The Influence of Vortex Agitation on Biphasic Phase Transfer Catalyzed Reactions: Carbene Addition to C-C Double Bonds

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Materials Science - Catalysts

General

- Biphasic processes in organic chemistry can be enhanced by the use of phase transfer catalysts. An example is the addition of a carbene to a C-C double bond to give a cyclopropane derivative.
- Agitation is a crucial variable in phase transfer catalytic reactions. The influence of reaction conditions such as agitation parameters, temperature, reaction time, and catalysts can be explored on an automated synthesizer.
- The use of Chemspeed's synthesizer for a phase transfer catalytic reaction was tested.

Reaction sketch and Objective

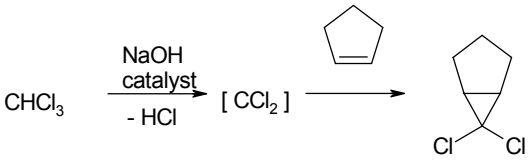


Figure 1

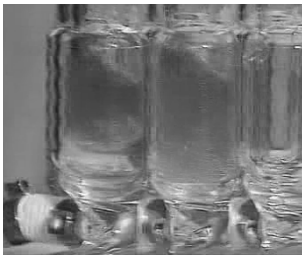
- Efficient product formation in phase transfer catalysis needs powerful agitation.
- Handling of viscous NaOH solution at low temperature is important for this reaction and has to be tested.
- Dispense of the reagents, run the temperature program of the reaction and the elaborate work-up with extraction and evaporation need to be performed, unattended in an overnight run.

Experimental Set-Up

- The phase transfer catalyst (tetrahexylammonium chloride) was placed into the reactors. Cyclopentene and chloroform were transfered into the reaction vessels.
- Viscous 50% NaOH solution in water was added to the reaction vessels at 0°C.
- Strong vortex for 1h at ambient temperature, subsequently for 5h at 40°C.
- Quench and automated solution-phase extraction of the reaction mixture.
- The experiment was carried out on a Chemspeed synthesizer equipped with 13mL double jacket reactors and reflux condensors.

Results

- The in-situ generated carbene reacted with the cyclopentene in a [2+1] cycloaddition reaction yielding 6,6-dichloro-bicyclo[3.1.0]hexane.



Picture 1

- The two phases were efficiently mixed with strong agitation (1300 rpm, Picture 1) at ambient and higher temperature (40°C).
- Successful transfer of a viscous 50% NaOH solution at 0°C.
- Dichlorocarbene was produced in-situ from the reaction of chloroform and NaOH.
- Efficient extraction was performed fully automated.

Analytics

- Analysis on a Voyager GC-MS instrument (Thermo Quest) revealed the pure product with the characteristic isotope pattern for two chlorine atoms in the ratio of 9:6:1 for $[M]^+$:$[M+2]^+$:$[M+4]^+$.

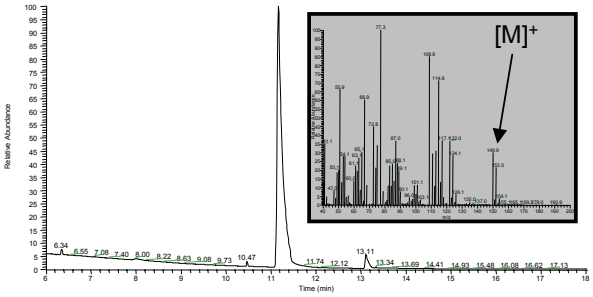


Figure 2

Summary

- Chemspeed's Synthesizers were proven to be very efficient for phase transfer catalysis with its crucial issues including agitation.
- High viscous NaOH solution can be handled at 0°C without difficulty.