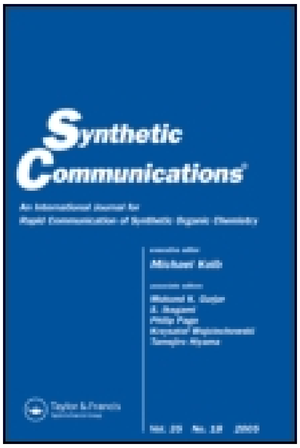

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Solvent-Free Iodination of Arenes using Iodine-Silver Nitrate Combination

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Abstract: A simple and environmentally safe general method of iodination of aromatic substrates under sovent-free conditions using the $I_2/AgNO_3$ combination in a solid state is reported. Both activated and deactivated aromatic compounds afford the respective aryl iodides in generally high yields (80–90%).

Keywords: aryl iodides, iodination, iodine, silver nitrate

INTRODUCTION

Aryl iodides are valuable precursors for various functional group transformations, and therefore the development of convenient procedures for iodination of aromatic compounds is an important field in synthetic organic chemistry.[1]

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Silver salts (e.g., Ag_2SO_4 and AgOTf) are commonly used as the reagents for the electrophilic iodination of arenes. Under strongly acidic conditions, silver salts can interact with iodine or iodine chloride, generating "superelectrophilic" I^+ species that are capable of iodinating even strongly deactivated aromatic substrates, whereas under neutral conditions an Ag^+/I_2 combination can serve as a mild iodinating reagent toward activated arenes.[2]

In contrast to Ag_2SO_4 and AgOTf, silver nitrite and silver nitrate are not commonly used as the reagents for electrophilic iodination. It has been reported, in particular, that iodine in the presence of $AgNO_2$ at room temperature in dichloromethane can slowly (60–70 h) iodinate benzene and alkylbenzenes, presumably via the intermediate formation of INO_2.[3] Silver nitrate is an even less common reagent for electrophilic iodination; the only published example involves the synthesis of 2-iodo-3,6-dimethoxybenzonitrile by the iodination of the appropriate aromatic substrate with the $I_2/AgNO_3$ combination.[4]

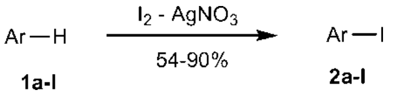
We report a simple and environmentally safe general method of iodination of aromatic substrates under sovent-free conditions using the $I_2/AgNO_3$ combination in solid state. It is important to note that only few examples of iodination of aromatic compounds by free-solvent reactions in solid phase have been reported in the literature.[5] These examples include the iodination of both activated and deactivated arenes by $Me_4N^+ICl_2^-$,[5a] oxidative iodination under the action of the silica-supported $I_2/Bi(NO_3)_3$,[5b] and iodination by ICl/*N*-iodosuccinimide[5c] or $I_2/PhI(OAc)_2$.[5d]

RESULTS AND DISCUSSION

We have found that gently blending a mixture of iodine, silver nitrate, and the aromatic substrate **1a–l** in an agate mortar at room temperature affords the respective iodides **2a–l** and AgI as a by-product (Scheme 1).

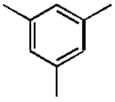
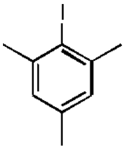
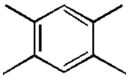
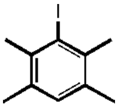
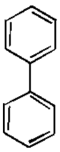
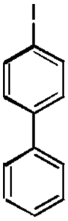
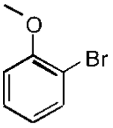
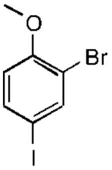
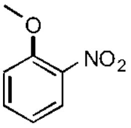
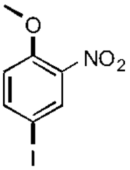
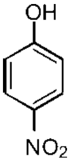
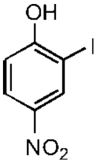
The best results were obtained when iodine and silver nitrate were initially ground for 1 min, then the aromatic substrate was added, and the blending was continued. A spontaneous heating and the formation of a brown mixture is observed upon initially blending iodine and silver nitrate. After addition of the aromatic substrate, the color of the mixture changes to grayish-green and then to yellow in about 30 min.

The reaction of compounds **1a–l** under these conditions afforded products of mono-iodination **2a–l** in 54–90% yield (Table 1). Under the same conditions, anisol gave a mixture of 4-iodoanisol and 2,4-diiodoanisol



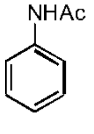
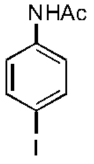
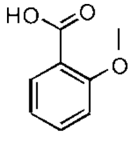
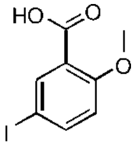
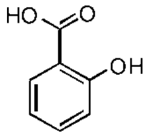
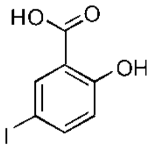
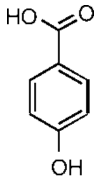
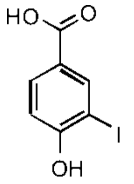
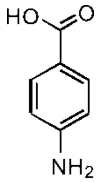
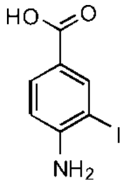
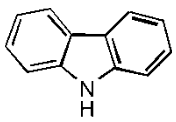
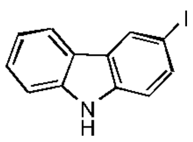
Scheme 1.

