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Photochemical Initiation and Reactions of Thiyl Radicals Studied with S_H2' Radical Traps

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A radical trapping method based on an S_H2' homolytic substitution reaction was applied to study the mechanism of a photochemical spirocyclisation of indole-ynones in the presence of thiols. Starting material, products and a range of trapped radical intermediates were simultaneously detected in reaction mixtures by mass spectrometry (MS). The trapped intermediates included both initiating and main chain propagating radicals. These data made it possible to propose a self-initiation mechanism consistent with the originally postulated photoexcitation of an intramolecular electron donor-acceptor complex of the substrate. The effect of thiol structure on the MS peak intensity of the reaction components was rationalised in terms of the relative stability of the radical intermediates. The results were compared to a simpler related reaction, a photochemical thiol-ene addition where reagents, products and trapped intermediate radicals were also detected by MS. Relative MS peak intensities were again explained by a combination of electronic and steric effects on the stability of intermediate radicals. Overall, S_H2' radical trapping was demonstrated to be a powerful experimental technique for providing mechanistic evidence on photochemical and other organic radical reactions.

Introduction

We have recently reported a visible-light-induced spirocyclisation of indole-ynones **S1** by a reaction with thiols **S2** (Figure 1a).[1] Based on the previous literature, the reaction was tentatively proposed to proceed via a radical chain mechanism which after initiation involves three propagation steps: thiyl radical addition to a triple bond, intramolecular radical addition to the indole ring and hydrogen atom transfer (HAT) from the starting thiol **S2** regenerating the thiyl radical. The spirocyclisation was initially studied under irradiation with blue LEDs in the presence of a Ru-based photocatalyst. Products were formed in good yields and the reaction was tolerant to a wide range of substituents. However, control experiments showed that while illumination is essential and the reaction does not proceed without light, it is equally efficient in the absence of a photocatalyst. This observation suggested that indole-ynones themselves act as photoinitiators. Indeed, unlike the parent indoles and ynones, the substrate **S1** showed light absorption in the visible region. We proposed therefore that **S1** formed an intramolecular electron donor-acceptor (EDA) complex **S1'** (Figure 1b). Photoinitiation of radical reactions using inter- and intramolecular EDA complexes has attracted much attention in the last few years, and mechanistic features of these reactions have in many cases been established.[2] We proposed that absorption of visible light by the intramolecular indole-ynone EDA complex led to the formation of a photoexcited state.

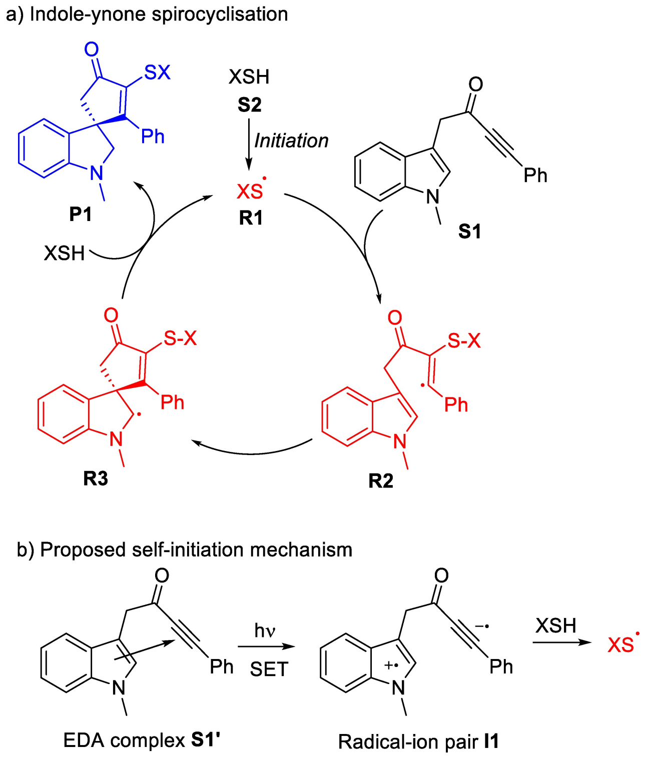

Figure 1. (a) Spirocyclisation of indole-ynones. (b) The originally proposed mechanism[1] of radical initiation via an intramolecular electron donor-acceptor (EDA) complex formation.

