Tetrahedron 68 (2012) 2899–2905

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Phosphonium salt-catalysed synthesis of nitriles from in situ activated oximes

Ross M. Denton *, Jie An, Petra Lindovska, William Lewis

School of Chemistry University of Nottingham, University Park, Nottingham NG7 2RD, UK

ARTICLE INFO

Article history:
Received 17 October 2011
Received in revised form 10 January 2012
Accepted 23 January 2012
Available online 30 January 2012

Keywords:
Nitriles
Oximes
Catalysis
Phosphonium salts
Phosphine oxides

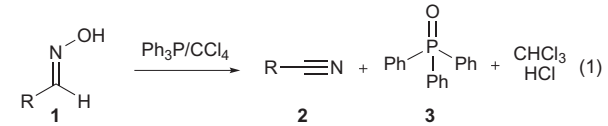
ABSTRACT

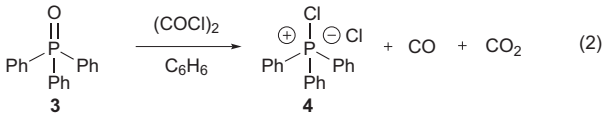
A metal-free catalytic method for the conversion of aromatic and aliphatic aldoximes to nitriles at room temperature using oxalyl chloride (1.2 equiv) in combination with 5 mol % of triphenylphosphine oxide is reported. Of the many potential pathways leading from oxime to nitrile a manifold involving chlorophosphonium salt-catalysed decomposition of oxime chlorooxalates formed in situ is shown to be operative.

1. Introduction

The nitrile functional group is fundamental to organic chemistry[1] and nitrile-containing molecules are also valuable end products in their own right.[2] The laboratory-scale[3] synthesis of aliphatic nitriles is usually accomplished by nucleophilic substitution of alkyl halides with inorganic cyanides,[4] while the synthesis of aryl nitriles can be achieved classically by direct cyanation of aryl halides using copper(I) cyanide[5] or more recently via palladium,[6] copper[7] or nickel[8] catalysis. An alternative method, applicable to the synthesis of both aliphatic and aromatic substrates, involves dehydration of primary amides or aldoximes. The latter can be achieved using stoichiometric reagents or,[9] more desirably, via catalysis.[9u,10] Of the documented stoichiometric methods the dehydration of aldoximes using in situ generated halophosphonium salts is attractive as these reactions take place at room temperature under mild conditions. Specific examples include the PPh_3/CCl_4 system[11] (Eq. 1) and the use of PPh_3/molecular halogen combinations.[12] A disadvantage of these methods is the production of phosphine oxides as stoichiometric by-products; however, recent work by others and us has involved the development of catalytic versions of reactions that are mediated by stoichiometric phosphorus(V) reagents.[13] These include the phosphine oxide-catalysed aza-Wittig reactions developed by Marsden,[14] the phosphine-catalysed Wittig reactions developed by O'Brien,[15] the phosphine-catalysed reduction of silyl peroxides by Woerpel[16] and the development of a catalytic Appel reaction for the synthesis of alkyl halides from alcohols[17] and epoxides[18] reported by us as well as by Rutjes and van Delft.[19]

At the outset of this study we reasoned, in analogy with our previous work,[17,18] that it might be possible to develop a catalytic aldoxime dehydration process by combining the conversion of aldoximes into nitriles (Eq. 1)[6] with the oxalyl chloride-mediated transformation of phosphine oxides into chlorophosphonium salts (Eq. 2).[20] In this way the phosphine oxide by-product derived from the dehydration could be converted back into the active halophosphonium salt to achieve a process, that is, catalytic with respect to the phosphorus component.





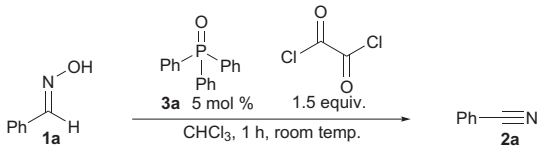
2. Results and discussion

We began by confirming that chlorotriphenylphosphonium chloride **4**, formed from triphenylphosphine oxide and oxalyl chloride, was effective for the stoichiometric dehydration of test substrate benzaldehyde oxime **1a** (Table 1, entry 1). The high yield and short reaction time were encouraging and an initial trial of the

* Corresponding author. Tel.: +44 115 951 4194; fax: +44 115 951 3564; e-mail address: ross.denton@nottingham.ac.uk (R.M. Denton).

0040-4020/$ – see front matter © 2012 Published by Elsevier Ltd.
doi:10.1016/j.tet.2012.01.067

Table 1
Development of catalytic aldoxime dehydration[a]



Entry	Catalyst loading (mol %)	$(COCl)_2$ (mol %)	Addition protocol	Time	Yield **2a** %
1	100	100	**1a** added to $(COCl)_2$ and **3** in one portion	3 min	91[b]
2	5	100	**1a** and $(COCl)_2$ added to **3** and $(COCl)_2$ over 1 h	2 h	73[c]
3	5	100	**1a** added to $(COCl)_2$ and **3** over 0.5 h	1 h	91[b]
4	5	120	**1a** added to $(COCl)_2$ and **3** over 0.5 h	1 h	99[b]
5	2	120	**1a** added to $(COCl)_2$ and **3** over 0.5 h	1 h	78[b]
6	0	120	**1a** added to $(COCl)_2$ over 0.5 h	1 h	0

[a] 1 mmol scale with respect to **1a**.
[b] Isolated yield.
[c] Yield determined by ^1H NMR using $C_2H_2Cl_4$ as an internal standard.

catalytic reaction with 5 mol % triphenylphosphine oxide and 1 equiv of oxalyl chloride followed (entry 2). A 73% yield of product was obtained with the remainder of the mass balance being the mono oxime ester **5a** derived from the reaction of the oxime with oxalyl chloride.

In this reaction both the oxalyl chloride and the oxime were added simultaneously (and separately) to a solution of 5 mol % of chlorophosphonium salt **4a** that had been preformed from triphenylphosphine oxide and oxalyl chloride. This protocol was adopted in an attempt to minimize the reaction between the oxime and oxalyl chloride that would result in the formation of mono and bis oxime esters **5a** and **6a** that we believed would be unreactive by-products. We were therefore surprised to observe that, upon addition of the oxime substrate to a solution of oxalyl chloride and triphenylphosphine oxide, the nitrile product was obtained in an improved 91% yield (entry 3). Increasing the amount of oxalyl chloride to 1.2 equiv improved the yield still further (entry 4) while decreasing the loading of triphenylphosphine oxide was detrimental (entry 5). Finally, no nitrile product was obtained in the absence of triphenylphosphine oxide (entry 6). That an increased yield was obtained using the addition protocol of entries 3–5 suggested a role for the oxime esters **5a** and **6a** in the formation of the nitrile product; however, before investigating the reactivity of **5a** and **6a** in more detail we first conducted a study of substrate scope using the optimal conditions from entry 4.

