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A new approach for the transformation of alkenes to pyrrolines via aziridine intermediates☆

K. Ajay Kumar, K. M. Lokanatha Rai* and K. B. Umesha

Department of Chemistry, University of Mysore, Manasagangotri, Mysore 570006, India

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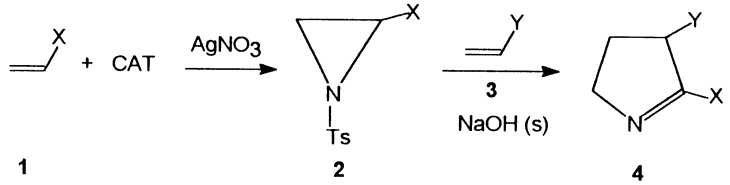
Abstract—Alkenes (**1**) reacts with chloramine-T in presence of the catalyst silver nitrate to afford aziridines (**2**). The aziridines underwent ring expansion with the acrylo nitrile or ethyl acrylate (**3**) in the presence of solid sodium hydroxide to form pyrrolines (**4**) in 40–58% yield.

1. Introduction

Azirine and aziridines can be regarded as representative of the first and most simple of *N*-heterocyclic systems and are used as a valuable intermediates in organic synthesis.[1] Apart from the usual synthesis from alkenes, the classical methods for the synthesis of aziridines via addition of INCO or IN_3 to olefins have been reported.[2] New routes to their preparation have been the focus of recent investigations with an emphasis on metal catalyzed processes.[3] Recently, a wide range of bromine sources have been used as catalysts for the aziridination of simple olefins using chloramine-T.[4]

As a consequence of the ring strain present in aziridines, ring opening and ring expansion reactions are the dominant feature of their chemistry.[1] For example, the anionic rearrangement of vinyl aziridine gave tetrahydropyridine and 1-pyrroline,[5] while Michael addition of vinyl aziridine to an acrylate produced a seven membered azepine ring system.[6] The direct synthesis of pyrrolines from alkenes has also been reported. For instance, in the presence of a catalytic amount of tributyl phosphine, substituted alkynoates or 2,3-allenoates reacted with electron deficient nitrile imines at room temperature to afford (3+2)-cycloaddition product pyrrolines in moderate to good yield.[7] Recently, Ishii and co-workers reported the selective synthesis of 3-pyrrolines using (*Z*)-allylic mesylates with sodium hydride.[8]

In continuation of our study on the applications of chloramine-T in organic synthesis, we successfully employed the new method for the generation of nitrene intermediates by the reaction of chloramine-T with silver nitrate as catalyst and trapped the in situ generated nitrene with olefins to produce aziridines. In a typical reaction, an equimolar mixture of an acrylo nitrile **1a**, chloramine-T trihydrate and a catalytic amount of silver nitrate in ethyl alcohol was stirred thoroughly at room temperature for 3 hours, which afforded the 2-substituted aziridine **2a** in 28% yield (Scheme 1). However, when the same reaction was carried out in benzene, dichloromethane or tetrahydrofuran, the yield was somewhat higher. For instance, **2a** was



Scheme 1. 4 (a) X=Y=CN; (b) X=Y=$COOC_2H_5$; (c) X=CN, Y=$COOC_2H_5$; (d) X=3,4-$(OCH_2O)C_6H_3CH_2$, Y=CN; (e) X=3,4-$(OCH_2O)C_6H_3CH_2$, Y=$COOC_2H_5$; (f) X=C_6H_5, Y=CN; (g) X=C_6H_5, Y=$COOC_2H_5$.

