The conversion of 2-cyano cyanothioformanilides into 3-aminoindole-2-carbonitriles using triphenylphosphine

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1. Introduction

Cyanothioformanilides (thioxanilonitriles) demonstrate herbicidal activity,1 and have been used extensively for the preparation of various heterocycles including pyrroles,2a,b imidazoles,3a–k oxazoles,3a–c 1,3,4-thiadiazoles,5 quinazolines6a and other fused heterocycles.7a–g Furthermore, cyanothioformanilides participate in Diels–Alder8a–c and ene9 reactions, can be N-arylated10 and on addition to the nitrite of H2O, H2S or NaN3 afford aminooxothioacetanilines, aminothiooxothioacetanilines (N-arylthiooxamides),11 or amidinothioformylanilines,12,12 respectively.

Cyanothioformanilides are traditionally prepared by the reaction of N-aryl isothiocyanates with cyanide,13–15 or bis(dialkylamino)acetanilides14 and also via dethiobhydration of N-aryldithiooxamides,15 thiomanation—dethiobhydration of N-aryldithiooxamides15 and thionation—dehydration of aryloxalamides.15 More recent methods involve treating 2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino)benzenes with either the oxidising agent m-CBBA,16 the reducing agent NaBH4CN,17 or with nucleophilic (thiophilic) reagents such asaq NaOH,18 NH2OH,19 tert-butylamine,20 tryptamine,21 o-aminophenethylamine and o-phenylenediamine,22 triphenylphosphoranylidene,23 triphenylphosphine in moist DCM24a–h and with the use of ethylmagnesium bromide (1 equiv).24i–k

Recently, we showed that treating 2-(4-chloro-5H-1,2,3-dithiazol-5-ylideneamino) benzonitriles 1 with triphenylphosphine (4 equiv) gave 3-aminoindole-2-carbonitriles 2 and not the expected 2-cyano cyanothioformanilides 3.26 The latter compounds could however, be prepared from the dithiazolimines 1 on treatment with DBU in high yield27 (Scheme 1).

2-Cyano cyanothioformanilide 3a reacts with triphenylphosphine in the presence of water to give 2-(cyanomethyleneamino)benzonitrile 4a. 2-(cyanomethylamino)benzonitrile 5, 3-aminoindole-2-carbonitrile 2a and (2-cyanoindol-3-yl)iminotriphenylphosphorane 6a. In the presence of p-toluenesulfonic acid in MeOH the reaction between 2-cyano cyanothioformanilide 3a and triphenylphosphine (2 equiv) gives 3-aminoindole-2-carbonitrile 2a in 90% yield. Under the same conditions 2-(cyanomethyleneamino)benzonitrile 4a gives anthranilonitrile 8a. 3-aminoindole-2-carbonitrile 2a and N-(2-cyano phenyl)formamide 9. In addition, substituted 2-cyano cyanothioformanilides 3b–f react with triphenylphosphine and p-toluenesulfonic acid in MeOH to give 3-aminoindole-2-carbonitriles 2b–f in 63–75% yields. Under analogous conditions 2-cyano-4,5-dimethoxycyanophanthydroformanilide 2g gives only 4,5-dimethoxynanthranilinonitrile 8g and 4,6,7-trimethoxyquinazoline-2-carbonitrile 14g, but in refluxing dry PhMe in the presence of p-toluenesulfonic acid 2-cyano-4,5-dimethoxycyanophanthydroformanilide 3g, (2-cyano-5,6-dimethoxyindol-3-yl)iminotriphenylphosphorane 6g and 2-(cyanomethyleneamino)-4,5-dimethoxybenzonitrile 4g are obtained. The structure of 2-(cyanomethyleneamino)-4,5-dimethoxybenzonitrile 4g is supported unambiguously via independent synthesis and comparison to the isomeric 6,7-dimethoxyquinazoline-2-carbonitrile 15. All new compounds are fully characterised and a tentative mechanism for the transformation of 2-cyano cyanothioformanilides to indoles is proposed.

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While a mechanism was not put forward for the formation of the indoles 2, our initial thoughts focused on the triphenylphosphine behaving as a typical thiophile and attacking the dithiazolimine S-2 ring sulfur (Scheme 2). This would be expected to lead to the 2-cyano cyanothioformanilide 3, however, as mentioned above this was not an observed.

