A sulfurfylative Hiyama cross-coupling reaction using gaseous SO$_2$ is described, using Pd-catalysts. The use of silicon-based nucleophiles leads to the formation of allyl sulfones under mild conditions with a broad functional group tolerance. Control experiments coupled with DFT calculations shed light on the key steps of the reaction mechanism, revealing the crucial role of a transient sulfinate anion.

Present in many contemporary pharmaceuticals, agrochemicals and materials (e.g. the antibiotic Thiamphenicol or the herbicide Pyroxasulfone), sulfones are also used as key intermediates in organic synthesis$^{1,2}$ (e.g. the Julia olefination$^3$ or the Ramberg-Bäcklund reaction$^4$). Given this combination of a prominent biological activity and an appealing synthetic utility, numerous methodologies have been developed for their preparation.$^1$ Because it has a high atom-efficiency, the insertion of a sulfur dioxide molecule upon coupling a nucleophile with an electrophile has recently emerged as a valuable route.$^5$ Organomagnesium,$^6$ organozinc$^7$ and organoboron$^8$ compounds were successively reported as nucleophiles; yet, they suffer from toxicity issues, functional group incompatibility, and/or air-sensitivity.$^9$

Because they are readily available, air-stable and show an improved functional-group tolerance, organosilanes were recently considered to produce sulfones from SO$_2$ or SO$_2$ surrogates.$^{10}$ However, up-to-date methods are still limited to sp$^3$-hybridized electrophiles, which react through $S$-alkylation after the formation of an intermediate sulfinate anion (Scheme 1). Unlocking the utilization of sp$^2$-hybridized electrophiles would require a change of mechanism; and, to tackle this issue, we report herein the first sulfonylative Hiyama cross-coupling affording sulfones from organosilanes, sulfur dioxide and aryl iodides, in a single-step reaction (Scheme 1). Mechanistic control experiments, combined with DFT calculations performed on the key reaction steps, provide insight into the mechanism of the reaction.

**Scheme 1.** Representative state-of-the-art of sulfone synthesis from SO$_2$ and organometallic compounds.

Shortly after the discovery of the eponymous coupling, Hiyama et al. reported the carbonylative coupling of aryl iodides with organosilanes in the presence of a palladium catalyst (Figure 1a).$^{11}$ SO$_2$ is both more electrophilic and nucleophilic than CO,$^{12}$ and its frontier orbitals are centered on the sulfur atom as they are on the carbon atom of carbon monoxide (Figure 1c). Besides, the migratory insertion of SO$_2$ in a Pd–C bond has already been reported by Goddard and co-workers (Figure 1b).$^{13}$ We hence hypothesized the feasibility of a sulfonylative Hiyama cross-coupling.

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Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x
We began our investigation by exploring the coupling of triethoxysilylalkanes (1a), 4-iodotoluene (2), and gaseous sulfur dioxide, generated by thermal decomposition of K₂SO₂ in a two-chamber apparatus (see Supporting Information). In the presence of Pd(acac)₂ as a catalyst and TBAF·3H₂O as a fluoride source to activate the weakly polar C–Si bond, the desired sulfone 3a was obtained in 12% yield (Table 1, entry 1). By contrast, the bench stable surrogate of SO₂, DABSO, popularized by Willis et al.,¹⁴ gave no desired product (Table 1, entry 2), presumably due to the coordination of the DABCO by palladium. Changing the fluoride source to the anhydrous tetrabutylammonium difluorophenyl-silicate (TBAT) improved the reaction efficiency (17% yield, Table 1, entry 3). While two equivalents of SO₂ increased the yield up to 26% (Table 1, entry 4), an excess of SO₂ was detrimental to the reaction (Table 1, entry 5), possibly because of a poisoning of the catalyst. After screening a variety of palladium sources and phosphine ligands (Table 1, entries 5–7 and Table S1), a set of conditions (Pd(acac)₂ 5 mol%, Xanthos 10 mol%, TBAT 1 eq.) gave the best results in our hands, yielding the desired sulfone 3a in 78% yield (Table 1, entry 7). No reaction took place without the catalyst, even after 24 h (Table S1).

