

Preparation of Aromatic Iodoacetyl Derivatives by Direct Iodination with a Potassium Iodide–Potassium Iodate–Sulfuric Acid System

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Synopsis. The reaction of aromatic acetyl derivatives with potassium iodide and potassium iodate in acetic acid in the presence of sulfuric acid at room temperature gave iodoacetyl derivatives in good yields.

α -Iodoketones are usually prepared from a halogen interchange reaction of bromo compounds with sodium iodide in acetone.¹⁾ They are also prepared by the reaction of *N*-iodosuccinimide with enol acetates, which are derived from ketones with acetic anhydride or isopropenyl acetate.²⁾ The treatment of enol silyl ether or enol acetates with iodine–copper(II) nitrate affords the corresponding α -iodo ketones.³⁾ The reaction of alkene with iodine–silver chromate,⁴⁾ iodine–pyridinium dichromate⁵⁾ or bis(2,4,6-trimethylpyridine) iodine(I) tetrafluoroborate–dimethyl sulfoxide⁶⁾ also afforded α -iodoketones. However, there has been only very little information concerning the direct α -iodination of ketones. Recently, Horiuchi and Satoh reported some novel α -iodination of ketones using iodine–copper(II) acetate in acetic acid,⁷⁾ and iodine–cerium(IV) ammonium nitrate in acetic acid or methanol.⁸⁾ Barluenga et al. have also reported on the direct α -iodination of carbonyl compounds with iodine–mercury(II) chloride.⁹⁾

During the course of our studies concerning direct α -halogenation of aromatic acetyl derivatives (**1**) with quaternary ammonium polyhalides, we found that the reaction of **1** with an equimolar amount of tetrabutylammonium tribromide (TBA Br₃) in dichloromethane–methanol gives bromoacetyl derivatives,¹⁰⁾ and that the reaction of **1** with an equimolar amount of benzyltrimethylammonium tetrachloroiodate (BTMA ICl₄)¹¹⁾ or with 2 molar amounts of benzyltrimethylammonium dichloroiodate (BTMA ICl₂)¹²⁾ in refluxing 1,2-dichloroethane–methanol gives chloroacetyl derivatives, respectively. However contrary to our expectations, the reaction of **1** with an equimolar amount of BTMA ICl₂ gave an inseparable mixture of **2** and chloroacetyl derivative.

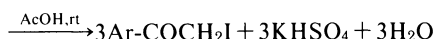
In the present paper we wish to report on the direct α -iodination of **1** with potassium iodide–potassium iodate in acetic acid in the presence of sulfuric acid.

Results and Discussion

The reaction of **1** with 2/3 molar amounts of potassium iodide and 1/3 molar amounts of potassium iodate in acetic acid in the presence of sulfuric acid (equimolar amount) at room temperature for 20–70 h gave **2** in good yields. The results are summarized in Table 1.



1



2

We believe that this method for the α -iodination of aromatic acetyl derivatives using KI–KIO₃–H₂SO₄ instead of I₂-salts of heavy metal (such as copper, cerium, and mercury) should prove to be useful, owing to its ease, safety, mildness of conditions, and good yields of the desired product.

As a limitation of this direct α -iodination method, reactive aromatic acetyl derivatives, such as amino- and hydroxy-substituted phenylethanones underwent oxidation by these reagents. Furthermore, the reaction of aliphatic ketones, such as RCH₂COCH₃ or RR'-CHCOCH₃ and cyclic ketones, with these reagents gave an inseparable mixture of several mono- and di-iodo derivatives, respectively.

Experimental

2-Iodo-1-phenyl-1-ethanone (2a); Typical Procedure: To a solution of 1-phenylethanone (**1a**) (0.72 g, 6 mmol) in acetic acid (40 ml) was added a solution of potassium iodide (0.66 g, 4 mmol) and potassium iodate (0.43 g, 2 mmol) in water (4 ml), and sulfuric acid (97%, 2 ml). After the black mixture was stirred at room temperature for 45 h, acetic acid was distilled off at 50 °C under reduced pressure. The residue was neutralized with aqueous NaHCO₃. The obtained mixture was extracted with dichloromethane (40 ml×3). The dichloromethane layer was dried over MgSO₄ and evaporated under reduced pressure to give **2a** as a colorless oil, which was confirmed by its NMR spectrum; yield 1.28 g (86%); bp 192 °C (760 Torr, 1 Torr=133.322 Pa) (lit.¹³⁾ mp 34.4 °C).

