MICROWAVE-INDUCED ORGANIC REACTION ENHANCEMENT (MORE) CHEMISTRY: TECHNIQUES FOR RAPID, SAFE AND INEXPENSIVE SYNTHESIS

A.K. BOSE*, M.S. MANHAS, B.K. BANIK AND E.W. ROBB

Department of Chemistry and Chemical Engineering, Stevens Institute of Technology, Hoboken, New Jersey 07030, U.S.A.

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Abstract—Synthetic organic reactions have been conducted under microwave irradiation in open vessels in unaltered domestic microwave ovens. Reaction times vary from a few seconds for sub-milligram reactions to about 15 minutes for reactions carried out on a scale of hundreds of grams. Promising results have been obtained for several condensations, as well as the Bischler-Napieralski reaction, the Wolff-Kishner reduction, free radical dehalogenation reactions, and other standard synthetic operations. Rapid catalytic transfer hydrogenation using ammonium formate as the source of hydrogen has been conducted at about 100-130 °C under microwave irradiation.

Meaningful, safe and inexpensive synthetic experiments for undergraduate and pre-college students have been developed and tested. The MORE chemistry techniques make it possible to use simple apparatus and very short reaction times.

Commercial microwave ovens are now essential equipment in our research and teaching laboratories [1-3]. These ovens are relatively inexpensive, easy to move from one laboratory and set up in another, and safe to operate. Glass, plastics, and ceramics are essentially transparent to microwaves whereas many organic compounds are dipolar in nature and absorb microwave energy readily. We have found that untraditional experimental arrangements are possible for conducting a wide variety of organic reactions in open vessels inside domestic microwave ovens. Depending on the quantity of reactants, most reactions (on a scale of milligrams to several grams) can be completed in minutes instead of hours. One important element of our "Microwave-induced Organic Reaction Enhancement" (MORE) chemistry is the proper choice of a microwave energy transfer agent as the reaction medium.

PREFERRED REACTION MEDIA

It is customary in most laboratories to choose an organic solvent as a reaction medium and conduct reactions under reflux to control the temperature of the reaction. For MORE chemistry the solvent of choice is one which absorbs microwave energy efficiently and is therefore heated rapidly under microwave irradiation and which has a boiling point that is at least 20-30 °C higher than the desired reaction temperature. The energy input into the reaction mixture is controlled in such a way as to prevent much vaporization of the
reaction mixture. This is comparatively easy since superheating of liquids is common under microwave irradiation.

We have found that N,N-dimethylformamide (DMF) (b.p. 160 °C) which has a high dielectric constant (ε = 36.7) is an excellent transfer agent for a variety of organic reactions. The reaction temperature can be raised to about 140 °C without much vaporization of DMF. This solvent seems to retain water formed in a reaction, thus obviating the need for a water separator (Dean-Stark tube). Formamide (b.p. 216 °C) can be used for some reactions if reaction temperature of 180-190 °C is desired.

Hydrocarbon solvents such as hexane, benzene, toluene and xylene are unsuitable as reaction media since they absorb microwave radiation poorly. In their place we have used chlorobenzene (b.p. 132 °C), 1,2-dichlorobenzene (b.p. 180 °C) and 1,2,4-trichlorobenzene (b.p. 214 °C) with success. For lower temperature reaction 1,2-dichloroethane (b.p. 83 °C) can be used.

For reactions that are usually conducted in alcohol solution we prefer ethylene glycol (b.p. 196 °C). Ether and tetrahydrofuran (THF) can be replaced by dioxane (b.p. 101 °C), diglyme (b.p. 162 °C) or triglyme (b.p. 216 °C).

**SIMPLE TECHNIQUES**

The preferred reaction vessel for MORE chemistry is a tall beaker, loosely covered, with a capacity much greater than the volume of the reaction mixture. Alternatively, a large Erlenmeyer flask with a funnel as a loose top, can be used. With proper adjustment of the energy level and intermittent heating there is little vaporization, and the upper part of the beaker or flask remains cool enough to touch.

Reactions on a scale of milligrams can be conducted in a reaction vial with a septum as a cap. If exclusion of air is desired, hypodermic needles can be used to replace the gas inside the capped reaction vial.

Domestic microwave ovens in the United States produce 2450 MHz radiation at a rate that is controlled by an on-off cycle. The 2450 MHz frequency, which was selected for efficient heating of water, is suitable for rapid heating of the solvents discussed above. When working with more than 5-10 g of reaction mixtures the on-off cycle may provide adequate temperature control. For smaller quantities of reactants we find it convenient to fine-tune the energy absorbed by the reaction by placing a beaker of water (or DMF) near the reaction vessel. This acts as a "heat sink" absorbing a suitable portion of the microwave energy in the oven.

**FAST MONITORING OF REACTIONS**

We [1] have found it convenient to monitor MORE chemistry experiments by thin-layer chromatography (TLC) followed by positive ion or negative ion chemical ionization mass spectrometry (CIMS). Spots on the TLC plate are rapidly and conveniently transferred