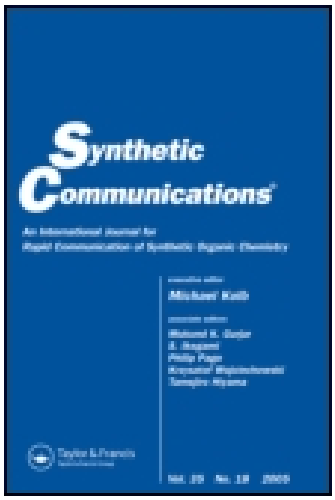

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A Simple and Selective Procedure for α-Bromination of Alkanones Using Hexamethylenetetramine-bromine Complex and Basic Alumina in Solvent-Free Conditions

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ABSTRACT

α-Bromoalkanones **2** were synthesized by the reaction of alkanones **1** with hexamethylenetetramine-bromine complex and basic alumina in solvent-free conditions under microwave irradiation.

Key Words: α-Bromoalkanones; HMTAB-bromine complex; Basic alumina; Solvent-free conditions; MW activation.

α-Bromoalkanones are the important synthons used for the synthesis of variety of biologically active heterocyclic compounds.[1–3] Generally, α-bromoalkanones have been synthesized by the reaction of alkanone

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with bromine in an appropriate solvent such as water, chloroform, carbon tetrachloride, acetic acid or *N*,*N*-dimethylformamide.[4] The reagents copper(II) bromide,[5] 1,4-dioxane bromooxonium bromide,[6] tribromoacetophenone[7] and *N*-bromosaccharin[8] have been used as alternate brominating agents instead of bromine. Furthermore, the solid organic ammonium tribromides, such as pyridinium,[9] phenyltrimethylammonium,[10] tetramethylammonium[11] and tetrabutylammonium tribromides[12] have also been used as selective brominating agents. All these reagents are quite expensive and when used make use of solvents. In these environmentally conscious days, researches have been directed to develop economic and environmentally friendly experimental procedures. Thus, there is a need to develop safe and economic method for α-bromination of alkanones.

Hexamethylenetetramine-bromine complex (HMTAB) has been used for selective oxidation[13] of primary and secondary alcohols to aldehydes and ketones, regeneration of ketones from oximes and tosylhydrazones,[14] and selective oxidation of sulfides to sulfoxides.[15] The HMTAB is yellow–orange, non-hygroscopic homogeneous solid, very stable at room temperature, not effected by ordinary exposure to light, air or water and has no offensive odour of bromine. Ease of work-up and stability of the reagent make it a safe and convenient source of active bromine. (For a review of positive halogens, see Ref.[16].) To our knowledge, HMTAB/basic alumina has not been used for α-bromination of alkanones under solvent-free conditions.

In recent years, the use of reagents impregnated over inorganic supports[17] has rapidly increased, as these reactions often involve milder conditions, easier work-up and higher selectivity than similar reactions using reagents in solution. Recently, an area of intense synthetic endeavor has emphasized the use and design of reagents without any solvent to reduce the amount of toxic waste and by-products arising from the chemical processes prompted by stringent environment protection laws. In continuation of our ongoing programme to develop synthetic protocols utilizing microwave irradiation under solvent-free conditions,[18] we wish to report here selective α-bromination of alkanones/cycloalkanones (Table 1) with HMTAB/basic alumina in solvent-free conditions under microwave irradiation.

The reaction in case of Entry 1 has been carried out using HMTAB under different conditions employing neat conditions as well as basic supports like K_2CO_3, $CaCO_3$, neutral alumina and basic alumina in order to obtain maximum yield in safer conditions. It has been found that under neat conditions lot of fumes were evolved and hence is not safe to carry out reaction in open vessel. Using K_2CO_3 and $CaCO_3$, only 20 and 30% con-

Table 1. Microwave-assisted synthesis of α-bromoalkanones/cycloalkanones using HMTAB and basic alumina (power = 300 W).

