Telluronium and Sulfonium Ylides for Organic Transformation

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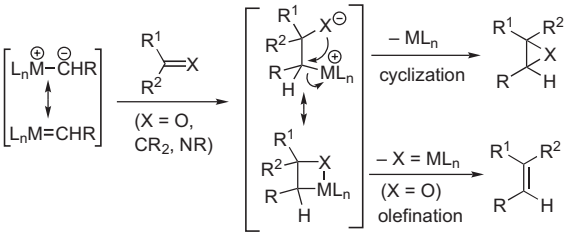
Abstract: This account briefly describes the development of ylide olefination, cyclopropanation, epoxidation and aziridination, achieved in our laboratory over the last several years.

Key words: catalytic Wittig-type reaction, telluronium ylide, cyclopropanation, epoxidation, aziridination

1 Introduction

An ylide can be viewed as a special carbanion neighbored with a positively charged heteroatom, which can act as a leaving group in a reaction. The reaction of an ylide with an electron-deficient C=C or C=X (X = N, O, etc.) double bond gives a betaine or oxetane intermediate, which can further eliminate the heteroatom-containing group in two modes to give the corresponding cyclization and olefination product, respectively, depending on the nature of ylides and the substrates (Scheme 1). Since the birth of the Wittig reaction in 1953,[1] the chemistry of ylides has grown rapidly and they have now become one of the most powerful and versatile synthetic tools in the arsenal of organic chemists.

In the past decades, considerable attention has been paid to the development of highly efficient catalysis and the control of selectivity in organic transformation. Despite the fact that ylides have developed into versatile reagents[2] for the preparation of olefins, small ring compounds and others, in most cases, ylide reactions are stoichiometric and not atom-economical.[2,3] In addition, the stereoselectivity for the preparation of vinyl-type small ring compounds via an ylide route is generally poor. Thus, our investigation has focused on the development of a catalytic and stereoselectively controllable ylide reaction. In this account, we describe our personal journey through the field of ylide chemistry, especially the synthetic chemistry of telluronium allylides and sulfonium allylides.



Scheme 1 Ylide cylization and olefination

2 Catalytic Wittig-Type Olefination

Highly efficient catalysis has become one of the most important frontiers in exploratory organic synthetic research. Although the ylide reaction is one of the most useful approaches in constructing C=C double bonds, surprisingly, only a few examples of catalytic Wittig-type reactions were reported in literature. The first example of catalytic Wittig-type reactions appeared in 1989, in which Huang et al. found that tributylarsine could be used as the catalyst in the presence of triphenyl phosphite.[4] Later on, they described the catalytic ylide olefination reactions mediated by dibutyl telluride.[5] In all of the reactions mentioned above, 20 mol% of the catalyst must be used. Reduction of the catalyst means low yield even if the reaction time was prolonged.[6] Needless to say, these processes need to be improved before it can be considered as a useful synthetic tool. In our studies on the application of ylides in organic synthesis, we first paid attention to catalytic efficiency of ylide olefination.

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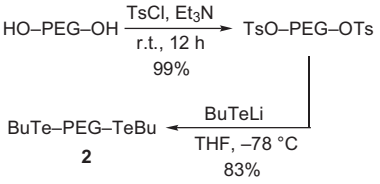
2.1 PEG-Supported Telluride

By analysis of the corresponding mechanism of Wittig-type olefination catalyzed by organotelluride, we proposed that the formation of ylide is probably the rate-determining step in the catalytic ylide olefination.[6] Improving the rate of ylide generation may essentially speed up the catalytic cycle. Thus, we initially designed telluride **1** containing an ammonium salt, which is supposed to improve the solubility of the inorganic base and to promote the deprotonation. Unfortunately, attempts to synthesize compound **1** failed. Considering that PEG[7] is expected to accelerate the reaction of ylide formation by self-assembling to form a half-opened crown ether[8] as shown in Figure 1, we prepared PEG-supported telluride **2** as a catalyst (Scheme 2).



Scheme 2 Synthesis of PEG-supported telluride **2**

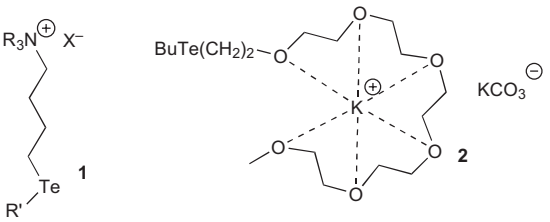


Figure 1 Designed catalyst for ylide olefination

In the presence of 10 mol% of PEG-supported telluride, disappointingly, only 58% yield was obtained when *p*-chlorobenzaldehyde was mixed with ethyl bromoacetate under the optimal conditions described in the literature,[5] using 20 mol% of dibutyl telluride as the catalyst. Further study showed that ethyl bromoacetate was destroyed under these conditions and thus, we examined the effects of solvents, bases as well as addition sequence of the reactants on the reaction. Finally, we found that the

Biographical Sketches

Yong Tang was born in September 1964 in Sichuan, China. He received his PhD degree in 1996 at Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences under the supervision of Prof. Yao-Zeng Huang and Prof. Li-Xin Dai. Having spent three years as a postdoctoral researcher in USA (at Colorado State University with Prof. Yian Shi, 1996–1997 and at Georgetown University with Prof. Alan Kozikowski, 1997–1999), he joined Shanghai Institute of Organic Chemistry, CAS in 1999 as an associate Professor. He was promoted to a full Professor in 2000. His current research interests are development of new synthetic methodology, design and synthesis of olefin polymerization catalyst.

Song Ye was born in Wuyuan, Jiangxi province, China, in 1973. He received his BSc degree in chemistry from the East China Normal University in 1995. He was enrolled as a graduate student of Shanghai Institute of Organic Chemistry, the Chinese Academy of Sciences (CAS), under the supervising of Professor Lin-Xin Dai and Professor Yong Tang in 1997, and obtained his PhD in organic Chemistry in 2002. Having been in National Institutes of Health, USA, as a post-doctoral visiting fellow in the group of Dr. Kenneth L. Kirk from 2002 to 2005, he returned to China and joined the Institute of Chemistry, CAS, as a faculty member in 2005.

