Synthesis of Iminonitriles by Oxone/TBAB-Mediated One-Pot Oxidative Three-Component Strecker Reaction

Jean-Baptiste Gualtierotti, Xavier Schumacher, Qian Wang, Jieping Zhu*

Institute of Chemical Sciences and Engineering, Ecole Polytechnique Fédérale de Lausanne, EPFL-SB-ISIC-LSPN, BCH 5304, 1015 Lausanne, Switzerland
Fax +41(21)6939740; E-mail: jieping.zhu@epfl.ch

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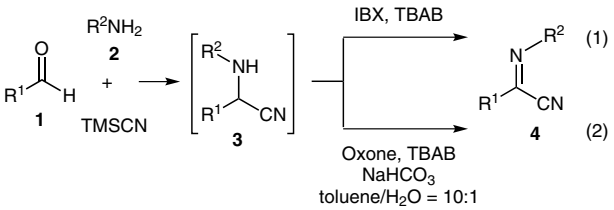
Abstract: Oxidative three-component reaction of aldehydes, amines, and TMSCN in a biphasic solvent system (toluene/H_2O) containing Oxone, tetra-*n*-butylammonium bromide (TBAB) and sodium bicarbonate afforded α-iminonitriles in good to excellent yields. This oxidative Strecker reaction was applicable to a wide range of aldehydes and amines, aromatic or aliphatic, of different electronic and steric properties. Substituted 1-aza-2-cyano-1,3-dienes were also accessible using α,β-unsaturated aldehydes as inputs.

Key words: α-iminonitrile, Oxone, α-aminonitrile, oxidative three-component Strecker reaction, multicomponent reaction



Scheme 1 Synthesis of iminonitriles by oxidative three-component Strecker reaction of aldehydes, amines, and TMSCN

α-Iminonitriles, also known as imidoyl cyanides, are interesting precursors for many functional groups including amides, keto acids, cyanoenamides, amidines, and *N*-keteneimines,[1] and are easily elaborated to diverse nitrogen-containing heterocycles.[2] In spite of their great synthetic potential, their use in organic synthesis is underexploited mainly due to the limited access to this chemical entity.[1–3] Indeed, reported methods are generally multistep processes leading to α-iminonitriles in low yields with severe limitation of scope. In 2008, our group reported a one-pot oxidative three-component Strecker reaction for the synthesis of α-iminonitriles from aldehydes, amines, and trimethylsilyl cyanide (TMSCN) using *o*-iodoxybenzoic acid (IBX)[4] as oxidant assisted by tetra-*n*-butylammonium bromide (TBAB) (Scheme 1, eq 1).[5] Subsequently, new syntheses of functionalized amides, indolizidines, and polysubstituted pyrroles were developed using α-iminonitriles as key intermediates.[1c,2f] In our continued efforts aimed at further developing the promising field of α-iminonitriles, a new user- and eco-friendly protocol with an even broader application scope was proved necessary. We report herein that the same oxidative multicomponent reaction[6,7] can be realized using innocuous Oxone as oxidizing agent in the presence of TBAB and sodium bicarbonate in a biphasic solvent system (toluene/H_2O) to afford the desired α-iminonitriles in good to excellent yields (Scheme 1, eq 2).

Oxone,[8] a potassium triple salt ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$), is a stable, cheap, and easy-to-handle source of potassium monopersulfate. It can oxidize a number of functional groups under mild conditions and is generally considered as a green oxidant as it generates nonpolluting by-products. It is known that Oxone can oxidize both 2-iodosobenzoic acid (IBA), a reduced form of IBX, and 2-iodobenzoic acid to IBX. Taking advantage of this observation, the groups of Vinod,[9] Giannis,[10] and Ishihara[11] have developed efficient protocols for the oxidation of alcohols to carbonyl compounds using a catalytic amount of either IBX, 2-iodobenzoic acid, or 2-iodobenzenesulfonic acid in the presence of Oxone. Based on these literature precedents, we were initially interested in performing the oxidative three-component Strecker synthesis of α-iminonitriles in the presence of a catalytic amount of IBX using Oxone as a terminal oxidant. To reach this goal, oxidation of aminonitrile **3a**, prepared by classical Strecker reaction of cinnamaldehyde, phenethylamine, and TMSCN, was chosen as a model reaction. Taking into account the importance of TBAB in our previous IBX-mediated oxidation process, the first trials were performed with IBX (0.1 equiv), Oxone (1.0 equiv), and TBAB (0.1 equiv) in different biphasic solvent systems [EtOAc/H_2O (10:1), wet MeCN, toluene/H_2O (10:1)] at different temperatures. Complete degradation occurred when the reaction was performed at 70 °C, the required temperature for oxidizing IBA to IBX, presumably due to the instability of the α-iminonitrile under these conditions. Interestingly, when the reaction was performed in toluene/H_2O (10:1) at room temperature, **4a** was isolated in 14% yield, which is slightly higher than the loading of IBX. Since IBX can not be regenerated under these conditions, we hypothesized that Oxone might also be able to oxidize α-aminonitriles to α-iminonitriles.

