Our initial efforts to explore the series were focused on the resynthesis of our hit compound TCMDC-143693. The synthesis of this compound has been already described ( <https://www.surechembl.org/document/US-20120121540-A1/>), therefore the same sequence of reactions was performed. The synthesis started with bromination at the 5-position of the 2-amino-3-(trifluoromethyl) pyridine ([**JBG28-1**](https://au-mynotebook.labarchives.com/share/Jessica%2520Baiget%2520Gonzalez/ODUuOHw2NTUvNjYvVHJlZU5vZGUvMjE3NzMwMzA3OHwyMTcuOA==)) followed by cyclisation with ethyl bromopyruvate to generate the imidazopyridine ring ([**JBG43-1**](http://openwhttps:/au-mynotebook.labarchives.com/share/Jessica%2520Baiget%2520Gonzalez/MTE1Ljd8NjU1Lzg5L1RyZWVOb2RlLzM2MTc2OTk3MjR8MjkzLjc=)), which was chlorinated at the 3-position with N-chlorosuccinimide ([**JBG45-1**](http://openwhttps:/au-mynotebook.labarchives.com/share/Jessica%2520Baiget%2520Gonzalez/MTE4LjN8NjU1LzkxL1RyZWVOb2RlLzIxMTc0MTE3NjZ8MzAwLjM=)). The resulting ester was hydrolysed with NaOH ([**JBG47-1**](https://au-mynotebook.labarchives.com/share/Jessica%2520Baiget%2520Gonzalez/MTIyLjJ8NjU1Lzk0L1RyZWVOb2RlLzEyMjE5MzA1ODl8MzEwLjI=)) to generate the corresponding acid, which could easily be converted to the amide by treatment with 2-(aminomethyl)thiophene and a coupling agent such as T3P ([**JBG48-1**](https://au-mynotebook.labarchives.com/share/Jessica%2520Baiget%2520Gonzalez/MTIzLjV8NjU1Lzk1L1RyZWVOb2RlLzM0NDcxMzE2NzJ8MzEzLjU=)). The last step, the palladium cyanylation reaction, was modified from the procedure described in the literature, with a longer reaction time and conventional heating instead of microwave irradiation improving the yield of the final compound ([**JBG50-1**](https://au-mynotebook.labarchives.com/share/Jessica%2520Baiget%2520Gonzalez/MTI2LjF8NjU1Lzk3L1RyZWVOb2RlLzQyNjE1NzcyMDR8MzIwLjE=)).

