XtalFluorE effects the C3H sulfenylation of indoles to form di indole sulfides

EurJOC
European Journal of Organic Chemistry

Research Article
doi.org/10.1002/ejoc.202101394

Chemistry Europe
European Chemical Societies Publishing

www.eurjoc.org

Special Collection

XtalFluor-E Enabled Regioselective Synthesis of Di-Indole Sulfides by C3–H Sulfenylation of Indoles

Nojus Cironis,[a] Kang Yuan,[a] Stephen P. Thomas,*[a] and Michael J. Ingleson*[a]

A simple, regioselective synthesis of di-indole sulfides by electrophilic aromatic substitution of the C3-position of indoles was achieved using Xtalfluor-E as the sulfenylating reagent. The addition of amine bases was found to have a significant effect on the reaction outcome, with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) switching off the reactivity of XtalFluor-E, while the hindered base 2,6-di*tert*butyl-4-methylpyridine (DBP) led to the formation of two di-indole-sulfur containing products, one S(II) and one S(IV). The optimal base for accessing the di-indole sulfides in high yield proved to be Hünigs base, EtN^iPr_2. While this amine formed a Lewis adduct with XtalFluor-E, adduct formation did not completely quench electrophilic reactivity indicating reversible coordination to the sulfur center. This is the first report utilizing XtalFluor-E in electrophilic aromatic substitution to form C–S bonds to our knowledge, and this process is applicable to a wide range of functionalized indoles and does not require N1-protection.

Introduction

Sulfur-fluorides are a well-established class of reagents widely used in fluorination reactions, with these transformations accepted to proceed by an electrophilic sulfur center activating a substrate towards fluoride transfer most often to form a new C–F bond.[1] Aminodifluorosulfinium salts ($[R_2NSF_2]^+$) are attractive members of this family as they are easier handled than earlier discovered S(IV) fluorination reagents, e.g. SF_4 and diethylaminosulfur trifluoride (DAST).[2] Indeed, the aminodifluorosulfinium salts, XtalFluor-E and XtalFluor-M (Figure 1), are commercially available salts whose improved thermal and chemical stability (relative to DAST) enable facile handling and storage, leading to increasingly widespread application.[2–6] XtalFluor salts are predominantly applied in combination with exogenous fluoride sources in the deoxyfluorination of alcohols and carbonyls,[2] but they have also been used in formylation,[3] ring expansion,[4] dehydration,[5] and cyclo-dehydration reactions,[6] amongst others.[7] The majority of these transformations involve oxygen-based nucleophiles, with S–O bond formation facilitating C–O cleavage/C–F formation. The utilization of XtalFluor salts as electrophiles to form other E–S bonds (E≠O) and thereby access other useful products (e.g. by C–S bond formation), is underexplored. To the best of our knowledge, XtalFluor salts have not been utilized in S_EAr-type reactions, despite sulfur cations being "soft" electrophiles with precedent to functionalize π nucleophiles. Key questions this work sought to answer included: Is S_EAr reactivity possible, and if so, what is the arene scope and what substituents remain bonded to sulfur post S_EAr? The latter is challenging to predict a priori as the Brønsted acid by-product from S_EAr using XtalFluor salts could lead to formation of HF, $H[BF_4]$ or HNR_2 (or $[baseH]^+$ if an exogenous base is added), with the usefulness of the product controlled by the substituents on sulfur in [S] (Figure 1).

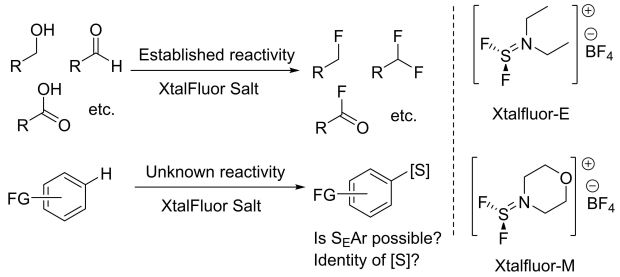


Figure 1. Structure of XtalFluor salts (right) and their established reactivity (top).

The formation of organosulfur compounds, including aryl sulfides, is of significant interest due to the prevalence of such structures in biologically active compounds[8] and functional materials,[9] with organosulfides also useful intermediates for accessing higher oxidation-state sulfur derivatives such as sulfoxides or sulfones. As a result, a plethora of methods have been developed to access aryl sulfides, predominantly by transition-metal-catalyzed routes.[10] The development of metal-free methodologies for the synthesis of aryl sulfides by direct C–H bond functionalization is an attractive alternative. This has been achieved by utilizing electrophilic sulfenylating reagents,

[a] N. Cironis, Dr. K. Yuan, Dr. S. P. Thomas, Prof. Dr. M. J. Ingleson
EaStCHEM School of Chemistry, University of Edinburgh
Edinburgh, EH9 3FJ, UK
E-mail: stephen.thomas@ed.ac.uk
michael.ingleson@ed.ac.uk
http://www.thomas.chem.ed.ac.uk/
http://www.ingleson.chem.ed.ac.uk/

Supporting information for this article is available on the WWW under https://doi.org/10.1002/ejoc.202101394

Part of the "EaSTCHEM" Virtual Institute Feature.

