A General Procedure to Selectively Prepare N-Alkylanilines by an Unexpected Reaction of (Z)-(tert-Butylsulfanyl)(aryl)diazenes with Alkyllithium Reagents

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Abstract: A general procedure has been set up to prepare, selectively, the N-monoalkylanilines, reacting (Z)-(tert-butylsulfanyl)(aryl)diazenes with alkyllithium. The reactions were carried out in anhydrous diethyl ether at 0 °C or –78 °C, depending on the reagent, and then at room temperature. In optimal conditions the yields of the pure products were from good to excellent: for 38 considered examples, 34 were positive with yields varying between 61% and 91% (average yield 78%). Collateral proofs were carried out to support a hypothesized reaction mechanism.

Key words: N-alkylanilines, amines, diazonium compounds, diazosulfides, alkyllithium

In the course of recent research directed towards the development of the synthetic potential of a new family of diazonium salts that are exceptionally stable in the dry state, namely the arenediazonium o-benzenedisulfonimides, we revisited the Stadler and Ziegler reactions used to prepare alkyl aryl and diaryl sulfides. In classical conditions the preparation of these sulfides consists in reacting arenediazonium salts in basic aqueous solution with aliphatic or aromatic thiols. As is known, the reactions proceed through the intermediate formation of the highly unstable (alkylsulfanyl or arylsulfanyl)(aryl)diazenes that, on decomposing in situ, give rise to sulfides. An exception, and a most important one, is found in (Z)-(tert-butylsulfanyl)(4-bromophenyl)diazene and their E diastereomers, that can be isolated and handled with no risk at all. The diazenes contain the diazonium group in a protected form, and acid treatment results in the easy restitution of the corresponding diazonium salts. This characteristic puts the diazenes with the better known 1-aryl-3,3-dialkyltriazenes. The present research began with the assumption that, given their easy accessibility, the diazenes could, like the triazenes, be used as intermediates in synthetic procedures involving reactions which required diazonium group protection. On this basis we attempted, by analogy to the positive triazene reactions, to react (Z)-(tert-butylsulfanyl)(4-bromophenyl)diazene with butyllithium, the aim being to obtain the lithium derivative, which could then be used in reactions with electrophiles.

To our great surprise, aqueous treatment of the reaction mixture obtained after the addition of butyllithium in hexane to 3j in anhydrous diethyl ether at –78 °C, gave N-ethyl-4-bromoaniline as the main product, not the expected hydrodemetallation product. To us this appeared an interesting result, one worthy of further investigation. Numerous procedures have been proposed for the preparation of N-monoalkylanilines, the most traditional being based on the direct N-alkylation of anilines using various reagents. However such procedures have major drawbacks, namely a high aniline/alkylating reagent ratio and the formation of N,N-dialkylation products alongside N-monoalkylation products. This prompted us to turn our re-
search towards the synthesis of \(N\)-monoalkylanilines via \((Z)-(\text{tert-butylsulfanyl})\)(aryl)diazenes 3, and to put aside, for the moment, our initial project. The overall new procedure is reported in Scheme 1.

The diazenes 3 were prepared through optimization of the procedure set up to prepare the simplest compound of the series, the \((Z)-(\text{tert-butylsulfanyl})(\text{phenyl})\)diazenes (3a), i.e. by reacting the salts 1 with sodium 2-methylpropane-2-thiolate in anhydrous methanol at room temperature for 30 min. The procedure gives the diazenes 3a–r easily and in good yield (Table 1), usually greater than 90%, and allows the recovery, in more than 80% yield, of the \(o\)-benzenedisulfonimide (5) that can be reused to prepare the salts 1.