Stimulated by this observation, a further survey of reaction conditions was conducted using in situ generated aminonitrile **3a** in aqueous toluene in the absence of IBX. As shown in Table 1, increasing the quantity of TBAB resulted in a faster reaction and an increase in yield (Table

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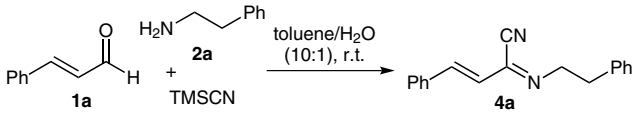
1, entry 1). It also became apparent that the concentration was a vital factor, with the best yield being obtained at $c = 0.75$ M (Table 1, entries 1–3). The stoichiometry and ratio of Oxone versus TBAB were also important. One equivalent each of Oxone and TBAB seemed to be optimum (entry 3). When the reaction was carried out in the presence of 0.5 equivalent of TBAB under otherwise identical conditions, the yield of **4a** went down to 25% (entries 7 vs 3).

Table 1 Survey of Reaction Conditions for the Synthesis of Iminonitriles[a]



Entry	Oxone/TBAB (equiv)	$NaHCO_3$	Concn (M)	Time (h)	Yield (%)[b]
1	1:1	–	0.25	3.5	57
2	1:1	–	0.5	1	65
3	1:1	–	0.75	0.5	75
4	1:2	–	0.75	2	68
5	2:1	–	0.75	0.3	61
6	2:2	–	0.75	0.2	79
7	1:0.5	–	0.75	2	25
8	0.55:1	–	0.75	2	29
9	0.55:0.5	–	0.75	3	10
10	1:1	1	0.75	0.75	83
11	1:1	1.5	0.75	0.5	88
12	1:1	2	0.75	0.7	86
13	1:1	1.5	0.75[c]	0.5	92

[a] Reaction conditions: To a solution of aldehyde **1** (0.1 mmol), amine **2** (0.1 mmol) and TMSCN (0.1 mmol) in toluene/H_2O (10:1) was added $NaHCO_3$ (0.15 mmol), Oxone (0.1 mmol), and TBAB (0.1 mmol) portionwise at r.t.
[b] Yield of isolated product.
[c] Reaction carried out at 0 °C.

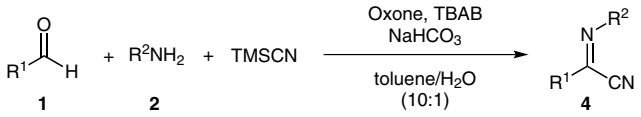
The acidity of the reaction mixture increased as Oxone was consumed and reached, at full conversion, around pH 1, which was much higher than that of the IBX protocol (pH 3). Knowing the acid vulnerability of α-iminonitriles, the reaction mixture was buffered with $NaHCO_3$. Satisfyingly, yields were indeed increased significantly (entries 10–13). Overall, the optimum conditions found consisted of performing the reaction in toluene/H_2O (1:1, $c = 0.75$ M) at 0 °C in the presence of Oxone (1.0 equiv), TBAB (1.0 equiv), and $NaHCO_3$ (1.5 equiv). Note that slow addition of inorganic salts under vigorous stirring, after the completion of the Strecker reaction, was also important in order to make a homogeneous solution, a prerequisite for a smooth oxidation reaction. Under these optimum conditions, iminonitrile **4a** was isolated in 92% yield directly from one equivalent each of cinnamaldehyde (**1a**), phenethylamine (**2a**), and TMSCN. The reaction was performed on a gram scale without erosion of the product yield.