Research Article
doi.org/10.1002/ejoc.202101394

including sulfonium salts.[11,12] Aryl sulfide synthesis via S_EAr with sulfonium salts was established by Belenkova and co-workers,[12] following this numerous isolated sulfonium salts (Scheme 1A),[13] and *in situ* formed sulfonium salts (Scheme 1B) have been used as electrophiles in S_EAr reactions.[14] The majority of these reactions form a single C–S bond, but it should be noted that 2-(fluorosulfonyl)difluoroacetic acid reacts as an electrophilic sulfur source in a double S_EAr reaction (Scheme 1C).[15] However, the use of S(IV) sulfenylating reagents for forming diaryl sulfide by a double S_EAr process, is not reported to the best of our knowledge. Herein we report the double C–H bond functionalization of indoles with XtalFluor-E to form di-indole sulfides (Scheme 1D) and under certain conditions di-aryl aza sulfonium species.

Results and Discussion

N-Methyl-indole (**1a**) was chosen as the initial nucleophilic partner for sulfenylation studies due to its relatively high nucleophilicity and our experience in the functionalization of indoles with main-group cations by S_EAr.[16] Our initial solvent screen indicated MeCN provided good solubility and reactivity without the observation of any deleterious side reactions. This was in contrast to the incompatibility of XtalFluor salts with MeCN in deoxyfluorination reactions reported by Couturier *et al.* where the promotion of Ritter-type chemistry was observed.[2] Using XtalFluor E and M we observed high selectivity for C-3 functionalization of two equivalents of *N*-Me-indole, with no mono-indole sulfide products observed. The reaction of two equivalents of indole **1a** and one equivalent of the XtalFluor salts proceeded at room temperature to give the di-indole sulfide **2a** in 68% and 70% yield, using the ethyl and

Mike Ingleson received his MChem. degree from the University of Bath in 2001 and received his PhD degree in organometallic chemistry in 2004 under the supervision of Prof. Andrew S. Weller. He then pursued postdoctoral studies in organometallic chemistry with Prof. Kenneth G. Caulton at Indiana University and in materials chemistry with Professor Matthew J. Rosseinsky at the University of Liverpool. He started his independent career at the University of Manchester in 2008 with a Royal Society University Research Fellowship. At Manchester, he was promoted to Reader in 2012 and Full Professor in 2018. He joined the University of Edinburgh as a Full Professor in 2019. His research interests include many aspects of main group chemistry, particularly catalytic and materials applications. He has a particular fondness for all things to do with boron.

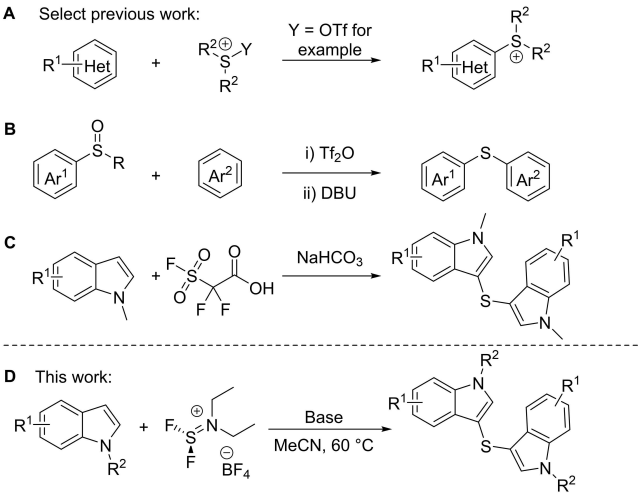
Stephen Thomas was born in Toronto, Canada, and completed his GCSEs at Court Fields Community School and A-levels at Richard Huish College in the South West of England. After completing his MChem at Cardiff University working with Prof. Nick Tomkinson, he moved to Churchill College, University of Cambridge for a PhD with Dr Stuart Warren. Postdoctoral work with Prof. Dr Andreas Pfaltz at the University of Basel, Switzerland, was shortly followed by a move to the University of Bristol to join Prof. Varinder Aggarwal FRS as his group Research Officer. In 2012 Stephen moved to the University of Edinburgh as a Chancellor's Research Fellow. In 2014 he was awarded a Royal Society University Research Fellowship. Stephen and the group have been awarded the 2016 Royal Society of Chemistry Hickinbottom Award, a Thieme Journal Award, a Pfizer Green Chemistry Research Award, the 2021 Royal Society of Chemistry Merck, Sharp and Dohme Award and was a UK Blavatnik Award Finalist 2022.

