

Communication

A Novel Synthesis of Bromobenzenes Using Molecular Bromine

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Received: 19 October 2007; in revised form: 6 November 2007 / Accepted: 6 November 2007 /

Published: 12 November 2007

Abstract: Certain substituted bromobenzenes have been synthesized in acceptable yields using a novel Sandmeyer type reaction. The reactions are relatively quick and possibly proceed via a radical mechanism.

Keywords: Sandmeyer reaction, bromination, bromobenzenes, diazonium salt, radical.

Introduction

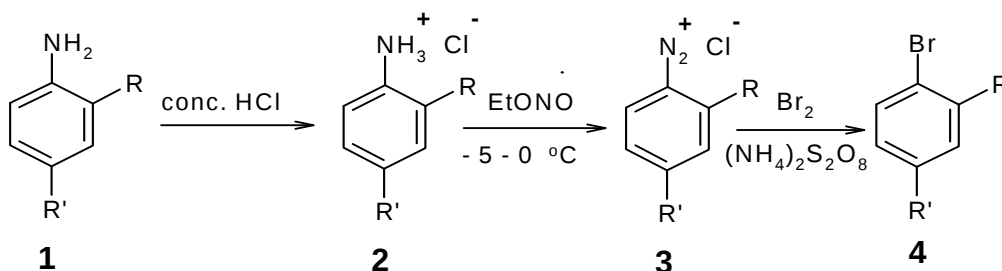
Halogenated aromatic compounds constitute an important class of chemicals that are also precursors to a number of organometallic species, which are useful in the synthesis of natural products and pharmaceutically important compounds. The manufacture of a wide range of bulk and fine chemicals, including flame retardants, disinfectants and antibacterial and antiviral drugs, involves bromination reactions [1]. Aryl bromides are often used in the syntheses of aryl esters, aryl olefins and other useful classes of compounds, consequently, numerous methods for the bromination of aromatics have been reported in the literature [2–14]. Some of the drawbacks of classical direct bromination of aromatic systems using elemental bromine as the reagent are the waste of bromine and the difficulties in selectively achieving monobromination (especially in the case of electron-rich compounds). Other methods of aromatic bromination involve the use of non-selective and hazardous acidic reagents, such

as mineral acids and metal halides, which can lead to separation difficulties and/or production of unacceptable levels of toxic and corrosive wastes. HBr had been proposed as a possible solution to overcome the difficulties confronted in direct bromination. Thus, in oxybromination, HBr is used as a bromine source and H_2O_2 /TBHP as oxidants. However, this approach has been only partially successful, since HBr is also considered highly toxic, corrosive and harmful to the environment. The well known Sandmeyer reaction [13] is another of the methods available for the preparation of halogen derivatives of aromatic compounds. The present report describes an alternative method to the Sandmeyer reaction that employs ammonium persulfate and molecular bromine instead of the classical cuprous bromide. Like the Sandmeyer reaction, the method presented requires arene diazonium salts, which are prepared in anhydrous ether media. This method gives aryl bromides in short times and in acceptable yields.

Results and Discussion

By means of the proposed method (Scheme 1), monobromobenzenes may be synthesized in the presence of other functional groups such as methyl, nitro, other halogens, etc.

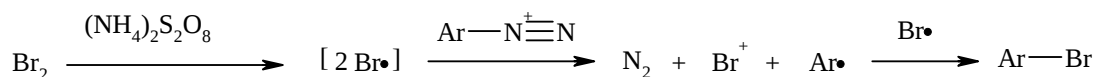
Scheme 1.



a) R: H, R': H; b) R: Cl, R': H; c) R: H, R': Cl; d) R: H, R': Br; e) R: H, R': I;
 f) R: NO_2 , R': H; g) R: H, R': NO_2 ; h) R: CH_3 , R': H; i) R: H, R': CH_3 ; j) R: COOH ,
 R': H; k) R: H, R': COOH

The reaction potentially proceeds by the sequence of reactions shown in Scheme 2, as evidenced by the fact that it does not occur thermally in the absence of persulfate acting as the radical initiator. Indeed, the reaction did not proceed at all with heat or light without any radical initiator present. The formation of gaseous BrCl was proven by sending the off-gas through a solution of AgNO_3 and observing the precipitation of silver halide.

Scheme 2.



Experimental

General

The substituted anilines and other chemicals were obtained from Merck Co. All the melting points reported were determined in sealed capillaries and are uncorrected. The boiling points were determined by simple distillation and then corrected according to the local pressure. The FT-IR spectra were recorded on a Matson 1000 spectrometer (KBr pellets). Nuclear magnetic resonance spectra were recorded on a Bruker instrument operating at 400 MHz.

Typical Procedure: Synthesis of 4-Nitrobromobenzene (**4g**)

4-Nitroaniline (1.38 g, 0.01 mol) and conc. HCl (2.7 mL, 0.04 mol) were slowly mixed. The 4-nitro anilinium salt formed was collected, dried, dissolved in absolute alcohol (30 mL) and the solution was cooled down to $-5 - 0^{\circ}\text{C}$. The mixture was then diazotized by the careful dropwise addition of ethyl nitrite (1 mL, 0.06 mol) over a period of 30 minutes. **Caution:** both the reaction mixture and the ethyl nitrite (bp 17°C) must be kept cold ($-5 - 0^{\circ}\text{C}$) during the addition. The diazonium salt formed (which precipitated upon addition of diethyl ether) was collected and washed with diethyl ether. A mixture of carbon tetrachloride (30 mL), bromine (1.6 g, 0.01 mol) and ammonium persulfate (0.1 g, 4.4×10^{-4} mol) was heated under reflux for 15 min. Then, the diazonium salt in ether was added portionwise to the bromine solution. The mixture was refluxed for 15 min. The carbon tetrachloride was evaporated on a rotary evaporator and the residue was suspended in a little amount of water and extracted with diethyl ether. The ethereal extract was dried over CaCl_2 and the ether was evaporated on a rotary evaporator. The residue was crystallized from absolute alcohol. The liquid products in cognate preparations were purified by distillation.

