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

Shoji Kajigaeshi,* Takaaki Kakinami,† Kazuhisa Inoue,† Manabu Kondo,†
Hiroko Nakamura,† Masahiro Fujikawa,† and Tsuyoshi Okamoto†
Department of Industrial Chemistry, Faculty of Engineering, Yamaguchi University, Tokiwadai, Ube 755
†Department of Industrial Chemistry, Ube Technical College, Tokiwadai, Ube 755

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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 Br_3) or tetrabutylammonium tribromide (TBA Br_3) 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 Br_3.

Results and Discussion

The reaction of aromatic amines **2** with BTMA Br_3 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 Br_3 (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 Br_3)

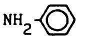
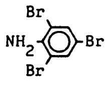
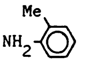
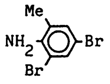
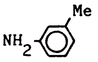
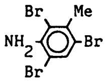
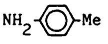
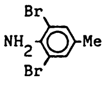
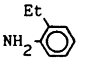
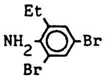
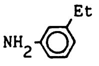
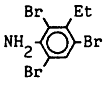
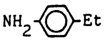
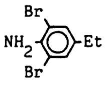
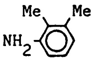
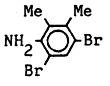
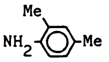
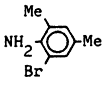
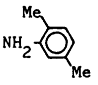
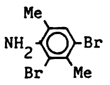
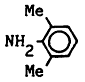
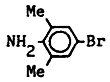
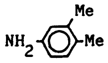
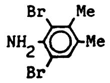
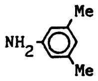
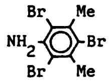
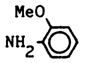
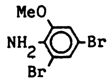
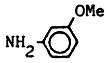
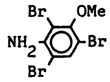
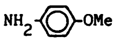
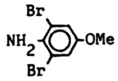
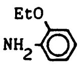
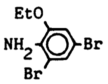
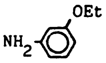
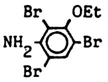
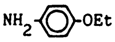
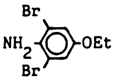
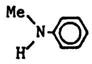
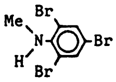
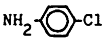
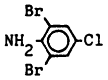
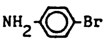
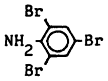
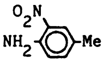
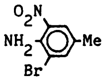
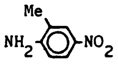
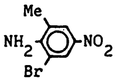
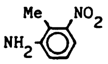
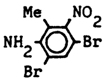
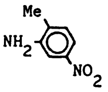
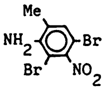
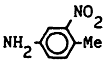
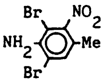
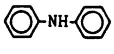
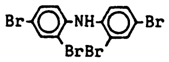
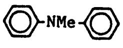
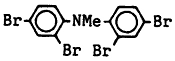
	Substrate **2**	Product **1**	Molar ratio (BTMA Br_3/**2**)	Yield[a)] %	Mp θ_m/°C Found	Mp θ_m/°C Reported
1			3.1	93	121—123	119—120[4)]
2			2.1	94	44—45	45—46[5)]
3			3.1	91	101—102	100—101.6[6)]
4			2.1	94	75—76	79[7)]
5			2.1	92	18—20	—
6			3.1	94	68—70	—
7			2.1	95	80—82	85[8)]
8			2.1	93	56—57	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 Br_3 is a useful para-selective monobrominating agent for aromatic amines.[3)] However, the reaction of aromatic amines with BTMA Br_3 gave polybromo-substituted aromatic amines since BTMA Br_3 is a stronger brominating agent than TBA Br_3.[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 Br_3 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 Br_3 (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); ^{1}H NMR ($CDCl_3$) δ=1.15 (3H, t, J=7Hz, CH_3), 2.38 (2H, q, J=7Hz, CH_2), 4.10 (2H, s, NH_2), 6.98 (1H, d, J=2Hz, 3-H), and 7.33 (1H, d, J=2Hz, 5-H). Found: C, 34.17; H, 3.09; N, 4.58; Br, 56.97%. Calcd for $C_8H_9NBr_2$: 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); ^{1}H NMR ($CDCl_3$) δ=1.12 (3H, t, J=7 Hz, CH_3), 4.00 (2H, q, J=7 Hz, CH_2), 4.50 (2H, br. s, NH_2), and 7.50 (1H, s, 5-H). Found: C, 26.75; H, 2.45; N, 4.16; Br, 67.09%. Calcd for $C_8H_8NBr_3$: 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); ^{1}H NMR ($CDCl_3$) δ=3.83 (3H, s, OCH_3), 4.63 (2H, br. s, NH_2), and 7.52 (1H, s, 5-H). Found: C, 23.37; H, 1.99; N, 4.15: Br, 66.46%. Calcd for $C_7H_6NOBr_3$: 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), ^{1}H NMR ($CDCl_3$) δ=1.44 (3H, t, J=7 Hz, CH_3), 4.00 (2H, q, J=7 Hz, CH_2), 4.50 (2H, s, NH_2), and 7.50 (1H, s, 5-H). Found: C, 25.64; H, 2.36; N, 3.97; Br, 64.25%. Calcd for $C_8H_8NOBr_3$: 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 Br_3 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 Br_3 under the same conditions described above gave a mixture of **1-*23*** and **2-*23*** (7:3 on its ^{1}H NMR spectrum).