Synthesis of Azirines Containing Aldehyde Functionality and their Utilization as Synthetic Tools for Five Membered Oxazoles and Isoxazoles

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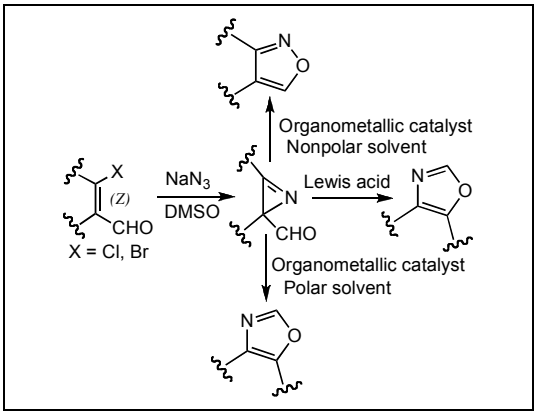

A simple and useful procedure for the synthesis of azirines containing aldehyde functionality from open chain bromo/chloro-aldehydes at room temperature is reported. The scope of the ring expansion reaction of a number of 3-substituted-2-formyl-azirines has been examined using different oraganometallic catalysts and a variety of Lewis acids.

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INTRODUCTION

Azirines bearing carbonyl functionality at 2-position are valuable intermediates in heterocyclic chemistry, undergoing thermal and photochemical rearrangements to produce larger ring heterocycles. The scope of these ring expansion reactions, of interest not only from the synthetic but also from the mechanistic point of view, has been actively invested [1,2].

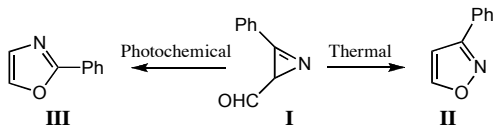
The most general method for the synthesis of azirines is the thermal or photochemical decomposition of vinyl azides involving vinyl nitrene as intermediates [3-6]. Padwa *et al.* synthesized azirines such as **3** by the addition of iodine azide to the dimethyl acetal of cinnamaldehyde followed by dehydrohalogenation, thermolysis and hydrolysis [7]. Following this sequence, the target 3-phenyl-2*H*-azirine-2-carboxaldehyde was obtained in 20% overall yield. Alajarin *et al.* has reported an approach to 3-aryl-2*H*-azirine-2-carboxaldehydes starting from cinamyl alcohols [8].

Much earlier, Isomura and co-workers had briefly reported [9] the synthesis of **3** by thermal decomposition of a mixture of (*E*)- and (*Z*)-β-azidocinamaldehyde in benzene at 50 °C followed by sublimation. Due to the synthetic versatility of 3-aryl-2*H*-azirine-2-carbox-aldehydes, short and efficient methods for their preparation are still in demand. Here, we have described a simple route to 3-substituted-2-formyl-azirines **3** and **7** from acyclic vinyl bromo/chloro-aldehydes **1** and **5** which is a useful alternative to those previously described methods.

Several research groups have reported convenient routes to isoxazoles and oxazoles [10,11] based on ring opening of 2*H*-azirine-2-carboxaldehydes, because they are a class of heterocyclic compounds having a remarkable number of applications and are useful synthetic intermediates in organic synthesis. The key feature of these heterocycles is that they possess the typical properties of an aromatic system. Isoxazole ring containing a weak N-O bond, which under certain conditions, particularly in reducing or basic conditions, is a potential site of ring cleavage. So our attention was next turned to the several routes for the catalytic conversion of azirine to isoxazole and oxazole.

Photochemical cleavage of C-C bond of the azirine ring accounts for the formation of 2-phenyl oxazole **III** from the irradiation of 2-formyl-3-phenyl-2*H*-azirine **I** [10b]. Heating of the same azirine for 24 h in toluene at 200 °C afforded 3-phenyl isoxazole **II** (Scheme 1).

Scheme 1

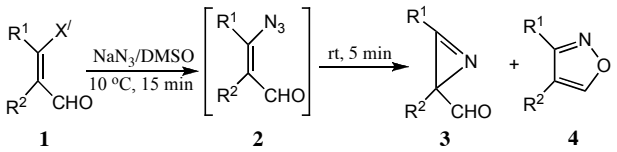


In continuation of our own investigation regarding synthesis of azirines, [12] we thought it would be of interest to investigate further the organometal and Lewis acid catalysed reactions of several azirines. In recent years, considerable interest has been given in the use of both organometallic reagent and catalysts for effecting ring cleavage of small ring systems [13]. Recently Padwa *et al*. reported several transition metal catalyzed ring-opening reactions of 2-phenyl-3-vinyl substituted 2*H*-azirines [14]. By comparison with the extensive studies carried out photochemically with 2*H*-azirines ring system, [15-18] its behavior toward organometallic reagent and other catalysts have been relatively unexplored.

