Supporting Information

Sulfur Ylides via Decarboxylation of Carboxymethylsulfonium Betaines: A Novel and Mild Protocol for the Preparation of Oxiranes

David C. Forbes,^{a,} Michael C. Standen,^{b,*} and Derrick L. Lewis^a*

^aDepartment of Chemistry, University of South Alabama, Mobile, AL 36688, USA

^bSynthetech, Albany, OR, 97321, USA

*corresponding authors: dforbes@jaguar1.usouthal.edu and mikes@synthetech.com

General Considerations. ¹H NMR (300 MHz) and ¹³C NMR (75 MHz) spectra were obtained as solutions in either CDCl₃ or D₂O. Chemical shifts were reported in parts per million (ppm, δ) and referenced to CHCl₃ (δ 7.27). Infrared spectra were recorded as a thin film on sodium chloride and absorptions were reported in wavenumbers (cm⁻¹). Melting points are uncorrected. Distillations were performed using a Kugelrohr ball-tube distillation apparatus. Gas chromatographic analyses were performed using an Agilent 6850 system (FID). Mass spectra were performed on a Shimadzu QP-5000 GC/MS. Combustion analyses were performed by Atlantic Microlabs. TLC analyses were performed on Whatman flexible polyester backed TLC plates with a fluorescent indicator. Detection was conducted by UV absorption (254 nm) and charring with 10% KMnO₄ in water. Baker silica gel (47-61 microns) was used for all chromatographic separations. Anhydrous organic solvents were dried and then distilled prior to use. All chemicals used for synthetic procedures were reagent grade or better. Solutions were concentrated in vacuo with a rotary evaporator and the residue was purified using a silica gel column unless specified otherwise.

Carboxymethyloctylsulfonium bromide (1)

Added to a 100 mL oven dried round bottom flask was 6.3 g methyl *n*-octyl sulfide (39.3 mmol, 1.0 equiv) and 10 mL acetone. A solution consisting of 6.0 g bromoacetic acid (43.2 mmol, 1.1 equiv) and acetone (15 mL) was added via syringe at room temperature dropwise. The solution was allowed to stir overnight under a stream of nitrogen at which time the crude reaction mixture was filtered and washed using TBME (3 x 10 mL). The crude salt (87% isolated yield) was carried on as is without further purification. A small sample was recrystallized (benzene) for spectral analysis (mp 40-1°C). ¹H NMR (300 MHz, CDCl₃); δ 8.50 (br s, 1H), 4.97 (q, *J* = 16.5, 2H), 3.74-3.68 (m, 2H), 3.23 (s, 3H), 1.90-1.75 (m, 2H), 1.55-1.47 (m, 2H), 1.36-1.26 (m, 8H), 0.87 (t, *J* = 6.6, 3H); ¹³C NMR (75.5 MHz, CDCl₃); δ 165.27, 44.66, 41.60, 31.78, 29.10, 28.51, 24.43, 23.30, 22.70, 14.18. IR (CH₂Cl₂) 3333, 2538, 2440, 1725, 1621 cm⁻¹. GC/MS (70 eV, LREI) M⁺ 160 (-CO₂, -CH₂). Analysis (C₁₁H₂₃BrO₂S) Calcd: C, 44.14%; H, 7.74%; S, 10.71%. Found: C, 43.49%; H, 7.75%; S, 10.60%.

Methyloctylsulfonioacetate (Methyloctylthetin) (2)

To an oven dried round bottom flask was added 751 mg sulfonium bromide (2.5 mmol, 1.0 equiv). The white crystalline salt was next dissolved in methanol (15 mL) to afford a clear and colorless solution. Next was added 872 mg of freshly prepared silver(I) oxide (3.76 mmol, 1.5 equiv) portionwise. The reaction mixture was allowed to stir overnight under a stream of nitrogen. After approximately 20 h, the crude reaction mixture was filtered and concentrated in vacuo without the assistance of any external heat. Control studies revealed significant levels of decarboxylation if heat ($>40^{\circ}\text{C}$) or non-polar aprotic solvents are employed. The glassy residue was crystallized via trituration using either diethyl ether or TBME (mp $104-7^{\circ}\text{C}$). ^1H NMR (300 MHz, CDCl_3); δ 4.44 (q, $J = 15.7$, 2H), 3.54-3.35 (m, 2H), 3.05 (s, 3H), 1.79-1.71 (m, 2H), 1.48-1.41 (m, 2H), 1.39-1.20 (m, 8H), 0.87 (t, $J = 6.6$, 3H); ^{13}C NMR (75.5 MHz, D_2O); δ 168.55, 46.43, 41.58, 31.08, 28.17, 28.01, 27.55, 23.30, 22.56, 22.10, 13.51. IR (CH_2Cl_2) 2969, 2923, 2859, 1641, 1337 cm^{-1} . GC/MS (70 eV, LRED) M^+ 160 ($-\text{CO}_2$, $-\text{CH}_2$). Analysis ($\text{C}_{11}\text{H}_{22}\text{O}_2\text{S}$) Calcd: C, 60.51%; H, 10.15%; S, 14.68%. Found: C, 55.97%; H, 10.30%; S, 13.48%.

