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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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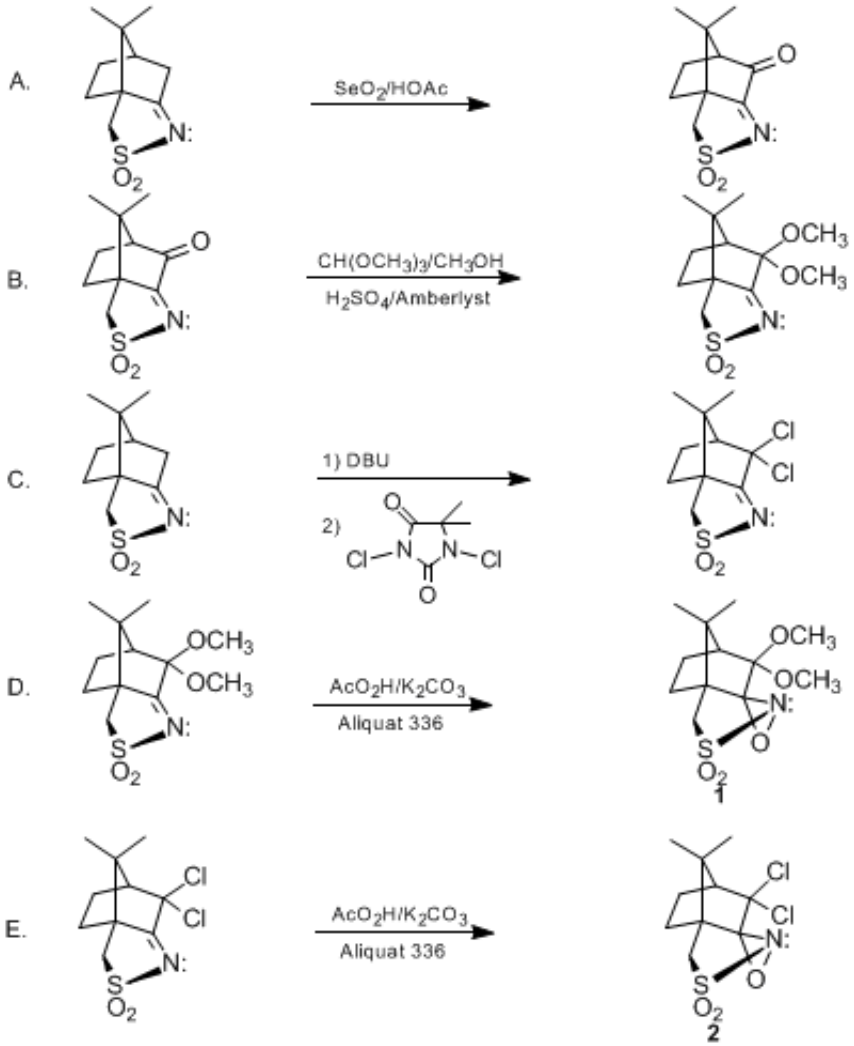
(+)-(2R,8aR)-[(8,8-DIMETHOXYCAMPHORYL)SULFONYL]OXAZIRIDINE AND (+)-(2R,8aR)-[(8,8-DICHLOROCAMPHORYL)SULFONYL]OXAZIRIDINE

[[4H-4a,7-Methanooxazirino[3,2-i][2,1]benzisothiazole, tetrahydro-8,8-dimethoxy-9,9-dimethyl-, 3,3-dioxide], [2R-(2α,4aα,7α,8aR)]- and [4H-4a,7-Methanooxazirino[3,2-i][2,1]benzisothiazole, 8,8-dichlorotetrahydro-9,9-dimethyl-, 3,3-dioxide, [2R-(2α,4aα,7α,8aR)]]



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1. Procedure

Caution! Reactions and subsequent operations involving peracids and peroxy compounds should be run behind a safety shield. Peroxy compounds should be added to the organic material, never the reverse. For relatively fast reactions, the rate of addition of the peroxy compound should be slow

enough so that it reacts rapidly and no significant unreacted excess is allowed to build up. The reaction mixture should be stirred efficiently while the peroxy compound is being added, and cooling should generally be provided since many reactions of peroxy compounds are exothermic. New or unfamiliar reactions, particularly those run at elevated temperatures, should be run first on a small scale. Reaction products should never be recovered from the final reaction mixture by distillation until all residual active oxygen compounds (including unreacted peroxy compounds) have been destroyed. Decomposition of active oxygen compounds may be accomplished by the procedure described in Korach, M.; Nielsen, D. R.; Rideout, W. H. Org. Synth. 1962, 42, 50 (Org. Synth. 1973, Coll. Vol. 5, 414). [Note added January 2011].

