PALLADIUM-CATALYSED SYNTHESIS OF PYRIMIDINES

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Abstract – Satisfactory yields of 4-substituted pyrimidines and bicyclic pyrimidines are produced from α-methyl or α-methylene ketones when reacted with formamide and tetrakis(triphenylphosphine)palladium(0) or a 1:2 mixture of palladium(II) acetate and triphenylphosphine as catalysts. Under the same reaction conditions pyridines or imidazole are formed from 1,3- or 1,2-diketones.

INTRODUCTION

Pyrimidines constitute an interesting group of naturally occurring diazines being found as pyrimidine and purine bases in nucleic acids and in the vitamin thiamine. Already in 1963 a number of pyrimidines were investigated with respect to their cytotoxic effect and since then important drugs e.g. the nucleoside analogue AZT used in AIDS therapy, acyclovir used in treatment of herpes infections and the prodrug capecitabine used in cancer therapy have been developed.

The intriguing properties and synthetic challenges of pyrimidines have fascinated chemists for a long time. Indeed a synthesis of 4-phenylpyrimidine was reported more than a hundred years ago by Reich. Unsurprisingly a multitude of synthetic methods have been developed since. Our interest stems from the discovery that pyrimidine was produced as a by-product in the Leuckart synthesis (Scheme 1).

Scheme 1

When optimizing the yield of the N-alkylformamide it was evident that the addition of water was advantageous and consequently, when water was omitted, more pyrimidine was produced. This agrees well
with the results of Wakamatsu et al.\textsuperscript{5} and Ochiai et al.\textsuperscript{6} who reported the synthesis of adenine under water free conditions from hydrogen cyanide and formamide respectively. Based on all of the above observations, together with the results showing that \(N\)-alkylformamide (2b) when treated with formamide did not produce any pyrimidine, we propose that four reactions are involved in the process (eqs. 1 – 4).

\[
\begin{align*}
\text{Ph} - \text{CHO} + \text{H}_2\text{NCHO} & \rightarrow \text{Ph-\text{\(N\)}\text{-CHO}} + \text{H}_2\text{O} \quad (1) \\
\text{H}_2\text{O} + \text{H}_2\text{NCHO} & \rightarrow \text{HCO}_2\text{NH}_4^+ \quad (2) \\
\text{Ph-\text{\(N\)}\text{-CHO}} + \text{HCO}_2\text{NH}_4^+ & \rightarrow \text{H}_{\text{\(N\)}\text{-CHO}} + \text{2 H}_2\text{O} \quad (3) \\
\text{Ph-\text{\(N\)}\text{-CHO}} + \text{H}_2\text{NCHO} & \rightarrow \text{\(N\)}\text{-\text{Pyrimidine}} + \text{2 H}_2\text{O} \quad (4)
\end{align*}
\]

Based on this hypothesis three different approaches can be employed in order to increase the yield of pyrimidine; (i) removal water formed in the reaction and thus inhibiting formation of ammonium formate, (eq. 2), (ii) increasing the rate of reaction between initially formed \(N\)-alkylideneformamide (2a) and formamide, making the amount of water found in the reaction mixture of minor importance (eq. 4) or (iii) removal of ammonium formate produced in the reaction, thus inhibiting the competing formation of \(N\)-alkylformamide (2b) (eq. 3). Attempts to remove water from the reaction mixture by drying agents such as molecular sieves or sodium carbonate failed, probably due to the high temperatures needed for the condensation. As a result a number of oxidizing agents were instead scanned in order to create sufficiently oxidizing conditions to prevent reduction of the intermediate \(N\)-alkylideneformamide (2a) to \(N\)-alkylformamide (2b). Utilizing cuprous chloride and molecular oxygen in the absence or presence of 1,10-phenanthroline, an oxidizing system described by Marco et al.,\textsuperscript{7} seemed to solve this problem.\textsuperscript{8} However, yields were not satisfactory, large amounts of catalyst were needed and reactions only took place at high temperatures. We determined therefore to reinvestigate the reaction.

