Synthesis of 3-Aryl-5-ethynlypyrazoles from Silyl-protected Aryl Butadiynyl Ketones

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In contrast to silylated ketones, $R-\text{CO}C\equiv C\equiv C\equiv \text{Si(CH}_3)_3$, which with hydrazine yield hydrazones\(^1\), aryl trimethylsilyl-butadiynyl ketones (1; readily prepared by Friedel Crafts reactions of bis-[trimethylsilyl]-butadiyne with acyl halides\(^2\)) upon treatment with hydrazine hydrate in acidified methanol give 3-aryl-5-trimethylsilylethynlypyrazoles (2) in moderate to good yield.

\[
\begin{align*}
\text{Ar} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} & \quad \text{Si(CH}_3)_3 \\
\text{O} & \\
1
\end{align*}
\]

\[
\begin{align*}
\text{Ar} & \quad \text{C} & \quad \text{C} & \quad \text{Si(CH}_3)_3 \\
\text{H} &
\end{align*}
\]

\[
\begin{align*}
\text{Ar} & \quad \text{C} & \quad \text{C} & \quad \text{CH} \\
\end{align*}
\]

\[
\begin{align*}
\text{N} &
\end{align*}
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\begin{align*}
\text{N} &
\end{align*}
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\begin{align*}
\text{N} &
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\begin{align*}
\text{N} &
\end{align*}
\]
Treatment of these silyl-protected products with aqueous methanolic alkali results in quantitative liberation of the 3-aryl-5-ethynylpyrazoles (3). The diketone likewise is converted to the dipyrrole 5.

![Chemical structure]

The reaction sequence usefully complements other routes to ethynyl pyrazoles based upon alternative means of protection, dehydrohalogenation, or upon cycloaddition of diazooalkanes to diacetylenes.

Table 3. 3-Aryl-5-trimethylsilyl ethynylpyrazoles (2) and 3-Aryl-5-ethynlypyrazoles (3) obtained from Silyl-Protected Aryl Butadiynyl Ketones

<table>
<thead>
<tr>
<th>Aryl</th>
<th>Yield of 2</th>
<th>2</th>
<th>m.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><img src="image1" alt="" /></td>
<td>43</td>
<td>103–104.5°</td>
<td>109–110.5°</td>
</tr>
<tr>
<td><img src="image2" alt="" /></td>
<td>44</td>
<td>144–145.5°</td>
<td>134–135.5°</td>
</tr>
<tr>
<td><img src="image3" alt="" /></td>
<td>25</td>
<td>132.5–133°</td>
<td>165–165.5°</td>
</tr>
<tr>
<td><img src="image4" alt="" /></td>
<td>80</td>
<td>189–190°</td>
<td></td>
</tr>
<tr>
<td><img src="image5" alt="" /></td>
<td>17</td>
<td>90.5–91.5°</td>
<td></td>
</tr>
<tr>
<td><img src="image6" alt="" /></td>
<td>38</td>
<td>85</td>
<td>250° (dec) (5)</td>
</tr>
</tbody>
</table>

4 Undistillable oil identified by N.M.R. and I.R.

Preparation of 3-Aryl-5-trimethylsilyl ethynylpyrazoles (2):
A solution of hydrazine hydrate (40 mmol) in methanol (50 ml) was added to a solution of the aryl trimethylsilylbutadiynyl ketone (30 mmol) in slightly acidified methanol (100 ml) and the mixture was boiled under reflux for 4 hr. Most of the methanol was then removed by rotary evaporation, water was added to the residue, and organic products were extracted with chloroform. The chloroform extracts were washed with water, then dried (Na₂SO₄), and concentrated under reduced pressure. The concentrate was chromatographed on silica gel (100 g) eluting initially with petroleum ether (40–60 fraction) and subsequently with petroleum ether containing up to 40% ether. Product-rich fractions (identified by I.R.) were combined and concentrated under reduced pressure and the residue was recrystallized from methanol/water containing a trace of hydrochloric acid.

Preparation of 3-Aryl-5-ethynylpyrazoles (3):
Aqueous 0.2 M sodium hydroxide (1 mol) was added to methanol (50 ml) containing 2 (1.2 mmol). The mixture was held at 20° for 15 min and was then poured into water (200 ml) and organic products were extracted with ether. The ether extracts were washed with water, then dried (Na₂SO₄), and concentrated by rotary evaporation to leave crude 3 which was purified by recrystallization from aqueous methanol.

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