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PREPARATION OF α-SUBSTITUTED *S*-PHENYLTHIO ESTERS FROM 2-NITRO-2-PHENYLTHIO OXIRANES

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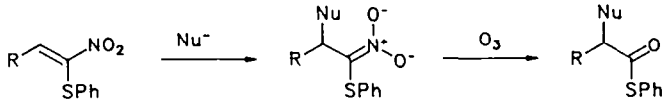
Summary: 2-Nitro-2-phenylthio oxiranes (3), prepared by nucleophilic epoxidation of 1-nitro-1-phenylthio alkenes (1), react with a variety of heteroatomic nucleophiles to give α-substituted S*-phenylthio esters (2). Of special note is the efficient reaction of 2-nitro-2-phenylthio oxiranes with boron trifluoride etherate in toluene at room temperature to give α-fluoro* S*-phenylthio esters (8).*

Nitroalkenes are widely used electrophilic reagents in synthesis.[1] The most generally useful process involves Michael addition of a nucleophile to a nitroalkene, followed by subsequent transformation of the nitro group to a carbonyl function, although many other possibilities exist.[2] The synthetic applications of nitroalkenes with further functionality on the double bond have only recently been investigated.[3,4,5] Nitroalkenes which have an additional phenylthio substituent at the 1-position are of special interest since these compounds exhibit high reactivity towards nucleophiles. This reactivity has been used in a furan annulation procedure,[5] and also in the synthesis of α-substituted *S*-phenylthio esters **(2)**.[6] In this latter application, nucleophiles are added to 1-nitro-1-phenylthio alkenes **(1)** to give the corresponding nitronate anions which, without isolation, can be converted to α-substituted *S*-phenylthio esters **(2)** by ozonolysis (Scheme 1). This methodology has been successfully employed in an approach to β-lactams,[7] and also in the synthesis of functionalised tetrahydrofurans and tetrahydropyrans.[8]



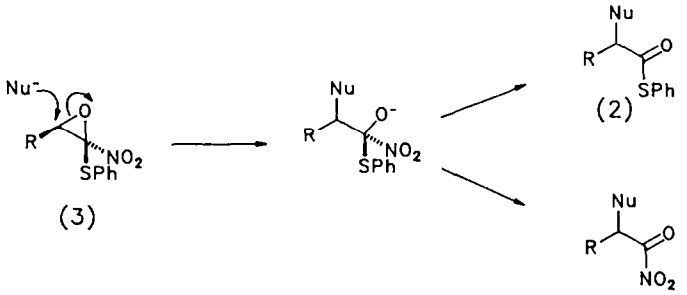
(1) (2)

Scheme 1

The principal precursor for the synthesis of 1-nitro-1-phenylthio alkenes is (phenylthio)nitromethane. Three published procedures for the synthesis of (phenylthio) nitromethane exist in the literature: reaction of ethyl nitroacetate with *N*-(phenylthio)

morpholine;[9] reaction of the dianion of (phenylthio)acetic acid with n-propyl nitrate;[5] and finally, reaction of the sodium salt of nitromethane with phenylsulphenyl chloride.[10] The latter procedure, recently adapted,[11] is the most convenient on a large scale and it is noteworthy in that a slurry of sodium nitromethylate in ethanol can be employed in the reaction with phenylsulphenyl chloride. This avoids the need to handle the anhydrous salt, which is a well-known explosive.[4] Although the nitration of the dianion of phenylthioacetic acid is conceptually attractive, both we, and others,[12] have experienced difficulties using this procedure, frequently obtaining low yields.

As part of our interest in the synthetic applications of heterosubstituted oxiranes,[13–17] we were attracted to the idea of developing a complimentary method for the conversion of 1-nitro-1-phenylthio alkenes **(1)** to α-substituted *S*-phenylthio esters **(2)**.[18] Rather than initial addition of a nucleophile to the alkene, with subsequent oxidation, we hoped to convert the alkene to an oxirane, and then investigate subsequent nucleophilic attack (Scheme 2). Although both 2-nitro oxiranes[19] and 2-phenylthio oxiranes[20] have been prepared, 2-nitro-2-phenylthio oxiranes **(3)** were unknown. Precedent drawn from the reactivity of 2-nitro oxiranes towards nucleophiles[19,21,22] suggested that nucleophilic attack on 2-nitro-2-phenylthio oxiranes **(3)** would occur at the carbon atom remote from the nitro group, although the fate of the initially formed tetrahedral intermediate was uncertain.

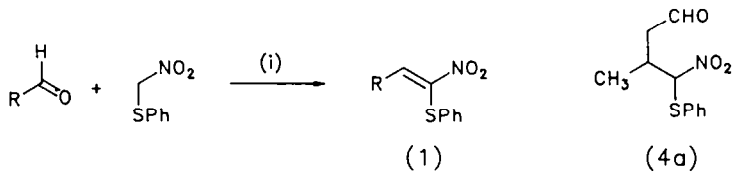


Scheme 2

Results and Discussion

The literature procedure for the synthesis of 1-nitro-1-phenylthio alkenes requires initial Henry reaction between (phenylthio)nitromethane and an aldehyde, followed by elimination of water using methanesulphonyl chloride and triethylamine.[5,6] Since this is a two-pot procedure, we decided to investigate the possibility that a one-pot Knoevenagel reaction might be useful. Indeed, reaction of (phenylthio)nitromethane and aldehydes in the presence of piperidinium acatate (5 mol. %) as catalyst in dichloromethane or toluene as solvent did give the desired 1-nitro-1-phenylthio alkenes **(1)** (Scheme 3). The alkenes were formed as single geometrical isomers, assigned the *Z* configuration on the basis of the chemical shift of the vinyl protons. In our earlier experiments with ethanal, we isolated significant amounts of the nitro aldehyde **(4a)** as a mixture of diastereoisomers. We presume that the adduct **(4a)** arises from Michael addition of ethanal to the alkene **(1a)** promoted by piperidinium acetate. Formation of analogous adducts with the other straight chain aldehydes was also observed.

