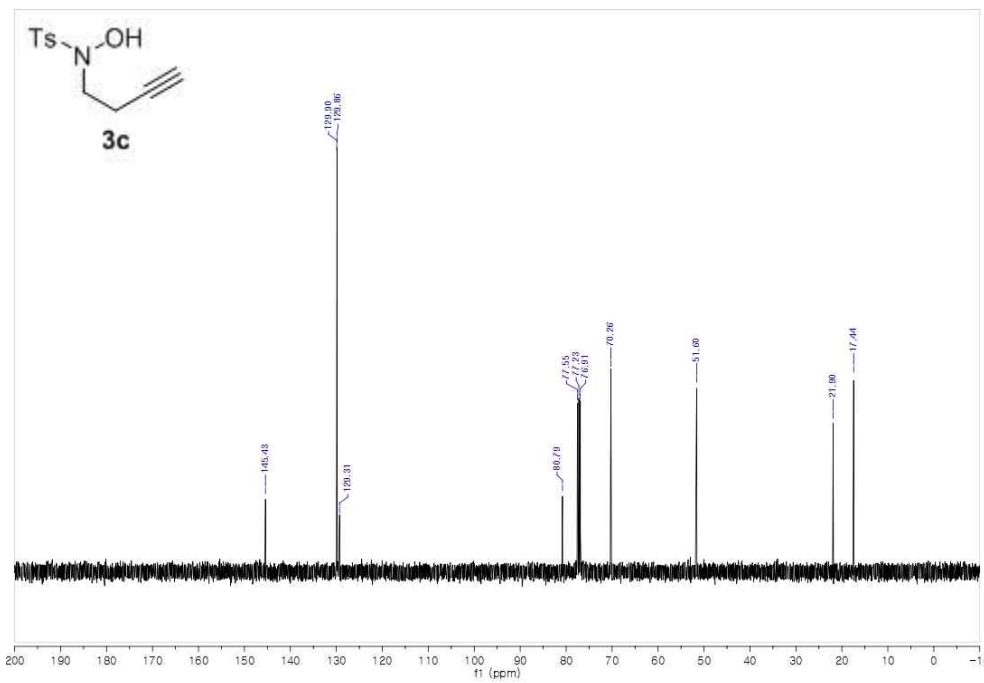
^{1}H NMR (400 MHz, $CDCl_3$) of **3b**



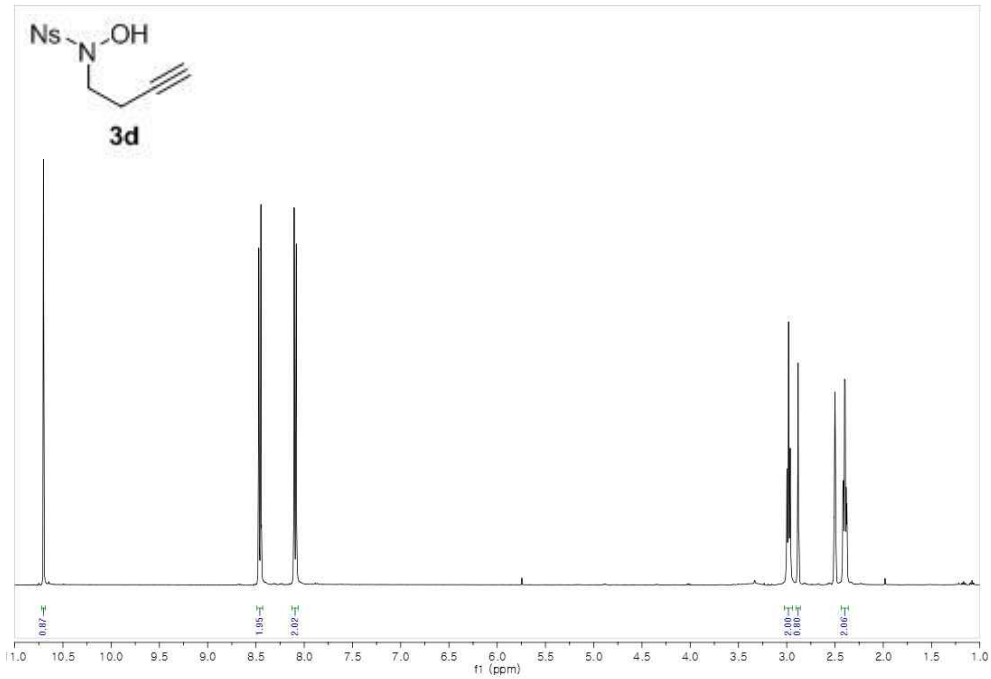
^{13}C NMR (100 MHz, $CDCl_3$) of **3b**



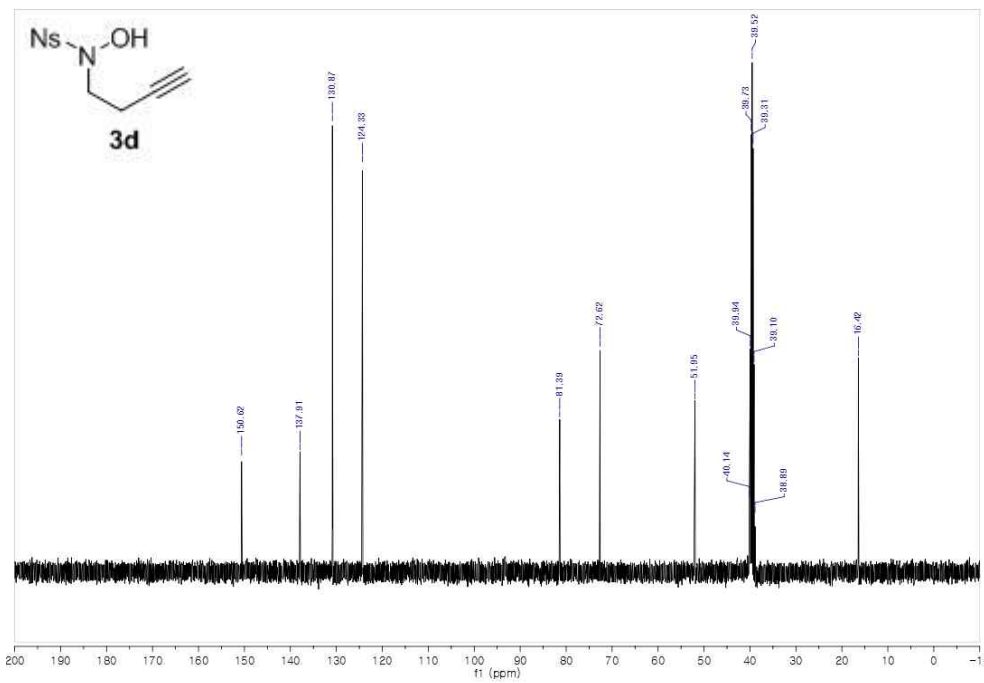
^{1}H NMR (400 MHz, $CDCl_3$) of **3c**



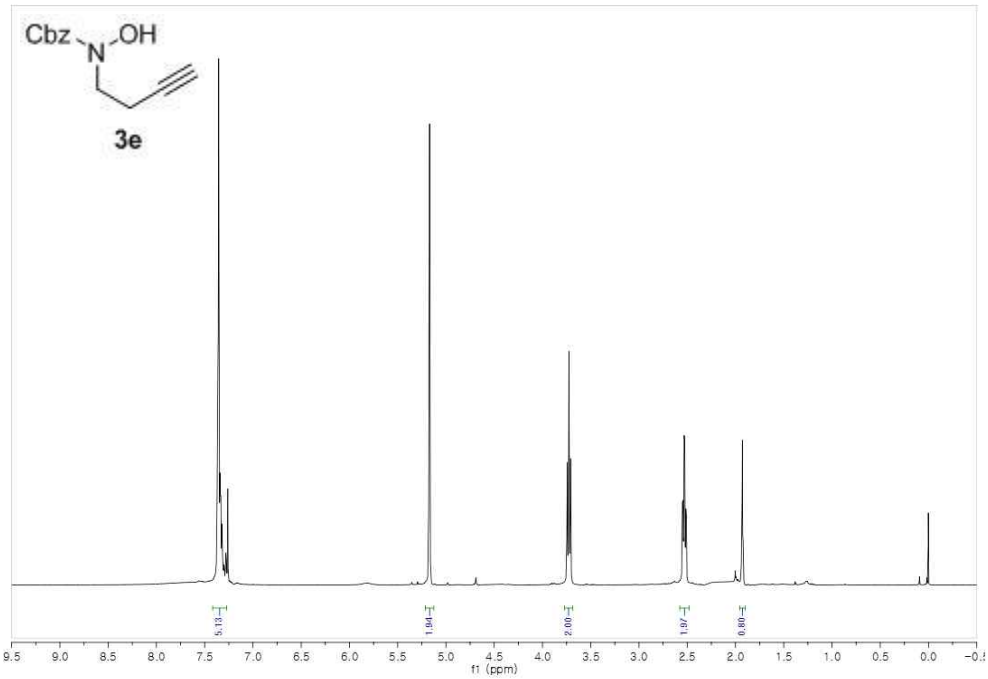
^{13}C NMR (100 MHz, $CDCl_3$) of **3c**



