Iodoaromatic compounds are useful synthetic building blocks in organic synthesis. They are valuable, versatile synthetic intermediates and have wide applications in medicine and biochemistry. One of the first and most commonly used methods for the preparation of iodoaromatics is the substitution of a diazo group by iodine (often called the Sandmeyer reaction). The fundamental advantage of this reaction, over other methods involving direct electrophilic iodination of aromatic compounds, is the selective introduction of iodine into a specific position of the aromatic ring, whereas direct electrophilic iodination frequently gives a mixture of isomers.

The process of diazotization–iodination is usually carried out with sodium nitrite at low temperature in two steps: diazotization of the amine in aqueous hydrochloric or sulfuric acid and a subsequent reaction with iodine and KI, sometimes in the presence of copper salts. As an alternative to these traditional methods, more expensive methods involving alkyl nitrites in the presence of diiodomethane acts more slowly than the Sandmeyer reaction. A slow reaction rate in the diazotization stage was clearly observed with 2,4,6-trichloroaniline (4a) which has two ortho-substituents. It is likely that the results of the reactions studied are influenced by a number of factors – amine basicity, water solubility, reagent diffusion rate into the polymeric matrix, product diffusion rate from the polymeric matrix, strength of interaction between starting arylammonium (and/or formed aryldiazonium) cations, and the polymeric matrix.

Reactions with all the studied amines proceeded smoothly at room temperature except for 4-methoxyaniline (6). Diazotization–iodination of 6 was successful only at 7–10 °C. Higher temperatures decreased the yield of 4-iodoanisole (6a) due to resification and a high degree of volatility of 6a.
Although water is safer, more convenient, and meets the ‘Green Chemistry’ requirements as a reaction medium, we also studied the possibility of using organic solvents such as DMSO and acetonitrile in this diazotization–iodination method. We found out that in these organic solvents, in contrast to aqueous medium, the diazotization stage for amines 1–11 proceeds with low conversion of the starting amines. This may be attributed to the hydrophilic nature of the cation-exchange resins used and their nonswelling ability in aprotic media.

Another attempt at carrying out the diazotization–iodination in water with cation-exchange resins in one stage, that is, with simultaneous treatment of NaNO₂ and KI, was in vain. During this procedure, we observed the release of elemental iodine and the formation of product mixtures with an incomplete conversion of the starting amines.

The yields of iodoarenes 1a–11a obtained by the developed method can be compared with the results of traditional diazotization-iodination methods, although the reactions proceed at a slower rate due to the polymeric nature of the acidic agent (Table 1). After iodination was completed, providing products 1a–11a, the sulfonic acid-based resin could be recycled without any significant loss in reactivity by washing with acetone, water, and then treating with aqueous hydrochloric acid.

It should be noted that the aryldiazonium cations, ArN₂⁺, prepared at the first stage have strong interactions with the polymeric resin matrix and the salts can be isolated by filtration. For example, after the diazotization stage the polymer-supported diazonium salt of amine 1 was filtered, washed with water, and then allowed to stand open at room temperature for nine days. After this period of time, the salt reacts with KI in an aqueous solution to give 4-iodonitrobenzene (1a) in a 71% yield, which is only a little less than that obtained under normal one-pot conditions (Table 1).

Previously, diazonium salts supported on sulfonic resins were obtained via the ion exchange of preliminarily synthesized aryldiazonium chlorides, ArN₂⁺Cl⁻, with the sodium form of sulfonic resin (Amberlyst A–15), and also revealed high storage stability and reactivity in obtaining an azo dye library.

In summary, we have demonstrated for the first time that, in the presence of sulfonic acid based cation-exchange resins, diazotization of aromatic amines successfully proceeds at room temperature in water. The resulting diazo-

### Table 1: The Diazotization–Iodination of Aromatic Amines 1–11 with NaNO₂ and Cation-Exchange Resins in Water at Room Temperature

