

Surfactant mediated oxygen reuptake in water for green aerobic oxidation: mass-spectrometric determination of discrete intermediates to correlate oxygen uptake with oxidation efficiency†

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A novel strategy of catalytic green aerobic oxidation by surfactant-mediated oxygen reuptake in water offers a new dimension to the applications of surfactants to look beyond as solubility aids and a conceptual advancement in understanding the role of surfactants in aquatic organic reactions through mass spectrometry guided identification of discrete intermediates.

Aerobic oxidation offers environmentally benign chemistries as toxic and corrosive stoichiometric oxidants (*e.g.*, peracids, iodoxyarenes, hydroperoxides or metallic oxidants such as lead tetraacetate, ceric ammonium nitrate *etc.*) can be replaced by dioxygen directly. However, this needs dioxygen activation¹ by various chemical models² and has a long-standing interest. A non-heme and transition-metal free model of dioxygen activation for green aerobic oxidation processes remains unexplored and is a challenging task. The adverse effect of chemical processes on the environment has put a thrust on sustainable development³ with major focus on the use of green reaction media.⁴ Water is most preferred on the basis of solvent selection guide of the pharmaceutical industry⁵ and its use in organic reactions has gained momentum.⁶ Yet its use is currently limited due to poor aqueous solubility of organic compounds and efforts are made to overcome the problem by using surfactants.⁷ However, the general assumption that ions in dissolved water have a strong effect on the bulk properties of liquid water led us to consider the role of surfactants beyond a solubility aid. Herein we report surfactant-induced direct fixation/activation of aerial oxygen by oxygen reuptake in water for an efficient strategy for green oxidation demonstrating that the role of surfactants extends beyond the solubility enhancing property.

We followed the cyclocondensation of benzaldehyde **1** (2.5 mmol) with 2-aminothiophenol **2** (2.5 mmol) in water in the presence and absence of surfactant by GCMS (Scheme 1).^{8,†}

Sodium dioctyl sulfosuccinate (SDOSS) showed 100% conversion to the desired 2-phenylbenzothiazole **3a** (96% isolated yield after purification) and was found to be the best promoter. Other surfactants afforded a mixture of **3a** and the 2-phenylbenzothiazoline **3b** with the **3a** : **3b** selectivity varying from 41 : 59 to 98 : 2 (**3a** was obtained in 32–91% yield after purification). Sodium dodecyl sulfate (SDS) and sodium

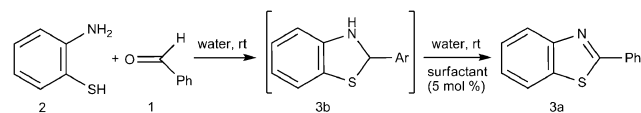
deoxycholate (SDC) were found to be the next best effective catalysts and exhibited **3a** : **3b** selectivities of 98 : 2 and 95 : 5 and afforded **3a** in 91 and 87% yields, respectively. Further studies on the optimization of the critical amount of SDOSS and the reaction time, revealed that the use of 5 mol% of SDOSS afforded 100% conversion to **3a** after 1 h at rt. The use of lesser quantities of SDOSS resulted in accumulation of some amount (4–15%) of **3b**.⁸ Elaborative GCMS studies on the SDOSS-catalysed reaction of **1** and **2** revealed that the use of water has two beneficial effects: (i) acceleration of the rate of cyclocondensation of **1** with **2** to form **3b** and (ii) enhancement of the rate of oxidation of **3b** to **3a** and that there is enhancement of oxygen transporter ability of water through oxygen uptake/reuptake mediated by SDOSS in accelerating the oxidative conversion of benzothiazoline to benzothiazole.⁸

To establish oxygen reuptake/activation as a specific role of the surfactant we measured the oxygen uptake property/ability of the surfactants to find any correlation between the oxygen uptake and the observed **3a** : **3b** selectivities (Fig. 1).^{8,†}

The oxygen content/uptake was found to be in higher amounts in the presence of SDOSS, SDS and SDC than that of the others⁸ and followed the order SDOSS > SDS > SDC which is in parallelism with the **3a** : **3b** selectivities observed in carrying out the cyclocondensation of **1** with **2** in water in the presence of these surfactants. A good correlation was also observed between the optimal oxygen content/uptake and the effective concentration/amount of SDOSS (Fig. 2). Maximum oxygen count/uptake was observed with 5 mol% of SDOSS which is evidently the critical micellar concentration to obtain the maximum conversion to benzothiazole.