The fact that formic acid and formates can be employed in catalytic hydrogen transfer hydrogenations catalysed by Pd/C,\textsuperscript{9} Raney Ni\textsuperscript{10} or magnesium\textsuperscript{11} led us to look for a suitable catalytic system that could assist in removing ammonium formate formed in the reaction. Akazome et al. have reported the condensation of formamide with 2-nitrophenyl ketones by a palladium(II) chloride and triphenylphosphine catalyst together with a co-catalyst.\textsuperscript{12} Furthermore, reports by Rajagopal and Spatola\textsuperscript{13} show that \(\alpha\)-chloro-
toluene can be hydrodehalogenated by formates with Pd/C catalysis and papers by Amatore et al.\textsuperscript{14} report the activation of aryl iodides by palladium(II) acetate/triphenylphosphine. Consequently, we decided to investigate palladium catalysis with iodobenzene as the hydrogen acceptor.

**RESULTS AND DISCUSSION**

The first successful homogenous catalyst employed was tetrakis(triphenylphosphine)palladium(0) resulting in 68\% of 4-phenylpyrimidine (Table 1). The yield was higher than that in the case of cuprous chloride catalysis and the temperature could be lowered from 180 °C to 160 °C. However, high temperatures were still necessary and we interpret this as the catalyst is not interacting with the actual formation of the \( \text{N-alkylideneformamide} \) or the pyrimidine but instead acts as hydrogen transfer catalyst (Scheme 2).

**Scheme 2**

\[
\begin{align*}
\text{Ph--I} & \quad \xrightarrow{\text{Pd}^0} \quad \text{NH}_4\text{HCO}_2 \quad \text{CO}_2 \\
\text{Ph--Pd--I} & \quad \text{NH}_4\text{I} + \text{Ph--Pd--H} \quad \longrightarrow \quad \text{p}^\text{d} + \text{Ph--H}
\end{align*}
\]

This is in agreement with the reports stating that palladium(II) acetate/triphenylphosphine results in a Pd(0) catalyst that activates iodobenzene\textsuperscript{14} and that formates are donating hydride to palladium followed by reduction of the hydrogen acceptor.\textsuperscript{13, 15} Other methyl ketones also reacted under the same reaction conditions, e.g. methyl cyclohexyl ketone (1b), indicating that the reaction is not limited only to aromatic ketones as has earlier been reported.\textsuperscript{16} Moreover, cyclic ketones, e.g. \( \alpha \)-tetralone (1c), also gave bicyclic product proving that a methylene functionality was tolerated. Since rigid ketones such as cycloheptanone (1d) reacted analogously it was surprising that cyclopentanone (1e) only gave small amounts of the expected product. We therefore wanted to investigate other palladium catalysts in order to see if yields could be improved and began by employing palladium(II) acetate together with triphenylphosphine. Under these changed conditions the yield of 6,7-dihydro-5H-cyclopentapyrimidine (3e) increased to 51\% and a number of other ketones were thus investigated under the same conditions giving pyrimidines in 22 - 82\% yield (Table 1). It was also found that reactions could be performed at somewhat lower temperatures than with the previous protocol and with lower loadings of catalyst. However, the prolonged reaction time combined with the sensitivity of the catalyst, sometimes causing the reaction to stop, led to our continuing with the previous conditions. As it seemed that there was no pronounced difference in the yield, whether a methyl- or a methylene group was situated at one side of the ketone, it was decided to investigate the regioselectivity of the reaction by reacting 2-acetyl cyclohexanone (4a) with formamide and palladium acetate catalysis. To our surprise it was neither of the expected products that were formed, but instead the
4-methyl-5,6,7,8-tetrahydroquinazoline (5a) was found as the main product in 58% yield (Table 2). The stoichiometry of the reaction implies that one equivalent of formamide and one equivalent of ammonia have reacted with the ketone and three equivalents of water have been expelled. Bredereck and co-workers have reported the same reaction, although in lower yield, proposing that the reaction proceeds through a β-ketoimine intermediate. A similar reaction has also been reported by Miller et al. where bis-(α-bromo ketones) gave imidazoles when reacted with formamide at elevated temperatures. However, the reaction of acetylacetone (4b) only gave traces of the symmetrical dimethylpyrimidine in some experiments and instead resulted in the formation of 1-(2,4,6-trimethylpyridin-3-yl)ethanone (5b).