During the screening process, the diallyl sulfone (4) was identified as a side-product. The relative proportion of 4 was found to depend directly on the nature of the substituents at the silicon atom (Table 2): the quantity of diallyl sulfone (4) increases with the fluoride-affinity of the organosilane (computed by the Gibbs free energy variation for the fluoride transfer from Me₂SiF₂⁻ to the allylsilane). As a result, tri(ethoxy)allyl silanes were selected to explore this new reaction, as it provides the best balance between selectivity and productivity (see SI).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Fluoride source (eq.)</th>
<th>SO₂ source (eq.)</th>
<th>Ligand (%)</th>
<th>Yield in 3a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TBAF·3H₂O (1)</td>
<td>SO₂²⁻ (1)</td>
<td>-</td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>TBAF·3H₂O (1)</td>
<td>DABSO (0.5)</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>TBAT (1)</td>
<td>SO₂²⁻ (1)</td>
<td>-</td>
<td>17</td>
</tr>
<tr>
<td>4</td>
<td>TBAT (1)</td>
<td>SO₂²⁻ (2)</td>
<td>-</td>
<td>26</td>
</tr>
<tr>
<td>5</td>
<td>TBAT (1)</td>
<td>SO₂²⁻ (4)</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>TBAT (1)</td>
<td>SO₂²⁻ (2)</td>
<td>XPhos (10)</td>
<td>41</td>
</tr>
<tr>
<td>7</td>
<td>TBAT (1)</td>
<td>SO₂²⁻ (2)</td>
<td>Xanthos (10)</td>
<td>78</td>
</tr>
<tr>
<td>8</td>
<td>TBAT (1)</td>
<td>SO₂²⁻ (2)</td>
<td>Xanthos (5)</td>
<td>65</td>
</tr>
<tr>
<td>9</td>
<td>TBAF·3H₂O (1)</td>
<td>SO₂²⁻ (2)</td>
<td>Xanthos (10)</td>
<td>71</td>
</tr>
</tbody>
</table>

Results obtained in THF at 80 °C during 4 h on a 0.1 mmol scale. *SO₂ was generated by thermal decomposition of K₂SO₂, see Supporting Information. TBAF = tetrabutyl ammonium fluoride; TBAT = tetrabutylammonium difluorophenyl-silicate. Yields measured by 'H NMR (internal standard: mesitylene).

The chosen reaction conditions enabled the synthesis of allyl aryl sulfones 3a–3e from aryl iodides bearing electron-donating substituents as well as electron-withdrawing in 38–82% yield. The reaction tolerates well the presence of a ketone group and mesitylene (Scheme 2). Interestingly, sulfones bearing electron-donating substituents 3a–3b were obtained in better yields (78–82%) than the ones bearing electron-withdrawing substituents (3d–3e, 38–45%, Scheme 2a), as reflected by a Hammett correlation with a slope of ρ = -0.39 (Scheme 2b). Alkenyl sulfone 3f was also prepared in 57% yield (Scheme 2a). Using aryl bromides, diallyl sulfone (4) was exclusively formed, presumably due to the more difficult activation of the C–Br bond by oxidative addition.

As regards the nucleophile, methyl-substituted allylsilanes 1e–1g successfully provided the desired sulfones in 33–74% yields, with the selective formation of the α-substituted sulfones from the corresponding γ-substituted allylsilanes, while the classical Hiyama cross-coupling reaction using substituted allylsilanes usually faces regioselectivity issues.¹⁵ Disappointingly, triethoxy(phenyl)ilane and triethoxy(vinyl)silane exhibited no reactivity (Scheme 3).
The formation of phenylsulfinate from triethoxy(phenyl)silane (5) is blocked (Scheme 4b). This finding was confirmed when diarylsulfone 7 was obtained in 24% yield from the preformed arylsulfinate 8c was exposed to phenyl iodide, in the presence of the palladium catalyst (Scheme 4c). All together, these data support path B in Scheme 4d, with the metal catalyst enabling the coupling between a transient sulfinate anion and the arylhalide electrophile.
In fact, the energy barrier computed for the reductive elimination of an allylsulfone from (allylSO2)–Pd(PMe3)2–Ph is high, at 37.1 kcal mol⁻¹ (compared to 23.2 kcal mol⁻¹ for allylPd(PMe3)2–Ph). Importantly, the DFT calculations also point to the lone pair of the sulfur atom with electron deficiency aryl partners. The inverse trends may be attributed to the lower nucleophilicity of the sulfinate anion compared to the thiolate anion, the lone pair of the sulfur atom being partly delocalized on the two oxygen atoms (Figure 2).

In conclusion, we have developed a practical palladium-catalyzed synthesis of allyl aryl sulfinones from readily available organosilanes, aryl halides, and sulfur dioxide. This process represents the first approach that introduces a sp²-hybridized electrophile with an organosilane in a sulfonoflative cross-coupling. Experimental and theoretical investigations have demonstrated the key role of transient sulfinate anions and their coupling with the aryl halides, mediated by palladium, and they highlight the challenges facing the synthesis of diaryl sulfinones from organosilanes.

Conflicts of interest

There are no conflicts to declare.

Notes and references

† As shown in Entry 9 of Table 1, TBAF (1M in THF) is a competent fluoride source and it was used for scaled-up experiments to avoid the formation of the allyl phenyl sulfone 3c from TBAT.
§ As shown in the SI, the unimolecular pathway has to be discarded, the fluoride transfer from the fluoride source to the organosilane and subsequent C–Si bond scission of the hypervalent species being too energetically demanding.
 §§ As already reported,¹⁰ and experimentally evidenced (see SI), the fluoride anion is actually transferred to SO2 to yield the stable anion FSO2⁻ which acts as the fluoride source.
8 Y. Chen and M. C. Willis, Chem. Sci., 2017, 8, 3249.