In light of this a pure sample of 2-cyano cyanothioformanilide 3a (R=H) was treated with triphenylphosphine to determine whether it was a possible intermediate in the dithiazole to indole conversion. Below we report our findings related to the treatment of 2-cyano cyanothioformanilides 3 with triphenylphosphine.

**Table 1**

<table>
<thead>
<tr>
<th>H₂O (equiv)</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Time (min)</th>
<th>Yields (%)</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>DCM</td>
<td>20</td>
<td>5</td>
<td>78</td>
</tr>
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<td>MeOH</td>
<td>60</td>
<td>5</td>
<td>52</td>
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While a mechanism was not put forward for the formation of the indoles 2, our initial thoughts focused on the triphenylphosphine behaving as a typical thiophile and attacking the dithiazolimine S-2 ring sulfur (Scheme 2). This would be expected to lead to the 2-cyano cyanothioformanilide 3, however, as mentioned above this was not an observed.

**2. Results and discussion**

**2.1. Reaction of 2-cyano cyanthioformanilides with triphenylphosphine**

Treatment of a solution of the cyanothioformanilide 3a in dry DCM at ca. 20 °C with triphenylphosphine (2 equiv) rapidly gave several products: Triphenylphosphine sulfide, 2-(cyanomethylamino)benzonitrile 5, the iminophosphorane 6a and triphenylphosphine oxide (Table 1). Interestingly 3-aminoindole-2-carbonitrile 2a was not observed, however, as the equivalents of water added to the reaction mixture were increased the yield of iminophosphorane 6a decreased while that of the 3-aminoindole 2a increased. The overall yields of indoles (2a + 6a) remained relatively steady. Furthermore, a new compound 4a was isolated in low yield, which was relatively unstable and identified as 2-(cyanomethyleneamino)benzonitrile 4a.

**Scheme 2.**

In light of this a pure sample of 2-cyano cyanthioformanilide 3a (R=H) was treated with triphenylphosphine to determine whether it was a possible intermediate in the dithiazole to indole conversion. Below we report our findings related to the treatment of 2-cyano cyanthioformanilides 3 with triphenylphosphine.
cyanothioformanilide 3a; the 2-(cyanomethyleneamino)benzonitrile 4a or the quinazoline-2-carbonitrile 7. Fortunately, the latter compound 7 is known [mp 162–164 °C, 1H NMR (CDCl3) δH 4.4 9.55 ppm] and had been prepared via an unambiguous route starting from 2-chloroquinazoline.28

When dry benzene or toluene was used as solvents, increasing the reaction temperature significantly raised the yield of the iminophosphorane 6a to 79 and 81%, respectively, and gave total indole recoveries (2a–6a) approaching 90%. In the presence of p-toluenesulfonic acid (PTSA) (1 equiv) the reaction in toluene at ca. 20 °C gave mainly 3-aminoindole-2-carbonitrile 2a rather than the iminophosphorane 6a. It was rationalised that the use of a protic solvent such as methanol could lead to the formation of lesser amounts of indole products and greater amounts of the cyamothylene 5 and this was indeed the case, although some indole products were still obtained. In this case, the addition of a catalytic quantity of PTSA (5 mol %) made little difference to the reaction time to 6 h led to the latter single crystal X-ray structure of the carbene. Similar thiaphosphiranes, have previously been proposed20 and recently the first single crystal X-ray structure of a thiaphosphirane was reported.21 Protonation of the zwitterion 10 could generate a new phosphonium species 11 that could then suffer a second attack by Ph3P on sulfur, followed by protonation, to release the observed (2-cyanomethylamino)benzonitrile 5. Alternatively, the phosphonium species 11 could eliminate triphenylphosphine sulfide to give the observed imine 4a although this could also form from the carbene 13 via a 1,2-H-shift (Scheme 4).

The formation of the indoles was more speculative. Tentatively the zwitterion 10 could add to the ortho cyano group either step-wise or via a cycloaddition to yield a heteroarene 12 that could fragment to the iminophosphorane 6a. Hydrolysis of the iminophosphoranes 6a can give the observed indole 2a and we have shown previously that these two species can be readily inter-converted in high yield.26 The proposed cycloadditions were tentatively supported by the high iminophosphorane recoveries in PhH and PhMe at reflux, while in MeOH and PTSA (1 equiv) the possibility that the ortho-cyano group was converted into an imidate prior to a step-wise cyclisation could explain the high yields of 3-aminoindole-2-carbonitrile 2a.