Entry	Reactant	Product	Time (min)	Yield[a] (%)	M.p. or b.p./ Lit. m.p. or b.p. (°C)
1	Acetophenone	Phenacyl bromide	6	75	46–47/48–51[19]
2	4′-Chloroacetophenone	2-Bromo-4′-chloroacetophenone	7	79	95–96/96–97[19]
3	4′-Nitroacetophenone	2-Bromo-4′-nitroacetophenone	6	80	99–100/100–101[19]
4	4′-Methylacetophenone	2-Bromo-4′-methylacetophenone	9	77	46–47/45–48[19]
5	4′-Bromoacetophenone	2-Bromo-4′-bromoacetophenone	5	76	107–108/108–110[19]
6	3′-Nitroacetophenone	2-Bromo-3′-nitroacetophenone	5	78	91–92/90–96[19]
7	4′-Methoxyacetophenone	2-Bromo-4′-methoxyacetophenone	6	73	69–70/69–71[19]
8	4′-Fluoroacetophenone	2-Bromo-4′-fluoroacetophenone	5	78	49–50/48–50[19]
9	4′-Ethoxyacetophenone	2-Bromo-4′-ethoxyacetophenone	7	80	59–60[b]
10	3′-Bromoacetophenone	2-Bromo-3′-bromoacetophenone	7	83	47–48[c]
11	4′-Cyclohexylacetophenone	2-Bromo-4′-cyclohexylacetophenone	8	75	69–70[d]
12	Cyclohexan-1-one	2-Bromocyclohexan-1-one	9	73	68–70/74[20](b.p.)
13	Cycloheptan-1-one	2-Bromocycloheptan-1-one	7	75	78–80/83[21](b.p.)
14	Cyclooctan-1-one	2-Bromocyclooctan-1-one	8	75	78/79–81[22](b.p.)
15	1-Tetralone	2-Bromo-1-tetralone	10	75	37–38/38–39[23]
16	4′-Hydroxyacetophenone	2-Bromo-4′-hydroxyacetophenone	10	70	128–129/130[24]

[a]Yield of isolated products.

[b]^{1}H NMR ($CDCl_3$): δ 1.5 (t, 3H, $-OCH_2CH_3$), 4.05 (q, 2H, $-OCH_2CH_3$), 4.5 (s, 2H, $-CH_2$), 6.60–7.10 (m, $2H_{arom}$), 8.05–8.50 (m, $2H_{arom}$). IR (KBr): 1675 cm^{-1}(C=O). *m/z*: 243 (M^+). Anal. calcd. for $C_{10}H_{11}BrO_2$: C, 49.38: H, 4.52. Found: C, 49.32; H, 4.57.

[c]^{1}H NMR ($CDCl_3$): δ 4.38 (s, 2H, $-CH_2$), 7.20–8.20 (m, $4H_{arom}$). ^{13}C NMR ($CDCl_3$): δ 190.6 (C=O), 137.46 (C1′), 132.43 (C2′), 131.09 (C5′), 130.2 (C4′), 128.1 (C6′), 123.8 (C3′), 31.46 (CH_2Br). IR (KBr): 1672 cm^{-1}(C=O). *m/z*: 278 (M^+). Anal. calcd. for $C_8H_6Br_2O$: C, 34.53; H, 2.15. Found: C, 34.48; H, 2.18.

[d]^{1}H NMR ($CDCl_3$): δ 1.0–2.1 (m, 10H, 5×$-CH_2$), 3.2 (m, 1H, CH_{hexyl}), 4.5 (s, 2H, $-CH_2$), 7.20–8.23 (m, $4H_{arom}$). IR (KBr): 1680 cm^{-1}(C=O). *m/z*: 281 (M^+). Anal. calcd. for $C_{14}H_{17}BrO$: C, 59.78; H, 6.04. Found: C, 59.73; H, 6.00.

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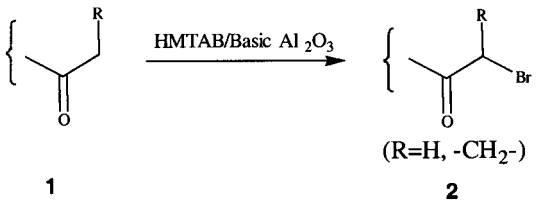

Scheme 1.

version takes place in 6 min respectively and rest products were burnt up. Further, with neutral alumina 50% conversion takes place in 5 min and rest 50% were the starting material. When basic alumina was used as support, 75% yield was obtained in 6 min. Thus, basic alumina was found to be highly efficient support compatible with HMTAB for α-bromination of alkanones/cycloalkanones (Sch. 1). No dibromination has been observed (TLC).

In conclusion, we have developed a rapid and high-yielding protocol for selective α-bromination of alkanones/cycloalkanones in the presence of HMTAB/basic alumina in solvent-free conditions under microwave irradiation. The new procedure is simple, inexpensive and eco-friendly, making it a useful alternative to existing methods.

EXPERIMENTAL

Melting points (uncorrected) were determined by Toshniwal melting point apparatus. IR spectra (ν_{max} in cm^{-1}) were recorded on Hitachi 270-30 spectrophotometer using KBr disc and ^{1}H NMR spectra on JNM-PMX 60 NMR (60 MHz) and ^{13}C NMR on Bruker DPX 200 (200 MHz) spectra in $CDCl_3$ (chemical shifts in δ, ppm) using TMS as an internal standard. The mass spectra were performed on Jeol D-300 spectrometer. Microwave irradiation was carried out using a BPL BMO 800T domestic oven having maximum power output of 800 W.

