

Halogenation Using Quaternary Ammonium Polyhalides. VI.¹⁾ Bromination of Aromatic Amines by Use of Benzyltrimethylammonium Tribromide

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Synopsis. The reaction of aromatic amines with benzyltrimethylammonium tribromide in dichloromethane-methanol containing calcium carbonate powder for 0.5 h at room temperature gave bromo-substituted aromatic amines in good yields.

It has recently been shown in our laboratories that quaternary ammonium polyhalides such as benzyltrimethylammonium tribromide (BTMA Br₃) or tetrabutylammonium tribromide (TBA Br₃) are useful brominating agents.²⁾ In the present paper, we wish to report on a facile synthetic method of bromo-substituted aromatic amines **1** by the use of BTMA Br₃.

Results and Discussion

The reaction of aromatic amines **2** with BTMA Br₃ in dichloromethane-methanol containing calcium carbonate powder for 0.5 h at room temperature gave **1** in good yields. In these cases, the calcium carbonate powder was used in order to neutralize a generating hydrogen bromide; the reaction was remarkably promoted by the presence of methanol, as shown in previous our reports.^{2b)}

The reagent BTMA Br₃ (stable orange crystals, mp 100—101 °C)^{2c)} has one merit in that it can be quantitatively treated, compared with liquid bromine, because

Table 1. Bromination of Aromatic Amines **2** using Benzyltrimethylammonium Tribromide (BTMA Br₃)

	Substrate 2	Product 1	Molar ratio (BTMA Br ₃ / 2)	Yield ^{a)} %	Mp θ _m /°C	
					Found	Reported
1			3.1	93	121—123	119—120 ⁴⁾
2			2.1	94	44—45	45—46 ⁵⁾
3			3.1	91	101—102	100—101.6 ⁶⁾
4			2.1	94	75—76	79 ⁷⁾
5			2.1	92	18—20	—
6			3.1	94	68—70	—
7			2.1	95	80—82	85 ⁸⁾
8			2.1	93	56—57	56 ⁹⁾
9			1.1	91	46—47	47—48 ¹⁰⁾
10			2.1	92	64.5—66	65 ¹¹⁾

Table 1. (Continued)

	Substrate 2	Product 1	Molar ratio (BTMA Br ₃ /2)	Yield ^{a)} %	Mp θ_m /°C	
					Found	Reported
11			1.1	83	47—48	49—50 ¹²⁾
12			2.1	95	58—59	63 ⁹⁾
13			3.1	91	196—197	195 ⁹⁾
14			2.1	68 ^{b)}	25—26	27 ¹³⁾
15			3.1	95	83—84	—
16			2.1	78 ^{b)}	79—80	81 ¹⁴⁾
17			2.1	71 ^{b)}	53.5—54.5	52.5 ¹⁵⁾
18			3.1	93	93—94	—
19			2.1	78 ^{b)}	72—73	80 ¹⁶⁾
20			3.1	93	37—39	39 ¹⁷⁾
21			2.1	95	93—94	94 ¹⁸⁾
22			2.1	91	121—123	119—120 ⁴⁾
23			1.1	93	65.5—66.5	64.5 ¹⁹⁾
24			1.1	91	183	180.3—181.3 ²⁰⁾
25			2.1	95	103—104	105 ²¹⁾
26			2.1	95	105.5	104 ²²⁾
27			2.1	80 ^{b)}	81—82	82 ²³⁾
28			4.1	90	189—190	182 ²⁴⁾
29			4.1	95	142	142 ²⁴⁾

a) Yield of isolated product. b) Product was isolated by column chromatography on alumina.

of its solid character. Furthermore, the end point of a reaction can be easily confirmed by a decolorization of the orange-colored solution. The results are summarized in Table 1.