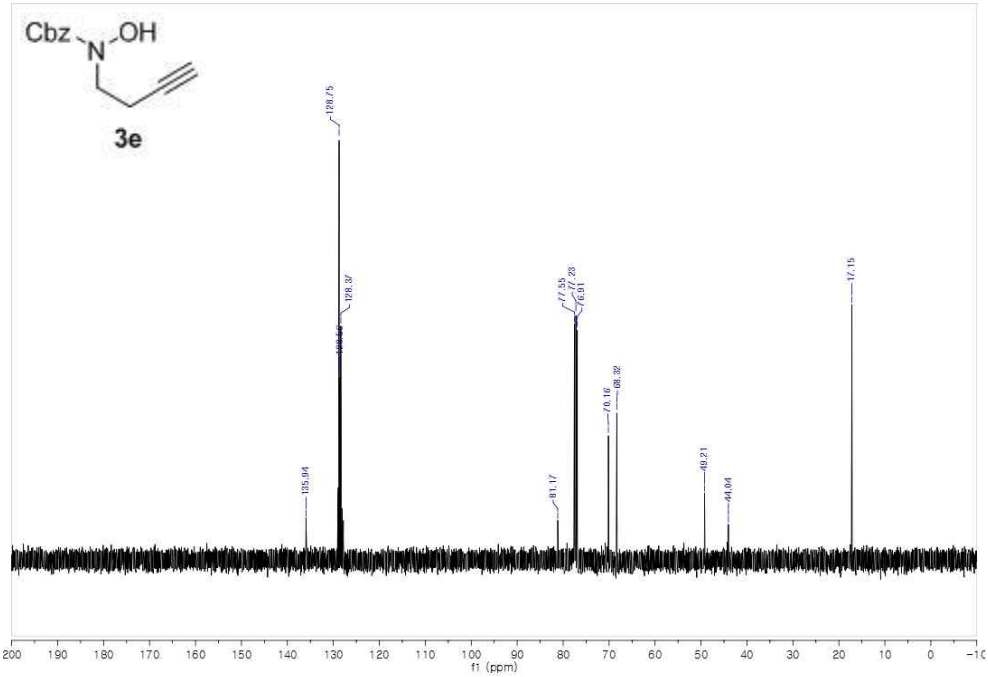
^{1}H NMR (400 MHz, DMSO) of **3d**



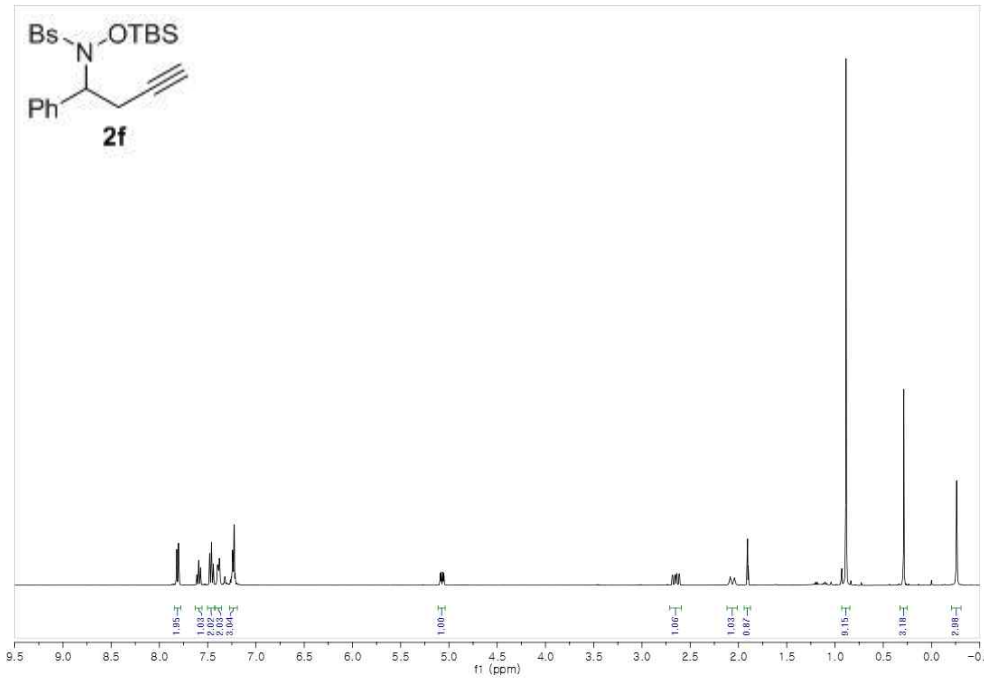
^{13}C NMR (100 MHz, DMSO) of **3d**



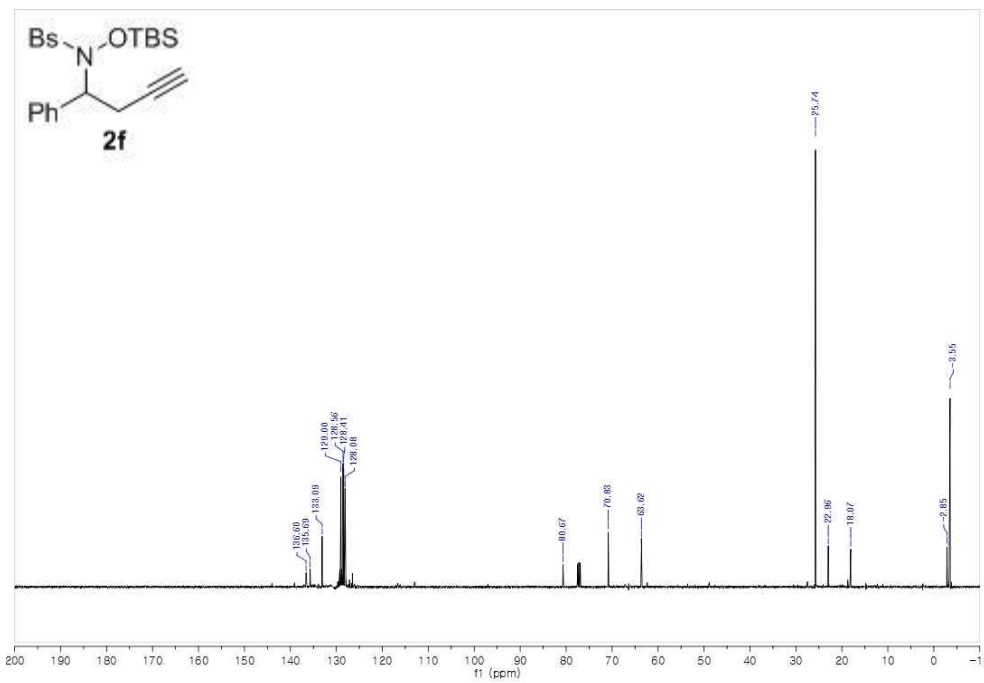
^{1}H NMR (400 MHz, $CDCl_3$) of **3e**



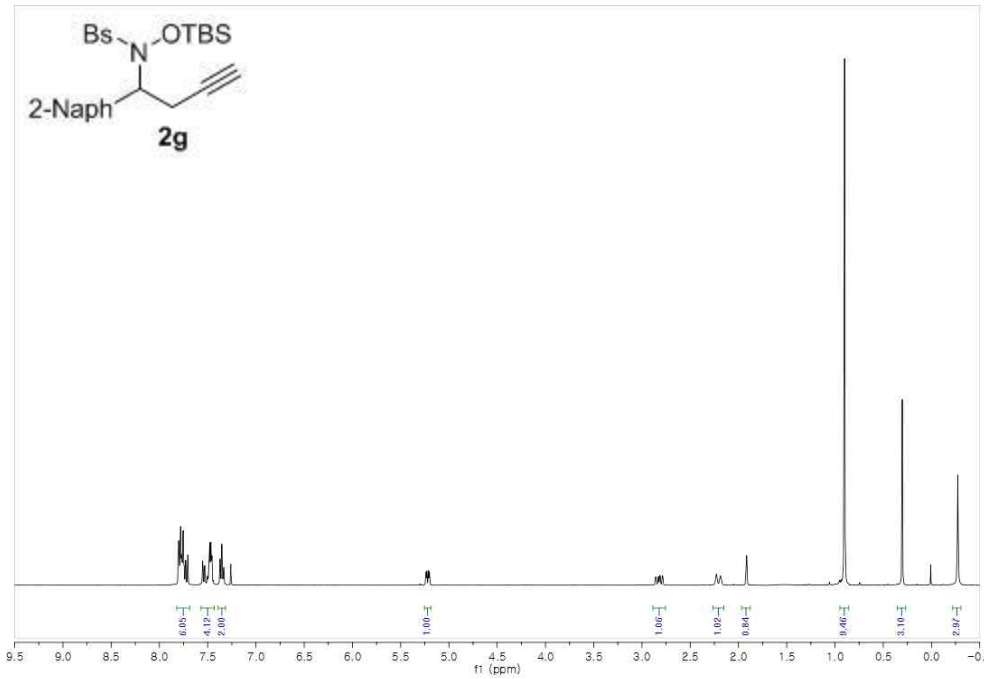
^{13}C NMR (100 MHz, $CDCl_3$) of **3e**



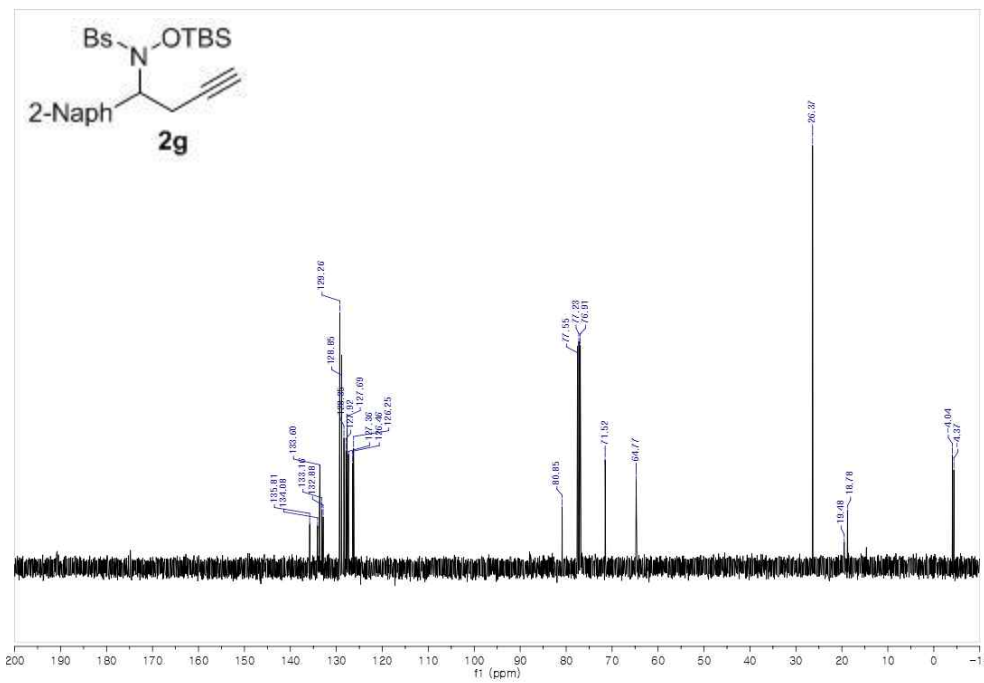
^{1}H NMR (400 MHz, $CDCl_3$) of **2f**



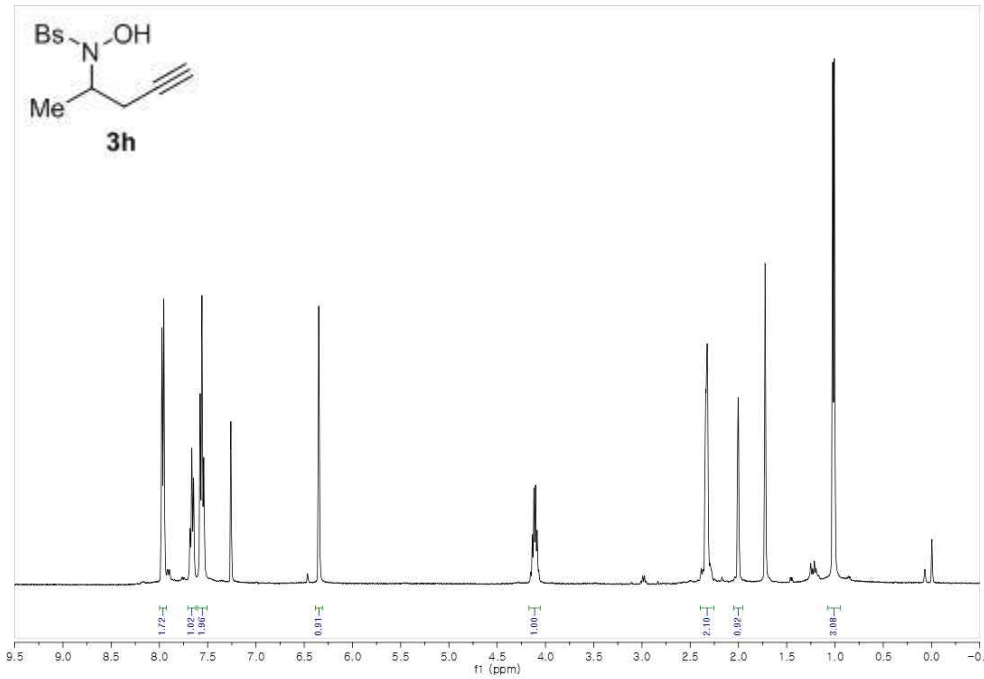
^{13}C NMR (100 MHz, $CDCl_3$) of **2f**



