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Pyrrolylsulfonium salts: stable, accessible and versatile pseudohalides for Stille couplings†

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Pyrrolyl halides can be difficult to synthesise in a regioselective manner and are often unstable, which has hampered their application in cross-coupling. Here we introduce pyrrolylsulfonium salts as advantageous pseudohalide coupling partners and showcase their applicability in Stille couplings. Benefits of these salts include their straightforward synthesis *via* an “interrupted Pummerer” process, their high stability, and the ability to selectively introduce the sulfonium group at either the pyrrole α - or β - position as required. The Stille coupling has been demonstrated for aryl, heteroaryl and alkynylstannanes, and the effect of the pyrrole substituents on the regioselectivity of S–C bond activation has been investigated. Conditions to effect *N*-desulfonylation of *N*-trisyl coupling products have been identified.

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Introduction

The pyrrole ring system is commonly found in organic materials,¹ as well as in natural products² and drug substances³ (Fig. 1). For example, GS70 is a pyrrole-based electron acceptor which has been used to fabricate organic solar cells that can achieve high power conversion efficiencies,⁴ P(DKPP-TPTH) is a pyrrole-containing polymer which has been used to construct organic field-effect transistors,⁵ and OCF₃-BnPyV is a viologen-substituted pyrrole which has been used in electrochromic devices.⁶ The natural products cycloprodigiosin⁷ and heronapyrrole A⁸ have immunosuppressant and antibiotic properties, respectively. The licensed drug vonoprazan⁹ is a potassium-competitive acid blocker indicated for gastro-duodenal ulcers and the investigational drug resminostat is in trials for oncology indications.¹⁰

Many synthetic strategies to access pyrrole-containing targets have been reported. These may be divided into *de novo* pyrrole syntheses¹¹ (where the pyrrole ring is formed with substituents already in place) and pyrrole functionalization approaches (where substituents are introduced onto a pre-existing pyrrole ring). In this latter category, S_EAr and pyrrole

metallation protocols are well developed.¹² Transition metal-catalysed cross-couplings have also been studied for pyrrole functionalization,¹³ although some shortcomings remain to be overcome. For example, the use of pyrrolyl halides as classical electrophilic cross-coupling partners may be hindered by difficulties of synthetic access and/or instability. Thus, halogenation of *N*-H pyrrole or simple *N*-alkyl/*N*-aryl derivatives with a variety of electrophilic halogen sources reportedly often leads to complex mixtures of mono- and polyhalopyrroles. Moreover, the parent *N*-H-2-halopyrroles are markedly unstable, decomposing upon attempted isolation (Scheme 1a).^{14,15} Selectivity for halogenation at C2 *vs.* C3 can also vary depending on the substrate and synthetic method, and separation is usually challenging. Whilst *N*-halosuccinimides can exhibit good selectivity for halogenation at C2 over C3, overreaction to the 2,4-dihalopyrrole can occur.¹⁴ To access 3-halopyrroles, an acid-mediated isomerization (“halogen dance”) of the 2-halo isomer can sometimes be employed, but this can also induce a degree of disproportionation (Scheme 1b).^{14,16} Halopyrroles substituted with electron-withdrawing groups can be more stable in some cases. For example, pyrroles bearing a carbonyl at C2 generally undergo electrophilic halogenation to give stable products, but regioselectivity between C4 and C5 depends on the halogenating agent and on the nature of the carbonyl (Scheme 1c).^{15,16a,17} Alternatively, use of an electron-withdrawing protecting group on nitrogen can sometimes increase stability. For example, considering bromopyrroles specifically, *N*-Boc-2-bromopyrrole¹⁸ can reportedly be stored as a solution in hexane at –10 °C,¹⁹ and *N*-tosyl-2-bromopyrrole²⁰ is stable in pure form. *N*-Tosyl-3-bromopyrrole may be synthesized by treating *N*-tosylpyrrole with Br₂ under acidic conditions,²¹ and *N*-Boc-3-bromo-

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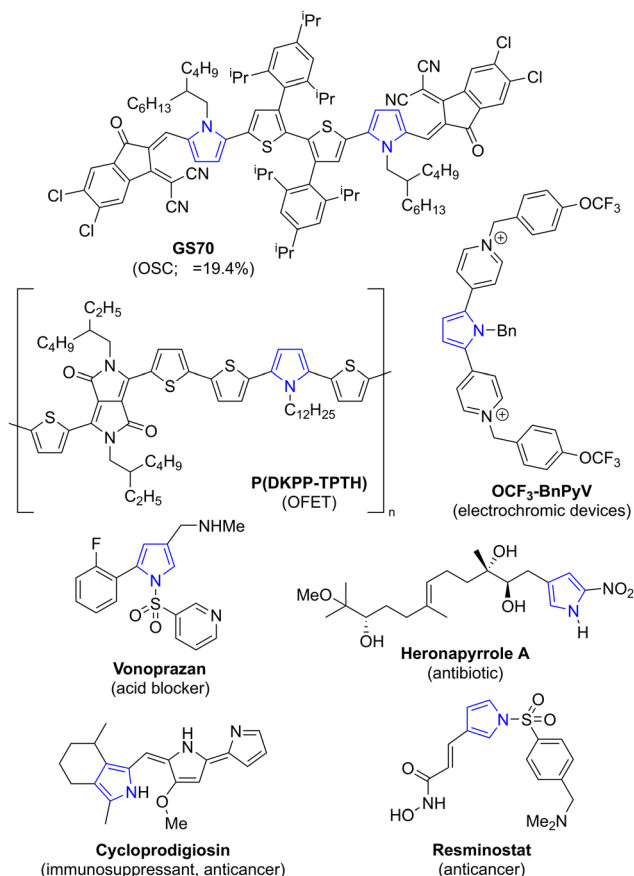
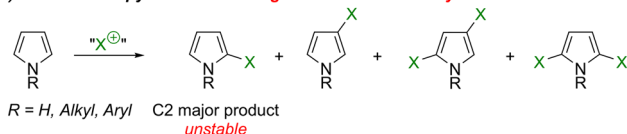
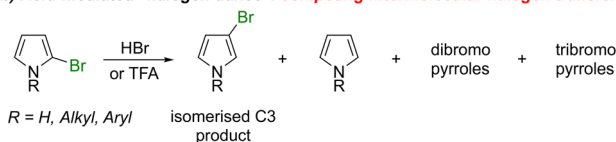


Fig. 1 A selection of pyrrole-containing molecules.

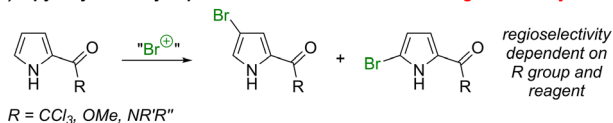
a) Electron-rich pyrroles: **overhalogenation and instability**



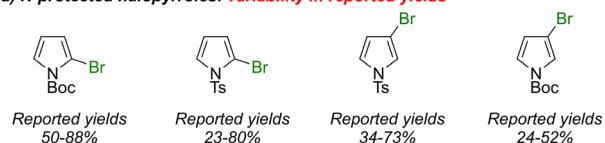
b) Acid-mediated "halogen dance": **competing intermolecular halogen transfer**



c) 2-pyrrolyl carbonyls: **products can be more stable but regioselectivity varies**



d) N-protected halopyrroles: **variability in reported yields**



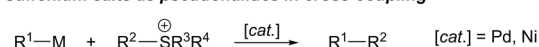
Scheme 1 Stability and selectivity problems in the formation of halopyrroles.

pyrrole is synthesized from *N*-TIPS-3-bromopyrrole by protecting group exchange²² (Scheme 1d). However, all of these examples have in common that the yields reported for their preparation (by the same procedure) vary appreciably.

Whilst some cross-couplings of halopyrroles such as those in Scheme 1 have been reported,²³ their more widespread utilisation has been hampered by the issues described above. An alternative approach is the use of a pyrrole pseudohalide for cross-coupling. Thus far, there are some examples of pyrrole triflates being used as pseudohalides in cross-couplings,²⁴ primarily in natural product total synthesis, but the preparation of the substrates has not been generalised. Pyrrole C-H functionalisation approaches have also been developed, each with varying scope in substrate, coupling partner, catalyst, *etc.*²⁵

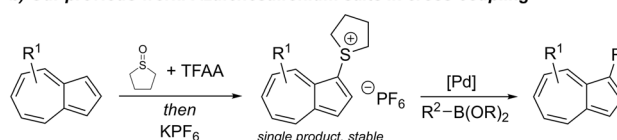
Sulfonium salts have become established as pseudohalides that can have advantages over classical halide coupling partners. Cross-coupling of sulfonium salts was first reported by Liebeskind *et al.*,²⁶ who demonstrated Stille, Suzuki-Miyaura and Negishi couplings with aryl, heteroaryl, alkenyl and benzyl sulfonium salts. Since then the scope of sulfonium salt cross-coupling has been expanded to include various other nucleophilic coupling partners, carbonylative couplings, reductive cross-electrophile couplings, *etc.*, employing both Pd and Ni (Scheme 2a).^{27,28} Sulfonium salts are also synthetically useful in other contexts, and their chemistry has been reviewed.²⁹ We previously reported the synthesis of azulenesulfonium salts and their use in cross-coupling.³⁰ These salts proved superior to azulene halides in terms of their stability and ease of syn-

a) Sulfonium salts as pseudohalides in cross-coupling

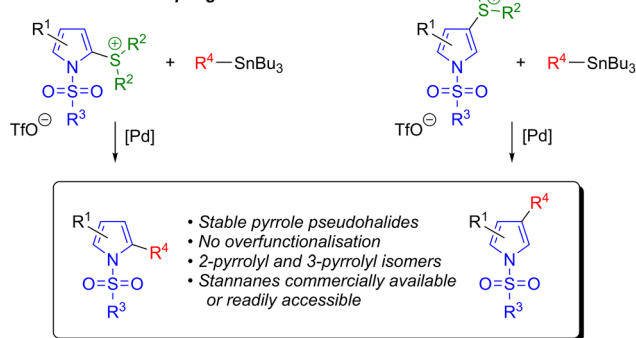


$M = \text{B, Zn, Sn, Cu, NH}_2$ (amination), $R^1 = \text{Ar, alkenyl, alkynyl, B(OR)}_2$
 OH/CO (carbonylation), $\text{C}\equiv\text{C}$ (Heck), $R^2 = (\text{het})\text{Ar, (het)ArCH}_2, \text{ alkenyl}$
 Ar (C-H activation) $R^3, R^4 = \text{Ar, alkyl, C}_m\text{F}_{2m+1}$

b) Our previous work: Azulen sulfonium salts in cross-coupling



c) This work: Pyrrolesulfonium salts in Stille cross-coupling



Scheme 2 Sulfonium salts are competent pseudohalides in cross-coupling.

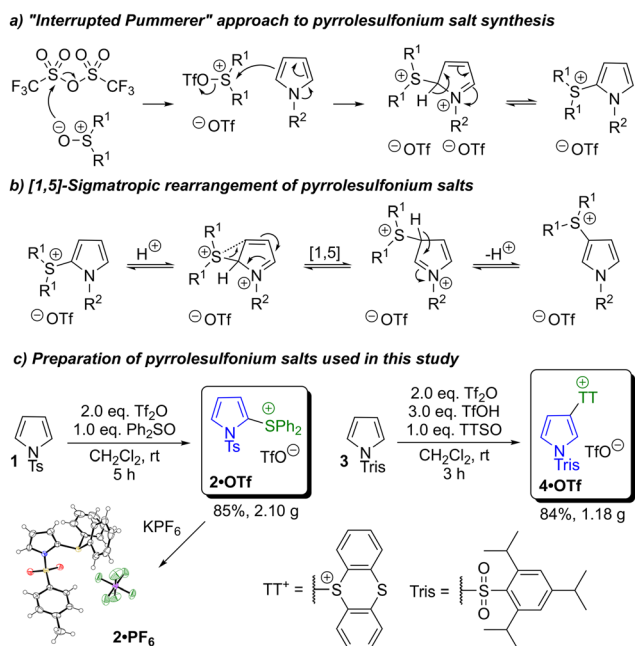
thesis. Synthesis of azulene halides by S_EAr reaction on the electron-rich five-membered ring typically leads to overhalogenation, and the products are unstable (unless electron-withdrawing groups are also present). In contrast azulen-sulfonium salts may be synthesised in good yield, as the sole products, and are stable without any special handling/storage precautions (Scheme 2b). The cationic sulfonium substituent serves to reduce the electron density of the aromatic system, thereby imparting stability. We recognised that many of the drawbacks of azulene halides (instability, difficulty of synthesis/purification) were shared with pyrrolyl halides, which also comprise an electron-rich five-membered aromatic ring. Therefore we sought to develop pyrrolylsulfonium salts for use in cross-coupling, anticipating that they would share the advantages of azulen-sulfonium salts. The results of these studies are reported here (Scheme 2c). Pyrrolylsulfonium salts are known,³¹ but to date they have been primarily used as radical precursors, in sigmatropic rearrangements or as substrates for dealkylation to give pyrrolyl thioethers.

