NOTES Bull. Chem. Soc. Jpn., 61, 600—602 (1988) [Vol. 61, No. 2

Halogenation Using Quaternary Ammonium Polyhalides. VII.[1) Iodination of Aromatic Amines by Use of Benzyltrimethylammonium Dichloroiodate(1−)

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(Received July 11, 1987)

Synopsis. The reaction of aromatic amines with benzyltrimethylammonium dichloroiodate(1−) in dichloromethane-methanol in the presence of calcium carbonate powder for several hours at room temperature gave selectively iodo-substituted aromatic amines in good yields.

Recent work in this series has shown that a new reagent, benzyltrimethylammonium dichloroiodate (1−) (BTMA ICl_2), is an excellent iodinating agent to phenols.[2) In the present paper we wish to also report on a selective iodination of aromatic amines **1** by the use of BTMA ICl_2.

Results and Discussion

The reaction of **1** with BTMA ICl_2 in dichloromethane-methanol in the presence of calcium carbonate powder for several hours at room temperature gave iodo-substituted aromatic amines **2** in good yields.

Usually, the reaction of aniline, toluidines and xylidines with calculated amounts of BTMA ICl_2 gave the desirable mono- and diiodo-substituted corresponding aromatic amines. For instance, the reaction of aniline (**1a**) with 1.0 equiv of BTMA ICl_2 gave 4-iodoaniline (**2a**) in 94% yield, and with 2.1 equiv of BTMA ICl_2 gave 2,4-diiodoaniline (**2b**) in 75% yield, respectively. That is, the iodination of these compounds first occurred at the para-position of the amino group and subsequent iodination at the ortho-position.

However, as a limitation of this new iodination method by use of BTMA ICl_2, the reaction was unsuccessfully carried out with less reactive nitroanilines. The results are summarized in Table 1.

We noticed that the presence of methanol markedly facilitated the iodination of **1**. In this case, the main active species which generates I^+ is probably methyl hypoiodite produced from a reaction of BTMA ICl_2 with methanol. The reaction of **1** with the active intermediate methyl hypoiodite must give **2** and methanol, which can be empolyed repeatedly. The generated hydrogen chloride should be neutralized by additional calcium carbonate.

$$\mathrm{PhCH_2(CH_3)_3N^+ICl_2^- + CH_3OH}$$
$$\mathrm{\rightarrow PhCH_2(CH_3)_3N^+Cl^- + CH_3OI + HCl}$$
$$\mathbf{1} + \mathrm{CH_3OI} \rightarrow \mathbf{2} + \mathrm{CH_3OH}$$

Experimental

Benzyltrimethylammonium Dichloroiodate(1−) (BTMA ICl_2): To a black solution of ICl (16.20 g, 0.1 mol) in dichloromethane (200 ml) was added dropwise a solution of benzyltrimethylammonium chloride (18.60 g, 0.1 mol) in water (100 ml) under stirring at room temperature. After the mixture was stirred for 30 min, the dichloromethane layer was separated and dried with magnesium sulfate, and then evaporated in vacuo to give a residue which was recrystallized from dichloromethane-ether (3 : 1) affording BTMA ICl_2 as stable brilliant yellow needles; yield 30.0 g (86%); Mp 125—125 °C. Found: C, 34.51; H, 4.67; N, 4.11%. Calcd for $C_{10}H_{16}NCl_2I$: C, 34.50; H, 4.63; N, 4.03%.

4-Iodoaniline (2a). Typical Procedure: To a solution of aniline (0.50 g, 5.37 mmol) in dichloromethane (50 ml)-methanol (20 ml) was added BTMA ICl_2 (1.87 g, 5.37 mmol) and calcium carbonate (0.7 g). The mixture was stirred for 30 min at room temperature, during which the color of the solution gradually changed from yellow to light brown. Excess calcium carbonate was filtered and filtrate was concentrated; then, to the obtained residue was added a $NaHSO_3$ solution (5%, 20 ml). The mixture was extracted with ether (40 ml×4). The ether layer was dried with $MgSO_4$ and evaporated in vacuo to give **2a** as colorless crystals (from 1 : 3 methanol-water); yield 1.13 g (96%); Mp 66 °C (lit,[3) Mp 67—68 °C).