2-Iodo-1-*m*-tolyl-1-ethanone (2b); Colorless oil; ¹H NMR (CDCl₃) δ =2.33 (3H, s, 3-Me), 4.20 (2H, s, CH₂I), and 7.20–7.97 (4H, m, ArH). Found: C, 41.88; H, 3.25%. Calcd for C₉H₉OI: C, 41.57; H, 3.49%.

1-*p*-Ethylphenyl-2-iodo-1-ethanone (2d); Colorless oil; ¹H NMR (CDCl₃) δ =1.23 (3H, t, *J*=7 Hz, CH₂–CH₃), 2.68 (2H, q, *J*=7 Hz, CH₂CH₃), 4.27 (2H, s, CH₂I), 7.20 (2H, d, *J*=4 Hz, 3- and 5-H), and 7.83 (2H, d, *J*=4 Hz, 2- and 6-H). Found: C, 46.50; H, 4.11%. Calcd for C₁₀H₁₁OI: C, 46.18; H, 3.88%.

1-(2,4-Dichlorophenyl)-2-iodo-1-ethanone (2g); Colorless oil; ¹H NMR (CDCl₃) δ =4.40 (2H, s, CH₂I), and 7.17–7.73 (3H, m, ArH). Found: C, 30.81; H, 1.59%. Calcd for C₈H₅OCl₂I: C, 30.51; H, 1.60%.

1-(3,4-Dichlorophenyl)-2-iodo-1-ethanone (2h); Colorless crystals (methanol–water (3:1)); mp 57–57.5 °C; ¹H NMR (CDCl₃) δ =4.32 (2H, s, CH₂I) and 7.38–8.00 (3H, m, ArH).

Table 1. α -Iodination of Aromatic Acetyl Derivatives with KI-KIO₃-H₂SO₄

	Substrate (1)	Reaction time/h	Product ^{a)} (2)	Yield ^{b)}	IR(KBr or Neat) $\nu_{C=O}(cm^{-1})$	Mp(°C) or Bp(°C)/Torr	
				%		Found	Reported
a		45		86	1665 (Neat)	192/760	34.4 ¹³⁾
b		46		90	1670 (Neat)	— ^{c)}	—
c		21		76	1660 (KBr)	43.5—44	44 ¹⁴⁾
d		26		82	1670 (Neat)	— ^{c)}	—
e		22		79	1660 (KBr)	57—57.5	61 ¹⁴⁾
f		22		87	1695 (KBr)	75.5—76	75.5 ¹⁵⁾
g		48		66	1680 (Neat)	— ^{c)}	—
h		70		83	1680 (KBr)	57—57.5	—
i		43		91	1690 (KBr)	92.5—93	95 ¹⁶⁾
j		26		87	1650 (KBr)	92—92.5	96 ¹⁷⁾
k		52		97	1685 (KBr)	94.5—95	97—98 ¹⁷⁾
l		42		99	1650 (KBr)	132.5—133	135 ¹⁸⁾
m		64		59	1650 (KBr)	87—87.5	91—91.5 ¹⁹⁾
n		23		83	1665 (KBr)	51—51.5	—
o		45		35	1670 (Neat)	— ^{c)}	48—49/1 ²⁰⁾

a) Known products were characterized by comparison with authentic material (¹H MMR and IR spectra and mp or bp). b) Yield of isolated product. c) It was not possible to make measurement of bp because of its liability.

Found: C, 30.59; H, 1.71%. Calcd for C₈H₅OCl₂I: C, 30.51; H, 1.60%.

2-Iodo-1-phenyl-1-propanone (2n): Colorless crystals (methanol-water (3:1)); mp 51—51.5°C; ¹H NMR (CDCl₃) δ =2.05 (3H, d, J =7 Hz, CH₁-CH₃), 5.48 (1H, q, J =7 Hz, CH₁-CH₃), and 7.23—8.27 (5H, m, ArH). Found: C, 41.36; H, 3.37%. Calcd for C₉H₉OI: C, 41.47; H, 3.49%.

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