이 학 박 사 학 위 논 문

Studies on Poly(3,4-dimethyl-5-vinylthiazolium) Iodide Catalyzed Organic Reactions

Poly(3,4−dimethyl−5−vinylthiazolium) Iodide 촉매 반응에 관한 연구

2018 년 8 월

서울대학교 대학원

화학부 무기화학전공

천 수 필

Studies on Poly(3,4-dimethyl-5-vinylthiazolium) Iodide Catalyzed Organic Reactions

Supervisor: Prof. Young Keun Chung

By

Supill Chun

A Thesis for Ph.D. Degree

in Inorganic Chemistry

2018

Department of Chemistry

Graduate School

Seoul National University

Studies on Poly(3,4-dimethyl-5-vinylthiazolium) Iodide Catalyzed Organic Reactions

지도 교수 정 영 근

이 논문을 이학박사 학위논문으로 제출함

2018 년 6 월

서울대학교 대학원

화학부 무기화학 전공

천 수 필

천 수 필의 박사학위논문을 인준함

2018 년 6 월

위 원 장 이연 (인)

부위원장 정영근 (인)

위 원 이홍근 (인)

위 원 강윤경 (인)

위 원 Soon Hyeok Hong (인)

Table of contents

Part II. Studies on Silver/NBS Catalyzed Organic Reaction

Chapter 5. Silver/NBS-Catalyzed Synthesis of α-Alkylated Aryl Ketones from Internal Alkynes and Benzyl Alcohols via Ether Intermediates

Abstract

Studies on Poly(3,4-dimethyl-5-vinylthiazolium) Iodide Catalyzed Organic Reactions

Supill Chun

Department of Chemistry

The Graduate School

Seoul National University

Part I. Various Synthetic Strategies using Poly(3,4-dimethyl-5-vinylthiazolium) Iodide as Catalyst

Chapter 2. Hydrothiolation of Alkenes and Alkynes Catalyzed by 3,4-Dimethyl-5-vinylthiazolium Iodide and Poly(3,4-dimethyl-5-vinyl-thiazolium) Iodide

Hydrothiolation reaction that is highly selective anti-Markovnikov addition of thiols to unsaturated carbon-carbon bonds has been developed using 3,4-dimethyl-5-vinylthiazolium iodide or its polymer, poly(3,4-dimethyl-5-vinylthiazolium) iodide as catalyst. A plausible mechanism involving a new model was confirmed by DFT calculations.

Chapter 3. Synthesis of Benzothiazoles from 2-Aminobenzenethiols in the Presence of a Reusable Polythiazolium Precatalyst under Atmospheric Pressure of Carbon Dioxide

Poly(3,4-dimethyl-5-vinylthiazolium) iodide based organocatalytic system could display activities in the cyclization of 2-aminobenzenethiols to benzothiazole in the presence of phenyl silane, 1,8-diazabicyclo [5.4.0] undec-7-ene (DBU), and 1 atm of carbon dioxide. The polymer catalyst reused 7 times in the cyclization reaction without any lose of activities.

Chapter 4. Transition-Metal-Free Poly(thiazolium) Iodide/1,8-Diazabicyclo[5.4.0]undec-7-ene/Phenazine-Catalyzed Esterification of Aldehydes with Alcohols

Esterification reactions of aldehydes with alcohols proceed using poly(3,4-dimethyl-5-vinylthiazolium) iodide and phenazine as an oxidant. The reaction performed under mild conditions, i. e. relatively low temperature (40 ^{o}C), reusable catalyst, and oxidant.

Part II. Studies on Silver/NBS Catalyzed Organic Reaction

Chapter 5. Silver/NBS- Catalyzed Synthesis of α-Alkylated Aryl Ketones from Internal Alkynes and Benzyl Alcohols via Ether Intermediates

α-Alkylated aryl ketones with a tertiary carbon center were synthesized from internal alkynes and benzyl alcohols using NBS and silver as respective catalysts. A plausible mechanism involving an ether intermediate is proposed based on reasonable experiments.

Keywords: hydrothiolation, thiol, carbon dioxide, benzothiazole, silane, reusable catalyst, esterification, phenazine, oxidant, poly(NHC), α-alkylated aryl ketone, silver hexafluoroantimonate ($AgSbF_6$)

Student Number: 2014-22414

Chapter 1. Introduction

1.1. Research Backgroud

Chemical bond forming reactions, such as carbon to carbon,[1] carbon to nitrogen, [2] and carbon to oxygen,[3] afford many important structures. Therefore, it is necessary to find a new strategy to create these compounds in chemical reactions under mild conditions. Depending on the role and use of the catalyst, the catalyst can be classified into two types: homogeneous and heterogeneous catalysts. Each of them has its own special advantages: homogeneous catalyst has advantages in selectivity, and heterogeneous catalyst shows advantages in reusability and recoverability.[4] Therefore, it is a very ideal to combine the advantages of both catalysts in terms of catalytic reaction.

Recently, organocatalysts related to environment-friendly chemistry have attracted much attentions.[5] Excellent publications and references represent all these things such as inexpensive, manageable, and non-toxic.[6] In particular, the organocatalytic reaction proceeds under inert reaction conditions, and the simple handling and storage of the catalyst can be its advantages. Furthermore, many organocatalytsts have commercially available and easy to transformation of their structure.[7] However, despite these advantages, organocatalysts still have drawbacks in re-use. Therefore, the reuse and recovery of the organocatalyst must be solved from the economic and efficiency point of view.

In order to overcome this obstacle, the heterogenized organocatalysts were synthesized by development of mesoporous support and polymerization of them.[8] However, most of these heterogeneous catalysts suffer from relatively

low yields and the poor selectivity under reaction conditions or the potential for poor recycling as a result of decomposition.

Thus, we studied the synthesis of poly(3,4-dimethyl-5-vinylthiazolium) iodide from 3,4-dimethyl-5-vinylthiazolium iodide. The resulting polymer had relatively higher reactivity than monomers and had the advantage of reusability due to the nature of the polymer. Above all, it could be applied to the catalytic reaction of the polymer salt itself (Chapter 2) and the reaction using the polymer as a precatalyst which acts as poly(NHC) (Chapter 3-4). The goals of the research are to demonstrate the new applications and reusability of polymers as organocatalysts. In the last part (Chapter 5), we show the study of the synthesis of α-alkylated aryl ketones via NBS/silver-catalyzed internal alkyne and primary alcohols on the extension line to form new bonds.

1.2. References

(1) (a) Boogaerts, I. I. F.; Nolan, S. P. *J. Am. Chem. Soc.* **2010**, *132*. 8858–8859. (b) Lipeng Wu, L; Liu, Q.; Fleischer, I.; Jackstell, R.; Beller, M. *Nature Commun.* **2014**, *5*, 3091.

(2) (a) Jacquet, O.; Frogneux, X.; Gomes, C. D. N.; Cantat, T. *Chem Sci.* **2013**, *4*, 2127. (b) Das, S.; Bobbink, F. D.; Laurenczy, G.; Dyson, P. J. *Angew. Chem. Int. Ed.* **2014**, *53*, 12876.

(3) Darensbourg, D.J.; Holtcamp, M.W. *Coord. Chem. Rev.* **1996**, *153*, 155.

(4) (a) Park, J. W.; Chung, Y. K. *ACS Catal*. **2015**, *5*, 4846-4850. (b) Park, J. H.; Yoon, J. C.; Chung, Y. K. *Adv. Synth. Catal*. **2009**, *351*, 1233-1237.

(5) Yang, Z.-Z.; He, L.-N.; Gao, J.; Liu, A.-H.; Yu, B. *Energy Environ Sci*. **2012**, *5*, 6602.

(6) (a) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; Benjamin, L. *Chem. Rev.* **2007**, *107*, 5471-5569. (b) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev*. **2007**, *107*, 5606-5655.

(7) Dalko, P. I.; Moisan, L. *Angew. Chem.* **2004**, *116*, 5248-5286.

(8) (a) Seo, U. R.; Chung, Y. K. *Adv. Synth. Catal.* **2014**, *356*, 1955. (b) Seo, U. R.; Chung, Y. K. *RSC Adv*. **2014**, *4*, 32371. (c) Chung, J. Y.; Seo, U. R.; Chun, S.; Chung, Y. K. *ChemCatChem* **2016**, *8*, 318.

Part I

Various Synthetic Strategies using Poly(3,4-dimethyl-5-vinylthiazolium) Iodide as Catalyst

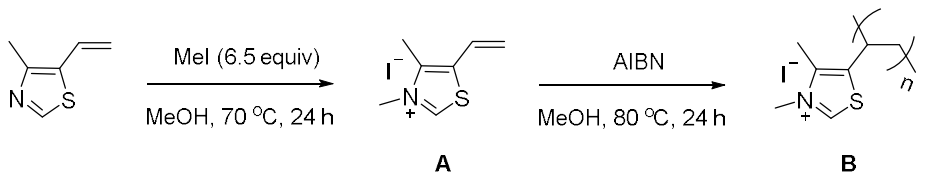
Chapter 2. Hydrothiolation of Alkenes and Alkynes Catalyzed by 3,4-Dimethyl-5-vinylthiazolium Iodide and Poly(3,4-dimethyl-5-vinylthiazolium) Iodide

2.1. Introduction

Since the first study of hydrothiolation by Posner,[1] many groups have studied the new C-S bond production of unsaturated carbon bonds and thiols.[2] For a long time, the sulfur-containing reaction methods have been applied not only to pharmaceutical products, but also to a polymer synthesis and linker for support.[3] Thus, the development of efficient catalytic systems that can promote hydrothiolation is an important challenge for synthetic organic chemists. Hydrothiolation can be catalyzed by strong bases,[4] strong acids, or free radicals.[4d] Recently, several metal compounds were revealed to catalyze hydrothiolation reactions and were reviewed.[5] However, some of the reported procedures have many disadvantages, such as unsatisfactory yields, long reaction times,[6] formation of unwanted byproducts, the use of highly carcinogenic and hazardous organic solvents,[7] and the use of expensive and/or difficult to obtain catalysts.[8] Thus, the development of a more efficient and convenient method for the hydrothiolation of alkenes and alkynes is necessary.

Recent interest in organic catalysts is increasing in that they can promote various types of reactions through different activation modes. These organocatalysts are readily available, robust and usually nontoxic.[9] However, they are not usually reusable because of the difficulties involved in their recovery. To overcome these limitations, a reusable organometallic catalyst was developed by a variety of support, such as silica gel and polymers, and by nanoparticles with support.[10]

As part of the context, we recently developed a polymer-based organocatalytic system,[11] poly(3,4-dimethyl-5-vinylthiazolium) iodide (**B**). We synthesized poly(vinylthiazolium) from 3,4-dimethyl-5-vinylthiazolium by using a radical initiator, that is, 2,2'-azobisisobutyronitrile (AIBN) (Scheme 2.1). 3,4-Dimethyl-5-vinylthiazolium (**A**) was prepared by reaction of 4-methyl-5-vinylthiazole, which is commercially available, with methyl iodide.



Scheme 2.1. Synthesis of poly(3,4-dimethyl-5-vinylthiazolium) iodide (**B**)

We discovered a simple and efficient protocol for the synthesis of linear and vinyl thioethers through the anti-Markovnikov addition of thiols to alkenes and alkynes by using ionic salt polymer catalysts, **A** and **B**. Our catalysts were highly effective, even in the presence of air, and did not requires the use of metal complexes or free-radical initiators. Interestingly, we also found that **A** and **B** were highly effective catalysts for the hydrothiolation of alkenes and alkynes under radical pathway (Typically, the thiol-ene reaction has been proceeded in a radical pathway reaction by photochemical conditions or radical initiator. The reaction to generate thiyl radical, the initiation step of hydrothiolation, is mainly driven by photoinitiators and radical initiators.).[4d] High turnover numbers were observed in the presence of polymeric catalyst **B**. To the best of our knowledge, catalyst **B** is the first successfully recyclable organic polymer catalyst for the hydrothiolation reaction.

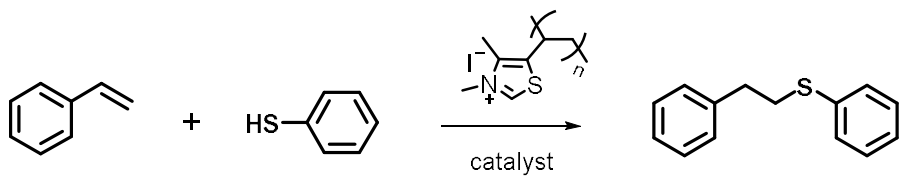
2.2. Results and Discussion

As a model reaction for hydrothiolation, we initially examined the reaction of styrene with thiophenol in the presence of polymeric **B** (1 mol%) for 60 min (Table 2.1). The reaction was highly sensitive to the medium and temperature. In CH_2Cl_2 and toluene, the expected product was not formed (Table 2.1, entries 1 and 2). However, upon changing the solvent to DMF at 40 ^oC, the expected product was formed, albeit in low yield (14 %; Table 2.1, entry 3). Increasing the amount of catalyst **B** to 2 mol% failed to produce any noticeable increase in yield (15 %; Table 2.1, entry 4). To optimize the reaction conditions further, we screened a range of temperatures. No reaction was observed at 25 ^oC. Upon increasing the reaction temperature to 60 ^oC, the yield increased dramatically to 82%. However, a further increase in the temperature to 70 ^oC was not helpful in increasing the yield (81 %; Table 2.1, entry 7). An increase in the reaction time to 90 min at 60 ^oC increased the yield of the product (96 %; Table 2.1, entry 8). The optimum reaction conditions were found to involve the use of **B** (1 mol%), **1a** (1 mmol), and **2a** (1.1 mmol) in DMF (1 mL) at 60 ^oC for 90 min. Moreover, the catalytic activity of **B** was higher than that of monomeric **A** (96:90; Table 2.1, entry8 vs. 9). The amount of catalyst **B** could be lowered to 0.01 mol% (Table 2.1, entry 10). A turnover number of 5800 was observed for the catalyst under our optimized conditions.[12] However, owing to experimental difficulties in measuring the turnover number with the small amount of catalyst **B** in our reaction system, the maximum turnover number was not investigated.

We also examined the reusability of **B** in successive reactions. For experimental feasibility, 5 mol% of **B** was used. Our catalytic system turned out to be quite

robust and could be reused up to four times without any loss of catalytic activity (96, 97, 97, and 95% in runs 1, 2, 3, and 4, respectively). Interestingly, under a nitrogen atmosphere a poor yield (9%) was observed (Table 2.1, entry 11).

Table 2.1. Optimization of the reaction conditions[a]



1a 2a 3a

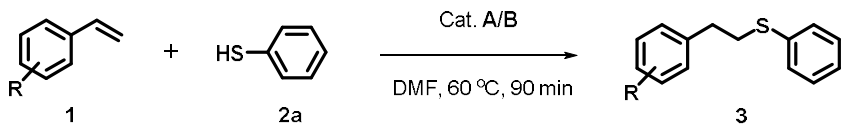
Entry	B (mol%)	Solvent	Temp (^{o}C)	Time (min)	Yield (%)[b]
1	1	CH_2Cl_2	40	60	N.R.
2	1	toluene	40	60	N.R.
3	1	DMF	40	60	14
4	2	DMF	40	60	15
5	1	DMF	25	60	N.R.
6	1	DMF	60	60	82
7	1	DMF	70	60	81
8	1	DMF	60	90	96
9	1	DMF	60	90	90[c]
10	0.01	DMF	60	90	58
11	1	DMF	60	60	9[d]

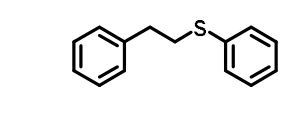
[a]Conditions: 1a (1 mmol), 2a (1.1 mmol), in air. [b]Yield of isolated product; N.R.=no reaction. [c]Catalyst A was used. [d]Under a N_2 atmosphere.

The hydrothiolation reaction under our standard reaction conditions tended to be quite clean and produced no significant side products. Next, the substrate scope of the hydrothiolation reaction with respect to the styrenes was examined under our optimized reaction conditions (Scheme 2.2). Using a standard thiol (thiophenol), reactions were performed with a variety of styrenes in the presence of both **A** and **B** as catalysts to compare their catalytic activities. For the substrates delivering products **3aa–ia**, except for **3ba** and **3da**, higher yields were observed in the presence of polymeric catalyst **B** than in the presence of monomeric **A**. Substrates with an electronwithdrawing substituent (e.g., CF_3, F, Cl, and Br) reacted smoothly with the thiol to afford the corresponding hydrothiolated products in good to high yields. If a methyl group was introduced to the position (see products **3ja** and **3ka**), the yield decreased and catalyst **A** became more active than catalyst **B**. The yields observed in the presence of **A** were slightly higher than those in the presence of **B** (product **3ja**, 76 and 65 %; product **3ka**, 77 and 70 %). This observation might be explained by considering the feasibility of the substrate encountering the catalytically active sites. In polymeric catalyst **B**, the catalytically active sites are densely situated on the polymer backbone and are quite effective for the reaction with ordinary substrates. However, **B** is less effective than **A** in reactions involving sterically hindered substrates. The active sites in monomeric catalyst **A** might be more accessible to sterically demanding substrates than the active sites in **B**. It is interesting that catalysts **A** and **B** are complementary in terms of the hydrothiolation reaction of thiophenol with various styrenes. Among substrates having a halogen substituent, the substrate bearing a bromine atom showed the highest yield (products **3ga–ia**: 78, 80, and 92%; products **3na** and **3ma**: 71 and 76%). 3-Chlorostyrene (91%) showed the highest yield among the 2-, 3-, and 4-chlorostyrenes. Interestingly, the formation of a β-nitrosulfide was observed in the

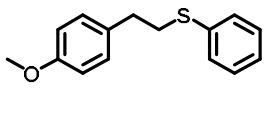
reaction of (E)-(2-nitrovinyl) benzene (**3la**).[13]

Scheme 2.2. Hydrothiolation of different styrenes with thiophenol[a]

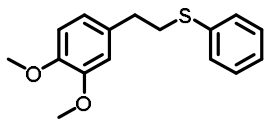




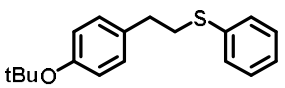
3aa, 90/96 %[b]



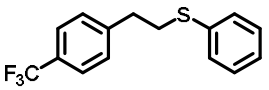
3ba, 95/89 %



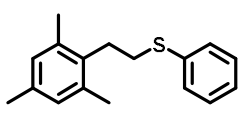
3ca, 78/85 %



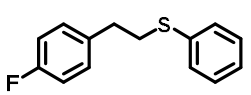
3da, 64/62 %[b]



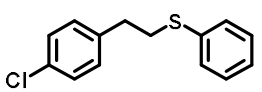
3ea, 59/82 %



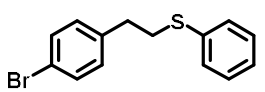
3fa, 75/84 %



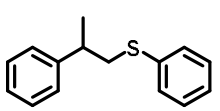
3ga, 73/78 %[b]



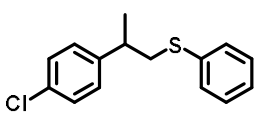
3ha, 67/80 %



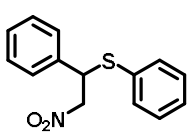
3ia, 74/92 %



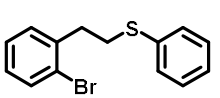
3ja, 76/65 %[c]



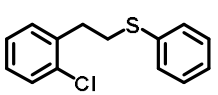
3ka, 77/70 %[d]



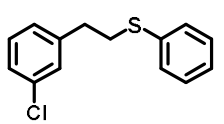
3la, 97/96 %[e]



3ma, 80/76 %



3na, 71/71 %

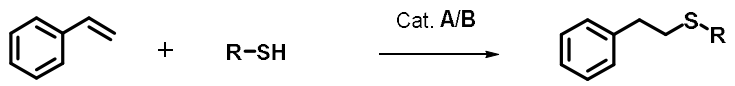


3oa, 73/91 %

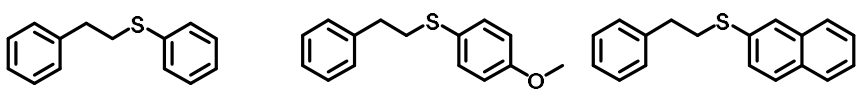
[a]Conditions: **1a** (1 mmol), **2** (1.1 mmol), **A** or **B** (1 mol%), DMF (1 mL), 60 °C, 90 min.

[b]Yield of isolated product (by **A/B**). [c]3 h. [d]**2** (2 equiv.). [e]α-Hydrothiolation.

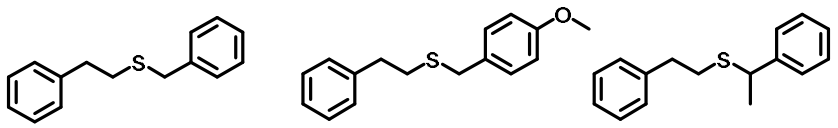
Scheme 2.3. Hydrothiolation of styrene with different thiols[a]



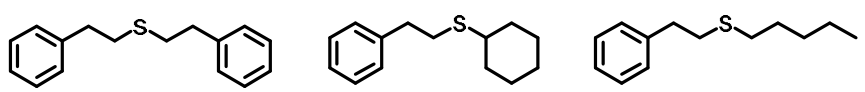
1a + **2** → **3**



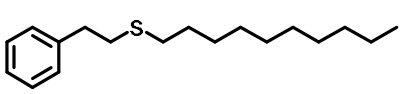
3ab, 81/83 %[b] **3ac**, 94/85 % **3ad**, 90/97 %[c]



3ae, 83/79 % **3af**, 86/77 %[d] **3ag**, 80/67 %



3ah, 57/42 %[d] **3ai**, 66[d]/38[e] % **3aj**, 62/38 %



3ak, 50/35 %

[a]Conditions: **1a** (1 mmol), **2a** (1.1 mmol), in air. [b]Yield of isolated product; N.R.=no reaction. [c]Catalyst A was used. [d]Under a N_2 atmosphere.

The scope of the reaction was then investigated further with a variety of thiols (Scheme 2.3). In general, high yields were observed for products **3ab–ag**. However,

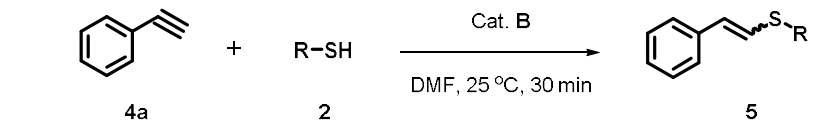
as the aliphatic character of the thiols increased, the yields decreased (products **3ae–ak**). Interestingly, higher yields were observed with monomeric catalyst **A** for most aliphatic thiols. For example, a poor yield (38%) was observed for pentanethiol in the presence of **B** (product **3aj**), but the yield increased to 62% in the presence of catalyst **A**. Upon using decane-1-thiol as the substrate in the presence of **A**, the yield was still moderate at 50% (product **3ak**). In the case of product **3ad**, the yield was calculated by ^{1}H NMR spectroscopy, because of difficulties in separating the product from the reactant. Unfortunately, 2-aminobenzenethiol and 2-chlorobenzenethiol were unreactive under our reaction conditions. Overall, the substrate scope of our hydrothiolation process suggests that both steric and electronic factors may play a major role in the reaction.

To expand the scope of this reaction to alkynes, we investigated the hydrothiolation of ethynylbenzene with various thiols under our optimized reaction conditions (Scheme 2.4). It was encouraging to observe that the reactions went to completion within 30 min. In most cases, the (E)-vinyl sulfide was the predominant product. The regioselectivity of the hydrothiolation varied depending upon the substrate.

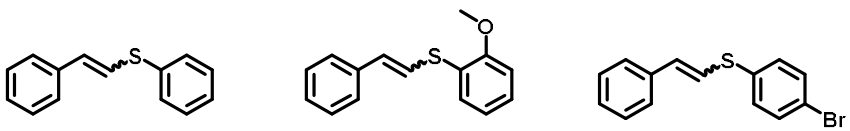
Introduction of a substituent on the thiophenol led to a decrease in the E/Z ratio from 89:11 to 80:20 (products **5aa**, **5al**, and **5am**). If an electron-donating group NH_2 was present on the thiophenol, the Z isomer was favored over the E isomer with a 91:9 ratio in a rather poor yield (31 %). It seemed that as the chain length of the aliphatic thiol increased (products **5ao**, **5aj**, and **5ak**), both the yield and the selectivity for the E isomer increased. However, if dodecane thiol was used, a poor regioselectivity was observed (E/Z= 42:58). The best E/Z ratio was observed upon using decane thiol. A branched alkane thiol such as 2-ethylhexane-1-thiol gave the E isomer as a major product. If a substrate with a bulky substituent, such as

(triisopropylsilyl)acetylene, was treated with thiophenol, a high E/Z ratio (product **5pa**; 90:10) was observed. In the reaction of 1,2-ethanedithiol, bis-hydrothiolation was observed, which resulted in the formation of 2-benzyl-1,3-dithiolane in 61% yield.[14]

Scheme 2.4. Hydrothiolation of different alkynes with thiols[a]



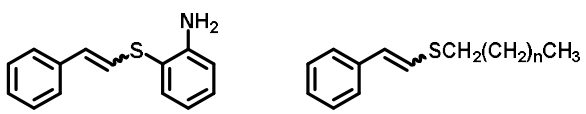
4a 2 5



5aa, 85 %[b] (89:11)[c]

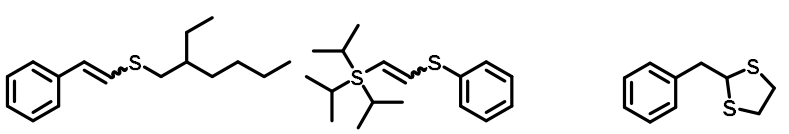
5al, 75 % (85:15)

5am, 81 % (80:20)



5an, 31 % (91:9)

5ao, n= 1 75 % (76:24)
5aj, n= 3 85 % (70:30)
5ak, n= 8 92 % (84:16)
5ap, n=10 87 % (42:58)



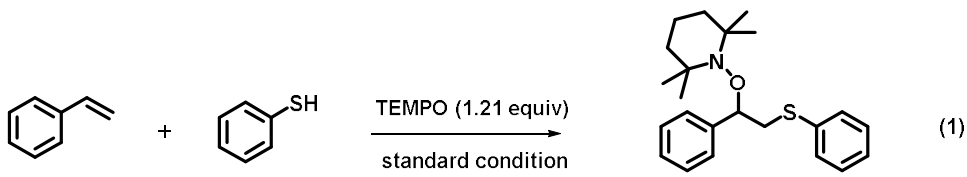
5aq, 85 % (85:15)

5pa, 68 % (90:10)

5ar, 61 %

[a]Conditions: **4a** (1 mmol), **2** (1.1 mmol), **B** (1 mol%), DMF (1 mL), RT, 30 min. [b]Yield of isolated product. [c]The E/Z ratio was determined by analysis of the isolated product by ^{1}H NMR spectroscopy.

To gain some insight into the reaction mechanism, we performed the reaction in the presence of a common radical trap [i.e., 2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO), 1.21 equiv.]. No hydrothiolation product was formed in this case. Instead, 2,2,6,6-tetramethyl-1-[1-phenyl-2-(phenylthio)ethoxy]piperidine[15] was obtained in a very low 9% yield (eq 1).

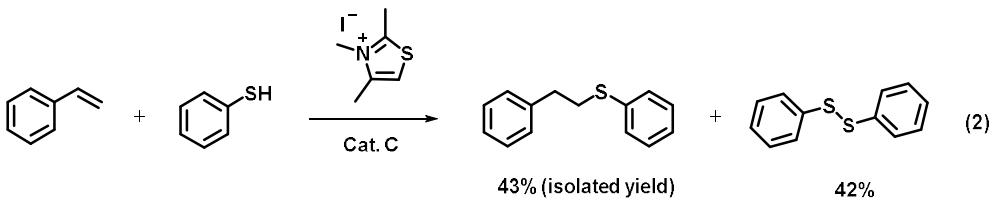


Only detected
9% (isolated yield)

(1)

Our observation that the hydrothiolation reaction could be performed in air suggested dioxygen as a radical initiator in our reaction.[16] Moreover, the formation of a product was not observed in the absence of catalyst **A**. This result suggests that catalyst **A** plays an important role in the reaction.

To gain further information about the reaction, we prepared **C** and tested it as a catalyst in the hydrothiolation of styrene with thiophenol. Reaction in the presence of **C** led to the formation of diphenyl disulphide (42%) and phenethyl phenyl sulfide (43%) (eq 2). This result shows that the substituent at the C2 position of the thiazolium highly affects the reaction; furthermore, the yield of the hydrothiolation product obtained in the presence of catalyst **A** with a hydrogen atom at the C2 position was much higher than that obtained in the presence of catalyst **C** with a methyl group at the C2 position.[17]



On the basis of our observations and those of others,[18] we suggest that the reaction follows a radical mechanism (Figure 2.1). The key point of the hydrothiolation is the role of the thiazolium, which interacts with the thiyl radical; this results in stabilization of the radical and enhances its addition to unsaturated c-c bonds.

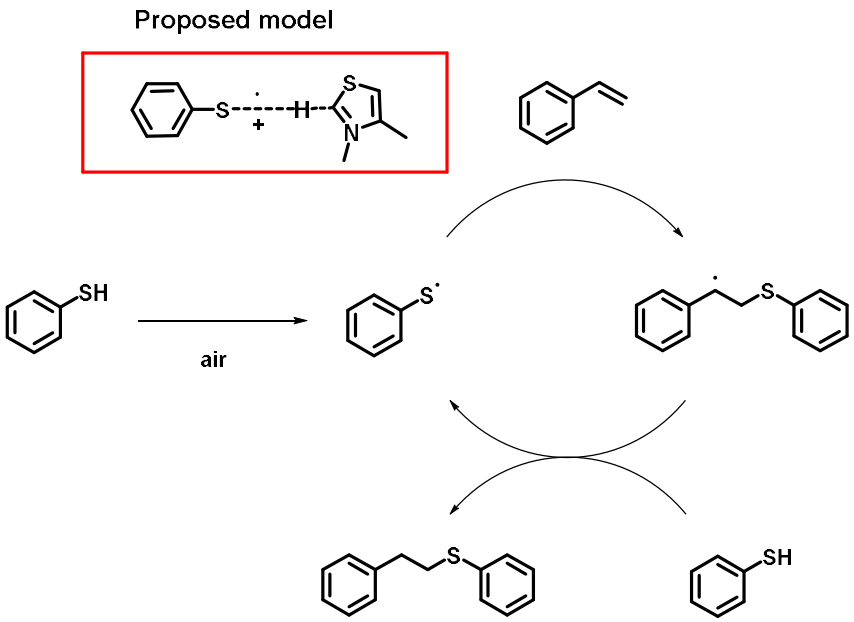


Figure 2.1. Plausible reaction mechanism for the hydrothiolation reaction.