After some optimisation it became clear that a two-fold excess of (phenylthio)nitromethane was necessary to suppress this further reaction. Formation of such Michael adducts is clearly not a problem in the case of either 2-methylpropanal or benzaldehyde. In the former case an excess of aldehyde can be used, and in the latter, one equivalent is satisfactory. The results are detailed in Table 1.



Scheme 3 (i) Piperidinium acetate

Table 1

R	Solvent	Time h	Temp.	Product	Yield %[a]
Me	CH_2Cl_2	2	0 °C	**(1a)**	57
Pr^n	CH_2Cl_2	2½	0 °C	**(1b)**	76
Pr^i [b]	CH_2Cl_2	7½	Reflux	**(1c)**	78
Bu	CH_2Cl_2	2½	0 °C	**(1d)**	75
Pent	CH_2Cl_2	2½	0 °C	**(1e)**	71
Hex	CH_2Cl_2	1½	0 °C	**(1f)**	56
Ph [c]	Benzene	5	Reflux	**(1g)**	79

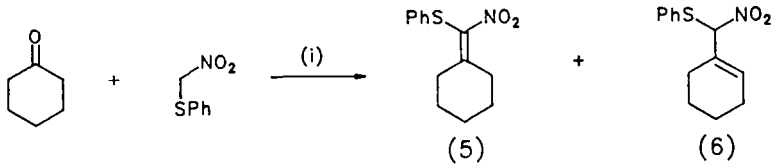
[a] Yield based on (phenylthio)nitromethane consumed.

[b] 1.5 equiv. of 2-methylpropanal used.

[c] 1.0 equiv. of benzaldehyde used.

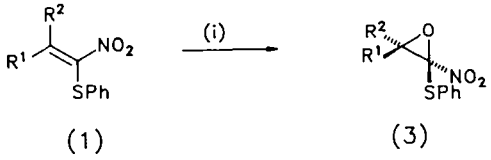
The one-pot Knoevenagel procedure is a useful alternative to the two-pot Henry reaction and elimination. For α-branched and aromatic aldehydes where (phenylthio)-nitromethane can be the limiting reagent, the Knoevenagel procedure offers some experimental advantages. In the case of simple straight chain aldehydes, most especially ethanal, the two-pot method is preferable.

In an effort to prepare more substituted 1-nitro-1-phenylthio alkenes, we have briefly investigated the Knoevenagel reaction of (phenylthio)nitromethane with cyclohexanone. As expected, no significant reaction was observed with piperidinium acetate catalysis.[23] However, use of N,N-dimethyl ethylenediamine and powdered molecular sieves in toluene at room temperature (a minor modification of Tamaru's procedure for the condensation of simple nitroalkanes with ketones[24]) did allow the isolation of poor yields of the 1-nitro-1-phenylthio alkene **(5)** (17 % based on (phenylthio)nitromethane consumed) and the corresponding allylic nitro compound **(6)** (17 %) (Scheme 4). Higher yields (up to 50 %) of the conjugated nitro alkene **(5)** could be obtained using dichloromethane as solvent and extended reaction times, although unidentified side reactions competed.



Scheme 4 (i) $Me_2NCH_2CH_2NH_2$, toluene, 4 Å sieves, r.t.

The usual method for the preparation of oxiranes bearing electron withdrawing groups involves nucleophilic epoxidation of the corresponding alkenes using basic hydrogen peroxide.[25] However, the presence of the oxidisable sulphur atom in 1-nitro-1-phenylthio alkenes mitigated against the use of this reagent. We had shown previously that epoxidation of 1-methyl-1-nitro-2-phenylethene proceeded in high yield using lithium *tert*-butyl hydroperoxide[26] under mild conditions,[27] and we therefore decided to investigate the nucleophilic epoxidation of 1-nitro-1-phenylthio alkenes **(1)** with this reagent. We were pleasantly surprised to discover that the epoxidation reaction for the aldehyde derived 1-nitro-1-phenylthio alkenes **(1)** proceeded smoothly within 1 hour at -78 °C to give the corresponding 2-nitro-2-phenylthio oxiranes **(3)** (Scheme 5). The ketone derived nitro alkene **(5)** required warming to -40 °C for reaction. The results are detailed in Table 2. The mild conditions for this process illustrate once again the highly electrophilic nature of 1-nitro-1-phenylthio alkenes. The oxiranes were all single diastereoisomers, and their relative configuration is depicted as arising from a stereospecific *cis* epoxidation, which has been shown to be the case for other epoxidations using lithium *tert*-butyl hydroperoxide.[15,26] The oxiranes derived originally from 2-methylpropanal and benzaldehyde were crystalline, although the latter was unstable at room temperature and could best be purified by low temperature crystallisation.



(1) (3)

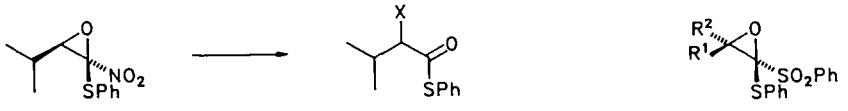
Scheme 5 (i) Bu^tOOH, Bu^nLi, THF, 1 h

Table 2

R^1	R^2	Alkene	Product	Yield %
Me	H	(1a)	(3a)	90[a]
Pr^n	H	(1b)	(3b)	80
Pr^i	H	(1c)	(3c)	91
Bu	H	(1d)	(3d)	78
Pent	H	(1e)	(3e)	77
Hex	H	(1f)	(3f)	80
Ph	H	(1g)	(3g)	66
$(CH_2)_5$		(5)	(3h)	57

[a] This is a crude yield, since the product is not stable to column chromatography.