Results and discussion

Aryl sulfonium salts can be synthesised by various approaches, including reaction of aryl thiols/thioethers with electrophiles, or activation of sulfoxides and attack by nucleophiles.^{29j} For the synthesis of pyrrolylsulfonium salts we opted to employ an “interrupted Pummerer” reaction,³² wherein a sulfoxide is activated by an acid anhydride, followed by attack at sulfur by a nucleophilic (*i.e.* electron-rich) arene, loss of an oxygen leaving group and rearomatisation (Scheme 3a). In Pummerer reac-

tions the sulfoxide is most commonly activated with a carboxylic acid anhydride, but in this case we employed a sulfonic acid anhydride (specifically triflic anhydride). This was due to our previous findings that use of a carboxylic acid anhydride can promote an alternative reaction pathway affording Δ^3 -pyrrol-2-one products.³³

A key advantage of pyrrolylsulfonium salts as reagents for cross-coupling is easy access to both the 2-pyrrolyl and 3-pyrrolyl regioisomers. The interrupted Pummerer process typically installs the sulfonium salt at the 2-position, in keeping with the established S_EAr reactivity of pyrrole. This product may then be isomerised to the 3-pyrrolylsulfonium salt *via* a Brønsted acid-catalysed [1,5]-sigmatropic rearrangement (Scheme 3b).^{31b-d} Analogous migrations of various other functional groups on the pyrrole ring have been reported,³⁴ although stability of the substrates to the highly acidic reaction conditions varies. In contrast, pyrrolylsulfonium salts are robust under these conditions and may be isomerised in high yield. Furthermore the interrupted Pummerer/rearrangement reaction cascade may be performed as a one-pot process. We prepared and screened multiple pyrrolylsulfonium salts to identify optimal reagents for cross-coupling that (a) are easily prepared in good yield on gram scale; (b) exhibit good stability; (c) have good solubility in the solvents to be used for cross-coupling; and (d) undergo oxidative addition into the correct C–S bond. From this screening we identified the novel salt diphenyl (*N*-(*p*-toluenesulfonyl)-1*H*-pyrrol-2-yl)sulfonium triflate **2-OTf** as an ideal reagent for the preparation of 2-substituted pyrroles, which was prepared on a gram scale (Scheme 3c). Reaction workup involved straightforward partitioning between MeCN and hexane,³⁵ followed by recrystallisation from methanol. The reaction generates an equivalent of triflic acid as a byproduct, which might be expected to catalyse the [1,5]-sigmatropic rearrangement shown in Scheme 3b. However, we found the specific combination of *N*-tosyl and diphenyl sulfonium substituents disfavoured the rearrangement under these reaction conditions, and hence 2-pyrrolyl (non-rearranged) salt **2-OTf** could be isolated in 85% yield. In contrast, we found that thianthrenium salts underwent the rearrangement more readily and that additional triflic acid facilitated the process. Formation of the 3-pyrrolylthianthrenium salt with an *N*-tosyl protecting group occurred in variable yield and the product was only sparingly soluble. Switching to a more sterically demanding *N*-trisyl group improved product solubility and rendered the synthesis reproducible and also scalable to gram scale. We thus identified the novel 5-(*N*-(2,4,6-triisopropylphenylsulfonyl)-1*H*-pyrrol-3-yl)-5*H*-thianthrenium triflate **4-OTf** as an ideal reagent for the preparation of 3-substituted pyrroles (Scheme 3c). Amongst the various sulfonium groups used as synthetic handles in the literature, the thianthrenium group has been extensively exploited due to its particular properties.^{36–38} For example, its introduction onto an aromatic ring typically proceeds in an exceptionally regioselective manner.^{28,39} In the case of *N*-trisyl pyrrole, NMR studies indicate that the initial thianthrenation affords a mixture of **4-OTf** and its 2-pyrrolyl regioisomer. This then



Scheme 3 Synthesis of sulfonium salts by “interrupted Pummerer” reaction and their isomerisation by [1,5]-sigmatropic rearrangement. TTSO = thianthrene-S-oxide.



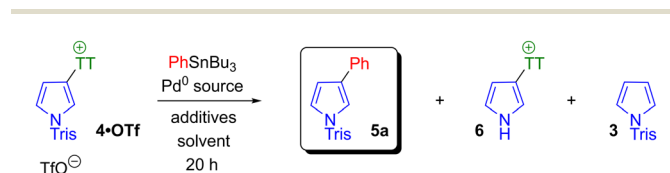
undergoes rearrangement to **4-OTf**, such that after 3 hours **4-OTf** is the only product present.^{31m,o} Introduction of a bulky group at nitrogen is known to favour 3-substituted products in pyrrole S_EAr reactions.²²

To establish the applicability of pyrrolylsulfonium salts **2-OTf** and **4-OTf** in cross-coupling, we employed them as pseudohalides in the Migita–Kosugi–Stille coupling.^{40,41} Examples of pyrrolyl halide Stille couplings are known,⁴² although competing dehalogenation can reportedly be significant in some cases.^{23p} Organostannanes are advantageous coupling partners due to their stability to air and moisture, as well as their availability from commercial sources or through straightforward syntheses.⁴³ The robust nature of the Stille coupling and its efficiency under mild reaction conditions mean it has proven successful in many instances where other cross-coupling methodologies have failed.⁴⁴ Whilst the (variable) toxicity of organostannanes⁴⁵ necessitates the thorough removal of tin residues from active pharmaceutical ingredients prepared through Stille coupling, methods to achieve this are well developed.⁴⁶

We selected phenyltributylstannane as an archetypal aryl stannane reagent for reaction optimisation. Reaction parameters were varied as shown in Scheme 4 and Table 1. Initial attempts using $Pd(PPh_3)_4$ and 1.3 equivalents of stannane showed the coupling was viable in DMF, toluene and *t*-butanol (entries 1–3). Desired product **5a** formed in each case, with the

highest conversion in DMF. Formation of byproducts was also observed, either as a result of *N*-sulfonyl group cleavage (giving **6**) or reductive cleavage of the thianthrenium group (giving **3**). This latter process is analogous to the dehalogenation sometimes observed with classical halide substrates. The beneficial effects of copper salt additives on Stille couplings are well documented,⁴⁷ so we evaluated the effect of CuI as an additive in DMF and toluene (entries 4 and 5), but no improvement in conversion was observed. Fluoride salts are also known to promote Stille couplings,⁴⁸ and synergistic effects arising from the presence of both copper and fluoride salts have been reported.⁴⁹ Multiple conditions including caesium fluoride as an additive were evaluated (entry 6), but formation of desired product **5a** was negligible in each case, with *N*-sulfonyl cleavage dominating instead to give **6**. Use of an alternative Cu(I) source did not increase conversion to **5a** (entries 7–10). Use of triphenylarsine as ligand⁵⁰ in conjunction with $Pd_2(dba)_3$ as palladium source in DMF gave greater conversion to **5a** (entries 11–15). Reaction temperature could be lowered to 50 °C without a reduction in conversion, and 2 mol% loading of $Pd_2(dba)_3$ (*i.e.* 4 mol% of Pd) was identified as optimal. Finally, a change in reaction stoichiometry to 2.2 equivalents of stannane increased conversion to 84% of **5a** and suppressed formation of byproducts **3** and **6** (entry 15).

An analogous reaction optimisation was carried out for the coupling of phenyltributylstannane with 2-pyrrolyl sulfonium salt **2-OTf**. Reaction parameters were varied as shown in Scheme 5 and Table 2. An initial attempt using $Pd(PPh_3)_4$ in DMF showed the coupling to be viable, with desired 2-phenylpyrrole **7a** forming in moderate yield (entry 1). Three byproducts were also identified, namely the *N*-sulfonyl cleavage product **8**, the sulfonium reductive cleavage product **1** and the parent pyrrole **9**. This latter byproduct (which was not observed in the coupling of **4-OTf**) presumably arises from *N*-sulfonyl cleavage from **1**, highlighting the greater stability of



Scheme 4 Stille coupling of **4-OTf** to form desired 3-phenylpyrrole **5a** and byproducts **6** and **3**.

Table 1 Optimisation of Stille coupling of 3-pyrrolyl thianthrenium salt **4-OTf**

Entry	Pd(0) source	PhSnBu ₃ (equiv.)	Additive	Ligand	Solvent	Conc. (M)	Temp. (°C)	Conv.% 5a	Conv.% 6	Conv.% 3
1	$Pd(PPh_3)_4$ (4 mol%)	1.3	—	—	DMF	0.12	110	64	<5	7
2	$Pd(PPh_3)_4$ (4 mol%)	1.3	—	—	Toluene	0.12	110	58	23	10
3 ^a	$Pd(PPh_3)_4$ (4 mol%)	1.3	—	—	<i>t</i> -BuOH	0.12	80	38	—	6
4	$Pd(PPh_3)_4$ (4 mol%)	1.3	CuI (16 mol%)	—	DMF	0.12	110	38	<5	8
5	$Pd(PPh_3)_4$ (4 mol%)	1.3	CuI (16 mol%)	—	Toluene	0.12	110	50	—	6
6	$Pd(PPh_3)_4$ (4 mol%)	1.3	CsF (2.2 eq.) with/without CuI	—	DMF/ toluene	0.12	80–110	<5	10–50	<5
7	$Pd(PPh_3)_4$ (4 mol%)	1.3	Cu(OTf)·Tol (16 mol%)	—	Toluene	0.12	110	46	<5	5
8	$Pd(PPh_3)_4$ (8 mol%)	1.3	Cu(OTf)·Tol (16 mol%)	—	Toluene	0.12	85	24	8	5
9	$Pd(PPh_3)_4$ (4 mol%)	1.3	Cu(OTf)·Tol (16 mol%)	—	Toluene	0.12	80	44	16	6
10	$Pd(PPh_3)_4$ (4 mol%)	1.3	Cu(OTf)·Tol (16 mol%)	—	Toluene	0.07	110	47	16	10
11	$Pd_2(dba)_3$ (2 mol%)	1.3	—	AsPh ₃ (16 mol%)	DMF	0.12	80	71	6	5
12	$Pd_2(dba)_3$ (2 mol%)	1.3	—	AsPh ₃ (16 mol%)	DMF	0.12	50	70	3	6
13	$Pd_2(dba)_3$ (1 mol%)	1.3	—	AsPh ₃ (16 mol%)	DMF	0.12	50	57	—	21
14	$Pd_2(dba)_3$ (4 mol%)	1.3	—	AsPh ₃ (16 mol%)	DMF	0.12	50	69	5	10
15	$Pd_2(dba)_3$ (2 mol%)	2.2	—	AsPh ₃ (16 mol%)	DMF	0.12	50	84	—	—

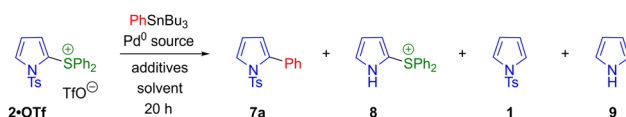
Conversions obtained from crude ¹H-NMR spectra by comparison to an internal standard (mesitylene). Cu(OTf)·Tol = copper(I) trifluoromethanesulfonate–toluene complex. ^a 13% of starting material **4** remained.



Table 2 Optimisation of Stille coupling of 2-pyrrolyl sulfonium salt 2-OTf

Entry	Pd(0) source	PhSnBu ₃ (equiv.)	Additive	Ligand	Solvent	Temp. (°C)	Conv% 7a	Conv% 8	Conv% 1	Conv% 9
1	Pd(PPh ₃) ₄ (4 mol%)	1.3	—	—	DMF	80	31	6	23	7
2	Pd(PPh ₃) ₄ (4 mol%)	1.3	CsF (2.2 eq.) Cu(OTf)·Tol (16 mol%)	—	DMF/ toluene	50–110	Trace	20–60	Trace	—
3	Pd ₂ (dba) ₃ (2 mol%)	1.3	—	AsPh ₃ (16 mol%)	DMF	50	64	14	15	—
4	Pd ₂ (dba) ₃ (4 mol%)	1.3	—	AsPh ₃ (16 mol%)	DMF	50	58	6	16	—
5	Pd ₂ (dba) ₃ (2 mol%)	1.3	—	AsPh ₃ (16 mol%)	DMF	80	53	10	18	—
6	Pd ₂ (dba) ₃ (2 mol%)	1.3	CuI (16 mol%)	AsPh ₃ (16 mol%)	DMF	50	24	16	25	6
7	Pd ₂ (dba) ₃ (2 mol%)	1.3	CuI (16 mol%)	AsPh ₃ (16 mol%)	DMF	25	7	—	12	3
8	Pd ₂ (dba) ₃ (2 mol%)	2.2	—	AsPh ₃ (16 mol%)	DMF	50	74	4	3	—

Conversions obtained from crude ¹H-NMR spectra by comparison to an internal standard (mesitylene). Cu(OTf)·Tol = copper(I) trifluoromethane-sulfonate-toluene complex.

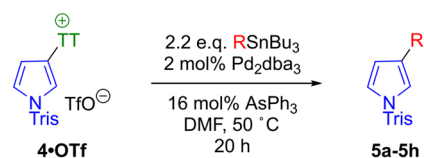
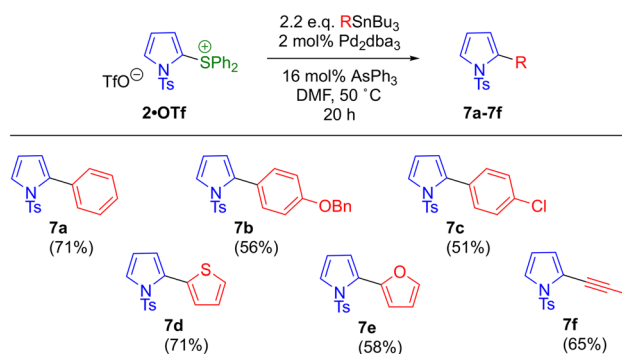
**Scheme 5** Stille coupling of 2-OTf to form desired 2-phenylpyrrole 7a and byproducts 8, 1 and 9.

the *N*-trisyl group compared to *N*-tosyl.[‡] Use of a fluoride additive with a copper(I) source was once again unproductive (entry 2). Use of AsPh₃/Pd₂(dba)₃ in DMF proved superior to the Pd(PPh₃)₄ system, and no increase in conversion was observed when the loading of Pd₂(dba)₃ was increased beyond 2 mol% or the temperature was increased beyond 50 °C (entries 3–5). With this palladium/ligand combination, copper(I) additives again proved deleterious (entries 6 and 7). However, a change in reaction stoichiometry to 2.2 equivalents of stannane was beneficial (as was the case for the coupling of 4-OTf), increasing conversion to 74% of 7a and minimising byproduct formation.

