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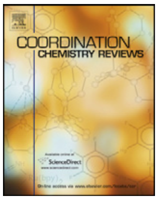

Review

Catalytic [2,3]-sigmatropic rearrangement of sulfur ylide derived from metal carbene

Yan Zhang[a], Jianbo Wang[a,b,*]

[a] *Beijing National Laboratory of Molecular Sciences (BNLMS), Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China*
[b] *State Key Laboratory of Organometallic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China*

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ABSTRACT

This paper reviews the most recent development of [2,3]-sigmatropic rearrangement of sulfur ylide generated from the reaction of sulfide with metal carbene. The metal carbene was formed from decomposition of diazo compounds catalyzed by transition metal complexes such as Cu(I) and Rh(II).

Abbreviations: $Rh_2(R\text{-BNP})_4$, dirhodium(II) tetrakis[(*R*)-binaphtholphosphate]; $Rh_2(R\text{-DDBNP})_4$, dirhodium(II) tetrakis[(*R*)-6,6′-didodecyl binapthol phosphate]; $Rh_2(S\text{-PTTL})_4$, dirhodium(II) tetrakis[(*S*)-*N*-phthaloyl-*tert*-leucinate]; $Rh_2(OAc)_4$, rhodium(II) acetate; $Rh_2(4R\text{-MEOX})_4$, dirhodium(II) tetrakis[methyl 2-oxooxazolidine-(4*R*)-carboxylate]; $Rh_2(4S\text{-MEOX})_4$, dirhodium(II) tetrakis[methyl 2-oxooxazolidine-(4*S*)-carboxylate]; $Rh_2(4S\text{-MPPIM})_4$, dirhodium(II) tetrakis[methyl 1-(3-phenylpropanoyl)-2-oxoimidazolidine-(4*S*)-carboxylate]; $Rh_2(S\text{-BPTV})_4$, dirhodium(II) tetrakis[(*S*)-*N*-benzene-fused phthaloyl-valinate]; Pybox, 2,6-bis(oxazolinyl)pyridine; $Rh_2(5S\text{-MEPY})_4$, dirhodium(II) tetrakis[methyl 2-pyrrolidine-(5*S*)-carboxylate]; $Rh_2(S\text{-TBSP})_4$, tetrakis[(2*S*)-1-[(4-*tert*-butylphenyl)-sulfonyl-pyrrolidinecarboxylate]dirhodium(II)]; $Rh_2(S\text{-DOSP})_4$, dirhodium(II) tetrakis[(*S*)-(−)-*N*-(*p*-dodecylphenylsulfonyl) prolinato]; $Rh_2({}^t\text{Bu-}(S)\text{-Pro})_4$, dirhodium(II) tetrakis[1-(4-*tert*-butylphenyl)-sulfonyl-(2*S*)-prolinate].

* Corresponding author at: Beijing National Laboratory of Molecular Sciences (BNLMS), Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China. Fax: +86 1062751708.
E-mail address: wangjb@pku.edu.cn (J. Wang).

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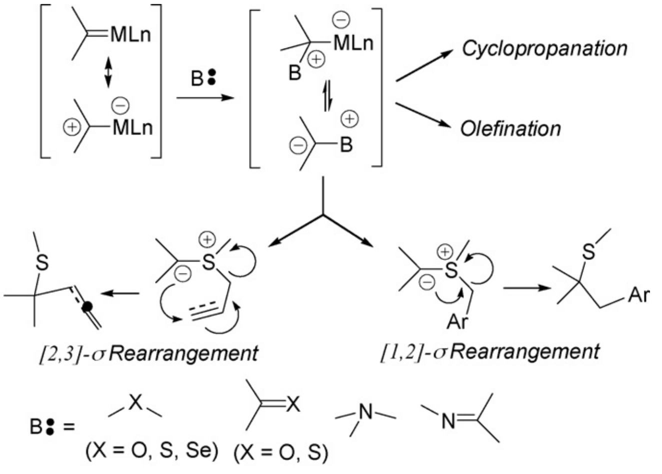
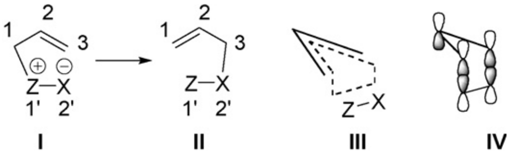
1. Introduction

Sulfur ylide can in general be formed through two main methods. One is the deprotonation of sulfonium salt promoted by base. Another way is the reaction of a sulfide with metal carbene, which can be generated by transition metal-catalyzed decomposition of diazo compounds (usually diazocarbonyl compounds). The latter method has been widely applied in organic chemistry. The divalent carbon of the metal carbene can form two new chemical bonds simultaneously and may produce new chiral center. Metal carbenes used as reactive intermediate in catalytic reactions play an important role in various transformations. Among the typical reaction of metal carbenes, the generation of a ylide species represents a unique process in that it can further lead to diverse transformations. The electron-deficient carbenic carbon easily reacts with nucleophiles such as Lewis base to generate a metal complex associated ylide or a free ylide. The typical reaction of the ylide intermediates falls into three main classes: (1) rearrangement reactions including [2,3]-sigmatropic rearrangement, [1,2]-sigmatropic rearrangement, Pummerer rearrangement, Sommelet–Hauser rearrangement, *etc.*; (2) cycloaddition including the formation of three membered rings such as cyclopropanation, epoxypropanation and aziridination; and five membered rings *via* [3 + 2] cycloaddition; (3) olefination reaction. The common Lewis bases that are used to react with metal carbene to generate ylides include esters, sulfides, amines, carbonyl compounds and imines (Scheme 1).

With various transformations, ylides can undergo intra- and intermolecular reactions, leading to the formation of products with increased complexity, especially those with heterocyclic structures. Therefore, this kind of reaction has significant applications in organic synthesis. Moreover, the recent development of asymmetric synthesis in this field opens more possibilities for their applications in the future. The metal carbene for reacting with Lewis bases to form ylides could be an unstable active intermediate that is generated *in situ*, or a stable Fisher carbene that undergoes subsequent reactions in a stoichiometric manner. Apparently, the catalytic transformations with the formation of unstable intermediates by transition metal-catalyzed decomposition of diazo compound are more attractive [1]. Sulfide groups easily interact with electron-deficient metal carbenes to generate the corresponding sulfur ylides. Useful reactions of the sulfonium ylides fall into two main classes: [2,3]-sigmatropic rearrangements and 1,2-shifts. The reactions of carbene-generated sulfur ylide have been reviewed previously [1], and most recently Sweenay has summarized the sigmatropic rearrangement of 'onium' ylides in a tutorial review which is closely related to its sulfur counterpart [2]. Herein in this review article we focus on the sigmatropic rearrangement of the sulfur ylides that are generated from metal carbene intermediates.



Scheme 1. Reactions of the ylide generated from metal carbene.



Scheme 2. Allyl-type ylide [2,3]-sigmatropic rearrangement process.

2. Catalytic [2,3]-sigmatropic rearrangement of sulfonium ylide generated from metal carbene

2.1. Introduction

[2,3]-Sigmatropic rearrangement is an orbital symmetry-controlled concerted reaction that undergoes rearrangement *via* an envelope transition state (Scheme 2). Sulfonium ylides generated from the reaction of metal carbene complexes and allyl, propargyl, or allenyl sulfides readily undergo [2,3]-sigmatropic rearrangements [3]. This type of rearrangement, known as the Doyle–Kirmse reaction, represents one of the most versatile bond re-organization processes in organic chemistry, and it is the most common type of reaction amongst the various sigmatropic rearrangements of sulfonium ylides. Moreover, high regioselectivity and stereoselectivity could be obtained from the ylide [2,3]-sigmatropic rearrangement because of the concerted nature of the reaction.