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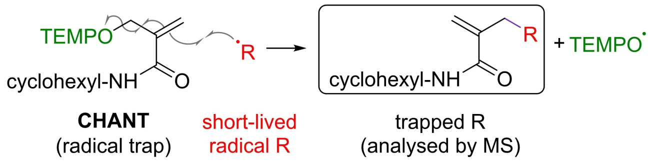
Following single electron transfer (SET), the radical ion pair was formed and then postulated to undergo a HAT reaction with the starting thiol **S2** to generate a thiyl radical and initiate the chain reaction. Although control experiments ruled out some potential alternative pathways and confirmed the correlation between the EDA formation/light absorption and the conversion/yields, the proposed radical initiation mechanism remained speculative. In particular, potential reactivity of the radical ion pair following the initial electron transfer in the photoexcited EDA complex was not explored. A deeper understanding of the mechanism could help optimise the reaction conditions, enhancing conversion rates and yields. Photochemical EDA-initiated reactions that operate under mild conditions and do not require metal catalysis are highly desirable, and expanding their applications will be facilitated by better understanding of underlying chemistry. Therefore, we undertook additional investigations to validate our mechanistic hypothesis.

In order to further probe the reaction mechanism, we sought evidence of intermediate radical formation. In typical synthetic radical reactions, the steady-state concentration of short-lived radicals is low which hinders their direct detection by conventional analytical techniques. Radical intermediates are therefore often detected indirectly, following a reaction with a radical trap added to the reaction mixture. In synthetic organic studies, (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) is often used for radical trapping. A fast reaction of TEMPO with carbon-centred radicals yields stable alkoxyamines which can be analysed by conventional techniques.[3] However, this method is usually not applicable to heteroatom-centred radicals, and addition of TEMPO to reaction mixtures could change the course of reaction. Arguably the most general method for detecting short-lived radicals in a range of different systems including synthetic chemistry is spin trapping.[4] In this technique, free radical intermediates are captured by addition to a nitrone or a nitroso derivative, yielding a persistent nitroxide adduct. Due to its stability, this adduct can accumulate to a relatively high concentration suitable for analysis. As nitroxide adducts are radicals, they are conventionally characterised by electron paramagnetic resonance (EPR) spectroscopy. This method however is complicated by artefacts (*e.g.*, false positives in the thiol-ene reaction can form by Forrester-Hepburn or inverse spin trapping mechanisms), it suffers from challenging deconvolution of signals from several simultaneously trapped radicals, and it usually provides limited structural information about the trapped radicals.[5]

We have recently developed an alternative approach to radical trapping, based on an S_H2' addition of radical intermediates to *O*-allyl-TEMPO derivatives, *e.g.*, **CHANT** (Figure 2).[6] In this method, the short-lived radicals add to a double bond of **CHANT**. Loss of stable radical TEMPO yields stable "trapped radical" products which can be characterised by conventional techniques such as mass spectrometry (MS), thus solving many of the disadvantages of conventional spin trapping (Figure 2).[6] The amide residue in the S_H2' traps can be tuned to give the trap the desired functionality. This radical trapping method has thus far demonstrated immunity to false positives. The S_H2' radical traps do not absorb visible light[6] which makes them suitable for studying photochemical reactions.[6,7] In a proof-of-principle experiment, we previously demonstrated the feasibility of trapping photogenerated thiyl radicals and their alkene adducts. The **CHANT**-trapped thiyl radical was also isolated in pure form and fully characterised.[6] The S_H2' trapping is therefore well-suited for unravelling the mechanisms of organic reactions thought to proceed via radical pathways. In particular, this method benefits from the ability to simultaneously detect many radicals as well as starting materials and products in a single measurement, and accurate masses of trapped radicals make it possible to unambiguously determine elemental composition and hence propose structural assignment (Figure 2). Here, we report a study on the radical intermediates in the spirocyclisation and related thiol-ene reactions, offering useful insights into their mechanisms.



Advantages of S_H2' trapping with MS detection:
- *Stable non-radical adducts*
- *Very high sensitivity (<nM adduct concentration)*
- *Inert to false positives (e.g., by nucleophilic attack)*
- *Accurate mass yields elemental composition*
- *Simultaneous detection of many adducts*

Figure 2. Homolytic substitution S_H2'-based radical trapping using allyl-TEMPO-based traps, and its advantages (e.g., as compared to conventional spin trapping).

