Novel organic-solvent-free aziridination of olefins: Chloramine-T–I_2 system under phase-transfer catalysis conditions

Daisuke Kano, Satoshi Minakata * and Mitsuo Komatsu *

*Department of Applied Chemistry, Graduate School of Engineering, Osaka University,
Yamadaoka 2-1, Suita, Osaka 565-0871, Japan*

Received (in Cambridge, UK) 5th June 2001, Accepted 31st October 2001
First published as an Advance Article on the web 19th November 2001

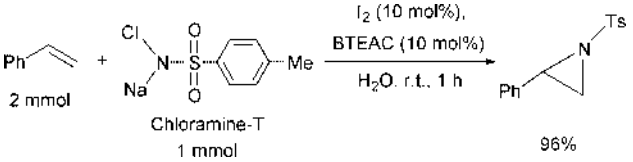
A variety of olefins could be aziridinated successfully by employing iodine-catalysed aziridination in water with a catalytic amount of a quaternary ammonium salt. Furthermore, the larger-scale process of styrene aziridination gives a highly pure aziridine in good yield *via* simple work-up.

Introduction

Aziridines,[1] as well as epoxides,[2] are useful synthetic intermediates and are often present as substructures of natural products in which they frequently show potent and diverse biological activities. From these reasons, a variety of methods for their preparation have been developed.[3–7] While a few methods for [2 + 1] aziridination require heavy metals,[4a,b,i] iodine, which is easy to handle, has been found, in our previous work,[6] to be an excellent catalyst for the aziridination of olefins, in which Chloramine-T (CT) is used as a potent nitrogen source. At nearly the same time, Sharpless reported an alternative aziridination of olefins using CT and trimethylphenylammonium tribromide (PTAB),[7a] as a catalyst. On the other hand, although there are a few examples of organic-solvent-free olefin epoxidation,[8] no olefin aziridination in such media has yet been reported, to the best of our knowledge.[9] In this paper, we report the first organic-solvent-free aziridination of olefins using a CT–I_2 system, wherein phase-transfer catalysts play a key role in the progress of the reaction in aqueous media.

Results and discussion

Our previously reported aziridination was run in acetonitrile or a mixture of acetonitrile and neutral buffer. In an effort to perform an organic-solvent-free aziridination, the reaction was carried out without those solvents. When two equivalents of styrene were treated with Chloramine-T and 10 mol% of iodine in water, no reaction was observed. Utilising the ionic character of CT, the addition of a catalytic amount of a quaternary ammonium salt, benzyltriethylammonium chloride (BTEAC), to the mixture led to a dramatic acceleration in the reaction to give the corresponding aziridine in 96% yield.



Scheme 1

In order to investigate the efficiency of the reaction, time courses for the aziridination of styrene under both reaction conditions (in acetonitrile/neutral buffer *vs.* in water with BTEAC) were examined as depicted in Fig. 1. It required about 10 h to complete the reaction under the former conditions, while our newly discovered PTC conditions gave the desired product quantitatively within only 1 h.

Table 1 Effect of several quaternary ammonium salts on the aziridination of styrene[a]

Quaternary ammonium salt	Yield/%[b]
$[(PhCH_2)Et_3N]$ Cl (BTEAC)	96
$[(PhCH_2)Et_3N]$ Br	97
$[(PhCH_2)Et_3N]$ I	85
$[(PhCH_2)Et_3N]$ OH	4[c]
(n-Bu_4N) Cl	89
Aliquat® 336[d]	88[c]

[a] Reaction conditions: styrene (2.0 mmol), CT (1.0 mmol), iodine (0.1 mmol), quaternary ammonium salt (0.1 mmol), in water (3.0 mL) at room temperature for 1 h. [b] Isolated yields based on Chloramine-T. [c] NMR yields. [d] $[Me(C_8H_{17})_3N]Cl$: mixture of C_8 and C_{10} chains with C_8 predominating.

