Photochemical Ring Editing: Access to Privileged 1,2,5-Thiadiazole Scaffolds *via* Efficient Carbon Excision from Thiadiazines Under Ambient, Aerobic Conditions

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Abstract

Thiadiazoles are a privileged motif in medicinal chemistry, however selective mono-oxidation of the endocyclic sulfur, without over oxidation, is challenging. Herein, we report the quantitative conversion of 1,2,6-thiadiazines to 1,2,5-thiadiazole 1-oxides in the presence of visible light and molecular oxygen under ambient conditions. Experimental and computational studies reveal a probable mechanistic pathway for the cycloaddition-ring contraction cascade: under visible light irradiation in the presence of molecular oxygen, 1,2,6-thiadiazines act as triplet photosensitisers that produce singlet oxygen and subsequently undergo an unprecedented, chemoselective [3 + 2] cycloaddition reaction. The resulting endoperoxide undergoes a ring contraction, with selective carbon atom excision and complete atom economy. The reaction was optimised under both batch and continuous-flow conditions and proven to be efficient in wide range of solvents, including green solvents. Flow conditions enabled precise control over irradiance exposure, enabling exclusive access to photosensitive thiadiazole products. A comprehensive scope of 1,2,6-thiadiazines provided 35 examples of novel, difficult-to-access 1,2,5-thiadiazole 1-oxide structures.

Introduction

Singlet oxygen ($^1O_2$) is a potent electrophile capable of selective oxidation of unsaturated hydrocarbons and electron rich heteroatoms. Since its discovery, the reactivity of $^1O_2$ has been well established; it has been shown to readily undergo pericyclic reactions with olefins and diene substrates, and selectively mono-oxidise sulfides and phosphines.[1] This unique reactivity has seen $^1O_2$ applied in the synthesis of a plethora of complex natural products and active pharmaceutical ingredients (Figure 1A).[2] Most famously, a $^1O_2$ mediated oxidation is a key step in the semi-synthesis of artemisinin, a vital anti-malarial drug which is manufactured on a >100 tonne per year scale (Sanofi).[3] Despite an increasing number of reports each year,[4] the known reactivity of $^1O_2$ has not expanded beyond the prototypical pericyclic reactions established in the late 20th century – with new reports largely focusing on the synthetic application of known $^1O_2$ reactivity towards complex synthetic targets.[2,5]

Whilst investigating 3,5-diphenyl-4*H*-1,2,6-thiadiazin-4-one (**1a**) as a potential photosensitiser for $^1O_2$ production, unusually rapid photobleaching of the chromophore was observed. Upon further analysis, it was revealed that thiadiazine **1a** had cleanly and quantitatively converted to 2-benzoyl-4-phenyl-1,2,5-thiadiazol-3(2*H*)-one 1-oxide (**1b**). The overall transformation had contracted the 6-membered heterocycle **1a** to a 5-membered ring in addition to oxidising one of the imine motifs to an imide and effecting the selective mono-oxidation of the ring sulfur to a stereogenic sulfoxide. It was remarkable that such a complex transformation, which clearly involved the cleavage of at least one C–C bond, could occur with only the substrate, solvent, visible light, and air present at ambient conditions.

Thiadiazoles are a privileged motif in nature and medicinal chemistry (Figure 1B),[6] with blockbuster drugs such as Timolol patented as early as 1968,[7] while reports and patents on 1,2,5-thiadiazole 1-oxides are rare. In 1982, a patent appeared describing 1,2,5-thiadiazole 1-oxides as elastase inhibitors for the treatments of diseases such as pancreatitis, emphysema and rheumatoid arthritis.[8] 1,2,5-Thiadiazole 1-oxides have also been applied as potent histamine H_2-receptor antagonists,[9] and for the inhibition of gastric acid secretion.[10] Despite their promising utility, there are relatively few reliable pathways to access 1,2,5-thiadiazole 1-oxides.[11–14] This is true for all sulfoxide-bearing scaffolds, as they are prone to overoxidation, and many chemoselective methods for their synthesis from sulfides use harsh reagents and high temperatures.[15] The ring contraction of 1,2,6-thiadiazines to access thiadiazoles has been previously reported, but generally involves high temperatures and the presence of acid to form non-S-oxidised 3,4-substituted-1,2,5-thiadiazole products.[16–20]

The most accessible synthetic pathways towards S-oxidised 1,2,5-thiadiazoles involve reacting thionyl chloride with *vic*-1,2-bisimines or bis(trimethylsilyl) derivatives,[21] but these reactions offer low to moderate yields. Weinstock *et al.*,[22] demonstrated that the lack of aromaticity of S-oxidised 1,2,5-thiadiazoles renders them highly electrophilic and thermally unstable. Therefore, the development of new mild and practical methods would allow researchers to explore this previously difficult to access chemical space.

The polyoxidation of thiadiazine **1a**, and specifically the selective oxidation of the sulfur atom to a sulfoxide, suggested to us that $^1O_2$ or other reactive oxygen species (ROS) must be involved in mediating this complex process. Herein, we describe an in-depth investigation of this transformation, which through a combination of detailed experimental and computational mechanistic studies, ultimately arrives at the discovery of an unprecedented, concerted [3 + 2] cycloaddition of $^1O_2$. The versatility and selectivity preferences of the reaction were explored through a comprehensive substrate scope of symmetric and asymmetric 1,2,6-thiadiazines, featuring 35 example structures (39-100%, 21 quantitative examples).

