Continuous flow ozonolysis using atmospheric plasma

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Ozonolysis is widely used in organic synthesis to obtain aldehydes and ketones from alkenes, a process of great interest, for example, for the pharmaceutical industry. This reaction is more environmentally accepted than other alternative oxidations and it has good atom efficiency. Ozonolysis, however, has an important drawback; the ozonides generated as intermediates in the process are unstable and pose a risk of explosion. To minimize this risk, continuous flow processing can be used, as this eliminates the accumulation of large amounts of hazardous intermediates, thereby offering an alternative to batch processing that greatly enhances the control and safety of the ozonolysis process.[1,2] Here we report on the results obtained with an air plasma-driven continuous-flow ozonolysis system.

A solution containing the starting material (see Fig. 1) flows along a semipermeable Teflon tube that is enclosed in a reaction vessel. The tube allows ozone generated in the vessel by an air dielectric barrier discharge to reach the solution inside the tube while preventing solvent and starting reagents to escape outside the tube. Reaction progress is inferred by nuclear magnetic resonance (NMR) analysis of processed samples. A typical NMR spectrum showing starting and final materials is shown in figure 1.

The feasibility of generating ozone to trigger the desired chemical reaction while controlling the temperature of the process was first tested by performing the ozonolysis with the reaction vessel on a batch configuration, i.e. by directly exposing a small volume of solution to the ozone generated in the vessel without the use of the tube. Fig. 2 shows the progress of the reaction as a function of time, which indicates that after ~48min the starting material had all been consumed. The temperature in the reaction vessel is seen to increase during this process due to the heating induced by the plasma source and it reaches a steady state value of ~45°C after ~20min.

Results in the continuous flow configuration confirm that the reaction takes place in the flow reactor and that the Teflon AF-2400 tube acts as a semipermeable membrane for this process.

[1] O'Brien, M.; Baxendale, I. R.; Ley, S. V. *Org. Lett*. **2010**, 12, 1596–1598.
[2] Irfan, M.; Glasnov, Toma N.; Kappe C.O. *Org. Lett*. **2011**, 13, 984–987.

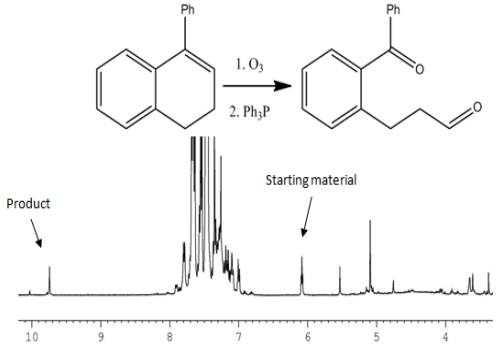

Figure 1. NMR spectrum showing partial conversion from starting material to product after 32 min of plasma exposure.

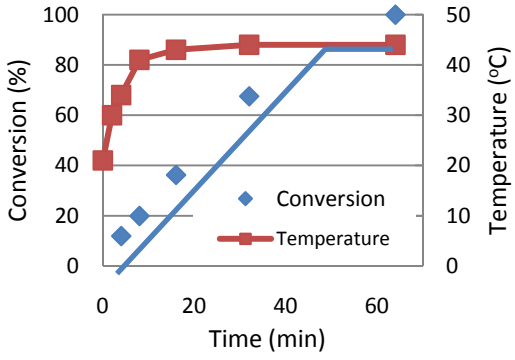

Figure 2. Temporal evolution of the ozonolysis progress and vessel temperature.