Kang Yuan received his BSc degree in 2013 from Sun Yat-sen University under the guidance of Prof. Ming-Liang Tong. Then, he moved to Canada to explore main group chemistry and obtained his PhD degree under the supervision of Prof. Suning Wang at Queen's University. In 2018, he joined the Ingleson group as a postdoctoral research associate. His current research focuses on developing new methods for constructing novel boron containing molecules.

Nojus grew up in Vilnius, Lithuania and obtained his MChem degree from the University of Nottingham working under supervision of Prof. Simon Woodward on copper mediated trifluoromethylation of aryl halides. Nojus started his PhD in September 2020 jointly supervised by Dr Stephen Thomas and Prof. Michael Ingleson and is now working on developing enantioselective main group catalysts for applications in organic synthesis.

Research Article
doi.org/10.1002/ejoc.202101394

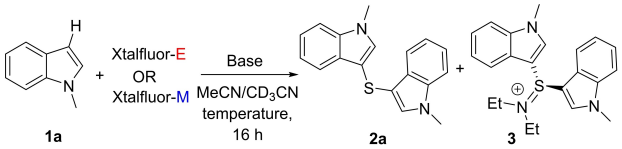
Chemistry Europe
European Chemical Societies Publishing



Scheme 1. Select previous examples of sulfoxonium cations (A and B) in S_EAr. C – use of a S(VI) compound in double S_EAr to form di-indolylsulfides. D – this work using XtalFluor-E in S_EAr.

morpholino analogues respectively (Table 1, entries 1 and 2). Heating these sulfenylation reactions led to decreased yields of di-indole sulfide **2a** due to indole oligomerization, while slow addition of XtalFluor-E to indole **1a** (in an attempt to minimize indole oligomer formation) did not result in a higher sulfide yield (entries 3 and 4). Lowering the temperature to −78 or −30 °C stopped reactivity completely and gradual warming to room temperature did not improve sulfide yield or lead to the formation of any mono-indole sulfide species (entry 5). Reactions at a 1:1 ratio of **1a** : XtalFluor-E/M resulted in the formation of complex mixtures at room temperature containing oligomerized indole products (entry 6, *see supporting information*).[17] The use of an excess of XtalFluor salt (2 eq.) led to indole decomposition within 1 hr at room temperature with minimal di-indole sulfide **2a** observed. During this initial screening, reactions with the morpholino analogue generally led to more complex reaction mixtures than the ethyl analogue. This is in agreement with the higher prevalence of XtalFluor-E in the literature due to the differences in stability and reactivity between these two salts.[2–6] As a result, only XtalFluor-E was used in further studies.

Table 1. Optimization of the S_EAr of N–Me indole (**1a**) with XtalFluor salts.



1a **2a** **3**

Entry[a]	T [°C]	Base [eq.]	**1a** [eq.]	Yield[b] [%] **2a**	**3**
1	rt	–	2	68	–
2[c]	rt	–	2	70	–
3[c]	60	–	2		–
4[d]	rt	–	2	50	–
5[e]	−30	–	2	–	–
6	rt	–	1	–	–
7	rt	DBP (1)	1	39	17
8[f]	rt	DBP (1)	1	38	35
9[g]	rt	DBU (1)	1	–	–
10[g]	100[h]	DBU (1)	1	–	–
11[g]	rt	EtN^iPr_2 (1)	1	47	–
12[g]	rt	EtN^iPr_2 (2)	1	22	–
13[g]	**60**[h]	**EtN^iPr_2 (1)**	**1**	**91**	–
14[g]	60[h]	EtN^iPr_2 (1)	2	61	–

[a] Reactions performed with XtalFluor-E (1 eq.) unless stated otherwise. [b] Yields based on indole and determined by ^1H NMR spectroscopy with dibromomethane as an internal standard. [c] Reaction performed with Xtalfluor-M (1 eq.). [d] Dropwise addition of XtalFluor-E. [e] No reaction. [f] Reaction performed with 2 eq. of XtalFluor-E. [g] Base and XtalFluor-E pre-mixed prior the addition of N–Me-indole. [h] Heated in a sealed tube.