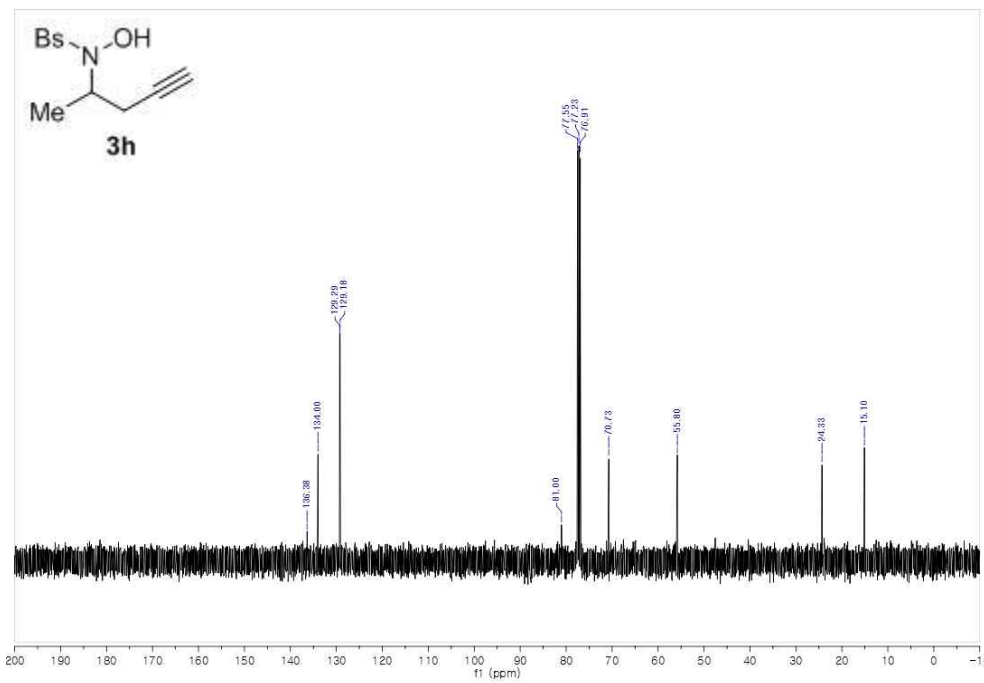
^{1}H NMR (400 MHz, $CDCl_3$) of **2g**



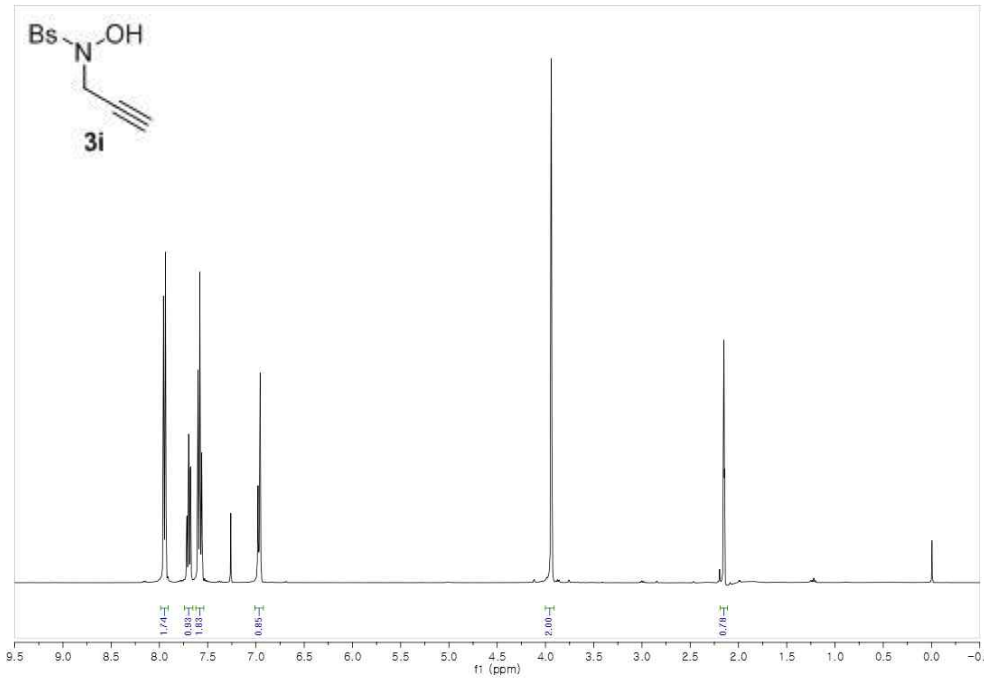
^{13}C NMR (100 MHz, $CDCl_3$) of **2g**



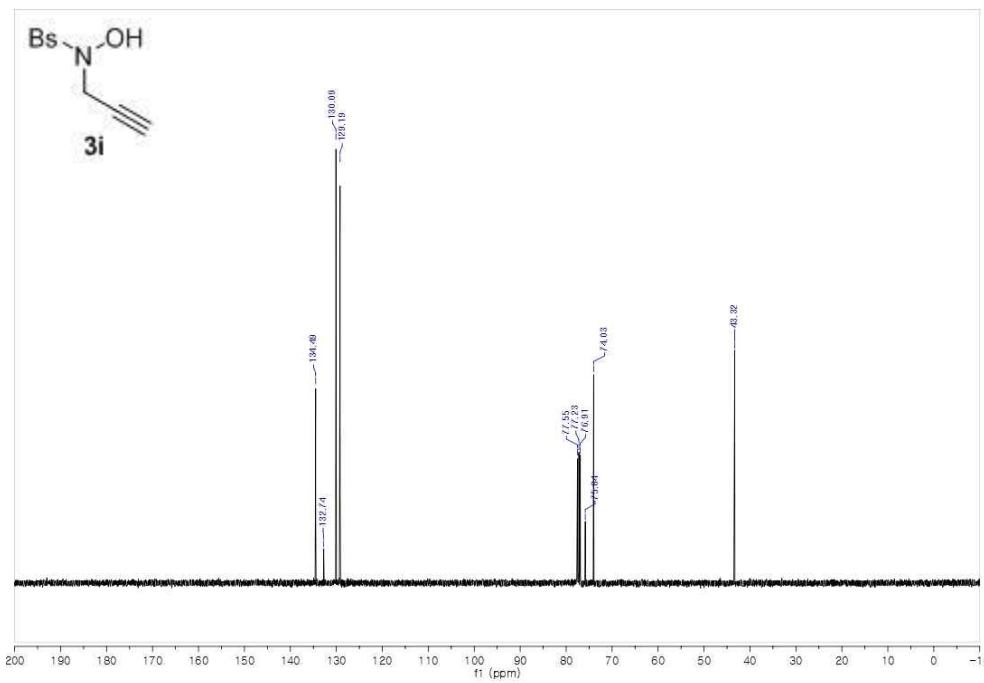
^{1}H NMR (400 MHz, $CDCl_3$) of **3h**



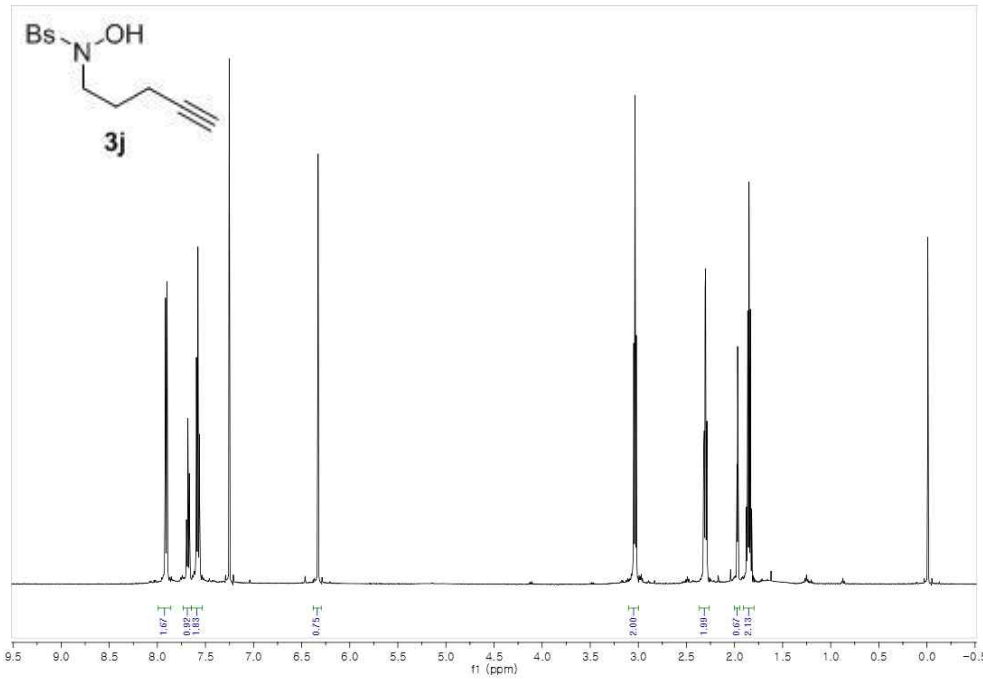
^{13}C NMR (100 MHz, $CDCl_3$) of **3h**