The scope of the reaction was investigated next (Table 2). The reaction was compatible with a variety of aliphatic, aromatic, and α,β-unsaturated aldehydes with different electronic properties, although the electron-rich aromatic aldehydes gave the corresponding α-iminonitriles with slightly reduced yield (Table 2, entries 6, 8, 16). The bulkiness of the aldehydes has no major impact to the reaction's outcome as 2,2-dimethylpropanal (entry 5) and 2,6-dichlorobenzaldehyde (entry 7) were well accepted substrates. Anilines, including highly oxidizable *p*-methoxyaniline, participated efficiently in this reaction (entry 14). Aliphatic amines including cyclopropylamine were tolerated. Interestingly, amino alcohols can be used directly without the competitive oxidation of the hydroxyl group, which was in situ protected to the trimethylsilyl ether under the reaction conditions (entry 3). Other common protective groups such as TBS ether (entry 8) and acetal (entry 17) withstood these conditions.

It is noteworthy that besides aldehydes[12] and amines,[13] both the double bonds[14] and imines[15] could potentially be oxidized by Oxone as an excess amount of oxidant was present in the reaction mixture. The chemoselectivity observed in this reaction was therefore truly remarkable.

Control experiments indicated that the presence of TBAB is important to the success of the process. As TBAB could potentially be oxidized to bromine,[16] an additional experiment using bromine as oxidant was performed. However, only complete degradation was observed. On the other hand, reaction of α-aminonitrile **3a** with preformed tetra-*n*-butylammonium–Oxone salt (TBA-Oxone)[17] in anhydrous toluene gave the desired α-iminonitrile **4a** in comparable yield to the developed method. Therefore, we assumed that TBAB served, under our conditions, simply as a phase-transfer agent. Indeed, reaction of **1a**, **2a**, and TMSCN using tetra-*n*-butylammonium hydrogen sulfate (TBAHS) instead of TBAB under otherwise identical conditions afforded the iminonitrile **4a** in comparable yield. The fact that cyclopropylamine participated in the reaction efficiently (entries 2, 13) allowed us to exclude the radical mechanism as cyclopropylamine cation radicals are known to undergo fragmentation leading to ring-opened products.[18] Without detailed mechanistic studies, we propose that the oxidation of α-aminonitriles to α-iminonitriles could go through the corresponding hydroxylamine intermediates.[19] Subsequent β-elimination of water would afford the α-iminonitriles.[7b]

Table 2 Synthesis of Iminonitriles by Oxone/TBAB-Mediated One-Pot Three-Component Oxidative Strecker Reaction[a]



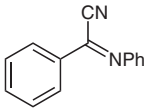
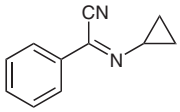
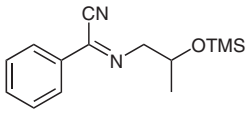
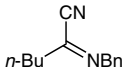
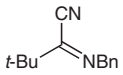
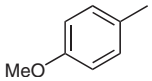
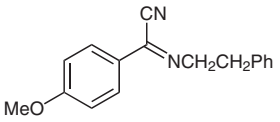
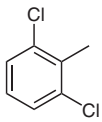
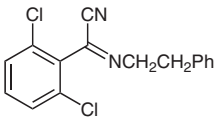
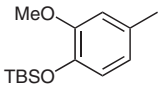
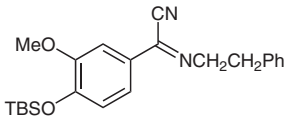
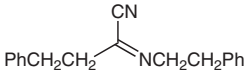
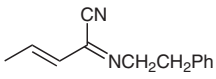
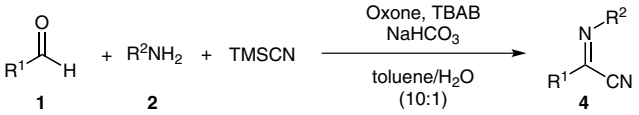
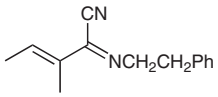
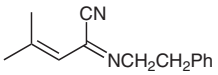
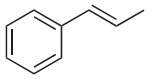
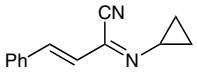
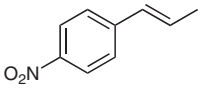
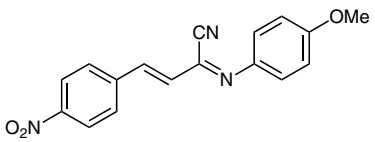
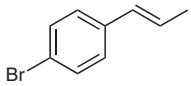
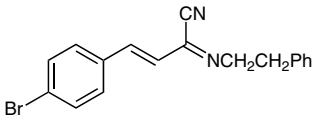
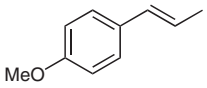
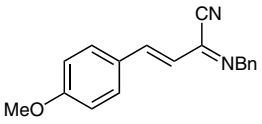
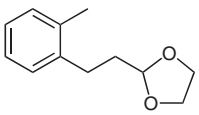
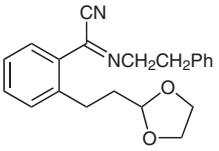
Entry	R^1	R^2	Product	Yield (%)[b]
1	Ph	Ph	 **4b**	89
2	Ph		 **4c**	87
3	Ph	$MeCH(OH)CH_2$	 **4d**	57
4	*n*-Bu	Bn	 **4e**	78
5	*t*-Bu	Bn	 **4f**	94
6		$PhCH_2CH_2$	 **4g**	70
7		$PhCH_2CH_2$	 **4h**	84
8		$PhCH_2CH_2$	 **4i**	75
9	$PhCH_2CH_2$	$PhCH_2CH_2$	 **4j**	95
10	MeCH=CH	$PhCH_2CH_2$	 **4k**	93

