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# A novel solid-phase equivalent to the triflate group and its application to traceless linking and cross-coupling-release strategies†

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**A solid-phase version of the triflate group has been developed and its use demonstrated in traceless linking of aromatics and cross-coupling release strategies.**

The upsurge in use of solid-phase organic synthesis (*e.g.* combinatorial chemistry and robotic parallel synthesis) has inspired the search for more versatile polymer supported reagents and linkers. "Traceless" linkers have proved particularly challenging but a number of successful strategies have been developed.<sup>1</sup> In this communication we wish to report a novel polymer linker that behaves like a "triflate" group.

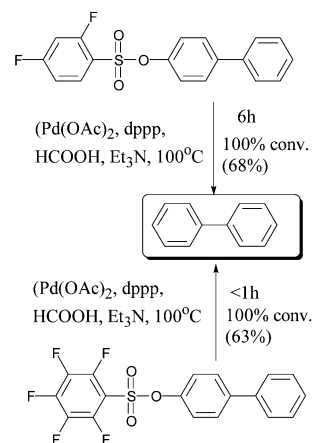
Organic triflates (trifluoromethane sulfonates) are widely employed in synthesis, effectively converting an OH group into a leaving group. Conversion of phenols into triflates renders the Ar–O bond sufficiently electron deficient (weak) to permit insertion of transition metals (such as Pd(0)) and their chemistry is akin to that of aryl bromides. As such there is a wealth of chemistry available. We,<sup>2</sup> and others, have used this chemistry for the deoxygenation of phenols by conversion to triflate and reduction with Pd(0)/HCOO<sup>–</sup>.<sup>3</sup> A polymer supported "triflate" equivalent would provide a means of attaching aryl residues (through phenolic OH) and removal from the resin in a traceless fashion (leaving Ar–H), or by employing other transition metal catalysed processes. An example of one such triflate equivalent has been reported by Holmes using a perfluoroalkylsulfonate.<sup>4</sup>

We wished to develop a solid-phase triflate equivalent using robust and simple chemistry and focused on aryl sulfonates. Polymer supported (simple) phenyl sulfonates have been employed in attempts to perform related chemistry but limited success was achieved.<sup>5</sup> The catalytic process required for reduction or cross-coupling relies on Pd(0) insertion into the Ar–O bond. Successful reactions require this bond to be weakened by either electron withdrawing groups on the Ar or on the sulfonate ester. Efficient reductive cleavage was therefore only observed when electron withdrawing groups were present on the aryl residue.

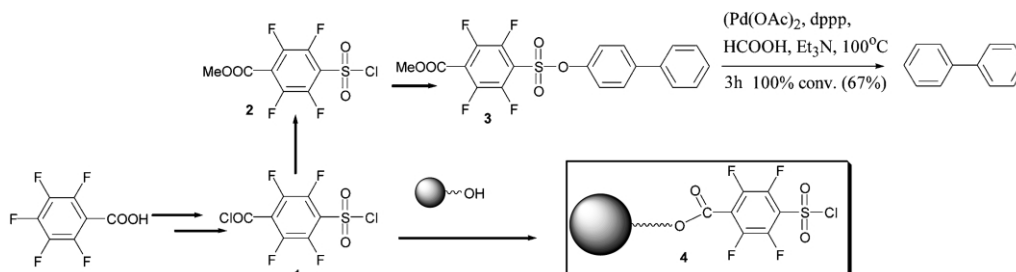
A more detailed solution phase study has been carried out by Cabri<sup>6</sup> who examined the effect of electron withdrawing groups on the sulfonate, ranking efficiency CF<sub>3</sub> > *p*-FAR > Ar, indicating the potential for polyfluorophenyl sulfonates. To establish the number of fluorines required for efficient Pd(0) insertion we performed further solution phase model reactions using 2,4-difluorophe-

nylsulfonyl chloride and pentafluorophenylsulfonyl chloride. The corresponding esters were prepared from phenylphenol and reduced using standard (for triflates) conditions (Pd(OAc)<sub>2</sub>, dppp, HCOOH, Et<sub>3</sub>N, 100 °C). Both reactions proceeded smoothly to give biphenyl as the only product (Scheme 1). The rates of the reactions were significantly different with the 2,4-difluorophenyl sulfonate requiring 6 h. The reaction employing the pentafluorophenyl sulfonate, in contrast, was complete in less than 1 h. This result indicates that 2 fluorine substituents are sufficient to enable reduction (Pd insertion) on electron-neutral residues, but the more powerfully electron deficient sulfonate permits reaction under milder conditions.

These model sulfonates are, of course, unsuitable for attachment to a solid support and require an additional linking functionality. We chose to link to a solid support *via* a carboxylic acid derivative, reasoning that the link group could serve also as a further electron withdrawing group, and that the synthesis of a suitable precursor would be straightforward. Di-acid chloride **1** was smoothly prepared following the procedure described by Fielding<sup>7</sup> starting from pentafluorobenzoic acid. Reaction of **1** with methanol at room temperature for 30 min gave the ester **2** (from reaction with the carboxylic acid chloride only) and this compound was used in a further solution state model analogous to that described previously (Scheme 2). Triflate equivalent **2** was reacted with phenylphenol to give **3** which was reduced under standard conditions. The reaction was complete in 3 h, giving biphenyl as the sole product.



**Scheme 1** Model studies towards a triflate-equivalent based on fluoroaryl sulfonates.



**Scheme 2** Synthesis of solid-phase (polymer supported) triflate equivalent and a related molecular derivative.

† Electronic Supplementary Information (ESI) available: typical experimental procedures and data for preparation of polymers and subsequent cleavage. See <http://www.rsc.org/suppdata/cc/b4/b408021a/>