**Table 1.** Isolated yield of products using different catalytic systems.

<table>
<thead>
<tr>
<th>Ketone</th>
<th>Product</th>
<th>Pd(PPh₃)₄</th>
<th>Pd(OAc)₂ / PPh₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>3a</td>
<td>68 %</td>
<td>80 %</td>
</tr>
<tr>
<td>1b</td>
<td>3b</td>
<td>50 %</td>
<td>60 %</td>
</tr>
<tr>
<td>1c</td>
<td>3c</td>
<td>47 %</td>
<td>82 %</td>
</tr>
<tr>
<td>1d</td>
<td>3d</td>
<td>46 %</td>
<td>54 %</td>
</tr>
<tr>
<td>1e</td>
<td>3e</td>
<td>&lt; 5 %</td>
<td>51 %</td>
</tr>
<tr>
<td>1f</td>
<td>3f</td>
<td>-</td>
<td>54 %</td>
</tr>
<tr>
<td>1g</td>
<td>3g</td>
<td>-</td>
<td>22 %&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Starting material was recovered in 50% yield
Other diketones with varying distance between the keto functionalities were also investigated, but results were not very encouraging except for the reaction of benzil (4c) that resulted in the formation of triphenylimidazole (5c) in 25% yield. The product is believed to be formed by a Heck coupling to intermediately formed diphenylimidazole (Scheme 3).

**Table 2.** Isolated yield of products from reaction of diketones.

<table>
<thead>
<tr>
<th>Ketone</th>
<th>Product</th>
<th>Pd(OAc)$_2$ / PPh$_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="4a.png" alt="Image" /></td>
<td><img src="5a.png" alt="Image" /></td>
<td>58%</td>
</tr>
<tr>
<td><img src="4b.png" alt="Image" /></td>
<td><img src="5b.png" alt="Image" /></td>
<td>50%</td>
</tr>
<tr>
<td><img src="4c.png" alt="Image" /></td>
<td><img src="5c.png" alt="Image" /></td>
<td>25%</td>
</tr>
</tbody>
</table>

Scheme 3

In view of the above results the reaction of cyclopentanone (1e) was re-examined. The resulting pyrimidine from reaction of cyclopentanone was isolated from the reaction mixture by chromatography on silica, but in order to obtain an analytically pure sample it was necessary to use HPLC. This also gave a new compound that according to mass spectral analysis and NMR spectroscopy was the tricyclic pyrimidine (6), in 14% yield which was later confirmed by X-Ray crystallography (Figure 1).
An explanation for this may be that the aldol product is formed followed by condensation with formaldehyde (Scheme 4). Similarly, the reactions between formamide and cyclohexanone (1f) or cycloheptanone (1d) gave tricyclic pyridines and work is in progress in investigating this reaction in more detail. It should however be noted that simple $\alpha,\beta$-unsaturated ketones, e.g. cyclopentenone and cyclohexenone did not give any expected product.

**Figure 1.** X-Ray structure of trifluoroacetic acid salt of 1,2,3,6,7,8-hexahydrodicyclopenta\[b,d\]pyridine (6).\(^{19}\)

![Diagram of X-Ray structure](image)

**Scheme 4**

\[
\begin{align*}
\text{1e} & \xrightarrow{H^+} \text{H$_2$NCHO} \\
\text{1e} & \xrightarrow{H^+} \text{6}
\end{align*}
\]

In our experience a limitation to the method is that only traces of pyrimidine have been detected when subjecting aldehydes or less rigid ketones to the same reaction conditions. Also, employing other nitrogen containing moieties such as benzonitrile did not yield any product similar to that what was reported by Herrera et al.\(^{20}\)

