The First Example of Catalytic Aziridination Mediated by Arsonium Ylides: Preparation of *trans*-Pentafluorophenyl-Containing Aziridines

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Received 25 February 2005

Abstract: Triphenylarsine catalyzes the formation of aziridines from tosyl imines and aromatic diazo compounds in a one-pot reaction. It is the first example of catalytic aziridination mediated by arsonium ylides. It gave aziridines in excellent diastereoselectivity with pentafluorophenyl diazomethane as the substrate. This catalytic reaction is complementary with the reaction mediated by sulfur ylides.

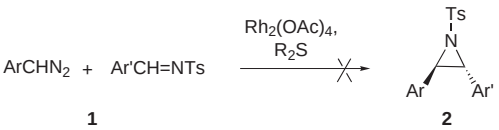
Key words: diazocompound, ylide, fluorine, aziridine, catalyze

Aziridines are synthetic intermediates that can be converted into important nitrogen containing functional groups.[1] Although several efficient synthesis of aziridines from olefins or imines have been reported, most methods are non-catalytic and result in low diastereoselectivities.[2] Aggarwal reported a novel catalytic and asymmetric process for aziridination mediated by sulfur ylides, however, the diastereoselectivities are low.[3] Moreover, the relative low reactivity of sulfur ylides limits the scope of their further applications. For example, sulfur ylides substituted with electron-withdrawing groups cannot react with imines to give the aziridines (see the details in this paper). Arsonium ylides have high reactivity with carbonyl compounds or electron-deficient alkenes and produce alkenes, epoxides, and cylcopropanes in high diastereoselectivity.[4] However, in the field of catalytic aziridination mediated by arsonium ylides, to the best of our knowledge, no examples have been reported.

Previously, we reported a catalytic procedure for the direct coupling of aldehydes with pentafluorophenyl benzaldehyde tosylhydrazone salts to give the *trans*-alkenes exclusively.[5] The reaction temperature (ca. 40 °C) and low yields (ca. 50%) severely limit its further applications. The inefficient decomposition of the sodium salt of pentafluorobenzaldehyde tosylhydrazone may account for the low yields. Therefore, development of an efficient method to generate the potentially hazardous diazo compound is necessary. Reese et al. reported that 2,4,6-triisopropylbenzenesulfonyl hydrazones are better intermediates than tosyl hydrazones in the preparation of aryldiazoalkanes.[6] Aryl diazomethane **1a** (Ar = C_6F_5) and **1b** (Ar = Ph), by using Reese's method, can be synthesized in more than 95% yield and 97% purity. The crude products aryl diazomethanes **1** could be used without further purification after general work-up. This procedure reduces the potential hazard significantly by avoiding heating the tosyl salt in vacuo.

The introduction of fluorine into organic molecules may profoundly influence their physical and biological properties. Recently, there has been growing interest in fluorine-containing aromatic compounds due to the unique physical properties of the fluorine atom. Herein, we report our attempts to prepare fluorine-containing aziridines catalytically from diazo compounds, mediated by arsonium ylides.

As we all know, sulfur ylides are well known for their abilities to react with aldehydes, electron-poor alkenes, and imines to form epoxides, cyclopropanes, and aziridines, respectively. Initially, to make sure that the sulfur ylide generated from pentafluorophenyl diazomethane (**1a**) could react with tosyl imines to give the corresponding aziridines, we used $Rh_2(OAc)_4$ to catalyze the decomposition of diazo compound **1a**, and tetrahydrothiophene to trap the metal carbenenoid. To our disappointment, no aziridine was isolated after several attempts (Equation 1). The imine was recycled in almost quantitative yield. The strong electron-withdrawing properties of fluorine atoms on the phenyl rings may be attributed to the failure of this transformation.

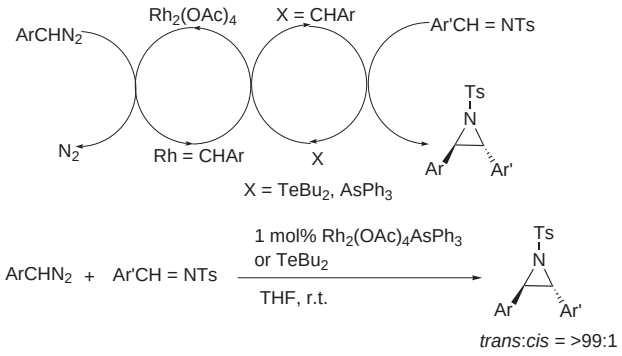


Equation 1

To resolve this problem, ylides with higher activity should be used. We know that tellurium ylides have similar chemical properties to sulfur ylides because they are situated in the same main group in the periodic table. Moreover, telluronium ylides are more reactive than the corresponding sulfur ylides. We assumed that the telluronium ylides generated in situ from the reaction of telluride and pentafluorophenyl diazomethane could react with tosyl imines to give aziridines. The reaction was carried out at room temperature by adding the diazo compound **1a** dissolved in THF dropwise to a solution of

