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Efficient Synthesis of α-Hydroxyacetophenone *via* Microwave Irradiation of α-Bromoacetophenone from Acetophenone

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Herein, we reported a new and efficient approach starting from acetophenone. In this work, α-hydroxyacetophenone was prepared under microwave irradiation of α-bromoacetophenone which was efficiently prepared by the use of HBr/H_2O_2 system.

Keywords: α-Hydroxyacetophenone, α-Bromoacetophenone, Acetophenone, Microwave.

INTRODUCTION

α-Hydroxyacetophenone is an important intermediates which is used for the synthesis of pharmaceuticals and agro-chemicals[1,2]. α-Hydroxyacetophenone was synthesized from enamine derivatives ketones and oxygen[7], ketone combined with iodobenzene diacetate in the presence of potassium hydroxide with methanol[8], α-hydroxylation of silylenol ethers react with chloroperbenzoic acid[9] and α-iodoketone with irradiation under a high-pressure mercury lamp also can product α-hydroxyacetophenone[10,11]. α-Bromoacetophenone was usually prepared by reaction of acetophenone with N-bromosuccinimide (NBS) or molecular bromine in the presence of Lewis acids such as NH_4OAc[3], $NaHSO_4{\cdot}SiO_2$[4], $Mg(ClO_4)_2$[5,6].

However, these methods have some drawbacks. For example, the bromine is toxic which corrodes the equipment. It is difficult handling and environmental pollution[12]. Besides, N-bromosuccinimide is easier handling, but it is unfortunately limited by low atom efficiency and the complex reprocessing[13]. Most importantly the common drawbacks in synthesis α-hydroxyacetophenone are the use of organic solvent[14], long reaction time and environmental problems[15].

Thus, it is necessary to search for a new methods to synthesize α-hydroxyacetophenone. In this work, HBr/H_2O_2 system was used as an efficient and environmentally friendly halogenation reagent in the synthesis of α-bromoacetophenone. Meanwhile, microwave synthesis was used to prepare α-hydroxyacetophenone from α-bromoacetophenone.

EXPERIMENTAL

Melting points were determined on a WPS-2 melting point apparatus and were uncorrected. ^{1}H NMR spectra were recorded on a Bruker Avance (400 MHz) spectrometer using $CDCl_3$ as the solvent. IR measurements were made on a Hitachi IR meter 260-10 for KBr pellets and only characteristic peaks were recorded. Spots were visualized with UV. HPLC (Shimadzu LC-10Avp Plus) and GC (Shimadzu GC-2014C) were utilized to determine product compositions. Microwave-assisted syntheses were carried out in a microwave reactor (IO keer WBFY-201) using a special 50 mL reaction vessel. All chemicals were analytical grade without further purification.

Typical procedure for bromination of acetophenone: To the acetophenone (2 mmol) in 1,4-dioxane (10 mL) was added 48 % aqueous solution of HBr (2 mmol) and 30 % aqueous solution of H_2O_2 (2.2 mmol). The solution was magnetically stirred at reflux temperature for 20 h. After completion the organic phase was extracted with dichloromethane for column chromatography.

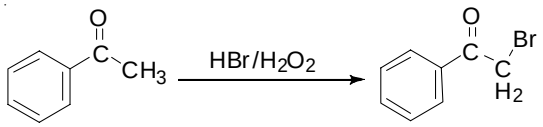
α-Bromoacetophenone: ^{1}H NMR δ, 8.27-8.10 (m, 2H), 7.89-7.78 (m, 1H), 7.65-7.60 (m, 2H), 4.39 (s, 2H); IR (KBr, ν_{max}, cm^{-1}), 3070, 3030, 1585, 1495, 1460, 3000, 1420, 1320, 1690, 1050.

Synthesis of α-hydroxyacetophenone by microwave process: To the mixture of α-bromoacetophenone (0.50 mmol) and water (8 mL) was added tetra-butylammonium chloride (0.10 mmol). Then the mxture was irradiated for 10 min by P_{50} microwaves. After completed the mixture was extracted with dichloromethane for column chromatography.