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* Corresponding author. Tel.: +91-821-515110; fax: +91-821-421263; e-mail: kmlrai@eth.net

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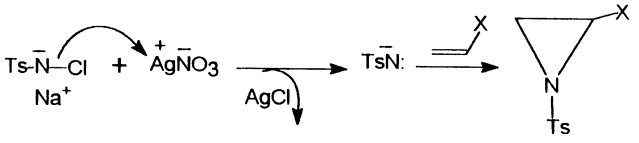
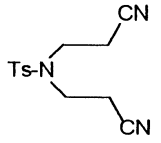


Scheme 2.

obtained in 30, 38 and 44%, respectively. From this observation it is concluded that, the aziridination in aprotic solvents affords better yields than in protic solvents. Also, we observed that the absence of catalyst during the reaction resulted in the double addition of olefin to chloramine-T afforded different product. For instance, the reaction of chloramine-T with acrylo nitrile in the absence of a catalyst silver nitrate formed **5** using a proton from the solvent. Furthermore, we carried out a ring expansion reaction of aziridines with acrylo nitrile and ethyl acrylate in the presence of solid sodium hydroxide as the base in tetrahydrofuran as the solvent under reflux conditions in a sealed tube and obtained 1-pyrrolines **4a**–**g** in 40–58% yield.



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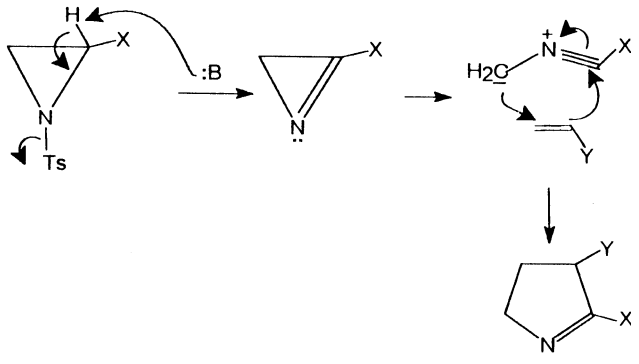
The structure proof of the aziridines was provided by IR and ^{1}H NMR spectral studies. For instance, all showed the two strong absorption peaks in the regions 1150–1176 and 1312–1334 cm^{-1} due to the sulfonamide S=O group. In addition to these peaks, **2b** showed a strong peak at 1741 cm^{-1} due to the ester group, while **2a** showed peaks at 2242 cm^{-1} due to the cyano group. ^{1}H NMR spectra of all aziridines gave the signals due to aromatic and substituent protons in the expected region. The signals due to the ring CH_2 protons were obtained as a doublet in the region δ 0.30–0.60 ppm, while the signal due to CH protons appear as triplet in the region δ 2.90–3.30 ppm. The signals belonging to the CH_2 and CH protons of the starting olefin in the region δ 4.50–6.0 and 5.0–8.0 ppm were absent.



Scheme 3.

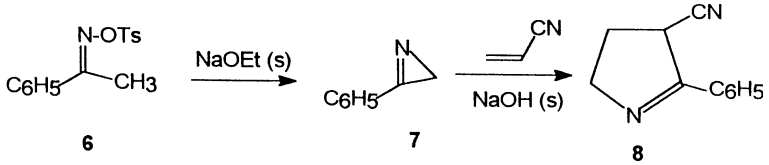
The probable mechanism for the formation of aziridine involves the interaction of chloramine-T with Ag^+ to form the reactive intermediate nitrene, followed by the addition of nitrene to alkenes (Scheme 2).

IR, ^{1}H NMR, ^{13}C NMR, MS studies and elemental analysis provided the structure proof of the pyrrolines. For instance, in the IR spectrum, pyrroline **4a** gave an absorption peak at 1685 cm^{-1} due to the newly formed C=N bond, while the peak expected at 1640–1645 cm^{-1} for the vinylic C=C bond was absent. Also it gave the absorption peak at 2245 cm^{-1} due to cyano group. All ^{1}H NMR spectra showed the signals due to the C_3–H as a triplet in the region δ 5.55–5.73 ppm, and those due to C_4 protons as a multiplet in the region δ 1.90–2.05 ppm and those due to C_5 protons as a triplet in the region δ 3.85–4.00 ppm.

In ^{13}C NMR spectra, all pyrrolines gave consistent signals for the newly formed ring carbons. For instance, the signals due to C_5 and C_4 carbons appear as triplets in the region δ 42.12–42.86 and 46.28–46.90 ppm, respectively, while, C_3 and C_2 carbons appear as a doublet and a singlet in the region δ 95.22–95.86 and 158.96–159.42 ppm, respectively. The relatively stable molecular ion peaks were observed in mass spectra, which supports the structure of the products. The possible fragmentation pattern involves some rearrangement with the loss of smaller molecules viz. H_2, HCN, etc. The formation of the products was further supported by correct elemental analysis.