SYNLETT 2005, No. 9, pp 1429–1432
Advanced online publication: 27.04.2005
DOI: 10.1055/s-2005-868498; Art ID: U05105ST

tosyl imine, dibutyl telluride, and a catalytic amount of $Rh_2(OAc)_4$ (1 mol%) in the same solvent. The reaction, which was monitored by TLC, was complete in four hours. The aziridines were isolated in moderate yields and diastereoselectivities after general work-up (Table 1, entries 1, 2). The tosyl imine of *trans*-cinnamaldehyde gave the aziridine **2c** in lower yield and diastereoselectivity than the saturated imines (Table 1, entry 3). The unpleasant odor and ready oxidation by air of $TeBu_2$ made this procedure very inconvenient.



Scheme 1 Catalytic cycle for the preparations of aziridines.

Discouraged by the above results, we turned our attention to the arsonium ylides. Arsonium ylides are known for their high reactivity and high diastereoselectivity in alkene, epoxide, and cyclopropane formation.[4] They have similar reactivity to the telluronium ylides, and in general exhibit higher diastereoselectivities than the latter. Moreover, the stability of triphenyl arsine in air may facilitate the experimental operations. Based on the above, we believed that arsonium ylides would produce the aziridines in higher yields and diastereoselectivities.

When a stoichiometric amount of triphenyl arsine was used instead of dibutyl telluride under the same reaction conditions, the starting material tosyl imine derived from benzaldehyde disappeared completely after four hours. The aziridine **2a** was obtained in almost quantitative yield and with complete *trans* stereoselectivity, which was in line with our prediction (Table 1, entry 4). Extension of the substrates showed that the yields of the aziridines are good to excellent for the imines of electron poor or neutral aromatic aldehydes (Table 1, entries 4–8), while moderate yields for those imines derived from electron rich aldehydes (Table 1, entries 9, 10). In particular, the low solubility of the tosyl imine derived from 4-nitrobenzaldehyde in THF resulted in moderate yield of aziridine (Table 1, entry 11). The reactions gave almost exclusive *trans* diastereoselectivities for all tosyl imines of aromatic aldehydes except *trans*-cinnamaldehyde. The *trans* stereoselectivities of aziridines were further confirmed by X-ray analysis (Figure 1).

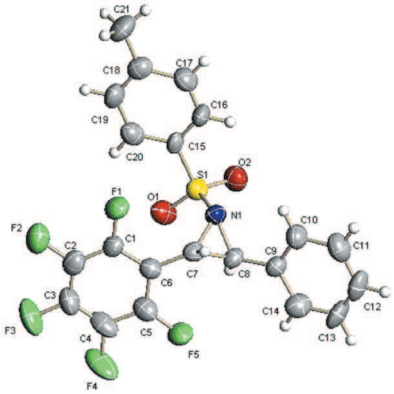


Figure 1

Table 1 Preparation of Aziridines from the Reaction of Tosyl Imines and Diazo Compound **1a**

Entry	Ar′CH=NTs (Ar′ =)	$TeBu_2$ or Ph_3As (mol%)	Products	Yield (%)[a]	*trans*/*cis*[b]
1	Ph	$TeBu_2$ (100)	**2a**	64	18:1
2	*p*-ClC_6H_4	$TeBu_2$ (100)	**2b**	49	9:1
3	*trans*-PhCH=CH	$TeBu_2$ (100)	**2c**	40	5:2
4	Ph	Ph_3As (100)	**2a**	98	>99:1
5	*p*-ClC_6H_4	Ph_3As (100)	**2b**	76	>99:1
6	*trans*-PhCH=CH	Ph_3As (100)	**2c**	90	25:2
7	*p*-BrC_6H_4	Ph_3As (100)	**2d**	73	>99:1
8	*o*-$NO_2C_6H_4$	Ph_3As (100)	**2e**	82	>99:1
9	*p*-$CH_3C_6H_4$	Ph_3As (100)	**2f**	55	>99:1
10	*p*-$CH_3OC_6H_4$	Ph_3As (100)	**2g**	63	>99:1
11	*p*-$NO_2C_6H_4$	Ph_3As (100)	**2h**	54	>99:1

[a] Isolated yield.
[b] Determined by ^1H NMR.