Table 1 \((\text{tert-Butylsulfanyl})(\text{aryl})\)diazenes 3

<table>
<thead>
<tr>
<th>Compd.</th>
<th>Ar</th>
<th>Yield a (%)</th>
<th>Oil or mp b (°C)</th>
<th>Lit.</th>
<th>(^1)H NMR (CDCl(_3)) (\delta (ppm), J (Hz))</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>Ph</td>
<td>96</td>
<td>48–50 (P)</td>
<td>48–49(^c)</td>
<td>1.60 (s, 9 H), 2.44 (s, 3 H), 6.87–6.91, 7.17–7.39 (2 m, 1:3, 4 H)</td>
</tr>
<tr>
<td>3b</td>
<td>2-MeC(_6)H(_4)</td>
<td>92</td>
<td>oil</td>
<td>oil(^d)</td>
<td>1.64 (s, 9 H), 6.93–7.03, 7.20–7.31 (2 m, 3:1, 4 H)</td>
</tr>
<tr>
<td>3c</td>
<td>4-MeC(_6)H(_4)</td>
<td>94</td>
<td>oil</td>
<td>oil(^d)</td>
<td>1.62 (s, 9 H), 6.66–6.93, 7.26–7.35, 7.45–7.49 (3 m, 1:2:1, 4 H)</td>
</tr>
<tr>
<td>3d</td>
<td>4-MeOC(_6)H(_4)</td>
<td>87</td>
<td>oil</td>
<td>oil(^e)</td>
<td>1.60 (s, 9 H), 6.61–6.78, 6.98–7.17, 7.41–7.48 (3 m, 1:2:1, 4 H)</td>
</tr>
<tr>
<td>3e</td>
<td>2-MeSC(_6)H(_4)</td>
<td>84(^f)</td>
<td>oil</td>
<td>(_)</td>
<td>(_)</td>
</tr>
<tr>
<td>3f</td>
<td>2-FC(_6)H(_4)</td>
<td>92</td>
<td>oil</td>
<td>(_)</td>
<td>(_)</td>
</tr>
<tr>
<td>3g</td>
<td>2-CIC(_6)H(_4)</td>
<td>94</td>
<td>oil</td>
<td>(_)</td>
<td>(_)</td>
</tr>
<tr>
<td>3h</td>
<td>2-BrC(_6)H(_4)</td>
<td>92</td>
<td>oil</td>
<td>(_)</td>
<td>(_)</td>
</tr>
<tr>
<td>3i</td>
<td>3-BrC(_6)H(_4)</td>
<td>100</td>
<td>oil</td>
<td>(_)</td>
<td>(_)</td>
</tr>
<tr>
<td>3j</td>
<td>4-BrC(_6)H(_4)</td>
<td>97</td>
<td>oil</td>
<td>oil(^e)</td>
<td>1.59 (s, 9 H), 6.96–7.01, 7.19–7.47 (2 m, 1:3, 4 H)</td>
</tr>
<tr>
<td>3k</td>
<td>4-NCC(_6)H(_4)</td>
<td>95</td>
<td>70–71</td>
<td>69–70(^e)</td>
<td>(_)</td>
</tr>
<tr>
<td>3l</td>
<td>4-MeOCOC(_6)H(_4)</td>
<td>80</td>
<td>88–89 (M)</td>
<td>(_)</td>
<td>(_)</td>
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<tr>
<td>3m</td>
<td>2.6-MeC(_6)H(_4)</td>
<td>94</td>
<td>oil</td>
<td>(_)</td>
<td>(_)</td>
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<tr>
<td>3n</td>
<td>2.6-F(_2)C(_6)H(_4)</td>
<td>91</td>
<td>oil</td>
<td>(_)</td>
<td>(_)</td>
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<tr>
<td>3o</td>
<td>2.6-Cl(_2)C(_6)H(_4)</td>
<td>94</td>
<td>72–73 (E)</td>
<td>(_)</td>
<td>(_)</td>
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<tr>
<td>3p</td>
<td>2.6-Br(_2)C(_6)H(_4)</td>
<td>94</td>
<td>84–85 (E)</td>
<td>(_)</td>
<td>(_)</td>
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<tr>
<td>3q</td>
<td>(_)</td>
<td>90–91(^b) (M)</td>
<td>(_)</td>
<td>(_)</td>
<td></td>
</tr>
<tr>
<td>3r</td>
<td>(_)</td>
<td>49–51(^b) (E)</td>
<td>(_)</td>
<td>(_)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) With the exceptions of 3e, 3q and 3r, yields refer to the crude diazosulfides, that had a satisfactory degree of purity (TLC, \(^1\)H NMR) and were directly used in the next step.
\(^b\) P = pentane; M = MeOH; E = EtOH.
\(^c\) Identical to that reported in ref. 1
\(^d\) Identical to that reported in ref. 11
\(^e\) Identical to that reported in ref. 26
\(^f\) Yield of pure product obtained by column chromatography (PE–Et\(_2\)O, 9.5:0.5).
\(^g\) Analytically pure samples obtained by column chromatography gave satisfactory microanalyses (C ± 0.12; H ± 0.010).
\(^h\) X = N=S=NSBu.
\(^i\) Molar ratio 1:2:2:2:2.
\(^j\) Yield of pure product obtained by column chromatography (PE–Et\(_2\)O, 8.5:1.5): its \(^1\)H NMR spectrum showed a mixture of diastereomers.
\(^k\) Mp refers to the major diastereomer obtained by crystallization.
The key reaction of the whole procedure was the addition of the chosen alkyllithium 6, at 0 °C or –78 °C depending on the reagent, to the diazenes 3 dissolved in anhydrous diethyl ether (molar ratio 3:6 = 1:1.5 or 1:2.2). After 30 min at low temperature, the reaction mixture was brought to room temperature in about 15–20 min, quenched with water and worked up simply to isolate the pure N-monoalkylanilines 7 by column chromatography. Table 2 shows examples and results.