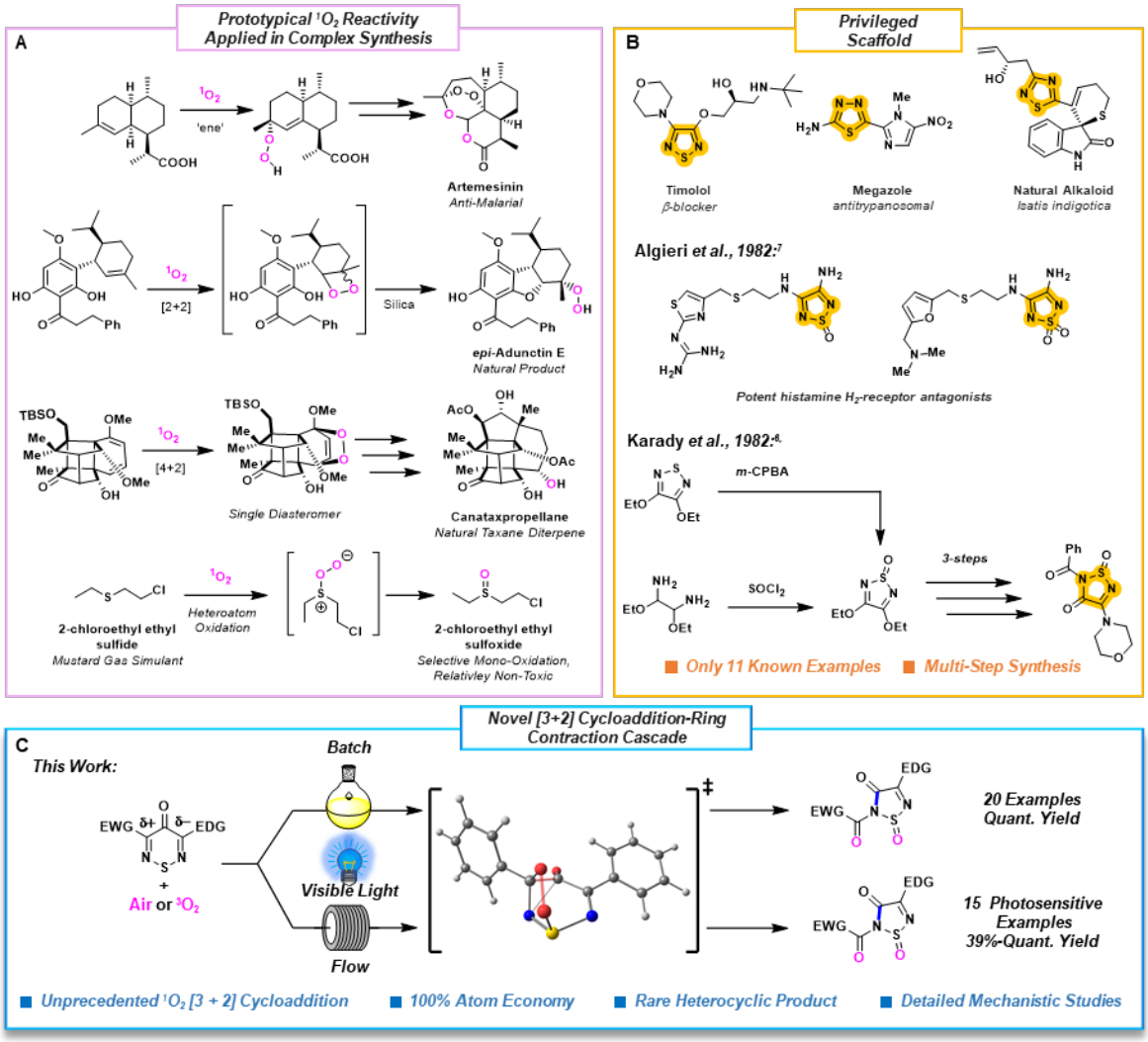


Figure 1. (**A**) Prototypical $^1O_2$ reactivity applied in the synthesis of complex natural products and active pharmaceutical ingredients. (**B**) Examples of active pharmaceutical ingredients featuring thiadiazole isomers and the only known reported synthetic route to 1,2,5-thiadiazole 1-oxides. (**C**) This work, describing a $^1O_2$ mediated oxidation and subsequent ring contraction to access 2,4-substituted 1,2,5-thiadiazole 1-oxides.

Optimisation and Mechanistic Studies

Following our initial discovery, we investigated the effects of various conditions to optimise the reaction and provide mechanistic insight. A series of control experiments confirmed that the reaction did not proceed in the absence of light or when irradiating with monochromatic light sources that did not overlap with the absorption spectrum of thiadiazine **1a**. Additionally, the reaction did not proceed under a N_2 atmosphere, confirming that $^3O_2$ was required and the source of the additional two oxygen atoms on the resulting thiadiazole **1b**. The reaction was repeated under an inert atmosphere while injecting varying volumes of $^3O_2$ to the reaction vessel, which gave a clear linear relationship with a gradient of ~1, indicating that the reaction proceeds *via* one equivalent of thiadiazine **1a** reacting with a single molecule of $^3O_2$ and providing 100% atom economy (Figure 2A).