The role of the thiazolium catalyst was confirmed by DFT calculations (Figure

2.2). The thiyl radical produced by the reaction with dioxygen is stabilized by catalyst **A** or **C** relative (stabilized by -10.53 and -7.86 kcal/mol in the presence of **A** and **C**, respectively, relative to the free thiyl radical), and the addition of the thiyl radical to styrene in the presence of **A** shows the lowest activation energy barrier 12.01 kcal/mol (TS_Cat. **A**). This is reflected in the high yield of the hydrothiolation product (90 %). In the absence of catalyst **A** or **C**, no reaction is observed within 90 min. However, in the presence of **C** or without any catalyst, the energy of the transition state does not match the trend in the yield. Thus, stabilization of the thiyl radical seems to be critical to the hydrothiolation reaction.

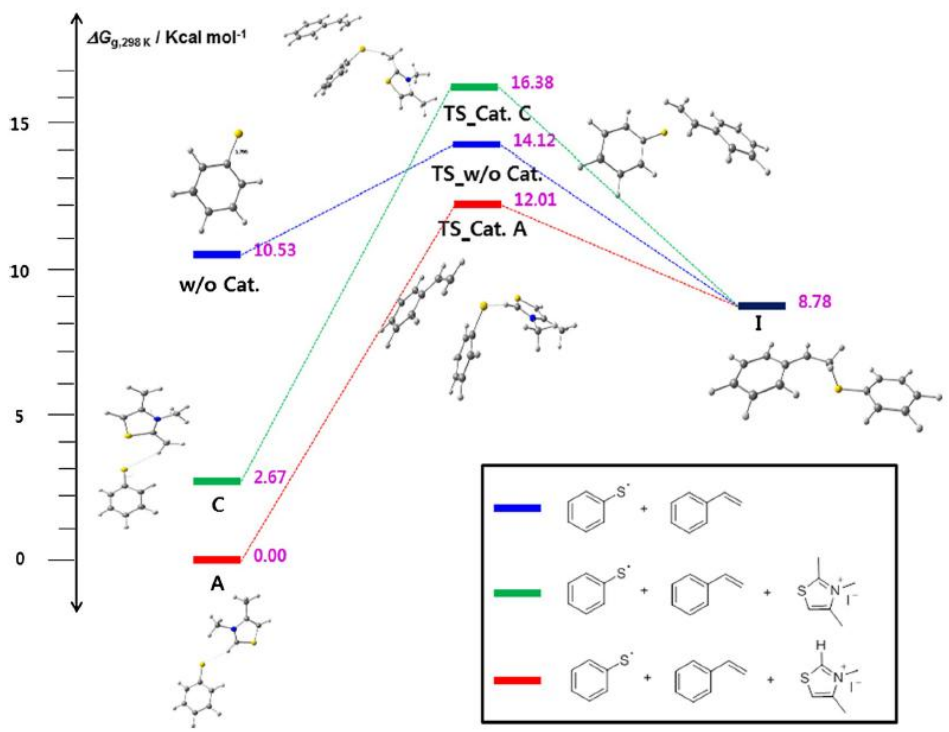


Figure 2.2. Energy profiles for the catalyzed and uncatalyzed thiol–ene reactions

2.3. Conclusion

We developed a robust method for the vinylthiazolium or poly(vinylthiazolium)-catalyzed hydrothiolation of alkenes and alkynes. The reaction can be employed for both aliphatic and aromatic thiols. Our optimized reaction conditions afforded linear thioethers from both activated and unactivated alkenes with aliphatic and aromatic thiol partners in good to excellent yields under metal-free, additive-free, and open-air conditions. For most aromatic thiols, higher yields were observed in the presence of polymer catalyst **B**, but with aliphatic thiols, higher yields were generally observed with monomeric catalyst **A**. The polymeric catalyst showed a high turnover number (5800) and was recyclable.

2.4. Experimental Section

General remarks

n-Hexanes and ethyl acetate were used without further purification. Other solvents were obtained by passing through activated alumina columns of solvent purification systems from Glass Contour. Reagents were purchased from Sigma-Aldrich, Alfa Aesar, Acros, and TCI and were used as received. DMF were used as a solvent. Reactions were carried out in a glassware equipped with a stirring under air condtions, unless otherwise indicated. Elevated temperatures were maintained in thermostat-controlled oil baths. The TLC plate was carried out on 0.25 mm E. Merck silica gel plates (60F-254) visualized by UV-light (254 nm) and treatment with acidic *p*-anisaldehyde and $KMnO_4$ stain followed by gentle heating. Workup procedures were done in air. Flash chromatography was carried out on Merck 60 silica gel (230 – 400 mesh). ^{1}H and ^{13}C NMR spectra were recorded with Varian spectrometer (400 MHz) spectrometer. ^{1}H NMR spectra were referenced to residual

TMS (0 ppm) and reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dt = doublets of triplets, td = triplet of doublets, qd = quartet of doublets, br s = broad singlet, m = multiplet). Chemical shifts of the ^{13}C NMR spectra were measured relative to $CDCl_3$ (77.16 ppm). Mass spectral data were obtained from the Korea Basic Science Institute (Daegu) on a Jeol JMS 700 high resolution mass

Procedure for the Hydrotiolation of Alkenes

Reactions were performed in a tube-type schlenk flask equipped with a stirring bar and the followings were placed in the flask in order: 1 mol% of catalyst **A** or **B** (2.6 mg, 1 mol%), styrene derivates (1 mmol), thiols (1.1~2 mmol), and 1 mL of DMF. The reaction mixture was heated at 60 ^{o}C for 90 minutes. After the solution was cooled to room temperature, the solvent was evaporated from the reaction mixture by using a rotary evaporator. Purification by flash chromatography on silica gel with n-hexane and ethyl acetate afforded thioether. The thioether products were characterized by ^{1}H NMR, ^{13}C NMR and HRMS.

Procedure for the Hydrotiolation of Alkynes

Reactions were performed in a tube-type schlenk flask equipped with a stirring bar and the followings were placed in the flask in order: 1 mol% of catalyst **B** (2.6 mg, 0.01 mmol), acetylene derivates (1 mmol), thiols (1.1 mmol), and 1 mL of DMF. The reaction mixture was reacted at room temperature for 30 minutes. After the solvent was evaporated from the reaction mixture by using a rotary evaporator, purification by flash chromatography on silica gel with n-hexane and ethyl acetate

afforded thioether. The thioether products were characterized by ^{1}H NMR, ^{13}C NMR and HRMS.

Recycling Test

A tube-type Schlenk flask was charged with 1 mmol of styrene (104 mg), 1.1 mmol of thiolphenol (121 mg), 5 mol% of catalyst **B** (13 mg, 0.05 mmol), and 1 mL of DMF. After the resulting solution was heated at 60 ^{o}C for 90 minutes, the solvent was evaporated from the reaction mixture by using a rotary evaporator. 80 mL of ethyl acetate was added to the residue. Then, the solution was filtered off to separate B. And, the recovered B was reused in the next experiment. The solvent was evaporated from the filtrate and the residue was purified by a flash column chromatograpy. The catalytic performance of poly(NHC) was well maintained during the four times of recycling with 95-97% isolated yields (1^{st} run, 96%; 2^{nd} run, 97%; 3^{rd} run, 97%; 4^{th}, 95%).

Characterization of compounds

3aa: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 7.8 Hz, 2 H), 7.20 (dt, J = 7.9, 3.3 Hz, 4 H), 7.16 – 7.04 (m, 4H), 3.10 – 3.04 (m, 2 H), 2.87 – 2.81 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.31, 136.48, 129.29, 129.04, 128.61, 126.56, 126.08, 35.75, 35.19 ppm. HRMS (EI) calc. for [$C_{14}H_{14}S$]: 214.0816, found: 214.0815; colorless oil.

3ba: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 2 H), 7.24 – 7.16 (m, 2 H), 7.14 – 7.08 (m, 1 H), 7.06 – 7.01 (m, 2 H), 6.80 – 6.72 (m, 2 H), 3.71 (s, 3 H), 3.19 – 3.01 (m, 2 H), 2.86 – 2.74 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.34, 136.57, 132.43, 129.60, 129.27, 129.04, 126.05, 114.04, 55.39, 35.49, 34.86 ppm. HRMS (EI) calc. for [$C_{15}H_{16}OS$]: 244.0922, found: 244.0919; colorless oil.

3ca: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.32 (m, 2 H), 7.32 – 7.13 (m, 3 H), 6.82 – 6.66 (m, 3 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 3.19 – 3.13 (m, 2 H), 2.91 – 2.84 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.97, 147.73, 136.52, 132.90, 129.29, 129.01, 126.06, 120.50, 111.92, 111.34, 56.01, 55.94, 35.42, 35.33 ppm. HRMS (EI) calc. for [$C_{16}H_{18}O_2S$]: 274.1028, found: 274.1027; colorless oil.

3da: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 2 H), 7.29 – 7.23 (m, 2 H), 7.18 – 7.12 (m, 1 H), 7.06 (d, J = 8.3Hz, 2 H), 6.90 (d, J = 8.3 Hz, 2 H), 3.12 (dd, J = 9.4, 6.6 Hz, 2 H), 2.90 – 2.83 (m, 2 H), 1.31 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.90, 136.56, 135.16, 129.23, 128.99, 128.93, 126.00, 124.29, 78.34, 35.26, 35.14, 28.93 ppm. HRMS (EI) calc. for [$C_{18}H_{22}OS$]: 286.1391, found: 286.1389; viscous oil.

3ea: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.5 Hz, 2 H), 7.27 (d, J = 7.8 Hz, 2 H), 7.16 (m, 5 H), 3.14 – 3.05 (m, 2 H), 2.89 (t, J = 7.5 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.26, 135.95, 129.70, 129.09 (d, J = 11.8 Hz), 128.78, 126.44, 125.54 (q, J = 3.8 Hz), 125.49, 123.04, 35.52, 35.02 ppm. HRMS (EI) calc. for [$C_{15}H_{13}F_3S$]: 282.0690, found: 282.0689; pale yellow oil.

3fa: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2 H), 7.20 (m, 2 H), 7.14 – 7.05 (m, 1 H), 6.73 (s, 2 H), 2.90 –2.84 (m, 2 H), 2.83 – 2.77 (m, 2 H), 2.13 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.45, 136.25, 135.84, 133.96, 129.91, 129.15, 128.99, 126.32, 32.88, 29.72, 20.93, 19.77 ppm. HRMS (EI) calc. for [$C_{17}H_{20}S$]: 256.1286, found: 256.1287; white solid.

3ga: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (m, 4 H), 7.16 – 7.03 (m, 3 H), 6.95 – 6.86 (m, 2 H), 3.07 (dd, J = 8.5, 6.9 Hz, 2 H), 2.85 – 2.79 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.72 (d, J = 245.2 Hz), 136.27, 135.94, 130.08 (d, J = 8.0

Hz), 129.46, 129.09, 126.23, 115.39 (d, J = 21.2 Hz), 35.41, 34.90 ppm. HRMS (EI) calc. for [$C_{14}H_{13}FS$]: 232.0722, found: 232.0720; colorless oil.

3ha: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.13 (m, 7 H), 7.07 (dd, J = 10.1, 3.7 Hz, 2 H), 3.10 (dd, J = 14.6, 7.3 Hz, 2 H), 2.86 (dd, J = 14.6, 6.9 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.64, 136.13, 132.29, 129.99, 129.47, 129.07, 128.67, 126.23, 35.12, 34.98 ppm. HRMS (EI) calc. for [$C_{14}H_{13}ClS$]: 248.0426, found: 248.0428; colorless oil.

3ia: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 8.3 Hz, 2 H), 7.21 (m, 4 H), 7.11 (d, J = 7.2 Hz, 1 H), 6.97 (d, J = 8.3 Hz, 2 H), 3.07 – 3.01 (m, 2 H), 2.81 – 2.75 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.21, 136.12, 131.69, 130.43, 129.57, 129.12, 126.32, 120.42, 35.14, 35.11 ppm. HRMS (EI) calc. for [$C_{14}H_{13}BrS$]: 291.9921, found: 291.9921; colorless oil.

3ja: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.24 (m, 4 H), 7.24 – 7.14 (m, 5 H), 7.14 – 7.08 (m, 1 H), 3.18 (ddd, J = 12.0, 5.8, 1.5 Hz, 1 H), 3.06 – 2.90 (m, 2 H), 1.36 (dd, J = 6.7, 1.7 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.61, 137.00, 129.17, 128.98, 128.64, 127.06, 126.70, 125.90, 42.11, 39.55, 21.14 ppm. HRMS (EI) calc. for [$C_{15}H_{16}S$]: 228.0973, found: 228.0974; pale yellow oil.

3ka: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.14 (m, 6 H), 7.12 – 7.01 (m, 3 H), 3.11 – 2.96 (m, 2 H), 2.88 (dd, J = 14.1, 7.0 Hz, 1 H), 1.29 (d, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.95, 136.62, 132.31, 129.41, 129.03, 128.73, 128.49, 126.12, 42.10, 39.09, 21.21 ppm. HRMS (EI) calc. for [$C_{15}H_{15}ClS$]: 262.0583, found: 262.0582; colorless oil.

3la: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 2 H), 7.28 – 7.22 (m, 5 H), 7.22 – 7.13 (m, 3 H), 4.83 – 4.72 (m, 2 H), 4.63 (m, 1 H) ppm. ^{13}C NMR (100 MHz,

$CDCl_3$) δ 136.38, 133.86, 131.97, 129.47, 129.09, 128.91, 128.75, 127.75, 78.62, 49.96 ppm. HRMS (EI) calc. for [$C_{14}H_{13}NO_2S$]: 259.0667, found: 259.0668; white solid.

3ma: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 8.0 Hz, 1 H), 7.31 (d, J = 7.5 Hz, 2 H), 7.21 (t, J = 7.6 Hz, 2 H), 7.16 – 7.08 (m, 3 H), 7.02 – 6.96 (m, 1 H), 3.11 – 3.06 (m, 2 H), 2.96 (dd, J = 9.5, 5.9 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.56, 136.17, 133.05, 131.00, 129.54, 129.05, 128.39, 127.66, 126.22, 124.44, 36.39, 33.41ppm. HRMS (EI) calc. for [$C_{14}H_{13}BrS$]: 291.9921, found: 291.9924; pale yellow oil.

3na: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 7.6 Hz, 2 H), 7.35 – 7.24 (m, 3 H), 7.23 – 7.12 (m, 4 H), 3.17 (dd, J = 9.5, 5.8 Hz, 2 H), 3.04 (dd, J = 9.4, 6.1 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.82, 136.21, 134.04, 130.98, 129.72, 129.40, 129.05, 128.14, 127.00, 126.17, 33.91, 33.22 ppm. HRMS (EI) calc. for [$C_{14}H_{13}ClS$]: 248.0426, found: 248.0429; colorless oil.

3oa: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.32 (m, 2 H), 7.31 – 7.26 (m, 2 H), 7.23 – 7.15 (m, 4 H), 7.07 – 7.03 (m, 1 H), 3.15 – 3.10 (m, 2 H), 2.90 – 2.85 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.22, 136.06, 134.33, 129.84, 129.57, 129.10, 128.77, 126.85, 126.75, 126.31, 35.38, 35.00 ppm. HRMS (EI) calc. for [$C_{14}H_{13}ClS$]: 248.0426, found: 248.0427; colorless oil.

3ab: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.17 (m, 4 H), 7.16 – 7.08 (m, 3 H), 7.06 – 7.03 (m, 2 H), 3.10 – 3.01 (m, 2 H), 2.87 – 2.77 (m, 2 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.46, 136.33, 132.60, 130.24, 129.85, 128.64, 128.61, 126.51, 35.96, 35.90, 21.16 ppm. HRMS (EI) calc. for [$C_{15}H_{16}S$]: 228.0973, found: 228.0971; colorless oil.

3ac: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.7 Hz, 2 H), 7.24 – 7.16 (m, 2 H), 7.15 – 7.03 (m, 3 H), 6.78 (d, J = 8.7 Hz, 2 H), 3.72 (s, 3 H), 3.02 – 2.95 (m, 2 H), 2.82 – 2.75 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.06, 140.50, 133.39, 128.64, 128.58, 126.46, 126.43, 114.73, 55.47, 37.37, 36.04 ppm. HRMS (EI) calc. for [$C_{15}H_{16}OS$]: 244.0922, found: 244.0920; colorless oil.

3ad: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.63 (m, 4 H), 7.44 – 7.32 (m, 3 H), 7.28 – 7.20 (m, 2 H), 7.19 – 7.09 (m, 3 H), 3.22 – 3.17 (m, 2 H), 2.93 – 2.87 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.36, 134.07, 133.98, 131.93, 128.69, 128.58, 127.87, 127.53, 127.20, 127.10, 126.70, 126.65, 125.79, 35.79, 35.21 ppm. HRMS (EI) calc. for [$C_{18}H_{16}S$]: 264.0973, found: 264.0974; colorless oil.

3ae: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.21 (m, 4 H), 7.20 – 7.10 (m, 4 H), 7.08 – 7.04 (m, 2 H), 3.63 (s, 2 H), 2.75 (dd, J = 9.1, 6.6 Hz, 2 H), 2.61 – 2.54 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.67, 138.55, 129.00, 128.62, 128.56, 127.11, 126.44, 36.61, 36.19, 32.93 ppm. HRMS (EI) calc. for [$C_{15}H_{16}S$]: 228.0973, found: 228.0973; colorless oil.

3af: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.19 (m, 2 H), 7.17 - 7.11 (m, 3 H), 7.11 – 7.06 (m, 2 H), 6.80 – 6.74 (m, 2 H), 3.72 (s, 3 H), 3.60 (s, 2 H), 2.76 (dd, J = 9.2, 6.5 Hz, 2 H), 2.62 – 2.54 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.74, 140.94, 130.49, 130.06, 128.64, 128.57, 126.44, 114.04, 55.43, 36.20, 35.95, 32.83 ppm. HRMS (EI) calc. for [$C_{16}H_{18}OS$]: 258.1078, found: 258.1081; colorless oil.

3ag: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.19 (m, 4 H), 7.18 – 7.12 (m, 3 H), 7.09 (t, J = 7.2 Hz, 1 H), 7.00 (d, J = 7.3 Hz, 2 H), 3.87 (q, J = 7.0 Hz, 1 H), 2.75 – 2.58 (m, 2 H), 2.52 – 2.39 (m, 2 H), 1.48 (d, J = 7.0 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.09, 140.77, 128.61, 128.57, 128.51, 127.42, 127.21, 126.36,

44.38, 36.28, 32.91, 22.70 ppm. HRMS (EI) calc. for [$C_{16}H_{18}S$]: 242.1129, found: 242.1129; colorless oil.

3ah: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.19 (m, 2 H), 7.17 – 7.07 (m, 3 H), 2.84 – 2.78 (m, 2 H), 2.74 – 2.68 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.69, 128.61, 126.49, 36.47, 33.93 ppm. HRMS (EI) calc. for [$C_{16}H_{18}S$]: 242.1129, found: 242.1131; colorless oil.

3ai: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.16 (m, 2 H), 7.16 – 7.04 (m, 3 H), 2.82 – 2.74 (m, 2 H), 2.73 – 2.66 (m, 2 H), 2.55 (m, 1 H), 1.88 (d, J = 10.2 Hz, 2 H), 1.67 (d, J = 5.5 Hz, 2 H), 1.52 (d, J = 6.5 Hz, 1 H), 1.29 – 1.11 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.93, 128.51, 128.51, 126.35, 43.75, 36.82, 33.79, 31.75, 26.23, 25.95 ppm. HRMS (EI) calc. for [$C_{14}H_{20}S$]: 220.1286, found: 220.1284; colorless oil.

3aj: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.20 (m, 2 H), 7.20 – 7.10 (m, 3 H), 2.81 (dd, J = 9.5, 6.3 Hz, 2 H), 2.70 (m, 2 H), 2.49 – 2.43 (m, 2 H), 1.57 – 1.47 (m, 2 H), 1.34 – 1.19 (m, 4 H), 0.83 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.87, 128.60, 128.59, 126.43, 36.56, 33.82, 32.44, 31.25, 29.50, 22.46, 14.13 ppm. HRMS (EI) calc. for [$C_{13}H_{20}S$]: 208.1286, found: 208.1284; colorless oil.

3ak: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.20 (m, 2 H), 7.19 – 7.08 (m, 3 H), 2.81 (dd, J = 9.3, 6.2 Hz, 2 H), 2.72 – 2.65 (m, 2 H), 2.49 – 2.42 (m, 2 H), 1.56 – 1.45 (m, 2 H), 1.36 – 1.27 (m, 2 H), 1.19 (s, 12 H), 0.81 (t, J = 6.8 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.86, 128.59, 128.58, 126.42, 36.56, 33.81, 32.46, 32.04, 29.80, 29.71, 29.68, 29.46, 29.39, 29.07, 22.83, 14.27 ppm. HRMS (EI) calc. for [$C_{18}H_{30}S$]: 278.2068, found: 278.2068; pale yellow oil.

5aa: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.38 (m, 1 H), 7.34 – 7.31 (m, 1 H), 7.26 – 7.11 (m, 8 H), 6.79 (d, J = 15.5 Hz, 0.90 H), 6.64 (d, J = 15.5 Hz, 0.89 H), 6.50 (d, J = 10.7 Hz, 0.11 H), 6.41 (d, J = 10.7 Hz, 0.11 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.03, 136.53, 135.24, 131.81, 129.83, 129.17, 129.07, 128.70, 127.60, 127.51, 127.16, 126.96, 126.03, 123.40 ppm. HRMS (EI) calc. for [$C_{14}H_{12}S$]: 212.0660, found: 212.0660; pale yellow oil.

5al: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.21 (m, 4 H), 7.16 – 7.09 (m, 2 H), 6.93 – 6.78 (m, 3 H), 6.65 (d, J = 15.5 Hz, 0.86 H), 6.53 (d, J = 10.8 Hz, 0.14 H), 6.36 (d, J = 10.8 Hz, 0.14 H), 3.80 (d, J = 1.7 Hz, 3 H), 3.79 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.17, 136.78, 132.30, 130.49, 129.00, 128.77, 128.38, 128.29, 127.85, 127.63, 126.15, 123.57, 122.52, 121.45, 110.93, 56.03 ppm. HRMS (EI) calc. for [$C_{15}H_{14}OS$]: 242.0765, found: 242.0763; pale yellow oil.

5am: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.31 (m, 3 H), 7.30 – 7.20 (m, 4 H), 7.19 – 7.14 (m, 2 H), 6.74 (d, J = 15.4 Hz, 0.79 H), 6.68 (d, J = 15.4 Hz, 0.8 H), 6.55 (d, J = 10.7 Hz, 0.22 H), 6.34 (d, J = 10.7 Hz, 0.2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.35, 134.73, 133.14, 132.34, 132.32, 131.53, 131.20, 128.90, 128.86, 128.47, 128.33, 127.99, 127.49, 126.24, 125.01, 122.34, 120.95 ppm. HRMS (EI) calc. for [$C_{14}H_{11}BrS$]: 289.9765, found: 289.9762; white solid.

5an: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.43 (m, 2 H), 7.38 – 7.26 (m, 3 H), 7.20 - 7.14 (m, 1 H), 7.11 – 7.05 (m, 1 H), 6.70 – 6.62 (m, 2 H), 6.59 (d, J = 15.5 Hz, 0.11 H), 6.43 (d, J = 10.8 Hz, 0.98 H), 6.27 (d, J = 15.5 Hz, 0.10 H), 6.10 (d, J = 10.8 Hz, 0.97 H), 4.15 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.79, 136.67, 135.34, 130.58, 128.88, 128.70, 128.47, 127.85, 127.12, 126.79, 125.84, 118.80, 117.91, 115.43 ppm. HRMS (EI) calc. for [$C_{14}H_{13}NS$]: 227.0769, found: 227.0767; dark yellow soild.

5ao: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.33 (m, 1 H), 7.32 – 7.26 (m, 3 H), 7.23 – 7.16 (m, 1 H), 6.73 (d, J = 15.6 Hz, 0.76 H), 6.48 (d, J = 15.6 Hz, 0.76 H), 6.44 (d, J = 11.0 Hz, 0.24 H), 6.25 (d, J = 11.0 Hz, 0.24 H), 2.82 – 2.75 (m, 2 H), 1.79 – 1.67 (m, 2 H), 1.05 (t, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.29, 128.75, 128.72, 128.34, 127.82, 126.89, 126.87, 126.69, 125.58, 125.47, 125.38, 38.04, 34.78, 23.70, 22.98, 13.55, 13.34 ppm. HRMS (EI) calc. for [$C_{11}H_{14}S$]: 178.0816, found: 178.0814; pale yellow oil.

5aj: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.24 (m, 1 H), 7.24 – 7.15 (m, 3 H), 7.14 – 7.06 (m, 1 H), 6.65 (d, J = 15.6 Hz, 0.7 H), 6.43 – 6.31 (m, 1 H), 6.16 (d, J = 10.9 Hz, 0.3 H), 2.70 (dd, J = 14.8, 7.3 Hz, 2 H), 1.69 – 1.55 (m, 2 H), 1.39 – 1.18 (m, 4 H), 0.83 (td, J = 7.2, 4.0 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.28, 137.17, 128.72, 128.70, 128.31, 127.82, 126.85, 126.71, 126.65, 125.54, 125.48, 125.31, 36.01, 32.70, 31.10, 30.86, 30.06, 29.26, 22.40, 14.10, 14.08 ppm. HRMS (EI) calc. for [$C_{13}H_{18}S$]: 206.1129, found: 206.1132; pale yellow oil.

5ak: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.23 (m, 1 H), 7.23 – 7.15 (m, 3 H), 7.13 – 7.04 (m, 1 H), 6.64 (d, J = 15.6 Hz, 0.84 H), 6.40 – 6.29 (m, 1 H), 6.15 (d, J = 10.9 Hz, 0.16 H), 2.69 (dd, J = 14.9, 7.4 Hz, 2 H), 1.60 (dt, J = 15.0, 7.3 Hz, 2 H), 1.38 – 1.09 (m, 14 H), 0.80 (t, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.29, 128.71, 128.30, 127.83, 126.84, 126.69, 126.64, 125.54, 125.49, 125.31, 36.04, 32.72, 32.03, 30.38, 29.69, 29.65, 29.57, 29.45, 29.33, 28.95, 28.72, 22.82, 14.26 ppm. HRMS (EI) calc. for [$C_{18}H_{28}S$]: 276.1912, found: 276.1912; yellow oil.

5ap: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.38 (m, 1 H), 7.31 – 7.25 (m, 1 H), 7.19 (dd, J = 13.9, 2.4 Hz, 2 H), 7.16 – 7.06 (m, 1 H), 6.65 (d, J = 15.6 Hz, 0.49 H), 6.43 – 6.30 (m, 1 H), 6.17 (d, J = 10.9 Hz, 0.67 H), 2.71 (dd, J = 14.4, 7.0 Hz, 2

H), 1.61 (dt, J = 15.0, 7.3 Hz, 2 H), 1.56 – 0.97 (m, 18 H), 0.81 (t, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.31, 137.19, 128.74, 128.72, 128.33, 127.84, 126.87, 126.75, 126.67, 125.57, 125.51, 125.34, 36.07, 32.76, 32.07, 30.40, 29.79, 29.78, 29.74, 29.66, 29.65, 29.59, 29.50, 29.34, 28.97, 28.74, 22.84, 14.28 ppm. HRMS (EI) calc. for [$C_{20}H_{32}S$]: 304.2225, found: 304.2226; yellow oil.

5aq: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.23 (m, 1 H), 7.22 – 7.01 (m, 4 H), 6.63 (d, J = 15.6 Hz, 0.85 H), 6.33 (dd, J = 21.2, 13.3 Hz, 1 H), 6.13 (d, J = 10.9 Hz, 0.15 H), 2.70 (dd, J = 6.3, 2.0 Hz, 2 H), 1.52 (td, J = 12.5, 6.3 Hz, 1 H), 1.45 – 1.13 (m, 8 H), 0.82 (tt, J = 8.6, 4.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.36, 128.72, 128.55, 128.31, 126.79, 126.60, 126.32, 126.13, 125.51, 124.99, 40.80, 39.97, 39.28, 39.06, 37.12, 35.58, 32.69, 32.49, 32.22, 28.95, 25.87, 25.71, 25.39, 23.10, 14.22, 10.95 ppm. HRMS (EI) calc. for [$C_{16}H_{24}S$]: 248.1599, found: 248.1601; pale yellow oil.

5pa: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.21 (m, 5 H), 7.18 (d, J = 13.3 Hz, 0.12 H), 6.70 (d, J = 18.3 Hz, 1.12 H), 5.87 (d, J = 18.3 Hz, 1.12 H), 5.80 (d, J = 13.3 Hz, 0.12 H), 1.15 – 1.07 (m, 3 H), 1.07 – 0.98 (m, 18 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.47, 134.90, 130.81, 129.28, 127.25, 124.75, 19.06, 18.73, 12.05, 11.10 ppm. HRMS (EI) calc. for [$C_{17}H_{28}SSi$]: 292.1681, found: 292.1682; colorless oil.

5ar: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.21 (m, 2 H), 7.20 – 7.15 (m, 3 H), 4.66 (t, J = 7.1 Hz, 1 H), 3.23 – 3.08 (m, 4 H), 3.05 (d, J = 7.1 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.22, 129.28, 128.52, 126.96, 55.05, 45.43, 38.71 ppm. HRMS (EI) calc. for [$C_{10}H_{12}S_2$]: 196.0380, found: 196.0379; colorless oil.

2.5. References

(1) Posner, T. *Ber. Dtsch. Chem. Ges*. **1905**, *38*, 646.

(2) (a) Skinner, E. K.; Whiffin, F. M.; Price, G. J. *Chem. Commun*. **2012**, *48*, 6800. (b) Pallela, V. R.; Mallireddigari, M. R.; Cosenza, S. C.; Akula, B.; Subbaiah, D. R. C. V.; Reddy, E. P.; Reddy, M. V. R. *Org. Biomol. Chem*. **2013**, *11*, 1964.

(3) (a) McReynolds, M. D.; Dougherty, J. M.; Hanson, P. R. *Chem. Rev*. **2004**, *104*, 2239. (b) de la Pradilla, R. F.; Tortosa, M.; Viso, A. *Top. Curr. Chem*. **2007**, 275, 103. (c) Kondo, T.; Mitsudo, T. *Chem. Rev*. **2000**, *100*, 3205. (d) Beletskaya, I. P.; Ananikov, V. P. *Chem. Rev*. **2011**, *111*, 1596. (e) Cui, Y.; Floreancig, P. E. *Org. Lett*. **2012**, *14*, 1720.