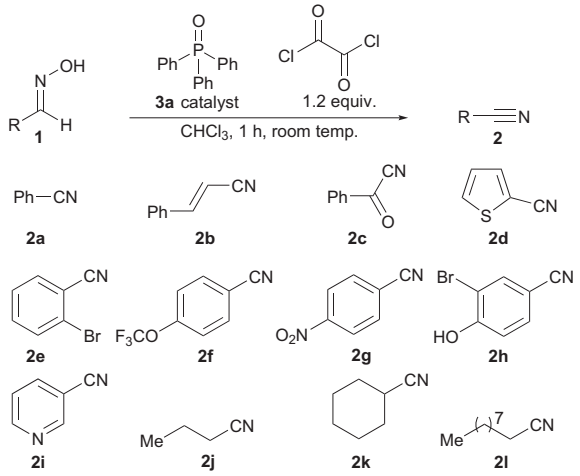
The results obtained show that the reaction is effective for a range of aliphatic, aromatic and heteroaromatic substrates and that good to excellent yields (73–99%) were obtained in all cases. Substrates that have basic/nucleophilic heteroatoms, such as **1h** and **1i** (entries 11 and 12) were also efficiently converted into nitriles; furthermore, nitro, ketone and trifluoromethoxy groups were also tolerated.

We next applied the reaction to the synthesis of a naturally occurring pyrrole from *Angelas oroides*.[21] The synthesis began with the double bromination of commercially available pyrrole **7**. The dibromide obtained after recrystallisation was then condensed with hydroxylamine hydrochloride to afford the corresponding oxime **1m**. Dehydration of this substrate using the conditions depicted in Table 2 afforded the natural product in 91% isolated yield (Scheme 1).

2.1. Mechanistic studies

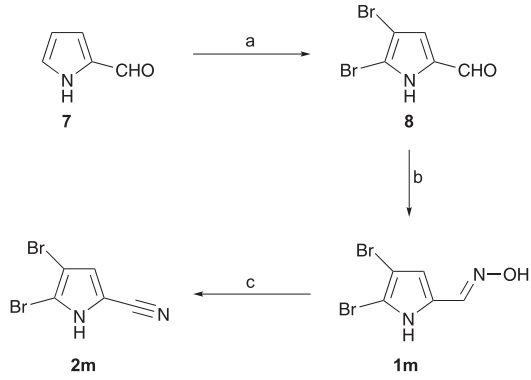
Having examined the scope of the reaction we examined in more detail the roles of the phosphine oxide and derived chlorophosphonium salt in the catalytic reaction. At the outset we envisaged a catalytic cycle of the type depicted as cycle 1 within Scheme 2 (resulting from the combination of Eqns. 1 and 2) in which the chlorophosphonium salt reacts with the oxime to provide intermediate **9** that undergoes conversion to the nitrile product. However, from the results presented in Table 1 it is apparent that the highest yields are obtained when the oxime substrate is added to a solution of 5 mol % triphenylphosphine oxide and 1.2 equiv of oxalyl chloride. Under this addition protocol, in which the oxime will be exposed to a large excess of oxalyl chloride, it is very likely that activated oxime esters of type **5** (shown in cycle 2 of Scheme 2) are formed and, further, that they are implicated in the formation of product through a second manifold (cycle 2,

Table 2
Substrate scope for catalytic dehydration of aldoximes[a]



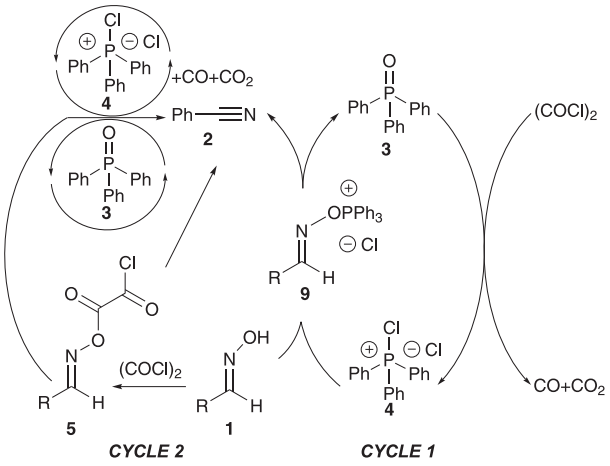
Entry	Oxime	Solvent	Method	Product	Yield **2** %
1	**1a**	$CHCl_3$	a	**2a**	99
2	**1a**	$CHCl_3$	b	**2a**	76
3	**1a**	$CHCl_3$	a	**2a**	94[b]
4	**1b**	$CHCl_3$	b	**2b**	90
5	**1c**	EtOAc	a	**2c**	93
6	**1d**	EtOAc	a	**2d**	95
7	**1d**	$CHCl_3$	b	**2d**	77
8	**1e**	EtOAc	a	**2e**	73
9	**1f**	$CHCl_3$	a	**2f**	82
10	**1g**	$CHCl_3$	b	**2g**	87
11	**1h**	$CHCl_3$	b	**2h**	85
12	**1i**	EtOAc	b	**2i**	77
13	**1j**	$CHCl_3$	a	**2j**	99
14	**1k**	$CHCl_3$	a	**2k**	88
15	**1l**	$CHCl_3$	a	**2l**	95

[a] 1 mmol scale with respect to **1**; all yields isolated yields except for **2j** (determined by ^1H NMR using $C_2H_2Cl_4$ as an internal standard).
[b] 10 mmol scale with respect to **1**. See Experimental section for details of methods a and b.



Scheme 1. Reagents and conditions: (a) Br_2, AcOH, $CHCl_3$, 50 °C, 16 h, 56%; (b) $NH_2OH{\cdot}HCl$, NaOH, EtOH, 1.5 h, 87%; (c) $(COCl)_2$ 1.2 equiv, Ph_3PO 5 mol %, $CHCl_3$, rt, 1 h, 91%.

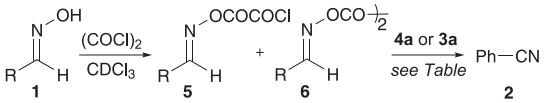
Scheme 2). In this pathway the activated oxime ester **5** may undergo non-catalysed or catalysed decomposition to the nitrile as shown.



Scheme 2.

In order to explore the various possible pathways we prepared and characterized the mono oxime ester[22] **5a** by slow addition of the relevant oxime to oxalyl chloride (Table 3). In this reaction the desired mono ester **5a** was obtained with (26%) of the corresponding bis ester **6a**. While the ester carbonyl carbon and azamethine ^{13}C NMR resonances associated with the mono ester were well resolved ($CDCl_3$ 100 MHz δ 160.2 and 159.3 ppm, respectively) a single peak at 158.4 was observed for the bis ester indicating overlap of these two resonances. This was confirmed by deliberate synthesis of the bis ester **6a**, X-ray crystallography[23] (Fig. 1) and subsequent NMR analysis.

Table 3
Synthesis and reactivity of oxime esters[a]



Entry	Oxime	Catalyst (loading mol %)	Yield **2** %
1	**1a**	**3a** (5)	74
2	**1a**	**4a** (5)	71
3	**1j**	No cat.	32
4	**1j**	**3a** (5)	97
5	**1j**	**4a** (5)	97

[a] Yield determined by ^1H NMR using $C_2H_2Cl_4$ as an internal standard.