Xiu-Li Sun was born in 1971 in Inner Mongolia, China. She received her PhD degree in 2000 at Nankai University under the supervision of Professor Xiu-Zhong Zhou. In 2000, she joined the group of Prof. Yong Tang at Shanghai Institute of Organic Chemistry as a research associate. She is currently an Associate Professor at the same institute. Her research interests focus on the development of new catalysts on olefin polymerization and organic synthesis.

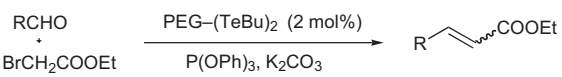
Wittig-type olefination product was isolated in 88% yield with excellent stereoselectivity using 1 mol% of telluride **2**.[9] In contrast, only 12% of the product was obtained under the same conditions in the presence of 2 mol% of dibutyl telluride instead of 1 mol% of telluride **2**, suggesting that the catalytic efficiency of this reaction was improved greatly compared with the reported catalytic ylide olefination.

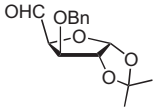
The generality of this reaction was investigated by employing a variety of structurally different aldehydes (Table 1) in the presence of 2 mol% of BuTe–PEG–TeBu **2**.[9] Both aliphatic and aromatic aldehydes worked well in reasonable yields with high *E* stereoselectivity. Aromatic aldehydes with an electron-withdrawing group or a weak electron-donating group in the *para* position as well as the heteroaromatic aldehydes were the most suitable substrates. All of these substrates can afford the desired products in excellent yields with high stereoselectivity. Although an aromatic aldehyde with a strong electron-donating group, such as *p*-methoxybenzaldehyde, was less active, 98% yield was obtained when 5 mol% of PEG-supported telluride was employed. Functionalized and unfunctionalized aliphatic aldehydes with different structures were also utilized in this reaction to give the corresponding olefins in moderate yields with high stereoselectivity. When only 0.5 mol% of the corresponding salt **3**, $\{PEG–[Te(Bu)CH_2CO_2Et]_2\}^{2+}2Br^-$, was taken as the catalyst instead of PEG telluride, the olefination reaction of *p*-chlorobenzaldehyde with ethyl α-bromo acetate could also give 94% yield.

To make this reaction more practical, we took our efforts to use inorganic reducing agents instead of $P(OPh)_3$. By optimizing the reaction conditions, sodium bisulfite was chosen and it was found that a variety of aldehydes, including some functionalized aldehydes such as an epoxy aldehyde, could react with *tert*-butyl bromoacetate in the presence of 2 mol% of PEG-supported telluride **2**. Thus, sodium bisulfite turned out to be another effective reducing reagent in this catalytic Wittig-type reaction. It is interesting that the use of $NaHSO_3$ improved the stereoselectivity of this reaction in the case of some functionalized aldehyde used (Table 2 vs. Table 1).

One feature of this reaction is that the product purification was very simple using $NaHSO_3$ as a reducing reagent. After the reaction was complete, almost pure product could be obtained just by filtering off the inorganic salts, followed by precipitation of the PEG-supported telluride **2** with diethyl ether. Further studies showed that the catalyst could be recovered quantitatively but partially lost its activity through multiple cycles. For an example, it was found that 2-furaldehyde reacted with *tert*-butyl bromoacetate in the presence of sodium bisulfite to afford the desired product in 90% yield when 2 mol% of PEG-supported telluride was used. The catalyst could be recovered in 100% yield by filtering off the solid of the reaction mixture, followed by addition of diethyl ether and collection of the precipitate. The recovered catalyst could be used in the second run, but only a 69% yield was obtained,

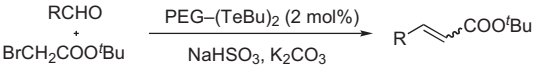
Table 1 Olefination of Aldehydes Catalyzed by PEG-Supported Telluride

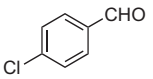
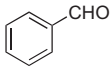
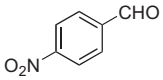
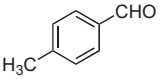
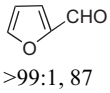
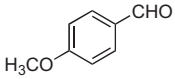
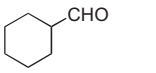
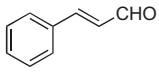
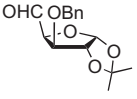
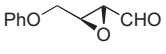


Entry	RCHO	Yield (%)[a]	*E*/*Z*[b]
1	*p*-ClC_6H_4CHO	98	>99:1
2	PhCHO	98	>99:1
3	*p*-$CF_3C_6H_4CHO$	74	>99:1
4	*p*-$CH_3C_6H_4CHO$	93	90:10
5	*p*-$CH_3OC_6H_4CHO$[c]	98	>99:1
6	2-Furaldehyde	96	>99:1
7	*E*-Cinnamic aldedyde	74	>99:1
8	Cyclohexylcarbaldehyde	70	>99:1
9	*n*-$C_9H_{19}CHO$	74	86:14
10		79	58:42
11[d]	*p*-ClC_6H_4CHO	94	>99:1

[a] Isolated yields.
[b] The ratio of *E*/*Z* isomers was determined by ^1H NMR.
[c] 5 mol% of catalyst was used.
[d] 0.5 mol% of PEG-supported telluronium salt was used.

Table 2 Olefination of Aldehydes Catalyzed by Telluride **2** in the Presence of $NaHSO_3$



E/*Z*, yield (%)	*E*/*Z*, yield (%)	*E*/*Z*, yield (%)
 >99:1, 93	 >99:1, 87	 >99:1, 88[a]
 94:6, 96	 >99:1, 87	 >99:1, 88[a]
 >99:1, 96	*n*-$C_9H_{19}CHO$ 95:5, 87	 >99:1, 89[a]
 >99:1, 65	 >99:1, 69	

[a] 5 mol% of catalyst was used.

probably due to the partial decomposition of PEG-supported telluride in the previous cycle of the catalytic olefination.[9b]

2.2 Oligoglycolic Telluronium Salt

To further improve the efficiency of catalytic ylide olefination as well as to increase the telluronium salt loading in the PEG carrier, several pentaerythritol-derived oligoglycols as a new type of catalyst carriers were designed. We successfully synthesized and characterized oligoglycol **4** (Figure 2) but failed to load telluronium salt to this potential carrier. The reason is that the hydroxyl groups of oligoglycol **4** could not be fully transformed into the corresponding tosylates or bromides under a variety of conditions. In all cases, disordered compounds were obtained and no pure product could be isolated. Thus, we prepared a simple telluride and its salts **5a** and **5b** (Figure 2) with a oligo(ethyleneglycol) skeleton for our study and evaluated their catalytic activity for Wittig-type olefinations.