A. *(−)-(3-Oxocamphorylsulfonyl)imine*. A 2-L, single-necked, round-bottomed flask, equipped with a condenser and magnetic stirring bar, is charged with 42.6 g (0.2 mol) of (−)-(camphorylsulfonyl)imine (Note 1), 30.0 g (0.27 mol) of selenium dioxide (Note 2), and 500 mL of reagent grade acetic acid (Note 3). The mixture is stirred at reflux for 14 hr (Note 4), and the black selenium metal that separates is removed by suction filtration of the hot reaction mixture using a 250-mL porcelain filter funnel. The funnel, flask and residue are washed with 50 mL of acetic acid. Removal of solvent using a rotary evaporator gives 43.0–47.0 g of crude (−)-(3-oxocamphorylsulfonyl)imine as a dark orange solid that is dried under reduced pressure overnight in a desiccator (Note 5) and (Note 6). This product is suitable for further reaction without purification.

B. *(+)-[(7,7-Dimethoxycamphoryl)sulfonyl]imine*. A 500-mL, single-necked, round-bottomed flask, equipped with a condenser, magnetic stirring bar, and nitrogen inlet, is charged with 22.8 g (0.1 mol) of the crude (−)-(3-oxocamphorylsulfonyl)imine prepared above, 125 mL of trimethyl orthoformate, 68 mL of methanol, and 5 mL of concd sulfuric acid. The mixture is heated to 85–90°C in an oil bath (Note 7) and (Note 8). After heating for 4 hr, during which time precipitation of the product is observed, the reaction mixture is cooled to room temperature, and an additional 30 mL of trimethyl orthoformate and 10 mL of methanol are added. Heating is continued for an additional hour, after which the reaction mixture is cooled to room temperature and transferred with the aid of 250 mL of methylene chloride to a 500-mL separatory funnel. The solution is washed successively with water (100 mL), aqueous 20% sodium bicarbonate solution (100 mL), water (4 × 100 mL), and brine (100 mL), and dried over anhydrous magnesium sulfate. Filtration and removal of the solvent under reduced pressure affords 22.8–23.0 g (83–85%) of the crude (+)-(7,7-dimethoxy camphorylsulfonyl)imine as a light pink solid, mp 179–184°C ((Note 9) and (Note 10)). This product is suitable for further reaction without purification.

C. *(+)-[(7,7-Dichlorocamphoryl)sulfonyl]imine*. A 1-L, three-necked, round-bottomed flask, equipped with a mechanical stirrer or magnetic stirring bar, thermometer, and 250-mL pressure-equalizing addition funnel with a nitrogen inlet, is placed under a nitrogen atmosphere and charged with a solution of 50 g (0.235 mol) of (−)-(camphorsulfonyl)imine (Note 1) in 250 mL of ethyl acetate. To this solution is added 71 g (0.47 mol) of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (Note 11) over 30 min, and the reaction mixture is stirred for 30 min at room temperature. To the resulting mixture is then added 51.5 g (0.26 mol) of 1,3-dichloro-5,5-dimethylhydantoin (Note 12) in portions over 90 min while maintaining the reaction temperature at 20–25°C by cooling with an ice-water bath. When the reaction is complete, typically 30–60 min as determined by HPLC or TLC (Note 13) and (Note 14), 400 mL of water is slowly added while keeping the temperature at 20–25°C. The pH of the reaction mixture is adjusted to 7–7.5 by the addition of ~25 mL of concd hydrochloric acid, and the ethyl acetate solvent is removed on the rotary evaporator at a maximum bath temperature of 60°C (Note 15). The resulting suspension is stirred for 1 hr at room temperature, then the solids are collected by suction filtration, washed with 500 mL of water, and dried in a draft oven at 50°C to a constant weight affording 62.0–63.0 g (94–95%) of white solid (+)-(7,7-dichlorocamphorylsulfonyl)imine (mp 170–175°C) (Note 16) and (Note 17). This product is suitable for further reaction without purification.

