Controlled oxidation of organic sulfides to sulfoxides under ambient conditions by a series of titanium isopropoxide complexes using environmentally benign H_2O_2 as an oxidant⁺

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Controlled oxidation of organic sulfides to sulfoxides under ambient conditions has been achieved by a series of titanium isopropoxide complexes that use environmentally benign H_2O_2 as a primary oxidant. Specifically, the $[N,N'-bis(2-oxo-3-R_1-5-R_2-phenylmethyl)-N,N'-bis(methylene-R_3)-ethylenediamine]-Ti(O'Pr)_2 [R_1 = t-Bu, R_2 = Me, R_3 = C_7H_5O_2 (1b); R_1 = R_2 = t-Bu, R_3 = C_7H_5O_2 (2b); R_1 = R_2 = Cl, R_3 = C_7H_5O_2 (3b) and R_1 = R_2 = Cl, R_3 = C_6H_5 (4b)] complexes efficiently catalyzed the sulfoxidation reactions of organic sulfides to sulfoxides at room temperature within 30 min of the reaction time using aqueous <math>H_2O_2$ as an oxidant. A mechanistic pathway, modeled using density functional theory for a representative thioanisole substrate catalyzed by 4b, suggested that the reaction proceeds *via* a titanium peroxo intermediate 4c', which displays an activation barrier of 22.5 kcal mol⁻¹ (ΔG^{\ddagger}) for the overall catalytic cycle in undergoing an attack by the S atom of the thioanisole substrate at its σ^* -orbital of the peroxo moiety. The formation of the titanium peroxo intermediate was experimentally corroborated by a mild ionization atmospheric pressure chemical ionization (APCI) mass spectrometric technique.

Introduction

The long standing interest in the sulfoxidation of organic sulfides is primarily fuelled by its utility in diverse areas of chemistry originating from the constant use of sulfoxide derived chiral auxiliaries in total synthesis,¹ to its use in medicinal chemistry² and biology,³ to its application in industrially important desulfurization processes.⁴ The use of environmentally benign oxidizing agents like H₂O₂⁵ or even molecular oxygen6 for achieving the sulfoxidation reaction under amenable conditions, as opposed to some very strong conditions like inorganic salts,⁷ thus, represent some of the foremost objectives of research in this area. Furthermore, achieving controlled oxidation of organic sulfides to sulfoxides over the fully oxidized sulfones represents yet another notable challenge of sulfoxidation. In this regard it is noteworthy that sulfoxides are high value targets owing to their application as chiral auxiliaries in organic synthesis as well as important functionalities in many biologically active molecules8 and consequently, new methods for the formation of sulfoxides, thus, remain always in demand. Because of the aforementioned reasons we became interested in looking into ways of devising highly efficient Lewis acid catalyzed controlled oxidation of organic sulfides to sulfoxides under amenable conditions employing an environmentally friendly

oxidizing agent like H_2O_2 . Our choice of H_2O_2 rests on several advantages it naturally possesses right from being considered a "green" oxidizing agent by virtue of eliminating H_2O as a by-product to being cheap and also atom efficient in carrying out the oxidation reactions.⁹

Pioneering work in this area was done by Kagan¹⁰ and Modena¹¹ who successfully employed a modified version of the "Katsuki Sharpless reagent" consisting of Ti(O'Pr)₄/diethyltartarate/alkyl hydroperoxide mixture for asymmetric oxidation of prochiral sulfides. The system however suffered from many disadvantages arising out of low activity requiring higher catalyst loading of 4-6 mol% and thereby decreasing its cost effectivity. Pasini12 employed a well characterized salen based titanium precatalyst namely {2,2'-[1,2-ethanediylbis-(nitrilomethylidene)]diphenoxy}TiO for the oxidation of thioanisole to the corresponding sulfoxide albeit in low enantioselectivity (20% ee). The second generation of salen based titanium precatalyst was reported by Katsuki13 for enantioselective sulfoxidation. Apart from these salen based complexes, the in situ formed titanium precatalysts of the chiral diol ligands *i.e.* 1,2-bis-(methoxypheny1)ethane-1,2diol¹⁴ and (R) 1,1'-binaphthyl-2,2'-diol¹⁴ and Ti(O'Pr)₄ have also been successfully employed in various sulfoxidation reactions. Recently Licini¹⁵ reported a highly active well characterized Ti(IV)-amine tris-phenolate complex namely, {phenoxy, 2,2',2"-[nitrilotris(methylene)]tris[6-(1,1-dimethylethyl)]Ti(O'Pr) that exhibited an increased turnover number (TON) of up to 8000 and turnover frequency (TOF) of up to 1700 h⁻¹ for sulfoxidation of organic sulfides at 0.01 mol% of the catalyst loading using H_2O_2 as an oxidant. Alongside the above mentioned development in homogeneous catalysis significant research has also been performed on heterogeneous systems.^{5a,5b,16} Besides these titanium complexes various other metals like Mn,¹⁷ V,¹⁸ Mo,¹⁹ Fe²⁰ etc. have been reported for the sulfoxidation reaction.

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[†] Electronic supplementary information (ESI) available: ORTEP plots of **2b–4b**, geometry optimized structures of **1b'–4b'**, **4c'**, **4e'–4g'** along with the B3LYP coordinates of the optimized geometries for **1b'–4b'** and **4c'–4h'**, molecular orbital interaction table, X-ray crystallographic parameters table, catalysis tables and natural charge analysis tables. CCDC reference numbers 654513, 679212, 690057 and 711908. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b921720g

In keeping with a key theme of our research on understanding various oxidation processes of chemical and biological worlds, we have recently reported several small molecule synthetic analogs of the copper enzyme galactose oxidase²¹ and the iron enzyme catechol dioxygenase²² that utilize molecular oxygen for the oxidation reactions similar to the respective enzymes. Thus, having successfully mimicked enzymes with these small molecule synthetic analogs, we set out to design transition metal based catalysts for a commercially important reaction particularly, the controlled oxidation of organic sulfides to sulfoxides. In the backdrop of a few prior reports of titanium isopropoxide complexes for sulfoxidation reactions involving organic hydroperoxides as oxidants,23 the Group (IV) elements being electron deficient and non-toxic in nature, became our metal of choice for accomplishing the controlled oxidation of organic sulfides to sulfoxide using "green" H₂O₂ oxidant.²⁴

Here in this contribution, we report a series of titanium(IV) isopropoxide complexes, [N, N'-bis(2-oxo-3-R₁-5-R₂-phenylmethyl)-N, N'-bis(methylene-R₃)-ethylenediamine]Ti(O'Pr)₂ $[R_1 = t$ -Bu, $R_2 = Me$, $R_3 = C_7H_5O_2$ (1b); $R_1 = R_2 = t$ -Bu, $R_3 = C_7H_5O_2$ (2b); $R_1 = R_2 = Cl$, $R_3 = C_7H_5O_2$ (3b) and $R_1 = R_2 = Cl$, $R_3 = C_6H_5$ (4b)], that efficiently catalyzed the sulfoxidation reactions of organic sulfides at ambient temperature using aqueous H_2O_2 as an oxidant (Fig. 1). The catalytic cycle of the sulfoxidation reaction as modeled using density functional theory studies revealed that the rate-determining step involved an attack by the S atom of the organic sulfide substrate at the σ^* -orbital of the peroxo moiety of a titanium peroxo intermediate.



Fig. 1 Titanium isopropoxide 1b–4b complexes supported over $[\rm N_2O_2]$ ligands $1a{-}4a.$

Results and discussion

With the intent of stabilizing titanium(IV) isopropoxide complexes, a series of tetradentate $[N_2O_2]$ ligands namely N,N'-bis(2-oxo-3- R_1 -5- R_2 -phenylmethyl)-N,N'-bis(methylene- R_3)-ethylenediamine $[R_1 = t$ -Bu, $R_2 = Me$, $R_3 = C_7H_5O_2$ (1a); $R_1 = R_2 = t$ -Bu, $R_3 = C_7H_5O_2$ (2a); $R_1 = R_2 = Cl$, $R_3 = C_7H_5O_2$ (3a) and $R_1 = R_2 = Cl$, $R_3 = C_6H_5$ (4a)] were synthesized. Specifically, the 1a–4a ligands were prepared by the Mannich condensation reaction of the N,N'-bis(methylene- R_3)-ethylenediamine $[R_3 = C_7H_5O_2, C_6H_5]$ with the respective 2,4-disubstituted phenol and aqueous formaldehyde (Scheme 1).

