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Synthesis of oxime ethers under single electron oxidation induced by radical cation tris(aryl)aminium salts: O-alkylation of oximes with *n*-vinyl lactams

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ABSTRACT

O-Alkylation of (*E*)- and (*Z*)-oxime was achieved via single electron oxidation of *N*-vinyl lactams by using a catalytic amount of tris(aryl)aminium salts as initiator, producing the corresponding oxime ethers in high yields under mild condition. A reaction mechanism based on electron transfer was proposed.

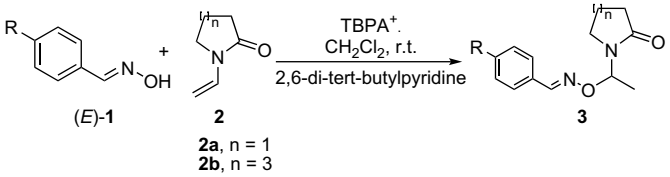
1. Introduction

Oximes and oxime ethers are important building blocks in organic synthesis. The addition of organometallic or radical species to oxime ethers is synthetically valuable protocol for the construction of C–C bonds, and various useful reactions are built through this methodology.[1,2] Generally, oxime ethers were prepared from *O*-alkyl hydroxylamines and the corresponding aldehydes. The direct preparation of oxime ethers from oximes has been commonly limited to the reaction of oximes with alkyl halides under basic conditions.[3] Recently, several new methods were discovered by using oximes in transition metal-catalyzed allylic substitution,[4] Michael addition[5] as well as Cu-catalyzed cross-coupling reaction,[6] but N-alkylation byproducts were inevitably produced under acidic conditions.[4b] Therefore, it is desirable to develop some new synthetic protocols for the preparation of oxime ethers under neutral or acidic conditions.

In connection with our present interests on exploring the synthetic potentials of cation radical induced reactions,[7] we have found that aza-Diels–Alder reactions could be efficiently induced by tris(4-bromophenyl)aminium cation radical salt ($TBPA^{+\bullet}$ $SbCl_6$) to accomplish the [4+2] cycloaddition of aromatic imines with electron-rich olefins.[7a,b] Besides, $TBPA^{+\bullet}$ as cation radical could readily induce the [3+2] cycloaddition of chalcone epoxides with imines[7f] or electron-rich olefins.[7d] Recently, we have reported that $TBPA^{+\bullet}$ can also efficiently initiate the O-alkylation of oximes with *N*-vinyl lactams, producing the corresponding oxime ethers in excellent yields.[7c] Herein, we will report the detailed investigations on the synthesis of oxime ethers via single electron oxidation induced by a catalytic amount of radical cation tris(aryl)aminium salts.

2. Results and discussion

In our previous studies,[7c] we found that the addition of the corresponding oximes and *N*-vinyl lactams can easily occur in the presence of 2,6-di-*tert*-butylpyridine as an acid scavenger (Scheme 1). A mechanism based on cation radical chain addition of **2** with (*E*)-**1** as the nucleophile was proposed (Scheme 2). In addition to the known ***route a*** in Scheme 2,[7c] there might be another alternative way to generate the oxime ethers **3** through ***route b*** starting from the distonic radical cation intermediate **4**. In ***route b***, intermediate **4** might undergoe a fast [1,3]-H shift via the four-membered transition state **6** leading to product **3**. To rule out this pathway, two isotopic experiments were then conducted. As demonstrated in Scheme 3, in the presence of *N*-vinyl-2-pyrrolidinone **2a**, *O*-deuterio-*p*-methylbenzaldehyde oxime **7** and *O*-deuteriopyridinebenzaldehyde oxime **8** were subjected to the standard reaction condition. After column chromatographic purification, however, only the final products **3c** and **9** were obtained in 95% and 67% yield, respectively,[7c] and no related deuterated derivatives were isolated. Clearly, these facts exclude the ***route b*** in



Scheme 1.

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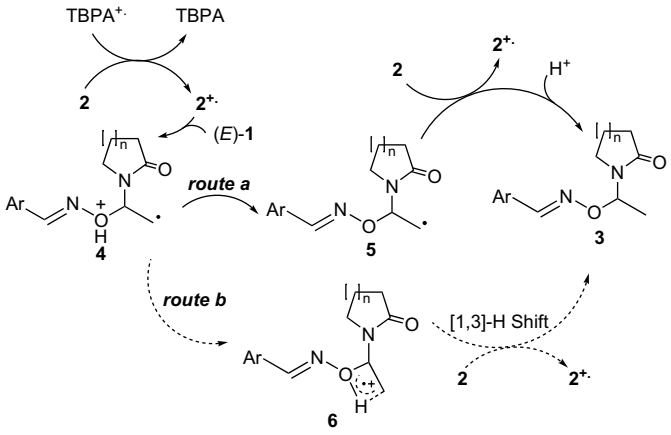
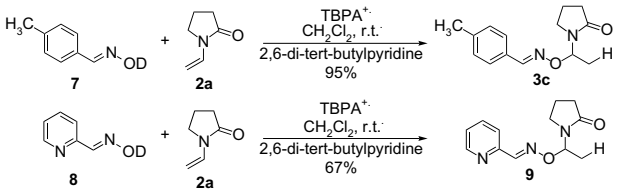


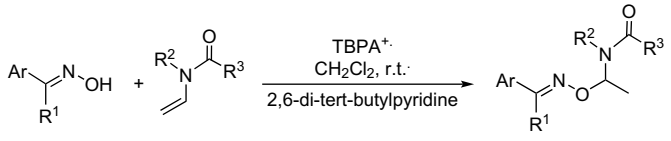
Scheme 2.



