A Convenient Procedure for the Preparation of Camphorsulfonyl Oxaziridines

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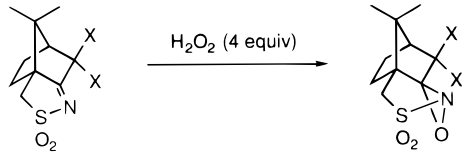
The preparation of a range of (camphorsulfonyl)oxaziridines is achieved in high yields in a simple and clean process by treatment of the (camphorsulfonyl)imines with commercial aqueous hydrogen peroxide.

Enantiomerically pure oxaziridines are versatile reagents which can be used to carry out asymmetric enolate hydroxylation, epoxidation, and oxidation of sulfides to sulfoxides and of selenides to selenoxides. Several of these reagents, including the most effective, derived from camphor, have been developed by Davis.[4] The preparation of the (camphorsulfonyl)imine precursors can be achieved with relative ease on a multigram scale.[5] The subsequent oxidation of the imines to oxaziridines however requires careful use of relatively powerful oxidants. Initially, concentrated MCPBA (>95%) was used in order to obtain good yields, but recently peracetic acid has been employed under phase transfer conditions.[6] Oxone has also been used, but has shown variable reactivity in the reaction, which also requires pH control.[5]

We have discovered that commercial aqueous hydrogen peroxide (30% w/v) can be used to prepare oxaziridines in a high-yielding, extremely simple, inexpensive, and environmentally friendly process. Unlike other methods of preparation, because the reactions are clean and there are no byproducts such as acids or bis-peroxides, minimum workup is required, and oxaziridines are readily isolated, often without the need for any further purification. The procedure is successful on a multigram scale even for the more sensitive oxaziridines.

Excellent yields of crystalline products are obtained from a number of camphorsulfonylimines (**1**−**5**) on a gram scale, including acetals of ((oxocamphor)sulfonyl)-oxaziridines, which have proved to be highly selective oxidants,[7,8] simply by treatment with commercial aqueous hydrogen peroxide in methanolic solution in the presence of potassium carbonate (Table 1, method A).

Table 1. Preparation of (Camphorsulfonyl)Oxaziridines



X, X		reaction time/h	method	yield/%
H	(1)[10]	3	A	91
OCH_2CH_2O	(2)	3	A	93
OMe	(3)	8	A	82
OEt	(4)	12	A	86
Cl	(5)[11]	3	B	76
OMe	(3)	3	B	97

Purification by chromatography is not required. The preparation of ((dichlorocamphor)sulfonyl)oxaziridine (**5**), which is particularly useful for enolate alkylation and which appears to be less stable under these reaction conditions, and larger scale preparations of other oxaziridines are best carried out under phase transfer conditions (Table 1, method B), which are successful on up to at least a 50 g scale.

Experimental Section

General Experimental Details. CH_2Cl_2 was dried by distillation from calcium hydride under an inert atmosphere. MeOH, anhydrous grade, was used as supplied. H_2O_2 was purchased as a 30% w/v solution in water. Other reagents were used as supplied. Organic extracts were dried over anhydrous $MgSO_4$.

Sample Procedures. Method A. (+)-((3-Oxocamphor)-sulfonyl)oxaziridine Ethylene Ketal (2). Commercial aqueous H_2O_2 (30% w/v) (*ca.* 15 mmol) was added to a stirred suspension of K_2CO_3 (1.0 g, 7.2 mmol) in MeOH (10 mL) at room temperature. (−)-((3-Oxocamphor)sulfonyl)imine ethylene ketal (1.00 g, 3.69 mmol) was then added and oxaziridine formation monitored by TLC. After 3 h, the reaction mixture was partitioned between saturated brine (50 mL) and CH_2Cl_2 (100 mL), the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic extracts were washed with aqueous sodium sulfite (10 mL) to destroy residual H_2O_2[9] and dried. Removal of the organic solvent *in vacuo* below 40 °C furnished **2** as a colorless crystalline solid (0.985 g, 93%): mp 176−178 °C (Found: C, 50.11; H, 5.96; N, 4.91. $C_{12}H_{17}NO_5S$ requires C, 50.17; H, 5.92; N, 4.88%); ν_{max} (CH_2Cl_2) 1332, 1308, 1164 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (3H, s), 1.35 (3H, s), 1.83−2.22 (5H, m), 3.11 (1H, d, J = 14 Hz), 3.33 (1H, d, J = 14 Hz), 3.84−4.15 (4H, m); ms *m/z* (EI) 287.08253 (M^+), $C_{12}H_{17}NO_5S$ requires 287.08273; $[\alpha]^{20}_D = +72°$ (c = 0.75, CH_2Cl_2).

