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Rapid Communication

Synthesis and characterization of novel (fenchonylsulfonyl) oxaziridine

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An efficient synthesis of (fenchonylsulfonyl) oxaziridine from commercially available fenchone is described. Several intermediates involved in the synthesis of oxaziridine *viz*. fenchonesulfonic acid, fenchonesulfonyl chloride, fenchone sulfonamide, fenchone sulfonimine have also been synthesized and characterized.

Keywords: Fenchone, fenchonesulfonic acid, sulfonyl chloride, sulfonamide, sulfonimine, (fenchonylsulfonyl) oxaziridine

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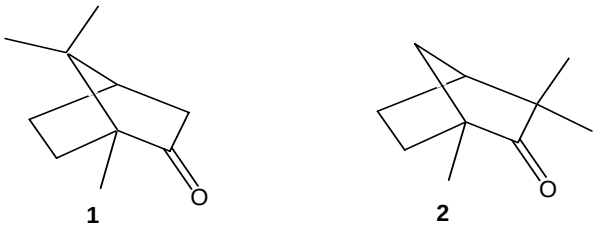
The synthesis and chemistry of oxaziridines has been widely studied[1-3]. Oxaziridines are aprotic, neutral oxidizing agents and have proved themselves to be efficient candidates for the oxidation of sulfides to sulfoxides[4], the asymmetric hydroxylation of enolates[5] and also useful in the stereo-selective epoxidation of olefins[6]. It has been established that the attack of a nucleophile occurs at either the oxygen or the nitrogen atom of the ring, depending upon the nature of the nucleophile and the substituents on the oxaziridine, especially at the nitrogen atom. Oxaziridines having electron-withdrawing substituents on the nitrogen atom or on both the nitrogen and the carbon atoms of the three-membered ring have the ability to transfer oxygen atoms to nucleophiles. N-Sulfonyl-oxaziridines[5,7] are among the best candidates, and fall in this category. Camphor **1** and fenchone **2** (**Figure 1**) and their derivatives are widely used as primary sources for chirality. This is because of the fact that the different position of the *gem*-dimethyl group in each derivative confers dissimilar topology, often reflected in the capacity for chirality transfer. Therefore, they are often employed as chiral reagents, intermediates or catalysts in asymmetric synthesis[8].



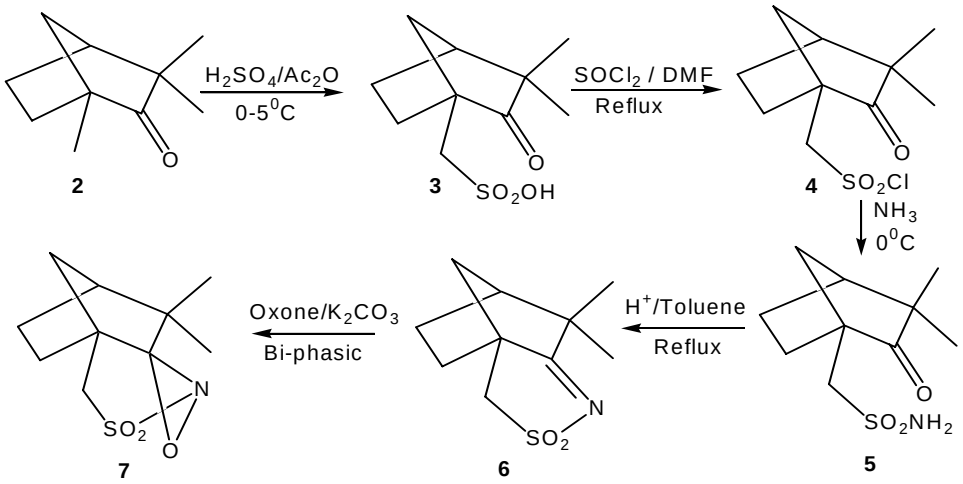
1 2

Figure 1

Over the last decade, the synthesis of a large number of fenchone derivatives has been reported[9-11]. Recently, synthesis and amination properties of fenchyl oxaziridine have also been described[12]. In the ongoing research program, it was intented to obtain a unique (fenchonylsulfonyl) oxaziridine **7** which could be a versatile reagent for many useful chemical transformations as compared with other N-sulfonyl-oxaziridines *e.g.* (camphorylsulfonyl) oxaziridine[13]. So far, the title compound has neither been synthesized nor probed[14]. This is due to the fact that most of C-10 substituted camphor derivatives are obtained from 10-camphorsulfonic acid whereas the corresponding key starting material 10-fenchone sulfonic acid is not commercially available[15]. In this communication, is described the first efficient synthesis of (fenchonylsulfonyl) oxaziridine **7** from commercially available fenchone **2** (**Scheme I**).

