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Sonocatalyzed facile and mild one pot synthesis of *gem*-dichloroaziridine derivatives under alkaline conditions

Hossein Naeimi *, Khadijeh Rabiei

Department of Organic Chemistry, Faculty of Chemistry, University of Kashan, Kashan 87317, Iran

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ABSTRACT

In this research, rapid and efficient preparation of 2,2-dichloro-1,3-diarylaziridines through the reaction of Schiff base compounds with dichlorocarbene yielded in situ from chloroform and sodium hydroxide without any phase transfer catalyst under ultrasonic irradiation is described. The advantages of this reaction are very short reaction times, excellent product yields, simplicity of the method and high purity of products.

1. Introduction

Aziridines, which are extremely important synthetic building blocks, are nitrogen equivalents of epoxides, and can be similarly opened in a stereo controlled manner with various nucleophiles, providing access to a wide range of important nitrogen-containing products [1]. These compounds are among the most fascinating intermediates in organic synthesis, acting as precursors of many complex molecules due to the strain incorporated in their skeletons [2]. Since the first synthesis of an aziridine reported by Gabriel in 1888 [3], the synthetic scope of aziridine chemistry has blossomed in recent years. Thus, obtaining aziridines, has become of great importance in organic chemistry. In particular, the antitumor and antibiotic properties of a great number of aziridine-containing compounds are of high significance among other biological properties, which make them attractive synthetic targets in their own right [4]. As a result, several methods for synthesis of *gem*-dichlo roaziridines have been reported. The preparation has been accomplished by the addition of dichlorocarbene generated from chloroform, hexachloroacetone or ethyltrichloroacetate with the appropriate base under phase transfer catalyst, to imines [5–10].

The use of ultrasonic waves in organic synthesis has been boosted in recent years [11–21]. Ultrasound is known to accelerate diverse types of organic reactions and it is established as an important technique in organic synthesis [17,19,22]. Sonication also increases the reaction rate and avoids the use of high reaction temperatures [19]. A number of organic reactions have been revisited by means of ultrasonic waves [17,19,22]. Also, some literatures on ultrasonically prepared dichlorocarbene have been reported [23–27]. Recently, syntheses of fluoro aziridines in the presence of phase transfer catalyst under ultrasonic irradiation have been reported [28]. The advantages of ultrasound procedures, such as, good yields, short reaction times and mild reaction conditions, are well documented [29].

In conjunction with ongoing work in our laboratory on the preparation of Schiff base derivatives [30–33], here we decided to report the synthesis of various dichloroaziridines through the reaction of various Schiff base compounds and chloroform without any phase transfer catalyst under ultrasonic irradiation.

2. Experimental section

2.1. Materials

All the materials were of commercial reagent grade. All the Schiff bases have been prepared according to the previously reported procedures [30,31].

2.2. Apparatus

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 tetramethylsilane as internal reference. Mass spectra were recorded on a Finnigan MAT

* Corresponding author. Tel.: +98 361 5912388; fax: +98 361 5552935.
E-mail address: naeimi@kashanu.ac.ir (H. Naeimi).

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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. The BANDELIN ultrasonic HD 3200 with probe model KE 76, 6 mm diameter, was used to produce ultrasonic irradiation and homogenizing the reaction mixture. Piezoelectric crystal of this kind of probe normally works in the range of 700 kHz, but using through some proper clamps the output frequency of piezoelectric crystal have controlled and reduced to 20 kHz. Therefore, the induced frequency of probe to the reaction mixture is equal to 20 kHz. By changing the power of Tip the cavitations rate is displaced. Meaning the Tip frequency under all amount of power is constant. Melting points obtained with a Yanagimoto micro melting point apparatus are uncorrected. The purity determination of the substrates and reaction monitoring were accomplished by TLC on silica-gel polygram SILG/UV 254 plates (from Merck Company).

2.3. The power measurement by calorimetric method

We assessed the cavitational energy applied by ultrasonication calorimetrically with water. The piezoelectric transducer was connected to the frequency generator, HD-3200 (with frequency; 20 kHz). The probe (KE-76) was dipped in a jacketed cylindrical vessel. For calorimetric measurement, the jacket was empty and connected to vacuum to minimize heat losses. In this method, by measuring the rate of temperature increase due to the conversion of ultrasound energy into heat and calculating $P_{acoustic}$ according to: $P = mc\Delta T/t$, where m is the mass of water (g), c is the specific heat capacity of water (4.18 $Jg^{-1}\,k^{-1}$), ΔT is the difference in temperature (k) and t is the sonication time(s).

