Reactivity in eliminative cleavage of activated four-membered rings. The behaviour of 3-hydroxythietane derivatives

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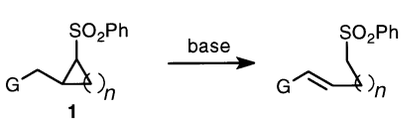
3-Hydroxythietane derivatives undergo retro-aldol ring fission in aqueous sodium hydroxide at a rate determined by the substituent (H or Ph) at the 3 position and by the oxidation state of sulfur. Reactions occur between 4 × 10^4 and 5 × 10^5 times faster than for the open chain analogues. These rate accelerations correlate with an expression of strain energy between 41% and 33% compared with approximately 26% for alkene-forming eliminations of cyclobutanes. These differences, together with the differences in relative sensitivities to α-phenyl substitution and uniformly positive values of entropies of activation for 3-hydroxythietane derivatives, suggest a greater degree of ring cleavage in the transition structure for thietanes than for cyclobutanes. Ring fission is, however, accompanied by concomitant protonation of the leaving carbon group as evidenced by the isotope discrimination value of 1.7 for reaction of 3e. 3-Hydroxythietane itself does not undergo retro-aldol ring cleavage but rather anionic polymerisation to yield polymer 9a.

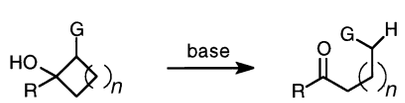
Introduction

The effect of strain on reactivity is a very familiar but rather poorly quantified phenomenon inviting questions such as: how much strain is harnessed on going from initial to transition structure and hence affects reactivity? Is the effect of strain on reactivity dependent on the reaction type and/or transition structure? In spite of the importance of strained systems in chemical synthesis,[1] materials chemistry[2] and biology[3] relatively little attention has been paid to quantification of strain effects and examination of the transition structures of the (often unusual) reactions that strained systems display. We[4] and others[5] have examined a variety of systems involving both strain release and strain increase in the relevant transition structures. The pattern which emerges is that four-membered rings, albeit of strain comparable with three-membered rings, both form[6] and open[7,8] much less readily with reactivity ratios up to 10^{10} being recorded.[7b] The ability to predict the extent of strain effects particularly, of course, for reactions for which transition structures are not well described, is still very limited. Calculations have been able to reproduce experimental results with astonishing accuracy in simple systems.[7b]

Our earlier work on the effect of strain on ring fission reactions used two systems **1** and **2** for alkene and carbonyl forming eliminations respectively (Scheme 1).



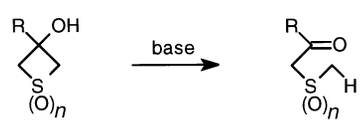
G = CN and SO_2Ph
n = 1 and 2



2a R = H, G = H, *n* = 1
b R = Ph, G = H, *n* = 1
c R = H, G = SPh, *n* = 1 (*cis*)
d R = H, G = SO_2Ph, *n* = 1 (*cis*)

Scheme 1

For system **1**, the three *versus* four reactivity ratio of typically 10^4 could be understood satisfactorily[7a] in terms of analysis of the components of the excess enthalpy differential for each of the ring systems and their relaxation as the ring opened. This was simply not possible for system **2** in which the huge (10^{10}) differentials between three and four membered rings could not be related to any simple picture of the transition structure and the dispersal of strain on ring fission.[7b] Against this background, we wished to examine the behaviour of a much more reactive system in which carbonyl-forming ring fission is involved. We chose the 3-hydroxythietane series **3** (Scheme 2)



3a R = H, *n* = 0
b R = Ph, *n* = 0
c R = H, *n* = 1 (*cis*)
d R = H, *n* = 1 (*trans*)
e R = Ph, *n* = 1
f R = H, *n* = 2
g R = Ph, *n* = 2

4

Scheme 2

in the expectation that leaving group stability (and hence, presumably, reactivity) would be greatly enhanced and that the leaving group stability could be tuned by alteration of the oxidation state of sulfur. An additional aspect of this system was that it also offered the opportunity to examine the timing of leaving group protonation *versus* ring fission as a function of the relative stabilities of the carbon leaving groups.