General Procedure for the Synthesis of α-Bromoalkanones/Cycloalkanones

Alkanone (3 mmol), HMTAB (5 mmol) and basic alumina (5 g) were grinded in a pestle mortar, when a homogeneous powder was obtained. This powder was then transferred in a borosil beaker (100-mL) and

irradiated in an unmodified domestic microwave oven at 300 watt for an appropriate time (Table 1, monitored by TLC). After irradiation, the contents were cooled to room temperature and extracted with methylene chloride (3×15 mL). The solid inorganic support material was filtered and the solvent was removed under reduced pressure to afford the product, which was purified by crystallization from petroleum ether (60–80°C).

The structures of the products were confirmed by IR, ^{1}H NMR, mass spectral data and comparison with authentic samples prepared according to literature methods.

REFERENCES

1. Shivarama Holla, B.; Gonsalves, R.; Sarojini, B.K.; Shenoy, S. Indian J. Chem. **2001**, *40B*, 475.
2. Martinez, R. J. Het. Chem. **1999**, *36*, 687.
3. Gupta, R.; Paul, S.; Sharma, M.; Sudan, S.; Somal, P.; Kachroo, P.L. Indian J. Chem. **1993**, *32B*, 1187.
4. (a) Levene, P.A. Org. Synth. **1943**, *II*, 88; (b) Rappe, C. Org. Synth. **1973**, *53*, 123; (c) Langley, W.D. Org. Synth. **1941**, *I*, 127; (d) Klingenberg, J.J. Org. Synth. **1963**, *IV*, 110; (e) Cowper, R.M.; Davidson, L.H. Org. Synth. **1943**, *II*, 480; (f) Pearson, D.I.; Poper, H.W.; Hargrove, W.E. Org. Synth. **1973**, *V*, 117.
5. King, L.C.; Ostrum, G.K. J. Org. Chem. **1964**, *29*, 3459.
6. Yanovskaya, L.A.; Terentev, A.P.; Belen, L.I. J. Gen. Chem. **1952**, *22*, 1594; Chem. Abstr. **1953**, *47*, 8032.
7. Krohnke, F.; Ellegast, K. Chem. Ber. **1953**, *86*, 1556.
8. Sanchez, E.I.; Fumarola, M.J. J. Org. Chem. **1982**, *49*, 1588.
9. Fieser, L.F.; Fieser, M. *Reagents for Organic Synthesis*; John Wiley and Sons: New York, 1967; Vol. I, p 967.
10. Visweswariah, S.; Prakash, G.; Bhushan, V.; Chandrasekaran, S. Synthesis **1982**, 309.
11. Avramoff, M.; Weiss, J.; Schachter, O. J. Org. Chem. **1963**, *28*, 3256.
12. Kajigaeshi, S.; Kakinami, T.; Okamoto, T.; Fujisaki, S. Bull. Chem. Soc. Jpn. **1987**, *60*, 1159.
13. Yavari, I.; Shaabani, A. J. Chem. Res. (S) **1994**, 274.
14. Bandgar, B.P.; Admane, S.B.; Jane, S.S. J. Chem. Res. (S) **1998**, 154.
15. Shaabani, A.; Teimouri, M.B.; Safaei, H.R. Synth. Commun. **2000**, *30*, 265.
16. Foucaud, A. Chem. Halides, Pseudohalides, Azides **1983**, *1*, 441.
17. Varma, R.S. Green Chem. **1999**, *1*, 43.

18. (a) Paul, S.; Nanda, P.; Gupta, R.; Loupy, A. Tetrahedron Lett. **2002**, *43*, 4261; (b) Paul, S.; Gupta, M.; Gupta, R.; Loupy, A. Synthesis **2002**, 75; (c) Paul, S.; Gupta, M.; Gupta, R.; Loupy, A. Tetrahedron Lett. **2001**, *42*, 3827; (d) Paul, S.; Gupta, R.; Loupy, A.; Rani, B.; Dandia, A. Synth. Commun. **2001**, *31*, 711; (e) Paul, S.; Gupta, M.; Gupta, M. Synlett **2000**, 1115.
19. *Aldrich Catalog Handbook of Fine Chemicals*; USA, 1999–2000.
20. Bedoukian, P.Z. J. Am. Chem. Soc. **1945**, *67*, 1430.
21. Corey, E.J. J. Am. Chem. Soc. **1953**, *75*, 2301.
22. Cope, A.C.; Johnson, H.E. J. Am. Chem. Soc. **1957**, *79*, 3889.
23. Kopping, F.S. Trans. J. Chem. Soc. **1894**, *65*, 500.
24. Buuhoi, N.P.; Xuong, N.D.; Lavit, D. J. Chem. Soc. **1954**, 1034.