**Table 2  N-Alkylanilines 7**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting compd.</th>
<th>R</th>
<th>Chromatographic solvent PE–Et₂O (ratio)</th>
<th>Yield (%)</th>
<th>MS m/z (M⁺)</th>
<th>Mp (°C) or bp (°C)/torr</th>
<th>¹H NMR (CDCl₃), δ (ppm), J (Hz) or Lit.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 3a</td>
<td>Ph</td>
<td>Me</td>
<td>9:1</td>
<td>78</td>
<td>107</td>
<td>80–82/15</td>
<td>79.2/12</td>
</tr>
<tr>
<td>2 3a</td>
<td>Bu</td>
<td>9.8:0.2</td>
<td>84</td>
<td>149</td>
<td>60–61/0.5</td>
<td>59–60/0.1</td>
<td></td>
</tr>
<tr>
<td>3 3a</td>
<td>s-Bu</td>
<td>9:1</td>
<td>76</td>
<td>149</td>
<td>74–75/0.15</td>
<td>106–108/12</td>
<td></td>
</tr>
<tr>
<td>4 3a</td>
<td>n-C₆H₁₃</td>
<td>9.8:0.2</td>
<td>84</td>
<td>177</td>
<td>88–89/0.1</td>
<td>84–86/0.1</td>
<td></td>
</tr>
<tr>
<td>5 3b</td>
<td>2-MeC₆H₄</td>
<td>Bu</td>
<td>9.5:0.5</td>
<td>71</td>
<td>163</td>
<td>72–73/0.5</td>
<td>258–260/771</td>
</tr>
<tr>
<td>6 3c</td>
<td>4-MeC₆H₄</td>
<td>Me</td>
<td>9:1</td>
<td>73</td>
<td>121</td>
<td>54–55/1</td>
<td>98–99/19</td>
</tr>
<tr>
<td>7 3c</td>
<td>Bu</td>
<td>9:1</td>
<td>89</td>
<td>163</td>
<td>70–71/0.5</td>
<td>74–79/0.5</td>
<td></td>
</tr>
<tr>
<td>8 3c</td>
<td>s-Bu</td>
<td>9:1</td>
<td>71</td>
<td>163</td>
<td>78–79/0.15</td>
<td>136–138/25</td>
<td></td>
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<tr>
<td>9 3c</td>
<td>n-C₆H₁₃</td>
<td>9.8:0.2</td>
<td>83</td>
<td>191</td>
<td>36–37 (P)</td>
<td>37.1–37.36</td>
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<tr>
<td>10 3d</td>
<td>4-MeOC₆H₄</td>
<td>Me</td>
<td>9:1</td>
<td>76</td>
<td>137</td>
<td>37–38 (P)</td>
<td>40/13</td>
</tr>
<tr>
<td>11 3d</td>
<td>Bu</td>
<td>9:1</td>
<td>80</td>
<td>179</td>
<td>80–81/0.5</td>
<td>142–145/67</td>
<td></td>
</tr>
<tr>
<td>12 3d</td>
<td>s-Bu</td>
<td>9:1</td>
<td>69</td>
<td>179</td>
<td>80–82/0.15</td>
<td>112–113/2/18</td>
<td></td>
</tr>
<tr>
<td>13 3d</td>
<td>n-C₆H₁₃</td>
<td>9:1</td>
<td>88</td>
<td>207</td>
<td>99–100/0.1</td>
<td>145/2/19</td>
<td></td>
</tr>
<tr>
<td>14 3e</td>
<td>2-MeSC₆H₄</td>
<td>Bu</td>
<td>9.5:0.5</td>
<td>84</td>
<td>195</td>
<td>87–88/0.5</td>
<td>96/13</td>
</tr>
<tr>
<td>15 3f</td>
<td>2-FC₆H₄</td>
<td>Bu</td>
<td>9.5:0.5</td>
<td>69</td>
<td>167</td>
<td>61–62/0.4</td>
<td>98/13</td>
</tr>
<tr>
<td>16 3g</td>
<td>2-CIC₆H₄</td>
<td>Bu</td>
<td>9:1</td>
<td>83</td>
<td>183</td>
<td>89–90/0.5</td>
<td>96/13</td>
</tr>
<tr>
<td>17 3h</td>
<td>2-BrC₆H₄</td>
<td>Bu</td>
<td>#</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 3i</td>
<td>3-BrC₆H₄</td>
<td>Bu</td>
<td>9.5:0.5</td>
<td>84</td>
<td>227</td>
<td>91–92/0.5</td>
<td>96/13</td>
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</table>
Table 2  \(N\)-Alkylanilines 7 (continued)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting Ar R</th>
<th>Chromatographic solvent PE–Et&lt;sub&gt;2&lt;/sub&gt;O (ratio)</th>
<th>Yield&lt;sup&gt;a&lt;/sup&gt; (%)</th>
<th>MS m/z (M&lt;sup&gt;+&lt;/sup&gt;)</th>
<th>Mp&lt;sup&gt;b&lt;/sup&gt; (°C) or bp (°C)/torr</th>
<th>(^1)H NMR (CDCl&lt;sub&gt;3&lt;/sub&gt;), δ (ppm), J (Hz)</th>
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</thead>
<tbody>
<tr>
<td>19</td>
<td>3j 4-BrC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>Me 9:1</td>
<td>71</td>
<td>185</td>
<td>70–71/1.2</td>
<td>137–138/14&lt;sup&gt;12&lt;/sup&gt;</td>
</tr>
<tr>
<td>20</td>
<td>3j Bu</td>
<td>9.5:0.5</td>
<td>91</td>
<td>227</td>
<td>95–96/0.5</td>
<td>0.93 (t, (J = 7.1, 3) H), 1.30–1.62 (m, 4 H), 3.05 (t, (J = 7.1, 2) H), 3.98 (br s, 1 H), 6.45, 7.22 (2 d, 1:1, (J = 9.2, 4) H)</td>
</tr>
<tr>
<td>21</td>
<td>3j s-Bu</td>
<td>9.5:0.5</td>
<td>79</td>
<td>227</td>
<td>103–104/0.8</td>
<td>0.91 (t, (J = 7.4, 3) H), 1.13–1.16 (m, 6 H), 3.27–3.36 (m, 1 H), 3.46 (br s, 1 H), 6.42, 7.19 (2 d, 1:1, (J = 8.8, 4) H)</td>
</tr>
<tr>
<td>22</td>
<td>3j n-C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;13&lt;/sub&gt;</td>
<td>9.5:0.5</td>
<td>86</td>
<td>255</td>
<td>118–119/0.2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.88 (t, (J = 6.3, 3) H), 1.20–1.44 (m, 6 H), 1.53–1.65 (m, 2 H), 3.07 (t, (J = 7.0, 2) H), 6.53, 7.25 (2 d, 1:1, (J = 8.8, 4) H)</td>
</tr>
<tr>
<td>23</td>
<td>3k 4-NCC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>Me 4:1</td>
<td>78</td>
<td>132</td>
<td>87–88 (M)</td>
<td>86&lt;sup&gt;22&lt;/sup&gt;</td>
</tr>
<tr>
<td>24</td>
<td>3k Bu</td>
<td>8.5:1.5</td>
<td>87</td>
<td>174</td>
<td>43–44 (M)</td>
<td>41&lt;sup&gt;12&lt;/sup&gt;</td>
</tr>
<tr>
<td>25</td>
<td>3k s-Bu</td>
<td>4:1</td>
<td>71</td>
<td>174</td>
<td>152–153/1.1</td>
<td>0.93 (t, (J = 7.4, 3) H), 1.16 (d, (J = 6.3, 3) H), 1.40–1.61 (m, 2 H), 3.37–3.46 (m, 1 H), 3.95 (br s, 1 H), 6.49, 7.37 (2 d, 1:1, (J = 8.8, 4) H)</td>
</tr>
<tr>
<td>26</td>
<td>3k n-C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;13&lt;/sub&gt;</td>
<td>8.5:1.5</td>
<td>85</td>
<td>202</td>
<td>38–39 (M)</td>
<td>35.1–35.7&lt;sup&gt;0&lt;/sup&gt;</td>
</tr>
<tr>
<td>27</td>
<td>3l 4-MeOCOC&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>Me 4:1</td>
<td>61</td>
<td>165</td>
<td>93–94 (M)</td>
<td>95.5&lt;sup&gt;12&lt;/sup&gt;</td>
</tr>
<tr>
<td>28</td>
<td>3l Bu</td>
<td>8.5:1.5</td>
<td>67</td>
<td>207</td>
<td>104 (M)</td>
<td>104–105&lt;sup&gt;25&lt;/sup&gt;</td>
</tr>
<tr>
<td>29</td>
<td>3l s-Bu</td>
<td>4:1</td>
<td>79</td>
<td>207</td>
<td>140–41/0.9&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.95 (t, (J = 7.4, 3) H), 1.19 (d, (J = 6.3, 3) H), 1.43–1.67 (m, 2 H), 3.42–3.52 (m, 1 H), 3.84 (s, 3 H), 3.92 (br s, 1 H), 6.51, 7.84 (2 d, 1:1, (J = 8.8, 4) H)</td>
</tr>
<tr>
<td>30</td>
<td>3l n-C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;13&lt;/sub&gt;</td>
<td>4:1</td>
<td>69</td>
<td>235</td>
<td>94–95 (M)</td>
<td>93–94&lt;sup&gt;40&lt;/sup&gt;</td>
</tr>
<tr>
<td>31</td>
<td>3m 2,6-Me&lt;sub&gt;2&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>Bu</td>
<td>4:1</td>
<td>69</td>
<td>235</td>
<td>94–95 (M)</td>
</tr>
<tr>
<td>32</td>
<td>3n 2,6-F&lt;sub&gt;2&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;3&lt;/sub&gt;</td>
<td>Bu 9.8:0.2</td>
<td>70</td>
<td>185</td>
<td>55–56/0.4</td>
<td>0.93 (t, (J = 7.1, 3) H), 1.33–1.58 (m, 4 H), 3.31 (t, (J = 7.1, 2) H), 3.52 (br s, 1 H), 6.57–6.83 (m, 3 H)</td>
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<td>33</td>
<td>3o 2,6-Cl&lt;sub&gt;2&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>Bu</td>
<td>4:1</td>
<td>69</td>
<td>235</td>
<td>94–95 (M)</td>
</tr>
<tr>
<td>34</td>
<td>3p 2,6-Br&lt;sub&gt;2&lt;/sub&gt;C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;4&lt;/sub&gt;</td>
<td>Bu</td>
<td>4:1</td>
<td>69</td>
<td>235</td>
<td>94–95 (M)</td>
</tr>
<tr>
<td>35</td>
<td>3q (MeNH&lt;sub&gt;2&lt;/sub&gt;)&lt;sub&gt;2&lt;/sub&gt;CH=CH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>7.5:2.5</td>
<td>82</td>
<td>226</td>
<td>55–56 (M)</td>
<td>54–55&lt;sup&gt;26&lt;/sup&gt;</td>
</tr>
<tr>
<td>36</td>
<td>3q (BuNH&lt;sub&gt;2&lt;/sub&gt;)&lt;sub&gt;2&lt;/sub&gt;CH=CH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>8.5:1.5</td>
<td>81</td>
<td>316</td>
<td>44–45 (M)</td>
<td>45&lt;sup&gt;27&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Yield determined by GLC.