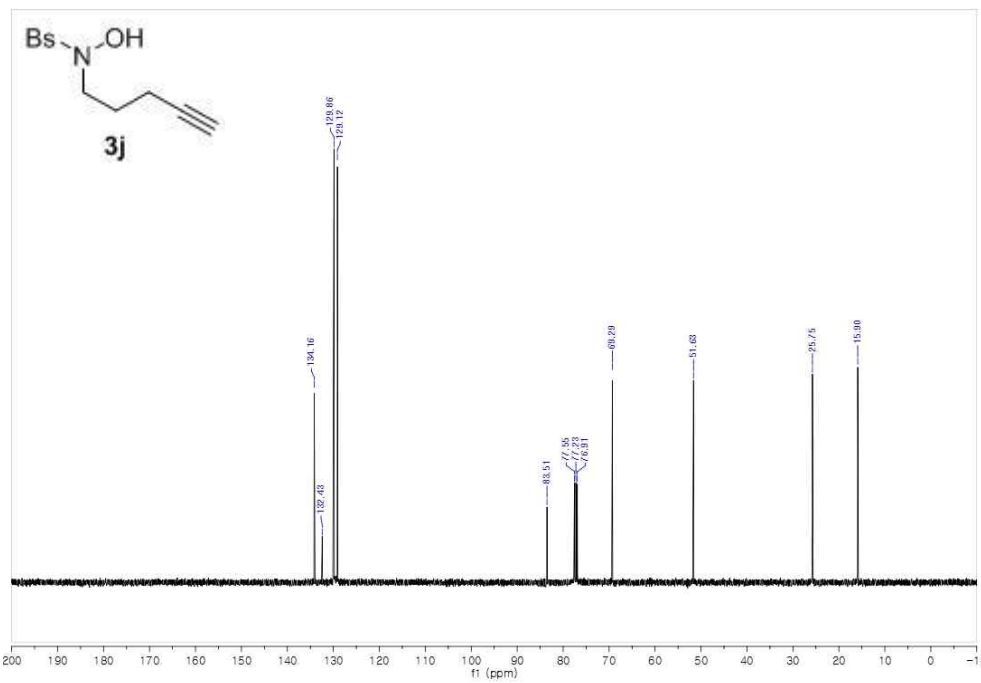
^{1}H NMR (400 MHz, $CDCl_3$) of **3i**



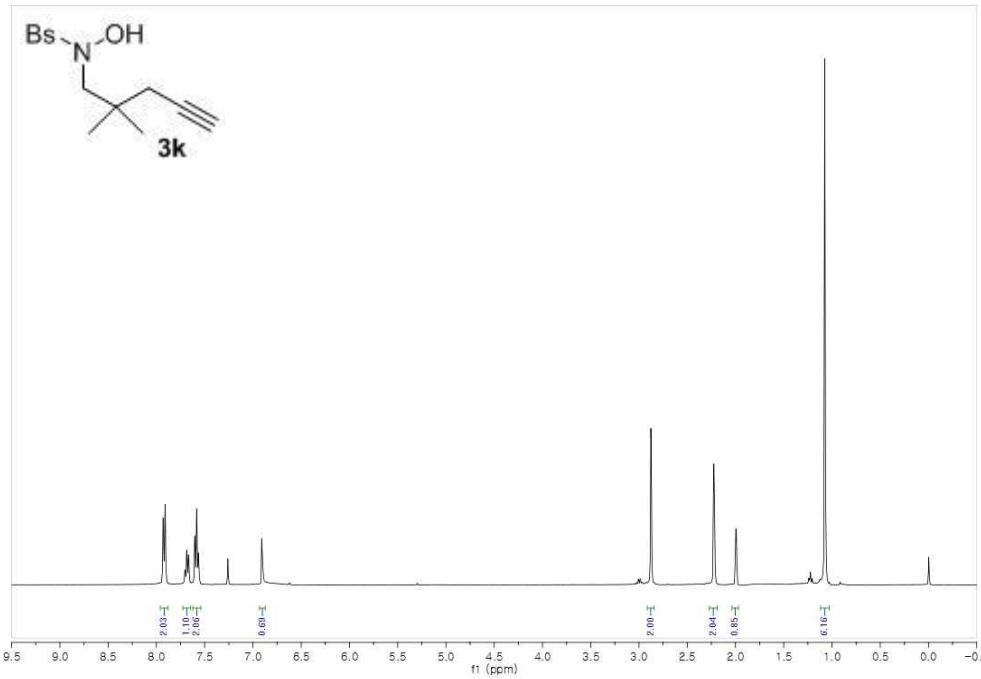
^{13}C NMR (100 MHz, $CDCl_3$) of **3i**



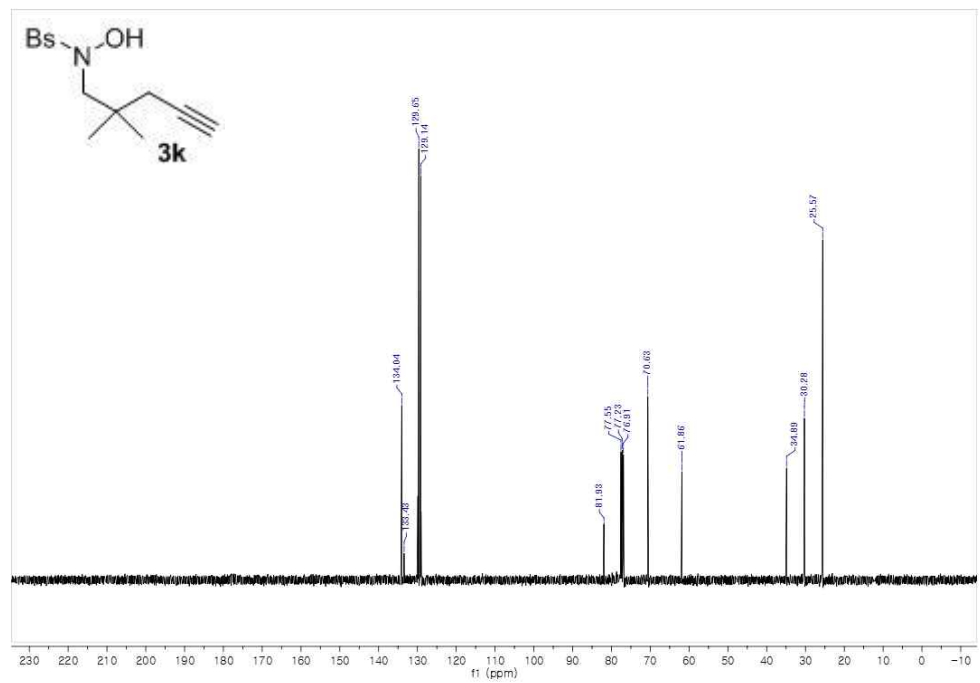
^{1}H NMR (500 MHz, $CDCl_3$) of **3j**



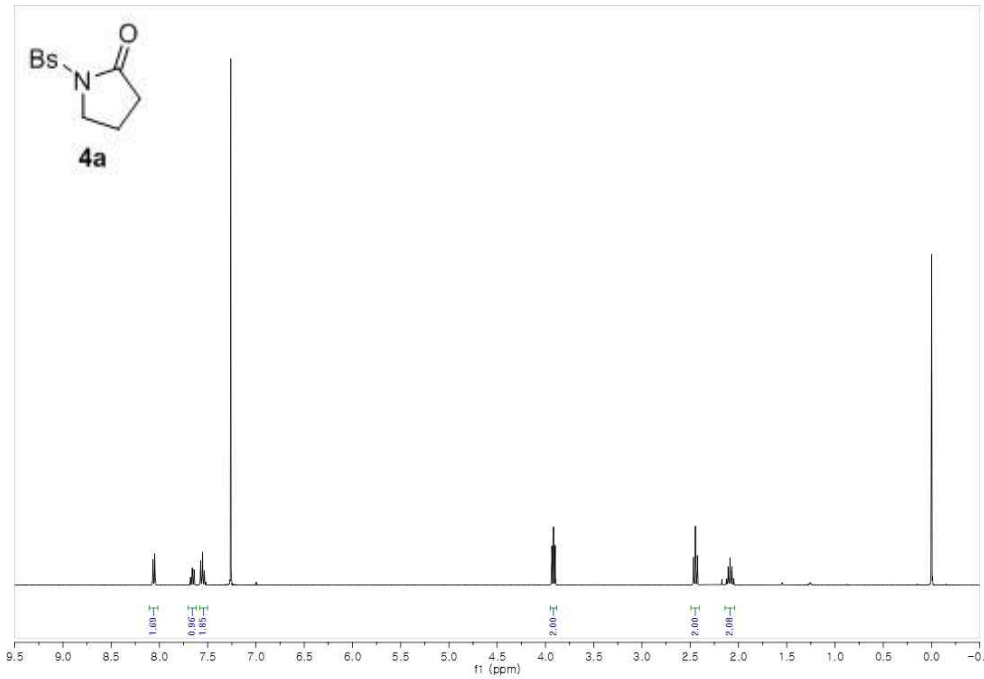
^{13}C NMR (100 MHz, $CDCl_3$) of **3j**



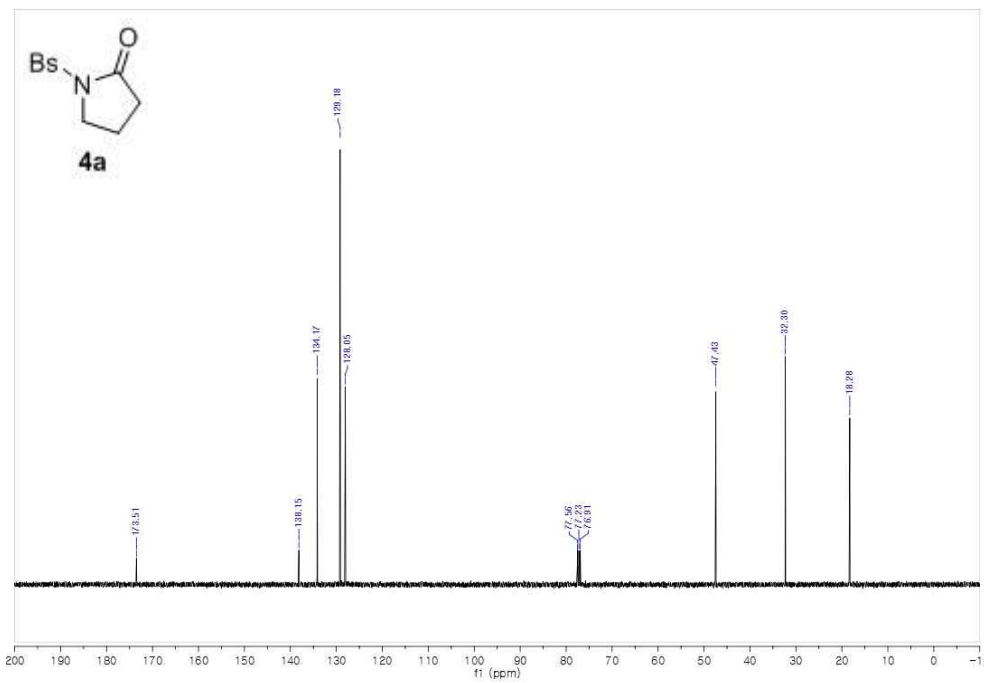
^{1}H NMR (400 MHz, $CDCl_3$) of **3k**



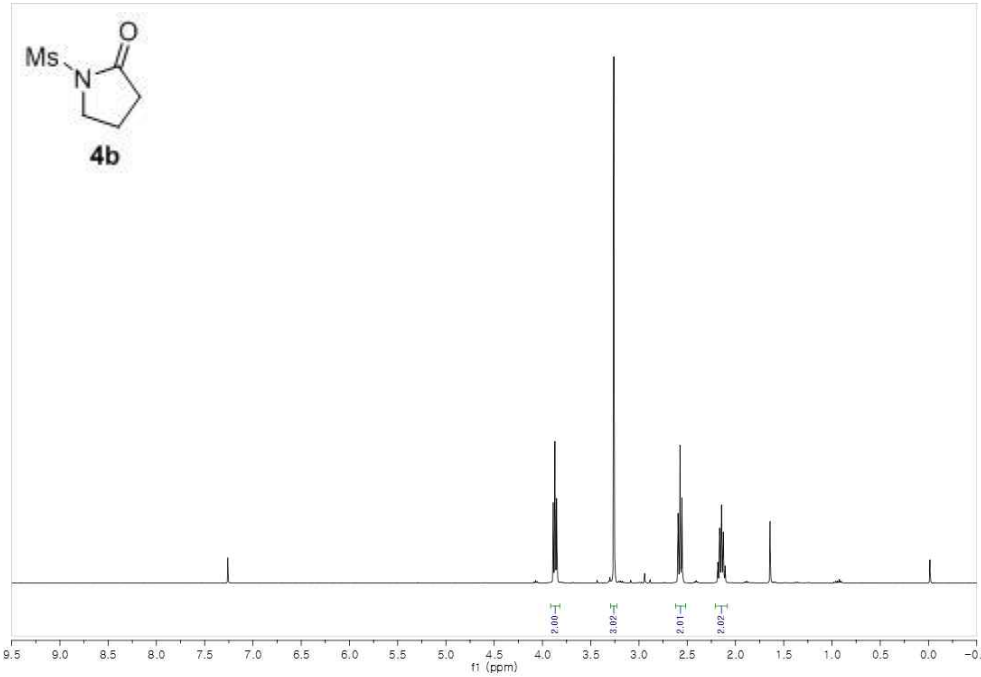
^{13}C NMR (100 MHz, $CDCl_3$) of **3k**