The role of the surfactant for oxygen activation/reuptake can be visualised by the formation of the non-covalent adducts **A** and **B**, as exemplified in the case of SDOSS and SDS, respectively, (Fig. 3).

The oxygen activation/fixation⁹ occurs *via* a cooperative hydrogen bond network involving (i) one hydrogen of water and the oxyanionic site of sulfonate/sulfate group of SDOSS/SDS due to a labile hydrogen bond network at the surface of water¹⁰ and the propensity of the anion of alkali metal salts to form hydrogen bonds with water molecules,¹¹ (ii) the other hydrogen of the water molecule and one of the oxygen atoms of O=O, akin to proton assisted O–O bond scission in



Scheme 1 Surfactant-induced reaction of **1** with **2** in water.

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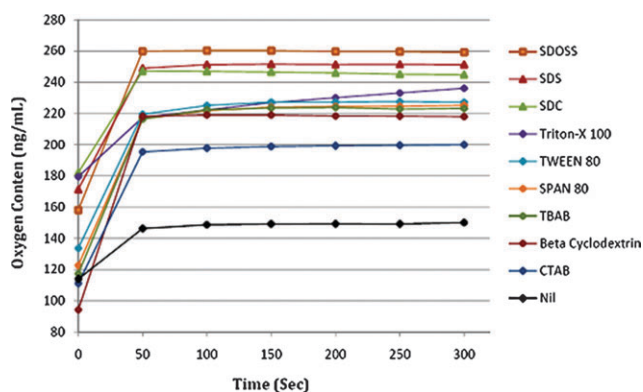


Fig. 1 Oxygen uptake by different surfactants.

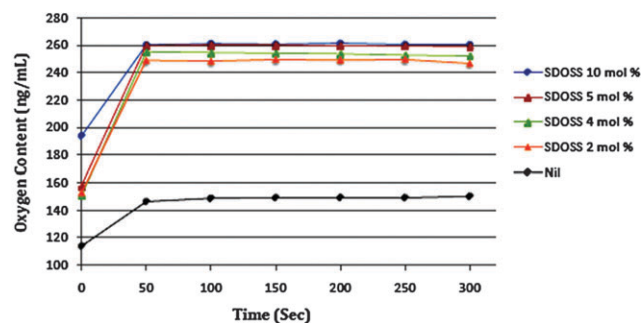


Fig. 2 Oxygen uptake with varying amounts of SDOSS.

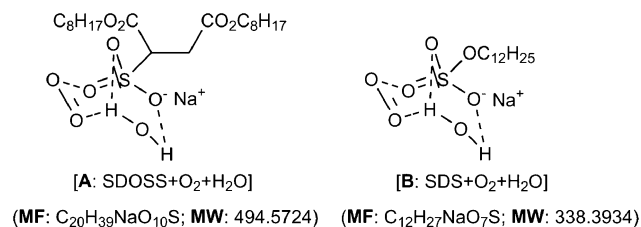


Fig. 3 The oxygen adducts of SDOSS (A) and SDS (B).

cytochrome P450,¹² followed by (iii) charge–charge interaction between the electron deficient (due to hydrogen bond formation of the other oxygen atom with the water molecule) oxygen atom of O=O and the oxygen lone pair of electrons in the S=O of SDOSS/SDS. The oxygen atom of one of the S=O groups forms a bridgehead through the bifurcated¹³ hydrogen bond with water and provides rigidity to the structure. The absence of such hydrogen bonds and charge–charge interaction network in organic solvents explains the poor conversion and low **3a:3b** selectivity observed in these solvents. Although a clear solution of SDOSS is formed in these solvents they are not conducive for oxygen uptake/reuptake due to the absence of the desired co-operative non-covalent hydrogen bond interactions. This further suggests that the role of SDOSS in aqueous medium extends beyond as its function as a solubility enhancer. These structures mimic the protein environment of water-assisted dioxygen activation for heme metabolism¹⁴ and constitute a non-heme and transition metal-free model.

