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Anthraquinone Sulfonates as Water-Soluble Photocatalysts: Synthetic Applications and Perspectives

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Anthraquinone sulfonates are water-soluble and cost-effective photocatalysts that have been attracting increasing interest due to their unique features. Their sulfonate groups unlock the application of the photoactive anthraquinone core in aqueous solution. Moreover, these readily available catalysts can engage with substrates through different activation modes, such as hydrogen atom transfer and proton-coupled electron transfer events. However, to date, their reactivity has not been fully explored and further applications are expected to emerge. Herein, the existing synthetic applications are outlined and the future perspectives are discussed.

1. Introduction

Organic photoredox catalysts have become cost-effective alternatives to metal-based catalysts for the C—H activation of organic molecules.[1–3] Herein, even relatively simple quinone derivatives, such as naphthoquinones,[4,5] anthraquinones,[6,7] or DDQ,[8,9] showcase a rich photochemistry as these are able to interact as catalysts with substrates through different activation modes, including hydrogen atom transfer (HAT), single electron transfer (SET), and triplet energy transfer.[4–9]

However, despite the versatility of these quinone-based photocatalysts, due to solubility issues in aqueous medium, their use is often restricted to organic solvents. Accordingly, introducing ionizable substituents into these scaffolds can be a fruitful strategy to unlock their application in water as a sustainable solvent.[10] An example of this approach is anthraquinone sulfonates (AQS), which gather several desirable properties. Their high solubility in aqueous environments, commercial availability, and tunable redox properties make them an interesting option for the development of photochemical reactions in water. Herein, the low pKa values of the sulfonate groups of AQS enable the full ionization of these substances in this medium. This simplifies their catalytic systems, as the existence of different species in equilibrium is precluded, as it is the case with other catalysts displaying phosphate or carboxylate groups, whose speciation in water depends on the pH of the solution.[11] Regarding their general structure, AQS display a photoactive anthraquinone core attached to one or multiple sulfonate groups commonly coupled to an ammonium or sodium countercation (**Scheme 1**). In organic synthesis, the most commonly used are sodium AQS (SAQS) such as sodium anthraquinone-2-sulfonate (**SAQS-1**), sodium anthraquinone-2,6-disulfonate (**SAQS-2**), sodium anthraquinone-2,7-disulfonate (**SAQS-3**), and sodium anthraquinone-1,5-disulfonate (**SAQS-4**). Herein, the number of sulfonate groups, the symmetry, and the substitution pattern have a great impact on the solubility of these catalysts in water, which ranges from 0.0197 M for the monosulfonated derivative **AQS-1** to 0.74 M for the disulfonated derivative **SAQS-3**.[11,12] Moreover, their commercial availability and easy preparation by sulfonating anthraquinone make these catalysts attractive options when developing new reactions in water.

The quinone/semiquinone/hydroquinone redox system is, to date, one of the most studied.[13] Due to their rapid redox kinetics and chemical tunability, AQS have found widespread application as electrolytes in the design of redox flow batteries[13–17] or as exogenous redox mediators for biological systems.[18–21]

The photophysical properties of AQS were investigated as early as the 1950s.[22] The valuable mechanistic understanding gathered during this stage laid the foundation for the later development of their synthetic photochemical applications. Initially, AQS were almost exclusively employed as catalysts for the photooxidation of alcohols[22] and as photoinitiators for polymerizations.[23–26] More recently, several catalytic functionalization protocols have been reported, including tandem processes and photoelectrochemistry.

The UV–Vis spectra of AQS (**Figure 1**) display broad absorption bands with maxima around 330 nm and exhibit tailing into the visible light region. These bands correspond to electronic π–π^* transitions, and as can be observed, the different substitution patterns of AQS have only a limited impact on them.[11] Upon irradiation with purple or blue LEDs (365–450 nm), the photoactive anthraquinone core leads to excited states that can engage with substrates via HAT or proton-coupled electron transfer (PCET) events. For the latter, the protonated excited states of AQS have been found to display oxidation potentials of up to +2.3 V in the case of **SAQS-1**.[27] Furthermore, due to their ability to generate reactive oxygen species (ROS),[28,29] AQS can be employed for the oxidation of organic compounds in water.[30,31] Thus, these photocatalysts have promising potential applications in environmental remediation.[7]

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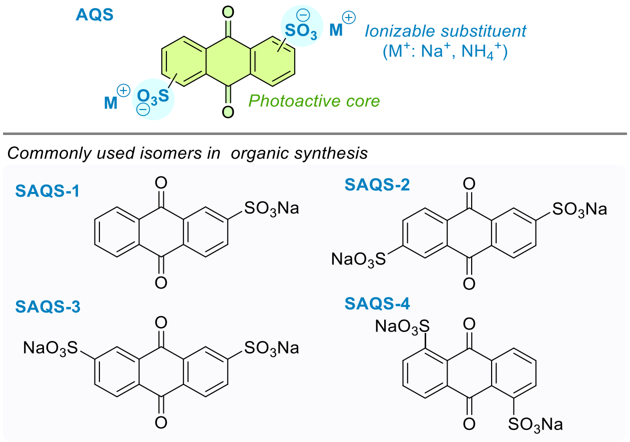


Scheme 1. General structure of AQS and most common isomers used in light-driven synthetic methodologies.

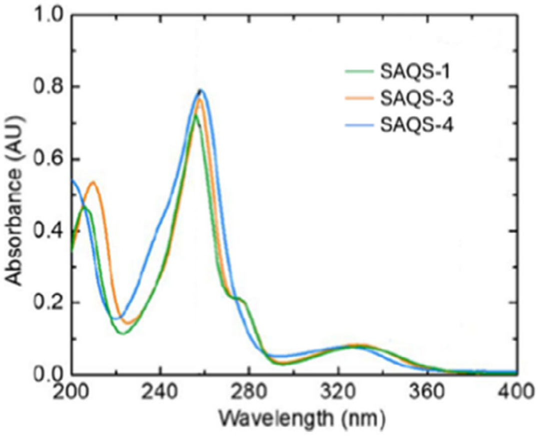


Figure 1. UV–Vis spectra of selected AQS derivatives in water. Reproduced under terms of the CC-BY license.[11] Copyright 2020, IOP Publishing.

To date, these substances have been predominantly employed as photoexcitable HAT agents for the activation of C—H bonds. However, in our opinion, the full potential of these water-soluble catalysts has not been fully explored yet. We expect significant progress in this field, especially as notable efforts are currently underway to further develop photochemical reactions in water.[10,32–38] Accordingly, our intention is to provide the reader with a roadmap of the multiple opportunities offered by AQS.