The formation of di-indole sulfide **2a** involves loss of both fluorides and the NEt_2 group from the sulfur center, this is presumably due in part to these groups acting as Brønsted bases in a S_EAr reaction. Indeed H–N containing species (e.g. $HNEt_2$) are observed by *in-situ* ^1H NMR spectra during formation of di-indole sulfide **2a**. Therefore, we added exogenous base in the reaction mixture in an attempt to sequester the protic by-product from S_EAr and access different indole-S containing products by maintaining the S–F and/or the S–NEt_2 bond(s). The initial base used was the highly hindered base, 2,6-di*tert*butyl-4-methyl-pyridine (DBP), to preclude nitrogen to sulfur dative bond formation (Lewis adduct formation is well-documented between amine base and other fluorosulfonium cations).[18] Strong dative bond formation significantly reduces the electrophilicity at sulfur.[2,19] The use of DBP led to formation of the di-indole diethylamino-sulfonium cation **3** alongside the di-indole sulfide **2a** (entry 7). Formation of diethylamino-sulfonium cation **3** was maximized when two equivalents of XtalFluor-E, one equivalent of indole **1a** and one equivalent of base were used, however we were not able to direct reactivity towards the clean formation of diethylamino-sulfonium cation **3** as the di-indole sulfide **2a** was always present in significant quantities (e.g. entry 8). XtalFluor salts have been used for deoxyfluorination in the presence of a range of amine bases, including 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and EtN^iPr_2,[2] indicating these weakly nucleophilic bases do not quench the reactivity of XtalFluor-E (in deoxy-fluorinations at least). Using these two bases pre-mixed with XtalFluor-E, led to disparate outcomes in C–S bond formation with *N*-methyl indole **1a**, with no sulfonium cation **3** observed at any point over the reaction course (as monitored by *in situ* ^{19}F and ^1H NMR spectroscopy). With DBU (entries 9 and 10) no C–S bond formation was observed at room temperature or at 100 °C, thus DBU-XtalFluor-E adduct formation (significant changes to the ^1H and ^{19}F NMR spectra consistent with adduct formation were observed) appears to quench XtalFluor-E reactivity towards indoles. In contrast, using EtN^iPr_2 gave slower but more selective (than in the absence of base) C–S bond formation to form di-indole sulfide **2a**, as observed at room temperature (entry 11). This reaction was retarded by the addition of further equivalents of base (entry 12) but accelerated at 60 °C, with EtN^iPr_2 and Xtalfluor-E pre-mixed in a 1:1 molar ratio to give di-indole sulfide **2a** in excellent yield at this temperature (entry 13). Notably, a 1:2 XtalFluor-E/*N*-Me-indole mixture (the ratio of S : indole present in product **2a**) led to lower yields of

Research Article
doi.org/10.1002/ejoc.202101394

di-indole sulfide **2a** (entry 14) even in the presence of EtN^iPr_2, suggesting that the additional XtalFluor-E is playing an important role in the reaction (possibly in enabling the reduction to S(II) in **2a**, vide infra).

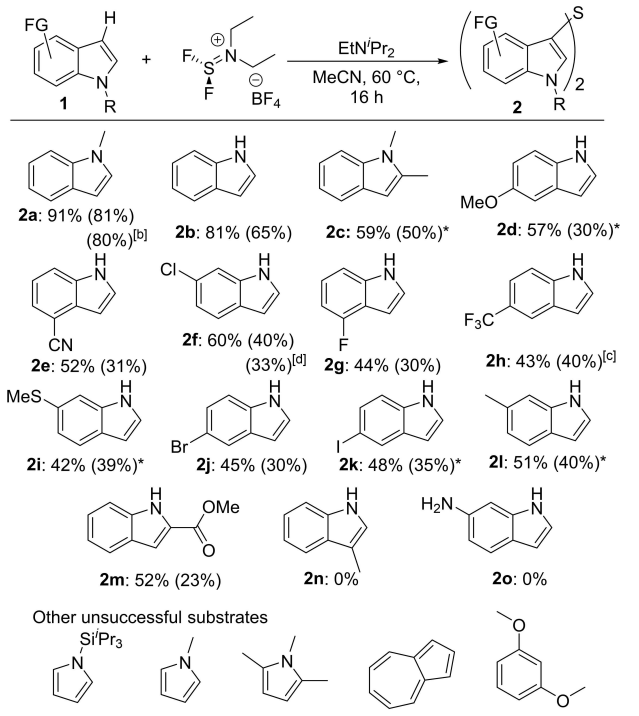
Using the optimized conditions (entry 13) the substrate scope of this methodology for forming symmetric di-aryl sulfides was explored. The double S_EAr reaction to form di-indole sulfides was applicable to a range of indoles (Table 2), including unprotected *N*-H-indoles (**1b**, **1d**–**m**), and was tolerant of electron-donating (**1c**–**d**, **1i** and **1l**) and electron-withdrawing functional groups (**1e**–**1h**, **1j**–**k**, **1m**) in a range of positions (C4: **1e**, **1g**, C5: **1d**, **1h**, **1j**, **1k**, C6: **1f**, **1i**, **1l**). Our method was also amenable to scale-up, with **1a** giving excellent di-aryl sulfide yield at a 20-fold increase in reagent loading. C–S bond formation was exclusively at the C3 position consistent with an S_EAr mechanism for the functionalization of indoles. It should be noted where competitive indole oligomerization was observed, a higher loading of indole was used to overcome this (**1c**, **1d**, **1i**, **1k**, **1l**). While indole substitution at the C-2 position did not negatively influence sulfide formation (with 2-methylindole and methyl 1*H*-indole-2-carboxylate reacting efficiently), substitution at the C-3 position (**1n**) led to complex intractable mixtures. Attempts to functionalize an amino substituted indole (**1o**) resulted in a rapid formation of complex mixtures. Finally, the reactivity appears to be limited to indoles as other nucleophilic (hetero)arenes did not lead to clean formation of diaryl-sulfides, this included pyrroles, azulene and 1,3-dimethoxybenzene, while no reaction was observed with less nucleophilic arenes.