In support of oxygen activation/uptake by SDOSS we planned to detect/identify the actual catalytic species (oxygen adduct A). Electrospray ionisation mass spectrometry

(ESI MS) has the ability to efficiently generate ions of non-covalent species in the gas phase¹⁵ and is the frontline biochemical research tool to study non-covalent interactions.¹⁶ We recently demonstrated ‘ion fishing’ by MALDI and ESI MS to detect/identify non-covalently formed supramolecular assemblies of small molecules.¹⁷

The total ion chromatogram (TIC) under (+ve) ESI MS (on linear ion trap) of aliquots of samples from a stock solution of 5 mol% (with respect to the aldehyde used for reaction) of SDOSS exhibited ion peaks at m/z 495.57, 494.58, 493.56 as $[A + H]^+$, $[A]^+$ and $[A - H]^+$, respectively.⁸ Further structural proof of the ion of m/z 494.57 was obtained by the MS–MS (MS²) that resulted in daughter ions $[A - H]^+$, $[A - C_8H_{17}]^+$ and $[A - 2C_8H_{17} + H]^+$ at m/z 493.52, 381.36 and 269.24, respectively.⁸ The characteristic ion peaks observed in the TIC of similar MS experiments on SDS indicated the involvement of B.⁸ More convincing evidences were obtained from the +ve ESI HRMS (on Q-TOF). The TIC (Fig. 4a) exhibited ion peaks at m/z 495.2469, 494.3898 and 493.3865 corresponding to $[A + H]^+$, $[A]^+$ and $[A - H]^+$, respectively. The MS² (Fig. 4b) of the ion of m/z 494.3898 resulted in daughter ions at m/z 493.3865, 467.2043 $[SDOSS + Na]^+$, 381.2597 $[A - C_8H_{17}]^+$ and 355.0814 $[SDOSS + Na - C_8H_{17} + H]^+$.

The poor catalytic ability of other surfactants can be accounted for their inefficiency to form the oxygen adduct and was demonstrated by the fact that when an aqueous soln (5 mol%) of Tween 80 and cetyl trimethyl ammonium bromide (CTAB), as representative surfactants that afforded poor conversion to benzothiazole, were subjected to (+ve) ESI MS, no ion peak corresponding to the respective oxygen adduct could be detected in the TIC. Additionally, these surfactants also showed inferior oxygen uptake, as measured with the microelectrode.

It was reasonably conceived that the catalytic efficiency of SDOSS should correspond to the amount/concentration of the oxygen adduct formed/present during the course of the reaction. Hence the estimation of the oxygen adduct was performed by measuring the ion current (represented by peak area)¹⁸ of ions at m/z 492.5–496.5 using a fixed amount (10 μ L)

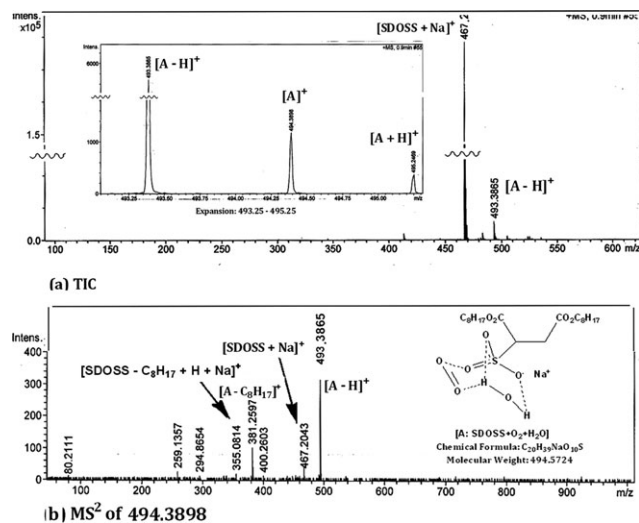


Fig. 4 (a) (+ve) ESI HRMS TIC of sample of 5 mol% SDOSS in 1 : 1 MeCN–water. (b) MS² of ion at m/z 494.3898 (TIC Fig. 4a).

