Acceleration of Tributyltin Hydride Reduction of Phenethyl Iodide and *m*-Methoxybenzyl Bromide by a Strong Magnetic Field

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Reduction reactions of phenethyl iodide and *m*-methoxybenzyl bromide with tributyltin hydride are accelerated by a strong (9.4 T) magnetic field.

An NMR spectrometer is an excellent tool not only for structural analysis but for investigating chemical reactions. This is because an NMR spectrometer is generally considered to be nondestructive to the samples and not to influence the chemical reactions. Study of kinetics of chemical reactions by NMR spectroscopy, however, would be valid only when the reaction is not affected by the strong magnetic field. The effects of magnetic fields on photochemical reactions have been reported.[1–4]

In our study of magnetic field effects on chemical reactions, the superconductive magnets of 400 MHz NMR spectrometers (Bruker ARX400 and JEOL GX400) generating a strong and extremely stable magnetic field (9.4 T [Tesla]) have been used.

Prior to the experiments, the temperature of the NMR probes, in which the samples were placed, was measured by a thermocouple (Yokogawa 2455) and the temperature of a water bath was set at the measured one. The typical procedure is as follows: An aliquot (named $S_{9.4T}$) of the reaction mixture was put in a 5-mm NMR sample tube and the tube was placed in the probe which was kept on 35 °C.[5] Throughout the reaction, the spinner and transmitter for a lock signal were turned off to avoid the effects other than the magnetic field. Other aliquots (named S_{0T}) were placed in the NMR sample tubes and they were set in the water bath (35 °C). The reaction course of $S_{9.4T}$ was monitored by measuring the NMR spectra at appropriate intervals. The reaction course of S_{0T} was monitored by exchanging $S_{9.4T}$ in the NMR probe with S_{0T}, and measuring the NMR spectrum (the number of accumulation = 32). After this, $S_{9.4T}$ and S_{0T} were put back in their original positions. This exchanging operation needed 5 min.

At first tributyltin hydride reduction of a halide was studied, because the reaction proceeds relatively slowly, and the reaction course can be followed by NMR spectroscopy. In the present case, reduction of phenethyl iodide with tributyltin hydride was examined both in the presence and absence of the magnetic field.

$$\text{Ph-CH}_2\text{CH}_2\text{-I} \xrightarrow{\text{TBTH}} \text{Ph-CH}_2\text{CH}_3$$

A solution of freshly distilled tributyltin hydride (TBTH: 50 µmol) and phenethyl iodide (34.5 µmol) in dry C_6D_6 (1.5 mL) was prepared. A 0.5 mL of this solution ($S'_{9.4T}$) was put in an NMR tube. The air in the tube was replaced with argon by repeated evacuation at –78 °C and filling with argon, and the tube was sealed and placed in the 400 MHz NMR probe. Another sealed NMR tube containing the 0.5 mL solution (S'_{0T}) was placed in a water bath. The temperature of the bath was set at 35 °C, which was the observed temperature of the probe. After the procedures described above, the results shown in Figure 1 were obtained.

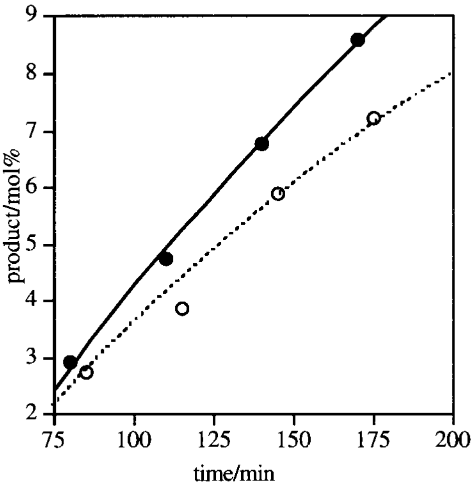

Figure 1. Plot of the yield (%) of ethylbenzene vs reaction time in the presence (solid) and absence (open) of 9.4T magnetic field.

This reaction turned out to be a secondary-order one, because the linear relation was observed between the reciprocal molar ratio (%) of phenethyl iodide and reaction time (Figure 2). An index $K_{9.4T/0T} = s_{9.4T}/s_{0T}$ (s: slope of the straight line) was introduced to show the effect of the magnetic field. In the present case, $K_{9.4T/0T} = 1.3$, which indicates that the tin hydride reduction is considerably accelerated by 9.4 T magnetic field.