2.4. Typical procedure for the synthesis of 2,2-dichloro-1, 3-diphenylaziridine

Measured quantities of NaOH (0.075 mol, 3 g) were dissolved in 30 ml of water and the obtained solution was introduced to a 100 ml flask. The ultrasonic probe was immersed directly in the reactor. Then, Schiff base (organic reactant; 0.028 mol, 8.2 g) dissolved in chloroform (0.07 mol, 8.3 ml) was gradually added drop wise to the NaOH solution under ultrasonic irradiation with power 67 W. The progress of the reaction was monitored by TLC. After the completion of the reaction in 15 min, the solution was separated and the portion of aqueous solution was extracted by diethylether. Magnesium sulfate was also added to adsorb the residual water. The organic solvent and other residues were stripped in a vacuum evaporator. The pale yellow solid, 2,2-dichloro-1, 3-diphenylaziri dine, was obtained in 96% yield, m.p. = 100–102 °C (reported [5,8–10], m.p. = 98–99 °C), All of the diarylaziridine products were identified by physical and spectroscopic data as following;

2,2-dichloro-1, 3-diphenylaziridine (2a); pale yellow solid; m.p. = 100–102 °C (m.p. = 98–99 °C) [5,8–10].

2,2-dichloro-1-(4-bromophenyl)-3-phenylaziridine (2b); white solid; m.p. = 143–145 °C; IR (KBr)/ υ(cm^{-1}): 3100, 2914, 1600, 1524 (C=C, Ar); ^1H NMR (DMSO)/ δ ppm: 4.34 (s, 1 H, HCN), 7.14 (d, 2 H, Ar), 7.45 (d, 2 H, Ar), 7.50–7.55 (m, 5 H, Ar); ^{13}C NMR/ ($CDCl_3$) / δ ppm: 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; m.p. = 72–74 °C (m.p. = 71–72 °C) [7].

2,2-dichloro-1, 3-bis(4-chlorophenyl)aziridine (2d); white solid; m.p. = 139–141 °C; IR (KBr)/ υ(cm^{-1}): 3085, 2910, 1600, 1504 (C=C, Ar); ^1H NMR (400 MHz, DMSO)/ δ ppm: 4.34 (s, 1 H, HCN), 7.14 (d, 2 H, Ar), 7.45 (d, 2 H, Ar), 7.50–7.58 (m, 4 H, Ar); ^{13}C NMR/ (100 MHz, DMSO)/ δ ppm: 53.15, 75.9, 122.3, 128.9, 129.3, 129.7, 130.1, 132.2, 134.1, 143.6; MS: m/z: 341 (M^{+8} + 8, 4), 337 (M^{+6} + 6,<3), 335 (M^{+4} + 4, 10), 333 (M^{+2} + 2, 25), 331 (M^+, 15), 298 (70), 296 (65), 174 (60), 172 (98), 161 (80), 159 (100), 77 (55); Anal. Calcd. For $C_{14}H_9NCl_4$: C, 50.45; H, 2.70; N, 4.20. Found: C, 50.48; H, 2.74; N. 4.21.

2,2-dichloro-1-(4-bromophenyl), 3-(4-chlorophenyl) aziridine (2e); white solid; m.p. = 134–136 °C; IR (KBr)/ υ(cm^{-1}): 3100, 2920, 1598, 1509 (C=C, Ar); ^1H NMR (400 MHz, DMSO)/δ ppm: 4.34 (s,1 H, HCN), 7.08 (d, 2 H, Ar), 7.50–7.56 (m, 4 H, Ar), 7.58 (d, 2 H, Ar); ^{13}C NMR/ (100 MHz, DMSO)/ δ ppm: 53.0, 76.9, 122.3, 129.1, 129.3, 130.1, 131.8, 134.5, 137.6, 150.1; MS: m/z: 381 (M^{+6} + 6, 6), 379 (M^{+4} + 4, 25), 377 (M^{+2} + 2, 34), 375 (M^+, 14), 342 (60), 340 (46), 218 (60), 216 (94), 205 (82), 203 (100); Anal. Calcd. For $C_{14}H_9NBrCl_3$: C, 44.62; H, 2.39; N, 3.72. Found: C, 44.64; H, 2.42: N, 3.73.