D. *(+)-(2R,8aR)-[(8,8-Dimethoxycamphoryl)sulfonyl]oxaziridine* (**1**). In a 500-mL, three-necked, Morton flask, equipped with a mechanical stirrer with a Teflon stirring blade and stirrer bearing, a thermometer, and a 250-mL pressure-equalizing addition funnel, is charged with 20.9 g (0.077 mol) of crude (+)-(7,7-dimethoxy camphorylsulfonyl)imine, 175 mL of methylene chloride, and 1.6 g of Aliquat 336 (Note 18). The reaction mixture is cooled in an ice bath to 0°C, efficient stirring is initiated, and a solution of 63 g (0.38 mol) of potassium carbonate in 120 mL of water is added at 0–10°C followed by

27.2 g (0.114 mol) of 32% peracetic acid (Note 19) dropwise such that the temperature is maintained at 3–5°C. After the addition is completed, the reaction mixture is allowed to warm to room temperature and stirred until reaction is complete (typically 40 hr) as determined by ^{1}H NMR (Note 4) and (Note 20). On completion, 0.6 g of sodium sulfite is added, the reaction mixture is stirred for 30 min, and 5 mL of aqueous 30% sodium hydroxide is introduced. The reaction mixture is transferred to a 500-mL separatory funnel with the aid of 50 mL of methylene chloride, the phases are separated, and the aqueous phase is extracted twice with 50 mL of methylene chloride. The combined organic extracts are washed successively with a saturated solution of sodium bicarbonate (50 mL) and water (2 × 50 mL), and then dried over anhydrous magnesium sulfate. The solvents are removed under reduced pressure while maintaining the temperature below 40°C which affords an off-white solid that is suspended in 100 mL hexane and collected by suction. The solids are washed on the filter with two additional 100-mL portions of hexane to give 15.1 g of (+)-(2R,8aR)-[(8,8-dimethoxycamphoryl)sulfonyl]oxaziridine (**1**) having mp 184–186°C (dec.) and $[\alpha]_D^{25}$ +91.6° ($CHCl_3$, c 3.39) (Note 21). A second crop is obtained by evaporating the filtrate to dryness and repeating the process which affords a total of 19.2–19.8 g (86–90%) of the oxaziridine (mp 184–186°C (dec.)). The product may be used as obtained for oxidations, but may be further purified, if desired, by recrystallization from 1400 mL of 95% ethanol.

This oxaziridine can also be prepared in ~4 hr by oxidation of the corresponding imine using 3-chloroperbenzoic acid (Note 22).

The antipode, (–)-(2S,8aR)-[(8,8-dimethoxycamphoryl)sulfonyl]oxaziridine, (mp 189°C (dec.); $[\alpha]_D^{20}$ –91.3° ($CHCl_3$, c 0.5)) was prepared in a similar manner starting from (+)-(camphorylsulfonyl)imine.

E. *(+)-(2R,8aR)-[(8,8-Dichlorocamphoryl)sulfonyl]oxaziridine* (**2**). A 1-L, three-necked, Morton flask, equipped with a mechanical stirrer with a Teflon stirring blade and stirrer bearing or a magnetic stirring bar, a thermometer, and a 250-mL pressure-equalizing addition funnel is charged with a solution of 48 g (0.17 mol) of (+)-[(7,7-dichlorocamphoryl)sulfonyl]imine in 300 mL of methylene chloride and 3.5 g of Aliquat 336 (Note 18). After cooling the resulting mixture to 0°C with an ice-bath, a solution of 119 g (0.86 mol) of potassium carbonate in 250 mL of water is added to the rapidly stirring reaction mixture while maintaining the temperature between 0–10°C. Then 45 g (0.188 mol) of 32% peracetic acid (Note 19) is added dropwise at such a rate (~30 min) that the temperature is maintained between 0–5°C. When the oxidation is complete, as determined by TLC (normally after stirring overnight) (Note 23), 1.3 g (0.099 mmol) of sodium sulfite is added between 0–10°C. After stirring for 30 min, 8 mL of 30% aqueous sodium hydroxide solution is added and the reaction mixture is warmed to room temperature. The organic phase is separated, the aqueous phase is extracted with methylene chloride (2 × 25 mL), and the combined organic phases are washed with saturated sodium bicarbonate solution (25 mL) and water (2 × 25 mL) (Note 24), and dried over anhydrous sodium sulfate. Approximately 210 mL of methylene chloride is evaporated from the organic phase under reduced pressure while maintaining the bath temperature below 40°C. During removal of the solvent crystallization occurs. The resulting slurry is diluted with 125 mL of hexane, cooled in an ice bath (0–5°C), and stirred for 1 hr. The product is collected by suction filtration, washed with hexane (100 mL), and dried at a maximum of 40°C in an air draft oven to yield 45.5–48.0 g (90–95%) of (+)-(2R,8aR)-[(8,8-dichlorocamphoryl)sulfonyl] oxaziridine (**2**) (mp 182–186°C; $[\alpha]_D^{20}$ +91.4° ($CHCl_3$, c 0.5)) ((Note 25) and (Note 26)).