<sup>b</sup> Compound sublimes.

<sup>c</sup> DMSO-CDCl<sub>3</sub> (6:4, v:v).

<sup>d</sup> Ref. 6<sup>c</sup>.

<sup>e</sup> Ref. 6<sup>i</sup>.

<sup>f</sup> Ref. 6<sup>j</sup>.

<sup>g</sup> Ref. 6<sup>12</sup>.

<sup>h</sup> Ref. 6<sup>15</sup>.

<sup>i</sup> Ref. 6<sup>16</sup>.

<sup>j</sup> Ref. 6<sup>24</sup>.
On the basis of the results (almost all positive for the examined reactions), the yields (34 cases, yield 61–91%; average yield: 78%) and the purity of the monoalkylanilines 7 (uncontaminated by N,N-dialkylamination products), and of the ease of operation and the mild conditions, it can be claimed that the procedure is, without any doubt, valid from the synthetic point of view. Moreover, the elevated reaction specificity allows the elevated reaction specificity allows the formation of the intermediates 10, which, by elimination of moisture. Instead, the singlet at δ = 1.64 corresponding to the tert-butyl group of the starting diazene 3m.o.p were recovered.

Apart from the undoubted synthetic usefulness, the reaction of (Z)-(tert-butylsulfanyl)(aryl)diazenes 3 with alkylithium reagents appears of interest also from the mechanistic point of view. Scheme 2 shows a suggested mechanistical mechanism.