2,2-dichloro-1-(4-bromophenyl), 3-(4-nitrophenyl) aziridine (2f); white solid; m.p. = 141–143 °C; IR (KBr)/ υ(cm^{-1}): 3080, 2924, 1600, 1522 (C=C, Ar); ^1H NMR (400 MHz, $CDCl_3$)/ δ ppm: 3.79 (s, 1 H, HCN), 6.95 (d, 2 H, Ar), 7.50 (d, 2 H, Ar), 7.71 (d, 2 H, Ar), 8.31 (d, 2 H, Ar); ^{13}C NMR (100 MHz, DMSO)/ δ ppm: 53.2, 75.9, 122.3, 128.9, 129.2, 129.7, 130.2, 132.2, 134.1, 143.6; MS: m/z: 392 (M^{+6} + 6, 7), 390 (M^{+4} + 4, 20), 388 (M^{+2} + 2, 50), 386 (M^+, 38), 353 (78), 351 (100), 307 (65), 305 (80), 218 (80), 216 (95), 77 (80); Anal. Calcd. For $C_{14}H_9N_2O_2BrCl_2$: C, 43.41; H, 2.33; N, 7.24. Found: C, 43.43; H, 2.35; N, 7.24.

2,2-dichloro-1-(4-methylphenyl), 3-(4-nitrophenyl) aziridine (2 g); yellow solid; m.p. = 140–142 °C; IR (KBr)/ υ(cm^{-1}): 3090, 2918, 1589, 1490 (C=C, Ar); ^1H NMR (400 MHz, DMSO)/ δ ppm: 2.29 (s, 3 H, CH_3) 4.45 (s, 1 H, HCN), 7.02 (d, 2 H, Ar), 7.21 (d, 2 H, Ar), 7.80 (d, 2 H, Ar)8.31 (d, 2 H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$)/ δ ppm: 20.9, 53.5, 75.1, 119.6123.7, 128.9, 134.6, 140.3, 141.7, 148.3; MS: m/z: 326 (M^{+4} + 4, 6), 324 (M^{+2} + 2, 29), 322 (M^+, 40), 289 (70), 287 (100), 243 (60), 241 (80), 154 (70), 152 (82), 91 (92); Anal. Calcd. For $C_{15}H_{12}N_2O_2Cl_2$: C, 55.73; H, 3.72; N, 8.67, Found: C, 55.75; H, 3.74; N, 8.67.

2,2-dichloro-1-(4-bromophenyl), 3-(4-methylphenyl) aziridine (2 h); yellow solid; m.p. = 146–148 °C; IR (KBr)/ υ(cm^{-1}): 3100, 2898, 1600, 1500 (C=C, Ar); ^1H NMR (400 MHz, $CDCl_3$)/ δ ppm: 2.38 (s, 3 H, CH_3) 3.41 (s, 1 H, HCN), 7.15 (d, 2 H, Ar), 7.21 (d, 2 H, Ar), 7.45 (d, 2 H, Ar), 7.84 (d, 2 H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$)/ δ ppm: 20.9, 51.0, 72.9, 120.1, 129.8, 130.1, 135.0, 136.7, 137.8, 149.3; MS: m/z: 361 (M^{+6} + 6,<2), 359 (M^{+4} + 4, 24), 357 (M^{+2} + 2, 47), 355 (M^+, 35), 322 (85), 320 (100), 218 (64), 216 (80), 91 (95); Anal. Calcd. For $C_{15}H_{12}NBrCl_2$: C, 50.56; H, 3.37; N, 3.93, Found: C, 50.59; H, 3.39; N, 3.94.

2,2-dichloro-1-(4-methylphenyl), 3-(4-chlorophenyl) aziridine (2i); white solid, m.p. = 128–130 °C; IR (KBr)/ υ(cm^{-1}); 3090, 2920, 1600, 1508 (C=C, Ar); ^1HNMR (400 MHz, $CDCl_3$)/ δ ppm: 2.36 (s, 3 H, CH_3) 3.65 (s, 1 H, HCN), 6.95 (d, 2 H, Ar), 7.18 (d, 2 H, Ar), 7.36–7.47 (m, 5 H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$)/ δ ppm: 21.5, 53.1, 73.1, 121.0, 128.5, 129.9, 130.1, 138.1, 138.5, 138.1, 139.0, 149.3; MS: m/z: 317 (M^{+6} + 6, 10), 315 (M^{+4} + 4, 20), 313 (M^{+2} + 2, 47), 311 (M^+, 50), 283 (96), 281 (100), 154 (80), 152 (84), 91 (98); Anal. Calcd. For $C_{15}H_{12}NCl_3$: C, 57.60; H, 3.84; N, 4.48, Found: C, 57.64; H, 3.88; N, 4.49.

3. Results and discussion

In this research, the ultrasonic irradiation as a phase transfer catalyzed reaction of dichloro aziridination of Schiff base compounds has been studied. When 0.028 mol of Schiff base compound was reacted with dichlorocarbene intermediate obtained in situ from the reaction of chloroform and base under ultrasonic irradiation, corresponding products, 2,2-dichloro-1, 3-diarylaziri-