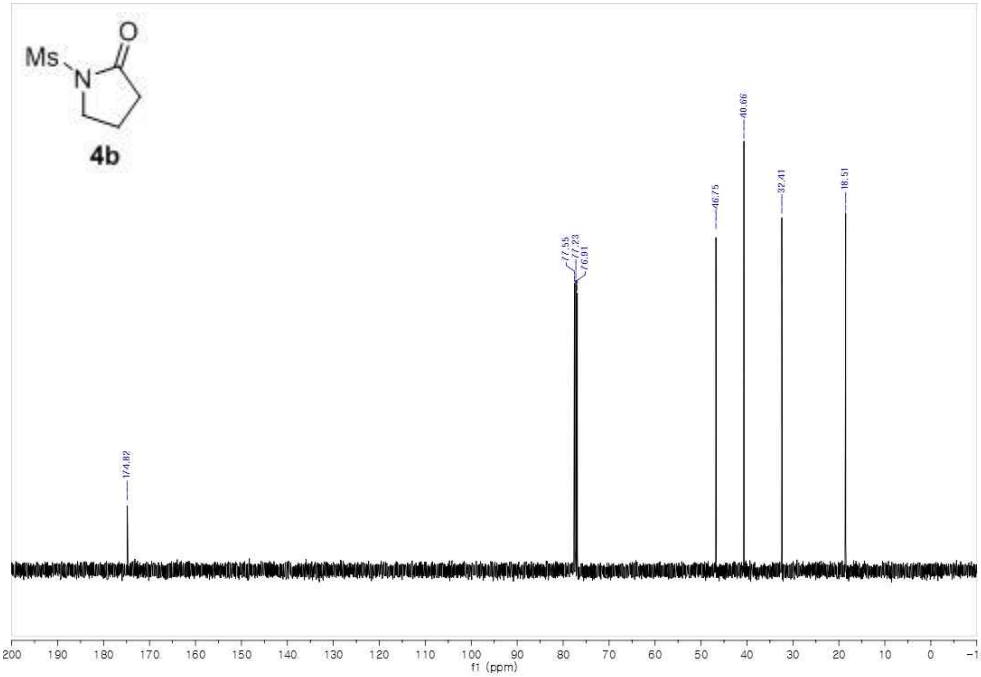
^{1}H NMR (400 MHz, $CDCl_3$) of **4a**



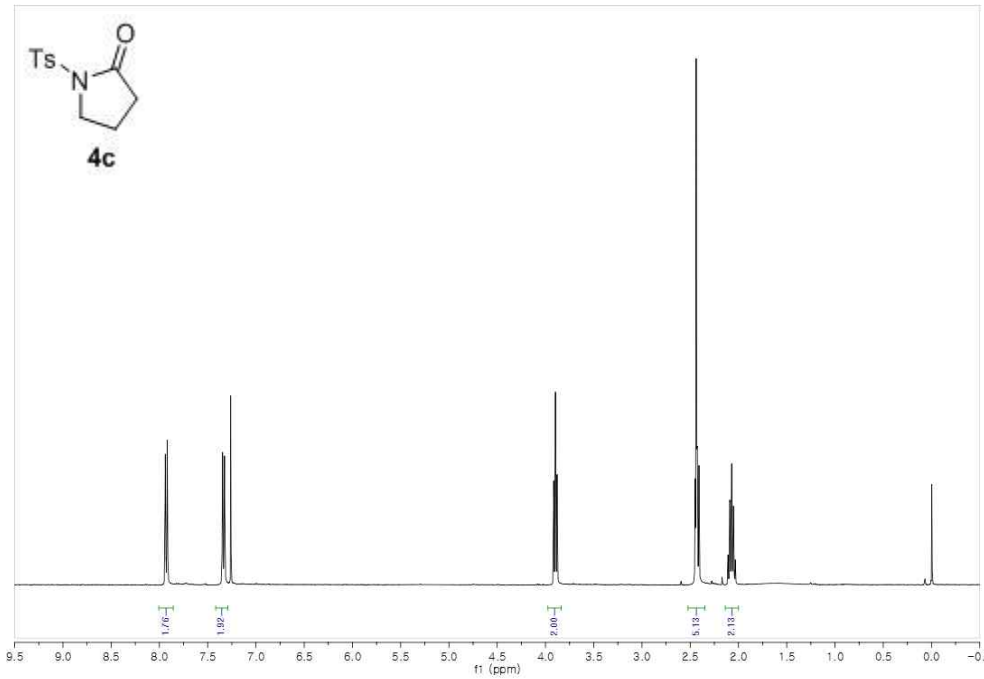
^{13}C NMR (100 MHz, $CDCl_3$) of **4a**



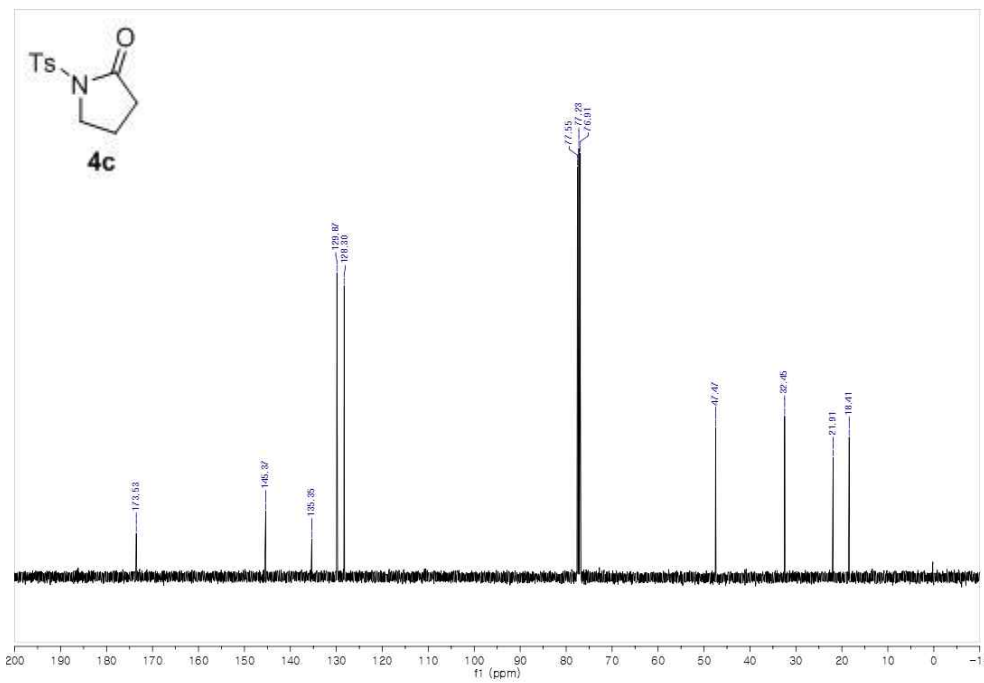
^{1}H NMR (400 MHz, $CDCl_3$) of **4b**



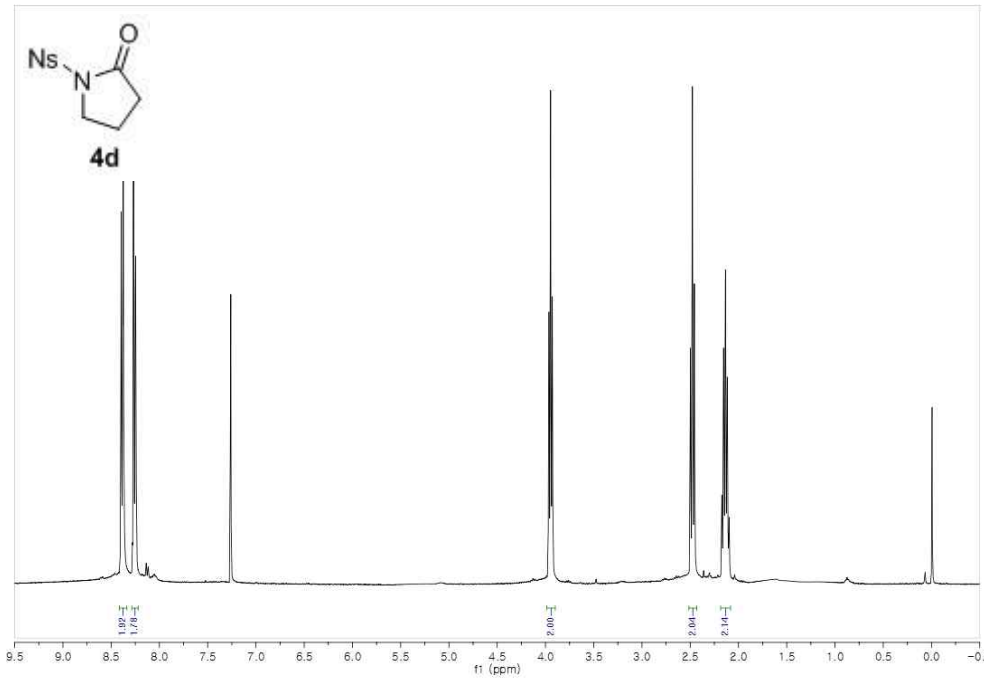
^{13}C NMR (100 MHz, $CDCl_3$) of **4b**