Table 1. Iodination of aromatic substrates in solid state with $AgNO_3/I_2$

			Yield,[a] (%)	Mp	Mp (lit. data)
1	 **1a**	 **2a**	90	29–30	29.5–30.5[10]
			58[b]	29–30	
2	 **1b**	 **2b**	87	78.5–79.5	78–79[11]
3	 **1c**	 **2c**	67	112–113	113–114[10]
4	 **1d**	 **2d**	76	80–82	—[12]
5	 **1e**	 **2e**	71	98–99	97–98[10]
6	 **1f**	 **2f**	71	84–86	86[13]

(*continued*)

Table 1. Continued

			Yield,[a] (%)	Mp	Mp (lit. data)
7	 **1g**	 **2g**	74	182–184	183–184[14]
8	 **1h**	 **2h**	84	152–153	—[15]
9	 **1i**	 **2i**	79	192–194	195[13]
10	 **1j**	 **2j**	74	175–176	175–176[16]
11	 **1k**	 **2k**	54	202–204	203–205[5a]
12	 **1l**	 **2l**	70	193–194	195–197[17]

[a] Yields of isolated and recrystallized products.

[b] $AgSO_4$ was used instead of $AgNO_3$.

[c] Mp not provided in this reference; product identified by NMR.

in a 1:4 ratio according to ^{1}H NMR data. The reaction of diphenylmethane was even less selective, affording an unseparable mixture of four products of mono- and diiodination in *ortho*- and *para*-positions. Our attempts to iodinate fluoren and 2,4-dinitroanisol were unsuccessful. Likewise, the iodination of 2- and 4-nitroanilines is very slow, and the conversion of the substrates to the iodinated products is very low (less than 5%). β-Naphthol, indol, and gallic acid react with $I_2/AgNO_3$ exothermically with a black tar formation.

The analysis of experimental data (Table 1) indicates that under solvent-free conditions the $I_2/AgNO_3$ system can be efficiently used to iodinate aromatic hydrocarbons, anisols with one electron-withdrawing substituent, and benzoic acids with one electron-donating substituent.

It can be assumed that INO_3 *in situ* is the actual electrophilic iodinating agent in the $I_2/AgNO_3$ system under solvent-free conditions, same as in the previously reported reactions of $I_2/AgNO_3$ and $ICl/AgNO_3$ in organic solvents (CH_2Cl_2, MeOH, chloroform-pyridine).[6] The inorganic by-products in this reaction are AgI and HNO_3. The presence of HNO_3, in particular, is indicated by the formation of trace amounts of 4-nitroanisol in the reaction of anisol with $I_2/AgNO_3$. Although INO_3 *in situ* is the most likely iodinating agent in this reaction, the presence of other inorganic iodinating species, such as $AgI_2^+NO_3^-$, or INO_2 (previously observed in systems I_2-KNO_3-CH_3COOH[7,8] and I_2-HNO_3[9]), cannot be excluded from possible consideration.

In conclusion, a simple and environmentally safe general method of iodination of aromatic substrates under sovent-free conditions using the $I_2/AgNO_3$ combination in solid state is reported. Both activated and deactivated aromatic compounds afford the respective aryl iodides in generally high yields (80–90%).

EXPERIMENTAL

All melting points were determined using a Boetius melting-point apparatus and are uncorrected. IR spectra were recorded on a Bruker Vector-22 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 NMR spectrometer. GC-MS spectra were obtained using a gas chromatograph equipped with quadrupole mass-spectrometer Hewlett Packard 5890/II as detector (EI, 70 eV).

Solid-State Iodination of Arenes using $AgNO_3/I_2$ Combination: General Procedure

A mixture of I_2 (127 mg, 0.5 mmol) and $AgNO_3$ (85 mg, 0.5 mmol) was gently blended in an agate mortar for 1 min, and then the aromatic substrate **1a–l** (0.5 mmol) was added. The resulting homogeneous mixture was additionally ground for 10 min, and then after a 2-min break, the grinding was continued for an additional 10–30 min. In the case of substrates **1 h–l**, three drops of acetic acid were added to the reaction mixture before the grinding was started. The resulting mixture was extracted with diethyl ether (2 × 5 mL), and the ether extract was filtered and concentrated on a rotary evaporator. Recrystallyzation of the residue from hexane-toluene mixtures (ratio of solvents between 10:1 and 3:1) afforded final products **2a–l**.

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