The antipode (–)-(2S,8aR)-[(8,8-dichlorocamphoryl)sulfonyl]oxaziridine (mp 182–186°C; $[\alpha]_D^{20}$ –92.3° ($CHCl_3$, c 0.5)) was prepared in a similar manner starting from (+)-(camphorylsulfonyl)imine.

2. Notes

1. (–)-(Camphorylsulfonyl)imine may be purchased from Aldrich Chemical Company, Inc., or prepared according to reference [5].
2. Selenium dioxide was purchased from Aldrich Chemical Company, Inc.
3. Reagent grade acetic acid was purchased from Aldrich Chemical Company, Inc.
4. The progress of the reaction was monitored using ^{1}H NMR by observing the disappearance of the two

methyl absorptions of (–)-(camphorylsulfonyl)imine at δ 0.88, and 1.09 in a sample obtained from a 0.5-mL aliquot which is concentrated to dryness on a rotary evaporator.

5. The crude product is of sufficient purity for the next step even if trace amounts of acetic acid and selenium dioxide are present. The material can be purified by crystallization from chloroform to provide product with mp 189–190°C (Lit.[6] mp 190–191°C) and $[\alpha]_D^{20}$ –178.5° (acetone, *c* 2.2).

6. The spectral properties of (–)-[(3-oxocamphoryl)sulfonyl]imine are as follows: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.95 (s, 3 H), 1.13 (s, 3 H), 1.76–1.87 (m, 1 H), 1.92–2.02 (m, 1 H), 2.16–2.36 (m, 2 H), 2.74 (d, 1 H, J = 4.8), 3.20 (d, 1 H, J = 13.5), 3.42 (d, 1 H, J = 13.5); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.41, 20.19, 22.28, 28.00, 44.65, 50.07, 59.04, 62.74, 181.38, 197.71; IR (KBr) cm^{-1}: 2950, 1761, 1654, 1340, 1166, 741.

7. Within 30 min of heating to 85–90°C, vigorous evolution of gas ensues.

8. The reaction was monitored using ^{1}H NMR by observing the disappearance of the two methyl absorptions at δ 0.95 and 1.13 of (–)-(3-oxocamphorylsulfonyl)imine.

9. This material can be purified by crystallization from absolute ethanol to give product with mp 186–7°C and $[\alpha]_D^{20}$ +7.2° ($CHCl_3$, *c* 3.6).

10. The spectral properties of (+)-[(7,7-dimethoxycamphoryl)sulfonyl]imine are as follows: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.94 (s, 3 H), 1.04 (s, 3 H), 1.73–2.02 (m, 4 H), 2.29 (d, 1 H, J = 1.4), 2.93 (d, 1 H, J = 13.3), 3.12 (d, 1 H, J = 13.3), 3.30 (s, 3 H), 3.39 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.4, 20.5, 20.6, 29.2, 46.0, 48.8, 50.3, 50.5, 52.0, 64.2, 103.0, 188.8; IR (KBr) cm^{-1}: 1620, 1340, 1160.

11. DBU was purchased from Fluka Chemie AG, Air Products, or Aldrich Chemical Company, Inc.

12. 1,3-Dichloro-5,5-dimethylhydantoin (DCDMH) was purchased from Aldrich Chemical Company and used without additional purification.