Results and Discussion

Detection of Initiator Radicals in Photochemical Self-Initiated Spirocyclisation

The thiyl radical mediated spirocyclisation reaction (Figure 1a) is known to operate via an efficient chain reaction and therefore high product yields can be achieved with a low flux of initiating radicals. This makes the detection of initiator radicals challenging. In the synthetic protocol for spirocyclisation, the high concentration of starting materials further reduces the lifetime of initiator radicals as they undergo a fast HAT reaction with thiol **S2**. It would be challenging for any radical trap to compete with this reaction. Therefore, detection of initiator radicals was attempted with various thiol concentrations, with the maximum concentration being equal to the first-reported synthesis. **CHANT** (0.1 eq.) was also added but conditions were otherwise kept the same as in the synthetic protocol.

Electrospray ionization (ESI) mass spectra of the reaction mixtures containing **CHANT**, indole-ynone **S1** and 3-methoxythiophenol **S2.1** indicated the presence of starting materials, products, and the trapped radicals **R1** and **R2**/**R3** involved in the main propagation cycle (Table 1). **R2** and **R3** have identical *m/z* ratios and hence their trapped radicals cannot be

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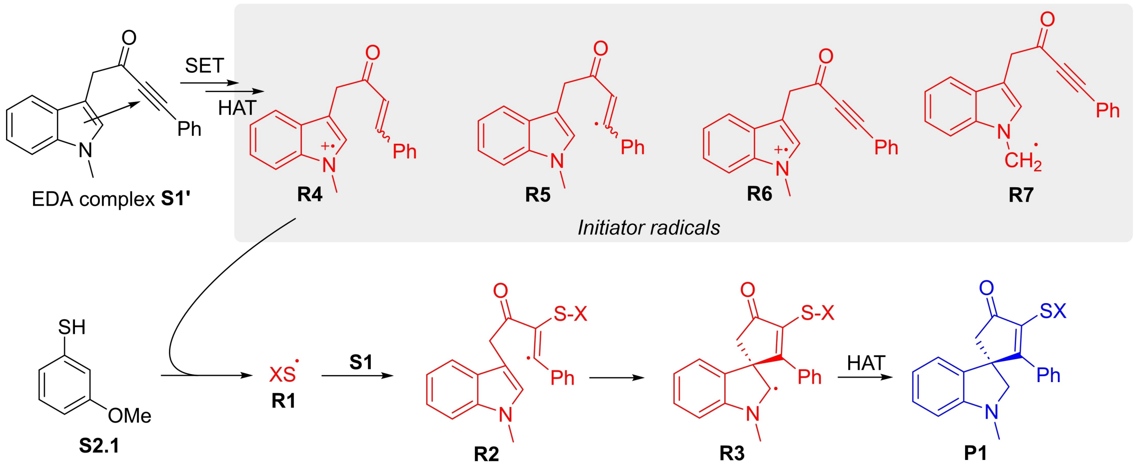
Table 1. Species identified from **CHANT** trapping of spirocyclisation in dichloroethane, using different quantities of 3-methoxythiophenol **S2.1** as substrate (0.0, 0.5 and 1.6 eq.) and MS for characterisation. Systematic *m/z* error = 0.0000; random *m/z* error = ±0.0025; 100% intensity = 5.45×10^9 absolute count.



Species		Predicted m/z	MS peak intensities relative to unreacted trap standard (%) for different quantities of **S2.1**		
			0.0 eq.	0.5 eq.	1.6 eq.
Trap	[**CHANT** + H]$^+$ ($C_{19}H_{35}N_2O_2$)	323.2698	100	0.206	0
Reactants	[**S1** + H]$^+$ ($C_{19}H_{16}NO$)	274.1232	3.93	0	0.411
	[**S1** + Na]$^+$ ($C_{19}H_{15}NONa$)	296.1051	22.6	0.353	0
Trapped main cycle radicals	[trapped **R1** + H]$^+$ ($C_{17}H_{24}NO_2S$)	306.1528	0.007	0.054	0.445
	[trapped **R1** + Na]$^+$ ($C_{17}H_{23}NO_2SNa$)	328.1347	0.015	0.139	0.678
	[trapped **R2**/**R3** + Na]$^+$ ($C_{36}H_{38}N_2O_3SNa$)	601.2501	0.001	0.784	0.086
Trapped initiation and solvent radicals	[trapped **R4**/(**R5** + H)]$^+$ ($C_{29}H_{33}N_2O_2$)	441.2542	0.006	0.002	0
	[trapped **R5** + Na]$^+$ ($C_{29}H_{32}N_2O_2Na$)	463.2361	0.043	0.010	0
	[trapped **R6**/(**R7** + H)]$^+$ ($C_{29}H_{31}N_2O_2$)	439.2385	0.021	0	0
	[trapped **R7** + Na]$^+$ ($C_{29}H_{30}N_2O_2Na$)	461.2205	0.024	0	0
	[trapped $C_2H_3Cl_2^\bullet$ + H]$^+$ ($C_{12}H_{20}Cl_2NO$)	264.0922	0.007	0	0
	[trapped $C_2H_3Cl_2^\bullet$ + Na]$^+$ ($C_{12}H_{19}Cl_2NONa$)	286.0741	0.017	0	0
Products	[**P1** + H]$^+$ ($C_{26}H_{24}NO_2S$)	414.1527	0.021	11.7	19.8
	[**P1** + Na]$^+$ ($C_{26}H_{23}NO_2SNa$)	436.1347	0.057	1.68	11.2