α-Hydroxyacetophenone: ^{1}H NMR δ, 8.01-7.94 (m, 2H), 7.70-7.64 (m, 1H), 7.58-7.56 (m, 2H), 4.79 (s, 2H); IR (KBr, ν_{max}, cm^{-1}), 3085, 3066, 3030, 1595, 1495, 1445, 3400, 2920, 1400, 1380, 1700, 550.

RESULTS AND DISCUSSION

Synthesis of α-bromoacetophenone with HBr/H_2O_2 system was shown in (**Scheme-I**). The effect of different solvents was evaluated and the results were summarized in (Table-1, entry1-7). When the reaction was carried out using ethers solvents (Table-1, entry 4, 6 and 7), the reaction conversion was higher. Correspondingly, the α-bromoacetophenone yield was higher. This may be due to the good solubility of α-bromoacetophenone in ether solvents caused by "polarily-matching rule". For 1,4-dioxane as solvent, the conversion was 73.2 % and the yield of α-bromoacetophenone got to 69.8 %. And with the reaction time increasing, the conversion and yield of α-bromoacetophenone also increased (Table-1, entry 7-9). In 20 h reaction, the conversion reached 73.2 % and the yield of α-bromoacetophenone was 69.8 %.



Scheme-I

TABLE-1
EFFECT OF SOLVENT IN THE SYNTHESIS OF α-BROMOACETOPHENONE[a]

Entry	Solvent	Time (h)	Conv. [b](%)	Yield [b](%)
1	Dichloromethane	20	23.0	18.7
2	*n*-Hexane	20	20.2	16.3
3	Cyclohexane	20	37.4	28.5
4	Ether	20	69.1	60.4
5	1,2-Dichloroethane	20	34.2	25.8
6	Tetrahydrofuran	20	69.5	67.7
7	1,4-Dioxane	20	73.2	69.8
8	1,4-Dioxane	16	60.1	52.7
9	1,4-Dioxane	22	74.0	69.1

[a]48 % HBr (2 mmol) and 30 % H_2O_2 (2.2 mmol) and acetophenone (2 mmol) in 1,4-dioxane (10 mL) were rapidly magnetically stirred at room temperature for 20 h; [b] Yield was determined by GC with 4-nitrotoluene an internal standard

The reaction temperature and the catalyst were also investigated to obtain the optimized condition. The results were summarized in Table-2.

With the reaction temperature rising, as shown in Table-2, the conversion and yield somewhat increased (Table-2, entry1-6). When at the refluxing temperature, the conversion of acetophenone (87.1 %) and the yield of α-bromoacetophenone obtained 86.2 %. In order to study the effect of catalyst, the catalyst was carried out under the same experimental conditions (Table-2, entry7-8). The results show that the conversion of acetophenone could be excellent, but the yield of α-bromoacetophenone got to only 12.6 and 20.7 % in the catalytic presence. Based on this result, we inferred that acetophenone has generated other products in the presence of catalyst and this suspicion has been confirmed by GC. Therefore, in the system of HBr/H_2O_2, the catalytic was useless.

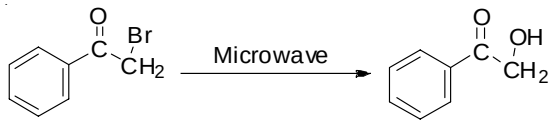
In summary, we developed a general method for the synthesis of α-bromoacetophenone using HBr/H_2O_2 system. However, α-bromoacetophenone was an intermediate and this method did not improve α-hydroxyacetophenone yield. So,

TABLE-2
EFFECT OF REACTION TEMPERATURE AND CATALYST IN THE SYNTHESIS OF α-BROMOACETOPHENONE[a]

Entry	Temp. (°C)	Conv. [b](%)	Yield [b](%)
1	25	73.2	69.8
2	40	73.3	70.2
3	50	77.1	70.6
4	65	79.3	76.2
5	75	78.8	75.0
6	Reflux	87.1	86.2
7[c]	Reflux	82.1	12.6
8[d]	Reflux	84.9	20.7

[a]48 % HBr (2 mmol) and 30 % H_2O_2 (2.2 mmol) and acetophenone (2 mmol) in 1,4-dioxane (10 mL) were rapidly magnetically stirred at room temperature for 30 min, then reflux for 20 h; [b]Yield was determined by GC using nitrobenzene as internal standard; [c]Added Tetrabutylammonium bromide for the catalytic; [d]Added polyethylene 400 for the catalytic

in order to improve the α-hydroxyacetophenone yield, the microwave synthesis method was used. It is well known that microwave heating can shorten the reaction time, accelerate the reaction rate and improve product yields[16-19]. And the synthesis of α-hydroxyacetophenone by microwave process was investigated (**Scheme-II**).