13. HPLC conditions were as follows: C_{18}-Novapak (Waters), 5μ; UV detector at 210 nm; mobile phase: acetonitrile/water (55/45) at a flow rate of 1 mL/min. Alternately, this reaction can be monitored by TLC: R_f = 0.42 using CH2Cl2 and 10% molybdophosphoric acid in ethanol as the developer.

14. During the reaction, the suspended solids dissolve giving a clear solution.

15. In the event that foaming takes place a few drops of 2-octanol are added.

16. This solid can be purified by crystallization from 2-propanol to give product with mp 177–179°C, and $[\alpha]_D^{20}$ +7.9° ($CHCl_3$, *c* 2.1), $[\alpha]_D^{20}$ +97.8° (CH_3CN, *c* 1).

17. The spectral properties of (+)-[(7,7-dichlorocamphoryl)sulfonyl]imine are as follows: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.12 (s, 3 H), 1.17 (s, 3 H), 1.75–1.93 (m, 1 H), 1.96–2.20 (m, 2 H), 2.23–2.38 (m, 1 H), 2.75 (d, 1 H, J = 3.5), 3.24 (d, 1 H, J = 13.5), 3.42 (d, 1 H, J = 13.5); ^{13}C NMR (75 MHz, CDCl3) δ: 21.8, 25.1, 27.4, 47.8, 50.8, 61.2, 64.1, 81.9, 189.2.

18. Aliquat 336 (tricaprylylmethylammonium chloride) was purchased from Aldrich Chemical Company, Inc.

19. Peracetic acid, 32% in acetic acid, was purchased from Aldrich Chemical Company, Inc.

20. The reaction was monitored using ^{1}H NMR by observing the disappearance of the two methyl absorptions at δ 0.94 and 1.04 of (–)-(7,7-dimethoxycamphoryl sulfonyl)imine.

21. The spectral properties of (+)-(2R,8aR)-[(8,8-dimethoxycamphoryl)sulfonyl]oxaziridine are as follows: ^{1}H NMR (300 MHz, $CDCl_3$) δ:1.02 (s, 3H), 1.28 (s, 3H), 1.70–1.95 (m, 4 H), 2.24 (d, 1 H, J = 4.0), 3.03 (d, 1 H, J = 14), 3.23 (s, 3 H), 3.24 (d, 1 H, J = 14), 3.30 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.5, 21.6, 28.1, 45.1, 47.4, 50.5, 50.8, 52.9, 54.6, 97.6, 102.8; IR (KBr) cm^{-1}: 1356, 1165.

22. Biphasic basic oxidation using technical grade (50–60%) 3-chloroperbenzoic acid affords this oxaziridine in ~4 hr: In a 2-L, three-necked, Morton-flask equipped with a mechanical stirrer was placed 22.6 g (0.083 mol) of crude (+)-[(7,7-dimethoxycamphoryl)sulfonyl]imine, 42.6 g (0.13 mol) of 3-chloroperoxybenzoic acid (50–60%) in 450 mL of methylene chloride, and 450 mL of saturated potassium carbonate solution. The reaction mixture was stirred vigorously until the oxidation was complete as indicated by TLC (Note 27) at which time 500 mL of water was added, the organic layer was separated and the aqueous layer was extracted with methylene chloride (2 × 500 mL). The combined

organic extracts were washed with saturated sodium sulfite (300 mL) and water (300 mL), and dried over anhydrous magnesium sulfate.
23. The reaction was monitored by TLC using silica gel plates (Kieselgel-60F, 254 nm, Merck), developing with CH_2Cl_2; for visualization spray with 5% molybdophosphoric acid in ethanol and heat.
24. The aqueous phases are monitored with Merckoquant 10011 test strips for their peroxide content prior to their disposal. The residual peroxide is neutralized (<1 ppm, the detection limit of the paper) by the addition of saturated sodium sulfite solution.
25. The spectral properties of (+)-(2R,8aR)-[(8,8-dichlorocamphoryl)sulfonyl]oxaziridine are as follows: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.16 (s, 3 H), 1.48 (s, 3 H), 1.86–2.18 (m, 3 H), 2.30–2.40 (m, 1 H), 2.73 (d, 1 H, J = 3.9), 3.23 (d, 1 H, J = 14), 3.45 (d, 1 H, J = 14); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.9, 23.31, 25.3, 26.8, 47.3, 49.4, 54.6, 62.5, 86.1, 99.1.
26. The product can be recrystallized from ethanol/ethyl acetate (1.5:1).
27. A 1-mL aliquot was removed from the organic layer, diluted with 2 mL of methylene chloride, and analyzed by TLC eluting with methylene chloride (I_2 visualization); imine R_f = 0.34, oxaziridine R_f = 0.51.

