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Mild, convenient and efficient synthesis of novel 2,2-dichloro-1, 3-diarylaziridines from Schiff bases by phase transfer CTAB catalysis under low concentration alkaline conditions

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Abstract

A mild and efficient method for preparation of novel 2,2-dichloro-1,3-diarylaziridines from Schiff base compounds in the presence of *N*-cetyl-*N,N,N*-trimethyl ammonium bromide (CTAB) as phase transfer catalyst has been described. The reaction is dramatically enhanced in the presence of quaternary ammonium salt. The corresponding products have been obtained in excellent yields, high purity and short reaction times.
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Keywords: Aziridine; Synthesis; Schiff base; CTAB; Phase transfer catalyst

Aziridines, three-membered nitrogen heterocycles, are highly reactive molecules, in part due to ring strain [1]. As a consequence of their high reactivity, these small heterocycles play an important role as intermediates in synthesis of both organic [2], pharmaceutical and natural product. Among three-membered heterocycles, aziridines constitute a particularly versatile class of molecule, and as discussed in recent book [3], both physical properties and chemical reactions of aziridines have been the subject of numerous theoretical and experimental investigations which have proved invaluable in understanding the mechanism of drug action of pharmaceuticals containing azriridine warheads [4]. The preparation of substituted aziridines and also, modern catalytic synthesis of aziridines from diazo compounds and imines has been extensively reviewed [5,6]. While, 2,2-dihalodiarylaziridines have been very poorly investigated. The development of new efficient syntheses of halogenated nitrogen heterocycles and their precursors is a rather persisting problem in organic chemistry [7–10].

Schiff bases that contain an imine or azomethine have prepared from condensation of primary amines with carbonyl compounds [11–13]. These compounds have been extensively studied in chemistry due to their facile syntheses, electronic properties, good solubility in common solvents and numerous applications in organic synthesis, pharmacology [14] and *etc.* Phase transfer catalysis (PTC) technology has recently been widely applied to synthesize specially chemicals from organic reactions [15,16]. Many chemists have investigated phase transfer catalysis in numerous reactions, such as: substitution, displacement, condensation, electro-reduction and *etc.* As a result, PTC considered having great potential for industrial-scale application [17,18].

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Because of these economical and environmental reasons and in conjunction with ongoing work in our laboratory on the preparation of Schiff base derivatives [19,20], here we decided to report the synthesis of various dichloroaziridines through the reaction of Schiff base compounds and chloroform in the presence of *N*-cetyl-*N,N,N*-trimethyl ammonium bromide (CTAB) as phase transfer catalyst under alkaline condition at room temperature.

1. Experimental

All the materials were of commercial reagent grade. All the Schiff bases have been prepared according with previously reported procedure [21,22]. IR spectra were recorded as KBr pellets on a Perkin-Elmer 781 spectrophotometer and an Impact 400 Nicolet FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR were recorded in DMSO/$CDCl_3$ solvents on a Bruker DRX-400 spectrometer with TMS as internal reference. Mass spectra were recorded on a Finnigan MAT 44S by electron ionization (EI) mode with an ionization voltage of 70 eV. The elemental analyses (C.H.N) were obtained from a Carlo ERBA Model EA 1108 analyzer. Melting points obtained with a Yanagimoto micro melting point apparatus are uncorrected.

Typical procedure for the synthesis of 2,2-dichloro-1,3-diphenylaziridine: NaOH (0.095 mol, 3.8 g) and CTAB (0.00082 mol, 0.3 g) were dissolved in 30 mL of water. The mixed solution was introduced to a 100 mL flask and uniformly agitated at isothermal condition for 10 min. Then, Schiff base (organic reactant; 0.027 mol) dissolved in 10 mL chloroform was gradually added drop wise to the mixed solution. The progress of the reaction was monitored by TLC. After the completion of the reaction, the solution was separated and the portion of aqueous solution was extracted twice by ether. Magnesium sulfate was also added to adsorb the residual water. The organic solvent (chloroform) and other residues were stripped in a vacuum evaporator. The pale yellow solid, 2,2-dichloro-1,3-diphenylaziridine, was obtained in 90% yield (0.024 mol). All of the diarylaziridine products were identified by physical and spectroscopic data as following:

2,2-Dichloro-1,3-diphenylaziridine (***2a***)*:* pale yellow solid; 0.024 mol; mp: 100–102 °C, (98–99 °C, Ref. [23,24]); IR (KBr)/υ (cm^{-1}): 3090, 2930, 1600, 1520 (C=C, Ar); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.20 (s, 1H, HCN), 7.01–7.80 (m, 10H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.1, 74.1, 119.0, 120.1, 125.1, 126.1, 127.1, 128.3, 134.2, 140.1; MS: *m/z* 267 (M^{+4} + 4, 7), 265 (M^{+2} + 2, 29), 263 (M^{+}, 45), 230 (67), 228 (100), 77 (95); Anal. Calcd. For $C_{14}H_{11}NCl_2$: C, 63.64 5; H, 4.17; N, 30, Found: C, 63.67; H, 4.19 5; N, 30.

2,2-Dichloro-1-(4-bromophenyl)-3-phenylaziridine (***2b***): white solid; 0.025 mol; mp: 110–112 °C; IR (KBr)/υ (cm^{-1}): 3100, 2914, 1600, 1524 (C=C, Ar); ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.34 (s, 1H, HCN), 7.14 (d, 2H, Ar), 7.45 (d, 2H, Ar), 7.50–7.55 (m, 5 H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 50.0, 71.0, 119.4, 122.7, 128.9, 129.0, 131.9, 132.3, 136.2, 151; MS: *m/z*: 347 (M^{+6} + 6, 8), 345 (M^{+4} + 4, 20), 343 (M^{+2} + 2, 45), 341 (M^{+}, 27), 308 (80), 306 (100), 229 (75), 227 (50), 77 (85); Anal. Calcd. For $C_{14}H_{10}NBrCl_2$: C, 49.12; H, 2.92; N. 4.11. Found: C, 49.15; H, 2.95; N. 4.12.

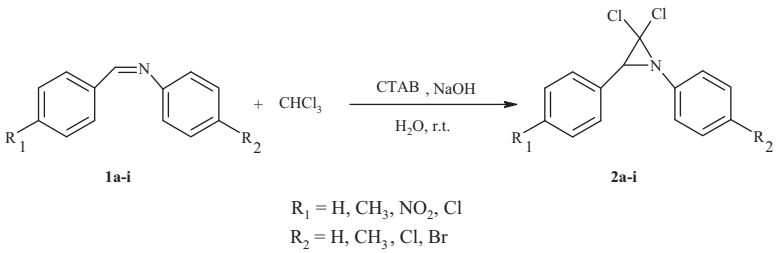
2,2-Dichloro-1-(4-chlorophenyl)-3-phenylaziridine (***2c***)*:* pale yellow solid; 0.0248 mol; mp: 72–74 °C, (71–72 °C, Ref. [25]); IR (KBr)/υ (cm^{-1}): 3090, 2900, 1598, 1499 (C=C, Ar); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.21 (s, 1 H, HCN), 7.10 (d, 2 H, Ar), 7.32 (d, 2 H, Ar), 7.48–7.55 (m, 5 H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.1, 76.9, 119.1, 120.8, 121.1, 127.9, 128.1, 130.1, 131.2, 135.1, 142.2; MS: *m/z* 233 (M^{+6} + 6, 7), 231 (M^{+4} + 4, 15), 299 (M^{+2}+2, 32), 297 (M^{+}, 35), 264 (96), 262 (100), 174 (75), 172 (80), 91 (95), 77 (45); Anal. Calcd. For $C_{14}H_{10}NCl_3$: C, 56.28; H. 3.35; N, 4.69, Found: C, 56.31; H. 3.38; N, 4.70.

2. Results and discussion

In this research, the phase transfer catalyzed reaction of dichloro aziridination of Schiff base compounds has been studied. When 0.027 mol of Schiff base compound was reacted with dichlorocarbene intermediate obtained in situ from the reaction of chloroform and base in the presence of CTAB as a phase transfer catalyst, corresponding products, 2,2-dichloro-1,3-diarylaziridine compounds was obtained at room temperature (Scheme 1).

Firstly, we have carried out this reaction in the presence and without of two-phase transfer catalysts, such as: CTAB and *N*-cetyl pyridinium bromide (CPB). The corresponding results are indicated in Table 1.

