The first efficient preparation of vinylaziridines *via* an ylide route

An-Hu Li, Li-Xin Dai* and Xue-Long Hou

Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China

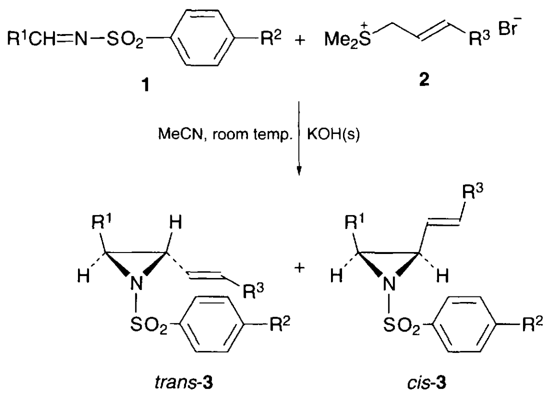
A simple and direct method for preparation of vinylaziridines *via* an ylide route is described; dimethylsulfonium allylides or dimethylsulfonium cinnamylides, produced *in situ* from the corresponding allylic sulfonium salts and solid potassium hydroxide in acetonitrile at room temperature, react efficiently with *N*-sulfonylimines to furnish vinylaziridines rapidly with excellent yields.

In view of the demonstrated utility of various functionalized aziridines in organic synthesis,[1,2] the chemistry of this type of versatile synthetic intermediates is an area of current interest. Among them, vinylaziridines are of special importance. By various transformations[3] and rearrangements,[4] vinylaziridines have been widely used as intermediates in the synthesis of pyrrolizidine alkaloids[4a,5] and other biologically active substances.[1a,3b,3c] However, methods for the preparation of vinylaziridines remain rather undeveloped. Common methods for the preparation of aziridines including the reaction of nitrenes with alkenes[6] or carbenes with imines[7] are not suitable for this purpose. One often obtains vinylaziridines *via* a multi-step sequence with low overall yields and troublesome operations.[3a,4a,4d] Thus, the development of simple but efficient methods for preparation of vinylaziridines is necessary.

In continuing our interest in the synthesis of useful polyfunctionalized compounds,[8] we turned our attention to vinylaziridines. We here disclose our new method for the preparation of vinylaziridines by the reaction of allylsulfonium ylides and activated imines (Scheme 1).†

It is known that olefination, cyclopropanation and epoxidation *via* an ylide route are the fields of extensive research.[9] Instead, ylide aziridination has attracted little attention due to the low reactivity of imines towards the attack of ylides compared with that of carbonyl compounds or Michael acceptors and only a few examples have been reported.[10] However, in the reports, imines did react with ylides of high reactivity, such as $Me_2S^+–CH_2^-$ or $Me_2S(O)^+–CH_2^-$, to give aziridines. That is, only the methylene group could be successfully transferred to the C=N bond.[11] Due to the easily occurring [2,3]-σ-rearrangement of sulfonium allylides, this kind of ylide has been rarely used in epoxidation[12] and cyclopropanation.[12a] No report concerning the aziridination involving them has appeared. It is reported[12c–e] that dimethylsulfonium allylide produced *in situ* from the corresponding sulfonium salt under phase transfer conditions reacted normally with aldehydes to give vinyloxiranes instead of the rearranged product. Unfortunately, under the same conditions, we found that no aziridination occurred with the usual imines.‡ Even the non-rearrangeable diphenylsulfonium allylide did not react with the usual imines.§ However, the aziridination is realized successfully when the activated imines¶ (*N*-sulfonylimines[13]) were submitted to this reaction.|| Results are summarized in Table 1.

This is a one-pot reaction without the need to preform the ylide by reacting **2** with a base. The reaction was carried out at room temperature with excellent yields, and, unusually no



Scheme 1

Table 1 Preparation of vinylaziridines **3** by the reaction of allylic sulfonium salts and *N*-sulfonylaldimines under phase transfer conditions[a]

Entry	R¹	R²	R³	Reaction time/min	(%) Yield[b]	*cis*-**3**/ *trans*-**3**[c]
1	*p*-nitrophenyl	Me	H	5	54 (**3a**)	53/47
2	*o*-methoxyphenyl	Me	H	15	92 (**3b**)	61/39
3	2,6-dichlorophenyl	Me	H	80	36 (**3c**)[d]	56/44
4	3-pyridinyl	Me	H	5	82 (**3d**)[e]	65/35
5	*p*-methylphenyl	H	H	5	84 (**3e**)	34/66
6	*p*-methoxyphenyl	H	H	15	95 (**3f**)	45/55
7	*p*-chlorophenyl	Me	Ph	5	96 (**3g**)	52/48
8	*p*-nitrophenyl	Me	Ph	5	75 (**3h**)	51/49
9	*p*-methylphenyl	H	Ph	5	89 (**3i**)	75/25
10	*p*-methoxyphenyl	H	Ph	5	94 (**3j**)	57/43
11	*trans*-PhCH=CH	H	Ph	5	92 (**3k**)	64/36