This is to say that the reaction could take place through the formation of the intermediates 10, which, by elimination of the lithium tert-butylthiolate (8), could give rise to the nitrenes 11. Subsequently, by adding water to 11 there would be the formation of the intermediates 12, which on dissociation, would form the N-alkylanilines 7 and hyponitrurous acid (9). The hypothesized mechanism is supported by the experimental results of two collateral proofs. In the first proof, given the hypothesis that alkylithium addition could lead to the formation and presence of the intermediates 10, there was realized, and monitored (1H NMR) in a non-hermetically sealed tube, the reaction of (Z)-(tert-butylsulfanyl)(aryl)diazene (3a) and methylithium (6, R = Me) carried out in THF-d8, first at 0 °C and then at room temperature (Experimental). After 10 min the spectrum of the reaction mixture showed two singlets of high intensity at δ = 2.07 and 1.17, attributable respectively to the methyl and tert-butyl groups of the intermediate 10 (Ar = Ph; R = Me), and a singlet of weak intensity at δ = 2.73, attributable to the N-methylaniline 7 (Ar = Ph, R = Me), which formed in small amounts in the presence of moisture. Instead, the singlet at δ = 1.64 corresponding to the tert-butyl group of the starting diazene.

### Table 2  N-Alkylanilines 7 (continued)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting Ar R</th>
<th>Chromatographic solvent PE–Et2O (ratio)</th>
<th>Yielda (%)</th>
<th>MS m/z (M+)</th>
<th>Mp°C or bp °C/torr</th>
<th>1H NMR (CDCl3), δ (ppm), J (Hz) or Lit.a</th>
</tr>
</thead>
<tbody>
<tr>
<td>37</td>
<td>3r</td>
<td>PE–Et2O</td>
<td>7:3</td>
<td>79</td>
<td>136</td>
<td>0.93 (t, J = 7.2, 6 H), 1.31–1.66 (m, 8 H), 2.86 (mr, 2 H), 3.08 (t, J = 7.2, 4 H), 5.95 (s, 1 H), 6.04–6.08 (m, 2 H), 6.98 (t, J = 7.9, 1 H)</td>
</tr>
<tr>
<td>38</td>
<td>3r</td>
<td>PE–Et2O</td>
<td>7:5:2:5</td>
<td>85</td>
<td>220</td>
<td>45–46 (M) or 165–170/1012</td>
</tr>
</tbody>
</table>

a Yields of pure products obtained by column chromatography.

b P = pentane; M = methanol.

c Spectral data are identical to those reported.

d Identical to that of a commercially available sample of analytical purity.

e Satisfactory microanalyses were obtained (C ± 0.12; H ± 1.11).

f Physical data are not reported.

g The reaction gave several products, no traces of N-butyl-2-bromoaniline were however present (GC–MS analysis).

h N-Hexylaniline is known, but physical and spectral data are not reported.

i Methyl N-(sec-buty1)benzoate is known, but physical and spectral data are not reported.

j The reaction failed and the starting diazoulsulfides 3m.o.p were recovered.

### Scheme 2

![Scheme 2](image)
3a was completely absent. Moreover, lithium tert-butanol- 
thiolate (8) began separating out as a white substance in the 
NMR-tube. With time there was the rapid diminishing of the 
two singlets at $\delta = 2.07$ and 1.17, both disappearing after 
about 30 min, while, contemporarily, the singlet at $\delta = 2.73$ and the precipitate 8 increased. Furthermore a 
singlet of weak intensity was evidenced at $\delta = 1.39$, attrib- 
tuable to the thiol 2 formed by the partial hydrolysis of the 
salt 8. This increased with time.

With regard to the second proof, it must be noted that the 
reaction products of all the reactions between the diazenes 
3 and the alkylolithium reagents 6 included, alongside the 
N-alkylanilines 7, traces of the corresponding hydrazines 
14. Thus a reaction took place between 3a and butyllithium 
(6, R = Bu) in high excess (molar ratio 3a:6 = 1:4) under argon, at −78 °C and then at room temperature 
(Experimental). On completion, the reaction, quenched 
with water and worked up appropriately, gave N-butyl-
niline and N,N'-dibutyl-N-phenylhydrazine (14; Ar = Ph, 
R = Bu) in yields of 50 and 31%, respectively.

The results of the two proofs are in good agreement with 
the mechanism reported in Scheme 2. Nevertheless, whereas the formation of the intermediates 10 is almost certainly substantiated, greater caution is needed with re-
card to accepting the formation of nitrene intermediates 
11.

In summary, we have developed a general procedure, 
starting from anilines, for the preparation of aryl alkyl 
amines containing primary and secondary alkyl radicals, 
through the intermediate formation of (Z)-(tert-butylsulfanyl)(aryl)diazenes 3. The alkylating reagent/diazen 
ratio is low, the yields are good to excellent and the N-
monoalkylanilines obtained are uncontaminated by N,N-
dialkyranilines. An interesting aspect of the studied reac-
tion concerns the umpolung of the nitrogen atom of the 
amino group, which, present in the diazene protected form, reacts exceptionally as an electrophile to carbanions 
instead of as nucleophile to electrophilic alkyls. The crude salts were virtually pure and could be used to prepare compounds 3, without further crystallization.

Dry Methylene-4,4'-bis(benzendiazonium) Bis(o-benzenedi- 
sulfonimide) [1; Ar = 4-(4-N-tert-C$_6$H$_4$CH$_3$)$_2$C$_6$H$_4$-O] (C$_6$H$_5$SO$_2$N- 
SO$_2$)

Prepared according to the procedure previously reported, diazotization of methylene-4,4'-dianiline (0.99 g, 5 mmol) was carried out with iso-
pentyl nitrite (1.29 g, 11 mmol) in the presence of o-benzenedi-
sulfonimide (5) (2.41 g, 11 mmol) in HCO$_2$H (20 mL) at 0–5 °C. 
Then anhyd Et$_2$O was added to complete the precipitation of the diazoni-
ium salt that was collected by filtration on a Buchner funnel and 
was kept several times on the funnel with anhyd Et$_2$O to complete 
the diminution of HCO$_2$H. After drying under reduced pressure, 
the virtually pure (1H NMR, decomposition point) dry title compound 
was obtained as a violet solid in 97% yield (3.19 g). For analytical 
purpose, a sample was purified by dissolution in hot HCO$_2$H and 
precipitation with anhyd Et$_2$O after cooling; decom. 97–98 °C.

