

Iodination of Aromatic Ethers by Use of Benzyltrimethylammonium  
Dichloroiodate and Zinc Chloride<sup>1)</sup>

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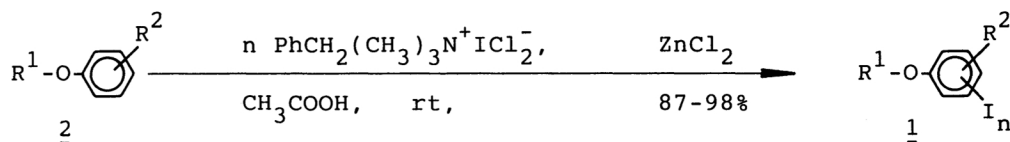
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The reaction of aromatic ethers with benzyltrimethylammonium dichloroiodate(1-) in acetic acid in the presence of zinc chloride at room temperature gave iodo-substituted aromatic ethers in good yields.

Usually, iodo-substituted aromatic ethers (1) have been obtained from the Sandmeyer reaction of alkoxyanilines,<sup>2)</sup> and from the O-alkylation of iodophenols with dialkyl sulfate.<sup>3)</sup> Otherwise, 1 have been obtained, in only limited cases, from the direct iodination of aromatic ethers (2) by use of a mixture of iodine and appropriate oxidizing agent such as mercuric oxide<sup>4)</sup> and hydrogen peroxide / strong mineral acid.<sup>5)</sup> A mixture of iodine and silver trifluoroacetate can be also used.<sup>6)</sup> Further, iodine monochloride (ICl) have considerably been used as an iodinating agent.<sup>7)</sup> In this case, as a source of ICl produced, dichloramine-T with NaI or HI have been employed.<sup>8)</sup>


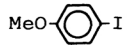

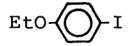

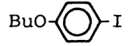

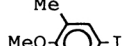

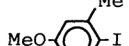
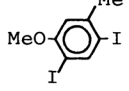
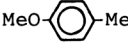
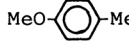
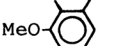
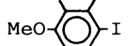
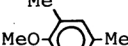
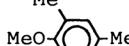
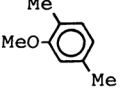
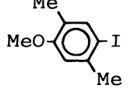
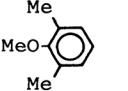
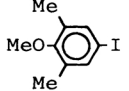
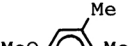
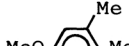
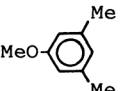
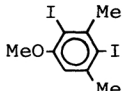

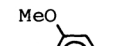
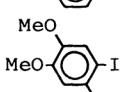
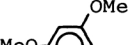
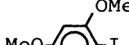
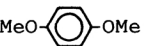
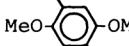
Recently, we found that benzyltrimethylammonium dichloroiodate(1-) (BTMA ICl<sub>2</sub>) was a highly useful reagent to obtain iodo-substituted phenols<sup>9)</sup> and aromatic α-chloroacetyl derivatives.<sup>10)</sup> In this paper, we wish to report on a facile synthesis of 1 from 2 by use of BTMA ICl<sub>2</sub>.

Reaction of 2 with BTMA ICl<sub>2</sub> in AcOH in the presence of ZnCl<sub>2</sub> at room temperature gave 1 in good yields. The results are summarized in Table 1.



BTMA ICl<sub>2</sub> is only slightly soluble in AcOH at room temperature. However, an addition of ZnCl<sub>2</sub> makes this reagent soluble in AcOH, and the iodination reaction of 2 proceeds smoothly under the mild conditions. The combined effect of BTMA ICl<sub>2</sub> and ZnCl<sub>2</sub> in AcOH thus provides a new excellent iodination procedure. Actually, in CH<sub>2</sub>Cl<sub>2</sub>-CH<sub>3</sub>OH which was well-suited solvent for these halogenations using quaternary

Table 1. Iodo Aromatic Ethers(1) from Aromatic Ethers(2) and BTMA ICl<sub>2</sub>

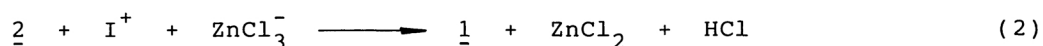
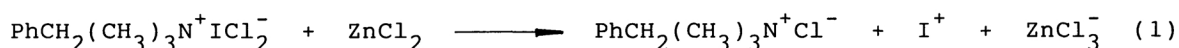
	Substrate (2)	Molar ratio (BTMA ICl <sub>2</sub> /2)	Reaction time	Product <sup>a)</sup> (1)	Yield <sup>b)</sup>	Mp/°C or Bp/°C	
					%	found	reported
a		1.1	3 h		92	53-54	52 <sup>8)</sup>
b		1.1	2 h		97	27-28	27 <sup>8)</sup>
c		1.1	4 h		98	277/760 mmHg	104-106/ <sup>11)</sup> 0.5 mmHg
d		1.1	30 min		97	77.5-78	75-76 <sup>3)</sup>
e		1.0	30 min		94	42-44	43-45 <sup>12)</sup>
f		2.1	24 h		96	102-103.5	-
g		1.1	6 h		94	30.5-31	30-31 <sup>7)</sup>
h		1.1	30 min		96	39-40	32-33 <sup>14)</sup>
i		1.1	8 h		91	255/760 mmHg	-
j		1.1	30 min		98	47	46-48 <sup>16)</sup>
k		1.1	8 h		96	259/760 mmHg	133-135/ <sup>17)</sup> 13 mmHg
l		1.1	30 min		92	57-58	57-58 <sup>18)</sup>
m		2.1	1 h		98	124	125 <sup>8)</sup>
n		1.0	30 min		97	33-34	34-35 <sup>19)</sup>
o		2.1	4 h		94	132-133.5	134 <sup>8)</sup>
p		2.1	10 min		98	200-201	198-199 <sup>8)</sup>
q		2.1	15 h		92	171-172	171 <sup>8)</sup>

