

Telluronium Ylides in Cyclopropanation and Catalytic Olefination

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ABSTRACT: Telluronium ylides are versatile reagents for cyclopropanation reaction and Wittig-type olefination. This review outlines the recent development in stereoselectivity of ylide cyclopropanation and catalytic olefination in our group. © 2002 Wiley Periodicals, Inc. Heteroatom Chem 13:463–466, 2002; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10076

INTRODUCTION

The birth of Wittig reaction marked the entry of ylides into the arsenal of important synthetic tools [1]. Because of their effectiveness and generality, ylides have not only become one of the most useful reagents in constructing carbon–carbon double bonds, but in some cases they have also been used in constructing small ring compounds such as epoxides, cyclopropanes and aziridines [2].

In our continuing studies on the application of ylides in organic synthesis, we have focused on telluronium ylides. In this account, we have summarized our recent results on cyclopropanation and catalytic olefination of telluronium ylides.

STEREOCONTROLLED SYNTHESIS OF VINYL CYCLOPROPANES

It was found that a silylated telluronium allylide, generated in situ from 3-trimethylsilylprop-2-enyldiisobutyltelluronium bromide (**1**) in the presence of lithium 2,2,6,6-tetramethylpiperidide (LTMP), reacted with methyl cinnamate (*trans*) to form *trans*-3-substituted-*trans*-2-trimethylsilylvinyl-1-methoxycarbonylcyclopropane (**2**) with very high selectivity [3]. Later on, we found that a one-pot reaction of the same ylide with *trans*-benzalacetophenone gave *trans*-3-substituted-*cis*-2-trimethylsilylvinyl-1-benzoylcyclopropane (**3**) with excellent stereoselectivity under solid–liquid phase-transfer catalysis (Scheme 1) [4].

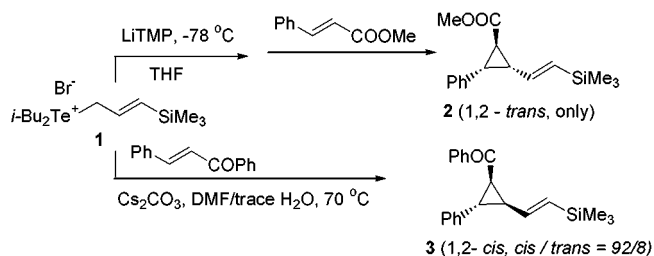
Further studies showed that the Lewis acid (the cation of the base) played a key role in determining the stereochemistry of this reaction. The allylic telluronium ylides reacted with α,β -unsaturated esters or amides in the presence of a lithium salt to afford *trans*-2-vinyl-*trans*-3-substituted cyclopropyl esters or amides **4**, respectively, with high selectivity and in excellent yields (Scheme 2). In the absence of lithium salts, the stereoselectivity of these reactions changed and *cis*-2-vinyl-*trans*-3-substituted cyclopropyl esters or amides **5** were obtained. It is shown that the reaction temperature is also a governing factor in the stereoselectivity of this reaction, a higher temperature being beneficial to the formation of *cis* compounds, but causing a lowering of the yields of products greatly. The solvent can influence the stereoselectivity, but less effectively than the lithium salts. In many cases, the ratio of the two isomers **4** and **5** can be inverted from 99:1 to

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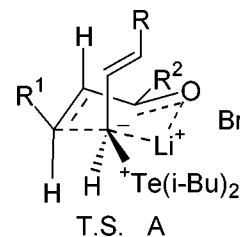
SCHEME 1 Ylide cyclopropanation of α,β -unsaturated ester and ketone.

1:99 by a proper choice of base and solvent. Moreover, not only the trimethylsilylated allylide could be used, but the unsubstituted allylide and corresponding crotonylide could also give good results [5].

The different stereoselectivity of the reaction of **1** with α,β -unsaturated esters and amides under different reaction conditions can be explained as follows: When $\text{KN}(\text{SiMe}_3)_3$ is used as the base, this cyclopropanation reaction is subject to thermodynamic control and the *cis*-2-vinyl isomer is the major product. In the presence of lithium salts, however, the reactions may proceed via a chelating six-membered ring transition state, which is formed by the coordination of lithium ion with the carbonyl oxygen and ylidic carbanion simultaneously (Scheme 3) to give *trans*-2-vinyl isomer.

This mechanistic insight suggested that it might be possible to control the stereoselectivity of such reactions by occupying the coordination site of lithium by an additional ligand. Hexamethylphosphoramide (HMPA) was first chosen as the additive because it is supposed to inhibit the formation of a lithium-mediated transition state in situ because of its strong coordinating ability with the lithium ion. As expected, without HMPA, silylated telluronium allylide reacted with α,β -unsaturated esters and amides to afford *trans*-2-vinyl-*trans*-3-substituted cyclopropanes (**4**) in high yield and with high selectivity. The same reaction provided *cis*-2-vinyl-*trans*-3-substituted cyclopropanes (**5**) when carried out in the presence of HMPA (Scheme 4) [6].