The titanium(IV) isopropoxide complexes, **1b–4b**, were synthesized by the direct reaction of the **1a–4a** ligands with Ti(O'Pr)₄ in 65–90% yields. Consistent with the formations of the isopropoxide derivative, the metal bound O*i*-Pr moiety appeared as a septet at 4.90–5.19 ppm (${}^{3}J_{\text{HH}} = 8 \text{ Hz}$) and as two doublets at 1.12–1.32 ppm

 $({}^{3}J_{\rm HH} = 8 \text{ Hz})$ and 1.07–1.30 ppm $({}^{3}J_{\rm HH} = 8 \text{ Hz})$ in the ${}^{1}\text{H}$ NMR spectrum while the corresponding carbon resonances appeared at 77.7–79.9 ppm, 26.1–26.9 ppm and 25.8–26.6 ppm respectively in the ${}^{13}\text{C}{}^{1}\text{H}$ NMR spectrum. Quite interestingly, two of the three methylene resonances of the **1b–4b** complexes were found to be diastereotopic in nature with each appearing as two sets of doublets at 4.15–4.29 ppm (${}^{2}J_{\rm HH} = 13 \text{ Hz}$) and 3.22–3.43 ppm (${}^{2}J_{\rm HH} = 13 \text{ Hz}$) and at 2.61–2.88 ppm (${}^{2}J_{\rm HH} = 10 \text{ Hz}$) and 2.31–2.44 ppm (${}^{2}J_{\rm HH} = 11 \text{ Hz}$).

The molecular structures of 1b-4b as determined by X-ray diffraction studies revealed the titanium center to be in a distorted octahedral geometry in these complexes (Fig. 2 and Fig. S1-S3, ESI^{\dagger}). The tetradentate [N₂O₂] ligand was seen chelated to the metal center through two phenolate-O atoms and two amine-N atoms, of which a pair of phenolate-O and amine-N atoms occupied adjacent equatorial sites while the other pair occupied adjacent equatorial and axial sites. The two Oi-Pr moieties occupied the remaining equatorial and axial sites thereby adopting a cis disposition to each other. Of particular interest are the Ti-O distances in the 1b-4b complexes as the two Ti-O(phenolate) bonds [1.896(2)–1.919(3) Å] are longer than the other two Ti-O(isopropoxide) bonds [1.775(4)-1.815(16) Å]. For comparison, the Ti-O single bond distance as obtained from the sum of the individual covalent radii is 1.984 Å.25 The shorter Ti-O(isopropoxide) distances in 1b-4b are a consequence of Ti-O π -donation arising out of an interaction of an oxygen lone pair with an empty d-orbital of the highly electron deficient titanium(IV) d^0 metal center in these complexes (Fig. 3). Further support in favor of the Ti–O π -donation in these 1b–4b complexes comes from density functional theory studies. In particular, the electronic structures (1b'-4b') of the 1b-4b complexes computed at B3LYP/LANL2DZ, 6-31G(d) level of theory using atomic coordinates adapted from X-ray analysis showed the presence of such Ti–O π -back donation as depicted by the molecular orbitals



Fig. 2 ORTEP of **1b**. Hydrogen atoms on carbon are omitted for clarity. Selected bond lengths (Å) and angles (°) are given: Ti1–O1 1.8961(16), Ti1–O2 1.8147(16), Ti1–O5 1.9036(16), Ti1–O6 1.8127(17), Ti1–N1 2.430(2), Ti1–N2 2.3942(19), O1–Ti1–O6 90.58(7), O2–Ti1–O6 107.58(8), O1–Ti1–N2 92.55(7), O2–Ti1–N2 159.13(7), O5–Ti1–N2 78.97(6), O6–Ti1–N2 91.62(7).



Scheme 1 General synthetic procedure of the 1b-4b complexes.



Fig. 3 Ti–O π -interaction in 1b–4b.

MO 189 (**1b**'), MO 212 (**2b**'), MO 184 (**3b**') and MO 165 (**4b**') (Fig. 3 and Table S1, ESI†). Similar short Ti–O(isopropoxide) distances have been observed in other structurally characterized titanium(IV) complexes namely, [*N*,*N*-bis(2-oxy-3,5-dimethylbenzyl)-*N'*,*N'*dimethylethanediamine]Ti(O'Pr)₂ [1.838(1) Å and 1.808(1) Å]²⁶ and [tris(3,5-di-*t*-butyl-2-oxybenzyl)amine]Ti(O'Pr) [1.778(4) Å]²⁷ complexes. The Ti–N(amine) distances [2.331(3)–2.394(3) Å] in the **1b–4b** complexes, on the other hand, display more of a single bond character as these distances are longer than the sum of the individual covalent radii of Ti and N (2.024 Å).²⁵

Quite significantly, the **1b–4b** complexes effectively carried out the sulfoxidation reaction of organic sulfides to sulfoxides at ambient temperature using H_2O_2 as an oxidant (Table 1 and eqn (1)). Specifically, when alkyl and aryl sulfides were treated with H_2O_2 in the presence of 0.5 mol% of the **1b–4b** catalysts, excellent conversions to sulfoxides were obtained within 30 min of the reaction time. In order to establish the practical efficacy of the sulfoxidation reaction, isolated yields for the all the substrates used in the catalysis were obtained for a representative **2b** precatalyst (Table S5, ESI†). Notably, the **1b–4b** complexes were highly active in a more competitive solvent like methanol using aqueous H_2O_2 as the primary oxidant (Table S6, ESI†). The better performance of **1b–4b** in methanol as a solvent assumes importance in the back drop of the fact that many of the reported sulfoxidation procedures use health and environmentally hazardous chlorohydrocarbons as solvents²⁸ and hence there exists a palpable need for improved protocols.

$$R_{1} \xrightarrow{S} R_{2} \xrightarrow{H_{2}O_{2}, RT} R_{1} \xrightarrow{O} R_{2} \xrightarrow{H_{2}O_{2}, RT} R_{1} \xrightarrow{O} R_{2} \xrightarrow{O} R_{1} \xrightarrow{O} R_{2}$$
(1)

The catalyst influence is very much evident when compared to the blank runs carried out in the absence of these catalysts which showed significantly subdued conversion to sulfoxides under analogous conditions (Table 1 and Table S2, ESI†). It is worth noting that control experiments performed with $Ti(O'Pr)_4$ showed a significantly higher buildup of sulfones in comparison to the **1b–4b** catalysts (Table 1 and Table S2, ESI†). Thus, the selective and near quantitative formation of sulfoxides in the case of **1b– 4b** highlights a key attribute of these catalysts. It is worth noting that sulfoxides are important, high valued synthetic intermediates of considerable commercial and biological interests²⁹ and hence the catalysts for selective oxidation of organic sulfides to the corresponding sulfoxides are in great demand. Lastly, the attempts to recover the catalyst after the catalysis runs proved to be unsuccessful for a representative precatalyst **2b**.

Another important attribute of these **1b–4b** catalysts is the convenience of the use of an environment friendly oxidant like aqueous H_2O_2 instead of organic peroxides or other harsh inorganic oxidants. For example, oxidation with an organic peroxide namely *m*-chloroperbenzoic acid (*m*-CPBA) for a representative substrate thioanisole by **1b** yielded *ca*. 52% of sulfoxide as compared to 90% with aqueous H_2O_2 under analogous conditions (Table S3, ESI†). Quite interestingly, the use of *t*-butyl hydroperoxide (TBHP) produced no sulfoxide product under analogous conditions. Lastly, similar attempts with aerial oxidation as well as by bubbling molecular oxygen showed no conversion even after 24 h.

A concentration dependence study showed that an increase in catalyst loading of 1b from 0.05 mol% to 0.5 mol% led

Table 1	Selected results of oxi	dation of thioether l	by aqueous H ₂ O ₂	catalyzed by 1b-4b
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			Conversion ^{a0} / ₂ (SO : SO ₂) ^b			
Entry	Substrate	Product	1b	2b	3b	4b
1.	∕_S	O S S	74 (3:1)	80 (4:1)	90 (9:1)	82 (5:1)
2.	∕S	O II S	90 (10:1)	82 (5:1)	96 (48:1)	82 (16:1)
3.	Y ^S Y		62 (9:1)	93 (31:1)	55 (>99:1)	66 (17:1)
4.	~~~ ^{\$} ~~~		82 (5:1)	90 (9:1)	91 (10:1)	79 (4:1)
5.	∕ ^S ∕∕∕∕	0 S	68 (8:1)	89 (22:1)	64 (21:1)	65 (13 : 1)
6.	∕~^S√∕∕	O S S	50 (7:1)	76 (25:1)	52 (>99:1)	63 (31:1)
7.	S_	o S S	90 (10 : 1)	77 (6:1)	84 (21 : 1)	66 (13:1)
8.	S	S S	95 (>99:1)	95 (>99:1)	76 (4:1)	54 (18:1)
9.	S S	o S S	65 (>99:1)	59 (>99:1)	32 (>99:1)	25 (>99:1)
10.	S	O S S	28 (>99:1)	16 (>99 : 1)	12 (>99:1)	7 (>99:1)

^{*a*} Reaction conditions: 2.00 mmol of substituted thioether, 2.00 mmol of H_2O_2 , 2.00 mmol of internal standard (1,2-dichlorobenzene) and 1.00×10^{-2} mmol Ti catalyst, in CH₃OH (5 mL) at room temperature (30 min). Products were quantified by GC analysis with respect to internal standard and identified by GCMS analysis. ^{*b*} Ratio of sulfoxide to sulfone is given in parenthesis under conversion.

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to an increase in sulfoxide formation from 26% to 90%, after which a decrease to 73% was observed at 1 mol% along with sulfone formation (15%) at this catalyst concentration (Table S4, ESI†). A similar trend is reflected in the time dependence study, carried out on thioanisole by **1b**, which showed an increase in sulfoxide formation along with a much reduced sulfone buildup with increase in time (Fig. S24, ESI†).