The effect of temperature provided the first evidence that $^1O_2$ may be involved in the reaction: the reaction displayed a negative, approximately linear relationship between conversion and temperature (Figure 2B). The lifetime of $^1O_2$ in $CHCl_3$ can be significantly extended at reduced temperatures,[23] providing more time for the substrate and $^1O_2$ to react and rationalising our

experimental observations. Although reduced temperatures were beneficial, the reaction achieved full conversion in less than 15 min under ambient conditions with irradiation from a 420 nm LED module (28 W), and in the interest of operational simplicity, we proceeded with our investigation using these optimised conditions.

The reaction kinetics were then screened in a variety of solvents, as the lifetime of $^1O_2$ strongly depends on the solvent environment.[24,25] Specifically, we compared the reaction rate between protonated and deuterated solvents as the latter prolong the lifetime of $^1O_2$ by reducing vibronic energy transfer between $^1O_2$ and the solvent, which consequently reduces non-radiative decay of $^1O_2$.[26,27] The full kinetic profile of the reaction was qualitatively similar for all solvents. The profiles did not perfectly fit either a 1st or 2nd order kinetic model as they transitioned between different kinetic regimes after achieving a certain conversion of thiadiazine **1a** to thiadiazole **1b**, consistent with our proposed mechanism (*vide infra*). Hence, the initial rate of reaction, between approximately 0-70% conversion, which fits relatively well to a 1st order kinetic model was used to compare the various solvents empirically.

As anticipated, the reaction rate displayed a strong dependence on solvent environment and the initial reaction rate in deuterated solvents was generally an order of magnitude greater than their protonated equivalent (Figure 2C). Dimethyl carbonate was trialled as a green solvent alternative and provided similar kinetics to ethyl acetate and dichloromethane. Although dimethyl carbonate does not provide the most efficient reaction kinetics, it is a sustainable solvent alternative that was compatible with the reaction and could be enhanced through flow chemistry (*vide infra*).[28] The observed initial rate constant for the reaction was plotted against literature values for the lifetime of $^1O_2$ in the various solvents, revealing a strong positive correlation (Figure 2D). We suggest this is compelling evidence for the involvement of $^1O_2$ in the reaction. Dimethyl sulfoxide (DMSO) displayed significantly slower kinetics, with an observed initial rate constant that was two orders of magnitude lower than other non-deuterated solvents. As well as DMSO providing the lowest $^1O_2$ lifetime (5.5 μs), it is also known that DMSO can react with $^1O_2$ to form dimethyl sulfone, providing a competitive process that removes $^1O_2$ and rationalises the significant decrease in reaction rate – providing further evidence of the involvement of $^1O_2$.[29]

The reaction's kinetic profile was also investigated while varying some additional parameters (Figure 2E): the reaction rate was enhanced when performed under an atmosphere of pure $^3O_2$ and reduced when the intensity of irradiance was reduced (1 *vs* 2 LED modules). Additionally, only the initial rate, and not the observed 1st order rate constant, was significantly affected when the initial concentration of **1a** was reduced by 60% (0.25 *vs* 0.1 mg/mL). The details of these experiments and extracted rate constants are presented in the Supporting Information (see Section S2.4). Following this, we performed a series of experiments with ROS traps to help confirm the presence of $^1O_2$ (see Supporting Information, Section S2.1). Notably, in the presence of $^1O_2$ traps such as α-terpinene and Ph_3P, full conversion of thiadiazine **1a** to thiadiazole **1b** required significantly longer reaction times (1 and 2 h, respectively) and the expected characteristic $^1O_2$-trapped adducts, ascaridole and Ph_3PO, were observed.[30–32] Performing the reaction in the absence of irradiation and with dark $^1O_2$ generator systems also enabled the conversion to thiadiazole **1b**, indicating that the reaction mechanism was not reliant on a photochemical rearrangement of thiadiazine **1a** or its electronic excited states. Finally, the reaction was performed in the presence of a known $^1O_2$ photosensitiser, methylene blue, which has a visible light absorption spectrum that is chromatically orthogonal to that of the substrate **1a** (Figure 1F). With 1 mol% loading of the orthogonal photosensitiser and red-light irradiation (620 nm), under otherwise identical conditions, full conversion to thiadiazole **1b** was achieved within 1 h.