[a] All reactions were carried out under solid–liquid phase transfer conditions at room temperature in a ratio of imine : sulfonium salt : KOH(s) = 1 : 1.2 : 1.2 at a 0.5 mmol scale in wet acetonitrile. [b] Isolated yields based on imine. [c] Determined by 300 MHz ^1H NMR analysis. [d] Imine (53%) was recovered. The yield could not be improved by lengthening the reaction time. [e] A 16% yield of 2-(pyridin-3-yl)-3-vinyloxirane (*trans*/*cis* = 2 : 1) from the reaction of ylide and aldehyde generated by the hydrolysis of imine was isolated.

moisture- and oxygen-free manipulations were required. Another feature of this reaction is the short reaction time. Usually, the reaction is completed within a few minutes, whereas no reaction occurs with common *N*-alkyl- or aryl-substituted imines even after a long time. Aryl-, heteroaryl-, and α,β-unsaturated *N*-sulfonylaldimines are useful substrates for this reaction. It is noteworthy that oxosulfonium methylide $Me_2S(O)^+{-}CH_2^-$, which reacted readily with common *N*-alkyl- or aryl-substituted imines[10e,10f] and *N*-sulfinimines[10a] to furnish aziridines, reacted with *N*-sulfonylimines to give azetidines instead of aziridines.[14] *N*-Sulfinimines also did not react with allylsulfonium ylides under these conditions.**

Financial supports from the National Natural Science Foundation of China and Chinese Academy of Sciences is gratefully acknowledged.

Footnotes

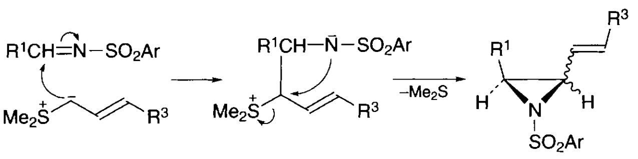
† General procedure for aziridination. A 25 cm^3 flask containing a magnetic stirring bar was charged with imine (**1**, 1.0 equiv.), sulfonium salt (**2**, 1.2 equiv.), and acetonitrile (4 cm^3, reagent grade; it need not be dried before use). Powdered potassium hydroxide (1.2 equiv.) was subsequently added under stirring. After the reaction was completed (by TLC), the reaction mixture was filtered on a short neutral Al_2O_3 column to remove inorganic salts. The filtrate was concentrated and chromatographed on a neutral Al_2O_3 column with a mixture of light petroleum (60–90°C), ethyl acetate and NEt_3 (8 : 1 : 1) as the eluent to give pure product.

‡ Cinnamyldimethylsulfonium bromide (1.2 equiv.), PhCH=NPh (1.0 equiv.), and powdered KOH (1.2 equiv.) were mixed in 4 cm^3 MeCN at room temperature. After stirring for 1 h, the rearranged product of dimethylsulfonium cinnamylide, 3-phenyl-4-methylthiobut-1-ene, was obtained quantitatively. No aziridination occurred.

§ An experiment was carried out at −78 °C in THF by reacting diphenylsulfonium allylide, generated from allyldiphenylsulfonium perchlorate and BuLi, with $PhCH{=}NCH_2Ph$, and no aziridine was detected.

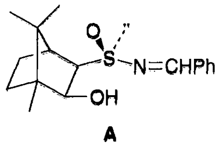
¶ The computation with AM1 (HYPERCHEM Release 3 from Hypercuban, Inc. and Autodesk, Inc., 1993) showed that the carbon connected with nitrogen of *N*-sulfonylimines was much more electrophilic than that of common *N*-alkyl- or *N*-aryl-substituted imines.

|| The possible mechanism of this reaction is shown in Scheme 2.



Scheme 2

** When A was submitted to reaction with cinnamyldimethylsulfonium bromide under our conditions, no aziridine was detected. There was, however, quantitative recovery of the imine and the rearranged product of the sulfonium ylide.



A

References

1 F. A. Davis, G. V. Reddy and H. Liu, *J. Am. Chem. Soc.*, 1995, **117**, 3651; C.-H. Wong, L. Provencher, J. A. Porco, Jr., S.-H. Jung, Y.-F. Wang, L. Chen, R. Wang and D. H. Steensma, *J. Org. Chem.*, 1995, **60**, 1492; J. M. Schkeryantz and S. J. Danishefsky, *J. Am. Chem. Soc.*, 1995, **117**, 4722.

2 For recent reviews on the chemistry of aziridines: D. Tanner, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 599.