In this perspective, we outline the general properties of AQS, present existing synthetic applications, showcase recent advances, and discuss future perspectives. For the different synthetic methods presented, selected substrate scope examples are provided, plausible reaction mechanisms are discussed, and their eventual application in the late-stage functionalization of natural products and pharmaceuticals is showcased.

2. Aqueous Photochemistry of AQS

Despite the many advantages provided by the solubility of AQS in water and their ability to engage with substrates via HAT and ET events, it is of utmost importance to understand the different ways in which AQS can react with water itself.

Photoinduced reactions between AQS and water have been attracting attention for over 50 years. In the late 1960s, it was observed that the irradiation of aqueous solutions of AQSs with near ultraviolet and visible light yields a mixture of hydroxylated anthraquinone sulfonate derivatives.[39,40] Multiple studies have been conducted to demystify the nature of this aqueous photoreactivity. In early reports,[39–41] the hydroxylating ability of AQS was explained by the generation of free hydroxy-radicals derived from water (Fenton-type chemistry). However more recent studies ruled out the formation of free hydroxyl radicals in the aqueous solution of AQS.[42–45] Although, until now, there is no consensus on the exact mechanism, elaborated spectroscopic studies (including laser flash photolysis) allow us to draw the following photoreaction scheme for **SAQS-2** (**Scheme 2**a).[43]

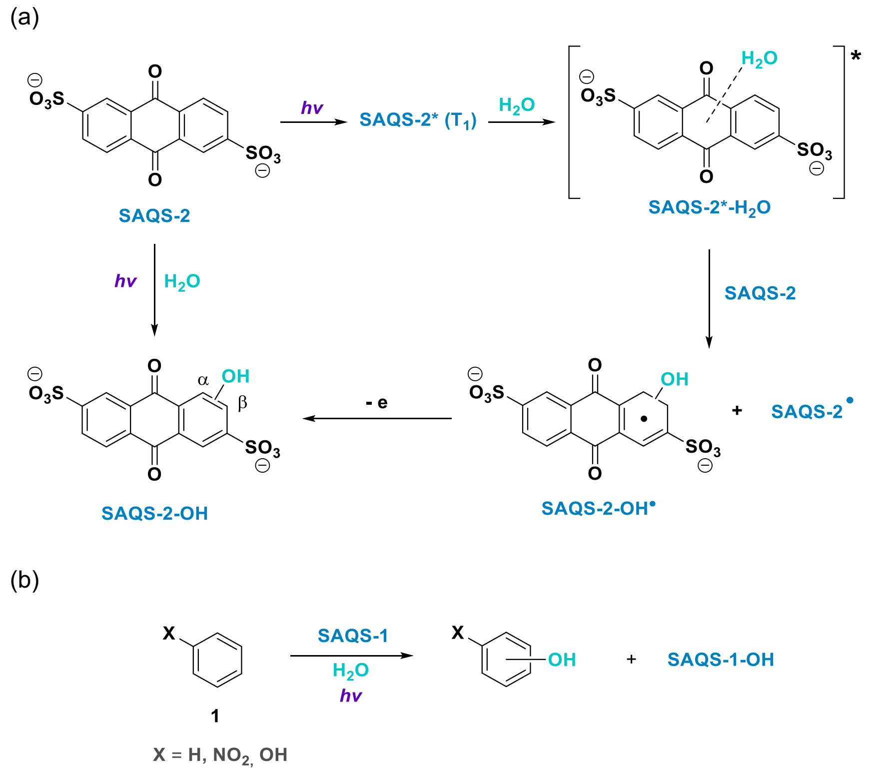
First, upon irradiation, **SAQS-2** undergoes photoexcitation to form the triplet species (**SAQS-2***) featuring a lifetime of less than 1 μs. Triplet **SAQS-2*** undergoes a fast reaction with water to form two spectroscopically distinct anthraquinone-water adducts **SAQS-2*-H_2O**.[46] Due to their short lifetimes, the exact structures of **SAQS-2*-H_2O** were not clearly determined. However, time-resolved resonance Raman spectroscopy provided some hints.[47] Further, **SAQS-2*-H_2O** might undergo oxidation by ground state **SAQS-2** to form an anthraquinone-hydroxy radical adduct **SAQS-2-OH$^•$** and semiquinone radical **SAQS-2$^•$**. The semiquinone species **SAQS-2$^•$** can then be quenched in the presence of oxygen, or, alternatively, under inert conditions, disproportionate to give the parent anthraquinone **SAQS-2** and the corresponding fully reduced hydroquinone (**SAQS-2-H_2**). Oxidation of **SAQS-2-OH$^•$** in aqueous solution by oxygen or another oxidant leads to the formation of stable hydroxylated products **SAQS-2-OH**. The α/β-OH regioisomer distribution depends on the pH of the solution and oxygen concentration.[40] Noteworthy, the photoreactivity and the intermediates observed for monosubstituted **SAQS-1** are almost equivalent to that proposed for disulfonate **SAQS-2**.[45,46,48–53]

Interestingly, light-excited **SAQS-1** species can induce hydroxylation of aromatic compounds (**1**) such as benzene, nitrobenzene, or phenols (Scheme 2b).[30,45] As a result, it is important to note that despite their many advantages, AQS also have an important drawback: they can react with water. Accordingly, these catalysts may not be suitable for reactions that require prolonged periods of time. Alternatively, an increased catalytic loading can be employed to account for these undesired catalyst losses. In contrast, the photohydroxylating ability of aqueous AQS toward substituted benzenes holds promise for synthetic application, especially if operated in a catalytic regime.

3. Photochemical Applications of AQS

3.1. Photooxidation of Alcohols

AQS absorb light in the near-UV and visible range to form excited states capable of engaging with substrates in HAT events through homolytic C—H bond cleavage. Some advantages of performing



Scheme 2. Aqueous photochemistry of AQS. a) Photohydroxylation of SAQS-2 in inaquesous solution.[43] b) Photohydroxylation of arenes SAQS-1.[30,45]

such reactions in water are the inert nature of this solvent towards HAT events (due to the high bond-dissociation energy (BDE) of its HO—H bond)[54] and the increased lifetimes of the formed open-shell species in this medium, as neutral C-centered radicals do not react with water.[37]