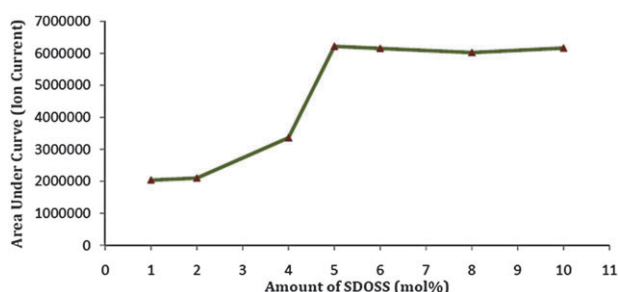


Fig. 5 Ion current of the species at m/z 492.5–496.5 measured using different amounts of SDOSS.

of stock solutions containing various amounts of SDOSS.^{8†} A good correlation was observed between the ion current and the critical amounts of SDOSS required for the formation of the benzothiazole (Fig. 5). An increasing trend of the ion current was observed with an increase in the concentration of SDOSS from 1–4 mol%. A sharp increase in the ion current was observed in changing the amount of SDOSS from 4 to 5 mol%. An optimum value of the ion current was obtained for the sample of the 5 mol% solution that also corresponds to the critical concentration/amount of SDOSS required to obtain the best conversion (100%) to **3a**.

In conclusion, the novel findings of catalytic aerial oxygen reuptake in aqueous medium offers a new dimension to the chemistry of surfactants to look beyond them as simply solubility aids. The identification of the non-covalent adduct as a discrete species in dioxygen activation and estimation/correlation of oxygen activation/uptake as a function of the ion current of the catalytic species makes the basis for rational selection of a surfactant for aerobic oxidation in aqueous medium and provides a non-heme and transition metal-free model for dioxygen activation under ambient conditions. Further implication of these findings is that it would provide insight into the microenvironment of reverse micelles that enable them to carry out various reactions in confinement, and the microscopic origin of the role of surfactants as solubility aids, and as to whether gaseous uptake is the prerequisite in imparting the solubility enhancing property of these materials!

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Notes and references

† Typical procedures. *Determination of benzothiazoline: benzothiazole selectivity during cyclocondensation of benzaldehyde with 2-aminothiophenol in the presence of surfactant*: To a magnetically stirred suspension of SDOSS (0.044 g, 5 mol%) in water (5 mL) was added benzaldehyde (0.21 g, 2 mmol) and 2-aminothiophenol (0.25 g, 2 mmol) and the mixture was stirred magnetically at rt. After completion of reaction (TLC, 1 h), the reaction mixture was diluted

with EtOAc (5 mL). An aliquot portion (500 μ L) of the supernatant EtOAc layer was taken out and subjected to GCMS to observe the benzothiazoline: benzothiazole selectivity of 2:98. *Determination of oxygen uptake by surfactants*: In a blank experiment ultrapure water (1 mL) (27 $^{\circ}$ C, 18.2 Ω) was taken into the cuvette of the Oxygraph and the oxygen content was recorded (0–5 min) at 70 rpm. Following a similar procedure the oxygen content/uptake of 1 mL freshly prepared 0.01 M solution of the surfactant in ultrapure water (27 $^{\circ}$ C, 18.2 Ω) was recorded. The actual oxygen content was determined by subtracting the blank reading from the corresponding reading of the analyte solution at 5 min and normalised to nmol mL^{-1} . *Determination of ion current of the oxygen adduct of SDOSS*: An aliquot portion (10 μ L) of a solution of SDOSS (0.022 g) in 5 mL of water–acetonitrile (1:1) was subjected to (+ve) ESI MS (linear ion trap) and the ion current was determined by measuring the area of the ion peak corresponding to the oxygen adduct of SDOSS.

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