Table 2 Synthesis of Iminonitriles by Oxone/TBAB-Mediated One-Pot Three-Component Oxidative Strecker Reaction[a] (continued)



1 2 4

Entry	R^1	R^2	Product	Yield (%)[b]
11	MeCH=C(Me)	$PhCH_2CH_2$	 **4l**	63
12	Me_2C=CH	$PhCH_2CH_2$	 **4m**	76
13			 **4n**	88
14		4-$MeOC_6H_4$	 **4o**	93
15[c]		$PhCH_2CH_2$	 **4p**	89
16		Bn	 **4q**	77
17[c]		$PhCH_2CH_2$	 **4r**	88

[a] Reaction conditions: A solution of aldehyde **1** (0.1 mmol), amine **2** (0.1 mmol), and TMSCN (0.1 mmol) in toluene was stirred until the complete consumption of starting materials. H_2O (10% by volume) was added, followed by portionwise $NaHCO_3$ (0.15 mmol), Oxone (0.1 mmol), and TBAB (0.1 mmol).
[b] Isolated yield after FCC on silanized silica gel.
[c] CH_2Cl_2/H_2O (10:1) was used as solvent for better solubility.

In summary, we have described an efficient, practical, and chemoselective method for the synthesis of α-iminonitriles by a one-pot oxidative three-component Strecker reaction. Oxone was used as oxidant in a biphasic solvent system in the presence of TBAB and $NaHCO_3$. Key features are: a) operational simplicity without the need of anhydrous and inert atmospheric conditions; b) use of relatively innocuous Oxone as oxidizing agent; c) the formation of harmless potassium salts as by-products; and d) broad application scope and good to excellent yields. This mild and simple protocol provides a valuable alternative to the existing methodologies and paves the way to further exploit the synthetic potential of α-iminonitriles.

Mass spectra were determined with a Waters ACQUITY H-class UPLC/MS ACQ-SQD by electron ionization (EI positive and negative) or a Finnigan TSQ7000 by electrospray ionization (ESI+). The accurate masses were done by the mass spectrometry service of

the EPFL by ESI-TOF using a QTOF Ultima from Waters. NMR spectra were recorded on a Bruker Avance III-400, Bruker Avance-400 or Bruker DPX-400 spectrometer at r.t.; ^{1}H frequency is at 400.13 MHz and ^{13}C frequency is at 100.62 MHz. Chemical shifts (δ) are reported in parts per million (ppm) from TMS. NMR experiments were carried out in $CDCl_3$. Standard abbreviations were used for denoting the multiplicities in the ^{1}H NMR spectra. Coupling constants (*J*) are reported in hertz (Hz). IR spectra were recorded in a Jasco FT/IR-4100 spectrometer outfitted with a PIKE technology. Melting points were determined using a Stuart SMP30 and are uncorrected. Flash column chromatography (FCC) was performed using Silicycle silica gel: 230–400 mesh (40–63 μm). Reactions were monitored using Merck Kieselgel 60 F254 on aluminum sheets. TLC analyses were visualized by UV fluorescence (254 nm), followed by one of the following: $KMnO_4$, ninhydrine, Pancaldi solution [molybdatophosphorus acid and Ce(IV) sulfate in 4% H_2SO_4]; *p*-anisaldehyde, or vanillin. All reagents were obtained from commercial suppliers, unless otherwise stated.