With optimised conditions in hand for the coupling of both salts, substrate scope for the couplings was examined using a range of commercially available stannanes. For the coupling of 4-OTf (Scheme 6), both (substituted) phenyl (5a–5e) and heteroaryl (5f–5g) products were isolated in good yield. In the formation of chlorophenyl pyrrole 5d, no evidence was seen of unwanted C–Cl bond activation in the product.⁵¹ Alkynyl stannanes were also competent coupling partners (5h–5i). Use of a bis(stannyl)thiophene effected a double coupling to give 5j. To the best of our knowledge, the heteroaryl triad in 5j with this particular connectivity (2,5-bis(3-pyrrolyl)thiophene) is a previously unknown structural motif outside the field of porphyrin chemistry.⁵²

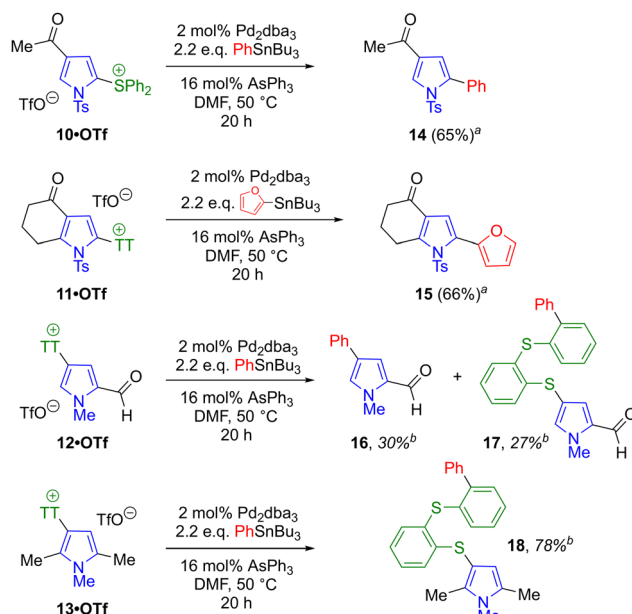
For the coupling of 2-OTf (Scheme 7), here also (substituted) phenyl (7a–7c), heteroaryl (7d–7e) and alkynyl (7f) products were accessible in good to moderate yield.

[‡]An alternative explanation for the formation of 9 would be by reductive cleavage of the sulfonium group from 8. However, this appears less likely since if the reductive cleavage occurs by Pd-mediated S–C bond activation in the first step, then in 8 this would be expected to favour the S–Ph bond over the S–pyrrole bond, on the basis of the results shown in Scheme 9.

**Scheme 6** Coupling of 4-OTf with a range of stannanes. Yields in parentheses are isolated yields.**Scheme 7** Coupling of 2-OTf with a range of stannanes. Yields in parentheses are isolated yields.

Preparation of sulfonium salts from C-substituted pyrroles was next attempted (Scheme 8). An *N*-tosyl pyrrole bearing a methyl ketone formed diphenylsulfonium salt **10-OTf** in low yield, along with byproducts potentially arising from enol triflate formation, although **10-OTf** was nevertheless isolable in pure form after chromatography. In contrast, a similar ketone-bearing substrate formed thianthrenium salt **11-OTf** in a much better yield. Here, the presence of electron-withdrawing groups at both N1 and C3 seemingly disfavours the migration of the sulfonium group. Pyrrole substrates lacking *N*-sulfonyl protection were also examined, with salts **12-OTf** and **13-OTf** forming from the corresponding *N*-methyl pyrroles. Salt **13-OTf** is the only regioisomer that can form from the corresponding substrate (1,2,5-trimethylpyrrole). However, **12-OTf** forms from 2-formyl-*N*-methylpyrrole, which has 3 potential sites of attachment. As such, the exclusive isolation of the product with the thianthrenium group at C4 is noteworthy, given that the regioselectivity of S_EAr reactions on 2-pyrrolyl carbonyls can vary (see Scheme 1c).

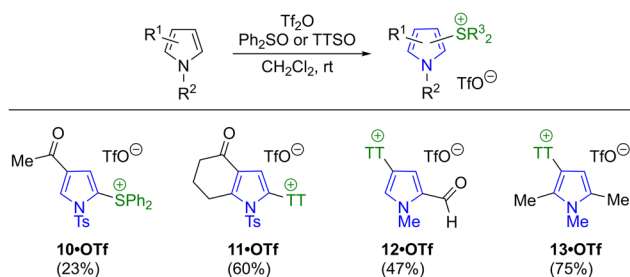
The successful cross-coupling of salts **2-OTf** and **4-OTf** requires that the initial oxidative addition step of the catalytic cycle is selective for the correct S–C bond. That is to say, palladium must insert into the bond between sulfur and the pyrrole ring, and not into a bond between sulfur and a phenyl ring (of the diphenyl sulfonium or thianthrenium group). During optimisation of the coupling conditions and during preparation of the products in Schemes 6 and 7, only products arising from activation of the correct S–C bond were isolated, and no products from coupling at the “wrong” S–C bond were ever detected. To determine the structural motif(s) responsible for regioselectivity in S–C bond activation, sulfonium salts from Scheme 8 were cross-coupled under the established conditions. Results with **2-OTf** and **4-OTf** indicate that with a sulfonium group at either C2 or C3, when the only other substituent is an electron-withdrawing (sulfonyl) group at N1, the desired regioselectivity is observed. Salts **10-OTf** and **11-OTf** are both substrates with a sulfonium handle at C2 as well as electron-withdrawing groups at N1 and C4. Coupling of **10-OTf** with PhSnBu_3 led to isolation of **14** and coupling of **11-OTf** with 2-furyl- SnBu_3 led to isolation of **15** as the sole product in each case (Scheme 9), illustrating that the desired regioselectivity is observed in this scenario also. In contrast, salt **12-OTf** possesses a sulfonium handle at C4 and an electron-



Scheme 9 Coupling of C-substituted pyrrolylsulfonium salts. ^aIsolated yield. ^bConversion by ¹H-NMR.

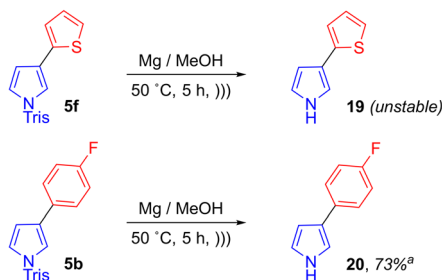
withdrawing group at C2, but lacks an electron-withdrawing group at N1. This salt underwent the coupling to give two products in approximately equal conversion, namely the desired product **16** and the product arising from ring cleavage of the thianthrenium motif, **17**. Under the same reaction conditions, salt **13-OTf** (lacking any electron-withdrawing groups) formed only the thianthrene ring cleavage product **18**, in high conversion.

Formation of the products depicted in Scheme 9 highlights the role of the *N*-sulfonyl group in ensuring that the desired regioselectivity in the S–C bond activation step is achieved. Therefore, since pyrrolylsulfonium couplings of the type reported here are likely to be carried out on *N*-sulfonyl substrates specifically, we investigated removal of the *N*-sulfonyl group from selected coupling products. For *N*-tosyl pyrroles of the type shown in Scheme 7, conditions for *N*-deprotection are widely reported in the literature using, for example, sodium hydroxide in ethanol.^{20a–c} However for *N*-trisyl pyrroles of the type shown in Scheme 6, the additional steric bulk renders the *N*-sulfonyl group much more resistant to removal. Attempted deprotection of thienylpyrrole **5f** under basic hydrolysis conditions ($\text{NaOH}/\text{MeOH}/\Delta$) led to recovery of starting material. A reported procedure for *N*-sulfonyl cleavage using triflic acid led to decomposition.⁵³ Attempts at reductive S–N bond cleavage using SmI_2 or complexes thereof also returned starting material.⁵⁴ However, use of Mg in MeOH at 50 °C under sonication⁵⁵ was successful at removing the *N*-trisyl group to give 3-(2-thienyl)pyrrole **19**. Instability of this substance in air or upon attempted purification hampered quantitation of its formation. Therefore a less electron-rich *N*-trisylpyrrole was selected for deprotection (*p*-fluorophenyl product **5b**). The resultant deprotection product **20** exhibited greater stability

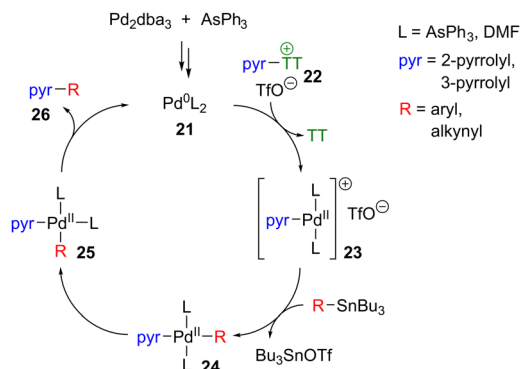


Scheme 8 Synthesis of sulfonium salts from substituted pyrroles. TTSO = thianthrene-S-oxide. Yields in parentheses are isolated yields.





Scheme 10 N-Deprotection of N-trisylpyrroles. ^aConversion by ¹H-NMR.



Scheme 11 Proposed mechanistic cycle for pyrrolylsulfonium Stille couplings.

than **19**, and it was determined to have formed in 73% conversion (Scheme 10).

A possible mechanism for a representative pyrrolylsulfonium Stille coupling is depicted in Scheme 11. The Pd⁰ active catalyst **21** will engage in oxidative addition into the C–S bond of a pyrrolylsulfonium salt such as **22** to give Pd^{II} complex **23**. Whereas oxidative addition with a classical halide coupling partner would form a neutral Pd^{II} complex with a Pd–X bond, we propose that use of pyrrolylsulfonium pseudohalide **22** may instead lead to a cationic tricoordinate complex of type **23**. In the specific case of thianthrenium salts, Ritter *et al.* have presented evidence that thianthrene (“TT”) is notably non-coordinating towards Pd^{II} complexes (less coordinating than triflate),⁵⁶ although this may not necessarily apply for other sulfonium salts such as the diphenylsulfonium salts **2-OTf** and **10-OTf**. Transmetalation with the stannane reagent would afford tetracoordinate **24**, which after isomerisation could undergo reductive elimination to give product **26**. DMF is reportedly a non-innocent solvent in Stille couplings, and transmetalation can occur from a Pd^{II} complex in which DMF occupies a coordination site (*i.e.* L = DMF).^{50b} Accordingly we do not speculate as to the specific identity of the “L” substituents in each of the complexes in Scheme 11. The mechanism shown is most likely a simplification of the true process, which may vary depending on the nature of the pyrrolylsulfonium salt and stannane used.^{40b,57} Accordingly the mechanism of this process merits further study.

Conclusions

We have described the straightforward synthesis of multiple pyrrolylsulfonium salts and demonstrated their applicability as pseudohalides in Stille couplings. The approach used for the synthesis of these salts allows for their regioselective installation at either the pyrrole α- or β-position, through the choice of appropriate sulfonium substituents and reaction conditions for the pyrrole in question. The salts are formed in good yield and exhibit good stability, and the synthesis is not prone to overfunctionalisation; these are all significant advantages over the classical pyrrolyl halide coupling partners. Additionally, we have identified reaction conditions that are able to effect the Stille coupling of the pyrrolylsulfonium salts with a range of (hetero)aryl- and alkynyl-stannanes. When the pyrrolylsulfonium salt possesses an N-sulfonyl substituent, cross-coupling occurs at the desired S–C bond only. The sulfide byproduct is therefore recoverable and could be recycled for the synthesis of additional pyrrolylsulfonium salt, if required. Both the N-tosyl and N-trisyl groups have been shown to be removable subsequent to the coupling step. Furthermore, variants of this methodology may be applicable to other heterocycles. For example, while Stille couplings of other arylthianthrenium salts are unknown so far, we note that indolyl thianthrenium salts have been reported.[§] For the reasons listed above we anticipate that the methodology described here may find applications in various synthetic contexts.

Author contributions

S.E.L. and J.L.H. conceived the project. J.L.H. carried out the synthesis. C.L.L. and J.L.H. acquired and interpreted NMR data. G.K.-K. carried out X-ray crystallography. S.E.L. wrote the manuscript with input from all authors.

Data availability

The data supporting this article have been included as part of the ESI.[†] Crystallographic data for **2-PF₆** and **5f** have been deposited at the CCDC under 2382855 and 2382856.[†]

Conflicts of interest

There are no conflicts to declare.

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[§]The synthesis of indol-3-ylthianthrenium tetrafluoroborate is reported in the ESI[†] for ref. 39.