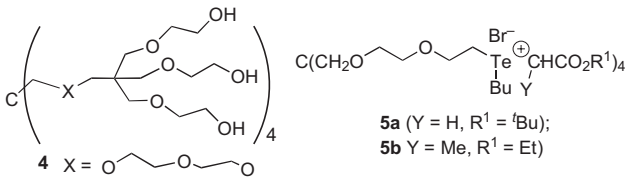


Figure 2

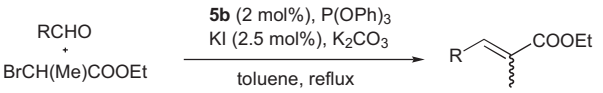
It was found that salt **5a** was a comparable catalyst to PEG-supported telluride for the Wittig-type reaction of aldehydes with bromoacetate. In the presence of $NaHSO_3$, both aromatic aldehydes and aliphatic aldehydes worked well when 1.25 mol% of catalyst **5a** was employed. All reactions gave *E* isomers with excellent stereoselectivity and in good to high yields. Notably, compared with the known dibutyltelluronium salt, $[Bu_2TeCH_2COO\textit{t}\text{-}Bu]^+ Br^-$ **6**, the newly synthesized tellurium salt **5a** was more efficient.[10]

Although several catalytic Wittig reactions have been developed, few involved the olefination of aldehydes with α-bromopropionate. It was found that moderate to good yields could be obtained when using the newly designed **5b** as the catalyst for the Wittig-type reaction of α-bromopropionate, although higher reaction temperature is required, compared with the corresponding olefination of bromoacetate. As shown in Table 3, both aromatic and aliphatic aldehydes were good substrates for this reaction. Aromatic aldehydes gave high stereoselectivity (entries 1–4), while inferior diastereoselectivity was observed when cyclohexylaldehyde was used (entry 5).[10]

2.3 Miscellaneous

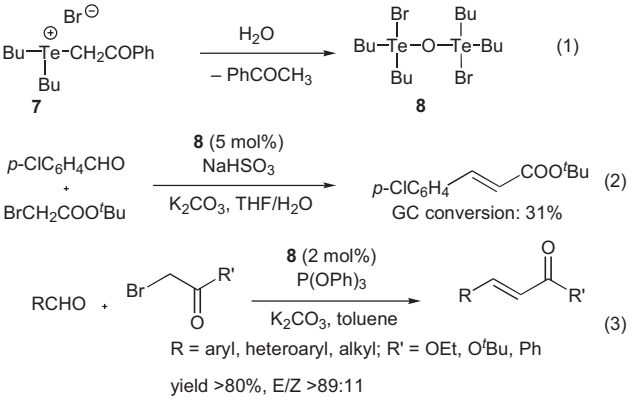
During our investigation of the mechanism of the Wittig-type olefination catalyzed by PEG-supported telluride, we found the telluronium salt **7** decomposed quickly in the presence of water and a stable odorless compound **8** was obtained (equation 1 in Scheme 3). Initially, we assumed that compound **8** was an inactive species and its formation would lead to the loss of the activity of dibutyl telluride in the catalytic cycle. This assumption could also explain the deactivation of the recovered PEG-supported telluride. To verify this assumption, we tried a catalytic reaction of 4-chlorobenzaldehyde with bromoacetate using compound **8** instead of dibutyltelluride. Unexpectedly, the reaction proceeded well and afforded the desired product in 31% yield (equation 2 in Scheme 3). After optimization, it was found that the olefination reaction of a variety of aldehydes could afford the corresponding products in excellent yields in the presence of 1 mol% of telluride **8** (equation 3 in Scheme 3) when $P(OPh)_3$ was used as the reducing agent. Furthermore, a dehalogenation reaction catalyzed by 1 mol% of telluride **7** is also developed.[11]

Table 3 Olefination of Aldehyde with α-Bromopropionate



Entry	Time (h)	R	*E*/*Z*[a]	Yield (%)
1	24	4-ClC_6H_4	96:4	72
2	24	Ph	97:3	69
3	24	4-$NO_2C_6H_4$	96:4	68
4	40	2-$CH_3OC_6H_4$	99:1	67
5	24	Cyclohexyl	70:30	6

[a] Determined by ^1H NMR.

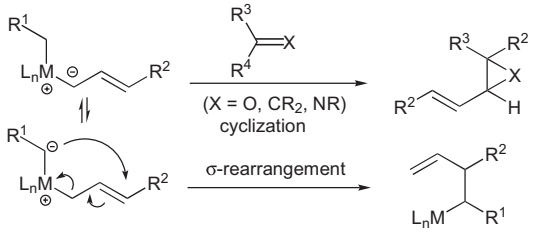


Scheme 3

3 Ylide Cyclopropanation

Vinylcyclopropane is a ubiquitous structural element of a variety of biologically active compounds, notably agrochemicals such as pyrethroids.[12] In addition, vinylcyclopropanes serve as diverse intermediates in organic synthesis.[13] In view of the difficulty associated with both the regioselective introduction of the vinyl group and the stereoselective formation of the multisubstituted cyclo-

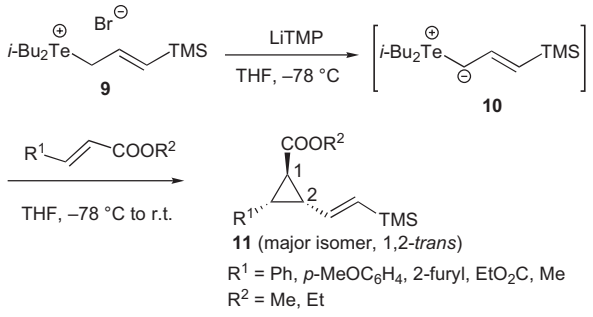
propane ring, synthesis of multisubstituted vinylcyclopropanes with high diastereoselectivity and enantioselectivity remains a challenging problem. Of the synthetic methods developed,[14] the addition of allylic ylides $L_nM^+CH^-CH=CHX$ to Michael acceptors represents a convenient and attractive method because ylides are readily available and L_nM is easily recovered and reused. The key point is to suppress the possible [2,3] σ-rearrangement of the allylide (Scheme 4), a competing reaction with the cyclopropanation.