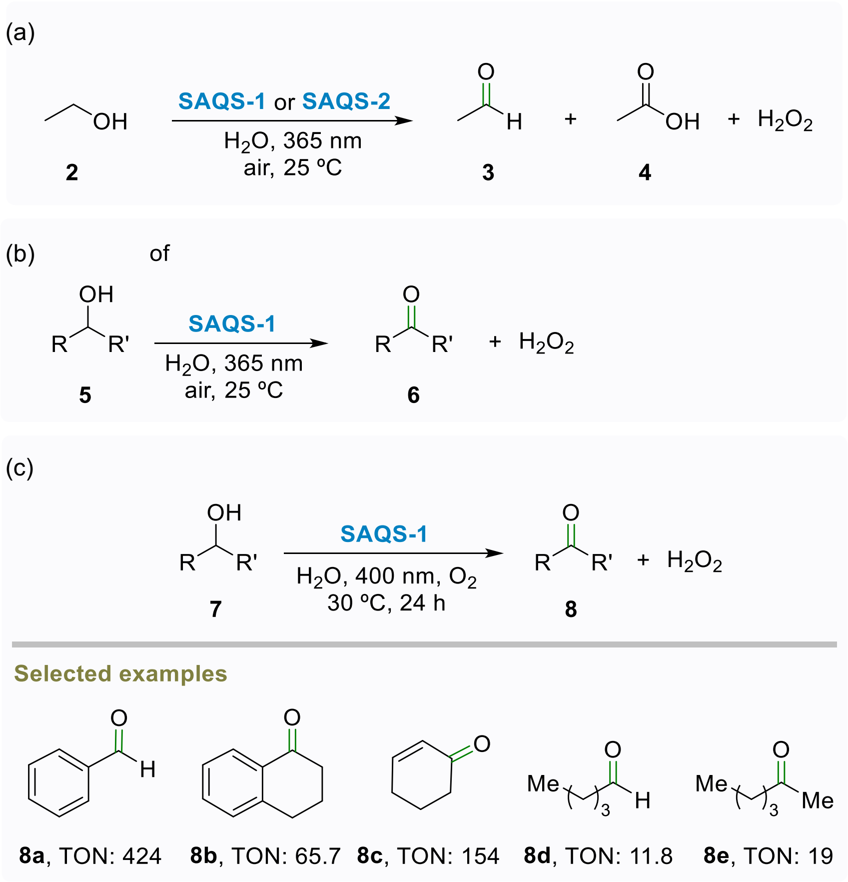
Once these C-centered radicals are formed by AQS, a wide array of transformations can be accessed depending on the presence of radical traps. For instance, molecular oxygen is prone to react with these open-shell species to form peroxyl radicals as reactive intermediates. These, due to their instability, can further collapse to form stable carbonyl derivatives (aldehydes and ketones) or carboxylic acid products upon hydrogen peroxide extrusion.[55,56] Therefore, it is of no surprise that the first synthetic applications of AQS were developed under air atmosphere, making use of this ubiquitous external oxidant. Additionally, this aerobic photooxidative approach has been proven efficient for the design of tandem sequences that utilize the formed carbonyl compounds as electrophilic reactants.

Due to the relatively low BDE displayed by α-alkoxy C—H bonds,[54] alcohols are particularly attractive substrates for HAT-based transformations. Moreover, the polarity of these functional groups allows us to employ small alcohol molecules in aqueous environments.

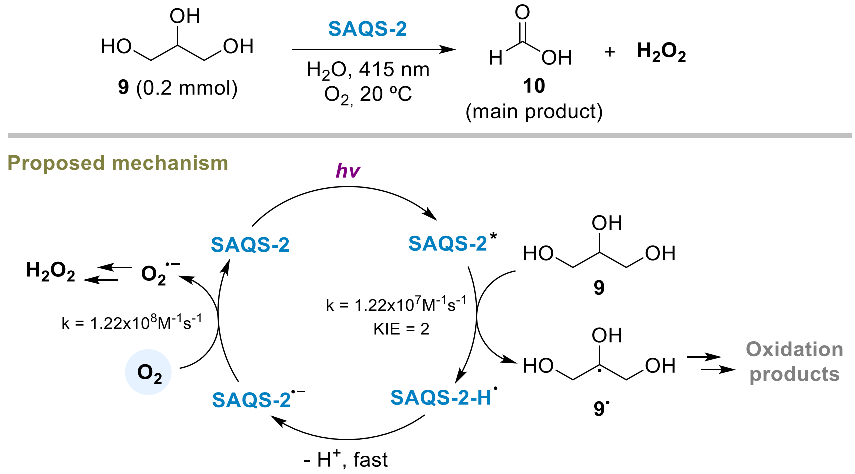
Pioneering work by the Cooper group in 1954 provided the first example of the application of AQS for the photooxidation of an alcohol.[22] The authors successfully employed sodium antraquinone-2,6-disulfonate (**SAQS-2**) in aqueous solution under aerobic conditions and 365 nm irradiation. Under these conditions, the photooxidation of ethanol (**2**) yielded a mixture containing acetaldehyde (**3**) as the main product, hydrogen peroxide as a by-product, and significant amounts of acetic acid (**4**) (**Scheme 3**a). The latter formed presumably due to the overoxidation of the formed acetaldehyde product, as the aldehydic C—H bond displays a rather low BDE, and therefore, is prone to undergo HAT in the presence of **SAQS-2**. Building on these results, Wells reported a series of kinetic experiments regarding the photooxidation of several alcohols (**5**) (methanol, ethanol, isopropanol, and *tert*-butanol) with **SAQS-1** in aqueous solution (Scheme 3b).[57,58] Accordingly, this work expanded the scope of the photooxidation of alcohols for the preparation of a ketone (**6**) (in this case, acetone, obtained by oxidizing isopropanol). Altogether, these initial findings were followed by significant mechanistic speculation, wherein, Newton concluded that the photooxidation of alcohols proceeded through H-atom abstraction from the alcohol by the electronically excited anthraquinone in its n,π^* triplet state.[59]

Inspired by the previously discussed findings, in 2017 Hollmann and coworkers developed a general method for the photooxidation of alcohols (**7**) using **SAQS-1** as HAT catalyst (Scheme 3c). By activating a wide array of benzylic (**7a** and **7b**), allylic (**7c**), and aliphatic (**7d** and **7e**) α-alkoxy C—H bonds, the corresponding aldehydes and ketones were successfully prepared (**8a**–**8e**) with reasonable turnover numbers (TON) (Scheme 3c).[60] Herein, the authors proposed a mechanism based on the quenching of C-centered radicals by oxygen and the formation of peroxyl radicals as key intermediates.

More recently, the Sartorel group reported a similar light-driven strategy for the oxidation of glycerol (**9**) in aqueous solution employing **SAQS-2** as the catalyst (**Scheme 4**).[61]



Scheme 3. AQS-catalyzed photooxidation of alcohols. a) Oxidation of primary alcohols.[22,59] b) Oxidation of secondary alcohols.[59] c) Scope expansion for alcohols.[60]



Scheme 4. AQS-catalyzed glycerol oxidation to formic acid.