Attempts to improve the transformation in MeOH by replacing PTSA by mild Lewis acids such as caesium carbonate or zinc chloride gave mainly (2-cyanomethylamino)benzonitrile 5 in 65–67% yields. Further work to understand the scope of this transformation is now underway.

### 2.3. Scope of the 2-cyano cyanothioformanilides to 3-aminoindole-2-carbonitrile transformation

Elucidating the reaction mechanisms for the above transformations still requires further work, however, investigating the effect of aryl substituents can provide useful data as well as identifying the reaction scope and limitations. As such several aryl substituted 2-cyano cyanothioformanilides 3a–g were treated with triphenylphosphine in MeOH in the presence of PTSA (1 equiv) at ca. 20 °C (Table 2).

![Scheme 3](image)

Scheme 3. Reagents and conditions: (i) Ph3P (2 equiv), PTSA (1 equiv) in MeOH at rt, 5 h.

In nearly all cases the expected 3-aminoindole-2-carbonitriles 2 were formed together with triphenylphosphine sulfide, triphenylphosphine oxide and some recovered substituted anthranilinonitriles 8. Some anomalous results were evident: First, the 2-cyano-4-nitro substituted cyanothioformanilide 3c gave a mixture of 3-amino-5-nitroindole-2-carbonitrile 2c (40%) together with the iminophosphorane 6c (21%) but extending the reaction time to 6 h led to the latter’s conversion into the 3-amino-5-nitroindole-2-carbonitrile 2c (65%). Secondly, the 4-chloro-2-cyano cyanothioformanilide 3e gave a moderate yield of 6-chloro-4-methoxyquinazoline-2-carbonitrile 14e (23%). Finally, and the most notable exception, 2-cyano-4,5-dimethoxyphenyl cyanothioformanilide 2g gave 4,5-dimethoxyanthranilinonitrile 8g (30%) and 4,6,7-trimethoxyquinazoline-2-carbonitrile 14g (19%) and no indole products in MeOH. Nevertheless, in anhydrous PhMe at reflux in the absence of PTSA 2-cyano-4,5-dimethoxyphenyl cyanothioformanilide 3g gave some...
(2-cyano-5,6-dimethoxyindol-3-yl)iminotriphenylphosphorane 6g (31%) together with some 2-(cyanomethyleneamino)-4,5-dimethoxybenzonitrile 4g (23%). While the 4-methoxy substituted quinazoline-2-carbonitriles have been previously prepared from cyanothioformanilides simply on treatment with base in MeOH,6c 2-(cyanomethyleneamino)-4,5-dimethoxybenzonitrile 4g had previously mistakenly been identified as 6,7-dimethoxyquinazoline-2-carbonitrile 15 and based on the above identification of 2-(cyanomethyleneamino)benzonitrile 4a this tentative assignment was put into doubt (see below).

Since the by-products from the 2-cyano cyanothioformanilide 3 into indole 2 transformation were in some cases similar or identical to those isolated from the dithiazoalmine 1 to indole 2 transformation it can be postulated that the latter transformation

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**Table 2**

Reaction of cyanothioformanilides 3a–g (0.10 mmol) with Ph$_3$P (2 equiv) in the presence of PTSA (1 equiv) in wet MeOH at rt under a CaCl$_2$ drying tube