(4) (a) Zeni, G.; Stracke, M. P.; Nogueira, C. W.; Braga, A. L.; Menezes, P. H.; Stefani, H. A. *Org. Lett.* **2004**, *6*, 1135. (b) Kondoh, A.; Takami, K.; Yorimitsu, H.; Oshima, K. *J. Org. Chem*. **2005**, *70*, 6468. (c) Duan, Z.; Ranjit, S.; Zhang, P.; Liu, X. *Org. Lett*. **2010**, *12*, 2430. (d) Minozzi, M.; Monesi, A.; Nanni, D.; Spagnolo, P.; Marchetti, N.; Massi, A. *J. Org. Chem*. **2011**, *76*, 450.

(5) (a) C. Munro-Leighton, S. A. Delp, N. M. Alsop, E. D. Blue, T. B. Gunnoe, *Chem. Commun*. **2008**, 111. (b) Castarlenas, R.; Di Giuseppe, A.; Pérez-Torrente, J. J.; Oro, L. A. *Angew. Chem. Int. Ed*. **2013**, *52*, 211; *Angew. Chem.* **2013**, *125*, 223. (c) Dondoni, A.; Marra, A. Eur. *J. Org. Chem*. **2014**, 3955.

(6) (a) Fadeyi, O. O.; Mousseau, J. J.; Feng, Y.; Allais, C.; Nuhant, P.; Chen, M. Z.; Pierce, B.; Robinson, R. *Org. Lett*. **2015**, *17*, 5756. (b) Degtyareva, E. S.; Burykina, J. V.; Fakhrutdinov, A. N.; Gordeev, E. G.; Khrustalev, V. N.; Ananikov, V. P. *ACS Catal*. **2015**, *5*, 7208.

(7) Kanagasabapathy, S.; Sudalai, A.; Benicewicz, B. C. *Tetrahedron Lett*. **2001**, *42*, 3791.

(8) (a) Yang, J.; Sabarre, A.; Fraser, L. R.; Patrick, B. O.; Love, J. A. *J. Org. Chem*. **2009**, *74*, 182. (b) Girijavallabhan, V.; Alvarez, C.; Njoroge, F. G. *J. Org.Chem*. **2011**, *76*, 6442.

(9) (a) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; Benjamin, L. *Chem. Rev.* **2007**, *107*, 5471-5569. (b) Shaikh, I. R. *J. Catal.* **2014**, 402860.

(10) (a) Seo, U. R.; Chung, Y. K. *Adv. Synth. Catal*. **2014**, *356*, 1955. (b) Seo, U. R.; Chung, Y. K. *RSC Adv*. **2014**, *4*, 32371. (c) Li, P; Wang, L.; Zhang, Y.; Wang, M. *Tetrahedron Lett*. **2008**, *49*, 6650. (d) Ranganath, K. V. S.; Kloesges, J.; Schäfer, A. H.; Glorius, F. *Angew. Chem. Int. Ed.* **2010**, *49*, 7786.

(11) Chung, J.; Seo, U. R.; Chun, S.; Chung, Y. K. *ChemCatChem* **2016**, *8*, 318.

(12) To measure the turnover number, 10 mmol of styrene and 11 mmol of thiophenol were used, and 27 mg of the catalyst was dissolved in 1 mL of DMSO. 0.01 mL of the catalyst solution was taken from the mother solution using a micro pipet to use in the catalytic reaction.

(13) Cason, L. F.; Wanser, C. C. *J. Am. Chem. Soc*. **1951**, *73*, 142.

(14) Bhadra, S.; Ranu, B. C. *Can. J. Chem*. **2009**, *87*, 1605.

(15) (a) Braslau, R.; Burrill II, L. C.; Siano, M.; Naik, N.; Howden, R. K.; Mahal, L. K. *Macromolecules* **1997**, *30*, 6445. (b) Braslau, R.; Burrill II, L. C.; Mahal, L. K.; Wedeking, T. *Angew. Chem. Int. Ed. Engl*. **1997**, *36*, 237; *Angew. Chem*. **1997**, *109*, 247. (c) C. St. Thomas, H. Maldonado-Textle, A. Rockenbauer, L. Korecz, N. Nagy, R. Guerrero-Santos*, J. Polym. Sci. Part A* **2012**, *50*, 2944.

(16) Zhang, Z. C.; Chung, T. C. M. *Macromolecules* **2006**, *39*, 5187.

(17) (a) Chabriere, E.; Vernede, X.; Guigliarelli, B.; Charon, M. H.; Hatchikian, E. C.; Camps, J. C. F. *Science* **2001**, *294*, 2559. (b) White, N. A.; Rovis, T. *J. Am. Chem. Soc*. **2014**, *136*, 14674. (c) Du, Y.; Wang, Y.; Li, X.; Shao, Y.; Li, G.; Webster, R. D.; Chi, Y. R. *Org. Lett*. **2014**, *16*, 5678. (d) Zhang, Y.; Du, Y.; Huang, Z.; Xu, J.; Wu, X.; Wang, Y.; Wang, M.; Yang, S.; Webster, R. D.; Chi, Y. R. *J. Am. Chem. Soc*. **2015**, *137*, 2416.

(18) (a) Jin, Z.; Xu, B.; Hammond, G. B. *Eur. J. Org. Chem*. **2010**, 168. (b) Postigo, A. *RSC Adv*. **2011**, *1*, 14. (c) Liu, K.; Jia, F.; Xi, H.; Li, Y.; Zheng, X.; Guo, Q.; Shen, B.; Li, Z. *Org. Lett*. **2013**, *15*, 2026.

Chapter 3. Synthesis of Benzothiazoles from 2-Aminobenzenethiols in the Presence of a Reusable Polythiazolium Precatalyst under Atmospheric Pressure of Carbon Dioxide

3.1. Introduction

A report on the separation of stable carbene by Bertrand[1] and Arduengo[2] had stimulated widespread interest in properties and reactivity of carbenes. N-heterocyclic carbenes (NHCs) have a strong electron donating power and are widely used owing to their high stability and outstanding application in homogeneous catalyst.[3] It can be used as a ligand and can also serve as organocatalyst. Despite these advantages, however, most can only be used once in a homogeneous reaction. They cannot be easily separated from the reaction system and cannot be reused, resulting in waste of expensive transition metals as well as problems of solution contamination. In order to overcome the problem, we were able to introduce a poly(NHC) using the synthesized polymer, poly(3,4-dimethyl-5-vinylthiazolium) iodide, as precatalyst.

Carbon dioxide (CO_2) is an abundant resource and an easily accessible C1 building block. However, due to its stability and inertness, rendering CO_2 to

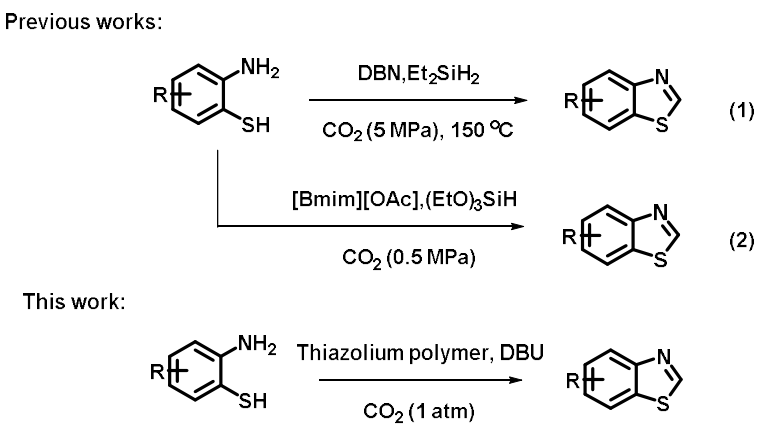
participate in chemical reactions is quite challenging.[4] Although there are several ways to activate CO_2, they usually require harsh reaction conditions such as high pressure and temperature. Thus, finding a new route to employ this compound in a chemical reaction under mild conditions would be necessary.

Recently, there has been a growing interest in the use of NHCs in CO_2 activation. Since 1999, a number of works related to the use of imidazolium derived NHCs in CO_2 activation have been reported.[5] The use of polymeric NHCs in CO_2 fixation was also published.[6] In 2009, Lu et al. developed an imidazolium polymer-based CO_2 adsorbent under mild conditions.[7] Our group also reported the use of poly(4-vinylimidazolium) iodide as a recyclable organocatalyst for the synthesis of cyclic carbonates from epoxides.[8] In 2016, Dyson et al. reported N-formylation of amines catalyzed by thiazolium carbene (CO_2 at atmospheric pressure).[9] However, few studies using thiazolium derived NHCs in organic synthesis have been reported to date. Therefore, it would be very interesting to develop a new reaction with carbon dioxide using thiazolium-derived NHCs as the precatalyst.

Benzothiazoles have diverse biological properties that are useful in pharmaceutical industries.[10] Considering their importance, it would be meaningful to develop a simple synthetic method. Numerous approaches are available for the synthesis of benzothiazoles starting from 2-aminobenzenethiols. These include a copper-catalyzed condensation reaction of 2-aminobenzenethiols with nitriles[11] or a reaction with β-diketone.[12] However, few works using 1 atm of CO_2 as a C1 source in the synthesis of benzothiazole exist to date (Scheme 3.1).

In 2014, Liu et al. synthesized benzothiazoles from 2-aminobenzenethiol using silane as a CO_2 fixing agent.[13] However, the harsh reaction conditions (5 MPa and

150 ºC) and limited substrate scope diminished the synthetic utility in practical application (eq 1). In 2015, they also published the synthesis of benzothiazole under 0.5 MPa of carbon dioxide and triethoxysilane at 60 ºC, employing imidazolium-based ionic liquids as a catalyst (eq 2).[14] However, this procedure still required a special reactor and a stoichiometric amount of catalyst. Our interest in the use of thiazolium-based catalysis prompted us to investigate the use of thiazolium-based NHCs as a catalyst in the formation of benzothiazoles from 2-aminobenzenethiols and carbon dioxide. Therefore, we studied and found that we could use poly(3,4-dimethyl-5-vinylthiazolium) iodide as a precatalyst and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base in the synthesis of benzothiazoles from 2-aminobenzenethiols and atmospheric pressure of carbon dioxide.

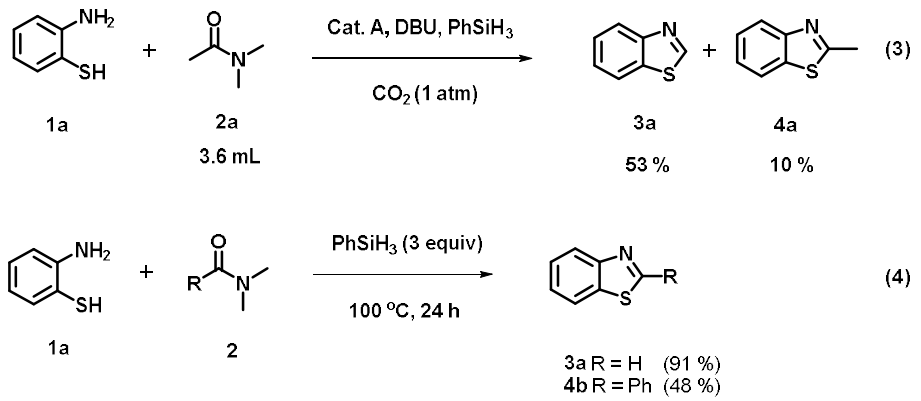


Scheme 3.1. Synthesis of benzothiazole using carbon dioxide as a building block.

3.2. Results and Discussion

The results from the synthesis of benzothiazole under various conditions, using 2-aminobenzenethiol as a model substrate, are listed in Table 3.1. Referring to the

above mentioned previous works, 3,4-dimethyl-5-vinylthiazolium iodide **A**, DBU, and $PhSiH_3$ were used as a catalytic system. We envisioned that Cat. **A** and phenylsilane acted as a CO_2 fixing agent and a hydride donor, respectively. All the reactions were conducted under 1atm of carbon dioxide (using a CO_2 balloon). When the reaction was conducted in DMF, benzothiazole was isolated in 71 % yield. In N,N-dimethylacetamide (DMA), the reaction afforded the product and 2-methylbenzothiazole in 53 % and 10 % yields, respectively (eq 3). However, without **A** and DBU, benzothiazoles, **3a** and **4b**, were isolated in 91% and 48% yields, respectively (eq 4).



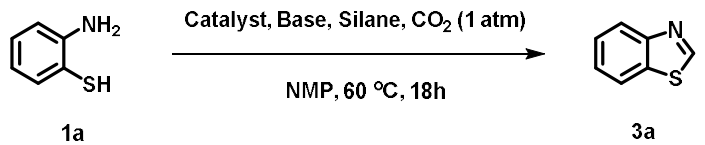
Scheme 3.2. Reaction of 2-aminothiophenol with phenylsilane in the presence/absence of Cat. **A** and DBU

This observation suggested that the amidic solvents reacted with 2-aminobenzenethiol in the presence of phenylsilane to afford benzothiazoles. Thus, the use of amidic solvent was thought to diminish the efficiency of the formation of a specific benzothiazole. However, no such problem was expected when a cyclic amide, N-methyl-2-pyrrolidone (NMP), was used as the solvent. As expected, the

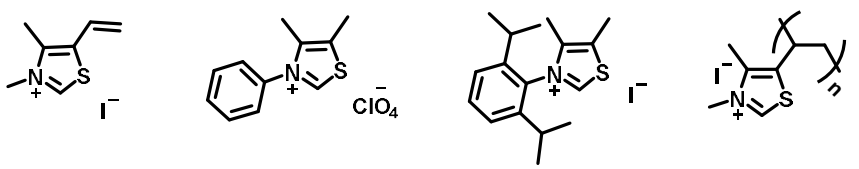
use of NMP as a reaction medium afforded a higher yield (61 %, entry 1). Thus, NMP was chosen as the reaction solvent. When the reaction was carried out in the absence of **A**, benzothiazole was isolated in low yield (44 %, entry 2). We next screened different reaction conditions. Raising the temperature from 50 to 60 ºC improved the yield slightly (71 %, entry 3). When other hydrosilanes such as Ph_2SiH_2, $(EtO)_3SiH$, and Et_2SiH_2 were screened, only a trace amount of benzothiazole was detected (entries 4–6, respectively), implying the superiority of phenylsilane in the proposed reaction system. Other thiazolium compounds, 4,5-dimethyl-3-phenylthiazolium perchlorate **B**, 3-(2,6-diisopropylphenyl)-4,5-dimethylthiazolium iodide **C**, and poly(3,4-dimethyl-5-vinylthiazolium) iodide **D**, bearing different substituents and counteranions, were screened as precatalysts (entries 7–9, respectively).[15] Thiazolium catalyst **B** exhibited activity comparable to that of **A**. Conversely, **C,** with a sterically bulky substituent, only afforded a trace amount of the product. This indicated that the reaction was highly sensitive to the steric bulkiness of the substituent on the phenyl ring of the thiazolium based NHCs. Interestingly, higher yields were observed in polymeric thiazolium catalyst **D** (75 %, entry 9) than **A**. It was also expected to be reusable as a polymer catalyst. Therefore, using **D** as the precatalyst, we next screened different reaction conditions. Increasing the reaction temperature did not improve the yield (65 %, entry 10). Conversely, reducing the amount (2 equiv) of phenylsilane significantly decreased the yield (entry 11), indicating the importance of the role of hydrosilane. Other organic and inorganic bases such as triethylamine and potassium carbonate did not prove to be as efficient as DBU (entries 12 and 13). The yield was highly sensitive to the reaction time. Shortening the reaction time from 18 to 15 h led to a remarkable decrease in yield (59 %, entry 14). The best GC yield (90 %; 76 % isolated yield, entry 15) was observed in the presence of **D** (9 mol%). From these

results, the optimum conditions were established as follows: 0.5 mmol of 2-aminobenzenethiol, 9–10 mol% **D**, 3 equiv of phenylsilane, 9–10 mol% DBU, 3.6 mL of NMP, 1 atm CO_2, at 60 ºC, for 18 h.

Table 3.1. Optimization of the reaction conditions[a]



1a 3a



A B C D

Entry	Catalyst	Base	Silane	Temp (ºC)	Yield (%)[b]
1	A	DBU	$PhSiH_3$	50	61
2		DBU	$PhSiH_3$	50	44
3	A	DBU	$PhSiH_3$	60	71
4	A	DBU	Ph_2SiH_2	60	Trace[c]
5	A	DBU	$(EtO)_3SiH$	60	Trace[c]
6	A	DBU	Et_2SiH_2	60	Trace[c]
7	B	DBU	$PhSiH_3$	50	63
8	C	DBU	$PhSiH_3$	50	Trace[c]

9	D	DBU	$PhSiH_3$	60	75
10	D	DBU	$PhSiH_3$	70	65
11	D	DBU	$PhSiH_3$	60	34
12	D	K_2CO_3	$PhSiH_3$	60	66
13	D	Et_3N	$PhSiH_3$	60	Tracec
14[e]	D	DBU	$PhSiH_3$	60	59
15[f]	D	DBU	$PhSiH_3$	60	76 (90[c])

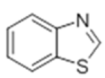
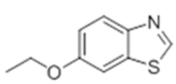
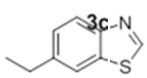
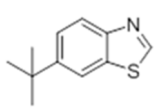
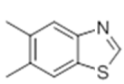
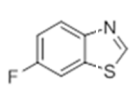
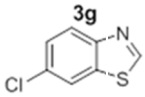
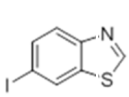
[a]Reaction conditions: 2-aminobenzenethiol (0.5 mmol), hydrosilane (1.5 mmol), catalyst (10 mol%), base (10 mol%), CO_2 (1 atm), N-methyl-2-pyrrilidone (3.6 mL), 18 h. [b]Isolated yields. [c]Yields determined by gas chromatography using mesitylene as an internal standard. [d]1 mmol of $PhSiH_3$. [e]15 h [f]9 mol% of catalyst and 9 mol% of base used.

With the optimized reaction conditions in hand, other benzothiazoles bearing different substituents were tested (Table 3.2). All the substrates listed afforded the corresponding benzothiazoles, under the standard conditions, in moderate to good yield. Reactions were held at 60 or 70 ºC depending on the substrate used. However, temperatures >70 ºC reduced the yield. The correlation between the electronic effect of the substrate and the yield was not clear. Reactions with substrates containing an alkoxy (methoxy or ethoxy) group proceeded well, affording alkoxybenzothiazole in good yield (entries 2 and 3). Moreover, 2-amino-5-methylbenzenethiol and 2-amino-5-ethylbenzothiazole afforded moderate yields (entries 4 and 5, respectively). However, the reaction was sluggish when 2-amino-

5-tert-butylbenzenethiol was employed (entry 6). In the case of 2-aminobenzenethiols with electron-withdrawing substrates, 2-amino-5-chlorobenzenethiol afforded the product in good yield (entry 9). Moreover, a trifluoromethoxy group was tolerable (entry 12). Fluoro, bromo, and iodo substituents exhibited an increase in yield when the temperature was raised from 60 to 70 ºC (entries 8, 10–11, respectively). Contrary to the substrates bearing functional groups at the C5 position, the reactions with substrates on the C3 position were relatively sluggish (entries 2 vs 13; 4 vs 14, respectively).[16] 4-Methoxybenzothiazole and 4-methylbenzothiazole were isolated in 33 %, and 54 % yield, respctively (entries 13 and 14).

This result may be attributed to steric effects. To our surprise, 3-substituted-2-aminobenzenethiols have not been used as substrates in the synthesis of 4-substituted benzothiazoles. Thus, these are the first example of the use of 3-substituted-2-aminobenzenethiols in the synthesis of 4-substituted benzothiazoles, although the yields were not high. Some additional factors were thought to affect the yield difference in the 3- or 5- methoxy substituent group. In order to interpret these experimental data, the electron densities of the two substrates were investigated by density functional theory calculations. The outcome was similar, but we discovered that the distance between the oxygen atom and the proton of the amino group was close, indicating the presence of hydrogen bonding. This hydrogen bonding is thought to stabilize 2-amino-3-methoxybenzenethiol, making it less likely to participate in the reaction.

Table 3.2. Substrate scope of benzothiazoles[a]

Entry	Product	Yield[b]	Entry	Product	Yield[b]
1	 **3a**	76 (90 [c, e])	2		73[c]
3	 **3c**	84 [c]	4		63
5	 **3e**	60	6	 **3f**	34
7	 **3g**	53	8	 **3h**	62
9	 **3i**	72[c]	10		62
11	 **3k**	66	12		73[d]
13		33	14		54

[a]Reaction conditions: 2-aminobenzenethiol (0.5 mmol), phenylsilane (1.5 mmol), Cat. D (9 mol%), DBU (9 mol%), CO_2 (1 atm), N-methyl-2-pyrrolidone (3.6 mL), 70 ^oC, 24 h. [b]Isolated yields. [c]60 ^oC and 18 h. [d]30 h. [e]Yields determined by gas chromatography using mesitylene as an internal standard

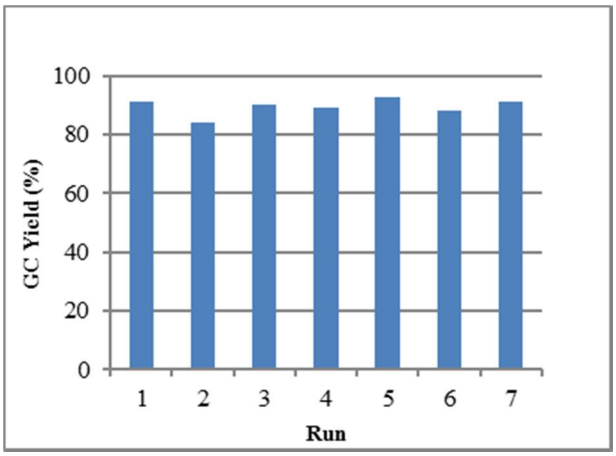


Figure 3.1. Reuse of poly(vinylthiazolium) iodide in the cyclization of 2-aminobenzenethiol to benzothiazole

Reusability of the thiazolium polymer was tested using 12 mol% of catalyst loading. The recovery of the precatalyst was successful achieved by adding excess hydroiodic acid. When methanol was added after eliminating the solvent, the precatalyst was precipitated. The recovered polymer precatalyst could be reused for 7 times without losing its activity (Figure 3.1, 84–93 % yields).

Based on these experimental results and previous studies, a possible reaction mechanism is proposed in Figure 3.2.[17] First, a free carbene generated by DBU

binds to carbon dioxide. This adduct reacts with phenylsilane to form an intermediate **I**. Then, the amino group of the substrate reacts with **I** to produce intermediate **II**. The thiol group on **II** condenses with the carbonyl group to form a heterocycle and a subsequent dehydration leads to the benzothiazole. In order to confirm the formation of intermediate **I**, a reaction was carried out without 2-aminothiophenol. ^{1}H NMR and ^{13}C NMR data of the reaction mixture showed the existence of **I** (See SI).[28]

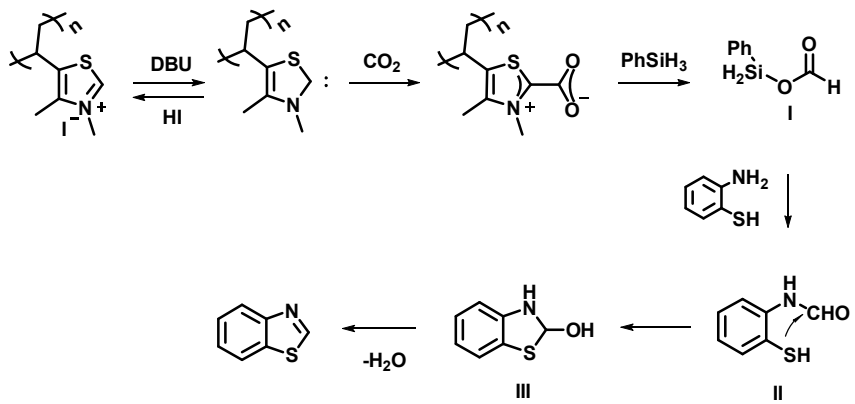


Figure 3.2. Plausible reaction mechanism of benzothiazole synthesis

3.3. Conclusion

We have developed a polythiazolium-based organocatalytic system that displays high catalytic activities in the cyclization of 2-aminobenzenethiol to benzothiazole in the presence of DBU and atmospheric pressure of carbon dioxide. The scope of the reaction is broad and its conditions are mild. Moreover, due to the feasibility of organocatalytic system **D** from commercially available A in one step, mild reaction conditions, and a simple purification procedure, together with the reusability of **D**, this method shows great potential for practical use in the synthesis of benzothiazoles from 2-aminobenzenethiols.

3.4. Experimental Section

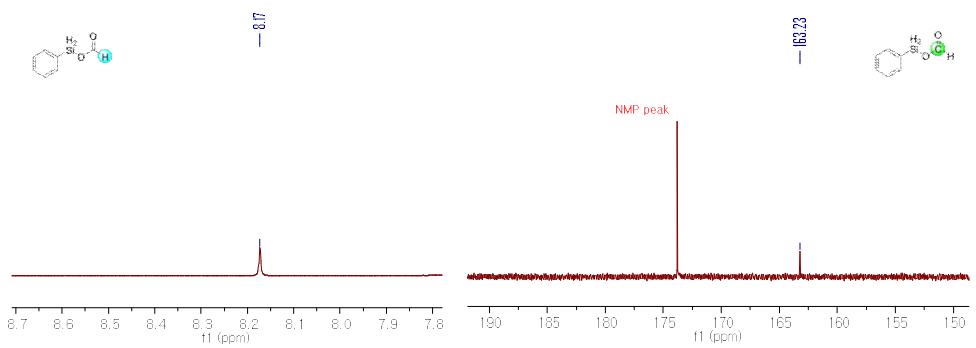
General Remarks

n-Hexanes and ethyl acetate were used without further purification. Other solvents were obtained by passing through activated alumina columns of solvent purification systems from Glass Contour. Reagents were purchased from Sigma-Aldrich, Alfa Aesar, Acros, and TCI and were used as received. N-methyl-2-pyrrolidone was used as a solvent. Reactions were carried out in a glassware equipped with a stirring under carbon dioxide conditions, unless otherwise indicated. Elevated temperatures were maintained in thermostat-controlled oil baths. The TLC plate was carried out on 0.25 mm E. Merck silica gel plates (60F-254) visualized by UV-light (254 nm) and treatment with acidic p-anisaldehyde and $KMnO_4$ stain followed by gentle heating. Workup procedures were done in air. Flash chromatography was carried out on Merck 60 silica gel (230 – 400 mesh). ^{1}H and ^{13}C NMR spectra were recorded with Varian spectrometer (400 MHz) spectrometer. 1H NMR spectra were referenced to residual TMS (0 ppm) and reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dt = doublets of triplets, td = triplet of doublets, qd = quartet of doublets, br s = broad singlet, m = multiplet). Chemical shifts of the ^{13}C NMR spectra were measured relative to $CDCl_3$ (77.16 ppm). Mass spectral data were obtained from the Korea Basic Science Institute (Daegu) on a Jeol JMS 700 high resolution mass spectrometer.

General procedure for the synthesis of benzothiazole derivatives

A tube-type Schlenk flask was charged with 0.045 mmol of catalyst **D**, 0.045 mmol of 1,8-diazabicyclo[5.4.0]undec-7-ene (7 μL), and 1 mL of N-methylpyrrolidone. The solution was stirred under nitrogen atmosphere at 60–70 °C for 30 minutes. And, 2 mL of N-methylpyrrolidone was added, followed by addition of a balloon charged with carbon dioxide gas. The solution was stirred at 60-70 °C for 30 minutes. Then, 2-aminobenzenethiol derivatives (0.5 mmol), phenylsilane (1.5 mmol) dissolved in 0.5 mL of N-methylpyrrolidone was added to the mixture. Reaction was carried out at 60–70 ºC for 18-30 hours. After the solution was cooled to room temperature, purification by flash chromatography on silica gel with n-hexane and ethyl acetate afforded benzothiazole derivatives. The products were characterized by ^{1}H NMR, ^{13}C NMR, and HRMS.

^{1}H NMR and ^{13}C NMR spectral data of Intermediate I



SI Figure 3.1. ^{1}H NMR spectral (left) and ^{13}C NMR spectral (right) of a reactionmixture of CO_2, $PhSiH_3$, Catalyst, DBU, and NMP (DMSO-d_6, 298 K)

Characterization of compounds

3a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.14 (d, J = 8.1 Hz, 1H), 7.94 (d, J = 7.9 Hz, 1H), 7.51 (t, J = 7.7 Hz, 1H), 7.42 (t, J = 7.5 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.96, 153.30, 133.76, 126.21, 125.59, 123.69, 121.94 ppm. HRMS (EI) calc. for [C_7H_5NS]: 135.0143, found: 135.0141; pale yellow oil.

3b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.94 (d, J = 9.0 Hz, 1H), 7.32 (d, J = 2.5 Hz, 1H), 7.05 (dd, J = 9.0, 2.5 Hz, 1H), 3.82 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.14, 151.53, 147.98, 135.23, 124.13, 115.97, 104.11, 55.92 ppm. HRMS (EI) calc. for [C_8H_7NOS]: 165.0248, found: 165.0250; pale yellow solid; MP 70 ºC.

3c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.99 (d, J = 8.9 Hz, 1H), 7.36 (d, J = 1.8 Hz, 1H), 7.10 (dd, J = 8.9, 2.0 Hz, 1H), 4.08 (q, J = 7.0 Hz, 2H), 1.45 (t, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.47, 151.38, 147.87, 135.18, 124.07, 116.33, 104.81, 64.21, 14.92 ppm. HRMS (EI) calc. for [C_9H_9NOS]: 179.0405, found: 179.0403; yellow oil.

3d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.94 (d, J = 8.3 Hz, 1H), 7.67 (s, 1H), 7.25 (d, J = 8.3 Hz, 1H), 2.43 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.97, 151.54, 135.82, 134.01, 127.96, 123.18, 121.66, 21.65 ppm. HRMS (EI) calc. for [C_8H_7NS]: 149.0299, found: 149.0302; yellow oil.

3e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.77 (s, 1H), 7.36 (d, J = 8.4 Hz, 1H), 2.80 (q, J = 7.6 Hz, 2H), 1.31 (t, J = 7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.08, 151.70, 142.24, 134.05, 126.92, 123.32, 120.46, 29.05, 15.97 ppm. HRMS (EI) calc. for [C_9H_9NS]: 163.0456, found: 163.0456; pale yellow oil.