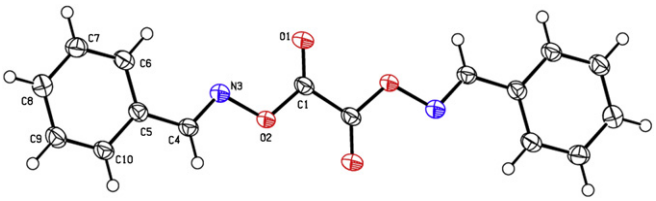


Fig. 1. Crystal structure of **6a**.

With both mono and bis oxime esters synthesized and characterized we investigated their reactivity with phosphine oxides and phosphonium salts (Table 3). In the first instance the mixture of **5a** and **6a** (74%:26%) obtained from the reaction depicted in entry 1 was treated with 5 mol % of triphenylphosphine oxide under the conditions employed in the catalytic reactions (entry 1). Complete conversion of **5a** into the nitrile product was observed while the bis ester present in the mixture remained unchanged. In an analogous reaction with chlorophosphonium salt **4a** (entry 2) we observed complete conversion into benzonitrile.[24] These results clearly indicated that the pathway involving decomposition of activated oximes of type **5** is feasible under the conditions of the catalytic reactions.

To gain further information we monitored the catalytic dehydration of benzaldehyde oxime to benzonitrile via multinuclear NMR. In this experiment the oxime was added to a solution of oxalyl chloride (1.2 equiv) and triphenylphosphine oxide (5 mol %) in one portion and ^1H, ^{13}C and ^{31}P spectra were recorded approximately every 10 min. Inspection of the ^{13}C NMR spectra recorded at 5 min (Fig. 2) revealed a mixture of mono ester **5a**, bis ester **6a**, oxalyl chloride and benzonitrile; the major species being **5a**. Subsequent spectra showed a decay of the carbonyl resonances associated with **5a** and an increase of those associated with the benzonitrile product while the peaks associated with the bis ester **6a** remained constant throughout.

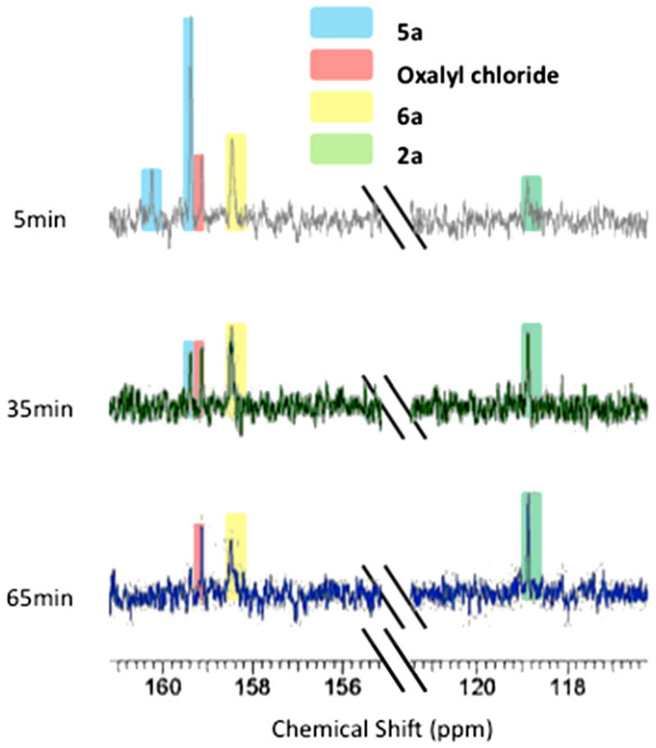
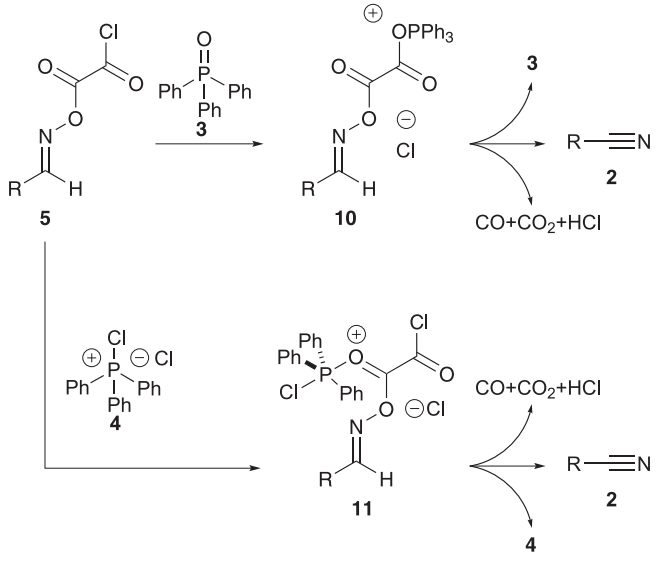


Fig. 2. NMR study of catalytic reaction.

Inspection of analogous ^{31}P NMR spectra showed chlorophosphonium salt **4a** but no triphenylphosphine oxide. While the conditions under, which the NMR data was acquired are not identical to those employed in all of the catalytic reactions (method a involves addition of the oxime to a solution of phosphine oxide and oxalyl chloride over 30 min) the results of this study provide strong support for catalysis occurring in cycle 2 of Scheme 2 and, specifically, for chlorophosphonium salt **4a** being responsible[25] for conversion of the activated oxime ester **5a** into the product. This is consistent with the results presented in Table 1, which showed that the highest yield of benzonitrile was obtained under conditions that expose the both oxime substrate and the phosphine oxide to an excess of oxalyl chloride (entry 3, Table 1). Catalysis in cycle 1 may be occurring when the oxime and oxalyl chloride are added simultaneously and separately to a preformed solution of phosphonium salt **4a** (entry 2, Table 1); however, it is clear that superior results are obtained from the activated ester pathway. We then repeated this study with the aliphatic oxime **1j**. In contrast to the above we noted, in this case, that the mono oxime ester **5j** undergoes slow conversion into the nitrile product in the absence of catalyst (32% after 1 h, entry 3).[26] A much-improved 97% yield of nitrile product was obtained when the mono ester was treated with 5 mol % of either triphenylphosphine oxide or chlorotriphenylphosphonium chloride. These results indicate that catalytic reactions with aliphatic substrates are also operating in cycle 2 but that some of the product may arise from direct conversion of **5j** to the product perhaps via a retro ene process in which oxalic acid mono chloride is generated as a an initial by-product.

Finally, we speculate on the role that the phosphine oxide and chlorophosphonium salt play in the conversion of the activated mono oxime ester **5** to nitrile (Scheme 3). In the case of the phosphine oxide activation of substrate **5** may occur via addition to the acid chloride followed by elimination to afford **10**. In the case of the chlorophosphonium salt **4** one tentative possibility is a Lewis acid/Lewis base interaction between the ester carbonyl oxygen and the phosphonium salt[25] resulting in the formation of a transient pentacoordinate phosphorane, such as **11**, which then decomposes to product returning the phosphonium salt.



Scheme 3.