The probable mechanism for the formation of pyrrolines is outlined below. It is expected that the base abstract the acidic proton from C_2 carbon, which in turn expels the Ts^- ion to form azirine. The azirine undergoes ring opening by a thermal process leading to formation of the nitrile ylide as a 1,3-dipole, which later cycloadds to alkenes to give 1-pyrroline (Scheme 3).

One of the more important approaches to the synthesis of 2*H*-azirines involves a base induced cycloelimination reaction of suitably functionalized ketone derivatives. An example of this cycloelimination involves the Neber rearrangement of oxime tosylates.[9] From the mechanistic studies on the Neber reaction, a 2*H*-azirine has been shown to be a distinct intermediate formed by the closure of a vinyl nitrene. The configurational stereospecificity in a modified Neber reaction has been studied with an oxime carbamate[10] in order to elucidate the mechanism of the reaction.



6 **7** **8**

Scheme 4.

In support of the formation of pyrrolines **4**, we carried out the base-induced cycloelimination reaction of oxime tosylate **6** in the presence of solid sodium ethoxide to form azirine **7**. Furthermore, the azirine **7** was subjected to ring expansion reaction with acrylo nitrile in the presence of solid sodium hydroxide as the base in tetrahydrofuran as the solvent under reflux conditions in a sealed tube and obtained pyrroline **8**[11] (Scheme 4), which supports the formation of the products **4**.

In summary, we have demonstrated for the first time that pyrrolines can be synthesized via silver nitrate catalyzed aziridination of alkenes using inexpensive chloramine-T followed by pyrolysis in presence of alkenes in a sealed tube.

2. Experimental

2.1. Data for compounds

2.1.1. A typical procedure for the preparation of 2-cyano-*N*-tosyl-aziridine 2a. To a well stirred mixture of chloramine-T trihydrate (1.4 g, 5.0 mmol), silver nitrate (0.34 g, 2 mmol) in tetrahydrofuran (20 mL), acrylo nitrile **1a** (0.26 g, 5 mmol) was added dropwise and the reaction mixture was kept in dark at room temperature for 6–8 h with constant stirring. The AgCl formed in the reaction was filtered off. The filtrate was extracted into ether (25 mL), washed successively with water (2×20 mL), brine solution (1×15 mL) and dried over anhydrous sodium sulphate. After usual workup, **2a** obtained as white solid in 42% (1.37 g) yield. Mp 83–85°C, IR (Nujol): in cm^{-1} 1161, 1322, 1748; ^1H NMR $CDCl_3$: δ 0.4 (d, 2H, CH_2, J=7.71 Hz), 2.3 (s, 3H, Ar–CH_3), 2.9 (t, 1H, CH, J=7.45 Hz), 7.2 (s, 4H, Ar–H). MS (relative abundance) *m/z*: 223 (MH^+, 71), 195 (52), 91 (100), 66 (16). Anal. Calcd for $C_{10}H_{10}N_2O_2S$: C, 54.05, H, 4.50, N, 12.61%. Found: C, 54.00, H, 4.41, N, 12.46%. The same procedure was used in all cases.

2.1.2. Ethyl-*N*-tosyl-aziridine-2-carboxylate 2b. Obtained from ethyl acrylate **1b** (0.49 g, 5.0 mmol), and chloramine-T (1.4 g, 5.0 mmol) as a colourless solid in 51% (0.82 g) yield. Mp 91–93°C, IR (Nujol): in cm^{-1} 1166, 1324, 1741; ^1H NMR $CDCl_3$: δ 0.3 (d, 2H, CH_2, J=7.74 Hz), 1.2 (t, 3H, CH_3, J=3.83 Hz), 2.35 (s, 3H, Ar–CH_3), 3.0 (t, 1H, CH, J=7.41 Hz), 4.50 (q, 2H, OCH_2, J=3.91 Hz), 7.3 (s, 4H, Ar–H). MS (relative abundance) *m/z*: 270 (MH^+, 62), 241 (38), 197 (44), 114 (12), 91 (100). Anal. Calcd for $C_{12}H_{15}NO_4S$: C, 53.53, H, 5.57, N, 5.20%. Found: C, 53.44, H, 5.41, N, 5.08%.