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References

- 1 C. Bulumulla, R. Gunawardhana, P. L. Gamage, J. T. Miller, R. N. Kularatne, M. C. Biewer and M. C. Stefan, Pyrrole-Containing Semiconducting Materials: Synthesis and Applications in Organic Photovoltaics and Organic Field-Effect Transistors, *ACS Appl. Mater. Interfaces*, 2020, **12**, 32209–32232.
- 2 (a) N. Singh, S. Singh, S. Kohli, A. Singh, H. Asiki, G. Rathee, R. Chandra and E. A. Anderson, Recent progress in the total synthesis of pyrrole-containing natural products (2011–2020), *Org. Chem. Front.*, 2021, **8**, 5550–5573; (b) I. S. Young, P. D. Thornton and A. Thompson, Synthesis of natural products containing the pyrrolic ring, *Nat. Prod. Rep.*, 2010, **27**, 1801–1839.
- 3 G. L. Petri, V. Spanò, R. Spatola, R. Holl, M. V. Raimondi, P. Barraja and A. Montalbano, Bioactive pyrrole-based compounds with target selectivity, *Eur. J. Med. Chem.*, 2020, **208**, 112783.
- 4 J. Wang, C. Wang, Y. Wang, J. Qiao, J. Ren, J. Li, W. Wang, Z. Chen, Y. Yu, X. Hao, S. Zhang and J. Hou, Pyrrole-Based Fully Non-fused Acceptor for Efficient and Stable Organic Solar Cells, *Angew. Chem., Int. Ed.*, 2024, **63**, e202400565.
- 5 R. Agneeswari, I. Shin, V. Tamilavan, D. Y. Lee, S. Cho, Y. Jin, S. H. Park and M. H. Hyun, Modulation of the properties of pyrrolo[3,4-*c*]pyrrole-1,4-dione based polymers containing 2,5-di(2-thienyl)pyrrole derivatives with different substitutions on the pyrrole unit, *New J. Chem.*, 2015, **39**, 4658–4669.
- 6 B. Deng, Y. Zhu, M. U. Ali, K. Li, X. Liu, X. Zhang, J. Ning, Z. Hu, H. Chen, J. He, Y. He and H. Meng, Pyrrole-based viologen derivatives with high contrast and magenta color for electrochromic-fluorescent devices, *Sol. Energy Mater. Sol. Cells*, 2023, **251**, 112149.
- 7 (a) R. Pandey, R. Chander and K. B. Sainis, Prodigiosins as anti cancer agents: living up to their name, *Curr. Pharm. Des.*, 2009, **15**, 732–741; (b) H. H. Wasserman and J. M. Fukuyama, The synthesis of (±)-cycloprodigiosin, *Tetrahedron Lett.*, 1984, **25**, 1387–1388; (c) E. E. Schultz and R. Sarpong, Application of In Situ-Generated Rh-Bound Trimethylenemethane Variants to the Synthesis of 3,4-Fused Pyrroles, *J. Am. Chem. Soc.*, 2013, **135**, 4696–4699; (d) R. E. Johnson, T. de Rond, V. N. G. Lindsay, J. D. Keasling and R. Sarpong, Synthesis of Cycloprodigiosin Identifies the Natural Isolate as a Scalemic Mixture, *Org. Lett.*, 2015, **17**, 3474–3477.
- 8 (a) R. Raju, A. M. Piggott, L. X. Barrientos Diaz, Z. Khalil and R. J. Capon, Heronapyrroles A–C: Farnesylated 2-Nitropyrroles from an Australian Marine-Derived *Streptomyces* sp., *Org. Lett.*, 2010, **12**, 5158–5161; (b) T. Matsuo, S. Hashimoto, K. Nishikawa, T. Kodama, S. Kikuchi, Y. Tachi and Y. Morimoto, Total synthesis and complete stereochemical assignment of heronapyrroles A and B, *Tetrahedron Lett.*, 2015, **56**, 5345–5348.
- 9 (a) K. P. Garnock-Jones, Vonoprazan: First Global Approval, *Drugs*, 2015, **75**, 439–443; (b) Y. Arikawa, H. Nishida, O. Kurasawa, A. Hasuoka, K. Hirase, N. Inatomi, Y. Hori, J. Matsukawa, A. Imanishi, M. Kondo, N. Tarui, T. Hamada, T. Takagi, T. Takeuchi and M. Kajino, Discovery of a Novel Pyrrole Derivative 1-[5-(2-Fluorophenyl)-1-(pyridin-3-ylsulfonyl)-1*H*-pyrrol-3-yl]-*N*-methylmethanamine Fumarate (TAK-438) as a Potassium-Competitive Acid Blocker (P-CAB), *J. Med. Chem.*, 2012, **55**, 4446–4456.
- 10 S. Mandl-Weber, F. G. Meinel, R. Jankowsky, F. Oduncu, R. Schmidmaier and P. Baumann, The novel inhibitor of histone deacetylase resminostat (RAS2410) inhibits proliferation and induces apoptosis in multiple myeloma (MM) cells, *Br. J. Haematol.*, 2010, **149**, 518–528.
- 11 (a) I. V. Efimov, L. N. Kulikova, A. R. Miftyakhova, M. D. Matveeva and L. G. Voskressensky, Recent Advances for the Synthesis of *N*-Unsubstituted Pyrroles, *ChemistrySelect*, 2021, **6**, 13740–13772; (b) S. C. Philkhana, F. O. Badmus, I. C. Dos Reis and R. Kartika, Recent Advancements in Pyrrole Synthesis, *Synthesis*, 2021, 1531–1555; (c) V. Estévez, M. Villacampa and J. C. Menéndez, Recent advances in the synthesis of pyrroles by multicomponent reactions, *Chem. Soc. Rev.*, 2014, **43**, 4633–4657; (d) M. A. Yurovskaya and R. S. Alekseyev, New Perspectives on Classical Heterocyclic Reactions Involving Pyrrole Derivatives, *Chem. Heterocycl. Compd.*, 2014, **49**, 1400–1425.
- 12 M. K. Hunjan, S. Panday, A. Gupta, J. Bhaumik, P. Das and J. K. Laha, Recent Advances in Functionalization of Pyrroles and their Translational Potential, *Chem. Rec.*, 2021, **21**, 715–780.
- 13 (a) E. M. Beck and M. J. Gaunt, Pd-catalyzed C-H bond functionalization on the indole and pyrrole nucleus, *Top. Curr. Chem.*, 2010, **292**, 85–121; (b) M. G. Banwell, T. E. Goodwin, S. Ng, J. A. Smith and D. J. Wong, Palladium-Catalysed Cross-Coupling and Related Reactions Involving Pyrroles, *Eur. J. Org. Chem.*, 2006, 3043–3060.
- 14 (a) H. M. Gilow and D. E. Burton, Bromination and chlorination of pyrrole and some reactive 1-substituted pyrroles, *J. Org. Chem.*, 1981, **46**, 2221–2225; (b) M. De Rosa, Acid catalyzed chlorination of pyrrole with *N*-chloroacetanilide, *J. Heterocycl. Chem.*, 1982, **19**, 1585.
- 15 (a) G. A. Cordell, 2-Halopyrroles. Synthesis and chemistry, *J. Org. Chem.*, 1975, **40**, 3161–3169; (b) V. Leen, E. Braeken, K. Luckermans, C. Jackers, M. van der Auweraer, N. Boens and W. Dehaen, A versatile, modular synthesis of mono-functionalized BODIPY dyes, *Chem. Commun.*, 2009, 4515–4517.
- 16 (a) F. Tutino, G. Papeo and F. Quartieri, Acid catalyzed halogen dance on deactivated pyrroles, *J. Heterocycl. Chem.*, 2010, **47**, 112–117; (b) E. Dvornikova and K. Kamińska-Trela, Synthesis of 2- and 3-Substituted *N*-Methylpyrroles, *Synlett*, 2002, 1152–1154.
- 17 (a) P. Belanger, Electrophilic substitutions on 2-trichloroacetylpyrrole, *Tetrahedron Lett.*, 1979, **20**, 2505–2508;



- (b) P. E. Sonnet, Preparation and properties of ternary iminium salts of pyrrole aldehydes and ketones. Synthesis of 4-substituted pyrrole-2-carboxaldehydes, *J. Org. Chem.*, 1972, **37**, 925–929; (c) O. Castillo-Aguilera, P. Depreux, L. Halby, N. Azaroual, P. B. Arimondo and L. Goossens, Regioselective and efficient halogenation of 4,5-unsubstituted alkyl 3-hydroxypyrrole/3-hydroxythiophene-2-yl-carboxylates, *Tetrahedron Lett.*, 2017, **58**, 2537–2541; (d) S. Gao, T. K. Bethel, T. Kakeshpour, G. E. Hubbell, J. E. Jackson and J. J. Tepe, Substrate Controlled Regioselective Bromination of Acylated Pyrroles Using Tetrabutylammonium Tribromide (TBABr₃), *J. Org. Chem.*, 2018, **83**, 9250–9255.
- 18 (a) P. Hernández-Lladó, K. Garrec, D. C. Schmitt and J. W. Burton, Transition Metal-Free, Visible Light-Mediated Radical Cyclisation of Malonyl Radicals onto 5-Ring Heteroaromatics, *Adv. Synth. Catal.*, 2022, **364**, 1724–1731; (b) R. F. Yilmaz, Y. Derin, B. A. Misir, V. E. Atalay, Ö. F. Tutar, S. Ökten and A. Tutar, Synthesis and spectral properties of symmetrically arylated BODIPY dyes: Experimental and computational approach, *J. Mol. Struct.*, 2023, **1291**, 135962; (c) W. Chen and M. P. Cava, Convenient synthetic equivalents of 2-lithiopyrrole and 2,5-dilithiopyrrole, *Tetrahedron Lett.*, 1987, **28**, 6025–6026.
- 19 W. Chen, E. K. Stephenson, M. P. Cava and Y. A. Jackson, 2-Substituted Pyrroles From *N*-tert-Butoxycarbonyl-2-bromopyrrole: *N*-tert-Butoxycarbonyl-2-trimethylsilylpyrrole, *Org. Synth.*, 1992, **70**, 151.
- 20 (a) D. W. Cho, M. Fujitsuka, J. H. Ryu, M. H. Lee, H. K. Kim, T. Majima and C. Im, S₂ emission from chemically modified BODIPYs, *Chem. Commun.*, 2012, **48**, 3424–3426; (b) J. H. Ryu, Y. K. Eom, J.-C. G. Bünzli and H. K. Kim, Ln(III)-cored complexes based on boron dipyrromethene (Bodipy) ligands for NIR emission, *New J. Chem.*, 2012, **36**, 723–731; (c) L. Knight, J. Huffman and M. Isherwood, 2-Bromo-*N*-(*p*-toluenesulfonyl)pyrrole: A Robust Derivative of 2-Bromopyrrole, *Synlett*, 2003, 1993–1996; (d) T. Koike, Y. Shinohara, T. Nishimura, M. Hagiwara, S. Tobinaga and N. Takeuchi, Condensation Reactions of a Nitrodienamine with Organocopper and Alkylolithium Reagents Prepared from Pyrrole Derivatives, *Heterocycles*, 2000, **53**, 1351–1359.
- 21 (a) T. Okumi, A. Mori and K. Okano, Regiocontrolled halogen dance of 2,5-dibromopyrroles using equilibrium between dibromopyrrolyllithiums, *Chem. Commun.*, 2023, **59**, 1046–1049; (b) L. Chumakova, A. Patron, C. Priest, D. S. Karanewsky, R. Kimmich, B. C. Boren, J. R. Hammaker, V. Chumakov, W. Zhao, A. Noncovich and J. Ung, Compounds useful as modulators of TRPM8, *World Pat*, WO2014130582, 2014; (c) C. Zonta, F. Fabris and O. de Lucchi, The Pyrrole Approach toward the Synthesis of Fully Functionalized Cup-Shaped Molecules, *Org. Lett.*, 2005, **7**, 1003–1006.
- 22 (a) B. L. Bray, P. H. Mathies, R. Naef, D. R. Solas, T. T. Tidwell, D. R. Artis and J. M. Muchowski, *N*-(Triisopropylsilyl)pyrrole. A progenitor “par excellence” of 3-substituted pyrroles, *J. Org. Chem.*, 1990, **55**, 6317–6328; (b) J. Leroy, E. Porhiel and A. Bondon, Synthesis and characterization of partially β -fluorinated 5,10,15,20-tetra-phenylporphyrins and some derivatives, *Tetrahedron*, 2002, **58**, 6713–6722; (c) K. Billingsley and S. L. Buchwald, Highly Efficient Monophosphine-Based Catalyst for the Palladium-Catalyzed Suzuki–Miyaura Reaction of Heteroaryl Halides and Heteroaryl Boronic Acids and Esters, *J. Am. Chem. Soc.*, 2007, **129**, 3358–3366; (d) F. J. Lopez-Tapia, L. E. Lowrie Jr and D. Nitzan, Arylsulfonyl pyrrolidines as 5-HT₆ inhibitors, *World Pat*, WO2008055847, 2008.
- 23 For selected examples, see: (a) Y. Okui, Y. Yasuda, A. Mori and K. Okano, Total Synthesis of Lamellarins U and A3 by Interrupting Halogen Dance, *Synthesis*, 2022, 2647–2660; (b) K. Cui, M. Gao, H. Zhao, D. Zhang, H. Yan and H. Huang, An Efficient Synthesis of Aryl-Substituted Pyrroles by the Suzuki–Miyaura Coupling Reaction of SEM-Protected Pyrroles, *Molecules*, 2019, **24**, 1594; (c) M. A. Schafroth, S. M. Rummelt, D. Sarlah and E. M. Carreira, Enantioselective Iridium-Catalyzed Allylic Cyclizations, *Org. Lett.*, 2017, **19**, 3235–3238; (d) S. J. Mishra, S. Ghosh, A. R. Stothert, C. A. Dickey and B. S. J. Blagg, Transformation of the Non-Selective Aminocyclohexanol-Based Hsp90 Inhibitor into a Grp94-Selective Scaffold, *ACS Chem. Biol.*, 2017, **12**, 244–253; (e) R. B. Alnoman, S. Rihn, D. C. O'Connor, F. A. Black, B. Costello, P. G. Waddell, W. Clegg, R. D. Peacock, W. Herrebout, J. G. Knight and M. J. Hall, Circularly Polarized Luminescence from Helically Chiral *N,N,O,O*-Boron-Chelated Dipyrromethenes, *Chem. – Eur. J.*, 2016, **22**, 93–96; (f) J. Thireau, J. Marteaux, P. Delagrangé, F. Lefoulon, L. Dufourny, G. Guillaumet and F. Suzenet, Original Design of Fluorescent Ligands by Fusing BODIPY and Melatonin Neurohormone, *ACS Med. Chem. Lett.*, 2014, **5**, 158–161; (g) R. Y. Huang, P. T. Franke, N. Nicolaus and M. Lautens, Domino C–H functionalization reactions of *gem*-dibromoolefins: synthesis of *N*-fused benzo[*c*]carbazoles, *Tetrahedron*, 2013, **69**, 4395–4402; (h) P. Kancharla and K. A. Reynolds, Synthesis of 2,2'-bipyrrole-5-carboxaldehydes and their application in the synthesis of B-ring functionalized prodiginines and tambjamines, *Tetrahedron*, 2013, **69**, 8375–8385; (i) N. Sakamoto, C. Ikeda, M. Yamamura and T. Nabeshima, α -Bridged BODIPY oligomers with switchable near-IR photoproperties by external-stimuli-induced foldamer formation and disruption, *Chem. Commun.*, 2012, **48**, 4818–4820; (j) H. K. Tanui, E. Hao, M. I. Ihachi, F. R. Fronczek, K. M. Smith and M. G. H. Vicente, Efficient synthesis and reactions of 1,2-dipyrrolylethynes, *J. Porphyrins Phthalocyanines*, 2011, **15**, 412–420; (k) G. Barker, J. L. McGrath, A. Klapars, D. Stead, G. Zhou, K. R. Campos and P. O'Brien, Enantioselective, Palladium-Catalyzed α -Arylation of *N*-Boc Pyrrolidine: In Situ React IR Spectroscopic Monitoring, Scope, and Synthetic Applications, *J. Org. Chem.*, 2011, **76**, 5936–5953; (l) Y. Matano, M. Fujita, A. Saito and H. Imahori, Synthesis, structures, optical and electrochemical properties, and