1H NMR (CD$_3$CN): $\delta = 4.49$ (s, 2 H), 7.66–7.78 (m, 12 H), 8.44 (d, 
J = 8.8 Hz, 4 H).

Anal. Calcd for C$_{35}$H$_{24}$O$_6$N$_x$: C, 55.88; H, 2.72; N, 12.69; S, 
19.54. Found: C, 55.80; H, 2.72; N, 12.69; S, 19.54.

Dry Benzenebis(1,3-diazonium) Bis(o-benzenedisulfonyl- 
nimide) [1; Ar = 3-N-tert-C$_6$H$_5$-O-(C$_6$H$_5$SO$_2$N-SO$_2$)$_2$]

Prepared according to the above procedure, starting from 1,3-phe-
nylenediamine (0.54 g, 5 mmol). The virtually pure (1H NMR, de-
comp. point) anhyd title compound was obtained as a beige solid in 
95% yield (2.70 g). For analytical purpose, a sample was purified 
by dissolution in hot HCO$_2$H and precipitation with anhyd Et$_2$O, after 
cooling; decom. 135–136 °C.

1H NMR (CD$_3$COOD): $\delta = 7.69$–7.72 (m, 8 H), 8.30 (t, J = 8.0 Hz, 
1 H), 9.20 (d, J = 8.0 Hz, 2 H), 9.94 (s, 1 H).

Anal. Calcd for C$_{55}$H$_{42}$O$_{14}$N$_x$: C, 38.02; H, 2.13; N, 14.78; S, 
22.56. Found: C, 38.13; H, 2.17; N, 14.70; S, 22.62.

CAUTION! In our laboratory there was no case of sudden decom-
position during the preparation, purification and handling of salts 1. 
Nevertheless it must be born in mind that all diazonium salts in 
the dry state are potentially explosive. Therefore they must be carefully 
stored and handled.

(Z)-(tert-Butylsulfonyl)(aryl)diazenes [or (Z)-tert-Butyl Aryl Di-
zasulfides] 3a–r

(Z)-(tert-Butylsulfonyl)(2-fluorophenyl)diazenes (3f); Representa-
tive Procedure

According to the procedure previously reported for the preparation 
of (Z)-(tert-butylsulfonyl)(phenyl)diazenes (3a), 2-fluorobenzenedi-
zonium o-benzenedisulfonimide (1, Ar = 2-FC$_6$H$_4$) (3.41 g, 
10 mmol) was added in one portion with vigorous stirring, to a 
soin of sodium 2-methylpropan-2-thiolate, prepared from 2-methylpropan-
2-thiol (2) (0.99 g, 11 mmol) and sodium methoxide (30% soln in 
MeOH: 2.00 g, 11 mmol) in anhyd MeOH (20 mL), at r.t. (20– 
25 °C). The salt dissolved at once and a yellow–orange soln was ob-
tained. No evolution of nitrogen was observed. Stirring was main-
tained until a test of azocoupling with 2-naphthol was negative (10
min). The reaction mixture was poured into Et₂O-sat. aq NaCl (200 mL; 1:1). The aq soln was separated and extracted with Et₂O (100 mL). The combined organic extracts were washed with sat. aq NaCl (2 × 100 mL), dried (Na₂SO₄), and evaporated under reduced pressure. The yellow oil obtained was the title compound (92% yield, 1.95 g). It was virtually pure (TLC, PE–Et₂O, 9.5:0.5) and was directly used in the next step.

1H NMR (CDCl₃): δ = 1.64 (s, 9 H); 6.13–7.03 and 7.20–7.31 (2 m, 3:1; 4 H).

The aq layer and the aq washings, containing the sodium o-benzene-disulfonimide (4), were collected and evaporated under reduced pressure. The residue was passed through a column (Dowex 50X8 ion-exchange resin; 4.5 g for 1 g of product), eluting with water. After removal of the water under reduced pressure, virtually pure (1H NMR) o-benzene-disulfonimide (5) was recovered.

Yield: 1.76 g (80%); mp 192–194 °C (toluene) (lit.,10 mp 192–194 °C).

With three only exceptions (3c, q, r), the obtained (tert-butylsulfanyl)diazenes 3a had a satisfactory degree of purity (TLC, 1H NMR) and could be used directly in the next step. Most of them were yellow or orange oily substances. Their further purification by distillation under reduced pressure was not possible, because of thermal decomposition. For analytical purposes, the samples were chromatographed on a short column: satisfactory microanalyses were always obtained. The solid substance could be further purified by crystallization. All the compounds could be stored in the freezer for a long time, ready for use. Compounds 3 gave a positive azo coupling test when they were treated with HBF₄–Et₂O, to free the diazonium salt, and then with an alkaline soln of 2-naphthol.

Moreover, compounds 3 restored the corresponding diazonium salts 1 in yields greater than 90%, when they were treated with o-benzene-disulfonimide (5) (molar ratio 3:5 = 1:1.1) in glacial MeCO₂H or HCO₂H (50 or 20 mL, respectively, for 10 mmol of 3). The reaction times for the preparation of the diazosulfides 3 varied from 10 (in the presence of electron-withdrawing groups) to 30 min (in the presence of electron-donating groups). o-Benzene-disulfonimide (5) was recovered from all the reactions, in 80–90% yields. Yields and physical and spectral data of compound 3a–r are reported in Table 1.