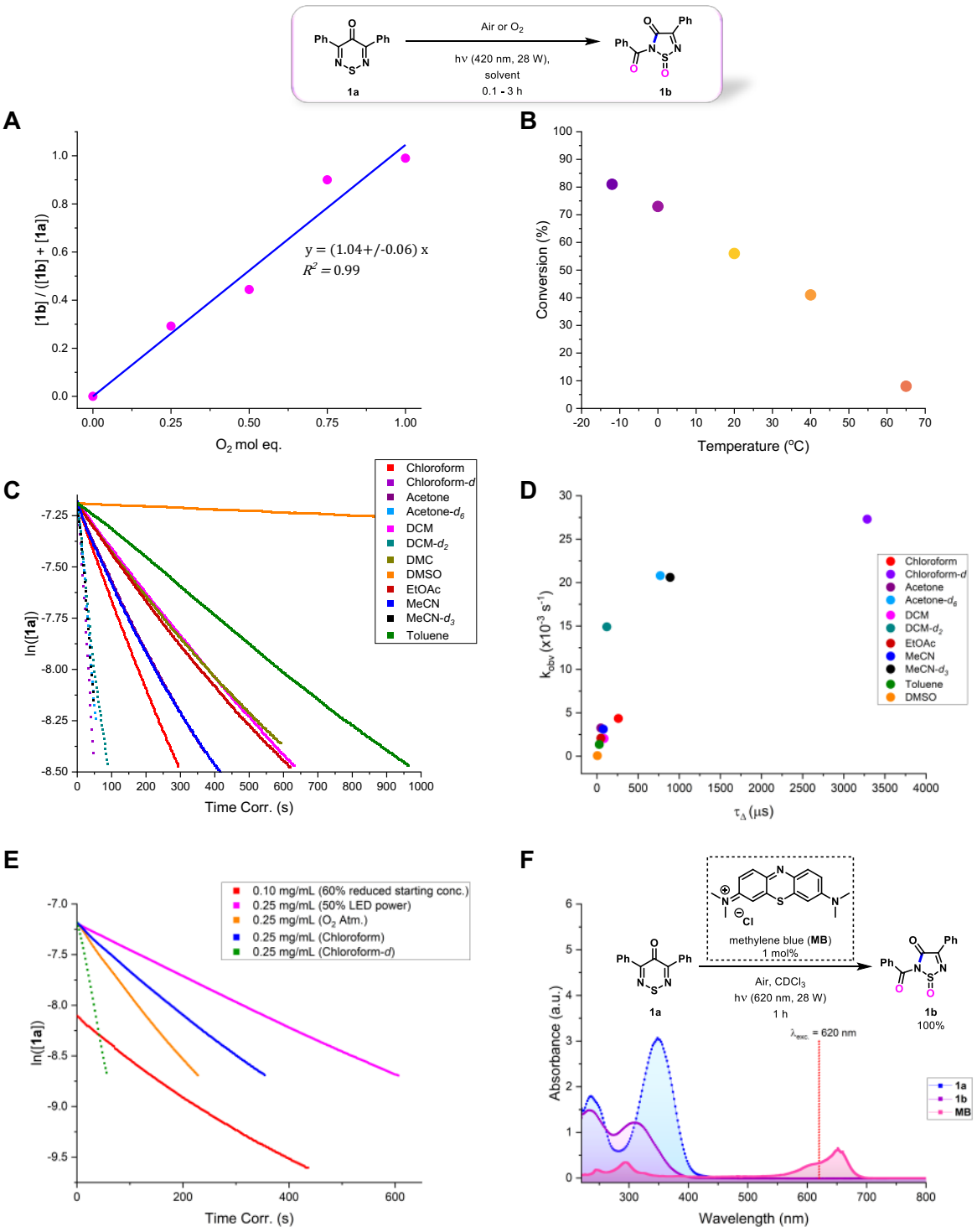


Figure 2. Series of plots showing the results of mechanistic and kinetic experiments for the general reaction scheme (top). (**A**) Plot of conversion *vs.* molar equivalents of oxygen injected to the reaction vessel. (**B**) Plot of conversion to **1b** *vs* reaction temperature. (**C**) Kinetic data of the conversion of **1a** under irradiation in various solvents, fit to a 1st order kinetic model. Monitored by UV-Vis. absorbance at 400 nm with continuous sampling (see Supporting Information, S2.4). (**D**) Plot of the observed 1st order rate constants in each of the solvents *vs* literature values for the lifetime of singlet oxygen in that solvent (τ_Δ). (**E**) 1st order kinetic models for the conversion of **1a** under various conditions, monitored by UV-Vis. Absorbance at 400 nm with continuous sampling. The blue trace is standard conditions under air. (**F**) Reaction scheme for the conversion of **1a** to **1b** using an orthogonal photosensitiser, methylene blue chloride (**MB**). The reaction scheme is superimposed over UV-Vis. spectra for **1a**, **1b** and **MB**, displaying that the visible light absorbances of the three compounds are orthogonal. The red dashed line indicates the excitation wavelength of maximum intensity for the monochromatic LED module used in the reaction.

This further suggests that $^1O_2$ can independently drive the reaction and enables the reaction to be performed with longer irradiation wavelengths that avoid excitation of more complex substrates containing chromophores.

To rule out the involvement of superoxide, the reaction was performed in the presence of dark superoxide generators and led to no conversion, with the starting material **1a** being fully recovered. Performing the reaction under standard conditions in the presence of 1,4-benzoquinone, a $O_2^{\cdot-}$ trapping species, achieved full conversion to thiadiazole **1b** within 45 min. However, the expected trapping adduct, hydroquinone, was not observed and suggests $O_2^{\cdot-}$ is not present.[33] Overall, we concluded that production of $O_2^{\cdot-}$ by thiadiazine **1a**, and its subsequent role in the reaction mechanism, was very unlikely.

Additionally, the reaction proceeded unhindered in the presence of Ph_2SeO, a trap for persulfoxide anions,[34] which shows the reaction does not proceed *via* the established mechanism of $^1O_2$ mediated sulfide oxidation to sulfoxides displayed in Figure 1A.