In this paper, we have reported some organometal and Lewis acid catalyzed rearrangement of azirine containing aldehyde functionality to oxazole and isoxazole using different solvents.

the major product presumably *via* the corresponding vinyl nitrenes (Scheme 2 and Table 1). We also obtained isoxazoles **4**, although in very low yield, that might have formed by a ring-opening/ring-closure process of azirines **3**. Only in case of **1g** and **1l**, were we able to isolate the azido-aldehyde intermediate and we finally obtained the corresponding azirines.

Scheme 2



1 **2** **3** **4**

Bis-bromo/chloro-aldehydes **5** [19a,20] also underwent this reaction in analogous fashion *i.e.*, giving mainly *bis*-

Table 1

Reaction of bromo/chloro-aldehysdes **1a-f** with Sodium azide in DMSO

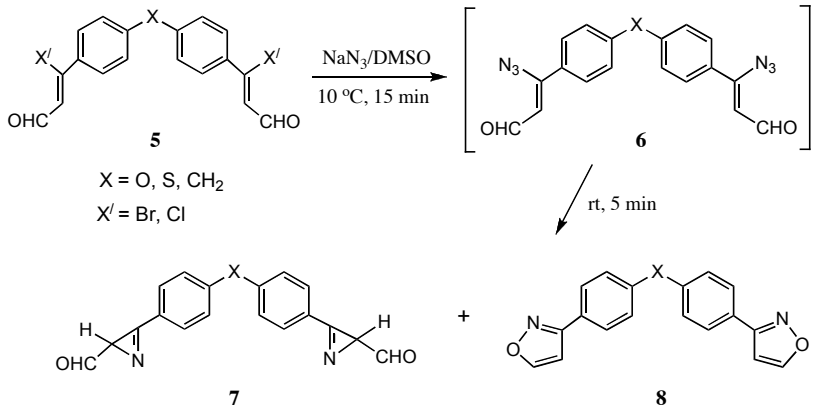
Entry	Substrates	Products	Yields (azirine, isoxazole)
1	**1a** (R^1 = Ph, R^2 = H $X^/$ = Cl)	**3a**, **4a**	65, 8
2	**1b** (R^1 = *p*-MeC_6H_4, R^2 = H, $X^/$ = Cl)	**3b**, **4b**	65, 8
3	**1c** (R^1 = 2-Naphthyl, R^2 = H, $X^/$ = Cl)	**3c**, **4c**	63, 7
4	**1d** (R^1 = *p*-ClC_6H_4, R^2 = H, $X^/$ = Cl)	**3d**, **4d**	65, 8
5	**1e** (R^1 = *p*-BrC_6H_4, R^2 = H, $X^/$ = Cl)	**3e**, **4e**	65, 8
6	**1f** (R^1 = Ph, R^2 = Ph, $X^/$ = Cl)	**3f**, **4f**	60, 6
7	**1g** (R^1 = Ph, R^2 = CH_3, $X^/$ = Cl)	**3g**	70
8	**1h** (R^1 = Ph, R^2 = H, $X^/$ = Br)	**3a**, **4a**	68, 8
9	**1i** (R^1 = *p*-MeC_6H_4, R^2 = H, $X^/$ = Br)	**3b**, **4b**	65, 8
10	**1j** (R^1 = Naphthyl, R^2 = H, $X^/$ = Br)	**3c**, **4c**	64, 6
11	**1k** (R^1 = Ph, R^2 = Ph, $X^/$ = Br)	**3f**, **4f**	61, 7
12	**1l** (R^1 = Ph, R^2 = CH_3, $X^/$ = Br)	**3g**	75

RESULTS AND DISCUSSION

In our synthesis, the acyclic bromo/chloro-aldehydes **1** [19] were reacted with sodium azide in DMSO at 10 °C to get the corresponding non-isolable 3-azido-aldehydes **2**, which at room temperature underwent spontaneous denitrogenation and ring closure to 2-formyl-azirines **3** as 2*H*-azirines **7** with minor amounts of isoxazoles **8** due to the same reason (Scheme 3 and Table 2).

Initially for the detection of unstable azido-aldehydes **2** and **6**, we performed the reaction of chloro-aldehyde **1** and **5** with sodium azide in an NMR tube using d_6-DMSO as solvent. For example, the ^{1}H NMR spectrum of chloroaldehyde **5a** showed a signal at δ

Scheme 3



5 **6** **7** **8**

10.10 for the aldehyde proton and at δ 6.94 for C*H*-CHO.

Table 2

Reaction of *bis*-bromo/chloro-aldehysdes **5a-f** with Sodium azide in DMSO

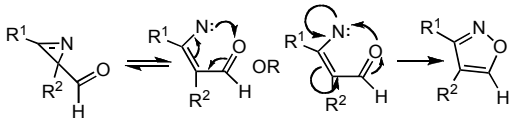
Entry	Substrates	Products	Yields (azirine, isoxazole)
1	**5a** (X = CH_2, X′ = Cl)	**7a**, **8a**	60, 8
2	**5b** (X = O, X′ = Cl)	**7b**, **8b**	57, 7
3	**5c** (X = S, X′ = Cl)	**7c**, **8c**	58, 6
4	**5d** (X = CH_2, X′ = Br)	**7d**, **8d**	47, 8
5	**5e** (X = O, X′ = Br)	**7e**, **8e**	42, 7
6	**5f** (X = S, X′ = Br)	**7f**, **8f**	44, 7

Immediately after the addition of NaN_3, these two peaks were shifted up field (δ 10.10 to δ 9.97 and δ 6.94 to δ 5.76 respectively), which clearly supported the formation of azido-aldehyde **6a**.