However, the stereochemical control of the reaction failed when the substrates were changed to



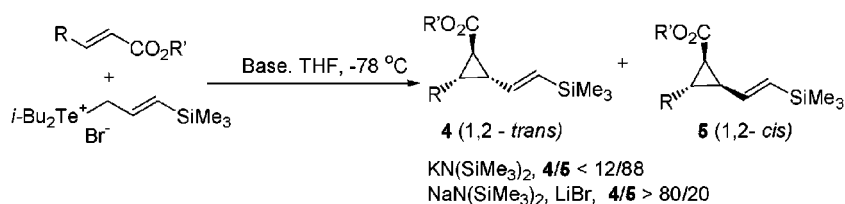
SCHEME 3 Possible transition state involving lithium ion.

α,β -unsaturated ketones. It was found that the stereochemistry of this reaction was almost independent of the lithium salt. The major products are **7**, but in which the trimethylsilylvinyl group and carbonyl group are on the same side of the ring and oriented *trans* with respect to the phenyl group. Moreover, the presence of a lithium salt reduced the yield significantly, and the product of the reaction of the ylide with a chalcone was complex due to the concomitant formation of some epoxides. Epoxide was the major product when toluene was selected as the solvent in the presence of lithium bromide.

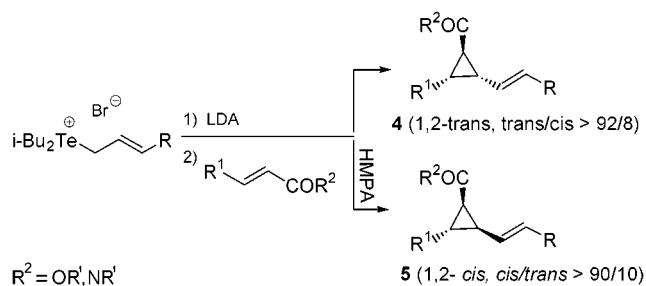
Fortunately, the corresponding allylic arsonium ylide [7] can also react smoothly with α,β -unsaturated ketones to furnish cyclopropanes in high yields with stereochemistry opposite to that which is obtained by the use of the corresponding telluronium ylides. In this case, isomer **6** was obtained with high stereoselectivity when an arsonium ylides was used. Thus, it provided an alternative path for the control of the stereoselectivity in the cyclopropanation reaction of ylides with Michael acceptors (Scheme 5).

(-)-8-Phenylmenthol is a powerful chiral auxiliary in asymmetric synthesis. It has also been proved to work well in the cyclopropanation of a telluronium allylide (Scheme 6) [8]. It was found that a variety of α,β -unsaturated esters could react with a silylated allylic telluronium ylide to provide silylvinylcyclopropane (**8**) with high diastereoselectivity and in high yield.

The high diastereoselectivities may be the result of a π -stacking effect between the phenyl and



SCHEME 2 Effect of base on the stereoselectivity.



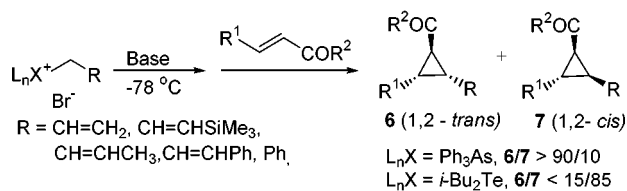
SCHEME 4 Tuning of stereoselectivity by HMPA.

dienyl group in (-)-8-phenylmenthyl esters of α,β -unsaturated acids. As shown in Scheme 7, the phenyl group was proposed to block the *si* face of the carbon-carbon double bond. The telluronium ylide attacked at C-3 at the *re* face, and compound **8** was formed as the major product.

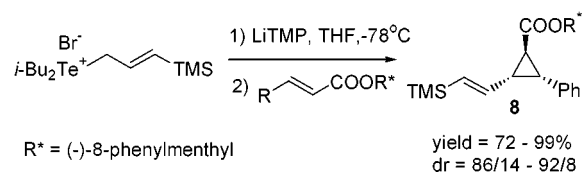
CATALYTIC WITTIG-TYPE REACTION

The Wittig olefination reaction was reported in 1953 by Wittig and his coworker [9]. To date, variants of this reaction are among the most powerful approaches in constructing carbon-carbon double bonds [1]. However, from the point of view of atom economy, it is not a perfect reaction [10]. A solution to this problem is to develop catalytic Wittig olefination reactions. Till date, there are few successful examples: the first example of a catalytic Wittig-type of olefination reaction was reported in 1989, in which Huang et al. found that tributylarsine could be used as the catalyst in the presence of triphenyl phosphite [11]. Later on, they described catalytic ylide olefination reactions mediated by dibutyl telluride or diisobutyl telluride [12]. Unfortunately, in both of the reactions mentioned above, 20 mol% of the catalyst must be used. Reduction of the amount of catalyst causes low yield, even if the reaction time is prolonged [13]. Compared to other catalytic reactions, obviously, low catalytic efficiency and use of triphenyl phosphite are the two serious drawbacks.

