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Organocatalytic sulfoxidation

Stuart C. Davidson,[a] Gabriel dos Passos Gomes,[b,c,d] Leah R. Kuhn,[b] Igor V. Alabugin,[b] Alan R. Kennedy[a] and Nicholas C. O. Tomkinson[a,*]

[a]Department of Pure and Applied Chemistry, WestCHEM, Thomas Graham Building, University of Strathclyde, 295 Cathedral Street, Glasgow, G1 1XL, U.K.

[b]Department of Chemistry and Biochemistry, Florida State University, Tallahassee, FL, 32306, USA.

[c]Department of Chemistry, University of Toronto, 80 St George St, Toronto, Ontario M5S 3H6, Canada.

[d] Department of Computer Science, University of Toronto, 214 College St., Toronto, Ontario M5T 3A1, Canada.

Nicholas.Tomkinson@strath.ac.uk

Abstract

Treatment of a sulfide with a catalytic amount of a 1,3-diketone in the presence of silica sulfuric acid as a co-catalyst and hydrogen peroxide (50% aq) as the stoichiometric oxidant leads to the corresponding sulfoxide product. The reaction is effective for diaryl, aryl-alkyl and dialkyl sulfides and is tolerant of oxidisable and acid sensitive functional groups. Investigations have shown that the *tris*-peroxide **2**, formed on reaction of pentane-2,4-dione with hydrogen peroxide under acidic reaction conditions, can oxidise two equivalents of sulfide using the exocyclic peroxide groups whereas the endocyclic peroxide remains intact. Calculations provide a mechanism consistent with experimental observations and suggest the reaction proceeds *via* an initial acid catalysed ring opening of a protonated *tris*-peroxide prior to oxygen transfer to a sulfur nucleophile.

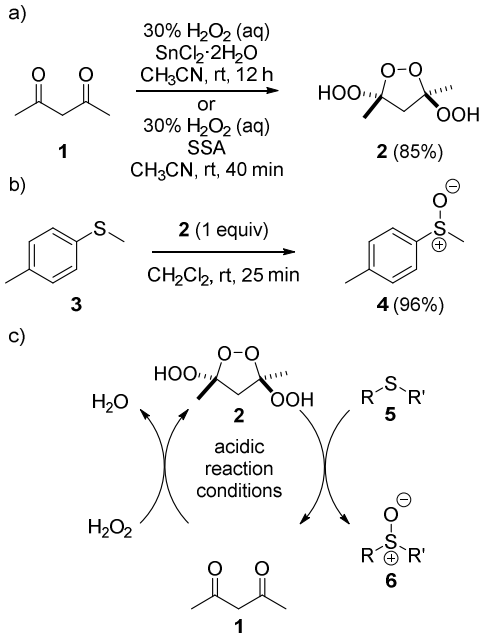
Introduction

Peroxides possess a rich and fascinating chemistry.[1] Of particular interest is their high reactivity and ability to act as effective reagents in a number of important oxidative transformations. One challenging aspect of peroxide chemistry is the high energy nature of these compounds.[2] Whilst this renders peroxides synthetically versatile, safety considerations have often limited the uptake and development of their chemistry.

The design and development of new catalytic procedures is a fundamental challenge for the synthetic community. Of specific relevance is the invention of benign procedures to perform functional group transformations in a clean and efficient manner.[3] The *in-situ* catalytic generation of active peroxide reagents represents a particularly useful way in which to harness the synthetic power of this important functional group whilst avoiding the challenges associated with handling and manipulating these compounds.

Perhydrates represent a readily accessible and versatile peroxide derivative of both ketones and aldehydes.[4] This functionality reversibly forms under a range of reaction conditions, allowing formation of an activated peroxide functionality *in situ*. For example, it has been shown that perhydrates of hexafluoroacetone, and its derivatives, can be used in a series of catalytic oxidation procedures including the epoxidation of alkenes,[5] the Bayer-Villager oxidation of ketones[6] and the oxidation of heteroatoms such as nitrogen[7] and sulfur.[8] More recently, Kokotos reported the use of trifluoroacetophenone in the presence of acetonitrile and hydrogen peroxide in a series of reactions including the oxidation of alkenes[9] as well as heteroatoms such as silicon,[10] nitrogen[11] and sulfur.[12] Mechanistic studies showed that the Payne reaction conditions[13] were key to the success of these transformations, through the generation of a highly reactive acetonitrile hydrogen peroxide adduct within the catalytic cycle.[14]

The high oxygen content perhydrate derivative **2**, formed by the condensation of three molecules of hydrogen peroxide with acetylacetone, was first reported by Reich in 1961[15] and was later characterised spectroscopically by Milas and co-workers.[16] 30 years later, Azarifar reported **2** to be an effective reagent for the oxidation of sulfides to sulfoxides.[17] In this report, the peroxide **2** was generated in one-step from acetyl acetone **1** by treatment with aqueous hydrogen peroxide in the presence of tin(II) chloride dihydrate and was assigned the *trans*-configuration based on ^{1}H NMR spectroscopy. Subsequent work showed this peroxide could also be prepared using silica-sulfuric acid (SSA)[18] (90% yield) providing a more benign and recyclable catalyst for peroxide generation.[19] Of particular note with this work were the rapid reaction times, mild conditions and selectivity for the sulfoxide product with no over oxidation to the corresponding sulfone being noted. Repeating this work, we were able to prepare the peroxide **2** (85%) and found this peroxide to be an effective reagent for the oxidation of 4-tolyl methyl sulfide **3** to the corresponding sulfoxide **4** (96%) (Scheme 1).



Scheme 1. a) Synthesis of acetylacetone derived peroxide **2**. b) Application of peroxide **2** in sulfoxidation. c) Potential catalytic cycle for sulfoxidation.

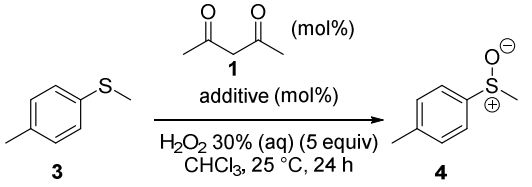
Based upon the findings of Azarifar, we saw potential to develop a novel catalytic oxidation procedure (Scheme 1c). This involved the *in-situ* generation of active peroxide **2** through the acid catalysed reaction of acetylacetone **1** with a source of hydrogen peroxide. To achieve success, we required the reaction of a substrate sulfide **5** with the peroxide reagent **2** to be compatible with the acidic conditions necessary to form the perhydrate. Within this manuscript we describe the development of this novel catalytic process, exploration of the scope of the transformation and the development of an understanding of the nature of the catalytically active species.

Results and discussion

Our investigation began with the oxidation of 4-tolyl methyl sulfide **3**, in the presence of H_2O_2 (30% aq, 5.0 equiv), acetylacetone **1** (100 mol%) and $SnCl_2 \cdot 2H_2O$ (20 mol%) (Table 1, entry 1). After stirring in chloroform at 25 °C for 24 h, the sulfoxide **4** was prepared in 98% yield as determined by a calibrated HPLC analysis. This result showed the sulfoxidation could occur under acidic conditions. We therefore performed the reaction in the presence of substoichiometric amounts of **1** (20 mol%) and $SnCl_2 \cdot 2H_2O$ (20 mol%), which led to the sulfoxide product **4** in 77% yield providing a novel catalytic procedure (entry 2). SSA also proved to be an effective co-catalyst for the transformation (entry 3; 54%) providing a more benign, easily removable and recyclable additive. Increasing the amount of SSA added to the

reaction mixture led to a more efficient transformation (entries 4 and 5). A brief examination of the reaction concentration suggested that whilst lower concentrations were less effective (entry 6; 54%) conducting the process at 0.4 M provided the product in 88% yield (entry 7). Whilst some background reaction was apparent within the transformation in the absence of **1** (entry 8; 20%), overall, this provided a simple and effective process for the oxidation of 4-tolyl methyl sulfide **3** to the sulfoxide **4** catalysed by the commercial diketone **1** under mild reaction conditions.