Due to the formation of NaCl, we could not take further clear NMR spectra. So after work up, followed by separation using preparative TLC, azirine **7a** (60%) and isoxazole **8a** (8%) were obtained. There are several reports about photolyses and pyrolyses of vinyl azides where the nitrene intermediate could not be detected [21,22].

The thermal transformations observed with aldehyde containing azirine system could be rationalized in terms of an equilibrium of the 2*H*-azirine with a transient vinyl nitrene, which subsequently rearranges to the five membered rings (Scheme 4).

Scheme 4



Nishiwaki and coworkers have demonstrated that a vinyl nitrene can be generated and trapped during the thermolysis of substituted 2*H*-azirine [23]. Several examples are also available in literature, which provide good analogy for the cyclization of butadienyl nitrene to a five-membered ring [24,25]. Here, we have investigated solvent variant several oraganometal catalyzed thermal conversion of azirine to oxazole and isoxazole and different Lewis acid catalyzed conversion of azirine to oxazole.

Scheme 5

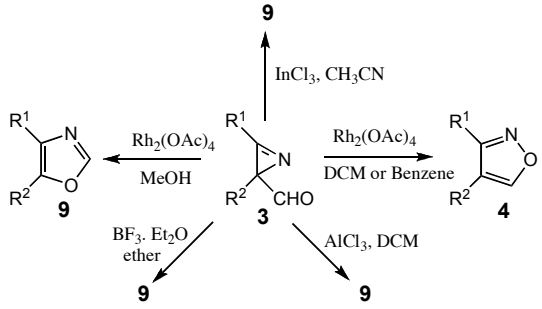


Table 3

Reaction of azirines under different reagents and conditions

Entry	Substrates	Reagents	Products	Time	Yield (%)
1	**3a**	$Rh_2(OAc)_4$	**4a**	6 h	70
2	**3b**	in DCM/	**4b**	6 h	72
3	**3c**	Benzene	**4c**	7 h	65
4	**3f**		**4f**	7 h	63
1	**3a**	$Rh_2(OAc)_4$	**9a**	1.5 h	70
2	**3b**	in MeOH	**9b**	6h	75
3	**3c**		**9c**	2 h	65
4	**3f**		**9f**	2.5 h	63
1	**3a**	$InCl_3$	**9a**	2 h	80
2	**3b**	in CH_3CN	**9b**	6 h	80
3	**3c**		**9c**	2.5 h	75
4	**3f**		**9f**	2.5 h	70
5	**3g**		**9g**	3 h	80
1	**3a**	$BF_3.Et_2O$	**9a**	20 min	95
2	**3b**	in Et_2O	**9b**	6 min	85
3	**3c**		**9c**	5-10 min	75
4	**3f**		**9f**	5-10 min	70
5	**3g**		**9g**	30 min	80
1	**3a**	$AlCl_3$	**9a**	5 min	80
2	**3b**	in DCM	**9b**	6 min	80
3	**3c**		**9c**	5-10 min	75
4	**3f**		**9f**	5-10 min	70
5	**3g**		**9g**	30 min	80

Being encouraged by this success we carried out the reaction of *bis*-azirines with different organometallics catalysts and a variety of Lewis acids (Scheme 6 and Table 4).

Scheme 6

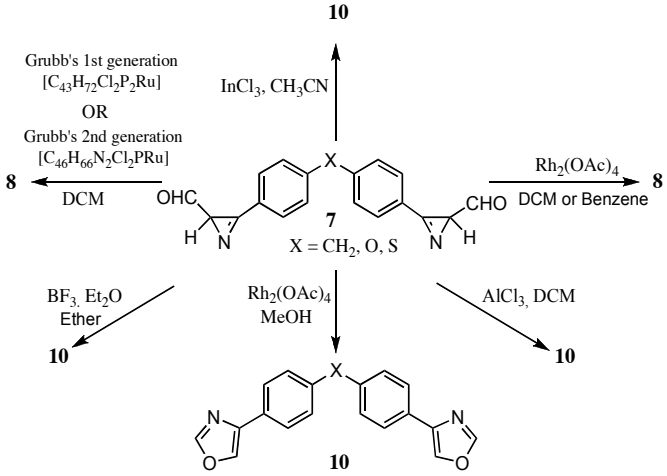


Table 4

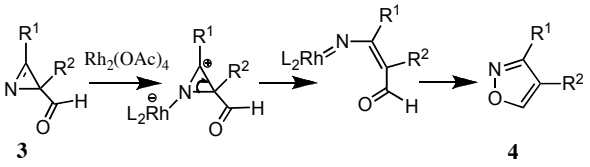
Reaction of *bis*-azirines under different reagents and conditions

