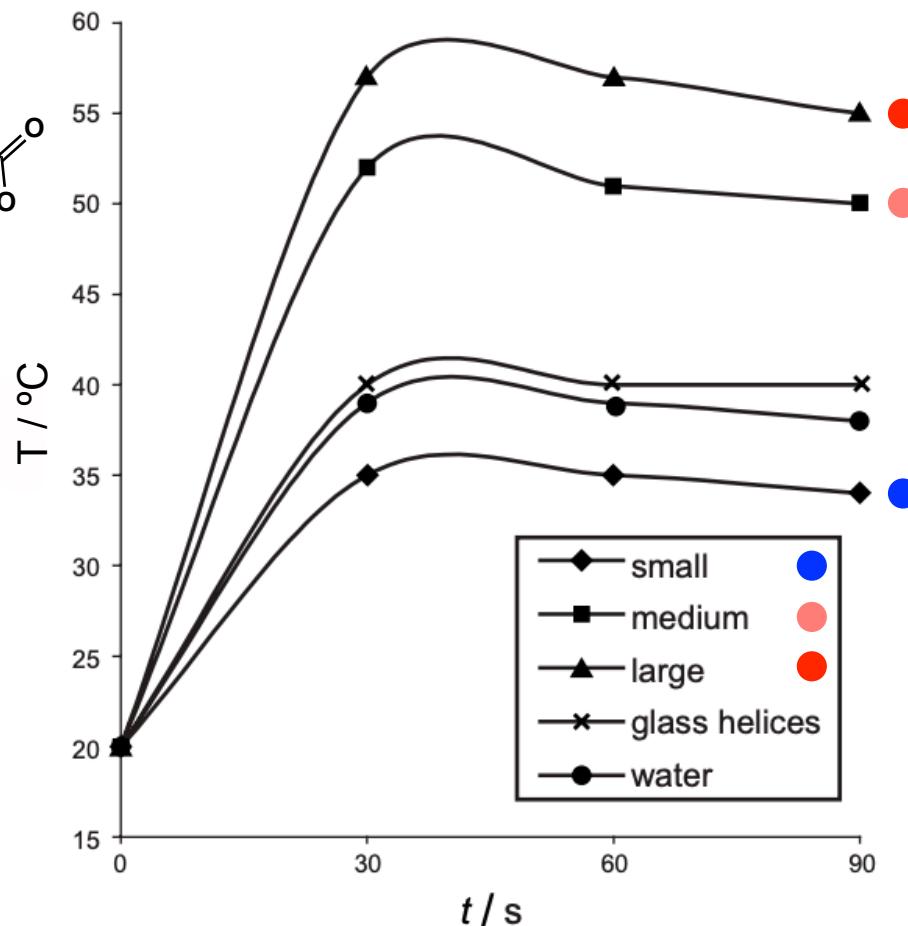
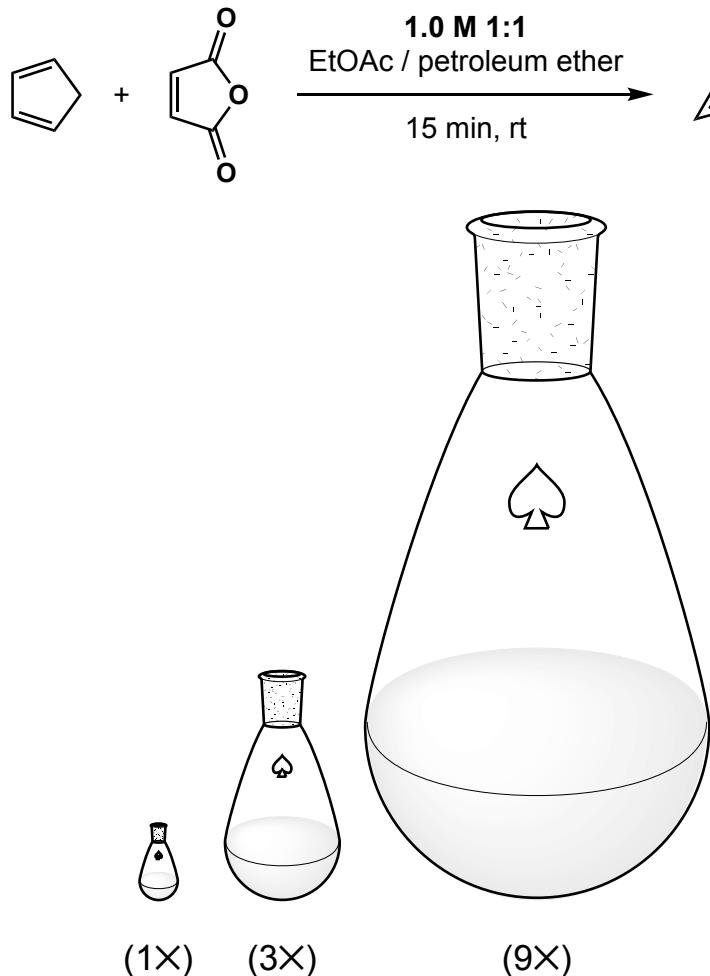


# safety moment: responsible reaction scale-up – the rule of three

small (0.75 g) → medium (7.5 g) → large (30 g)



**Figure 1.** Dependence of reaction temperature on reaction size and the presence of glass helices or water in the Diels–Alder reaction between cyclopentadiene and maleic anhydride.

# safety moment: responsible reaction scale-up – the rule of three

**small** (100 mg : 1 mmol of MW = 100 g/mol)  
 → **medium** (300 mg) → **large** (1.0 g)

with Lori Digal

**consider:** reaction exotherm potential, stirring and ventilation challenges, reaction solvent (heat capacity) and solvent level (headspace), reaction heterogeneity, available equipment, cost of starting materials vs. another method (even if more steps), ...