Important is the comparison of the efficiency of our catalyst 1b-4b with other reported examples particularly with those of the well-defined titanium based ones. Quite interestingly, the precatalyst 1b-4b exhibited superior activity in comparison to a structurally characterized titanium binapthyl-bridged salen based precatalyst namely [2,2'-bis(3-t-Bu-2-hydroxybenzylideneimino)-1,1'-binaphthyl]TiCl₂,³⁰ which exhibited 60% conversion for the p-tolylmethyl sulfide in 1200 min at 1 mol% of the precatalyst loading using H₂O₂ as an oxidant while the precatalyst 1b-4b exhibited 54-95% conversion for the same substrate at half the precatalyst loading of 0.5 mol% in 30 min. The precatalyst 1b-4b were, however, found to be less active than that of the another {phenoxy, 2,2',2"-[nitrilotris(methylene)]tris[6-(1,1dimethylethyl)}Ti(O'Pr) precatalyst,15a which exhibited conversion of 92% in 30-60 min for the phenylmethyl sulfide substrate using H₂O₂ as oxidant at 1 mol% precatalyst loading as compared to the 1b-4b precatalyst displaying 66-90% conversions for the same substrate at 0.5 mol% of the precatalyst loading in 30 min. In this context it is worth noting that many of the other reported examples of titanium mediated sulfoxidation reactions were performed under "Ligand Assisted Catalysis" (LAC) conditions employing *in situ* generation of the catalyst,^{5b,10b,10d,24,31} in the reaction mixture quite unlike the case of the well-defined precatalyst **1b–4b** employed in the present study.

Further insight into the mechanism of the sulfoxidation reaction by the **1b–4b** complexes came from density functional theory studies. Specifically, the sulfoxidation of thioanisole by a representative complex **4b** was modeled at B3LYP/LANL2DZ, 6-31G(d) level of theory by applying suitable modifications to the starting geometry optimized **4b'** structure, computed using atomic coordinates obtained from X-ray analysis data of **4b**, to generate the catalytically relevant species, and which were subjected to subsequent geometry optimization followed by single-point calculation to obtain the desired stationary and the transition states of the catalytic cycle.

In this regard, an oxygen transfer mechanism has been proposed for the sulfoxidation reaction as opposed to an electron transfer mechanism, the possibility of which was ruled out based on UV-visible spectroscopy studies. UV-visible spectroscopy studies showed the absence of any d–d transitions and thereby negating the existence of a paramagnetic species that may possibly result in an electron transfer pathway. It is worth noting that the electrophilic oxygen transfer from a d⁰ titanium-peroxo complexes to an organic sulfides has been reported earlier.^{23a,32}

The initiation of the catalytic cycle is proposed to proceed with the formation of a titanium peroxo intermediate 4c' from the reaction of 4b' with H₂O₂ (Scheme 2 and Fig. S8, ESI[†]) as opposed to an alternative higher energy hydroperxo pathway (see Fig. S9,



Scheme 2 Mechanism of the sulfoxidation reaction catalyzed by a representative precatalyst 4b.



Fig. 4 Computed free energy (ΔG) profile (in red) and total energy (E) with zero-point energy (ZPE) correction (E + ZPE) profile (in blue) along reaction coordinate of the catalytic cycle of oxidation of thioanisole.

ESI[†]). The peroxo intermediate **4c'** displayed distorted octahedral geometry at titanium similar to that in **4b'**. The Ti–O(peroxo) distances of 1.833 Å and 1.836 Å are shorter than the sum of the individual covalent radii of Ti and O (1.984 Å).²⁵ The peroxo moiety is characterized by a O1–O4 distance of 1.444 Å that is slightly longer than a O–O single bond distance (1.32 Å).²⁵

Significantly enough, crucial evidence in favor of the proposed Ti–peroxo species came from mass spectrometric studies. It is worth noting that the mild ionization technique like atmospheric pressure chemical ionization (APCI) has become an important tool in detecting the reaction intermediates in various catalytic processes.³³ After rigorous mass spectrometric experiments we found that the APCI method in both the positive and negative ion modes are more suitable for the detection of our proposed Ti–peroxo species involved in the catalytic cycle. Indeed, the convincing evidence in favor of the formation of the proposed Ti–peroxo species were observed in both the positive and negative ion modes for two representative precatalysts, **1b** and **2b**, when treated with H_2O_2 (50 equivalent) in a CHCl₃–CH₃CN (10:1) mixed solvent (see Fig. S10–S17, ESI†).

The intermediate 4c' undergoes a nucleophilic attack at the peroxo-O atom by the S atom of the thioanisole to give a transition state 4d' that is 22.5 kcal mol⁻¹ higher in energy (ΔG value) (Fig. 4 and 5). Significant elongation of the O1 \cdots O4 distance (1.802 Å) observed in the 4d' structure relative to that in 4c' (1.444 Å) is in concurrence with the nucleophilic attack by the S atom of the thioanisole occurring at the σ^* -orbital of the peroxo (O1–O4) bond resulting in a linear S1 \cdots O1 \cdots O4 orientation. A similar linear S \cdots O \cdots O type transition state has been proposed for the asymmetric sulfoxidation reaction of imidazole based prochiral sulfides.³⁴ Indeed, the natural charge analysis of intermediate 4c' and the transition state 4d', revealed that the thioanisole-S mediated nucleophilic attack at the peroxo-O moiety in the transition state 4d' led to the increase in the electron density on



Fig. 5 Fully optimized transition state **4d**'. Selected bond lengths (Å) and angles (°): Ti1–O1 1.872, Ti1–O2 1.898, Ti1–O3 1.906, Ti1–O4 1.730, O1–O4 1.802, O1–S1 2.214, O1–Ti1–O4 59.9, O2–Ti1–O3 146.8, S1–O1–O4 174.6.

the O1 and O4 atoms of the peroxo moiety in 4d' relative to 4c' along with the concomitant decrease in electron density on the S1 center of the thioanisole moiety in the 4d' relative to that of the free thioanisole molecule (Tables S19 and S20, ESI†). Quite expectedly, the thioanisole moiety as a whole too showed similar reduction of electron density upon coordination to the metal center (see Fig. S18 and S19, ESI†).

Quite interestingly, similar nucleophilic attack by the S atom of organic sulfide at the peroxy-O of a metal bound peroxo species resulting in a linear $S \cdots O \cdots O$ transition state having an activation barrier of *ca*. 25 kcal mol⁻¹ has earlier been predicted by Jøgersen.³⁵ The experimental support in favor of the nucleophilic attack by S atom of organic sulfide on the peroxy-O of the metal bound peroxo species, however, comes from the observation of negative Hammett ρ value for the oxidation of organic sulfides to sulfoxides by a variety of oxidants like H₂O₂ or organic hydroperoxides.^{32a,36}

The complete cleavage of the O1...O4 bond of the peroxo moiety occurs subsequent to the transition state 4d' resulting in a lower energy intermediate 4e' containing a Ti=O moiety and a weakly coordinated methyl phenyl sulfoxide moiety (Fig. S20, ESI[†]). The observed Ti–O4(oxo) distance [1.646 Å], being double bonded in character is significantly shorter than the other Ti-O1(methyl phenyl sulfoxide) distance [2.079 Å] of the weakly bound methyl phenyl sulfoxide moiety in the 4e' intermediate. Quite expectedly, the S1-O1 distance [1.564 Å] falls between S-O single (1.70 Å) and double (1.56 Å) bond distances.²⁵ Our attempt to detect the formation of the titanium coordinated sulfoxide species by ¹H NMR experiments, performed both at low and ambient temperatures, proved to be unsuccessful suggesting either a rapid exchange of the coordinated sulfoxide moiety or the formation of the same in minute amounts occurring in the catalytic cycle. Similar fast exchange of the coordinated sulfoxide moiety had earlier been observed in the literature.³⁷ Specifically, the ¹H NMR spectrum of a representative precatalyst, **1b**, when treated with H_2O_2 in the presence of thioanisole in CDCl₃ at room temperature, showed the formation of the partially oxidized sulfoxide, as evidenced by a peak at 2.73 ppm and the fully oxidized sulfone as observed by a peak at 3.05 ppm, in 3:1 ratio within the first 5 min of the reaction time. It is worth noting that very little shift was observed of the sulfoxide methyl resonances in the reaction mixture with respect to its free form, thereby suggesting either a rapid exchange in the NMR time-scale or the formation in minute amounts in the catalytic cycle. However, complete conversion to the fully oxidized sulfone product was seen in 15 min of the reaction time. The analogous experiment performed at low temperature of -40 °C showed much slower conversion with similar formation of sulfone and sulfoxide products along with unreacted sulfide in a 1:1:6 ratio within 5 min of the reaction time. However, very little progress of the reaction was observed even after 15 min of the reaction time as the ratio of sulfoxide, sulfone and the unreacted sulfide slightly increased to be 1.6:1:5.3 in favor of the oxidized products.