3. Conclusions

In summary we have developed a metal-free catalytic method for the dehydration of aromatic and aliphatic aldoximes that takes place at room temperature using inexpensive and readily available reagents. In contrast to our original design, which was based on dehydration under Appel conditions, the dehydration reaction takes place via in situ activation of the oxime with oxalyl chloride followed by chlorophosphonium salt-catalysed decomposition to product.

4. Experimental

4.1. General information

Glassware was dried in an oven overnight before use. Thin layer chromatography was carried out on Polgram SIL G/UV254 silica-aluminium plates and plates were visualised using ultra-violet light (254 nm) and $KMnO_4$ solution. For flash column chromatography Fluorochem silica gel 60, 35–70 μ was used. NMR data was collected at either 270, or 400 MHz. Data was manipulated directly from the spectrometer or via a networked PC with appropriate software. All samples were analysed in $CDCl_3$ unless otherwise stated. Reference values for residual solvent were taken as δ=7.27 ($CDCl_3$) for ^1H NMR; δ=77.1 ($CDCl_3$) for ^{13}C NMR. Multiplicities for coupled signals we designated using the following abbreviations: s=singlet, d=doublet, t=triplet, q=quartet, quin=quintet, sex=sextet and br=broad signal, and coupling constants are given in hertz. Where appropriate, COSY, HMQC and HMBC experiments were performed to aid assignment. ^{31}P NMR was recorded with decoupling. Single crystal X-ray diffraction was carried out by the X-ray crystallography department at the University of Nottingham using a Bruker SMART 1000 CCD area detector diffractometer. All solvents and reagents were obtained from commercial sources and used as supplied.

4.2. General procedure to determine the yield via ^1H NMR

The crude reaction mixture was dissolved in $CDCl_3$ and transferred to a volumetric flask (two washings of the original flask were done after transfer) that was subsequently made up to the correct volume with further $CDCl_3$. To a 1 mL aliquot of this solution was added 1,1,2,2-tetrachlorethane (accurately approximately 15–80 mg). The ^1H NMR spectrum was recorded and the mass of the product calculated according to the equation below:

$$\text{mass}_{\text{product}} = \left(\text{area}_{\text{product}}/\text{area}_{\text{standard}}\right) \times \left(\text{MW}_{\text{product}}/\text{MW}_{\text{standard}}\right) \times \text{mass}_{\text{standard}} \times \text{purity factor}_{\text{standard}} \times n \times m$$

where n corrects for the amount of the crude reaction mixture used and m corrects for the number of protons associated with the resonance used.

4.3. Synthesis of nitriles

4.3.1. Method a. To a solution of triphenylphosphine oxide (14 mg, 0.050 mmol) in either $CHCl_3$, $CDCl_3$ or EtOAc (2.0 mL) was added oxalyl chloride (102 μL, 1.21 mmol) and the reaction mixture was stirred for 5 min. The appropriate oxime (1.00 equiv) as solution in either $CHCl_3$, $CDCl_3$ or EtOAc (1.0 mL) was then added over 0.5 h via syringe pump at room temperature and the reaction mixture was stirred for a further 0.5 h at room temperature after which the solvent was removed in vacuo. Purification by flash chromatography (silica, 10–100% Et_2O/pet. ether) gave the pure nitriles.

4.3.2. Method b. To a solution of triphenylphosphine oxide (14 mg, 0.050 mmol) in either $CHCl_3$, $CDCl_3$ or EtOAc (3.0 mL) was added oxalyl chloride (102 μL, 1.21 mmol) and the reaction mixture was stirred for 5 min. The appropriate oxime (1.00 equiv) was then

added in one portion and the reaction mixture was stirred for 1.0 h at room temperature after which the solvent was removed in vacuo. Purification by flash chromatography (silica, 10–100% Et_2O/pet. ether) gave the pure nitriles.

4.3.3. Benzonitrile ***2a***.[27] The following reagents were combined in the amounts indicated according to method a. (*E*)-benzaldehyde oxime (121 mg, 0.999 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (14 mg, 0.050 mmol) and $CHCl_3$ (3.0 mL). Purification by flash column chromatography (silica, 10% Et_2O/pet. ether) afforded **2a** as a colourless oil (102 mg, 99%). R_f (17% Et_2O/pet. ether) 0.57; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69–7.58 (m, 3H, Ar**H**), 5.52–7.44 (m, 2H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.7, 132.1, 129.1, 118.8, 112.3.

4.3.4. Benzonitrile ***2a*** *[27] large-scale reaction.* To a solution of triphenylphosphine oxide (139 mg, 0.499 mmol) in $CHCl_3$ (20.0 mL) was added oxalyl chloride (1.02 mL, 12.1 mmol) and the reaction mixture was stirred for 5 min (*E*)-benzaldehyde oxime (1.21 g, 10.0 mmol) as solution in $CHCl_3$ (10.0 mL) was then added simultaneously over 45 min via pressure equalizing dropping funnel at room temperature. The reaction mixture was stirred for another 0.5 h at room temperature. The solvent was then removed in vacuo. Purification by flash column chromatography (silica, 10% Et_2O/pet. ether) afforded **2a** as a colourless oil (965 mg, 94%). R_f (17% Et_2O/pet. ether) 0.57.

4.3.5. Cinnamonitrile ***2b***.[28] The following reagents were combined in the amounts indicated according to method b. (*E*/*Z*) cinnamylaldehyde oxime (147 mg, 0.999 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (14 mg, 0.050 mmol) and $CHCl_3$ (3.0 mL). Purification by flash column chromatography (silica, 100% Et_2O) afforded **2b** as a colourless oil (116 mg, 90%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.36 (m, 6H, 5× Ar**H** and ArC**H**), 5.89 (d, *J*=16.7 Hz, 1H, C**H**CN); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.6, 133.5, 131.2, 129.1, 127.4, 118.2, 96.4.

4.3.6. Benzoyl cyanide ***2c***.[29] The following reagents were combined in the amounts indicated according to method a. 2-Isonitrosoacetophenone (149 mg, 0.999 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (14 mg, 0.050 mmol) and EtOAc (3.0 mL). Purification by flash column chromatography (silica, 100% Et_2O) afforded **2c** as a yellow oil (122 mg, 93%). ^1H NMR (270 MHz, $CDCl_3$) δ 8.18–8.13 (m, 2H, Ar**H**), 7.83–7.77 (m, 1H, Ar**H**), 7.65–7.59 (m, 2H, Ar**H**); ^{13}C NMR (68 MHz, $CDCl_3$) δ 167.9, 136.9, 133.3, 130.5, 129.5, 112.7.

4.3.7. Thiophene-2-carbonitrile ***2d***.[30] The following reagents were combined in the amounts indicated according to method b. Thiophene-2-carboxaldoxime (127 mg, 0.999 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (14 mg, 0.050 mmol) and $CHCl_3$ (3.0 mL). Purification by flash column chromatography (silica, 20% Et_2O/pet. ether) afforded **2d** as a colourless oil (84 mg, 77%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.66–7.60 (m, 2H, SCH**CH**C**H**); 7.16–7.11 (m, 1H, SC**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 132.6, 127.7, 114.3, 109.9.

