

Selective Monoiodination of Aromatic Compound with Electrochemically Generated I^+ Using Micromixing

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General Remarks. GC analysis was performed on a gas chromatograph (SHIMADZU GC-14B) equipped with a flame ionization detector using a fused silica capillary. Coldspray ionization (CSI)-MS measurements were performed with JEOL JMS-T100CSK, equipped with the CSI source. All reactions were carried out under Ar atmosphere unless otherwise noted.

Materials. Tetrabutylammonium tetrafluoroborate was purchased from TCI and dried at 50 °C/1 mmHg overnight before use. Acetonitrile was distilled from CaH₂ to remove a trace amount of acid, and stored over molecular sieves 3A.

Product Identification. All products in this paper are identified by comparison with the reported spectral data in the literature.¹

Electrochemical Generation of I^+ . Typical Procedure. The anodic oxidation was carried out in an H-type divided cell (4G glass filter) equipped with a platinum plate anode and cathode (40 mm x 20 mm). In the anodic chamber was placed a solution of iodine (127 mg, 0.500 mmol) in 0.3 M Bu₄NBF₄/CH₃CN (8.0 mL). In the cathodic chamber were placed 0.3 M Bu₄NBF₄/CH₃CN (8.0 mL) and trifluoromethanesulfonic acid (79 mg, 0.526 mmol). The constant current electrolysis (8 mA) was carried out at 0 °C with magnetic stirring until 2.1 F/mol of electricity was consumed.

A Typical Iodination Procedure Using Batch Mixing. A solution of I^+ (cooled at 0 °C) generated from iodine (127 mg, 0.500 mmol) by using electrochemical oxidation was added to a solution of 1,3-dimethoxybenzene (113 mg, 0.818 mmol) in CH₃CN (8 mL, cooled at 0 °C) by syringe. (At this time the solutions of I^+ was quickly transferred to syringes, which were kept cool with dry ice, and immediately used. Decomposition of I^+ was thus avoided.) The reaction mixture was stirred for 1 h at 0 °C. The solvent was removed under reduced pressure. The

residue was quickly filtered through a short column (10 cm) of silica gel to remove Bu_4NBF_4 . The silica gel was washed with ether (100 mL). The solvent was removed under reduced pressure and the residue was dissolved in hexane (50 mL). The organic phase was washed with sat. NaHCO_3 (30 mL) and then was separated. The solvent was removed to give a crude mixture (179.4 mg). Yields of 4-iodo-1,3-dimethoxybenzene (monoiodo product) and 4,6-diiodo-1,3-dimethoxybenzene (diiodo product) were determined by GC analysis: 4-iodo-1,3-dimethoxybenzene 45% (96.8 mg, 0.367 mmol, t_R 9.75 min, column, CBP-1; 0.22 mm ϕ x 0.25 μm x 25 m; oven temperature, 100 °C; rate of temperature increase, 10 °C/min): 4,6-diiodo-1,3-dimethoxybenzene 18% (58.0 mg, 0.149 mmol, t_R 14.3 min, column, CBP-1; 0.22 mm ϕ x 0.25 μm x 25 m; oven temperature, 100 °C; rate of temperature increase, 10 °C/min).

A Typical Iodination Procedure Using Micromixing. A solution of 1,3-dimethoxybenzene (112 mg, 0.811 mmol) in CH_3CN and an I^+ solution (8 mL, cooled at 0 °C), generated from I_2 (127 mg, 0.500 mmol) using the electrochemical method described above, were simultaneously introduced to an IMM single mixer (version 2) having a Si inlet (channel width = 50 μm), which was dipped in a coolant at 0 °C, using syringe pumps (flow rate is 3.0 mL/min each). Then, the reaction mixture coming out from the outlet of the micromixer was collected with a 100 mL round bottom flask, containing sat. NaHCO_3 (30 mL), sat. $\text{Na}_2\text{S}_2\text{O}_3$ (1 mL), and Et_2O (30 mL), with magnetic stirring. The organic layer was separated and the solvent was removed under reduced pressure. The residue was quickly filtered through a short column (10 cm) of silica gel to remove Bu_4NBF_4 . The silica gel was washed with Et_2O (100 mL). The solvent was removed under reduced pressure and the residue was dissolved in hexane (50 mL). The organic phase was washed with sat. NaHCO_3 (30 mL) and then was separated. The solvent was removed to give a crude product (204 mg). Yields of 4-iodo-1,3-dimethoxybenzene (monoiodo product) and 4,6-diiodo-1,3-dimethoxybenzene (diiodo product) were determined by GC analysis: 4-iodo-1,3-dimethoxybenzene 78% (167 mg, 0.632 mmol): 4,6-diiodo-1,3-dimethoxybenzene 4% (13 mg, 0.033 mmol).

Reference

1. K. Orito, T. Hatakeyama, M. Takeo and H. Suginome, *Syntheis*, 1995, 1273.