Computational Studies & Proposed Mechanism

The mechanism of the reaction of thiadiazine **1a** with singlet oxygen was investigated computationally (see Supporting Information, S3 for full details). Figure 3 shows that the initial addition of $^1O_2$ to thiadiazine **1a** can occur in two ways to give a common endoperoxide intermediate **I** at 7.4 kcal/mol: i) a concerted [3 + 2] addition across the C(Ph)–N=S moiety, *via* **TS(1a-1b)2** at 9.6 kcal/mol; or ii) an end-on addition of $^1O_2$ onto C3 *via* **TS(1a-1b)1** at 18.7 kcal/mol followed by barrierless S–O bond formation. From **I**, O–O bond cleavage occurs with concomitant ring contraction in a single step *via* **TS(1a-1b)3** at 21.7 kcal/mol. This process entails the simultaneous cleavage of the O–O and C3–C4 bonds as well as the formation of a new amide bond between N2 and C4 (see Figure 3). The formation of the thiadiazole in **2a** is very exergonic (ΔG = -85.7 kcal/mol) and proceeds with an overall barrier of 21.7 kcal/mol, consistent with the room temperature reactivity observed experimentally. **TS(1a-1b)3** will be both the rate-determining and selectivity-determining transition state.

We present in the Supporting Information (see S2.5 for details) a mechanism that we believe contains the minimum number of elementary steps to be consistent with the findings of the experimental and computational mechanistic studies and kinetics. In summary (Figure 3), the mechanism includes absorption by the substrate, thiadiazine **1a**; energy transfer from excited **1a** to $^3O_2$ to generate $^1O_2$ and return ground state **1a**; $^1O_2$ then subsequently reacts with the substrate to form the product, thiadiazole **1b**, *via* the [3 + 2] cycloaddition-ring contraction cascade discussed above; quenching of the $^1O_2$ by the solvent; and quenching of the excited state of the substrate, either by the solvent or by self-quenching. Assuming that establishment of a photostationary state is rapid relative to reaction, and with appropriate relative rates of other processes, this mechanism is consistent with the observed switch from approximately 1st order to 2nd order kinetics during the course of the reaction and with the observed sensitivity of the rate to other parameters (O_2 concentration, light intensity, and temperature).

To the best of our knowledge, concerted [3 + 2] cycloadditions with $^1O_2$ are unprecedented, with its existence previously only being tentatively suggested.[35] The discovery of this reactivity expands the already rich diversity of $^1O_2$ applications in chemical synthesis (*cf.* Figure 1A), unlocking new potential to achieve complex targets and novel chemical structures.

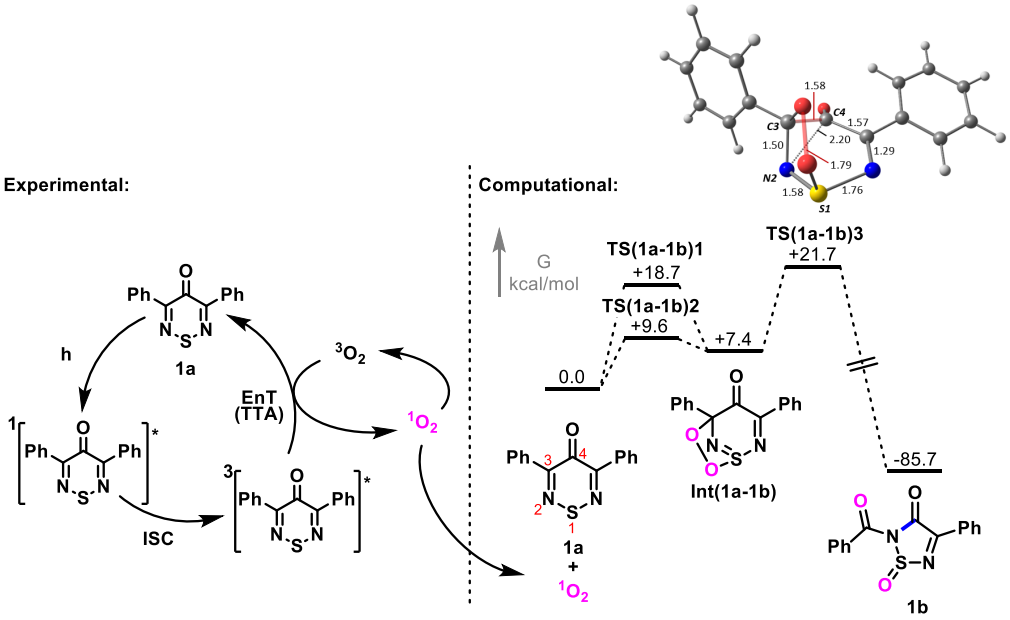


Figure 3. Proposed mechanism for the light mediated ring contraction of 1,2,6-thiadiazines to 1,2,5-thiadiazole 1-oxides. Computed free energy profiles (CASPT2(16,13)/6-31G**//UB3LYP($CHCl_3$)/6-31G**; kcal/mol) for the reaction of $^1O_2$ with thiadiazine **1a** to form thiadiazole **1b**. Geometry of **TS(1a-1b)3**. Breaking bonds in red, forming bond as a fragmented line. Key distances in Å.