<table>
<thead>
<tr>
<th>3a–g (R)</th>
<th>Time (h)</th>
<th>Yields (%)</th>
<th>8</th>
<th>4</th>
<th>14</th>
<th>2</th>
<th>6</th>
<th>Ph$_3$P=O</th>
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<tbody>
<tr>
<td>3a (R=H)</td>
<td>0.17</td>
<td>72</td>
<td>8a (8)</td>
<td>4a (0)</td>
<td>14a (0)</td>
<td>2a (90)</td>
<td>6a (0)</td>
<td>80</td>
</tr>
<tr>
<td>3b (R=3-Me)</td>
<td>1</td>
<td>80</td>
<td>8b (24)</td>
<td>4b (0)</td>
<td>14b (0)</td>
<td>2b (75)</td>
<td>6b (0)</td>
<td>82</td>
</tr>
<tr>
<td>3c (R=4-Cl)</td>
<td>1</td>
<td>77</td>
<td>8c (24)</td>
<td>4c (0)</td>
<td>14c (0)</td>
<td>2c (40)</td>
<td>6c (21)</td>
<td>78</td>
</tr>
<tr>
<td>3d (R=4-O$_2$N)</td>
<td>1</td>
<td>80</td>
<td>8d (25)</td>
<td>4d (0)</td>
<td>14d (0)</td>
<td>2d (65)</td>
<td>6d (0)</td>
<td>77</td>
</tr>
<tr>
<td>3e (R=4-Cl)</td>
<td>1</td>
<td>68</td>
<td>8e (0)</td>
<td>4e (0)</td>
<td>14e (23)</td>
<td>2e (75)</td>
<td>6e (0)</td>
<td>76</td>
</tr>
<tr>
<td>3f (R=4-MeO)</td>
<td>1</td>
<td>80</td>
<td>8f (37)</td>
<td>4f (0)</td>
<td>14f (0)</td>
<td>2f (63)</td>
<td>6f (0)</td>
<td>76</td>
</tr>
<tr>
<td>3g (R=4,5-(MeO)$_2$)</td>
<td>1</td>
<td>59</td>
<td>8g (27)</td>
<td>4g (0)</td>
<td>14g (19)</td>
<td>2g (0)</td>
<td>6g (0)</td>
<td>62</td>
</tr>
<tr>
<td>3h (R=4,5-(MeO)$_2$)</td>
<td>1*</td>
<td>52</td>
<td>8h (0)</td>
<td>4g (23)</td>
<td>14g (0)</td>
<td>2g (0)</td>
<td>6g (31)</td>
<td>50</td>
</tr>
</tbody>
</table>

* The reaction took place in PhMe at reflux.
involved a cyanothioformanilide intermediate or at least a closely related structure. The overall yields of the cyanothioformanilide to indole conversion were notably higher (63–90%) than those reported for the related dithiazoline reaction (7–75), presumably owing to a shorter reaction pathway. Despite this, the dimethoxy substituted cyanothioformanilide 3g gave very low yields of indoles 2g (0%), 3g (31%), similar to the analogous dithiazoline reaction. Electron donating substituents such as methoxy groups clearly did not favour the formation of the antici-
pipated indoles.

2.4. Independent synthesis of 2-(cyanomethyleneamino)-4,5-
dimethoxybenzonitrile 4g and 6,7-dimethoxyquinazoline-2-
carbonitrile 15

Unlike 2-(cyanomethyleneamino)benzonitrile 4a the 4,5-dime-
thoxy analogue 4g was considerably more stable and a sample was prepared independently via the mild oxidation of 2-(cyanomethyl-
amino)-4,5-dimethoxybenzonitrile 16 using either NBS or CaOCl.
Furthermore, treatment of 2-(cyanomethyleneamino)-4,5-dime-
thoxybenzonitrile 4g with NaBH4 in dry MeOH led to its facile con-
version back to 2-(cyanomethyleneamino)-4,5-dimethoxybenzonitrile

Scheme 5. Reagents and conditions: (i) NBS (1 equiv), CaCl2 (0.5 equiv), Ca(OH)2 (2.1 equiv) in CCl4 at 55 \( ^\circ\)C, 10 min (91%); (ii) CaOCl (1.5 equiv), CaCl2 (0.2 equiv), Ca(OH)2 (2 equiv) in DCM at rt. 4 d (50%); (iii) NaBH4 (1.2 equiv) in dry MeOH, rt, 10 min (91%).

To eliminate any possibility of error a pure sample of 6,7-
dimethoxyquinazoline-2-carbonitrile 15 was also prepared from 2-chloro-6,7-dimethoxyquinazoline 17 using sodium cyanide (2 equiv) and DABCO (1 equiv) in DMSO (Scheme 6).

Scheme 6. Reagents and conditions: (i) NaCN (2 equiv), DABCO (1 equiv) in DMSO at 75 \( ^\circ\)C, 10 h (38%), or at rt. 7 d (40%).