Scheme 3.

Scheme 2, and indicate that the deprotonation takes place, producing the radical species **5**, and then the electron transfer occurs between **5** and **2**, giving the oxime ethers **3**.

To extend the generality of this methodology, some acyclic *N*-vinyl lactams (**10a**–**10c**) as well as various aromatic oximes (**1a**–**1g**) were investigated (Scheme 4).



10a (R^2 = R^3 = Me)
10b (R^2 = H, R^3 = Me)
10c (R^2 = R^3 = H)

Scheme 4.

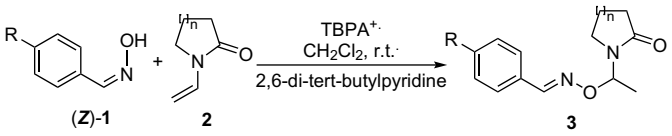
From Table 1, it could be seen that the current addition reaction proceeded readily in good to excellent yields. In the presence of different aldehyde oximes **1a**–**1d**, *N*-vinyl acetamides (**10a** and **10b**) and *N*-vinyl formamide (**10c**) as acyclic substrates behaved in an efficient manner similar to that of *N*-vinyl-2-pyrrolidinone **2a** as a model cyclic substrate (entries 1–10, Table 1). While using acyclic *N*-vinyl lactam **10a**, the ketone oxime **1e** (entry 11) and the heteroaromatic aldehyde oximes **1f**–**1g** (entries 12 and 13) are also effective in the current radical cation-induced addition reaction. In previously reported literatures, oximes can act as nitrogen nucleophilic reagents to accomplish the synthesis of nitrones,[4b,8] but under our radical cation condition mentioned above, no N-alkylation products were isolated.

In addition to the utilization of (*E*)-oximes (**1a**–**1g**, **7**, and **8**), several (*Z*)-oximes which were prepared according to the literature[9] were also examined in the current addition reaction

Table 1
$TBPA^{+\cdot}SbCl_6^-$ initiated addition of oximes **1** with *N*-vinyl lactams **10**

Entry	Substrates				Products	Yield[a] (%)
		Ar	R^1	10		
1	**1a**	Ph	H	**10a**	**11a**	96
2	**1b**	*p*-$C_6H_4NO_2$	H	**10a**	**11b**	86
3	**1b**	*p*-$C_6H_4NO_2$	H	**10b**	**11c**	84
4	**1b**	*p*-$C_6H_4NO_2$	H	**10c**	**11d**	88
5	**1c**	*p*-C_6H_4Cl	H	**10a**	**11e**	97
6	**1c**	*p*-C_6H_4Cl	H	**10b**	**11f**	92
7	**1c**	*p*-C_6H_4Cl	H	**10c**	**11g**	90
8	**1d**	*p*-$C_6H_4CH_3$	H	**10a**	**11h**	98
9	**1d**	*p*-$C_6H_4CH_3$	H	**10b**	**11i**	95
10	**1d**	*p*-$C_6H_4CH_3$	H	**10c**	**11j**	95
11	**1e**	Ph	CH_3	**10a**	**11k**	82
12	**1f**	2-furyl	H	**10a**	**11l**	97
13	**1g**	2-pyridyl	H	**10a**	**11m**	71

[a] Isolated yields based on **1**.



Scheme 5.

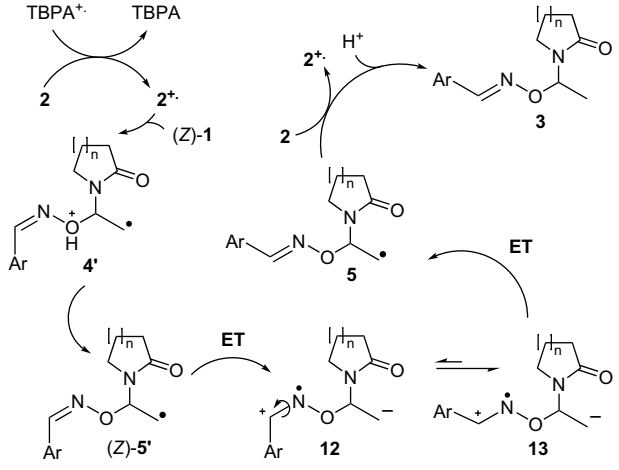
Table 2
$TBPA^{+\cdot}SbCl_6$ initiated addition of oximes (*Z*)-**1** with *N*-vinyl lactams **2**

Entry	Substrates		Products	Yield[a] (%)
	R	2		
1	Cl	**2a**	**3a**	85
2	Cl	**2b**	**3b**	80
3	CH_3	**2a**	**3c**	90
4	CH_3	**2b**	**3d**	89

[a] Isolated yields based on (*Z*)-**1**.

