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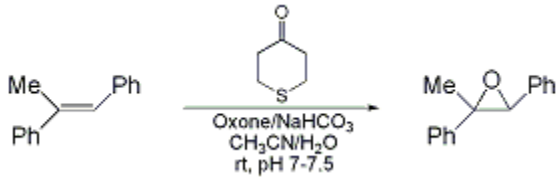
September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.078.0225

Organic Syntheses, Coll. Vol. 10, p.537 (2004); Vol. 78, p.225 (2002).

IN SITU CATALYTIC EPOXIDATION OF OLEFINS WITH TETRAHYDROTHIOPYRAN-4-ONE AND OXONE: trans-2-METHYL-2,3-DIPHENYLOXIRANE

[Oxirane, 2-methyl-2.3-diphenyl-, trans-]



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Checked by Jason M. Diffendal and Rick L. Danheiser.

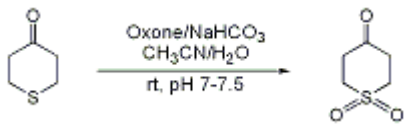
1. Procedure

Caution! This procedure should be conducted in an efficient fume hood to assure the adequate removal of oxygen.

A 250-mL, round-bottomed flask equipped with a Teflon-coated magnetic stirring bar is charged with 3.89 g (20.0 mmol) of trans-α-methylstilbene (Note 1), 0.12 g (1.0 mmol) of tetrahydrothiopyran-4-one (Note 2), 90 mL of acetonitrile (Note 3) and 60 mL of aqueous 4×10^{-4} M ethylenediaminetetraacetic acid, disodium salt (Na_2·EDTA) solution (Note 4). To this stirred mixture is added in portions a mixture of 18.4 g (30.0 mmol) of Oxone ® (Note 5) and 7.8 g (93 mmol) of sodium bicarbonate over a period of 3 hr at room temperature. A slow evolution of gas bubbles is observed (Note 6). The reaction is complete in 3.5 hr as shown by TLC analysis (Note 7). The contents of the flask are poured into a 250-mL separating funnel and extracted with three 50-mL portions of ethyl acetate . The combined organic layers are washed with 25 mL of saturated sodium chloride (NaCl) solution, dried over anhydrous magnesium sulfate , filtered, and concentrated under reduced pressure. The residue is purified by flash column chromatography (Note 8) to afford 4.10-4.18 g (98-99%) of 2-methyl-2,3-diphenyloxirane as a colorless oil that solidifies on standing to a white solid (Note 9).

2. Notes

1. trans-α-Methylstilbene was purchased from Aldrich Chemical Company, Inc. and used without further purification.
2. Tetrahydrothiopyran-4-one was purchased from Acros Chemical Company, Inc. and used without further purification. Oxone ® rapidly converts this ketone to 1,1-dioxotetrahydrothiopyran-4-one , which functions as the catalyst for the epoxidation (Figure 1).[2]



3. Analytical reagent grade acetonitrile was obtained from Labscan Ltd. or Mallinckrodt Inc. , and was used as received.
4. An aqueous 4×10^{-4} M Na_2·EDTA solution is prepared by dilution of 37.2 mg of ethylenediaminetetraacetic acid disodium salt hydrate (Acros Chemical Company, Inc.) with deionized water to the mark in a 250-mL volumetric flask.
5. Oxone ® ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) was purchased from Aldrich Chemical Company, Inc. , and was used as received.

6. Oxygen is formed as by-product in two processes, the decomposition of Oxone ® by dioxiranes and self-decomposition of Oxone ® .
7. The progress of the reaction is monitored by thin layer chromatography. A 0.1-mL sample is removed and dissolved in 2 mL of hexane . The solution is spotted on a TLC plate (1 cm × 4 cm, silica gel 60 F_{254}, Merck), and the plate is developed in 1:20 ethyl acetate/hexane .Visualization by short-wavelength ultraviolet light shows the olefin at $R_f = 0.50$ and the epoxide at $R_f = 0.35$.
8. Flash column chromatography[3] is performed on Merck silica gel 60 (230-400 mesh ASTM) with 5% ethyl acetate in hexane as eluent.
9. trans-2-Methyl-2,3-diphenyloxirane exhibits the following physical and spectroscopic characteristics: mp 43.5-44.5°C; lit.[4] 46-47°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.47 (s, 3 H), 3.97 (s, 1 H), 7.28-7.48 (m, 10 H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 16.9, 63.3, 67.3, 125.3, 126.7, 127.7, 127.9, 128.4, 128.7, 136.1, 142.5 ; EIMS (20 eV) m/z 210 (M^+, 91), 209 (52), 195 (44), 181 (39), 167 (100) ; HRMS for $C_{15}H_{14}O$ (M^+), calcd 210.1045, found 210.1047 .