Reaction Scope

The standard reaction conditions were re-optimised under continuous flow (see Supporting Information, S1.4). Optimisation of the flow system was initially performed with the green solvent, dimethyl carbonate, to examine the potential intensification of a sustainable process. Optimal process conditions were identified and the thiadiazole **1b** could be obtained in excellent yield (>98%) within 10 minutes residence time of the flow photo reactor, comparable to the optimised batch conditions in $CDCl_3$. When the optimised conditions were applied with $CDCl_3$ solvent, product **1b** could be isolated in quantitative yield after only 1 min residence time of the UV-150 reactor coil with a back pressure of 3 bar and using pure $^3O_2$ - a 15-fold reduction in reaction time from the batch protocol. The successful flow synthesis enables the continuous production of thiadiazole **1b** without concern over light attenuation effects that typically hinder the scale-up of photochemical processes in batch.[32]

The reaction generality was then explored on various 1,2,6-thiadiazine substrates. We chose to prioritise the batch protocol for substrate screening and reserved the flow procedure for more challenging substrates.

A selection of 3,5-diaryl-substituted thiadiazines were screened. Methyl-, methoxy- and chlorophenyl substituents were all tolerated well and provided the ring contracted products **2b**-**10b** in quantitative yields regardless of substitution pattern. The *m*-tolyl derivative **3b** photo-decomposed under batch conditions but could be isolated through the flow protocol in 97% yield. This highlights the benefit of precise control over irradiation exposure when performing a photochemical process with flow chemistry.[36]

In general, the reaction rates followed *para* > *meta* >> *ortho*. Additionally, *para*-substituted benzylether **11b** and methoxycarbonyl **12b** also followed this trend and were isolated in quantitative yield after 15 mins of irradiation in batch. As the resulting electronics of the aryl systems varies dramatically between the different substituents and ring positions, the most rational cause of this effect would derive from steric hindrance. However, as we propose the

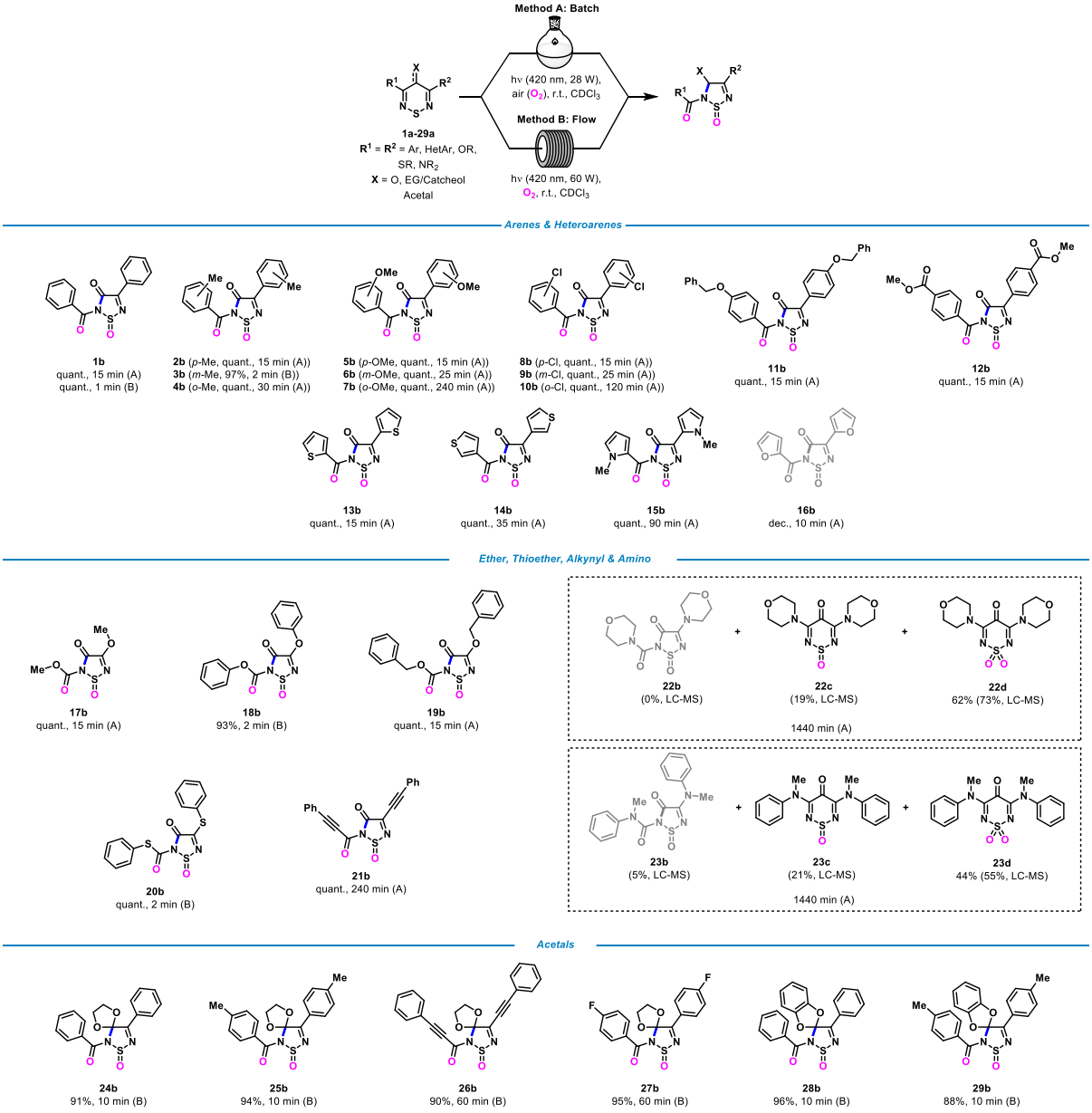
reaction is photoinitiated, it is possible that more complex photophysical phenomena are involved and the rate of reaction with various substrates could be tied to their relative inherent ability to generate $^1O_2$.