(Scheme 5). Under the standard condition, the reaction of (*Z*)-oximes and *N*-vinyl lactams was performed (Table 2). Interestingly, only the oxime ethers **3** with *E*-configuration were isolated in good yields (80–90%), and we did not observe the *Z*-configuration oxime ethers or the N-alkylation product nitrones.

To rationalize this observed inversion of the stereochemistry at the C=N double bond during this transformation, a possible mechanism based on the electron transfer (**ET**) process is shown in Scheme 6. Analogous to the mechanistic description in Scheme 2,



Scheme 6.

the distonic radical cation intermediate **4′** formed through the oxidative addition of **2** with oximes (*Z*)-**1** under the inducement of $TBPA^{+\bullet}$. The swift deprotonation resulted in the formation of the radical intermediate **5′**, and then the intramolecular electron transfer occurred from the C═N double bond to the radical moiety, giving the zwitterionic radical species **12**. Subsequently, the rotation of C–N bond followed by the electron transfer gave rise to the thermodynamic stable radical intermediate **5** with the reversed configuration of C═N double bond. Then, the redox process between **5** and **2** via single electron transfer gave the corresponding oxime ethers **3** with *E*-configuration. Currently, further mechanistic insight into the addition of (*Z*)-oximes to *N*-vinyl lactams under the catalysis of radical cation tris(aryl)aminium salts is underway in this laboratory.

3. Conclusion

In conclusion, we have discovered an O-alkylation reaction of oximes with *N*-vinyl lactams under the induction of radical cation salts, smoothly delivering the oxime ethers in good to excellent yields. The substrate scope and reaction generality were examined in detail, wherein the desired reactivity of different substrates (e.g., cyclic and acyclic *N*-vinyl lactams, aldehyde and ketone oximes as well as (*Z*)-aldehyde oximes) was demonstrated. In comparison with the previous reports, this method on preparing the synthetically useful oxime ethers is featured by the utilization of catalytic amount of racial cation initiator (5 mol %), the mild condition (at ambient temperature), the short reaction time (within 10–15 min), the high chemical yields, and especially no strong bases needed. Further investigations in this area are being actively carried out in our laboratory.

4. Experimental

4.1. General

Melting points were determined on a Yanagimoto melting point apparatus and uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury Plus 300 NMR at 300 MHz (^{1}HNMR) and 75 MHz (^{13}C NMR). Chemical shifts are given in parts per million with reference to internal TMS. EIMS spectra were recorded on an HP 5988A spectrometer. High-resolution mass spectra (HRMS) were recorded on a Bruker Daltonics APEX II 47e spectrometer by ESI. All commercially available substrates were used as received. *Z*-Oximes was synthesized according to the literature.

4.2. General procedure for $TBPA^{+\bullet}$ induced reaction of oximes 1 and *N*-vinyl lactams

An anhydrous CH_2Cl_2 solution (20 mL) of oxime (**1**, 1 mmol), *N*-vinyl lactam (1 mmol), and 2,6-di-*tert*-butyl-pyridine (0.1 mmol as base) was added dropwise to a CH_2Cl_2 solution (20 mL) of a catalytic amount of tris(4-bromophenyl)aminium hexachloroantimonate ($TBPA^{+\bullet}$ $SbCl_6^-$, 0.05 mmol) at ambient temperature under stirring. After completion of the reaction as monitored by TLC (10 min), the reaction was quenched with sodium carbonate methanol solution. Pour the mixture into a separator funnel with the addition of excess methylene chloride, and then the crude organic solution was extracted three times with water to remove inorganic salts. The organic phase was then dried over anhydrous magnesium sulfate, filtered, and the solvent was removed under reduced pressure and the products were separated by silica gel column chromatography eluted with hexane/acetone (v/v 10:1) to afford the pure oxime ether as the unique product.

4.3. Synthesis of *O*-deuterio-*p*-methylbenzaldehyde oxime and *O*-deuteriopyridinebenzaldehyde oxime

Oxime (1 mmol) was added to CH_3OH-d_4 under stirring and the solution was stirred overnight. The solvent was removed under reduced pressure and the products were used without further purified. According to ^1H NMR (300 MHz, DMSO-d_6), 85% oximes were deuterated.

*4.3.1. (E)-O-1-(2-Oxopyrrolidin-1-yl)-ethyl-4-chlorobenzaldehyde oxime (**3a**)*

Colorless oil.
^1H NMR (300 MHz, $CDCl_3$): δ 1.41 (d, J=6.3 Hz, 3H), 1.86–1.93 (m, 2H), 2.27–2.33 (m, 2H), 3.28–3.34 (m, 2H), 6.03 (q, J=6.3 Hz, 1H), 7.19 (d, J=8.7 Hz, 2H), 7.39 (d, J=8.7 Hz, 2H), 7.91 (s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 17.0, 18.2, 31.8, 41.7, 80.7, 128.5, 129.0, 130.7, 135.9, 148.4, 175.7.
EIMS *m*/*z* (rel int., %): 155 (7.3), 113 (11.1), 112 (100).
HR-ESI-MS calcd for $C_{13}H_{15}N_2O_2Cl+H^+$: 267.0897; found: 267.0897.