2.1.3. 2-(3′,4′-Methylenedioxybenzyl)-*N*-tosyl-aziridine 2c. Obtained from 4-allyl-(1,2-methylenedioxy)benzene **1c** (0.80 g, 5.0 mmol) and chloramine-T (1.4 g, 5.0 mmol) as a white solid in 45% (0.86 g) yield. Mp 119–121°C, IR (Nujol): in cm^{-1} 1171, 1328; ^1H NMR $CDCl_3$: δ 0.6 (d, 2H, CH_2, J=7.78 Hz), 2.45 (s, 3H, Ar–CH_3), 2.75 (s, 2H, Ar–CH_2), 3.3 (t, 1H, CH, J=7.38 Hz), 5.90 (s, 2H, OCH_2O), 7.2–7.4 (m, 7H, Ar–H). MS (relative abundance) *m/z*: 332 (MH^+, 64), 175 (40), 135 (100). Anal. Calcd for $C_{17}H_{17}NO_4S$: C, 61.63, H, 5.13, N, 4.22%. Found: C, 61.51, H, 5.02, N, 4.13%.

2.1.4. 2-Phenyl-*N*-tosyl-aziridine 2d. Obtained from styrene **1d** (0.51 g, 5.0 mmol) and chloramine-T (1.4 g, 5.0 mmol) as a white solid in 58% (0.94 g) yield. Mp 113–115°C, IR (Nujol): in cm^{-1} 1162, 1318; ^1H NMR $CDCl_3$: δ 0.55 (d, 2H, CH_2, J=7.71 Hz), 2.6 (s, 3H, Ar–CH_3), 3.35 (t, 1H, CH, J=7.36 Hz), 7.3–7.5 (m, 9H, Ar–H). MS (relative abundance) *m/z*: 274 (MH^+, 52), 181 (28), 117 (48), 77 (100). Anal. Calcd for $C_{15}H_{15}NO_2S$: C, 65.93, H, 5.49, N, 5.12%. Found: C, 65.81, H, 5.39, N, 4.97%.

2.1.5. Typical procedure for the preparation of 2,3-dicyano-1-pyrroline 4a. A mixture of **2a** (0.44 g, 2.0 mmol) and alkene **3a** (0.10 g, 2.0 mmol) and sodium hydroxide (1–2 pellets) in tetrahydrofuran (10 mL) were refluxed on a water bath in a sealed tube for 3 h. The mixture was then cooled to room temperature and the solvent was concentrated in vacuo. The pasty mass was extracted into ether (50 mL). The ethereal solution was washed successively with 10% aqueous sodium hydroxide (2×15 mL), water (2×20 mL), and brine solution (1×15 mL) and dried over anhydrous sodium sulphate. Evaporation of the solvent yielded an oily substance. The TLC of the product showed one major spot corresponding to the product and one minor spot related to the unreacted starting materials, which was purified by column chromatography using hexane/ethyl acetate (8:2) as eluent, which afforded **4a** as a colourless oil in 56% (0.125 g) yield. IR (Nujol) in cm^{-1}: 1685, 2245; ^1H NMR $CDCl_3$: δ 1.90 (m, 2H, 4-H), 3.90 (t, 2H, 5-H, J=5.26 Hz), 5.67 (t, 1H, 3-H, J=6.42 Hz). ^{13}C NMR ($CDCl_3$): δ 42.12 (t, 1C, 5-C), 46.28 (t, 1C, 4-C), 95.22 (d, 1C, 3-C), 115.62 (s, 1C, CN), 117.28 (s, 1C, CN), 159.42 (s, 1C, 2-C). MS (relative abundance) *m/z*: 119 (M^+, 16), 117 (33), 92 (100), 67 (54). Anal. Calcd for $C_6H_5N_3$: C, 60.50, H, 4.20, N, 35.29%. Found: C, 60.42, H, 4.10, N, 35.21%. The same procedure was used in all cases.