Since the oxirane **(3c)** derived originally from 2-methylpropanal was crystalline, stable and especially easy to prepare, we chose to explore the reactivity of the 2-nitro-2-phenylthio oxirane function in this compound. Our initial investigations involved treatment of the oxirane **(3c)** with lithium or magnesium halides,[28] and gave good yields of the corresponding α-halo *S*-phenylthio esters **(2a-c)** (Scheme 6).[29] The efficient formation of the *S*-phenylthio esters clearly demonstrates the superior leaving group ability of a nitro group compared with a phenylthio group. We have since discovered that 2-phenylsulphonyl-2-phenylthio oxiranes **(7)** behave in a similar manner (although they are slightly less reactive), and are superior precursors to α-halo *S*-phenylthio esters, since most of the intermediates are crystalline and all are stable.[14] More interestingly, on treatment of the oxirane **(3c)** with trifluoroacetic acid in toluene at reflux, we obtained a good yield of the trifluoroacetate **(2d)**. Analogous reaction with methanesulphonic acid gave the methanesulphonate **(2e)**. The success of these reactions, which involve the addition of a poor nucleophile, are indicative of considerable carbocationic character in the ring-opening step.[30] Our results are summarised in Table 3.



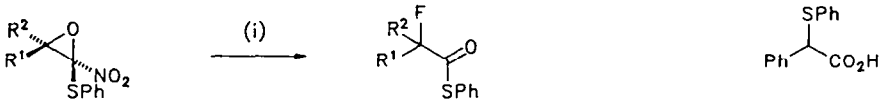
(3c) (2a-e) (7)

Scheme 6

Table 3

Reagent	Solvent	Time h	Temp.	Product	(X)	Yield %
LiCl	Acetone	1½	20 °C	**(2a)**	Cl	78
$MgBr_2.Et_2O$	Et_2O	2½	20 °C	**(2b)**	Br	85
MgI_2	Et_2O	½	0 °C	**(2c)**	I	91
CF_3CO_2H	Toluene	6	Reflux	**(2d)**	CF_3CO_2	69
CH_3SO_3H	Toluene	½	Reflux	**(2e)**	CH_3SO_3	76

In an attempt to investigate Lewis acid catalysed rearrangements of 2-nitro-2-phenylthio oxiranes, the oxirane **(3c)** was treated with boron trifluoride etherate in toluene at room temperature. However, the product obtained in high yield was the α-fluoro *S*-phenylthio ester **(8c)**. Use of diethyl ether as solvent resulted in no reaction. Both *tetra*-n-butylammonium fluoride in tetrahydrofuran and potassium fluoride/18-crown-6 in toluene gave lower yields of the α-fluoro *S*-phenylthio ester, together with other unidentified products. Since there appeared to be no general methods for the synthesis of α-fluoro *S*-phenylthio esters,[31] we decided to explore the scope of the reaction between 2-nitro-2-phenylthio oxiranes **(3)** and boron trifluoride etherate. Simple aliphatic oxiranes react cleanly to give the corresponding α-fluoro *S*-phenylthio esters **(8)** (Scheme 7). It is interesting that the oxirane derived from cyclohexanone also reacted efficiently. Our results are summarised in Table 4. However, the 3-phenyl oxirane **(3g)** underwent migration of the phenylthio group, presumably to give an acyl nitro compound which was subsequently hydrolysed leading to α-phenylthio phenylacetic acid **(9)** (65 %).



(3) (8) (9)

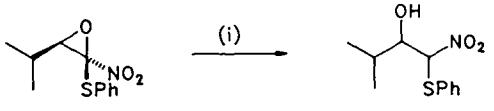
Scheme 7 (i) $BF_3.OEt_2$, toluene, r.t.

Table 4

R^1	R^2	Epoxide	α-Fluoro Thio ester	Yield %
Me	H	**(3a)**	**(8a)**	80
Pr^n	H	**(3b)**	**(8b)**	86
Pr^i	H	**(3c)**	**(8c)**	96
Pent	H	**(3e)**	**(8e)**	88
Hex	H	**(3f)**	**(8f)**	91
$(CH_2)_5$		**(3h)**	**(8h)**	87

Ring-opening of simple oxiranes with boron trifluoride etherate to give fluorohydrins has only been reported in steroidal examples. Even in these cases, the course of the reaction is often complicated and mixtures of products result.[32] Usually, the presence of hydrogen fluoride is required for efficient reaction.[31,33] The 2-nitro-2-phenylthio oxirane function seems to be uniquely susceptible to the fluorination reaction with boron trifluoride etherate: the analogous 2-phenylsulphonyl-2-phenylthio oxiranes **(7)** react to give mixtures of products.[34] Although the nitro group is a poor ligand,[35] it is possible that some interaction between the nitro group and the boron atom is responsible for the observed reactivity.

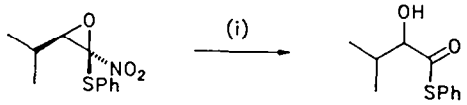
In an attempt to introduce carbon nucleophiles, the 2-nitro-2-phenylthio oxirane **(3c)** was treated with the higher order cuprate $(Bu_2CuCN)Li_2$[36] in tetrahydrofuran at -40 °C. Interestingly, the major product (45 %) obtained from this reaction was the β-hydroxy nitro derivative **(10)**, whose structure was confirmed by conversion to the 1-nitro-1-phenylthio alkene **(1c)**.[6] It appears that reduction of the oxirane by the cuprate is the major reaction pathway (Scheme 8).[37]



(3c) (10)

Scheme 8 (i) $(Bu_2CuCN)Li_2$, THF, - 40 °C

Reaction of the oxirane **(3c)** with triphenylphosphine led, in moderate yield (42 %), to the α-hydroxy thioester **(11)** (Scheme 9). This product is formally that of hydroxide ion attack. A reasonable mechanism for the formation of **(11)** involves reduction of the nitro group to a nitroso group, oxirane ring opening and hydrolysis.



