Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

# Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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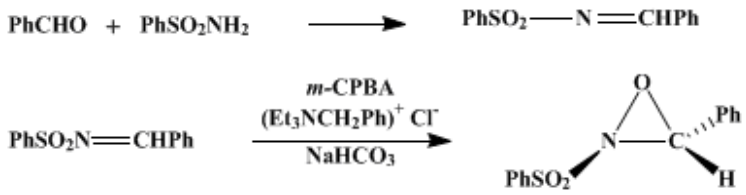
# (±)-*trans*-2-(PHENYLSULFONYL)-3-PHENYLOXAZIRIDINE

## [Oxaziridine, 3-phenyl-2-(phenylsulfonyl)-]

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Checked by James Pribish and Edwin Vedejs.

## 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. *N-Benzylidenebenzenesulfonamide*. A 3-L, one-necked, round-bottomed flask is equipped with a mechanical stirrer (Note 1), Dean–Stark water separator (Note 2), a double-walled condenser attached to an argon gas inlet, and outlet needle connectors through a mineral oil bubbler. Into the flask are placed 150 g of Linde 5A powdered molecular sieves (Note 3), 2.0 g of Amberlyst 15 ion-exchange resin (Note 4), 157 g of benzenesulfonamide (Note 5), 1650 mL of dry toluene, and 107.5 g (1.014 mol) of freshly distilled benzaldehyde (Note 5). The reaction mixture is stirred and heated at reflux under an argon atmosphere. Water that separates during the reaction is periodically removed and refluxing is continued until water separation ceases (ca. 16 hr). The reaction mixture is cooled to room temperature without stirring and the insoluble materials are filtered through a 500-mL-capacity sintered-glass funnel of medium porosity. The residue in the filter funnel is washed thoroughly with another 700 mL of toluene in three portions. The collected filtrate is concentrated with a rotary evaporator to give a thick, yellow, oily residue that usually solidifies on standing. The residue is triturated with 800 mL of distilled pentane and the solid is broken into a powder with the aid of a flat-ended glass rod. The solid is separated by filtration through a 500-mL sintered-glass funnel of medium porosity, washed with distilled pentane (2 × 100 mL), and air-dried. The yield is 212 g (87%); mp 76–80°C (Note 6).

Although of sufficient purity for the next step, the sulfonimine can be further purified by recrystallization. In a 2-L Erlenmeyer flask containing 150 mL of ethyl acetate is dissolved, with warming, 212 g of the crude sulfonimine. After the mixture is cooled to room temperature, about 400 mL of pentane is added and the solution is allowed to stand at room temperature for 2–3 hr. The colorless crystalline product is collected by filtration, washed with 100 mL of pentane, and air-dried to give 191.5 g (78%), mp 78–80°C. The washings and filtrate are combined and the volume reduced by about one-third using a rotary evaporator. A second crop of crystals, 20.2 g (8%), mp 75–79°C, was obtained on standing for several hours.

B. *(±)-trans-2-(Phenylsulfonyl)-3-phenyloxaziridine*. (See (Note 7).) A 5-L, three-necked flask is equipped with a mechanical stirrer and a 500-mL pressure-equalizing addition funnel. Into the flask are placed 500 mL of saturated aqueous sodium bicarbonate solution, 12.5 g (0.055 mol) of benzyltriethylammonium chloride (BTEAC), and 122.5 g (0.50 mol) of *N-*