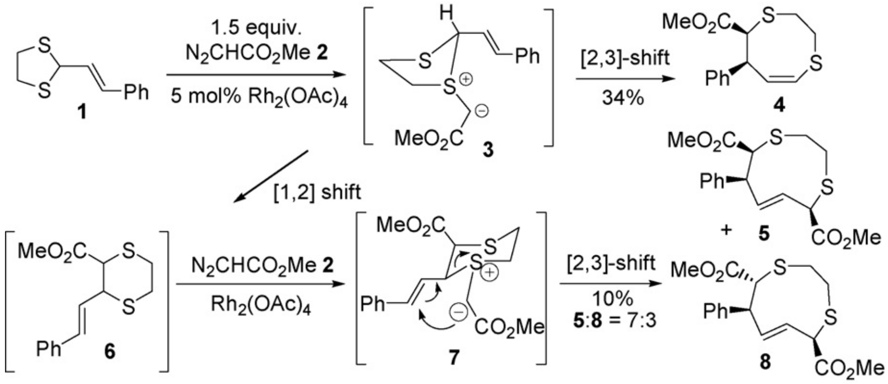
2.2. Recent examples of [2,3]-sigmatropic rearrangement of sulfonium ylide

Copper and rhodium complexes are the most efficient catalysts for diazo decomposition reactions, including ylide transformation [1]. Many examples utilizing these two types of catalyst in sulfur ylide transformations have appeared in the literature in recent years. For example, in the case of copper catalysts, Gulea et al. reported a $Cu(acac)_2$-catalyzed [2,3]-sigmatropic Wittig rearrangement of a sulfonium ylide intermediate generated from the reaction of diazomethanephosphonate with allylic sulfides. α-Phosphorylated γ, δ-unsaturated sulfides were produced in 60–75% yields [4a]. Khanova et al. disclosed their study on $Cu(OTf)_2$-catalyzed reaction of diazomethane with substituted 1,3-oxathiolanes to afford the corresponding 2,3,5,6-tetrahydro-1,4-oxathiocines formed *via* the [2,3]-sigmatropic rearrangement of the sulfonium ylide intermediates [4b].

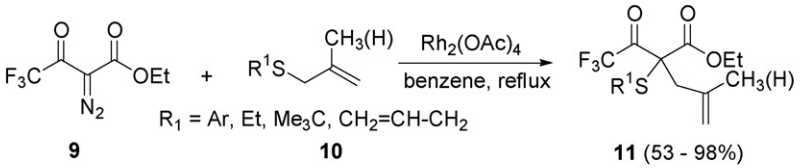
For the Rh(II) catalysts, Hanson et al. reported a $Rh_2(OAc)_4$-catalyzed reaction of α-diazophosphonate with diallyl sulfide, which affords [2,3]-sigmatropic rearrangement products in high yield [5].

An interesting reaction of sulfur ylide catalyzed by $Rh_2(OAc)_4$ is reported by Kostikov and co-workers recently. In this transformation, which is depicted in Scheme 3, the [1,2]-shift and [2,3]-sigmatropic rearrangement of the ylide intermediate are competing with each other [6]. Ditholane **1** and methyl diazoacetate (MDA, 2) can undergo a [2,3]-sigmatropic rearrangement to give **4** as the major product. Alternatively, a [1,2]-shift followed by another [2,3]-sigmatropic rearrangement can occur to generate products **5** and **8** as the minor products. The author pointed out that no signals corresponding to [1,2]-shift product dithiane **6** was observed in ^1H NMR.

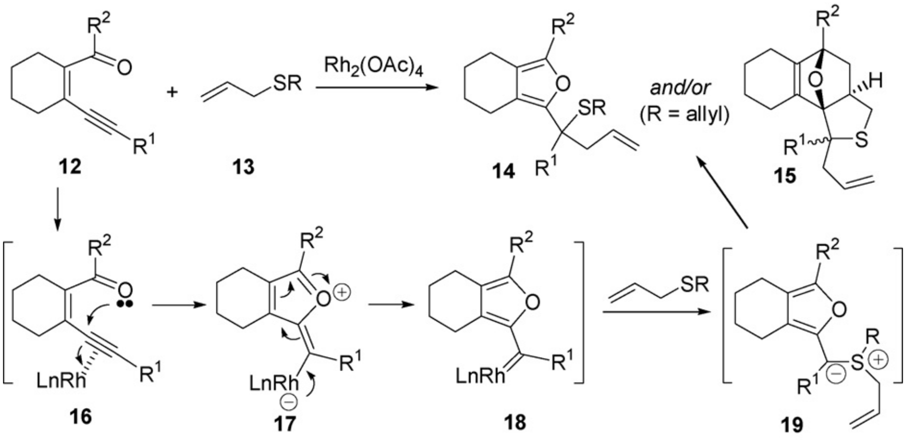
The sulfur ylide [2,3]-sigmatropic rearrangement has been used for the preparation of fluoro-containing sulfide compounds **11**. Zhu et al. reported an efficient Rh(II)-catalyzed rearrangement of



Scheme 3. [1,2]-Shift *versus* [2,3]-sigmatropic rearrangement.



Scheme 4. [2,3]-Sigmatropic rearrangement of fluoro-containing sulfur ylide.



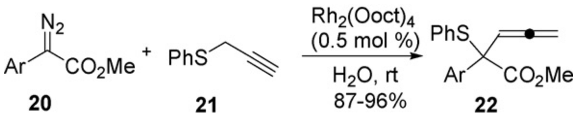
Scheme 5. Diazoalkane-free Doyle–Kirmse reaction of sulfonium ylide.

trifluoroacetyl-containing sulfur ylides in high yield. As expected, the electron donating groups on the aromatic ring of the sulfides were found to enhance reactivity, but the reaction also worked with a weakly electron-withdrawing group such as chloro on the aromatic ring, albeit in low yield (Scheme 4) [7].

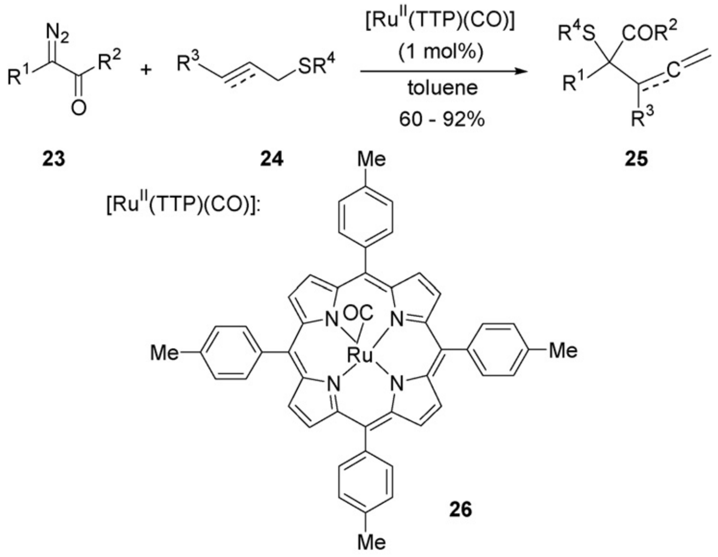
To further extend the pool of carbene precursors, there are some reports on developing alternative precursors other than diazo compounds for metal carbene generation. An interesting case of diazoalkane-free Doyle–Kirmse reaction has been reported by Uemura and co-workers. With $Rh_2(OAc)_4$ as catalyst, (2-furyl)carbenoid species is generated from conjugated ene-yne-carbonyl compounds **12** through the activation of the triple bond and the subsequent intramolecular nucleophilic attack by carbonyl oxygen (**16**–**17**). The Rh(II) carbene species **18** is trapped by allyl sulfides to form a sulfur ylides **19**, which undergo [2,3]-sigmatropic rearrangement to afford furan derivatives **14** in good yields. It is worth noticing that the intramolecular Diels–Alder reaction occurs to yield **15** ($R^2 = H$) if the reaction is carried out under reflux (Scheme 5) [8].

The Doyle–Kirmse reaction is usually performed in anhydrous organic solvent under inert atmosphere in order to avoid side reactions. However, it has been recently demonstrated that [2,3]-sigmatropic rearrangement of sulfur ylide derived from Rh(II) carbene and sulfide **21** can be efficiently performed in water to afford allene derivatives **22** (Scheme 6) [9]. Although the O–H insertion is a well known transformation of Rh(II) carbenes, the O–H insertion product is not identified in this reaction. This results may serve as an excellent example of “on water” reaction [10].

Besides the traditional Cu(I) and Rh(II) catalysts, other transition metal catalysts are also explored in this area in recent years. Che’s group studied ruthenium porphyrin complex $[Ru^{II}(TTP)(CO)]$ (*meso*-tetrakis(*p*-tolyl)porphyrinatoruthenium(II) carbonyl, **26**) catalyzed [2,3]-sigmatropic rearrangement of sul-



Scheme 6. [2,3]-Sigmatropic rearrangement “on water”.