Scheme-II

As shown in Table-3, the microwave heating significantly improve the reaction yield and shorten the reaction time in comparison with heat conditions (Table-3, entry 4 and 5). With the reaction time rising (Table-3 entry 1-4), the conversion and the yield increased. Undoubtedly, microwave systhesis of α-hydroxyacetophenone is preferable.

TABLE-3
EFFECT OF REACTION TIME IN THE MICROWAVE SYNTHESIS OF α-HYDROXYACETOPHENONE[a]

Entry	Time (min)	Reaction type	Conv. [b](%)	Yield [b](%)
1	5	MW P_{10}	-	-
2	10	MW P_{10}	5.1	4.6
3	15	MW P_{10}	9.0	8.3
4	20	MW P_{10}	14.5	13.2
5[c]	20	Reflux	-	-
6[c]	300	Reflux	> 99	99

[a]α-Bromoacetophenone (0.5 mmol) in water (10 mL) was irradiated by MW power; [b]Yields were determined by GC with 4-nitrotoluene as internal standard; [c]α-Bromoacetophenone (0. 5 mmol) in water (10 mL) was reaction by heat

The phase transfer catalyst were further developed by microwave synthesis. Results were summarized in Table-4.

As the results in Table-4 indicated, when the reaction was carried out with phase transfer catalyst, the conversion and the yield were higher than the system of α-bromoacetophenone in water under microwaves alone (Table-4, entry 1-2, 3-4). It was found that catalysts play rather important roles in the synthesis of α-hydroxyacetophenone. In order to find a better phase transfer catalyst to improve reaction conversion and

TABLE-4
EFFECT OF CATALYST TYPE IN THE SYNTHESIS OF α-HYDROXYACETOPHENONE[a]

Entry	Reaction type	Catalyst	Conv. (%)[b]	Yield (%)[b]
1	MW P_{10}	-	5.1	4.6
2	MW P_{10}	Tetrabutylammonium chloride	38.3	36.4
3	MW P_{30}	-	29.7	27.3
4	MW P_{30}	Tetrabutylammonium chloride	51.6	49.8
5	MW P_{30}	Tetrabutylammonium bromide	32.8	30.1
6	MW P_{30}	Polyethylene 400	36.4	35.0
7	MW P_{30}	Benzyltriphenylphonium ammonium chloride	35.7	34.3
8	MW P_{30}	Polyethylene 20000	40.9	39.2
9[c]	MW P_{50}	Tetrabutylammonium chloride	85.7	83.7

[a]α-Bromoacetophenone (0. 5 mmol) in water (10 mL) was irradiated by microwave for 10 min; [b]Yields were determined by GC with 4-nitrotoluene as internal standard; [c]α-Bromoacetophenone (0. 5 mmol) in water (10 mL) was irradiated by microwave

yield, several phase transfer catalysts were also tested (Table-4, entry 4-8). When the reaction was carried out with tetrabutylammonium chloride as phase transfer catalyst, the conversion and yield were higher than others and the conversion got to 85.7 %, the yield of α-hydroxy acetophenone obtained 83.7 %. This could be ascribed to that tetrabutylammonium chloride was better dissolving in both aqueous phase and organic phase than other catalysts, it accelerated the hydrolysis of α-bromoacetophenone and improved the yields.

It was also found that microwave power played an important role in improvement of the reaction. The conversion and yield of α-hydroxyacetophenone under different microwave power in water were summarized in Table-5.