Differential scanning calorimetric studies (5 \( ^\circ\)C/min) of isomers 4g and 15 gave considerably different thermal behaviour; the cyanomethyleneamino 4g gave no melting point and only a de-
composition peak at 177 \( ^\circ\)C (onset 173.4 \( ^\circ\)) while the quinazoline 15 showed a sharp melting point at 303.4 \( ^\circ\)C (onset 303.1 \( ^\circ\)) and was followed by an immediate decomposition at 310.3 \( ^\circ\)C (onset 305.7 \( ^\circ\)). Furthermore, unlike the cyanomethyleneamino 4g the isomer 6,7-dimethoxyquinazoline-2-carbonitrile 15 was stable to NaBH4 in dry MeOH. The spectral data of the independently pre-
pared sample of isomer 4g was identical to that isolated from the reaction of 2-cyano-4,5-dimethoxyphenyl cyanothioformanilide 3g with triphenylphosphine.

3. Conclusions

2-Cyano cyanothioformanilide reacts with triphenylphosphine (2 equiv) in either MeOH in the presence of PTSA (1 equiv) or in refluxing toluene to give 3-amino indole-2-carbonitrile in good yield. The reaction in MeOH/PTSA tolerated electron withdrawing substituents but not the strongly electron releasing dimethoxy substituents on the aren moiety. Several minor by-products provided insight into a possible reaction mechanism. Furthermore, 2-(cyanomethyleneamino)benzonitrile treated with triphenyl-
phosphine, PTSA in MeOH also surprisingly gave indole. The success of this transformation suggested that 2-cyano cyanothio-
formanilide could be an intermediate in the related triphenylphosphine mediated dithiazole to indole transformation.

4. Experimental

4.1. General methods and materials

DCM was freshly distilled from CaH2 under argon. Reactions were protected from atmospheric moisture by CaC2 drying tubes. Anhy-
drous Na2SO4 was used for drying organic extracts, and all volatiles were removed under reduced pressure. All reaction mixtures and column eluents were monitored by TLC using commercial glass backed thin layer chromatography (TLC) plates (Merck Kieselgel 60 F254). The plates were observed under UV light at 254 and 365 nm. The technique of dry flash chromatography was used throughout for all non-TLC scale chromatographic separations using Merck Silica Gel 60 (less than 0.063 mm). Melting and decomposition points were determined using either a PolymerTherm-A, Wagner & Munz, Koefler-Hotstage Microscope apparatus or where noted using a TA Instruments DSC Q1000 with samples hermetically sealed in alu-
minium pans under an argon atmosphere; using heating rates of 5 \( ^\circ\)C/min. Solvents used for recrystallisation are indicated after the melting point. UV spectra were obtained using a Perkin–Elmer Lambda–25 UV/vis spectrophotometer and inflections are identified by the abbreviation ‘inf’. IR spectra were recorded on a Shimadzu FTIR–NIR Prestige-21 spectrometer with a Pike Miracle Ge ATR ac-
cessory and strong, medium and weak peaks are represented by s, m and w, respectively. \( ^1\)H and \( ^13\)C NMR spectra were recorded on a Bruker Avance 300 machine (at 300 and 75 MHz, respectively). \( ^13\)C DEPT-135 NMR was used to identify quaternary and tertiary carbons, respectively. Deuterated solvents were used for homonuclear lock and the signals are referenced to the deuterated solvent peaks. Low resolution (EI) mass spectra were recorded on a Shimadzu QP2010 GC/MS with direct inlet probe. 2-Cyano cyanothioformanilides 3a–g, \( ^7\)N-(2-cyano phenyl)formamide 9 and 2-chloro-6,7-dime-
thoxyquinazoline 17 were prepared according to literature pro-
cedures. The isolated reaction by-products, triphenylphosphine sulfide, triphenylphosphine oxide and the anthranilonitriles 8a–g were identical to authentic samples.