4.3.8. Thiophene-2-carbonitrile ***2d***.[28] The following reagents were combined in the amounts indicated according to method a. Thiophene-2-carboxaldoxime (127 mg, 0.999 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (14 mg, 0.050 mmol) and EtOAc (3.0 mL). Purification by flash column chromatography (silica, 20% Et_2O/pet. ether) afforded **2d** as a colourless oil (104 mg, 95%).

4.3.9. 2-Bromobenzonitrile ***2e***.[31] The following reagents were combined in the amounts indicated according to method a. 2-Bromobenzaldoxime (200 mg, 1.00 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (14 mg, 0.050 mmol) and EtOAc (3.0 mL). Purification by flash column chromatography (silica, 50% Et_2O/pet. ether) afforded **2e** as a white solid (133 mg, 73%). Mp 54 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73–7.65 (m, 2H, Ar**H**), 7.51–7.41 (m, 2H, Ar**H**); ^{13}C NMR (400 MHz, $CDCl_3$) δ 134.3, 134.0, 133.2, 127.7, 125.3, 117.2, 115.8.

4.3.10. 4-(Trifluoromethoxy)benzonitrile ***2f***.[32] The following reagents were combined in the amounts indicated according to method a. 4-(Trifluoromethoxy)benzaldehyde oxime (103 mg, 0.502 mmol), oxalyl chloride (51 μL, 0.60 mmol), triphenylphosphine oxide (7.0 mg, 0.025 mmol) and $CHCl_3$ (1.5 mL). Purification by flash column chromatography (silica, 17% Et_2O/pet. ether) afforded **2f** as a colourless oil (76 mg, 82%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.76–7.70 (m, 2H, Ar**H**), 7.35–7.29 (m, 2H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 134.2, 121.2, 120.2 (q, *J*=258 Hz), 117.7, 110.9.

4.3.11. 4-Nitrobenzonitrile ***2g***.[33] The following reagents were combined in the amounts indicated according to method b. 4-Nitrobenzaldehyde oxime (166 mg, 0.999 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (14 mg, 0.050 mmol) and $CHCl_3$ (3.0 mL). Purification by flash column chromatography (silica, 100% Et_2O) afforded **2g** as a white solid (129 mg, 87%). Mp 146–147 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.40–8.34 (m, 2H, Ar**H**), 7.93–7.87 (m, 2H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.0, 133.5, 124.3, 118.3, 116.8.

4.3.12. 3-Bromo-4-hydroxybenzonitrile ***2h***.[34] The following reagents were combined in the amounts indicated according to method b. 3-Bromo-4-hydroxybenzaldehyde oxime (216 mg, 1.00 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (14 mg, 0.050 mmol) and $CHCl_3$ (3.0 mL). Purification by flash column chromatography (silica, 83% Et_2O/pet. ether) afforded **2h** as a white solid (168 mg, 85%). Mp 156 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J*=2.0 Hz, 1H, Ar**H**), 7.55 (dd, *J*=8.4 Hz and 2.0 Hz, 1H, Ar**H**), 7.1 (d, *J*=8.4 Hz, 1H, Ar**H**), 6.07 (s, 1H, O**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 136.1, 133.5, 117.6, 117.0, 110.7, 105.6.

4.3.13. Nicotinonitrile ***2i***.[30] To a solution of triphenylphosphine oxide (14 mg, 0.050 mmol) in EtOAc (3.0 mL) was added oxalyl chloride (102 μL, 1.21 mmol) and the reaction mixture was stirred for 5 min. 3-Pyridinealdoxime (122 mg, 0.999 mmol) was then added in a single portion. The reaction mixture was stirred for 1.0 h at room temperature before being quenched with water (5.0 mL) and extracted with Et_2O (5.0 mL). The aqueous phase was adjusted to pH=9 using NaOH (3 drops of a 50% aqueous solution) and extracted with Et_2O (2×5 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed in vacuo. Purification by flash chromatography (silica, 67% Et_2O/pet. ether) afforded **2i** as a white solid (80 mg, 77%). Mp 50 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.91–8.87 (m, 1H, Ar**H**), 8.84–8.80 (m, 1H, Ar**H**), 8.00–7.94 (m, 1H, Ar**H**), 7.47–7.41 (m, 1H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 152.6, 139.3, 123.7, 116.6, 110.2.

4.3.14. Butyronitrile ***2j***.[35] The following reagents were combined in the amounts indicated according to method a. Butyraldoxime (87 mg, 1.0 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (14 mg, 0.050 mmol) and $CDCl_3$ (3.0 mL) gave **2j** (68 mg, 99%) by ^1H NMR. ^1H NMR (400 MHz, $CDCl_3$) δ 2.33 (*t*, *J*=7.1 Hz, 2H, C**H**$_2$CN), 1.75–1.65 (m, 2H, C**H**$_2$CH$_2$CN), 1.08 (t, *J*=7.4 Hz, 3H, C**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 119.7, 19.2, 19.1, 13.4.

4.3.15. Cyclohexanecarbonitrile ***2k***.[31] The following reagents were combined in the amounts indicated according to method a. Cyclohexanecarboxaldehyde oxime (127 mg, 0.999 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (14 mg,

0.050 mmol) and $CDCl_3$ (3 mL). Purification by flash column chromatography (silica, 33% Et_2O/pet. ether) afforded **2k** as a colourless oil (96 mg, 88%). ^1H NMR (400 MHz, $CDCl_3$) δ 2.67–2.58 (m, 1H, C**H**CN), 1.91–1.36 (m, 10H, 5× C**H$_2$**); ^{13}C NMR (400 MHz, $CDCl_3$) δ 122.7, 29.5, 28.0, 25.3, 24.1.

4.3.16. Decanenitrile ***2l***.[36] The following reagents were combined in the amounts and method indicated according to method a. Decanal aldoxime[3] (171 mg, 0.998 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (14 mg, 0.050 mmol) and $CHCl_3$ (3.0 mL). Purification by flash column chromatography (silica, 50% Et_2O/pet. ether) afforded **2l** as a colourless oil (146 mg, 95%). ^1H NMR (400 MHz, $CDCl_3$) δ 2.33 (t, J=7.2 Hz, 2H, C**H$_2$**CN), 1.70–1.60 (m, 2H, C**H$_2$**CH$_2$CN), 1.49–1.39 (m, 2H, C**H$_2$**CH$_2$CH$_2$CN), 1.36–1.21 (m, 10H, CH$_3$C**H$_2$**C**H$_2$**C**H$_2$**C**H$_2$**C**H$_2$**), 0.88 (t, J=7.1 Hz, 3H, C**H$_3$**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 119.9, 31.8, 29.3, 29.2, 28.8, 28.7, 25.4, 22.7, 17.1, 14.1.

4.3.17. 4,5-Dibromo-1H-pyrrole-2-carbaldehyde ***8n***.[37] Pyrrole-2-carboxaldehyde (951 mg, 10.0 mmol), was dissolved in chloroform (30 mL) and glacial acetic acid (4.5 mL). Bromine (1.02 mL, 19.9 mmol) was slowly added at room temperature to the resulting cloudy solution and, once addition was complete, the reaction mixture was heated at 50 °C for 16 h. After cooling to room temperature the reaction mixture was quenched with $NaHCO_3$ (150 mL of a saturated aqueous solution) and extracted with Et_2O (50 mL×4). The combined organic layer was dried over $MgSO_4$, filtered and the solvent was removed in vacuo. The crude product crystallized (EtOAc/pet. ether) affording **8n** as pale pink powder (1.42 g, 56%). Mp 153–154 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 10.25 (br, 1H, N**H**), 9.36 (s, 1H, C**HO**), 6.89 (d, J=2.6 Hz, 1H, NHC=C**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 133.2, 123.0, 112.9, 101.9.