**EXPERIMENTAL**

Cycloheptanone (\(>99\%\)) and 4-phenylpyrimidine (\(>96\%\)) were supplied by Aldrich, 2-acetylnaphthalene (\(>99\%\)) was supplied by EGA Chemie and formamide (\(>99\%\)) was supplied by Merck. All other chemicals were supplied by Fluka and were of minimum 99% purity except for, 2-acetylcyclohexanone (\(>97\%\)), palladium(II) acetate (purum), triphenylphosphine (\(>97\%\)), $\alpha$-tetralone (\(>95\%\)). All chemicals were used as
delivered. Melting points were measured on a Büchi 535. GC analyses were performed on a Varian 3300 gas chromatograph equipped with a Supelco Equity-5 (30 m, 0.25 mm i.d.) column. IR spectra were recorded on a Perkin Elmer model 1600 FT-IR. NMR spectra were recorded on a Varian Mercury 400 plus (399.65/100.54 MHz) spectrometer with CDCl₃ as solvent. MS analyses were performed on a VG Quatro mass spectrometer connected to a Hewlett Packard 5890 gas chromatograph equipped with an Agilent HP-5 (30 m, 0.25mm i.d.) column. Compounds (3d) and (3e) were purified by preparative reversed phase high performance liquid chromatography (RP-HPLC) using a C₁₈-column (Delta-Pak™ C₁₈, 100 Å, 15 µm, 25 x 100 mm, Waters Corp., Milford, MA, USA) with a mixture of water and acetonitrile (both containing 0.1% v/v trifluoroacetic acid) as the mobile phase, a flow rate of 7.0 mL/min and UV-detection at 254 nm. A linear gradient varying from 10% to 30% acetonitrile in 30 min effected separation and fractions containing the pure (3d) and (3e) were pooled and the solvent was removed under reduced pressure. The TFA-salt of (3d), (3e) and (6) were diluted with a 10% sodium hydrogen carbonate solution and extracted into an ether phase, dried over magnesium sulfate before solvent removal under reduced pressure.

**General procedure**

To a round bottomed flask charged with palladium(II) acetate (40 mg, 0.18 mmol) and triphenylphosphine (95 mg, 0.36 mmol) were added formamide (5.0 g, 110 mmol), iodobenzene (2.0 g, 10 mmol) and ketone (3.6 mmol) and the resulting mixture was heated at 160 ºC for 8 hrs. The reaction mixture was diluted with ether (50 mL) and extracted with three 25 mL portions of a 2M aqueous solution of hydrogen chloride. The combined aqueous phase was basified by addition of solid sodium hydroxide or a 4M aqueous solution of sodium hydroxide. The combined layers were extracted with ether (2 x 50 mL) and washed with water and brine before drying over sodium carbonate. The solvent was removed under vacuum to give the clean crude yield. Analytically pure samples were obtained by flash chromatography with ethyl acetate or dichlormethane:methanol (19:1) except for compounds (3d) and (3e) which were purified by RP-HPLC.

**4-Phenylpyrimidine (3a)**

Isolated as slightly discolored white crystals (530mg, 80 %), with spectral properties as for commercial material.

**4-Cyclohexylpyrimidine (3b)**

Isolated as a slightly brown oil (320 mg, 60%), IR and MS spectra in accordance with earlier reported material.²¹ ¹H NMR (400 MHz, CDCl₃, δ, ppm): 9.12 (1H, s), 8.61 (1H, d, J = 4.8 Hz), 7.18 (1H, dd, J = 1.0, 5.0 Hz), 2.66 (1H, m), 1.95 (2H, m), 1.88 (2H, m), 1.77 (1H, m), 1.46 (4H, m), 1.30 (1H, m); ¹³C NMR (100 MHz, CDCl₃, δ, ppm): 174.62, 158.61, 156.86, 118.87, 45.97, 32.06, 26.22, 25.87
5,6-Dihydrobenzo[\(h\)]quinazoline (3c)
Isolated as a light yellow crystals (530 mg, 82%); mp 47-49 °C (from ethyl acetate) lit.,\(^{22}\) 54-55 °C; MS (m/z): 183 (25), 182 (88), 181 (100), 180 (14), 179 (5), 155 (12), 154 (57), 153 (11), 152 (7), 140 (6), 129 (6), 128 (37), 127 (65), 126 (36), 117 (8), 116 (11), 102 (8), 101 (7), 90 (6), 89 (12), 78 (8), 77 (27), 76 (13), 75 (13), 74 (9), 64 (27), 63 (23), 62 (6), 52 (6), 51 (19), 50 (9); \(^1\)H NMR (400 MHz, CDCl\(_3\), \(\delta\), ppm): 9.13 (1H, s), 8.56 (1H, s), 8.36 (1H, m), 7.42 (2H, m), 7.27 (1H, m), 2.97 (4H, m); IR (film \(\nu\), cm\(^{-1}\)): 3052, 2983, 1576, 1544, 1446, 1423, 1397, 750; X-Ray.\(^{19}\)