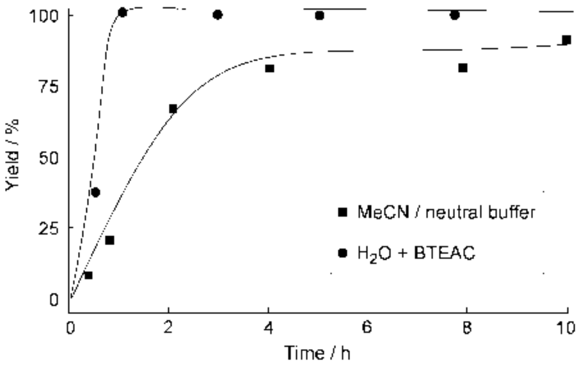


Fig. 1 Time courses for the aziridination of styrene under two different reaction conditions.

The influence of PTC was further examined *via* the use of several types of quaternary ammonium salts for the aziridination of styrene. The results are summarised in Table 1. When benzyltriethylammonium salts with a different counteranion were employed in the reaction, the salts containing a halide ion were effective in producing the desired compound in excellent yield, but the reaction scarcely proceeded in the case of the hydroxide salt. Tetrabutylammonium chloride and Aliquat® 336 were also good catalysts for the reaction. On the other hand, when a catalytic amount of PTAB[7a] was employed in the present aqueous media system instead of BTEAC and iodine only a trace amount of the desired product was obtained, although PTAB might have the ability to act as a PTC. Thus, the present system, which uses iodine and an ammonium salt as a co-catalyst, was found to be one of the most suitable methods for olefin aziridination in aqueous media.

As shown in Table 2, the reaction is dependent on the molar ratio of styrene and CT. A reaction involving equimolar amounts of styrene with CT for 1 h gave the desired product in moderate yield, but the yield was improved when a longer reaction time was employed. The aziridination proceeded efficiently even in 1 h when an excess of styrene was used and, in the case of two equivalents of styrene, an excellent yield was obtained. On the other hand, the use of an excess of CT had no noticeable effect on the yield of the product.

The aziridination of various olefins other than styrene was also successfully performed by using the CT–I_2–quaternary ammonium salt system (Table 3). When oct-1-ene was treated with CT and 20 mol% of iodine in the presence of 10 mol% of Aliquat® 336 in water, 2-hexyl-*N*-(*p*-tolylsulfonyl)aziridine was obtained in 77% yield (run 1). Other acyclic and cyclic aliphatic olefins such as *E*- and *Z*-oct-2-ene, 2-methylhept-2-ene and cyclohexene could be effectively converted to the corresponding aziridines in moderate to good yields (runs 2–5). It is noteworthy that a high stereospecificity was observed in the aziridination of the geometric isomers of oct-2-ene. Although conjugated olefins with an aromatic ring were also aziridinated in good yields (runs 6–8), the stereoselectivities of *E*- and *Z*-β-methylstyrene were rather low compared with the cases of oct-2-ene (runs 7 and 8). In order to improve the stereoselectivity, the reaction of *Z*-β-methylstyrene with CT in the presence of 30 mol% iodine was carried out at 0 °C, resulting in the corresponding *cis*-aziridine with no detectable formation of the *trans*-isomer. Functionalised olefins, such as allylic alcohols, were stereospecifically converted to the corresponding aziridines in good yields. The present method led to increased yields and/or shorter reaction time of these aziridinations compared with our previously reported method.[6]

Table 2 Influence of the amount of CT on the aziridination of styrene[a]

Styrene/mol	CT/mol	Time (*t*/h)	Yield/%[b]
1	1	1	58
1	1	3	80
1	1	8	79
1.5	1	1	77
2	1	1	96[c]
1	2	1	60

[a] Reaction conditions: styrene (1.0–2.0 mmol), CT (1.0–2.0 mmol), iodine (0.1 mmol), BTEAC (0.1 mmol), in water (3.0 mL) at room temperature. [b] NMR yields. [c] Isolated yield.

To establish the applicability of this aqueous media system to larger-scale processes in the case of styrene, a 0.1 mol-scale reaction of styrene (20.8 g) was undertaken with CT (28.2 g), a catalytic amount of iodine (2.5 g), and 10 mol% of Aliquat® 336 (4.0 g) in water (300 mL). After a 1.5 h-reaction, the water layer was decanted and the residual solid was recrystallised from hot MeOH to give the desired highly pure aziridine in good yield (23.5 g, 86% yield, >99% purity).