(3c) (11)

Scheme 9 (i) PPh_3, toluene, reflux

In conclusion, 2-nitro-2-phenyl oxiranes **(3)** may be readily prepared from the corresponding 1-nitro-1-phenylthio alkenes **(1)**. These oxiranes exhibit high reactivity towards acidic systems leading to α-substituted *S*-phenylthio esters, and allow the efficient incorporation of relatively non-nucleophilic counterions. This reactivity is complimentary to that shown by 1-nitro-1-phenylthio alkenes **(1)**, which require more nucleophilic reagents for efficient reaction.[5-8]

Experimental

Unless otherwise stated all new compounds were homogeneous by t.l.c.; n.m.r. spectra were run in $CDCl_3$ and recorded for ^1H at 60 MHz on a Perkin Elmer R24-B , and at 200 or 300 MHz on Bruker instruments, and ^{13}C spectra were recorded at 50.3 MHz. Infrared spectra were obtained on a Nicolet 20SX as capillary films (for oils) or KBr disks (for solids), and mass spectra were measured on either an AEI MS9 or a Kratos MS80 using the E.I. Method. Peaks due to ^{35}Cl and ^{79}Br only are recorded. Piperidinium acetate was obtained by addition of acetic acid to a solution of piperidine in diethyl ether, filtration and drying. All solvents were distilled: petrol refers to that fraction with boiling point between 40 and 60 °C; dry CH_2Cl_2 was distilled from P_2O_5; dry THF was distilled from potassium benzophenone ketyl; dry diethyl ether was distilled from sodium benzophenone ketyl. (Phenylthio)nitromethane was prepared either from phenylthioacetic acid[5] or, more conveniently, from phenylsulphenyl chloride.[11] All aldehydes were distilled prior to use. Anhydrous solutions of *tert*-butyl hydroperoxide in toluene were obtained by azeotropic drying, and concentrations were determined by ^1H n.m.r.[38] Organic extracts were dried over $MgSO_4$, and then concentrated using a rotary evaporator.

1-Nitro-1-phenylthiopropene (1a): Piperidinium acetate (29 mg, 0.2 mmol) and powdered 4 Å molecular sieves (0.5 g) were added to a solution of (phenylthio)nitromethane (1.363 g, 8.05 mmol) and ethanal (229 μl, 181 mg, 4.1 mmol) in dichloromethane (15 ml) at 0 °C under nitrogen. The reaction mixture was stirred for 2½ hours at 0 °C, and then filtered to remove the molecular sieves. The solution was washed with hydrochloric acid (1 *M*, 5 ml), saturated aqueous sodium chloride (10 ml), dried and concentrated. The residue was purified by flash chromatography using petrol/dichloromethane (4:1) as eluent to give the nitroalkene **(1a)** as an oil (0.467 g, 57 %) and recovered (phenylthio)nitromethane (0.648 g, 3.83 mmol). Spectral data for **(1a)** correspond to those reported.[5,6] In a similar experiment using 1 equivalent of (phenylthio)nitromethane, the nitroalkene **(1a)** (29 %) together with 3-methyl-4-nitro-4-phenylthiobutanal **(4a)** (15 %) as a mixture of diastereoisomers was also isolated: ν_{max} 1728, 1552, and 1360 cm^{-1}; δ_H (300 MHz) 1.17 (d, J = 6 Hz) and 1.21 (d, J = 6 Hz) (total 3H), 2.56-3.07 (3H, m), 5.56 (d, J = 6 Hz) and 5.62 (d, J = 5 Hz) (total 1H), 7.32-7.55 (5H, m),

and 9.76 (t, J = 2 Hz) and 9.79 (t, J = 2 Hz) (total 1H); δ_C (75 MHz) 16.55 and 16.95, 31.9 and 32.0, 46.75 and 46.95, 99.1 and 99.4, 129.5, 129.6, 129.7, 129.8, 129.9, 133.35, 133.40, 199.2.

General Procedure for Preparation of 1-Nitro-1-phenylthio Alkenes (1b, 1d–1f): piperidinium acetate (53.5 mg) and powdered 4 Å molecular sieves (1 g) were added to a solution of (phenylthio)nitromethane (2.496 g, 14.75 mmol) and aldehyde (7.37 mmol) in dichloromethane (25 ml) at 0 °C under nitrogen. The mixture was stirred at 0 °C for the time indicated in Table 1 (see discussion), and then filtered to remove the molecular sieves. The filtrate was washed with hydrochloric acid (1 *M*, 10 ml), saturated aqueous sodium chloride (20 ml), dried and concentrated. The residue was purified by flash chromatography using petrol/dichloromethane (4:1) as eluent to give the nitroalkene **(1b, 1d–f)** as an oil and recovered (phenylthio)nitromethane. The yields in Table 1 are based on the amount of (phenylthio)nitromethane consumed.

1-Nitro-1-phenylthio-1-pentene (1b): (Found: M^+, 223.0655. $C_{11}H_{13}NO_2S$ requires 223.0667); ν_{max} 1530, 1324 cm^{-1}; δ_H (60 MHz) 0.9 (3H, t, J = 7 Hz), 1.2–1.8 (2H, m), 2.5 (2H, q, J = 7.5 Hz), 7.2 (5H, br. s), and 7.75 (1H, t, J = 7.5 Hz); m/z 223 (M^+, 25 %), 177 ($M^+ - NO_2$, 64).

1-Nitro-1-phenylthio-1-hexene (1d): (Found: M^+, 237.0832. $C_{12}H_{15}NO_2S$ requires 237.0823); ν_{max} 1532, 1325 cm^{-1}; δ_H (300 MHz) 0.94 (3H, t, J = 7.2 Hz), 1.34–1.59 (4H, m), 2.60 (2H, q, J = 7.6 Hz), 7.21–7.35 (5H, m), and 7.77 (1H, t, J = 7.8 Hz); m/z 237 (M^+, 6 %), 191 ($M^+ - NO_2$, 15).

