

NOTE

Selective Iodination of Some Phenols, Anilines and Methoxyarenes by Molecular Iodine in the Presence of 1-Butyl-3-methylimidazolium Hydrogen Sulphate

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A simple, mild and regioselective method for the iodination of some phenols, anilines and methoxyarenes by using molecular iodine in presence of 1-butyl-3-methylimidazolium hydrogen sulphate ([bmim]-HSO₄) in acetonitrile as solvent is reported. One-pot synthesis, mild reaction conditions, short reaction times and excellent yields of the products are noteworthy.

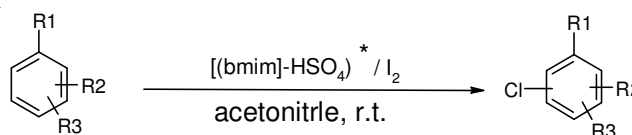
Key Words: Iodination, Phenols, Methoxyarenes, Anilines, 1-Butyl-3-methylimidazolium hydrogen sulphate.

Direct iodination of aromatic compounds have been the subject of numerous studies. Due to the low reactivity of iodine compared to chloride and bromine in electrophilic substitution reaction, direct introduction of iodine into the aromatic rings by the conventional methods is difficult. Therefore, new strategies have been developed to overcome this limitation. Most of the recent methods use a source of iodine as molecular iodine or iodide salts together with an oxidizing reagent or an acid (inorganic or Lewis acid). Other alternatives use reagents in which both the source of halogen and the oxidant or acid or both are present. Still other combinations of the mentioned protocols are also reported.

Among the conventional methods for the iodination, direct iodination methods usually employ I₂-tetrabutylammonium peroxydisulphate, I₂-diiodine pentoxide, I₂-silver sulphate, I₂-mercury salts (I₂/HgX₂), I₂-CrO₃ in acidic solution, I₂-lead acetate, I₂-thallium acetate, I₂-F-TEDA-BF₄, HNO₃/H₂SO₄, HIO₃ or HIO₄/H₂SO₄, KMnO₄/H₂SO₄, vanadium salts/CF₃SO₃H, ICl/Ag₂SO₄/H₂SO₄, NIS/CF₃CO₂H, N-iodosuccinimide (NIS), NIS-CF₃SO₃H, NIS-CF₃COOH, iodine monochloride, BuLi-F₃CCH₂I, NaOCl-NaI, bis(symcollidine)-iodine(I) hexafluorophosphate, bis(pyridine)-iodonium(I) tetrafluoroborate-CF₃SO₃H and NaI ammonium hexanitrocerate, Pb(OAc)₄/HOAc, NIS/CF₃SO₃H and NIS/CH₃CN. Most of these methods are complicated, costly or use toxic heavy metal catalysts with potential environmental problems due to the generation of hazardous waste and some of the reported procedures need harsh reaction conditions. Therefore, new methods have been developed in which regioselectivity,

high reaction yields, mild reaction conditions and environmentally benign considerations have been the subject of study¹⁻⁷.

In continuation of our research in the halogenation of aromatic compounds^{8,9}, we have used here an ionic liquid as the acid and molecular iodine in the iodination of some reactive aromatic compounds. The results showed good to excellent regioselectivity. We first prepared the acidic ionic liquid; 1-butyl-3-methylimidazolium hydrogen sulphate ([bmim]-HSO₄), which was supposed to be able to act as acid according to the previously reported methods. The prepared ionic liquid and molecular iodine were used in the acetonitrile as solvent at room temperature for selective iodination of some phenols, anilines and methoxyarenes. The progress of reactions was monitored by TLC or GC. According to the obtained results, this method can be used as a useful addition to the present methodologies for direct, mild and regioselective iodination of phenols, anilines and methoxyarenes (Table-1, **Scheme-I**).



* 1-Butyl-3-Methylimidazolium Hydrogen Sulfate

R₁=OMe, OH, NHMe, NMe₂
R₂= H, OH, OMe, Me, Cl, NO₂
R₃= OMe

Scheme-I

TABLE-1
IODINATION OF SOME PHENOLS, ANILINES AND METHOXYARENES IN THE PRESENCE OF 1-BUTYL-3-METHYLIMIDAZOLIUMHYDROGEN SULPHATE ([bmim]-HSO₄)^a IN ACETONITRILE AS SOLVENT^b

Entry	Substrate	Product(s)	Time (min)
1			Imm. ^c
2			15
3			10
4			Imm.
5			Imm.
6			60
7			Imm.
8			60
9			Imm.
10			Imm.
11			Imm.
12			Imm.
13			30
14			45
15		No reaction	75

^aIonic liquid/I₂/substrate ratio: 1:1:1, ^b100 % conversion, ^cImmediately.

All the reactions were performed at room temperature. According to the obtained results, most of the phenols and some methoxyarenes tested gave the corresponding products in excellent yields in short reaction times (Table-1, entries 1, 2, 4, 5, 7, 9, 10, 11 and 12). Most of the other methoxyarenes, phenols or anilines produced the corresponding products after the appropriate amount of time in excellent yields (Table-1, entries 2, 6, 8, 13 and 14). 2-Nitrophenol, however, was recovered unreacted after 75 min at room temperature (Table-1, entry 15). Comparing to the previously reported methods, this research has the advantages of being environmentally benign procedure which uses ionic liquid instead of hazardous Lewis acids or heavy metals at room temperature producing iodinated products in short reaction times.

In conclusion the easy procedure, simple work-up, mild reaction conditions and excellent yields of the products will make this method a useful addition to the available methodologies.

Preparation of 1-butyl-3-methylimidazolium hydrogen sulphate ([bmim]-HSO₄): 1-Butyl-3-methylimidazolium hydrogen sulphate [bmim][HSO₄] was synthesized according to the previously reported procedure¹⁰.

General procedure

Iodination of some aromatic compounds in the presence of 1-butyl-3-methylimidazolium hydrogen sulphate ([bmim]-HSO₄) in acetonitrile: To a mixture of aromatic compounds (1 mmol) in acetonitrile (5 mL), I₂ (1 mmol) and ionic liquid (1 mmol) was added and the resulting mixture was stirred at room temperature for 1-75 min. The progress of the reaction was monitored by TLC (eluent: ether/CCl₄) or GC (capillary column). After completion of the reaction, the solvent was separated by rotary evaporator and the excess of iodine was neutralized by sodium thiosulphate solution. Then diethyl ether (5 mL) was added and the product was extracted in organic layer. Evaporation of the solvent by rotary evaporator under reduced pressure gave the pure product.

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