4.2. Reaction of 2-cyano cyanothioformanilide 3a with \( \text{Ph}_3\text{P} \)

To stirred solution of 2-cyano cyanothioformanilide 3a (50 mg, 0.27 mmol) in dry PhH (2 mL) at ca. 20 \( ^\circ\)C, was added \( \text{Ph}_3\text{P} \) (142 mg, 0.54 mmol). The reaction mixture was then allowed to stir at ca. 20 \( ^\circ\)C for 5 min, until no starting materials remained (TLC). The re-
action mixture was adsorbed onto silica and chromatography (hexane/DCM, 5:5) gave triphenylphosphine sulfide (134 mg, 84%) as colourless needles, mp 161–162 \( ^\circ\)C (from cyclohexane), \( \text{Rf} \) (hex-
ane/DCM, 5:5) 0.60, identical to an authentic sample. Further elution (hexane/DCM, 2:8) gave 2-(cyanomethyleneamino)benzonitrile 4a (4 mg, 11%) as colourless cotton fibres, mp 75–76 \( ^\circ\)C (from cyclo-
hexane), \( \text{Rf} \) (hexane/DCM, 2:8) 0.70; (found: C, 69.7; H, 3.3; N, 27.0, \( \text{C}_9\text{H}_5\text{N}_3 \) requires C, 69.0; H, 3.8; N, 27.1%), \( \lambda_{\text{max}} \) (DCM)/nm 229 inf (log e 3.03), 237 inf (3.08), 243 (3.12), 253 inf (2.96), 321 (2.54); \( \nu_{\text{max}} \) cm\(^{-1}\) 3096w, 3067w and 3032w (Ar CH), 2926w, 2234m (\( \text{C}_9\text{H}_5\text{N}_3 \)).
Further elution (DCM, 100%) gave 3-aminoindole-2-carbonitrile 2a (1 mg, 3%) as light yellow cotton, mp 172–173 °C (lit., 26 172–173 °C) (from cyclohexane/EtOH), \( R_f \) (hexane/DCM, 2:8) 0.50, identical to an authentic sample. Further elution (DCM, 100%) gave 3-aminoindole-2-carbonitrile 2b (1 mg, 3%) as light yellow cotton, mp 172–173 °C (lit., 26 172–173 °C) (from cyclohexane/EtOH), \( R_f \) (hexane/DCM, 2:8) 0.50, identical to an authentic sample. Further elution (DCM/EtBr/Me2SO, 7:3) gave triphenylphosphine oxide (120 mg, 80%) as colourless needles, mp 154–155 °C (from cyclohexane), \( R_f \) (DCM/EtBr/Me2SO, 7:3) 0.50, identical to an authentic sample.

### 4.3. Reaction of 2-cyano cyanothioformamidines with triphenylphosphine and PTSA in MeOH. (Typical procedure)

#### Table 2

<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield</th>
<th>Rf (DCM/EtBr/Me2SO, 7:3)</th>
<th>mp (°C)</th>
<th>Spectral data</th>
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<tr>
<td>Triphenylphosphine powder</td>
<td>43%</td>
<td>0.05</td>
<td>210</td>
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<tr>
<td>Triphenylphosphine oxide</td>
<td>80%</td>
<td>0.50</td>
<td>139</td>
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</tbody>
</table>

To stirred solution of 2-cyano cyanothioformamide 3a (50 mg, 0.27 mmol) in MeOH (2 mL) at ca. 20 °C, was added PTSA (46.4 mg, 0.27 mmol) and the mixture was left to stir ca. 20 °C for 30 min. Then \( \text{Ph}_3\text{P} \) (142 mg, 0.54 mmol) was added and the mixture was then allowed to stir at ca. 20 °C for 50 min, until no starting material remained (TLC). The reaction mixture was adsorbed onto silica and chromatography (hexane/DCM, 5:5) gave triphenylphosphine sulfide (114 mg, 72%) as colourless needles, mp 161–162 °C (from cyclohexane), \( R_f \) (hexane/DCM, 5:5) 0.60, identical to an authentic sample. Further elution (hexane/DCM, 2:8) gave triphenylphosphine oxide (120 mg, 80%) as colourless needles, mp 154–155 °C (from cyclohexane), \( R_f \) (DCM/EtBr/Me2SO, 7:3) 0.50, identical to an authentic sample.

### 4.3.1. 3-Amino-4-methylindole-2-carbonitrile 2b. (35 mg, 75%) yellow cotton, mp 156–157 °C (lit., 26 156–157 °C) (from cyclohexane/EtOH) identical to an authentic sample.