3f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.06 (d, J = 8.7 Hz, 1H), 7.95 (s, 1H), 7.59 (dd, J = 8.6, 1.5 Hz, 1H), 1.41 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.40, 151.36, 149.20, 133.92, 124.61, 123.01, 117.96, 35.22, 31.71 ppm. HRMS (EI) calc. for [$C_{11}H_{13}NS$]: 191.0769, found: 191.0766; yellow oil.

3g: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 7.90 (s, 1H), 7.70 (s, 1H), 2.42 (s, 3H), 2.40 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.90, 152.22, 135.62, 135.23, 131.24, 123.77, 121.80, 20.36, 20.34 ppm. HRMS (EI) calc. for [C_9H_9NS]: 163.0456, found: 163.0454; white solid; MP 108 ºC.

3h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.01 (dd, J = 9.0, 4.8 Hz, 1H), 7.59 – 7.55 (m, 1H), 7.23 – 7.16 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.89 (d, J = 246.1 Hz), 153.71 (d, J = 2.5 Hz), 150.07, 133.65 (d, J = 265.6 Hz), 124.70 (d, J = 9.4 Hz), 115.18 (d, J = 25.0 Hz), 108.07 (d, J = 26.0 Hz) ppm. HRMS (EI) calc. for [C_7H_4FNS]: 153.0048, found: 153.0046; white solid; MP 58 ºC.

3i: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.04 (d, J = 8.7 Hz, 1H), 7.94 (d, J = 1.7 Hz, 1H), 7.48 (dd, J = 8.7, 2.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.43, 151.97, 135.10, 131.81, 127.21, 124.50, 121.61 ppm. HRMS (EI) calc. for [C_7H_4ClNS]: 168.9753, found: 168.9752; pale yellow solid; MP 42 ºC.

3j: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.03 (d, J = 1.7 Hz, 1H), 7.92 (d, J = 8.7 Hz, 1H), 7.57 – 7.53 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.45, 152.29, 135.59, 129.89, 124.87, 124.57, 119.50 ppm. HRMS (EI) calc. for [C_7H_4BrNS]: 212.9248, found: 212.9248; white solid; MP 55 ºC.

3k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.30 (d, J = 0.9 Hz, 1H), 7.87 (d, J = 8.6 Hz, 1H), 7.80 (dd, J = 8.6, 1.1 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ

154.41, 152.79, 136.03, 135.45, 130.56, 125.23, 90.31 ppm. HRMS (EI) calc. for [C_7H_4INS]: 260.9109, found: 260.9107; white solid; MP 81 ºC.

3l: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.14 (d, J = 8.9 Hz, 1H), 7.83 (s, 1H), 7.40 (d, J = 8.9 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.14, 151.88, 146.99 (d, J = 2.1 Hz), 134.78, 124.63, 120.65 (d, J = 257.8 Hz), 120.36, 114.49 (d, J = 0.5 Hz) ppm. HRMS (EI) calc. for [$C_8H_4F_3NOS$]: 218.9966, found: 218.9963; colorless oil.

3m: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 7.52 (d, J = 8.1 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 6.93 (d, J = 7.9 Hz, 1H), 4.06 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.05, 152.43, 143.74, 135.65, 126.70, 113.87, 106.57, 56.11 ppm. HRMS (EI) calc. for [C_8H_7NOS]: 165.0248, found: 165.0249; white solid; MP 104 ºC.

3n: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H), 7.80 (d, J = 7.0 Hz, 1H), 7.37 – 7.31 (m, 2H), 2.80 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.86, 152.71, 133.72, 133.62, 126.81, 125.62, 119.45, 18.53 ppm. HRMS (EI) calc. for [C_8H_7NS]: 149.0299, found: 149.0297; yellow oil.

3.5. References

(1) Bourissou, D.; Guerret, O.; Gabba1, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39.

(2) A historical review: Arduengo, A. J., III; Krafczyk, R. *Chem. Unserer Zeit*. **1998**, *32*, 6.

(3) (a) Darensbourg, D. J.; Holtcamp, M. W. *Coord. Chem. Rev.* **1996**, *153*, 155. (b) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606. (c) Marion, N.; Díez-González, S.; Nolan, S. P. *Angw. Chem., Int. Ed.* **2007**, *46*, 2988. (d) Hopkinson, M. N.; Richter, C.; Schedler, M.; Glorius, F. *Nature.* **2014**, *510*, 485.

(4) Leitner, W. *Angw. Chem., Int. Ed. Engl.* **1995**, *34*, 2207.

(5) Yang, L.; Wang, H. *ChemSusChem*. **2014**, *7*, 962.

(6) Pinaud, J.; Vignolle, J.; Gnanou, Y.; Taton, D. *Macromolecules*. **2011**, *44*, 1900.

(7) Zhou, H.; Zhang, W.-Z.; Wang, Y.-M.; Qu, J.-P.; Lu, X.-B. *Macromolecules*. **2009**, *42*, 5419.

(8) Seo, U. R.; Chung, Y. K. *Adv. Synth. Catal.* **2014**, *356*, 1955.

(9) Das, S.; Bobbink, F. D.; Bulut, S.; Soudani, M.; Dyson, P. J. *Chem. Commun.* **2016**. *52*, 2497.

(10) Raju, G. N. *J. Chem. Pharm. Res.* **2015**, *7*, 286.

(11) Sun, Y.; Jiang, H.; Wu, W.; Zeng, W.; Wu, X. *Org.Lett.* **2013**, *15*, 1598.

(12) Mayo, M. S.; Yu, X.; Zhou, X.; Feng, X.; Yamamoto, Y.; Bao, M. *Org. Lett.* **2014**, *16*, 764.

(13) Gao, X.; Yu, B.; Zhao, Y.; Hao, L.; Liu, Z. *RSC Adv.* **2014**, *4*, 56957.

(14) Gao, X.; Yu, B.; Yang, Z.; Zhao, Y.; Zhang, H.; Hao, L.; Han, B.; Liu, Z. *ACS Catal.* **2015**, *5*, 6648.

(15) Piel, I.; Pawelczyk, M. D.; Hirano, K.; Fröhlich, R.; Glorius, F. *Eur. J. Org. Chem.* **2011**, *28*, 5475.

(16) Gao, X.; Yu, B.; Mei, Q.; Yang, Z.; Zhao, Y.; Zhang, H.; Hao, L.; Liu, Z. *New J. Chem.* **2016**, *40*, 8282.

(17) Hao, L.; Zhao, Y.; Yu, B.; Yang, Z.; Zhang, H.; Han, B.; Gao. X.; Liu, Z. *ACS Catal.* **2015**, *5*, 4989.

(18) (a) Mukherjee, D.; Sauer, D. F.; Zanardi, A.; Okuda, J. *Chem. Eur. J.* **2016**, *22*, 7730. (b) Zhang, S.; Mei, Q.; Liu, H.; Zhang, Z.; Han, B. *RSC Adv.* **2016**, *6*, 32370.

Chapter 4. Transition Metal-Free Poly(thiazolium) Iodide/1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU)/Phenazine Catalyzed Esterification of Aldehydes with Alcohols

4.1. Introduction

In Chapter 3, we showed that poly(NHC) displayed high catalytic activities in the cyclization of 2-aminobenzenethiol to benzothiazole catalyzed activity and showed good results in terms of reusability. These polymeric catalysts were successfully recovered and reused several times without any decrease in performance. As such, we sought to expand the applications of the poly(thiazolium)iodide/base/phenazine system in the esterification of aldehydes with alcohols.

Esters are ubiquitous motifs in natural products and pharmaceuticals. They are also used as building blocks and protecting groups in the synthesis of many biologically active compounds.[1] Thus, the synthesis of esters has garnered

considerable attention and many useful methods have been established.[2] Among them, the direct transformation of aldehydes with alcohols to esters (oxidative esterification) is attractive in terms of atom-economy.[3] Extensive efforts have been put forth to identify efficient and practical methods for oxidative esterification, and several viable methods have been reported.[4] Air was used as a clean oxidant in some transition metal catalyzed oxidative esterification reactions.[5] Nevertheless, many reported methods involve harsh reaction conditions, have limited substrate scopes, and require transition metal catalysts that are difficult to prepare. Such requirements restrict the utility of these methods. Thus, metal-free catalysts have garnered considerable interest.

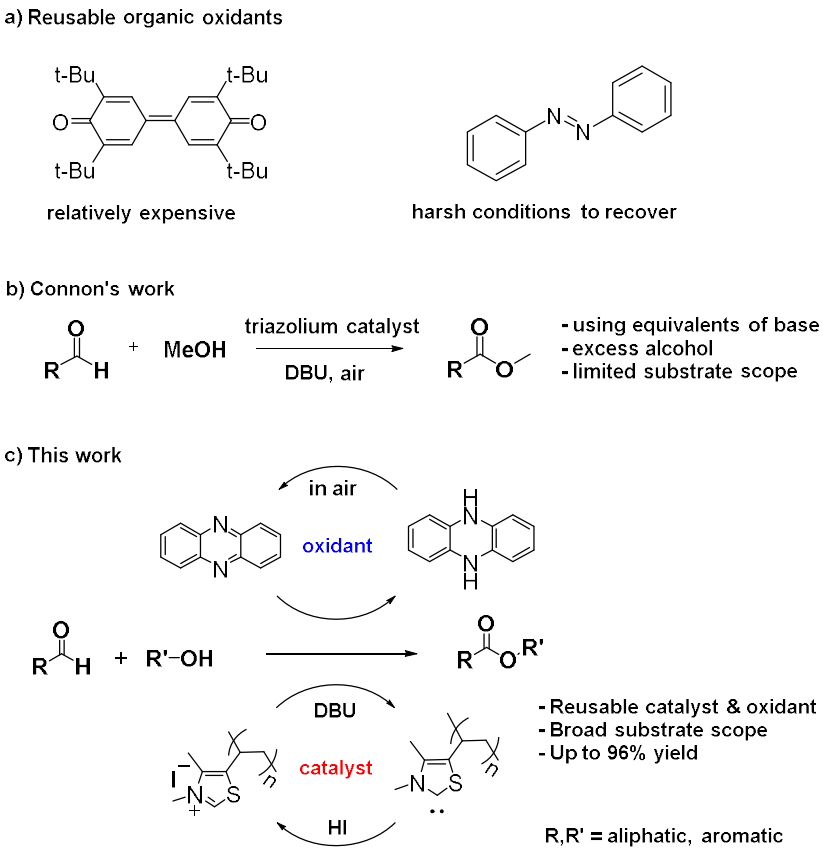
Recently, N-heterocyclic carbene (NHC)-catalyzed redox esterification of aldehydes with alcohols has emerged as a powerful strategy for the formation of esters.[6] Examples of metal-free NHC-catalyzed[7] and NHC transition metal-catalyzed[5,8] esterifications have been reported. However, the use of stoichiometric amounts of oxidants is required in NHC-catalyzed reactions. Several years ago, Studer et al. had reported[7f] an oxidative esterification using 1,3-dimethyltriazolium iodide as a precatalyst in the presence of DBU and 3,3',5,5'-tert-butyldiphenoqinone. However, the catalytic system utilized an expensive quinone as the oxidant although it was readily recovered by oxidation in air (Scheme 4.1a).

In 2011, Zeitler et al. also reported[7h] an oxidative lactonization using a thiazolium precatalyst with azobenzene as the oxidant, but the oxidant recovery process required harsh conditions and the reaction was only applicable to intramolecular esterification (Scheme 4.1a). In 2013, Connon et al. reported[6d] an oxidative esterification in the presence of a triazolium precatalyst and excess base (DBU, 110 mol %) in air, albeit with limited substrate scope (Scheme 4.1b). Despite these

important advances, significant challenges remain for the synthesis of esters under atom-economic, eco-friendly, and mild reaction conditions from readily available materials in the presence of a reusable catalyst.[9,10]

In this chapter, we will discuss a highly efficient method for the oxidative esterification of aldehydes with alcohols, which employs a polymer-based organocatalyst, poly(3,4-dimethyl-5-vinylthiazolium) iodide, as the precatalyst and phenazine as the reusable external oxidant (Scheme 4.1c). A simple, efficient, ligand-free, transition-metal-free, high-yielding, direct esterification of aldehydes and alcohols in the presence of a reusable poly(thiazolium) precatalyst and DBU was thus developed in this study.

Scheme 4.1. Examples of reusable organic oxidants and NHC- catalyzed esterification reactions[6,7]

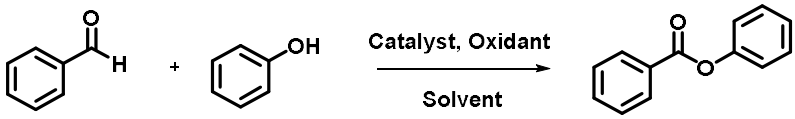


4.2. Results and Discussion

As a model reaction, we initially examined the reaction of benzaldehyde with phenol (a weak nucleophile) in the presence of the thiazolium polymer precatalyst (5 mol %), phenazine (1.2 equiv), and DBU (10 mol %) in DMSO at room temperature for 18 h (Table 4.1). The initial reaction conditions were adopted from a previous study.[12a] After the reaction, the expected ester was isolated in 70% yield (entry 1). The amount of catalyst influenced the yield of the reaction (entries 1-3). The yield of the reaction was slightly dependent on the reaction temperature (the yield at 25 °C (entry 2) and 40 °C (entry 4) were 77% and 88%, respectively). The

use of oxidants such as phenazine, azobenzene, and benzoquinone afforded the corresponding esters in 88%, 85%, and 8% yields, respectively (entries 4-6). Changing the reaction solvent from DMSO to acetone and DMF gave the corresponding esters in 15% and 78% yields, respectively (entries 7 and 8, respectively). Increasing the amount of phenol led to no noticeable change in the yield (entry 10). However, when 1.2 equiv of the aldehyde was used, the best yield (93%) was observed (entry 11). When the amount of oxidant (phenazine) was decreased to 0.6 equiv, the desired product was obtained in 53% yield (entry 12). No reaction was observed in the absence of a catalyst or phenazine. When a monomer ((3,4-dimethyl-5-vinylthiazolium) iodide) was used as the precatalyst instead of the polymer precatalyst, the product was isolated in 78% yield (entry 13). The optimum reaction conditions were as follows: 7 mol % precatalyst, 14 mol % DBU, 1.2 equiv phenazine, 1.0 mL DMSO at 40 °C for 18 h.

Table 4.1. Screening of esterification reaction of benzaldehyde with phenol[a]

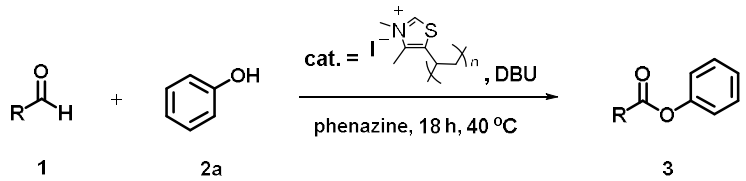


1a 2a 3a

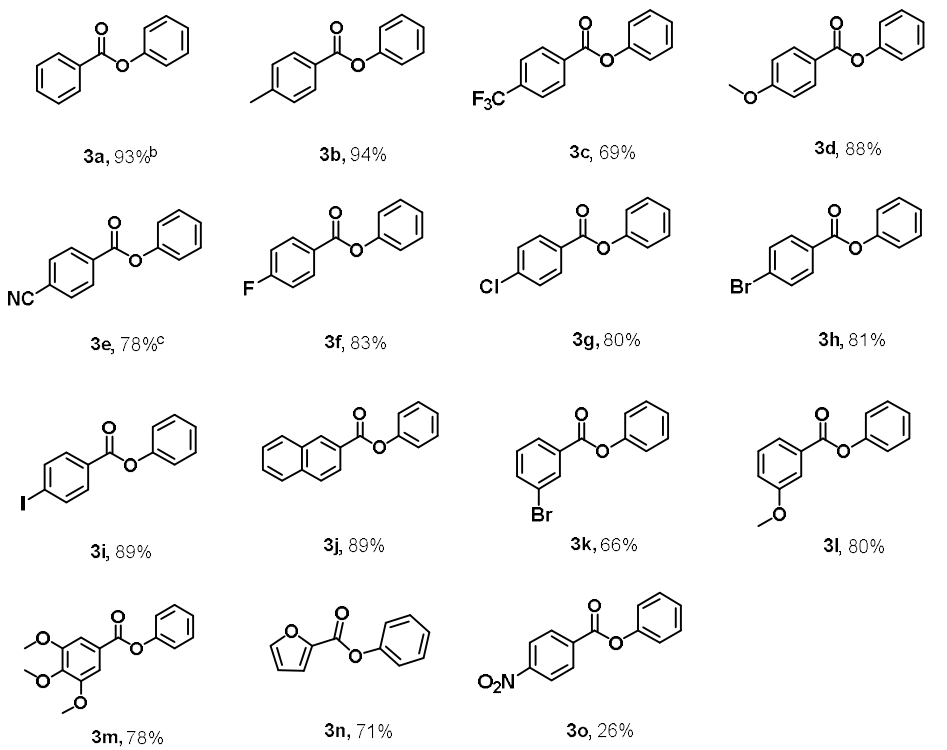
Entry	Oxidant	Solvent[b]	Catalyst (mol%)	Temp (°C)	Yield[c] (%)
1	Phenazine	DMSO	5	25	70
2	Phenazine	DMSO	7	25	77
3	Phenazine	DMSO	10	25	75
4	Phenazine	DMSO	7	40	88
5	Phenazine	DMSO	7	40	85
6	Benzoquinone	DMSO	7	40	8
7	Phenazine	Acetone	7	40	15
8	Phenazine	DMF	7	40	78
9	Phenazine	DMSO	7	60	85
10[d]	Phenazine	DMSO	7	40	83
11[e]	Phenazine	DMSO	7	40	93
12	Phenazine[f]	DMSO	7	40	53
13[g]	Phenazine	DMSO	7	40	78

[a]Conditions: benzaldehyde (0.5 mmol), phenol (0.6 mmol), DBU (2 equiv of catalyst), oxidant (0.6 mmol), 18 h, catalyst = poly(3,4-dimethyl-5-vinylthiazolium) iodide. [b]1 mL used. [c]Isolated yield. [d]Phenol (1 mmol) used. [e]Benzaldehyde (0.6 mmol), phenol (0.5 mmol) used. [f]0.3 mmol used [g]3,4-Dimethyl-5-vinylthiazolium iodide used as a catalyst.

Scheme 4.2. Esterification reactions of phenol with aromatic aldehydes[a]



1 2a 3



3a, 93%[b] **3b**, 94% **3c**, 69% **3d**, 88%

3e, 78%[c] **3f**, 83% **3g**, 80% **3h**, 81%

3i, 89% **3j**, 89% **3k**, 66% **3l**, 80%

3m, 78% **3n**, 71% **3o**, 26%

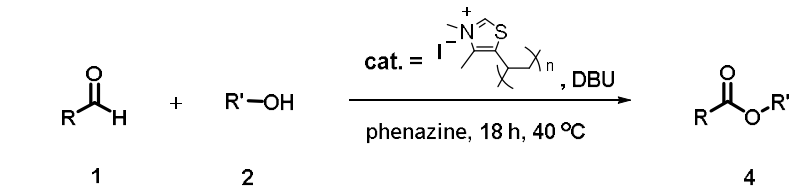
[a]Conditions: aldehyde (0.6 mmol), phenol (0.5 mmol), cat. (7 mol %), DBU (14 mol %), phenazine (0.6 mmol), DMSO (1 mL). [b]Isolated yield. [c]60 °C.

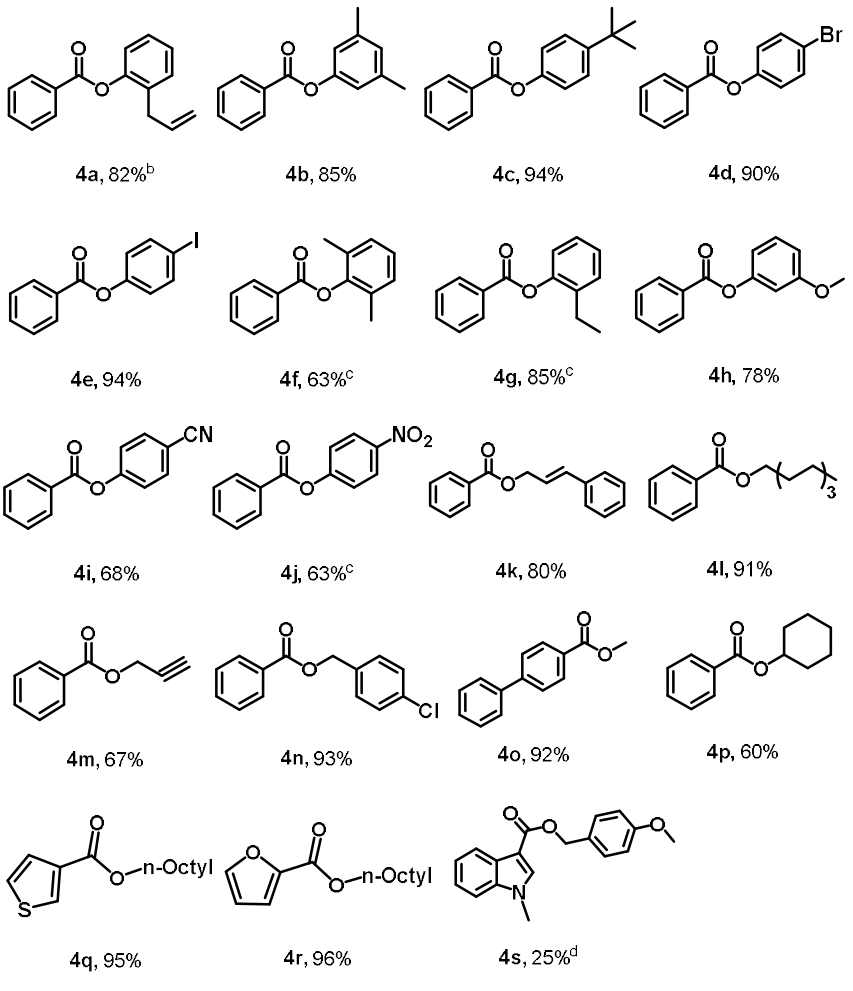
With the optimized reaction conditions in hand, we investigated the activity of the catalyst in the reaction of phenol with a variety of aryl aldehydes (Scheme 4.2). Benzaldehydes having alkyl, ether, nitrile, or halogen group(s) and 2-naphthaldehyde were converted into the corresponding phenyl esters in good to excellent yields (**3a-3j**, 69-94%). Benzaldehydes having electron donating (3-OMe,

3l) and electron withdrawing (3-Br, **3k**) groups could be transformed into esters. Notably, 3,4,5-trimethoxy substituted benzaldehyde (**3m**, 78%) and furan-2-carbaldehyde (**3n,** 71%) were good substrates. However, 4-nitrobenzaldehyde turned out to be a poor substrate (**3o**, 26%).

Next, the esterification of benzaldehyde with various types of alcohols was investigated (Scheme 4.3). Neither alcohol oxidation nor aldol condensation was observed under the reaction conditions. Various phenols containing alkyl, alkene, halogen, nitrile, or nitro group(s) afforded high to excellent yields of the corresponding esters (**4a**-**4j**). Sterically shielded phenol or phenol bearing a nitro group provided lower yields at 40 °C (**4f**, 48%; **4j**, 29%). In both cases, elevated temperatures (60 °C) were required to drive the reaction to obtain higher yields of 63%. Aliphatic alcohols, such as 3-phenylprop-2-en-1-ol, *n*-octanol, propargyl alcohol and (4-chlorophenyl) methanol also worked well for this reaction. Interestingly, double and triple bonds were tolerated in the oxidative esterification (**4k** and **4m**). In the reaction of benzaldehyde with methanol, the expected ester was produced in a high yield. However, during the purification, some of the ester evaporated. Thus, [1,1'-biphenyl]-4-carbaldehyde was used instead of benzaldehyde in the reaction with methanol, and the expected product (**4o**) was isolated in 92% yield. A secondary alcohol, cyclohexanol, was also a good substrate (**4p**, 60%). However, a tertiary alcohol, *tert*-butanol, was unreactive under the reaction conditions. Heteroaromatic aldehydes containing furan or thiophene moieties were good substrates for the esterification with aliphatic alcohols (**4q** and **4r**). However, in the case of indole-3-carboxaldehyde, an N-methylated ester, **4s**, was isolated in 25% yield.

Scheme 4.3. Esterification of aromatic aldehydes with various alcohols[a]





4a, 82%[b] 4b, 85% 4c, 94% 4d, 90%

4e, 94% 4f, 63%[c] 4g, 85%[c] 4h, 78%

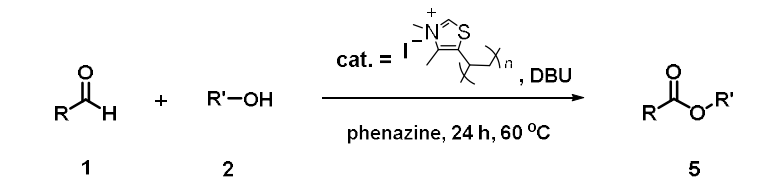
4i, 68% 4j, 63%[c] 4k, 80% 4l, 91%

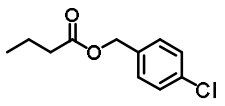
4m, 67% 4n, 93% 4o, 92% 4p, 60%

4q, 95% 4r, 96% 4s, 25%[d]

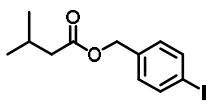
[a]Conditions: aldehyde (0.6 mmol), alcohol (0.5 mmol), cat. (7 mol %), DBU (14 mol %), phenazine (0.6 mmol), DMSO (1 mL). [b]Isoated yield. [c]60 °C. [d]Cat. (11 mol %), DBU (21 mol %), 38 h, 80 °C.

Scheme 4.4. Ester bond formation with aliphatic aldehydes and alcohols[a]

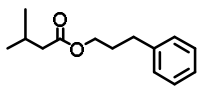




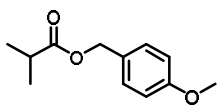
5a, 69%[b]



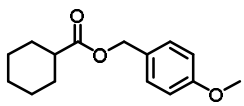
5b, 77%



5c, 69%[c]



5d, 96%

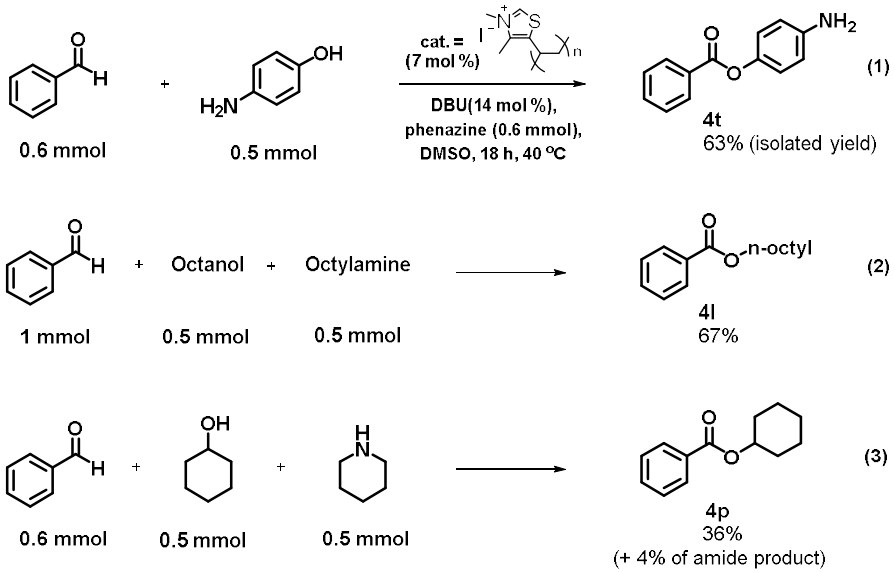


5e, 86%[d]

[a]Conditions: aldehyde (2.2 mmol), alcohol (0.5 mmol), cat. (11 mol %), DBU (21 mol %), phenazine (0.6 mmol), 24 h, 60 °C, DMSO (1 mL). [b]Isolated yield. [c]30 h, 80 °C. [d]Aldehyde (0.6 mmol), alcohol (0.5 mmol), cat. (7 mol %), DBU (14 mol %), 18 h, 40 °C.

Reactions between aliphatic aldehydes and aliphatic alcohols were also examined (Scheme 4.4). Aliphatic aldehydes, including primary-, secondary-, and cyclic aldehydes were good substrates and afforded high yields (69-96%) of the corresponding esters. Relatively higher yields were observed for secondary aldehydes (**5d** and **5e**: 96 and 86%**)** as compared to primary aldehydes (**5a-5c**: 69-77%).

Scheme 4.5. Chemoselective esterification of benzaldehyde over amidation



In order to extend the utility of the developed system, the chemical selectivity was examined by studying the reaction of 4-aminophenol with benzaldehyde (eq 1). An ester was isolated as a major product and a trace amount of an amide was formed (eq 1). Thus, this method is useful for the selective functionalization of OH groups in the presence of NH_2 groups. To determine the selectivity between nucleophiles, a competition experiment between octanol and octylamine with benzaldehyde was carried out (eq 2). The ester (67%) was formed in preference to the amide. A similar experiment with cyclohexanol and piperidine showed a 9:1 preference for the ester (overall yield: 40%) (eq 3).

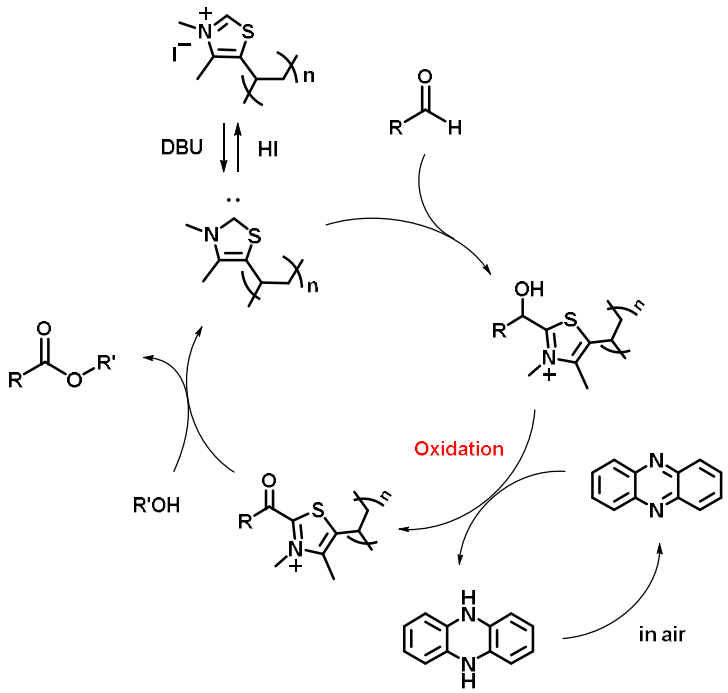


Figure 4.1. Proposed mechanism for esterification reaction

A possible mechanism for the poly(thiazolium)/base/phenazine-catalyzed esterification reaction based on the widely accepted mechanism is depicted in Figure 4.1.[4b] The benzylic alcohol intermediate is generated upon reaction of the carbene with the aldehyde. Finally, nucleophilic substitution by the alcohol takes place to give the desired esters.