The scope limitation is distinct to other sulfonium cations which have greater (hetero)arene scope and suggests that XtalFluor-E is a weaker electrophile than these cations, presumably due to the presence of significant N=S double bond character. Indeed DFT calculations at the M06-2X/6-311G(d,p) level with a polarizable continuum model (DCM) revealed that the LUMO of XtalFluor-E is significantly higher in energy than sulfonium cation, **A**, with **A** having a broader arene scope (the LUMO for both XtalFluor-E and **A** have significant sulfur character, for XtalFluor-E it is predominantly a SN π* orbital, while for **A** the LUMO has significant S-OTf σ* character (Figure 2)). It should be noted that **A** does not affect the S_EAr of indoles, instead indole oxidation and oligomerization occurs, which is only observed as a minor outcome using XtalFluor-E/indole combinations.[13a]

With the scope defined we were interested in determining the composition of XtalFluor-E/EtN^iPr_2 mixtures, with Lewis adduct formation hypothesized. While there is precedence for amine adducts with $[SF_3]^+$ and SF_4, no amine adducts with XtalFluor salts are reported to our knowledge, though it should be noted that the interaction of XtalFluor-E with oxo-bases (via dative bond formation) has been proposed as the initial step in deoxyfluorination reactions.[18,20] The combination of 1:1 XtalFluor-E/EtN^iPr_2 in MeCN led to a downfield shift and broadening of the resonances for EtN^iPr_2 and an upfield shift of the resonances for NEt_2 (of XtalFluor-E) in the ^1H NMR spectrum. These changes are consistent with formation of Lewis adduct **4** (Scheme 2). The ^{19}F NMR spectrum for this 1:1 mixture contained one major broad resonance at +28 ppm at room temperature (along with minor sharp resonances assigned to impurities in XtalFluor-E and observed throughout this study), with no XtalFluor-E resonance observed ($\delta_{19F} = +13$ ppm).

To gain more insight these 1:1 mixtures were cooled in MeCN which resulted in the initially broad ^{19}F resonance attributed to adduct **4** sharpening significantly, and at −10 °C appearing as a well resolved sharp resonance at $\delta_{19F} = 33$ ppm.

Table 2. Synthesis of di-indole sulfides.[a]



[a] Reaction conditions: 0.2 mmol of (hetero)arene, 0.2 mmol of EtN^iPr_2, 0.2 mmol of Xtalfluor-E in MeCN (1.2 mL) at 60 °C. Yields based on indole determined by ^1H NMR spectroscopy with dibromomethane as internal standard. Isolated yields showed in parentheses. [b] Reaction scaled-up 20 fold. [c] Yield based on indole determined by ^{19}F NMR spectroscopy with 1,3,5-trifluorobenzene as internal standard. [d] Reaction scaled-up 7.5 fold. *Reaction performed with 2 eq. of arene.