Method B. (+)-((8,8-Dimethoxycamphoryl)sulfonyl)oxaziridine (3).[7a] Aliquat 336 (tri-*n*-octylmethylammonium chloride) (5.0 mL, 10.9 mmol) was added to a stirred solution of (+)-((8,8-dimethoxycamphoryl)sulfonyl)imine (50 g, 183 mmol) in CH_2Cl_2 (250 mL) at 0 °C. Aqueous K_2CO_3 (50 g, 362 mmol, in 100 mL) was added and the two-phase mixture agitated. After 5 min, commercial aqueous H_2O_2 (30% w/v) (83 mL, 732 mmol) was added dropwise over 30 min, and the reaction mixture was allowed to reach room temperature over 3 h. The organic layer was separated and the aqueous phase extracted with CH_2Cl_2 (3 × 100 mL). Residual H_2O_2 was destroyed by careful addition of

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(9) The reaction of hydrogen peroxide and sodium sulfite is exothermic and may require cooling when carried out on a large scale.

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aqueous sodium sulfite.[9] The combined organic layers were washed with aqueous sodium sulfite (5 g in 100 mL) and brine (100 mL) and dried. Removal of the organic solvent *in vacuo* below 40 °C furnished the oxaziridine contaminated with a little imine. Recrystallization from ethanol gave **3** as a colorless crystalline solid (51.3 g, 97%): mp 188−190 °C; ν_{max} (CH_2Cl_2) 1367, 1345, 1165 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.06 (3H, s), 1.32 (3H, s), 1.75−2.30 (5H, m), 3.08 (1H, d, J = 12 Hz), 3.27 (3H, s), 3.29 (1H, d, J = 12 Hz), 3.34 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 20.5, 21.6, 28.1, 29.3, 45.1, 47.4, 50.5, 50.8, 52.9, 54.6, 97.6, 102.8; ms m/z (CI) 290.10619 (MH^+), $C_{12}H_{20}NO_5S$ requires 290.10622; $[\alpha]^{20}_D$ = +91° (c = 3.00, $CHCl_3$).

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Additions and Corrections

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Leonid A. Rozov, Patrice W. Rafalko, Suzanne M. Evans, Linda Brockunier, and Keith Ramig*. Asymmetric Synthesis of the Volatile Anesthetic 1,2,2,2-Tetrafluoroethyl Chlorofluoromethyl Ether Using a Stereospecific Decarboxylation of Unusual Stereochemical Outcome.

Page 1319. It has come to our attention that the assignment of absolute configuration to the anesthetic desflurane (1,2,2,2-tetrafluoroethyl difluoromethyl ether) has been reversed. (See: Polavarapu, P. L.; Cholli, A. L.; Vernice, G. G. *J. Pharm. Sci.* **1997**, *86*, 267. Schurig, V.; Juza, M.; Green, B. S.; Horakh, J.; Simon, A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1680.) The original erroneous assignment was used to assign absolute configurations to compounds **2**, **3**, **9**, **10**, and **12**. Thus, the absolute configuration of all these compounds is actually (*R*)-(−)/(*S*)−(+). A consequence of this is that the decarboxylation reactions shown in Scheme 3 actually proceed with retention of configuration.

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