In this approach, formic acid (**10**) was obtained as the main product (30% yield, 79% selectivity), along with a mixture of other oxidation products (including dihydroxyacetone, glycolic acid, glyceric acid, and carbon dioxide) and hydrogen peroxide as a by-product. In this case, the authors provided substantial evidence for the proposed HAT-driven mechanism, including spectroscopic and computational investigations, which were consistent with previously reported findings. Transient absorption spectroscopy (TAS), for instance, allowed to detect the triplet excited state of the photocatalyst (**SAQS-2***; $t \approx 0.9$ µs), formed upon irradiation. This species was postulated to abstract a hydrogen atom from the activated C2 position of **9** (bimolecular rate constant $k = 1.22 \times 10^7$ $M^{-1}s^{-1}$, KIE = 2) giving a C-centered radical (**9**$^{\cdot}$) and a ketyl radical (**SAQS-2-H**$^{\cdot}$). The former radical then

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undergoes oxidative degradation, yielding a mixture of glycerol oxidation products, including **10**. The latter species, **SAQS-2-H$^•$**, rapidly loses a proton to generate the corresponding semiquinone radical (**SAQS-2-H$^{•-}$**), as confirmed by TAS and electron paramagnetic resonance. Lastly, under aerobic conditions, SAQS-2-H$^{•-}$ is reoxidized by oxygen to **SAQS-2** (bimolecular rate constant $k = 1.2 \times 10^8\ M^{-1}s^{-1}$) accompanied by hydrogen peroxide formation, thus, closing the catalytic cycle.

3.2. Oxygenation of Aliphatic C—H Bonds

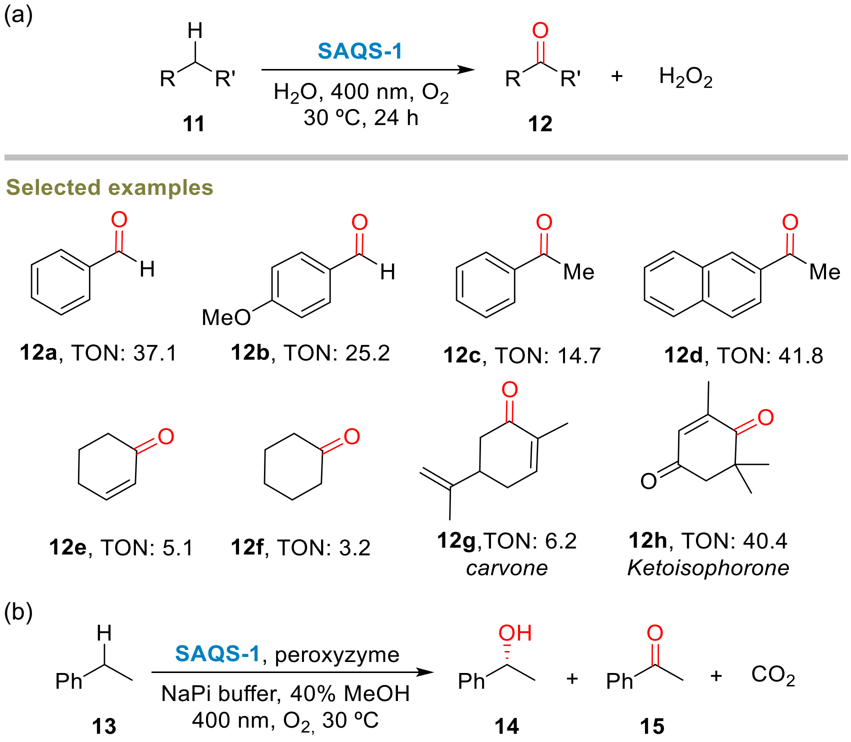
Additionally, the Hollman group applied the same approach with **SAQS-1** for the oxygenation of aliphatic C—H bonds (**11**) to give the corresponding carbonyl products (**12a–h**) (**Scheme 5**a).[60] Herein, the experiments performed with alkyl benzenes (**12a–d**) delivered the best TON for **SAQS-1**, presumably due to the relatively low BDEs displayed by their benzylic C—H bonds. Less activated C—H bonds displaying notably higher BDEs proved to be suitable as well (**12e–h**), although with notably lower TON, as showcased, for instance, by the oxidation of cyclohexene (**12e**) or cyclohexane (**12f**). Furthermore, the methodology was successfully applied for the selective oxygenation of two natural terpenes: limonene (**11g**) to carvone (**12g**) and isophorone (**11h**) to ketoisophorone (**12h**). Similar to the photooxidation of alcohols to carbonyl compounds, Hollmann suggested the formation of peroxyl radicals in the presence of oxygen. However, the oxygenation of aliphatics by anthraquinones is still the subject of ongoing investigations and mechanistic speculation.[62]

In a later publication, Hollman and coworkers reported **SAQS-1** as an efficient catalyst for driving the peroxygenase-catalyzed oxygenation of ethylbenzene (**13**) to give 1-phenylethanol (**14**) and acetophenone (**15**) (Scheme 5b), showcasing the combined advantages of water-solubility, excellent reactivity, and compatibility with peroxyzymes as enzymatic systems.[63] Moreover, the initial oxidation of ethylbenzene (**13**) to 1-phenylethanol (**14**) was performed in an asymmetric fashion, although with low enantioselectivity (34% ee). This same approach was applied to the oxidation of cyclohexane to cyclohexanol and cyclohexanone with similar results.

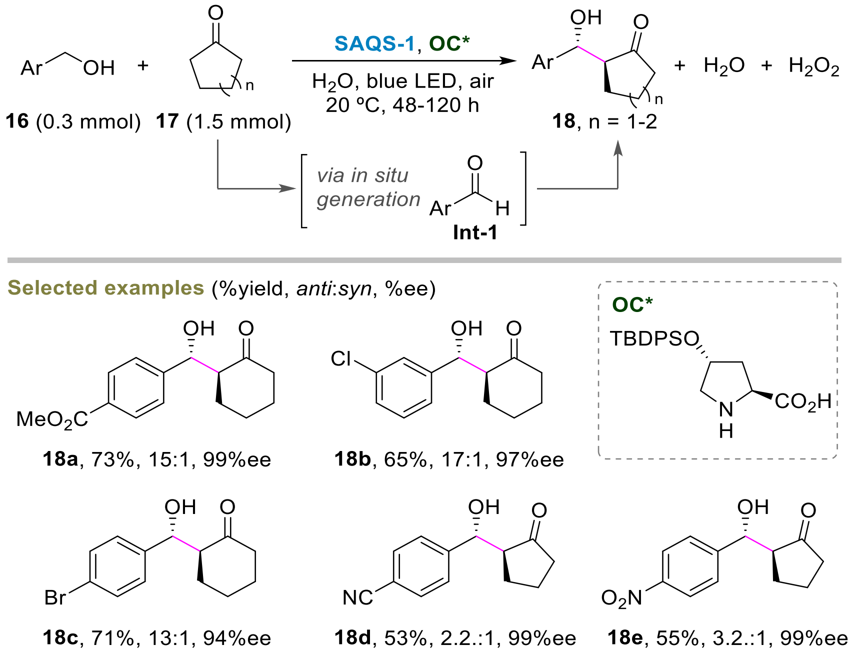
3.3. Tandem Photooxidative Processes

Based on the facile photooxidation of alcohols to carbonyls by AQS, such transformations can be coupled to additional steps, thus, utilizing the formed aldehydes as reactive electrophilic intermediates. As a result, tandem photooxidative processes (TPP) in alignment with the principles of green chemistry[64,65] can be easily designed, thus, circumventing tedious intermediate purification steps.