- complexation of 2,5-bis(pyrrol-2-yl)phospholes, *C. R. Chim.*, 2010, **13**, 1035–1047; (m) A. A. Kanakis and V. Sarli, Total Synthesis of (±)-Marinopyrrole A via Copper-Mediated *N*-Arylation, *Org. Lett.*, 2010, **12**, 4872–4875; (n) A. Gagnon, M. Duplessis, P. Alsabeh and F. Barabé, Palladium-Catalyzed Cross-Coupling Reaction of Tricyclopropylbismuth with Aryl Halides and Triflates, *J. Org. Chem.*, 2008, **73**, 3604–3607; (o) A. Dinsmore, D. G. Billing, K. Mandy, J. P. Michael, D. Mogano and S. Patil, Magnesium Employing Grignard Reagents and Catalytic Amine. Application to the Functionalization of *N*-Phenylsulfonylpyrrole, *Org. Lett.*, 2004, **6**, 293–296; (p) S. T. Handy, H. Bregman, J. Lewis, X. Zhang and Y. Zhang, An unusual dehalogenation in the Suzuki coupling of 4-bromopyrrole-2-carboxylates, *Tetrahedron Lett.*, 2003, **44**, 427–430; (q) H. Miyaji, W. Sato, J. L. Sessler and V. M. Lynch, A 'building block' approach to functionalized calix[4]pyrroles, *Tetrahedron Lett.*, 2000, **41**, 1369–1373; (r) L. H. Thoresen, H. Kim, M. B. Welch, A. Burghart and K. Burgess, Synthesis of 3,5-Diaryl-4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY®) Dyes, *Synlett*, 1998, 1276–1278; (s) P. A. Jacobi and S. Rajeswari, Tetrapyrroles. IV. A highly efficient synthesis of homochiral dihydropyrromethenones via Pd⁰ mediated coupling of iodopyrroles and acetylenic amides, *Tetrahedron Lett.*, 1992, **33**, 6235–6238; (t) S. Martina and A. D. Schlüter, Soluble polyarylenes with alternating sequences of alkyl-substituted phenylene and pyrrolic or terpyrrolic units, *Macromolecules*, 1992, **25**, 3607–3608.
- 24 For selected examples, see: (a) S. Doniz Kettenmann, M. White, J. Colard-Thomas, M. Kraft, A. T. Feßler, K. Danz, G. Wieland, S. Wagner, S. Schwarz, A. Wiehe and N. Kulak, Investigating Alkylated Prodigiosenes and Their Cu(II)-Dependent Biological Activity: Interactions with DNA, Antimicrobial and Photoinduced Anticancer Activity, *ChemMedChem*, 2022, **17**, e202100702; (b) E. Marchal, D. A. Smithen, M. I. Uddin, A. W. Robertson, D. L. Jakeman, V. Mollard, C. D. Goodman, K. S. MacDougall, S. A. McFarland, G. I. McFadden and A. Thompson, Synthesis and antimalarial activity of prodigiosenes, *Org. Biomol. Chem.*, 2014, **12**, 4132–4142; (c) I. Kholod, O. Vallat, A.-M. Buciumas, A. Neels and R. Neier, *Eur. J. Org. Chem.*, 2014, 7865–7877; (d) C. Minard, C. Palacio, K. Cariou and R. H. Dodd, Selective Suzuki–Miyaura Monocouplings with Symmetrical Dibromoarenes and Aryl Ditriflates for the One-Pot Synthesis of Unsymmetrical Triaryls, *Eur. J. Org. Chem.*, 2014, 2942–2955; (e) H. Kamiyama, Y. Kubo, H. Sato, N. Yamamoto, T. Fukuda, F. Ishibashi and M. Iwao, Synthesis, structure–activity relationships, and mechanism of action of anti-HIV-1 lamellarin α 20-sulfate analogues, *Bioorg. Med. Chem.*, 2011, **19**, 7541–7550; (f) K. Yoshida, K. Hayashi and A. Yanagisawa, Construction of Carbocyclic Ring of Indoles Using Ruthenium-Catalyzed Ring-Closing Olefin Metathesis, *Org. Lett.*, 2011, **13**, 4762–4765; (g) S. Hirao, Y. Yoshinaga, M. Iwao and F. Ishibashi, A formal total synthesis of the telomerase inhibitor dictyodendrin B, A General Method for the Synthesis of *N*-Unsubstituted 3,4-Diarylpyrrole-2,5-dicarboxylates, *Tetrahedron Lett.*, 2010, **51**, 533–536; (h) T. Fukuda, Y. Hayashida and M. Iwao, A General Method for the Synthesis of *N*-Unsubstituted 3,4-Diarylpyrrole-2,5-dicarboxylates, *Heterocycles*, 2009, **77**, 1105–1122; (i) J. T. Reeves, A Concise Synthesis of Butylcycloheptylprodigiosin, *Org. Lett.*, 2007, **9**, 1879–1881; (j) J. T. Tomlinson, G. Park, J. A. Misenheimer, G. L. Kucera, K. Hesp and R. A. Manderville, Photoinduced Cytotoxicity and Thioadduct Formation by a Prodigiosin Analogue, *Org. Lett.*, 2006, **8**, 4951–4954; (k) A. Fürstner, K. Radkowski and H. Peters, Chasing a Phantom by Total Synthesis: The Butylcycloheptylprodigiosin Case, *Angew. Chem., Int. Ed.*, 2005, **44**, 2777–2781; (l) A. Fürstner, J. Grabowski and C. W. Lehmann, Total Synthesis and Structural Refinement of the Cyclic Tripyrrole Pigment Nonylprodigiosin, *J. Org. Chem.*, 1999, **64**, 8275–8280; (m) R. D'Alessio and A. Rossi, Short synthesis of undecylprodigiosine. A new route to 2,2'-bipyrrolyl-pyrromethene systems, *Synlett*, 1996, 513–514.
- 25 For selected examples, see: (a) L. Filippini, M. Gusmeroli and R. Riva, Palladium-catalyzed cross-coupling of pyrrolyl anions with organic halides, *Tetrahedron Lett.*, 1992, **33**, 1755–1758; (b) R. D. Rieth, N. P. Mankad, E. Calimano and J. P. Sadighi, Palladium-Catalyzed Cross-Coupling of Pyrrole Anions with Aryl Chlorides, Bromides, and Iodides, *Org. Lett.*, 2004, **6**, 3981–3983; (c) X. Wang, B. S. Lane and D. Sames, Direct C-Arylation of Free (NH)-Indoles and Pyrroles Catalyzed by Ar–Rh(III) Complexes Assembled In Situ, *J. Am. Chem. Soc.*, 2005, **127**, 4996–4997; (d) N. R. Deprez, D. Kalyani, A. Krause and M. S. Sanford, Room Temperature Palladium-Catalyzed 2-Arylation of Indoles, *J. Am. Chem. Soc.*, 2006, **128**, 4972–4973; (e) P. Forgione, M.-C. Brochu, M. St-Onge, K. H. Thesen, M. D. Bailey and F. Bilodeau, Unexpected Intermolecular Pd-Catalyzed Cross-Coupling Reaction Employing Heteroaromatic Carboxylic Acids as Coupling Partners, *J. Am. Chem. Soc.*, 2006, **128**, 11350–11351; (f) B. Liégault, D. Lapointe, L. Caron, A. Vlassova and K. Fagnou, Establishment of Broadly Applicable Reaction Conditions for the Palladium-Catalyzed Direct Arylation of Heteroatom-Containing Aromatic Compounds, *J. Org. Chem.*, 2009, **74**, 1826–1834; (g) D. T. Gryko, O. Vakuliuk, D. Gryko and B. Koszarna, Palladium-Catalyzed 2-Arylation of Pyrroles, *J. Org. Chem.*, 2009, **74**, 9517–9520; (h) F. Jafarpour, S. Rahiminejadan and H. Hazrati, Triethanolamine-Mediated Palladium-Catalyzed Regioselective C-2 Direct Arylation of Free NH-Pyrroles, *J. Org. Chem.*, 2010, **75**, 3109–3112; (i) A. García-Rubia, B. Urones, R. Gómez Arrayás and J. C. Carretero, PdII-Catalysed C–H Functionalisation of Indoles and Pyrroles Assisted by the Removable *N*-(2-Pyridyl)sulfonyl Group: C2-Alkenylation and Dehydrogenative Homocoupling, *Chem. – Eur. J.*, 2010, **16**, 9676–9685; (j) E. T. Nadres, A. Lazareva and O. Daugulis, Palladium-



- Catalyzed Indole, Pyrrole, and Furan Arylation by Aryl Chlorides, *J. Org. Chem.*, 2011, **76**, 471–483; (k) N. Thies, C. G. Hrib and E. Haak, Ruthenium-Catalyzed Functionalization of Pyrroles and Indoles with Propargyl Alcohols, *Chem. – Eur. J.*, 2012, **18**, 6302–6308; (l) Y. Xu, L. Zhao, Y. Li and H. Doucet, Palladium-Catalysed Regioselective Sequential C-5 and C-2 Direct Arylations of 3-Acetylpyrroles with Aryl Bromides, *Adv. Synth. Catal.*, 2013, **355**, 1423–1432; (m) R. Jin, K. Yuan, E. Chatelain, J.-F. Soulé and H. Doucet, Palladium-Catalysed Direct Desulfurative Arylation of Pyrroles using Benzenesulfonyl Chlorides as Alternative Coupling Partners, *Adv. Synth. Catal.*, 2014, **356**, 3831–3841; (n) W. Chen, H.-J. Li, Y.-F. Cheng and Y.-C. Wu, Direct C2-arylation of *N*-acyl pyrroles with aryl halides under palladium catalysis, *Org. Biomol. Chem.*, 2021, **19**, 1555–1564; (o) M. Petkovic, M. Jovanovic, P. Jovanovic, M. Simic, G. Tasic and V. Savic, Dual Role of the Arylating Agent in a Highly C(II)-Selective Pd-Catalysed Functionalisation of Pyrrole Derivatives, *Synthesis*, 2022, 2839–2848; (p) W. Chen and M. Liu, A Highly Active Palladium System Catalyzed C2-Arylation of *N*-Acyl Pyrroles with Aryl Halides and Their Biological Activity, *Asian J. Org. Chem.*, 2023, **12**, e202200648; (q) N. Munir, N. Gürbüz, M. N. Zafar, E. Evren, B. Şen, M. Aygün and İ. Özdemir, Plausible PEPPSI catalysts for direct C–H functionalization of furans and pyrroles, *J. Mol. Struct.*, 2024, **1295**, 136679; (r) K. Jiang, X. Li, L. Wang and J. Han, Basicity-Controlled Reactivity of meta-OTf-Substituted Diaryliodonium Salts for Direct Arylation or Diels-Alder Cycloaddition of Pyrrole Derivatives, *Asian J. Org. Chem.*, 2024, **13**, e202400139; (s) J. Märsh, S. Reiter, T. Rittner, R. E. Rodriguez-Lugo, M. Whitfield, D. J. Scott, R. J. Kutta, P. Nuernberger, R. de Vivie-Riedle and R. Wolf, Cobalt-Mediated Photochemical C–H Arylation of Pyrroles, *Angew. Chem., Int. Ed.*, 2024, **63**, e202405780.
- 26 (a) C. Savarin, J. Srogl and L. S. Liebeskind, Thiol Ester–Boronic Acid Cross-Coupling. Catalysis Using Alkylative Activation of the Palladium Thiolate Intermediate, *Org. Lett.*, 2000, **2**, 3229–3231; (b) S. Zhang, D. Marshall and L. S. Liebeskind, Efficient Pd-Catalyzed Heterobenzylic Cross-Coupling Using Sulfonium Salts as Substrates and (PhO)₃P as a Supporting Ligand, *J. Org. Chem.*, 1999, **64**, 2796–2804; (c) J. Srogl, G. D. Allred and L. S. Liebeskind, Sulfonium Salts. Participants *par Excellence* in Metal-Catalyzed Carbon–Carbon Bond-Forming Reactions, *J. Am. Chem. Soc.*, 1997, **119**, 12376–12377.
- 27 For selected examples, see: (a) J.-W. Song, F. Xia, X.-L. Zhang and C.-P. Zhang, Pd-catalyzed relay Heck arylation of alkenyl alcohols with arylsulfonium salts, *Org. Chem. Front.*, 2024, **11**, 4219–4230; (b) S. Ni, J. Yan, S. Tewari, E. J. Reijerse, T. Ritter and J. Cornella, Nickel Meets Aryl Thianthrenium Salts: Ni(I)-Catalyzed Halogenation of Arenes, *J. Am. Chem. Soc.*, 2023, **145**, 9988–9993; (c) M. Gao and C. Gosmini, Co-Catalyzed Reductive Cross-Couplings of Csp³–S with C_{allyl}–O Electrophiles to form Csp³–Csp³ Bonds, *Adv. Synth. Catal.*, 2023, **365**, 3597–3602; (d) Y. Ye, J. Zhu, H. Xie and Y. Huang, Rhodium-Catalyzed Divergent Arylation of Alkenylsulfonium Salts with Arylboroxines, *Angew. Chem., Int. Ed.*, 2022, **61**, e202212522; (e) W. Wang, K. Yao and F. Wu, Nickel-Catalyzed Reductive Cross-Coupling of Benzylic Sulfonium Salts with Aryl Iodides, *Synlett*, 2022, 361–366; (f) N.-N. Ma, J.-A. Ren, X. Liu, X.-Q. Chu, W. Rao and Z.-L. Shen, Nickel-Catalyzed Direct Cross-Coupling of Aryl Sulfonium Salt with Aryl Bromide, *Org. Lett.*, 2022, **24**, 1953–1957; (g) C. Chen, M. Wang, H. Lu, B. Zhao and Z. Shi, Enabling the Use of Alkyl Thianthrenium Salts in Cross-Coupling Reactions by Copper Catalysis, *Angew. Chem., Int. Ed.*, 2021, **60**, 21756–21760; (h) A. Selmani, A. G. Gevondian and F. Schoenebeck, Transition-Metal-Free, Formal C–H Germylation of Arenes and Styrenes via Dibenzothiophenium Salts, *Org. Lett.*, 2021, **23**, 4779–4784; (i) Y. Ye, J. Zhu and Y. Huang, Diverse C–P Cross-Couplings of Arylsulfonium Salts with Diarylphosphines via Selective C–S Bond Cleavage, *Org. Lett.*, 2021, **23**, 2386–2391; (j) Y. Wu, Y.-H. Huang, X.-Y. Chen and P. Wang, Site-Selective Silylation of Arenes Mediated by Thianthrene S-Oxide, *Org. Lett.*, 2020, **22**, 6657–6661; (k) A. Selmani, A. G. Gevondian and F. Schoenebeck, Germylation of Arenes via Pd(I) Dimer Enabled Sulfonium Salt Functionalization, *Org. Lett.*, 2020, **22**, 4802–4805; (l) J. Wu, Z. Wang, X.-Y. Chen, Y. Wu, D. Wang, Q. Peng and P. Wang, *Para*-selective borylation of monosubstituted benzenes using a transient mediator, *Sci. China: Chem.*, 2020, **63**, 336–340; (m) K. Kafuta, A. Korzun, M. Böhm, C. Golz and M. Alcarazo, Synthesis, Structure, and Reactivity of 5-(Aryl)dibenzothiophenium Triflates, *Angew. Chem., Int. Ed.*, 2020, **59**, 1950–1955; (n) T. Yanagi, R. J. Somerville, K. Nogi, R. Martin and H. Yorimitsu, Ni-Catalyzed Carboxylation of C(sp²)–S Bonds with CO₂: Evidence for the Multifaceted Role of Zn, *ACS Catal.*, 2020, **10**, 2117–2123; (o) Z.-Y. Tian and C.-P. Zhang, Ullmann-type *N*-arylation of anilines with alkyl(aryl)sulfonium salts, *Chem. Commun.*, 2019, **55**, 11936–11939; (p) H. Minami, K. Nogi and H. Yorimitsu, Palladium-Catalyzed Alkoxyacylation of Arylsulfoniums, *Org. Lett.*, 2019, **21**, 2518–2522; (q) H. Minami, K. Nogi and H. Yorimitsu, Palladium-Catalyzed Homo-Coupling of Heteroarylsulfoniums via Borylation/Suzuki-Miyaura Coupling Sequence, *Heterocycles*, 2018, **97**, 998–1007; (r) M. H. Aukland, F. J. T. Talbot, J. A. Fernandez-Salas, M. Ball, A. P. Pulis and D. J. Procter, An Interrupted Pummerer/Nickel-Catalysed Cross-Coupling Sequence, *Angew. Chem., Int. Ed.*, 2018, **57**, 9785–9789; (s) Z.-Y. Tian, S.-M. Wang, S.-J. Jia, H.-X. Song and C.-P. Zhang, Sonogashira Reaction Using Arylsulfonium Salts as Cross-Coupling Partners, *Org. Lett.*, 2017, **19**, 5454–5457; (t) H. Kawashima, T. Yanagi, C.-C. Wu, K. Nogi and H. Yorimitsu, Regioselective C–H Sulfanylation of Aryl Sulfoxides by Means of Pummerer-Type Activation, *Org. Lett.*, 2017, **19**, 4552–4555; (u) S.-M. Wang, H.-X. Song,