1-Nitro-1-phenylthio-1-heptene (1e): (Found: M^+, 251.0976. $C_{13}H_{17}NO_2S$ requires 251.1017); ν_{max} 1531, 1323 cm^{-1}; δ_H (300 MHz) 0.83 (3H, t, J = 7.0 Hz), 1.23–1.33 (4H, m), 1.43–1.54 (2H, m), 2.53 (2H, q, J = 7.5 Hz), 7.14–7.30 (5H, m), and 7.70 (1H, t, J = 7.8 Hz); m/z 251 (M^+, 15 %), 205 ($M^+ - NO_2$, 11), 95 (100).

1-Nitro-1-phenylthio-1-octene (1f): ν_{max} 1533, 1325 cm^{-1}; δ_H (200 MHz) 0.91 (3H, t, J = 6.5 Hz), 1.27–1.41 (6H, m), 1.48–1.59 (2H, m), 2.61 (2H, q, J = 7.6 Hz), 7.23–7.33 (5H, m), and 7.79 (1H, t, J = 7.6 Hz); m/z 265 (M^+, 15 %), 219 ($M^+ - NO_2$, 18), 149 (95), 109 (100).

3-Methyl-1-nitro-1-phenylthio-1-butene (1b): Piperidinium acetate (0.187 g, 1.3 mmol) was added to a solution of (phenylthio)nitromethane (4.37 g, 25.84 mmol) and 2-methylpropanal (3.52 ml, 2.79 g, 38.76 mmol, 1.5 eq.) in dichloromethane (70 ml), and the mixture was refluxed under nitrogen for 7½ h. The solution was cooled, washed with hydrochloric acid (1 *M*, 10 ml), saturated aqueous sodium chloride (20 ml), dried and concentrated. The residue was purified by flash chromatography using petrol/dichloromethane 4:1 as eluent to give the nitroalkene **(1b)** (4.38 g, 76 %) as an oil which solidified on scratching to give an orange solid, m.p. 30 °C. Spectral data for **(1b)** correspond to those reported.[6]

1-Nitro-2-phenyl-1-phenylthioethene (1g): Piperidinium acetate (43 mg, 0.29 mmol) was added to a solution of (phenylthio)nitromethane (1.985 g, 11.7 mmol) and benzaldehyde (1.20 ml, 1.25

g, 11.7 mmol) in benzene (35 ml). The mixture was heated to reflux, with azeotropic removal of water using a Dean–Stark trap. After being refluxed for 5 h, the reaction mixture was cooled, the solvent removed on a rotary evaporator, and the residue purified by flash chromatography using petrol/dichloromethane (4:1) as eluent to give the nitroalkene **(1g)** (2.39 g, 79 %) as an oil. Residual traces of benzaldehyde were removed by heating at < 100 °C under vacuum. On scratching, the oil crystallised to a yellow solid, m.p. 65 °C (Found: M^+, 257.0505. $C_{14}H_{11}NO_2S$ requires 257.0560); ν_{max} 1597, 1520, 1312 cm^{-1}; δ_H 7.2–7.34 (5H, m), 7.4–7.55 (3H, m), 7.9–8.0 (2H, m), and 8.59 (1H, s); *m/z* 257 (M^+, 6 %), 211 (M^+ – NO_2, 80).

Condensation of (Phenylthio)nitromethane with Cyclohexanone: A solution of (phenylthio)nitromethane (0.29 g, 1.71 mmol), cyclohexanone (0.18 ml, 0.17 g, 1.74 mmol) and N,N–dimethyl ethylenediamine (14 μl, 0.011 g, 0.13 mmol) in toluene (5 ml) was stirred in the presence of 4 Å molecular sieves (0.25 g) at r.t. for 6 h. A further portion of molecular sieves (0.25 g) was then added, and stirring continued for 2 h. The sieves were removed by filtration, and the fitrate was diluted with dichloromethane (10 ml), washed with hydrochloric acid (1 *M*, 5 ml), dried and evaporated. The residue was purified by flash chromatography to give 1–[nitro(phenylthio)methylidene]cyclohexane **(5)** (40 mg, 17 %) and 1–[nitro(phenylthio)–methyl]cyclohexene **(6)** (40 mg, 17 %) and recovered (phenylthio)nitromethane (130 mg). Spectral data for **(5)**: (Found: M^+, 249.0849. $C_{13}H_{15}NO_2S$ requires 249.0824); ν_{max} 1582, 1524, 1352 cm^{-1}; δ_H (300 MHz) 1.61–1.81 (6H, m), 2.41 (2H, t, J = 5.5 Hz), 2.64 (2H, t, J = 5.4 Hz), 7.2–7.5 (5H, m); *m/z* 249 (M^+, 8 %), 203 (M^+– NO_2, 80), 169 (47). Spectral data for **(6)**: δ_H (300 MHz) 1.3–1.9 (4H, m), 2.2–2.7 (4H, m), 4.97 (1H, t, J = 4.0 Hz), 6.31 (1H, d, J = 1.5 Hz), and 7.2–7.6 (5H, m); *m/z* 249 (M^+), 203 (M^+– NO_2), 110 (PhSH), 109 (PhS).

General Procedure for the Preparation of 2–Nitro–2–Phenylthio Oxiranes (3a–h): A solution of *tert*–butyl hydroperoxide (2.81 ml, 3.4 *M* in toluene, 9.55 mmol) was diluted under a nitrogen atmosphere with dry THF (20 ml). The mixture was cooled to –78 °C and *n*–butyllithium (6.1 ml, 1.1 *M*, 6.71 mmol) was added slowly. The 1–nitro–1–phenylthio alkene **(1a–g)** (6.36 mmol) in dry THF (10 ml) was then added, and the reaction mixture was stirred at –78 °C for 1 h (–40 °C in the case of **(5)**). The reaction was quenched with sodium sulphite (1.0 g), and then aqueous ammonium chloride (10 ml, 10 %) was added, and the mixture allowed to warm to r.t. The mixture was extracted with dichloromethane (3 x 20 ml), and the combined organic extracts dried and evaporated. The residue was then purified by flash chromatography using petrol/dichloromethane (4:1) as eluent (for **(3b–f,** and **3h)**).