unambiguously distinguished. Tandem MS data were consistent with the structural assignments of trapped **R1** and **R2/R3** but also could not distinguish between trapped **R2** and **R3** (Tables SI5, SI6). The intramolecular spirocyclisation of **R2** to **R3** likely occurs faster than the HAT reaction, and the trapped radical is therefore more likely to result from **R3** rather than **R2**.

In addition to **R1**–**R3**, we detected radicals (**R4**–**R7**) deriving from the indole-ynone **S1** which are likely to be the initiating species of the overall chain reaction. These results provide evidence for the self-initiation of the photocatalytic spirocyclisation and make it possible to propose potential initiation pathways consistent with the detection of trapped **R4**–**R7** (Table 1). We note that [trapped **R4**]$^+$ has the same *m/z* peak as [trapped **R5** + H]$^+$ and hence the structure of **R4** cannot be unambiguously proven. **R5** however can be positively identified by the observation of the [trapped **R5** + Na]$^+$ which cannot be formed from **R4**. Similarly, **R6** and **R7** have identical *m/z* peaks but **R7** can be unambiguously identified by the observation of the [trapped **R7** + Na]$^+$. The proposed initiation pathway starts with the formation of an intramolecular EDA complex **S1′** in the excited state which can either directly generate a thiyl radical **R1** by electron transfer, or undergo other proton/electron transfers prior to initiation (Figure 3).[8]

Analysis of trends in Table 1 further supports this mechanism. For instance, increasing the concentration of 3-methoxythiophenol **S2.1** resulted in an increase in peak intensity for the product **P1**, and reduced starting indole-ynone **S1** peak intensity. An increase in peak intensity of the trapped main cycle radicals (**R1** and **R2**/**R3**) was also observed. This is expected as the product is formed in the chain reaction, which involves 3-methoxythiophenol **S2.1**, and consumes **S1** via radicals **R1**–**R3**. However, the intensity of the trapped initiator radicals decreased with the increased concentration of thiol **S2.1**. This can be rationalised by the fast reaction of **S2.1** with initiator radicals leading to their consumption and reducing the trapping efficiency. Consumption of the indole-ynone **S1** in the