N-Alkylanilines (7; R = Bu, s-Bu, n-C₃H₇); N-Benzylaniline; Typical Procedures

Method 1

Under the optimum conditions of entry 2 of Table 2, a yellow soln of (Z)-(tert-butylsulfonyl)(phenyl)diazone (3a) (1.94 g, 10 mmol) in anhyd Et₂O (20 mL) was cooled to −78 °C. BuLi (1.6 M soln in hexane; 13.75 mL, 22 mmol) was added dropwise during 10 min, and the resulting brown soln was stirred at the same temperature for an additional 30 min. Then, the cooling bath was removed and the reaction mixture was allowed to warm to r.t. (ca. 15–20 min). A TLC analysis showed the complete disappearance of the starting diazocarbonyl (14a, R = Bu, Ar = Ph) [MS: m/z = 136 (M⁺)]. No traces of N,N-dimethyl-N-phenylhydrazine (14) were identified by GC–MS in the first fraction collected from the column.

The reaction was directly quenched with H₂O (50 mL); at once the organic soln cleared to pale yellow. The aq layer was separated and extracted with Et₂O (2 × 80 mL). The combined organic extracts were washed with H₂O (2 × 50 mL), dried (Na₂SO₄), and evaporated under reduced pressure. TLC (PE–Et₂O, 9.8:0.2), GC and GC–MS analyses of the crude residue showed the presence of N-butylaniline, as major product [MS: m/z = 149 (M⁺)], besides some by-products. Among them, one was identified as N,N′-dibutyl-N-phenylhydrazine (14: R = Bu, Ar = Ph) [MS: m/z = 220 (M⁺)]. No traces of N,N-dibutylaniline were present. Column chromatography of the residue afforded the pure (TLC, GC, GC–MS, 1H NMR) title compound in 84% yield (1.25 g). Traces of the by-product 14 were identified by GC–MS in the first fraction collected from the column.

The aq layer and the aq washings were collected and a starch-iodide paper was immersed. At once the test was negative. The blue color develops only after 15–20 min. The basic aq soln was acidified with aq HCl (1 M), treated with I₂ (2.54 g, 10 mmol) and stirred at r.t. for 30 min. Usual work up afforded tert-butyl disulfide.

Yield: 0.73 g (82%).

MS: m/z = 178 (M⁺).

1H NMR (CDCl₃): δ = 1.32 (s), identical to that of an authentic sample of commercial origin.

When the reaction was carried out at 0 °C instead of −78 °C, pure N-butylaniline was isolated in a yield a little lower than that obtained above (1.16 g, 78%).

Method 2

Starting from the diastereomer of 3a, i.e. (E)-(tert-butylsulfanyl)(phenyl)diazene, the above procedure afforded N-butylaniline in comparable yield.

Methods 3 and 4

BuLi was used in an 1.1 (6.88 mL) or, respectively, 1.5 molar amount (9.38 mL) in respect to the diazosulfide 3a. Working as described above, both the reactions did not complete even after prolonged reaction times (3a was recovered in about 24% and 12% yield) and N-butylaniline was isolated in lower yields (41% and 62%) and moreover it was less pure.

All the N-butylanilines listed in Table 2 were prepared according to Method 1. In entries 36 and 38, the amount of BuLi was doubled (27.50 mL, 44 mmol).

N-(sec-Butyl)anilines (7, R = s-Bu) and N-Hexylanilines (7, R = n-C₆H₁₄)

Prepared according to Method 1, using sec-BuLi (1.3 M soln in cyclohexane; 16.92 mL, 22 mmol) or, respectively, hexyllithium (2.3 M soln in hexane; 9.56 mL, 22 mmol) instead of BuLi. The results are reported in Table 2.

The reactions failed when tert-BuLi (1.7 M soln in pentane) was used.

N-Methylaniline

In the optimum conditions of entry 1 of Table 2, a yellow soln of (Z)-(tert-butylsulfonyl)(phenyl)diazene (3a) (1.94 g, 10 mmol) in anhyd Et₂O (20 mL) was cooled to 0 °C. Methyllithium (1.6 M soln in Et₂O; 9.37 mL, 15 mmol) was added dropwise during 10 min, and the resulting black soln was stirred at the same temperature for an additional 5 min. Then, the cooling bath was removed and the reaction mixture was allowed to warm to r.t. (ca. 15–20 min). A TLC analysis showed the complete disappearance of the starting diazosulfide 3a. The reaction was directly quenched with H₂O (50 mL); at once the organic soln cleared to brown. The reaction mixture was worked up as described above for entry 2. TLC (PE–Et₂O, 9.5:0.5), GC and GC–MS analyses of the crude residue showed the presence of N-methylaniline as major product [MS: m/z = 108 (M⁺)] besides some by-products. Among them, one was identified as N,N′-dime-thyl-N-phenylhydrazine (14: R = Me, Ar = Ph) [MS: m/z = 136 (M⁺)]. No traces of N,N-dimethylaniline were present. Column chromatography of the residue afforded the pure (TLC, GC, GC–MS, 1H NMR) title compound in 78% yield (0.84 g). Traces of the by-product 14 were identified by GC–MS in the first fraction collected from the column.

The reaction was not complete when carried out at lower temperatures (variable between −78 °C and −20 °C). Using a molar ratio 3a:MeLi = 1:2.2, the title compound was obtained in lower yield and purity (0.56 g, 52%; about 75% purity). When the molar ratio was 1:1.2, the reaction did not proceed to completion.
All the N-methylanilines listed in Table 2 were prepared according to the procedure described above. In entries 35 and 37, the amount of MeLi was doubled (18.75 mL, 30 mmol).