### 4.3.2. 3-Amino-5-nitroindole-2-carbonitrile 2c. (35.5 mg, 65%) red cotton fibres, mp 310–311 °C (lit., 26 310–311 °C) (from Ph3P) identical to an authentic sample.

### 4.3.3. N-(2-Cyano-5-nitroindole-3-yl)formamidophosphonate 6c. (21 mg, 21%) red powder, mp 300 °C (from Ph3P); (found: C, 70.1; H, 4.1; N, 12.2; \( \text{C}_6\text{H}_9\text{NO}_3\text{P} \) requires C, 70.1; H, 4.1; N, 12.1%; \( \text{m} \text{ax} \text{m} \text{m} \text{ax} \text{m} \text{i} \text{m} \text{m} \text{i} \text{m} \text{i} \text{m} \text{i} \text{m} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{i} \text{"""Author's personal copy"""
3.87 (3H, s, C(3)), 3.71 (1H, s, Ph H), 3.31 (1H, s, Ph H) 3.87 (3H, s, C(3)), 3.86 (3H, s, C(3)O), 7.85 (3H, s, C(3)O); δ(C(75 MHz) 152.9, 150.2, 143.9, 137.4 (Ar C), 116.8, 116.0, 114.5 (Ar C), 102.2, 101.8 (Ar C), 56.4 (CH(3)O); m/z (EI) 215 (M+, 100%), 200 (72), 172 (33), 157 (45), 129 (11), 117 (25), 104 (29), 102 (49), 90 (39), 88 (23), 78 (57), 76 (58), 64 (33), 53 (30). Further elution (DCM/ t-BuOMe, 8:2) gave triphenylphosphine oxide (55 mg, 50%) as colourless needles, mp 154–155 °C (from cyclohexane), Rf (DCM/ t-BuOme, 8:2) 0.50, identical to an authentic sample. Further elution (hexane/EtOH, 7:3) gave (2-cyano-5,6-dimethoxyindol-3-yl) iminotriphenylphosphorane 6g (30 mg, 31%) as red rims, mp 157–158 °C (from cyclohexane/EtOH), Rf (hexane/EtOH, 7:3) 0.60; (found: C, 73.0; H, 5.1; N, 8.8%); Rmax(DCM)/nm 230 (log ε 3.47), 256 (3.22), 318 (3.22), 351.5 inf (2.79); δH(300 MHz; CD2Cl2) 7.80 (1H, s, Ph H), 7.65 (1H, br s, NCH), 7.51 (1H, s, Ph H), 7.31 (1H, s, PhH), 7.26 (1H, s, Ph H), 2.85 (3H, s, C(3)O); δ(C(75 MHz; CDCl3) 150.7, 145.3, 141.3, 133.0 (d, Jp=9.8, Ph P=3.3), 132.7, 132.3 (d, Jp=3.0, Ph P=4.6), 129.0 (d, Jp=12.0, Ph P=6.2), 117.7 (d, Jp=23.2, indole C=11), 117.3 (d, Jp=9.0 indole C=3), 102.3 (indole CH), 95.7 (d, Jp=15.8, indole CH=2, CC=2), 94.5 (indole CH=1), 56.1 (CH(3)O), 56.0 (CH(3)O); δ(C(13)C) (from cyclohexane/eud) 152.9, 157.4, 152.5, 147.4, 138.5, 121.7, 117.1 (C=C=1), 106.2 (Ar C=5 or 8), 105.1 (Ar C=5 or 8), 56.7 (CH(3)O), 56.4 (CH(3)O); m/z (EI) 477 (M+, 100%), 464 (43), 455 (82), 292 (6), 265 (17), 262 (8), 239 (7.5), 183 (37), 108 (14), 77 (3). 4.2. 2-(4-Methylamino)-4,5-dimethoxybenzonitrile 14a via oxidation of 2-(4-carbanilamino)-4,5-dimethoxybenzonitrile 16

4.2.1. Using NBS. To a stirred solution of NBS (27 mg, 0.20 mmol) in CC14 (1 mL) at ca. 55 °C, was added a solution of 2-(4-carbanilamino)-4,5-dimethoxybenzonitrile 16 (36 mg, 0.20 mmol) in CC14 (1 mL). The mixture was left to stir at ca. 55 °C for 5 min and then Ca(OH)2 (31 mg, 0.42 mmol) and CaCl2 (11 mg, 0.1 mmol) were added to the solution. The mixture was left to stir at this temperature for 2 h, until no starting material remained (TLC) and then collected onto silica. Chromatography (DCM, 100%) gave 2-(4-carbanilamino)-4,5-dimethoxybenzonitrile 14a (14 mg, 32%) as yellow cotton fibres, mp 170–171 °C (from cyclohexane), Rf (DCM, 100%) 0.50, identical that described above.

