

Bromination of Aromatic Amines by Use of Benzyltrimethylammonium Chlorobromate (1-)¹⁾

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Abstract

The reaction of aromatic amines with benzyltrimethylammonium chlorobromate (1-) in dichloromethane-methanol containing calcium carbonate powder at room temperature easily gave bromo-substituted aromatic amines in good yields.

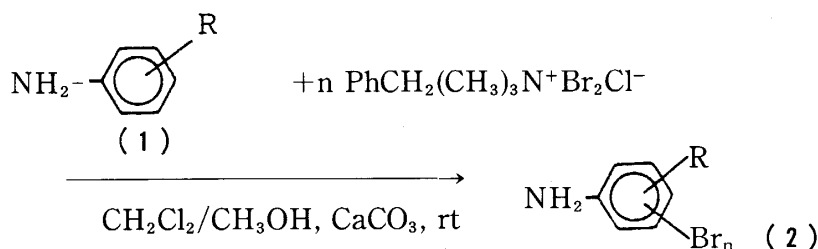
Introduction

Recent work in this series has shown that the reaction of aromatic amines (1) with benzyltrimethylammonium tribromide (BTMA Br₃) in dichloromethane-methanol containing calcium carbonate powder at room temperature readily gave bromo-substituted aromatic amines (2).²⁾ In this paper, we wish to report a bromination of 1 by use of a more effective reagent, benzyltrimethylammonium chlorobromate (1-) (BTMA Br₂Cl).

Results and Discussion

The reagent, BTMA Br₂Cl, was prepared from the reaction of benzyltrimethylammonium chloride with equimolar amount of bromine in dichloromethane, as shown in previous our report.³⁾

The reaction of 1 with BTMA Br₂Cl in dichloromethanemethanol in the presence of calcium carbonate powder for several minutes at room temperature gave 2 in good yields. The results are summarized in Table 1.




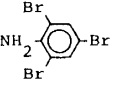
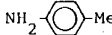
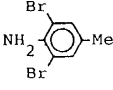
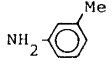
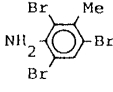

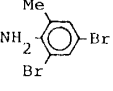
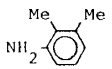
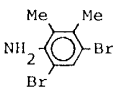
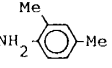
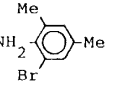
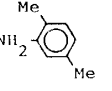
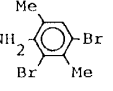

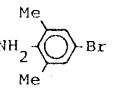
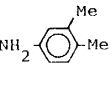
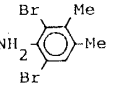
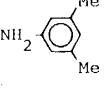
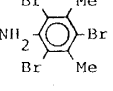
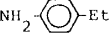
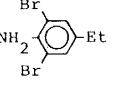
We noticed that the presence of methanol markedly facilitated the bromination of 1. In these cases, the main active species is probably methyl hypobromite produced from

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Table 1 Bromination of Aromatic Amines by Use of BTMA Br₂Cl

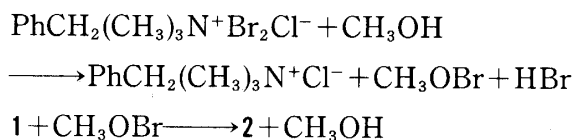
Substrate (1)	Product ^{a)} (2)	Molar ratio (BTMA Br ₂ Cl/1)	Reaction time/min	Yield ^{b)} %	Mp(°C)		¹ H NMR (CDCl ₃) δ=ppm
					found	reported	
a 		3.1	2	90	121-123	119-120 ⁴⁾	4.33(2H, br.s, NH ₂) 7.47(2H, s, 3,5-H)
b 		2.1	5	94	76-77	79 ⁵⁾	2.15(3H, s, CH ₃) 4.38(2H, br.s, NH ₂) 7.11(2H, s, 3, 5-H)
c 		3.1	5	93	102-104	100-101.6 ⁶⁾	2.47(3H, s, CH ₃) 4.45(2H, br.s, NH ₂) 7.52(1H, s, 5-H)
d 		2.1	5	93	50-51	45-46 ⁷⁾	2.02(3H, s, CH ₃) 3.91(2H, br.s, NH ₂) 7.00(1H, s, 5-H) 7.33(1H, s, 3-H)
e 		2.1	5	91	62-63	56 ⁸⁾	2.10(3H, s, 6-CH ₃) 2.28(3H, s, 5-CH ₃) 3.91(2H, br.s, NH ₂) 7.42(1H, s, 3-H)
f 		1.1	5	94	44-46	47-48 ⁹⁾	2.11(3H, s, 6-CH ₃) 2.15(3H, s, 4-CH ₃) 3.82(2H, br.s, NH ₂) 6.76(1H, s, 5-H) 7.07(1H, s, 3-H)
g 		2.1	5	92	65-67	65 ¹⁰⁾	2.08(3H, s, 6-CH ₃) 2.47(3H, s, 3-CH ₃) 4.00(2H, br.s, NH ₂) 7.08(1H, s, 5-H)
h 		1.1	5	87	51-53	49-50 ¹¹⁾	2.10(6H, s, CH ₃) 3.44(2H, br.s, NH ₂) 6.98(2H, s, 3, 5-H)
i 		2.1	5	99	65-66	63 ⁸⁾	2.19(3H, s, 4-CH ₃) 2.29(3H, s, 3-CH ₃) 4.44(2H, br.s, NH ₂) 7.17(1H, s, 5-H)
j 		3.1	5	92	196-198	195 ⁸⁾	2.56(6H, s, CH ₃) 4.63(2H, br.s, NH ₂)
k 		2.1	5	97	81-83	85 ¹²⁾	1.18(3H, t, J = 7.8 Hz, CH ₂ CH ₃) 2.50(2H, dd, J = 6.0 Hz, CH ₂ CH ₃) 4.34(2H, br.s, NH ₂) 8.22(2H, s, 3, 5-H)