Scheme 7. Ru-catalyzed [2,3]-sigmatropic rearrangement.

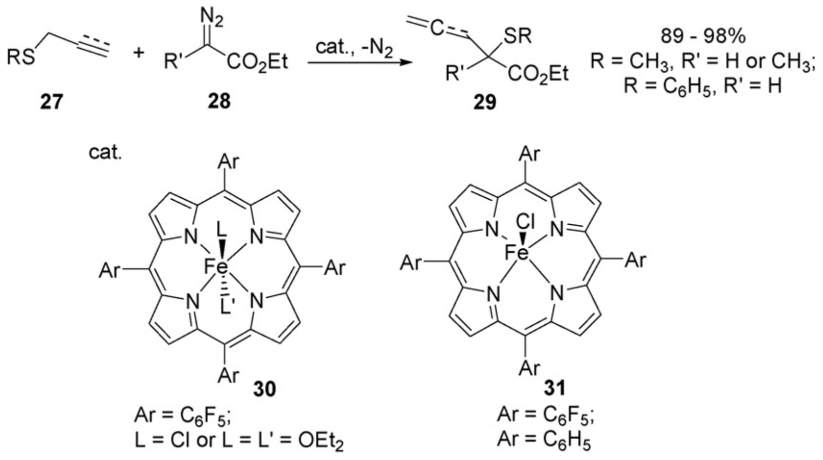
fur ylide generated from a metal carbene. Exclusive formation of [2,3]-sigmatropic rearrangement products **25** (70–80% yields) was observed, without any [1,2]-shift products being detected. The result was applied to the synthesis of (±)-platynecine [11] (Scheme 7). [2,3]-Sigmatropic rearrangement of sulfur ylide catalyzed by ruthenium compound has also been investigated by Xiao and Wang [12].

Due to the low cost of the metal, iron complexes are plausible candidates for catalysts in organic reactions. However, the chemistry of iron catalysts has been less developed in comparison with many other transition metal catalysts. In recent years, iron catalyzed reactions have received increasing attention. One present example of Iron catalysis is the iron(III)-catalyzed [2,3]-sigmatropic rearrangement of sulfonium ylide. Iron(III) corroles **30** and porphyrins complexes **31** were proved to be efficient for this reaction (Scheme 8) [13].

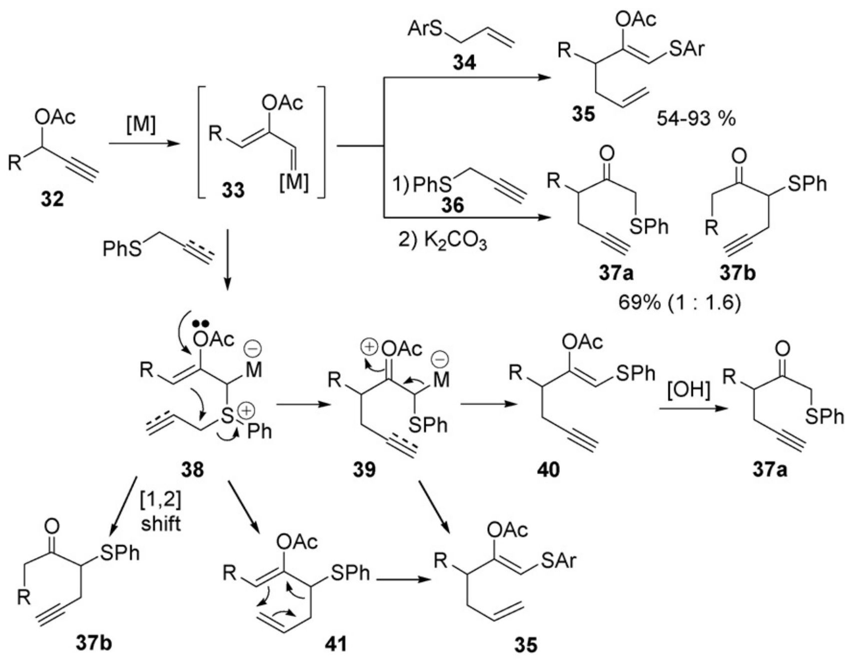
The past few years have witnessed explosive development of gold-catalyzed reactions. Gold compound is also an efficient catalyst in [2,3]-sigmatropic rearrangement of sulfur ylide. As a consequence, propargylic carboxylates **32**, which are widely applied in gold catalysis, were employed as precursors for the generation of gold carbenes. In the presence of allyl sulfide **34** or propargyl sulfide **36**, the sulfur ylides were generated to rearrange. Interestingly, in this reaction AuCl had to be applied to the reaction of allyl sulfide **34**, while $AuCl_3$ was used for the reaction with propargyl thioether **36**, respectively (Scheme 9) [14]. The mechanism of the first reaction involves [2,3]-sigmatropic rearrangement of the allyl fragment in **38**, generating intermediate **41**, which then undergoes a Cope rearrangement to give the final products **35**. Alternatively, **35** might be formed through oxygen-assisted 1,4-shift to give intermediate **39**, followed by subsequent elimination of the metal catalyst. For the reaction with propargyl thioether **36**, one pathway is the direct [1,2]-shift, which affords product **37b**. **37a** is formed through intermediate **40**, followed by hydrolysis. This investigation not only represents the first example of gold catalysis in this area, but also demonstrates the possibility to utilize propargylic carboxylates as metal carbene precursor in this type of reaction.

SmI_2 was also used for [2,3]-rearrangement of allyl sulfonium ylides by the reaction of allyl sulfides with samarium carbenoid, generated from CH_2I_2 and SmI_2 in THF [15].

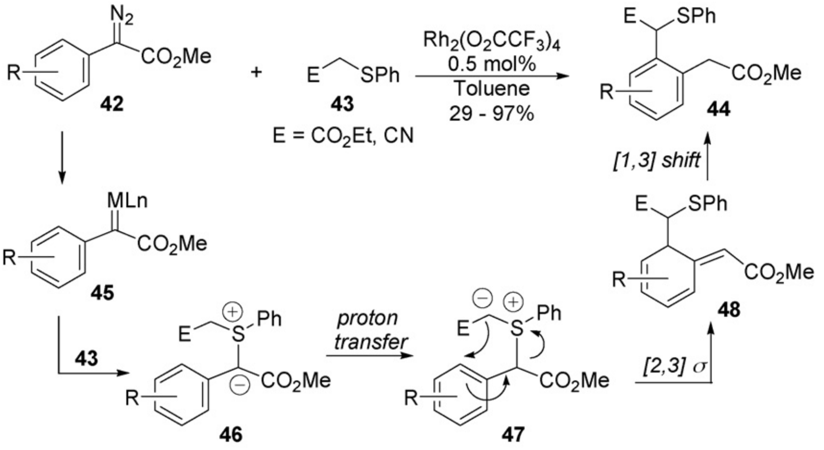
The aromatic double bond can also be involved in sulfur ylide [2,3]-sigmatropic rearrangement. Recently, the first example of Rh(II)-catalyzed Sommelet–Hauser rearrangement of sulfonium ylide has been reported [16]. The reaction gives ylide **46** through interaction of Rh(II) carbene **45** with the sulfide **43**, which is



Scheme 8. Fe-catalyzed [2,3]-sigmatropic rearrangement.



Scheme 9. Au-catalyzed [2,3]-sigmatropic rearrangements.

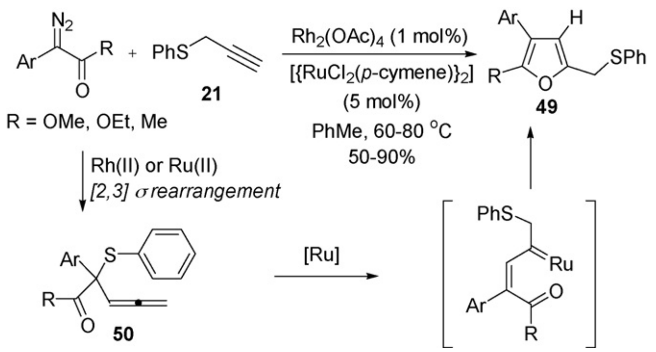


Scheme 10. Rh(II)-catalyzed Sommelet–Hauser rearrangement of sulfonium ylide.