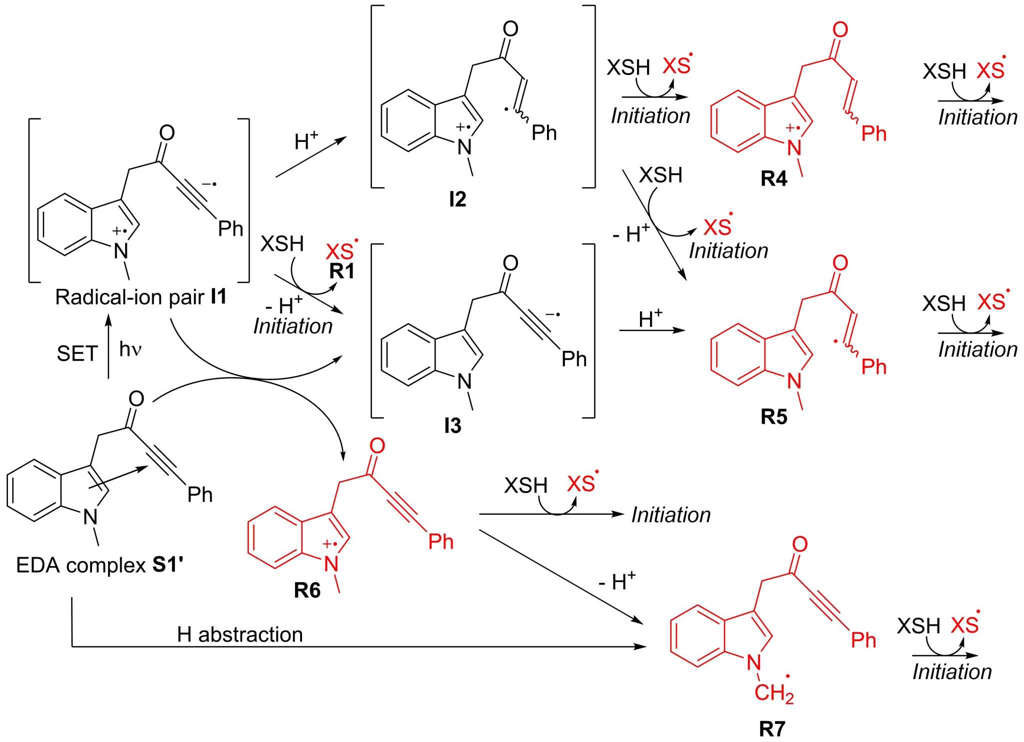


Figure 3. Potential mechanisms of radical initiation by the intramolecular EDA complex **S1′**. Radicals highlighted in red have been detected by S_H2' trapping.

chain reaction in the presence of **S2.1** further contributes to the reduction of the concentration of initiator radicals. Dichloroethane solvent ($C_2H_3Cl_2^{\bullet}$) and substrate (**R7**) radicals are not observed in the presence of 3-methoxythiophenol **S2.1** as its fast reaction with these radicals outcompetes trapping. Control experiments in which no trap was added validated that these trapped radicals were only observed in presence of radical trap (Table SI2). Furthermore, they demonstrated that overall conversion of the starting material was reduced in the presence of the trap as the trapping process breaks the radical chain (Table SI2). All observations are therefore consistent with the proposed self-initiated radical chain mechanism where photoexcitation of an intramolecular EDA complex of indole-ynone **S1** results in charge transfer and consequent reaction with thiol **S2** to form a thiyl radical **R1** and start the propagation cycle. Homolytic S_H2' trapping can thus be a highly effective method for mechanistic elucidation of radical initiation and propagation cycles.

These results prompted us to explore reactivity of indole-ynone **S1** with a range of structurally different thiols **S2.1**, **S2.2**, **S2.5**, **S2.6** (Table 2) which were previously shown to give variable yields of spirocyclic products.[1] In these examples, we were not focussing on the initiator radicals and therefore the reactions used the same thiol concentration and other conditions as in the synthetic protocol[1] with the addition of 0.1 equivalent of **CHANT**. In all cases, we were able to detect reactants, products and trapped intermediate main cycle radicals (Table 2).

Trapped **R1** were observed more intensely for thiophenols (**S2.1, S2.2**) whilst trapped **R2**/**R3** were generally observed more intensely for alkyl thiols (**S2.5**, **S2.6**). Peak intensity of trapped radicals does not directly report on the radical concentration due to (i) potentially different rates of trapping of different radicals (which is true for any radical trapping technique) and (ii) the sensitivity of MS ionisation efficiency to the composition of the reaction mixtures. However, the trends in MS peak intensity can be qualitatively examined. The high MS peak intensity of trapped **R1** for aromatic thiols could be explained by the resonance stabilisation of **R1** by the aromatic ring which facilitates the HAT reaction of the parent thiol and slows down the rate of **R1** addition to the triple bond.[9,10] The same argument can be used to explain stronger intensity of **R2**/**R3** for alkyl thiols, as poorer stability of aliphatic thiyl radicals leads to slower hydrogen abstraction from the thiol by **R3** thus extending its lifetime.

