Microwave-Assisted Reduction of Acetophenones Using Ni–Al Alloy in Water

Akira Miyazawa,*[1] **Masashi Tashiro,**[1]
G. K. Surya Prakash,[2] **and George A. Olah**[2]

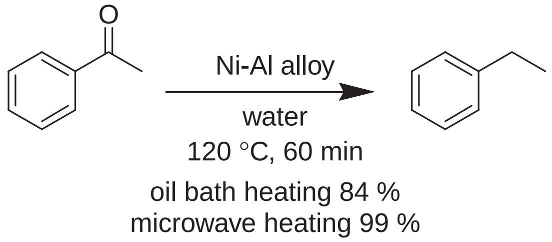
[1]National Institute of Advanced Industrial Science and
Technology (AIST), AIST Tsukuba Central 5,
1-1-1 Higashi, Tsukuba 305-8565

[2]Loker Hydrocarbon Research Institute,
University of Southern California,
Los Angeles, California 90089-1661, U. S. A.

Received October 19, 2005; E-mail: a.miyazawa@aist.go.jp

The reduction of acetophenones using a Ni–Al alloy catalyst in water (H_2O and D_2O) under microwave irradiation proceeded to give the corresponding (deuterated) alkylbenzenes in good yields.

Utilization of water as a chemical reagent such as a hydrogen and oxygen source or an alternative to organic solvents is an essential aspect of "Green Chemistry."[1] The reductions of carbonyl compounds is a fundamental organic transformation in synthetic organic chemistry. The Clemmensen[2,3] and the Wolf-Kishners[4] reductions are convenient and frequently used protocols to selectively reduce carbonyl groups. However, the former protocol cannot be applied to base sensitive substrates and a high reaction temperature is required, while the latter is conducted under strongly acidic conditions and occasionally uses poisonous mercury. Very recently, we reported that the reduction of acetophenones carried out in water in the presence of Ni–Al alloy[5] gives the corresponding alkylbenzene in good yields.[6] Our method for the reduction of carbonyl groups is simple and safe since organic solvents and a hydrogen gas cylinder are unnecessary. On the other hand, this decade has seen a tremendous increase in the number of reports on microwave-assisted chemistry.[7–9] Microwave irradiation drastically accelerates the reaction rate and occasionally enhances the selectivity. Thus, microwave irradiation should be a powerful tool in the field of Green Chemistry. To achieve more environmentally benign chemical processes, we have introduced microwave irradiation into our reduction system. Herein, we wish to report the microwave-assisted reductions of acetophenones with a Ni–Al alloy in water.



Scheme 1.

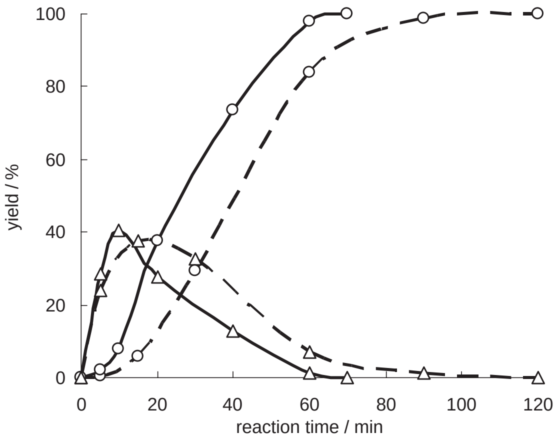


Fig. 1. Plots of yield versus reaction time in the reduction of acetophenone. Reaction conditions are noted in Scheme 1. - -△- - 1-phenylethanol, oil bath heating; - -○- - ethylbenzene, oil bath heating; —△— 1-phenylethanol, microwave heating; —○— ethylbenzene, microwave heating.

The reactions were conducted in the presence of a Ni–Al alloy in water at 120 °C using a preheated oil bath or microwave irradiation in a pressure resistant glass ampoule. During the reaction, the temperature of the ampoule was maintained at 120 °C by varying the irradiation power of the microwaves between 10 and 100 W. Scheme 1 shows the preliminary results using both heating methods. Upon microwave irradiation, acetophenone was completely consumed within 60 min and was converted to ethylbenzene in an almost quantitative yield. The reaction rate was fast compared to heating with a conventional oil bath heating. Figure 1 shows the reaction profiles for the formation of ethylbenzene and the intermediate 1-phenylethanol. In the initial stage of the reaction, both conditions (microwave irradiation and oil bath heating) had similar 1-phenylethanol formation rates. After the yields of 1-phenylethanol reached 40%, microwave heating decreased the rate of 1-phenylethanol faster than heating with the oil bath. It appears that the rates of hydrogen addition to the carbonyl group are nearly the same, but that microwave irradiation accelerates the hydrogenolysis step from 1-phenylethanol to ethylbenzene.