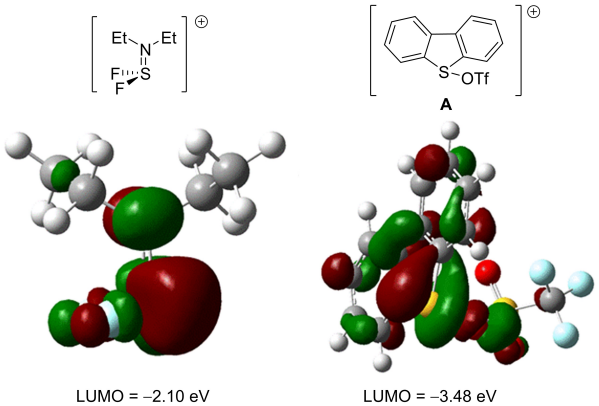
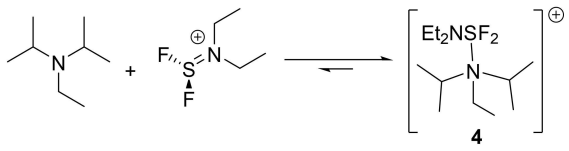


Figure 2. LUMO of XtalFluor-E and **A**.

Research Article
doi.org/10.1002/ejoc.202101394



Scheme 2. Proposed Lewis adduct formation between EtN^iPr_2 and XtalFluor-E.

At lower temperatures (−40 °C) this singlet converts to two broad resonances (with no coupling visible) and one very broad resonance, the broadness indicates fluxional processes that have not been frozen out at the low temperature limit in acetonitrile. At no temperature in MeCN was a ^{19}F resonance for free XtalFluor-E observed. We interpret this data as indicating reversible adduct formation with an equilibrium position favoring the Lewis adduct. Presumably adduct formation slows reactivity towards indole, consistent with additional equivalents of EtN^iPr_2 retarding the C–S bond formation reaction (entry 12). Attempts to crystallize the putative adduct **4** (and other Lewis adducts e.g. from 1:1 XtalFluor-E/amine mixtures where amine = Et_3N, 4-DMAP, DBU in borosilicate glass and in PTFE lined vessels) were unsuccessful in our hands. Inspection of these 1:1 mixtures indicated consumption of XtalFluor-E in each case, and formation of ^1H and ^{19}F NMR spectra consistent with Lewis adduct formation (see *supporting information*). The poor performance of DBU in these C–S bond forming reactions is consistent with its relatively high nucleophilicity towards soft electrophiles, which may preclude cleavage of the dative bond under these conditions.[21]

With adduct formation indicated by these experiments, we attribute the higher yielding formation of di-indole sulfide **2a** using XtalFluor E/EtN^iPr_2 (to that observed in the absence of base) to two effects: (i) the amine sequestering Brønsted acidic species (present as impurities or evolved during the S_EAr reaction); (ii) amine coordination preventing one-electron oxidation of indoles (as observed with sulfonium **A**). Consistent with the report on using **A** to form C–S bonds, we also disfavor a radical-mediated pathway as reactions carried out using putative adduct **4** in the presence of one equivalent of TEMPO still affords significant amounts of di-indole sulfide **2a** (30%), supporting a closed shell S_EAr mechanism. A key remaining question was how the sulfur(II) compound, **2**, is formed given that the initial sulfur reagent is a sulfonium cation (sulfur(IV)). Our initial hypothesis was based on sulfonium **3** acting as a precursor to sulfide **2** by reduction. However, combination of sulfonium **3** (1 eq.) with diethyl amine, EtN^iPr_2 or *N*-Me-indole (as potential reductants), all led to no reaction. As a result, the redox reaction leading to sulfide **2** remains unknown, and may proceed by formation of a S(VI) compound concomitantly to sulfide **2** consistent with the requirement for an excess of XtalFluor-E to give the highest yields (see Table 1, entries 13 and 14). Note, sulfonium cation **A** has been previously observed to react to form S(VI) and S(II) compounds under certain conditions, supporting this hypothesis.[13a] Regarding the formation of sulfonium **3**, it should be noted that **3** is not formed by oxidation of sulfide **2** with Xtalfluor-E followed by substituent transfer, as no reaction is observed by combining sulfide **2** and XtalFluor-E. These results suggest that the sulfide **2** and sulfonium **3** are formed by distinct pathways, possibly involving different protonation sites during the S_EAr reaction (e.g. deprotonation of an arenium cation with external base, by formation of HF or by formation of $HNEt_2$). This is consistent with the observation of significant amounts of sulfonium **3** only in the presence of the non-interacting exogenous base DBP, which may prevent protonation of the NEt_2 unit and thus maintain the S–N bond during the S_EAr reaction.