benzylidenebenzenesulfonamide dissolved in 380 mL of chloroform (Note 8). The reaction mixture is stirred vigorously at 0–5°C in an ice bath while a solution of 111.6 g (0.55 mol) of 85% *m*-chloroperoxybenzoic acid (MCPBA) dissolved in 1000 mL of chloroform is added dropwise. After the addition of the peracid, which takes about 1 hr, the reaction mixture is stirred for an additional hour at this temperature. A 3-L separatory funnel is used to separate the chloroform solution and wash it successively with 600 mL of cold water, 600 mL of aqueous 10% sodium sulfite, water (2 × 600 mL) and 250 mL of a saturated sodium chloride solution (Note 9). After the chloroform solution is dried over anhydrous potassium carbonate for 2 hr (Note 10), it is filtered and solvent is removed with a rotary evaporator, keeping the water-bath temperature below 40°C. The resulting white solid residue is washed with a small portion of pentane, dissolved in a minimum of ethyl acetate (about 700–800 mL) without heating, and filtered through fluted filter paper; 400 mL of pentane is added to the filtrate. After the white crystalline oxaziridine is cooled in the refrigerator overnight, it is separated by filtration, transferred to a 500-mL Erlenmeyer flask, washed with 200 mL of pentane, filtered, and air-dried for 1 hr. The yield is 83.5 g; mp 92–94°C. The mother liquor is reduced to about 300 mL and cooled in the refrigerator to give 36.6 g of a light-yellow solid; mp 87–90°C. This second crop is placed in a 250-mL Erlenmeyer flask and triturated with 50 mL of anhydrous ether followed by the addition of 60 mL of pentane. The oxaziridine is isolated by filtration to give 31.1 g; mp 94–95°C (dec) (Note 11) and (Note 12). The combined yield is 114.6 g (88%).

The 2-sulfonyloxaziridine can be stored in a brown bottle in the refrigerator. Storage at room temperature is potentially hazardous (Note 13).

## 2. Notes

1. A Teflon-coated, heavy duty, oval-shaped spin bar was used by the submitters for efficient stirring.
2. A Dean–Stark water separator equipped with a Teflon stopcock for water removal was used.
3. Linde powdered 5-Å molecular sieves were used as obtained from the supplier.
4. Amberlyst 15 ion-exchange resin is a strongly acidic, macroreticular resin purchased from Aldrich Chemical Company, Inc. The reaction fails in the absence of the acid catalysts.
5. Benzenesulfonamide, *m*-chloroperoxybenzoic acid, and benzaldehyde were obtained from the Aldrich Chemical Company, Inc. and, with the exception of the latter, used without additional purification.
6. The $^1$H NMR spectrum of *N*-benzylidenebenzenesulfonamide is as follows: ($CDCl_3$) δ: 7.6 (m, 6 H), 8.0 (m, 4 H), 9.05 (s, 1 H).
7. A more convenient oxidation method has since been developed.[2]
8. Analytical reagent-grade chloroform, Fisher Scientific Company, was used as obtained.
9. It is necessary to wash with a 10% $NaHCO_3$ solution, before the sodium chloride wash, if a large excess of *m*-chloroperoxybenzoic acid is used.
10. If the solution is dried for long times over potassium carbonate, decomposition of the oxaziridine sometimes occurs.
11. The $^1$H NMR spectrum of *trans*-2-(phenylsulfonyl)-3-phenyloxaziridine is as follows: ($CDCl_3$) δ: 5.5 (s, 1 H), 7.4 (s, 5 H), 7.6–7.8 (m, 3 H), 8.05 (br d, 2 H, $J$ = 7.1).
12. Careful recrystallization from ethyl acetate (saturated solution at 25°C; cool to –20°C) gave colorless crystals, ca. 20% recovery, mp 95–95.5°C.
13. Exothermic decomposition of a 500-g quantity after 2 weeks of storage at room temperature is reported by Dr. G. C. Crockett of Aldrich Chemical Company, Inc. Sufficient force was generated to shatter the container and char the oxaziridine.

## 3. Discussion

This procedure is representative of a general procedure for the synthesis of *trans*-2-sulfonyloxaziridines previously reported on a small scale (Table I).[3] *trans*-2-(Phenylsulfonyl)-3-(*p*-nitrophenyl)oxaziridine was prepared on a 0.16-molar scale in greater than 85% yield. The Baeyer–Villiger-type oxidation of the sulfonimine affords only the *trans*-oxaziridine. The synthesis of the sulfonimine ($PhSO_2N{=}CHPh$) directly from the sulfonamide and aromatic aldehyde is described here. This modification avoids use of the intermediate diethyl acetal used in earlier preparations of these compounds.[3]; [4]

2-Sulfonyloxaziridines are useful aprotic and neutral oxidizing reagents that, in general, afford greater selectivity for oxidations than do peracids. 2-Sulfonyloxaziridines have been employed in the oxidation of sulfides to sulfoxides,[5] disulfides to thiosulfinates,[5] selenides to selenoxides,[6] thiols to sulfenic acids

(RSOH),[7] organometallic reagents to alcohols and phenols,[8] ketone and ester enolates to α-hydroxy carbonyl compounds,[9] in the epoxidation of alkenes,[10] and in the conversion of chiral amide enolates to optically active α-hydroxy carboxylic acids (93–99% ee).[11,12] These reagents can be used in the study of reactive oxidation intermediates and for mechanistic studies of oxygen-transfer reactions because of the ease with which the course of the oxidation can be monitored by proton NMR.