Table 1. Initial optimisation of reaction conditions.



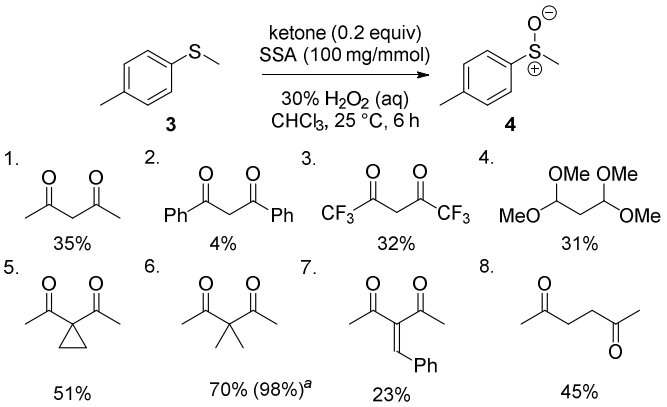
entry	**1** (mol%)	additive (mol%)	[ ] M	**4** (% yield)[a]
1	100	$SnCl_2 \cdot 2H_2O$ (20)	0.2	98
2	20	$SnCl_2 \cdot 2H_2O$ (20)	0.2	77
3	20	SSA (30)	0.2	54
4	20	SSA (60)	0.2	70
5	20	SSA (140)	0.2	89
6	20	SSA (60)	0.1	54
7	20	SSA (60)	0.4	88
8	0	SSA (60)	0.4	20

[a]Determined by HPLC analysis

In order to optimise the ketone used within the transformation a number of dicarbonyl compounds were examined, a selection of which are shown in Table 2, that revealed some key features of the conversion of **3** to **4**. Electron withdrawing groups were introduced α- to the reactive ketone functionality to increase the electrophilicity of the carbonyl groups. Whilst trifluoromethyl groups had little effect on the reaction outcome (entry 3; 32%), phenyl groups proved detrimental to the process (entry 2; 4%). Believing the origin of this observation to reside in the steric hindrance around the ketone, we examined a bis-acetal (entry 4; 31%) which showed no improvement in reactivity. Postulating that the presence of a readily enolisable proton in the diketone would reduce the electrophilicity of the carbonyl groups we sought to prevent this from happening (entries 5–7). Whilst benzylidene substitution was ineffective (entry 7; 23%), cyclopropylidene (entry 5; 51%) and dimethyl substitution (entry 6; 70%)[20] proved significantly more effective. A 1,4 diketone (entry 8; 45%) was more effective than a 1,3-diketone (entry 1; 35%), however, further optimisation of

this structure did not reach the efficiency of entry 6. Changing to 50% H_2O_2 (aq) resulted in complete conversion of the substrate sulfide **3** to the corresponding sulfoxide **4** in 2.5 h.

Table 2. Effect of ketone structure.

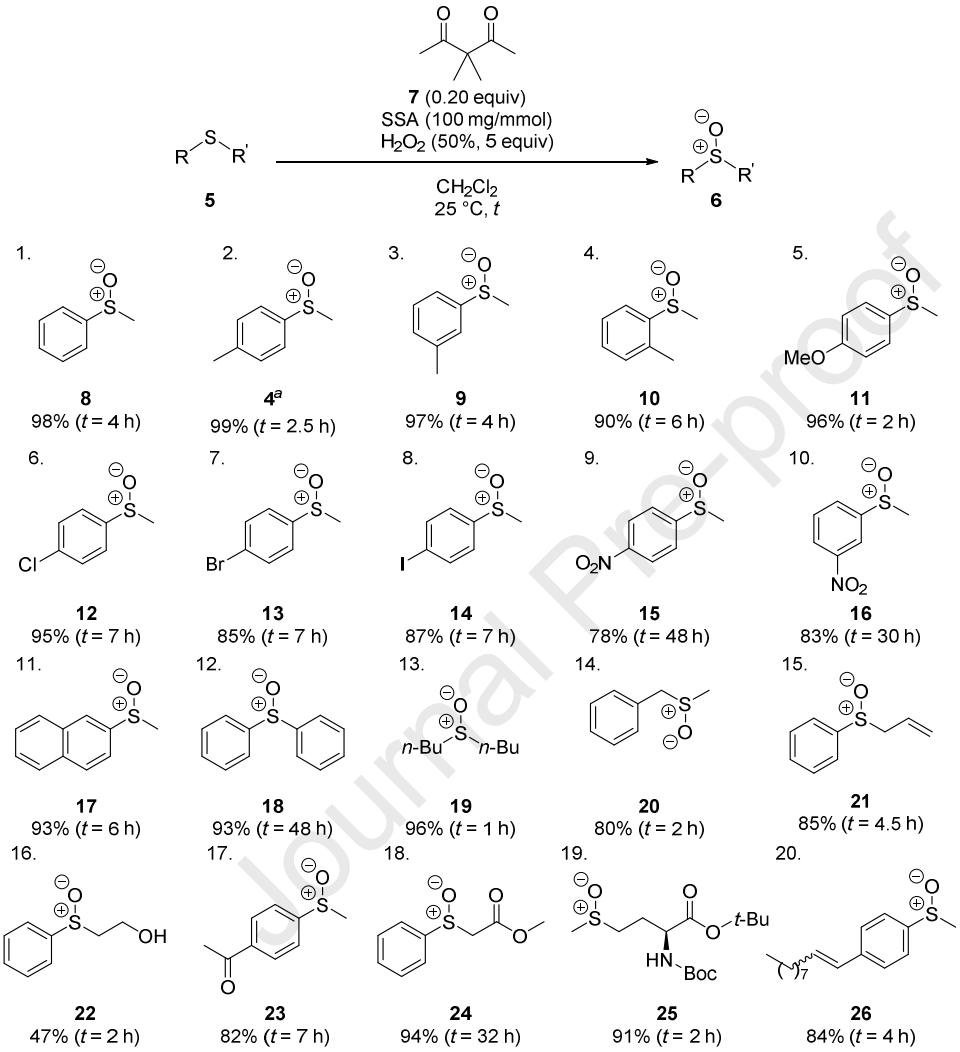


[a]Reaction carried out with 50% H_2O_2 (aq) for 2.5 h.

Having developed effective conditions for the oxidation of 4-tolyl methyl sulfide **3** we went on to examine the scope of the procedure (Scheme 2). The reaction was effective for aryl-alkyl (entries 1–11, 14–18 and 20), diaryl (entry 12) and dialkyl (entries 13 and 19) sulfides. Reactions with electron rich sulfides (*e.g.* entries 5 and 13) proceeded considerably faster than reactions with electron deficient sulfides (*e.g.* entry 9). The reaction rate was also affected by steric interactions with larger substituents around the sulfide (*e.g.* entry 12; 48 h) reacting considerably slower than sulfides with smaller substituents (*e.g.* entry 1; 4 h). Substitution of the aryl group was tolerated in all positions (entries 2–4) and functional groups including ether, nitro, chloride, bromide, iodide, ketone, alcohol, alkene, carbamate and ester did not significantly alter the reaction outcome (entries 5–10 and 15–20). Acid sensitive groups such as methyl and *tert*-butyl esters (entries 18 and 19) and *N*-Boc carbamate (entry 19) remained unaffected during the oxidation and oxidisable groups including alkene (entries 15 and 20), alcohol (entry 16) and ketone (entry 22) were compatible with the process. Conducting the reaction of 4-tolyl methyl sulfide on a 10 mmol scale lead to the expected sulfoxide **4** in a 96% isolated yield after the same reaction time of 2.5 h (*cf.* entry 2) suggesting this catalytic process should be scalable. Overall, this simple and effective catalytic oxidation occurs under mild reaction conditions, on a variety of substrates in excellent yield and selectivity with no apparent over oxidation to the corresponding sulfone, a challenge associated with many sulfur oxidation procedures. Oxidation to the sulfone did prove possible through the use of extended reaction times. For example, reaction of 4-tolyl methyl sulfide with H_2O_2 (50% aq, 5 equiv), SSA (100 mg $mmol^{-1}$) at 25 °C for 7 days gave

the corresponding sulfone in 85% isolated yield (see experimental section for full details), confirming that the second oxidation step was significantly slower using the catalytic procedure described.