6,7,8,9-Tetrahydro-5\(H\)-cycloheptapyrimidine (3d)
Isolated as a yellow oil (280 mg, 54%). \(^1\)H NMR spectrum in accordance with that of earlier reported material.\(^{21}\) A pure sample was prepared by RP-HPLC (t\(_R\) 19.8 min); MS: (m/z) 149 (12), 148 (100), 147 (44), 134 (4), 133 (38), 131 (8), 121 (7), 120 (28), 119 (63), 118 (5), 94 (11), 93 (9), 92 (15), 91 (12), 81 (9), 80 (41), 79 (35), 78 (12), 77 (19), 67 (16), 66 (29), 65 (47), 64 (13), 63 (16), 54 (12), 53 (27), 52 (39), 51 (28), 50 (11); \(^{13}\)C NMR (100 MHz, CDCl\(_3\), \(\delta\), ppm): 171.36, 156.40, 155.52, 135.56, 39.08, 32.35, 31.96, 27.48, 25.79; IR (film \(\nu\), cm\(^{-1}\)): 2922, 2851, 1572, 1552, 1450, 1397, 919, 779, 718.

6,7-Dihydro-5\(H\)-cyclopentapyrimidine (3e)
Isolated as a yellow oil (240 mg, 51%).\(^{21}\) A pure sample was prepared by RP-HPLC (t\(_R\) 9.4 min); MS (m/z): 121 (11), 120 (100), 119 (71), 94 (3), 93 (28), 92 (20), 80 (8), 67 (8), 66 (36), 65 (31), 64 (14), 63 (14); \(^1\)H NMR (400 MHz, CDCl\(_3\), \(\delta\), ppm): 8.97 (1H, s), 8.53 (1H, m), 3.00 (4H, m), 2.16 (2H, m); \(^{13}\)C NMR (100 MHz, CDCl\(_3\), \(\delta\), ppm): 174.78, 156.93, 151.99, 135.00, 31.78, 25.57, 22.48; IR (film \(\nu\), cm\(^{-1}\)): 3037, 2956, 1590, 1557, 1454, 1393, 732.

5,6,7,8-Tetrahydroquinazoline (3f)
Isolated as a slightly yellow oil (260 mg, 54%).\(^{21}\) MS (m/z): 135 (14), 134 (100), 133 (46), 119 (13), 107 (19), 106 (20), 105 (8), 92 (6), 80 (38), 79 (33), 78 (9), 77 (16), 66 (7), 66 (7); \(^1\)H NMR (400 MHz, CDCl\(_3\), \(\delta\), ppm): 8.89 (1H, s), 8.37 (1H, s), 2.85 (2H, t, J = 6.9 Hz), 2.73 (2H, t, J = 6.3 Hz), 1.89 (2H, m), 1.82 (2H, m); \(^{13}\)CNMR (100 MHz, CDCl\(_3\), \(\delta\), ppm): 165.93, 156.80, 156.0, 130.34, 31.78, 25.57, 22.13, 21.97; IR (film \(\nu\), cm\(^{-1}\)): 3028, 2936, 2861, 1579, 1553, 1454, 1453, 1396, 726.

4-Naphthalen-2-ylpyrimidine (3g)
Isolated as white crystals (160 mg, 22%); mp 122.5-124 °C (from ethyl acetate); MS (m/z): 207 (17), 206 (100), 205 (20), 180 (3), 179 (13), 178 (9), 177 (3), 154 (3), 153 (9), 152 (19), 151 (10), 150 (4), 127 (6),
125 (6), 103 (8), 89 (6), 77 (3), 76 (8), 75 (5); $^1$H NMR (400 MHz, CDCl$_3$, δ, ppm): 9.37 (1H, d, J = 1.2 Hz), 8.85 (1H, d, J = 5.2 Hz), 8.68 (1H, d, J = 2.0 Hz), 8.22 (1H, dd, J = 1.8, 8.6 Hz), 8.02 (2H, m), 7.93 (2H, m), 7.61 (2H, m); $^{13}$C NMR (100 MHz, CDCl$_3$, δ, ppm): 163.85, 159.20, 157.56, 134.69, 133.74, 133.27, 129.10, 128.94, 127.82, 127.63, 127.60, 126.79, 127.38, 117.28; IR (film ν, cm$^{-1}$): 3052, 2984, 1577, 1421, 1389, 895; Anal. Calcd for C$_{14}$H$_{10}$N$_2$: C, 81.53; H, 4.89; N, 13.58. Found: C, 79.80; H, 4.96; N, 13.19; X-Ray.$^{19}$