4,6-Diiodo-2-methylaniline (2d): Mp 80—81 °C (1 : 3 methanol-water); ^{1}H NMR ($CDCl_3$) δ= 2.20 (3H, s, CH_3), 4.10 (2H, br. s, NH_2), 7.30 (1H, d, J=3 Hz, 3-H), and 7.80 (1H, d, J=3 Hz, 5-H). Found: C, 23.40; H, 1.87; N, 3.69%. Calcd for $C_7H_7NI_2$: C, 23.42; H, 1.97; N, 3.90%.

4-Iodo-2,3-dimethylaniline (2i): Mp 56 °C (1 : 3 methanol-water); ^{1}H NMR ($CDCl_3$) δ=2.15 (3H, s, 2-CH_3), 3.33 (3H, s, 3-CH_3), 3.59 (2H, s, NH_2), 6.33 (1H, d, J=8 Hz, 6-H), and 7.50 (1H, d, J=8 Hz, 5-H). Found: C, 38.90; H, 3.96; N, 5.59%. Calcd for $C_8H_{10}NI$: C, 38.89; H, 4.08; N, 5.67%.

4,6-Diiodo-2,3-dimethylaniline (2j): Mp 89—90 °C (1 : 3 methanol-water); ^{1}H NMR ($CDCl_3$) δ= 2.23 (3H, s, 2-CH_3), 2.41 (3H, s, 3-CH_3), 3.94 (2H, br. s, NH_2), and 7.95 (1H, s, 5-H). Found: C, 25.83; H, 2.48; N, 3.85%. Calcd for $C_8H_9NI_2$: C, 25.76; H, 2.43; N, 3.76%.

4-Iodo-2,5-dimethylaniline (2k): Mp 69 °C (1 : 3 methanol-water); ^{1}H NMR ($CDCl_3$) δ=2.06 (3H, s, 2-CH_3), 2.29 (3H, s, 5-CH_3), 3.55 (2H, s, NH_2), 6.69 (1H, s, 6-H), and 7.44 (1H, s, 3-H). Found: C, 38.96; H, 4.09; N, 5.64%. Calcd for $C_8H_{10}NI$: C, 38.89; H, 4.08; N, 5.67%.

4,6-Diiodo-2,5-dimethylaniline (2l): Mp 105—106 °C (1 : 3 methanol-water); ^{1}H NMR ($CDCl_3$) δ= 2.25 (3H, s, 2-CH_3), 2.83 (3H, s, 5-CH_3), 4.25 (2H, br. s, NH_2), and 7.52 (1H, s, 3-H). Found: C, 25.82; H, 2.45; N, 3.87%. Calcd for $C_8H_9NI_2$: C, 25.76; H, 2.43; N, 3.76%.

4-Iodo-3,5-dimethylaniline (2m): Mp 112—113 °C (1 : 3 methanol-water); ^{1}H NMR ($CDCl_3$) δ=2.36 (6H, s, 3 and 5-CH_3), 3.53 (2H, br. s, NH_2), and 6.44 (2H, s, 2 and 6-H). Found: C, 38.99; H, 4.10; N, 5.53%. Calcd for $C_8H_{10}NI$: C, 38.89; H, 4.08; N, 5.67%.