In order to recycle the catalytic system, the catalyst was recovered by addition of hydroiodic acid.[12a] Moreover, we also recovered phenazine from the reaction mixture to overcome the potential drawback of its stoichiometric use. To our delight, separation of the reduced dihydrophenazine from the product in organic solvents under air afforded the reoxidized, active oxidant phenazine (96-99% in each cycle). Thus, the recovered catalytic system could be successfully reused

without considerable decrease in performance over five cycles (each time, 81-91% yield) (see SI).

4.3. Conclusion

We have developed a novel poly(thiazolium) iodide/DBU-catalyzed oxidative esterification of aldehydes with alcohols. The catalytic system showed high activity with a variety of aromatic and aliphatic aldehydes and alcohols. The methodology described herein has several advantages, including being a metal-free catalytic system, and the recovery and reusability of the organic precatalyst and phenazine oxidant. The polymer precatalyst exhibited higher catalytic activity than the monomeric analog and could be reused five times without a considerable decrease in activity.

4.4. Experimental Section

General Remarks

n-Hexanes and ethyl acetate were used without further purification. Other solvents were obtained by passing through activated alumina columns of solvent purification systems from Glass Contour. Reagents were purchased from Sigma-Aldrich, Alfa Aesar, Acros, and TCI and were used as received. Dimethyl sulfoxide was used as a solvent. Reactions were carried out in a flame dried glassware equipped with a stirring bar and capped with a rubber septum under N_2, unless otherwise indicated. Elevated temperatures were maintained in thermostat-controlled oil baths. The TLC plate was carried out on 0.25 mm E. Merck silica gel plates (60F-254) visualized by UV-light (254 nm) and treatment with acidic *p*-anisaldehyde and $KMnO_4$ stain followed by gentle heating. Workup procedures were done in air. Flash chromatography was carried out on Merck 60 silica gel (230 – 400 mesh). ^1H and ^{13}C NMR spectra were recorded with Varian spectrometer (400, 500 MHz) spectrometer. ^1H NMR spectra were referenced to residual TMS (0 ppm) and reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dt = doublets of triplets, td = triplet of doublets, qd = quartet of doublets, br s = broad singlet, m = multiplet). Chemical shifts of the ^{13}C NMR spectra were measured relative to $CDCl_3$ (77.16 ppm). Mass spectral data were obtained from the Korea Basic Science Institute (Daegu) on a Jeol JMS 700 high resolution mass spectrometer.

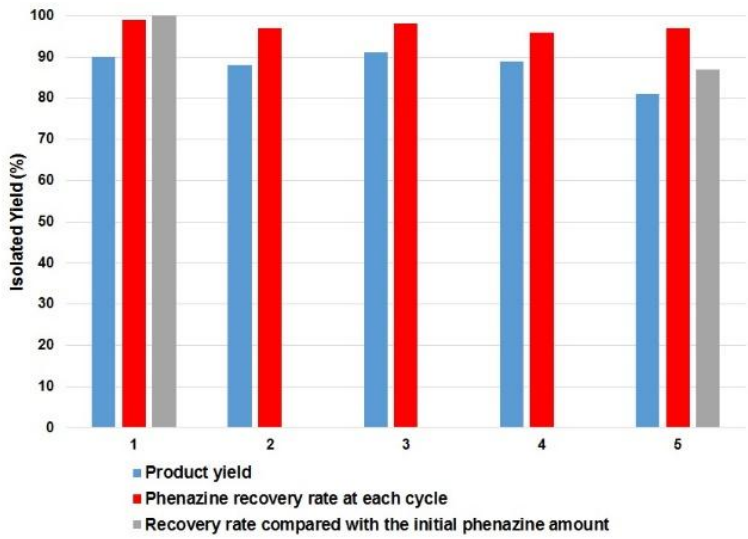
General procedure for for the Synthesis of Various Esters

Reactions were performed in a tube-type schlenk flask equipped with a stirring bar and capped with a rubber cap and the followings were placed in the tube-type flask: 7-11 mol % of thiazolium polymer precatalyst, 14-21 mol % of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), aldehyde (0.6-2.2 mmol), alcohol (0.5 mmol), phenazine (0.6 mmol), and 1 mL of DMSO at 40-80 °C for 18-38 hours. Purification by flash chromatography on silica gel with *n*-hexane and ethyl acetate afforded ester products. The products were characterized by ^{1}H NMR, ^{13}C NMR, and HRMS.

Recycling test

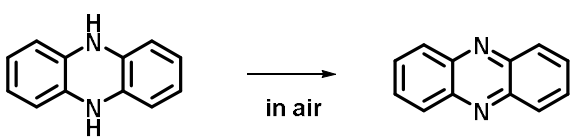
A tube-type schlenk flask was charged with benzaldehyde (25 μL, 0.25 mmol), octanol (51 μL, 0.3 mmol), phenazine (71.2 mg, 0.4 mmol), thiazolium polymer catalyst (13 mg, 20 mol %), DBU (7 μL, 20 mol %), and DMSO (0.35 mL). After stirring for 18 h at 40 °C, hydroiodic acid (0.5 mmol) was added to the reaction mixture, and the resulting solution was stirred for 30 min. Addition of 15 mL of methanol to the Schlenk flask led to precipitate the catalyst, and the supernatant was collected by using a centrifuge. This process repeated 10 times. The precipitate (catalyst) was recovered by filtration. After removal of methanol by a rotary evaporator, the residue was column-chromatographed to separate product and phenazine. The recovered catalyst was completely dried by a vacuum and was used for the next reaction with the recovered phenazine.

The catalytic performance of polymer precatalyst was maintained during the five times recycling with 81-91% isolated yields (1st run, 90%; 2nd run, 88%; 3rd run, 91%; 4th, 89% (at 60 °C); 5th, 81% (at 60 °C)) and phenazine was also recovered 5 times (1st run, 99%; 2nd run, 97%; 3rd run, 98%; 4th, 96%; 5th, 97%;).



SI Figure 4.1. Recycling of poly(3,4-dimethyl-5-vinylthiazolium) iodide and phenazine

Recycling of phenazine



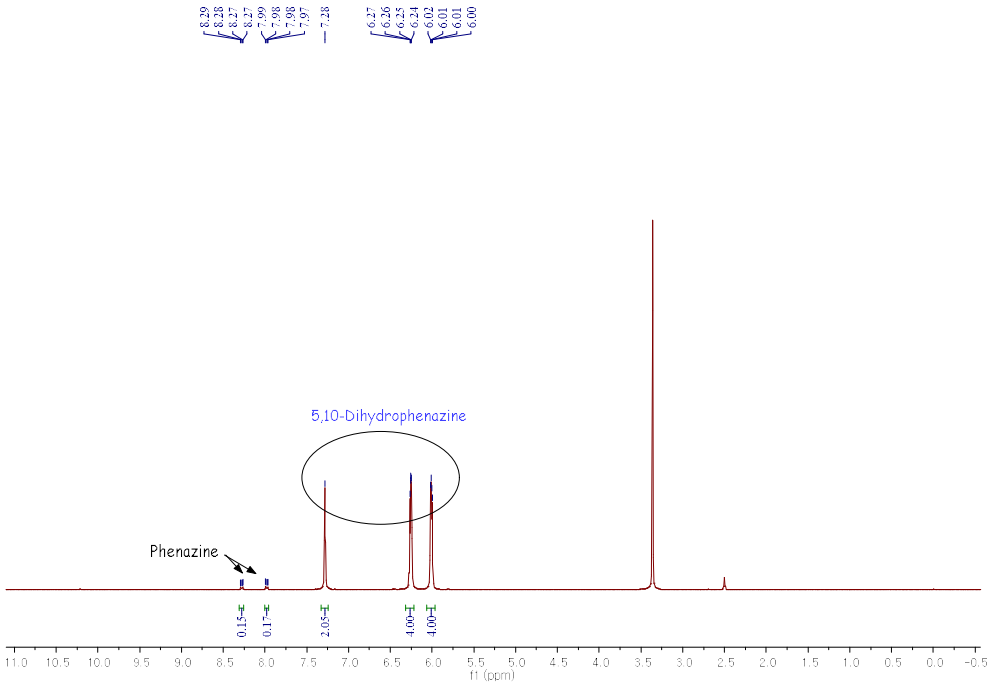
30 mg

Entry	Solvent	Solvent volume (mL)	Time
1	Acetone	6	5 h
2*	Methanol	6	1 h
3*	Dichloromethane (DCM)	6	12 h <

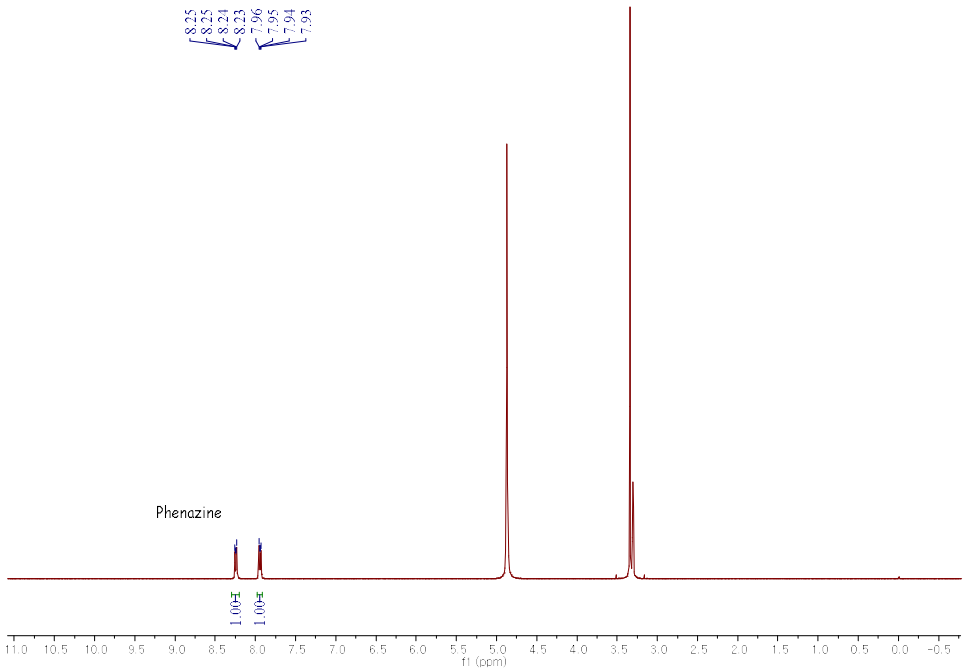
4*	Ethyl acetate	6	12 h <
5	Acetone	50	35 min
6	Acetone	100	13 min
7	Methanol (MeOH)	100	10 min

The conversion from 5,10-dihydrophenazine to phenazine was checked by TLC plate (DCM:MeOH = 10:1) using UV-light (254 nm) and ^{1}H NMR spectroscopy.

* Only partially dissolved.

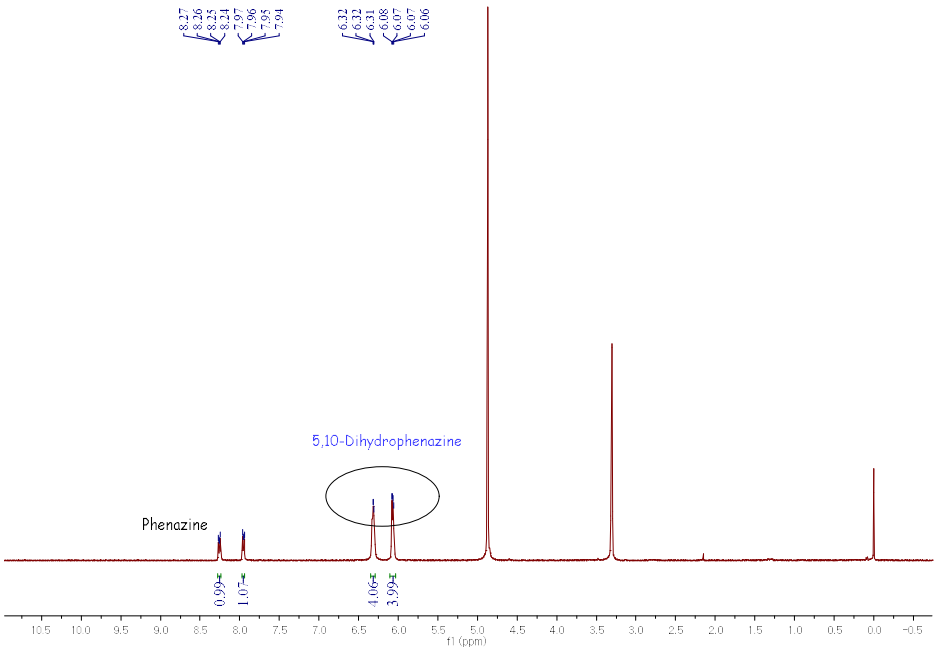


SI Figure 4.2. ^{1}H NMR spectral of 5,10-dihydrophenazine (DMSO-d_6, 298 K)



SI Figure 4.3. ^{1}H NMR spectrum of 5,10-dihydrophenazine after 1 hour in air (MeOH-d_4, 298 K)

(We could confirm that 5,10-dihydrophenazine is fully converted to phenazine.)



SI Figure 4.4. ^{1}H NMR spectrum of 5,10-dihydrophenazine after 1 hour under N_2 atmosphere

(5,10-dihydrophenazine:phenazine = 4:1) (MeOH-d_4, 298 K)

Characterization of compounds

3a: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.17 – 8.05 (m, 2 H), 7.53 (d, *J* = 5.8 Hz, 1 H), 7.45 – 7.37 (m, 2 H), 7.33 (d, *J* = 5.7 Hz, 2 H), 7.21 – 7.16 (m, 1 H), 7.13 (d, *J* = 5.6 Hz, 2 H) ppm. **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.3 ,151.1, 133.7, 130.3, 129.7, 129.6, 128.7, 126.0, 121.8 ppm. **HRMS (EI)** calc. for [$C_{13}H_{10}O_2$]: 198.0681, found: 198.0680; white solid; MP 70.3 ºC.

3b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.8 Hz, 2 H), 7.32 (t, *J* = 7.6 Hz, 2 H), 7.23 – 7.14 (m, 3 H), 7.11 (d, *J* = 7.6 Hz, 2 H), 2.33 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 151.1, 144.5, 130.3, 129.5, 129.4, 126.9, 125.9, 121.8, 21.8 ppm. HRMS (EI) calc. for [$C_{14}H_{12}O_2$]: 212.0837, found: 212.0836; white solid; MP 75.3 ºC.

3c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 7.8 Hz, 2 H), 7.67 (d, *J* = 7.7 Hz, 2 H), 7.35 (t, *J* = 7.1 Hz, 2 H), 7.20 (t, *J* = 7.2 Hz, 1 H), 7.13 (d, *J* = 7.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 150.8, 135.1 (q, *J* = 32.7 Hz), 134.0, 130.7, 129.7, 126.3, 125.7 (q, *J* = 3.7 Hz), 123.7 (q, *J* = 272.7 Hz), 121.7 ppm. HRMS (EI) calc. for [$C_{14}H_9F_3O_2$]: 266.0555, found: 266.0553; white solid; MP 90.4 ºC.

3d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (m, 2 H), 7.33 (t, *J* = 7.6 Hz, 2 H), 7.17 (t, *J* = 7.2 Hz, 1 H), 7.12 (d, *J* = 7.7 Hz, 2 H), 6.89 (m, 2 H), 3.79 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.0, 151.2, 132.4, 129.5, 125.8, 121.9, 113.9, 55.6 ppm. HRMS (EI) calc. for [$C_{14}H_{12}O_3$]: 228.0786, found: 228.0788; white solid; MP 75.8 ºC.

3e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.5 Hz, 2 H), 7.71 (d, *J* = 7.5 Hz, 2 H), 7.35 (t, *J* = 7.2 Hz, 2 H), 7.21 (t, *J* = 7.4 Hz, 1 H), 7.13 (d, *J* = 7.7 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 150.6, 133.4, 132.4, 130.7, 129.7, 126.4, 121.5, 117.9, 117.00 ppm. HRMS (EI) calc. for [$C_{14}H_9NO_2$]: 223.0633, found: 223.0634; white solid; MP 89.9 ºC.

3f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (m, 2 H), 7.38 – 7.29 (m, 2 H), 7.18 (m, 1 H), 7.15 – 7.03 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3 (d, *J* = 254.6 Hz), 164.3, 151.0, 132.9 (d, *J* = 9.4 Hz), 129.6, 126.0, 125.9 (d, *J* = 2.3 Hz), 121.8,

115.9 (d, J = 22.1 Hz) ppm. HRMS (EI) calc. for [$C_{13}H_9FO_2$]: 216.0587, found: 216.0588; white solid; MP 64.7 ºC.

3g: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (m, 2 H), 7.41 – 7.30 (m, 4 H), 7.18 (t, J = 7.4 Hz, 1 H), 7.11 (d, J = 7.7 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 150.9, 140.2, 131.6, 129.6, 129.0, 128.1, 126.1, 121.7 ppm. HRMS (EI) calc. for [$C_{13}H_9ClO_2$]: 232.0291, found: 232.0294; white solid; MP 104.9 ºC.

3h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.7 Hz, 2 H), 7.53 (d, J = 7.7 Hz, 2 H), 7.31 (d, J = 7.1 Hz, 2 H), 7.21 – 7.14 (m, 1 H), 7.10 (d, J = 7.4 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 150.8, 132.0, 131.7, 129.6, 128.9, 128.5, 126.1, 121.7 ppm. HRMS (EI) calc. for [$C_{13}H_9BrO_2$]: 275.9786, found: 275.9784; white solid; MP 119.2 ºC.

3i: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.86 (m, 4 H), 7.44 (t, J = 7.7 Hz, 2 H), 7.29 (t, J = 7.3 Hz, 1 H), 7.22 (d, J = 7.9 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 150.8, 138.1, 131.6, 129.6, 129.1, 126.1, 121.7, 101.7 ppm. HRMS (EI) calc. for [$C_{13}H_9IO_2$]: 323.9647, found: 323.9648; white solid; MP 101.0 ºC.

3j: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.08 (d, J = 8.6 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.82 – 7.75 (m, 2H), 7.52 – 7.40 (m, 2H), 7.33 (t, J = 7.9 Hz, 2H), 7.16 (d, J = 8.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 151.1, 135.9, 132.6, 132.0, 129.6, 129.6, 128.7, 128.5, 127.9, 126.9, 126.8, 126.0, 125.5, 121.9 ppm. HRMS (EI) calc. for [$C_{17}H_{12}O_2$]: 248.0837, found: 248.0835; white solid; MP 97.7 ºC.

3k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1 H), 8.07 (d, J = 7.6 Hz, 1 H), 7.69 (d, J = 7.9 Hz, 1 H), 7.37 (t, J = 7.3 Hz, 2 H), 7.31 (d, J = 7.8 Hz, 1 H), 7.22 (t, J = 7.1

Hz, 1 H), 7.15 (d, *J* = 7.9 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 150.8, 136.6, 133.2, 131.6, 130.3, 129.7, 128.8, 126.2, 122.8, 121.7 ppm. HRMS (EI) calc. for [$C_{13}H_9BrO_2$]: 275.9786, found: 275.9785; white solid; MP 58.5 ºC.

3l: ^1H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.7 Hz, 1 H), 7.60 – 7.57 (m, 1 H), 7.30 (m, 2 H), 7.28 (d, *J* = 2.4 Hz, 1 H), 7.14 (t, *J* = 7.4 Hz, 1 H), 7.09 (d, *J* = 7.7 Hz, 2 H), 7.04 (m, 1 H), 3.73 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 159.8, 151.0, 130.9, 129.7, 129.6, 126.0, 122.6, 121.8, 120.2, 114.6, 55.6 ppm. HRMS (EI) calc. for [$C_{14}H_{12}O_3$]: 228.0786, found: 228.0784; white solid; MP 61.1 ºC.

3m: ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 2 H), 7.33 (d, *J* = 7.9 Hz, 2 H), 7.18 (t, *J* = 7.3 Hz, 1 H), 7.12 (d, *J* = 8.0 Hz, 2 H), 3.86 (s, 3 H), 3.84 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 153.1, 151.0, 142.8, 129.6, 126.0, 124.5, 121.8, 107.4, 61.0, 56.4 ppm. HRMS (EI) calc. for [$C_{16}H_{16}O_5$]: 288.0998, found: 288.1001; white solid; MP 102.3 ºC.

3n: ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.33 (t, *J* = 7.8 Hz, 2 H), 7.29 (d, *J* = 3.5 Hz, 1 H), 7.17 (m, 1 H), 7.13 (d, *J* = 8.3 Hz, 2 H), 6.50 (d, *J* = 1.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 150.3, 147.2, 144.1, 129.6, 126.2, 121.7, 119.5, 112.3 ppm. HRMS (EI) calc. for [$C_{11}H_8O_3$]: 188.0473, found: 188.0470; white solid; MP 41.2 ºC.

3o: ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 – 8.24 (m, 4 H), 7.37 (t, *J* = 7.6 Hz, 2 H), 7.23 (t, *J* = 7.3 Hz, 1 H), 7.15 (d, *J* = 7.9 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 151.0, 150.6, 135.1, 131.4, 129.8, 126.5, 123.8, 121.5 ppm. HRMS (EI) calc. for [$C_{13}H_9NO_4$]: 243.0532, found: 243.0531; white solid; MP 128.3 ºC.

4a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.0 Hz, 2 H), 7.52 (t, *J* = 7.3 Hz, 1 H), 7.40 (t, *J* = 7.3 Hz, 2 H), 7.19 (d, *J* = 7.0 Hz, 2 H), 7.13 (d, *J* = 6.7 Hz, 1 H), 7.07 (d, *J* = 7.2 Hz, 1 H), 5.89 – 5.75 (m, 1 H), 5.02 – 4.83 (m, 2 H), 3.26 (d, *J* = 6.0 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 149.2, 135.9, 133.7, 132.2, 130.5, 130.2, 129.6, 128.7, 127.6, 126.3, 122.6, 116.4, 34.8 ppm. HRMS (EI) calc. for [$C_{16}H_{14}O_2$]: 238.0944, found: 238.0996; colorless liquid.

4b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 7.6 Hz, 2 H), 7.65 (t, *J* = 7.2 Hz, 1 H), 7.53 (t, *J* = 7.5 Hz, 2 H), 6.94 (s, 1 H), 6.87 (s, 2 H), 2.38 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 151.0, 139.4, 133.6, 130.2, 129.8, 128.6, 127.7, 119.4, 21.4 ppm. HRMS (EI) calc. for [$C_{15}H_{14}O_2$]: 226.0994, found: 226.0994; colorless liquid.

4c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.1 Hz, 2 H), 7.66 (t, *J* = 7.4 Hz, 1 H), 7.54 (t, *J* = 7.6 Hz, 2 H), 7.49 (d, *J* = 8.6 Hz, 2 H), 7.20 (d, *J* = 8.6 Hz, 2 H), 1.39 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 148.7, 148.7, 133.6, 130.2, 129.8, 128.6, 126.5, 121.1, 34.6, 31.5 ppm. HRMS (EI) calc. for [$C_{17}H_{18}O_2$]: 254.1307, found: 254.1306; white solid; MP 81.9 ºC.

4d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.3 Hz, 2 H), 7.65 (t, *J* = 7.4 Hz, 1 H), 7.58 – 7.48 (m, 4 H), 7.13 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 150.1, 133.9, 132.6, 130.3, 129.3, 128.8, 123.7, 119.1 ppm. HRMS (EI) calc. for [$C_{13}H_9BrO_2$]: 275.9786, found: 275.9789; white solid; MP 103.6 ºC.

4e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.0 Hz, 2 H), 7.74 (d, *J* = 7.9 Hz, 2 H), 7.65 (t, *J* = 7.0 Hz, 1 H), 7.52 (t, *J* = 7.6 Hz, 2 H), 7.01 (d, *J* = 7.9 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 150.9, 138.6, 133.9, 130.3, 129.3,

128.7, 124.0, 90.0 ppm. HRMS (EI) calc. for [$C_{13}H_9IO_2$]: 323.9647, found: 323.9647; white solid; MP 119.5 ºC.

4f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 7.8 Hz, 2 H), 7.68 (d, *J* = 6.9 Hz, 1 H), 7.57 (t, *J* = 7.2 Hz, 2 H), 7.19 – 7.12 (m, 3 H), 2.26 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 148.4, 133.7, 130.4, 130.2, 129.4, 128.7, 128.7, 126.0, 16.5 ppm. HRMS (EI) calc. for [$C_{15}H_{14}O_2$]: 226.0994, found: 226.0995; white solid; MP 43.1 ºC.

4g: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 – 8.09 (m, 2 H), 7.59 – 7.50 (m, 1 H), 7.43 (t, *J* = 6.8 Hz, 2 H), 7.28 – 7.12 (m, 3 H), 7.09 – 7.03 (m, 1 H), 2.53 (q, *J* = 7.5 Hz, 2 H), 1.12 (t, *J* = 7.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 149.1, 136.1, 133.7, 130.2, 129.7, 129.6, 128.7, 127.0, 126.4, 122.4, 23.4, 14.4 ppm. HRMS (EI) calc. for [$C_{15}H_{14}O_2$]: 226.0994, found: 226.0994; colorless liquid.

4h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.5 Hz, 2 H), 7.50 (t, *J* = 7.3 Hz, 1 H), 7.37 (t, *J* = 7.6 Hz, 2 H), 7.20 (t, *J* = 8.1 Hz, 1 H), 6.75 – 6.65 (m, 3 H), 3.67 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 160.6, 152.0, 133.6, 130.2, 129.9, 129.6, 128.6, 114.0, 111.9, 107.7, 55.5 ppm. HRMS (EI) calc. for [$C_{14}H_{12}O_3$]: 228.0786, found: 228.0788; colorless liquid.

4i: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.5 Hz, 2 H), 7.72 (d, *J* = 8.1 Hz, 2 H), 7.67 (t, *J* = 7.2 Hz, 1 H), 7.53 (t, *J* = 7.3 Hz, 2 H), 7.37 (d, *J* = 7.5 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 154.3, 134.2, 133.7, 130.3, 128.8, 128.7, 123.0, 118.3, 109.8 ppm. HRMS (EI) calc. for [$C_{14}H_9NO_2$]: 223.0633, found: 223.0636; white solid; MP 94.3 ºC.

4j: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (m, 2 H), 8.21 (d, *J* = 7.5 Hz, 2 H), 7.69 (t, *J* = 7.4 Hz, 1 H), 7.55 (t, *J* = 7.7 Hz, 2 H), 7.43 (m, 2 H) ppm. ^{13}C NMR (100 MHz,

$CDCl_3$) δ 164.4, 155.9, 145.5, 134.4, 130.5, 128.9, 128.7, 125.4, 122.8 ppm. HRMS (EI) calc. for [$C_{13}H_9NO_4$]: 243.0532, found: 243.0532; white solid; MP 140.5 ºC.

4k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.2 Hz, 2 H), 7.46 (t, *J* = 7.4 Hz, 1 H), 7.34 (m, 4 H), 7.23 (t, *J* = 7.4 Hz, 2 H), 7.19 – 7.14 (m, 1 H), 6.65 (d, *J* = 15.9 Hz, 1 H), 6.31 (dt, *J* = 15.9, 6.4 Hz, 1 H), 4.89 (d, *J* = 6.4 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 136.3, 134.3, 133.1, 130.3, 129.7, 128.7, 128.5, 128.2, 126.7, 123.3, 65.6 ppm. HRMS (EI) calc. for [$C_{16}H_{14}O_2$]: 238.0994, found: 238.0995; colorless liquid.

4l: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.7 Hz, 2 H), 7.54 (t, *J* = 7.3 Hz, 1 H), 7.43 (t, *J* = 7.6 Hz, 2 H), 4.32 (t, *J* = 6.6 Hz, 2 H), 1.82 – 1.70 (m, 2 H), 1.50 – 1.21 (m, 10 H), 0.89 (t, *J* = 6.2 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 132.9, 130.7, 129.6, 128.4, 65.2, 31.9, 29.4, 29.3, 28.8, 26.2, 22.8, 14.2 ppm. HRMS (EI) calc. for [$C_{15}H_{22}O_2$]: 234.1620, found: 234.1622; colorless liquid.

4m: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.9 Hz, 2 H), 7.56 (t, *J* = 7.0 Hz, 1 H), 7.44 (t, *J* = 7.5 Hz, 2 H), 4.92 (s, 2 H), 2.53 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 133.4, 129.9, 129.5, 128.5, 77.8, 75.1, 52.5 ppm. HRMS (EI) calc. for [$C_{10}H_8O_2$]: 160.0524, found: 160.0524; colorless liquid.

4n: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.1 Hz, 2 H), 7.57 (t, *J* = 7.4 Hz, 1 H), 7.45 (t, *J* = 7.7 Hz, 2 H), 7.38 (m, 4 H), 5.34 (s, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 134.6, 134.2, 133.2, 130.0, 129.7, 129.6, 128.8, 128.5, 65.9 ppm. HRMS (EI) calc. for [$C_{14}H_{11}ClO_2$]: 246.0448, found: 246.0450; colorless liquid.

4o: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.3 Hz, 2 H), 7.67 (d, *J* = 8.3 Hz, 2 H), 7.63 (d, *J* = 7.3 Hz, 2 H), 7.47 (t, *J* = 7.4 Hz, 2 H), 7.40 (t, *J* = 7.3 Hz, 1 H),

3.95 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 145.7, 140.1, 130.2, 129.0, 128.2, 127.4, 127.1, 52.2 ppm. HRMS (EI) calc. for [$C_{14}H_{12}O_2$]: 212.0837, found: 212.0835; white solid; MP 117.4 ºC.

4p: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.96 (m, 2 H), 7.47 (t, *J* = 7.4 Hz, 1 H), 7.36 (t, *J* = 7.7 Hz, 2 H), 5.00 – 4.92 (m, 1 H), 1.92 – 1.83 (m, 2 H), 1.72 (dd, *J* = 9.5, 3.4 Hz, 2 H), 1.56 – 1.47 (m, 3 H), 1.44 – 1.26 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 132.8, 131.1, 129.7, 128.4, 73.2, 31.8, 25.6, 23.8 ppm. HRMS (FAB) calc. for [$C_{13}H_{16}O_2$] [M+H]$^+$: 205.1229, found: 205.1233; colorless liquid.