To determine the effect of the microwave irradiation, we investigated the reaction of a Ni–Al alloy with water. When the suspension of Ni–Al alloy in water was heated at 120 °C for 10 min using a preheated oil bath or microwave irradiation, the resulting hydrogen pressure in each ampoule was 165 and 207 kPa, respectively (Scheme 2). These results indicate that microwave irradiation directly influences hydrogen generation in the reaction of the Ni–Al alloy with water. Microwaves collide with the Ni–Al alloy and cause hydrogen to be rapidly generated since aluminum is a good microwave absorber that reacts with water to generate hydrogen.[10,11] Thus, this rapid generation of hydrogen seemed to be a key step of the acceleration of acetophenone reduction.

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$$H_2O \xrightarrow[\text{120 °C} \\ \text{10 min}]{\text{Ni-Al alloy}} H_2\uparrow$$

	H_2 pressure
oil bath heating	165 kPa
microwave heating	207 kPa

Scheme 2.

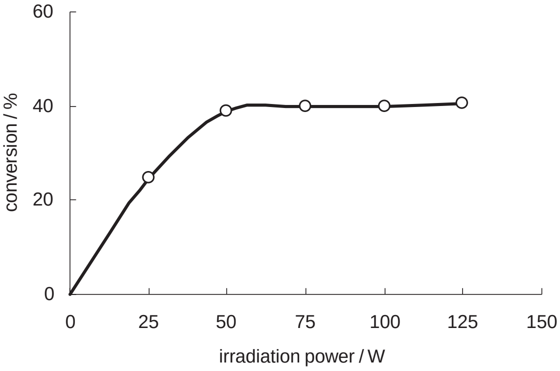


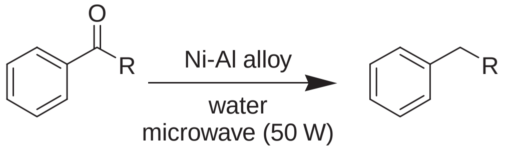
Fig. 2. Plots of conversion against irradiation power in the reaction of Ni–Al alloy and water.

As previously mentioned, to generate isothermal reaction conditions, the irradiation power was automatically fluctuated. Therefore, we investigated this microwave-assisted reduction under the conditions at constant power with continuous irradiation in more detail.

Figure 2 plots the microwave irradiation power against the acetophenone conversion. Although the acetophenone conversion was increased as the microwave irradiation power increased up to 50 W, more powerful irradiation did not affect the conversion. When the reaction of the Ni–Al alloy with water was conducted with continuous microwave irradiation of 50 W under the same conditions described in Scheme 2, the hydrogen pressure was 413 kPa.

Table 1 lists the results of acetophenone and propiophenone reduction using the Ni–Al alloy catalyst in water (H_2O and D_2O) under continuous microwave irradiation at 50 W. When microwaves were continuously irradiated at a fixed power (50 W), the reaction time was up to 10 min shorter than the isothermal conditions (120 °C) and the corresponding alkylbenzenes were obtained in good yields (Entries 1 and 2). D_2O was also applicable to this reaction as a deuterium source and solvent. Although the reaction required a longer time than H_2O, the expected ethylbenzene-d_5 and *n*-propylbenzene-d_7 were obtained in quantitative yields (Entries 3 and 4). GC-MS analysis was used to determine the amount of deuterium introduced.

Table 1. Preliminary Results of Acetophenon and Propiophenon Reduction with Ni–Al Alloy in Water (H_2O and D_2O)[a)]



Entry	R	Water	Time/min	Yield/%
1	Me	H_2O	10	quant
2	Et	H_2O	10	81
3	Me	D_2O	30	quant
4	Et	D_2O	30	quant

a) Conditions: starting ketones (200 mg), Ni–Al alloy (1.0 g), and water (2 mL) were used.

In summary, we have demonstrated the convenient reduction of acetophenones using a Ni–Al alloy with water under microwave irradiation. The presently developed method should be very useful since the reaction proceeds very rapidly and can be used as a deuteration.

Experimental

The Ni–Al alloy (50 wt % of Ni and Al, Wako Chemical Ltd.) was used as received. Other chemicals purchased were used as received without further purification. D_2O (99% D-content) was used for the deuteration reaction. The microwave apparatus (CEM Discover, 2.45 GHz frequency, CEM Corporation, NC U.S.A.) was used for irradiation. GC analyses were performed using a Shimadzu GC-14A with a capillary column (DB-1, 50 m). The GC-MS measurements were conducted with a Nippon Denshi SUN-200 spectrometer (electron impact system with a 70 eV ionization energy).

A typical microwave irradiation experiment (i.e. Scheme 1) used 200 mg (1.67 mmol) of acetophenone, 1.0 g of Ni–Al alloy, and 2 mL of H_2O in a pressure resistant glass ampoule equipped with a rubber septum and an aluminum cap. The loaded ampoule (10 mL capacity) was introduced into the cavity of the microwave apparatus and irradiated with microwaves for 60 min at 120 °C. The ampoule was cooled in an ice/water bath and the organic materials were extracted with ether. The ether fraction was analyzed by GC and GC-MS to identify and quantify the products.

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