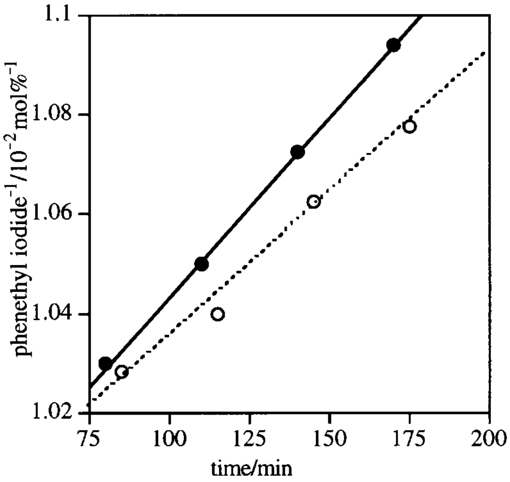

Figure 2. Plot of the reciprocal molar ratio (%) of phenethyl iodide vs reaction time: for symbols, see Figure 1.

Interestingly, this reaction proceeded without a radical initiator, AIBN (2,2'-azobisisobutyronitrile). When AIBN was added to the reaction mixture, no good reproducibility of the reaction rates was obtained. It is plausible that oxygen, present in the solvent and/or argon, plays a role as a radical initiator. A minor amount (28 % of ethylbenzene) of phenethyl alcohol was found in the product.[6] The production rate of phenethyl alcohol is also accelerated by the magnetic field in the same order as that of ethylbenzene.

The present experiments may have an intrinsic drawback. The reaction rate of S'_{0T} was determined by the NMR instrument; the sample might have been affected by the magnetic field during measurement of the spectrum. Therefore, the reaction course was investigated by HPLC.

One of the two NMR tubes containing C_6H_6 solutions of TBTH (179 μmol) and *m*-methoxybenzyl bromide (149 μmol) was placed in the NMR probe (35 °C; $S''_{9.4T}$) and another in the water bath (35 °C; S''_{0T}). The tubes were capped instead of sealed. The reaction course was monitored by taking out 10 μL portions of the mixture and analyzing them by HPLC (LiChrosorb®, hexane : AcOEt = 99.8 : 0.2, UV: 260 nm). The yield (X) of 3-methoxytoluene was calculated according to $X = B/(A+B)$, where A and B were the peak intensities of *m*-methoxybenzyl bromide and 3-methoxytoluene, respectively.

The HPLC analysis (Figure 3) indicates that the magnetic field increases the reaction rate ($K_{9.4T/0T} = 1.7$) as well. The average enhancement of the reaction rate, obtained after repeating 20 experiments, was $K_{9.4T/0T} = 1.58 \pm 0.16$.

On the other hand, when the butyltin hydride reduction of phenethyl iodide was performed in the presence of 0.4 T magnetic field (a neodymium magnet), no acceleration is observed.

The substitution reaction of phenethyl methanesulfonate with sodium iodide in acetone-d_6 was not accelerate by the magnetic field (9.4 T), either.

The acceleration mechanism of the magnetic effect on the present reaction is not clear so far, and experiments to study the mechanism to interpret the present findings are in progress.

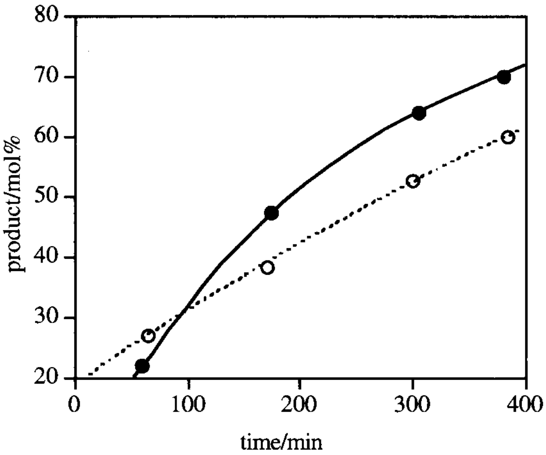

Figure 3. Plot of the yield (%) of 3-methoxytoluene vs reaction time: for symbols, see Figure 1.

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References and Notes

1 R. De, Y. Fujiwara, B. Zhang, and Y. Tanimoto, *Bull. Chem. Soc. Jpn.*, **73**, 1573 (2000).

2 R. Nakagaki and K. Mutai, *Bull. Chem. Soc. Jpn.*, **69**, 261 (1996).

3 R. Nakagaki, M. Yamaoka, O, Takahashi, Y. Fujiwara, and Y. Tanimoto, *J. Phys. Chem. A*, **101**, 556 (1997).

4 Y. Fujiwara, K. Yoda, T. Tomonari, T. Aoki, Y. Akimoto, and Y. Tanimoto, *Bull. Chem. Soc. Jpn.*, **72**, 1705 (1999).

5 It was found that the tin hydride reduction proceeded in a moderate rate at 35 °C. Therefore, the NMR probe was heated at this temperature.

6 Even though evacuation and filling with argon of the NMR tube were repeated several times, the yield of the phenethyl alcohol did not change. It seems that a considerable amount of oxygen is tightly trapped in the benzene.