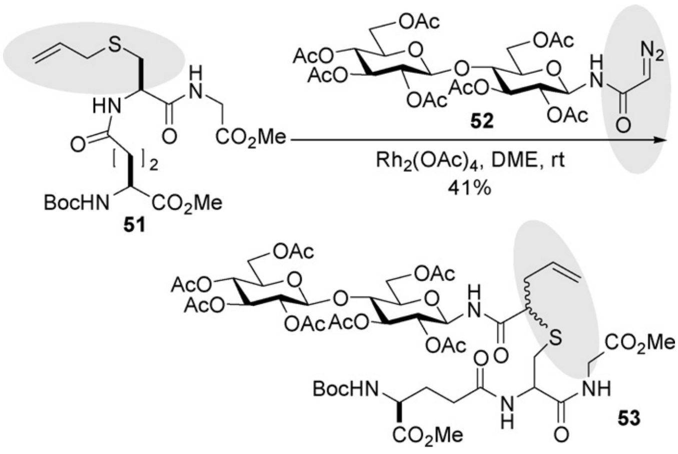
followed by proton transfer to generate ylide **47**. From **47**, the [2,3]-sigmatropic rearrangement occurs to form dearomatized intermediate **48**. Finally, the [1,3] hydrogen shift affords the final product **44**. The entire catalytic process was facile, and the rearrangement products were obtained in good to excellent yields. This reaction serves as a unique method for the preparation of *ortho*-substituted aromatic compounds (Scheme 10).

The allenyl sulfides **50**, obtained from the [2,3]-sigmatropic rearrangement of sulfonium ylides generated from Rh(II) carbene and propargyl sulfide **21**, can be further applied in a Ru(II) catalyzed reaction to afford furan derivatives through a 1,4 migration of the sulfanyl group and generation of Ru carbene intermediates. This discovery leads to a one-pot sequential catalytic transformation of α-diazocarbonyl compounds to furan derivatives **49** (Scheme 11) [17].

Sulfur [2,3]-sigmatropic rearrangement has also been applied in the field of bioorganic chemistry. For example, Crich and co-workers have used this rearrangement as a tool for amino-acid and peptide modification in the presence of $Rh_2(OAc)_4$ (Scheme 12) [18]. Even though there are many potential sites which may interact with Rh(II) carbene, such as N-H bonds and carbonyl groups in both the allyl sulfide **51** and the diazo substrate **52**, the sulfur ylide [2,3]-sigmatropic rearrangement product **53** is still formed in reasonable yield. This demonstrates that the reaction of Rh(II) carbene



Scheme 11. [2,3]-Sigmatropic rearrangement followed by 1,4 migration of the sulfanyl group.



Scheme 12. Sulfur [2,3]-sigmatropic rearrangement in peptide modification.

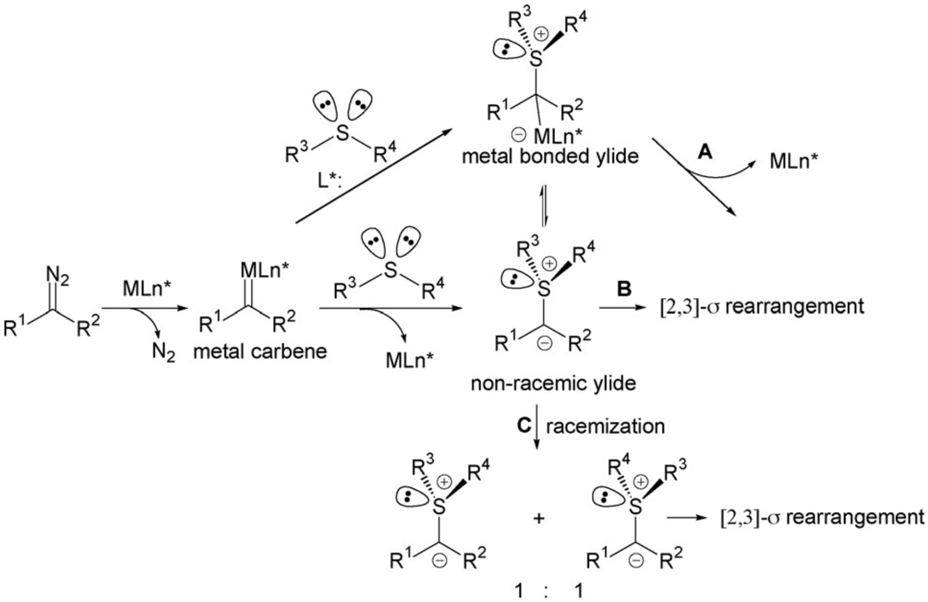
and sulfide and the subsequent [2,3]-sigmatropic rearrangement are highly preferred processes.

3. Asymmetric [2,3]-sigmatropic rearrangement of sulfonium ylide

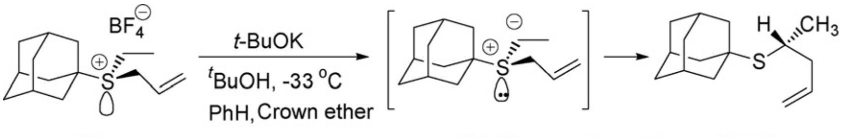
3.1. Introduction

As mentioned earlier, metal carbenes are generated by decomposition of diazo compounds catalyzed by transition metal complexes, which would further react with Lewis base to generate ylide and undergo subsequent rearrangement. When chiral metal complexes are applied to this type of reaction, there are three possible routes for the following rearrangement of the ylide intermediate (Scheme 13) [1g,3c]. (A) Chiral catalyst is associated with ylide during the rearrangement, which means sigmatropic rearrangement would be completed with chiral catalyst-associated ylide. In such case, the chiral catalyst may affect the stereochemistry of the rearrangement product. Thus, asymmetric catalysis is possible under such circumstance. (B) Chiral catalyst has been released already when the rearrangement occurs, but the ylide may retain the chirality which is induced in the previous step by the reaction of chiral metal carbene with sulfide. Asymmetric induction is also possible in this case because the [2,3]-sigmatropic rearrangement occurs through a concerted process. This requires that the racemization of the sulfur chiral center to be slower than the [2,3]-sigmatropic rearrangement process [19]. (C) Chiral catalyst is already released and the inversion at sulfur (racemization) is much faster than the following sigmatropic rearrangement. In this case, the chiral catalyst will not bring any asymmetric induction to the product.

In the early days asymmetric [2,3]-sigmatropic rearrangement of sulfonium ylide was realized by substrate-control method. The key issue in these studies was the transfer of chirality from sulfur to carbon. Trost and Hammen reported the first [2,3]-sigmatropic rearrangement of asymmetric sulfonium ylide in 1973 [20]. Starting from optically pure sulfonium salt **54**, they prepared chiral sulfonium ylide (*S*)-**55** through deprotonation. Ylide (*S*)-**55** subsequently underwent [2,3]-sigmatropic rearrangement, giving the product (*R*)-**56** with 94% ee (Scheme 14). Trost pointed out that the transfer of chirality from sulfur to carbon was due to the fact that the rearrangement occurred by a concerted mechanism *via* an envelope transition state.

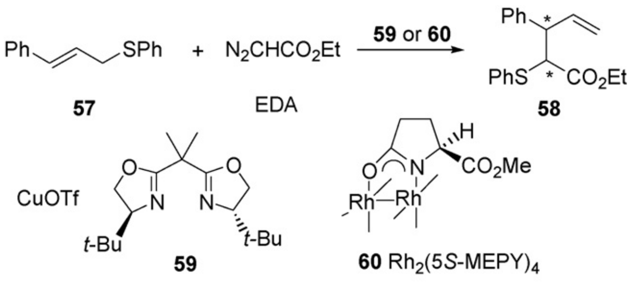


Scheme 13. Mechanistic analysis on [2,3]-sigmatropic rearrangement processes.