4q: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 3.0, 1.0 Hz, 1 H), 7.44 (dd, *J* = 5.0, 1.0 Hz, 1 H), 7.21 (dd, *J* = 5.0, 3.1 Hz, 1 H), 4.18 (t, *J* = 6.7 Hz, 2 H), 1.70 – 1.60 (m, 2 H), 1.38 – 1.30 (m, 2 H), 1.28 – 1.16 (m, 8 H), 0.80 (t, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 134.1, 132.5, 128.0, 126.0, 64.9, 31.9, 29.34, 29.29, 28.8, 26.1, 22.7, 14.2 ppm. HRMS (EI) calc. for [$C_{13}H_{20}O_2S$]: 240.1184, found: 240.1186; colorless liquid.

4r: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1 H), 7.14 (d, *J* = 3.4 Hz, 1 H), 6.51 – 6.44 (m, 1 H), 4.27 (t, *J* = 6.8 Hz, 2 H), 1.78 – 1.66 (m, 2 H), 1.44 – 1.36 (m, 2 H), 1.35 – 1.21 (m, 8 H), 0.85 (t, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 146.2, 145.0, 117.7, 111.8, 65.2, 31.9, 29.29, 29.25, 28.8, 26.0, 22.7, 14.2 ppm. HRMS (EI) calc. for [$C_{13}H_{20}O_3$]: 224.1412, found: 224.1413; colorless liquid.

4s: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 6.9 Hz, 1 H), 7.68 (s, 1 H), 7.33 (d, *J* = 8.4 Hz, 2 H), 7.24 – 7.15 (m, 3 H), 6.83 (d, *J* = 8.4 Hz, 2 H), 5.23 (s, 2 H), 3.72 (s, 3 H), 3.69 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 159.5, 137.3, 135.5, 130.0, 129.1, 126.8, 122.9, 122.0, 121.8, 114.0, 109.9, 107.0, 65.4, 55.4,

33.5 ppm. HRMS (EI) calc. for [$C_{18}H_{17}NO_3$]: 295.1208, found: 295.1211; colorless liquid.

4t: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.2 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.00 (d, *J* = 8.7 Hz, 2H), 6.71 (d, *J* = 8.7 Hz, 2H), 3.66 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 144.4, 143.1, 133.5, 130.2, 129.9, 128.6, 122.4, 115.8 ppm. HRMS (EI) calc. for [$C_{13}H_{11}NO_2$]: 213.0790, found: 213.0788; white solid; MP 151.4 ºC.

5a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (m, 4 H), 4.99 (s, 2 H), 2.25 (t, *J* = 7.4 Hz, 2 H), 1.59 (m, 2 H), 0.86 (t, *J* = 7.4 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 134.8, 134.1, 129.6, 128.8, 65.3, 36.2, 18.5, 13.8 ppm. HRMS (EI) calc. for [$C_{11}H_{13}ClO_2$]: 212.0604, found: 212.0603; colorless liquid.

5b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.1 Hz, 2 H), 7.09 (d, *J* = 8.1 Hz, 2 H), 5.04 (s, 2 H), 2.23 (d, *J* = 7.1 Hz, 2 H), 2.17 – 2.05 (m, 1 H), 0.94 (d, *J* = 6.6 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 137.7, 135.9, 130.1, 93.9, 65.3, 43.4, 25.8, 22.5 ppm. HRMS (EI) calc. for [$C_{12}H_{15}IO_2$]: 318.0117, found: 318.0117; colorless liquid.

5c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.4 Hz, 2 H), 7.20 (t, *J* = 7.3 Hz, 3 H), 4.11 (t, *J* = 6.5 Hz, 2 H), 2.74 – 2.66 (m, 2 H), 2.21 (d, *J* = 6.7 Hz, 2 H), 2.18 – 2.06 (m, 1 H), 2.01 – 1.93 (m, 2 H), 0.98 (d, *J* = 6.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 141.3, 128.6, 128.5, 126.1, 63.6, 43.6, 32.3, 30.4, 25.9, 22.6 ppm. HRMS (EI) calc. for [$C_{14}H_{20}O_2$]: 220.1463, found: 220.1460; pale yellow liquid.

5d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.5 Hz, 2 H), 6.89 (d, *J* = 8.6 Hz, 2 H), 5.05 (s, 2 H), 3.80 (s, 3 H), 2.63 – 2.51 (m, 1 H), 1.17 (d, *J* = 7.0 Hz, 6 H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 159.6, 129.9, 128.5, 114.0, 66.0, 55.4, 34.1, 19.1 ppm. HRMS (EI) calc. for [$C_{12}H_{16}O_3$]: 208.1099, found: 208.1100; pale yellow liquid.

5e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.4 Hz, 2 H), 6.80 (d, *J* = 8.5 Hz, 2 H), 4.96 (s, 2 H), 3.72 (s, 3 H), 2.29 – 2.18 (m, 1 H), 1.88 – 1.78 (m, 2 H), 1.70 – 1.53 (m, 3 H), 1.42 – 1.31 (m, 2 H), 1.25 – 1.08 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 159.6, 129.9, 128.6, 114.0, 65.8, 55.4, 43.3, 29.1, 25.9, 25.5 ppm. HRMS (EI) calc. for [$C_{15}H_{20}O_3$]: 248.1412, found: 248.1415; pale yellow liquid.

4.5. References

(1) (a) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; John Wiley & Sons: New York, 1991. (b) Otera, J. *Esterification: Methods Reactions and Applications*; Wiley: New York, 2003. (c) Otera, J.; Nishikido, J *Esterification: Methods, Reactions, and Applications*, 2nd ed.; Wiley-VCH: Weinheim, 2010.

(2) (a) Ogawa, T.; Matsui, M. *J. Am. Chem. Soc.* **1976**, *98*, 1629. (b) Larock, R. C. *Comprehensive Organic Transformation*; VCH: New York, 1989. p840; McDonald, C.; Holcomb, H.; Kennedy, K.; Kirkpatrick, E.; Leathers, T.; Vanemon, P. *J. Org. Chem.* **1989**, *54*, 1213. (c) Humphrey, J. M.; Chamberlin, A. R. *Chem. Rev.* **1997**, *97*, 2243. (d) Ishuhara, K. *Tetrahedron* **2009**, *65*, 1085. (e) Gaspa, S.; Porcheddu, A.; De Luca, L. *Org. Lett.* **2015**, *17*, 3666.

(3) (a) Haruta, M.; Kobayashi, T.; Sano, H.; Yamada, N. *Chem. Lett.*, **1987**, 405. (*b*) Haruta, M.; Yamada, N.; Kobayashi, T.; Iijima, S. *J. Catal.* **1989**, *115*, 301.

(4) (a) Ekoue-Kovi, K.; Wolf, C. *Chem. Eur. J.* **2008**, *14*, 6302. (b) Tang, S.; Yuan, J.; Liu, C.; Lei, A. *Dalton Trans.* **2014**, *43*, 13460. (c) Gaspa, S.; Porcheddu, A.; De Luc, L. *Tetrahedron Lett.* **2016**, *57*, 3433.

(5) (a) Zhang, M.; Zhang, S.; Zhang, G.; Chen, F.; Cheng, J. *Tetrahedron Lett.* **2011**, *52*, 2480. (b) Zhao, J.; Much-Lichtenfeld, C.; Studer, A. *Adv. Synth. Catal.* **2013**, *355*, 1098. (c) Marsden, C.; Taarning, E.; Hansen, D.; Johansen, L.; Klitgaard, S. K.; Egeblad, K.; Christensen, C. H. *Green Chem.* **2008**, *10*, 168.

(6) (a) Maki, B. E.; Scheidt, K. A. *Org. Lett.* **2008**, *10*, 4331. (b) Delany, E. G.; Fagan, C.-L.; Gundala, S.; Zeitler, K.; Connon, S. J. *Chem. Commun.* **2013**, *49*, 6513. (c) Alanthadka, A.; Maheswari, C. *Adv. Synth. Catal.* **2015**, *357*, 1199; (d) Delany, G. D.; Fagan, C.-L.; Gundala, S.; Mari, A.; Broja, T.; Zeitler, K.; Connon, S. J. *Chem. Commun.* **2013**, *49*, 6510.

(7) (a) Sohn, S. S.; Bode, J. W. *Org. Lett.,* **2005**, *7*, 3873. (b) Reynolds, N. T.; Rovis, T. *J. Am. Chem. Soc.* **2005**, *127*, 16406. (c) Chan, A.; Scheidt, K. A. *Org. Lett.* **2005**, *7*, 905. (d) Zeitler, K. *Org. Lett.* **2006**, *8*, 637. (e) Sohn, S. S.; Bode, J. W. *Angew. Chem., Int. Ed.* **2006**, *45*, 6021. (f) Sarkar, S. D.; Grimme, S.; Studer, A. *J. Am. Chem. Soc.* **2010**, *132*, 1190. (g) Maji, B.; Vedachalan, S.; Ge, X.; Cai, S.; Liu, X.-W. *J. Org. Chem*., **2011**, *76*, 3016. (h) Rose, C. A.; Zeitler, K. *Org. Lett.* **2010**, *12*, 4552. (i) Finney, E. E.; Ogawa, K. A.; Boydston, A. J. *J. Am. Chem. Soc.* **2012**, *134*, 12374.

(8) (a) Rosa, J. N.; Reddy, R. S.; Candeias, N. R.; Cal, P. M. S. D.; Gois, P. M. P. *Org. Lett.* **2010**, *12*, 2686. (b) Reddy, R. S.; Rosa, J. N.; Veiros, L. F.; Caddick, S.; Gois, P. M. P. *Org. Biomol. Chem.* **2011**, *9*, 3126.

(9) Miyamura, H.; Yasukawa, T.; Kobayashi, S. *Green Chem.* **2010**, *12*, 776.

(10) Suzuki, K.; Yamaguchi, T.; Matsushita, K.; Iitsuka, C.; Miura, J.; Akaogi, T.; Ishida, H. *ACS Catal*. **2013**, *3*, 1845.

(11) (a) Seo, U. R.; Chung, Y. K. *Adv. Synth. Catal.* **2014**, *356*, 1955. (b) Seo, U. R.; Chung, Y. K. *RSC Adv*. **2014**, *4*, 32371.

(12) (a) Chung, J. Y.; Seo, U. R.; Chun, S.; Chung, Y. K. *ChemCatChem* **2016**, *8*, 318. (b) Chun, S.; Chung, J. Y.; Chung, Y. K. *ChemCatChem* **2016***, 8,* 2476.

Part I I

Studies on Silver/NBS Catalyzed Organic Reaction

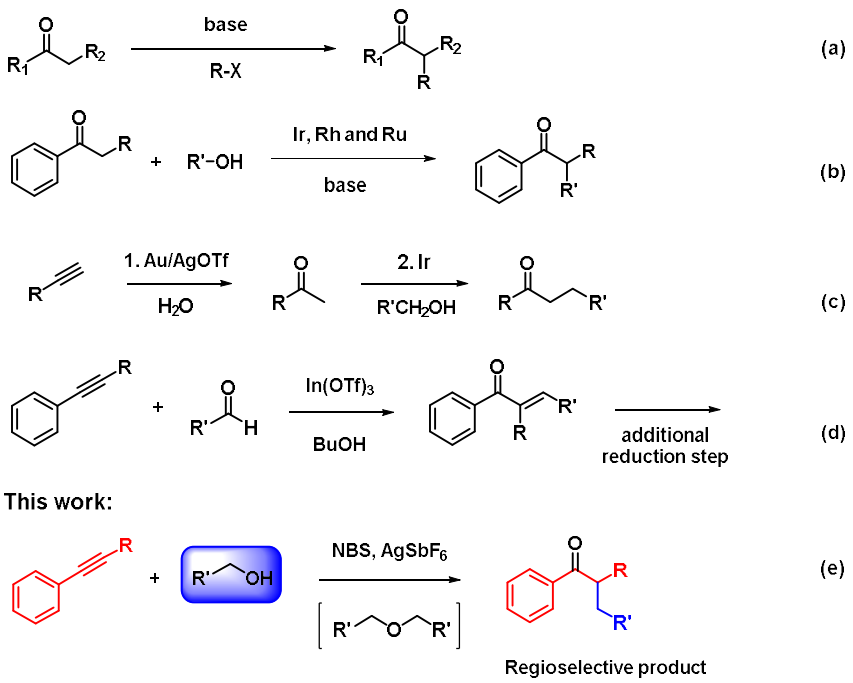
Chapter 5. Silver/NBS-Catalyzed Synthesis of α-Alkylated Aryl Ketones from Internal Alkynes and Benzyl Alcohols via Ether Intermediates

5.1. Introduction

In part I, we synthesized polymers and discussed their catalytic activities in some reactions. The use of polymer catalysts has led to the improvement of existing synthetic methodologies. In this context, the study in Chapter 5 focuses on recognizing limitations of exsting synthetic strategies and solving them via an introduction of new concepts.

Scheme 5.1. Various synthesis strategies for α-alkylated aryl ketone

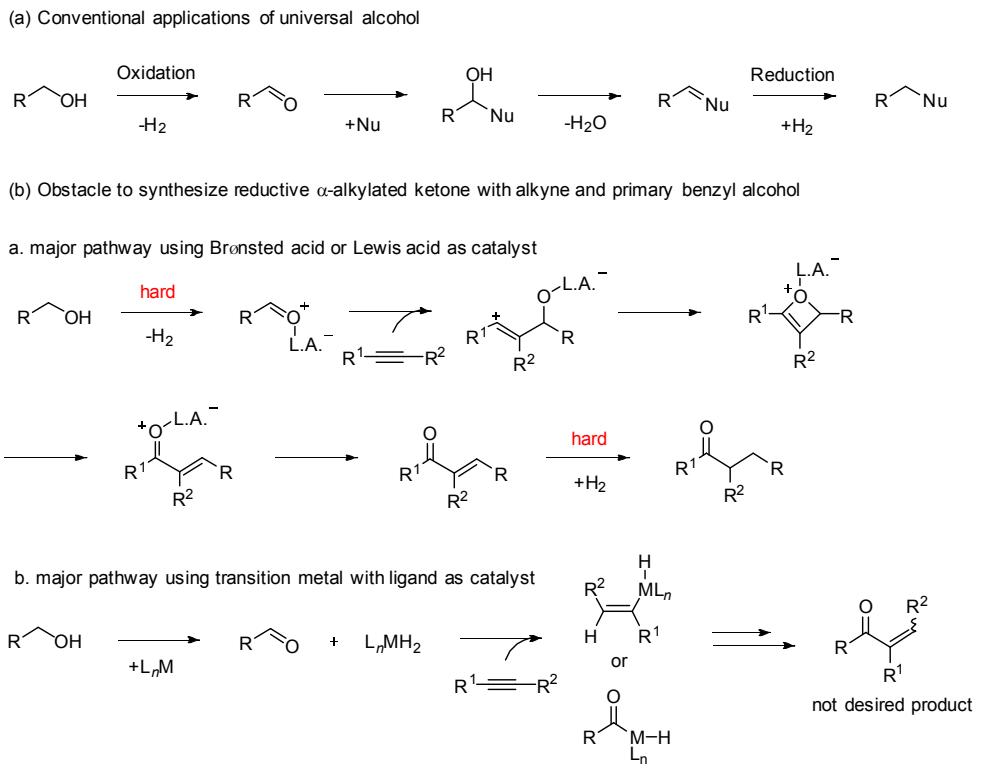
Previous works:



α-Alkylated aryl ketones are a very important class of compounds that have a wide range of pharmacological and physiological activities.[1] Their activities have attracted much research interest in the synthesis of α-alkylated aryl ketones in many groups. Although many methodologies have been developed, there is still interest in exploring new reaction systems.[2] α-Alkylated aryl ketones are synthesized via α-alkylation of nucleophilic enolates derived from ketones with electrophilic alkylating agents in the presence of at least a stoichiometric amount of a strong base (Scheme 5.1a).[3] However, these procedures suffer from toxicity of the alkylating agents and the generation of a large amount of harmful waste salts. Thus, the α-alkylation of ketones with alcohols (Scheme 5.1b) has attracted much attention[4] because alcohols can be used as an alkylating agent in the reaction with α-functionalized carbonyl compounds via a hydrogen borrowing process[5] in the presence of transition metal catalysts.[6] Recently, the α-alkylation of methylene

ketones with alcohol electrophiles has been also studied to prepare α-alkylated aryl ketones.[7] Several years ago, a strategy for the synthesis of α-alkylated ketones via a catalytic hydration of terminal alkynes and α-alkylation with primary alcohols was reported (Scheme 5.1c).[8] However, no reaction occurred with internal alkynes such as 5-decyne or diphenylacetylene.[9] The use of in situ generated α-substituted ketones from internal alkynes to form α-branched alkylation products is less developed. Aryl ketones may be synthesized by alkyne hydration,[10] however, reactions of internal alkynes often lead to a mixture of ketone regioisomers.[11] Thus, the regioselective functionalization of unsymmetrically substituted alkynes is of fundamental importance in organic synthesis.[12] The coupling of internal alkynes with aldehydes affording α,β-unsaturated ketones has been studied (Scheme 5.1d).[13] However, in order to get α-alkylated aryl ketones, they must be hydrogenated. Therefore, a new synthetic strategy with a conceptually different reaction pathway is required. We envisioned that the α-alkylation of internal alkynes with alcohols could be a highly desirable strategy for the synthesis of α-alkylated aryl ketones (Scheme 5.1e) if an alkylating agent could be catalytically generated from primary alcohols and were regioselectively added to internal alkynes.

Scheme 5.2. Synthesis strategies



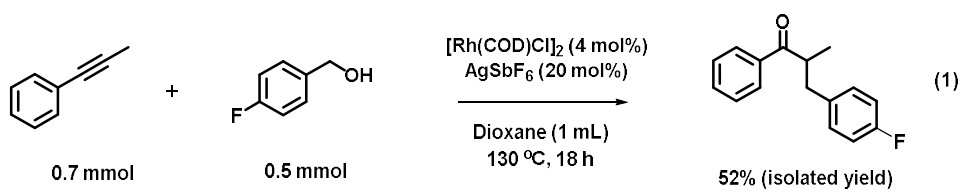
Most of the strategies to consume primary alcohol effectively apply the hydrogen borrowing strategy. Alcohols are first dehydrogenated to form aldehydes with the generation of hydrogen or metal hydride species. Then, the Lewis or Brønsted acid-mediated coupling between the resulting aldehydes and alkynes occurs to afford α,β-unsaturated ketones, which undergo reduction by the metal hydride species to give the final α-alkylated ketones (Scheme 5.2a). Although this method is apparently attractive, there are obstacles. Both the first (oxidation) and last (reduction) steps seem to be difficult to carry out in the presence of Lewis or Brønsted acid. When the reaction is carried out in the presence of transition metal catalyst via a hydrogen borrowing strategy, a coupling between the resulting

aldehydes and alkynes affords unwanted α,β-unsaturated ketones (Scheme 5.2b).

Very recently, $AgSbF_6$/NBS was found to be an excellent catalytic system for the synthesis of α-alkylated aryl ketones bearing a tertiary carbon center from internal alkynes and benzyl alcohols. The reaction is regioselective and applicable to a variety of internal alkynes and benzyl alcohols. A dibenzyl ether was generated in situ as a key intermediate, and a radical pathway, quite different from those proposed by previous studies,[8,13] was proposed. The present protocol provides a green, concise, and benign method to access α-alkylated aryl ketones. We communicate our preliminary results herein.

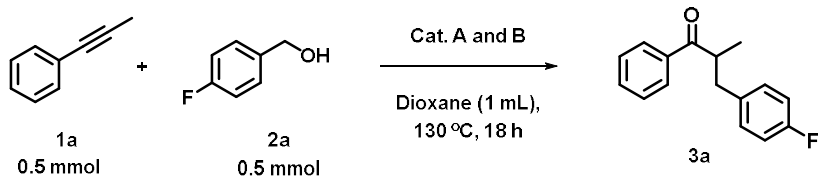
5.2. Results and Discussion

As a model reaction for the synthesis of α-alkylated aryl ketones, we initially examined the reaction of prop-1-yn-1-ylbenzene with (4-fluorophenyl)methanol in the presence of $[Rh(COD)Cl]_2$ and $AgSbF_6$ (eq 1).



After workup, an α-alkylated aryl ketone, 3-(4-fluorophenyl)-2-methyl-1-phenylpropan-1-one, was isolated in 52% yield. Encouraged by the above result, we screened several transition metal compounds (see Supporting Information). It seemed that the reaction was not sensitive to the identity of the metal, but was quite sensitive to the presence of the silver salt, $AgSbF_6$.

Table 5.1. Optimization of the reaction conditions for synthesis of α-alkylated aryl ketone



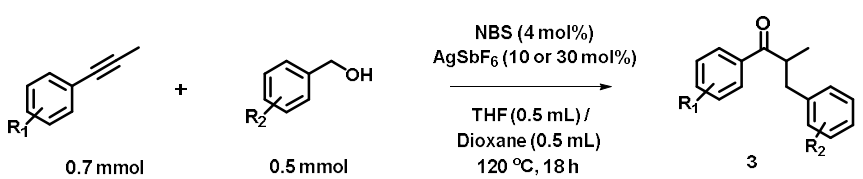
Entry	cat. A (mol%)	cat. B (mol%)	Yield[a] (%)
1	NBS (20)	$AgSbF_6$ (20)	50
2	NIS (20)	$AgSbF_6$ (20)	46
3	NCS (20)	$AgSbF_6$ (20)	50
4	-	$AgSbF_6$ (20)	N.R.
5	NBS (20)	-	N.R.
6	NBS (20)	$AgNTf_2$(20)	36
7[b]	NBS (20)	$AgSbF_6$ (30)	57
8[b]	NBS (4)	$AgSbF_6$ (30)	67
9[c]	NBS (4)	$AgSbF_6$ (30)	75

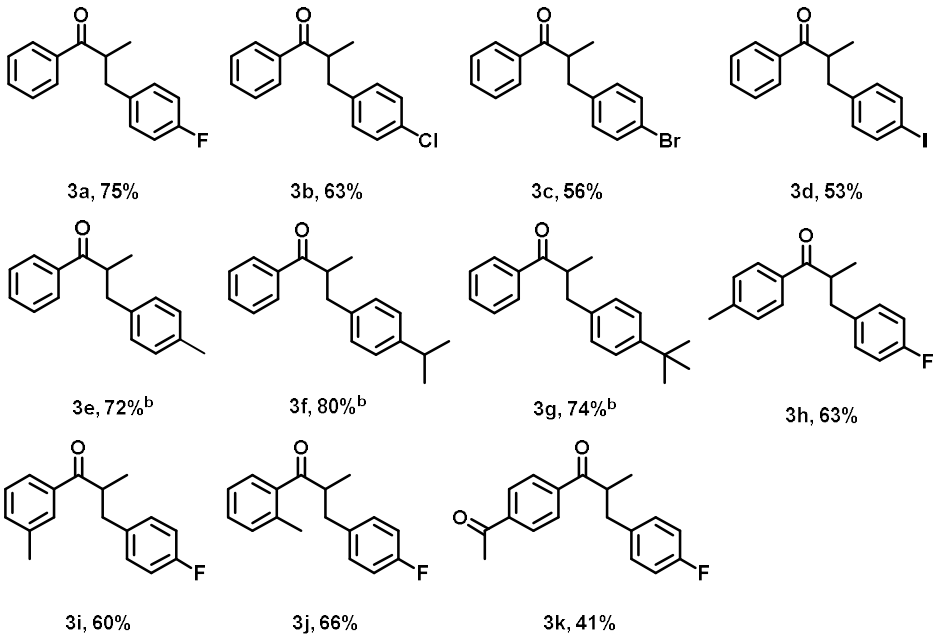
[a]Isolated yields. [b]**1a** (0.7 mmol), 120 °C. [c]**1a** (0.7 mmol), dioxane (0.5 mL)/THF (0.5 mL), 120 °C.

Organic halogenation compounds such as *N*-bromosuccinimide (NBS, 50%, entry 1), *N*-chlorosuccinimide (NCS, 46%, entry 2), and *N*-iodosuccinimide (NIS, 50%, entry 3) were screened as the catalyst (Table 5.1). As expected, without NBS or $AgSbF_6$, no reaction occurred even at 130 °C (entries 4 and 5). When Bu_4PF_6, $AgClO_4$, AgO_2CCF_3, $NaSbF_6$, or $[(4\text{-}BrC_6H_4)_3N]SbCl_6$ was used instead of $AgSbF_6$, no reaction was observed. When $AgNTf_2$ was used for the reaction, a certain

amount of reaction proceeded (36%, entry 6), but the best activity in terms of efficiency was observed when $AgSbF_6$ was used. The amounts of the alkyne and the alcohol used also had influence on the yield of the reaction (57%, entry 7). We chose the ratio of alkyne to alcohol to be 0.7:0.5 mmol in 1.0 mL of 1,4-dioxane. The yields of the reaction were dependent upon the amounts of NBS and $AgSbF_6$ used. The amount of NBS could be cut down to 4 mol%, but the amount of $AgSbF_6$ was fixed at 30 mol% (67%, entry 8). The yield of the reaction was also highly sensitive to the reaction medium (entries 9 - 11). The best yield (75%, entry 11) was observed when the reaction was carried out in a solvent mixture of THF and 1,4-dioxane with a ratio of 1:1. Thus, we established the optimum reaction conditions to obtain an α-alkylated aryl ketone from 1-phenyl-1-propyne and 4-fluorobenzyl alcohol.

Scheme 5.3. Synthesis of α-alkylated aryl ketones using methyl aryl acetylenes with various alcohols[a]





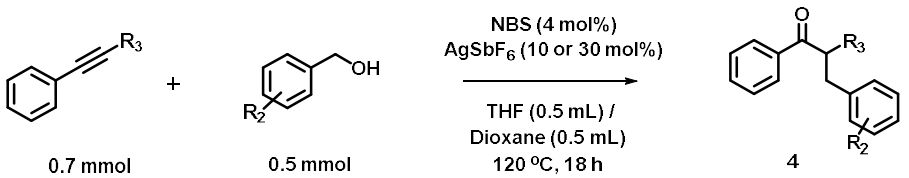
[a]30 mol% of $AgSbF_6$ was used and all the products were isolated by column chromatography. [b]10 mol% of $AgSbF_6$ was used and 1 mL of THF was used as solvent.

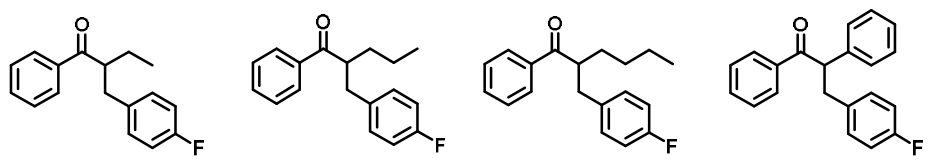
With the optimum reaction conditions for the synthesis of α-alkylated aryl ketones at hand, the substrate scope was investigated (Scheme 5.3). We first tested a reaction between 1-phenyl-1-propyne with 4-substituted benzyl alcohols in the presence of NBS and $AgSbF_6$ (entries **3a–3g**). The corresponding α-alkylated aryl ketones were isolated in 53–80% yields. In the reaction with 4-halobenzyl alcohols, the yield was dependent on the identity of the halogen. The highest yield (**3a**, 75%) was observed with a fluoro group and the lowest (**3d**, 53%) with an iodo group. Interestingly, in the reaction with 4-alkyl benzyl alcohols, the yield was rather insensitive to the identity of the alkyl group (**3e**–**3g**, 58–60%). When the same reaction was carried out in THF for 18 h, the yields dramatically improved (**3e**, 59 → 72%; **3f**, 60 → 80%; **3g**, 58 → 74%) even with a sterically bulky substituent.

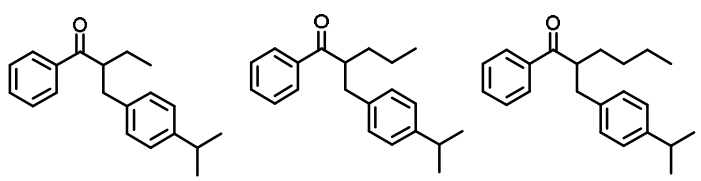
Next, we studied a reaction between prop-1-yn-1-yl substituted benzenes and 4-fluorobenzyl alcohol in the presence of NBS and $AgSbF_6$ (**3h**–**3k**). The yield of the reaction was rather insensitive to the position of a methyl group on the benzene ring (ortho, 66%; meta, 60%; para, 63%). However, a rather lower yield (**3k**, 41%) was observed with an acetyl group on the benzene ring.

Other internal alkynes, including 1-phenyl-1-butyne, 1-phenyl-1-pentyne, 1-phenyl-1-hexyne, and 1,2-diphenylethyne, were also good substrates to react with 4-fluorobenzyl alcohol in the presence of NBS and $AgSbF_6$, affording the corresponding α-alkylated aryl ketones in 60–72% yields (**4a**–**4g**, Scheme 5.4). In the reaction of 1,2-diphenylethyne, lengthening the reaction time improved the yield from 45% to 60% (**4d**). Notably, the reaction of benzyl alcohol having an iso-propyl substituent with internal alkynes in THF produced relatively higher yields (**4e**–**4f**; 68–71%, Scheme 5.4).

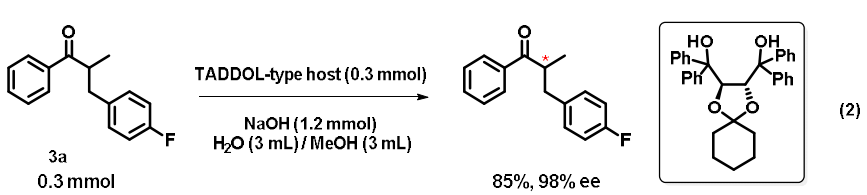
Scheme 5.4. Variation of the acetylene alkyl group in the synthesis of α-alkylated aryl ketones[a]







[a] 30 mol% of $AgSbF_6$ was used unless otherwise noted and all the products were isolated by column chromatography. [b]24 h. [c]10 mol% of $AgSbF_6$ was used and 1 mL of THF was used as solvent.