4-Methyl-5,6,7,8-tetrahydroquinazoline (5a)
Isolated as red-brown crystals (290 mg, 58%); mp 56-60 °C (from ethyl acetate); MS (m/z): 149 (24), 148 (100), 147 (72), 145 (8), 133 (33), 132 (6), 121 (8), 120 (48), 119 (8), 108 (9), 107 (48), 106 (16), 95 (6), 94 (38), 93 (22), 91 (6), 81 (42), 80 (42), 79 (66), 78 (16), 77 (36), 68 (6), 67 (11), 66 (14), 65 (15), 64 (6), 63 (8), 54 (8), 53 (29), 52 (50), 51 (29), 50 (12); $^1$H NMR (400 MHz, CDCl$_3$, δ, ppm): 8.84 (1H, s), 2.92 (2H, s), 2.70 (2H, s), 2.48 (3H, s), 1.91 (4H, m); $^{13}$C NMR (100 MHz, CDCl$_3$, δ, ppm): 165.35, 164.94, 154.52, 128.76, 32.10, 24.97, 22.26, 21.96, 21.42; IR (film ν, cm$^{-1}$): 3048, 2938, 1566, 1424, 1264, 739; Anal. Calcd for C$_9$H$_{12}$N$_2$: C, 72.94; H, 8.16; N, 18.90. Found: C, 72.62; H, 8.37; N, 18.49.

1-(2,4,6-Trimethylpyridin-3-yl)ethanone (5b)
Isolated as yellow oil (203 mg, 50%); MS (m/z): 164 (11), 163 (72), 149 (23), 148 (100), 121 (19), 120 (93), 118 (6), 104 (5), 93 (24), 91 (16), 80 (6), 79 (32), 78 (51), 65 (11), 63 (9), 53 (19), 52 (12), 51 (19), 50 (6), 43 (26); $^1$H NMR (400 MHz, CDCl$_3$, δ, ppm): 6.28 (1H, s), 2.48 (3H, s), 2.46 (3H, s), 2.42 (3H, s), 2.19 (3H, s); $^{13}$C NMR (100 MHz, CDCl$_3$, δ, ppm): 206.59, 157.74, 151.66, 142.64, 135.04, 122.34, 32.19, 24.10, 22.43, 18.78; IR (film ν, cm$^{-1}$): 2960, 2922, 1696, 1590, 1443, 1383, 1256, 1184; Anal. Calcd for C$_{10}$H$_{13}$NO: C, 73.59; H, 8.03; N, 8.58; O, 9.80. Found: C, 68.79; H, 6.96; N, 8.80; O, 15.44.

2,4,5-Triphenyl-1H-imidazole (5c)
Isolated as white crystals (210 mg, 25%) with spectral data similar to earlier reported material.$^{23}$

1,2,3,6,7,8-Hexahydrobicyclo[2.2.1]octa[2,3]dine (6)
The compound was found as a by-product in the synthesis of 3e and was purified by RP-HPLC (t$_R$ 16.6 min). Isolated as a colorless oil (36 mg, 14%) after treatment with sodium hydrogen carbonate; MS (m/z): 160 (9), 159 (72), 158 (100), 157 (6), 156 (10), 143 (5), 131 (13), 130 (19), 117 (5), 115 (5) 77 (10); $^1$H NMR (400 MHz, CDCl$_3$, δ, ppm): 8.21 (1H, s), 3.0-2.77 (8H, m), 2.16-2.05 (4H, m); $^{13}$C NMR (100 MHz, CDCl$_3$, δ, ppm): 163.33, 149.82, 143.44, 137.82, 133.11, 34.23, 31.42, 30.49, 29.48, 25.50, 23.48; X-Ray of TFA-salt.$^{19}$
ACKNOWLEDGEMENTS

Professor Lars Kristian Hansen is gratefully acknowledged for the X-Ray analysis and Frederick Leeson for linguistic assistance.

REFERENCES

3. For a comprehensive review see e.g. S. von Angerer, *Methods of Synthesis*, 2004, 16, 379.
19. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications CCDC 273297 (3c), CCDC 273295 (3g) and CCDC 273296 (6). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: (+44) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).