Entry	Substrates	Reagents	Products	Time	Yield (%)
1	**7a**	$Rh_2(OAc)_4$	**8a**	8 h	60
2	**7b**	in DCM/Benzene	**8b**	9 h	56
3	**7c**		**8c**	8 h	56
1	**7a**	$Rh_2(OAc)_4$	**10a**	8 h	60
2	**7b**	in MeOH	**10b**	9h	56
3	**7c**		**10c**	9 h	50
1	**7a**	Grubb's 2nd generation	**8a**	5 min	96
2	**7b**	catalyst in DCM	**8b**	7 min	95
3	**7c**		**8c**	10 min	93
1	**7a**	$InCl_3$	**10a**	1.5 h	95
2	**7b**	in CH_3CN	**10b**	2 h	90
3	**7c**		**10c**	2.5 h	92
1	**7a**	$BF_3.Et_2O$	**10a**	20 min	60
2	**7b**	in Et_2O	**10b**	15 min	56
3	**7c**		**10c**	25 min	56
1	**7a**	$AlCl_3$	**10a**	3 min	70
2	**7b**	in DCM	**10b**	5 min	65
3	**7c**		**10c**	5-8 min	60

Possible mechanism for the azirine-$Rh_2(OAc)_4$ involves the initial π-complexation of Rh(II) catalyst with the imino bond (Scheme 7). Ring opening by C-N bond cleavage would give intermediate, which then afford **4** by the loss of rhodium complex [26].

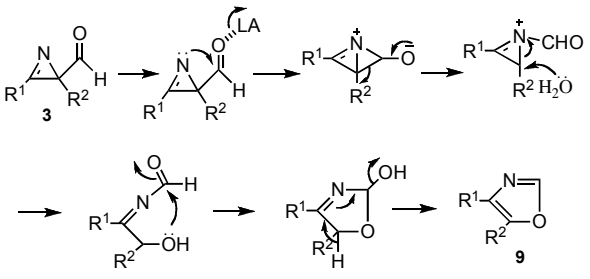
Probable mechanism:

Scheme 7



Though the mechanism for azirine in presence of Lewis acid is not clear, perhaps it involves co-ordination of azirine oxygen with Lewis acid in the first step. After that lone pair of azirine nitrogen attacks aldehyde carbon to form an intermediate. Subsequent addition of water followed by dehydration gave the product (Scheme 8).

Scheme 8



This work reveals that open chain vinyl bromo/chloro-aldehydes could be converted to 3-substituted 2-formyl-azirines at room temperature in moderate yields. Moreover, we have reported several methods for the conversion of azirines having aldehyde functionality to oxazoles and isoxazoles. Particularly the methodology for the formation oxazole using Lewis acid offered several opportunities for process improvement over the reported procedure.

EXPERIMENTAL

^1H (200 MHz) NMR spectra were recorded on a BRUKER-AC 200 MHz spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: 7.26 ppm). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constant (Hz). ^{13}C (50 MHz) NMR spectra were recorded on a BRUKER-AC 200 MHz. Spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: 77.0 ppm). ESIMS (70 eV) spectra were taken using a VG Autospec M mass spectrometer. Elemental analysis was carried out by using an Elemental Analyzer VARIO EL instrument.

All reactions were carried out under an argon atmosphere. Purification by preparative TLC [silica gel GF-254]. For reaction monitoring, precoated silica gel 60 F254, TLC sheets (Merck) were used. Petroleum ether refers to the fraction boiling in the range 60-80 °C. All the dry solvents used for reactions were purified according to the standard protocols. Sodium azide, $Rh_2(OAc)_4$, and indium(III) chloride (98%), $BF_3.Et_2O$, $AlCl_3$ were purchased from Lancaster.

General procedure for syntheses of substituted 2-formyl-azirines: To an ice-cold solution of sodium azide (2.5 mmol) in DMSO (15 ml), a solution of bromo- or chloro-aldehydes **1** (1 mmol) dissolved in DMSO were added dropwise. The mixture

was stirred for 15 min at 10 ºC and then for 5 min at rt (25-30 ºC). Then the reaction mixture was decomposed with water and the aqueous portion was extracted with DCM. Removal of the solvent under reduced pressure followed by purification by preparative TLC [silica gel GF-254, hexane-ethyl acetate (7:1) as eluent] gave 2-formyl-azirines **3** (60-68 %) and the isoxazoles **4** (6-8 %) as the only isolable products. *Bis*-2*H*-azirines **7** were prepared in a similar manner.