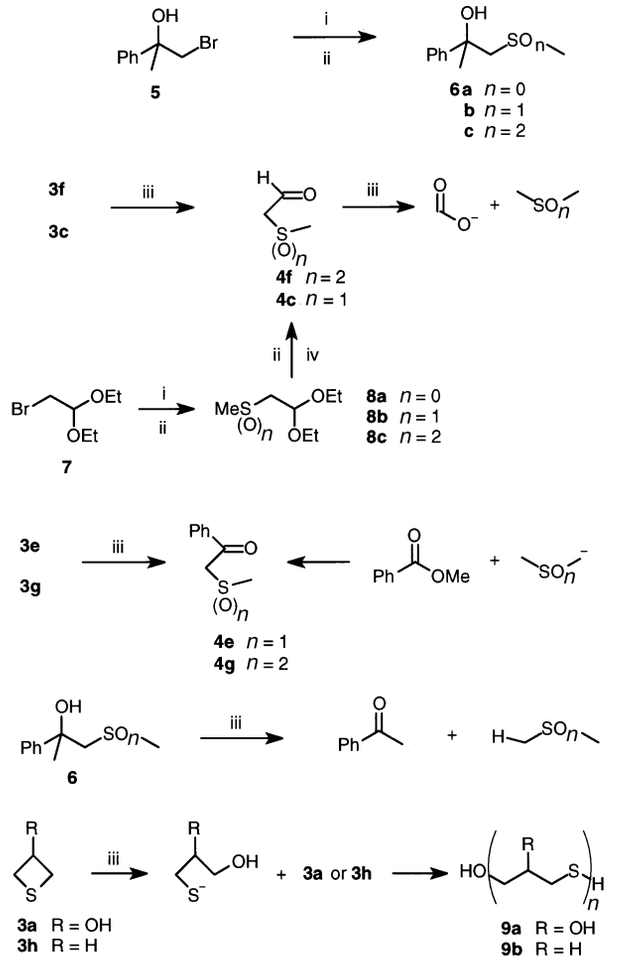
Results

Synthesis

Thietanes **3a**,[9] **3b**,[10] **3f**[9] and **3g**[10] have been described previously. The *cis* sulfoxide **3c** was separated from the diastereoisomeric mixture of sulfoxides obtained by oxidation of **3a** while the *trans* isomer **3d** was generated *in situ* from the acetoxy derivative.[11] Oxidation of **3b** gave **3e**, the *cis* isomer, only. The open chain series **6** were prepared by reaction of methanethiolate ion with bromo alcohol **5** and subsequent oxidation.

Reactions of 3-hydroxythietanes with base

All of the 3-hydroxythietanes, except **3a**, on treatment with



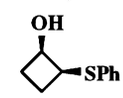
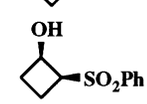
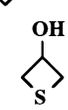
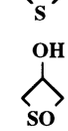
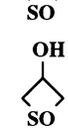
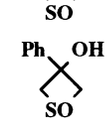
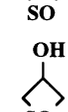
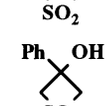
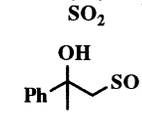
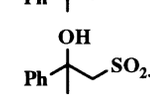
Scheme 3 *Reagents:* i, MeSNa/EtOH; ii, oxidation; iii, aq. NaOH; iv, H^+

