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An Efficient and Fast Method for the Preparation of Benzylic Bromides

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ABSTRACT

A mixture of triphenylphosphine and *N*-bromosuccinimide system is found to promote efficient conversion of benzylic alcohols into benzylic bromides under microwave irradiation conditions.

Key Words: Benzyl alcohol; Bromide; Microwave; Phosphine.

INTRODUCTION

The conversion of benzylic alcohols into the corresponding benzylic bromides is a fundamental reaction in the synthesis of a variety of organic compounds.^[1,2] Generally, the reagent systems of bromotrimethylsilanes,^[3] Ph₃P/Br₂,^[4] and dimethylsulfide/*N*-bromosuccinimide^[5] were commonly utilized to effect this transformation in various organic solvents.

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In recent years, microwave promoted organic transformations in solventfree conditions received much attention due to its environmentally very friendly conditions.^[6] In connection with our interests on microwave accelerated organic reactions, we wanted to develop an efficient method for conversion of benzylic alcohols into the corresponding benzylic bromide under solvent-free conditions. To our best knowledge, the only previous example of microwave promoted bromination of benzylic alcohols into benzyl bromides under microwave irradiation conditions was reported by using sodium bromide doped on K10 clay for the 6-9 min reaction time.^[7] However, in view of very fast heating nature of microwave irradiation conditions, the required reaction time of 9 min under strong acidic conditions in this method might be considered somewhat drastic in certain reactions. It is often preferable to conduct microwave induced reactions under neutral conditions at shorter reaction time due to the prolonged reaction time under excessive heating often could potentially lead to product decomposition. Thus, there is a need to develop a more fast and improved microwave promoted synthetic method under neutral reaction conditions for the preparation of benzylic bromides. After extensive search for suitable reagent system for the bromination of benzylic alcohols, we found the combination of triphenylphosphine/ N-bromosuccinimide to be most suitable for the solvent-free microwave irradiation conditions. Thus, microwave irradiation to the neat mixture of benzyl alcohol, triphenylphosphine (1.5 equiv.), and N-bromosuccinimide (1.5 equiv.) afforded benzyl bromide in just 10 sec (Sch. 1). A series of benzylic alcohols was reacted under the same reaction conditions and results are summarized in Table 1. All reactions studied were completed in less than 30 sec in very high yields. As can be seen in Table 1, primary benzyl alcohols generally afforded much higher yields than secondary alcohols (entries 5-7), which probably results from steric hindrance between phosphonium alkoxide intermediate and nucleophilic bromide ion.

In summary, the microwave promoted reaction of various benzylic alcohols with triphenylphosphine/*N*-bromosuccinimide under solvent-free conditions gave benzylic alcohols with high yields in very short reaction time. The neutral conditions and rapid reaction conditions together with eco-friendly solvent-free conditions should make present protocol an important alternative to other classical methods.

ArCHR'OH

PPh₃/NBS

ArCHR'Br

MWI, 10 - 30 sec

Scheme 1.

Entry	Substrate	Time (sec)	Product	Yield ^a (%)
1	∕_СН₂ОН	10	CH ₂ Br 1a	88
2	СІ—∕_СН₂ОН	10	CI-CH ₂ Br 2a	98
3	H₃C-∕_−СH₂ОН	20	H ₃ C-CH ₂ Br 3a	96
4	O ₂ N-CH ₂ OH	20	O ₂ N-CH ₂ Br 4a	98
5	СН(СН ₃)ОН	30	CH(CH ₃)Br 5a	76
6	Н₃С-∕СН(СН₃)ОН	30	H ₃ C-CH(CH ₃)Br 6a	75
7	CI-CH(CH ₃)OH	30	CI-CH(CH ₃)Br 7a	71
8	НОН ₂ С СН ₂ ОН	20	BrH ₂ C CH ₂ Br 8a	90

Table 1. Microwave promoted preparation of benzylic bromides.

^aIsolated yield.

EXPERIMENTAL

All reactions were performed in a commercial domestic microwave oven (Samsung RE-21C). ¹H NMR spectra were obtained on a Varian Gemini 2000-300 MHz spectrometer.

General Procedure

A mixture of benzylic alcohol (1.0 mmol), *N*-bromosuccinimide (0.26 g, 1.5 mmol), and triphenylphosphine (0.39 g, 1.5 mmol) was placed in a 50 mL of glass tube. The reaction mixture was inserted in an alumina bath inside a domestic microwave oven and irradiated (700 W) indicated time in Table 1. On completion of the reaction, the product was extracted with dichloromethane and washed with water (40 mL). The organic layer was separated and dried over MgSO₄. After evaporation of solvent, the product

was purified by flash column chromatography on silica gel using *n*-pentane as eluent to furnished pure benzylic bromide.

1a. ¹H-NMR (300 MHz, CDCl₃): δ 4.50 (s, 2H), 7.26–7.39 (m, 5H).

2a. ¹H-NMR (300 MHz, CDCl₃): δ 4.45 (s, 2H), 7.26–7.32 (m, 5H).

3a. ¹H-NMR (300 MHz, CDCl₃): δ 2.34 (t, 3H), 4.49 (s, 2H), 7.13–7.16 (m, 2H), 7.26–7.30 (m, 2H).

4a. ¹H-NMR (300 MHz, CDCl₃): δ 4.52 (s, 2H), 7.54–7.57 (m, 2H), 8.19–8.20 (m, 2H).

5a. ¹H-NMR (300 MHz, CDCl₃): δ 2.06 (d, 3H), 5.24 (q, 1H), 7.31–7.49 (m, 5H).

6a. ¹H-NMR (300 MHz, CDCl₃): δ 2.02 (d, 3H), 2.33 (s, 3H), 5.18 (q, 1H), 7.13–7.16 (m, 2H), 7.32–7.34 (m, 2H).

7a. ¹H-NMR (300 MHz, CDCl₃): δ 2.02 (d, 3H), 5.16 (q, 1H), 7.27–7.39 (m, 4H).

8a. ¹H-NMR (300 MHz, CDCl₃): δ 4.48 (s, 4H), 7.26–7.42 (m, 3H).

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