54 (*S*)-55 (*R*)-56

Scheme 14. [2,3]-Sigmatropic rearrangement of chiral sulfonium ylide.



cat.	condition	yield (%)	ee of **58** (%)
Cu(I)	toluene, 0 °C, 20 h	41	65/35 (20/14)
Rh(II)	CH_2Cl_2, 40 °C, 20 h	49	60/40 (18/17)

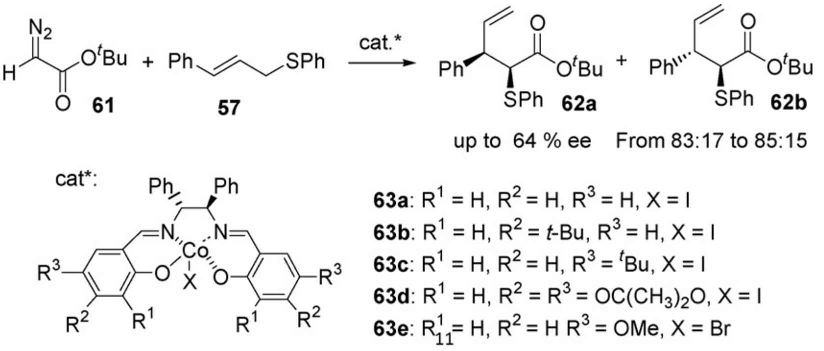
Scheme 15. Chiral Cu/Rh compound-catalyzed reaction of cinnamyl phenyl sulfide and EDA.

3.2. Early developments in asymmetric catalysis of sulfonium ylide [2,3]-sigmatropic rearrangement

In the following years, research in this area focused on the substrate-control approach [21]. Until 1995, Uemura et al. first reported the asymmetric [2,3]sigmatropic rearrangement of sulfonium ylide between (*E*)-cinnamyl phenyl sulfide **57** and ethyl diazoacetate (EDA) (Scheme 15) [22]. The diazo compound was decomposed by catalytic amount of Cu(I)/chiral ligand **59** or chiral Rh(II) catalyst **60** to generate the chiral metal carbene species, which further reacted with sulfide to form the corresponding sulfonium ylide. The ylide then underwent asymmetric [2,3]-sigmatropic rearrangement to afford the final product **58**. The enantioselectivity of this reaction is not high, but it is the first example of asymmetric induction in this type of reaction.

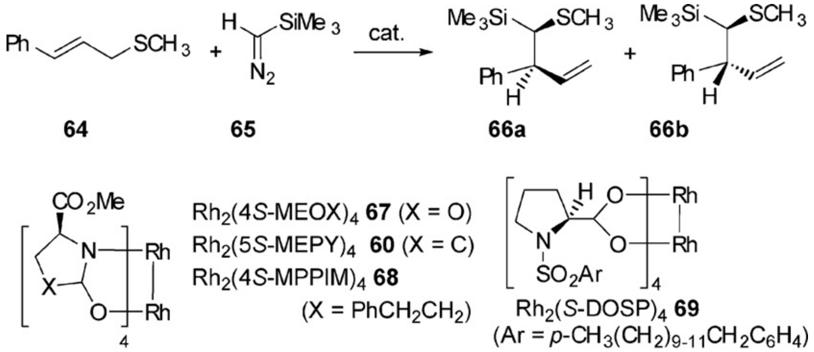
In 1997 and 1999, Katsuki et al. reported the asymmetric sigmatropic rearrangement of sulfonium ylide catalyzed by Co(III)/Salen type ligand **63a–e** (Scheme 16) [23]. They used a similar system as Uemura's and obtained higher enantioselectivity (up to 64% ee) with the chiral salen ligand **63e**. Katsuki suggested that the differentiation of the enantiotopic lone pair electrons on the sulfur atom was dictated by the chirality of the Co-salen complex. They also found that chiral ligands almost had no effect on the diastereoselectivity. According to the previous analysis, the chiral catalyst will affect the diastereoselectivity of the final product if the metal catalyst is still associated with the ylide intermediate when the [2,3]-sigmatropic rearrangement takes place. Thus, Katsuki's result supports a free ylide mechanism.

However, the results disclosed by Aggarwal et al. supported a different reaction mechanism. They reported the [2,3]-sigmatropic rearrangement of sulfonium ylide between (*E*)-cinnamyl methyl



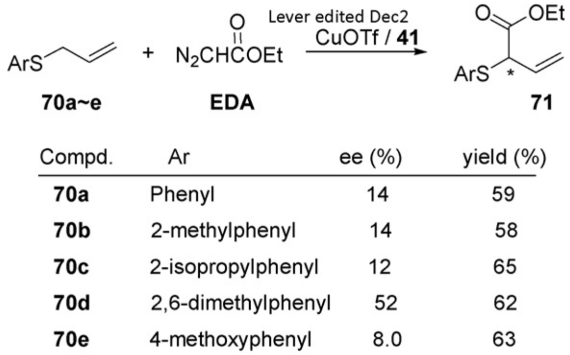
63a: R^1 = H, R^2 = H, R^3 = H, X = I
63b: R^1 = H, R^2 = *t*-Bu, R^3 = H, X = I
63c: R^1 = H, R^2 = H, R^3 = ^{t}Bu, X = I
63d: R^1 = H, R^2 = R^3 = $OC(CH_3)_2O$, X = I
63e: R^1_{11}= H, R^2 = H R^3 = OMe, X = Br

Scheme 16. Reaction of cinnamyl phenyl sulfide and *t*-butyl diazoacetate catalyzed by chiral Co(III) complexes.



cat.	yield (%)	**66a** : **66b** [ee(%)]
$Rh_2(OAc)_4$	90	90 : 10
Rh_2(4*S*-MEOX)$_4$ **67**	74	53(10) : 47(≤5)
Rh_2(5*S*-MEPY)$_4$ **60**	94	49(13) : 51(15)
Rh_2(4*S*-MPPIM)$_4$ **68**	73	68(≤5) : 32(≤5)
Rh_2(*S*-DOSP)$_4$ **69**	82	80(≤5) : 20(≤5)
$Cu(CH_3CN)_4PF_6$/**59**	96	88(≤5) : 12(18)

Scheme 17. Reaction of cinnamyl methyl sulfide and trisilyl diazomethane catalyzed by chiral Cu(I) or Rh(II).



Compd.	Ar	ee (%)	yield (%)
70a	Phenyl	14	59
70b	2-methylphenyl	14	58
70c	2-isopropylphenyl	12	65
70d	2,6-dimethylphenyl	52	62
70e	4-methoxyphenyl	8.0	63

Scheme 18. Chiral Cu(I)-catalyzed reaction of allyl sulfide and EDA.

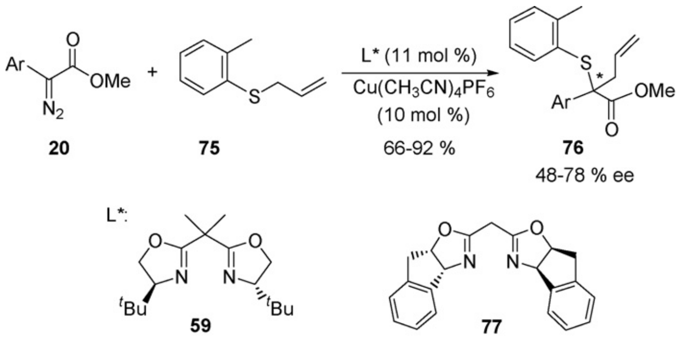
sulfide **64** and trimethylsilyldiazomethane **65** with various chiral metal complexes (Scheme 17). Although the enantioselectivity was not high in general, they found the diastereoselectivity relied on the chiral catalysts employed in the reaction system [24]. These results are consistent with the mechanism that [2,3]-sigmatropic rearrangement occurs through metal catalyst-associated ylide. Thus, this is contradictory to Katsuki's experimental results.

McMillen et al. demonstrated that the structure of sulfide had influence on the enantioselectivity of rearrangement product (Scheme 18) [25]. For the Cu(I)-catalyzed reaction of EDA with aryl sulfide, they observed that the enantioselectivity could be increased up to 52% ee when the aryl group in allyl sulfide **70e** was 2,6-dimethylphenyl.

On the other hand, Hashimoto found that the structure of the diazo compound apparently affected the diastereoselectivity of the rearrangement product. With the catalyst $Rh_2(PTPI)_4$ **74** that was developed in their group, the reaction of diazoacetate **72** with (*E*)-cinnamyl phenyl sulfide **57** gave the sulfur [2,3]-sigmatropic rearrangement product with 53% ee when the R group of diazo compound was 2,6-dimethyl-3-pentyl (Scheme 19) [26].