*4.3.2. (E)-O-1-(Caprolactam-N-yl)ethyl-4-chlorobenzaldehyde oxime (**3b**)*

Colorless oil.
^1H NMR (300 MHz, $CDCl_3$): δ 1.25 (d, J=6.6 Hz, 3H), 1.47–1.53 (m, 6H), 2.40–2.42 (m, 2H), 3.18–3.20 (m, 2H), 6.45 (q, J=6.6 Hz, 1H), 7.16 (d, J=8.7 Hz, 2H), 7.37 (d, J=8.7 Hz, 2H), 7.87 (s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 17.4, 23.6, 29.2, 30.1, 37.9, 41.7, 82.8, 128.5, 129.0, 130.7, 135.9, 148.4, 176.2.
EIMS *m*/*z* (rel int., %): 155 (1.8), 141 (8.5), 140 (100), 112 (13.0).
HR-ESI-MS calcd for $C_{15}H_{19}N_2O_2Cl+H^+$: 295.1208; found: 295.1208.

*4.3.3. (E)-O-1-(2-Oxopyrrolidin-1-yl)ethyl-4-methylbenzaldehyde oxime (**3c**)*

Colorless oil.
^1H NMR (300 MHz, $CDCl_3$): δ 1.35 (d, J=6.3 Hz, 3H), 1.82–1.92 (m, 2H), 2.23 (s, 3H), 2.27–2.32 (m, 2H), 3.29–3.34 (m, 2H), 6.02 (q, J=6.3 Hz, 1H), 7.04 (d, J=7.5 Hz, 2H), 7.36 (d, J=7.5 Hz, 2H), 7.92 (s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 16.7, 17.8, 21.2, 31.4, 41.3, 80.0, 126.9, 128.9, 129.1, 140.0, 149.2, 175.3.
EIMS *m*/*z* (rel int., %): 135 (4.4), 113 (7.9), 112 (100).
HR-ESI-MS calcd for $C_{14}H_{18}N_2O_2+H^+$: 247.1441; found: 247.1439.

*4.3.4. (E)-O-1-(Caprolactam-N-yl)ethyl-4-methylbenzaldehyde oxime (**3d**)*

Colorless oil.
^1H NMR (300 MHz, $CDCl_3$): δ 1.38 (d, J=6.3 Hz, 3H), 1.55–1.67 (m, 6H), 2.34 (s, 3H), 2.52–2.54 (m, 2H), 3.31–3.34 (m, 2H), 6.57 (q, J=6.3 Hz, 1H), 7.15 (d, J=8.1 Hz, 2H), 7.47 (d, J=8.1 Hz, 2H), 8.02 (s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 17.1, 21.2, 23.2, 28.7, 29.8, 37.5, 41.2, 82.2, 126.9, 128.9, 129.1, 140.0, 149.2, 175.8.
EIMS *m*/*z* (rel int., %): 141 (8.8), 140 (100), 112 (16.6).
HR-ESI-MS calcd for $C_{16}H_{22}N_2O_2+H^+$: 275.1748; found: 275.1754.

*4.3.5. (E)-O-1-(2-Oxopyrrolidin-1-yl)ethyl-2-pyridinecarboxaldehyde oxime (**9**)*

Colorless oil.
^1H NMR (300 MHz, $CDCl_3$): δ 1.30 (d, J=6.0 Hz, 3H), 1.77–1.87 (m, 2H), 2.20–2.25 (m, 2H), 3.16–3.25 (m, 2H), 6.00 (q, J=6.0 Hz, 1H),

7.07 (m, 1H), 7.48 (t, J=7.8 Hz, 1H), 7.68 (d, J=7.8 Hz, 1H), 7.97 (s, 1H), 8.39 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 16.9, 18.0, 31.6, 41.4, 80.8, 120.8, 124.2, 136.5, 149.2, 150.3, 151.4, 175.6.
EIMS m/z (rel int., %): 122 (3.5), 113 (7.5), 112 (100).
HR-ESI-MS calcd for $C_{12}H_{15}N_3O_2$+H^+: 234.1228; found: 234.1237.

4.3.6. (E)-O-1-(N-Methyl-N-acetamino-1-yl)ethylbenzaldehyde oxime (**11a**)

^{1}H NMR (300 MHz, $CDCl_3$): rotamer **A** (major): δ 1.27 (d, J=6.0 Hz, 3H), 2.17 (s, 3H), 2.70 (s, 3H), 5.77 (q, J=6.0 Hz, 1H), 7.19–7.24 (m, 3H), 7.39–7.46 (m, 2H), 7.93 (s, 1H); rotamer **B** (minor): δ 1.23 (d, J=6.3 Hz, 3H), 2.00 (s, 3H), 2.67 (s, 3H), 6.50 (q, J=6.3 Hz, 1H), 7.19–7.24 (m, 3H), 7.39–7.46 (m, 2H), 7.96 (s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): rotamer **A** (major): δ 17.3, 21.6, 24.9, 85.9, 126.8, 128.2, 130.5, 131.5, 149.5, 170.7; rotamer **B** (minor): δ 16.3, 22.0, 25.0, 81.5, 126.8, 129.6, 130.5, 131.3, 148.2, 170.7.
EIMS m/z (rel int., %): 121 (1.5), 116 (3.0), 100 (85.8), 58 (100).
ESI-HRMS m/z calcd for $C_{12}H_{16}N_2O_2$+Na: 243.1104; found: 243.1104.