By analysis of the mechanism corresponding to that reported (Scheme 8), probably the formation of



SCHEME 5 Different selectivity of telluronium and arsonium ylide.



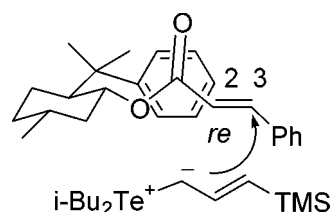
SCHEME 6 Asymmetrical synthesis of vinylcyclopropanes mediated by (-)-8-phenylmenthol.

ylide is a rate-determining step in the catalytic ylide olefination [14].

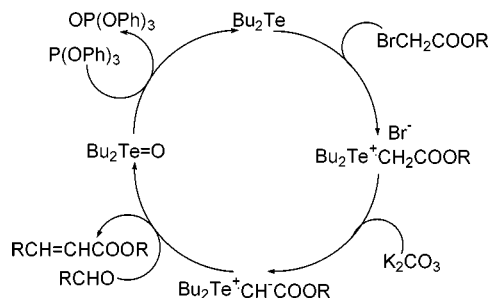
Improving the rate of ylide generation may be essential to speed up this catalytic cycle. Thus, we designed PEG-telluride as the catalyst for the following considerations. Firstly, the PEG may interact with potassium ion, as in a crown ether [13], by self-assembly to form a half-open crown ether as shown in Fig. 1. PEG could be proposed not only to play a role as a phase-transfer catalyst but also to increase the basicity of the potassium carbonate in the reaction system. Thus, it is expected to accelerate the reaction of ylide formation and to enhance the catalytic activity. Secondly, soluble PEG is being developed as an alternative matrix for organic synthesis owing to the advantages of homogeneous solution chemistry as against those of solid phase methods [15]. The soluble PEG-supported telluride catalyst can be recovered easily and reused.

When *p*-chlorobenzaldehyde was mixed with ethyl bromoacetate in the presence of triphenyl phosphite and 1 mol% of PEG-supported telluride in toluene at 80°C, we found that the Wittig-type reaction product was obtained in 88% yield with excellent stereoselectivity. This meant that the catalytic efficiency of this reaction was improved greatly compared with other catalytic ylide reactions reported to date. By optimization of the reaction conditions, the desired olefin could be obtained in quantitative yield when 2 mol% of PEG-supported telluride was used. To determine the generality of this reaction, a variety of structurally different aldehydes were employed.

It was found that both aliphatic and aromatic aldehydes worked well with high *E*-stereoselectivity and in reasonable yields. Aromatic aldehydes with



SCHEME 7 Model for chiral induction.



SCHEME 8 Proposed mechanism for catalytic Wittig-type reaction.

an electron-withdrawing group or a weak electron-donating group in the *p*-position as well as the heteroaromatic aldehydes were the most suitable substrates. All of these can afford the desired products in excellent yields with high stereoselectivity. Although an aromatic aldehyde with a strong electron donor group, such as *p*-methoxybenzaldehyde, was less active, it still worked well 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. Ethyl 2-bromopropanoate could also react with an aldehyde to afford a trisubstituted olefin with high stereoselectivity in moderate yield.

Finally, in order to make this reaction more practical, we extended our efforts to use inorganic reducing reagents instead of $P(OPh)_3$. By optimizing the reaction conditions, we chose *tert*-butyl bromoacetate instead of the ethyl ester and obtained a 99% yield of the corresponding olefin under the same conditions. Even if 1 mol% of catalyst was used, the yield was still 81%. A variety of structurally different 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 when using $NaHSO_3$ as the cocatalyst. Thus, $NaHSO_3$ turned out to be another effective reducing reagent in this catalytic Wittig-type reaction. It is interesting that the

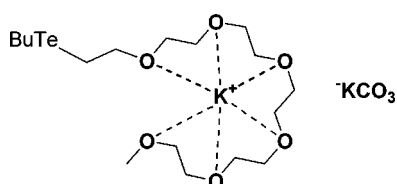


FIGURE 1 Catalyst for ylide olefination.

use of $NaHSO_3$ improved the stereoselectivity of this reaction.

It is noteworthy that the product isolation procedure was very simple after this modification. 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 with ether.

Further studies showed that the catalyst could be recovered quantitatively but partially lost its activity through multiple cycles. We found that 2-furaldehyde (10.85 mmol) reacted with *t*-butyl bromoacetate in the presence of sodium bisulfite to afford the desired product in 90% yield when 2 mol% of PEG-telluride was used. The catalyst could be recovered in 100% yield by filtering off the solid of the reaction mixture, followed by addition of ether and collection of the precipitate. The recovered catalyst could be used in the second run, but only a 69% yield was obtained, probably because of the decomposition of PEG-telluride during the catalytic olefination [16].

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