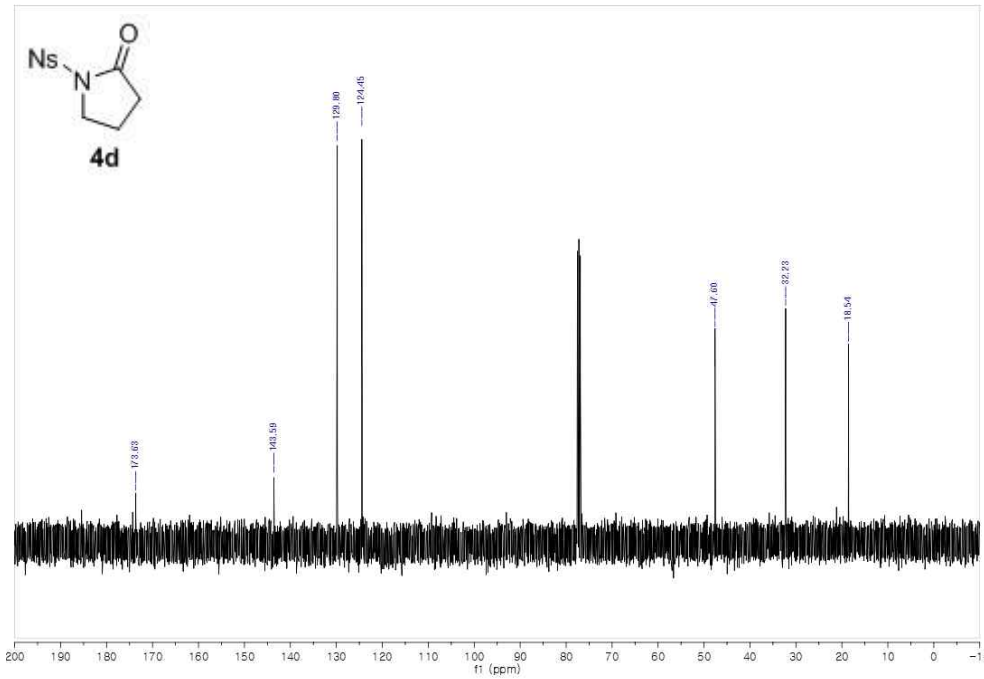
^{1}H NMR (400 MHz, $CDCl_3$) of **4c**



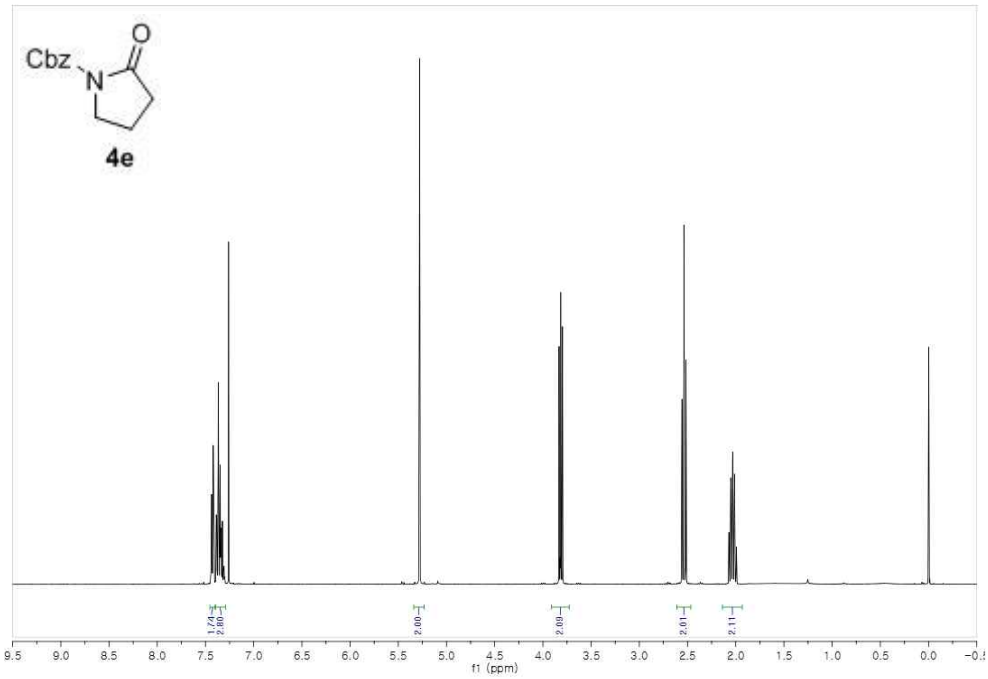
^{13}C NMR (100 MHz, $CDCl_3$) of **4c**



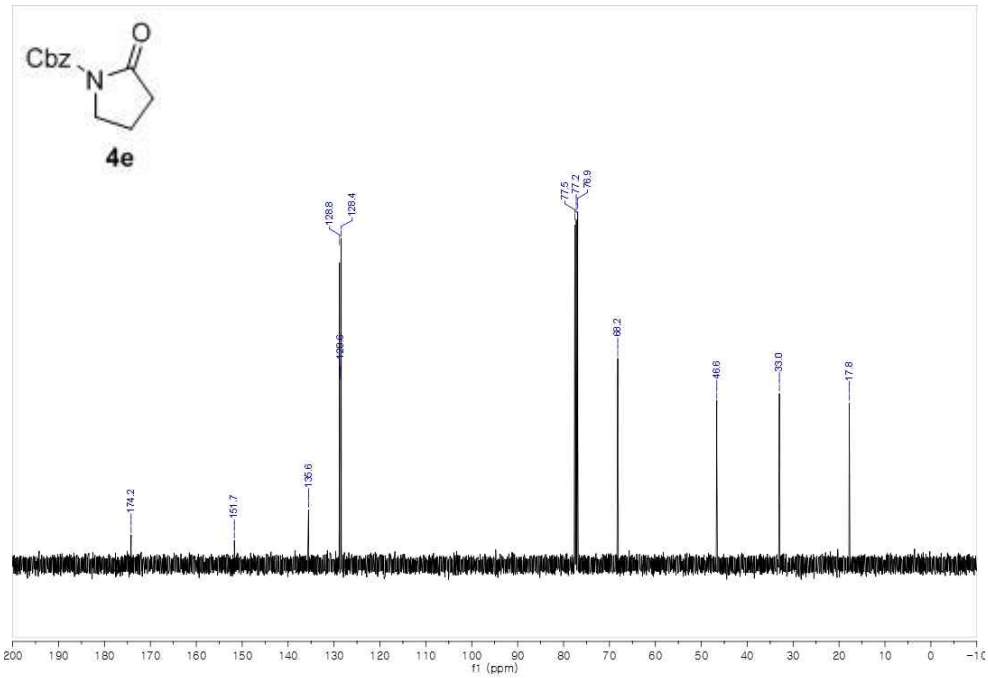
^{1}H NMR (400 MHz, $CDCl_3$) of **4d**



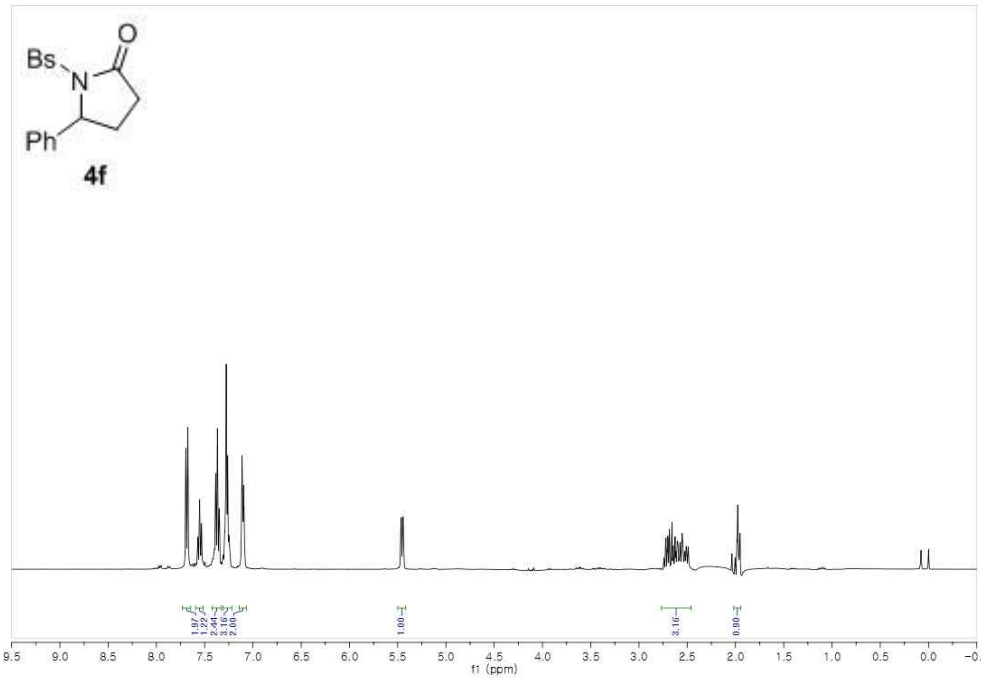
^{13}C NMR (100 MHz, $CDCl_3$) of **4d**