3.3. Sulfonium ylide [2,3]-sigmatropic rearrangement of aryldiazoacetate

As shown in the studies that are mentioned in Section 3.2, only low to moderate enatioselectivity has been achieved for the sulfur [2,3]-sigmatropic rearrangement reactions with diazoacetates as substrates. By contrast, Davies et al. have recently reported a series of asymmetric catalysis in C–H insertion and cyclopropanation of aryldiazoacetate derivatives, which demonstrated exceptionally high enantioselectivity [27]. Therefore, it is plausible to investigate the asymmetric sulfur [2,3]-sigmatropic rearrangement with aryldiazoacetates as substrates.



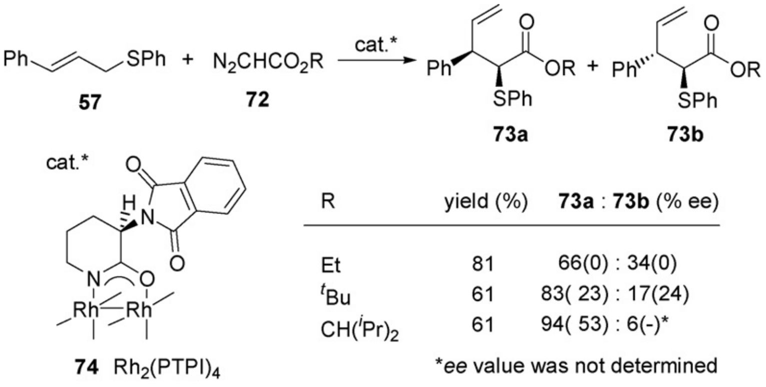
Scheme 20. Chiral metal complex-catalyzed reaction of aryl diazo **20** and allyl aryl sulfide **75**.

Wang and co-workers have reported the asymmetric sulfonium ylide [2,3]-sigmatropic rearrangements between methyl aryldiazoacetate **20** and allyl 2-methylphenyl sulfide **75** catalyzed by chiral Cu(I) complex. The enantioselectivity of the product reaches moderate level (up to 78% ee) when $Cu(CH_3CN)_4PF_6$/ligand **59** is used as catalyst (Scheme 20) [28]. This is a significant improvement as compared with the previous studies.

Previous investigation indicated that propargyl sulfides were also useful starting materials for sulfur [2,3]-sigmatropic rearrangements to afford allene derivatives [29]. Thus, asymmetric catalysis using propargyl sulfide as substrate with both chiral Cu(I) and Rh(II) complexes was investigated [30]. The results indicate that good asymmetric induction can be realized and up to 81% ee can be achieved in the reaction of 2-chlorophenyl propagyl sulfide **78** and different methyl aryldiazoacetates catalyzed by Cu(I)-based catalyst **59** or Rh(II) catalyst **80** and **69** (Scheme 21).

Considering the difference between organic solvents and water, it was proposed that the enantioselectivity of the asymmetric catalytic [2,3]-sigmatropic rearrangement of sulfonium ylides might be improved when the reaction was carried out in water. Thus, the same reaction of methyl aryldiazoacetate **20** (in the case when Ar is *p*-methoxylphenyl) and 2-chlorophenyl propargyl sulfide **79** was repeated in toluene/water catalyzed by different chiral rhodium(II) catalysts [9]. The rearrangement reaction could be efficiently carried out in water without O–H insertion product being detected. However, the enantioselectivity was unfortunately lower than those performed in toluene even under lower temperature. The results suggest that aqueous media may not improve the enantioselectivity in this type of reaction.

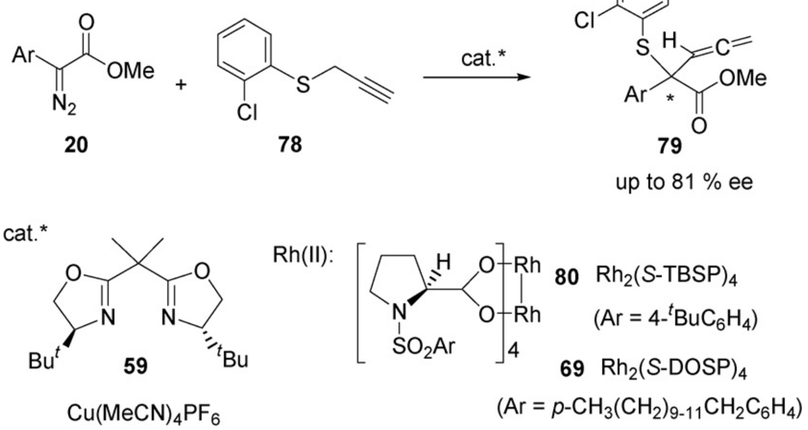
Allenic sulfide could also be transformed into alkyne derivatives *via* sulfonium ylide [2,3]-sigmatropic rearrangement. Wang and co-workers further studied the asymmetric sulfonium ylide [2,3]-sigmatropic rearrangement of methyl aryldiazoacetate **20**



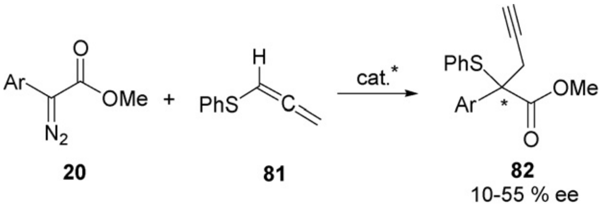
R	yield (%)	**73a** : **73b** (% ee)
Et	81	66(0) : 34(0)
^tBu	61	83(23) : 17(24)
$CH(^iPr)_2$	61	94(53) : 6(-)*

**ee* value was not determined

Scheme 19. Reaction of cinnamyl(phenyl)sulfide and diazoacetate catalyzed by chiral Rh(II) complex.



Scheme 21. Chiral metal complex-catalyzed reaction of methyl aryldiazoacetate **20** and propargyl sulfide **78**.



Scheme 22. Chiral metal complex-catalyzed reaction of aryl diazo **20** and allenic sulfide **81**.

and phenyl allenic sulfide **81** (Scheme 22) [31]. Although asymmetric induction is also possible for this type of reaction, the enantioselectivities are much lower when applying the same chiral catalytic system as in the reaction of propargyl sulfide.

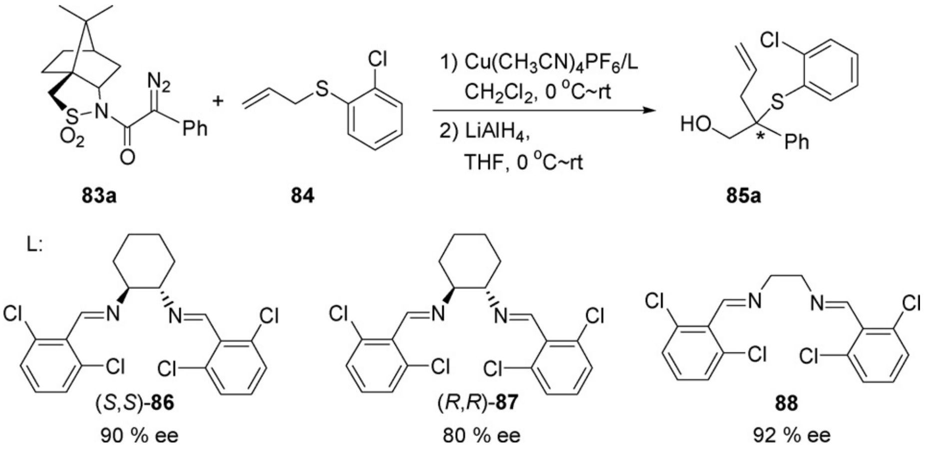
3.4. Double asymmetric induction

Although the asymmetric catalysis of the sulfur ylide [2,3]-sigmatropic rearrangement has achieved considerable success, it becomes rather difficult to further improve the selectivity regardless of extensive optimization efforts. Aiming at this problem, a double asymmetric approach is conceived which combines diazo substrate bearing chiral auxiliary and chiral metal catalyst. After screening a number of chiral auxiliaries, it was found that high enantioselectivity could be achieved by combining diazo compound **83a** with chiral 2,10-camphor sultam auxiliary, chiral complex Cu(MeCN)$_4$PF$_6$/ligand (*S*,*S*)-**86** and 2-chlorophenyl allyl sulfide **84**. The rearrangement product was treated with LiAlH$_4$ without isolation to remove the chiral auxiliary and compound **85a** in 90% ee was obtained.