4.3.18. (Z)/(E)-4,5-Dibromo-1H-pyrrole-2-carbaldehyde oxime ***1m***.[38] A suspension of 4,5-dibromo-1*H*-pyrrole-2-carbaldehyde (1.23 g, 4.86 mmol), $NH_2OH{\cdot}HCl$ (677 mg, 9.74 mmol) and NaOH (390 mg, 9.75 mmol) in EtOH (50 mL) was heated at 80 °C for 1.5 h. After cooling to room temperature H_2O (50 mL) was added and the reaction mixture was extracted with EtOAc (3×50 mL). The combined organic layers were washed with brine (2×50 mL), dried over $MgSO_4$, filtered and the solvent was removed in vacuo. Purification by flash column chromatography (silica, 33% EtOAc/pet. ether) afforded **1m** as a pale yellow powder (1.13 g, 87%). (*Z*)-isomer ^1H NMR (400 MHz, CD_3CN) δ 10.55 (br, 1H), 9.35 (br, 1H), 7.81 (s, 1H, C**H**=NOH), 6.61 (d, J=2.3 Hz, 1H, NHC=C**H**); ^{13}C NMR (100 MHz, CD_3CN) δ 141.0, 128.4, 117.5, 104.7, 100.4; (*E*)-isomer ^1H NMR (400 MHz, CD_3CN) δ 10.12 (br, 1H), 8.75 (s, 1H), 7.14 (s, 1H, C**H**=NOH), 6.40 (d, J=2.9 Hz, 1H, NHC=C**H**); ^{13}C NMR (100 MHz, CD_3CN) δ 137.3, 127.1, 115.0, 104.4, 100.0.

4.3.19. 2-Cyano-4,5-dibromopyrrole ***2m***.[21] To a solution of triphenylphosphine oxide (3.5 mg, 0.13 mmol) in EtOAc (1.0 mL) was added oxalyl chloride (51 μL, 0.60 mmol) and the reaction mixture was stirred for 5 min (*Z*)/(*E*)-4,5-dibromo-1*H*-pyrrole-2-carbaldehyde oxime (134 mg, 0.500) as solution in EtOAc (0.5 mL) was then added over 0.5 h via syringe pump and the reaction mixture was stirred for 0.5 h at room temperature after which the solvent was removed in vacuo. Purification by flash chromatography (silica, 17% EtOAc/pet. ether) gave **2m** as a white solid (114 mg, 91%). Mp 176 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.26 (br, 1H, N**H**), 6.86 (d, J=2.9 Hz, 1H, NHC=C**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 122.8, 112.3, 107.4, 103.2, 100.7.

4.3.20. Control reactions.

4.3.20.1. Table 1 entry 7. To a solution of oxalyl chloride (102 μL, 1.21 mmol) in $CHCl_3$ (2.0 mL) was added (*E*)-benzaldehyde oxime (121 mg, 0.999 mmol) as solution in $CHCl_3$ (1.0 mL) over 0.5 h via syringe pump at room temperature and the reaction mixture was stirred for 0.5 h at room temperature. Gave (*E*)-2-(benzylideneaminooxy)-2-oxoacetyl chloride **5a** (86%), bis ester **6a** (14%), benzonitrile **2a** (0%) by ^1H NMR. (*E*)-2-(Benzylideneaminooxy)-2-oxoacetyl chloride **5a**.[39] ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H, ArC**H**), 7.77–7.72 (m, 2H, Ar**H**), 7.58–7.52 (m, 1H, Ar**H**), 7.50–7.45 (m, 2H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ.160.2, 159.3, 154.1, 132.9, 129.2, 128.9, 128.6; bis ester **6a**[40] ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 2H, 2× ArC**H**), 7.78–7.73 (m, 4H, Ar**H**), 7.57–7.51 (m, 2H, Ar**H**), 7.50–7.43 (m, 4H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.4 (2C), 132.6, 129.2, 129.1, 128.8.

4.3.20.2. Table 3 entry 1. To a solution of triphenylphosphine oxide (14 mg, 0.050 mmol) in $CHCl_3$ (2.0 mL) was added (*E*)-2-(benzylideneaminooxy)-2-oxoacetyl chloride **5a** (212 mg, 1.00 mmol) as solution in $CHCl_3$ (1.0 mL) over 0.5 h via syringe pump at room temperature and the reaction mixture was stirred for 0.5 h at room temperature. The solvent was removed in vacuo. Purification by flash column chromatography (silica, 10% Et_2O/pet. ether) afforded benzonitrile **2a** as a colourless oil (76 mg, 74%).

4.3.20.3. Table 3 entry 2. To a solution of triphenylphosphine oxide (14 mg, 0.050 mmol) and oxalyl chloride (17 μL, 0.20 mmol) in $CHCl_3$ (2.0 mL) was added (*E*)-2-(benzylideneaminooxy)-2-oxoacetyl chloride **5a** (212 mg, 1.00 mmol) as a solution in $CHCl_3$ (1.0 mL) over 0.5 h via syringe pump at room temperature and the reaction mixture was stirred for 0.5 h at room temperature. The solvent was removed in vacuo. Purification by flash column chromatography (silica, 10% Et_2O/pet. ether) afforded benzonitrile **2a** as a colourless oil (73 mg, 71%).

4.3.20.4. Table 3 entry 3. To a solution of oxalyl chloride (102 μL, 1.21 mmol) in $CHCl_3$ (2.0 mL) was added butyraldoxime (87 mg, 1.0 mmol) as solution in $CHCl_3$ (1.0 mL) over 0.5 h via syringe pump at room temperature and the reaction mixture was stirred for 0.5 h at room temperature. Gave butyronitrile **2j** (32%) by ^1H NMR.

4.3.20.5. Table 3 entry 4. To a solution of oxalyl chloride (102 μL, 1.21 mmol) in $CHCl_3$ (2.0 mL) was added butyraldoxime (87 mg, 1.0 mmol) as a solution in $CHCl_3$ (1.0 mL) over 0.5 h via syringe pump at room temperature. Triphenylphosphine oxide **3a** (14 mg, 0.050 mmol) was then added and the reaction mixture was stirred for 1 h. Gave butyronitrile **2j** (97%) by ^1H NMR.

4.3.20.6. Table 3 entry 5. To a solution of oxalyl chloride (102 μL, 1.21 mmol) in $CHCl_3$ (2.0 mL) was added butyraldoxime (87 mg, 1.0 mmol) as solution in $CHCl_3$ (1.0 mL) over 0.5 h via syringe pump at room temperature. Triphenylphosphine oxide **3a** (14 mg, 0.050 mmol) and oxalyl chloride (4 μL, 0.05 mmol) were then added and the reaction mixture was stirred for 1 h. Gave butyronitrile **2j** (97%) by ^1H NMR.