aqueous sodium hydroxide underwent ring opening by retro-aldol carbonyl forming elimination to give aldehydes or ketones which were isolated directly or characterised as 2,4-dinitrophenylhydrazones (Scheme 3). Thietane dioxide **3f** yielded the conjugate base of the aldehyde sulfone **4f** which slowly decomposed to dimethyl sulfone and formate ion[12] both characterised *in situ* by ^{13}C NMR spectroscopy. Enolate **4f** was also characterised directly as its 2,4-dinitrophenylhydrazone, identical to that obtained from bromoacetal **7**. Thietane oxide **3c** behaved similarly and formate ion and dimethyl sulfoxide were again identified by ^{13}C NMR spectroscopy. Efforts to isolate the aldehyde **4c** directly or as the 2,4-dinitrophenylhydrazone were unsuccessful. Thietane oxide **3e** gave the keto sulfide **4e** isolated directly and identical to that obtained from dimsyl† anion and ethyl benzoate. The corresponding sulfone **3g** likewise gave the sulfonyl ketone **4g** also obtained from dimethylsulfonyl anion and ethyl benzoate. The open chain analogues **6b** and **6c** similarly underwent retro-aldol cleavage to yield acetophenone mixed, in the case of **6c**, with an equimolar amount of dimethylsulfone.

The thietane **3a** did not undergo base-catalysed ring fission but rather yielded a polymeric product whose ^{1}H NMR spectrum was consistent with poly(3-hydroxythietane) **9a**. This product is consistent with nucleophilic ring fission of **3a** producing the much more nucleophilic thiolate which then propagates the chain anionic polymerisation. This sequence is not followed for any of the other thietane derivatives for which the sulfur anion would be much less carbon-nucleophilic and the alternative carbanions much more stabilised. The polymerisation of thietane **3h** itself with thiolates has been reported[13] and we observed that prolonged treatment of **3h** with aqueous sodium hydroxide at high temperature provided a viscous gel whose spectral characteristics were consistent with polythietane **9b**.

† Dimsyl = methyl sulfoxide.

Table 1 Retro-aldol cleavage of cyclobutanols **2**, thietanols **3** and open-chain analogues **6**

Compound	Structure	k (25 °C)[a]	$\Delta H^{\ddagger}$[b]	$\Delta S^{\ddagger}$[c]
2a[d]		1.3×10^{-12}	132 (±1)	−29 (±4)
2b[d]		1.1×10^{-12}	125 (±1)	−54 (±4)
2c[d]		9.0×10^{-8}	117 (±2)	+12 (±5)
2d[d]		7×10^{-1}[e]	—	—
3a		5×10^{-6}[f]	—	—
3c *cis*		5.33×10^{-5}	103 (±2)	+17 (±5)
3d *trans*[g]		4.87×10^{-5}	109 (±4)	+37 (±2)
3e *cis*		6.27×10^{-3}	88 (±1)	+8 (±3)
3f		1.40×10^{-2}	99 (±1)	+50 (±1)
3g		6.22×10^{-1}	94 (±0.1)	+67 (±0.6)
6b		1.21×10^{-8}[h]	96 (±2)	−74 (±5)
6c		1.57×10^{-5}	87 (±1)	−46 (±3)

[a] $dm^3\ mol^{-1}\ s^{-1}$ in NaOH–H_2O. [b] kJ mol^{-1}. [c] J $K^{-1}\ mol^{-1}$. [d] Values from ref. 7*b*. [e] Minimum value. [f] Not elimination, see text. [g] Generated *in situ* from *O*-acetyl compound. [h] Estimated from reactions in sealed tubes in the temperature range 67–97 °C.

Kinetics

Kinetics of reactions of the hydroxythietanes and open-chain analogues with large excesses of aqueous sodium hydroxide were followed by UV spectroscopy and obeyed a first-order rate law in each case. The $>10^7$ span of reactivity required the use of stop-flow apparatus at one extreme and sealed tubes at elevated temperatures at the other. Results are in Table 1.

Isotope discrimination

The release of a strongly basic carbon leaving group in the ring fission reactions examined offered the opportunity to determine an isotope effect and isotope discrimination factor pertaining to the protonation of the carbanion leaving group. Reactions

of thietane **3e** were performed in NaOH–H_2O and NaOD–D_2O and provided an observed inverse kinetic isotope effect of $k_{OH^-/OD^-} = 0.72$. By repeating the same reaction in varying mixtures of H_2O and D_2O and calculating the proportion of deuterium incorporation (mass spectrometry and ^{1}H NMR spectroscopy) relative to the proportion of deuteriated solvent, an isotope discrimination value of 1.7 ± 0.2 was obtained.