Radical Intermediates in Intermolecular Photochemical Thiol-Ene Reactions

In order to gain further understanding of the factors controlling radical reactivity, we compared spirocyclisation with a simpler photochemical thiol-ene reaction. In this reaction, thiyl radical addition to an unsaturated bond is not complicated by further radical addition steps (Figure 4),[11] expanding on previously reported data.[3,12] Radical trapping was examined for a range of thiols and alkene substrates. Similarly to the spirocyclisation, less product was observed in the presence of the **CHANT** trap after a given time (Table SI7). Trapped **R1** was observed most intensely in the absence of alkene. Both these observations are

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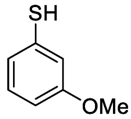
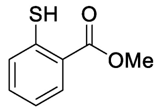
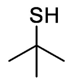
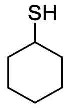
Table 2. Species identified from **CHANT** trapping of spirocyclisation using different thiols as substrates (1.6 eq.) and MS for characterisation. Systematic *m/z* error = 0.0000; random *m/z* error = ±0.0026; 100 % intensity = 5.45×10^9 absolute count.

					
		S2.1	**S2.2**	**S2.5**	**S2.6**
P1 yield[a]/%		94	54	37	74
Species		MS peak intensities relative to unreacted trap standard/%			
Trap	$[\mathbf{CHANT}+H]^+$ ($C_{19}H_{35}N_2O_2$)	0.012	0.017	0.013	0
Reactants	$[\mathbf{S1}+H]^+$	0.763	1.44	0.280	0.492
	$[\mathbf{S1}+Na]^+$	0.006	0	0.416	0.276
Trapped radicals	[trapped **R1** + H]$^+$	0.661	0.980	0.874	0.546
	[trapped **R1** + Na]$^+$	1.01	3.49	1.41	1.25
	[trapped **R2/R3** + H]$^+$	0.015	0.013	0.188	0.141
	[trapped **R2/R3** + Na]$^+$	0.127	0.005	2.00	1.32
Products	$[\mathbf{P1}+H]^+$	29.5	61.3	81.7	121
	$[\mathbf{P1}+Na]^+$	16.7	32.9	7.96	15.7

[a] Yields from ref. [1].

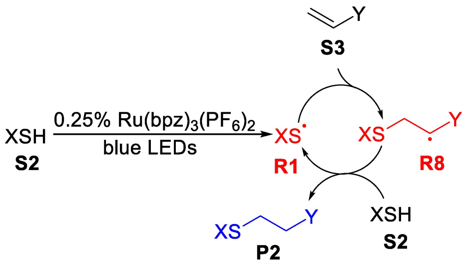
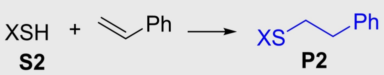
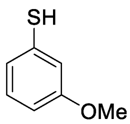
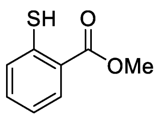
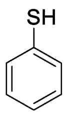
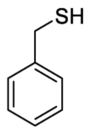
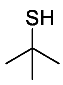
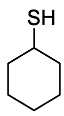


Figure 4. Photochemical thiol-ene reaction.

consistent with the competition between the alkene and the trap for the thiyl radicals. A small quantity of trapped **R1** was observed in the absence of catalyst and in the absence of light. This can be tentatively explained by the propensity of thiols for self-initiation, *e.g.*, via reaction with molecular oxygen or trace transition metal ions.[13]

As these reactions were carried out for all thiols under the same conditions with styrene as the common alkene substrate, relative trends in the MS intensity of detected compounds can be interpreted in terms of chemical reactivity. For instance, unreacted **CHANT** intensity was significantly lower and trapped **R1** intensity higher for thiophenols **S2.1**–**S2.3** than for alkyl thiols **S2.4**–**S2.6** (Table 3). This suggests that thiophenols undergo initiation more rapidly than alkyl thiols, probably due to the resonance stabilisation of aromatic thiyl radicals, consistent

Table 3. Species identified from **CHANT** trapping of Ru-photocatalysed radical thiol-ene addition after 24 h, using different thiols and styrene as substrates and MS for characterisation. Systematic *m/z* error = −0.0004; random *m/z* error = ±0.0006; 100 % intensity = 2.55×10^9 absolute count.