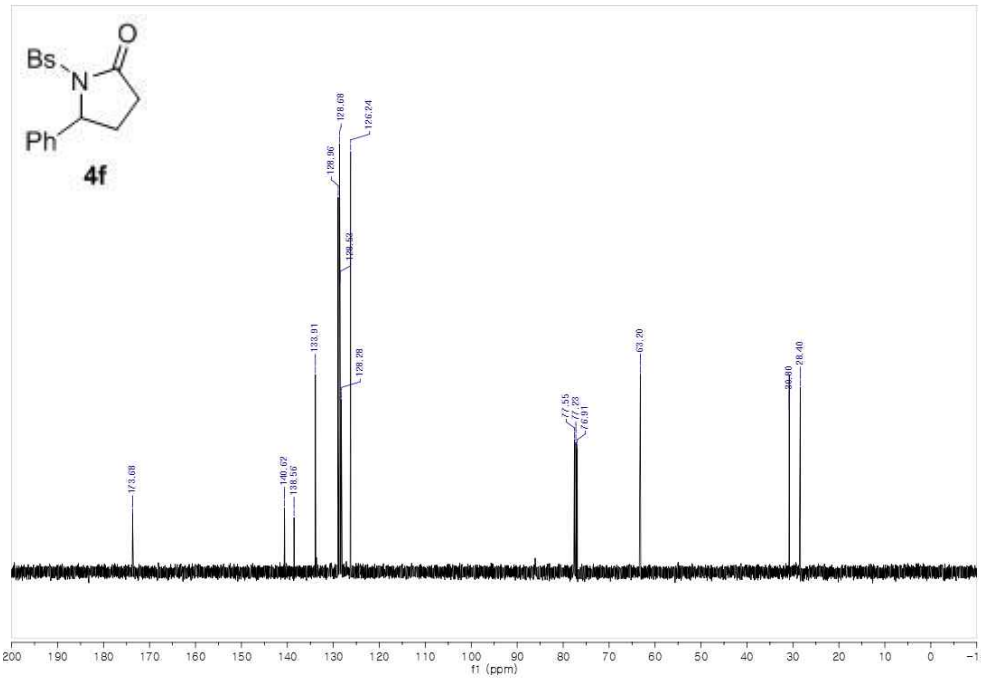
^{1}H NMR (400 MHz, $CDCl_3$) of **4e**



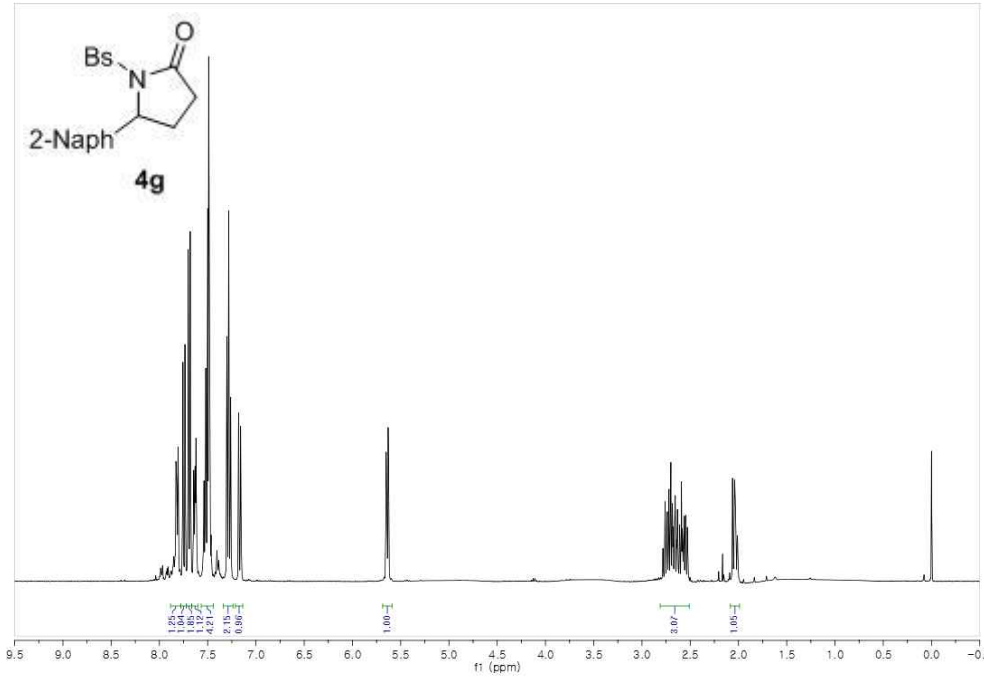
^{13}C NMR (100 MHz, $CDCl_3$) of **4e**



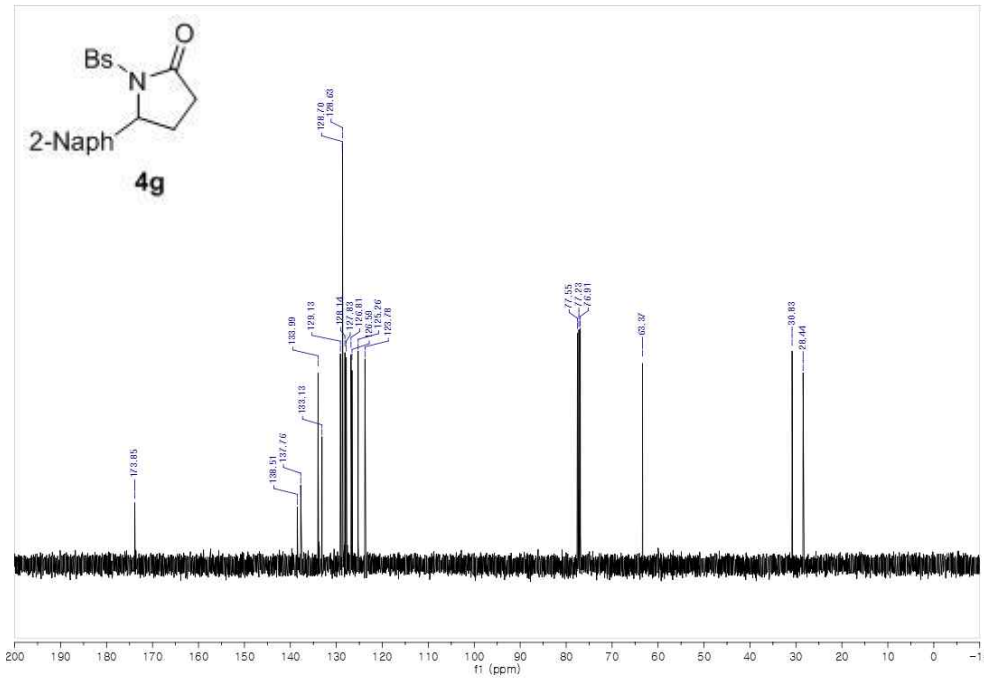
^{1}H NMR (400 MHz, $CDCl_3$) of **4f**



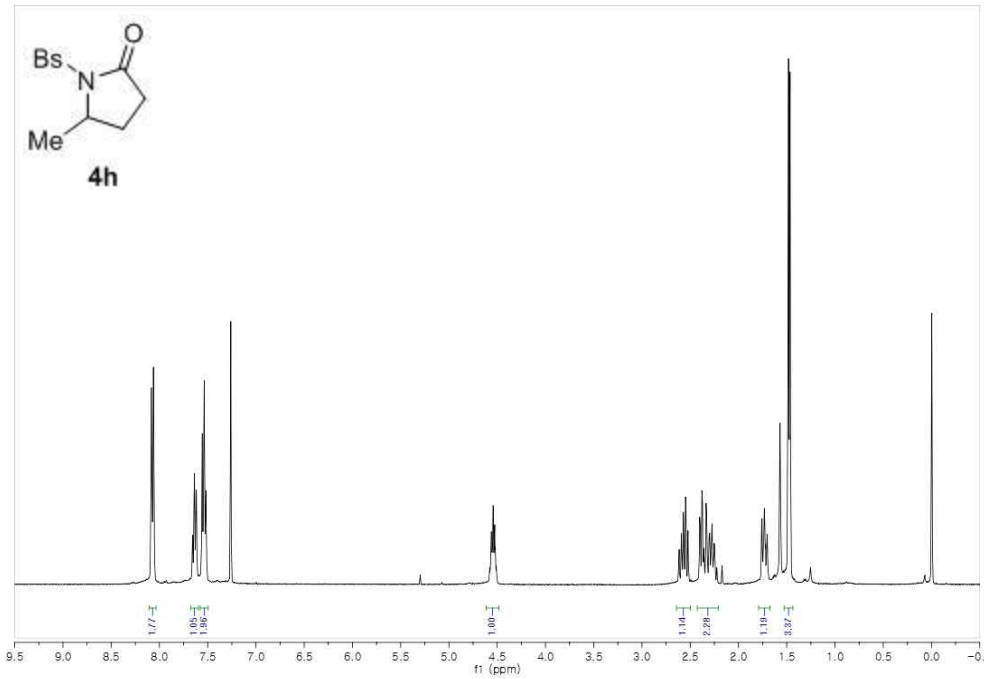
^{13}C NMR (100 MHz, $CDCl_3$) of **4f**



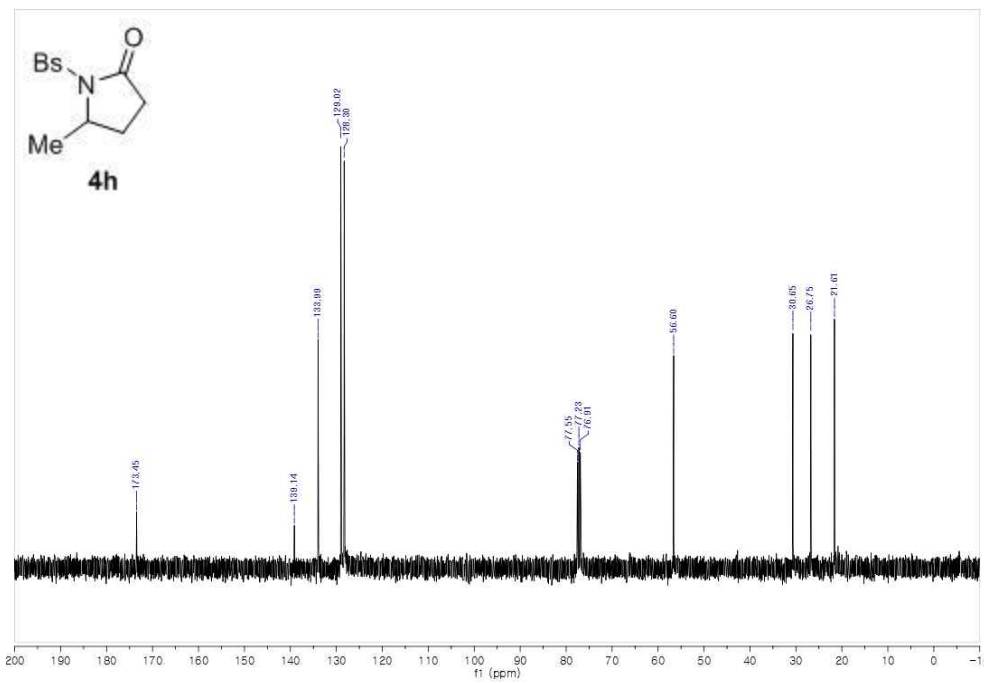
^{1}H NMR (400 MHz, $CDCl_3$) of **4g**



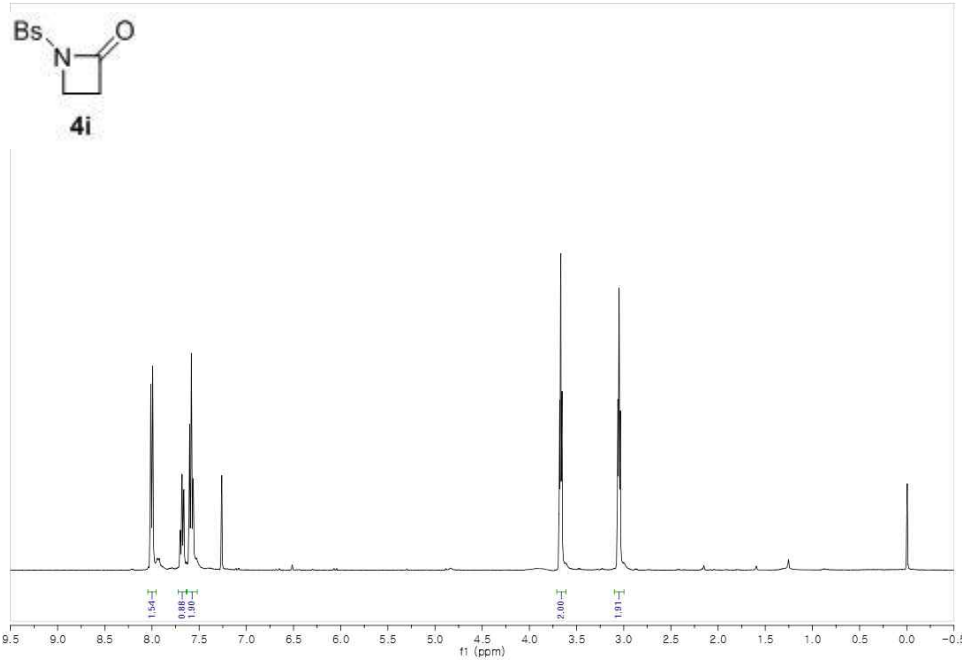
^{13}C NMR (100 MHz, $CDCl_3$) of **4g**