Collateral Proofs

Proof A

A soln of MeLi in Et₂O (1.6 M; 0.94 mL, 1.5 mmol) was cooled to –78 °C and maintained under a nitrogen flow until evaporation of the solvent. The white solid of MeLi so obtained was dissolved in THF-d₈ (2.5 mL) and the temperature was allowed to rise to 0 °C. (Z)-(tert-Butylsulfanyl)(phenyl)diazene (3a) (0.19 g, 1 mmol) was added, under stirring, and then the reaction mixture was allowed to warm to r.t. A sample was drawn with a syringe and put into an NMR-tube that was sealed, but not hermetically, and the progress of the reaction was monitored by using ¹ H NMR. The spectrum recorded after 10 min showed the absence of the peak at δ = 1.64, corresponding to the starting diazofluorene (3a), and the presence of the intermediate (R = Me, Ar = Ph), as major product, and of a small amount of the N-methylaniline [δ = 1.17 (s, t-Bu), 2.07 (s, Me₂NN), 2.73 (s, MeNH), 6.44–6.57, 6.63–6.91, 7.00–7.08 (3 m)].

Because of the rapid progress of the reaction, it was not possible to quantify the peaks. Moreover, a white precipitate of lithium 2–methylthioprop-2-thiol (8) began to form. In time, the peaks at δ = 1.17, 2.07 and 6.63–6.91 decreased rapidly until disappearance after ca. 30 min, and simultaneously the peaks at δ = 2.73, 6.44–6.57 and 7.00–7.08 and the precipitate 8 increased. At this point the NMR spectrum highlighted also a peak at δ = 1.39 (s), corresponding to thiol (2) formed by partial hydrolysis of 8. This increased over time.

Proof B

According to the conditions reported in (1) for entry 2 of Table 2, (Z)-(tert-butylsulfanyl)(phenyl)diazene (3a) (1.94 g, 10 mmol) was treated with an excess of BuLi (1.6 M soln in hexane; 25.00 mL, 40 mmol) at –78 °C and then r.t. GC–MS analysis of the crude residue, obtained after a work up identical to that described above, showed the presence of two major products, i.e. N,N′-dibutyl-N-phenylhydrazine (14; R = Bu, Ar = Ph) [MS: m/z = 220 (M⁺)], and N-butyllanilnine [MS: m/z = 149 (M⁺)], besides some unidentified byproducts. The two major products were separated by flash chromatography [PE–acetone (9:9:0.1)]. The first eluted product was 14, which was further purified by a second flash chromatography [PE–Et₂O, (9:8:0.2)].

Yield: 0.69 g (31%); bp 101–102 °C/0.5 torr.

¹H NMR (CDCl₃, δ): δ = 0.96 (t, J = 7.1 Hz, 3 H), 0.98 (t, J = 7.3 Hz, 3 H), 1.25–1.68 (m, 8 H), 2.33 (dt, J₁ = 7.4, J₂ = 5.3 Hz, 2 H), 3.71 (t, J = 7.0 Hz, 2 H), 6.76–6.89 and 7.17–7.30 (2 m, 2, 3, 5 H).

¹³C NMR (CDCl₃, 400 MHz, δ): δ = 147.71 (CN), 129.05 (CH), 119.35 (2 CH), 114.22 (2 CH), 45.23, 35.23, 29.78, 26.97, 20.93, 20.41 (CH₂), 14.01, 13.88 (CH₃).

Anal. Calcd for C₁₄H₂₄N₂: C, 76.45; H, 11.05; N, 12.66.

The second eluted product was the pure (TLC, GC, GC–MS, ¹H NMR) N-butyllanilnine.

Yield: 0.75 g (50%).

Yields remained unchanged when the reaction time at r.t. was prolonged to 16 h; yields comparable to those reported above were obtained when the reaction was carried out under an atmosphere of argon.

Yield 14: 0.79 g (36%).

Yield N-butyllanilnine: 0.72 g (48%).

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References


(6) Some recent examples on the synthesis of N-
monoalkylanilines, apart from N-monoalkylation of
anilines: (a) Mićočević, I. V.; Ivanović, M. D.; Piantak, D. M.;
Rennels, R. A.; Buchwald, S. L. Angew. Chem., Int. Ed.
Engl. 1995, 34, 1348. (c) Wolfe, J. P.; Buchwald, S. L. J.
6066. (f) Bernardi, P.; Dembech, P.; Fabbri, G.; Ricci, A.;
Seconi, G. J. Org. Chem. 1999, 64, 641; and references
therein. (g) Beletskaya, I. P.; Bessmertnykh, A. G.; Guilard,
R. Synlett 1999, 1459. (h) Bae, J. W.; Cho, Y. J.; Lee, S. H.;
(i) Wolfe, J. P.; Buchwald, S. L. J. Org. Chem. 2000, 65,
1144; and references therein. (j) Periasamy, M. M.;
Natarajan Jayakumart, K.; Bharathi, P.-L.; Basselier, J.-J.


(8) Barbero, M.; Degani, I.; Fochi, R.; Regondi, V. Gazz.

1969, 34, 3434.

(10) (a) Barbero, M.; Degani, I.; Fochi, R.; Perracino, P. National
Abstr. 1998, 129, 24494. (b) Barbero, M.; Crisma, M.;
(c) Barbero, M.; Degani, I.; Dughera, S.; Fochi, R.;

(11) Dell’Erba, C.; Novi, M.; Petrillo, G.; Tavani, C. Tetrahedron
1992, 48, 325.

10.1; Chapman & Hall Electronic Publishing Division: