Communication

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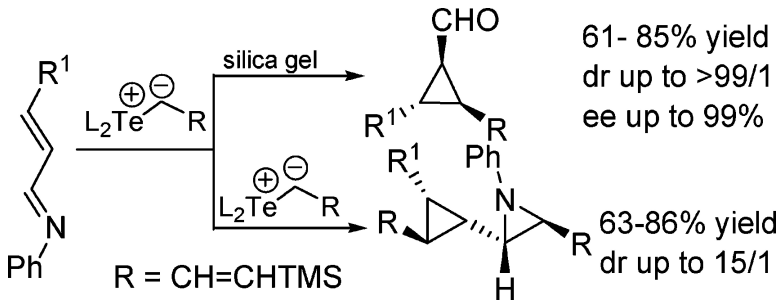

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The Michael Addition−Elimination of Ylides to α,β-Unsaturated Imines. Highly Stereoselective Synthesis of Vinylcyclopropanecarbaldehydes and Vinylcyclopropylaziridines

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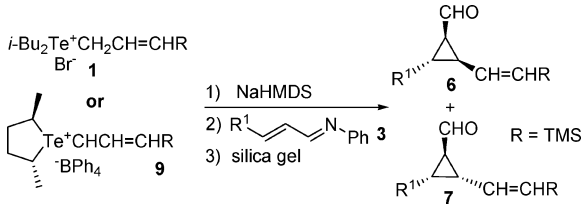
Much attention has been paid to the construction of multisubstituted cyclopropanes, the basic structural elements in a wide range of biologically active compounds as well as important intermediates in organic synthesis.[1] The tandem Michael addition−elimination of ylides to electron-deficient alkenes provides easy access to functionalized cyclopropanes.[2] However, few examples were reported on the preparation of cyclopropanecarbaldehydes[3] via ylide cyclopropanation of α,β-unsaturated aldehydes, except those related to stabilized ylides,[2c,4] due to the difficulty associated with the control of the chemoselectivity (C=C versus C=O). Our group described a method for the one-step enantioselective synthesis of 1,3-disubstituted-2-vinylcyclopropanes[3,5] with high diastereoselectivity from α,β-unsaturated esters, amides, ketones, and nitriles via a sulfur or tellurium ylide.[6] However, switching the substrate to α,β-unsaturated aldehyde gave epoxide in lieu of the desired cyclopropanecarbaldehyde.[7] We recently sought a solution to this problem and developed the first example of ylide cylopropanation of α,β-unsaturated imines, leading to a highly stereoselective synthesis of vinylcyclopropanecarbaldehydes and vinylcyclopropylaziridines. In this communication, we wish to report the preliminary results.

The reactions of ylides with α,β-unsaturated imines were well-studied and documented to afford aziridines as the products via a 1,2-addition.[8] To the best of our knowledge, no example of ylide cyclopropanation of α,β-unsaturated imines via a 1,4-addition has been described in the literature. Fortunately, we found that telluronium salt **1**, after deprotonation by NaHMDS, could react with imine **3a** in a 1,4-addition manner to afford cyclopropanecarbaldehyde[9] **6a** and **7a** with excellent chemoselectivity and diastereoselectivity (**6a**/**7a** > 99/1) in 85% yield (entry 1, Table 1). Further studies showed that the *N*-substituents strongly affected the chemoselectivity. When *N*-sulfonyl or *N*-sulfinyl imine was selected as a substrate instead of the *N*-phenyl imine, only aziridine was obtained. Therefore, the chemoselectivity of the reaction of the ylide with α,β-unsaturated imine could be controlled by a reasonable choice of the *N*-substituents (Scheme 1).

Having established the feasibility of and optimal conditions for the cyclopropanation, we surveyed the scope of the α,β-unsaturated imines. As shown in Table 1, β-aryl and β-heteroaryl α,β-unsaturated imines were good substrates to afford the desired products with high diastereoselectivities (up to >99/1) in good yields (entries 1−7, Table 1), providing easy access to vinylcyclopropanecarbaldehydes that could not be prepared by a direct reaction of α,β-unsaturated aldehydes with allylic ylides due to the problem of the chemoselectivity. Substitution on the aryl ring with both electron-withdrawing and electron-donating groups proved to be well-tolerated, notably, with an ester group attached to the aromatic substituent.

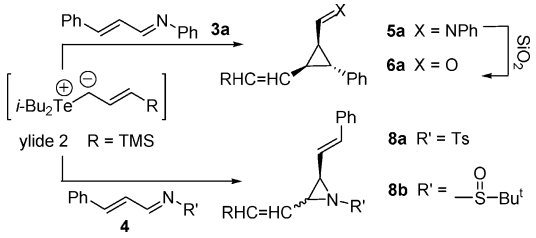
Table 1. Selective Cyclopropanation between Unsaturated Imines and Telluronium Ylide[7]



entry	salt	**3** (R^1)	**6**/**7**[a]	yield (%)[b]	ee (%)[c]
1	**1**	**3a** (C_6H_5)	>99/1	85	−
2	**1**	**3b** (4-ClC_6H_4)	>99/1	75	−
3	**1**	**3c** (4-$CF_3C_6H_4$)	>99/1	85	−
4	**1**	**3d** (4-$MeOC_6H_4$)	>99/1	68	−
5	**1**	**3e** (4-$MeO_2CC_6H_4$)	>99/1	80	−
6	**1**	**3f** (2-furanyl)	>99/1	68	−
7	**1**	**3g** (2,4-$Cl_2C_6H_3$)	>32/1	88	−
8	**9**	**3a** (C_6H_5)	>60/1	85	99
9	**9**	**3b** (4-ClC_6H_4)	>60/1	73	95
10	**9**	**3c** (4-$CF_3C_6H_4$)	>36/1	83	95
11	**9**	**3d** (4-$MeOC_6H_4$)	>99/1	68	95
12	**9**	**3f** (2-furanyl)	>99/1	61	95

[a] Determined by 300 M ^{1}H NMR. [b] Isolated yield. [c] Determined by chiral HPLC for compound **6** when salt **9** was used.

Scheme 1



In a previous study,[6a] it was demonstrated that chiral telluronium salt **9** was good for the highly enantioselective synthesis of vinylcyclopropane derivatives. For both β-aryl and β-heteroaryl unsaturated imines, the reaction with chiral salt **9** instead of salt **1** gave the desired cyclopropanes with both excellent diastereoselectivity and enantioselectivity in good yields (entries 8−12, Table 1), providing a new method for the preparation of optically active vinylcyclopropanecarbalehydes in one-pot.

It was a great surprise to us that vinylcyclopropylaziridines **10a** and **11a** were isolated in 82% overall yield when increasing the equivalent ratio between telluronium salt **1** and imine **3a** to 3 to 1, because aliphatic *N*-phenylaldimines were found to be inert to ylide **2** in our previous study.[10] This experimental result also demonstrated the formation of intermediate **5a**, suggesting that the cyclopropyl-

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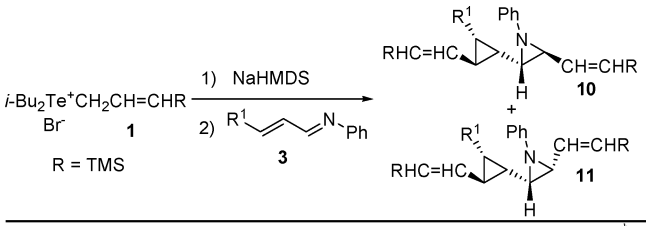
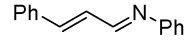
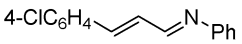
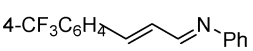
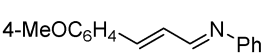
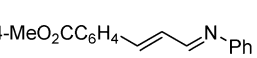
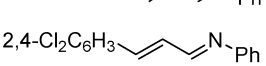
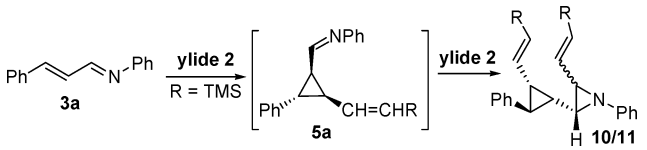
Table 2. One-Pot Synthesis of Cyclopropylaziridines[7]



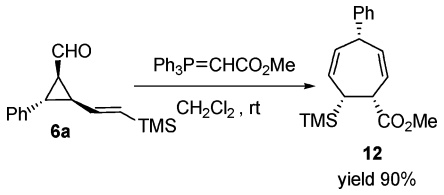
Entry		3	10/11[a]	Yield(%)[b]
1	**3a**		13/1	82
2	**3b**		13/1	80
3	**3c**		13/1	81
4	**3d**		8/1	63[c]
5	**3e**		15/1	82
6	**3g**		13/1	86

[a] Determined by 300 M ^{1}H NMR. [b] Isolated yield. [c] Products are not very stable on silica gel, and 4 equiv of salt **1** was used. When **3f** was selected as a substrate, the products were completely decomposed on column.

Scheme 2



Scheme 3. Tandem Reaction from Vinylcyclopropanecarbaldehyde **6a** to Cycloheptadiene **12**[7]



aziridines were produced via a Michael addition−elimination, followed with an aziridination reaction by a second ylide attack (Scheme 2).

By employing 3−4 equiv of salt **1** relative to imine **3**, we found that the desired product with cumulated three-membered rings could be synthesized with good diastereoselectivity (up to 15/1) in reasonable yields (Table 2). Again, β-aryl and β-heteroaryl α,β-unsaturated imines worked well in the sequential cyclopropanation−aziridination. Entry 5 is noteworthy, indicating that the ester group is compatible with the reaction.

In summary, we have developed a new protocol for the preparation of vinylcyclopropanecarbaldehydes as well as cyclopropylaziridines via allylic ylides using readily available α,β-unsaturated imines as starting materials. The high diastereoselectivity, excellent enantioselectivity, and in particular the unique chemoselectivity make this reaction potentially useful. For example, the aldehyde **6a** was easily transformed into a seven-membered ring compound **12** through a Wittig reaction, followed by a [3,3] σ-rearrangement (Scheme 3).

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Supporting Information Available: Synthesis and characterization of key compounds, chiral HPLC data of **6** (PDF, CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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