Iminonitriles 4; General Procedure

To a solution of aldehyde **1** (0.1 mmol, 1.0 equiv) in toluene (1.3 mL, *c* = 0.75 M) was added amine **2** (0.1 mmol, 1.0 equiv) at r.t. The mixture was stirred until the disappearance of the starting materials (1 min for most aldehydes, up to 4 h for electron-rich aromatic aldehydes) before TMSCN (0.1 mmol, 1.0 equiv) was added. The mixture was stirred for 5 min before the portionwise addition of H_2O (10% by volume), $NaHCO_3$ (0.15 mmol, 1.5 equiv), Oxone (0.1 mmol, 1.0 equiv), and TBAB (0.1 mmol, 1.0 equiv) at 0 °C. The biphasic mixture was then stirred vigorously at r.t. until the disappearance of the intermediate; the biphasic mixture was then partitioned between sat. aq $NaHCO_3$ (20 mL) and EtOAc (20 mL). The aqueous phase was extracted with EtOAc (2 ×) and the combined organic phases were washed with brine, dried (Na_2SO_4), and concentrated in vacuum. The residue was purified by FCC (pentane then PE–EtOAc, 95:5) to yield the respective pure α-iminonitrile **4**.

***N*-Phenethylcinnamimidoyl Cyanide (4a)**

Yield: 23.9 mg (92%); yellow crystals; mp 56–58 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56–7.25 (m, 11 H), 6.98 (d, *J* = 16 Hz, 1 H), 4.17 (t, *J* = 8.0 Hz, 2 H), 3.09 (t, *J* = 8.0 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.8, 142.6, 138.7, 134.5, 130.3, 129.1, 129.0, 128.6, 128.4, 127.8, 126.6, 125.8, 60.3, 36.9.

***N*-Phenylbenzimidoyl Cyanide (4b)**

Yield: 20.4 mg (99%); yellow solid, mixture of isomers.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23–8.09 (m, 2 H), 7.65–7.44 (m, 5 H), 7.36–7.04 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.3, 148.1, 140.4, 140.0, 133.8, 133.5, 133.3, 133.0, 132.6, 129.4, 129.3, 129.2, 128.5, 128.4, 127.5, 122.3, 121.1, 120.5, 111.0, 110.8.

***N*-Cyclopropylbenzimidoyl Cyanide (4c)**

Yield: 14.8 mg (87%); clear oil.

IR (film): 3014, 2216, 1575, 1443, 1268, 1181, 1008, 949, 771, 690 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 8.1, 2.0 Hz, 2 H), 7.51–7.41 (m, 3 H), 3.68–3.62 (m, 1 H), 1.32–1.25 (m, 2 H), 1.25–1.19 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.7, 133.7, 131.6, 128.9, 127.0, 110.8, 41.3, 12.1.

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{11}N_2^+$ [M + H]$^+$: 171.0917; found: 171.0919.

***N*-{2-[(Trimethylsilyl)oxy]propyl}benzimidoyl Cyanide (4d)**

Yield: 14.8 mg (57%); clear oil.

IR (film): 2960, 1605, 1452, 1251, 1096, 1006, 839, 689 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02–7.98 (m, 2 H), 7.56–7.42 (m, 3 H), 4.22 (m, 1 H), 3.96 (d, *J* = 6.0 Hz, 2 H), 1.31 (d, *J* = 6.0 Hz, 3 H), 0.09 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.8, 133.8, 132.4, 129.1, 127.8, 110.1, 68.1, 66.6, 22.4, 0.4.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{21}N_2OSi^+$ [M + H]$^+$: 261.1418; found: 261.1427.

***N*-Benzylpentanimidoyl Cyanide (4e)**

Yield: 15.6 mg (78%); clear oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.28 (m, 5 H), 4.93 (s, 2 H), 2.61 (t, *J* = 7.5 Hz, 2 H), 1.74–1.67 (m, 2 H), 1.44–1.35 (m, 2 H), 0.96 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.0, 137.4, 128.7, 128.0, 127.6, 110.7, 62.3, 38.5, 27.7, 22.0, 13.7.