2,4-Diiodo-3,5-dimethylaniline (2n): Mp 95—96 °C (1 : 3 methanol-water); ^{1}H NMR ($CDCl_3$) δ=2.35 (3H, s, 5-CH_3), 2.80 (3H, s, 3-CH_3), 4.02 (2H, s, NH_2), and 6.50 (1H, s, 6-H). Found: C, 25.83; H, 2.45; N, 3.87%. Calcd for $C_8H_9NI_2$: C,

Table 1. Iodo Aromatic Amines **2** from Aromatic Amines **1**

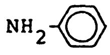
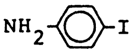
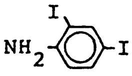
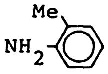
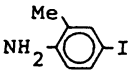
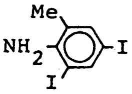
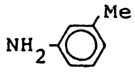
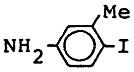
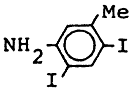
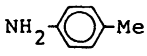
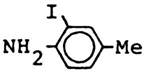
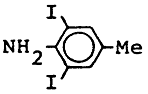
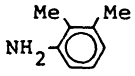
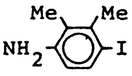
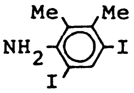
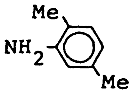
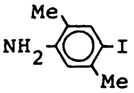
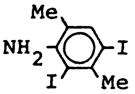
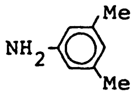
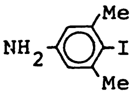
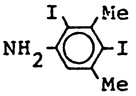
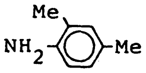
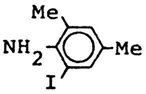
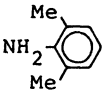
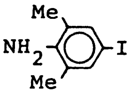
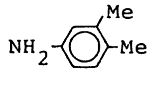
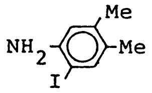
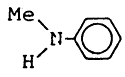
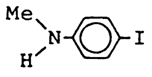
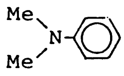
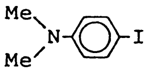
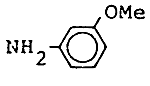
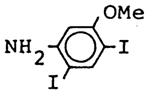
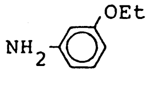
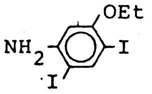
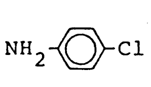
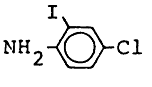
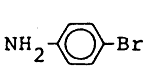
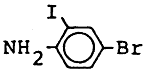
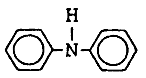
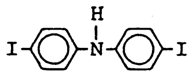
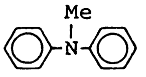
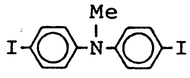
	Substrate **1**	Product **2**	Molar ratio (BTMA ICl_2/**1**)	Reaction time/h	Yield[a]	Mp θ_m/°C	
					%	Found	Reported
a			1.0	0.5	94	66	67—68[3]
b			2.1	2.0	75	94—94.5	95—95.5[4]
c			1.0	2.0	92	88.5—89.5	86—88[5]
d			2.1	4.0	89	80—81	—
e			1.0	1.0	81	46.5—47	46[6]
f			2.1	8.0	96	68—71	73—74[7]
g			1.0	2.5	77	37—39	40[8]
h			2.1	4.0	73	123.5—125	124.5[4]
i			1.0	0.5	75	56	—
j			2.1	8.0	94	89—90	—
k			1.0	0.5	87	69	—
l			2.1	8.0	95	105—106	—
m			1.0	0.5	96	112—113	—
n			2.1	1.0	86	95—96	—
o			1.1	1.0	82	64.5—65.5	65[9]
p			1.1	1.0	96	56	52—53[9]

Table 1. (Continued)

	Substrate **1**	Product **2**	Molar ratio (BTMA ICl_2/**1**)	Reaction time/h	Yield[a) %]	Mp θ_m/°C Found	Mp θ_m/°C Reported
q			1.1	0.5	87	51—52.5	—
r			1.0	0.5	88	31.5	—
s			1.0	1.0	85	73—74	78—79[8)]
t			2.1	8.0	92	120—121	—
u			2.1	8.0	96	70.5—71.5	—
v			1.1	8.0	86	39.5—40.5	46[10)]
w			1.1	8.0	89	71	71[10)]
x			2.1	4.0	96	123—124	—
y			2.1	4.0	96	122—123	—

a) Yield of isolated product.