Such an approach was successfully implemented with **SAQS-1** by the Itoh group in 2015.[66] Herein, the photooxidation of benzyl alcohols (**16**) to benzaldehydes (**Int-1**) under aerobic conditions was coupled with a subsequent aldol condensation with cyclic ketones (**17**). Accordingly, the authors prepared several *β*-hydroxy ketones from benzyl alcohols displaying various substitution patterns and cyclic ketones of different ring sizes (**18a–e**) (**Scheme 6**). Furthermore, by employing a derivative of L-proline as a water-soluble asymmetric organocatalyst (**OC***), the corresponding products were obtained with high diastereo- and enantioselectivities. For this tandem process, the authors proposed the in situ generation of benzaldehydes (**Int-1**) accompanied by concomitant hydrogen peroxide formation as a key



Scheme 5. AQS-driven oxygenation methodologies. a) Oxygenation of aliphatic C—H bonds;[60] b) AQS-driven peroxygenase-catalyzed oxygenation.[63]



Scheme 6. Asymmetric photooxidative aldol condensation of benzyl alcohols.

step. The formed aldehyde is proposed to undergo a condensation reaction with the enolate of the cyclic ketone. This final step is catalyzed by **OC***, which transfers its chiral information to the substrate, thereby allowing the nucleophilic attack of the enolate to occur in an asymmetric fashion.

More recently, the König group applied a similar strategy for the preparation of benzylidenemalononitrile derivatives (**21**) from benzyl alcohols (**19**) and malononitrile (**20**) (**Scheme 7**).[67] For this, the photooxidation of the benzyl alcohols to the corresponding benzaldehydes intermediates was coupled with a Knoevenagel condensation reaction. As a result, hydrogen peroxide and water are generated as by-products. This dual catalytic system comprises **SAQS-4** as HAT catalyst and β-alanine as a green and inexpensive organocatalyst. Regarding the substrate scope, benzyl alcohol and its derivatives displaying electron-donating groups gave particularly good results in terms of yield and short reaction times (**19a**,**b**). Additionally, the system was found to be compatible with various other substituents (**19c**–**e**). Moreover, this methodology was demonstrated to be efficient for the selective functionalization of benzylic over aliphatic alcohols (**19f**). Due to the low solubility of the formed products in aqueous medium, in most cases, these can be easily isolated by filtering the reaction mixture, resulting in an operationally simple protocol. Referring to the results published by Hollmann[60] and Itoh,[66] the König group proposed a plausible reaction mechanism for this transformation.

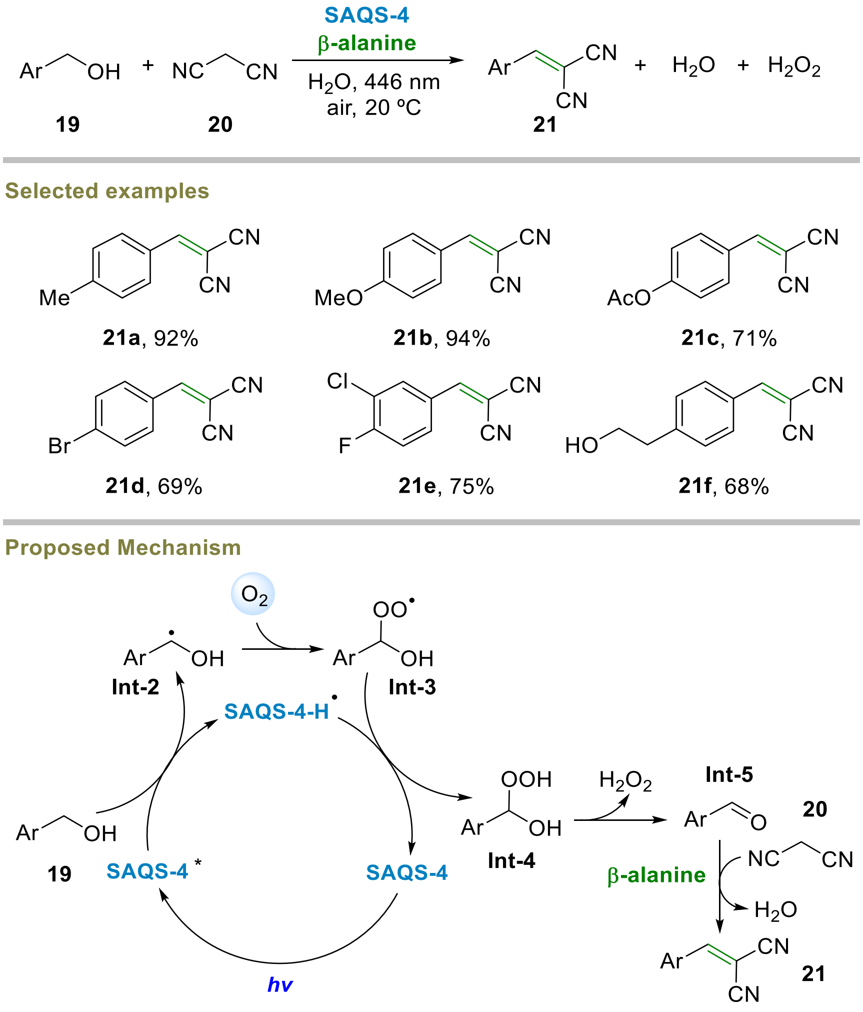
First, the photoexcited anthraquinone sulfonate (**SAQS-4***) engages with the benzyl alcohol (**17**) via HAT to generate an α-alkoxy benzylic radical (**Int-2**). This species can then be quenched by molecular oxygen to generate a peroxyl radical (**Int-3**). The resulting O-centered radical is proposed to convert **SAQS-4-H** to its ground state (**SAQS-4**) and the formed peroxide intermediate (**Int-4**) to decompose to the corresponding aldehyde (**Int-5**), releasing hydrogen peroxide. The aldehyde, in the presence of β-alanine as an organocatalyst, undergoes condensation with malononitrile (**20**), which results in the formation of the corresponding benzylidenemalononitrile product (**21**).