Discussion

The results we have obtained for the reactivities of a series of hydroxythietanes are to be considered in relation to the following questions. (i) How does reactivity in ring fission, occurring with release of strain in the four-membered ring, compare with that in the open-chain (unstrained) analogues? (ii) How does the inherent reactivity of thietanols compare with that of the cyclobutanols studied earlier, taking into account the carbanion stabilising substituents in each case? (iii) How is strain energy expressed in terms of rate acceleration in each case?

The results obtained in this work are presented in Table 1, together with our earlier data on cyclobutanols. With respect to the effect of strain on reactivity, the comparison of **3e** with **6b** gives an acceleration of 5.2×10^5 while **3g** reacts at 4.0×10^4 the rate of **6c**. Assuming strain in thietanes (81.9 kJ mol^{-1}) to be relatively unaffected by substituent[14] and oxidation state, the strain energy is expressed to the extent of about 41% for the sulfoxide and 33% for the sulfone. By comparison, 26% of strain energy is estimated to be expressed in the acceleration of alkene-forming eliminations of cyclobutanes[7a] and 46% for the corresponding reaction of cyclopropanes.[7a] We have previously postulated that this difference between cyclopropane and cyclobutane ring fission is due to alternative modes of strain release as a consequence of the different ring strain components in each case.[7a] This argument assumed an equivalent degree of bond fission in the transition state for each reaction and could accurately account for the large rate variance observed; a variance which cannot be simply explained by the differential in ring strain (*ca.* 6 kJ mol^{-1}). In comparing thietanes with cyclobutanes, however, the assumption of equivalently positioned transition states does not appear valid, as evidenced by the differential sensitivity towards α-phenyl substitution. The heat of formation of a phenyl ketone is *ca.* 15 kJ mol^{-1} greater than that of the benzylic isomer[15] and so the almost equivalent reaction rates of ring fission for cyclobutanol **2a** and its α-phenyl counterpart **2b** suggests an early transition state. By comparison, the rate enhancements of sulfoxide **3e** and sulfone **3g**, relative to unsubstituted **3c** and **3f**, are 117 and 44, respectively, which suggests a more advanced transition state. This interpretation is supported by the larger contribution of strain energy to acceleration and by the uniformly positive values of the entropies of activation.

Perhaps unsurprisingly, the inherently less reactive sulfoxide **3e** shows the larger acceleration by comparison with the sulfone **3f** and it is noticeable that the ring fission reaction is a factor of 10 less sensitive to the sulfur oxidation state than the open chain comparator. The open-chain comparators show a rate-ratio corresponding to a $\Delta\Delta E_A$ of about 18 kJ mol^{-1}. The ΔpK_a (sulfoxide–sulfone) value[16] of 4 units if fully expressed would give a $\Delta\Delta E_A$ value of about 23 kJ mol^{-1}.

In relation to the mechanism of ring fission in the thietanes, reaction of sulfoxide **3e** showed an observed inverse kinetic isotope effect of $k_{OH^-/OD^-} = 0.72$. Reactions are effectively zero-order in base (Table 1) and so this is not a primary kinetic isotope effect. This value is the balance of opposing effects on changing from H_2O to D_2O which increases the 'internal nucleophilicity' of the alkoxide ion while decreasing the rate of protonation on the leaving carbon atom. Although thietane oxides are much more reactive than the corresponding unsubstituted cyclobutanols as a result of the carbanion-stabilising group, the isotope discrimination value of 1.7 ± 0.2 demonstrates that the reaction does not generate a free carbanion but rather that ring fission occurs with concomitant protonation of the leaving carbon and points to enforced catalysis of the overall reaction as seen by Thibblin and Jencks in the cleavage of cyclopropanols.[17]

Finally, the 24.3 kJ mol^{-1} lower strain energy of thietane relative to cyclobutane is reflected in the decreased reactivity of thietane **3a** relative to cyclobutyl sulfide **2c** and thietane dioxide **3f** relative to phenylsulfone **2d** which bear essentially equivalent carbanion stabilising groups. Indeed, the low reactivity of thietane **3a** towards retro-aldol ring fission is such that anionic polymerisation is the exclusive process.