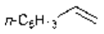
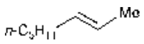
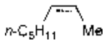
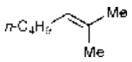
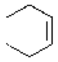
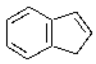
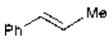
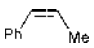
In conclusion, we provide details on the organic-solvent-free aziridination of olefins using the CT–I_2 system in the presence of a catalytic amount of a quaternary ammonium salt. A variety of olefins were successfully aziridinated in good to excellent yields by employing the method. The process possesses some advantages over our previously reported procedure[6] in that it involves an organic-solvent-free system, provides higher yields, and requires a shorter reaction time. Furthermore, the aziridination system in aqueous media is applicable to a larger-scale process and the product is easily isolated in good yield in a high state of purity *via* a simple work-up. The procedure is practical for the synthesis of aziridines where it involves an organic-solvent-free system and no heavy metals.

Experimental

General

Melting points were determined on a Yanagimoto micro melting-point apparatus and are uncorrected. IR spectra were obtained on a JASCO FT/IR-410 Fourier transform infrared spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded on a JEOL FT-NMR JNM EX 270 spectrometer (^{1}H-NMR, 270 MHz; ^{13}C-NMR, 68 MHz) using tetramethylsilane as internal standard. Mass spectra were measured on a Shimadzu

Table 3 Aziridination of various olefins in aqueous media[a]

Run	Olefin	I_2/mol%	Time (*t*/h)	Yield (*cis* : *trans*)/%[b]
1		20	5	77
2		15	5	52 (<5 : >95)
3		15	5	81[c] (>95 : <5)
4		10	5	43
5		20	3	74
6		20	2	56
7		10	1	87 (25 : 75)
8		10	5	91 (34 : 66)
9[d]		30	5	36 (>95 : <5)
10		10	3	79 (<5 : >95)
11[e]		10	3	72 (>95 : <5)

[a] Reaction conditions: olefin (2.0 mmol), CT (1.0 mmol), a catalytic amount of iodine, Aliquat® 336 (0.1 mmol), in water (3.0 mL) at room temperature. [b] Isolated yields based on CT. [c] The reaction was performed using 2.5 mmol of the olefin. [d] The reaction was carried out at 0 °C. [e] BTEAC was used instead of Aliquat® 336.

Model GCMS-QP5000 spectrometer. High-resolution mass spectral data were obtained on a JEOL DX-303 mass spectrometer. Flash column chromatography (FCC) was performed using silica gel BW-300 (Fuji Silysia Chemical Co.). Preparative gel-permeation liquid chromatography (GPLC) was performed on a JAI (Japan Analytical Industry) LC-908 instrument with JAIGEL 1H-2H columns and chloroform as eluent. High-performance liquid chromatography (HPLC) was performed on a Hitachi instrument with Hitachi L-4200 (UV-VIS Detector), Hitachi L-6250 (Intelligent pump), Hitachi L-2500 (Chromato-Integrator), RP-18 GP 150–4.6 Mightysil (reversed-phase column) and methanol/distilled water as eluent. Analytical thin layer chromatography (TLC) was performed using EM reagent 0.25 mm silica gel 60-F plates. Visualisation was accomplished with UV light and ethanolic phosphomolybdic acid solution followed by heating. Characteristics of all aziridines in this paper (aziridines from indene,[7b] allylic alcohols,[7a] *E*- and *Z*-oct-2-ene,[6] 2-methylhept-2-ene,[6] and the others[4c]) were found to be identical to those published previously.

General procedure for preparation of aziridines

To a mixture of iodine (0.1 mmol, 10 mol%), Chloramine-T (1.0 mmol), and a quaternary ammonium salt (0.1 mmol, 10 mol%) in distilled water (3.0 mL) was added the appropriate olefin (2.0 mmol). The mixture was stirred at room temperature from 1 to 5 hours under an ambient atmosphere. After the addition of Et_2O (40 mL), the organic layer was washed with brine (60 mL). The aqueous phase was extracted with Et_2O (20 mL × 1). The combined organic extracts were dried over K_2CO_3 and concentrated to give the crude product. Purification by flash column chromatography (silica gel; 10% ethyl acetate in hexane) gave the corresponding aziridine as a white crystalline solid or colorless oil.