Scheme 4 Competing σ-rearrangement and cyclization of allylide

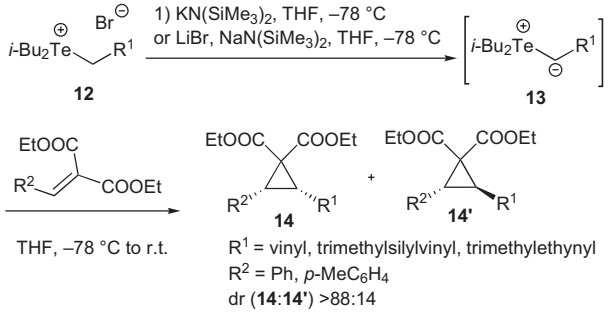
3.1 Cyclopropanation via Telluronium Allylide

Osuka et al. found that telluronium allylide could react with aldehydes at –78 °C to produce oxiranes.[15] Later on, Huang and coworkers described an epoxidation of aldehydes or ketones with allylic telluronium salts in the presence of base.[16] These results suggested that telluronium allylide is much stable and not prone to rearrangement at low temperature, compared with the corresponding sulfur ylides. Thus, we explored the reaction of telluronium allylide towards Michael acceptors and found that trimethylsilylated telluronium ylide **10**, generalized in situ from the telluronium salt **9** with lithium 2,2,6,6-tetramethylpiperidide (LiTMP), reacted with α,β-unsaturated esters to give the trimethylsilylvinylcyclopropane derivatives **11** in good yields (Scheme 5).[17] It is noteworthy that allylide **10** reacted with β-aryl-α,β-unsaturated esters with exclusive diastereoselectivity but with methyl crotonate or methyl methylacrylate, the same reaction gave poor selectivity with a ratio of around 1:1.



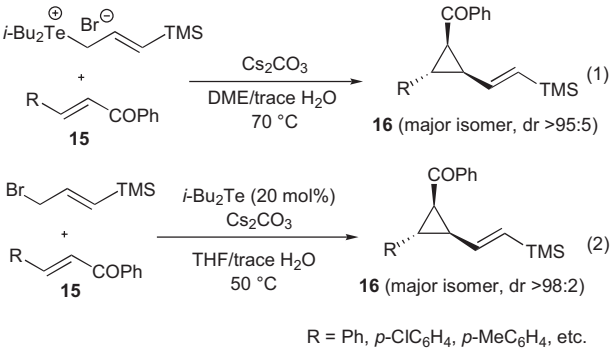
Scheme 5 The cyclopropanation of telluronium allylide with α,β-unsaturated esters

Further study showed that ylide **10** or its analogue **13** could react with alkylidene malonate to afford the vinylcyclopropane 1,1-dicarboxylic esters **14** (Scheme 6).[18]



Scheme 6 Cyclopropanation of telluronium ylide with alkylidene malonates

Telluronium salt **9** proved to react with α,β-unsaturated ketones to produce the cyclopropane derivative in the presence of cesium carbonate (equation 1 in Scheme 7).[19] One feature of this ylide cyclopropanation is that diisobutyltelluride is regenerated after the cyclization, and may be further transformed to ylide. On the basis of this consideration, we successfully developed a catalytic ylide cyclopropanation mediated by diisobutyltelluride (equation 2 in Scheme 7). In the presence of 20 mol% of diisobutyltelluride, a variety of α,β-unsaturated ketones could react with 3-trimethylsilylallyl bromide smoothly to afford the trimethylsilylvinylcyclopropane derivatives with high diastereoselectivity (dr > 98:2).[19]

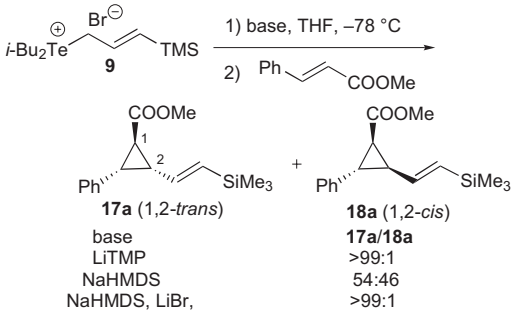


Scheme 7 Cyclopropanation of telluronium allylide with α,β-unsaturated ketones

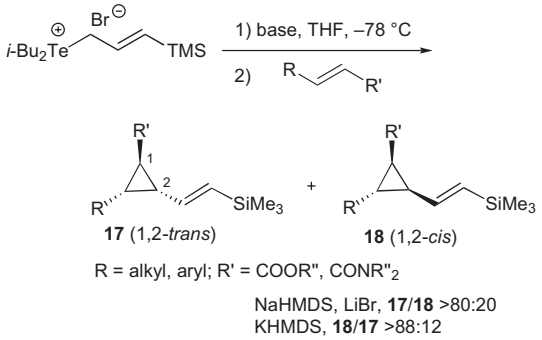
3.2 Control of the Diastereoselectivity

During the study on ylide cyclopropanation, we noticed that the cyclopropanation reaction of telluronium allylide **10** with α,β-unsaturated esters and ketones featured the different diastereoselectivity in the major products: in the case of α,β-unsaturated ester as a substrate, the trimethylvinyl group and the ester group were located *trans* to each other but the trimethylvinyl group was located at the *cis*-position of COR^2 when switching the substrate to the corresponding ketones. This encouraged us to develop a strategy to control the disastereoselectivity of these cyclopropanations.