Scheme 2. Substrate scope.

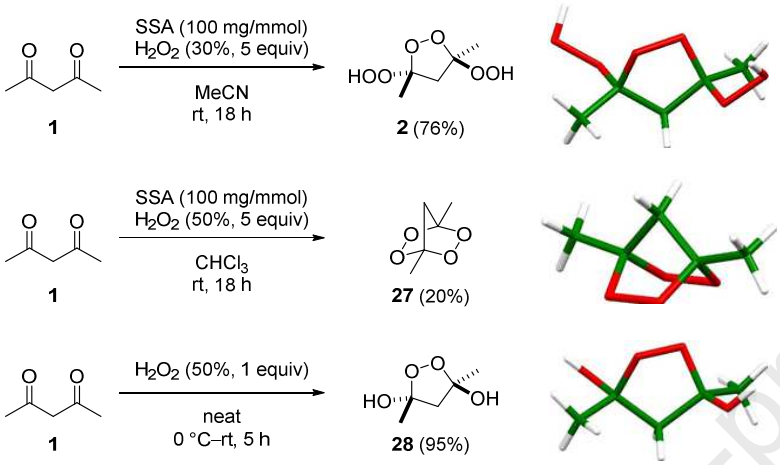


[a]96% isolated yield after 2.5 h when conducted on a 10 mmol scale.

To gain an understanding of the transformation we prepared and characterised a series of peroxides we considered could be the reactive species within the catalytic cycle (Scheme 3). *Tris*-peroxide **2** was made in 76% isolated yield by the reaction of an acetonitrile solution of acetylacetone with H_2O_2 (30% aq) in the presence of SSA (100 mg/mmol). Conducting the reaction in chloroform with H_2O_2 (50% aq) allowed isolation of the tetraoxane **27** in 20% yield. The endocyclic *mono*-peroxide **28** was prepared in 95% yield by the reaction of **1** with 50% aq H_2O_2 in the absence of an organic solvent (95%).[16] The structures of each of these peroxides (**2**, **27** and **28**) were confirmed by single crystal X-ray analysis which showed **2** and **28** unequivocally had the *trans*-relationship of their exocyclic oxygen substituents. Exposure

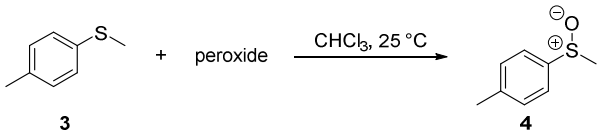
of each of these peroxides to the catalytic reaction conditions (SSA 100 mg/mmol, H_2O_2 50 mol% (aq) 5 equiv, $CDCl_3$, 25 °C) and monitoring by ^1H NMR spectroscopy showed each of these species to be in equilibrium.

Scheme 3. Preparation and single crystal X-ray structure of potential reactive species.



Reaction of either the endocyclic *mono*-peroxide **28** or the tetraoxane **27** with 4-tolyl methyl sulfide **3** in chloroform under anhydrous reaction conditions resulted in recovery of both unreacted sulfide and peroxide in each case (Table 3, entries 1 and 2). This suggests that these peroxides were not the active species within our catalytic cycle. In stark contrast, reaction of the *tris*-peroxide **2** (1.0 equiv) with 4-tolyl methyl sulfide **3** in anhydrous chloroform gave the sulfoxide **4** in 92% after 6 h (entry 3). More interestingly, conducting the reaction in the presence of 0.5 equiv peroxide **2** gave the sulfoxide product in 79% (entry 4), in the presence of 0.33 equiv peroxide **2** the product **4** was isolated in 60% yield (entry 5) and in the presence of 0.2 equiv peroxide the product **4** was formed in 39% (entry 6). These results suggest that the *tris*-peroxide **2** transfers two equivalents of oxygen to the sulfide substrate **3**. We believe that it is the exocyclic peroxide groups contained within **2** which oxidise the substrate. This is consistent with the results using peroxides **27** and **28** which contain endocyclic peroxide groups and which were unreactive to the sulfide nucleophile **3**.

Table 3. Oxidation of sulfide **3** with peroxides **2**, **27** and **28**.

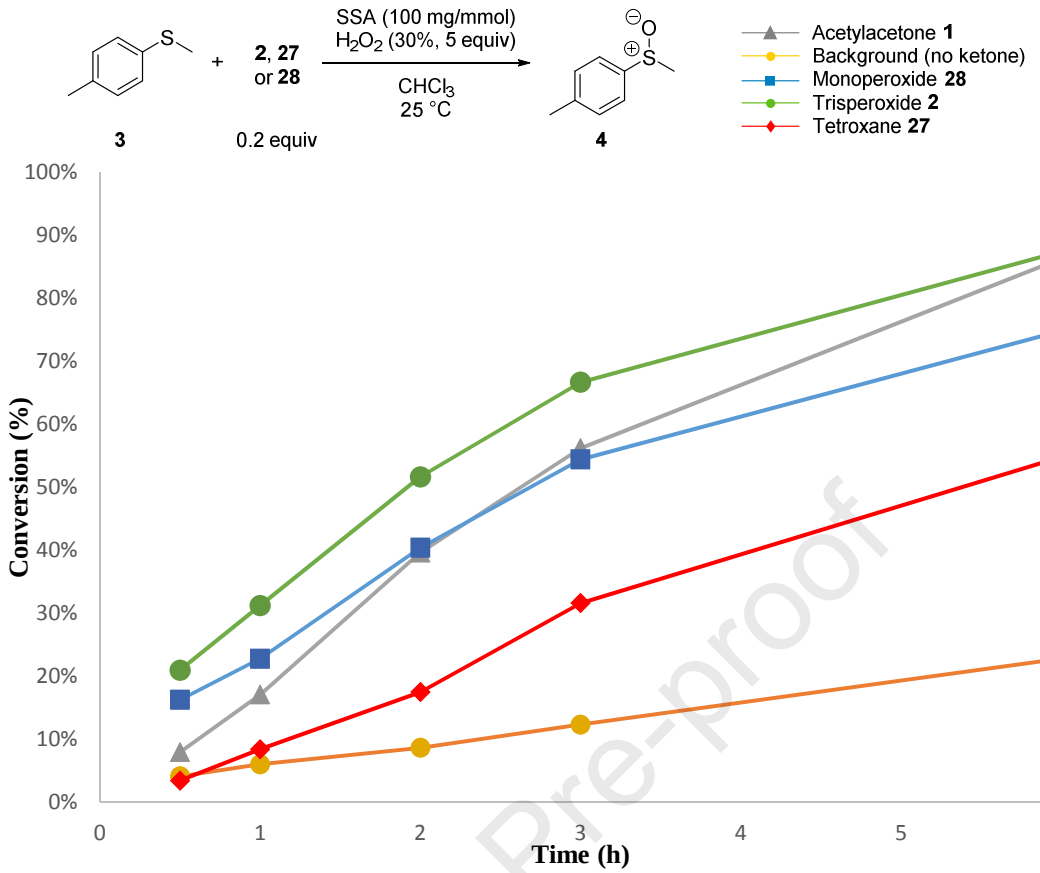


3 **4**

entry	peroxide (mol%)	time (h)	**4** (% yield)
1	**28** (100)	6	<5
2	**27** (100)	6	<5
3	**2** (100)	6	92
4	**2** (50)	6	79
5	**2** (33)	6	60
6	**2** (20)	6	39

