Direct Amidation of carboxylic acids using a Borate Ester

Answers

1. Thinking of the other parameters discussed earlier (i.e. solvents; waste; energy; health and safety; work-up and isolation; catalysts; elemental sustainability):

   a. Can you identify any ‘hot-spots’ or potential issues with the reaction?

      For example:

      2 equivalents of the Borate ester are used
      DCM is used in the work-up – hazardous solvent
      Waste contaminated with fluorinated material is generated
      Reflux – 15 hours – energy intensive

   b. Where is the reaction performing well in terms of its ‘green credentials’?

      For example:

      Direct amidation – no prior activation step is needed
      One to one stoichiometric ratio of reactants
      No critical elements used
      Work-up is fairly straightforward (no chromatography)

2. What other factors would you need to consider in order to assess the overall greenness of the reaction?

   For example:

   How is the reagent tris(2,2,2-trifluoroethyl)borate prepared? (May have hidden upstream issues)
3. Which areas would you target to further improve the green credentials of this research?

For example:

- Solvent screen
- Less MI work-up
- Lower amount of reagent or look for catalytic method