4.3.7. (E)-O-1-(N-Methyl-N-acetamino-1-yl)ethyl-4-nitrobenzaldehyde oxime (**11b**)

^{1}H NMR (300 MHz, $CDCl_3$): rotamer **A** (major): δ 1.56 (d, J=6.3 Hz, 3H), 2.31 (s, 3H), 2.85 (s, 3H), 5.97 (q, J=6.3 Hz, 1H), 7.71 (d, J=9.0 Hz, 2H), 8.15 (s, 1H), 8.20 (d, J=9.0 Hz, 2H); rotamer **B** (minor): δ 1.44 (d, J=5.7 Hz, 3H), 2.18 (s, 3H), 2.88 (s, 3H), 6.68 (q, J=5.7 Hz, 1H), 7.75 (d, J=9.3 Hz, 2H), 8.15 (s, 1H), 8.23 (d, J=9.3 Hz, 2H).
^{13}C NMR (75 MHz, $CDCl_3$): rotamer **A** (major): δ 16.5, 17.6, 21.9, 87.0, 123.8, 127.3, 137.6, 147.8, 171.0 (one ^{13}C signal lost for overlap); rotamer **B** (minor): δ 16.5, 22.3, 25.4, 82.5, 123.9, 127.7, 137.6, 147.4, 171.0 (one ^{13}C signal lost for overlap).
EIMS m/z (rel int., %): 166 (15.4), 149 (4.5), 136 (2.6), 100 (100).
ESI-HRMS m/z calcd for $C_{12}H_{15}N_3O_4$+Na: 288.0956; found: 288.0955.

4.3.8. (E)-O-1-(N-Acetamino-1-yl)ethyl-4-nitrobenzaldehyde oxime (**11c**)

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.53 (d, J=6.4 Hz, 3H), 2.05 (s, 3H), 6.06–6.16 (m, 1H), 6.28 (br, 1H), 7.75 (d, J=8.8 Hz, 2H), 8.11 (s, 1H), 8.82 (d, J=8.8 Hz, 2H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 19.7, 23.4, 79.8, 123.9, 127.7, 131.5, 138.2, 147.2, 169.7.
EIMS m/z (rel int., %): 103 (1.5), 86 (41.1), 44 (100).
ESI-HRMS m/z calcd for $C_{11}H_{13}N_3O_4$+Na: 274.0798; found: 274.0797.

4.3.9. (E)-O-1-(N-Formamino-1-yl)ethyl-4-nitrobenzaldehyde oxime (**11d**)

^{1}H NMR (300 MHz, $CDCl_3$): rotamer **A** (major): δ 1.60 (d, J=6.4 Hz, 3H), 5.55–5.62 (m, 1H), 6.76 (br, 1H), 7.73 (d, J=8.8 Hz, 2H), 8.12 (s, 1H), 8.23 (d, J=8.8 Hz, 2H), 8.42 (d, J=11.6 Hz, 1H); rotamer **B** (minor): δ 1.56 (d, J=6.0 Hz, 3H), 6.16–6.20 (m, 1H), 6.40 (br, 1H), 7.75 (d, J=9.2 Hz, 2H), 8.11 (s, 1H), 8.22 (d, J=9.2 Hz, 2H), 8.26 (s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): rotamer **A** (major): δ 19.2, 83.4, 123.9, 127.8, 137.7, 147.8, 160.5, 165.1; rotamer **B** (minor): δ 19.6, 78.2, 124.0, 127.8, 138.0, 147.5, 148.5, 165.1.
EIMS m/z (rel int., %): 166 (1.5), 103 (2.5), 89 (1.9), 72 (100), 44 (70.1).
ESI-HRMS m/z calcd for $C_{10}H_{11}N_3O_4$l+Na: 260.0642; found: 260.0646.

4.3.10. (E)-O-1-(N-Methyl-N-acetamino-1-yl)ethyl-4-chlorobenzaldehyde oxime (**11e**)

^{1}H NMR (300 MHz, $CDCl_3$): rotamer **A** (major): δ 1.47 (d, J=6.6 Hz, 3H), 2.23 (s, 3H), 2.67 (s, 3H), 5.79 (q, J=6.6 Hz, 1H), 7.22 (d, J=10.2 Hz, 2H), 7.37 (d, J=10.2 Hz, 2H), 7.92 (s, 1H); rotamer **B** (minor): δ 1.30 (d, J=6.3 Hz, 3H), 2.02 (s, 3H), 2.80 (s, 3H), 6.52 (q, J=6.3 Hz, 1H), 7.21 (d, J=9.6 Hz, 2H), 7.36 (d, J=9.6 Hz, 2H), 7.94 (s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): rotamer **A** (major): δ 17.4, 22.2, 25.1, 86.2, 128.0, 128.6, 129.9, 135.8, 148.5, 170.8; rotamer **B** (minor): δ 16.5, 22.2, 25.2, 81.8, 128.2, 128.7, 130.2, 135.6, 148.2, 170.9.
EIMS m/z (rel int., %): 155 (7.3), 138 (4.3), 111 (11.6), 100 (96.3), 58 (100).
ESI-HRMS m/z calcd for $C_{12}H_{16}ClN_2O_2$+Na: 277.0714; found: 277.0715.

