



Topic 2 Summary Questions

1. Read the experimental section of the following paper on the synthesis of Rabeprazole:
<http://www.researchgate.net/publication/229060684>

- a. The improved version provides superior yield, atom economies, reaction mass efficiencies and process mass intensities to the patented version. However there are still areas of improvement. Using the solvent selection guide, identify the solvents of major issues to be substituted.

Answer: chloroform, dichloromethane, diisopropyl ether

- b. Justifying your answers, from the same paper [1] explain what would be suitable replacements for the solvents of major concern.

As all the solvents in question are classed as non-polar, suggestions could include other non-polar solvents such as cyclohexane or heptane. THF, 2-methyl THF, CPME could all be suggested as replacement ethers if opting to go for the same class of molecule; as they all have similar dipole moments to the solvents in question. Ethyl acetate could similarly be suggested on this factor. Crucially, none of these solvents (at present) are in the hazardous or highly hazardous categories on any of the solvent guides – though all except ethyl acetate are listed as problematic with substitution requested on some guides – thereby presenting an incremental improvement. Any answer which replaces ‘highly hazardous’ or ‘banned’/‘black listed’ solvents with less problematic ones, justified by physical properties or reference to scores on the selection guides, is acceptable.

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