When a substoichiometric amount of $AsPh_3$ (20 mol%) was used to catalyze the reaction, the aziridines were obtained in similar diastereoselectivity, but with a slightly reduced yield (Table 2).

Table 2 Preparation of the Aziridines from the Reaction of Tosyl Imines and Diazo Compound **1a** Using a Catalytic Amount of $AsPh_3$ (20%)

Entry	Ar′CH=NTs (Ar′ =)	Yield (%)[a]	*trans*/*cis*[b]
1	Ph	**2a** (61)	>99:1
2	*p*-ClC_6H_4	**2b** (49)	>99:1
3	*trans*-PhCH=CH	**2c** (59)	12:1
4	*p*-BrC_6H_4	**2d** (45)	>99:1
5	*o*-$NO_2C_6H_4$	**2e** (61)	>99:1
6	*p*-$CH_3OC_6H_4$	**2g** (51)	>99:1

[a] Isolated yield.
[b] Determined by ^1H NMR spectroscopy.

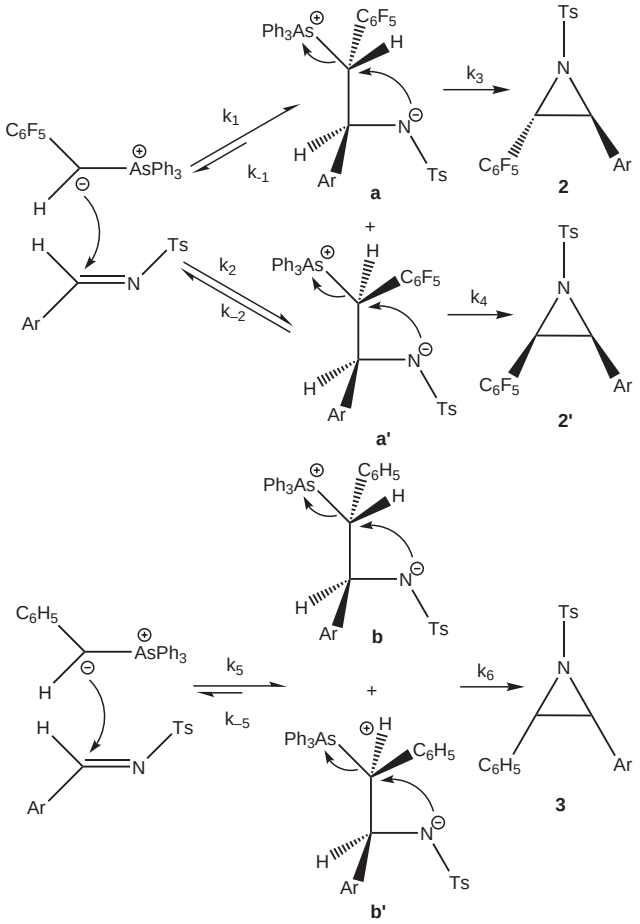
Encouraged by the above results, we then tried to extend this method to the preparation of non-fluoroaziridines. The corresponding non-fluoroaziridine **3a** was prepared in quantitative yield under the same reaction conditions by using a stoichiometric amount of Ph_3As and diazo compound **1b** (Table 3, entry 1), unfortunately with complete loss of diastereoselectivity. Reducing the amount of $AsPh_3$ to a substoichiometric amount (20 mol%), it gave the aziridines in excellent yields but again no diastereoselectivity resulted (Table 3, entries 2, 3).

Table 3 Preparation of Aziridines from the Reaction of Tosyl Imines and Diazo Compound (**1b**)

Entry	Ar′CH=NTs (Ar′ =)	Ph_3As (mol%)	Yield (%)[a]	*trans*/*cis*[b]
1	Ph	100	**3a** (100)	51:49
2	Ph	20	**3a** (97)	53:47
3	*p*-ClC_6H_4	20	**3b** (83)	1:1

[a] Isolated yield.
[b] Determined by ^1H NMR spectroscopy.

To account for the different diastereoselectivities between these two types of arsonium ylides, possible reaction mechanisms were proposed (Scheme 2). The reaction of the arsonium ylides with the tosyl imines to form the aziridines should be stepwise, and the first step giving the intermediates should be reversible. Due to the strong electronegativity of the fluorine atom, the negative charge on the intermediate species can be efficiently stabilized by the pentafluorophenyl. The thermodynamically unstable intermediate **a′** would then convert back to the starting materials ylide and imine. As for the thermodynamically stable intermediate **a**, $k_1 >> k_{-1}$, therefore the *trans*-aziridine will form without reversible reaction. This means that the reaction gives mainly the thermodynamic stable isomers **2** diastereoselectively. As for the intermediates **b** and **b′**, due to the high activity of triphenyl arsin-phenylmethylene, the rate constant k_5 is much greater than k_{-5} ($k_5 >> k_{-5}$), as a result a mixture of *trans*- and *cis*-aziridines are formed.