Larger-scale process of styrene aziridination

To a mixture of iodine (10 mmol, 10 mol%), Chloramine-T (100 mmol), and Aliquat® 336 (10 mmol, 10 mol%) in distilled water (300 mL) was added styrene (200 mmol). The mixture was stirred at room temperature under an ambient atmosphere for 1.5 hours. After the decantation of water, the crude product was obtained as a brown solid. The resultant solid was purified by recrystallisation from methanol (100 mL) to give the corresponding aziridine 86% yield (purity: >99% by HPLC). Analytical HPLC was performed using RP-18 GP 150-4.6 Mightysil reversed-phase column on a Hitachi instrument. UV detection was at 230 nm, and 10% methanol in distilled water was run at 1.0 mL min^{-1} flow rate.

Acknowledgements

This work was supported, in part, by the Sasakawa Scientific Research Grant from The Japan Science Society and a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan. We also acknowledge the Instrumental Analysis Center, Faculty of Engineering, Osaka University.

References

1 (*a*) J. A. Deyrup, in *The Chemistry of Heterocyclic Compounds*, ed. A. Hassner, Wiley, New York, 1983, vol. 42, Part 1, p. 1; (*b*) A. Padwa and A. D. Woolhouse, in *Comprehensive Heterocyclic Chemistry*, ed. W. Lwowski, Pergamon Press, Oxford, 1984, vol. 7, p. 47; (*c*) W. H. Pearson, B. W. Lian and S. C. Bergmeier, in *Comprehensive Heterocyclic Chemistry II*, ed. A. Padwa, Pergamon Press, Oxford, 1996, vol. 1A, p. 1; (*d*) K. M. L. Rai and A. Hassner, in *Comprehensive Heterocyclic Chemistry II*, ed. A. Padwa, Pergamon Press, Oxford, 1996, vol. 1A, p. 61.

2 (*a*) M. Bartók and K. L. Láng, in *The Chemistry of Heterocyclic Compounds*, ed. A. Hassner, Wiley, New York, 1984, vol. 42, Part 3, p. 1; (*b*) E. G. Lewars, in *Comprehensive Heterocyclic Chemistry*, ed. W. Lwowski, Pergamon Press, Oxford, 1984, vol. 7, p. 96; (*c*) I. Erden, in *Comprehensive Heterocyclic Chemistry II*, ed. A. Padwa, Pergamon Press, Oxford, 1996, vol. 1A, p. 97; (*d*) I. Edren, in *Comprehensive Heterocyclic Chemistry II*, ed. A. Padwa, Pergamon Press, Oxford, 1996, vol. 1A, p. 145.

3 (*a*) D. Tanner and P. Somfai, *Tetrahedron*, 1988, **44**, 619; (*b*) D. Tanner and C. Birgersson, *Tetrahedron Lett.*, 1991, **32**, 2533; (*c*) S. C. Bergmeier, W. K. Lee and H. Rapoport, *J. Org. Chem.*, 1993, **58**, 5019; (*d*) D. Tanner, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 599.