As can be seen in this Table, desired product was obtained with excellent yield in the presence of CTAB rather than CPB as phase transfer catalyst. Also, any product was obtained in the reaction without phase transfer catalyst in alkaline solution (Table 1, entries 9 and 10). It has also been investigated the reaction in the presence of various



Scheme 1. Preparation of 2,2-dichloro-1,3-diarylaziridine compounds from Schiff bases.

amounts of sodium hydroxide. The optimum amount of used NaOH was resulted 12.6 wt% in which 2,2-dichloro-1,3-diphenylaziridine was obtained in excellent yield and appropriate reaction time.

With attention to above results, several Schiff base compounds were reacted with $CHCl_3$ in the presence of mixture of NaOH (12.6%) and CTAB as phase transfer catalyst and desired dichloroaziridine derivatives were prepared. The results are summarized in Table 2. As shown in this Table, the reaction of the various Schiff bases with chloroform and optimum amount of NaOH, were catalyzed by CTAB as two-phase transfer. The corresponding products were obtained in excellent yields and appropriate reaction times.

Table 1
Enhancement of phase transfer catalyst (PTC) and amount of NaOH on the formation of 2,2-dichloro-1-(4-bromophenyl),3-(4-chlorophenyl) aziridine.

Entry	PTC	NaOH (%)	Time (h)	Yield (%)
1	CTAB	8	12	10
2	CTAB	10	9	25
3	CTAB	11	6	55
4	CTAB	12.6	2.3	98
5	CTAB	14	2.3	98
6	CPB	12.6	12	10
7	CPB	12.6	16	15
8	CPB	12.6	24	20
9	None	22.5	96	–
10	None	30	96	–

Table 2
Synthesis of 2,2-dichloro-1,3-diarylaziridines in the presence of CTAB catalyst and 12.6 wt% NaOH.

Entry	Substrate		Product	M.P. (°C)	Time (h)	Yield[a] (%)
	R_1	R_2				
1	H	H	**2a**	100–102	4	90, (61)[b], (55)[c]
2	H	Br	**2b**	110–112	3.20	94
3	H	Cl	**2c**	72–74	3.25, (16)[d]	92,(68)[d]
4	Cl	Cl	**2d**	139–141	2.40	98
5	Cl	Br	**2e**	134–136	2.30	98
6	NO_2	Br	**2f**	141–143	4.40	90
7	NO_2	CH_3	**2g**	140–142	4.45	92
8	CH_3	Br	**2h**	146–148	3.45	96
9	Cl	CH_3	**2i**	128–130	3.30	97

[a] Isolated yields.
[b] By hexachloroacetone and sodium methoxide, Ref. [23].
[c] By sodium methoxide and chloroform, Ref. [24].
[d] By potassium *t*-butoxide and chloroform, Ref. [25].

The structure of products has been confirmed by physical and spectroscopic data such as; IR, ^{1}H NMR, ^{13}C NMR, Mass spectroscopy and C. H. N. analyses. In the IR spectra of compound **2b**, the stretching frequency of aromatic C=C is formed in the region 1587 cm^{-1} and 1487 cm^{-1}. The stretching vibration of C–H in the alkyl groups was appeared at region 2928 cm^{-1}. In the ^{1}H NMR spectra, one proton of CH–N was appeared in δ 4.34 as a singlet. Two aromatic protons were appeared in δ 7.14 as a doublet. The appeared signal in δ 7.45 is belong to another two aromatic protons. The signals around δ 7.50–7.55 are assigned by other five protons of aromatic rings. In the ^{13}C NMR spectra, one carbon of C–N has chemical shift in δ 50.0 and the signal in δ 71.0 is assigned by one carbon of CCl_2 of aziridine ring. The signal around δ 119.4–150.0 is assigned by carbons of aromatic rings. Appearance of molecular ion peak with *m/z* 341was confirmed the formation of this product.

In conclusion, we have synthesized dichloroaziridine derivatives through the reaction of various Schiff base compounds with chloroform in the presence of CTAB at room temperature. The corresponding products have been obtained in excellent yields, high purity and short reaction times. The products have been confirmed by physical and spectroscopic data such as; IR, ^{1}H NMR, ^{13}C NMR, MS spectroscopy and C. H. N. analyses.

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