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

In the Radex study, samples of oxaziridine **2** were heated in open glass tubes at 60°C/hr from ambient temperature to 260°C under atmospheric conditions. It was found that there is a strong exotherm with an onset at 165°–190°C (neat), at 135–158°C upon addition of stainless steel, and at 73°–84°C upon addition of $FeCl_3 \cdot H_2O$. Furthermore, the onset temperature in the $FeCl_3 \cdot H_2O$ study was found to be dependent on the concentration of ferric ion. In each case as the exotherm occurred, each sample frothed violently out of the sample tube as a gas was produced.

3. Discussion

(–)-[(3-Oxocamphoryl)sulfonyl]imine has been prepared independently by Glahsl and Herrmann in 70% yield in a similar manner using dioxane as solvent, but the reaction required two weeks for completion.[7] The submitters observed that using acetic acid as the solvent dramatically reduces the time to ~14 hr and improves the yield to 90%.[6] (+)-[(7,7-Dimethoxycamphoryl)sulfonyl]imine has been prepared in a similar manner in 70% yield.[8] This procedure affords this material in 83–88% yield.[6] Chlorination of the aza enolate of (+)-(camphorylsulfonyl)imine, prepared by treatment with sodium bis(trimethylsilyl)amide, with N-chlorosuccinimide affords (+)-[(7,7-dichlorocamphoryl)sulfonyl]imine in 74% yield.[9] The procedure described here uses inexpensive DBU and 1,3-dichloro-5,5-dimethylhydantoin to give this imine in 95% yield and is applicable to large scale preparations.[10]

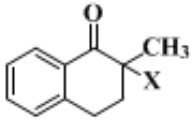
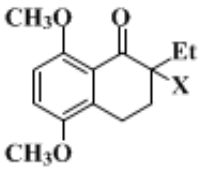
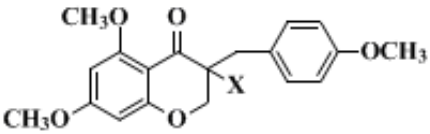
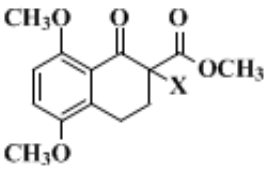
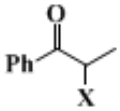
Oxidation of (+)-[(7,7-dimethoxycamphoryl)sulfonyl]imine (96%)[6] and (+)-[(7,7-dichlorocamphoryl)sulfonyl]imine (98%)[10] with 3-chloroperbenzoic acid has been reported. The procedure described here uses less hazardous and less expensive peracetic acid with the aid of Aliquat 336.[10] However, this system requires 40 hr vs. 4 hr using 3-chloroperbenzoic acid for oxidation of (+)-[(7,7-dimethoxycamphoryl)sulfonyl]imine to the oxaziridine.

N-Sulfonyloxaziridines are an important class of selective, neutral, and aprotic oxidizing reagents.[11,12] Enantiopure N-sulfonyloxaziridines have been used in the asymmetric hydroxylation of enolates to enantiomerically enriched α-hydroxy carbonyl compounds,[9,11,12,13,14] the asymmetric oxidation of sulfides to sulfoxides,[15,16] selenides to selenoxides,[17] sulfenimines to sulfinimines,[18] and the epoxidation of alkenes.[19]

