Supporting Information

for

The in situ generation and reactive quench of diazonium compounds in the synthesis of azo compounds in microreactors

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Additional diagrams and NMR spectra

Azo coupling reaction in the synthesis of Sudan II azo dye in Little Things Factory microreactors

Statistical Model validation for the predictive multiple regression model fitted in the investigation of reaction parameters, i.e., flow rate, temperature and pH which have an effect on the azo coupling reaction in the synthesis of Sudan II azo dye.

Predicted conversion (%) = - 42.4512 + 27.9443 * pH - 6.5854 * Flow rate + 0.3187 * Temperature - 1.6268 * pH² - 0.0061 * Temperature²

It was also found that about 85% of the variation seen in the observed data can be explained by the model.
Figure S1: Normal probability plot.
Figure S2: Scatter plot of predicted values vs. residual values

Azo coupling reaction in the synthesis of 4-(2-(4-nitrophenyl)diazenyl)-N-phenylbenzenamine in Little Things Factory microreactors

Statistical Model validation for the predictive multiple regression model fitted in the investigation of reaction parameters, i.e., flow rate, temperature and pH which have an effect on the azo coupling reaction in the synthesis of 4-(2-(4-nitrophenyl)diazenyl)-N-phenylbenzenamine in LTF-MS microreactors.

Model fitting was performed using statistica-12 Statsoft program where a Logit model transformation was carried out on the response which in this case was the percentage conversion. Three outliers (Cases 18, 24 and 25) were removed from the raw data set.

The predictive multiple regression model obtained was as follows;

Predicted conversion (%) = 8.14853 - 4.48258 * pH + 0.01204 * Temperature + 0.61041 * Flow rate + 0.43744 * pH²

It was also found that about 75% of the variation seen in the observed data can be explained by the model.
Figure S3: Scatter plot of predicted values vs residual values.

Figure S4: Normal probability plot.
Continuous flow synthesis of Sudan II azo dye in LTF-MS microreactors

**Table S1:** Summary of statistical multiple regression data analysis

<table>
<thead>
<tr>
<th></th>
<th>Regression Summary for Dependent Variable: Conversion % R= .54875331 R²= .30113019 Adjusted R²= .17009210</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=20</td>
<td>b*</td>
</tr>
<tr>
<td>Intercept</td>
<td>96.2480</td>
</tr>
<tr>
<td>Amine + HCl (l/min)</td>
<td>0.387552</td>
</tr>
<tr>
<td>Sodium Nitrite (l/min)</td>
<td>-0.072019</td>
</tr>
<tr>
<td>Coupler (l/min)</td>
<td>-0.382741</td>
</tr>
</tbody>
</table>

**Figure S5:** Normal probability plot.

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Figure S6: Scatter plot of predicted values vs residual values.
$^1$H and $^{13}$C NMR spectra of principle compounds synthesized from the model reactions used in the optimized synthesis of azo compounds in continuous flow systems.

Compound: 1-((2,4-dimethylphenyl)azo)naphthalen-2-ol

$^1$H NMR spectra
$^{13}$C NMR spectra
Compound: 4-(2-(4-nitrophenyl)diazenyl)-N-phenylbenzenamine

$^1$H NMR spectra
$^{13}$C NMR spectra
\(^1\text{H}\) and \(^{13}\text{C}\) NMR spectra of selected azo compounds as shown in Table 9 of this paper

**Compound Entry: 1**

\(^1\text{H}\) NMR spectra
$^{13}$C NMR spectra
Compound Entry: 4

$^1$H NMR spectra
$^{13}C$ NMR spectra
Compound Entry: 7

$^1$H NMR spectra
$^{13}$C NMR spectra
Compound Entry: 9

$^1$H NMR spectra
$^{13}$C NMR spectra

Other reactions were only followed by HPLC by monitoring consumption of the relevant starting materials.