3-Phenyl-2*H*-azirine-2-carbaldehyde 3a. Yellow solid; mp 47-50 °C (from ether) (lit mp 49-51 °C) [7]; IR (KBr) ν_{max} 1773, 1710, 1451, 1116 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.53 (d, *J* = 6.5 Hz, 1H, NC*H*), 6.75-6.99 (m, 3H, Ar-*H*), 7.15-7.34 (m, 2H, Ar-*H*), 8.70 (d, *J* = 6.4 Hz, 1H, C*H*O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 39.01, 122.49, 129.32, 130.51, 134.35, 159.32, 199.86; Mass (ES^+): m/z 146 [MH^+, 100%], 117 [M^+-CO].

3-Phenyl isoxazole 4a. Pale yellow viscous liquid; IR (KBr) ν_{max} 3050, 2967, 1670, 1608 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 6.66 (d, *J* = 1.7 Hz, 1H, NCC*H*), 7.42-7.47 (m, 3H, Ar-*H*), 7.80-7.85 (m, 2H, Ar-*H*), 8.45 (d, *J* = 1.7 Hz, 1H, OC*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 102.43, 126.89, 128.80, 128.93, 130.02, 158.85, 161.51; Mass (ES^+): m/z 146 [MH^+, 100%]; HRMS (ES^+) calcd for C_9H_7NO (MH^+) 146.0528 found 146.0663.

3-(*p*-Tolyl)-2*H*-azirine-2-carbaldehyde 3b. Pale yellow solid; mp 32-34 °C (from ether) (lit mp 31-32 °C) [8]; IR (KBr) ν_{max} 1773, 1710, 1451, 1116 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.52 (s, 3H, CH_3), 2.87 (d, *J* = 6.7 Hz, 1H, NC*H*), 7.45- 7.50 (m, 2H, Ar-*H*), 7.87-8.03 (m, 2H, Ar-*H*), 8.99 (d, *J* = 6.6 Hz, 1H, C*H*O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.02, 39.01, 122.49, 129.32, 130.51, 144.35, 159.32, 199.86; Mass (ES^+): m/z 160.07 [MH^+, 100%].

3-(*p*-Tolyl)isoxazole 4b. Colorless solid; mp 53-55 °C (from DCM) (Lit. 55-56 °C) [27]; IR (KBr): 3030, 2921, 1612, 1557, 1520, 1121 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.30 (s, 3H, CH_3), 6.63 (d, J = 1.6 Hz, 1H, NCC*H*), 7.28 (d, J = 8.1 Hz, 2H, Ar-*H*), 7.76 (d, J = 8.1 Hz, 2H, Ar-*H*), 8.43 (d, J = 1.6 Hz, 1H, OC*H*).

3-Naphthalen-2-yl-2*H*-azirine-2-carbaldehyde 3c. Yellow solid, mp 60-62 °C (from DCM); IR (KBr) ν_{max}: 1771, 1706, 1279, 1110, 819 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) [12]: δ = 2.89 (d, *J* = 2.7 Hz, 1H, NC*H*), 7.53-7.63 (m, 3H, Ar-*H*), 7.86-7.97 (m, 4H, Ar-*H*) 8.92 (d, *J* = 6.7 Hz, 1H, C*H*O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 26.63, 123.86, 126.73, 127.74, 128.40, 129.51, 130.14, 132.49, 134.48, 135.56, 198.06; Mass (ES^+): m/z 196[MH^+, 100%], 167[M^+-CO]; HRMS (ES^+) calcd for $C_{13}H_9NO$ (MH^+) 196.0684 found 196.0785.

3-Naphthalen-2-yl-isoxazole 4c. Yellow viscous liquid; IR (KBr) ν_{max} 3040, 2968, 1611, 1561cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 6.80 (d, *J* = 1.5 Hz, 1H, NCC*H*), 7.51-7.59 (m, 2H, Ar-*H*), 7.87-7.97 (m, 4H, Ar-*H*), 8.27 (s, 1H, Ar-*H*), 8.50 (d, *J* = 1.5 Hz, 1H, OC*H*),; Mass (ES^+): m/z 196 [MH^+, 100%]; Elemental analysis calcd for $C_{13}H_9NO$: C, 80.07; H, 4.65; N, 7.18. Found C, 79.92; H, 4.70; N, 7.2.

3-(*p*-chlorophenyl)-2*H*-azirine-2-carboxaldehyde 3d. Pale yellow solid, mp 87-90 °C (from ether) (lit mp 88-89 °C) [8]; IR (KBr) ν_{max}: 1770, 1710, 1680, 1125, 990 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.87 (d, *J* = 6.4 Hz, 1H, NC*H*), 7.63 (d, *J* = 8.0 Hz, 2H, Ar-*H*), 7.86 (d, *J* = 8.1 Hz, 2H, Ar-*H*), 8.95 (d, *J* = 6.7 Hz, 1H, C*H*O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 38.92, 122.49, 129.45, 130.51, 139.35, 159.31, 199.86.

3-(*p*-bromophenyl)-2*H*-azirine-2-carboxaldehyde 3e. Pale yellow solid, mp 107-109 °C (from ether) (lit mp 109-110 °C) [8]; IR (KBr) ν_{max}: 1773, 1715, 1690, 1119, 988 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.87 (d, *J* = 6.4 Hz, 1H, NC*H*), 7.61 (d, *J* = 8.1 Hz, 2H, Ar-*H*), 7.85 (d, *J* = 8.2 Hz, 2H, Ar-*H*), 8.95 (d, *J* = 6.7 Hz, 1H, C*H*O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 38.92, 122.49, 129.45, 130.51, 134.35, 159.31, 199.86.

2,3-Diphenyl-2*H*-azirine-2-carbaldehyde 3f. White solid, mp 99-102 °C (from DCM); IR (KBr) ν_{max}: 1764, 1707, 1599, 1447, 1232 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 7.17-7.84 (m, 2H, Ar-*H*), 7.63-7.94 (m, 8H, Ar-*H*), 9.32 (s, 1H, C*H*O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 127.59, 128.14, 128.30, 128.48, 128.84, 129.32, 129.63, 130.20; 130.68, 133.34, 134.02, 134.41, 141.81, 150.05, 193.85; Mass (ES^+): m/z 222.07 (MH^+, 100 %).

4,5-Diphenyl-isoxazole 4f. Yellow viscous compound; IR (KBr) ν_{max}: 2960, 1610, 1575, 1440 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) [28]: δ = 7.26-7.42 (m, 6H, Ar-*H*), 7.75 (d, *J* = 7.6 Hz, 2H, Ar-*H*), 7.89 (s, 1H, OC*H*), 8.04-8.06 (m, 2H, Ar-*H*); Mass (ES^+): m/z 222 (MH^+, 100 %); Elemental analysis calcd for $C_{15}H_{11}NO$: C, 81.43; H, 5.01; N, 6.33. Found C, 81.51; H, 5.29; N, 6.38.

3-Azido-2-methyl-3-phenyl propenal 2g. Pale yellow oil; IR (KBr) ν_{max}: 2114, 1773, 1701, 1654, 1560, 1508, 1458 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 1.87 (s, 3H, CH_3), 7.45-7.87 (m, 3H, Ar-*H*), 7.26-7.37 (m, 2H, Ar-*H*), 9.27 (s, 1H, C*H*O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 40.79, 128.40, 128.89, 129.39, 130.14, 156.26, 164.90, 200.38; Mass (ES^+): m/z 160 (MH^+-N_2, 100 %); Elemental analysis calcd for $C_{10}H_9N_3O$: C, 64.16; H, 4.85; N, 22.45. Found C, 63.89; H, 4.79; N, 22.38.

2-Methyl-3-phenyl-2*H*-azirine-2-carbaldehyde 3g. Yellow oil; IR (KBr) ν_{max}: 1760, 1703, 1599, 1440; ^1H NM (200 MHz, $CDCl_3$): δ = 1.51 (s, 3H, CH_3), 7.55-7.72 (m, 3H, Ar-*H*), 7.83 (d, *J* = 1.9 Hz, 1H, Ar-*H*), 7.87 (d, *J* = 1.43 Hz, 1H, Ar-*H*), 8.84 (s, 1H, C*H*O); Elemental analysis calcd for $C_{10}H_9NO$: C, 75.45; H, 5.70; N, 8.80. Found C, 75.53; H, 4.81; N, 9.02.

***Bis*-4,4'-[3-(2*H*-azirine-2-formyl)]phenylmethane 7a.** Pale yellow solid mp 89-91 °C (from DCM); IR (KBr) ν_{max}: 1738, 1618 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.87 (d, *J* = 6.4 Hz, 2H, NC*H*), 4.21 (s, 2H, CCH_2C), 7.44 (d, *J* = 8.1 Hz, 4H, Ar-*H*), 7.88 (d, *J* = 8.1 Hz, 4H, Ar-*H*), 8.95 (d, *J* = 6.4 Hz, 2H, C*H*O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 29.67, 38.95, 42.19, 129.34, 130.63, 146.70, 158.93, 200.00; DEPT-135: 38.95 (**C**H_2), 42.18 (N**C**H); Mass (FAB): m/z 303 [M^++H, 40%]; HRMS (ES^+) calcd for $C_{19}H_{14}N_2O_2$ (MH^+) 303.1056 found 303.1113.

***Bis*-4,4'-(3-isoxazole)phenylmethane 8a.** Pale yellow semisolid; (KBr) ν_{max} 3010, 1601, 1556 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 4.07 (s, 2H, CCH_2C), 6.62 (d, *J* = 1.5 Hz, 2H, NCC*H*), 7.28 (d, *J* = 10.3 Hz, 4H, Ar-*H*), 7.75 (d, *J* = 10.3 Hz, 4H, Ar-*H*), 8.43 (d, *J* = 1.5 Hz, 2H, OC*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 39.02, 119.17, 130.07, 157.89, 159.78; Mass (ES^+): m/z 303 (MH^+); Elemental analysis calcd for $C_{19}H_{14}N_2O_2$: C, 75.48; H, 4.67; N, 9.27. Found C, 75.55; H, 4.68; N 9.19.