TABLE-5
EFFECT OF MICROWAVE POWER IN THE SYNTHESIS OF α-HYDROXYACETOPHENONE[a]

Entry	Reaction type	Conv. (%)[b]	Yield (%)[b]
1	MW P_{10}	-	-
2	MW P_{30}	40.1	37.6
3	MW P_{50}	85.7	83.7
4	MW P_{80}	89.3	77.2
5	MW P_{50}	88.9	73.1

[a]α-Bromoacetophenone (0. 5 mmol) in water (10 mL) was irradiated by microwave for 5 min; [b]Yields were determined by GC with 4-nitrotoluene as internal standard

As can be seen from Table-5, it was found that with the microwave power rising, the conversion and yield were significantly increasing (Table-5, entry1-5). But when the microwave power was MW P_{80} and MW P_{100} (Table-5, entry4-5), the yield of α-hydroxyacetophenone were decline. Based on this result, we inferred that when the microwave power was MW P_{80} and MW P_{100}, the reaction temperature got too high and α-hydroxyacetophenone was decomposition. Therefore, we selectted the microwave power as MW P_{50}.

Conclusion

In summary, α-bromoacetophenon was highly selectively prepared in high yield with a HBr/H_2O_2 system in the presence of 1,4-dioxane. HBr/H_2O_2 system has many advantages, such as simple experimental procedure, high yields of α-bromoacetophenone, a lower impact on the environment since bromine is generated *in situ* from HBr/H_2O_2. The synthesis of α-hydroacetophenone is also simple, clean and environment friendly. Microwave reaction was found significantly to improve the α-hydroacetophenone yield and shorten the reaction time of the key step reactions.

REFERENCES

1. A. Podgoršek, S. Stavber, M. Zupan and J. Iskra, *Tetrahedron Lett*., **65**, 4429 (2009).
2. C.J. Li and T.H. Chan, *Tetrahedron Lett*., **55**, 11149 (1999).
3. K. Tanemura, T. Suzuki, Y. Nishida, K. Satsumabayashi and T. Horaguchi, *Chem. Commun.*, 470 (2004).
4. B. Das, K. Venkateswarlu, G. Mahender and I. Mahender, *Tetrahedron Lett*., **46**, 3041 (2005).
5. D. Yang, Y.-L. Yan and B. Lui, *Org. Chem*., **67**, 7429 (2002).
6. I.E. Baciocch, I.M. Biett and M.F. Gerini, L. Manduchi, M. Salamone and S. Steenken, *Chemistry*, **9**, 153 (2001).
7. T. Cuvigny, G. Valette, M. Larcheveque and H.J. Normant, *Org. Chem*., **155**, 147 (1978).
8. R.M. Moriarty, H. Hu and S.C. Gupta, *Tetrahedron Lett*., **22**, 1283 (1981).
9. Y. Horiguchi, E. Nakamura and I. Kuwajima, *Tetrahedron Lett*., **30**, 3323 (1989).
10. C.A. Horiuchi, A. Takeda, W. Chai, K. Ohwada, S.J. Ji and T.T. Takahashi, *Tetrahedron Lett*., **44**, 9307 (2003).
11. W. Chai, A. Takeda, M. Hara, S.-J. Ji and C.A. Horiuchi, *Tetrahedron Lett*., **61**, 2453 (2005).
12. X. Beebe, A.M. Nilius, P.J. Merta, N.B. Soni, M.H. Bui, R. Wagner and B.A. Beutel, *Chem. Lett*., **13**, 3133 (2003).
13. S. Navath, *Synlett*, 1267 (2008).
14. T. Utsukihara, H. Nakamura, M. Watanabe and C.A. Horiuchi, *Tetrahedron Lett*., **47**, 9359 (2006).
15. A. Podgoršek, M. Zupan and J. Iskra, *Angew. Chem*., **48**, 8424 (2009).
16. K. Bougrin, A. Loupy and M.J. Soufiaoui, *Photochem. Photobiol. C*, **6**, 139 (2005).
17. G.W. Kabalka, L. Wang, V. Namboodiri and R.M. Pagni, *Tetrahedron Lett*., **41**, 5151 (2000).
18. R.K. Arvela, N.E. Leadbeater, T.L. Mack and C.M. Kormos, *Tetrahedron Lett*., **47**, 217 (2006).
19. R.K. Arvela and N.E.J. Leadbeater, *Org. Chem*., **70**, 1786 (2005).