Along with the *tris*-peroxide **2**, both the *mono*-endocyclic peroxide **28** and the tetraoxane **27** were shown to be catalytically competent within the sulfoxidation process (Scheme 4). Using **2** or **27** or **28** (20 mol%) in chloroform in the presence of SSA (100 mg/mmol) and H_2O_2 (30% aq, 5 equiv) converted the sulfide **3** into the corresponding sulfoxide **4**. The oxidation with *tris*-peroxide **2** was faster than the reaction with acetyl acetone **1**, the endocyclic *mono*-peroxide **28** or the tetroxane **27**. We believe this is because the active peroxide is added directly to the reaction mixture rather than being prepared *in situ*. The initial rate of reaction with tetroxane **27** was substantially slower than the reaction using **2** or **28**, however, over time this rate improved. We believe this is due to the equilibration of tetroxane **27** and the active *tris*-peroxide **2** under the reaction conditions. The oxidation of 4-tolyl methyl sulfide **3** using *tris*-peroxide **2** was found to obey second order kinetics with a first order dependence in both **2** and **3** (k = 3.17 M^{-1} s^{-1}, 25 °C, $CHCl_3$) (see the supporting information for full details).

Scheme 4. Relative activity of peroxides **2**, **27** and **28** within the catalytic sulfoxidation process.

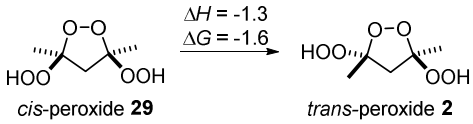


Within the optimised catalytic procedure (**7** 0.2 equiv, SSA 100 mg/mmol, 50% H_2O_2 5 equiv, CH_2Cl_2, 25 °C), on completion of the reaction, we were unable to gain evidence for the starting diketone **7** through ^{1}H NMR spectroscopy on the crude reaction mixture, presumably due to the presence of excess hydrogen peroxide within the reaction mixture, which led to the formation of further peroxide derivatives. In order to recover the diketone **7**, we treated the crude reaction mixture from a sulfoxidation procedure with sodium sulfate and then triphenylphosphine, continuing stirring for 18 h. This resulted in a 49% recovery of the diketone **7** after aqueous workup and purification by column chromatography (see supporting information for full details). Repeating this protocol with polymer supported triphenyl phosphine[21] returned the diketone in a similar 51% yield (see supporting information for full details). We believe this reduced recovery of the diketone **7** is primarily due to a pinacol rearrangement of the active peroxide leading to pivalic acid and acetic acid as described by Payne.[22]

To support and rationalise the synthetic work we examined the *tris*-peroxide **2** using DFT calculations at the (SMD=$CHCl_3$)/M06-2X(D3)/6-311++G(d,p)/int=ultrafine, level of theory. The *tris*-peroxide can exist in two diastereomeric forms, the *cis*-isomer **29** and the *trans*-isomer **2**. The *trans*-isomer **2** was found to be 1.6 kcal mol^{-1} lower in energy than the

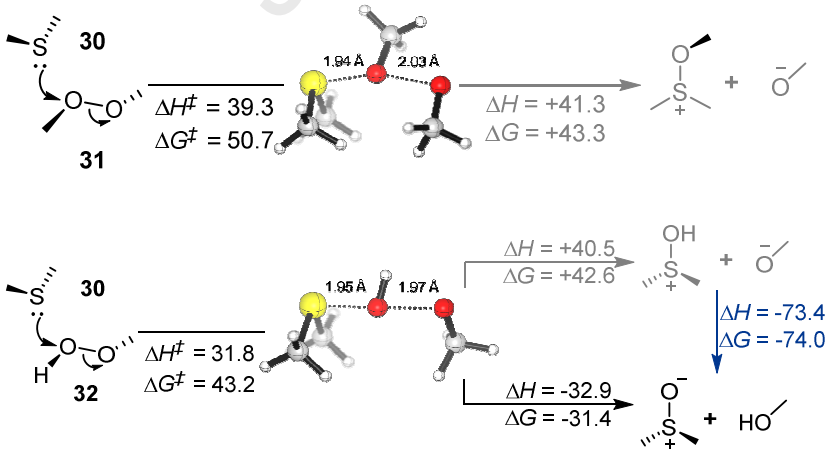
corresponding *cis*-isomer **29** (Scheme 5). Given this difference, and the observed reactivity of **2** with a sulfide, all subsequent calculations were performed with this isomer.

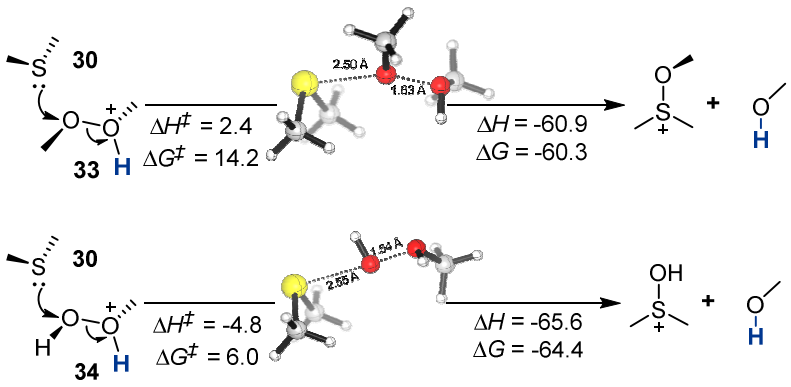
Scheme 5. Stability of *tris*-peroxide isomers.



To investigate the importance of acid catalysis in peroxide reactions, we compared the S_N2 reactions of dimethyl sulfide **30** with MeOOMe **31** and with MeOOH **32**, i.e., the parent organic peroxide and the parent hydroperoxide (Scheme 6). For the neutral peroxides, the reactions are >40 kcal/mol endergonic and, as a consequence, have an even higher activation barrier. This thermodynamic penalty results from the unfavorable charge separation associated with the formation of the two charged products. However, the charge-separated products of the MeOOH/Me_2S reaction can "neutralise" each other *via* a highly exergonic proton transfer. These simple calculations illustrate the intrinsic preference of hydroperoxides over peroxides as the O-transfer agents and suggest that a path that avoids charge separation should be intrinsically much more favorable. Indeed, the reactions of dimethyl sulfide **30** with the two protonated peroxides **33** or **34** proceed through the much lower (6–14 kcal/mol) barriers and are highly exergonic.

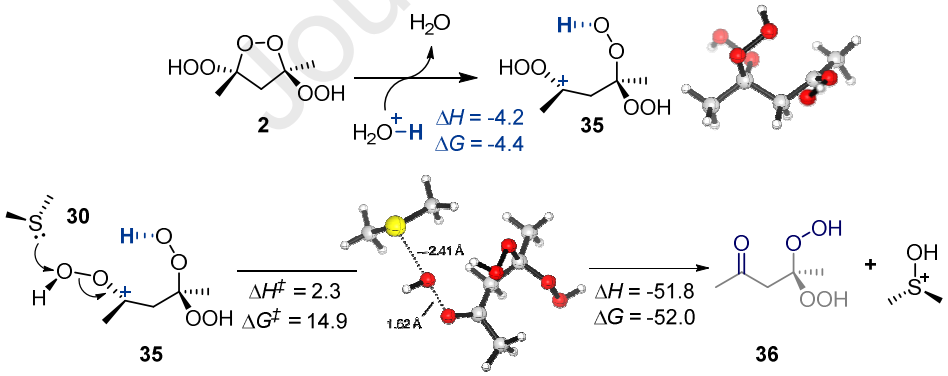
Scheme 6. Reactions of dimethyl sulfide **30** with neutral and protonated parent organic peroxide and hydroperoxide.