l			2.1	5	99	oil	18-20 ²⁾	1.16(3H, t, J = 7.5 Hz, CH ₂ CH ₃) 2.43(2H, dd, J = 7.5 Hz, CH ₂ CH ₃) 4.13(2H, br.s, NH ₂) 7.08(1H, s, 5-H) 7.37(1H, s, 3-H)
m			2.1	5	75	81-82	81 ¹⁵⁾	3.70(3H, s, OCH ₃) 4.16(2H, br.s, NH ₂) 7.00(2H, s, 3, 5-H)
n			3.1	5	82	84-87	83-84 ²⁾	3.89(3H, s, OCH ₃) 4.66(2H, br.s, NH ₂) 7.60(1H, s, 5-H)
o			2.1	5	75	oil	27 ¹⁴⁾	3.88(3H, s, OCH ₃) 4.25(2H, br.s, NH ₂) 6.88(1H, d, J = 1.5 Hz, 5-H) 7.25(1H, d, J = 1.5 Hz, 3-H)
p			2.1	5	57	74-75.5	80 ¹⁵⁾	1.36(3H, t, J = 7.8 Hz, OCH ₂ CH ₃) 3.97(2H, dd, J = 6.0 Hz, OCH ₂ CH ₃) 4.23(2H, br.s, NH ₂) 7.11(2H, s, 3, 5-H)
q			2.1	10	93	97-98	94 ¹⁶⁾	4.44(2H, br.s, NH ₂) 7.40(2H, s, 3, 5-H)
r			2.1	10	91	122-124	119-120 ⁴⁾	4.54(2H, br.s, NH ₂) 7.51(2H, s, 3, 5-H)
s			2.1	30	90	206-207	206-207 ¹⁷⁾	6.80(2H, br.s, NH ₂) 8.35(2H, s, 3, 5-H)
t			2.1	23 (hr)	96	131-132	127 ¹⁸⁾	7.31(2H, br.s, NH ₂) 8.04(1H, d, J = 1.5 Hz, 3-H) 8.19(1H, d, J = 1.5 Hz, 5-H)
u			2.5	30	98	107.5-108	104 ¹⁹⁾	2.22(3H, s, CH ₃) 4.39(2H, br.s, NH ₂) 7.22(1H, s, 5-H)
v			2.5	30	84	106.5-107	105 ²⁰⁾	2.16(3H, s, CH ₃) 4.44(2H, br.s, NH ₂) 7.65(1H, s, 3-H)
w			2.5	2.5 (hr)	99	82.5-83.5	82 ²¹⁾	2.20(3H, s, CH ₃) 4.70(2H, br.s, NH ₂) 7.32(1H, s, 5-H)

a) Structures of known products were also confirmed by their ¹H NMR spectra.

b) Yield of isolated product.

the reaction of BTMA Br₂Cl with methanol. In fact, we confirmed the evolution of hydrogen bromide by the addition of BTMA Br₂Cl into methanol at room temperature. The reaction of **1** with the active intermediate methyl hypobromite must give **2** and methanol which can be employed repeatedly. Hydrogen bromide generated should be neutralized by added calcium carbonate.



As shown in Table 1, the reaction times for the bromination of **1** using BTMA Br₂Cl are quite short compared with BTMA Br₃.²⁾ That is, BTMA Br₂Cl is a stronger brominating agent for **1** than BTMA Br₃.

Although exhaustive dibromination of nitroanilines (e.g., **1s**, **1t**) with 2 equiv. of BTMA Br₃ was not so easy, no matter how long a time was taken,²²⁾ reaction of the nitroanilines with 2 equiv. of BTMA Br₂Cl gave desired dibromo-substituted nitroanilines (e.g., **2s**, **2t**) in good yields (see Table 1). That is, BTMA Br₂Cl is particularly useful and effective brominating agents for relatively inactive aromatic amines such as nitroaniline derivatives.

However, as a limitation of the procedure using BTMA Br₂Cl, attempts at the selective mono-bromination of **1** were unsuccessful.

Experimental

2,4,6-Tribromoaniline (**2a**), Typical Procedure.

To a solution of aniline (**1a**) (0.50g, 5.37 mmol) in dichloromethane (50 ml)–methanol (20ml) was added BTMA Br₂Cl (5.75g, 16.64 mmol) and calcium carbonate powder (2g) at room temperature. The mixture was stirred for only 2 min until a fading of the orange color took place. Excess calcium carbonate was filtered and the filtrate was concentrated; then, to the obtained residue was added a sodium hydrogensulfite solution (5%, 20ml). The mixture was extracted with ether (40ml × 4). The ether layer was dried with magnesium sulfate and evaporated in vacuo to give a residue which was recrystallized from methanol–water (1 : 3) affording **2a** as colorless crystals; yield 1.59g (90%); mp 121–123°C (Lit.,⁴⁾ mp 119–120°C).

References and Notes

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- 22) The treatment of 2-nitroaniline (1t) with BTMA Br₃ instead of BTMA Br₂Cl under the similar conditions (see Table), gave a mixture of the starting material 1t, 2-nitro-4-bromoaniline and 2t in the ratio of 1 : 2 : 6 on its ¹H NMR spectrum.