Initially, it was found that silylated telluronium allylide **10**, generated in situ from telluronium bromide **9** with LiTMP, reacted with methyl cinnamate to form *trans*-2-phenyl-*trans*-3-[2-(trimethylsilyl)vinyl]-1-(methoxycarbonyl)cyclopropane exclusively. However, using $NaN(SiMe_3)_2$ instead of LiTMP as the base to generate ylide **10**, the same reaction gave poor diastereoselectivity and the ratio of the two diastereomers was nearly 1:1. Notably, using the same base $NaN(SiMe_3)_2$ but in the presence of LiBr, the reaction became diastereospecific again (Scheme 8). These results suggested that the lithium salt was one of the main factors controlling the stereoselectivity. And thus, we focused on the effect of the base on the reaction stereoselectivity. Finally, we demonstrated that the choice of the bases played an important role in controlling the diastereoselectivity of this reaction (Scheme 9).[20] The allylic telluronium ylide **10**, generated in situ from corresponding telluronium salt **9** in the presence of a lithium salt, reacted with α,β-unsaturated esters or amides to afford *trans*-2-vinyl-*trans*-3-substituted cyclopropyl esters or amides **17**, respectively, with high selectivity in excellent yields. On the other hand, in the absence of lithium ion, the stereoselectivity of these reactions changed to give *cis*-*2*-vinyl-*trans*-3-substituted cyclopropyl esters or amides **18**.[20]



Scheme 8



Scheme 9 Tuning of the diastereoselectivity by the choice of base

The different stereoselectivity of the reaction of **9** with α,β-unsaturated esters and amides under different reaction conditions can be explained as follows: when $KN(SiMe_3)_3$ is used as the base, this cyclopropanation reaction is subject to thermodynamic control and the *cis*-2-vinyl isomer **18** is the major product. In the presence of lithium salt, however, the reactions may proceed via a chelating six-membered ring transition state (Figure 3), which is formed by the coordination of lithium ion with the carbonyl oxygen and ylidic carbanion simultaneously to give *trans*-2-vinyl isomer **17**. This mechanistic insight suggested that it might be possible to control the stereoselectivity of this reaction by taking lithium ion away in situ. Hexamethylphosphoramide (HMPA) is first chosen for this purpose because of its strong coordinating ability with the lithium ion. As expected, without HMPA, silylated telluronium allyllide reacted with α,β-unsaturated esters and amides to afford *trans*-2-vinyl-*trans*-3-substituted cyclopropanes **17** in high yield and with high selectivity. The same reaction provided *cis*-2-vinyl-*trans*-3-substituted cyclopropanes **18** when carried out in the presence of HMPA (Scheme 10).[21]

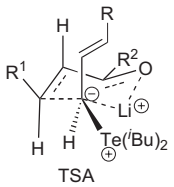
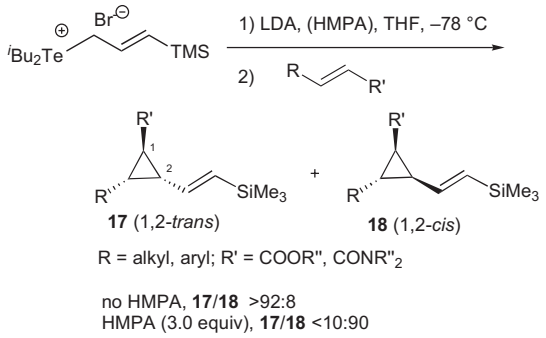
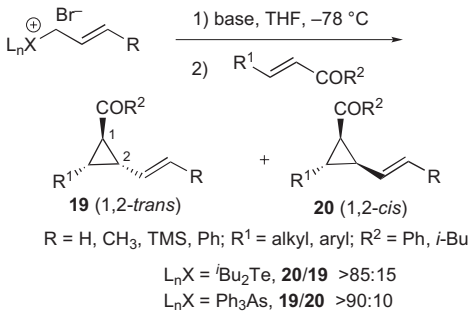


Figure 3 Possible transition state involving lithium ion



Scheme 10 Tuning of the diastereoselectivity by HMPA

After successfully controlling the diastereoselectivity of the cyclopropanation reaction of α,β-unsaturated ester, we tried to extend the strategy to the cyclopropanation of α,β-unsaturated ketones. However, it turns out that the stereochemistry of this reaction is almost independent of the lithium salts and the *cis*-isomer **20** is the major product under both reaction conditions. Fortunately, the corresponding allylic arsonium ylide proves to react smoothly with α,β-unsaturated ketones to furnish cyclopropanes in high yields with diastereoselectivity opposite to the isomers obtained by the use of the corresponding telluronium ylides. Thus, it provided an alternative path for the control of the diastereoselectivity in the cyclopropanation reaction of ylides with Michael acceptors (Scheme 11).[22]



Scheme 11 Controlling the diastereoselectivity by the choice of telluronium or arsonium ylide

3.3 Asymmetric Cyclopropanation via a Chiral Sulfonium Ylide

The allylides prove to be good reagents to prepare the vinylcyclopropane derivatives, leading us to an attempt to develop chiral ylides for the synthesis of optically active cyclopropanes. Based on the mechanistic insight of the stereoselective tuning by lithium ion, chiral sulfonium ylide **21** was designed since it is possible to form a rigid transition state via the hydroxyl group and a metal ion, probably beneficial to improve the enantioselectivity (Figure 4).

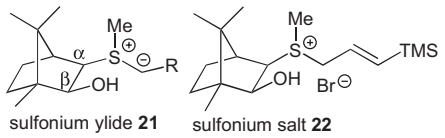
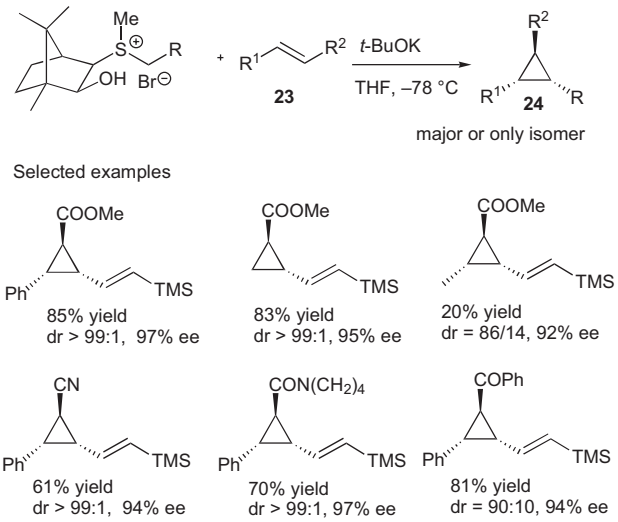