Experimental

General instructions have been given.[4d] Stopped flow kinetics were measured with a Durrum Gibson spectrometer.

Synthesis of substrates

3-Hydroxythietane **3a**,[9] 3-phenyl-3-hydroxythietane **3b**,[10] 3-hydroxythietane 1,1-dioxide **3f**,[9] 3-phenyl-3-hydroxythietane 1,1-dioxide **3g**[10] and *trans*-3-acetoxythietane 1-oxide[11] were prepared as described previously.

3-Hydroxythietane 1-oxide 3c. Chloroperbenzoic acid (16.7 mmol) in dichloromethane (90 cm^3) was slowly added to a stirred solution of thietane **3a** (1.77 g, 16.7 mmol) in dichloromethane (90 cm^3) at 0 °C. After addition, the solution was stirred at 20 °C for 16 h and then cooled to −80 °C to precipitate *m*-chlorobenzoic acid. Filtration, evaporation of the dichloromethane and Kugelrohr distillation of the resulting oil (oven temp. 170 °C, 0.005 Torr) provided an isomeric mixture of **3c** and **3d** (77% yield) in the ratio 3:2 (Found: C, 34.0; H, 6.1. $C_3H_6O_2S$ requires C, 34.0; H, 5.7); **3c** δ_C(22.5 MHz; $CDCl_3$) 55.10 and 62.64; **3d** δ_C(22.5 MHz; $CDCl_3$) 60.04 and 63.93.[18] Radial chromatography on silica (chloroform as eluent) followed by crystallisation (chloroform–light petroleum) yielded **3c**, mp 80.5–81 °C.

***cis*-3-Hydroxy-3-phenylthietane 1-oxide 3e.** Thietane **3b** was oxidised with 30% hydrogen peroxide in the presence of sodium tungstate dihydrate as previously reported for the conversion of **3a** to the corresponding dioxide.[9] Approximately 30 min after peroxide addition, a white solid began to precipitate from the aqueous solution and was collected after a further 16 h at 20 °C. Two recrystallisations (ethanol–light petroleum) provided **3e** (47% yield), mp 159.5–160 °C (Found: C, 59.0; H, 5.8. $C_9H_{10}O_2S$ requires C, 59.3; H, 5.5); ν_{max}/cm^{-1} (KBr disc) 3275, 1209 and 1031; δ_H(90 MHz; CD_3OD) 3.61 (dd, 2 H), 4.39 (dd, 2 H), 4.81 (s, 1 H) and 7.48 (s, 5 H); δ_C(22.5 MHz; CD_3OD) 67.05 (C), 67.44 (CH_2), 125.40 (CH), 128.39 (CH), 129.17 (CH) and 144.50 (C).

1-Methylthio-2-phenylpropan-2-ol 6a. Bromoalcohol **5**[19] (10.9 g, 50.4 mmol) was added dropwise to a well stirred solution of sodium ethoxide (prepared from sodium, 2.5 g and absolute ethanol, 30 cm^3) saturated with methanethiol. The solution was heated for 1 h at 60 °C and stirred for a further 16 h at room temperature. It was then poured into water (60 cm^3) and extracted thoroughly with dichloromethane. Evaporation of the solvent and Kugelrohr distillation of the resulting oil (oven temp. 160 °C/0.45 Torr) provided the sulfide as a clear oil (83.4% yield) (Found: C, 65.7; H, 7.7. $C_{10}H_{14}OS$ requires C, 65.9; H, 7.7); δ_H(90 MHz; $CDCl_3$) 1.59 (s, 3 H), 1.85 (s, 3 H), 2.91 (AB q, 2 H), 3.24 (s, 1 H) and 7.12–7.60 (m, 5 H).