- X.-Y. Wang, N. Liu, H.-L. Qin and C.-P. Zhang, Palladium-catalyzed Mizoroki–Heck-type reactions of $[\text{Ph}_2\text{SR}_{\text{fn}}][\text{OTf}]$ with alkenes at room temperature, *Chem. Commun.*, 2016, **52**, 11893–11896; (v) D. Vasu, H. Yorimitsu and A. Osuka, Base-Free Palladium-Catalyzed Cross-Coupling of Arylsulfonium Salts with Sodium Tetraarylborates, *Synthesis*, 2015, 3286–3291; (w) D. Vasu, H. Yorimitsu and A. Osuka, Palladium-Assisted “Aromatic Metamorphosis” of Dibenzothiophenes into Triphenylenes, *Angew. Chem., Int. Ed.*, 2015, **54**, 7162–7166; (x) M.-L. Xu and W. Huang, Metal-free carbon–carbon cross-couplings between the ion pairs in sulfonium tetraphenylborates, *Tetrahedron Lett.*, 2014, **55**, 4230–4232; (y) H. Lin, X. Dong, Y. Li, Q. Shen and L. Lu, Highly Selective Activation of Vinyl C–S Bonds Over Aryl C–S Bonds in the Pd-Catalyzed Coupling of (*E*)-(β -Trifluoromethyl)vinylidiphenylsulfonium Salts: Preparation of Trifluoromethylated Alkenes and Dienes, *Eur. J. Org. Chem.*, 2012, 4675–4679; (z) C. Vanier, F. Lorge, A. Wagner and C. Mioskowski, Traceless, Solid-Phase Synthesis of Biaryl methane Structures through Pd-Catalyzed Release of Supported Benzylsulfonium Salts, *Angew. Chem., Int. Ed.*, 2000, **39**, 1679–1683.
- 28 F. Berger, M. B. Plutschack, J. Riegger, W. Yu, S. Speicher, M. Ho, N. Frank and T. Ritter, Site-selective and versatile aromatic C–H functionalization by thianthrenation, *Nature*, 2019, **567**, 223–228.
- 29 For reviews, see: (a) S. Timmann, Z. Feng and M. Alcarazo, Recent Applications of Sulfonium Salts in Synthesis and Catalysis, *Chem. – Eur. J.*, 2024, **30**, e202402768; (b) X. Wu, P. Gao and F. Chen, Synthetic Applications of Sulfonium Salts as Aryl Radical Precursors, *Eur. J. Org. Chem.*, 2023, e202300864; (c) L. van Dalsen, R. E. Brown, J. A. Rossi-Ashton and D. J. Procter, Sulfonium Salts as Acceptors in Electron Donor-Acceptor Complexes, *Angew. Chem., Int. Ed.*, 2023, **62**, e202303104; (d) Z.-Y. Tian, Y. Ma and C.-P. Zhang, Alkylation Reactions with Alkylsulfonium Salts, *Synthesis*, 2022, 1478–1502; (e) G. J. P. Perry and H. Yorimitsu, Sulfur (IV) in Transition-Metal-Free Cross-Couplings for Biaryl Synthesis, *ACS Sustainable Chem. Eng.*, 2022, **10**, 2569–2586; (f) Q.-Z. Li, W.-L. Zou, Z.-Q. Jia and J.-L. Li, Recent Advances on Annulation Reactions with Allyl and Propargyl Sulfonium Salts, *Synthesis*, 2022, 67–78; (g) H. Xu, J. Zhang, J. Zuo, F. Wang, J. Lü, X. Hun and D. Yang, Recent Advances in Visible-Light-Catalyzed C–C Bonds and C–Heteroatom Bonds Formation Using Sulfonium Salts, *Chin. J. Org. Chem.*, 2022, **42**, 4037–4059; (h) R. Melngaile and J. Veliks, Synthetic Applications of Monofluoromethylsulfonium Salts, *Synthesis*, 2021, 4549–4558; (i) R. Fan, C. Tan, Y. Liu, Y. Wei, X. Zhao, X. Liu, J. Tan and H. Yoshida, A leap forward in sulfonium salt and sulfur ylide chemistry, *Chin. Chem. Lett.*, 2021, **32**, 299–312; (j) H. Yorimitsu, Catalytic Transformations of Sulfonium Salts via C–S Bond Activation, *Chem. Rec.*, 2021, **21**, 3356–3369; (k) S. I. Kozhushkov and M. Alcarazo, Synthetic Applications of Sulfonium Salts, *Eur. J. Inorg. Chem.*, 2020, 2486–2500; (l) Á. Péter, G. J. P. Perry and D. J. Procter, Radical C–C Bond Formation using Sulfonium Salts and Light, *Adv. Synth. Catal.*, 2020, **362**, 2135–2142; (m) D. Kaiser, I. Klose, R. Oost, J. Neuhaus and N. Maulide, Bond-Forming and -Breaking Reactions at Sulfur(IV): Sulfoxides, Sulfonium Salts, Sulfur Ylides, and Sulfinate Salts, *Chem. Rev.*, 2019, **119**, 8701–8780; (n) Z.-Y. Tian, Y.-T. Hu, H.-B. Teng and C.-P. Zhang, Application of arylsulfonium salts as arylation reagents, *Tetrahedron Lett.*, 2018, **59**, 299–309.
- 30 (a) P. Cowper, Y. Jin, M. D. Turton, G. Kociok-Köhn and S. E. Lewis, Azulenesulfonium Salts: Accessible, Stable, and Versatile Reagents for Cross-Coupling, *Angew. Chem., Int. Ed.*, 2016, **55**, 2564–2568; (b) C. M. López-Alled, F. J. O. Martin, K.-Y. Chen, G. Kociok-Köhn, T. D. James, J. Wenk and S. E. Lewis, Azulenesulfonium and azulenebis (sulfonium) salts: Formation by interrupted Pummerer reaction and subsequent derivatisation by nucleophiles, *Tetrahedron*, 2020, **76**, 131700.
- 31 (a) F. Franco, R. Greenhouse and J. M. Muchowski, Novel syntheses of 5-aryl-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]pyrrole-1-carboxylic acids, *J. Org. Chem.*, 1982, **47**, 1682–1688; (b) K. Hartke and D. Strangemann, Sulfonioidolides and Sulfoniopyrrolides, *Heterocycles*, 1986, **24**, 2399–2402; (c) K. Hartke, D. Teuber and H.-D. Gerber, Indole- and pyrrole-sulfonium ylides, *Tetrahedron*, 1988, **44**, 3261–3270; (d) H. H. Wendebourg and K. Hartke, 3-Pyrrolylsulfonium Salts and 3-Pyrrolylsulfonium Ylides, *Synthesis*, 1989, 329–331; (e) D. K. Bates, R. T. Winters and J. A. Picard, Intramolecular capture of Pummerer rearrangement intermediates. 3. Interrupted Pummerer rearrangement: capture of tricoordinate sulfur species generated under Pummerer rearrangement conditions, *J. Org. Chem.*, 1992, **57**, 3094–3097; (f) F. Bellesia, F. Ghelfi, R. Grandi, U. M. Pagnoni and A. Pinetti, The reaction of pyrroles with trimethylhalosilanes-dialkyl sulfoxides, *J. Heterocycl. Chem.*, 1993, **30**, 617–621; (g) D. K. Bates and K. A. Tafel, Sulfenylation Using Sulfoxides. Intramolecular Cyclization of 2- and 3-Acylpyrroles, *J. Org. Chem.*, 1994, **59**, 8076–8080; (h) J. A. Picard, S. Chen and D. K. Bates, Intramolecular Sulfenylation Using Sulfoxides. Preparation of 5*H*-Pyrrolo [1,2-*a*][3,1]benzothiazines, *Heterocycles*, 1994, **38**, 1775–1789; (i) N. E. Shevchenko, A. S. Karpov, E. P. Zakurdaev, V. G. Nenajdenko and E. S. Balenkova, Synthesis of methylthiosubstituted heterocycles using the complex of trifluoromethanesulfonic anhydride with dimethyl sulfide, *Chem. Heterocycl. Compd.*, 2000, **36**, 137–143; (j) N. E. Shevchenko, V. G. Nenajdenko and E. S. Balenkova, Triflic Anhydride-Promoted Cyclization of Sulfides: A Convenient Synthesis of Fused Sulfur Heterocycles, *Synthesis*, 2003, 1191–1200; (k) A. Thompson, R. J. Butler, M. N. Grundy, A. B. E. Laltoo, K. N. Robertson and T. S. Cameron, Sulfur-Based Protecting Groups for Pyrroles and the Facile Deprotection of 2-(2,4-Dinitrobenzene)sulfinyl and Sulfonyl Pyrroles, *J. Org. Chem.*, 2005, **70**, 3753–3756; (l) L. M. Yagupolskii, A. V. Matsnev, R. K. Orlova, B. G. Deryabkin and