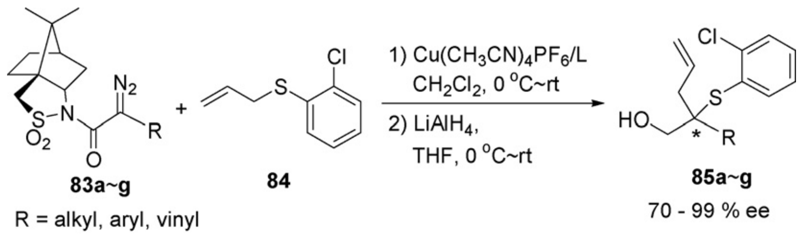
In order to study the match/mismatch relationship between catalyst and chiral auxiliary group, the same reaction with ligand (*R*,*R*)-**87** was performed and 80% ee of product **85a** was obtained. The interesting issue was that the same absolute configuration of major products was obtained with either (*S*,*S*)-**86** or (*R*,*R*)-**87** as the ligand for the catalyst, indicating that the chiral auxiliary group of the diazo compound determined the absolute configuration in the asymmetric induction, instead of the chiral ligand. Consistent with this argument, the catalyst with achiral ligand **88** could also give the product with 92% ee (Scheme 23) [32].

The scope of the reaction involving diazo compounds **83b–g** bearing chiral auxiliary group and 2-chlorophenyl allyl sulfide **84** catalyzed by Cu(I) bearing both chiral and achiral ligands has been investigated (Scheme 24). The sulfide substrate has also been extended to propargyl sulfide (Scheme 25). Up to 96% ee was obtained [32].

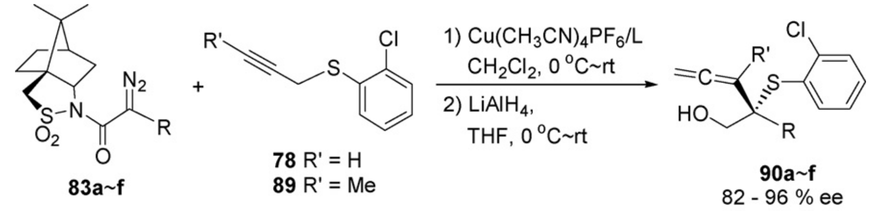
The absolute configuration of chiral center of the product is confirmed by X-ray of the single crystal of the intermediate, which bears chiral auxiliary group (Scheme 26). From this result, the stereochemistry of the newly generated chiral center was the same no matter whether the R group was alkyl or aryl group.



Scheme 23. Cu(I)-catalyzed [2,3]-sigmatropic rearrangement of chiral diazo compound **83a**.



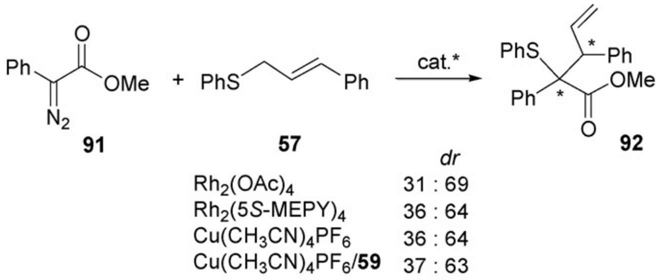
Scheme 24. Scope of the catalytic reaction with different chiral diazo compounds **83a–g** and sulfide **84**.



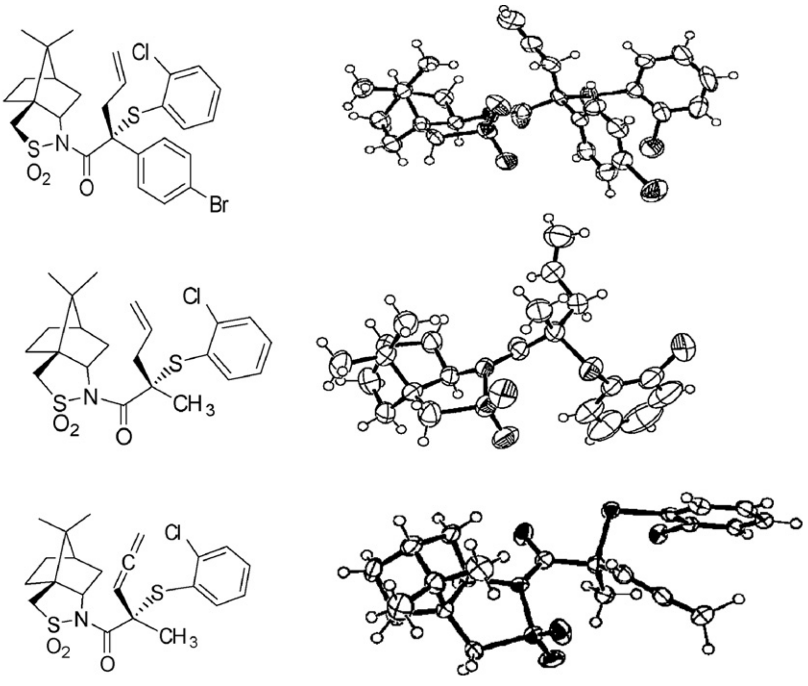
Scheme 25. Reaction of different chiral diazo compounds **83a–f** and sulfides **78**, **89**.

3.5. Discussion on the reaction mechanism

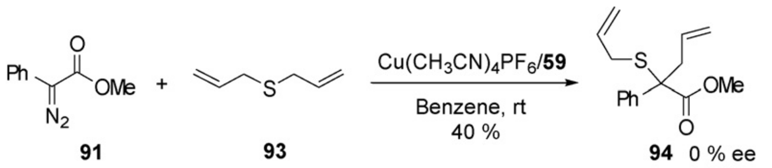
The key issue of the reaction mechanism for asymmetric induction in sulfur ylide [2,3]-sigmatropic rearrangements is whether the rearrangement proceeds through free ylide or the metal catalyst-associated ylide. Uemura, Katsuki and Aggarwal have discussed this problem in their study and reached contradictory conclusions [22–24]. The results from Wang's group also provide perspectives on the mechanism of the reaction. First of all, the diastereoselectivity of product derived from the reaction of methyl phenyldiazoacetate and (*E*)-cinnamyl phenyl sulfide with a series of chiral Cu(I) or Rh(II) catalysts is investigated (Scheme 27). The diastereoselectivity of rearrangement products seemed not to be significantly affected by the different catalysts employed in the reaction. This is in agreement with Uemura and Katsuki's observation, which supports the rearrangement *via* free ylide.



Scheme 27. Reaction of diazoacetate and cinnamyl(phenyl)sulfide with chiral or achiral metal complex.



Scheme 26. Confirmation of absolute configuration with X-ray analysis of single crystal.



Scheme 28. Reaction of methyl phenyldiazoacetate and diallyl sulfide **93** catalyzed by chiral Cu(I).

Next, symmetric diallyl sulfide **93** was prepared. The ylide formed was achiral in this case, thus the rearrangement should proceed *via* metal complex-associated ylide if the product was stereoselective. However, the product obtained is found without any enantioselectivity, which is again in agreement with a rearrangement that proceeds through free ylide species (Scheme 28) [28].