1-Methylsulfinyl-2-phenylpropan-2-ol 6b. Sodium periodate oxidation[11] of sulfide **6a** (0.5 g, 2.7 mmol) followed by extraction with dichloromethane provided the diastereoisomeric sulfoxides (0.54 g, 100% yield) in equal amounts. Recrystallisation (chloroform–light petroleum) provided one diastereoisomer (24% yield), mp 124–126 °C (Found: C, 60.8; H, 7.4. $C_{10}H_{14}O_2S$ requires C, 60.6; H, 7.1); ν_{max}/cm^{-1} (KBr disc) 3150 and 1005; δ_H(90 MHz; $CDCl_3$) 1.61 (s, 3 H), 2.52 (s, 3 H), 3.12 (s, 2

H), 4.78 (s, 1 H) and 7.15–7.57 (m, 5 H). Despite successive recrystallisations of the diastereoisomeric mixture, the other diastereoisomer could only be obtained 80% isomerically pure, as a clear oil; δ_H(90 MHz; $CDCl_3$) 1.74 (s, 3 H), 2.46 (s, 3 H), 3.08 (s, 2 H), 5.01 (s, 1 H) and 7.15–7.57 (m, 5 H).

1-Methylsulfonyl-2-phenylpropan-2-ol 6c. Hydrogen peroxide–tungstic acid oxidation[9] of sulfide **6a** followed by extraction with dichloromethane provided the sulfone **6c** as a clear oil (100% yield) after evaporation of the solvent under reduced pressure (Found: C, 56.2; H, 6.8. $C_{10}H_{14}O_3S$ requires C, 56.1; H, 6.6); ν_{max}/cm^{-1} (KBr disc) 3460, 1305 and 1117; δ_H(90 MHz; $CDCl_3$) 1.69 (s, 3 H), 2.45 (s, 2 H), 3.47 (AB q, 2 H), 4.31 (s, 1 H) and 7.20–7.65 (m, 5 H).

Characterisation of cleavage products

Cleavage of thietane dioxide 3f. Ring fission of this substrate in 1.0 mol dm^{-3} NaOH provided the intermediate β-sulfonyl enolate of **4f** (λ_{max}/nm = 232, ε/dm^3 mol^{-1} = *ca.* 14 500) which slowly decomposed to give dimethyl sulfate and sodium formate[12]; δ_C(22.5 MHz; 1 mol dm^{-3} NaOH–D_2O) 42.62 (CH_3SO_2-CH_3) and 171.91 ($NaHCO_2$). This intermediate was isolated as the 2,4-dinitrophenylhydrazone. Compound **3f** (50.8 mg, 0.42 mmol) was dissolved in 1.0 mol dm^{-3} NaOH solution (5 cm^3). After 10 min at 18 °C the reaction was quenched with a solution of 2,4-dinitrophenylhydrazine (0.25 g) and concentrated sulfuric acid (1 cm^3) in methanol (5 cm^3). Yellow–orange crystals precipitated immediately and after 10 min these were collected and recrystallised twice from ethanol to provide 71.8 mg (57.1% yield) of methylsulfonylacetaldehyde-2,4-dinitrophenylhydrazone (mp 201.5–202 °C) identified by comparison of the IR spectrum with an authentic sample (prepared as described below) and a mixed melting point.