3–Methyl–2–nitro–2–phenylthio Oxirane (3a): obtained as an oil, which was unstable to chromatography ν_{max} 1560, 1336; δ_H (200 MHz) 1.53 (3H, d, J = 5.3 Hz), 3.61 (1H, q, J = 5.3 Hz), 7.2–7.5 (5H, m).

2–Nitro–2–phenylthio–3–propyl Oxirane (3b): obtained as an oil (Found: M^+, 239.0625. $C_{11}H_{13}NO_3S$ requires 239.0616); ν_{max} 1563, 1339, 1277 cm^{-1}; δ_H 1.03 (3H, t, J = 7.3 Hz), 1.5–1.65 (2H, m), 1.85–1.96 (2H, m), 3.61 (1H, t, J = 6.1 Hz), 7.25–7.4 (3H, m), and 7.5–7.6 (2H, m); *m/z* 239 (M^+), 193 (M^+ – NO), 165 (M^+– NO – CO), 110 (PhSH), 109 (PhS).

3-(1-Methylethyl)-2-nitro-2-phenylthio Oxirane (3c): obtained as a white crystalline solid, m.p. 55–56 °C (from diethyl ether/petrol) (Found: C, 55.5; H, 5.5; N, 5.8. $C_{11}H_{13}NO_3S$ requires C, 55.2; H, 5.5; N, 5.85; ν_{max} 1560, 1345, 1271 cm^{-1}; δ_H (200 MHz) 1.09 (3H, d, J = 6.8 Hz), 1.19 (3H, d, J = 6.7 Hz), 2.00 (1H, m), 3.31 (1H, d, J = 9.5 Hz), 7.26–7.43 (3H, m), and 7.52–7.62 (2H, m); *m/z* 239 (M^+), 193 ($M^+ - NO_2$), 165 ($M^+ - NO_2 - CO$), 110 (PhSH), 109 (PhS).

3-Butyl-2-nitro-2-phenylthio Oxirane (3d): obtained as an oil (Found: M^+, 253.0790. $C_{12}H_{15}NO_3S$ requires 253.0773); ν_{max} 1563, 1341, 1211 cm^{-1}; δ_H (200 MHz) 0.96 (3H, t, J = 7.0 Hz), 1.38–1.62 (4H, m), 1.87–1.98 (2H, m), 3.60 (1H, t, J = 6.1 Hz), 7.25–7.42 (3H, m), and 7.5–7.6 (2H, m); *m/z* 253 (M^+), 207 ($M^+ - NO_2$), 179 ($M^+ - NO_2 - CO$), 110 (PhSH), 109 (PhS).

2-Nitro-3-pentyl-2-phenylthio Oxirane (3e): obtained as an oil (Found: M^+, 267.0892. $C_{13}H_{17}NO_3S$ requires 267.0929); ν_{max} 1564, 1339, 1211 cm^{-1}; δ_H (60 MHz) 0.9 (3H, t, J = 7 Hz), 1.3–2.0 (8H, m), 3.6 (1H, t, J = 7 Hz), 7.2–7.6 (5H, m); *m/z* 267 (M^+), 221 ($M^+ - NO_2$), 193 ($M^+ - NO_2 - CO$), 110 (PhSH), 109 (PhS).

3-Hexyl-2-nitro-2-phenylthio Oxirane (3f): obtained as an oil: (Found: $M^+ - NO_2$, 235.1115. $C_{14}H_{19}SO$ requires 235.1156); ν_{max} 1564, 1339, 1277 cm^{-1}; δ_H (200 MHz) 0.91 (3H, t, J = 6.4 Hz), 1.20–1.60 (8H, m), 1.9–2.0 (2H, m), 3.60 (1H, t, J = 6.1 Hz), 7.26–7.41 (3H, m), and 7.5–7.6 (2H, m); *m/z* 235 ($M^+ - NO_2$, 78 %), 207 ($M^+ - NO_2 - CO$, 70), 110 (PhSH, 86), 109 (PhS, 100).

2-Nitro-3-phenyl-2-phenylthio Oxirane (3g): obtained as yellow crystals from diethyl ether/petrol at −20 °C. The compound is unstable at room temperature and could not be purified by chromatography. Neither a m.p. nor a satisfactory microanalysis could be obtained. Spectral data: ν_{max} 1562, 1332, 1271 cm^{-1}; δ_H (200 MHz) 4.65 (1H, s), 7.25–7.52 (10H, m); *m/z* 273 (M^+), 244, 226 ($M^+ - HNO_2$), 199 ($M^+ - NO_2 - CO$), 110 (PhSH), 109 (PhS).

2-Nitro-2-phenylthio-1-oxaspiro[2.5]octane (3h): obtained as an oil (Found: M^+, 265.0756. $C_{13}H_{15}NO_3S$ requires 265.0773); ν_{max} 1557, 1341, 1254 cm^{-1}; δ_H (200 MHz) 1.52–1.88 (8H, m), 1.90–2.04 (2H, m), 7.25–7.40 (3H, m), and 7.50–7.56 (2H, m); 265 (M^+), 219 ($M^+ - NO_2$), 191 ($M^+ - NO_2 - CO$), 110 (PhSH), 109 (PhS).

Reactions of 3-(1-Methylethyl)-2-nitro-2-phenylthio Oxirane (3c).

***S*-Phenyl 2-Chloro-3-methyl(thiobutanoate) (2a):** The oxirane **(3c)** (87 mg, 0.363 mmol) was dissolved in acetone (2 ml) and lithium chloride (40 mg, 0.94 mmol) was added. The mixture was stirred at r.t. for 1½ h, and then the solvent was removed using a rotary evaporator. The residue was dissolved in petrol (5 ml), washed with water, dried and concentrated to give the thioester **(2a)** (65 mg, 78 %) as an oil, homogeneous by t.l.c. (Found: M^+, 228.0383. $C_{11}H_{13}ClOS$ requires 228.0376); ν_{max} 1689 cm^{-1}; δ_H (300 MHz) 1.07 (3H, d, J = 6.7 Hz), 1.10 (3H, d, J = 6.8 Hz), 2.42–2.53 (1H, m), 4.37 (1H, d, J = 5.3 Hz), 7.42 (5H, s); *m/z* 228

(M^+), 144, 119, 110 (PhSH).