The first step of synthesis consists of the reaction of **2** with conc.H_2SO_4/Ac_2O at 0ºC to give 10-fenchonesulfonic acid **3**. Several attempts were made to convert the sulfonic acid **3** into sulfonylchloride **4** by using various chlorinating reagents such as Cl_2, PCl_5, SO_2Cl_2 and $SOCl_2$ but they all failed. A mixture of $SOCl_2$ and DMF (Vilsmeier reagent) afforded the desired product at reflux temperature. 10-Fenchonesulfonyl chloride **4** on subsequent treatment with NH_3 gas at 0ºC in $CHCl_3$ resulted in the formation of 10-fenchonesulfonamide **5** in very good yield. Dehydration of sulfonamide **5** in the presence of Amberlyst 15 ion exchange resin (an acid catalyst) in toluene provided fenchonesulfonimine **6**. Sulfonimine **6** was oxidized using oxone/K_2CO_3 in bi-phasic medium and gave corresponding (fenchonylsulfonyl) oxaziridine **7**. All the compounds have been characterized by usual spectroscopic techniques.

To summarize, the first synthesis of (fenchonyl-sulfonyl) oxaziridine has been achieved, *via* a number of synthetic intermediates. Investigations on the



Scheme I

comparative chemical and optical properties of the compound are under progress.

Experimental Section

Melting points were determined on S D Fine Electrotherm-9100 melting point apparatus and are uncorrected. IR spectra were recorded in KBr pellets on Perkin-Elmer model BXII FTIR spectrophotometer. ^{1}H NMR spectra were recorded on Bruker (400 MHz) spectrometer and chemical shifts were expressed on the δ scale against TMS as internal standard. The GC-MS analysis was performed on Varian 3400GC coupled to a TSQ 7000 mass spectrometer (Finnigan Mat.). All reagents were of commercial quality from ACROS Organics and used as received without further purification. Distilled water was used for all purposes.

Preparation of 10-fenchonesulfonic acid 3. In a three necked round bottom flask fitted with a powerful slow-speed stirrer having a teflon blade, a dropping funnel, and a thermometer arranged to dip in to the liquid was placed conc. H_2SO_4 15.2 mL (0.25 mole). The flask was cooled by an ice-salt mixture, the stirring started and 50 mL (0.507 mole) of acetic anhydride was added at such a rate so that the temperature did not exceed above 20ºC. Fenchone 40 mL (0.249 mole, diluted with 20 mL of acetic anhydride) was added dropwise. Stirring was continued at this temperature for 3 hr and then at RT for another 6 hr The reaction mixture was kept at RT for three days. Then the reaction mixture was poured into cold diethyl ether. 10-Fenchonesulfonic acid got precipitated which was washed with diethyl ether to remove acid impurities, followed by the evaporation of solvent over rotatory evaporator which resulted in a brown colored viscous product. Yield 30%. IR (KBr): 3418, 2974, 1727, 1186, and 1041 cm^{-1}; ^{1}H NMR (CD_3OD): δ 4.9 (s, OH, 1H), 3.71 and 3.64 (dd, CH_2SO_2, 2H), 2.24-1.25 (m, 7H), 1.0 (d, CH_3, 6H). EIMS was recorded of the methyl ester of the acid, which was obtained by reacting acid with diazomethane. EIMS: m/z(%) 246 (M^+, 2), 151 (M^+ - SO_2OCH_3, 6), 123 (100), 109 (2), 91 (10.5), 81 (70), 79 (96), 67 (22), 53 (12), 41 (43.9).

Preparation of 10-fenchonesulfonyl chloride 4. To compound **3** (12.0 g, 0.051 mole in 350 mL) in $CHCl_3$, a mixture of $SOCl_2$ (7.0 mL, 1.9 eq. 0.096 mol) and DMF (0.6 mL, 0.006 mole was added dropwise and the resultant mixture refluxed for 4 hr to get the sulfonylchloride **4**. The reaction mixture was washed with ice-cold water and dried over anhydrous Na_2SO_4. Removal of solvent on a rotatory evaporator produced a viscous product. Yield 2.5 g (20%). IR(KBr): 2971, 2931, 1744, 1373, 1166, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.20 and 3.80 (dd, CH_2SO_2, 2H), 2.09 -1.30 (m, 7H), 0.9 (d, CH_3, 6H); EIMS: m/z(%) 250 [M^+, (^{35} Cl), 2], 252 [M^++2, (^{37} Cl), 0.66], 151 (M^+- SO_2Cl), 123 (100), 93 (4), 81 (84), 79 (26), 67 (26), 55 (10.5), 41 (29).