1,1-Diethoxy-2-methylsulfonylethane 8c. A solution of 30% hydrogen peroxide (23.4 cm^3) containing ammonium molybdate (0.5 g) was slowly added to a well stirred solution of sulfide **8a**[20] (6.0 g, 37.0 mmol) in methanol (250 cm^3). The reaction mixture was stirred at room temperature for 16 h and then concentrated to approximately 50 cm^3 under reduced pressure, diluted with brine (50 cm^3) and extracted thoroughly with dichloromethane. The combined organic extracts were washed with 5% sodium hydrogen sulfite, dried (Na_2SO_4) and the solvent removed under reduced pressure. Kugelrohr distillation (oven temp. 160 °C, 0.2 Torr) provided 6.32 g (88.2% yield) of the sulfone **8c** as a clear oil which solidified (mp 24.5–25 °C) on standing (Found: C, 42.7; H, 8.4. $C_7H_{16}O_4S$ requires C, 42.8; H, 8.2); δ_H(90 MHz; $CDCl_3$) 1.22 (t, 6 H), 2.98 (s, 3 H), 3.27 (d, 2 H), 3.62 (m, 4 H) and 4.95 (t, J = 5.6 Hz, 1 H); δ_C(22.5 MHz; $CDCl_3$) 15.20 (CH_3), 42.49 (CH_3), 58.22 (CH_2), 62.89 (CH_2) and 98.11 (CH).

Methylsulfonylacetaldehyde-2,4-dinitrophenylhydrazone. Concentrated sulfuric acid (1.0 cm^3) was carefully added to a suspension of 2,4-dinitrophenylhydrazine (0.25 g) in methanol (5 cm^3). The solution was filtered and refluxed with sulfone **8c** (0.172 g) for 1 h. After being cooled in ice, the crude hydrazone was collected by vacuum filtration and recrystallised (ethanol) to provide 0.179 g (67.5% yield) of yellow–orange crystals (mp 203–204 °C) (Found: C, 35.9; H, 3.3; N, 18.4. $C_9H_{10}N_4O_6S$ requires C, 35.8; H, 3.3; N, 18.5); ν_{max}/cm^{-1} (KBr disc) 1616, 1336, 1306 and 1140.

Cleavage of sulfoxide 3c. Ring fission of this substrate in 1.0 mol dm^{-3} NaOH provided an enolate intermediate [(λ_{max}/nm = 235, ε/dm^3 mol^{-1} = *ca.* 3300[20]); δ_C(22.5 MHz; 1.0 mol dm^{-3} NaOH–D_2O) 40.11, 101.84 and 173.57] which slowly decomposed to dimethyl sulfoxide (δ_C 39.89) and sodium formate (δ_C 171.91). This data is consistent with the initial formation of **4c** enolate. Attempts to isolate the intermediate aldehyde directly or as the 2,4-dinitrophenylhydrazone were unsuccessful, as were attempts to prepare it independently by the acid-catalysed hydrolysis of the corresponding diethylacetal, **8b**.

Table 2 UV absorptions of products generated *in situ* from cleavage of **3** and **6** in 1.0 mol dm^{-3} NaOH solution

Substrate	λ_{max}/nm	ε/dm^3 mol^{-1}
3c, **3d**	235	3300
3e	287	7600
3f	232	14 500
3g	280	7300
6b	245	10 000
6c	245	10 000

Cleavage of sulfoxide 3e. This substrate (100 mg, 0.55 mmol) was dissolved in 1.5 mol dm^{-3} NaOH (4 cm^3) and after approximately 20 min at 18 °C the reaction was quenched with 1.0 mol dm^{-3} HCl (6 cm^3) and extracted with dichloromethane. The combined organic extracts were dried (Na_2SO_4) and evaporated to yield α-methylsulfinylacetophenone **4e** (96 mg, 96.0% yield), identified by comparison of the ^{1}H and ^{13}C spectra with those of an authentic sample (prepared from the reaction of dimsyl anion and ethyl benzoate[21]).

Cleavage of sulfone 3g. This substrate (51 mg, 0.26 mmol) was dissolved in 1.5 mol dm^{-3} NaOH (2 cm^3) and after approximately 2 min at 18 °C the reaction was quenched with 1.0 mol dm^{-3} HCl (3 cm^3) and extracted thoroughly with dichloromethane. The combined organic extracts were dried (Na_2SO_4) and evaporated to yield α-methylsulfonylacetophenone **4g** (51 mg, 100% yield), identified by comparison of the ^{1}H and ^{13}C spectra with those of an authentic sample (prepared from the reaction of dimethylsulfonyl anion and ethyl benzoate[22]).