- Y. L. Yagupolskii, A new method for the synthesis of trifluoromethylating agents—Diaryltrifluoromethylsulfonium salts, *J. Fluorine Chem.*, 2008, **129**, 131–136; (m) J. Kobayashi, S.-Y. Nakafuji, A. Yatabe and T. Kawashima, A novel ylide-stabilized carbene; formation and electron donating ability of an amino(sulfur-ylide)carbene, *Chem. Commun.*, 2008, 6233–6235; (n) A. J. Eberhart, C. Cicoira and D. J. Procter, Nucleophilic *ortho*-Allylation of Pyrroles and Pyrazoles: An Accelerated Pummerer/Thio-Claisen Rearrangement Sequence, *Org. Lett.*, 2013, **15**, 3994–3997; (o) H. Steinert, C. Schwarz, A. Kroll and V. H. Gessner, Towards the Preparation of Stable Cyclic Amino(ylide)Carbenes, *Molecules*, 2020, **25**, 796; (p) D. Wang, C. G. Carlton, M. Tayu, J. J. W. McDouall, G. J. P. Perry and D. J. Procter, Trifluoromethyl Sulfoxides: Reagents for Metal-Free C–H Trifluoromethylthiolation, *Angew. Chem., Int. Ed.*, 2020, **59**, 15918–15922; (q) E. M. Alvarez, T. Karl, F. Berger, L. Torkowski and T. Ritter, Late-Stage Heteroarylation of Hetero(aryl)sulfonium Salts Activated by α -Amino Alkyl Radicals, *Angew. Chem., Int. Ed.*, 2021, **60**, 13609–13613; (r) W. Zhang, T. Liu, H. T. Ang, P. Luo, Z. Lei, X. Luo, M. J. Koh and J. Wu, Modular and Practical 1,2-Aryl (Alkenyl) Heteroatom Functionalization of Alkenes through Iron/Photoredox Dual Catalysis, *Angew. Chem., Int. Ed.*, 2023, **62**, e202310978; (s) Y. Guo, L. Wei, H. Jiang and C. Qi, Palladium-Catalyzed Carbonylation of Aryl Sulfonium Salts with CO₂ as a CO Surrogate, *Asian J. Org. Chem.*, 2024, **13**, e202400142.
- 32 For reviews, see: (a) Y. Liang and B. Peng, Revisiting Aromatic Claisen Rearrangement Using Unstable Aryl Sulfonium/Iodonium Species: The Strategy of Breaking Up the Whole into Parts, *Acc. Chem. Res.*, 2022, **55**, 2103–2122; (b) K. Higuchi and M. Tayu, The Interrupted Pummerer Reaction: Design of Sulfoxides and Their Utility in Organic Synthesis, *Heterocycles*, 2021, **102**, 783–824; (c) X. Zhao, J. Zeng, L. Meng and Q. Wan, Application of Interrupted Pummerer Reaction Mediated (IPRm) Glycosylation in Natural Product Synthesis, *Chem. Rec.*, 2020, **20**, 743–751; (d) Z. He, A. P. Pulis, G. J. P. Perry and D. J. Procter, Pummerer chemistry of benzothiophene *S*-oxides: Metal-free alkylation and arylation of benzothiophenes, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2019, **194**, 669–677; (e) T. Yanagi, K. Nogi and H. Yorimitsu, Recent development of *ortho*-C–H functionalization of aryl sulfoxides through [3,3] sigmatropic rearrangement, *Tetrahedron Lett.*, 2018, **59**, 2951–2959; (f) H. Yorimitsu, Cascades of Interrupted Pummerer Reaction-Sigmatropic Rearrangement, *Chem. Rec.*, 2017, **17**, 1156–1167; (g) L. H. S. Smith, S. C. Coote, H. F. Sneddon and D. J. Procter, Beyond the Pummerer Reaction: Recent Developments in Thionium Ion Chemistry, *Angew. Chem., Int. Ed.*, 2010, **49**, 5832–5844.
- 33 J. L. Hann, C. L. Lyall, G. Kociok-Köhn, C. Faverio, G. D. Pantoş and S. E. Lewis, Unusual Regio- and Chemoselectivity in Oxidation of Pyrroles and Indoles Enabled by a Thianthrenium Salt Intermediate, *Angew. Chem., Int. Ed.*, 2024, **63**, e202405057.
- 34 (a) O. Carmona, R. Greenhouse, R. Landeros and J. M. Muchowski, Synthesis and rearrangement of 2-(aryl-sulfinyl)- and 2-(alkylsulfinyl)pyrroles, *J. Org. Chem.*, 1980, **45**, 5336–5339; (b) J. R. Carson and N. M. Davis, Acid-mediated rearrangement of acylpyrroles, *J. Org. Chem.*, 1981, **46**, 839–843; (c) J. DeSales, R. Greenhouse and J. M. Muchowski, Synthesis and rearrangement of pyrrolyl sulfides and sulfones, *J. Org. Chem.*, 1982, **47**, 3668–3672; (d) M. Kakushima, P. Hamel, R. Frenette and J. Rokach, Regioselective synthesis of acylpyrroles, *J. Org. Chem.*, 1983, **48**, 3214–3219; (e) M. C. Pina, V. A. Budilin, M. Rodrigues and Y. G. Bundel, Synthesis and prototropic isomerization of 1-nitrophenyl-2-acylpyrroles, *Chem. Heterocycl. Compd.*, 1989, **25**, 268–271; (f) J.-H. Mirebeau, M. Haddad, M. Henry-Ellinger, G. Jaouen, J. Louvel and F. Le Bideau, Rearrangement of 2,5-Bis(silylated)-*N*-Boc Pyrroles into the Corresponding 2,4-Species, *J. Org. Chem.*, 2009, **74**, 8890–8892.
- 35 B. Altundas, S. Kumar and F. F. Fleming, Acetonitrile–Hexane Extraction Route to Pure Sulfonium Salts, *ACS Omega*, 2020, **5**, 13384–13388.
- 36 For reviews, see: (a) F. Berger and T. Ritter, Site-Selective Late-Stage C–H Functionalization via Thianthrenium Salts, *Synlett*, 2022, 339–345; (b) X.-Y. Chen, Y. Wu and P. Wang, Recent Advances in Thianthrenation/Phenoxathiination Enabled Site-Selective Functionalization of Arenes, *Synthesis*, 2022, 3928–3940; (c) H. Meng, M.-S. Liu and W. Shu, Organothianthrenium salts: synthesis and utilization, *Chem. Sci.*, 2022, **13**, 13690–13707; (d) M. Kim, K. Targos, D. E. Holst, D. J. Wang and Z. K. Wickens, Alkene Thianthrenation Unlocks Diverse Cation Synthons: Recent Progress and New Opportunities, *Angew. Chem., Int. Ed.*, 2024, **63**, e202314904.
- 37 For selected examples, see: (a) L. Zhang, Y. Xie, Z. Bai and T. Ritter, Suzuki–Miyaura coupling of arylthianthrenium tetrafluoroborate salts under acidic conditions, *Nat. Synth.*, 2024, DOI: [10.1038/s44160-024-00631-4](https://doi.org/10.1038/s44160-024-00631-4); (b) F. Jin, Q. Hu, Q. Wang, J. Sun, K. Huang, C.-G. Yan, Y. Han, H. Fei and L. Wang, Synthesis of Sulfoxides by Palladium-Catalyzed Arylation of Sulfenate Anions with Aryl Thianthrenium Salts, *J. Org. Chem.*, 2024, **89**, 13319–13328; (c) R. Kumar, A. Sharma and A. Sharma, Mechanochemically Induced Thianthrenium Salts-Based Arylation of Diverse Heterocyclic Scaffolds, *ACS Sustainable Chem. Eng.*, 2024, **12**, 12808–12818; (d) M. Jiao, J. Zhang, M. Wang, H. Lu and Z. Shi, Metallaphotoredox deuteroalkylation utilizing thianthrenium salts, *Nat. Commun.*, 2024, **15**, 5067; (e) G. Bao, X. Song, Y. Li, Z. He, Q. Zuo, R. E. T. Yu, K. Li, J. Xie, W. Sun and R. Wang, Orthogonal bioconjugation targeting cysteine-containing peptides and proteins using alkyl thianthrenium salts, *Nat. Commun.*, 2024, **15**, 6909; (f) P. Hartmann, K. Bohdan, M. Hommrich, F. Juliá, L. Vogelsang, J. Eirich, R. Zangl, C. Farès, J. B. Jacobs, D. Mukhopadhyay, J. M. Mengeler, A. Vetere, M. S. Sterling,



H. Hinrichs, S. Becker, N. Morgner, W. Schrader, I. Finkemeier, K.-J. Dietz, C. Griesinger and T. Ritter, Chemoselective umpolung of thiols to episulfoniums for cysteine bioconjugation, *Nat. Chem.*, 2024, **16**, 380–388; (g) S. R. Nasireddy, G. C. Upreti and A. Singh, Photochemical Trifluoromethylative Difunctionalization of Styrenes and Phenylacetylenes via a Catalytic EDA Platform, *Eur. J. Org. Chem.*, 2024, e202400114; (h) Y. Fang, Q. Liang, L. Shi, J. Wen, X. Liu, X. Hong, X. Zha and F. Ji, Site-Selective S-Arylation of 1-Thiosugars with Aryl Thianthrenium Salts through Copper(I)-Mediated, Photoredox-Catalyzed Reactions, *Adv. Synth. Catal.*, 2024, **366**, 2344–2351; (i) B. Mondal, A. Chatterjee, N. C. Saha, M. Jana and J. Saha, Thianthrenation-promoted photo-induced alkene difunctionalization and aryl allylation with Morita–Baylis–Hillman adducts, *Chem. Commun.*, 2024, **60**, 7184–7187; (j) G. Magagnano, V. Poirier, F. Romoli, D. Corbisiero, F. Calogero, P. G. Cozzi and A. Gualandi, Dielectrophilic Approach to Sequential Heterofunctionalization of Ethylene from Vinylthianthrenium Salt, *Eur. J. Org. Chem.*, 2024, e202400224; (k) P. Sarró, A. Gallego-Gamo, R. Pleixats, A. Vallribera, C. Gimbert-Suriñach and A. Granados, Access to Benzyl Oxindoles via Electron Donor-Acceptor Complex Photoactivation Using Thianthrenium Salts and Potassium Carbonate, *Adv. Synth. Catal.*, 2024, **366**, 2587–2595; (l) J. Zhang, M. Jiao, Z. Lu, H. Lu, M. Wang and Z. Shi, Hydrodeuteroalkylation of Unactivated Olefins Using Thianthrenium Salts, *Angew. Chem., Int. Ed.*, 2024, **63**, e202409862; (m) Z. He and P. Dydio, Photoinduced Cu(II)-Mediated Decarboxylative Thianthrenation of Aryl and Heteroaryl Carboxylic Acids, *Angew. Chem., Int. Ed.*, 2024, **63**, e202410616; (n) G. Zhang, Z. Luo, G. Mei, H. Wang and C. Ding, EDA Complex from BCP-Thianthrenium Salt: A Catalyst-Free Strategy To Access 1-Trifluoromethyl-3-quinoline Derivatives Bicyclo[1.1.1]pentanes, *Eur. J. Org. Chem.*, 2024, e202400386; (o) D. Dupommier, M. Vuagnat, J. Rzaev, S. Roy, P. Jubault and T. Besset, Site-Selective *Ortho/Ipsa* C–H Difunctionalizations of Arenes using Thianthrene as a Leaving Group, *Angew. Chem., Int. Ed.*, 2024, **63**, e202403950; (p) H. Moon, J. Jung, J.-H. Choi and W.-J. Chung, Stereospecific *syn*-dihalogenations and regio-divergent *syn*-interhalogenation of alkenes via vicinal double electrophilic activation strategy, *Nat. Commun.*, 2024, **15**, 3710; (q) M.-S. Liu, H.-W. Du, H. Meng, Y. Xie and W. Shu, Unified metal-free intermolecular Heck-type sulfonylation, cyanation, amination, amidation of alkenes by thianthrenation, *Nat. Commun.*, 2024, **15**, 529; (r) Z. Zhang, X. Chen, Z.-J. Niu, Z.-J. Niu, Z.-M. Li, Q. Li, W.-Y. Shi, T. Ding, X.-Y. Liu and Y.-M. Liang, A Practical and Regioselective Strategy for Aromatic C–H Difunctionalization via Site-Selective C–H Thianthrenation, *Org. Lett.*, 2024, **26**, 1813–1818; (s) W. Qi, S. Gu and L.-G. Xie, Reductive Radical-Polar Crossover Enabled Carboxylative Alkylation of Aryl Thianthrenium Salts with CO₂ and Styrenes, *Org. Lett.*, 2024, **26**, 728–733; (t) F. Xiang,

D. Wang, K. Xu and C.-C. Zeng, Paired Electrolysis Enabled Trifluoromethylheteroaromatization of Alkenes and Alkyne with Trifluoromethyl Thianthrenium Triflate (TT-CF₃⁺OTf[−]) as a Bifunctional Reagent, *Org. Lett.*, 2024, **26**, 411–415; (u) J. Zhang, L.-C. Wang, Y. Wang, B.-H. Teng and X.-F. Wu, Site-selective carbonylation of arenes via C(sp²)-H thianthrenation: Palladium-catalyzed direct access to α,β -unsaturated ketones, *J. Catal.*, 2024, **432**, 115454; (v) L.-Z. Qin, M.-Y. Wu, X. Yuan, H. Sun, X. Duan, J.-K. Qiu and K. Guo, The development and application of a novel trideuterium methylation reagent, *Cell Rep. Phys. Sci.*, 2024, **5**, 101843; (w) B. Kerwin, S. E. Liu, T. Sadhukhan, A. Dasgupta, L. O. Jones, R. López-Arteaga, T. T. Zeng, A. Facchetti, G. C. Schatz, M. C. Hersam and T. J. Marks, Trifluoromethylation of 2D Transition Metal Dichalcogenides: A Mild Functionalization and Tunable p-Type Doping Method, *Angew. Chem., Int. Ed.*, 2024, **63**, e202403494; (x) X.-B. Hu, Q.-Q. Fu, X.-Y. Huang, X.-Q. Chu, Z.-L. Shen, C. Miao and W. Chen, Hydroxylation of Aryl Sulfonium Salts for Phenol Synthesis under Mild Reaction Conditions, *Molecules*, 2024, **29**, 831; (y) T. Zhang, J. Rabeah and S. Das, Red-light-mediated copper-catalyzed photoredox catalysis promotes regioselectivity switch in the difunctionalization of alkenes, *Nat. Commun.*, 2024, **15**, 5208; (z) T. Liu, T. Li, Z. Y. Tea, C. Wang, T. Shen, Z. Lei, X. Chen, W. Zhang and J. Wu, Modular assembly of arenes, ethylene and heteroarenes for the synthesis of 1,2-arylheteroaryl ethanes, *Nat. Chem.*, 2024, **16**, 1705–1714.

38 For further selected examples, see: (a) D. E. Holst, C. Dorval, C. K. Winter, I. A. Guzei and Z. K. Wickens, Regiospecific Alkene Aminofunctionalization via an Electrogenated Dielectrophile, *J. Am. Chem. Soc.*, 2023, **145**, 8299–8307; (b) A. Dewanji, L. van Dalsen, J. A. Rossi-Ashton, E. Gasson, G. E. M. Crisenza and D. J. Procter, A general arene C–H functionalization strategy via electron donor–acceptor complex photoactivation, *Nat. Chem.*, 2023, **15**, 43–52; (c) W. Liu, H. Hou, H. Jing, S. Huang, W. Ou and C. Su, Photoinduced Phosphination of Arenes Enabled by an Electron Donor–Acceptor Complex Using Thianthrenium Salts, *Org. Lett.*, 2023, **25**, 8350–8355; (d) B. Li, D. Xing, X. Li, S. Chang, H. Jiang and L. Huang, Chemo-divergent Cyano Group Migration: Involving Elimination and Substitution of the Key α -Thianthrenium Cyano Species, *Org. Lett.*, 2023, **25**, 6633–6637; (e) X.-Y. Chen, Y.-N. Li, Y. Wu, J. Bai, Y. Guo and P. Wang, Cu-Mediated Thianthrenation and Phenoxathiination of Arylborons, *J. Am. Chem. Soc.*, 2023, **145**, 10431–10440; (f) G. Zhang, Z. Luo, C. Guan, X. Zhang and C. Ding, Nickel-Catalyzed Selective C–H Cyanation via Aromatic Thianthrenium Salts, *J. Org. Chem.*, 2023, **88**, 9249–9256; (g) H. Xu, X. Li, Y. Dong, S. Ji, J. Zuo, J. Lv and D. Yang, Thianthrenium-Enabled Phosphorylation of Aryl C–H Bonds via Electron Donor–Acceptor Complex Photoactivation, *Org. Lett.*, 2023, **25**, 3784–3789; (h) S. Ni, J. Yan, S. Tewari, E. J. Reijerse, T. Ritter and J. Cornella, Nickel Meets Aryl Thianthrenium Salts: Ni(I)-Catalyzed