4.3.11. (E)-O-1-(N-Acetamino-1-yl)ethyl-4-chlorobenzaldehyde oxime (**11f**)

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.50 (d, J=6.0 Hz, 3H), 2.02 (s, 3H), 6.00–6.06 (m, 1H), 6.38 (br, 1H), 7.32 (d, J=8.4 Hz, 2H), 7.48 (d, J=8.4 Hz, 2H), 8.00 (s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 19.8, 23.4, 79.2, 128.3, 128.8, 130.6, 135.7, 148.2, 169.7.
EIMS m/z (rel int., %): 113 (0.9), 111 (2.6), 86 (23.5), 44 (100).
ESI-HRMS m/z calcd for $C_{11}H_{13}N_2O_2Cl$+Na: 263.0558; found: 263.0565.

4.3.12. (E)-O-1-(N-Formamino-1-yl)ethyl-4-chlorobenzaldehyde oxime (**11g**)

^{1}H NMR (300 MHz, $CDCl_3$): rotamer **A** (major): δ 1.55 (d, J=6.0 Hz, 3H), 5.47–5.54 (m, 1H), 6.65 (br, 1H), 7.31 (d, J=8.8 Hz, 2H), 7.49 (d, J=8.8 Hz, 2H), 8.00 (s, 1H), 8.40 (d, J=11.2 Hz, 1H); rotamer **B** (minor): δ 1.55 (d, J=6.0 Hz, 3H), 6.09–6.13 (m, 1H), 6.34 (br, 1H), 7.33 (d, J=8.4 Hz, 2H), 7.51 (d, J=8.4 Hz, 2H), 8.02 (s, 1H), 8.22 (s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): rotamer **A** (major): δ 19.2, 82.9, 128.9, 130.1, 136.1, 148.8, 160.4, 165.2; rotamer **B** (minor): δ 19.7, 77.9, 128.3, 129.0, 130.1, 135.9, 148.6, 160.4.
EIMS m/z (rel int., %): 229 (2.1), 158 (1.5), 156 (5.0), 138 (4.9), 111 (6.9), 89 (8.8), 72 (95.9), 44 (100).
ESI-HRMS m/z calcd for $C_{10}H_{11}N_2O_2Cl$+Na: 249.0401; found: 249.0408.

4.3.13. (E)-O-1-(N-Methyl-N-acetamino-1-yl)ethyl-4-methylbenzaldehyde oxime (**11h**)

^{1}H NMR (300 MHz, $CDCl_3$): rotamer **A** (major): δ 1.43 (d, J=6.0 Hz, 3H), 2.25 (s, 3H), 2.28 (s, 3H), 2.76 (s, 3H), 5.81 (q, J=6.0 Hz, 1H), 7.09 (d, J=7.8 Hz, 2H), 7.34 (d, J=7.8 Hz, 2H), 7.94 (s, 1H); rotamer **B** (minor): δ 1.31 (d, J=6.3 Hz, 3H), 2.90 (s, 3H), 2.03 (s, 3H), 2.78 (s, 3H), 6.50 (q, J=6.3 Hz, 1H), 7.09 (d, J=7.8 Hz, 2H), 7.39 (d, J=7.8 Hz, 2H), 7.97 (s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): rotamer **A** (major): δ 17.7, 21.4, 22.0, 25.4, 86.2, 126.8, 127.0, 128.8, 140.5, 149.9, 171.2; rotamer **B** (minor): δ 16.7, 21.4, 22.0, 25.4, 82.1, 126.8, 127.1, 129.3, 140.5, 149.6, 171.2.

EIMS *m*/*z* (rel int., %): 135 (2.1), 138 (4.9), 100 (100), 58 (98.8).
ESI-HRMS *m*/*z* calcd for $C_{13}H_{18}N_2O_2$+Na: 257.1260; found: 257.1262.

4.3.14. (E)-O-1-(N-Acetamino-1-yl)ethyl-4-methylbenzaldehyde oxime (**11i**)

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.50 (d, J=6.0 Hz, 3H), 2.01 (s, 3H), 2.35 (s, 3H), 6.00–6.05 (m, 1H), 6.36 (br, 1H), 7.16 (d, J=8.0 Hz, 2H), 7.46 (d, J=8.0 Hz, 2H), 8.02 (s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 19.8, 21.4, 23.4, 79.7, 127.0, 129.3, 140.1, 149.5, 169.6 (one ^{13}C signal lost for overlap).
EIMS *m*/*z* (rel int., %): 135 (1.0), 103 (1.3), 86 (21.7), 44 (100).
ESI-HRMS *m*/*z* calcd for $C_{12}H_{16}N_2O_2$+Na: 243.1104; found: 243.1106.