<table>
<thead>
<tr>
<th>Substrate: NaNO₂: KI (mmol)</th>
<th>Substrate</th>
<th>Reaction time (min)</th>
<th>Product</th>
<th>Yield (%)</th>
<th>Mp (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:2:2.5</td>
<td>4-NO₂C₆H₄NH₂</td>
<td>25/65</td>
<td>4-NO₂C₆H₄I</td>
<td>81</td>
<td>172–173 (171–173)</td>
</tr>
<tr>
<td>1:2:2.5</td>
<td>2-NO₂C₆H₄NH₂</td>
<td>30/60</td>
<td>2-NO₂C₆H₄I</td>
<td>71</td>
<td>52–53 (49–51)</td>
</tr>
<tr>
<td>1:2:2.5</td>
<td>4-MeCO₂C₆H₄NH₂</td>
<td>40/50</td>
<td>4-MeCO₂C₆H₄I</td>
<td>75</td>
<td>84–85 (82–84)</td>
</tr>
<tr>
<td>1:2:2.5</td>
<td>4-IC₆H₄NH₂</td>
<td>55/300</td>
<td>1,4-IC₆H₄</td>
<td>50</td>
<td>128–129 (131–133)</td>
</tr>
<tr>
<td>1:2:2.5</td>
<td>2-IC₆H₄NH₂</td>
<td>45/95</td>
<td>1,2-IC₆H₄</td>
<td>90</td>
<td>oil (oil)</td>
</tr>
<tr>
<td>1:2:2.5</td>
<td>4-MeOC₂H₆NH₂</td>
<td>40/60</td>
<td>4-MeOC₂H₆I</td>
<td>61</td>
<td>51–52 (50–53)</td>
</tr>
<tr>
<td>1:2:2.5</td>
<td>4-NH₂C₆H₄CO₂H</td>
<td>140/600</td>
<td>4-NH₂C₆H₄CO₂H</td>
<td>98</td>
<td>269–270 (270–273)</td>
</tr>
<tr>
<td>1:2:2.5</td>
<td>2-NH₂C₆H₄CO₂H</td>
<td>180/190</td>
<td>2-NH₂C₆H₄CO₂H</td>
<td>65</td>
<td>161–162 (160–162)</td>
</tr>
<tr>
<td>1:2:2.5</td>
<td>2,4,6-Cl₃C₆H₂NH₂</td>
<td>420/100</td>
<td>2,4,6-Cl₃C₆H₂I</td>
<td>53</td>
<td>50–51 (53–54)</td>
</tr>
<tr>
<td>1:2:2.5</td>
<td>4-CNC₆H₄NH₂</td>
<td>100/80</td>
<td>4-CNC₆H₄I</td>
<td>56</td>
<td>125–127 (124–128)</td>
</tr>
<tr>
<td>1:2:2.5</td>
<td>4-PhC₆H₄NH₂</td>
<td>100/85</td>
<td>4-PhC₆H₄I</td>
<td>50</td>
<td>112–113 (110–114)</td>
</tr>
</tbody>
</table>

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*An amount of 5 g of cation-exchange resin was used with 2 mmol of the substrate.
*Yield of isolated product.
*Reference 8.
*The reaction proceeded at 7–10 °C.
nium salts are generally stable and readily react with KI to form iodoarenes in moderate to high yields. This new method has a number of advantages over traditional diazotization–iodination methods with sodium nitrite. These advantages include the use of water as solvent, strong acid–free conditions, mild reactions at room temperature, ease of separation of the intermediates and products from the reaction mixture, and the possibility of recycling the resins.

Commercially available reagents and solvents were used as received without further purification. Column chromatography was performed using silica gel 60 (40–63 μm mesh). Merck silica gel 60 F254 aluminum sheets were used for analytical TLC. 1H and 13C NMR spectra were recorded in CDCl3 on a Bruker AC 300 MHz spectrometer. Melting points were determined on a Bülchi B-540 apparatus and are uncorrected. Commercially available sulfonic acid-based cation-exchange resins KU-2-8 (Russia) and Trilite SPC-160H (South Korea) with exchange capacity of 4.9–5.1 mg equiv/g were treated in the following way for subsequent reactions.

**Cation Exchange Resins**

**KU-2-8 Resin:** At first the resin (200 g) was allowed to swell in sat. aq NaCl (250 mL). Then, the crude cation exchange resin KU-2-8 in the Na-form (200 g) was treated with aq 5% NaOH (250 mL) for 3–4 h with frequent shaking. Treatment with a 5% solution of NaOH was repeated until the color of the solution faded. After the alkaline treatment, the cation exchange resin was washed with 10 volumes of distilled H2O and then aq HCl: first, 5 volumes of a 5% solution, then 5 volumes of a 10% solution, and finally, by a 15% solution until the complete absence of ferrous ions in the solution (test by ammonium thiocyanate). After the acid treatment, the cation exchange resin was thoroughly washed with distilled H2O until the pH reached 6–7.

**Trilite SPC-160H Resin:** The cation exchange resin Trilite SPC-160H (South Korea) in H-form was washed with distilled H2O until the pH reached 6–7.

**Iodoarenes 1a–11a; General Procedure**

The respective aromatic amine 1–11 (2.0 mmol) was added to the cation-exchange resin (5.0 g) in H2O (50 mL). After stirring for 10 min, NaNO2 (4.0 mmol, 0.276 g) was added to the mixture. Then, the mixture was stirred for the time specified in Table 1, and the process was accompanied by the substrate dissolution. The reaction was followed by monitoring the complete disappearance of starting aromatic amine by TLC. Then, KI (5.0 mmol, 0.830 g) was added to the mixture and stirred for the time specified in Table 1. The reaction was monitored by the β-naphthol color test. The formation of iodoarene precipitates was observed in most reactions. After the iodination was complete, the reaction mixture was treated with aq 10% Na2SO3 (15 mL). The solid products and cation-exchange resins were filtered and washed with H2O, and then treated with acetone (10 mL). To this acetone solution was added H2O to precipitate the iodoarene products, which were then collected by filtration and dried. In the case of liquid products, the mixture extracted with Et2O (3 × 15 mL) and worked up in the usual way. All the products were characterized by comparison of melting points with the literature values (Table 1).

**Acknowledgment**

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**References**

6. Preparing KU-2-8 (Russia) and Trilite SPC-160H (South Korea) with exchange capacity of 4.9–5.1 mg equiv/g were treated in the following way for subsequent reactions.

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