- Halogenation of Arenes, *J. Am. Chem. Soc.*, 2023, **145**, 9988–9993; (i) N. Kaplaneris, A. Puet, F. Kallert, J. Pöhlmann and L. Ackermann, Late-stage C–H Functionalization of Tryptophan-Containing Peptides with Thianthrenium Salts: Conjugation and Ligation, *Angew. Chem., Int. Ed.*, 2023, **62**, e202216661; (j) R. A. Roberts, B. E. Metze, A. Nilova and D. R. Stuart, Synthesis of Arynes via Formal Dehydrogenation of Arenes, *J. Am. Chem. Soc.*, 2023, **145**, 3306–3311; (k) P. Angyal, A. M. Kotschy, Á. Dudás, S. Varga and T. Soós, Intertwining Olefin Thianthrenation with Kornblum/Ganem Oxidations: Ene-type Oxidation to Furnish α,β -Unsaturated Carbonyls, *Angew. Chem., Int. Ed.*, 2023, **62**, e202214096; (l) M. J. Cabrera-Afonso, A. Granados and G. A. Molander, Sustainable Thioetherification via Electron Donor–Acceptor Photoactivation Using Thianthrenium Salts, *Angew. Chem., Int. Ed.*, 2022, **61**, e202202706; (m) M.-S. Liu, H.-W. Du, J.-F. Cui and W. Shu, Intermolecular Metal-Free Cyclopropanation and Aziridination of Alkenes with XH_2 ($\text{X}=\text{N}$, C) by Thianthrenation, *Angew. Chem., Int. Ed.*, 2022, **61**, e202209929; (n) S. Liu, H.-W. Du and W. Shu, Metal-free allylic C–H nitrogenation, oxygenation, and carbonation of alkenes by thianthrenation, *Chem. Sci.*, 2022, **13**, 1003–1008; (o) Y. Zhao, C. Yu, W. Liang, I. L. Atodiresi and F. W. Patureau, TEMPO-mediated late stage photochemical hydroxylation of biaryl sulfonium salts, *Chem. Commun.*, 2022, **58**, 2846–2849; (p) C. Chen, Z.-J. Wang, H. Lu, Y. Zhao and Z. Shi, Generation of non-stabilized alkyl radicals from thianthrenium salts for C–B and C–C bond formation, *Nat. Commun.*, 2021, **12**, 4526.
- 39 F. Juliá, Q. Shao, M. Duan, M. B. Plutschack, F. Berger, J. Mateos, C. Lu, X.-S. Xue, K. N. Houk and T. Ritter, High Site Selectivity in Electrophilic Aromatic Substitutions: Mechanism of C–H Thianthrenation, *J. Am. Chem. Soc.*, 2021, **143**, 16041–16054.
- 40 For reviews, see: (a) C. Cordovilla, C. Bartolomé, J. M. Martínez-Ilarduya and P. Espinet, The Stille Reaction, 38 Years Later, *ACS Catal.*, 2015, **5**, 3040–3053; (b) P. Espinet and A. M. Echavarren, The Mechanisms of the Stille Reaction, *Angew. Chem., Int. Ed.*, 2004, **43**, 4704–4734; (c) V. Farina, V. Krishnamurthy and W. J. Scott, The Stille Reaction, *Org. React.*, 1997, **50**, 1–652; (d) J. K. Stille, The Palladium-Catalyzed Cross-Coupling Reactions of Organotin Reagents with Organic Electrophiles, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 508–524.
- 41 For initial reports, see: (a) M. Kosugi, K. Sasazawa, Y. Shimizu and T. Migita, Reactions of allyltin compounds III. Allylation of aromatic halides with allyltributyltin in the presence of tetrakis(triphenylphosphine)palladium(0), *Chem. Lett.*, 1977, 301–302; (b) D. Milstein and J. K. Stille, A general, selective, and facile method for ketone synthesis from acid chlorides and organotin compounds catalyzed by palladium, *J. Am. Chem. Soc.*, 1978, **100**, 3636–3638; (c) D. Milstein and J. K. Stille, Palladium-catalyzed coupling of tetraorganotin compounds with aryl and benzyl halides. Synthetic utility and mechanism, *J. Am. Chem. Soc.*, 1979, **101**, 4992–4998.
- 42 For selected examples, see: (a) H. Muraoka, S. Kubota and S. Ogawa, Synthesis and Emission Properties of a Series of 2,3,4,5-Tetrakis(5-aryl-2-thienyl)-1-phenylpyrroles as a Sterically-crowded Star-shaped $\text{D}(\pi\text{-A})_4$ Molecule, *Chem. Lett.*, 2020, **49**, 10–13; (b) A. Rana, Y. Hong, T. Y. Gopalakrishna, H. Phan, T. S. Herng, P. Yadav, J. Ding, D. Kim and J. Wu, Stable Expanded Porphycene-Based Diradicaloid and Tetradiradicaloid, *Angew. Chem., Int. Ed.*, 2018, **57**, 12534–12537; (c) A. H. Antropow, K. Xu, R. J. Buchsbaum and M. Movassaghi, Synthesis and Evaluation of Agelastatin Derivatives as Potent Modulators for Cancer Invasion and Metastasis, *J. Org. Chem.*, 2017, **82**, 7720–7731; (d) J. Shi, I. Murtaza, S. Shao, X. Zhu, Y. Zhao, M. Zhu, O. Goto and H. Meng, Tetra-EDOT substituted 3D electrochromic polymers with lower band gaps, *Sci. China: Chem.*, 2017, **60**, 90–98; (e) B. J. Hale, M. Elshobaki, R. Gebhardt, D. Wheeler, J. Stoffer, A. Tomlinson, S. Chaudhary and M. Jeffries-EL, Evaluating the influence of heteroatoms on the electronic properties of aryl[3,4-*c*]pyrroledione based copolymers, *Polymer*, 2017, **109**, 85–92; (f) G. Anguera, B. Kauffmann, J. I. Borrell, S. Borrós and D. Sánchez-García, Stable 5,5'-Substituted 2,2'-Bipyrroles: Building Blocks for Macrocyclic and Materials Chemistry, *J. Org. Chem.*, 2017, **82**, 6904–6912; (g) M. Jouanneau, B. McClary, J. C. P. Reyes, R. Chen, Y. Chen, W. Plunkett, X. Cheng, A. Z. Milinichik, E. F. Albone, J. O. Liu and D. Romo, Derivatization of agelastatin A leading to bioactive analogs and a trifunctional probe, *Bioorg. Med. Chem. Lett.*, 2016, **26**, 2092–2097; (h) X.-B. Ding, D. P. Furkert, R. J. Capon and M. A. Brimble, Total Synthesis of Heronapyrrole C, *Org. Lett.*, 2014, **16**, 378–381; (i) M. G. Banwell, B. L. Flynn, E. Hamel and D. C. R. Hockless, Convergent syntheses of the pyrrolic marine natural products lamellarin-O, lamellarin-Q, lukianol-A and some more highly oxygenated congeners, *Chem. Commun.*, 1997, 207–208; (j) J. Wang and A. I. Scott, An efficient synthesis of 3-vinylpyrroles by Stille coupling reaction of 3-iodopyrroles with vinyltributyltin, *Tetrahedron Lett.*, 1995, **36**, 7043–7046.
- 43 (a) A. S.-Y. Lee and W.-C. Dai, A facile and highly efficient sonochemical synthesis of organostannane via Barbier reaction, *Tetrahedron*, 1997, **53**, 859–868; (b) R. A. Rossi, Recent advances in the synthesis of stannanes and the scope of their posterior chemical transformations, *J. Organomet. Chem.*, 2014, **751**, 201–212.
- 44 J. A. Ragan, J. W. Raggon, P. D. Hill, B. P. Jones, R. E. McDermott, M. J. Munchhof, M. A. Marx, J. M. Casavant, B. A. Cooper, J. L. Doty and Y. Lu, Cross-Coupling Methods for the Large-Scale Preparation of an Imidazole–Thienopyridine: Synthesis of [2-(3-Methyl-3H-imidazol-4-yl)-thieno[3,2-*b*]pyridin-7-yl]-(2-methyl-1H-indol-5-yl)-amine, *Org. Process Res. Dev.*, 2003, **7**, 676–683.
- 45 I. J. Boyer, Toxicity of dibutyltin, tributyltin and other organotin compounds to humans and to experimental animals, *Toxicology*, 1989, **55**, 253–298.
- 46 E. Le Grogne, J.-M. Chrétien, F. Zammattio and J.-P. Quintard, Methodologies Limiting or Avoiding



- Contamination by Organotin Residues in Organic Synthesis, *Chem. Rev.*, 2015, **115**, 10207–10260.
- 47 (a) L. S. Liebeskind and R. W. Fengl, 3-Stannylcyclobutenediones as nucleophilic cyclobutenedione equivalents. Synthesis of substituted cyclobutenediones and cyclobutenedione monoacetals and the beneficial effect of catalytic copper iodide on the Stille reaction, *J. Org. Chem.*, 1990, **55**, 5359–5364; (b) S. Gronowitz, P. Björk, J. Malm and A.-B. Hörnfeldt, The effect of some additives on the Stille Pd⁰-catalyzed cross-coupling reaction, *J. Organomet. Chem.*, 1993, **460**, 127–129; (c) V. Farina, S. Kapadia, B. Krishnan, C. Wang and L. S. Liebeskind, On the Nature of the “Copper Effect” in the Stille Cross-Coupling, *J. Org. Chem.*, 1994, **59**, 5905–5911; (d) X. Han, B. M. Stoltz and E. J. Corey, Cuprous Chloride Accelerated Stille Reactions. A General and Effective Coupling System for Sterically Congested Substrates and for Enantioselective Synthesis, *J. Am. Chem. Soc.*, 1999, **121**, 7600–7605.
- 48 M. Hervé, G. Lefèvre, E. A. Mitchell, B. U. W. Maes and A. Jutand, On the Triple Role of Fluoride Ions in Palladium-Catalyzed Stille Reactions, *Chem. – Eur. J.*, 2015, **21**, 18401–18406.
- 49 (a) S. P. H. Mee, V. Lee and J. E. Baldwin, Stille Coupling Made Easier—The Synergic Effect of Copper(I) Salts and the Fluoride Ion, *Angew. Chem., Int. Ed.*, 2004, **43**, 1132–1136; (b) S. P. H. Mee, V. Lee and J. E. Baldwin, Significant Enhancement of the Stille Reaction with a New Combination of Reagents—Copper(I) Iodide with Cesium Fluoride, *Chem. – Eur. J.*, 2005, **11**, 3294–3308; (c) V. Lee, Application of copper(I) salt and fluoride promoted Stille coupling reactions in the synthesis of bioactive molecules, *Org. Biomol. Chem.*, 2019, **17**, 9095–9123.
- 50 (a) V. Farina and B. Krishnan, Large rate accelerations in the stille reaction with tri-2-furylphosphine and triphenylarsine as palladium ligands: mechanistic and synthetic implications, *J. Am. Chem. Soc.*, 1991, **113**, 9585–9595; (b) C. Amatore, A. A. Bahsoun, A. Jutand, G. Meyer, A. N. Ntepe and L. Ricard, Mechanism of the Stille Reaction Catalyzed by Palladium Ligated to Arsine Ligand: PhPdI(AsPh₃)(DMF) is the Species Reacting with Vinylstannane in DMF, *J. Am. Chem. Soc.*, 2003, **125**, 4212–4222.
- 51 J. Jing, Y. Hu, Z. Tian, Y. Wang, L. Yao, L. Qiu, L. Ackermann, K. Karaghiosoff and J. Li, C–S-Selective Stille-Coupling Enables Stereodefined Alkene Synthesis, *Angew. Chem., Int. Ed.*, 2024, **63**, e202408211.
- 52 (a) J. Song, S. Y. Jang, S. Yamaguchi, J. Sankar, S. Hiroto, N. Aratani, J.-Y. Shin, S. Easwaramoorthi, K. S. Kim, D. Kim, H. Shinokubo and A. Osuka, 2,5-Thienylene-Bridged Triangular and Linear Porphyrin Trimers, *Angew. Chem., Int. Ed.*, 2008, **47**, 6004–6007; (b) J. Song, N. Aratani, H. Shinokubo and A. Osuka, A β -to- β 2,5-thienylene-bridged cyclic porphyrin tetramer: its rational synthesis and 1:2 binding mode with C₆₀, *Chem. Sci.*, 2011, **2**, 748–751; (c) S. Tokuji, H. Yorimitsu and A. Osuka, Preferential Formation of Cyclic Trimers by Palladium-Catalyzed Oxidative Coupling Reactions of 2,18-Diethynylporphyrins, *Angew. Chem., Int. Ed.*, 2012, **51**, 12357–12361; (d) S. Omomo, Y. Maruyama, K. Furukawa, T. Furuyama, H. Nakano, N. Kobayashi and Y. Matano, Optical, Electrochemical, and Magnetic Properties of Pyrrole- and Thiophene-Bridged 5,15-Diazaporphyrin Dimers, *Chem. – Eur. J.*, 2015, **21**, 2003–2010; (e) I. Nishimura, T. Higashino and H. Imahori, Synthesis of thiophene-fused porphyrin dimers as effective π -extended helical chromophores, *Chem. Commun.*, 2021, **57**, 9606–9609.
- 53 T. Javorskis and E. Orentas, Chemoselective Deprotection of Sulfonamides Under Acidic Conditions: Scope, Sulfonyl Group Migration, and Synthetic Applications, *J. Org. Chem.*, 2017, **82**, 13423–13439.
- 54 (a) T. Yamagishi, H. Ichikawa, T. Haruki and T. Yokomatsu, Diastereoselective Synthesis of α,β' -Disubstituted Aminomethyl(2-carboxyethyl)phosphinates as Phosphinyl Dipeptide Isosteres, *Org. Lett.*, 2008, **10**, 4347–4350; (b) T. Ankner and G. Hilmersson, Instantaneous Deprotection of Tosylamides and Esters with SmI₂/Amine/Water, *Org. Lett.*, 2009, **11**, 503–506; (c) M. Szostak, M. Spain and D. J. Procter, Determination of the Effective Redox Potentials of SmI₂, SmBr₂, SmCl₂, and their Complexes with Water by Reduction of Aromatic Hydrocarbons. Reduction of Anthracene and Stilbene by Samarium(II) Iodide–Water Complex, *J. Org. Chem.*, 2014, **79**, 2522–2537.
- 55 B. Nyasse, L. Grehn and U. Ragnarsson, Mild, efficient cleavage of arenesulfonamides by magnesium reduction, *Chem. Commun.*, 1997, 1017–1018.
- 56 D. Zhao, R. Petzold, J. Yan, D. Muri and T. Ritter, Tritiation of aryl thianthrenium salts with a molecular palladium catalyst, *Nature*, 2021, **600**, 444–449.
- 57 A. L. Casado, P. Espinet and A. M. Gallego, Mechanism of the Stille Reaction. 2. Couplings of Aryl Triflates with Vinyltributyltin. Observation of Intermediates. A More Comprehensive Scheme, *J. Am. Chem. Soc.*, 2008, **130**, 10518–10520.