r		2.1	10 min		91	110	-
s		2.1	10 min		97	133.5	-
t		2.1	48 h		87	140-141	139 <sup>22)</sup>
u		1.1	2 h		90	61-62	62-63 <sup>23)</sup>
v		2.1	4 h		95	177-178	175-177 <sup>24)</sup>

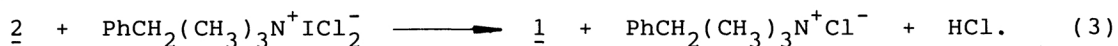
a) Structures of known products were also confirmed by their <sup>1</sup>H NMR spectra.

b) Yield of isolated product.

ammonium polyhalides, the reaction of 2 with BTMA ICl<sub>2</sub> did not proceed at all, even under reflux for many hours. The reaction scheme which affords 1 (monoiodo-substituted ethers) can be presented as follows;



overall:



We emphasize that the synthetic procedure for the direct iodination of 2 by use of BTMA ICl<sub>2</sub> and ZnCl<sub>2</sub> in AcOH is a useful method owing to its ease, simplicity, mildness of conditions, and good product yields.

As limitation of these methods, the less reactive 2 such as nitroanisoles gave no product. The reactions of 3,5-dimethylmethoxybenzene (2m), 1,3-dimethoxybenzene (2p), 1,4-dimethoxybenzene (2q), 1,3-diethoxybenzene (2r), and 1,3,5-trimethoxybenzene (2s) with equimolecular amounts of BTMA ICl<sub>2</sub> were so vigorous that the mixtures of mono-, and di-iodinated products were obtained, respectively.

The following is a typical procedure for the synthesis of 4-iodomethoxybenzene (1a): To a solution of methoxybenzene (2a) (0.50 g, 5.09 mmol) in AcOH (30 ml) were added BTMA ICl<sub>2</sub> (1.77 g, 5.10 mmol) and anhydrous ZnCl<sub>2</sub> (ca. 1 g). The mixture was stirred for 3 h at room temperature. A yellow color of the solution gradually changed to light brown. To the mixture was added water (20 ml) and then aqueous NaHSO<sub>3</sub> (5%, 20 ml). The mixture was extracted with hexane (50 ml x 3). The organic layer was dried with MgSO<sub>4</sub>, and passed through a short alumina-column. The hexane solution was concentrated in vacuo to give 1a as colorless crystals; yield 0.99 g.

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- 13) 2,4-Diiodo-5-methyl-methoxybenzene (1f): mp 102.5-103.5 °C (from aq EtOH (3:1)).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$ = 2.33 (3H, s,  $\text{CH}_3$ ), 3.78 (3H, s,  $\text{OCH}_3$ ), 6.60 (1H, s, 2-H), 8.00 (1H, s, 5-H). Found: C, 25.44; H, 2.04%. Calcd for  $\text{C}_8\text{H}_8\text{OI}_2$ : C, 25.70; H, 2.16%.
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- 15) 2-Iodo-4,6-dimethyl-methoxybenzene (1i): bp 255 °C/760 mmHg.  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$ = 2.08 (3H, s, 6- $\text{CH}_3$ ), 2.27 (3H, s, 4- $\text{CH}_3$ ), 3.68 (3H, s,  $\text{OCH}_3$ ), 6.87 (1H, s, 5-H), 7.10 (1H, s, 3-H). Found: C, 41.47; H, 4.07%. Calcd for  $\text{C}_9\text{H}_{11}\text{OI}$ : C, 41.25; H, 4.23%.
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- 21) 2,4-Diiodo-1,3,5-trimethoxybenzene (1s): mp 133.5 °C (from aq EtOH (3:1)).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$ = 3.47 (3H, s, 3- $\text{OCH}_3$ ), 3.85 (6H, s, 1 and 5- $\text{OCH}_3$ ), 6.16 (1H, s, 6-H). Found: C, 25.58; H, 2.36%. Calcd for  $\text{C}_9\text{H}_{10}\text{O}_3\text{I}_2$ : C, 25.74; H, 2.40%.
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