HRMS (ESI): *m*/*z* calcd for $C_{13}H_{17}N_2^+$ [M + H]$^+$: 201.1386; found: 201.1381.

***N*-Benzylpivalimidoyl Cyanide (4f)**

Yield: 18.6 mg (93%); clear oil.

IR (film): 2969, 1699, 1631, 1456, 1367, 1261, 1161, 1088, 736, 696 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.20 (m, 5 H), 4.96 (s, 2 H), 1.30 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.9, 137.8, 128.6, 127.7, 127.4, 109.7, 61.7, 39.5, 27.0.

HRMS (ESI): *m*/*z* calcd for $C_{13}H_{17}N_2^+$ [M + H]$^+$: 201.1386; found: 201.1381.

4-Methoxy-*N*-phenethylbenzimidoyl Cyanide (4g)

Yield: 18.4 mg (70%); white powder; mp 77–78 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92–7.90 (m, 2 H), 7.32–7.23 (m, 5 H), 6.98–6.95 (m, 2 H), 4.18 (t, *J* = 8.0 Hz, 2 H), 3.87 (s, 3 H), 3.09 (t, *J* = 8.0 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.9, 141.4, 139.1, 129.4, 129.2, 128.6, 126.6, 126.5, 114.4, 109.8, 60.1, 55.7, 37.0.

2,6-Dichloro-*N*-phenethylbenzimidoyl Cyanide(4h)

Yield: 25.5 mg (84%); clear oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.22 (m, 8 H), 4.36 (t, *J* = 7.2 Hz, 2 H), 3.17 (t, *J* = 7.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.4, 137.8, 134.4, 132.3, 131.9, 129.0, 128.8, 128.4, 126.8, 109.1, 60.8, 36.4.

4-[(*tert*-Butyldimethylsilyl)oxy]-3-methoxy-*N*-phenethylbenzimidoyl Cyanide (4i)

Yield: 29.6 mg (75%); clear oil.

IR (film): 2931, 2858, 2337, 2226, 1699, 1594, 1509, 1288, 912, 841 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 2.1 Hz, 1 H), 7.42 (dd, *J* = 8.2, 2.1 Hz, 1 H), 7.31–7.19 (m, 5 H), 6.89 (d, *J* = 8.2 Hz, 1 H), 4.16 (t, *J* = 7 Hz, 2 H), 3.06 (t, *J* = 7 Hz, 2 H), 3.85 (s, 3 H), 0.99 (s, 9 H), 0.17 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.6, 149.4, 141.6, 139.1, 129.2, 128.6, 127.6, 126.6, 122.2, 120.9, 109.8, 109.7, 60.0, 55.6, 37.0, 25.8, 18.6, –4.4.

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{31}N_2O_2Si^+$ [M + H]$^+$: 395.2149; found: 395.2156.

***N*-Phenethyl-3-phenylpropanimidoyl Cyanide (4j)**

Yield: 24.89 mg (95%); light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.17 (m, 10 H), 3.99 (m, 2 H), 2.97–2.93 (m, 4 H), 2.83–2.79 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.8, 139.6, 138.7, 129.1, 128.8, 128.6, 128.6, 126.7, 110.4, 60.1, 40.3, 36.6, 31.8.

(2*E*)-*N*-Phenethylbut-2-enimidoyl Cyanide (4k)
Yield: 18.4 mg (93%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.22 (m, 5 H), 6.70 (dq, *J* = 16.1, 6.8 Hz, 1 H), 6.34 (dd, *J* = 16.1, 1.4 Hz, 1 H), 4.09 (t, *J* = 7.2 Hz, 2 H), 3.04 (t, *J* = 7.2 Hz, 2 H), 1.99 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.6, 142.2, 138.8, 129.9, 129.0, 128.6, 126.6, 109.0, 59.8, 36.8, 18.6.

(2*E*)-2-Methyl-*N*-phenethylbut-2-enimidoyl Cyanide (4l)
Yield: 13.3 mg (63%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.19 (m, 5 H), 6.65–6.55 (m, 1 H), 4.09 (t, *J* = 7.4 Hz, 2 H), 3.03 (t, *J* = 7.4 Hz, 2 H), 2.11 (s, 3 H), 1.94 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.2, 139.2, 137.8, 135.2, 129.1, 128.5, 126.5, 109.3, 59.7, 37.0, 14.9, 12.0.