Acknowledgements

This work was supported by the University of Nottingham New Researcher's Fund NF5012 and The Nuffield Foundation Bursary to P.L. We are grateful to Dr. Deborah Kays (University of Nottingham) for the loan of a Young's NMR tube.

Supplementary data

Supplementary data related to this article can be found online at doi:10.1016/j.tet.2012.01.067.

References and notes

1. (a) Friedrich, K.; Wallenfels, K. In *The Chemistry of the Cyano Group*; Rappaport, Z., Ed.; Wiley-Interscience: New York, NY, 1970; p 67; (b) Fatiadi, A. In *Preparation and Synthetic Applications of Cyano Compounds*; Patai, S., Rappaport, Z., Eds.; Wiley: New York, NY, 1983; p 1057.
2. For reviews on naturally occurring nitriles, see (a) Scheuer, P. J. *Acc. Chem. Res.* **1992**, *25*, 433–439; (b) Fleming, F. F. *Nat. Prod. Rep.* **1999**, *16*, 597–606; See also; (c) Kleeman, A.; Engel, J.; Kutscher, B.; Reichert, D. *Pharmaceutical Substances: Syntheses, Patents, Applications*, 4th ed.; Georg Thieme: Stuttgart, 2001; (d) Collier, S. J.; Langer, P. *Sci. Synth.* **2004**, *19*, 403–425.
3. Oxidation of amines 'ammoxidation' is employed on industrial scale. See (a) Stevenson, A. C. *Ind. Eng. Chem.* **1949**, *41*, 1846–1851; (b) Denton, W. I.; Bishop, R. B.; Cadwell, H. P.; Chapman, H. D. *Ind. Eng. Chem.* **1950**, *42*, 796–800.
4. (a) Mowry, D. T. *Chem. Rev.* **1948**, *42*, 189–283; (b) Kiefel, M. J. In *Comprehensive Organic Functional Group Transformations*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Pergamon: Cambridge, UK, 1995; p 641.
5. (a) Rosenmund, K. W.; Struck, E. *Ber. Dtsch. Chem. Ges.* **1919**, *2*, 1749–1756; (b) Lindley, J. *Tetrahedron* **1984**, *40*, 1433–1456; (c) Ellis, G. P.; Romney-Alexander, T. M. *Chem. Rev.* **1987**, *87*, 779–794.
6. For reviews, see (a) Sundermeier, M.; Zapf, A.; Mutyala, S.; Baumann, W.; Sans, J.; Weiss, S.; Beller, M. *Chem.—Eur. J.* **2003**, *9*, 1828–1836; (b) Takagi, K. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley: Hoboken, NJ, 2002; Vol. 1; p 657.
7. For selected references, see (a) Zanon, J.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 2890–2891; (b) Cristau, H.-J.; Ouali, A.; Spindler, J.-F.; Taillefer, M. *Chem.—Eur. J.* **2005**, *11*, 2483–2492.
8. For selected references on nickel-catalyzed cyanation of aryl halides, see (a) van Soolingen, J.; Brandsma, L.; Kruse, C. G. EP Patent 613,719, 1993; (b) Arvela, R. K.; Leadbeater, N. E. *J. Org. Chem.* **2003**, *68*, 9122–9125; (c) Schareina, T.; Zapf, A.; Mägerlein, W.; Müller, N.; Beller, M. *Chem.—Eur. J.* **2007**, *13*, 6249–6254; (d) Ren, Y. L.; Liu, Z. F.; Zhao, S.; Tian, X. Z.; Wang, J. J.; Yin, W. P.; He, S. B. *Catal. Commun.* **2009**, *10*, 768–771.
9. For selected stoichiometric methods, see (a) Chakrabarti, J. K.; Terrence, M. H. *J. Chem. Soc., Chem. Commun.* **1972**, 1226–1227; (b) Saraine, T.; Ishiguro, T.; Kawashima, K.; Morita, R. K. *Tetrahedron Lett.* **1973**, 2121–2124; (c) Foley, H. G.; Dalton, D. R. *J. Chem. Soc., Chem. Commun.* **1973**, 628–629; (d) Cacchi. *J. Org. Chem.* **1973**, *38*, 1060–1061; (e) Vowinkel, E.; Bartel, J. *Chem. Ber.* **1974**, *107*, 1221–1227; (f) Ho, T. L.; Wong, C. M. *Synth. Commun.* **1975**, *5*, 423–425; (g) Krause, J. G.; Shaikh, S. *Synthesis* **1975**, 502–504; (h) Hendrickson, J. B.; Bair, K. W.; Keehn, P. M. *Tetrahedron Lett.* **1976**, 603–604; (i) Carotti, A.; Campagna, F.; Ballini, R. *Synthesis* **1979**, 56–58; (j) Olah, G. A.; Vankar, Y. D.; Garcia-Luna, A. *Synthesis* **1979**, 227–228; (k) Denis, J. A.; Krief, A. *J. Chem. Soc., Chem. Commun.* **1980**, 544–545; (l) Olah, G. A.; Narang, S. C.; Garcia-Luna, A. *Synthesis* **1980**, 659–660; (m) Dulcere, J. P. *Tetrahedron Lett.* **1981**, *22*, 1599–1602; (n) Molina, P.; Alajain, M.; Vilaplana, M. J. *Synthesis* **1982**, 1016–1017; (o) Saednya, A. *Synthesis* **1983**, 748–749; (p) Akananchi, K. G. *Synth. Commun.* **1999**, *29*, 1741–1745; (q) Jose, B.; Sulatha, M. S.; Pillai, P. M.; Prathapan, S. *Synth. Commun.* **2000**, *30*, 1509–1514; (r) Bourah, M.; Konwar, D. *J. Org. Chem.* **2002**, *67*, 7138–7139; (s) Jie, Z.; Rammoorty, V.; Fischer, B. *J. Org. Chem.* **2002**, *67*, 711–719; (t) Narsaiah, A. V.; Nagaiah, K. *Adv. Synth. Catal.* **2004**, *346*, 1271–1274; (u) Augustine, J. K.; Kumar, R.; Bombrun, A.; Mandal, A. B. *Tetrahedron Lett.* **2011**, *52*, 1074–1077.