Figure 4 Designed chiral sulfonium ylide for the asymmetric cyclopropanation

The ylide precursor **22** is found to be easily prepared from D-camphor in three steps.[23a] We are pleased to find that ylide **21**, generated in situ from the corresponding salt **22** and *t*-BuOK (3.0 equiv), could react with methyl cinnamate in one pot to afford vinylcyclopropane **24a** with 97% ee in 85% yield. A variety of α,β-unsaturated esters, amides, ketones and nitriles are all worked well to afford the cyclopropanation products in good yields except for methyl crotonate. The diastereoselectivities are good to excellent with the β-aryl substrates. The enantiomeric excesses of all reactions are higher than 92%, and as high as 99% (Scheme 12).[23b]

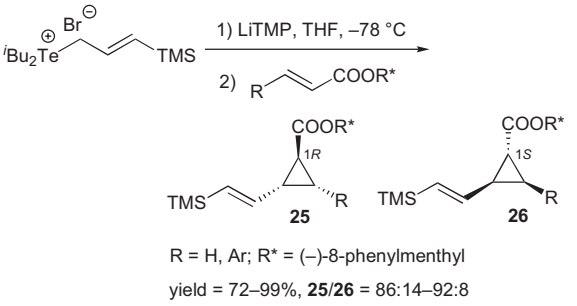
3.4 Asymmetric Cyclopropanation Using a Chiral Auxiliary

It is reported that (–)-8-phenylmenthol is a powerful chiral auxiliary in Michael addition reaction. The first step of ylide cyclopropanation is usually considered to be a Michael addition, so we carried out the asymmetric ylide cyclopropanation with (–)-8-phenylmenthol as a chiral auxiliary.[24] It was found that silylated telluronium allylide



Scheme 12 Enantioselective synthesis of vinylcyclopropanes mediated by chiral sulfonium salt

could react with (–)-8-phenylmenthyl α,β-unsaturated esters to afford the chiral vinylcyclopropanes with high diastereoselectivity in high yields (Scheme 13).



Scheme 13 Asymmetric synthesis of vinylcyclopropanes via (–)-8-phenylmenthol

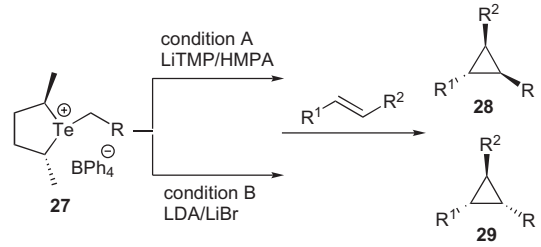
By comparing the different reaction results with (–)-menthyl, (–)-8-(2-naphthyl)menthyl and (–)-8-phenylmenthyl as the chiral auxiliaries, it is proposed that the possible π-stacking effect between the aryl of chiral auxiliary and dienyl group of α,β-unsaturated esters is involved in this diastereoselective cyclopropanation.[24]

3.5 Asymmetric Cyclopropanation via Chiral Telluronium Ylides[25]

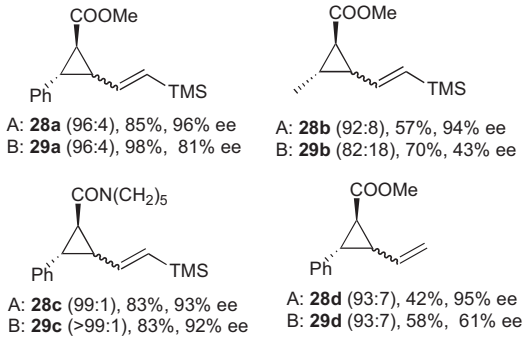
Encouraged by the successful tuning of the diastereoselectivity of the cyclopropanation of diisobutyltelluride ylide with Michael acceptors described in section 3.2, we were interested in extending this methodology to the enantioselective synthesis of vinylcyclopropanes. The C_2-symmetric telluronium salt **27** is designed and readily prepared from (2*S*,5*S*)-2,5-hexanediol-dimethanesulfonate. Gratifyingly, we found that the salt **27**, after deprotonation

by LiTMP/HMPA, could react with a variety of α,β-unsaturated esters, amides, ketones to afford vinylcyclopropanes with high diastereoselectivity and enantioselectivity (Method A, Scheme 14). It is noteworthy that the reaction of α,β-unsaturated ketones give cyclopropanes in high regioselectivity without epoxides detected.

Noticeably, when generated by LDA/LiBr, the same ylide could react with a variety of α,β-unsaturated esters and amides to give the desired products but with opposite diastereoselectivity compared with those reactions using LiTMP/HMPA as a base (Method B, Scheme 14). In most cases, β-aryl-α,β-unsaturated esters and amides give good to high diastereoselectivities and enantioselectivities. The reaction with methyl crotonate is less enantioselective, and only 43% ee is reached.[25]

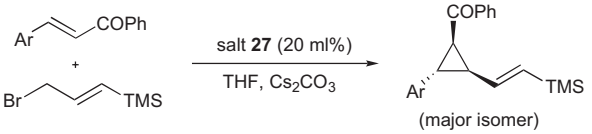


selected examples: condition A or B, major isomer (dr) yield, ee



Scheme 14 Diastereoselectively controllable enantioselective synthesis of vinylcyclopropanes via chiral telluronium ylides

Considering the regeneration of the organotelluride after the cyclopropation, we tried a catalytic version of this reaction. Using 20 mol% of salt **27** as a catalyst, the reaction of chalcones with silylated allylic bromide in THF gave the desired cyclopropane in high yield with high diastereoselectivity and up to 89% ee (Scheme 15).[25]



Ar = Ph, 91% yield, dr = 90:10, 86% ee
Ar = *p*-ClC_6H_4, 94% yield, dr = 91:9, 89% ee

Scheme 15 Enantioselective synthesis of vinylcyclopropane mediated by a catalytic amount of telluronium salt