3-Methyl-*N*-phenethylbut-2-enimidoyl Cyanide (4m)
Yield: 16.1 mg (76%); clear oil.

IR (film): 2923, 2215, 1643, 1591, 1453, 1269, 1032, 746, 699 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.20 (m, 5 H), 5.99–5.96 (m, 1 H), 4.07 (t, *J* = 7.3 Hz, 2 H), 3.03 (t, *J* = 7.3 Hz, 2 H), 2.11 (s, 3 H), 1.94 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.7, 140.1, 139.1, 129.1, 128.6, 126.5, 121.7, 111.0, 59.6, 36.9, 28.0, 20.3.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{17}N_2^+$ [M + H]$^+$: 213.1386; found: 213.1389.

***N*-Cyclopropylcinnamimidoyl Cyanide (4n)**
Yield: 17.2 mg (88%); white crystals; mp 44–45 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.49 (m, 2 H), 7.42–7.36 (m, 3 H), 7.32 (d, *J* = 16.0 Hz, 1 H), 6.91 (d, *J* = 16.0 Hz, 1 H), 3.56–3.51 (m, 1 H), 1.29–1.21 (m, 2 H), 1.20–1.14 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.3, 139.6, 134.9, 129.6, 129.1, 127.7, 126.0, 110.1, 41.3, 12.4.

***N*-(4-Methoxyphenyl)-3-(4-nitrophenyl)acrylimidoyl Cyanide (4o)**
Yield: 22.7 mg (74%); orange crystals; mp 135–138 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32–8.27 (m, 2 H), 7.76–7.70 (m, 2 H), 7.56 (d, *J* = 16.4 Hz, 1 H), 7.41–7.36 (m, 2 H), 7.27 (d, *J* = 16.4 Hz, 1 H), 7.02–6.96 (m, 2 H), 3.89 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.5, 148.4, 141.3, 140.9, 139.3, 135.3, 131.3, 128.5, 124.5, 124.0, 114.7, 111.2, 55.7.

3-(4-Bromophenyl)-*N*-phenethylacrylimidoyl Cyanide (4p)
Yield: 31.2 mg (92%); white crystals; mp 57–61 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.52 (m, 2 H), 7.40–7.36 (m, 2 H), 7.34–7.28 (m, 3 H), 7.26–7.21 (m, 3 H), 6.93 (d, *J* = 16.4 Hz, 1 H), 4.14 (t, *J* = 7.2 Hz, 2 H), 3.06 (t, *J* = 7.3 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.7, 141.3, 138.7, 133.5, 132.4, 129.3, 129.1, 128.6, 126.7, 126.5, 124.7, 108.9, 60.3, 36.9.

(2*E*)-*N*-Benzyl-3-(4-methoxyphenyl)acrylimidoyl Cyanide (4q)
Yield: 21.2 mg (77%); orange crystals; mp 68–75 °C.

IR (film): 2930, 2839, 2363, 1604, 1579, 1513, 1248, 1174, 1031, 824 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.30 (m, 8 H), 6.94–6.90 (m, 3 H), 5.05 (s, 2 H), 3.85 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.6, 143.1, 142.9, 137.8, 129.6, 128.9, 128.3, 127.7, 127.4, 123.9, 114.7, 109.5, 62.5, 55.6.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{17}N_2O^+$ [M + H]$^+$: 277.1335; found: 277.1333.

2-[2-(1,3-Dioxolan-2-yl)ethyl]-*N*-phenethylbenzimidoyl Cyanide (4r)
Yield: 29.4 mg (88%); yellow oil.

IR (film): 3027, 2951, 2880, 1604, 1494, 1454, 1250, 1139, 1030, 945, 898, 769, 749, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66–7.61 (m, 1 H), 7.45–7.20 (m, 8 H), 4.81 (t, *J* = 4.7 Hz, 1 H), 4.26 (t, *J* = 7.2 Hz, 2 H), 4.02–3.92 (m, 2 H), 3.91–3.83 (m, 2 H), 3.14 (t, *J* = 7.3 Hz, 2 H), 2.99 (m, 2 H), 1.96–1.88 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.5, 141.7, 139.0, 132.7, 131.5, 131.1, 130.5, 129.1, 128.7, 126.7, 126.6, 110.3, 104.0, 65.1, 60.7, 36.7, 34.9, 28.2.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{23}N_2O_2^+$ [M + H]$^+$: 335.1754; found: 335.1760.

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