4.3.15. (E)-O-1-(N-Formamino-1-yl)ethyl-4-methylbenzaldehyde oxime (**11j**)

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.52 (d, J=5.2 Hz, 3H), 2.34 (s, 3H), 5.47 (q, J=5.2 Hz, 1H), 6.08 (br, 1H), 7.15 (d, J=8.0 Hz, 2H), 7.43 (d, J=8.0 Hz, 2H), 7.99 (s, 1H), 8.38 (s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 19.2, 21.4, 82.7, 127.1, 129.0, 140.2, 149.8, 160.5, 165.4.
EIMS *m*/*z* (rel int., %): 206 (2.1), 135 (14.9), 72 (78.8), 44 (100).
ESI-HRMS *m*/*z* calcd for $C_{11}H_{14}N_2O_2$+Na: 229.0950; found: 229.0950.

4.3.16. (E)-O-1-(N-Methyl-N-acetamino-1-yl)ethylacetophenone oxime (**11k**)

^{1}H NMR (300 MHz, $CDCl_3$): rotamer **A** (major): δ 1.38 (d, J=6.3 Hz, 3H), 2.10 (s, 3H), 2.18 (s, 3H), 2.70 (s, 3H), 5.78 (q, J=6.3 Hz, 1H), 7.19–7.21 (m, 3H), 7.43–7.54 (m 2H); rotamer **B** (minor): δ 1.28 (d, J=6.3 Hz, 3H), 1.94 (s, 3H), 2.10 (s, 3H), 2.70 (s, 3H), 6.51 (q, J=6.3 Hz, 1H), 7.19–7.21 (m, 3H), 7.43–7.54 (m, 2H).
^{13}C NMR (75 MHz, $CDCl_3$): rotamer **A** (major): δ 11.8, 17.4, 21.6, 28.0, 85.8, 127.9, 128.8, 128.9, 135.6, 155.2, 170.1; rotamer **B** (minor): δ 12.0, 16.4, 22.0, 28.0, 81.5, 125.6, 127.9, 128.8, 135.6, 154.7, 170.7.
EIMS *m*/*z* (rel int., %): 135 (2.2), 118 (5.6), 100 (100), 58 (99.9).
ESI-HRMS *m*/*z* calcd for $C_{13}H_{18}N_2O_2$+Na: 257.1260; found: 257.1263.

4.3.17. (E)-O-1-(N-Methyl-N-acetamino-1-yl)ethyl-2-furaldehyde oxime (**11l**)

^{1}H NMR (300 MHz, $CDCl_3$): rotamer **A** (major): δ 1.48 (d, J=6.0 Hz, 3H), 2.18 (s, 3H), 2.71 (s, 3H), 5.83 (q, J=6.0 Hz, 1H), 6.43 (s, 1H), 7.10–7.12 (m, 1H), 7.33 (s, 1H), 7.38 (s, 1H); rotamer **B** (minor): δ 1.36 (d, J=6.3 Hz, 3H), 2.02 (s, 3H), 2.74 (s, 3H), 6.43 (s, 1H), 6.69 (q, J=6.3 Hz, 1H), 7.10–7.12 (m, 1H), 7.33 (s, 1H), 7.38 (s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): rotamer **A** (major): δ 17.4, 21.6, 25.1, 86.6, 111.9, 117.6, 136.8, 143.3, 144.5; 170.8; rotamer **B** (minor): δ 16.3, 22.0, 27.9, 82.1, 111.9, 117.5, 136.9, 143.1, 144.7, 170.8.
EIMS *m*/*z* (rel int., %): 111 (1.6), 100 (77.8), 58 (100).
ESI-HRMS *m*/*z* calcd for $C_{10}H_{14}N_2O_3$+Na: 233.0897; found: 233.0899.

4.3.18. (E)-O-1-(N-Methyl-N-methylacetamino-1-yl)ethyl-2-pyridinecarboxaldehyde oxime (**11m**)

^{1}H NMR (300 MHz, $CDCl_3$): rotamer **A** (major): δ 1.45 (d, J=6.0 Hz, 3H), 2.44 (s, 3H), 2.75 (s, 3H), 5.85 (q, J=6.0 Hz, 1H), 7.17–7.21 (m, 1H), 7.56–7.61 (m, 1H), 7.62 (d, J=7.5 Hz, 1H), 8.08–8.09 (m, 1H), 8.50 (s, 1H); rotamer **B** (minor): δ 1.33 (d, J=6.3 Hz, 3H), 2.23 (s, 3H), 2.79 (s, 3H), 6.57 (q, J=6.3 Hz, 1H), 7.17–7.21 (m, 1H), 7.56–7.61 (m, 1H), 7.78 (d, J=7.8 Hz, 1H), 8.08–8.09 (m, 1H), 8.51 (s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): rotamer **A** (major): δ 17.4, 21.8, 25.2, 86.5, 120.4, 124.1, 136.3, 149.3, 150.4, 151.0, 170.9; rotamer **B** (minor): δ 16.4, 22.2, 28.2, 82.1, 120.6, 124.1, 136.3, 149.5, 150.6, 151.3, 170.9.
EIMS *m*/*z* (rel int., %): 122 (6.3), 100 (78.6), 58 (100).
ESI-HRMS *m*/*z* calcd for $C_{11}H_{15}N_3O_2$+Na: 244.1056; found: 244.1048.

