100 G TO 1 KG – THE FORGOTTEN SCALE?

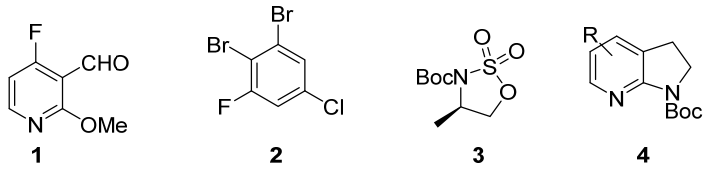
Achim Porzelle

Apollo Scientific Ltd. Whitefield Road, Bredbury, Stockport, Cheshire, SK6 2QR, UK;
achim.porzelle@apolloscientific.co.uk

As chemists we all are very familiar with small scale reactions ranging from a couple of milligrams to a few grams, for example in academia or in hit to lead optimisations in medicinal chemistry projects. On the other hand large scale process chemistry projects, *e.g.* the synthesis of API's on industrial scale, are well established and documented in the primary literature and patents. Interestingly, looking at the scale in between, reactions on 10s of grams to 1 kg are relatively scarce in the literature and, as I find, typically underrepresented at conferences and symposia.

This presentation will focus on the unique challenges synthesis on this scale presents us with on a daily basis, including the choice of reagents, the difficulties of reaction analysis of highly substituted arenes and a discussion on purification vs. turnover/yield. An emphasis is placed on the available purification techniques (what do you do if you can't chromatograph your way out of it?) and their big influence on the route design to new products.

The presentation will feature several recent projects to make novel compounds e.g. **1** and will include large scale lithiations and the "halogen dance", medium and large scale regioselective Grignard reactions on di-bromoarenes **2**, and an unexpected result of ring opening of *tert*-butyl 1,2,3-oxathiazolidine-3-carboxylate 2,2-dioxide **3** that led to ω-fluoroalky amines. The final part of the talk will be looking at 7-azaindolines **4** and their synthesis in batch and flow.



1 **2** **3** **4**

Figure 1. Compounds featuring in the presentation