4 (*a*) J. T. Groves and T. Takahashi, *J. Am. Chem. Soc.*, 1983, **105**, 2073; (*b*) R. S. Atkinson and B. J. Kelly, *J. Chem. Soc., Chem. Commun.*, 1988, 624; (*c*) D. A. Evans, M. M. Faul and M. T. Bilodeau, *J. Org. Chem.*, 1991, **56**, 6744; (*d*) R. E. Lowenthal and S. Masamune, *Tetrahedron Lett.*, 1991, **32**, 7373; (*e*) Z. Li, K. R. Conser and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1993, **115**, 5326; (*f*) D. A. Evans, M. M. Faul, M. T. Bilodeau, B. A. Anderson and D. M. Barnes, *J. Am. Chem. Soc.*, 1993, **115**, 5328; (*g*) H. Nishikori and T. Katsuki, *Tetrahedron Lett.*, 1996, **37**, 9245; (*h*) H. M. I. Osborn and J. Sweeny, *Tetrahedron, Asymmetry*, 1997, **8**, 1693; (*i*) S.-M. Au, W.-H. Fung, M.-C. Cheng, C.-M. Che and S.-M. Peng, *Chem. Commun.*, 1997, 1655; (*j*) M. J. Södergren, D. A. Alonso, A. V. Bedekar and P. G. Andersson, *Tetrahedron Lett.*, 1997, **38**, 6897; (*k*) T. Ando, S. Minakata, I. Ryu and M. Komatsu, *Tetrahedron Lett.*, 1998, **39**, 309.

5 (*a*) P. Baret and H. B. J.-L. Pierre, *Bull. Soc. Chim. Fr.*, 1972, 2493; (*b*) A. J. Hubert, A. Feron, R. Warin and P. Teyssie, *Tetrahedron Lett.*, 1976, 1317; (*c*) K. B. Hansen, N. S. Finney and E. N. Jacobsen, *J. Chem. Soc., Chem. Commun.*, 1995, 676; (*d*) K. G. Rasmussen and K. A. Jørgensen, *J. Chem. Soc., Chem. Commun.*, 1995, 1401; (*e*) M. Moran, G. Bernardinelli and P. Müller, *Helv. Chim. Acta*, 1995, **78**, 2048; (*f*) Z. Zhu and J. H. Espenson, *J. Org. Chem.*, 1995, **60**, 7090; (*g*) M. C. McMills, D. L. Wright, J. D. Zubkowski and E. J. Valente, *Tetrahedron Lett.*, 1996, **37**, 7205; (*h*) V. K. Aggarwal, A. Thompson, R. V. H. Jones and C. H. Standen, *J. Org. Chem.*, 1996, **61**, 8368; (*i*) J. M. Mohan, B. S. Uphade, V. R. Choudhary, T. Ravindranathan and A. Sudalai, *Chem. Commun.*, 1997, 1429; (*j*) K. G. Rasmussen and K. A. Jørgensen, *J. Chem. Soc., Perkin Trans. 1*, 1997, 1287; (*k*) S. Nagayama and S. Kobayashi, *Chem. Lett.*, 1998, 685; (*l*) M. F. Mayer and M. M. Hosain, *J. Org. Chem.*, 1998, **63**, 6839; (*m*) J. C. Antilla and W. D. Wulff, *J. Am. Chem. Soc.*, 1999, **121**, 5099; (*n*) K. Juhl, R. H. Hazell and K. A. Jørgensen, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2293; (*o*) T. Kubo, S. Sakaguchi and Y. Ishii, *Chem. Commun.*, 2000, 625.

6 T. Ando, D. Kano, S. Minakata, I. Ryu and M. Komatsu, *Tetrahedron*, 1998, **54**, 13485.

7 (*a*) J. U. Jeong, B. Tao, I. Sagasser, H. Henniges and K. B. Sharpless, *J. Am. Chem. Soc.*, 1998, **120**, 6844; (*b*) S. L. Ali, M. D. Nikalje and A. Sudalai, *Org. Lett.*, 1999, **1**, 705; (*c*) A. V. Gontcharov, H. Liu and K. B. Sharpless, *Org. Lett.*, 1999, **1**, 783.

8 (*a*) K. Sato, M. Aoki, M. Ogawa, T. Hashimoto and R. Noyori, *J. Org. Chem.*, 1996, **61**, 8310; (*b*) K. Sato, M. Aoki, M. Ogawa, T. Hashimoto, D. Panyella and R. Noyori, *Bull. Chem. Soc. Jpn.*, 1997, **70**, 905.

9 Only one example of solvent-free aziridination of conjugated nitroalkenes has been reported. See S. Fioravanti, L. Pellacani, S. Stabile, P. A. Tardella and R. Ballini, *Tetrahedron*, 1998, **54**, 6169.