References and notes

1. (a) Miyabe, H.; Yamaoka, Y.; Naito, T.; Takemoto, Y. *J. Org. Chem.* **2003**, *68*, 6745; (b) Hanessian, S.; Lu, P. P.; Sanceau, J. Y.; Chemla, P.; Gohda, K.; Fonne-Pfiser, R.; Prade, L.; Cowan-Jacob, S. W. *Angew. Chem., Int. Ed.* **1999**, *38*, 3159; (c) Bernardi, L.; Cere, V.; Femoni, C.; Pollicino, S.; Ricci, A. *J. Org. Chem.* **2003**, *68*, 3348; (d) Kakiya, H.; Yagi, K.; Shinokubo, H.; Oshima, K. *J. Am. Chem. Soc.* **2002**, *124*, 9032; (e) Moody, C. J.; Lightfoot, A. P.; Gallagher, P. T. *Synlett* **1997**, 659; (f) Marco, J. A.; Carda, M.; Murga, J.; Gonzalez, F.; Falomir, E. *Tetrahedron Lett.* **1997**, *38*, 1841.
2. (a) Kim, S.; Song, H. J.; Choi, T. L.; Yoon, J. Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 2524; (b) Miyabe, H.; Ueda, M.; Yashioka, N.; Yamakawa, K.; Naito, T. *Tetrahedron* **2000**, *56*, 2413; (c) Miyabe, H.; Ueda, M.; Nishimura, A.; Naito, T. *Org. Lett.* **2002**, *4*, 131; (d) Miyabe, H.; Ushiro, C.; Naito, T. *Chem. Commun.* **2000**, 1789; (e) Miyabe, H.; Ueda, M.; Naito, T. *Synlett* **2004**, 1140; (f) Mcnabb, S. B.; Ueda, M.; Naito, T. *Org. Lett.* **2004**, *6*, 1911; (g) Ryu, I.; Kuriyama, H.; Minakata, S.; Komatsu, M.; Yoon, J.-Y.; Kim, S. *J. Am. Chem. Soc.* **1999**, *121*, 12190.
3. (a) Bull, S. D.; Davies, S. G.; Domingez, S. H.; Jones, S.; Price, A. J.; Sellers, T. G. R.; Thomas, G. R.; Smith, A. D. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2141; (b) Davis, S. G.; Fox, J. F.; Jones, S.; Price, A. J.; Sanz, M. A.; Sellers, T. G. R.; Smith, A. D.; Teixeira, F. C. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1757; (c) Koenig, S. G.; Leonard, K. A.; Lowe, R. S.; Austin, D. J. *Tetrahedron Lett.* **2000**, *41*, 9393.
4. (a) Miyabe, H.; Matsumura, A.; Yoshida, K.; Yamauchi, M.; Takemoto, Y. *Synlett* **2004**, 2123; (b) Miyabe, H.; Yoshida, K.; Reddy, V. K.; Matsumura, A.; Takemoto, Y. *J. Org. Chem.* **2005**, *70*, 5630; (c) Miyabe, H.; Matsumura, A.; Moriyama, K.; Takemoto, Y. *Org. Lett.* **2004**, *6*, 4631.
5. Bhuniya, D.; Moban, S.; Narayanan, S. *Synthesis* **2003**, 1018.
6. De, P.; Nonappa; Pandurangan, K.; Maitra, U.; Wailes, S. *Org. Lett.* **2007**, *9*, 2767.
7. (a) Jia, X. D.; Lin, H. C.; Huo, C. D.; Zhang, W.; Lü, J. M.; Yang, L.; Zhao, G. Y.; Liu, Z. L. *Synlett* **2003**, 1707; (b) Jia, X. D.; Han, B.; Zhang, W.; Jin, X. L.; Yang, L.; Liu, Z. L. *Synthesis* **2006**, 2831; (c) Jia, X. D.; Da, Y. X.; Yang, C. X.; Yang, L.; Liu, Z. L. *Tetrahedron Lett.* **2008**, *49*, 1786; (d) Huo, C. D.; Jia, X. D.; Zhang, W.; Yang, L.; Lü, J. M.; Liu, Z. L. *Synlett* **2004**, 251; (e) Zhang, W.; Jia, X. D.; Yang, L.; Liu, Z. L. *Tetrahedron Lett.* **2002**, *43*, 9433; (f) Huo, C. D.; Wei, R.; Zhang, W.; Yang, L.; Liu, Z. L. *Synlett* **2005**, 161; (g) Zhang, W.; Guo, Y. P.; Liu, Z. G.; Jin, X. L.; Yang, L.; Liu, Z. L. *Tetrahedron* **2005**, *61*, 1325.
8. (a) Francois, D.; Maden, A.; Murray, W. V. *Org. Lett.* **2004**, *6*, 1931; (b) Nakama, K.; Seki, S.; Kanemasa, S. *Tetrahedron Lett.* **2001**, *42*, 6719; (c) Nakama, K.; Seki, S.; Kanemasa, S. *Tetrahedron Lett.* **2002**, *43*, 829; (d) Buehler, E. *J. Org. Chem.* **1967**, *32*, 261.
9. Schoenewaldt, E. F.; Kinnel, R. B.; Paul, D. *J. Org. Chem.* **1968**, *33*, 4270.