Conclusion

In summary, XtalFluor-E reacts as a source of electrophilic sulfur for the synthesis of di-indole sulfides directly from indoles. This reaction affords C3-functionalised indoles consistent with an S_EAr mechanism. It is applicable to a range of functionalized indoles and does not require indole N-protection. Notably, the reaction outcome was highly dependent on the exogenous base added, with a di-indole diethylamino-sulfonium cation (3) observed only in the presence of 2,6-di*t*Bu-4-Me-pyridine base, indicating the deprotonation process can have a significant effect on product outcome. The reversible formation of a Lewis adduct between an amine and XtalFluor-E is proposed to be essential for high yielding formation of di-indole sulfides, with the bulky base EtN^iPr_2 proving optimal. We attribute this to EtN^iPr_2 forming a reversible, dative bond to XtalFluor-E (preventing unwanted side reactions), but not irreversibly quenching the electrophilicity at S, presumably by EtN^iPr_2 dissociation which would represent frustrated Lewis pair type reactivity.[22] In contrast, more nucleophilic amines, e.g. DBU, preclude S_EAr using XtalFluor presumably due to stronger Lewis adduct formation. Thus variation in the basic partner when using XtalFluor salts should be carefully considered given the drastic effect that has been seen in this chemistry.

Acknowledgements

The University of Edinburgh is thanked for a PhD. studentship (N.C) and S.P.T. thanks the Royal Society for a University Research Fellowship (URF/R/191015). We thank Juraj Bella for the assistance with low temperature NMR experiments as well as Mass Spectrometry facility (SIRCAMS) at the University of Edinburgh for carrying out MS analysis.

Conflict of Interest

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: Arylsulfides · C–H functionalization · Indole · Lewis adduct · XtalFluor