Further reaction of the titanium oxo intermediate 4e' with another molecule of H₂O₂ results in the formation of a transition state 4f' in which a proton transfer is seen to occur from the H₂O₂ molecule to the Ti1–O4 moiety (Fig. S21, ESI†). Consequently, a much elongated Ti–O4 distance [1.729 Å] was observed in the transition state 4f' as compared to the same in the immediately preceding 4e' species, [Ti1–O4(oxo) = 1.646 Å], containing a Ti=O moiety.

The transition state **4f'** subsequently leads to a lower energy titanium–(hydroxo)(hydroperoxo) intermediate **4g'** (Fig. S22, ESI†). The Ti1–O4(hydroxo) [1.843 Å] and the Ti1–O5(hydroperoxo) [1.896 Å] distances are more consistent with a single bond character.

Finally, the last step involves a proton transfer between a titanium bound hydroperoxo moiety to an adjacent titanium bound hydroxo moiety *via* a transition state **4h'** along with the elimination of the much desired methyl phenyl sulfoxide product (Fig. S23, ESI†). Additionally, the transition state **4h'** eliminates a molecule of H_2O to regenerate back the starting titanium peroxo intermediate **4c'**, whereby marking the completion of the catalytic

cycle. Quite interestingly, the transition state **4h'** is more of a product-like transition state with its structure closely resembling the final peroxo intermediate **4c'** as reflected in the Ti–O and O–O bond lengths in **4h'** [Ti1–O1 1.852 Å, Ti1–O4 2.062 Å, and O1–O4 1.447 Å] and **4c'** [Ti1–O1 1.836 Å, Ti1–O4 1.833 Å, and O1–O4 1.444 Å].

The energy landscape of the catalytic cycle was modeled in free energy (ΔG) as well as in total energy (ΔE) with zero-point energy (ZPE) correction (ΔE + ZPE) surfaces (Fig. 4). Both the free energy (ΔG) and the total energy with zero-point energy correction (ΔE + ZPE) profiles showed the rate-determining step of the catalytic cycle to be the nucleophilic attack of the S atom of thioanisole on the σ^* -molecular orbital of the peroxo moiety as represented by the transition state 4d' which displayed an activation barrier of 22.5 kcal mol⁻¹ on the free energy (ΔG) surface and of 10.1 kcal mol⁻¹ on the (ΔE + ZPE) surface. In this regard it is worth noting that the free energy activation barrier for similar sulfoxidation of imidazole based sulfide has been estimated to vary in the range 14.7–24.5 kcal mol⁻¹ depending upon the proposed reaction pathways.³⁴ Furthermore, the difference in energy at both ends of the free energy profile show an overall negative free energy $(-36.3 \text{ kcal mol}^{-1})$ for the oxidation of thioanisole with H_2O_2 to methyl phenyl sulfoxide, thereby indicating its exergonic nature and at the same time also pointing towards the irreversibility of the sulfoxidation processes.

Conclusions

In summary, a series of titanium(IV) isopropoxide complexes namely, $[N,N'-bis(2-oxo-3-R_1-5-R_2-phenylmethyl)-N,N'$ bis(methylene- R_3)-ethylenediamine]Ti(O'Pr)₂ [$R_1 = t$ -Bu, $R_2 =$ Me, $R_3 = C_7H_5O_2$ (1b); $R_1 = R_2 = t$ -Bu, $R_3 = C_7H_5O_2$ (2b); $R_1 = R_2 = Cl, R_3 = C_7 H_5 O_2$ (3b) and $R_1 = R_2 = Cl, R_3 = C_6 H_5$ (4b)] that efficiently carry out sulfoxidation reactions of organic sulfides at ambient temperature using environmentally friendly aqueous H_2O_2 as an oxidant, have been designed. The catalytic cycle modeled using density functional theory studies for the reaction of thioanisole with H_2O_2 catalyzed by a representative complex 4b suggests that the catalysis proceeds via a titanium peroxo intermediate 4c' that undergoes nucleophilic attack by the S atom of thioanisole at the σ^* -orbital of the peroxo moiety and which also represents the rate-determining step of the catalytic cycle displaying an activation barrier of 22.5 kcal mol⁻¹. The APCI mass spectrometry studies corroborate the formation a peroxo intermediate in the catalysis cycle.

Experimental

General procedures

All manipulations were carried out using a combination of standard schlenk techniques and glove box. Solvents were purified and degassed by standard procedures. The 2,4-di-*t*-butylphenol, 2-*t*-butyl-4-methylphenol, 2,4-*di*-chlorophenol, piperonal and Ti(O'Pr)₄ were purchased from Sigma Aldrich, Germany and used without any further purification. The N,N'-bis(2-hydroxo-3,5-*di*-chlorophenylmethyl)-N,N'-dibenzylethylenediamine (**4a**) was prepared by following a modified literature procedure.³⁸ ¹H and ¹³C{¹H} NMR spectra were recorded on a Varian 400 MHz NMR

Table 2 X-Ray crystallographic parameters for 1b-4b

Compound	1b	2b	3b	4b
Lattice	Triclinic	Monoclinic	Trigonal	Orthorhombic
Formula	$C_{62}H_{80}N_2O_8Ti$	$C_{61}H_{84}N_2O_8Ti$	$C_{19}H_{20}Cl_2NO_4Ti_{0.50}$	$C_{36}H_{40}Cl_4N_2O_4Ti$
Formula weight	1029.18	1021.20	421.21	754.40
Space group	$P\overline{1}$	$P-2_1/c$	$R\bar{3}c$	$P2_{1}2_{1}2_{1}$
a/Å	11.8560(3)	19.743(4)	25.514(4)	11.1277(4)
b/Å	16.7553(6)	18.552(4)	25.514(2)	15.5670(7)
c/Å	16.9088(6)	16.993 (4)	30.429(2)	21.1098(7)
$\alpha/^{\circ}$	62.844(4)	90.000(17)	90.00	90.00
$\beta/^{\circ}$	86.881(3)	113.19(2)	90.00	90.00
$\gamma/^{\circ}$	70.612(3)	90.000(17)	120.00	90.00
$V/Å^3$	2800.27(16)	5721(2)	17154(3)	3656.7(2)
Z	2	4	36	4
T/K	150(2)	150(2)	150(2)	150(2)
Radiation $(\lambda/\text{\AA})$	0.71073	0.71073	0.71073	0.71073
ρ (calcd.)/g cm ⁻³	1.221	1.186	1.468	1.370
μ (Mo K α)/mm ⁻¹	0.209	0.204	0.560	0.567
$\theta \max/^{\circ}$	25.00	25.00	25.00	25.00
Reflection collected/unique	25 227/9773	28 748/9986	44 655/3359	21722/6330
<i>R</i> (int)	0.0389	0.0997	0.2281	0.0864
Data/restraints/parameters	9733/0/672	9986/0/666	3359/0/242	6330/0/428
R indices (all data)	$R_1 = 0.0822$	$R_1 = 0.1315$	$R_1 = 0.1029$	$R_1 = 0.0913$
	$WR_2 = 0.1307$	$WR_2 = 0.1324$	$WR_2 = 0.2152$	$WR_2 = 0.0836$
Final K indices $I > 2\sigma(I)$	$K_1 = 0.0488$	$K_1 = 0.056 /$	$K_1 = 0.0853$	$K_1 = 0.050/$
COF	$WK_2 = 0.1188$	$WK_2 = 0.1112$	$WK_2 = 0.2020$	$WK_2 = 0.0/11$
Flack x parameter	0.945	0.885	1.12/ —	0.962 0.0340 (0.0387)

spectrometer. ¹H NMR peaks are labeled as singlet (s), doublet (d), triplet (t) and septet (sept). Infrared spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrometer. Mass spectrometry measurements were done on a Micromass Q-Tof spectrometer. X-Ray diffraction data were collected on a Bruker P4 difractometer equipped with a SMART CCD detector. The crystal data collection and refinement parameters are summarized in Table 2. The structures were solved using direct methods and standard difference map techniques, and were refined by fullmatrix least-squares procedures on F^2 with SHELXTL (version 6.10).³⁹ GC spectra were obtained on a PerkinElmer Clarus 600 equipped with a FID. GCMS spectra were obtained on a PerkinElmer Clarus 600 T equipped with an EI source. APCI/MS experiments were performed with a Varian Proctar 500-LCMS instrument, with upper mass limit of m/z 2000, through direct infusion via a syringe pump. Standard experimental conditions in the LCMS was at the given capillary voltage 80 V, syringe pressure 10 Psi, temperature 320 °C, flow rate 10 µL min⁻¹, RF loading 80%, nebulizing gas, helium. Elemental analysis was carried out on Thermo Quest FLASH 1112 SERIES (CHNS) Elemental Analyzer. Melting points of the compounds were recorded on a Buchi Melting Points B-545 instrument.