							
		S2.1	**S2.2**	**S2.3**	**S2.4**	**S2.5**	**S2.6**
Species		MS peak intensities relative to unreacted trap standard/%					
Trap	$[\mathbf{CHANT}+H]^+$ ($C_{19}H_{16}NO$)	0.016	1.22	0.093	91.2	113	93.3
Trapped radicals	[trapped **R1** + H]$^+$	0.705	3.67	7.32	0.029	0.015	0.083
	[trapped **R1** + Na]$^+$	11.6	22.8	12.2	1.05	0.051	0.181
	[trapped **R8** + H]$^+$	0.013	0.031	0.016	0.03	0.095	0.056
	[trapped **R8** + Na]$^+$	0.014	0.126	0.011	0.078	0.204	0.068
	[**R8**−TEMPO + H]$^+$	10.7	10.8	17.9	2.24	2.18	1.15
Products	$[\mathbf{P2}+Na]^+$	0.031	1.158	0.009	0.017	0	0.008

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with the similar trend observed for spirocyclisation. **R8** gave highest intensity peaks by recombination with TEMPO$^{\bullet}$ (released during the trapping reaction, Figure 2), as carbon-centred radicals rapidly react with nitroxide radicals.[14] TEMPO adducts of **R2**/**R3** were not observed for spirocyclisation, presumably due to steric hindrance.[15] Just like in spirocyclisation, in the thiol-ene reaction the intensity of trapped **R8** was higher for aliphatic than for aromatic thiols suggesting that these trends have general applicability and that the mechanisms of both these reactions share common features.

We also tested the alkene substituent effects on the reaction using benzyl mercaptan **S2.4** as the thiol substrate (Table 4). The results were consistent with the previously observed trends and could be interpreted by considering the reaction mechanism and the stability of the intermediate radicals. For instance, styrene **S3.1** reacted with thiyl radical the fastest and much of the **CHANT** trap therefore remained unreacted. The intensity of trapped **R1** was low for the same reason. The intensity of trapped **R8** was relatively high for styrene due to stability of the conjugated **R8**.[9] Alkyne **S3.4** reacted with thiyl radical the slowest hence the corresponding **R1** consumed most of the **CHANT** trap, consistent with the low intensity of **CHANT** and high intensity of trapped **R1**. Sterically-hindered **S3.2** and **S3.3** gave the lowest intensity of trapped **R8**, presumably because of the slow trapping rate of the corresponding radicals.[16] All these observations validate existing mechanistic understanding and further demonstrate how S_H2' trapping can be used as a useful tool for mechanism elucidation.

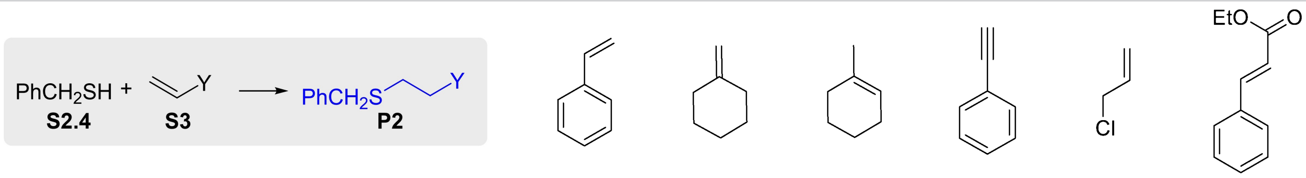
Conclusions

We have applied a recently-developed homolytic substitution S_H2'-based radical trapping method to explore the mechanistic features of self-initiated spirocyclisation reactions of indole-tethered ynones. Several substrate-derived radical intermediates were trapped and characterised by mass spectrometry (MS). Their observation confirmed the proposed initiation mechanism which involves photochemical excitation of the intramolecular EDA complex of the substrate. In addition, starting material, products and trapped thiyl and addition radicals were detected for a range of substituted starting materials. Although the MS results are qualitative, the observed MS peak intensities could be correlated with the reactivity trends. The spirocyclisation was compared to a simpler reaction with a similar mechanism, a photochemical thiol-ene addition. The MS intensity of trapped intermediate radicals in both reactions was affected by similar factors (*e.g.*, radical stability and steric hindrance). Overall, the S_H2' radical trapping method proved highly valuable in the characterisation of radical intermediates in synthetic reaction mixtures, and hence in the elucidation of the reaction mechanisms. The main advantages compared to traditional indirect radical detection methods include improved structural information, no false positives, simultaneous detection of multiple radical intermediates as well as starting materials and products. S_H2' radical trapping could therefore be a useful tool for the optimisation of the reaction conditions, enhancing conversion rates and yields.