Heteroaryl-substituted thiadiazines were also well tolerated, providing ring-contracted products **13b**-**15b** in quantitative yield. In contrast, furyl-substituted thiadiazine **16b** decomposed, likely due to the known propensity of such species to undergo [4 + 2] cycloadditions with $^1O_2$ to produce endoperoxide species that readily ring open to form hydroxy lactones or carbonyl substituted olefins.[37,38] This tentatively supported our proposed mechanism involving $^1O_2$.

We then explored a series of thiadiazines with alternative, non-aromatic functional groups as 3,5-substitutents. Ethers and thioethers were tolerated and provided the ring-contracted thiadiazoles **17b**-**20b** in quantitative yields. Phenylether **18b** and thioether **20b** photo-decomposed using the batch protocol but were obtained in excellent yields under flow. Finally for this series, the alkynyl thiadiazine **23a** was also tolerated and afforded the thiadiazole **23b** in quantitative yield. However, the reaction was relatively sluggish, requiring 4 h of irradiation.

Amine derivatives were not well tolerated and were either unreactive or rapidly decomposed under both batch and flow conditions (see Supporting Information, S2.6). Tertiary amines did not yield the desired ring contracted products, however, batch irradiation for 24 h yielded significant quantities (62% and 44%, respectively) of the thiadiazine sulfones **22d** and **23d**, which were isolated and characterised. The sulfoxide derivatives **22c** and **23c** were also tentatively identified by LC-MS of the crude reaction mixture, however, thiadiazoles **22b** and **23b** were not identified within the crude reaction mixture.

Protection of the pre-existing C4 ring carbonyl with ethylene glycol and catechol acetal derivatives was then explored. In general, all the acetal protected thiadiazoles **24b**-**29b** displayed reduced photostability: the reversible photo-induced cleavage of acetal-protected benzaldehydes with UV irradiation has been reported previously, which may factor into the instability of these compounds when over-irradiated in batch,[39] However, acetal-protected thiadiazoles could be isolated in excellent yields (~90%) using the flow protocol. No significant differences in stability or reactivity between the ethylene glycol and catechol acetals were observed.

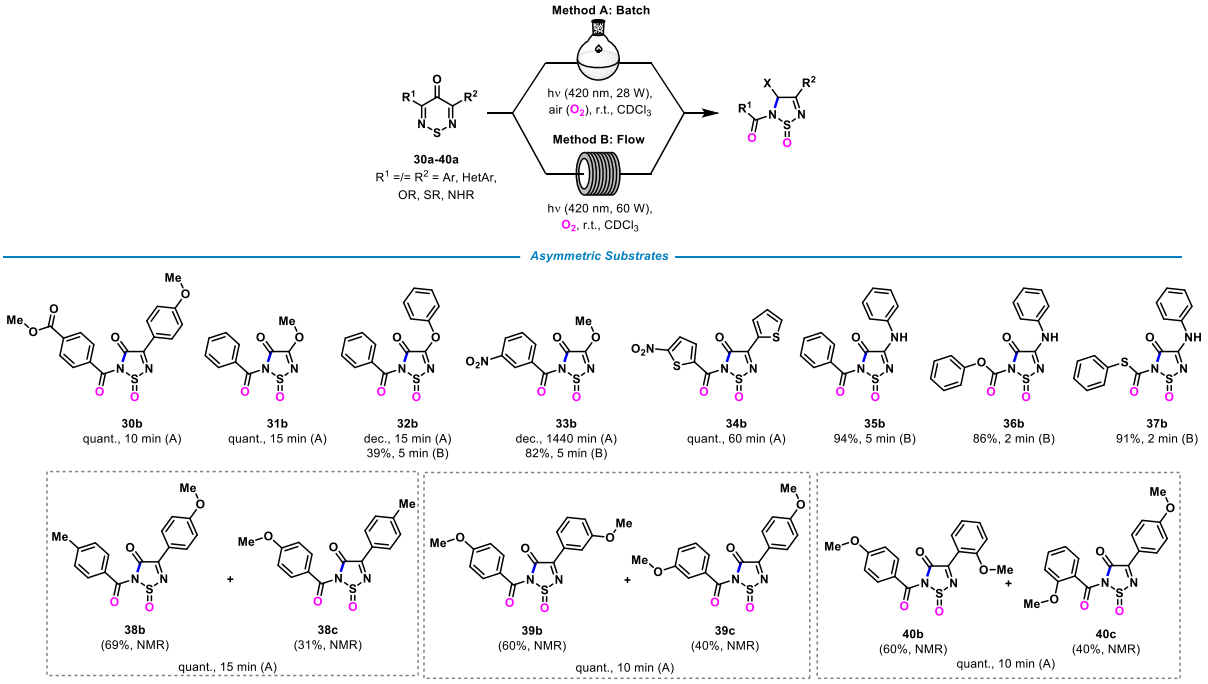


Scheme 1. Reaction scope of the ring contraction. Conditions: SM (0.0376 mmol), $CDCl_3$ (37.5 mM), 420 nm LED, rt. Isolated yields are reported.