Guided by these results, we investigated sulfoxidation pathways starting from a protonated peroxide species. Interestingly, protonation of an endocyclic oxygen atom of the peroxide **2** leads to a ring-opened peroxycarbenium ion **35** (Scheme 7). Although peroxycarbenium ions are generally relatively high energy reactive intermediates,[23] this particular cation is more stable than the isomeric cyclic peroxonium ion, perhaps due to the strain relief associated with the ring opening. The subsequent reaction of the peroxycarbenium cation with the sulfide nucleophile is > 50 kcal/mol exergonic and forms the protonated sulfoxide product through a low activation barrier (~15 kcal/mol). The bis-peroxide **36** can quickly close into a cyclic bis-peroxide[24] prior to undergoing a second similar O-transfer reaction.

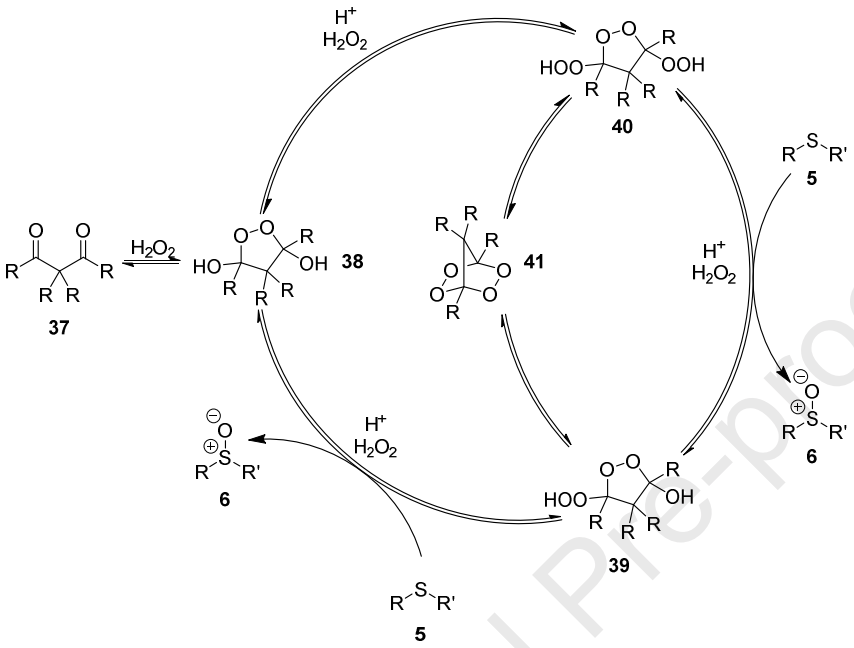
Scheme 7. Protonation of endocyclic oxygen in peroxide **2** leads to a favourable reaction with the sulfide nucleophile.



Based upon these mechanistic insights we propose the reaction is proceeding through the catalytic cycle outlined in Scheme 8. Reaction of hydrogen peroxide with a diketone **37** leads to the endocyclic *mono*-peroxide **38**. This can react with either one or two equivalents of hydrogen peroxide to give the reactive species **39** or **40**. Loss of water from **39** or hydrogen peroxide from **40**, under the acidic reaction conditions, followed by intramolecular cyclisation leads to the tetroxane **41**, which is not active in the sulfoxidation process. Each of

the peroxides **38**, **39**, **40** and **41** are in a dynamic equilibrium under the reaction conditions. Reaction of an exocyclic peroxide from **39** or **40** with a sulfide nucleophile leads to the oxidised product **6**.

Scheme 8. Proposed catalytic cycle.



Conclusions

In summary, we have developed a novel catalytic procedure for the oxidation of sulfides to sulfoxides. Treatment of a sulfide with a catalytic amount of a diketone in the presence of a silica sulfuric acid co-catalyst and hydrogen peroxide (50% aq) leads to the corresponding sulfoxide. Investigations have shown that the *tris*-peroxide **2** can oxidise two equivalents of sulfide using the exocyclic peroxide groups whereas endocyclic peroxides are not reactive within this transformation. Electronic structure calculations suggest that oxidation of the substrate proceeds *via* an initial acid catalysed ring opening of the protonated *tris*-peroxide **2** prior to oxygen transfer to the sulfur nucleophile. Peroxide **2** has also been used as a stoichiometric reagent in a number of alternative transformations including the oxidation of alcohols to ketones,[25] oxidative cleavage of alkenes,[26] halogenation of aromatic rings,[27] epoxidation of α,β-unsaturated carbonyl compounds,[28] oxidation of heterocycles[29] and the synthesis of nitriles.[30] Ongoing work within the laboratory to apply our knowledge to these transformations will be reported in due course.

Experimental section

General information: Commercially available solvents and reagents were used without further purification. Flash chromatography was carried out using Merck Kieselgel 60 H silica or Matrex silica 60. Analytical thin layer chromatography was carried out using aluminium-backed plates coated with Merck Kieselgel 60 GF254 that were visualised under UV light (at 254 and/or 360 nm). Reactions were heated using an oil bath. Nuclear magnetic resonance (NMR) spectra were recorded in $CDCl_3$ at 18 °C unless otherwise stated and were reported in ppm; *J* values were recorded in Hz and multiplicities were expressed by the usual conventions. Low-resolution mass spectra (MS) were determined using atmospheric pressure chemical ionisation (APCI) unless otherwise stated. ES refers to electrospray ionisation, CI refers to chemical ionisation (methane) and EI refers to electron ionisation. High-resolution mass spectra were obtained courtesy of the EPSRC Mass Spectrometry Service at University of Wales, Swansea, U.K. using the ionisation methods specified. *In vacuo* refers to evaporation at reduced pressure using a rotary evaporator and diaphragm pump, followed by the removal of trace volatiles using a vacuum (oil) pump. Melting points were determined with a Gallenkamp SG92 melting point apparatus and are uncorrected.

Synthesis of SSA

Chlorosulfonic acid (13.5 mL, 203 mmol) was added *via* dropping funnel, under a constant flow of N_2, over 1.5 hours to stirred silica (60 g). The exhaust from the reaction vessel was run through 4 M NaOH to quench the HCl gas generated. The silica was allowed to stir for a further hour to give silica sulfuric acid (SSA) (77 g). Titration with NaOH gave a H^+ concentration of 5.6 mmol/g.

General procedure for catalytic sulfoxidation

$H_2O_{2(aq)}$ (50%, 285 µL, 5.00 mmol, 5 equiv) was added to a solution of sulfide (1.00 mmol, 1 equiv), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol, 0.2 equiv) and SSA (100 mg) in $CHCl_3$ (2.5 mL). The resulting biphasic solution was stirred at 25 °C for the time indicated and monitored by TLC or HPLC. The reaction was filtered into saturated $Na_2S_2O_{5(aq)}$ (2 mL) and H_2O (10 mL) and the solid washed with EtOAc (3 × 5 mL). The aqueous layer was further extracted with EtOAc (2 × 15 mL). The combined organics were washed with brine (10 mL), dried with $MgSO_4$ and filtered. The solvent was removed *in vacuo* and the crude material was then purified by silica gel chromatography (petrol:EtOAc) to obtain the target products. All oxidations were run in duplicate and presented results are an average of 2 runs.

1-Methyl-4-(methylsulfinyl)benzene 4[31]

Reaction of methyl(*p*-tolyl)sulfane (135 µL, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 2.5 hours according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 1:1) to give the *title compound* **7** (Run 1: 152 mg, 0.99 mmol, 99%, Run 2: 153 mg, 0.99 mmol, 99%, Average Yield: 99%) as an orange oil which crystallised to a yellow solid upon cooling; mp 40–42 °C [Lit = 52–54 °C][31] IR (ATR)/cm^{-1} 2991, 2922, 1496, 1040; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 2.70 (s, 3H), 2.41 (s, 3H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.7, 141.6, 130.2, 123.7, 44.1, 21.5; LRMS (GCMS-CI) *m/z* 154.9 $[M+H]^+$.