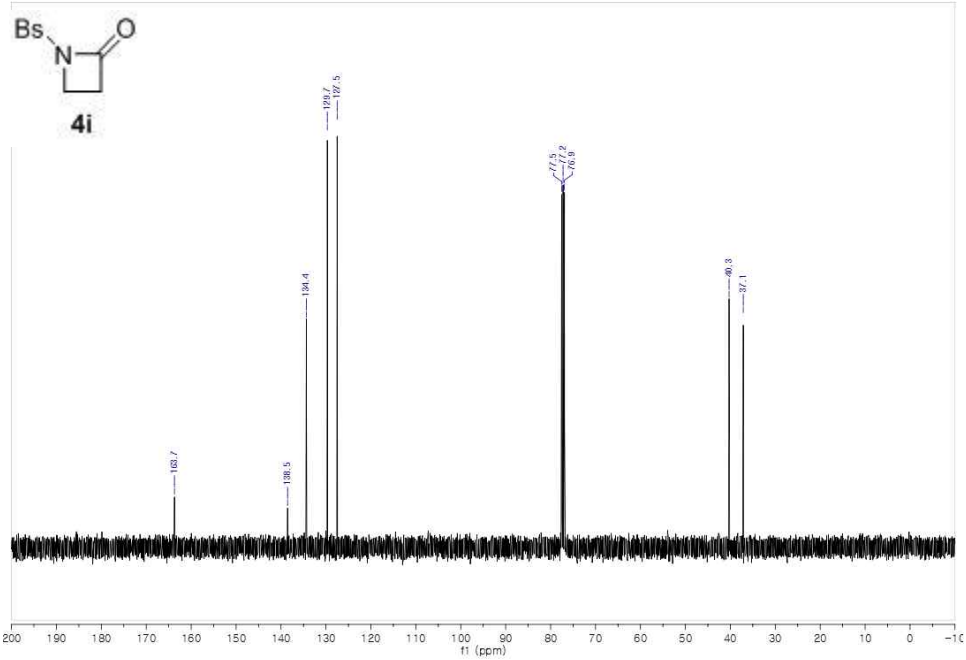
^{1}H NMR (400 MHz, $CDCl_3$) of **4h**



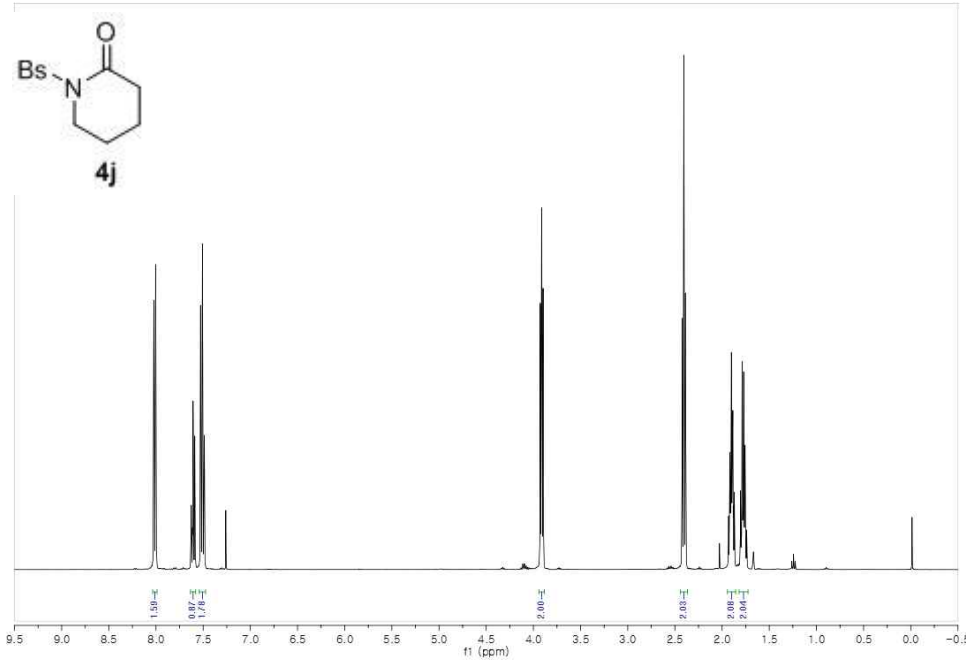
^{13}C NMR (100 MHz, $CDCl_3$) of **4h**



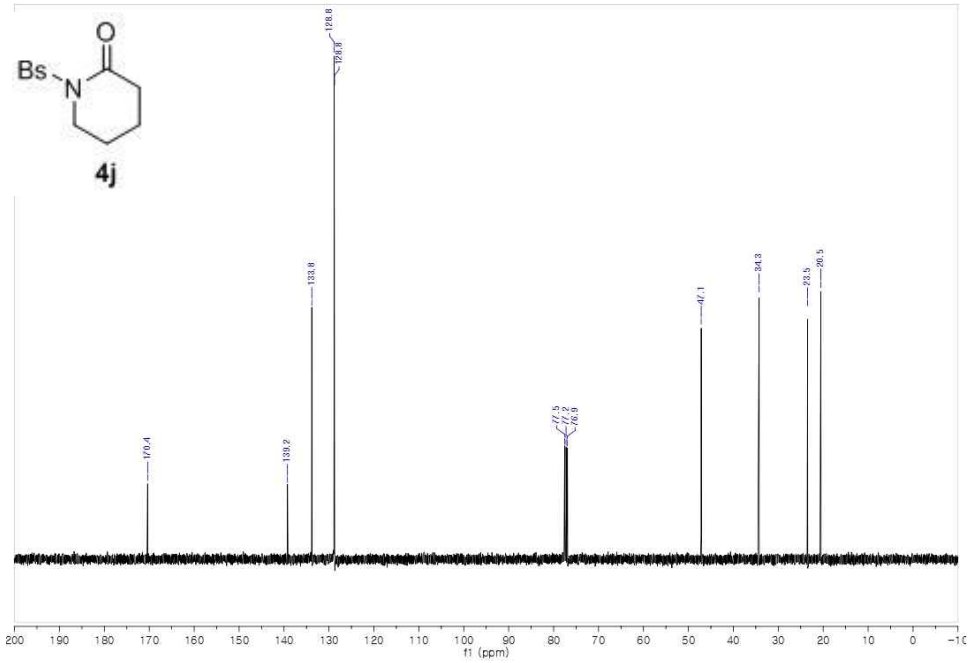
^{1}H NMR (400 MHz, $CDCl_3$) of **4i**



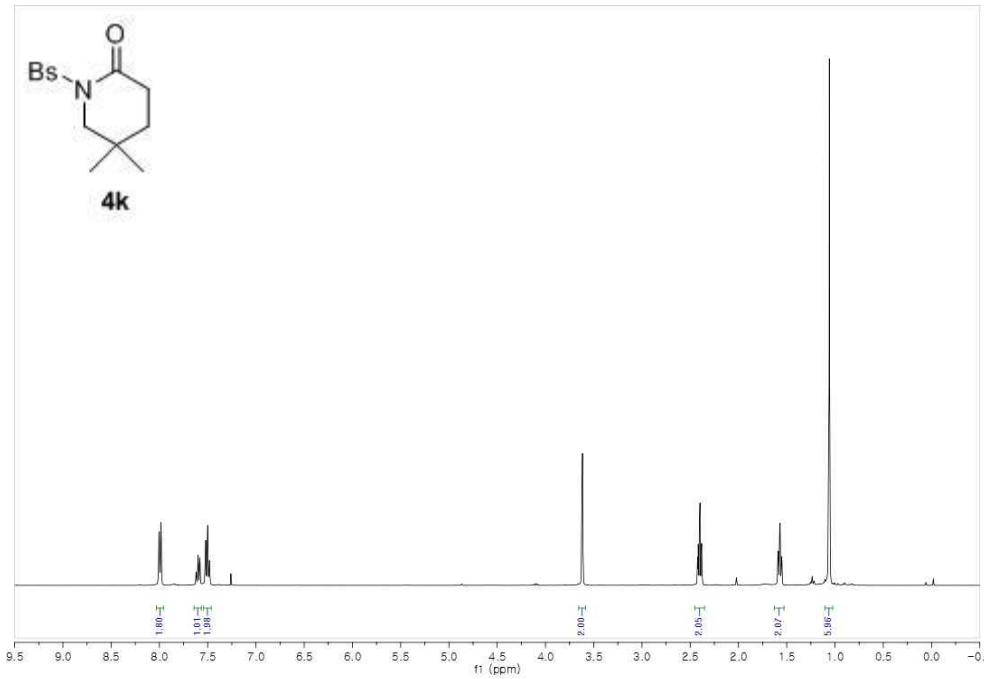
^{13}C NMR (100 MHz, $CDCl_3$) of **4i**



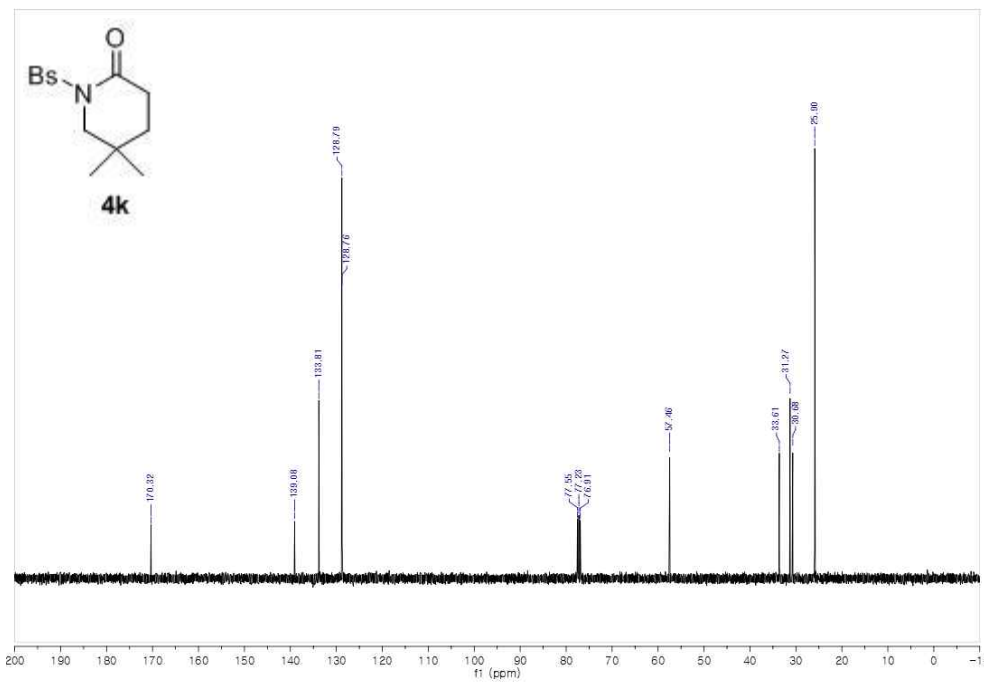
^{1}H NMR (400 MHz, $CDCl_3$) of **4j**



^{13}C NMR (100 MHz, $CDCl_3$) of **4j**



^{1}H NMR (400 MHz, $CDCl_3$) of **4k**



^{13}C NMR (100 MHz, $CDCl_3$) of **4k**