***S*-Phenyl 2-Bromo-3-methyl(thiobutanoate) (2b)**: The oxirane **(3c)** (173 mg, 0.725 mmol) and magnesium bromide etherate (280 mg, 1.08 mmol) were dissolved in dry diethyl ether (5 ml). the mixture was stirred for 2½ h at r.t. and then washed with water (2 ml). The aqueous layer was extracted with ether (5 ml), and the combined organic extracts dried and evaporated to give the thioester **(2b)** (168 mg, 85 %), homogeneous by t.l.c. (Found: M^+, 271.9893. $C_{11}H_{13}BrOS$ requires 271.9870); ν_{max} 1697 cm^{-1}; δ_H (300 MHz) 1.10 (3H, d, J = 6.8 Hz), 1.13 (3H, t, J = 6.7 Hz), 2.31–2.41 (1H, m), 4.34 (1H, d, J = 6.9 Hz), 7.43 (5H, s); *m/z* 272 (M^+), 188, 135, 110 (PhSH), 109 (PhS).

***S*-Phenyl 2-Iodo-3-methyl(thiobutanoate) (2c)**: Iodine (334 mg, 1 mmol) was added to magnesium turnings (90 mg, 3.7 mmol) in dry diethyl ether (10 ml), and the mixture stirred for 30 min, when it was colourless, and then cooled to 0 °C. The oxirane **(3c)** (200 mg, 0.837 mmol) was then added and the mixture was stirred for 30 min at 0 °C. The mixture was diluted with petrol (10 ml), and washed with saturated aqueous sodium thiosulphate (5 ml). The organic extracts were dried and evaporated, to give the thioester **(2c)** (245 mg, 91 %) as a yellow light sensitive oil, homogeneous by t.l.c. (Found: M^+, 319.9759. $C_{11}H_{13}IOS$ requires 319.9732); ν_{max} 1705 cm^{-1}; δ_H (200 MHz) 1.09 (3H, d, J = 6.6 Hz), 1.12 (3H, d, J = 6.6 Hz), 2.00–2.10 (1H, m), 4.46 (1H, d, J = 8.0 Hz), 7.44 (5H, m); *m/z* 320 (M^+), 137, 110 (PhSH), 109 (PhS).

***S*-Phenyl 2-Trifluoroacetoxy-3-methyl(thiobutanoate) (2d)**: The oxirane **(3c)** (240 mg, 1.004 mmol) and trifluoroacetic acid (115 μl, 170 mg, 1.49 mmol) were dissolved in toluene (4 ml) and the mixture heated at reflux for 6 h. After being cooled, the mixture was concentrated and then purified by Kugelrohr distillation (oven temp. 180 °C, 0.3 mm Hg) to give the thioester **(2d)** (212 mg, 69 %) as an oil ν_{max} 1793, 1705 cm^{-1}; δ_H (60 MHz) 1.1 (6H, d, J = 7 Hz), 2.2–2.5 (1H, m), 5.3 (1H, d, J = 5 Hz), 7.3 (5H, s); *m/z* 306 (M^+), 169, 110 (PhSH), 109 (PhS).

***S*-Phenyl 2-Methanesulphonyloxy-3-methyl(thiobutanoate) (2e)**: The oxirane **(3c)** (163 mg, 0.684 mmol) was dissolved in toluene (3 ml) and methanesulphonic acid (75 μl, 111 mg, 1.15 mmol) was added. The mixture was heated at reflux for 30 min, and then cooled. After evaporation of the solvent, the residue was purified by Kugelrohr distillation to give the thioester **(2e)** (150 mg, 76 %) as an oil (Found: M^+, 288.0507. $C_{12}H_{16}O_4S_2$ requires 288.0490); ν_{max} 1701, 1367, 1180 cm^{-1}; δ_H (60 MHz) 1.10 (3H, d, J = 7 Hz), 1.15 (3H, d, J = 7 Hz), 2.2–2.6 (1H, m), 3.05 (3H, s), 4.8 (1H, d, J = 5 Hz), 7.3 (5H, s); *m/z* 288 (M^+, 8 %), 188 (45), 151 (78), 109 (PhS).

General Procedure for the Preparation of 2-Fluoro Thioesters (8): The 2-nitro-2-phenylthio oxirane (3.68 mmol) was dissolved in toluene (15 ml), and boron trifluoride etherate (0.68 ml, 5.53 mmol) was added. The reaction mixture was stirred for 12 h at r.t. and then treated with saturated aqueous sodium bicarbonate (30 ml). The aqueous layer was separated and extracted with petrol (30 ml) and dichloromethane (10 ml). The combined organic extracts were dried

and concentrated to give the 2-fluoro thioester (**8**). Purification by flash chromatography was possible using petrol/dichloromethane (3:1) as eluent, but generally led to some decomposition.

***S*-Phenyl 2-Fluoro(thiopropanoate) (8a):** an oil (Found: M^+, 184.0378. C_9H_9FOS requires 184.0358); ν_{max} 1705, 1483, 1445, 1155, 1090, 1073, 970 cm^{-1}; δ_H (200 MHz) 1.635 (3H, dd, J_H = 6.8, J_F = 24 Hz), 5.13 (1H, dq, J_F = 49, J_H = 6.8 Hz), 7.45 (5H, s); *m/z* 184 (M^+, 50 %), 110 (PhSH, 100), 109 (PhS).