Synthesis of N, N'-bis(2-hydroxo-3-*t*-butyl-5-methylphenylmethyl)-N, N'-bis(1,3-benzodioxol-5-ylmethyl)ethylenediamine (1a)

A solution of N,N'-bis(1,3-benzodioxol-5-ylmethyl)ethylenediamine (0.603 g, 1.84 mmol), 2-*t*-butyl-4-methylphenol (0.602 g, 3.67 mmol) and aqueous formaldehyde (39% w/v, 0.605 g, 7.34 mmol) in methanol (*ca.* 30 mL) was refluxed for 24 h. The white precipitate formed was filtered, washed with methanol (*ca.* 4×20 mL) and then dried in vacuum to obtain product **1a** as a white solid (0.718 g, 58%). ¹H NMR (CDCl₃, 400 MHz, 25 °C): δ 10.4 (s, 2H, OH), 6.98 (s, 2H, C₆H₂{2-OH, 3-C(CH₃)₃, 5- CH_3), 6.68 (s, 2H, C_6H_2 {2-OH, 3-C(CH_3)_3, 5-CH_3), 6.67 (s, 2H, $C_7H_5O_2$), 6.60–6.57 (m, 4H, $C_7H_5O_2$), 5.89 (s, 4H, $C_7H_5O_2$), 3.60 (s, 4H, CH₂), 3.38 (s, 4H, CH₂), 2.62 (s, 4H, CH₂), 2.22(s, 6H, CH₃), 1.40 (s, 18H, C(CH₃)₃). ${}^{13}C{}^{1}H$ NMR (CDCl₃, 100 MHz, 25 °C): δ 154.0 (C_6H_2 {2-OH,3-C(CH₃)₃,5-CH₃}), $147.9(C_7H_5O_2), 147.2(C_7H_5O_2), 136.6(C_6H_2\{2-OH,3-C(CH_3)_3,5-C(CH_3)_$ CH₃}), 130.6 $(C_7H_5O_2)$, 127.5 $(C_6H_2\{2\text{-OH},3\text{-C}(CH_3)_3,5\text{-}$ CH_3), 127.4 (C_6H_2 {2-OH,3-C(CH_3)_3,5-CH_3}), 126.9 (C_6H_2 {2-OH,3-C(CH₃)₃,5-CH₃}), 122.9 (C₇H₅O₂), 121.9 (C₆H₂{2-OH,3- $C(CH_3)_3, 5-CH_3$), 109.8 ($C_7H_5O_2$), 108.1 ($C_7H_5O_2$), 101.1 $(C_7H_5O_2)$, 58.9 (CH₂), 58.2 (CH₂), 50.1 (CH₂), 34.7 (C(CH₃)₃), 29.7 (C(CH₃)₃), 20.9 (CH₃). Melting point: 115–116 °C. IR (KBr pellet cm⁻¹): 3430 (m), 2913 (w), 2833 (s), 1608 (m), 1493 (s), 1444 (s), 1400 (w), 1365 (w), 1351 (w), 1249 (s), 1232 (s), 1103 (w), 1035 (s), 971 (w), 825 (w), 810 (w), 765 (s), 644 (w), 600 (w). HRMS (ES): m/z 681.3911 [(ligand + H)]⁺, Calcd. 681.3904.

Synthesis of [N,N'-bis(2-oxo-3-*t*-butyl-5-methylphenylmethyl)-N,N'-bis(1,3-benzodioxol-5-ylmethyl)ethylenediamine]Ti(O^{*i*}Pr)₂ (1b)

To a solution of N,N'-bis(2-hydroxo-3-*t*-butyl-5-methylphenylmethyl)-N,N'-bis(1,3-benzodioxol-5-ylmethyl)ethylenediamine **1a** (0.204 g, 0.299 mmol) in toluene (*ca.* 10 mL), a solution of Ti(O'Pr)₄ (0.169 g, 0.595 mmol) in toluene (*ca.* 1 mL) was added. The resulting solution was stirred at 50 °C for 4 h after which the volatiles were removed under reduced pressure. The residue was washed with hexane (*ca.* 2 mL) and dried under vacuum to obtain product **1b** as a yellow solid (0.203 g, 80%). ¹H NMR (CDCl₃, 400 MHz, 25 °C): δ 6.98 (d, 2H, ⁴J_{HH} = 2 Hz, $C_6H_2O{3-C(CH_3)_3, 5-CH_3}), 6.76 (d, 2H, {}^3J_{HH} = 7 Hz, C_7H_5O_2),$ 6.54 (d, 2H, ${}^{4}J_{HH} = 2$ Hz, $C_{6}H_{2}O\{3-C(CH_{3})_{3}, 5-CH_{3}\})$, 6.50 (d, 2H, ${}^{3}J_{HH} = 7$ Hz, $C_{7}H_{5}O_{2}$), 6.48 (s, 2H, $C_{7}H_{5}O_{2}$), 5.96 (m, 4H, $C_7H_5O_2$), 4.90 (sept, 2H, ${}^3J_{HH} = 7$ Hz, OCH(CH₃)₂), 4.24 (d, 2H, ${}^{2}J_{HH} = 13$ Hz, CH₂), 4.12 (s, 4H, CH₂), 3.31 (d, 2H, ${}^{2}J_{\rm HH} = 13$ Hz, CH_{2}), 2.88 (d, 2H, ${}^{2}J_{\rm HH} = 10$ Hz, CH_{2}), 2.35 (d, 2H, ${}^{2}J_{HH} = 10$ Hz, CH₂), 2.20 (s, 6H, CH₃), 1.48 (s, 18H, $C(CH_{3})_{3}$, 1.26 (d, 6H, ${}^{3}J_{HH} = 7$ Hz, $OCH(CH_{3})_{2}$), 1.13 (d, 6H, ${}^{3}J_{\text{HH}} = 7 \text{ Hz}, \text{ OCH}(\text{CH}_{3})_{2}$). ${}^{13}\text{C}\{{}^{1}\text{H}\} \text{ NMR} (\text{CDCl}_{3}, 100 \text{ MHz},$ 25 °C): δ 159.6 (C₆H₂O{3-C(CH₃)₃,5-CH₃}), 147.7 (C₇H₅O₂), 147.6 $(C_7H_5O_2)$, 136.8 $(C_7H_5O_2)$, 128.5 $(C_6H_2O\{3-C(CH_3)_3,5-C(CH_$ CH₃}), 127.4 (C_6H_2O {3-C(CH₃)₃,5-CH₃}), 126.3 ($C_7H_5O_2$), 126.1 $(C_6H_2O{3-C(CH_3)_3, 5-CH_3})$, 125.4 $(C_6H_2O{3-C(CH_3)_3, 5-CH_3})$ CH₃}), 124.0 (C₆H₂O{3-C(CH₃)₃,5-CH₃}), 112.6 (C₇H₅O₂), 108.1 $(C_7H_5O_2)$, 101.3 $(C_7H_5O_2)$, 77.7 $(OCH(CH_3)_2)$, 59.7 (CH_2) , 58.9 (CH₂), 44.9 (CH₂), 35.0 (C(CH₃)₃), 30.6 (C(CH₃)₃), 26.9 (OCH(CH₃)₂), 26.6 (OCH(CH₃)₂), 20.9 (CH₃). Melting point: 270–272 °C dec. IR (KBr pellet cm⁻¹): 3431 (m), 2964 (w), 2612 (w), 1608 (w), 1490 (s), 1467 (s), 1442 (s), 1360 (s), 1249 (s), 1125 (s), 1041 (m), 930 (m), 841 (m), 608 (m), 564 (m). Anal. Calcd. for C₄₈H₆₄N₂O₈Ti: C, 68.23; H, 7.64, N, 3.32. Found: C, 68.53; H, 8.15, N, 3.37.

Synthesis of N,N'-bis(2-hydroxo-3,5-*di-t*-butylphenylmethyl)-N,N'-bis(1,3-benzodioxol-5-ylmethyl)ethylenediamine (2a)

A solution of N, N'-bis(1,3-benzodioxol-5-ylmethyl)ethylenediamine (1.00 g, 3.08 mmol), 2,4-di-t-butylphenol (1.27 g, 6.15 mmol) and aqueous formaldehyde (39% w/v, 1.08 g, 13.1 mmol) in methanol (ca. 30 mL) was refluxed for 24 h. The white precipitate obtained was filtered, washed with methanol (ca. 4×20 mL) and then dried in vacuum to obtain product 2a as white solid (1.14 g, 49%). ¹H NMR (CDCl₃, 400 MHz, 25 °C): δ 10.3 (s, 2H, OH), 7.13 (s, 2H, C₆H₂{2-OH,3,5- $C(CH_3)_3$), 6.73 (s, 2H, C_6H_2 {2-OH, 3, 5-C(CH_3)_3}), 6.66-6.64 (m, 4H, $C_7H_5O_2$), 6.57 (m, 2H, $C_7H_5O_2$), 5.92 (s, 4H, $C_7H_5O_2$), 3.62 (s, 4H, CH₂), 3.40 (s, 4H, CH₂), 2.65 (s, 4H, CH₂), 1.39 (s, 18H, $C(CH_3)_3$), 1.25 (s, 18H, $C(CH_3)_3$). ¹³ $C{^1H}$ NMR (CDCl₃, 100 MHz, 25 °C): δ 153.9 (C₆H₂{2-OH,3,5- $C(CH_3)_3$), 147.9 ($C_7H_5O_2$), 147.2 ($C_7H_5O_2$), 140.9 (C_6H_2 {2-OH,3,5-C(CH₃)₃), 135.9 (C_6H_2 {2-OH,3,5-C(CH₃)₃}), 130.6 $(C_7H_5O_2)$, 123.8 $(C_6H_2\{2\text{-OH},3,5\text{-C}(CH_3)_3\})$, 123.2 $(C_6H_2\{2\text{-}$ OH,3,5-C(CH₃)₃), 123.1 ($C_7H_5O_2$), 121.2 (C_6H_2 {2-OH,3,5- $C(CH_3)_3$), 109.9 ($C_7H_5O_2$), 108.2 ($C_7H_5O_2$), 101.2 ($C_7H_5O_2$), 59.3 (CH₂), 58.1 (CH₂), 50.2 (CH₂), 35.0 (C(CH₃)₃), 34.3 (C(CH₃)₃), 31.9 (C(CH₃)₃), 29.8 (C(CH₃)₃). Melting point: 141–143 °C. IR (KBr pellet cm⁻¹): 3396 (m), 2956 (s), 2902 (s), 2864 (s), 1600 (m), 1501 (m), 1489 (m), 1441 (s), 1388 (w), 1363 (w), 1352 (w), 1242 (s), 1208 (w), 1164 (w), 1124 (w), 1096 (w), 1072 (w), 1036 (s), 994 (w), 928 (m), 881 (w), 845 (w), 805 (w), 774 (w), 761 (w), 723 (w), 684 (w), 649 (w). HRMS (ES): m/z 765.4857 [(ligand + H)]⁺, Calcd. 765.4843.