***Bis*-4,4'-[3-(2*H*-azirine-2-formyl)]phenylether 7b.** Yellow solid, mp 93-95 °C (from DCM); IR (KBr) ν_{max}: 1706, 1592, 1494, 1244 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.90 (d, *J* = 6.2 Hz, 2H, NC*H*), 7.25-7.30 (m, 4H, Ar-*H*) , 7.92-7.97 (m, 4H, Ar-*H*), 8.98 (d, *J* = 6.3 Hz, 2H, C*H*O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 30.67, 43.19, 128.34, 132.63, 150.70, 156.93, 198.00; Mass (ES^+): m/z 305 (MH^+); HRMS (ES^+) calcd for $C_{18}H_{12}N_2O_3$ (MH^+) 305.0848 found 305.0921.

***Bis*-4,4'-(3-isoxazole)phenylether 8b.** Yellow viscous liquid; IR (KBr) ν_{max} 3035, 1620, 1560 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 6.66 (d, *J* = 1.5 Hz, 2H, NCC*H*), 7.12-7.22 (m, 4H, Ar-*H*), 7.86-7.95 (m, 4H, Ar-*H*), 8.48 (d, *J* = 1.8 Hz, 2H, OC*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 120.07, 132.07, 158.29, 160.70,;

Mass (ES^+): m/z 305 (MH^+); Elemental analysis calcd for $C_{18}H_{12}N_2O_3$: C, 71.04; H, 3.97; N, 9.21. Found C, 70.91; H, 4.15; N, 9.32.

***Bis*-4,4'-[3-(2*H*-azirine-2-formyl)]phenylsulphide 7c.** Yellow viscous liquid; IR (KBr) ν_{max}: 1745, 1620 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.91 (d, J = 6.3 Hz, 2H, NCC*H*), 7.57 (d, J = 8.1 Hz, 4H, Ar-*H*), 7.91 (d, J = 10.1 Hz, 4H, Ar-*H*), 8.98 (d, J = 6.4 Hz, 2H, C*H*O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 29.67, 42.19, 129.34, 130.63,146.70, 158.93, 200.00; Mass (ES^+): m/z 321; HRMS (ES^+) calcd for $C_{18}H_{12}N_2O_2S$ (MH^+) 321.0620 found 321.0673.

***Bis*-4,4'-(3-isoxazole) phenyl sulphide 8c.** Pale yellow semisolid; IR (KBr) ν_{max} 2095, 1617, 1565 cm-1; ^1H NMR (200 MHz, $CDCl_3$): δ = 6.70 (d, J = 1.9 Hz, 2H, NCC*H*), 7.35-7.58 (m, 4H, Ar-*H*), 7.74-7.94 (m, 4H, Ar-*H*), 8.51 (d, J = 1.9 Hz, 2H, OC*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 118.59, 131.87, 159.28, 162.70,; Mass (ES^+): m/z 321 (MH^+); Elemental analysis calcd for $C_{18}H_{12}N_2O_2S$: C, 67.48; H, 3.78; N, 8.74. Found C, 67.43; H, 3.87; N, 8.52.

General procedure for the formation of isoxazole/oxazole from the reaction of azirine and $Rh_2(OAc)_4$. Azirines **3** and **7** (1mmol) were dissolved in DCM or benzene (Caution: carcinogenic) /methanol and 5 mol % of $Rh_2(OAc)_4$ was added to it. Then the reaction mixture was refluxed and monitored by TLC. Removal of solvent under reduced pressure followed by purification by preparative TLC [Silica Gel GF-254, hexane-ethylacetate (7:1 and 1:3) as eluent] gave isoxazoles/oxazoles in moderate yield.

General procedure for the formation of oxazole from the reaction of azirine and $InCl_3$. Azirines **3** and **7** (1 mmol) were dissolved in acetonitrile and $InCl_3$ (1.5 mmol/3 mmol) was added to it. Then the reaction mixture was refluxed and monitored by TLC. After removal of solvent under reduced pressure, the reaction mixture was decomposed with water and the aqueous portion was extracted with DCM. Followed by purification by preparative TLC [Silica Gel GF-254, hexane-ethylacetate (7:1 and 1:3) as eluent] gave oxazoles (**9** and **10**) in moderate yield.

General procedure for the formation of oxazole from the reaction of azirine and $BF_3.Et_2O$. Azirines **3** and **7** (1 mmol) were dissolved in ether and $BF_3.Et_2O$ (1.5 mmol/3 mmol) was added to it at -50 ºC and then stirred at rt for few minutes. Then the reaction mixture was dried under reduced pressure, the reaction mixture was decomposed with water and the aqueous portion was extracted with ether. Removal of solvent under reduced pressure followed by purification by preparative TLC [Silica Gel GF-254, hexane-ethylacetate (7:1 and 1:3) as eluent] gave oxazole (**9** and **10**) in excellent yield.