3.4. Bromination of Arenes

As an alternative to HAT activation, the excited triplet state of AQS can engage in sequential PCET processes. These sequences are initiated by an SET event between the excited AQS and an aromatic substrate with an accessible oxidation potential. The generated radical aryl cation intermediate then undergoes subsequent proton transfer (PT). Despite the great oxidative power of AQS, the synthetic applications of this activation mode are limited to just a few examples.

Due to their carbonyl groups, the electron density of anthraquinones can be easily altered by protonation, leading to modifications in their redox properties. As a result, particularly high redox potentials can be achieved, which would otherwise be almost exclusively attainable by notably more expensive photocatalysts, such as iridium complexes or acridinium dyes.

This strategy was successfully implemented by the König's group for the bromination of electron-rich arenes (**22**) via aromatic C—H activation through PCET (**Scheme 8**).[27] By protonating **SAQS-1** with trifluoroacetic acid, the authors claimed to achieve a redox potential of +2.3 V, able to engage with a variety of arenes via ET. The generated radical cation aryl species (**Int-6**) are postulated to undergo nucleophilic attack in the presence of bromide anions. As a result, the corresponding aryl bromide (**23**) is formed, while hydrogen peroxide is formed as a by-product of the process since oxygen is used as an external oxidant for the regeneration of the photocatalyst. This example showcases the versatility of AQS, as their redox properties can be easily tuned in the presence of certain additives such as acids.



Scheme 7. Tandem synthesis of benzylidenemalononitriles in/on water under visible light.

However, to date, the modification of the redox properties of these catalysts via protonation of hydrogen-bonding events remains relatively unexplored. Regarding the substrate scope, the methodology was successfully applied for the preparation of a wide array of products (**23a–g**), including bioactive molecules such as phenazone (**23 d**), tramadol (**23e**), lidocaine (**23f**), and gemfibrozil (**23g**). Interestingly, a similar enhancement in reactivity by protonation was reported for AQS in the photooxygenation process of alkanes.[62]

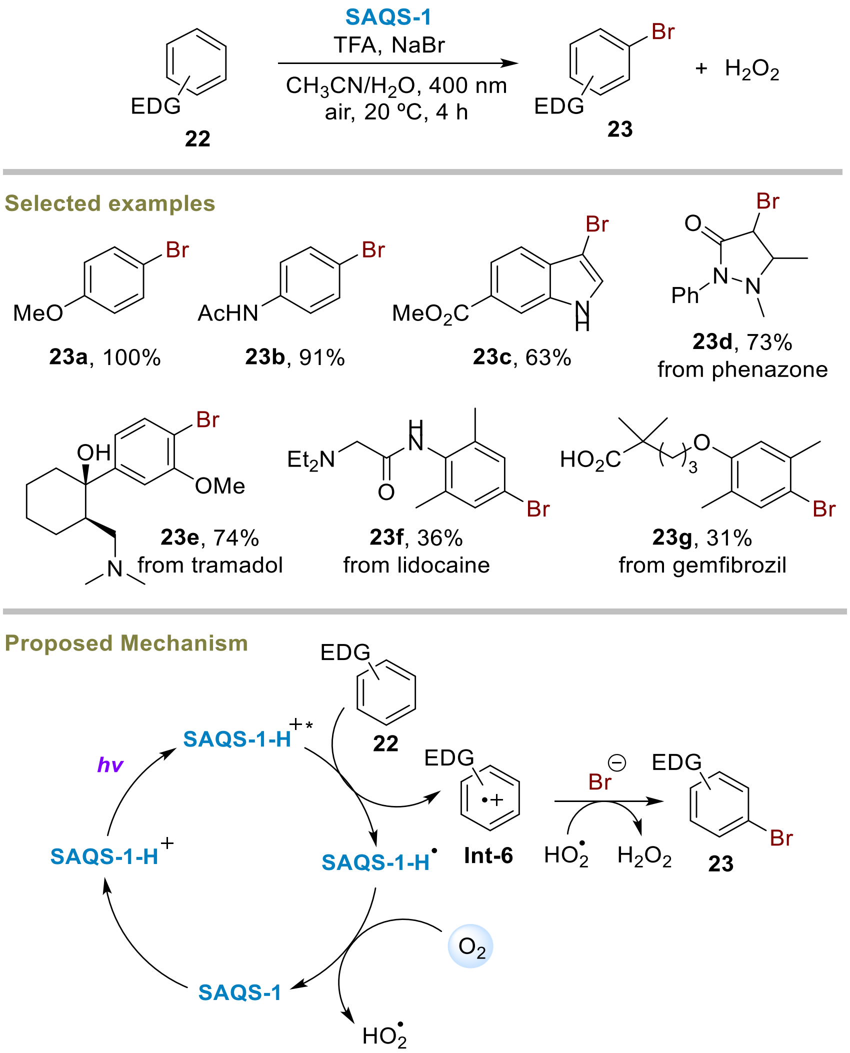
Regarding AQS-driven brominations, more recently, the Hollmann group demonstrated the application of **SAQS-1** for the bromination of thymol (**24**) using a peroxidase (**Scheme 9**), proceeding through the in situ generation of hypobromite as an oxidizing agent.[63] Herein, methanol is used as the sacrificial electron donor to drive this bromination process.

3.5. Photoelectrochemical Asymmetric Cyanation of Benzylic C—H Bonds

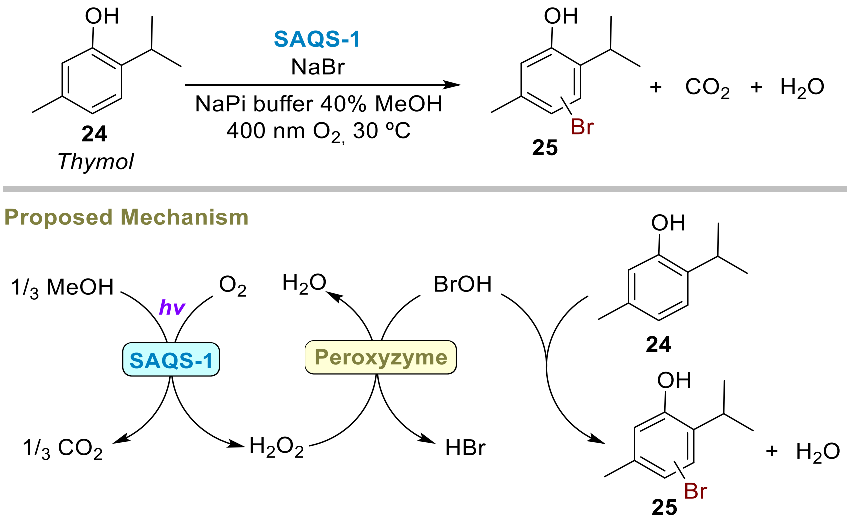
Another interesting application of AQS is their combination with photoelectrochemistry. Herein, the Xu group disclosed a versatile cyanation protocol for benzylic C—H bonds (**26**).[68] While trimethylsilyl cyanide (TMSCN) is used as cyanation agent, the dual catalytic system is based on the interplay between **SAQS-3** for benzylic radical generation and a copper complex employed for radical trapping (**Scheme 10**). As an alternative to other cyanation protocols based on photoinduced HAT,[69–71] Xu and coworkers employed **SAQS-3** for a two-step sequential electron/proton transfer. In this process, the applied current was used for regenerating both catalysts. By employing a chiral ligand (**L1***) in combination with a copper salt, the transformation was conducted asymmetrically, with high enantioselectivities. In addition, formic acid was employed for enhancing the reactivity of **SAQS-3** by increasing its oxidation potential, a similar strategy that has already been discussed for the bromination of electron-rich arenes by **SAQS-1**.[27]