[1] a) W. R. Hasek, W. C. Smith, V. A. Engelhardt, *J. Am. Chem. Soc.* **1960**, *82*, 543–551; b) W. J. Middleton, *J. Org. Chem.* **1975**, *40*, 574–578; c) G. S. Lal, G. P. Pez, R. J. Pesaresi, F. M. Prozonic, H. Cheng, *J. Org. Chem.* **1999**, *71*, 7048–7054; d) J. M. Shreeve, R. P. Singh, *Synthesis* **2002**, *17*, 2561–2578.
[2] a) A. L'Heureux, F. Beaulieu, C. Bennett, D. Bill, S. Clayton, F. LaFlamme, M. Mirmehrabi, S. Tadayon, D. Tovell, M. Couturier, *J. Org. Chem.* **2010**, *75*, 3401–3411; b) F. Beaulieu, L. Beauregard, G. Courchesne, M. Couturier, F. LaFlamme, A. L'Heureux, *Org. Lett.* **2009**, *11*, 5050–5053.
[3] M. Roudias, F. Vallée, J. Martel, J. Paquin, *J. Org. Chem.* **2018**, *83*, 8731–8738.
[4] A. Cochi, D. Gomez Pardo, J. Cossy, *Org. Lett.* **2011**, *13*, 4442–4445.
[5] M. Keita, M. Vandamme, O. Mahé, J. Paquin, *Tetrahedron Lett.* **2015**, *56*, 461–464.
[6] M. Pouliot, L. Angers, J. Hamel, J. Paquin, *Org. Biomol. Chem.* **2012**, *10*, 988–993.
[7] a) Y. Yi, H. Gholami, M. Morrow, B. Borhan, *Org. Biomol. Chem.* **2017**, *15*, 9570–9574; b) O. Mahé, J. Desroches, J. Paquin, *Eur. J. Org. Chem.* **2013**, *2013*, 4325–4331.
[8] a) K. Dunbar, D. Scharf, A. Litomska, C. Hertweck, *Chem. Rev.* **2017**, *117*, 5521–5577; b) M. Feng, B. Tang, S. H. Liang, X. Jiang, *Curr. Top. Med. Chem.* **2016**, *16*, 1200–1216.
[9] H. Iino, T. Usui, J.-I. Hanna, *Nat. Commun.* **2015**, *6*, 6828.
[10] C. Lee, Y. Liu, S. Badsara, *Chem. Asian J.* **2014**, *9*, 706–722.
[11] For an example with sulfur dichloride see: a) M. Barbier, M. Devys, *J. Heterocycl. Chem.* **1989**, *26*, 265–267. For an example with thiols see: b) S. Parumala, R. Peddinti, *Green Chem.* **2015**, *17*, 4068–4072. For an example with di-sulfides see: c) C. Prasad, S. Balkrishna, A. Kumar, B. Bhakuni, K. Shrimali, S. Biswas, S. Kumar, *J. Org. Chem.* **2013**, *78*, 1434–1443. For an example with *N*-(thio)succinimides see: d) T. Hostier, V. Ferey, G. Ricci, D. Gomez Pardo, J. Cossy, *Org. Lett.* **2015**, *17*, 3898–3901. For an example with sulfonyl hydrazines see: e) Pang, X. Liu, X. Li, L. Xiang, G. Huang, *J. Org. Chem.* **2014**, *79*, 10605–10610. For an example with sulfonyl chlorides see: f) Q. Wu, D. Zhao, X. Qin, J. Lan, J. You, *Chem. Commun.* **2011**, *47*, 9188–9190.
[12] a) V. Nenajdenko, P. Vertelezkij, I. Gridnev, N. Shevchenko, E. Balenkova, *Tetrahedron* **1997**, *53*, 8173–8180; b) N. Shevchenko, A. Karpov, E. Zakurdaev, V. Nenajdenko, E. Balenkova, *Chem. Heterocycl. Compd.* **2000**, *36*, 137–143; c) V. Nenaidenko, E. Balenkova, *Russ. J. Org. Chem.* **2003**, *39*, 291–330.
[13] a) K. Kafuta, A. Korzun, M. Böhm, C. Golz, M. Alcarazo, *Angew. Chem. Int. Ed.* **2020**, *59*, 1950–1955; *Angew. Chem.* **2020**, *132*, 1966–1971; b) S. Kozhushkov, M. Alcarazo, *Eur. J. Inorg. Chem.* **2020**, *2020*, 2486–2500; c) P. Xu, D. Zhao, F. Berger, A. Hamad, J. Rickmeier, R. Petzold, M. Kondratiuk, K. Bohdan, T. Ritter, *Angew. Chem. Int. Ed.* **2020**, *59*, 1956–1960; *Angew. Chem.* **2020**, *132*, 1972–1976; d) F. Juliá, Q. Shao, M. Duan, M. Plutschack, F. Berger, J. Mateos, C. Lu, X. Xue, K. Houk, T. Ritter, *J. Am. Chem. Soc.* **2021**, *143*, 16041–16054.
[14] J. Fernández-Salas, A. Pulis, D. Procter, *Chem. Commun.* **2016**, *52*, 12364–12367.
[15] Y. Li, L. Shi, W. Zhu, H. Li, Q. Zhang, *Synlett* **2018**, *29*, 1847–1850.
[16] a) M. Grundy, K. Yuan, G. Nichol, M. Ingleson, *Chem. Sci.* **2021**, *12*, 8190–8198; b) S. Iqbal, K. Yuan, J. Cid, J. Pahl, M. Ingleson, *Org. Biomol. Chem.* **2021**, *19*, 2949–2958; c) S. Iqbal, J. Cid, R. Procter, M. Uzelac, K. Yuan, M. Ingleson, *Angew. Chem. Int. Ed.* **2019**, *58*, 15381–15385; *Angew. Chem.* **2019**, *131*, 15525–15529; d) J. McGough, J. Cid, M. Ingleson, *Chem. Eur. J.* **2017**, *23*, 8180–8184.
[17] For acid-promoted polymerisation of indoles see: G. Smith, in: *Advances in Heterocyclic Chemistry*, vol. 2 (Eds: A. R. Katritzky) Academic Press, New York, **1963**, pp. 287–309.
[18] For $[SF_3]^+$/amine adducts see: a) D. Turnbull, P. Chaudhary, P. Hazendonk, S. Wetmore, M. Gerken, *Inorg. Chem.* **2021**, *60*, 3893–3901. For Sulfur Trifluoride Cation $[SF_3]^+$ Affinities of Pyridines in gas phase see: b) P. Wong, S. Ma, S. Yang, R. Cooks, F. Gozzo, M. Eberlin, *J. Am. Soc. Mass Spectrom.* **1997**, *8*, 68–75.
[19] Couturier et al. reported DBU retarding the reactivity in deoxyfluorination reactions of alcohols if pre-mixed with XtalFluor reagent prior the addition of the alcohol – see reference 2.
[20] For SF_4/amine adducts see: a) Chaudhary, J. Goettel, H. Mercier, S. Sowlati-Hashjin, P. Hazendonk, M. Gerken, *Chem. Eur. J.* **2015**, *21*, 6247–6256; b) J. Goettel, P. Chaudhary, P. Hazendonk, H. Mercier, M. Gerken, *Chem. Commun.* **2012**, *48*, 9120; c) N. Kostiuk, J. Goettel, M. Gerken, *Inorg. Chem.* **2020**, *59*, 8620–8628.
[21] B. Maji, M. Breugst, H. Mayr, *Angew. Chem. Int. Ed.* **2011**, *50*, 6915–6919.
[22] a) C. Martin, M. Jennings, M. Ferguson, P. Ragogna, *Angew. Chem. Int. Ed.* **2009**, *48*, 2210–2213; b) F. Tsao, A. Waked, L. Cao, J. Hofmann, L. Liu, S. Grimme, D. Stephan, *Chem. Commun.* **2016**, *52*, 12418–12421.

Manuscript received: November 17, 2021
Revised manuscript received: February 10, 2022
Accepted manuscript online: February 11, 2022