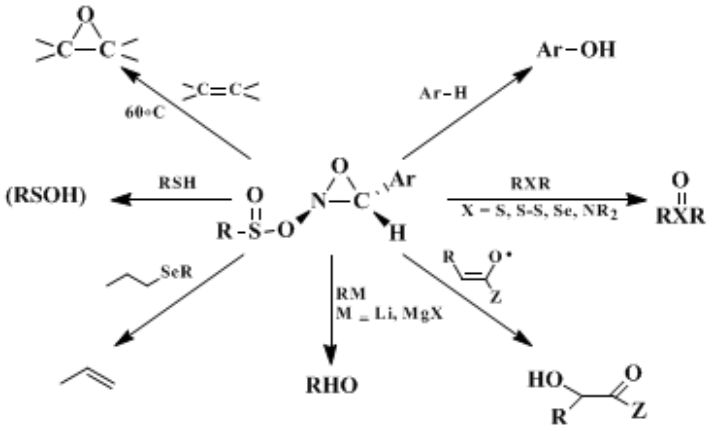
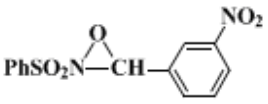
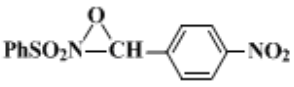
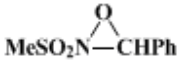
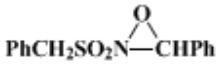



TABLE I
PREPARATION OF 2-SULFONYLOXAZIRIDINES[3a,b]

| RSO$_2$N—CHAr | Yield (%) | mp (°C, dec) |
|---|---|---|
|  | 83 | 113–115 |
| R = Ph, Ar = 3-NO$_2$Ph | | |
|  | 80 | 134–136 |
| R = Ph, Ar = 4-NO$_2$Ph | | |
|  | 85 | 59–61 |
| R = Me, Ar = Ph | | |
|  | 90 | 118–119 |
| R = PhCH$_2$, Ar = Ph | | |

Oxidation of chiral sulfonimines (R*SO$_2$N=CHAr)[13] and chiral sulfamylimines (R*RNSO$_2$N=CHAr)[14] affords optically active 2-sulfonyloxaziridines and 2-sulfamyloxaziridines, respectively. These chiral, oxidizing reagents have been used in the asymmetric oxidation of sulfides to sulfoxides (15–68% ee),[13,14,15] selenides to selenoxides (8–9% ee),[16] enolates to α-hydroxycarbonyl

compounds (8–37% ee),[17] and in the asymmetric epoxidation of alkenes (15–40% ee).[18] The synthetic applications of these reagents has been reviewed.[19]

## References and Notes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## Appendix
## Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

m-chloroperoxybenzoic acid (MCPBA)

Linde 5A

sulfonimine

benzyltriethylammonium chloride (BTEAC)

2-sulfonyloxaziridine

trans-2-sulfonyloxaziridines

diethyl acetal

2-Sulfonyloxaziridines

2-sulfamyloxaziridines

potassium carbonate (584-08-7)

ethyl acetate (141-78-6)

ether (60-29-7)

sodium sulfite (7757-83-7)

chloroform (67-66-3)

sodium bicarbonate (144-55-8)

sodium chloride (7647-14-5)

benzaldehyde (100-52-7)

toluene (108-88-3)

Pentane (109-66-0)

Benzenesulfonamide (98-10-2)

argon (7440-37-1)

oxaziridine,
trans-oxaziridine

Oxaziridine, 3-phenyl-2-(phenylsulfonyl)-,
trans-2-(phenylsulfonyl)-3-phenyloxaziridine,
(±)-trans-2-(Phenylsulfonyl)-3-phenyloxaziridine (63160-13-4)

m-chloroperoxybenzoic acid (937-14-4)

N-Benzylidenebenzenesulfonamide (13909-34-7)

trans-2-(Phenylsulfonyl)-3-(p-nitrophenyl)oxaziridine