Due to the mild reaction conditions, the system exhibited broad functional group tolerance (**27a–i**). Its scope included, for instance, a peptide derivative (**27d**) and substrates bearing highly reactive groups such as azides (**27e**) or epoxides (**27f**). Furthermore, the methodology was applied for the late-stage functionalization of bioactive molecules such as ibuprofen-(**27g**) D-glucose-(**27h**) or penicillanic acid (**27i**) derivatives.

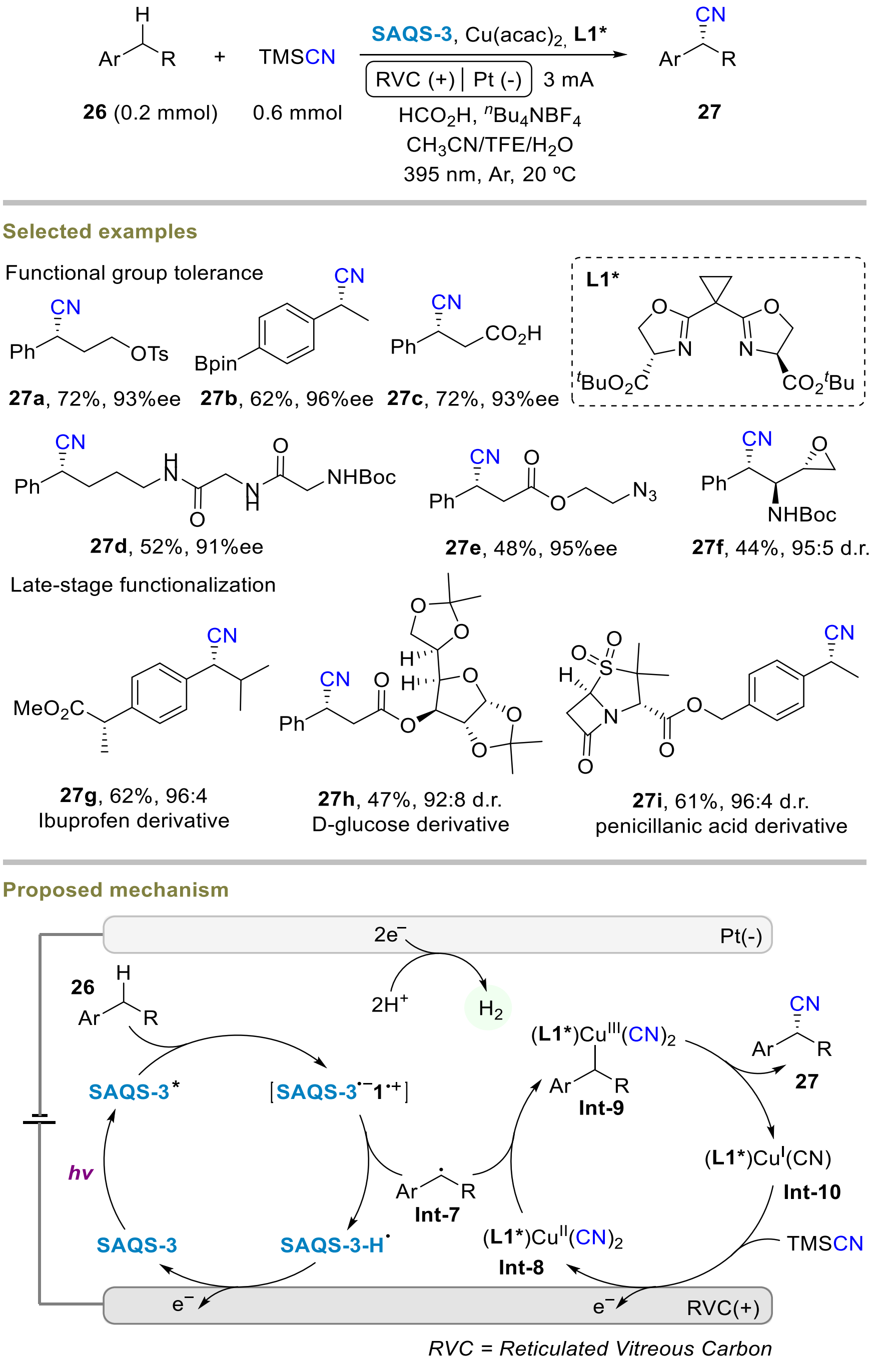
Regarding the proposed mechanism, the catalytic cycle is initiated with **SAQS-3** being excited by light to give **SAQS-3*,** which



Scheme 8. Photocatalytic bromination of electron-rich arenes.



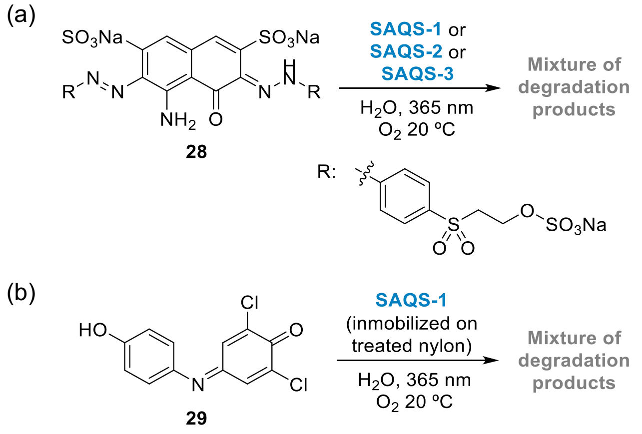
Scheme 9. AQS-driven peroxidase catalyzed bromination of thymol.