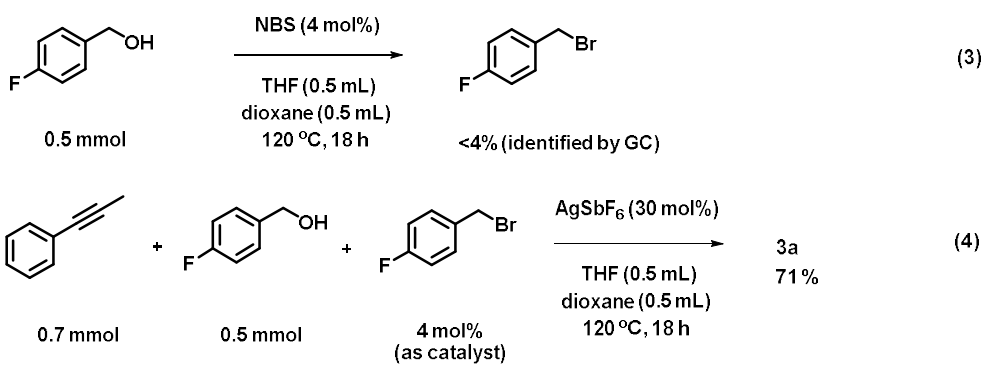


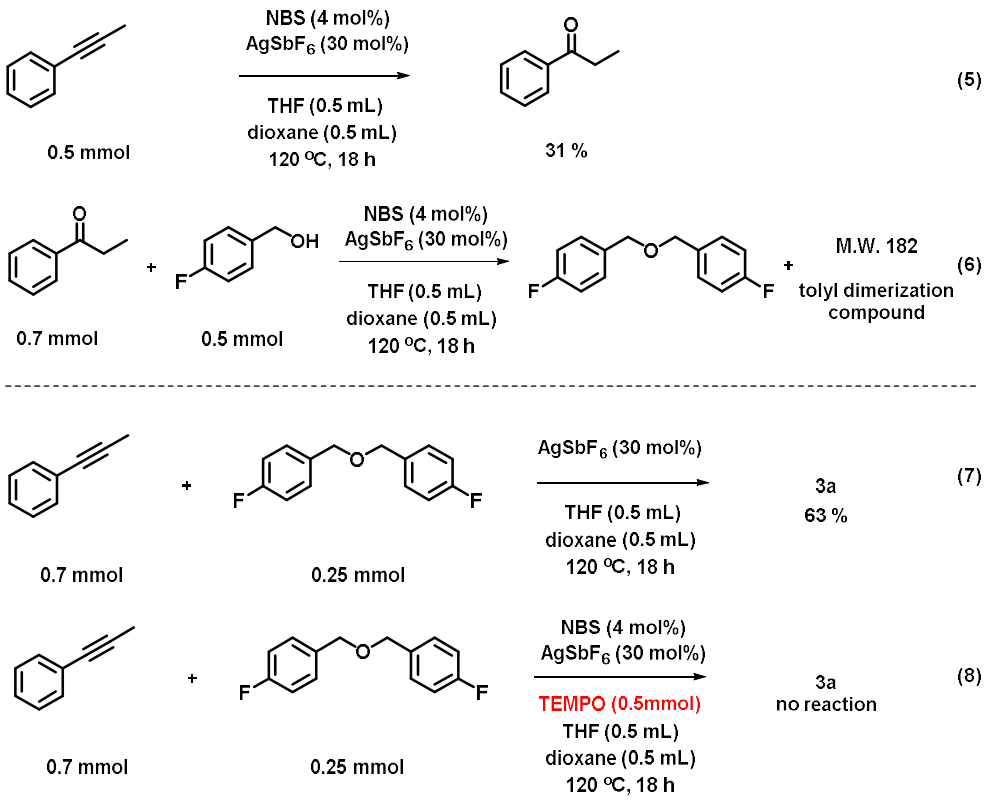
α-Alkylated aryl ketones are particularly useful due to the possibility of a stereogenic center at the α-position to the ketone group. The synthetic utility of our strategy could be enhanced, provided racemic ketones could be transformed into

the optically active α–benzyl ketones. Fortunately, several years ago, Tsunoda and coworkers reported[14] the conversion of racemic ketones bearing a stereogenic center α to the carbonyl group into optically active ketones in the presence of TADDOL-type host molecules in H_2O/MeOH in suspension in basic media. Thus, 3-(4-fluorophenyl)-2-methyl-1-phenylpropan-1-one (**3a**) was treated with base in aqueous MeOH in the presence of (-)-(2*R*,3*R*)-*trans*-2,3-bis(hydroxyldiphenylmethyl)-1,4-dioxaspiro[5.4]decane (eq 2). After workup, a highly optically pure ketone was isolated in 85% yield with 98% ee.

While we were studying the $AgSbF_6$/NBS-mediated synthesis of **3a** from the reaction of 1-phenyl-1-propyne with 4-fluorobenzylalcohol, the formation of a symmetric ether, 1,1′-[oxybis(methylene)]bis[4-fluorobenzene], was always observed. Furthermore, formation of toluene was observed by ^{1}H NMR. $AgSbF_6$/NBS was also found to be a catalyst in the etherification of benzyl alcohol (see SI). It seems that alcohols can be activated via halogenation reactions to give more reactive organohalides, and further serve as the alkylating reagents to afford symmetric ethers.

Scheme 5.5. Control experiments





To further validate the reaction mechanism, additional experiments were performed (eq 3-8). When 4-fluorobenzyl alcohol was treated with 4 mol% of NBS in a solvent mixture of THF (0.5 mL) and 1,4-dioxane (0.5 mL) at 120 °C for 18 h, the formation of 4-fluorobenzyl bromide was identified by GC analysis (eq 3). When 1-phenyl-1-propyne was reacted with 4-fluorobenzyl bromide in the presence of $AgSbF_6$ (30 mol%) in a solvent mixture of THF (0.5 mL) and 1,4-dioxane (0.5 mL) at 120 °C for 18 h, **3a** was isolated in 71% yield (eq 4). When 1-phenyl-1-propyne was reacted under our reaction conditions, ethyl phenyl ketone was isolated in 31% yield (eq 5). However, when ethyl phenyl ketone was treated with 4-fluorobenzyl alcohol in the presence of NBS (4 mol%) and $AgSbF_6$ (30 mol%) in a solvent mixture of THF (0.5 mL) and 1,4-dioxane (0.5 mL) at 120 °C

for 18 h, no desired product was observed (eq 6). Instead, formation of 1,1′-[oxybis(methylene)]bis[4-fluorobenzene] and 1,2-diphenylethane (a tolyl dimerized compound) was observed. This observation suggests that a direct transformation of 1-phenyl-1-propyne to ethyl phenyl ketone did not occur during the reaction. When 1-phenyl-1-propyne was reacted with 1,1′-[oxybis(methylene)]bis[4-fluorobenzene] in the presence of $AgSbF_6$ in a solvent mixture of THF (0.5 mL) and 1,4-dioxane (0.5 mL) at 120 °C for 18 h, **3a** was isolated in 63% yield (eq 7), indicating that an ether was probably the reaction intermediate. However, when 0.5 mmol of TEMPO was added to the above solution, no reaction was not observed (eq 8). In the same way, no reaction was observed in the presence of 2,6-di-*tert*-butyl-4-methylphenol. The observation of the formation of toluene and the dimerized tolyl product may provide some evidence that the reaction proceeds via a radical pathway.

Based on our findings and previous studies,[15] we propose a possible mechanism as depicted in Figure 5.1. Two catalytic cycles may operate: one is the generation of ether and oxonium bromide intermediates, and the other is the generation of α-alkylated aryl ketones through a radical process. Thus, benzyl alcohol is transformed into benzyl bromide in the presence of NBS. Benzyl bromide then reacts with another benzyl alcohol in the presence of $AgSbF_6$ to afford dibenzyl ether via oxonium bromide intermediates.[16] The in situ-generated benzyl radical from benzyl bromide (see SI) or dibenzyl ether in the presence of $AgSbF_6$ adds to the triple bond of 1-phenyl-1-propyne regioselectively, providing a vinyl radical intermediate **I**. The generation of the benzyl radical could be indirectly verified by the observation of toluene. The vinyl radical **I** must be oxidized to the vinyl cation by Ag(**II**). Sequential reaction of the vinyl cation with water would produce an enol intermediate **II**, which subsequently undergoes a keto-enol tautomerism to

produce the product.

Two catalytic cycles may operate: one is the generation of ether and oxonium bromide intermediates, and the other the generation of α-alkylated aryl ketones through a radical process. Thus, benzyl alcohol is transformed into benzyl bromide in the presence of NBS. Benzyl bromide then reacts with another benzyl alcohol in the presence of $AgSbF_6$ to afford dibenzyl ether via oxonium bromide intermediates. The in situ-generated benzyl radical from benzyl bromide (see SI) or dibenzyl ether in the presence of $AgSbF_6$ adds to the triple bond of prop-1-yn-1-ylbenzene regioselectively, providing vinyl radical intermediate I. Sequential reaction of the vinyl radical with water would produce enol intermediate II, which subsequently undergoes keto-enol tautomerism to produce the product.

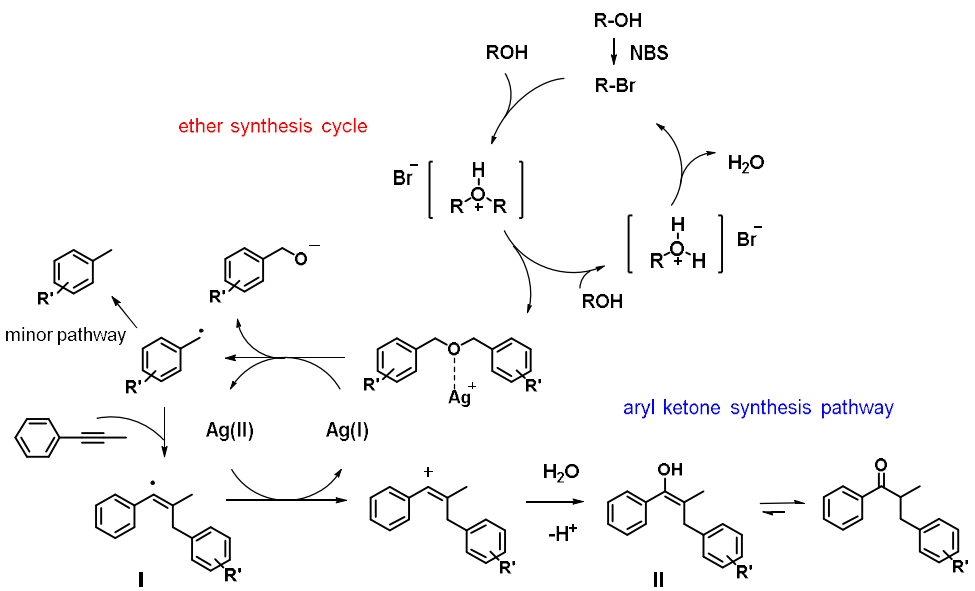


Figure 5.1. Proposed mechanism for synthesis of α-alkylated aryl ketones using alkynes and alcohols

5.3. Conclusion

We have developed a silver/NBS-mediated synthesis of α-alkylated aryl ketones with a tertiary carbon center from internal alkynes and benzyl alcohols. Thus, an atom-economic direct functionalization of internal alkynes was achieved by using alcohol as both a hydration and alkylation source.

5.4. Experimental Section

General remarks

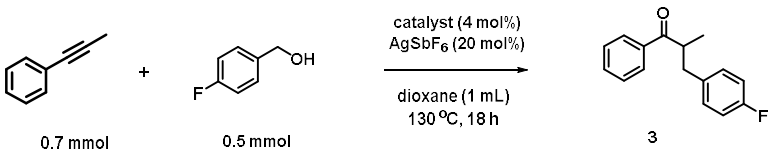
Hexanes and diethyl ether were used without further purification. THF was obtained by passing through activated alumina columns of solvent purification systems from Glass Contour and dioxane was purchased from Sigma-Aldrich. Reagents were purchased from Sigma-Aldrich, Alfa Aesar, Acros, and TCI and were used as received. Reactions were carried out in a flame-dried glassware equipped with a stirring bar and capped with a rubber septum under N_2, unless otherwise indicated. Elevated temperatures were maintained in thermostat-controlled oil baths. The TLC plate was carried out on 0.25 mm E. Merck silica gel plates (60F-254) visualized by UV-light (254 nm) and treatment with acidic *p*-anisaldehyde and $KMnO_4$ stain followed by gentle heating. Workup procedures were done in air. Flash chromatography was carried out on Merck 60 silica gel (230 – 400 mesh). ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded with Agilent 400-MR DD2 Magnetic Resonance System (400 MHz) and a Varian/Oxford As-500 (500 MHz) spectrophotometer. ^{1}H NMR spectra were referenced to residual TMS (0 ppm) and reported as follows: chemical shift, multiplicity (s = singlet, d =

doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dt = doublets of triplets, td = triplet of doublets, qd = quartet of doublets, br s = broad singlet, m = multiplet), and coupling constants and an integration of the peaks were followed. Chemical shifts of the ^{13}C NMR spectra were measured relative to $CDCl_3$ (77.16 ppm). Mass spectral data were obtained from the Korea Basic Science Institute (Daegu) on a Jeol JMS 700 high resolution mass spectrometer. GC-MS analyses were performed with a HP-6890 series with a HP-5 capillary column (30 m x 0.25 mm; coating thickness 0.25 μm) and Agilent 5973 Network Mass Selective detector. Analytical condition – initial temperature: 50 ^oC, raising temperature 10 ^oC / min, final temperature: 280 ^oC, He gas, Pressure: 7.56 psi, Total flow: 53.7 mL / min. IR spectra were measured on a Thermo Scientific Nicolet 6700 spectrometer. Specific rotations were obtained on a JASCO P-1030 polarimeter. Chiral HPLC spectra were obtained on a HPLC Hewlett Packard 1100 Series.

Optimization of the reaction conditions

Reactions were performed in a tube-type Schlenk flask equipped with a stirring bar and the followings were placed in the tube-type flask: 4 mol% of catalyst, 20 mol% of $AgSbF_6$, alkyne (0.7 mmol), alcohol (0.5 mmol) and 1 mL of dioxane. The reaction mixture was heated at 130 °C for 18 h. Purification by flash chromatography on silica gel with hexanes and diethyl ether afforded ketone products.

SI Table 5.1. Optimization of the reaction conditions using transition metal for synthesis of α-alkylated aryl ketone



0.7 mmol 0.5 mmol 3

Entry	Catalyst	Yield (%)	Entry	Catalyst	Yield (%)
1	$[Rh(COD)Cl]_2$	52	5	$MgCl_2$	46
2	$CuCl_2$	49	6	CuI	46
3	$FeCl_3$	47	7	NaCl	N.R.
4	$CaCl_2$	50		AgCl	N.R.

Procedure for the synthesis of α-alkylated aryl ketones

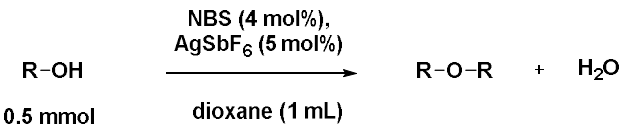
Reactions were performed in a tube-type Schlenk flask equipped with a stirring bar and the followings were placed in the tube-type flask: 4 mol% of NBS, 30 mol% of $AgSbF_6$, alkyne (0.7 mmol), halide substituted alcohol (0.5 mmol) and 0.5 mL of dioxane/0.5 mL of THF or 4 mol% of NBS, 10 mol% of $AgSbF_6$, alkyne (0.7 mmol), alkyl substituted alcohol (0.5 mmol) and 1 mL of THF. The reaction mixture was heated at 120 °C for 18 h. Purification by flash chromatography on silica gel with hexanes and diethyl ether (100:1) afforded ketone products. The products were characterized by ^{1}H, ^{13}C, and ^{19}F NMR, and HRMS.

Synthesis of symmetrical ether

Reactions were performed in a tube-type Schlenk flask equipped with a stirring bar and the followings were placed in the tube-type flask: 4 mol% of NBS, 5 mol% of

$AgSbF_6$, alcohol (0.5 mmol) and 1 mL of dioxane. The reaction mixture was heated at 100 - 150°C for 0.25 - 15 h. Purification by flash chromatography on silica gel with hexanes and diethyl ether (100:1) afforded ether products.

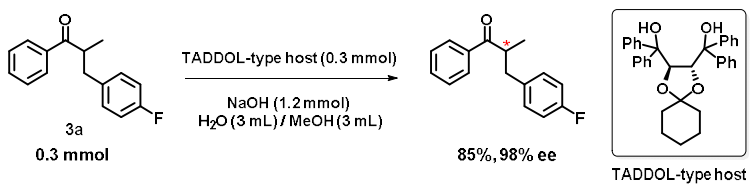
SI Table 5.2. Synthesis of symmetrical ether using various alcohols without alkyne[a]



Entry	R	Time	Temp (°C)	Yield (%)
1	$PhCH_2$	3 h	100	82(86[a])
2	$4\text{-}MeC_6H_4CH_2$	15 min	100	80
3	$4\text{-}(CH_3)_2CHC_6H_4CH_2$	15 min	100	81(84[b])
4	$4\text{-}(CH_3)_3CC_6H_4CH_2$	15 min	100	74
5	$4\text{-}FC_6H_4CH_2$	5 h	100	84 (87[c])
6	$4\text{-}ClC_6H_4CH_2$	5 h	100	80
7	$4\text{-}BrC_6H_4CH_2$	5 h	100	70
8	$2\text{-}IC_6H_4CH_2$	5 h	100	45
9	$Ph(CH_2)_2CH_2$	15 h	150	50
10	$CH_3(CH_2)_5CH_2$	15 h	150	47(55[d])

[a]$AgSbF_6$ (30 mol%). [b]1 h. [c]dioxane (0.3 mL), 24 h. [d]NBS (10 mol%), $AgSbF_6$ (30 mol%). [e]dioxane (0.3 mL).

Introduction of a stereogenic center to 3-(4-fluorophenyl)-2-methyl-1-phenylpropan-1-one (3a)

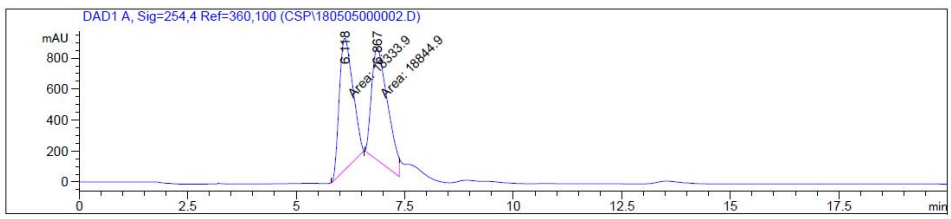


Reactions were performed in a tube-type Schlenk flask equipped with a stirring bar. **3a** (72.6 mg, 0.3 mmol), distilled H_2O (3 mL) and, NaOH (48 mg, 1.2 mmol) were added to a solution of TADDOL-type host (152 mg, 0.3 mmol) in MeOH (3 mL) in a flask.

The resulting suspension was stirred at room temperature for 2 days. The mixture was filtered, and the residue was washed with a mixture of H_2O/MeOH (1:1; 4 x 2 mL). The resulting white solid was dissolved in diethyl ether, and the resulting solution was dried with $MgSO_4$ and filtered. After removal of the solvent by a rotary evaporator, the residue was suspended again in a fresh mixture of H_2O/MeOH (v/v, 1:1; total 6 mL) and left at ambient temperature for 1 d. After filtration followed by washing with H_2O/MeOH (v/v, 1:1; 4 x 2 mL), the residue was dissolved in diethyl ether. The resulting solution was dried with $MgSO_4$ and filtered, and the solvent was removed by a rotary evaporator. The residue was purified by silica gel column chromatography (hexanes/diethyl ether, 100/1) to give chiral **3a** (61.7 mg, 85 %; 98 % ee) as a colorless oil.

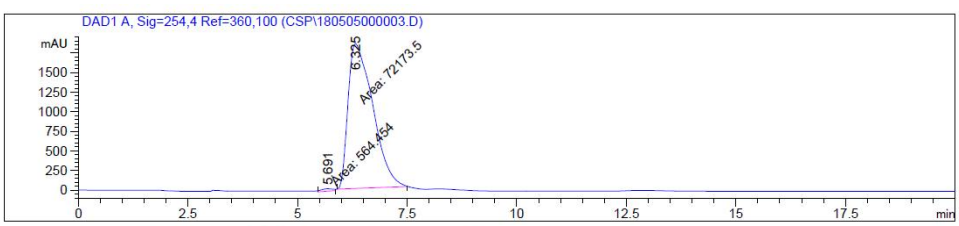
Chiral HPLC Analysis

$[\alpha]_D^{20}$ = +64.5 (*c* = 1, $CHCl_3$); HPLC separation: (CHIRALCEL OD-H, Hexanes: iPrOH = 99:1, 1.0 mL/min, tR (minor) = 5.691 min, tR (major) = 6.325 min); column dimension – ID 4.6 mm, Length 250 mm, Particle size 5 µm



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.118	MM	0.3589	1.83339e4	851.40076	49.3127
2	6.867	MM	0.4353	1.88449e4	721.52344	50.6873
Totals :				3.71788e4	1572.92419	

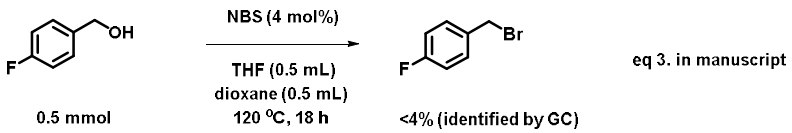


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.691	MM	0.3154	564.45367	29.82826	0.7760
2	6.325	MM	0.6513	7.21735e4	1846.78857	99.2240
Totals :				7.27380e4	1876.61684	

Further mechanism study

1) Additional data of the mechanism study

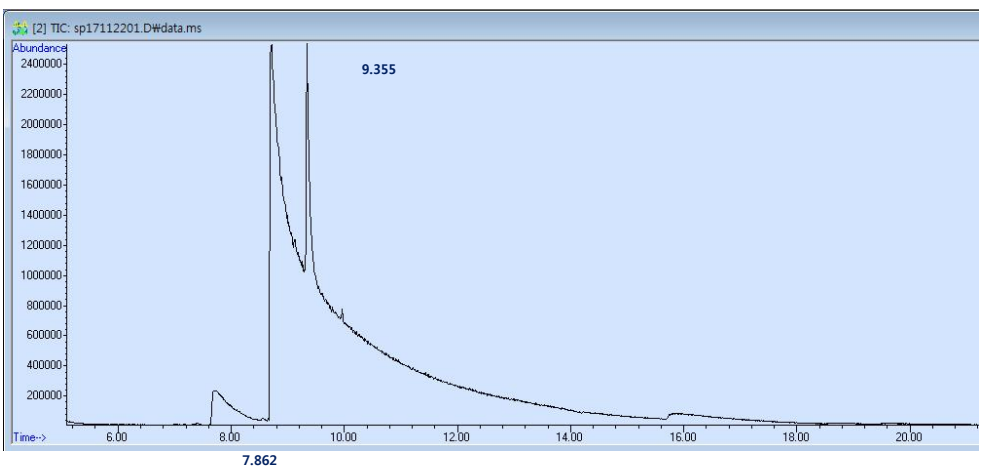


0.5 mmol

<4% (identified by GC)

eq 3. in manuscript

The role of NBS is to convert benzyl alcohol into benzyl bromide. The reaction mechanism will be as shown below. In fact, some aldehydes were found by analyzing GC-MS.



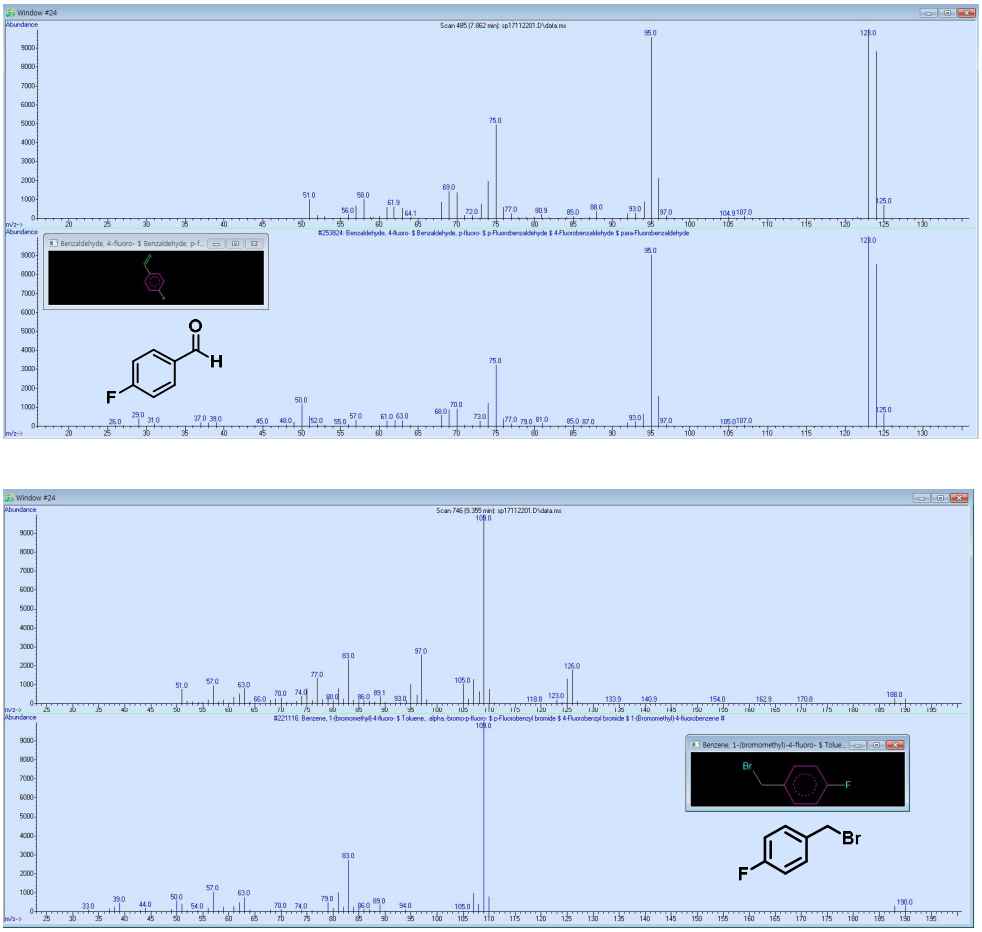


Figure S1. GC-MS data of control experiment eq 3

Retention times – 7.862 min: 4-fluoro benzaldehyde

8.720 min: 4-fluorobenzyl alcohol

9.355 min: 1-(bromomethyl)-4-fluorobenzene

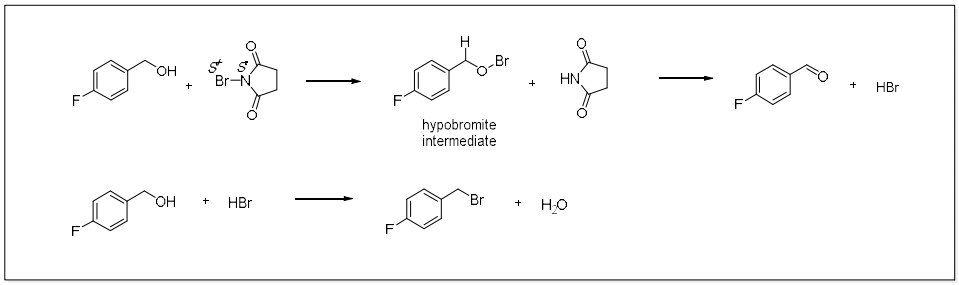
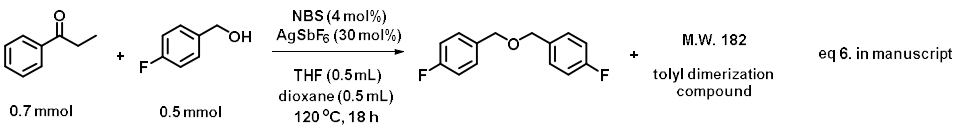
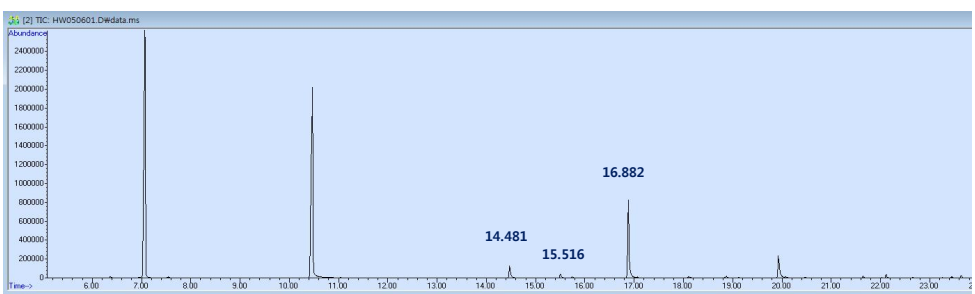
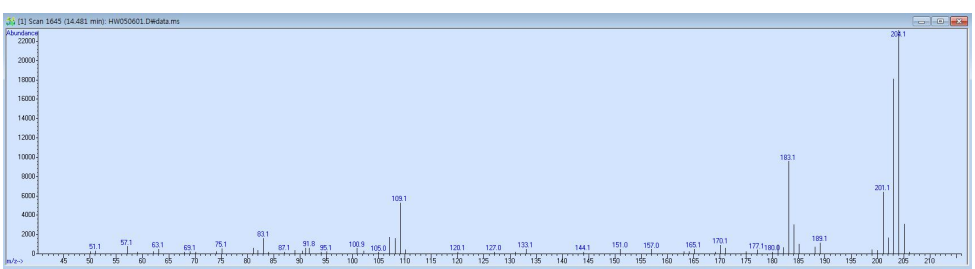


Figure S2. Proposed pathway for 1-(bromomethyl)-4-fluorobenzene



This reaction seems to proceed via a the radical pathway, which can be partially proved by experiments with a radical scavenger and by detection of dimerized tolyl products.