JEOL

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X : parts per Million : 13C

JEOL

--- PROCESSING PARAMETERS ---

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X : parts per Million : 1H

Typical Procedure for the Preparation of Oxiranes 3a-e

An oven dried round bottomed flask was equipped with stir bar, septum and drying tube. To this system was added aldehyde (1.0 equiv) and 1,2-dichloroethane (0.1 M, 3.0 mL). The system was externally heated to 60°C (sand bath) at which time a solution of betaine (2.0 equiv) in 1,2-dichloroethane (0.1M, 4.0 mL) was added via syringe pump over a period of 1.0 h. The reaction mixture was allowed to stir for an additional period of 2.0 h. After cooling to room temperature, the reaction mixture was concentrated in vacuo and immediately purified by silica gel chromatography using a gradient eluent system of hexanes and EtOAc (three column equivalents per solvent combination) to afford analytically pure oxirane [hexanes/EtOAc, 100:0, 64:1, 32:1, 16:1, 10 x 30 mm SiO₂, 10 mL fractions].

2-(2,6-Dichlorophenyl)oxirane (3a)

From the combination of 2,6-dichlorobenzaldehyde (46.3 mg, 0.26 mmol) and methyloctylthetin (115.5 mg, 0.53 mmol), 2-(2,6-dichlorophenyl)oxirane **3a** was obtained after purification by silica gel chromatography in 42.4 mg (0.22 mmol, 85% yield). Spectral data are in agreement with that previously reported.¹

2-(4-Nitrophenyl)oxirane (3b)

From the combination of 4-nitrobenzaldehyde (45.8 mg, 0.30 mmol) and methyloctylthetin (132.3 mg, 0.61 mmol), 2-(4-nitrophenyl)oxirane **3b** was obtained after purification by silica gel chromatography in 45.9 mg (0.28 mmol, 84% yield). Spectral data are in agreement with that previously reported.²

2-(4-Chlorophenyl)oxirane (**3c**)

From the combination of 4-chlorobenzaldehyde (24.1 mg, 0.17 mmol) and methyloctylthetin (74.9 mg, 0.34 mmol), 2-(4-chlorophenyl)oxirane **3c** was obtained after purification by silica gel chromatography in 16.4 mg (0.11 mmol, 62% yield). Spectral data are in agreement with that previously reported.²

2-Phenyloxirane (**3d**)

From the combination of benzaldehyde (44.5 mg, 0.42 mmol) and methyloctylthetin (183.2 mg, 0.84 mmol), 2-phenyloxirane **3d** was obtained after purification by silica gel chromatography in 27.4 mg (0.23 mmol, 55% yield). Spectral data are in agreement with that previously reported.³

1,2-Epoxy-4-phenylbutane (**3e**)

From the combination of dihydrocinnamaldehyde (45.3 mg, 0.34 mmol) and methyloctylthetin (147.0 mg, 0.67 mmol), 1,2-epoxy-4-phenylbutane **3e** was obtained after purification by silica gel chromatography in 22.5 mg (0.15 mmol, 45% yield). Spectral data are in agreement with that previously reported.⁴

In Situ Generation of 2-(4-Nitrophenyl)oxirane (unoptimized)

An oven dried round bottomed flask was equipped with stir bar, septum and drying tube. To this system was added 4-nitrobenzaldehyde (13 mg, 1.0 equiv), silver carbonate on Celite (approx. 2 equiv) and 1,2-dichloroethane (0.1 M, 3.0 mL). Added next to the solution was silver carbonate on Celite (2.0 equiv) and methyl octyl sulfide (29 mg, 2.0 equiv). The system was externally heated to 60°C (sand bath) at which time a solution of bromoacetic acid (25 mg, 2.0 equiv) in 1,2-dichloroethane (1.0 mL) was added via syringe pump over a period of 1.0 h. The reaction mixture was allowed to stir for an additional period of 2.0 h. After cooling to room temperature, the reaction mixture was filtered using a Celite plug and analyzed by GC. Revealed was the presence of oxirane (40% conversion) and unreacted aldehyde.

References

- (1) Anderson, M. W.; Jones, R. C. F.; Saunders, J. J. *Chem. Soc. Perkin Trans I* **1986**, 205.
- (2) Pedragosa-Moreau, S.; Morisseau, C.; Zylber, J.; Archelas, A.; Baratti, J.; Furstoss, R. *J. Org. Chem.* **1996**, 61, 7402.
- (3) Aggarwal, V. K.; Ali, A.; Coogan, M. P. *J. Org. Chem.* **1997**, 62, 8628.
- (4) (a) Ooi, T.; Kagoshima, N.; Maruoka, K. *J. Am. Chem. Soc.* **1997**, 119, 5754. (b) Cho, I. S.; Lee, B.; Alper, H. *Tetrahedron Lett.* **1995**, 36, 6009.