Recently, Berthelot et al. reported that TBA Br₃ is a useful para-selective monobrominating agent for aromatic amines.³⁾ However, the reaction of aromatic amines with BTMA Br₃ gave polybromo-substituted aromatic amines since BTMA Br₃ is a stronger brominating agent than TBA Br₃.²⁵⁾ Syntheses of bromomethoxyanilines and bromomethylnitroanilines are usually difficult. Our method easily gave these compounds in good yields.

We believe that the procedure for the bromination of aromatic amines using BTMA Br₃ is a highly useful method owing to its ease, simplicity, mildness of conditions, and good product yields.

Experimental

2,4,6-Tribromoaniline (1-1); General procedure: To a solution of aniline (2-1) (0.50 g, 5.37 mmol) in dichloromethane (50 ml)-methanol (20 ml) was added BTMA Br₃ (6.49 g, 16.64 mmol) and calcium carbonate powder (2 g) at room temperature. The mixture was stirred for 30 min until a fading of the orange color took place. The solid calcium carbonate was filtered off, the filtrate was concentrated and to the obtained residue was added water (20 ml). The mixture was extracted with ether (40 ml×4). The ether layer was then dried with magnesium sulfate and evaporated in vacuo to give a residue which was recrystallized from methanol-water (1:3) affording 1-1 as colorless crystals; yield 1.65 g (93%); Mp 121–123 °C (lit.⁴⁾ Mp 119–120 °C).

2,4-Dibromo-6-ethylaniline (1-5): Mp 18–20 °C (1:3 methanol-water); ¹H NMR (CDCl₃) δ=1.15 (3H, t, J=7 Hz, CH₃), 2.38 (2H, q, J=7 Hz, CH₂), 4.10 (2H, s, NH₂), 6.98 (1H, d, J=2 Hz, 3-H), and 7.33 (1H, d, J=2 Hz, 5-H). Found: C, 34.17; H, 3.09; N, 4.58; Br, 56.97%. Calcd for C₈H₉NBr₂: C, 34.44; H, 3.25; N, 5.02; Br, 57.28%.

2,4,6-Tribromo-3-ethylaniline (1-6): Mp 68–70 °C (1:3 methanol-water); ¹H NMR (CDCl₃) δ=1.12 (3H, t, J=7 Hz, CH₃), 4.00 (2H, q, J=7 Hz, CH₂), 4.50 (2H, br. s, NH₂), and 7.50 (1H, s, 5-H). Found: C, 26.75; H, 2.45; N, 4.16; Br, 67.09%. Calcd for C₈H₈NBr₃: C, 26.85; H, 2.25; N, 3.91; Br, 66.96%.

2,4,6-Tribromo-3-methoxyaniline (1-15): Mp 83–84 °C (1:3 methanol-water); ¹H NMR (CDCl₃) δ=3.83 (3H, s, OCH₃), 4.63 (2H, br. s, NH₂), and 7.52 (1H, s, 5-H). Found: C, 23.37; H, 1.99; N, 4.15; Br, 66.46%. Calcd for C₇H₆NOBr₃: C, 23.37; H, 1.68; N, 3.89; Br, 66.61%.

2,4,6-Tribromo-3-ethoxyaniline (1-18): Mp 93–94 °C (1:3 methanol-water); ¹H NMR (CDCl₃) δ=1.44 (3H, t, J=7 Hz, CH₃), 4.00 (2H, q, J=7 Hz, CH₂), 4.50 (2H, s, NH₂), and

7.50 (1H, s, 5-H). Found: C, 25.64; H, 2.36; N, 3.97; Br, 64.25%. Calcd for C₈H₈NOBr₃: C, 25.70; H, 2.16; N, 3.75; Br, 64.12%.

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- 25) For instance, the reaction of 4-methyl-2-nitroaniline (2-23) with an equimolecular amount of BTMA Br₃ in dichloromethane-methanol for 0.5 h at room temperature gave 2-bromo-4-methyl-6-nitroaniline (1-23) in 93% yield. However, the treatment of 2-23 with TBA Br₃ under the same conditions described above gave a mixture of 1-23 and 2-23 (7:3 on its ¹H NMR spectrum).