25.76; H, 2.43; N, 3.76%.

6-Iodo-3,4-dimethylaniline (2o): Mp 51—52.5 °C (1:3 methanol-water); ^{1}H NMR ($CDCl_3$) δ=2.12 (6H, s, 3 and 4-CH_3), 3.73 (2H, s, NH_2), 6.58 (1H, s, 2-H), and 7.42 (1H, s, 5-H). Found: C, 38.79; H, 4.17; N, 5.57%. Calcd for $C_8H_{10}NI$: C, 38.89; H, 4.08: N, 5.67%.

4-Iodo-*N*-methylaniline (2r): Mp 31.5 °C (1:3 methanol-water); ^{1}H NMR ($CDCl_3$) δ=2.79 (3H, s, CH_3), 3.73 (1H, br. s, NH), 6.36 (2H, d, J=8 Hz, 2 and 6-H), and 7.41 (2H, d, J=8 Hz, 3 and 5-H). Found: C, 35.90; H, 3.61; N, 5.78%. Calcd for C_7H_8NI: C, 36.08; H, 3.46; N, 6.01%.

4,6-Diiodo-3-methoxyaniline (2t): Mp 120—121 °C (1:3 methanol-water); ^{1}H NMR ($CDCl_3$) δ=3.37 (3H, s, OCH_3), 3.98 (2H, br. s, NH_2), 6.23 (1H, s, 2-H), and 7.83 (1H, s, 5-H). Found: C, 22.44; H, 1.84; N, 3.70%. Calcd for $C_7H_7NOI_2$: C, 22.42; H, 1.88; N, 3.74%.

4,6-Diiodo-3-ethoxyaniline (2u): Mp 70.5—71.5 °C (1:3 methanol-water); ^{1}H NMR ($CDCl_3$) δ=1.38 (3H, t, J=11 Hz, CH_3), 3.87 (2H, q, J=11 Hz, CH_2), 4.20 (2H, br. s, NH_2), 6.18 (1H, s, 2-H), and 7.80 (1H, s, 5-H). Found: C, 24.82; H, 2.08; N, 3.75%. Calcd for $C_8H_9NOI_2$: C, 24.70; H, 2.33; N, 3.60%.

4,4′-Diiododiphenylamine (2x): Mp 123—124 °C (1:3 methanol-water); ^{1}H NMR ($CDCl_3$) δ=4.72 (1H, br. s, NH), 6.83 (4H, d, J=15Hz, 2,2′,6,6′-H), and 7.53 (4H, d, J=15 Hz, 3,3′,5,5′-H). Found: C, 34.44; H, 2.00; N, 3.35%. Calcd for $C_{12}H_9NI_2$: C, 34.23; H, 2.15; N, 3.33%.

4,4′-Diiodo-*N*-methyldiphenylamine (2y): Mp 122—123 °C (1:3 methanol-water); ^{1}H NMR ($CDCl_3$) δ=3.37 (3H, s, CH_3), 6.90 (4H, d, J=15 Hz, 2,2′,6,6′-H), and 7.63 (4H, d, J=15 Hz, 3,3′5,5′-H). Found: C, 35.88; H, 2.39; N, 3.06%. Calcd for $C_{13}H_{11}NI_2$: C, 35.89; H, 2.55; N, 3.22%.

We wish to thank Dr. Mamoru Nakai and Mr. Katsumasa Harada, Ube Laboratory, Ube Industries, Ltd., for elemental analysis.

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