Preparation of 10-fenchonesulfonamide 5. Compound **4** (2.5 g, 0.01 mole) in 100 mL of $CHCl_3$ was cooled down to 0ºC and ammonia gas was passed through the cooled solution for 25 min and the progress of reaction was monitored with the help of TLC (toluene/acetone= 9:1). The reaction mixture was stirred for 3hr at 0ºC and then at RT for an additional 2hr The solution was filtered, washed with water and dried over anhydrous Na_2SO_4. Evaporation of the solvent on a rotatory evaporator gave **5** as a brownish solid product which on purification by recrystallization from DCM/Petroleum ether

(40-60ºC) afforded the pure compound. Yield 1.5 g (65%). m.p. 100-02ºC; IR (KBr): 3348, 3262, 2972, 1739, 1317, 1166 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.83 (bs, SO_2NH_2, 2H), 3.70 and 3.30 (dd, CH_2SO_2, 2H, *J*= 16Hz), 2.31 (m, CH, 1H), 2.01 (m, CH_2, 2H), 1.75 (m, CH_2, 2H), 1.6 (m, CH_2, 2H), 1.02 (d, CH_3, 6H, *J*= 12Hz); EIMS: m/z (%) 231 (M^+, 4), 151 (M^+ - SO_2NH_2, 9), 123 (100), 122 (14), 79 (55), 67 (17), 55 (9), 43 (12).

Preparation of fenchone sulfonimine 6. 10-Fenchonesulfonamide **5** (1.5 g, 6.49 mmole) was dissolved in 100 mL of toluene and 0.3 g of Amberlyst 15 (ion exchange resin) was added to this solution. The reaction mixture was refluxed for 4 hr. Water formed during this reaction was removed by using Dean-Stark condensor. After completion of reaction (monitored by TLC, toluene/acetone = 9:1), the reaction mixture was allowed to reach RT. The solution was filtered and the residue was washed with DCM. The combined organic layer (Toluene and DCM) was concentrated to give solid product which on purification by recrystallization from DCM/Petroleum ether (40-60ºC) afforded the pure brownish solid compound **6**, yield (0.95 g, 70%). m.p. 138-42ºC; IR (KBr): 2970, 1637, 1326, 1161 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.30 and 3.20 (dd, CH_2SO_2, 2H, *J*= 12Hz), 2.20 (m, CH, 1H), 1.84 (m, CH_2, 2H), 1.73 (m, CH_2, 2H), 1.64 (m, CH_2, 2H), 1.20 (d, CH_3, 6H, *J*= 12Hz); Q-TOF-MS-MS: m/z (%) 214 (M^++1, 32), 150 (59), 133 (38), 109 (27), 81 (100), 67 (19).

Preparation of (fenchonylsulfonyl) oxaziridine 7. In a two necked round-bottom flask, compound **6** (4.14 mmoles) was taken in toluene (100 mL) and K_2CO_3 (15 g, 0.108 mole) in 30 mL of distilled water. The reaction mixture was cooled to 0ºC in an ice bath and stirred vigorously; a solution of 10.0 g (0.016 mole) of oxone in 40 mL of distilled water was added dropwise. After addition of the oxone, the reaction mixture was warmed to RT. Stirring was continued and progress of reaction was monitored by TLC (toluene/acetone = 9:1). Potassium carbonate was added to adjust and maintain the *p*H of the reaction mixture at *p*H 9. After the completion of the reaction, the reaction mixture was stirred vigorously for an additional 1 hr, filtered and transferred into a separating funnel. The toluene layer was separated, and the aqueous layer was extracted with DCM. The organic extracts were combined, washed with water and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded solid product which on purification by recrystallization from DCM/Petroleum ether (40-60ºC) gave a white coloured crystalline compound. Yield 0.70 g (70%). m.p.116-20ºC; IR (KBr): 2962, 2920, 1464, 1358, 1184 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.35 and 3.25 (dd, CH_2SO_2, 2H, *J*= 12Hz), 2.22 (m, CH, 1H), 1.80 (m, CH_2, 2H), 1.70 (m, CH_2, 2H), 1.62 (m, CH_2, 2H), 1.25 (d, CH_3, 6H, *J*= 12Hz); EIMS: m/z(%) 229 (M^+, 0.1), 214 (6), 150 (13), 135 (15), 123 (18), 107 (58), 93 (57), 81 (75), 79 (100), 69 (55), 67 (33), 55 (31).

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