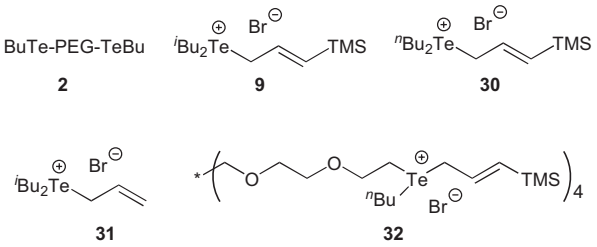
4 Ylide Epoxidation and Aziridination

4.1 Catalytic Ylide Epoxidation

Vinyl epoxides have proven utility as building blocks[26] for the preparation of pharmaceutical targets and natural products. Of the methods available for their synthesis, ylide epoxidation is especially attractive as it involves the regioselective construction of the vinyl epoxide unit with concomitant formation of a carbon–carbon bond. However, in contrast to the reactions of benzylide with aldehydes in which considerable progress has been made, the addition of allylides to aldehydes to form vinyl epoxides is still less developed.[2d] This is probably due to the difficulties associated with [2,3] σ-rearrangement and stereoselectivity. Reports from both the Osuka[15] and Huang groups[16,27] demonstrated that allylic telluronium ylides could react with aldehydes to afford desired compounds. Dai described that the stereoselectivity of ylide epoxidation could be tuned in some cases by changing both the reaction conditions and the ligands of the sulfur ylides.[28] To the best of our knowledge, only a few catalytic versions involved in allylides were documented. However, the catalyst loading is 20 mol% and reduction of catalyst loading resulted in low yields.

4.1.1 Organotelluride

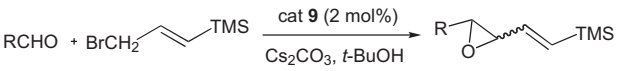
In our studies on ylide chemistry, it is found that the PEG-supported telluride **2** is a better catalyst for the ylide olefination reaction. We also try to explore these catalysts and their analogues to the reaction of ylide expoxidation. The potential catalysts in Scheme 16 were tested in the epoxidation of 4-chlorobenzaldehyde with silylated allylic bromide under various reaction conditions.



Scheme 16

Telluronium salts **9** and **30** proved to be good catalysts for this epoxidation with cesium carbonate as a base in *t*-BuOH.[29] Under optimal conditions, as shown in Table 4, both electron-rich and electron-deficient aromatic aldehydes give vinyl-type epoxides in excellent yields (entries 1–8). Compared with aromatic aldehydes, aliphatic aldehydes such as cyclohexanecarboxaldehyde and nonylaldehyde are usually less active in catalytic ylide reactions, but they worked well (entries 9, 10) in our conditions in the presence of 20 mol% of salt **9**. It is worth noting that allyl bromide also is good for this reaction to give the desired epoxide in excellent yield (entry 11).

Table 4 Catalytic Expoxidation of Aldehydes with Silylated Allylic Bromide



Entry	Catalyst	R	*cis*/*trans*	Yield (%)[a]
1	30	4-ClC_6H_4	49:51	82
2	9	4-ClC_6H_4	49:51	86
3	30	C_6H_5	51:49	88
4	30	4-$CH_3C_6H_4$	50:50	83
5	9	4-$CH_3C_6H_4$	49:51	88
6	30	4-$NO_2C_6H_4$	51:49	78
7	30	2-ClC_6H_4	45:55	82
8	30	2-Naphthyl	52:48	92
9 [b]	9	*n*-C_9H_{19}	54:46	83
10[b]	9	Cyclohexyl	58:42	73
11[c]	31	4-ClC_6H_4	55:45	92

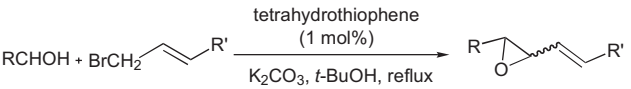
[a] Isolated yield.
[b] 20 mol% of catalyst was used.
[c] Allylic bromide is used to give the non-silylated compound.

4.1.2 Tetrahydrothiophene

Sulfur ylides, particularly sulfur benzylides, have been developed as good reagents[2d] for the preparation of oxirane, cyclopropane and aziridine derivatives since Johnson et al. found the reaction of sulfur ylide with aldehydes in 1958.[30] Although vinyloxiranes are versatile building blocks and precursors of functionalized four-carbon sequences, the reactions of allylic sulfur ylide with aldehydes, imines and electron-deficient alkenes were less explored than other ylide reactions due to its easy [2,3]-sigmatropic rearrangement.

By careful analysis of the reaction of allylic sulfur ylide in the presence of aldehyde, we reasoned that it is possible to realize catalytic ylide epoxidation when high concentrations of both aldehyde and allylic bromide are used in a one-pot reaction because the high concentration of allylic bromide is beneficial to the formation of sulfur salt and the high concentration of aldehyde could probably lead to the reaction of aldehydes with the sulfur ylide before the ylide rearranges. As alcoholic solvents are found to activate the aldehyde probably due to the formation of hydrogen bonds between solvent and aldehyde, we chose *t*-BuOH as the solvent and used 5 mol% tetrahydrothiophene as the catalyst to start our study. As expected, in the presence of 5 mol% tetrahydrothiophene, the reaction of 4-chlorobenzaldehyde with allylbromide at reflux gave the desired product in quantitative yield when either Cs_2CO_3 or K_2CO_3 was used as the base.[31]

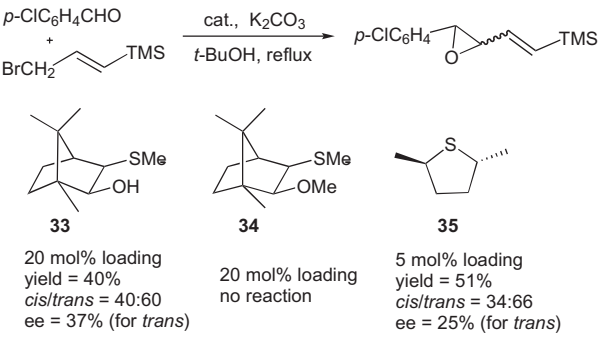
Table 5 Reactions of Aldehydes with Allylic Bromides Catalyzed by Tetrahydrothiophene[a]



Entry	R	R^1	*cis*/*trans*[c]	Yield (%)
1	4-ClC_6H_4	H	36:64	94
2	C_6H_5	H	33:67	85
3	4-$NO_2C_6H_4$	H	38:62	96
4[b]	4-$CH_3OC_6H_4$	H	30:70	85
5[b]	*n*-C_9H_{19}	H	55:45	75
6	4-ClC_6H_4	TMS	25:75	83
7	C_6H_5	TMS	24:76	89
8	4-$NO_2C_6H_4$	TMS	30:70	85
9	2-ClC_6H_4	TMS	27:73	85
10[b]	*n*-C_9H_{19}	TMS	42:58	88
11[b]	Cyclohexyl	TMS	50:50	78

[a] All reactions were carried out in one pot at reflux using tetrahydrothiophene (0.06 mmol), β-trimethylsilylallyl bromide (9.75 mmol) [or allylbromide (19.4 mmol)], aldehyde (6.5 mmol), K_2CO_3 (7.8 mmol), *t*-BuOH (2 mL) under dry N_2 atmosphere.
[b] 5 mol% of catalyst was used.
[c] Determined by GC.
[d] Isolated yield.

