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SHORT COMMUNICATIONS

A Simple and Efficient Procedure for Diazotization–Iodination of Aromatic Amines in Aqueous Pastes by the Action of Sodium Nitrite and Sodium Hydrogen Sulfate

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One of the most widely used methods of synthesis of aromatic iodides is based on diazotization–iodination of aromatic amines. The diazotization is generally carried out using accessible sodium nitrite in strongly acidic medium at reduced temperature [1–5]. Alternative procedures involve more expensive alkyl nitrites as diazotizing agents in the presence of diiodomethane or other sources of iodine [6, 7]. We previously proposed simple procedures for diazotization–iodination with sodium nitrite at room temperature in weakly acidic media created by *p*-toluenesulfonic acid [8] or sulfonated cation exchangers [9]. We recently described successful diazotization–iodination in aqueous pastes by grinding substituted anilines with *p*-toluenesulfonic acid [10]. In the present communication we report on facile diazotization of a large number of substituted anilines **I–XIV** and 5-aminouracil (**XIV**) with sodium nitrite in aqueous paste by the action of more accessible and ecologically safe acidic reagent, sodium hydrogen sulfate; the subsequent iodination is effected by addition of potassium iodide.

$$\underset{\textbf{I–XV}}{\mathrm{ArNH_2}} \xrightarrow{\text{(1) NaHSO}_4\text{, NaNO}_2\text{; (2) KI; aqueous paste, 18–20°C, 20–30 min}} \underset{\textbf{XVI–XXX}}{\mathrm{ArI}}$$

I–XIV, **XVI–XXIX**, Ar = RC_6H_x; **XV**, **XXX**, Ar = 2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl (38%); **I**, **XVI**, R = 4-O_2N (68%); **II**, **XVII**, R = 2-O_2N (68%); **III**, **XVIII**, R = 4-Ac (75%); **IV**, **XIX**, R = 2-Ac (76%); **V**, **XX**, R = 4-I (52%); **VI**, **XXI**, R = 2-I (67%); **VII**, **XXII**, R = 2-HOCO (80%); **VIII**, **XXIII**, R = 4-HOCO (84%), **IX**, **XXIV**, R = 3-HO-4-HOCO (80%); **X**, **XXV**, R = 3-NC (70%); **XI**, **XXVI**, R = 4-NC (75%); **XII**, **XXVII**, R = 4-MeO (61%); **XIII**, **XXVIII**, R = 4-Ph (79%); **XIV**, **XXIX**, R = 2,4-$(O_2N)_2$ (30%).

An aromatic amine (2 mmol) was ground with solid sodium hydrogen sulfate (6 mmol) in the presence of 0.2 ml of water in an agate mortar over a period of several minutes. Sodium nitrite (5 mmol) was then added, and the diazotization process was complete in approximately 10 min on occasional grinding. The formation of diazonium salt was confirmed by a test with β-naphthol. When the diazotization was complete, potassium iodide (5 mmol) was added to the paste-like diazonium salt, and the mixture was intermittently ground over a period of 10–20 min. The iodination process started instantaneously; immediately after addition of potassium iodide the volume of the paste-like mixture increased due to evolution of nitrogen. On the whole, the diazotization–iodination process took 20–30 min. The aqueous pastes containing aryl iodides **XVI–XXX** were treated with water and a solution of sodium sulfite, and the pure products were isolated by recrystallization or column chromatography; the yields were moderate to good. Compounds **XVI–XXX** were identified by comparing their melting points and ^1H and ^{13}C NMR spectra with the corresponding parameters of authentic samples.

The reaction is general, and the procedure is applicable to most anilines having both electron-donating and electron-withdrawing substituents, though the diazotization of weakly basic amines **XIV** and **XV** was incomplete, and the yield of the corresponding iodides was lower. On the other hand, anilines **II**, **IV**, **VI**, **VII**, and **IX** having one *ortho* substituent gave rise to the corresponding iodides in high yield. As a rule, the yields of aryl iodides **XVI–XXX** were comparable with those obtained in the diazotization–iodination in aqueous pastes with *p*-toluenesulfonic acid [10].

The proposed procedure is applicable for enlarged syntheses; for example, increase in the amount of *p*-aminobenzoic acid (**VIII**) to 15 mmol did not result in reduced yield of 4-iodobenzoic acid (**XXIII**). To ensure successful diazotization–iodination, the above sequence of reactant mixing is necessary. When potassium iodide was added simultaneously with sodium nitrite, complex mixtures of products were obtained, and the yields of aryl iodides were considerably lower.

Kaupp et al. [11] described a procedure according to which grinding of a dry diazonium nitrate with potassium iodide leads to quantitative formation of the corresponding aryl iodide. However, this procedure required gaseous reagents in the diazotization step, and long time was necessary for the iodination step. Moreover, dry diazonium salts are explosive materials, unlike reactions with “wet” salts or performed in solvents. The diazotization procedure proposed by us is safe, for the reactions occur in aqueous pastes. Furthermore, arenediazonium sulfates are stable and nonexplosive [1–5, 10, 12]. Our procedure is experimentally simple, and it largely conforms to the “green chemistry” principles.

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