(Methylsulfinyl)benzene 8[32]

Reaction of thioanisole (117 µL, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 4 hours according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 1:1) to give the *title compound* **8** (Run 1: 139 mg, 0.99 mmol, 99%, Run 2: 136 mg, 0.97 mmol, 97%, Average Yield: 98%) as a yellow oil; IR (ATR)/cm^{-1} 3055, 2997, 1444, 1035; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.62 (m, 2H), 7.56–7.47 (m, 3H), 2.72 (s, 3H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.8, 131.2, 129.5, 123.6, 44.0; LRMS (GCMS-CI) *m/z* 140.9 $[M+H]^+$.

1-Methyl-3-(methylsulfinyl)benzene 9

Reaction of methyl(*m*-tolyl)sulfane (138 mg, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 4 hours according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 1:1) to give the *title compound* **9** (Run 1: 152 mg, 0.99 mmol, 99%, Run 2: 144 mg, 0.94 mmol, 94%, Average Yield: 97%) as a colourless oil; IR (ATR)/cm^{-1} 2993, 2921, 1415, 1042; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.40 (app d, *J* = 5.1 Hz, 2H), 7.32–7.28 (m, 1H), 2.71 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.6, 139.8, 132.0, 129.3, 123.9, 120.7, 44.1, 21.6; LRMS (GCMS-CI) *m/z* 154.9 $[M+H]^+$; HRMS (ASAP) calculated for $C_8H_{11}OS$ $[M+H]^+$ 155.0531, found 155.0532.

1-Methyl-2-(methylsulfinyl)benzene 10

Reaction of methyl(*o*-tolyl)sulfane (138 mg, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 6 hours according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 1:1) to give the *title compound* **10** (Run 1: 139 mg, 0.90 mmol, 90%, Run 2: 137 mg, 0.89 mmol, 89%, Average Yield: 90%) as a colourless oil; IR (ATR)/cm^{-1} 3051, 2978, 1474, 1035; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.45 (app td, *J* = 7.6, 0.8 Hz, 1H), 7.39 (td, *J* = 7.4, 1.5 Hz, 1H), 7.20 (app d, *J* = 7.4 Hz, 1H), 2.68 (s, 3H), 2.37 (s, 3H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 134.1, 130.9, 130.8, 127.6, 123.1, 42.2, 18.2; LRMS (GCMS-CI) *m/z* 154.9 $[M+H]^+$; HRMS (ASAP) calculated for $C_8H_{11}OS$ $[M+H]^+$ 155.0531, found 155.0532.

1-Methyl-4-(methylsulfinyl)benzene 11[33]

Reaction of (4-methoxyphenyl)(methyl)sulfane (154 mg, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 2 hours according to the General Procedure. The crude material was purified by silica gel chromatography (EtOAc) to give the *title compound* **11** (Run 1: 165 mg, 0.97 mmol, 97%, Run 2: 161 mg, 0.95 mmol, 95%, Average Yield: 96%) as a colourless solid; mp 47–49 °C [Lit = 43–47 °C][33]; IR (ATR)/cm^{-1} 2989, 2958, 1249, 1022; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dt, *J* = 8.9, 2.9 Hz, 2H), 7.03 (dt, *J* = 8.9, 2.9 Hz, 2H), 3.86 (s, 3H), 2.70 (s, 3H). ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 136.8, 125.6, 115.0, 55.7, 44.2; LRMS (GCMS-CI) *m/z* 171.0 $[M+H]^+$.

1-Chloro-4-(methylsulfinyl)benzene 12[33]

Reaction of (4-chlorophenyl)(methyl)sulfane (130 µL, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 7 hours according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 1:1) to give the *title compound* **12** (Run 1: 164 mg, 0.94 mmol, 94%, Run 2: 165 mg, 0.95 mmol, 95%, Average Yield: 95%) as a colourless oil; IR (ATR)/cm^{-1} 3081, 2913, 1478, 1040, 742; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dt, *J* = 8.9, 2.3 Hz, 2H), 7.51 (dt, *J* = 8.9, 2.2 Hz, 2H), 2.72 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.4, 137.4, 129.8, 125.1, 44.2; LRMS (GCMS-CI) *m/z* 174.9 $[M+H]^+$.

1-**Bromo-4-(methylsulfinyl)benzene 13**

Reaction of (4-bromophenyl)(methyl)sulfane (203 mg, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 7 hours according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 1:1) to give the *title compound* **13** (Run 1: 188 mg, 0.86 mmol, 86%, Run 2: 180 mg, 0.83 mmol, 83%, Average Yield: 85%) as a colourless solid; mp 89–91 °C; IR (ATR)/cm^{-1} 2989, 2911, 1422, 1038, 817; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (dt, *J* = 8.9, 2.3 Hz, 2H), 7.52 (dt, *J* = 9.0, 2.2 Hz, 2H), 2.72 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 132.7, 125.6, 125.3, 44.1.; LRMS (GCMS-CI) *m/z* 218.9 [M(Br^{79})+H]; HRMS (ASAP) calculated for $C_7H_8OS(Br^{79})$ $[M+H]^+$ 218.9475, found 218.9479.

1-Iodo-4-(methylsulfinyl)benzene 14 Reaction of (4-iodophenyl)(methyl)sulfane (250 mg, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 7 hours according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 1:1) to give the *title compound* **14** (Run 1: 230 mg, 0.86 mmol, 86%, Run 2: 231 mg, 0.87 mmol, 87%, Average Yield: 87%) as a colourless solid; mp 117–119 °C; IR (ATR)/cm^{-1} 2989, 2911, 1422, 1033, 811; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dt, *J* = 8.8, 2.1 Hz, 2H), 7.39 (dt, *J* = 8.8, 2.2 Hz, 2H), 2.71 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.9, 138.6, 125.3, 97.5, 44.1; LRMS (GCMS-CI) *m/z* 266.9 $[M+H]^+$; HRMS (ASAP) calculated for C_7H_8OSI $[M+H]^+$ 266.9341, found 266.9344.

1-(Methylsulfinyl)-4-nitrobenzene 15[32]

Reaction of methyl(4-nitrophenyl)sulfane (169 mg, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 48 hours according to the General Procedure. The crude material was purified by silica gel chromatography (EtOAc) to give the *title compound* **15** (Run 1: 147 mg, 0.79 mmol, 79%, Run 2: 142 mg, 0.76 mmol, 76%, Average Yield: 78%) as an off-white solid; mp 156–158 °C [Lit = 153–155°C][32]; IR (ATR)/cm^{-1} 3101, 2922, 1517, 1342, 1048; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (dt, *J* = 9.1, 2.2 Hz, 2H), 7.84 (dt, *J* = 9.1, 2.3 Hz, 2H), 2.79 (s, 3H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.4, 149.7, 124.8, 124.6, 44.0.; LRMS (GCMS-CI) *m/z* 185.9 $[M+H]^+$.

1-(Methylsulfinyl)-3-nitrobenzene 16

Reaction of methyl(3-nitrophenyl)sulfane (169 mg, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 30 hours according to the General Procedure. The crude material was purified by silica gel chromatography (EtOAc) to give the *title compound* **16** (Run 1: 154 mg, 0.83 mmol, 83%, Run 2: 153 mg, 0.83 mmol, 83%, Average Yield: 83%) as a pale yellow solid; mp 122–124 °C; IR (ATR)/cm^{-1} 3094, 2922, 1521, 1348, 1072; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (app t, *J* = 1.9 Hz, 1H), 8.36 (ddd, *J* = 8.2, 2.2, 1.0 Hz, 1H), 8.01 (ddd, *J* = 7.8, 1.5, 1.1 Hz, 1H), 7.76 (t, *J* = 7.9 Hz, 1H), 2.80 (s, 3H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.9, 148.8, 130., 129.41, 125.9, 119.1, 44.2.; LRMS (GCMS-CI) *m/z* 185.9 $[M+H]^+$; HRMS (ASAP) calculated for $C_78_7NO_3S$ $[M+H]^+$ 186.0225, found 186.0222.