10. For selected catalytic methods, see (a) Attanasi, O.; Palma, P.; Serra-Zanetti, F. *Synthesis* **1983**, 741–742; (b) Hart-Davis, J.; Battioni, P.; Boucher, J.-L.; Mansuy, D. *J. Am. Chem. Soc.* **1998**, *120*, 12524–12530; (c) Barman, D. C.; Thakur, A. J.; Prajapati, D.; Sandhu, J. S. *Chem. Lett.* **2000**, 1196–1197; (d) Yang, S. H.; Chang, S. *Org. Lett.* **2001**, *3*, 4209–4211; (e) Choi, E.; Lee, C.; Na, Y.; Chang, S. *Org. Lett.* **2002**, *4*, 2369–2371; (f) Ishihara, K.; Furuya, Y.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2002**, *41*, 2983–2986; (g) Yan, P.; Batamack, P.; Prakash, G. K. S.; Olah, G. A. *Catal. Lett.* **2005**, *101*, 141–143; (h) Yamaguchi, K.; Fujiwara, H.; Ogasawara, Y.; Kotani, M.; Mizuno, N. *Angew. Chem., Int. Ed.* **2007**, *46*, 3922–3925; (i) Anand, N.; Owston, N. A.; Parker, A. J.; Slatford, P. A.; Williams, J. M. J. *Tetrahedron Lett.* **2007**, *48*, 7761–7763; (j) Kim, H. S.; Kim, S. H.; Kim, J. N. *Tetrahedron Lett.* **2009**, *50*, 1717–1719; (k) See Ref 36. For catalytic dehydration using propylphosphonic anhydride, see; (l) See Ref. 9v. For an interesting approach to catalysis of the Beckmann rearrangement, see; (m) Vanos, C. M.; Lambert, T. H. *Chem. Sci.* **2010**, *1*, 705–708.
11. (a) Appel, R.; Kleinstück, R.; Ziehn, K. D. *Chem. Ber.* **1971**, *104*, 1030–1034.
12. (a) Cooper, D.; Trippet, S. *Tetrahedron Lett.* **1979**, 1725–1726; (b) Sosnovsky, G.; Krogh, J. A. *Z. Naturforsch., B: Chem. Sci.* **1979**, *34*, 511–515; (c) Gawley, R. E. In *Organic Reactions*; Kende, A. S., Ed.; Wiley-Interscience: Hoboken, NJ, United States, 1988; Vol. 35; p 1; (d) Narsaiah, A. V.; Sreenu, D.; Nagaiah, K. *Synth. Commun.* **2006**, *36*, 137–140; (e) Moussa, Z.; Ahmed, S. A.; ElDouhaibi, A. S.; Al-Raqa, S. Y. *Tetrahedron Lett.* **2010**, *51*, 1826–1831; (f) Singh, M. K.; Lakshman, M. K. *J. Org. Chem.* **2009**, *74*, 3079–3084 For a direct conversion of aldehydes to nitriles using the T3P reagent, see; (g) Augustine, J. K.; Atta, R. N.; Ramappa, B. K.; Boodappa, C. *Synlett* **2009**, 3378–3382.
13. For mini review articles on catalysis of the Wittig and aza-Wittig reactions, see (a) Marsden, S. P. *Nat. Chem.* **2009**, *1*, 685–687 and; (b) Fairlamb, I. J. S. *ChemSusChem* **2009**, *2*, 1021–1024.
14. McGonagle, A. E.; Marsden, S. P.; McKever-Abbas, B. *Org. Lett.* **2008**, *10*, 2589–2591.
15. O'Brien, C. J.; Tellez, J. L.; Nixon, Z. S.; Kang, L. J.; Carter, A. L.; Kunkel, S. R.; Przeworski, K. C.; Chass, C. G. *Angew. Chem., Int. Ed.* **2009**, *48*, 6836–6839.
16. Harris, J. R.; Haynes, M. T., II; Thomas, A. M.; Woerpel, K. A. *J. Org. Chem.* **2010**, *75*, 5083–5091.
17. (a) Denton, R. M.; An, J.; Adeniran, B. *Chem. Commun.* **2010**, 3025–3027; (b) Denton, R. M.; An, J.; Adeniran, B.; Blake, A. J.; Lewis, W.; Poulton, A. *J. Org. Chem.* **2011**, *76*, 6749–6767.
18. Denton, R. M.; Tang, X.; Przelack, A. *Org. Lett.* **2010**, *12*, 4678–4681.
19. van Kalkeren, H. A.; Leenders, S. H. A. H.; Hommersom, C. R. A.; Rutjes, F. P. J. T.; van Delft, F. L. *Chem.—Eur. J.* **2011**, *17*, 11290–11295.
20. (a) Masaki, M.; Fukui, K. *Chem. Lett.* **1977**, *6*, 151–155; (b) Yano, T.; Hoshino, M.; Kuroboshi, M.; Tanaka, H. *Synlett* **2010**, 801–803; (c) Yano, T.; Kuroboshi, M.; Tanaka, H. *Tetrahedron Lett.* **2010**, *51*, 698–701.
21. Koenig, G. M.; Wright, A. D.; Linden, A. *Planta Med.* **1998**, *64*, 443–447.
22. (a) Scanlan, E. M.; Walton, J. C. *Chem. Commun.* **2002**, 2086–2087; (b) Portela-Cubillo, F.; Lymer, J.; Scanlan, E. M.; Scott, J. S.; Walton, J. C. *Tetrahedron* **2008**, *64*, 11908–11916.
23. The following crystal structure has been deposited at the Cambridge Crystallographic Data Centre. Deposition number CCDC 834121.
24. The remainder of the mass balance was the bis oxime ester **6a** that was formed during the reaction of the oxime with oxalyl chloride.
25. For a review on phosphonium salt organocatalysis, see Werner, T. *Adv. Synth. Catal.* **2009**, *351*, 1469–1481.
26. A similar result was obtained for substrates **1k** and **1m**. In these cases a 26% yield of **2k** was obtained in the absence of catalyst (compared to 88% with catalyst) and a 30 % yield of **2m** was obtained in the absence of catalyst (compared to 91% with catalyst).
27. Zhu, J.-L.; Lee, F.-Y.; Wu, J.-D.; Kuo, C.-W.; Shia, K.-S. *Synlett* **2007**, 1317–1319.
28. Ranu, B. C.; Jana, R. *J. Org. Chem.* **2005**, *70*, 8621–8624.
29. Duplais, C.; Bures, F.; Sapountzis, I.; Korn, T. J.; Cahiez, G.; Knochel, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 2968–2970.
30. Anbarasan, P.; Neumann, H.; Beller, M. *Chem.—Eur. J.* **2011**, *17*, 4217–4222.
31. Kokare, N. D.; Shinde, D. B. *Monatsh. Chem.* **2009**, *140*, 185–188.
32. Anbarasan, P.; Neumann, H.; Beller, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 519–522.
33. Sasson, R.; Rozen, S. *Org. Lett.* **2005**, *7*, 2177–2179.
34. Kavala, V.; Naik, S.; Patel, B. K. *J. Org. Chem.* **2005**, *70*, 4267–4271.
35. Nacario, R.; Kotakonda, S.; Fouchard, D. M. D.; Tillekeratne, L. M. V.; Hudson, R. A. *Org. Lett.* **2005**, *7*, 471–474.
36. Heravi, M. M.; Sadjadi, S.; Hekmatshoar, R.; Oskooie, H. A.; Bamoharram, F. F. *Chin. J. Chem.* **2009**, *27*, 607–609.
37. Handy, S. T.; Sabatini, J. J. *Org. Lett.* **2006**, *8*, 1537–1539.
38. Bailey, D. M.; (Sterling Drug, USA). US, 1976; Vol. US 3932458.
39. Scanlan, E. M.; Walton, J. C. *Helv. Chim. Acta* **2006**, *89*, 2133–2143.
40. Jochims, J. C.; Hehl, S.; Herzberger, S. *Synthesis* **1990**, *12*, 1128–1133.