***S*-Phenyl 2-Fluoro(thiopentanoate) (8b):** an oil (Found: M^+, 212.0680. $C_{11}H_{13}FOS$ requires 212.0671); ν_{max} 1705, 1482, 1445, 1145, 1075 (br), 1025 cm^{-1}; δ_H (200 MHz) 0.98 (3H, t, J = 7.3 Hz), 1.49–1.65 (2H, m), 1.79–2.04 (2H, m), 5.01 (1H, ddd, J_F = 49, J = 5.2, 6.1 Hz), 7.42 (5H, s); *m/z* 212 (M^+), 110 (PhSH, 100 %), 109 (PhS).

***S*-Phenyl 2-Fluoro-3-methyl(thiobutanoate) (8c):** an oil (Found: M^+, 212.0637. $C_{11}H_{13}FOS$ requires 212.0671); ν_{max} 1703, 1442, 1137, 1082, 1008 cm $^{-1}$; δ_H (200 MHz) 1.15 (3H, dd, J = 0.5, 6.8 Hz), 1.07 (3H, d, J = 7 Hz), 2.14–2.36 (1H, m), 4.77 (1H, dd, J_F = 49, J_H = 3.8 Hz), 7.38 (5H, s); *m/z* 212 (M^+, 15 %), 110 (PhSH, 100), 109 (PhS, 53).

***S*-Phenyl 2-Fluoro(thioheptanoate) (8e):** an oil (Found: M^+, 240.0996. $C_{13}H_{17}FOS$ requires 240.0984); ν_{max} 1704, 1479, 1465, 1142, 1079 cm^{-1}; δ_H (200 MHz) 0.91 (3H, t, J = 6.8 Hz), 1.27–1.37 (4H, m), 1.46–1.61 (2H, m), 1.82–2.06 (2H, m), 5.05 (1H, ddd, J_F = 49.5, J_H = 5.4, 6.6 Hz), 7.44 (5H, s); *m/z* 240 (M^+, 60 %), 110 (PhSH, 100), 109 (60).

***S*-Phenyl 2-Fluoro(thiooctanoate) (8f):** an oil (Found: M^+, 254.1114. $C_{14}H_{19}FOS$ requires 254.1141); ν_{max} 1705, 1478, 1440, 1072 cm^{-1}; δ_H (200 MHz) 0.90 (3H, t, J = 6.5 Hz), 1.27–1.53 (6H, m), 1.54–1.65 (2H, m), 1.82–2.06 (2H, m), 5.05 (1H, dt, J_F = 49.3, J_H = 5.9 Hz), 7.44 (5H, s); *m/z* 254 (M^+, 47 %), 110 (PhSH, 100), 109 (80).

1-Fluoro-1-phenylthiocarbonyl cyclohexane (8h): an oil (Found: M^+, 238.0839. $C_{13}H_{15}FOS$ requires 238.0828); ν_{max} 1703, 1557, 1442, 1162, 1133 cm^{-1}; δ_H (200 MHz) 1.48–1.97 (10H, m), 7.34 (5H, s); *m/z* 238 (M^+, 45 %), 191 (50), 110 (PhSH, 100), 109 (75).

Phenylthiophenylethanoic acid (9): The oxirane (**3g**) (223.4 mg, 0.82 mmol) was dissolved in toluene (7 ml) and the solution cooled to −10 °C, before boron trifluoride etherate (0.15 ml, 173 mg, 1.22 mmol) was added. The mixture was kept at 4 °C for 15 h, and then aqueous sodium bicarbonate (3 ml) was added. The mixture was extracted with petrol (5 ml), and the aqueous layer was then acidified with hydrochloric acid (1 *M*). The acidified aqueous layer was then extracted with ethyl acetate (2 x 10 ml), and the combined extracts were dried and concentrated to yield the acid (**9**) (130 mg, 65 %) as a crystalline solid, m.p. 99–100 °C (lit.[39] 100 °C). The spectral data for (**9**) were identical to those in the literature.[39]

Reaction of Oxirane (3c) with $(Bu_2CuCN)Li_2$: n-Butyllithium (1.74 ml, 1.32 *M*, 2.3 mmol) was added dropwise to a suspension of dry CuCN (103 mg, 1.15 mmol) in dry THF (20 ml) at −50 °C. The solution was stirred at −50 °C for 6 min, and then the oxirane (**3c**) (0.25 g, 1.05

mmol) in THF (10 ml) was added slowly. The mixture was stirred for 25 min between -50 to -40 °C and then quenched with aqueous ammonium chloride (10 %, 10 ml). The organic layer was separated, and the aqueous layer extracted with ethyl acetate (2 x 20 ml). The combined organic extracts were dried and concentrated. Flash chromatography of the residue using petrol/ethyl acetate (4:1) as eluent gave 1-nitro-1-(phenylthio)-2-propanol (113 mg, 45 %), identified by comparison with published data,[5] and by conversion to 3-methyl-1-nitro-1-phenylthio-1-butene (**1c**) using the published procedure.[5,6]

***S*-Phenyl 2-Hydroxy-3-methyl(thiobutanoate) (11):** A solution of the oxirane (**3c**) (120 mg, 0.5 mmol) and triphenylphosphine (133 mg, 0.5 mmol) in toluene (1 ml) was heated to reflux for 1 h. An initial exotherm was observed. The reaction mixture was cooled, and then solvent evaporated. The residue was purified by flash chromatography using petrol/ethyl acetate (5:1) as eluent to give the thioester (**11**) (44 mg, 42 %) as an oil (Found: M^+, 210.0701. $C_{11}H_{14}O_2S$ requires 210.0714); ν_{max} 3520, 1705 cm^{-1} ; δ_H (200 MHz) 0.96 (3H, d, J = 6.8 Hz), 1.11 (3H, d, J = 6.9 Hz), 2.18-2.33 (1H, m), 2.81 (1H, br. d, J = 3.5 Hz), 4.25 (1H, br. t), 7.43 (5H, s); δ_C (50.3 MHz) 15.6, 19.3, 33.0, 82.2, 127.1, 129.4, 129.6, 134.8, 201.8; *m/z* 210 (M^+), 182, 110 (PhSH), 109 (PhS).

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