1-Methyl-4-(methylsulfinyl)benzene 17[33]

Reaction of methyl(naphthalen-2-yl)sulfide (174 mg, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 6 hours according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 1:1) to give the *title compound* **17** (Run 1: 170 mg, 0.89 mmol, 89%, Run 2: 182 mg, 0.96 mmol, 96%, Average Yield: 93%) as a colourless solid; mp 113–115 °C [Lit = 92–99 °C][33]; IR (ATR)/cm^{-1} 3058, 2991, 1420, 1035; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 1.4 Hz, 1H), 7.99 (d, *J* = 8.6 Hz, 1H), 7.97–7.89 (m, 2H), 7.63–7.58 (m, 3H), 2.80 (s, 3H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.9, 134.6, 133.1, 129.8, 128.7, 128.2, 128.0, 127.5, 124.2, 119.6, 44.0; LRMS (LCMS-ESI) *m/z* 191.0 $[M+H]^+$.

Sulfinyldibenzene 18[31]

Reaction of diphenylsulfide (165 µL, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 48 hours according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 3:1) to give the *title compound* **18** (Run 1: 182 mg, 0.90 mmol, 90%, Run 2: 192 mg, 0.95 mmol, 95%, Average Yield: 93%) as a colourless solid; mp 71–73 °C [Lit = 67–68 °C][31]; IR (ATR)/cm^{-1} 3051, 1442, 1024; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68–7.62 (m, 4H), 7.50–7.42 (m, 6H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.73, 131.21, 129.48, 124.94, 77.16.; LRMS (GCMS-CI) *m/z* 203.0 $[M+H]^+$.

1-(Butylsulfinyl)butane 19[31]

Reaction of di-*n*-butylsulfide (175 µL, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 1 hour according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 1:1) to give the *title compound* **19** (Run 1: 155 mg, 0.96 mmol, 96%, Run 2: 154 mg, 0.95 mmol, 95%, Average Yield: 96%) as a colourless oil; IR (ATR)/cm^{-1} 2960, 2932, 1022; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.72–2.57 (m, 4H), 1.80–1.68 (m, 4H), 1.56–1.39 (m, 4H), 0.95 (t, *J* = 7.4 Hz, 6H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 52.3, 24.7, 22.2, 13.8.; LRMS (GCMS-CI) *m/z* 163.0 $[M+H]^+$.

((Methylsulfinyl)methyl)benzene 20[33]

Reaction of benzyl(methyl)sulfane (135 µL, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 2 hours according to the General Procedure. The crude material was purified by silica gel chromatography (EtOAc) to give the *title compound* **20** (Run 1: 120 mg, 0.78 mmol, 78%, Run 2: 126 mg, 0.82 mmol, 82%, Average Yield: 80%) as a colourless solid; mp 61–63 °C [Lit = 53–59 °C][33]; IR (ATR)/cm^{-1} 3034, 2967, 1498, 1037; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.27 (m, 5H), 4.06 (d, *J* = 12.8 Hz, 1H), 3.92 (d, *J* = 12.8 Hz, 1H), 2.45 (s, 3H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.3, 130.2, 129.2, 128.6, 60.5, 37.5.; LRMS (LCMS-ESI) *m/z* 155.1 $[M+H]^+$.

(Allylsulfinyl)benzene 21[33]

Reaction of allyl(phenyl)sulfane (150 µL, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 4.5 hours according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 3:1) to give the *title compound* **21** (Run 1: 141 mg, 0.85 mmol, 85%, Run 2: 139 mg, 0.84 mmol, 84%, Average Yield: 85%) as a colourless oil; IR (ATR)/cm^{-1} 3055, 2980, 1636, 1446, 1040; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62–7.58 (m, 2H), 7.55–7.47 (m, 3H), 5.65 (ddt, *J* = 17.6, 10.2, 7.5 Hz, 1H), 5.33 (app d, *J* = 10.1, 1H), 5.19 (dq, J = 17.0, 1.2 Hz, 1H), 3.57 (ddq, *J* = 12.8, 7.5, 0.5 Hz, 1H), 3.51 (ddq, *J* = 12.8, 7.5, 0.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.1, 131.2, 129.2, 125.4, 124.5, 124.0, 61.0; LRMS (LCMS-ESI) *m/z* 167.0 $[M+H]^+$.

2-(Phenylsulfinyl)ethan-1-ol 22

Reaction of of 2-(phenylthio)ethan-1-ol (135 µL, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 2 hours according to the General Procedure. The crude material was purified by silica gel chromatography (EtOAc) to give the *title compound* **22** (Run 1: 74 mg, 0.44 mmol, 44%, Run 2: 84 mg, 0.49 mmol, 49%, Average Yield: 47%) as a colourless oil; IR (ATR)/cm^{-1} 3341, 2924, 1446, 1020; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.63 (m, 2H), 7.58–7.50 (m, 3H), 4.17 (ddd, *J* = 11.8, 8.7, 2.9 Hz, 1H), 4.04 (ddd, *J* = 12.3, 5.4, 3.9 Hz, 1H), 3.27 (bs, 1H), 3.19 (ddd, *J* = 13.6, 8.7, 3.8 Hz, 1H), 2.87 (ddd, *J* = 13.6, 5.7, 3.0 Hz, 1H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.1, 131.4, 129.6, 124.1, 57.9, 57.5; LRMS (LCMS-ESI) *m/z* 171.0 $[M+H]^+$.

1-(4-(Methylsulfinyl)phenyl)ethan-1-one 23 Reaction of 1-(4-(methylthio)phenyl)ethan-1-one (166 mg, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 7 hours according to the General Procedure. The crude material was purified by silica gel chromatography (EtOAc) to give the *title compound* **23** (Run 1: 148 mg, 0.81 mmol, 81%, Run 2: 150 mg, 0.82 mmol, 82%, Average Yield: 82%) as a white solid; mp 114–116 °C; IR (ATR)/cm^{-1} 2986, 2919, 2850, 1671, 1266, 1046; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13–8.09 (dt, *J* = 8.6, 1.8 Hz, 2H), 7.76–7.72 (dt, *J* = 8.6, 1.7 Hz, 2H), 2.76 (s, 3H), 2.65 (s, 3H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.1, 151.1, 139.2, 129.3, 123.9, 44.0, 26.9; LRMS (GCMS-EI) *m/z* 182.1 $[M+H]^+$; HRMS (ASAP) calculated for $C_9H_{11}O_2S$ $[M+H]^+$ 183.0480, found 183.0476.

Methyl 2-(phenylsulfinyl)acetate 24

Reaction of methyl 2-(phenylthio)acetate (155 µL, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 32 hours according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 1:1) to give the *title compound* **24** (Run 1: 190 mg, 0.96 mmol, 96%, Run 2: 183 mg, 0.92 mmol, 92%, Average Yield: 94%) as a colourless oil; IR (ATR)/cm^{-1} 3058, 2954, 1733, 1437, 1264, 1046; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71–7.66 (m, 2H), 7.57–7.52 (m, 2H), 3.85 (d, *J* = 13.7 Hz, 1H), 3.71 (s, 3H), 3.67 (d, *J* = 13.7 Hz, 1H).; ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3, 143.2, 132.0, 129.6, 124.3, 61.8, 52.9; LRMS (GCMS-CI) *m/z* 198.9 $[M+H]^+$.