Scheme 2 Probable mechanisms of the reaction to prepare aziridines.

In summary, we have reported that arsonium ylides, generated in situ from the reaction of triphenyl arsine with aromatic diazomethane catalyzed by $Rh_2(OAc)_4$, mediated aziridination of the tosyl imine. It could give, selectively, completely *trans*-perfluorophenyl-containing aziridines starting from the tosyl imines of saturated aromatic aldehydes. Due to the high reactivity, the diastereoselectivity disappeared completely when using phenyl diazomethane as the substrate, although the yield is excellent. To the best of our knowledge, it is the first report that arsonium ylide mediated aziridination from imines. It is complementary to the sulfur ylides which have lower reactivity for the preparation of aziridines. This base-free, catalytic, diastereoselective and mild reaction will be the method of choice in many instances.

Acknowledgment

The authors thank the National Natural Science Foundation of China (NNSFC) (No. 20372077 and 20472106).

References

(1) (a) van Santen, R. A.; Kuipers, H. P. C. *Adv. Catal.* **1987**, *35*, 265. (b) Zwanenburg, B.; ten Holte, P. In *Stereoselective Heterocyclic Synthesis III*, Vol. 216; Metz, P., Ed.; Topics in Current Chemistry, Springer: Berlin, **2001**, 93–124.
(2) Müller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905.
(3) Aggarwal, V. K.; Alonson, E.; Fang, G.; Ferrara, M.; Hynd, G.; Porcelloni, M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599.
(4) (a) Aggarwal, V. K.; Patel, M.; Studley, J. *Chem. Commun.* **2002**, 1514. (b)Tewari, R. S.; Chaturvedi, S. C. *Tetrahedron Lett.* **1977**, *43*, 3843. For reviews on arsonium ylides: (c) Lloyd, D.; Gosney, I.; Ormiston, R. A. *Chem. Soc. Rev.* **1987**, *16*, 45. (d) Huang, Y.; Sheng, Y. *Adv. Organomet. Chem.* **1982**, *20*, 113. (e) Johnson, A. W. *Ylide Chemistry*; Academic Press: New York, **1966**.
(5) Zhu, S. F.; Liao, Y. X.; Zhu, S. Z. *Org. Lett.* **2004**, *6*, 377.
(6) Dudman, C. C.; Reese, C. B. *Synthesis* **1982**, 419.
(7) (a) Ramachandran, P. V. In *Asymmetric Fluoroorganic Chemistry: Synthesis Applications and Future Directions, ACS Symposium Series 746*; American Chemical Society: Washington DC, **2000**. (b) Ojima, I.; McCarthy, J. R.; Welch, J. T. In *Biomedical Frontiers of Fluorine Chemistry, ACS Symposium Series 639*; American Chemical Society: Washington DC, **1996**. (c) Kukhar', V. P.; Soloshonok, V. A. In *Fluorine-containing Amino Acids: Synthesis and Properties*; Wiley: New York, **1995**. (d) Welch, J. T. In *Selective Fluorination in Organic and Bioorganic Chemistry, ACS Symposium Series 456*; American Chemical Society: Washington DC, **1991**. (e) Welch, J. T.; Eswarakrishnan, S. In *Fluorine in Bioorganic Chemistry*; Wiley & Sons: New York, **1991**.
(8) (a) Strehmel, B.; Sarker, A. M.; Malpert, J. H.; Strehmel, V.; Seifert, H.; Neckers, D. C. *J. Am. Chem. Soc.* **1999**, *121*, 1226. (b) Brooke, G. M.; Mawson, S. D. *J. Fluorine Chem.* **1990**, *50*, 111. (c) Feast, W. J.; Lovenich, P. W.; Puschmann, H.; Taliani, C. *Chem. Commun.* **2001**, 505. (d) Yu, L.; Bao, Z. *Adv. Mater.* **1994**, *6*, 156. (e) Coates, G. W.; Dunn, A. R.; Henling, L. M.; Ziller, J. W.; Lobkovskey, E. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **1998**, *120*, 3641. (f) Krebs, F. C.; Jensen, T. *J. Fluorine Chem.* **2003**, *120*, 77.