

Iodination of Aromatic Ethers by Use of Benzyltrimethylammonium
Dichloroiodate and Zinc Chloride¹⁾

Shoji KAJIGAESHI,* Takaaki KAKINAMI,[†] Masayuki MORIWAKI, Masakazu WATANABE,[†]
Shizuo FUJISAKI, and Tsuyoshi OKAMOTO[†]

Department of Industrial Chemistry, Faculty of Engineering,
Yamaguchi University, Tokiwadai, Ube 755

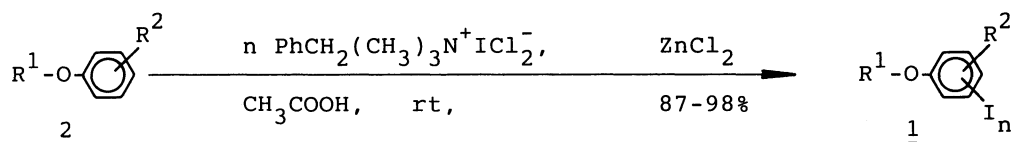
[†]Department of Industrial Chemistry, Ube Technical College, Tokiwadai, Ube 755

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,²⁾ and from the O-alkylation of iodophenols with dialkyl sulfate.³⁾ 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 oxide⁴⁾ and hydrogen peroxide / strong mineral acid.⁵⁾ A mixture of iodine and silver trifluoroacetate can be also used.⁶⁾ Further, iodine monochloride (ICl) have considerably been used as an iodinating agent.⁷⁾ In this case, as a source of ICl produced, dichloramine-T with NaI or HI have been employed.⁸⁾


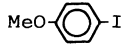

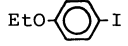

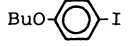

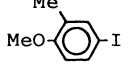

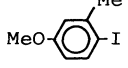
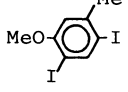
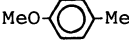
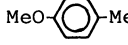
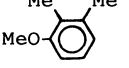
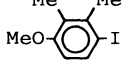
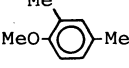
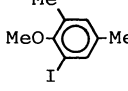
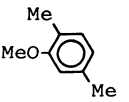
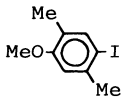
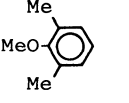
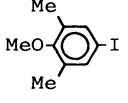
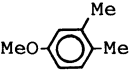
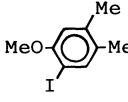
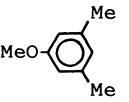
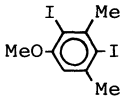

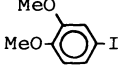
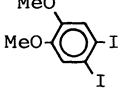
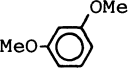
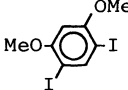
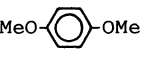
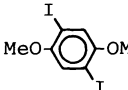
Recently, we found that benzyltrimethylammonium dichloroiodate(1-) (BTMA ICl₂) was a highly useful reagent to obtain iodo-substituted phenols⁹⁾ and aromatic α -chloroacetyl derivatives.¹⁰⁾ In this paper, we wish to report on a facile synthesis of 1 from 2 by use of BTMA ICl₂.

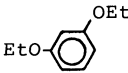
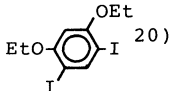
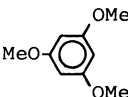
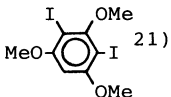
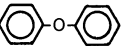
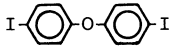
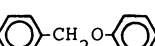
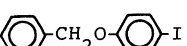
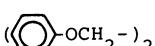
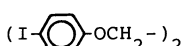
Reaction of 2 with BTMA ICl₂ in AcOH in the presence of ZnCl₂ at room temperature gave 1 in good yields. The results are summarized in Table 1.