Synthesis of [N,N'-bis(2-oxo-3,5-di-t-butylphenylmethyl)-N,N'-bis(1,3-benzodioxol-5-ylmethyl)ethylenediamine]Ti(O'Pr)₂ (2b)

To a solution of N,N'-bis(2-hydroxo-3,5-*di*-*t*-butylphenylmethyl)-N,N'-bis(1,3-benzodioxol-5-ylmethyl)ethylenediamine **2a**

(0.261 g, 0.341 mmol) in toluene (ca. 10 mL), a solution of Ti(O'Pr)₄ (0.184 g, 0.648 mmol) was added. The resulting solution was stirred at 50 °C for 4 h after which the volatiles were removed under reduced pressure. The residue was washed with hexane (ca. 2 mL) and dried under vacuum to obtain product 2b as a yellow solid (0.283 g, 89%). ¹H NMR (CDCl₃, 400 MHz, 25 °C): δ 7.08 (d, 2H, ${}^{4}J_{\text{HH}} = 2$ Hz, C₆H₂O₂{3,5-C(CH₃)₃}), 6.65 (d, 2H, ${}^{3}J_{HH} = 8$ Hz, $C_{7}H_{5}O_{2}$), 6.52 (d, 2H, ${}^{4}J_{HH} = 2$ Hz, $C_6H_2O_2\{3,5-C(CH_3)_3\}), 6.41 (d, 2H, {}^3J_{HH} = 8 Hz, C_7H_5O_2), 6.37$ (s, 2H, $C_7H_5O_2$), 5.87 (m, 4H, $C_7H_5O_2$), 4.85 (sept, 2H, ${}^3J_{HH} =$ 7 Hz, OCH(CH₃)₂), 4.15 (d, 2H, ${}^{2}J_{HH} = 13$ Hz, CH₂), 4.03 (s, 4H, CH₂), 3.22 (d, 2H, ${}^{2}J_{HH} = 13$ Hz, CH₂), 2.74 (d, 2H, ${}^{2}J_{HH} =$ 10 Hz, CH_2), 2.31 (d, 2H, ${}^2J_{HH} = 10$ Hz, CH_2), 1.42 (s, 18H, $C(CH_3)_3$, 1.20 (s, 18H, $C(CH_3)_3$), 1.12 (d, 6H, ${}^{3}J_{HH} = 7$ Hz, OCH(CH₃)₂), 1.07 (d, 6H, ${}^{3}J_{HH} = 7$ Hz, OCH(CH₃)₂). ${}^{13}C{}^{1}H{}$ NMR (CDCl₃, 100 MHz, 25 °C): δ 159.7 ($C_6H_2O\{3, 5-C(CH_3)_3\}$), 147.6 $(C_7H_5O_2)$, 147.5 $(C_7H_5O_2)$, 138.9 $(C_6H_2O\{3,5-C(CH_3)_3\})$, 135.8 $(C_6H_2O{3,5-C(CH_3)_3})$, 129.2 $(C_7H_5O_2)$, 126.6 $(C_7H_5O_2)$, 126.0 $(C_6H_2O{3,5-C(CH_3)_3}), 124.4 (C_6H_2O{3,5-C(CH_3)_3}),$ 123.6 $(C_6H_2O{3,5-C(CH_3)_3})$, 112.5 $(C_7H_5O_2)$, 108.1 $(C_7H_5O_2)$, 101.3 (C₇H₅O₂), 77.7 (OCH(CH₃)₂), 60.0 (CH₂), 59.4 (CH₂), 46.2 (CH₂), 35.3 (C(CH₃)₃), 34.3 (C(CH₃)₃), 31.9 (C(CH₃)₃), 30.6 (C(CH₃)₃), 26.9 (OC(CH₃)₂), 26.5 (OCH(CH₃)₂). Melting point: 279-282 °C dec. IR (KBr pellet cm⁻¹): 3446 (m), 3356 (m), 3118 (m), 2963 (s), 2865 (m), 2544 (s), 1658 (w), 1598 (w), 1503 (w), 1491 (m), 1441 (m), 1411 (w), 1392 (w), 1361 (w), 1270 (s), 1243 (s), 1203 (w), 1168 (w), 1124 (m), 1041 (m), 992 (w), 930 (m), 914 (w), 878 (w), 846 (s), 811 (w), 776 (w), 748 (w), 697 (w), 650 (w), 610 (m), 553 (m), 470 (m). Anal. Calcd. for C₅₄H₇₆N₂O₈Ti: C, 69.81; H, 8.25, N, 3.02. Found: C, 69.49; H, 8.37, N, 3.10.

Synthesis of N, N'-bis(2-hydroxo-3,5-*di*-chlorophenylmethyl)-N, N'-bis(1,3-benzodioxol-5-ylmethyl)ethylenediamine (3a)

A solution of N, N'-bis(1,3-benzodioxol-5-ylmethyl)ethylenediamine (1.00 g, 3.05 mmol), 2,4-di-chlorophenol (0.998 g, 6.12 mmol) and aqueous formaldehyde (39% w/v, 1.01 g, 12.2 mmol) in methanol (ca. 30 mL) was refluxed for 24 h. The white precipitate formed was filtered, washed with cold methanol $(ca. 4 \times 20 \text{ mL})$ and then dried in vacuum to obtain product **3a** as a white solid (1.20 g, 58%). ¹H NMR (CDCl₃, 400 MHz, 25 °C): δ 11.4 (s, 2H, OH), 7.25 (d, 2H, ${}^{4}J_{HH} = 2$ Hz, C₆H₂{2-OH,3,5-Cl₂}), 6.81 (d, 2H, ${}^{4}J_{HH} = 2$ Hz, C₆H₂{2-OH,3,5-Cl₂}), 6.73 (d, 2H, ${}^{3}J_{HH} = 8$ Hz, $C_{7}H_{5}O_{2}$), 6.65 (s, 2H, $C_{7}H_{5}O_{2}$), 6.58 (d, 2H, ${}^{3}J_{\text{HH}} = 8 \text{ Hz}, \text{ C}_{7}H_{5}\text{O}_{2}$), 5.96 (s, 4H, $\text{C}_{7}H_{5}\text{O}_{2}$), 3.64 (s, 4H, $\text{C}H_{2}$), 3.44 (s, 4H, CH_2), 2.63 (s, 4H, CH_2). ¹³C{¹H} NMR (CDCl₃, 100 MHz, 25 °C): δ 152.2 (C_6 H₂{2-OH,3,5-Cl₂}), 148.2 (C_7 H₅O₂), 147.7 ($C_7H_5O_2$), 129.1 (C_6H_2 {2-OH,3,5-Cl₂}), 129.0 ($C_7H_5O_2$), 126.9 (C₆H₂{2-OH,3,5-Cl₂}), 123.9 (C₆H₂{2-OH,3,5-Cl₂}), 123.8 $(C_6H_2\{2\text{-OH},3,5\text{-Cl}_2\}), 123.0 (C_7H_5O_2), 121.7 (C_6H_2\{2\text{-OH},3,5\text{-}$ Cl_2), 109.6 ($C_7H_5O_2$), 108.5 ($C_7H_5O_2$), 101.4 ($C_7H_5O_2$), 58.9 (CH₂), 57.9 (CH₂), 50.2 (CH₂). Melting point: 175–176 °C. IR (KBr pellet cm⁻¹): 3459 (w), 3070 (w), 2896 (w), 2842 (w), 2597 (w), 1670 (w), 1599 (m), 1501 (s), 1452 (s), 1391 (m), 1378 (m), 1283 (m), 1250 (s), 1232 (m), 1170 (m), 1103 (m), 1044 (s), 933 (m), 884 (m), 865 (m), 849 (m), 806 (m), 725 (s), 661 (w), 547 (w), 494 (w). HRMS (ES): m/z 677.0806 [(ligand + H)]⁺, Calcd. 677.0780.