Scheme 10. Photoelectrochemical asymmetric cyanation of benzylic C—H bonds.

can engage through ET with the alkyl-arene substrate. As a result, an ion–radical pair is formed between the benzylic radical cation and the reduced semiquinone radical. Next, a PT event takes place between both species which results in the formation of a benzylic radical (**Int-7**). Subsequently, this open-shell species can be trapped by the copper (II) complex (**Int-8**) to form a copper (III) intermediate (**Int-9**). This complex then releases the desired cyanated product (**27**), simultaneously getting reduced to a copper (I) intermediate (**Int-10**), which is further oxidized by the anode and reacts with TMSCN to regenerate the copper (II) complex (**Int-8**). Similarly, the previously formed semiquinone species is also oxidized by the anode, thus closing the photocatalytic cycle. The electrons gained during both steps are used for proton reduction at the cathode.

Although, as mentioned, there are alternative photochemical cyanation methodologies available employing a HAT approach,[69–71] Xu's system showcases a clear advantage over these by regenerating the photocatalyst electrochemically. Furthermore, similarly to Itoh's work,[66] the combination of AQS photocatalysts with asymmetric catalysts has proven to be an efficient strategy for the preparation of products with high enantioselectivities.



Scheme 11. AQS-catalyzed degradation or organic dyes. a) Photooxidative degradation of Reactive Black 5.[28] b) Photooxidative degradation of DCIP.[31]

3.6. Environmental Applications

As discussed, upon irradiation, AQS can reach excited states from which they can react as strong oxidants via SET or as excellent HAT agents. Moreover, these catalysts stand out for their ability to generate ROS species[7,28,29] in water.

In addition, various AQS derivatives have been successfully employed for the degradation of organic dyes such as Reactive Black 5 (**28**) (**Scheme 11**a)[28] or 2,6-dichloroindophenol (**29**) (Scheme 11b).[31] Based on a series of mechanistic studies, the authors proposed the in situ generation of several ROS, including singlet oxygen, hydroxyl radicals, and peroxyl radicals. As a result, the potential application of these photocatalysts in wastewater may be promising. Furthermore, **SAQS-1** has also been reported as an efficient microbial photosensitizer for the removal of inorganic pollutants, such as nitrates, from aqueous solution. Herein, Zhou and coworkers reported a semiartificial system involving this catalyst as a photosensitizer for bacterial denitrification reactions.[72]

4. Future Perspectives

The current trends in synthetic organic chemistry point toward the further development of photocatalysis as an indispensable tool for performing organic transformations in a sustainable fashion. Prioritizing the use of green solvents is another key pillar of this strategy. However, in the case of water, the options regarding available photocatalysts are limited. Consequently, the demand for water-soluble catalysts is increasing. In this context, AQS are emerging as promising candidates contributing to this shift in organic synthesis, unlocking the application of the photoactive anthraquinone to the aqueous medium. Accordingly, these catalysts enable adapting quinone photochemistry to water such as benzylic or aromatic functionalizations.

Although for AQS, this feature is relatively underexplored, if we direct our attention toward other sulfonated photocatalysts, it becomes apparent that their water-solubility can be a significant advantage when aiming to transform highly polar biologically derived molecules. An excellent example of this application is provided by the structurally resembling photocatalysts to AQS, benzophenone-3,3′-bis(sodium sulfonate). Herein, this catalyst has been successfully employed as a HAT agent for the alkylation of α,β-unsaturated compounds[73,74] and the isomerization of aldoses.[75] Hereof, an example that might support a potentially similar application of AQS in the future is the recent report by the Murai group on the oxidation of ascorbic acid by anthraquinone-2,6-disulfonate.[76]

Another feature of AQS that might be further exploited is their excellent compatibility with other catalysts. To date, AQS have been successfully employed in combination with a wide array of other catalysts, ranging from simple organocatalysts, such as β-alanine,[67] to more complex catalysts, such as the proline derivative employed by the Itoh group,[66] or the chiral copper complex reported by Xu and coworkers.[68] This compatibility is also extended to biological systems, in which, due to the low pKa values of the sulfonate groups, speciation issues are precluded. Herein, apart from their application as electron shuttles in biological systems,[19] AQS have also been employed for synthetic purposes in the presence of enzymes[63] or as bacterial photosensitizers for denitrification processes.[72]

Furthermore, as showcased by Xu's cyanation protocol,[67] the application of electric current can be a fruitful strategy for the regeneration of AQS and the design of transformations with high atom economies. Although this approach remains relatively underexplored to date, it also holds great potential, as photoelectrochemistry is rising as a powerful tool for synthetic purposes.[77,78] Herein, the pioneering work by the Xu group might serve as inspiration for the development of more sustainable methodologies, precluding the need for sacrificial oxidants.

The ability of AQS, to generate a wide array of ROS species and their compatibility with biological systems, such as bacteria, has enabled the application of these photosensitizers for the degradation of a wide array of pollutants ranging from organic molecules, such as organic dyes,[31] to inorganic pollutants such as nitrates.[72] Herein, AQS might be a metal-free and more cost-effective alternative to other photocatalysts that have been investigated for similar purposes, such as the decatungstate anion, previously reported for the photodegradation of pesticides in water.[79]

In contrast, a particularly interesting but underexplored feature of AQS is the modification of their reactivity by protonation. This strategy was showcased by the bromination and cyanation protocols reported by the König[27] and Xu[68] groups, respectively, and it can render excellent results in the dramatic enhancement of the oxidative power of these catalysts by the addition of acids. AQS can easily replace certain oxidative catalysts as an inexpensive and water-compatible option. Moreover, the protonation of AQS significantly enables these photocatalysts to target a much broader range of substrates, thus, expanding the synthetic chemist's toolbox.

Lastly, in our opinion, the photophysical properties of AQS should be further investigated to provide valuable insights and guidance in the selection of different AQS isomers depending on their synthetic applications. Accordingly, the combination of experimental results, spectroscopic studies, and computational investigations might be a good strategy for getting valuable insights and drawing relationships between structure and reactivity of these promising photocatalysts.

5. Conclusions

AQS entail a class of photoorganocatalysts with outstanding properties and great potential applications in organic synthesis. To date, their application in oxygenation reactions has been particularly prominent, being TPP of great interest, as they allow to build molecular complexity from relatively simple molecules. Moreover, AQS have been successfully combined with chiral catalysts, enabling the development of asymmetric transformations in aqueous media. Furthermore, the electrochemical regeneration of these photocatalysts appears to point to the future development of more sustainable photoelectrochemical reactions. Additionally, due to the ability of AQS to generate ROS, their application for the degradation of organic compounds in water holds great potential. Altogether, we expect that further investigations and a better understanding of the reactivity of these catalysts might bolster the development of their synthetic applications in water in the upcoming years.

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Conflict of Interest

The authors declare no conflict of interest.

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