2.1.6. Diethyl-1-pyrrolinyl-2,3-dicarboxylate 4b. Obtained from **2b** (0.49 g, 2.0 mmol) and **3b** (0.20 g, 2.0 mmol) as a colourless oil in 46% (0.19 g) yield. IR (Nujol) in cm^{-1}: 1682, 1742; ^1H NMR $CDCl_3$: δ 1.20–1.30 (m, 6H, CH_3), 1.95 (m, 2H, 4-H), 3.23 (q, 2H, CH_2, J=3.91 Hz), 3.90 (t, 2H, 5-H, J=5.31 Hz), 5.67 (t, 1H, 3-H, J=5.09 Hz). ^{13}C NMR ($CDCl_3$): δ 13.52 (CH_3), 42.86 (t, 1C, 5-C), 46.86 (t, 1C, 4-C), 62.32 (t, 1C, CH_2), 95.86 (d, 1C, 3-C), 158.96 (s, 1C, 2-C), 168.72 (s, 1C, CO). MS (relative abundance) *m/z*: 213 (M^+, 12), 211 (48), 184 (10), 140 (08), 139 (100). Anal. Calcd for $C_{10}H_{15}NO_4$: C, 56.33, H, 7.04, N, 6.97%. Found: C, 56.24, H, 6.97, N, 6.86%.

2.1.7. Ethyl-2-cyano-1-pyrrolinyl-3-carboxylate 4c. Obtained from **1a** (0.62 g, 1.5 mmol) and **3b** (0.15 g, 1.5 mmol) as a colourless oil in 42% (0.180 g) yield. IR (Nujol) in cm^{-1}: 1680, 1745, 2230; ^1H NMR $CDCl_3$: δ 1.35 (t, 3H, CH_3, J=3.86 Hz), 1.90 (m, 2H, 4-H), 3.30 (q, 2H, CH_2, J=3.94 Hz), 4.0 (t, 2H, 5-H, J=5.24 Hz), 5.67 (t, 1H, 3-H, J=5.23 Hz). ^{13}C NMR ($CDCl_3$): δ 13.65 (q, 1C, CH_3), 42.56 (t, 1C, 5-C), 46.66 (t, 1C, 4-C), 62.46 (t, 1C, CH_2), 95.47 (d, 1C, 3-C), 115.26 (s, 1C, CN), 159.22 (s, 1C,

2-C), 168.86 (s, 1C, CO). Anal. Calcd for $C_8H_{10}N_2O_2$: C, 57.83, H, 6.02, N, 16.86%. Found: C, 57.69, H, 5.92, N, 16.74%.

2.1.8. 2-(2′,3′-Methylenedioxybenzyl)-3-cyano-1-pyrroline 4d. Obtained from **2c** (0.47 g, 1.5 mmol) and **3a** (0.08 g, 1.5 mmol) as a colourless oil in 52% (0.167 g) yield. IR (Nujol) in cm^{-1}: 1676, 2252; ^1H NMR $CDCl_3$: δ 2.0 (m, 2H, 4-H), 3.85 (t, 2H, 5-H, J=5.14 Hz), 5.57 (t, 1H, 3-H, J=5.36 Hz), 5.90 (s, 2H, OCH_2O), 7.18 (m, 3H, Ar–H). ^{13}C NMR ($CDCl_3$): δ 42.62 (t, 1C, 5-C), 46.36 (t, 1C, 4-C), 61.86 (t, 1C, CH_2), 95.74 (d, 1C, 3-C), 101.32 (t, 1C, OCH_2O), 106.57 (s, 1C, 5′-C), 108.21 (s, 1C, 2′-C), 115.21 (s, 1C, CN), 122.62 (s, 1C, 6′-C), 132.2 (s, 1C, 1′-C), 148.2 (s, 1C, 4′-C), 149.3 (s, 1C, 3′-C), 158.58 (s, 1C, 2-C). MS (relative abundance) m/z: 228 (M^+, 10), 226 (58), 201 (100). Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.42, H, 5.26, N, 12.28%. Found: C, 68.19, H, 5.22, N, 12.02%.