Cleavage of sulfoxide 6b. This substrate (200 mg, 1.01 mmol) was sealed in a glass ampoule with 1.0 mol dm^{-3} NaOH (7 cm^3) at 130 °C. After 3 h the reaction was acidified with dilute HCl and extracted thoroughly with dichloromethane. The combined organic extracts were dried (Na_2SO_4) and evaporated to provide acetophenone (120 mg, 100% yield) [δ_H(90 MHz; $CDCl_3$) 2.55 (s, 3 H), 7.45 (m, 3 H) and 7.96 (m, 2 H)].

Cleavage of sulfone 6c. This substrate (150 mg, 0.70 mmol) in methanol (2 cm^3) was stirred with 1.5 mol dm^{-3} NaOH (2 cm^3) at 69 °C. After 1 h, the reaction was acidified with dilute HCl and extracted thoroughly with dichloromethane. The combined organic extracts were dried (Na_2SO_4) and evaporated to provide 150 mg of material which consisted of dimethyl sulfone [δ_H(90 MHz; $CDCl_3$) 2.95, s] and acetophenone in equal amounts.

Cleavage of sulfide 3a. This substrate (1.0 g) was refluxed in 3.0 mol dm^{-3} NaOH (11 cm^3). After 69 h the solution was acidified with dilute HCl and extracted thoroughly with dichloromethane. The combined organic extracts were dried (Na_2SO_4) and evaporated to yield 0.1 g of starting material. Insoluble in both the organic and aqueous phases was a clear, viscous gel (0.6 g); ν_{max}/cm^{-1} (KBr disc) 3350 (br); δ_C(22.5 MHz; [$^2H_6$]DMSO) 38.46 (CH_2) and 70.17 (CH). This data is consistent with the formation of polymer **9a**.

Cleavage of thietane 3h. Thietane (0.5 g) and 1.5 mol dm^{-3} NaOH (15 cm^3) were sealed in a glass ampoule and heated at 125 °C. After 18 h the heterogenous mixture was acidified with dilute HCl and extracted with dichloromethane. The combined organic extracts were dried (Na_2SO_4) and evaporated to yield a clear, viscous gel (0.3 g); δ_H(90 MHz; $CDCl_3$) 1.70 (m, 2 H) and 2.50 (t, 4 H); δ_C 29.11 (CH_2) and 30.80 (CH_2). This data is consistent with the formation of polymer **9b**.[13]

Kinetic measurements

With 1.0 mol dm^{-3} NaOH in the reference cell, substrate (sufficient to give a maximum absorbance of 1–1.5) was mixed with a large excess of 1.0 mol dm^{-3} NaOH and added to the thermostatted sample cell. Stop-flow mixing was required to measure the rate of reaction for sulfone **3g**. The corresponding reactions of **6b** required elevated temperatures and were performed in sealed ampoules. The increase of absorbance was monitored at the wavelengths indicated in Table 2. All reactions

obeyed a first-order rate equation and rate constants were, in general, the average of three reactions.

Isotope discrimination experiments

Sulfoxide **3e** (32 mg) was dissolved in 2.0 mol dm^{-3} NaOH (0.5 cm^3) containing either a 1:1 or 2:1 ratio of H_2O to D_2O. After 15 min at 20 °C the solution was quenched with 1.0 mol dm^{-3} HCl (1 cm^3) and extracted with dichloromethane. The organic extracts were combined, dried (Na_2SO_4) and the solvent removed under reduced pressure to provide deuteriated **4e** almost quantitatively. The procedure was then repeated with 1.0 mol dm^{-3} NaOH to remove deuterium incorporated into the methylene group. The proportion of deuterium incorporated into the methyl group was determined by mass spectrometry and by integration of the high field ^{1}H NMR spectrum.

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