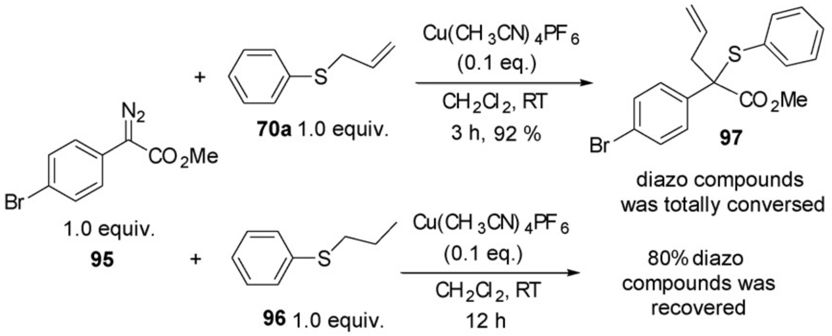
Previous experimental results seem to show that sulfonium ylide rearrangement proceeds *via* free ylide without bonded metal complex. However, the following investigations showed that Cu(I) easily coordinates with sulfonium ylide. The reaction of allyl sulfide **70a** and methyl *p*-bromophenyldiazoacetate **95** was compared with the same reaction of another sulfide **96** which bears a propyl group instead of allyl group. The reaction with sulfide **70a** proceeds normally, while the [2,3]-sigmatropic rearrangement with sulfide **96** is not possible. In the latter case, if the copper catalyst can be released from the ylide, it will enter the catalytic cycle to decompose another diazo substrate. This will lead to the complete transformation of the diazo substrate and the sulfide to the ylide. On the other hand, if the copper catalyst strongly bonds to the ylide, then the catalyst will be deactivated and most of the diazo substrate will remain intact. Experimental results indicated that diazo compound disappeared and the product was obtained in a yield of 92% after 3 h with the reaction of sulfide **70a** catalyzed by Cu(I) complex. Meanwhile, 80% of the diazo compound was recovered from the reaction of **96** under the same catalytic system (Scheme 29).

The result indicated that Cu(I) complex could not enter the catalytic cycle and decompose all the diazo compounds in the case of sulfide **96**. Therefore it is suggested that equilibrium exists between metal catalyst-associated ylide **98** and free ylide **99**. The equilibrium strongly favored the metal catalyst-associated ylide **98**. Thus, most of the Cu(I) complex can not be released to enter another catalytic cycle (Scheme 30).

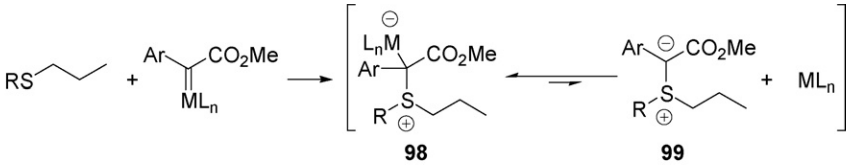
The direct evidence of Cu(I)-associated ylide comes from the studies on the infrared spectra. Free ylide **102** was synthesized by deprotonation of sulfide **101** and the stretching vibration of its carbonyl group appears at 1587 cm^{-1}. The C=O frequency occurs at 1587 cm^{-1} with a significant blue shift caused by the conjugation with carbanion (Scheme 31).

The Cu(I) complex was then added to the solution of free ylide and the IR spectra were measured again. The C=O absorption in the IR spectrum is now shifted from 1587 cm^{-1} to 1736 cm^{-1}. This is due to the fact that the coordination with Cu(I) complex makes the conjugation of carbonyl group with carbanion not feasible. Thus, the stretching vibration returns to normal C=O again (Scheme 32).

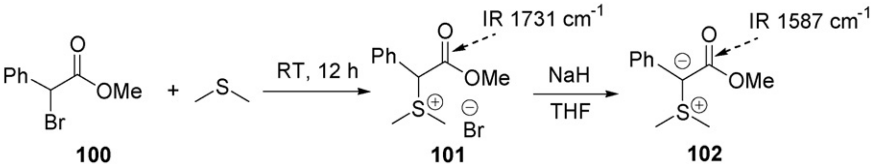
In another experiment diazo compound **91**, dimethyl sulfide and Cu(I) was mixed stoichiomically. The C=O stretching absorption was at 1736 cm^{-1} after the diazo compound disappeared on



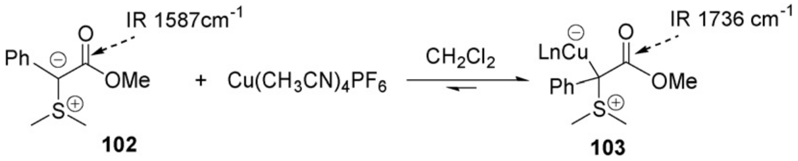
Scheme 29. Comparison of the reaction of ally sulfide **70a** with propyl sulfide **96**.



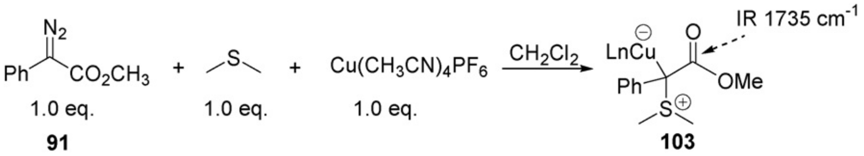
Scheme 30. Equilibrium between Cu(I)-associated ylide and free ylide.



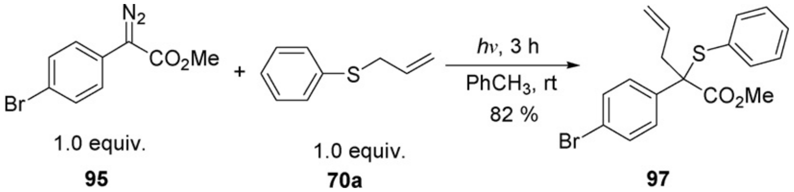
Scheme 31. IR absorption of free ylide.



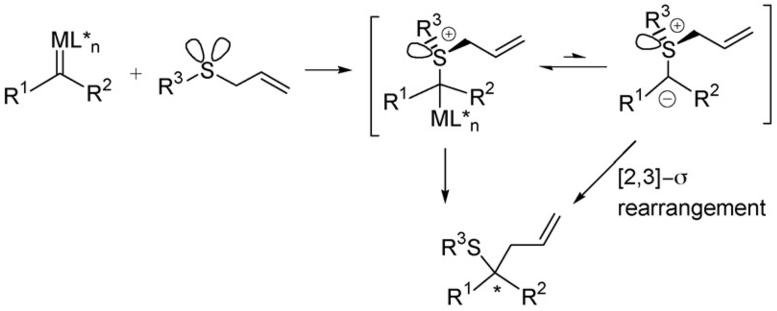
Scheme 32. Infrared absorption of Cu(I)-associated ylide **103**.



Scheme 33. IR absorption of sulfonium ylide derived from Cu(I)-catalyzed decomposition of diazo compound.



Scheme 34. Photoreaction of sulfonium ylide [2,3]-sigmatropic rearrangement.



Scheme 35. Mechanism of sulfur ylide [2,3]-sigmatropic rearrangement *via* metal carbene.

TLC (Scheme 33). This absorption could be assigned to the metal complex-associated ylide **103**.

Finally, free carbene was prepared through photo-induced reaction and was treated with sulfide to afford free ylide. The reaction of diazo compound **95** and sulfide **70a** was completed after 3 h with irradiation and the rearrangement product **97** was obtained in 82% yield (Scheme 34). The result exhibits that free sulfur ylide can readily proceed through the subsequent [2,3]-sigmatropic rearrangement, which is in accordance with Trost's previous work.

According to the previous experimental results it is evident that the interaction of metal carbene and sulfide preferable generates the metal catalyst-associated sulfur ylide as major product. There is an equilibrium between free ylide and metal catalyst-associated ylide and this equilibrium is largely shifted to the latter. However, based on the results of study on diastereoselectivity, it is believed that the rearrangement occurs through free ylide. Although the free ylide is in low concentration, according to Curtin–Hammett principle, the rearrangement can still proceed to completion if the [2,3]-sigmatropic rearrangement is a very fast process, which has been supported by many experimental results. Therefore, the asymmetric induction for the overall reaction is due to the chirality of the sulfur in ylide species, which undergo slow racemization process as compared with the [2,3]-sigmatropic rearrangement (Scheme 35).

4. Summary

Sulfur ylide reactions *via* metal carbene have been widely applied in organic synthesis as a special C–C bond forming method. Catalytic asymmetric ylide [2,3]-sigmatropic rearrangements have been developed in recent years. Although the enantioselectivity of asymmetric ylide [2,3]-sigmatropic rearrangements was still rather low as compared with other asymmetric metal carbene reactions such as cyclopropanations, the results have changed the view on this type of reaction and advanced this chemistry to a new level. So far most of the enantioselectivity of sulfur [2,3]-sigmatropic rearrangement product is not quite satisfactory. Furthermore, the mechanistic study of this kind of reaction was still in its infancy. There is room for further improvement of the reaction through optimizing the design of chiral metal catalysts and other factors that may affect the stereoselectivity. It is expected that with further development this kind of reaction can be applied in the synthesis of compounds of biological and medicinal interests.

Acknowledgments

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