2.1.9. Ethyl-2-(2′,3′-methylenedioxybenzyl)-1-pyrrolinyl-3-carboxylate 4e. Obtained from **2d** (0.47 g, 1.5 mmol) and **3b** (0.15 g, 1.5 mmol) as a colourless oil in 49% (0.19 g) yield. IR (Nujol) in cm^{-1}: 1686, 1746; ^1H NMR $CDCl_3$: δ 2.05 (m, 2H, 4-H), 4.0 (t, 2H, 5-H, J=5.31 Hz), 5.67 (t, 1H, 3-H, J=5.34 Hz), 5.95 (s, 2H, OCH_2O), 7.18–7.22 (m, 3H, Ar–H). MS (relative abundance) m/z: 273 (M^+, 09), 271 (48), 244 (06), 200 (08), 199 (100). Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.93, H, 5.49, N, 5.12%. Found: C, 65.69, H, 5.32, N, 5.01%.

2.1.10. 2-Phenyl-3-cyano-1-pyrroline 4f. Obtained from **2e** (0.41 g, 1.5 mmol) and **3a** (0.08 g, 1.5 mmol) as a colourless oil in 58% (0.15 g) yield. IR (Nujol) in cm^{-1}: 1688, 2250; ^1H NMR $CDCl_3$: δ 1.95 (m, 2H, 4-H), 3.90 (t, 2H, 5-H, J=5.40 Hz), 5.59 (t, 1H, 3-H, J=5.13 Hz), 7.60 (s, 5H, Ar–H). ^{13}C NMR ($CDCl_3$): δ 42.78 (t, 1C, 5-C), 46.72 (t, 1C, 4-C), 95.68 (d, 1C, 3-C), 122.32 (d, 2C, 2′,6′-C), 115.28 (s, 1C, CN), 127.12 (d, 2C, 3′,5′-C), 128.22 (s, 1C, 1′-C), 130.82 (s, 1C, 4′-C), 159.28 (s, 1C, 2-C). MS (relative abundance) m/z: 170 (M^+, 21), 168 (56), 143 (100). Anal. Calcd for $C_{11}H_{10}N_2$: C, 77.64, H, 5.88, N, 16.47%. Found: C, 77.57, H, 5.74, N, 16.40%.

2.1.11. Ethyl-2-phenyl-1-pyrrolinyl-3-carboxylate 4g. Obtained from **2f** (0.41 g, 1.5 mmol) and **3b** (0.15 g, 1.5 mmol) as a colourless oil in 52% (0.17 g) yield. IR (Nujol) in cm^{-1}: 1685, 1740; ^1H NMR $CDCl_3$: δ 1.98 (m, 2H, 4-H), 3.94 (t, 2H, 5-H, J=5.30 Hz), 5.63 (t, 1H, 3-H, J=4.96 Hz), 7.65 (s, 5H, Ar–H). MS (relative abundance) m/z: 21 7 (M^+, 14), 215 (46), 188 (09), 143 (100). Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.88, H, 6.91, N, 6.45%. Found: C, 71.77, H, 6.79, N, 6.34%.

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11. Compound **8** obtained as a colourless oil showed peaks at 1686, 2251 cm^{-1} in IR spectrum; ^1H NMR $CDCl_3$: δ 1.95 (m, 2H, 4-H), 3.92 (t, 2H, 5-H, J=5.42 Hz), 5.60 (t, 1H, 3-H, J=5.14 Hz), 7.61 (s, 5H, Ar–H). MS (relative abundance) m/z: 170 (M^+, 22), 168 (54), 143 (100). Anal. Calcd for $C_{11}H_{10}N_2$: C, 77.64, H, 5.88, N, 16.47%. Found: C, 77.54, H, 5.76, N, 16.38%.