Synthesis of [N,N'-bis(2-oxo-3,5-*di*-chlorophenylmethyl)-N,N'-bis(1,3-benzodioxol-5-ylmethyl)ethylenediamine $[Ti(O'Pr)_2$ (3b)

To a solution of N,N'-bis(2-hydroxo-3,5-di-chlorophenylmethyl)-N, N'-bis(1,3-benzodioxol-5-ylmethyl)ethylenediamine 3a (0.302 g, 0.445 mmol) in toluene (ca. 10 mL), a solution of Ti(O^{*i*}Pr)₄ (0.251 g, 0.883 mmol) in toluene (ca. 1 mL) was added. The resulting solution was stirred at 50 °C for 4 h after which the volatiles were removed under reduced pressure. The residue was washed with hexane (ca. 3 mL) and dried under vacuum to obtain product **3b** as a yellow solid (0.242 g, 65%). ¹H NMR (CDCl₃, 400 MHz, 25 °C): δ 7.29 (d, 2H, ${}^{4}J_{\rm HH}$ = 3 Hz, C₆H₂O{3,5-Cl₂}), 6.84 (d, 2H, ${}^{4}J_{\rm HH} = 3$ Hz, C₆H₂O{3,5-Cl₂}), 6.79 (d, 2H, ${}^{3}J_{\rm HH} =$ 8 Hz, $C_7H_5O_2$), 6.57 (s, 2H, $C_7H_5O_2$), 6.55 (s, 2H, $C_7H_5O_2$), 5.99 (m, 4H, $C_7H_5O_2$), 5.19 (sept, 2H, ${}^3J_{HH} = 6$ Hz, OCH(CH₃)₂), 4.25 (d, 2H, ${}^{2}J_{HH} = 14$ Hz, CH₂), 4.13 (s, 4H, CH₂), 3.43 (d, 2H, ${}^{2}J_{HH} = 14$ Hz, CH₂), 2.61 (d, 2H, ${}^{2}J_{HH} = 11$ Hz, CH₂), 2.42 (d, 2H, ${}^{2}J_{HH} = 11$ Hz, CH₂), 1.32 (d, 2H, ${}^{3}J_{HH} = 6$ Hz, OCH(CH₃)₂), 1.28 (d, 2H, ${}^{3}J_{HH} = 6$ Hz, OCH(CH₃)₂). ${}^{13}C{}^{1}H{}$ NMR (CDCl₃, 100 MHz, 25 °C): δ 157.8 (C₆H₂O{3,5-Cl₂}), 147.9 $(C_7H_5O_2)$, 147.8 $(C_7H_5O_2)$, 129.4 $(C_6H_2O\{3,5-Cl_2\})$, 128.2 $(C_6H_2O{3,5-Cl_2})$, 126.7 $(C_7H_5O_2)$, 125.9 $(C_6H_2O{3,5-Cl_2})$ Cl_2), 125.8 (C_6H_2O {3,5- Cl_2 }), 122.6 (C_6H_2O {3,5- Cl_2 }), 121.3 $(C_7H_5O_2)$, 112.3 $(C_7H_5O_2)$, 108.3 $(C_7H_5O_2)$, 101.4 $(C_7H_5O_2)$, 79.8 (OCH(CH₃)₂), 58.9 (CH₂), 57.2 (CH₂), 47.7 (CH₂), 26.1 $(OCH(CH_3)_2)$, 25.8 $(OCH(CH_3)_2)$. Melting point: 261–262 °C dec. IR (KBr pellet cm⁻¹): 3437 (m), 2967 (m), 2901 (w), 1503 (m), 1490 (s), 1461 (s), 1443 (s), 1376 (w), 1362 (m), 1319 (m), 1300 (m), 1240 (m), 1217 (w), 1177 (w), 1127 (m), 1040 (m), 1022 (m), 928 (w), 864 (s), 779 (s), 755 (m), 592 (w), 572 (w), 534 (w), 503 (w), 482 (w). Anal. Calcd. for $C_{38}H_{40}Cl_4N_2O_8Ti$: C, 54.18; H, 4.79, N, 3.33. Found: C, 53.77; H, 5.69, N, 3.06.

Synthesis of N, N'-bis(2-hydroxo-3,5-*di*-chlorophenylmethyl)-N, N'-dibenzylethylenediamine (4a)

A solution of N,N'-dibenzylethane-1,2-diamine (1.00 g, 4.16 mmol), 2,4-dichlorophenol (1.36 g, 8.34 mmol) and formaldehyde (39% w/v, 1.36 g, 16.4 mmol) in methanol (ca. 20 mL) was refluxed for 24 h. A white precipitate was formed which was filtered and washed with methanol (ca. 4×20 mL) and then dried over vacuum to obtain product 4a as a white powder (2.03 g, 83%). ¹H NMR (CDCl₃, 400 MHz, 25 °C): δ 11.5 (S, 2H, OH), 7.32–7.30 (m, 6H, C_6H_5), 7.25 (d, 4H, ${}^{3}J_{HH} = 8$ Hz, C_6H_5 , 7.14 (d, 2H, ${}^4J_{HH} = 2$ Hz, C_6H_2 {2-OH,3,5-Cl₂}), 6.80 (d, 2H, ${}^{4}J_{\rm HH} = 2$ Hz, $C_{6}H_{2}\{2\text{-OH},3,5\text{-Cl}_{2}\}$), 3.64 (s, 4H, CH_{2}), 3.54 (s, 4H, CH_2), 2.63 (s, 4H, CH_2). ¹³C{¹H} NMR (CDCl₃, 100 MHz, 25 °C): δ 152.3 (C₆H₂{2-OH,3,5-Cl₂}), 135.4 (C₆H₅), 129.5 (C₆H₅), 129.2 (C₆H₅), 129.1 (C₆H₅), 128.4 (C₆H₂{2-OH,3,5- Cl_2), 127.0 (C_6H_2 {2-OH,3,5-Cl₂}), 124.0 (C_6H_2 {2-OH,3,5-Cl₂}), 123.9 (C_6H_2 {2-OH,3,5-Cl₂}), 121.8 (C_6H_2 {2-OH,3,5-Cl₂}), 59.2 (CH₂), 58.2 (CH₂), 50.3 (CH₂). Melting point: 169-171 °C. IR Data (KBr pellet cm⁻¹): 3429 (m), 3079 (w), 3028 (w), 2925 (w), 2856 (w), 2542 (w), 1600 (w), 1452 (s), 1392 (w), 1362 (w), 1272 (w), 1249 (w), 1211 (w), 1169 (m), 1065 (w), 1019 (w), 966 (w), 864 (m), 846 (m), 749 (s), 728 (s), 705 (m), 672 (w), 612 (w), 483 (w). HRMS (ES): m/z 589.0973 [(ligand + H)]⁺, Calcd. 589.0983.

Synthesis of [N,N'-bis(2-oxo-3,5-di-chlorophenylmethyl)-N,N'-dibenzylethylenediamine]Ti(O'Pr)₂ (4b)

To a solution of N,N'-bis(2-hydroxo-3,5-di-chlorophenylmethyl)-N,N'-dibenzylethylenediamine 4a (0.205 g, 0.347 mmol) in toluene (ca. 5 mL), a solution of Ti(O'Pr)₄ (0.196 g, 0.614 mmol) in toluene (ca. 1 mL) was added. The resulting solution was stirred at 50 °C for 4 h after which the volatiles were removed under reduced pressure. The residue was washed with hexane (ca. 2 mL) and dried under vacuum to obtain product 4b as a yellow solid (0.208 g, 80%). ¹H NMR (CDCl₃, 400 MHz, 25 °C): δ 7.33-7.31 (m, 6H, C₆ H_5), 7.28 (d, 2H, ${}^{4}J_{HH} = 2$ Hz, C₆H₂O{3,5-Cl₂}), 7.08 (m, 4H, C₆ H_5), 6.79 (d, 2H, ${}^4J_{\rm HH} = 2$ Hz, C₆H₂O{3,5-Cl₂}), 5.18 (sept, 2H, ${}^{3}J_{HH} = 6$ Hz, OCH(CH₃)₂), 4.29 (d, 2H, ${}^{2}J_{HH} = 13$ Hz, CH_2), 4.19 (s, 4H, CH_2), 3.41 (d, 4H, ${}^{3}J_{HH} = 13$ Hz, CH_2), 2.62 (d, 2H, ${}^{2}J_{HH} = 11$ Hz, CH₂), 2.44 (d, 2H, ${}^{2}J_{HH} = 11$ Hz, CH₂), 1.33 (d, 6 H, ${}^{3}J_{HH} = 6$ Hz, OCH(CH₃)₂), 1.30 (d, 6H, ${}^{3}J_{HH} =$ 6 Hz, OCH(CH₃)₂). ¹³C{¹H} NMR (CDCl₃, 100 MHz, 25 °C): δ 157.9 $(C_6H_2O\{3,5-Cl_2\})$, 132.5 $(C_6H_2O\{3,5-Cl_2\})$, 132.4 (C_6H_5) , 129.5 (C_6H_5), 128.6 (C_6H_5), 128.5 (C_6H_5), 128.3 (C_6H_2O {3,5- Cl_2), 126.8 ($C_6H_2O\{3,5-Cl_2\}$), 122.7 ($C_6H_2O\{3,5-Cl_2\}$), 121.3 $(C_6H_2O{3,5-Cl_2}), 79.9 (OCH(CH_3)_2), 59.3 (CH_2), 57.3 (CH_2),$ 47.9 (CH₂), 26.2 (OCH(CH₃)₂), 25.9 (OCH(CH₃)₂). Melting point: 229–230 °C dec. IR (KBr pellet cm⁻¹): 3436 (m), 3063 (w), 3028 (w), 2966 (w), 2924 (w), 2860 (w), 2377 (w), 1583 (w), 1462 (s), 1441 (s), 1374 (w), 1312 (m), 1217 (w), 1178 (w), 1125 (m), 1070 (w), 1016 (m), 987 (m), 869 (m), 785 (w), 769 (m), 732 (w), 704 (m), 623 (w), 613 (w), 570 (w), 485 (m). Anal. Calcd. for C₃₆H₄₀Cl₄N₂O₄Ti: C, 57.32; H, 5.34, N, 3.71. Found: C, 56.98; H, 5.27, N, 3.82.