Waste Disposal Information

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

3. Discussion

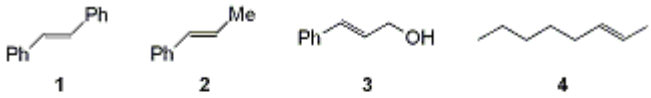
Dioxiranes[5] are powerful oxidants for epoxidation of olefins under mild and neutral reaction conditions.[6] These epoxides are important and versatile intermediates in organic synthesis.[7] The most commonly used dioxiranes, i.e., dimethyldioxirane and methyl(trifluoromethyl)dioxirane , can be obtained by distillation.[8] For preparative epoxidation, an operationally simple method is to generate dioxiranes in situ from ketones and Oxone ® . Compared with acetone , 1,1,1-trifluoroacetone is much more reactive for in situ epoxidation although a 10-fold excess is usually used.[9] Therefore, it will be desirable to employ commercially available ketones in low catalyst loading with a minimal amount of Oxone ® for epoxidation.

The procedure described here provides a simple and convenient method for the preparation of a variety of epoxides. It uses Oxone ® , an inexpensive, safe, and easily handled reagent as the terminal oxidant. The epoxidation reactions are environmentally acceptable processes as Oxone ® only produces non-toxic potassium hydrogen sulfate and oxygen as the by-products.

As shown in the Table, with 5 mol% of 1,1-dioxotetrahydrothiopyran-4-one as catalyst,[10] epoxidation of various olefins (2-mmol scale) in a homogeneous acetonitrile-water solvent system with 1.5 equiv of Oxone ® at room temperature can be achieved in a short period of time with excellent yields of epoxides (80-97%) isolated by flash column chromatography.[2] As the pH of the reaction is maintained at 7-7.5 by sodium bicarbonate , acid- or base-labile epoxides (entries 12-14) can be easily isolated without decomposition. More importantly, the in situ epoxidation of olefins can be performed on a large scale directly with 5 mol% of tetrahydrothiopyran-4-one , which is oxidized immediately by Oxone ® to 1,1-dioxotetrahydrothiopyran-4-one during the epoxidation reactions. For example, with 5 mol% of tetrahydrothiopyran-4-one , substrates **3**, **5** (20 mmol each) and **11** (100 mmol) were epoxidized with excellent isolated yields of epoxides (91-96%).

TABLE
IN SITU EPOXIDATION OF OLEFINS

Substrates:



Entry	Substrate	Reaction Time (hr)[a]	Epoxide Yield (%)[b]
1	**1**	5	95
2	**2**	4.5	87
3	**3**	1.5 (1.7[c])	95 (96[c])
4	**4**	1.5	81
5	**5**	4 (3.5[c])	97 (91[c])
6	**6**	2.5	94
7	**7**	0.5	83
8	**8**	4	95
9	**9**	2.5	85
10	**10**	3	96
11	**11**	0.5 (2[d])	96 (92[d])
12	**12**	4.5	80
13	**13**	3.5	95
14	**14**	2.5	92

[a]Time for epoxidation to be completed as shown by TLC or GC analysis.
[b]Isolated yield.
[c]20-mmol scale reaction with 5 mol% of tetrahydrothiopyran-4-one .
[d]100-mmol scale reaction with 5 mol% of tetrahydrothiopyran-4-one .

References and Notes

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10. Although 1,1-dioxotetrahydrothiopyran-4-one acts as a catalyst for epoxidation and can be recovered (≈80%) by column chromatography (see reference 2), it is more convenient to use tetrahydrothiopyran-4-one directly for epoxidation.

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

Tetrahydrothiopyran-4-one:
4H-Thiopyran-4-one, tetrahydro- (8,9); (1072-72-6)

Oxone:
Peroxymonosulfuric acid, monopotassium salt, mixt. with
dipotassium sulfate and
potassium hydrogen sulfate (9) (37222-66-5)

trans-2-Methyl-2,3-diphenyloxirane:
Oxirane, 2-methyl-2,3-diphenyl-, trans- (9); (23355-99-9)

trans-α-Methylstilbene:
Stilbene, α-methyl-, (E)-;
Benzene, 1,1'-(1-methyl-1,2-ethenediyl)bis-, (E)- (9); (833-81-8)

Acetonitrile (8,9); (75-05-8)

Ethylenediaminetetraacetic acid, disodium salt, dihydrate:
Acetic acid, (ethylenedinitrilo)tetra-, disodium salt, dihydrate (8);
Glycine, N,N'-1,2-ethanediylbis[N-(carboxymethyl)-, disodium salt, dihydrate (9); (6381-92-6)