The scope of acetal derivatives confirms that the reaction is not prevented by the protection of cyclic ketone moiety. Therefore, we confirm: *(i)* the additional oxygen atoms installed through the reaction result on the ring sulfur and external amide carbonyl; *(ii)* the C4 centred carbonyl does not migrate and; *(iii)* the cleavage of the C–C bond during the ring contraction does not depend on Norrish-type radical processes induced by direct excitation of the carbonyl.[40]

To assess the selectivity preferences for the reaction, with respect to the excised carbon, we screened a series of asymmetric thiadiazines **30a**-**40a** with different R-groups substituted at the 3- and 5-ring positions. Pleasingly, most asymmetric compounds showed excellent chemoselectivity and a single product was isolated. Bisaryl thiadiazine **30a** displayed accelerated reactivity and complete selectivity for excising the carbon bound to the more

electron deficient *para*-(methoxycarbonyl)phenyl. Thiadiazines **31b**-**33b**, bearing a 3-ether and 5-phenyl substituent, were also tolerated, and selectively contracted by excising the phenyl-bearing carbon atom. Thiadiazine **34a** bearing nitrothienyl and thienyl substituents was also well tolerated but required longer irradiation times (1 h), and again showed complete selectivity for excising the carbon bound to the more electron deficient heteroarene. In contrast to the symmetric amino thiadiazines, asymmetric secondary amine bearing thiadiazines **35a**-**37a** were also tolerated. In all three cases, the non-amine bound carbon was selectively excised and a single thiadiazolone product, **35b**-**37b** was obtained in excellent yield.



Scheme 2. Reaction scope of asymmetric thiadiazines. Conditions: SM (0.0376 mmol), $CDCl_3$ (37.5 mM), 420 nm LED, rt. Isolated yields are reported.

Interestingly, a set of three asymmetric 3,5-bisphenyl thiadiazines **38a-40a**, bearing ring substituents with similar electron donating character, did lead to the formation of mixtures of both potential ring contracted products. In the case of 3-(4-methoxyphenyl)-5-(4-tolyl)thiadiazine **38a**, the tolyl bound carbon was preferentially excised, leading to an approximate 67:33 mixture of thiadiazoles **38b** and **38c**, respectively. Asymmetric methoxyphenyl-substituted thiadiazines **39a** and **40a** allowed a comparison of the preference of carbon excision with respect to the *ortho*, *meta* and *para* position of the methoxy group. Despite significant differences in the reactivity of symmetrical *ortho*-, *meta*- and *para*-methoxyphenyl-substituted thiadiazines, both thiadiazines **39a** and **40a** showed only a slight preference for contracting at the *para*-methoxyphenyl bound carbon, leading to 60:40 mixtures of thiadiazoles **39b/c** and **40b/c**, respectively.

To the best of our knowledge, all the resulting 1,2,5-thiadiazole 1-oxides accessed *via* this transformation are unreported compounds. Considering that thiadiazole isomers are privileged motifs in natural products and drug compounds (Figure 1B),[6] we believe these structures could possess untapped potential and provide new chemical architectures for fine chemical industries.

Conclusions

In conclusion, we report the photochemical ring editing of 1,2,6-thiadiazines under ambient, aerobic conditions, which provides a sustainable and atom economic ring editing route to afford elusive 1,2,5-thiadiazole 1-oxides in generally quantitative yields and chromatography-free purification.

The reaction mechanism was elucidated through comprehensive experimental and computational studies, revealing that the reaction is driven through auto-photosensitisation of $^1O_2$ which subsequently undergoes a chemoselective [3 + 2] cycloaddition with the substrate, before ring-contracting to form the product. $^1O_2$ [3 + 2] cycloadditions are unprecedented and unique from its prototypical reactivity. This presents an opportunity to explore this reactivity in other chemical systems and expand on the already impressive utility of $^1O_2$ in complex synthesis.

The reaction tolerated a variety of functional groups, providing 35 examples of previously un-accessed 1,2,5-thiadiazole 1-oxides. Flow chemistry enabled a reliable method to control irradiation exposure and provided exclusive access to products that were prone to photodecomposition in batch. The reaction was proven to be viable in a variety of solvents, including the green solvent dimethyl carbonate. Slower reaction kinetics in this solvent could be overcome through process intensification in flow, enabling a sustainable, continuous process with comparable kinetics to the batch synthesis in exotic deuterated and halogenated solvents.

Additionally, asymmetric 1,2,6-thiadiazines bearing non-equivalent 3,5-substituent groups with moderate differences in electronic induction, react with complete selectivity for excising the more electron deficient endocyclic carbon atom to produce a single product. The efficient synthesis of these compounds under ambient, aerobic conditions enables chemists to easily explore their untapped potential, as an extension of thiadiazole privileged scaffolds for medicinal, agrochemical and materials chemistry.

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Supplementary Materials

Materials and Methods

Supplementary Text

Figs. S1 to S16

Tables S1 to S5

References (S1-S28)