Computational methods

Density functional theory (DFT) calculations were performed using GAUSSIAN 0340 suite of quantum chemical programs on the 1b-4b complexes, with respective computed structures designated by 1b'-4b' (Fig. S4-S7, ESI[†]) and on the various derived intermediates and transition states namely, 4c'-4h', pertaining to a proposed mechanistic pathway. The Becke three parameter exchange functional in conjunction with Lee-Yang-Parr correlation functional (B3LYP) has been employed in this study.41 The LANL2DZ basis set was used for the Ti atom while all other atoms are treated with 6-31G(d) basis set.^{37,42} The geometry of the transition state structures were optimized in the first order saddle point using Gaussian 03 program suite. Stationary points were characterized as minima by evaluating Hessian indices on the respective potential energy surfaces using tight SCF convergence (10⁻⁸ a.u). Fully optimized transition state structures have been characterized by a single imaginary frequency, while rest of the optimized structures possesses only real frequency. Natural bond orbital (NBO) analysis43 was performed using the NBO 3.1 programs implemented in the Gaussian 03 package (Tables S7-S16, ESI[†]).

General procedure for sulfoxidation catalysis

In a typical run, to a solution of thioether (2.00 mmol), catalyst **1b–4b** (0.01 mmol) and internal standard 1,2-dichlorobenzene (2.00 mmol) in dry degassed methanol (5 mL), 50% aq. H_2O_2 (2.00 mmol) was added and the reaction mixture was allowed

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to stirred at room temperature under nitrogen atmosphere for 30 min. The products in the solution were quantified by gas chromatography (PerkinElmer Clarus 600) and subsequently identified by GC-MS (PerkinElmer Clarus 600 T) analysis.

Control catalysis experiment performed in absence of H₂O₂

A solution of thioether (2 mmol), catalyst **1b** (0.01 mmol) and internal standard 1,2-dichlorobenzene (2 mmol) in dry degassed methanol (5 mL) was allowed to stirred at room temperature under nitrogen atmosphere for 30 min in the absence of any added H_2O_2 . The reaction mixture was analyzed by gas chromatography (PerkinElmer Clarus 600) which showed no formation of the sulfoxide product. The same blank experiment when carried out in presence of air also showed no formation of the desired sulfoxide product.

Control catalysis experiment performed using molecular oxygen as oxidant

To a solution of thioether (2 mmol), catalyst **1b** (0.01 mmol) and internal standard 1,2-dichlorobenzene (2 mmol) in dry degassed methanol (5 mL), oxygen gas was bubbled through and the reaction mixture was allowed to stir at room temperature for 30 min. The reaction mixture was analyzed by gas chromatography and which showed no formation of the desired sulfoxide product.

Catalyst recovery experiment

To a solution of thioether (6.00 mmol), catalyst **2b** (0.03 mmol) in dry degassed methanol (5 mL), 50% aq. H_2O_2 (6.00 mmol) was added and the reaction mixture was allowed to stir at room temperature under nitrogen atmosphere for 30 min. The volatiles were removed under reduced pressure and the product mixture was analyzed by ¹H NMR spectra which showed no peak characteristic of the precatalyst **2b**.

UV-Vis experiment

In order to investigate the possibility of the sulfoxidation reaction proceeding *via* an electron transfer process the following UVvisible experiment was performed. To a 1×10^{-2} M solution of **1b** in CHCl₃ (1 mL) was added 1 mL of 2×10^{-2} M methanolic solution of H₂O₂ and 1 mL methanol and the UV-visible spectrum was recorded at room temperature. In a subsequent experiment, to a mixture of 1×10^{-2} M solution of **1b** in a CHCl₃ (1 mL) and 1 mL of 2×10^{-2} M methanolic solution of H₂O₂, was added 1 mL of $2 \times$ 10^{-2} M methanolic solution of thioanisole and the reaction was monitored by UV-visible spectroscopy in different time intervals up to 35 min. No additional bands corresponding to any redox intermediate or any radical species were observed upon addition of thioanisole, thereby ruling out the possibility of an electron transfer mechanism occurring in the sulfoxidation reaction.^{32b}

APCI/MS experiment for detection of the proposed peroxo species

The APCI/MS experiments were performed in both positive and negative ion modes to detect the proposed Ti(Iv)-peroxo species of the sulfoxidation catalytic cycle by **1b–4b**. In a typical experiment, a solution of the precatalyst **1b** or **2b**, and H_2O_2 (50 equivalent) in

CHCl₃–CH₃CN (10:1) mixture was injected in the LCMS(APCI) instrument and the spectrum was collected in both positive and negative ion modes. Specifically, the positive ion mode spectrum of **1b** and H₂O₂ showed a peak at m/z 759 (10% of the base peak) corresponding to the desired Ti-peroxo species (see Fig. S10–S11, ESI†). Additionally, a peak at m/z 680 (100%) of ligand **1a**, a cleaved product, and a peak at m/z 785 (25%) corresponding to the cationic species derived from **1b** by loss of one O'Pr moiety were observed. Similarly, the spectrum of **1b** and H₂O₂ in the negative ion mode showed the Ti-peroxo species at m/z 758 (20%) along with a more intense peak at m/z 793 (35%) that corresponded to its Cl⁻ adduct (Fig. S12–S13, ESI†). In this regard it should be mentioned that similar Cl⁻ adducts have been reported previously in the literature.⁴⁴

The APCI/MS in positive ion mode spectrum of **2b** and H_2O_2 showed a small peak at m/z 842 (2% of the base peak) corresponding to the desired Ti-peroxo species. Additionally, a peak at m/z 765 (100%) of the ligand **2a**, a cleaved product, and a peak at m/z 870 (2.5%) corresponding to the cationic species derived from **2b** by loss of one O'Pr moiety were observed (see Fig. S14–S15, ESI†). As observed earlier, the spectrum of **2b** and H_2O_2 in the negative ion mode showed the Ti-peroxo species at m/z 842 (10%) along with an intense peak at m/z 877 (25%) that corresponded to its Cl⁻ adduct (see Fig. S16–S17, ESI†).

¹H NMR experiment for detecting coordinated sulfoxide species at room temperature

 H_2O_2 (12 µL, 0.212 mmol) was added to a mixture of **1b** (0.029 g, 0.035 mmol) and thioanisole (0.013 g, 0.106 mmol) in CDCl₃ (0.7 mL) in an NMR tube and the reaction was monitored by ¹H NMR spectroscopy at room temperature. Within the first 5 min, the formation of sulfoxide, characterized by a peak at 2.73 ppm and the sulfone characterized by a peak at 3.05 ppm, in 3 : 1 ratio was observed and complete conversion to sulfoxide methyl proton, between its coordinated and free forms, was observed in the ¹H NMR spectrum suggested the rapid exchange between the coordinated and the free sulfoxide at room temperature or the formation of the coordinated sulfoxide species in trace amounts.

1H NMR experiment for detecting coordinated sulfoxide species at $-40\ ^\circ C$

 H_2O_2 (12 µL, 0.212 mmol) was added to a mixture of **1b** (0.030 g, 0.035 mmol) and thioanisole (0.013 g, 0.106 mmol) in CDCl₃ (0.7 mL) in an NMR tube and the reaction was monitored by ¹H NMR spectroscopy at -40 °C. The formation of both sulfoxide and sulfone was observed in the reaction mixture as their methyl resonances appeared at 2.79 ppm and 3.29 ppm respectively along with the unreacted sulfide in 1:1:6 ratios after 5 min of the reaction time. However, the observation of no significant shift of the sulfoxide methyl proton may be ascribed to the rapid exchange between the coordinated and the free sulfoxide even at low temperature (-40 °C). Concentration of sulfide, sulfoxide and sulfone were determined by the integration of the methyl group signals in the recorded spectra.

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