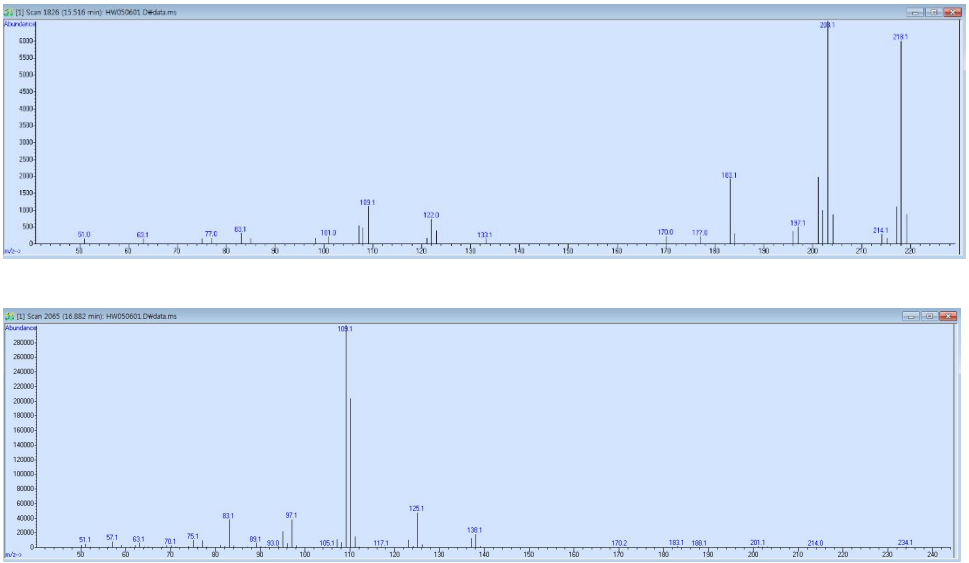
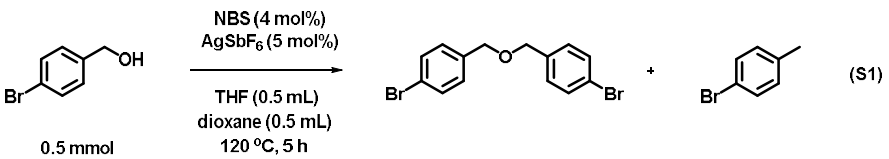


Figure S3. GC-MS data of dimerized tolyl product

Retention time – 14.481 min: M.W. 204.1

15.516 min: dimerized tolyl product (M.W. 218.1)

16.882 min: 4,4'-(oxybis(methylene))bis(fluorobenzene)



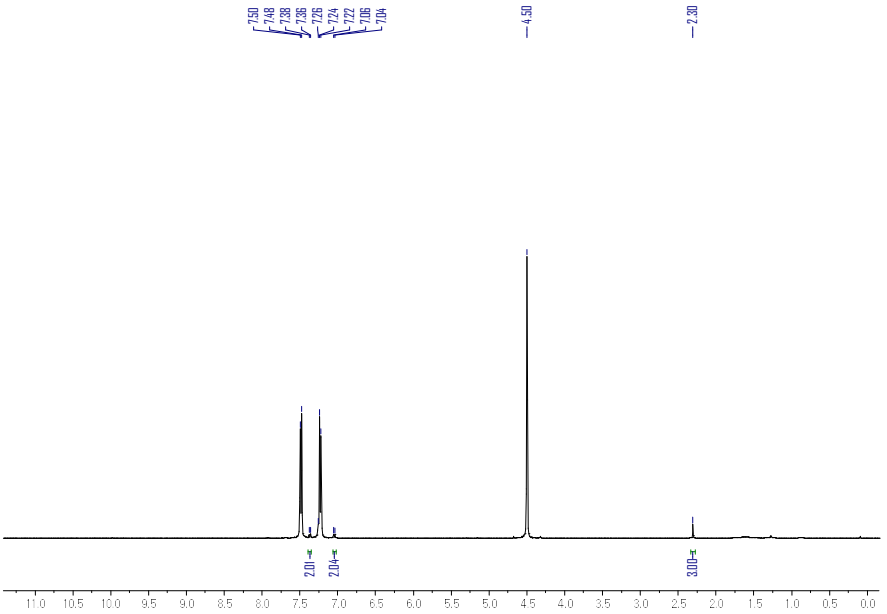
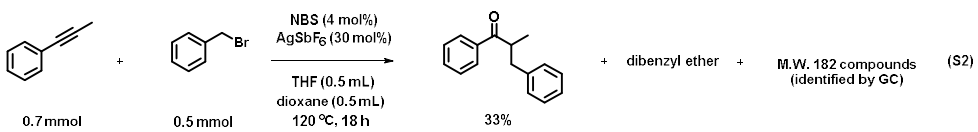


Figure S4. ^{1}H NMR of 4-bromotoluene



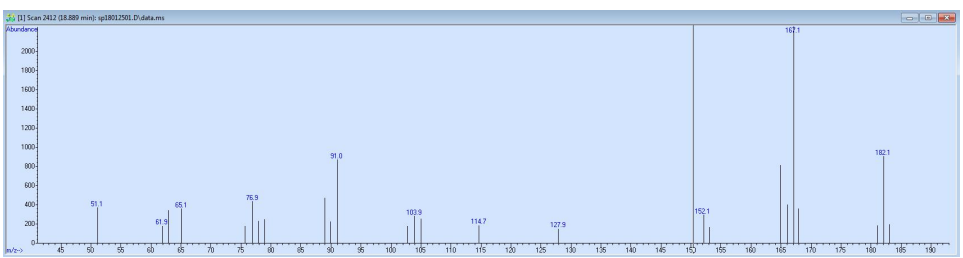
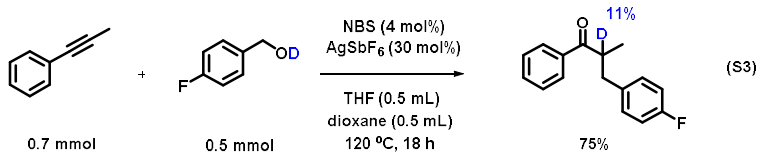


Figure S5. GC-MS data of tolyl dimerized compound

Retention time – 18.889 min: M.W. 182.1



This experiment (eq S3) suggested that most of H_2O used as the nucleophile was from the solvent rather than that produced in the ether formation.

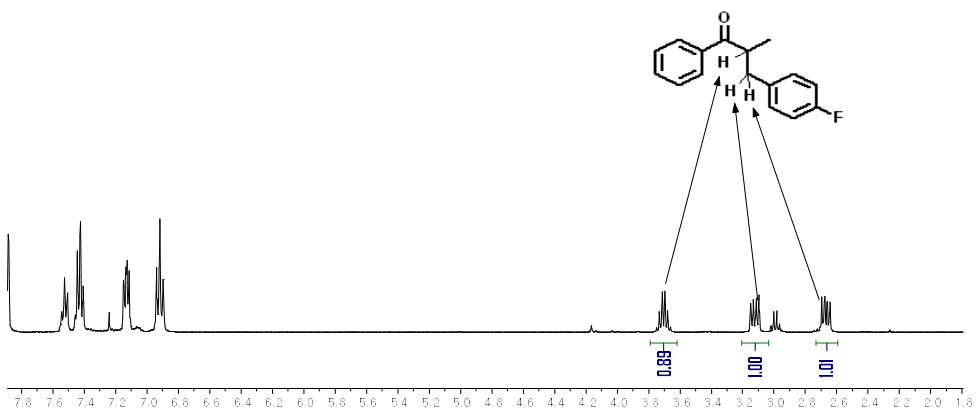
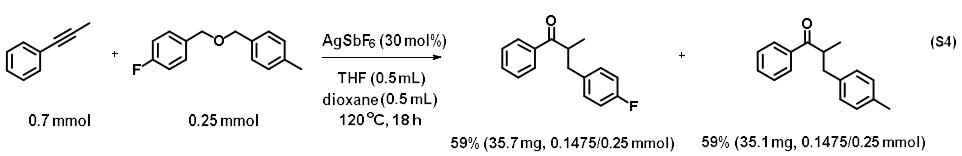
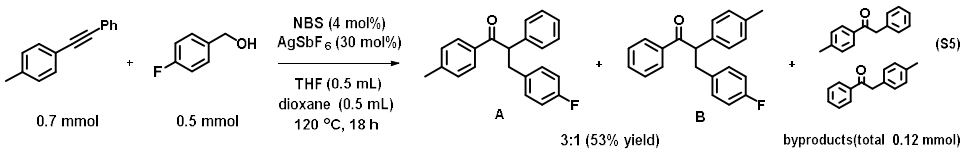


Figure S6. ^{1}H NMR of deuterium substituted product (3a')

2) Selectivity study



A selectivity test for ether cleavage was carried out, but no specific result was obtained.



A and B were generated in a ratio of 3: 1, which could be explained by the stability of the vinyl cation as a reaction intermediate. As a side reaction, ketones were produced by a reaction between alkyne and water.

Characterization of compounds

3a: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.7 Hz, 2H), 7.46 (t, *J* = 7.3 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.10 – 7.02 (m, 2H), 6.85 (t, *J* = 8.5 Hz, 2H), 3.68 – 3.59 (m, 1H), 3.06 (dd, *J* = 13.8, 6.7 Hz, 1H), 2.60 (dd, *J* = 13.8, 7.4 Hz, 1H), 1.12 (d, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.7, 161.6 (d, *J* = 244.1 Hz), 136.5, 135.7 (d, *J* = 3.2 Hz), 133.1, 130.6 (d, *J* = 7.9 Hz), 128.8, 128.4, 115.3 (d, *J* = 21.2 Hz), 43.0, 38.6, 17.7 ppm. HRMS (EI) calc. for [$C_{16}H_{15}FO$]: 242.1107, found: 242.1104; colorless oil.

3b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 3.78 –

3.66 (m, 1H), 3.14 (dd, J = 13.7, 6.8 Hz, 1H), 2.68 (dd, J = 13.8, 7.4 Hz, 1H), 1.20 (d, J = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 138.5, 136.4, 133.2, 132.1, 130.6, 128.8, 128.6, 128.4, 42.8, 38.7, 17.7 ppm. HRMS (EI) calc. for [$C_{16}H_{15}ClO$]: 258.0811, found: 258.0815; colorless oil.

3c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.3 Hz, 2H), 7.55 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 8.2 Hz, 2H), 3.77 – 3.66 (m, 1H), 3.12 (dd, J = 13.7, 6.8 Hz, 1H), 2.66 (dd, J = 13.7, 7.4 Hz, 1H), 1.20 (d, J = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 139.1, 136.4, 133.2, 131.5, 130.9, 128.8, 128.4, 120.1, 42.7, 38.7, 17.7 ppm. HRMS (EI) calc. for [$C_{16}H_{15}BrO$]: 302.0306, found: 302.0306; colorless oil.

3d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.5 Hz, 2H), 7.57 (d, J = 8.2 Hz, 2H), 7.45 (t, J = 7.6 Hz, 2H), 7.26 (s, 1H), 6.95 (d, J = 8.1 Hz, 2H), 3.76 – 3.66 (m, 1H), 3.11 (dd, J = 13.8, 6.7 Hz, 1H), 2.65 (dd, J = 13.7, 7.4 Hz, 1H), 1.20 (d, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 139.8, 137.6, 136.4, 133.2, 131.3, 128.8, 128.4, 91.5, 42.7, 38.9, 17.8 ppm. HRMS (EI) calc. for [$C_{16}H_{15}IO$]: 350.0168, found: 350.0164; colorless oil.

3e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.2 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.5 Hz, 2H), 7.11 – 7.05 (m, 4H), 3.77 – 3.67 (m, 1H), 3.13 (dd, J = 13.7, 6.1 Hz, 1H), 2.64 (dd, J = 13.7, 8.0 Hz, 1H), 2.30 (s, 3H), 1.19 (d, J = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.9, 136.9, 136.6, 135.8, 133.0, 129.2, 129.1, 128.8, 128.4, 43.0, 39.0, 21.2, 17.4 ppm. HRMS (EI) calc. for [$C_{17}H_{18}O$]: 238.1358, found: 238.1357; colorless oil.

3f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.6 Hz, 2H), 7.54 (t, J = 7.3 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.12 (s, 4H), 3.78 – 3.66 (m, 1H), 3.13 (dd, J = 13.7, 6.1

Hz, 1H), 2.92 – 2.78 (m, 1H), 2.66 (dd, *J* = 13.7, 7.9 Hz, 1H), [1.22, 1.21, 1.19] (3H and 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 146.9, 137.4, 136.6 133.0, 129.1, 128.7, 128.4, 126.5, 42.9, 39.1, 33.8, 24.2, 17.5 ppm. HRMS (EI) calc. for [$C_{19}H_{22}O$]: 266.1671, found: 266.1667; colorless oil.

3g: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.3 Hz, 2H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 3.78 – 3.68 (m, 1H), 3.13 (dd, *J* = 13.8, 6.1 Hz, 1H), 2.66 (dd, *J* = 13.8, 7.9 Hz, 1H), 1.29 (s, 9H), 1.20 (d, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 149.1, 137.0, 136.6, 133.0, 128.9, 128.7, 128.4, 125.4, 42.9, 39.0, 34.5, 31.5, 17.5 ppm. HRMS (EI) calc. for [$C_{20}H_{24}O$]: 280.1827, found: 280.1825; colorless oil.

3h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.14 (dd, *J* = 8.4, 5.6 Hz, 2H), 6.93 (t, *J* = 8.7 Hz, 2H), 3.75 – 3.63 (m, 1H), 3.12 (dd, *J* = 13.8, 6.8 Hz, 1H), 2.67 (dd, *J* = 13.8, 7.4 Hz, 1H), 2.40 (s, 3H), 1.18 (d, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.3, 161.6 (d, *J* = 243.7 Hz), 144.0, 135.8 (d, *J* = 3.0 Hz), 134.0, 130.6 (d, *J* = 7.9 Hz), 129.5, 128.5, 115.2 (d, *J* = 21.1 Hz), 42.8, 38.7, 21.8, 17.8 ppm. HRMS (EI) calc. for [$C_{17}H_{17}FO$]: 256.1263, found: 256.1260; colorless oil.

3i: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.38 – 7.29 (m, 2H), 7.14 (dd, *J* = 8.3, 5.6 Hz, 2H), 6.93 (t, *J* = 8.6 Hz, 2H), 3.76 – 3.64 (m, 1H), 3.13 (dd, *J* = 13.8, 6.8 Hz, 1H), 2.67 (dd, *J* = 13.8, 7.4 Hz, 1H), 2.39 (s, 3H), 1.19 (d, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.9, 161.6 (d, *J* = 244.1 Hz), 138.6, 136.6, 135.8 (d, *J* = 3.2 Hz), 133.9, 130.6 (d, *J* = 7.8 Hz), 128.9, 128.7, 125.6, 115.2 (d, *J* = 21.1 Hz), 43.0, 38.7, 21.5, 17.8ppm. HRMS (EI) calc. for [$C_{17}H_{17}FO$]: 256.1263, found: 256.1264; colorless oil.

3j: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.7 Hz, 1H), 7.33 (t, *J* = 7.1 Hz, 1H), 7.24 – 7.17 (m, 2H), 7.14 (dd, *J* = 8.4, 5.6 Hz, 2H), 6.94 (t, *J* = 8.7 Hz, 2H), 3.57 – 3.48 (m, 1H), 3.12 (dd, *J* = 13.7, 7.1 Hz, 1H), 2.62 (dd, *J* = 13.7, 7.3 Hz, 1H), 2.38 (s, 3H), 1.15 (d, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.0, 161.6 (d, *J* = 244.0 Hz), 138.6, 137.9, 135.8 (d, *J* = 3.3 Hz), 131.8, 131.0, 130.6 (d, *J* = 7.8 Hz), 127.6, 125.7, 115.3 (d, *J* = 21.1 Hz), 46.5, 38.4, 20.9, 17.2 ppm. HRMS (EI) calc. for [$C_{17}H_{17}FO$]: 256.1263, found: 256.1264; colorless oil.

3k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.3 Hz, 2H), 7.95 (d, *J* = 8.3 Hz, 2H), 7.14 (dd, *J* = 8.1, 5.6 Hz, 2H), 6.94 (t, *J* = 8.6 Hz, 2H), 3.77 – 3.67 (m, 1H), 3.13 (dd, *J* = 13.8, 7.0 Hz, 1H), 2.70 (dd, *J* = 13.8, 7.2 Hz, 1H), 2.63 (s, 3H), 1.21 (d, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 197.5, 161.6 (d, *J* = 244.3 Hz), 140.2, 139.8, 135.4 (d, *J* = 3.2 Hz), 130.6 (d, *J* = 7.9 Hz), 128.7, 128.5, 115.3 (d, *J* = 21.1 Hz), 43.5, 38.6, 27.0, 17.6 ppm. HRMS (EI) calc. for [$C_{18}H_{17}FO_2$]: 284.1213, found: 284.1214; colorless oil.

4a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.4 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.12 (dd, *J* = 8.3, 5.5 Hz, 2H), 6.90 (t, *J* = 8.7 Hz, 2H), 3.68 – 3.58 (m, 1H), 3.07 (dd, *J* = 13.7, 8.0 Hz, 1H), 2.76 (dd, *J* = 13.7, 6.2 Hz, 1H), 1.86 – 1.74 (m, 1H), 1.64 – 1.56 (m, 1H), 0.89 (t, *J* = 7.4 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.8, 161.5 (d, *J* = 243.9 Hz), 137.6, 135.8 (d, *J* = 3.2 Hz), 133.0, 130.5 (d, *J* = 7.8 Hz), 128.7, 128.2, 115.2 (d, *J* = 21.2 Hz), 49.9, 36.9, 25.5, 11.8ppm. HRMS (EI) calc. for [$C_{17}H_{17}FO$]: 256.1263, found: 256.1260; colorless oil.

4b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.78 (m, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.11 (dd, *J* = 8.4, 5.6 Hz, 2H), 6.89 (t, *J* = 8.7 Hz, 2H), 3.74 – 3.65 (m, 1H), 3.07 (dd, *J* = 13.7, 8.2 Hz, 1H), 2.75 (dd, *J* = 13.7, 6.0 Hz,

1H), 1.84 – 1.71 (m, 1H), 1.56 – 1.47 (m, 1H), 1.38 – 1.18 (m, 2H), 0.86 (t, J = 7.3 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 161.5 (d, J = 243.9 Hz), 137.6, 135.8 (d, J = 3.2 Hz), 133.0, 130.5 (d, J = 7.8 Hz), 128.7, 128.2, 115.2 (d, J = 21.1 Hz), 48.4, 37.5, 34.9, 20.7, 14.3 ppm. HRMS (EI) calc. for [$C_{18}H_{19}FO$]: 270.1420, found: 270.1419; colorless oil.

4c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 7.3 Hz, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.11 (dd, J = 8.3, 5.6 Hz, 2H), 6.89 (t, J = 8.7 Hz, 2H), 3.72 – 3.63 (m, 1H), 3.07 (dd, J = 13.7, 8.1 Hz, 1H), 2.75 (dd, J = 13.7, 6.1 Hz, 1H), 1.90 – 1.68 (m, 1H), 1.61 – 1.44 (m, 1H), 1.32 – 1.17 (m, 4H), 0.83 (t, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 161.5 (d, J = 243.9 Hz), 137.6, 135.8 (d, J = 3.2 Hz), 133.0, 130.5 (d, J = 7.8 Hz), 128.7, 128.2, 115.2 (d, J = 21.1 Hz), 48.6, 37.5, 32.4, 29.6, 23.0, 14.0 ppm. HRMS (EI) calc. for [$C_{19}H_{21}FO$]: 284.1576, found: 284.1574; colorless oil.

4d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 7.4 Hz, 2H), 7.44 (t, J = 7.4 Hz, 1H), 7.34 (t, J = 7.6 Hz, 2H), 7.28 – 7.15 (m, 5H), 7.01 (dd, J = 8.4, 5.6 Hz, 2H), 6.86 (t, J = 8.7 Hz, 2H), 4.75 (t, J = 7.3 Hz, 1H), 3.51 (dd, J = 13.8, 7.4 Hz, 1H), 3.04 (dd, J = 13.8, 7.1 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.2, 161.6 (d, J = 244.0 Hz), 139.0, 136.8, 135.5 (d, J = 3.2 Hz), 133.1, 130.7 (d, J = 7.9 Hz), 129.1, 128.8, 128.6, 128.4, 127.4, 115.1 (d, J = 21.1 Hz), 56.2, 39.4 ppm. HRMS (EI) calc. for [$C_{21}H_{17}FO$]: 304.1263, found: 304.1265; colorless oil.

4e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 7.3 Hz, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.09 (s, 4H), 3.69 – 3.59 (m, 1H), 3.06 (dd, J = 13.7, 7.3 Hz, 1H), 2.90 – 2.79 (m, 1H), 2.74 (dd, J = 13.7, 6.8 Hz, 1H), 1.88 – 1.74 (m, 1H), 1.68 – 1.56 (m, 1H), 1.20 (d, J = 6.9 Hz, 6H), 0.87 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.1, 146.8, 137.7, 137.4, 132.9, 129.1, 128.7, 128.3,

126.5, 49.9, 37.5, 33.8, 25.3, 24.2, 11.8 ppm. HRMS (EI) calc. for [$C_{20}H_{24}O$]: 280.1827, found: 280.1825; colorless oil.

4f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.3 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.08 (s, 4H), 3.76 – 3.61 (m, 1H), 3.06 (dd, *J* = 13.7, 7.6 Hz, 1H), 2.89 – 2.77 (m, 1H), 2.73 (dd, *J* = 13.7, 6.5 Hz, 1H), 1.84 – 1.70 (m, 1H), 1.57 – 1.48 (m, 1H), 1.37 – 1.25 (m, 2H), 1.20 (t, *J* = 8.6 Hz, 6H), 0.85 (t, *J* = 7.3 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.3, 146.8, 137.8, 137.4, 132.9, 129.0, 128.6, 128.3, 126.5, 48.4, 38.0, 34.7, 33.8, 24.2, 20.8, 14.4 ppm. HRMS (EI) calc. for [$C_{21}H_{26}O$]: 294.1984, found: 294.1986; colorless oil.

4g: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.2 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.08 (s, 4H), 3.80 – 3.58 (m, 1H), 3.06 (dd, *J* = 13.7, 7.5 Hz, 1H), 2.89 – 2.78 (m, 1H), 2.73 (dd, *J* = 13.7, 6.5 Hz, 1H), 1.86 – 1.70 (m, 1H), 1.59 – 1.44 (m, 1H), 1.31 – 1.22 (m, 4H), 1.19 (d, *J* = 6.9 Hz, 6H), 0.82 (t, *J* = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.2, 146.7, 137.7, 137.4, 132.8, 129.0, 128.6, 128.3, 126.5, 48.5, 38.0, 33.8, 32.2, 29.7, 24.1, 23.0, 14.0 ppm. HRMS (EI) calc. for [$C_{22}H_{28}O$]: 308.2140, found: 308.2142; colorless oil.

5.5. References

(1) (a) Franck, H. G.; Stadelhofer, J. W. *Industrial Aromatic Chemistry*; Springer: Berlin, **1988**. (b) Surburg, H.; Panten, J. *Common Fragrance and Flavor Materials*; Wiley-VCH: Weinheim, **2006**, 5th ed. (c) Dieter, R. K. *Tetrahedron* **1999**, *55*, 4177–4236. (d) Wang, X. J.; Zhang, L.; Sun, X.; Xu, Y.; Krishnamurthy, D.; Senanayake, C. H. *Org. Lett.* **2005**, *7*, 5593–5595. (e) Batt, D. G.; Goodman, R.;

Jones, D. G.; Kerr, J. S.; Mantegna, L. R.; McAllister, C.; Newton, R. C.; Nurnberg, S.; Welch, P. K.; Covington, M. B. *J. Med. Chem.* **1993**, *36*, 1434–1442.

(2) (a) Xu, Z.-F.; Cai, C.-X.; Liu, J.-T. Org. Lett. 2013, 15, 2096-2099. (b) Huang, L.; Rudolph, M.; Rominger, F.; Hashmi, A.S.K. *Angew. Chem. Int. Ed.* **2016**, *55*, 4808−4813.

(3) (a) Caine, D. In *Comprehensive Organic Synthesis: Carbon-Carbon σ-Bond Formation*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; Vol. 3. (b) Cho, C. S. *J. Mol. Catal. A: Chem.* **2005**, *240*, 55–60. (c) Gansäuer, A., Fielenbach, D.; Stock, C.; Geich-Gimbel, D. *Adv. Synth. Catal.* **2003**, *345*, 1017–1030.

(4) (a) Pan, S.; Shibata, T. *ACS Catal.* **2013**, *3*, 704−712. (b) Gunanathan, C.; Milstein, D. *Science* **2013**, *341*, 1229712. (c) Ketcham, J. M.; Shin, I.; Montgomery, T. P.; Krische, M. J. *Angew. Chem. Int. Ed.* **2014**, *53*, 9142−9150. (d) Obora, Y. *ACS Catal.* **2014**, *4*, 3972−3981. (e) Huang, F.; Liu, Z.; Yu, Z. *Angew. Chem. Int. Ed.* **2016**, *55*, 862−875.

(5) (a) Guillena, G.; Ramon, D. J.; Yus, M. *Angew. Chem. Int. Ed.* **2007**, *46*, 2358–2364. (b) Nixon, T. D.; Whittlesey, M. K.; Williams, J. M. J. *Dalton Trans.* **2009**, 753–765. (c) Dobereiner, G. E.; Grabtree, R. H. *Chem. Rev.* **2010**, *110*, 681–703. (d) Guillena, G.; Ramon, D.; Yus, M. *Chem. Rev.* **2010**, *110*, 1611–1641. (e) Bähn, S.; Imm, S.; Neubert, L.; Zhang, M.; Neumann, H.; Beller, M. *ChemCatChem* **2011**, *3*, 1853–1864.

(6) (a) Taguchi, K.; Nakagawa, H.; Hirabayashi, T.; Sakaguchi, S.; Ishii, Y. *J. Am. Chem. Soc.* **2004**, *126*, 72–73. (b) Onodera, G.; Nishibayashi, Y.; Uemura, S. *Angew. Chem. Int. Ed.* **2006**, *45*, 3819–3822. (c) Kuwahara, T.; Fukuyama, T.; Ryu, I. *Org. Lett.* **2012**, *14*, 4703–4705. (d) Kwon, M. S.; Kim, N.; Seo, S. H.; Park, I. S.;

Cheedrala, R. K.; Park, J. *Angew. Chem. Int. Ed.* **2005**, *44*, 6913–6915. (e) Buil, M. L.; Esteruelas, M. A.; Herrero, J.; Izquierdo, S.; Pastor, I. M.; Yus, M. *ACS Catal.* **2013**, *3*, 2072–2075.

(7) (a) Schlepphorst, C.; Maji, B.; Glorius, F. *ACS Catal.* **2016**, *6*, 4184–4188. (b) Frost, J. R.; Cheong, C. B.; Akhtar, W. M.; Caputo, D. F. J.; Stevenson, N. G.; Donohoe, T. J. *J. Am. Chem. Soc.* **2015**, *137*, 15664−15667. (c) Yan, F.-X.; Zhang, M.; Wang, X.-T.; Xie, F.; Chen, M.-M.; Jiang, H. *Tetrahedron* **2014**, *70*, 1193−1198.

(8) Ma, J.; Wang, N.; Li, F. *Asian J. Org. Chem.* **2014**, *3*, 940–947.

(9) Thuong, M. B. T.; Mann, A.; Wagner, A. *Chem. Commun.* **2012**, *48*, 434–436.

(10) (a) Alonso, F.; Beletskaya, I. P.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079–3160. (b) Beller, M.; Seayad, J.; Tillack, A.; Jiao, H. *Angew. Chem. Int. Ed.* **2004**, *43*, 3368–3398.

(11) (a) Hartman, J. W.; Hiscox, W. C.; Jennings, P. W. *J. Org. Chem.* **1993**, *58*, 7613–7614. (b) Jennings, P. W.; Hartman, P. J. W.; Hiscox, W. C. *Inorg. Chim. Acta* **1994**, *222*, 317–322. (c) Hintermann, L.; Labonne, A. *Synthesis* **2007**, 1121–1150. (d) Tani, K.; Kataoka, Y. in *Catalytic Heterofunctionalisation* (Eds.: Togni, A.; Grützmacher, H.), Wiley-VCH, Weinheim, **2001**, 171–216. (e) Inu, K.; Imai, K.; Utimoto, K. *Tetrahedron Lett.* **1987**, *28*, 3127–3130. (f) Israelsohn, O.; Vollhardt, K. P. C.; Blum, J. *J. Mol. Catal. A: Chem.* **2002**, *184*, 1–10.

(12) Zheng, G.; Li, Y.; Han, J.; Xiong, T.; Zhang, Q. *Nature Commun.* **2015**, *6*, 7011.

(13) (a) Miura, K.; Yamamoto, K.; Yamanobe, A.; Ito, K.; Kinoshita, H.; Ichikawa, J.; Hosomi, A. *Chem. Lett.* **2010**, *39*, 766–767. (b) Yadav, J.S.; Subba Reddy, B.V.; Vishnumurthy, P. *Tetrahedron Lett.* **2008**, *49*, 4498–4500.

(14) Kaku, H.; Imai, T.; Kondo, R.; Mamba, S.; Watanabe, Y.; Inai, M.; Nishii, T.; Horikawa, M.; Tsunoda, T. *Eur. J. Org. Chem.* **2013**, 8208–8213.

(15) Malpani, Y. R.; Biswas, B. K.; Han, H. S.; Jung, Y.-S.; Han, S. B. *Org. Lett.* **2018**, *20*, 1693-1697.

(16) Xu, Q.; Xie, H.; Chen, P.; Yu, L.; Chena, J.; Hu, X. *Green Chem*. **2015**, *17*, 2774–2779.

국 문 초 록

Poly(3,4-dimethyl-5-vinylthiazolium) Iodide 촉매 반응에 관한 연구

제 1 부. Poly(3,4-dimethyl-5-vinylthiazolium) Iodide 을 촉매로 이용한 다양한 합성 전략

제 2 장

3,4-Dimethyl-5-vinylthiazolium iodide 또는 Poly(3,4-dimethyl-5-vinylthiazolium) iodide 을 촉매로 사용하여 불포화 탄소-탄소 결합에 대한 싸이올의 선택성이 높은 안티마르코브니코브 첨가 형태인 하이드로싸이올레이션 반응을 개발하였다. 새롭게 제안한 분자 모델이 포함된 메커니즘은 DFT 계산에 의해 확인되었다.

제 3 장

Poly(3,4-dimethyl-5-vinylthiazolium) iodide 을 기반으로 페닐실레인, DBU, 1 기압의 이산화탄소 등을 포함하는 촉매시스템은 2-아미노벤젠싸이올에서 벤조싸이아졸 합성이 가능한 활성을 보여주었다. 고분자 촉매는 또한 활성 변화없이 7 번의 재사용이 가능하였다.

제 4 장

고분자 촉매와 산화제인 페나진의 사용을 통해 알데하이드와 알코올의 에스터화 반응을 진행하였다. 반응은 상대적으로 낮은 온도에서 수월하게 진행되었으며, 산화제를 재사용한다는 장점을 가진다.

제 2 부. 은/NBS 를 촉매로 이용한 합성 전략

제 5 장

알파 위치에 알킬이 도입된 케톤을 합성하기 위해 내부 알카인과 벤질알코올, 그리고 촉매시스템으로 NBS 와 은을 사용하였다. 합리적인 실험들을 통해 에테르 중간체를 가지는 메커니즘 또한 제시하였다.

주요어: 하이드로싸이올레이션, 황, 이산화탄소, 벤조싸이아졸, 실레인, 재사용이 가능한 촉매, 에스터화, 페나진, 산화제, 폴리(nhc), 알파 위치에 알킬이 도입된 케톤, 실버헥사플루오르안티모네이트.

학번: 2014-22414