(+)-(2R,8aR)-[(8,8-Dimethoxycamphoryl)sulfonyl]oxaziridine (**1**) and (+)-(2R,8aR)-[(8,8-dichlorocamphoryl)sulfonyl]oxaziridine (**2**) are most effective for the hydroxylation of 2-substituted 1-tetralone enolates to 2-substituted 2-hydroxy-1-tetralones. The former oxaziridine, **1**, gives higher ee's (>90%) with tetralones having an 8-methoxy group, while the dichloro reagent **2** is more effective with those enolates lacking this substituent. For example (+)-**1** has been employed in highly enantioselective syntheses of (+)- and (–)-5,7-O-dimethyleucomol (>96% ee),[20] the AB-ring segments for γ-rhodomycinone and α-citromycinone (94% ee),[6] and (R)-(–)-2-acetyl-5,8-dimethoxy-1,2,3,4-tetrahydro-2-naphthol (>95% ee), a key intermediate in the synthesis of anthracyclinones.[21] The asymmetric synthesis of the AB ring of aklavinone (>95% ee)[22] and the homoisoflavanoids (+)-O-trimethylsappanone (94% ee) and (+)-O-trimethylbrazilin (92% ee) used oxaziridine (+)-**2**. Some representative examples using these reagents are given in the Table.

TABLE

ASYMMETRIC HYDROXYLATION OF TETRALONE AND PROPIOPHENONE ENOLATES USING (CAMPHORYLSULFONYL)OXAZIRIDINES **1** AND **2**

Oxaziridine	Ketone (X=H)	Base	Temp. (°C)	α-Hydroxy Tetralone (X=OH) %Yield[a]	%ee (Config.)	Ref.
(+)–**1**		NHMDS[a]	–78	66	36(R)	6,9,22
(+)–**2**		NHMDS	–78	66	>95(R)	6,9,22
(+)–**1**		NHMDS	–78	58	60(R)	6,22
		LDA[b]	0	66	94(R)	
(+)–**2**		LDA	–78	55	73(R)	
(+)–**1**		NHMDS	–78	75	77(R)	20
		LDA	–78	72	≥96(R)	
(+)–**2**		NHMDS	–78	66	88(R)	
(+)–**1**		NHMDS	0	73	56(S)	21
		LDA	0		No Reaction	
		KHMDS[c]	–78	70	≥95(S)	
(+)–**2**		NHMDS	0	63	47(S)	
(+)–**1**		NHMDS	–78	73	79(S)	6,9,22
(+)–**2**		NHMDS	–78	70	95(S)	9

[a]Isolated yields. [b]NHMDS = Sodium bis(trimethylsilyl)amide. [b]LDA = Lithium diisopropylamide. [c]KHMDS = Potassium bis(trimethylsilyl)amide.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 10, 378

References and Notes

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5. Towson, J. C.; Weismiller, M. C.; Lal, G. S.; Sheppard, A. C.; Davis, F. A. *Org. Synth., Coll. Vol. VIII* **1993**, 104.
6. Davis, F. A.; Kumar, A.; Chen, B.-C. *J. Org. Chem.* **1991**, *56*, 1143.
7. Glahsl, G.; Herrmann, R. *J. Chem. Soc., Perkin Trans. I* **1988**, 1753.
8. Verfürth, U.; Herrmann, R. *J. Chem. Soc., Perkin Trans. I* **1990**, 2919.
9. Davis, F. A.; Weismiller, M. C.; Murphy, C. K.; Thimma Reddy, R.; Chen. B.-C. J. *Org. Chem.* **1992**, *57*, 7274.
10. Mergelsberg. I.; Gala, D.; Scherer, D.; DiBenedetto, D.; Tanner, M. *Tetrahedron Lett.*, **1992**, *33*, 161.
11. For reviews on the chemistry of N-sulfonyloxaziridines, see: a) Davis, F. A.; Sheppard, A. C. *Tetrahedron* **1989**, *45*, 5703;
12. Davis, F. A.; Chen, B.-C. *Chem. Rev.*, **1992**, *92*, 919.
13. Davis, F. A.; Sheppard, A. C.; Chen, B.-C.; Haque, M. S. *J. Am. Chem. Soc.* **1990**, *112*, 6679.
14. Davis, F. A.; Weismiller, M. C. *J. Org. Chem.* **1990**, *55*, 3715.
15. Davis, F. A.; Thimma Reddy, R.; Weismiller, M. C. *J. Am. Chem. Soc.* **1989**, *111*, 5964.
16. Davis, F. A.; Thimma Reddy, R.; Han, W. Carroll, P. J. *J. Am. Chem. Soc.* **1992**, 114, 1428.
17. Davis, F. A.; Thimma Reddy, R. *J. Org. Chem.* **1992**, *57*, 2599.
18. Davis, F. A.; Thimma Reddy, R.; Reddy, R. E. *J. Org. Chem.* **1992**, *57*, 6387.
19. Davis, F. A.; Thimma Reddy, R.; McCauley, Jr., J. P; Przeslawski, R. M.; Harakal, M. E.; Carroll, P. J. *J. Org. Chem.* **1991**, *56*, 809.
20. Davis, F. A.; Chen, B.-C. *Tetrahedron Lett.* **1990**, *31*, 6823.
21. Davis, F. A.; Clark, C.; Kumar, A.; Chen, B.-C. *J. Org. Chem.* **1994**, *59*, 1184.
22. Davis, F. A.; Kumar, A. *Tetrahedron Lett.* **1991**, *3*

Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

(–)-(Camphorsulfonyl)imine

(+)-[(7,7-Dimethoxycamphoryl)sulfonyl]imine

(+)-[(7,7-Dichlorocamphoryl)sulfonyl]imine

(-)-[(3-Oxocamphoryl)sulfonyl]imine

[4H-4a,7-Methanooxazirino[3,2-i][2,1]benzisothiazole, tetrahydro-8,8-dimethoxy-9,9-dimethyl-, 3,3-dioxide], [2R-(2α,4aα,7α,8aR)]-

[4H-4a,7-Methanooxazirino[3,2-i][2,1]benzisothiazole, 8,8-dichlorotetrahydro-9,9-dimethyl-, 3,3-dioxide, [2R-(2α,4aα,7α,8aR)]

(–)-(3-Oxocamphorylsulfonyl)imine

(−)-(camphorylsulfonyl)imine

(+)-(7,7-dimethoxy camphorylsulfonyl)imine

(+)-(7,7-dichlorocamphorylsulfonyl)imine

(−)-(2S,8aR)-[(8,8-dimethoxycamphoryl)sulfonyl]oxaziridine

(+)-(camphorylsulfonyl)imine

(−)-(2S,8aR)-[(8,8-dichlorocamphoryl)sulfonyl]oxaziridine

(−)-(7,7-dimethoxycamphoryl sulfonyl)imine

$FeCl_3 \cdot H_2O$

(−)-5,7-O-dimethyleucomol

(R)-(−)-2-acetyl-5,8-dimethoxy-1,2,3,4-tetrahydro-2-naphthol

(+)-O-trimethylsappanone

(+)-O-trimethylbrazilin

ethanol (64-17-5)

potassium carbonate (584-08-7)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ethyl acetate (141-78-6)

methanol (67-56-1)

acetonitrile (75-05-8)

sodium sulfite (7757-83-7)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

sodium bicarbonate (144-55-8)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

selenium dioxide (7446-08-4)

2-propanol (67-63-0)

methyl (2229-07-4)

N-chlorosuccinimide (128-09-6)

methylene chloride (75-09-2)

2-Octanol (123-96-6)

Propiophenone (93-55-0)

magnesium sulfate (7487-88-9)

dioxane (123-91-1)

selenium tetralone (529-34-0)

peracetic acid (79-21-0)

hexane (110-54-3)

1,3-dichloro-5,5-dimethylhydantoin (118-52-5)

Molybdophosphoric acid (51429-74-4)

lithium diisopropylamide (4111-54-0)

tricaprylylmethylammonium chloride (5137-55-3)

trimethyl orthoformate (149-73-5)

1,8-diazabicyclo[5.4.0]undec-7-ene,
DBU (6674-22-2)

(+)-(2R,8aR)-[(8,8-DIMETHOXYCAMPHORYL)SULFONYL]OXAZIRIDINE (131863-82-6)

(+)-(2R,8aR)-[(8,8-DICHLOROCAMPHORYL)SULFONYL]OXAZIRIDINE,
(+)-(2R,8aR)-[(8,8-dichlorocamphoryl)sulfonyl] oxaziridine (127184-05-8)

3-chloroperoxybenzoic acid, 3-chloroperbenzoic

acid (937-14-4)

Sodium bis(trimethylsilyl)amide (1070-89-9)

Potassium bis(trimethylsilyl)amide (40949-94-8)