BTMA ICl₂ is only slightly soluble in AcOH at room temperature. However, an addition of ZnCl₂ makes this reagent soluble in AcOH, and the iodination reaction of 2 proceeds smoothly under the mild conditions. The combined effect of BTMA ICl₂ and ZnCl₂ in AcOH thus provides a new excellent iodination procedure. Actually, in CH₂Cl₂-CH₃OH which was well-suited solvent for these halogenations using quaternary

Table 1. Iodo Aromatic Ethers(1) from Aromatic Ethers(2) and BTMA ICl_2

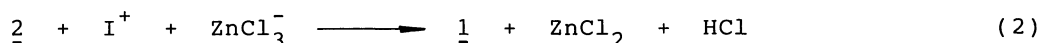
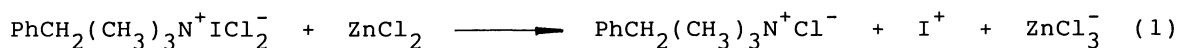
	Substrate (<u>2</u>)	Molar ratio (BTMA ICl_2 / <u>2</u>)	Reaction time	Product ^{a)} (<u>1</u>)	Yield ^{b)} %	Mp/°C or Bp/°C	
						found	reported
a		1.1	3 h		92	53-54	52 ⁸⁾
b		1.1	2 h		97	27-28	27 ⁸⁾
c		1.1	4 h		98	277/760 mmHg	104-106/ ¹¹⁾ 0.5 mmHg
d		1.1	30 min		97	77.5-78	75-76 ³⁾
e		1.0	30 min		94	42-44	43-45 ¹²⁾
f		2.1	24 h		96	102-103.5	-
g		1.1	6 h		94	30.5-31	30-31 ⁷⁾
h		1.1	30 min		96	39-40	32-33 ¹⁴⁾
i		1.1	8 h		91	255/760 mmHg	-
j		1.1	30 min		98	47	46-48 ¹⁶⁾
k		1.1	8 h		96	259/760 mmHg	133-135/ ¹⁷⁾ 13 mmHg
l		1.1	30 min		92	57-58	57-58 ¹⁸⁾
m		2.1	1 h		98	124	125 ⁸⁾
n		1.0	30 min		97	33-34	34-35 ¹⁹⁾
o		2.1	4 h		94	132-133.5	134 ⁸⁾
p		2.1	10 min		98	200-201	198-199 ⁸⁾
q		2.1	15 h		92	171-172	171 ⁸⁾

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

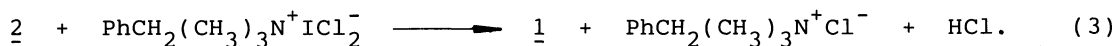
a) Structures of known products were also confirmed by their ¹H NMR spectra.

b) Yield of isolated product.

ammonium polyhalides, the reaction of 2 with BTMA ICl₂ 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 ICl₂ and ZnCl₂ 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 ICl₂ 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 ICl₂ (1.77 g, 5.10 mmol) and anhydrous ZnCl₂ (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 NaHSO₃ (5%, 20 ml). The mixture was extracted with hexane (50 ml x 3). The organic layer was dried with MgSO₄, 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)). ^1H NMR (CDCl_3) δ = 2.33 (3H, s, CH_3), 3.78 (3H, s, 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. ^1H NMR (CDCl_3) δ = 2.08 (3H, s, 6- CH_3), 2.27 (3H, s, 4- CH_3), 3.68 (3H, s, 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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- 20) 2,4-Diiodo-1,5-diethoxybenzene (1r): mp 110 °C (from aq EtOH (3:1)). ^1H NMR (CDCl_3) δ = 1.43 (6H, t, J =10 Hz, 2CH_3), 4.00 (4H, q, J =10 Hz, 2CH_2), 6.25 (1H, s, 6-H), 7.97 (1H, s, 3-H). Found: C, 28.59; H, 2.80%. Calcd for $\text{C}_{10}\text{H}_{12}\text{O}_2\text{I}_2$: C, 28.73; H, 2.89%.
- 21) 2,4-Diiodo-1,3,5-trimethoxybenzene (1s): mp 133.5 °C (from aq EtOH (3:1)). ^1H NMR (CDCl_3) δ = 3.47 (3H, s, 3- OCH_3), 3.85 (6H, s, 1 and 5- 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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