Experimental Section

Mass spectrometry. SolariX XR FTMS mass spectrometer in a positive ion mode electrospray ionisation was used for analysis. Samples were dissolved in 1:1 CH_3CN:H_2O and diluted with 0.1%/

Table 4. Species identified from **CHANT** trapping of Ru-photocatalysed radical thiol-ene addition under standard conditions after 24 h, using benzyl mercaptan **S2.4** and different alkenes as substrates and MS for characterisation. Systematic *m/z* error = −0.0005; random *m/z* error = ±0.0012; 100% intensity = 2.11×10^9 absolute count.



Species		S3.1	S3.2	S3.3	S3.4	S3.5	S3.6
		MS peak intensities relative to unreacted trap standard/%					
Trap	[**CHANT** + H]$^+$	72.2	7.91	9.79	1.50	10.1	7.78
Trapped radicals	[trapped **R1** + H]$^+$	0.176	0.260	0.139	1.26	0.138	0.400
	[trapped **R1** + Na]$^+$	1.43	2.45	3.28	7.29	1.19	2.48
	[trapped **R8** + H]$^+$	0.317	0	0	0.049	0.006	0
	[trapped **R7** + Na]$^+$	0.314	0	0	0	0.014	0
	[**R8** − TEMPO + H]$^+$	5.13	0.008	0.017	0.240	0.044	0.209
Products	[**P2** + H]$^+$	0.031	0.008	0	0.015	0	0.061
	[**P2** + Na]$^+$	0.045	0	0	0.027	0	0.500

1:1 $HCOOH/CH_3CN:H_2O$. HPLC-MS used an Agilent-1200 HPLC instrument equipped with a Waters Symmetry C18 3.5 μm, 4.6×75 mm reverse phase column, connected to the mass spectrometer.

Spirocyclisaion standard reaction procedure. Indole-tethered ynone **S1** (27.3 mg, 100 μmol, 1.0 eq.) was placed in a transparent 2 mL vial and dissolved in degassed dichloroethane (1.0 mL, 0.10 M). If undertaking radical trapping, **CHANT** (3.22 mg, 10 μmol, 0.1 eq.) was also added. For all reaction mixtures, the solution was sparged with argon for 5 min, whilst stirring. Required quantity of thiol **S2** was added and an aliquot removed (0.10 mL). The remaining solution was irradiated with blue LEDs (60 W, 455 nm) for 16 h, whilst stirring. Another aliquot was removed (0.10 mL) and all aliquots had solvent removed in vacuo and were MS characterised.

Thiol-ene standard reaction procedure. Alkene or alkyne **S3** (100 μmol, 1.0 eq.) was placed in a transparent 2 mL vial and dissolved in $Ru(bpz)_3(PF_6)_2$ solution (0.50 mM in dry acetonitrile, 0.50 mL, 0.25 μmol, 0.0025 eq.). If undertaking radical trapping, **CHANT** (3.22 mg, 10 μmol, 0.10 eq.) was also added. For all reaction mixtures, thiol **S2** (200 μmol, 2.0 eq.) was added and an aliquot removed (5.0 μL). The remaining solution was irradiated with blue LEDs (60 W, 455 nm) for 1–72 h. Another aliquot was removed (5.0 μL) and all aliquots characterised by MS.

Supporting Information Summary

Full experimental details and procedures including control experiments and tandem MS data are given in Supplementary Information.

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: Radical reactions · Radicals · Photochemistry · Reaction mechanisms · Radical trapping

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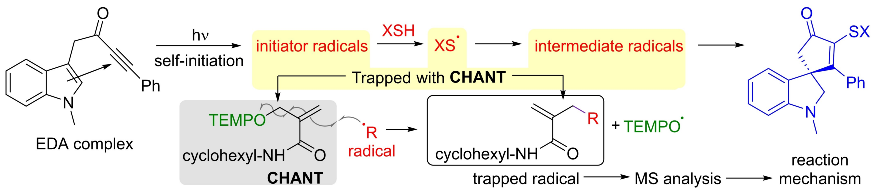

S_H2'-based radical traps were used to probe the mechanisms of photochemical spirocyclisation of indole-ynones with thiols and a relate thiol-ene reaction. The observation of trapped initiator radicals by electrospray ionisation mass spectrometry (ESI-MS) was consistent with the proposed formation of an intramolecular electron donor-acceptor indole-ynone complex. Trends in MS intensity of trapped intermediate radicals were rationalised in terms of radical reactivity.

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Photochemical Initiation and Reactions of Thiyl Radicals Studied with S_H2' Radical Traps