Characterization data

Bromobenzene (4a): Yield: 65 %; bp 154°C (lit. bp 156°C [15]); IR (KBr): 3070 cm^{-1} ; $^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta=7.5$ (m, 5H, Ar-H); MS (EI, 70 eV): m/z (%) 155 (65) [M^+ , Ar- ^{79}Br], 157 (63) [$\text{M}+2^+$, Ar- ^{81}Br].

2-Chlorobromobenzene (4b): Yield: 70 %; bp 206°C (lit bp 204°C [15]); IR (KBr): 3030 cm^{-1} ; $^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta=7.4$ (d, 1H, Ar-H), 7.6 (d, 1H, Ar-H), 7.1-7.3 (m, 2H, Ar-H); MS (EI, 70 eV): m/z (%) 190 (85) [M^+ , Ar- $^{79}\text{Br}^{35}\text{Cl}$], 192 (100) [$\text{M}+2^+$, Ar- $^{79}\text{Br}^{37}\text{Cl}$ or Ar- $^{81}\text{Br}^{35}\text{Cl}$], 194 (25) [M^+2+2 , Ar- $^{81}\text{Br}^{37}\text{Cl}$].

4-Chlorobromobenzene (4c): Yield: 68 %; mp. $65-66^{\circ}\text{C}$ (lit. mp. $66-68^{\circ}\text{C}$ [15]); IR (KBr): 3047 cm^{-1} ; $^1\text{H-NMR}$ (400 MHz, CDCl_3): $\delta=7.2$ (m, 4H, Ar-H); MS (EI, 70 eV): m/z (%) 190 (20) [M^+ , Ar- $^{79}\text{Br}^{35}\text{Cl}$], 192 (18) [$\text{M}+2^+$, Ar- $^{79}\text{Br}^{37}\text{Cl}$ or Ar- $^{81}\text{Br}^{35}\text{Cl}$], 194 (8) [M^+2+2 , Ar- $^{81}\text{Br}^{37}\text{Cl}$].

1,4-Dibromobenzene (4d): Yield: 63 %; Mp 85-88 °C (lit. mp. 87-89 °C [15]); IR (KBr): 3060 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ= 6.5 (m, 4H, Ar-H); MS (EI, 70 eV): m/z (%) 234 (50) [M⁺, Ar-⁷⁹Br⁷⁹Br], 236 (100) [M+2⁺, Ar-⁸¹Br⁷⁹Br], 238 (45) [M⁺ 2+2 , Ar-⁸¹Br⁸¹Br].

4-Iodobromobenzene (4e): Yield: 72 %; mp. 89-91 °C (lit. mp. 92 °C [15]); IR (KBr): 3040 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ=7.5 (m, 4H); MS (m/z): 282 (100) [M⁺, Ar-⁷⁹Br], 284 (95) [M+2⁺, Ar-⁸¹Br].

2-Nitrobromobenzene (4f): Yield: 75 %; mp. 41-42 °C (lit. mp. 42-43 °C [15]); IR (KBr): 3065 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ= 7.8-7.9 (dd, 2H, Ar-H), 7.5 (m, 2H, Ar-H); MS (m/z): 201 (100) [M⁺, Ar-⁷⁹Br], 203 (97) [M+2⁺, Ar-⁸¹Br].

4-Nitrobromobenzene (4g): Yield: 80 %; mp. 127 °C (lit. mp. 127 °C [15]); IR (KBr): 3050 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ= 7.8 (m, 4H, Ar-H); MS (m/z): 201 (12) [M⁺, Ar-⁷⁹Br], 203 (18) [M+2⁺, Ar-⁸¹Br].

2-Methylbromobenzene (4h): Yield: 55 %; bp. 178 °C (lit. bp. 182 °C [15]); IR (KBr): 3100, 2960 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ= 7.00-7.45 (m, 4H, Ar-H), 2.40 (s, 3H, CH₃); MS (m/z): 170 (40) [M⁺, Ar-⁷⁹Br], 172 (38) [M+2⁺, Ar-⁸¹Br].

4-Methylbromobenzene (4i): Yield: 60 %; mp. 25-26 °C (lit. mp. 25-27 °C [15]); IR (KBr): 3055 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ= 7.00 (m, 4H, Ar-H), 2.0 (s, 3H, CH₃); MS (m/z): 170 (60) [M⁺, Ar-⁷⁹Br], 172 (100) [M+2⁺, Ar-⁸¹Br].

2-Bromobenzoic acid (4j): Yield: 75 %; mp. 148-149 °C (lit. mp. 149-150 °C [15]); IR (KBr): 3400, 3000, 1680 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ= 7.7 (d, 2H, Ar-H), 8.1 (d, 2H, Ar-H); MS (m/z): 119 (100) [M⁺ - ⁸¹Br], 120 (20) [M⁺ - ⁷⁹Br].

4-Bromobenzoic acid (4k): Yield: 70 %; mp. 250-252 °C (lit. mp. 252-254 °C [15]); IR (KBr): 3425, 3020, 1684 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃): δ= 7.97 (d, 2H, Ar-H), 7.64 (d, 2H, Ar-H); MS (m/z): 200 (10) [M⁺, Ar-⁷⁹Br] , 202 (12) [M+2⁺, Ar-⁸¹Br].

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Sample Availability: Samples of compounds **4a-k** are available from the authors.

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