3 (*a*) A. Satake, I. Shimizu and A. Yamamoto, *Synlett*, 1995, 64; (*b*) X. Tian, T. Hudlicky and K. Königsberger, *J. Am. Chem. Soc.*, 1995, **117**, 3643; (*c*) T. Hudlicky, X. Tian, K. Königsberger and J. Rouden, *J. Org. Chem.*, 1994, **59**, 4037; (*d*) T. Ibuka, K. Nakai, H. Habashita, Y. Hotta, N. Fujii, N. Mimura, Y. Miwa, T. Taga and Y. Yamamoto, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 652; (*e*) G. W. Spears, K. Nakanishi and Y. Ohfune, *Synlett*, 1991, 91; (*f*) D. Tanner and P. Somfai, *Bioorg. Med. Chem. Lett.*, 1993, **3**, 2415.

4 For vinylaziridine to pyrroline rearrangement: (*a*) T. Hudlicky and J. W. Reed, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 5, pp. 899–970; For aza-[2,3]-Wittig rearrangement: (*b*) J. Åhman and P. Somfai, *J. Am. Chem. Soc.*, 1994, **116**, 9781; (*c*) P. Somfai and J. Åhman, *Tetrahedron Lett.*, 1995, **36**, 1953; (*d*) J. Åhman and P. Somfai, *Tetrahedron Lett.*, 1995, **36**, 303.

5 T. Hudlicky, F. Rulin, T. C. Lovelace and J. W. Reed, in *Studies in Natural Product Chemistry, Stereoselective Synthesis*, ed. Atta-ur-Rahman, Elsevier, Amsterdam, 1989, vol. 3, part B, p. 3.

6 Z. Li, K. R. Conser and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1993, **115**, 5326; D. A. Evans, M. M. Faul and M. T. Bilodeau, *J. Org. Chem.*, 1991, **56**, 6744; D. A. Evans, M. M. Faul, M. T. Bilodeau, B. A. Anderson and D. M. Barnes, *J. Am. Chem. Soc.*, 1993, **115**, 5328; R. S. Atkinson and E. Barker, *J. Chem. Soc., Chem. Commun.*, 1995, 819 and references cited therein.

7 K. B. Hansen, N. S. Finney and E. N. Jacobsen, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 676; H. Yamanaka, J. Kikui, K. Teramura and T. Ando, *J. Org. Chem.*, 1976, **41**, 3794.

8 L.-X. Dai, B.-L. Lou and Y.-Z. Zhang, *J. Am. Chem. Soc.*, 1988, **110**, 5195; J.-Y. Lai, F.-S. Wang, G.-Z. Guo and L.-X. Dai, *J. Org. Chem.*, 1993, **58**, 6944; J.-Y. Lai, X.-X. Shi and L.-X. Dai, *J. Org. Chem.*, 1992, **57**, 3485.

9 W.-F. Huang, *Ylide Chemistry*, Central China Normal University Press, Wuhan, 1993 (Book in Chinese).

10 (*a*) J. L. G. Ruano, I. Fernandez and C. Hamdouchi, *Tetrahedron Lett.*, 1995, **36**, 295; (*b*) P. Mosset and R. Grée, *Synth. Commun.*, 1985, **15**, 749; (*c*) R. S. Tewari, A. K. Awasthi and A. Awasthi, *Synthesis*, 1983, 330; (*d*) B. C. Elmes, *Tetrahedron Lett.*, 1971, 4139. (*e*) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, 1965, **87**, 1353; (*f*) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, 1962, **84**, 3782; (*g*) V. Franzen and H.-E. Driesen, *Chem. Ber.*, 1963, **96**, 1881; (*h*) A. G. Hortmann and D. A. Robertson, *J. Am. Chem. Soc.*, 1967, **89**, 5974; (*i*) A. G. Hortmann and D. A. Robertson, *J. Am. Chem. Soc.*, 1972, **94**, 2758.

11 One example of the transferring of an ethylidene group from sulfoximine ylide to a C=N bond has also appeared: C. R. Johnson and E. R. Janiga, *J. Am. Chem. Soc.*, 1973, **95**, 7692.

12 (*a*) R. W. LaRochelle, B. M. Trost and L. Krepski, *J. Org. Chem.*, 1971, **36**, 1126; (*b*) M. Tanaka, K. Tomioka and K. Koga, *Tetrahedron Lett.*, 1985, **26**, 6109; (*c*) M. J. Hatch, *J. Org. Chem.*, 1969, **34**, 2133; (*d*) J.-C. Paladini and J. Chuche, *Bull. Soc. Chim. Fr.*, 1974, 187; (*e*) K. S. Feldman and T. E. Fisher, *Tetrahedron*, 1989, **45**, 2969.

13 Recent methods for preparation of *N*-sulfonylimines: B. E. Love, P. S. Raje and T. C. Williams II, *Synlett*, 1994, 493; D. L. Boger and W. L. Corbett, *J. Org. Chem.*, 1992, **57**, 4777; B. M. Trost and C. Marrs, *J. Org. Chem.*, 1991, **56**, 6468; D. L. Boger, W. L. Corbett, T. T. Curran and A. M. Kasper, *J. Am. Chem. Soc.*, 1991, **113**, 1713.

14 U. K. Nadir and V. K. Koul, *Synthesis*, 1983, 554.

Received, 13th September 1995; Com. 5/06048F