General procedure for the formation of oxazole from the reaction of azirine and $AlCl_3$. Azirines **3** and **7** (1mmol) were dissolved in DCM and $AlCl_3$ (1mmol/2 mmol or little excess) was added to it at -40 ºC. The reaction was completed rapidly at this temperature producing oxazole in 95 % yield. Then the reaction mixture was decomposed with ice water and the aqueous portion was extracted with DCM. Removal of solvent under reduced pressure gave oxazole (**9** and **10**) in excellent yield.

4-Phenyl-oxazole 9a. Pale yellow viscous liquid product; [29] IR (KBr) ν_{max}: 1638, 1445, 1261, 1020 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 7.23 (s, 1H, NCC*H*), 7.42-7.48 (m, 3H, Ar-*H*), 7.71 (s, 1H, NC*H*), 8.02-8.07 (m, 2H, Ar-*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 124.06, 128.21, 128.31, 128.84, 129.02, 137.84, 148.74; Mass (ES^+): m/z 146 (MH^+, 100%).

4-(*p*-Methylphenyl)-oxazole 9b. Pale yellow viscous liquid product; IR (KBr) ν_{max}: 1630, 1444, 1265 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.52 (s, 3H, CH_3), 7.22 (s, 1H, NCC*H*), 7.40-7.47 (m, 2H, Ar-*H*), 7.69 (s, 1H, NC*H*), 7.85-8.02 (m, 2H, Ar-*H*); Mass (ES^+): m/z 160 (MH^+, 8.8%), 159 (M^+, 100%)

4- Naphthalen-2-yl-oxazole 9c. IR (KBr) ν_{max}: 1630, 1460 cm^{-1}; [29] ^1H NMR (200 MHz, $CDCl_3$): δ = 7.53-7.62 (m, 3H, Ar-*H*), 7.65 (s, 1H, NCC*H*), 7.98 (s, 1H, NC*H*), 8.00-8.91 (m, 4H, Ar-*H*); m/z 196 (HM^+, 100%); Elemental analysis calcd for $C_{13}H_9NO$: C, 79.98; H, 4.65; N, 7.17. Found C, 80.01; H, 4.63; N, 7.21.

4,5-Diphenyl-oxazole 9f. Pale yellow liquid product, [30] soon solidified; mp 40-43 °C (from DCM) (lit mp 42-44 °C); IR (KBr) ν_{max}: 1635, 1505, 1408 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 7.20-7.49 (m, 10H, Ar-*H*), 7.90 (s, 1H, NC*H*); Mass (ES^+): m/z 222 (MH^+, 100%).

5-Methyl-4-phenyl-oxazole 9g. Pale yellow viscous liquid [31]; IR (KBr) ν_{max}: 1655, 1535, 1415 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.50 (s, 3H), 7.42 (s, 1H), 7.97-8.02 (m, 5H);

***Bis*-4,4'-(4-oxazole)phenylmethane 10a.** Yellow liquid product, solidified at 4 °C; IR (KBr) ν_{max}: 1645, 1440, 1270 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 4.05 (s, 2H, CCH_2C), 7.15 (d, J = 8.2 Hz, 4H, Ar-*H*), 7.23 (s, 2H, NCC*H*), 7.70 (s, 2H, NC*H*), 8.01 (d, J = 8.1 Hz, 4H, Ar-*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 39.11, 121.07, 128.17, 130.07, 140.09, 146.68, 151.18, 158.90; Mass (ES^+): m/z 303 (MH^+); Elemental analysis calcd for $C_{19}H_{14}N_2O_2$: C, 75.48; H, 4.67; N, 9.27. Found C, 75.35; H, 4.71; N, 9.17.

***Bis*-4,4'-(4-oxazole)phenylether 10b.** Pale yellow viscous liquid; IR (KBr) ν_{max}: 1655, 1458 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 6.94 (d, J = 8.7 Hz, 4H, Ar-*H*), 7.04 (s, 2H, NCC*H*), 7.57 (s, 2H, NC*H*), 7.87 (d, J = 8.7 Hz, 4H, Ar-*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 118.60, 121.57, 133.17, 139.19, 153.11, 159.70, 158.30; Mass (ES^+): m/z 305 (MH^+); Elemental analysis calcd for $C_{18}H_{12}N_2O_3$: C, 71.04; H, 3.97; N, 9.21. Found C, 70.85; H, 4.21; N, 9.01.

***Bis*-4,4'-(4-oxazole)phenylsulphide 10c.** Yellow viscous liquid; IR (KBr) ν_{max}: 1656, 1460 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 7.11 (d, J = 8.7 Hz, 4H, Ar-*H*), 7.15 (s, 2H, NCC*H*), 7.50 (s, 2H, NC*H*), 7.82 (d, J = 8.2 Hz, 4H, Ar-*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 119.06, 126.57, 133.17, 139.09, 153.89, 158.29, 160.03; Mass (ES^+): m/z 321 (MH^+); Elemental analysis calcd for $C_{18}H_{12}N_2O_2S$: C, 67.50; H, 3.75; N, 8.745. Found: C, 67.29; H, 3.80; N, 8.45.

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