4.2.2. Using calcium hypochlorite. To a stirred solution of 2-(carbanilamino)-4,5-dimethoxybenzonitrile 16 (36 mg, 0.20 mmol) in DCM (2 mL) was added CaOCl (43 mg, 0.30 mmol) and CaCl2 (11 mg, 0.1 mmol). The mixture was left to stir at ca. 20 °C for 5 min and then Ca(OH)2 (30 mg, 0.40 mmol) was added to the solution. The mixture was left to stir at this temperature for 4 h, until no starting material remained (TLC) and then collected onto silica. Chromatography (DCM, 100%) gave 2-(4-carbanilamino)-4,5-dimethoxybenzonitrile 14a (21.5 mg, 50%) as yellow cotton fibres, mp 170–171 °C (from cyclohexane), Rf (DCM, 100%) 0.50, identical to that described above.

4.2. 2-(4-Methylamino)-4,5-dimethoxybenzonitrile 14a via reduction of 2-(4-carbanilamino)-4,5-dimethoxybenzonitrile 16

4.2.1. Using NBS. To a stirred solution of 2-(4-carbanilamino)-4,5-dimethoxybenzonitrile 16 (36 mg, 0.20 mmol) in DCM (2 mL) was added CaOCl (43 mg, 0.30 mmol) and CaCl2 (11 mg, 0.1 mmol). The mixture was left to stir at ca. 20 °C for 5 min and then Ca(OH)2 (30 mg, 0.40 mmol) was added to the solution. The mixture was left to stir at this temperature for 4 h, until no starting material remained (TLC) and then collected onto silica. Chromatography (DCM, 100%) gave 2-(4-carbanilamino)-4,5-dimethoxybenzonitrile 14a (21.5 mg, 50%) as yellow cotton fibres, mp 170–171 °C (from cyclohexane), Rf (DCM, 100%) 0.50, identical to that described above.

4.2.2. Using calcium hypochlorite. To a stirred solution of 2-(carbanilamino)-4,5-dimethoxybenzonitrile 16 (36 mg, 0.20 mmol) in DCM (2 mL) was added CaOCl (43 mg, 0.30 mmol) and CaCl2 (11 mg, 0.1 mmol). The mixture was left to stir at ca. 20 °C for 5 min and then Ca(OH)2 (30 mg, 0.40 mmol) was added to the solution. The mixture was left to stir at this temperature for 4 h, until no starting material remained (TLC) and then collected onto silica. Chromatography (DCM, 100%) gave 2-(4-carbanilamino)-4,5-dimethoxybenzonitrile 14a (21.5 mg, 50%) as yellow cotton fibres, mp 170–171 °C (from cyclohexane), Rf (DCM, 100%) 0.50, identical to that described above.

4.2. 2-(4-Methylamino)-4,5-dimethoxybenzonitrile 14a in DCM (2 mL) via reduction of 2-(4-carbanilamino)-4,5-dimethoxybenzonitrile 16

4.2.1. Using NBS. To a stirred solution of 2-(4-carbanilamino)-4,5-dimethoxybenzonitrile 16 (36 mg, 0.20 mmol) in DCM (2 mL) was added CaOCl (43 mg, 0.30 mmol) and CaCl2 (11 mg, 0.1 mmol). The mixture was left to stir at ca. 20 °C for 5 min and then Ca(OH)2 (30 mg, 0.40 mmol) was added to the solution. The mixture was left to stir at this temperature for 4 h, until no starting material remained (TLC) and then collected onto silica. Chromatography (DCM, 100%) gave 2-(4-carbanilamino)-4,5-dimethoxybenzonitrile 14a (21.5 mg, 50%) as yellow cotton fibres, mp 170–171 °C (from cyclohexane), Rf (DCM, 100%) 0.50, identical to that described above.
Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.06.020.

References and notes