As described in Table 5, both electron-rich and electron-deficient aromatic aldehydes give the desired epoxides in excellent yields (entries 1–4). Compared with aromatic aldehydes, aliphatic aldehydes such as cyclohexanecarboxaldehyde and decylaldehyde always are less active in catalytic ylide reactions. However, under our conditions, they worked well (entries 5, 10 and 11). Although the stereoselectivity is not good, the isomers could be separated easily as a single *cis* and/or *trans* isomer by flash chromatography. Noticeably, β-trimethylsilylallyl bromide is also good to give the corresponding epoxides in excellent yields using only 1 mol% or 5 mol% of catalyst (entries 6–11).[31]



Scheme 17 Asymmetric ylide epoxidation catalyzed by sulfide

We also tried a catalytic asymmetric ylide epoxidation with chiral sulfides **33**, **34** and **35** as a catalyst but only moderate yield was achieved in the presence of sulfide **33** or **35**. The enantioselectivities were low to moderate. Sulfide **34** could not catalyze this reaction, probably because the formation of the salt was very difficult (Scheme 17).

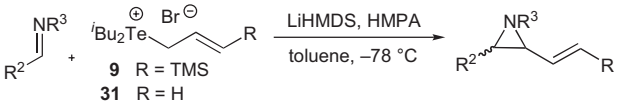
4.2 Aziridination via Telluronium Allylides

Vinylaziridines have proven to be very useful building blocks in organic synthesis and are important subunits in a number of biologically active compounds.[32] The development of synthetic protocols for direct preparation of vinylaziridines from readily available materials is especially attractive. Carbene or nitrene approaches are generally recognized as the most efficient methods for the preparation of aziridines,[33] but generally they are less effective for vinyl-type aziridines due to the difficulty associated with the regioselectivity control. Of the synthetic methods via ylide routes, the reaction between allylic ylide and imines proved to be one of the most convenient methods as it involves the regioselective construction of vinylaziridine unit. Dai and Hou found that sulfur allylides could react with *N*-tosyl arylimines under phase-transfer conditions to give aziridines.[34] Later on, they described that the stereoselectivity of the reaction of arylimines with allylic sulfur ylides could be controlled by the choice of both reaction conditions and ylides.[35] Aggarwal et al. reported that silylated sulfur allylide could react with N–SES phenylimine to afford *trans*-trimethylsilylvinylaziridine.[36] Unlike the arylimines activated by tosyl or diphenylphosphinoyl, *N*-phenylaldimine is less active and no aziridine was detected when it was treated with dimethyl sulfur silylated allylide probably due to ylide rearrangement. Furthermore, few reports appeared in literature on the reaction of allylic ylide with aliphatic imines but *tert*-butyl *N*-tosyl imine.

Considering that allylic telluronium ylide is more active and less prone to rearrangement than the corresponding sulfur ylide, we tried the aziridination of telluronium allylide with less active imines.[34] It was found that this reaction of *N*-phenylaldimine with telluronim allylide proceeds well to give the desired aziridines with high stereoselectivity. Moreover, we also found that a variety of *N*-Boc alkylimines with different structures are also good substrates for this ylide aziridination.

As shown in Table 6, all the aromatic *N*-phenylaldimines are good substrates to afford the desired products in moderate to high yields. In all cases, excellent *trans*-selectivity is observed. Allylic telluronium salt **31** also worked to give the vinylaziridine but both the yield and selectivity decreases slightly (entry 7). Usually, aliphatic imines are regarded as less active than aromatic imines. They are easily isomerized into enamine under the reaction conditions and a few alkylimines but particularly *tert*-butyl *N*-tosylimine is applied to the ylide aziridination. By a one-pot strategy, we are pleased to find that telluronium allylide could react with *N*-Boc-aliphatic imines to afford *cis*-*N*-Boc-aziridines in good yields with good stereoselectivity (entries 8–10). And, thus, this strategy greatly extends the substrate scope of ylide aziridination.[37]

Table 6 Stereoselective Synthesis of Aziridines[a]



Entry	R	R^2	R^3	Yield (%)[b]	*trans*/*cis*[c]
1[d]	TMS	Ph	Ph	84	98:2
2	TMS	*p*-MeC_6H_4	Ph	70	99:1
3	TMS	*p*-$MeOC_6H_4$	Ph	52	96:4
4	TMS	*o*-$MeOC_6H_4$	Ph	71	99:1
5	TMS	*p*-ClC_6H_4	Ph	83	98:2
6[d]	TMS	*p*-$CF_3C_6H_4$	Ph	64	98:2
7	H	Ph	Ph	37	80:20
8[e]	TMS	$(CH_3)_2CH$	Boc	77	9:91
9[e]	TMS	Cyclohexyl	Boc	71	7:93
10[e]	TMS	*n*-Bu	Boc	50	14:86

[a] Reaction were carried out at –78 °C, imine/salt/base = 1:1.4:1.4 and 3 equiv of HMPA used.
[b] Isolated yields based on imines.
[c] Determined by ^1H NMR.
[d] In THF at –78 °C.
[e] In THF at –78 °C and NaHMDS as the base.

5 Summary and Outlook

Catalysis and selectivity are two of the major challenges in current ylide chemistry. In the past several years, we attempted to develop catalytic and selective ylide reactions and discovered that the PEG-supported telluride is a very efficient catalyst for the Wittig-type olefination of aldehydes. The diastereoselectively controllable and asymmetric ylide cyclopropanation were also developed. The catalytic and selective ylide reactions with high efficiency for the preparation of multisubstituted small ring compounds are still a challenge and await new strategies.

Acknowledgment

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