***t*-Butyl(*2S*)-2-((*t*-butoxycarbonyl)amino)-4-(methylsulfinyl)butanoate 25**

Reaction of *t*-butyl(*t*-butoxycarbonyl)-*L*-methioninate (305 mg, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 2 hours according to the General Procedure. The crude material was purified by silica gel chromatography (EtOAc) to give the *title compound* **25** (Run 1: 285 mg, 0.89 mmol, 89%, Run 2: 294 mg, 0.92 mmol, 92%, Average Yield: 91%) as a viscous yellow oil as a 1:1 mixture of diastereomers; IR (ATR)/cm^{-1} 3253, 2973, 2926, 1708, 1366, 1151, 1020; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.31–5.15 (m, 1H), 4.36–4.20 (m, 1H), 2.85–2.64 (m, 2H), 2.57 (app d, J = 2.0 Hz, 3H), 2.38–2.25 (m, 1H), 2.10–1.98 (m, 1H), 1.47 (app d, J = 1.2 Hz, 9H), 1.44 (s, 9H).; ^{13}C NMR (101 MHz, $CDCl_3$) some signals doubled due to diastereomeric mixture δ 170.8, 155.6, 83.0, 82.9, 80.2, 53.4, 53.0, 51.0, 50.7, 38.9, 38.8, 28.4, 28.1, 26.4; LRMS (LCMS-ESI) *m/z* 344.0 $[M+Na]^+$.

1-(Dec-1-en-1-yl)-4-(methylsulfinyl)benzene 26

Reaction of (4-(dec-1-en-1-yl)phenyl)(methyl)sulfane (262 mg, 1 mmol, 1:1 mixture of *E*:*Z*), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 4 hours according to General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 2:1) to give the *title compound* **26** (Run 1 226 mg, 0.81 mmol, 81%, Run 2: 243 mg, 0.87 mmol, 87%, Average Yield: 84%) as a viscous yellow oil which was a 1:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$, mixture of diastereomers) δ 7.60 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 6.43–6.39 (m, 2H), 6.34 (dt, *J* = 15.8, 6.6 Hz, 1H), 5.77 (dt, *J* = 11.7, 7.3 Hz, 1H), 2.73 (s, 3H), 2.71 (s, 3H), 2.31 (qd, *J* = 7.5, 1.7 Hz, 2H), 2.23 (q, *J* = 6.8 Hz, 2H), 1.50–1.43 (m, 4H), 1.37–1.21 (m, 20H), 0.89–0.86 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.7, 143.5, 141.2, 141.0, 135.6, 134.1, 129.7, 128.7, 127.7, 126.9, 124.0, 123.6, 44.1, 44.1, 33.2, 32.0, 32.0, 30.0, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 28.9, 22.8, 14.2; LRMS (LCMS-ESI) *m/z* 295.0 $[M+NH_4]^+$; HRMS (NSI) calculated for $C_{17}H_{27}OS$ $[M+H]^+$ 279.1777, found 279.1775.

1-Methyl-4-(methylsulfonyl)benzene 42[34]

Reaction of methyl(*p*-tolyl)sulfide (135 µL, 1.00 mmol), 3,3-dimethylpentane-2,4-dione **7** (26 µL, 0.20 mmol), SSA (100 mg) and $H_2O_{2(aq)}$ (50% aq, 285 µL, 5.00 mmol) in $CHCl_3$ (2.5 mL) at 25 °C for 7 days according to the General Procedure. The crude material was purified by silica gel chromatography (petrol:EtOAc, 1:1) to give the *title compound* **43** (145 mg, 0.85 mmol, 85%) as an amorphous solid; IR (ATR)/cm^{-1}: 2926, 1286, 1143; ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.83 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 3.03 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1, 137.6, 130.1, 127.6, 44.8; LRMS (GCMS-CI) *m/z* 171 $[M+H]^+$.

3,5-Dihydroperoxy-3,5-dimethyl-1,2-dioxolane 2[17]

$H_2O_{2(aq)}$ (30%, 10.0 mL, 100 mmol) was added to a solution of acetylacetone **1** (2.00 mL, 20 mmol) and SSA (2 g) in MeCN (80 mL) at room temperature. The resulting solution was stirred at room temperature for 18 hours. The reaction was diluted with H_2O (50 mL) and the aqueous was extracted with EtOAc (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and filtered. The solvent was removed *in vacuo* to give the *title compound* **2** as a white solid (2.52 g, 15.2 mmol, 76%); mp 100–102 °C [Lit: 98–100 °C][17]; IR (ATR)/cm^{-1} 3338, 3004, 2952, 1433, 1381, 1165; ^1H NMR (400 MHz, CD_3CN) δ 9.64 (bs, 2H), 2.59 (s, 2H), 1.50 (s, 6H); ^{13}C NMR (101 MHz, CD_3CN) δ 113.1, 52.2, 18.1.

1,4-Dimethyl-2,3,5,6-tetraoxabicyclo[2.2.1]heptane 27[35]

$H_2O_{2(aq)}$ (50%, 2.85 mL, 50 mmol) was added to a solution of acetylacetone **1** (200 μL, 2 mmol) and SSA (1.00 g) in $CHCl_3$ (25 mL). The resulting biphasic solution was stirred at room temperature for 18 hours. Saturated $Na_2S_2O_{5(aq)}$ (25 mL) was added dropwise at 0 °C. The resulting layers were separated and the aqueous was further extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were dried over $MgSO_4$ and filtered. The solvent was removed *in* vacuo and the crude material was purified by silica gel chromatography (petrol:EtOAc, 5:1) to afford the *title compound* as a white solid (50 mg, 0.38 mmol, 19%); mp 121–123 °C [Lit: 123–125 °C][35]; IR (ATR)/cm^{-1} 2956, 2919, 2852, 1467, 1368; ^1H NMR (400 MHz, $CDCl_3$) δ 2.74 (s, 2H), 1.67 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 110.0, 50.7, 10.8.

3,5-Dihydroxy-3,5-dimethyl-1,2-dioxolane 28[16]

$H_2O_{2(aq)}$ (50%, 0.57 mL, 10.0 mmol) was added every 5 minutes in 0.1 mL portions to acetylacetone **1** (1.00 mL, 10.0 mmol) which was cooled to 0 °C with regular shaking. The vessel was maintained at 0 °C for 4 hours with regular shaking. After warming to rt, the now crystalline material was vacuum dried over P_2O_5 overnight giving the *title compound* **27** (1.27 g, 9.62 mmol, 96%) as a white solid; mp 89–91 °C [Lit: 90–91 °C][16]; IR (ATR)/cm^{-1} 3350, 2931, 2864; ^1H NMR (400 MHz, CD_3CN) δ 2.57 (s, 2H), 2.38 (bs, 2H), 1.46 (s, 6H); ^{13}C NMR (101 MHz, CD_3CN) δ 106.4, 59.4, 23.3; LRMS.

Calculations

All DFT calculations were performed at the (SMD=$CHCl_3$)M06-2X(D3)/6-311++G(d,p)/int=ultrafine, level of theory. All energies are in kcal/mol.

In order to compare the contributions of different basic sites in these multifunctional molecules, we employed the ("Geometry, Frequency, Noncovalent, eXtended Tight Binding") GFN-xTB method by Grimme and coworkers[36] for an automated search and energy-ranking of protomers.[37] GFN-xTB is semiempirical (TB) method for the calculation of structures, vibrational frequencies, and noncovalent interactions of large molecular system stakes. After placing a proton on each heteroatom, each geometry was optimised by GFN-xTB, and ranked by energies within a threshold of 50 kcal/mol. These calculations took implicit solvation into account using GBSA (Generative Born Surface Area)[38] for chloroform. The lowest energy protomers were then fully optimised at our standard level of theory.

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Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: