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Direct oxidative conversion of aldehydes and alcohols to 2-imidazolines and 2-oxazolines using molecular iodine

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Abstract—Aldehydes were converted to the corresponding 2-imidazolines and 2-oxazolines in good yields by the reaction with ethylenediamine and aminoethanol, respectively, using molecular iodine and potassium carbonate. Moreover, primary alcohols were directly converted to the corresponding 2-imidazolines and 2-oxazolines via aldehydes in one-pot manner with ethylenediamine and aminoethanol, respectively, using molecular iodine and potassium carbonate.

1. Introduction

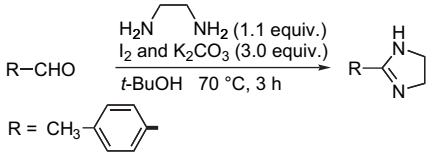
Preparation of 2-substituted imidazolines and oxazolines has become of great interest and importance because of their pharmaceutical[1] and synthetic material applications.[2] To date, there are several synthetic methods for 2-imidazolines and 2-oxazolines starting from mainly nitriles,[3] esters,[4] carboxylic acids,[5] and acyl benzotriazoles.[6] Aldehydes can also be used as the starting substrate, such as for BF_3-promoted oxazoline formation from the reaction of azidoalcohols with aldehydes,[7] and 2-arylmethyl imidazolines formation from the reaction of 2-aryl-1,1-dibromoethenes with ethylenediamine.[8] More recently, preparation of 2-imidazolines[9,10] and 2-oxazolines[10] could be performed by the reaction of aldehydes with ethylenediamine and aminoethanol, respectively, with NXS[9] (X=Cl, Br, and I) and pyridinium hydrobromide perbromide.[10] Once 2-imidazolines and 2-oxazolines are formed, they can be smoothly oxidized to the corresponding 2-imidazoles and 2-oxazoles by oxidants such as MnO_2,[11a] NiO_2,[11b] Pd/C,[11c] DMSO,[3f] $KMnO_4$,[11d] trichloroisocyanuric acid,[11e] $(COCl)_2$–DMSO,[8] and IBX,[11f] etc. As a part of our basic study of molecular iodine for organic synthesis, previously we reported an efficient preparation of various alcohols to esters[12] and nitriles,[13] and very recently we reported the preparation of 2-imidazolines and 2-imidazoles from aldehydes with molecular iodine and (diacetoxyiodo)benzene as a preliminary study.[14] Here, we would like to report as a full form for the preparation of 2-imidazolines and 2-oxazolines from aldehydes, and direct one-pot oxidative conversion of primary alcohols to the corresponding 2-imidazolines and 2-oxazolines with ethylenediamine and aminoethanol, respectively, using molecular iodine in the presence of potassium carbonate.

2. Results and discussion

2.1. Preparation of 2-imidazolines and 2-oxazolines from aldehydes

The addition of molecular iodine to a mixture of *p*-tolualdehyde and ethylenediamine in the presence of K_2CO_3 provided the corresponding 2-(4-methylphenyl)imidazoline, and the use of 1.25 equiv of molecular iodine gave the product quantitatively as shown in Table 1 (entry 3). According to our previously reported reaction conditions using molecular iodine,[12b] *t*-BuOH was used as a solvent in the present reaction. ICl also works; however, molecular iodine is much

Table 1. Formation of 2-(4-methylphenyl)imidazoline from *p*-tolualdehyde with ethylenediamine and iodine



Entry	I_2 (equiv)	Yield (%)[a]
1	0.75	82
2	1.00	89
3	1.25	100
4	1.50	100
5	2.5[b]	83

[a] Isolated yield.
[b] ICI was used, instead of I_2.

Keywords: 2-Imidazoline; 2-Oxazoline; Iodine; Alcohol; Aldehyde; Ethylenediamine; Aminoethanol.
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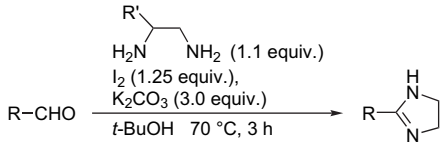
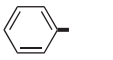
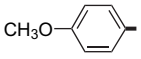
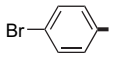
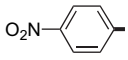
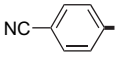
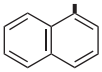
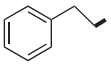
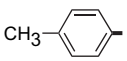
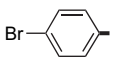
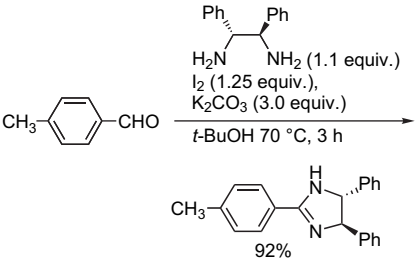
more efficient in terms of operational utility of the reagent and the yield (entry 5). The same treatment of *p*-tolualdehyde with (diacetoxyiodo)benzene (DIB), instead of molecular iodine, gave a complicated reaction mixture, and 2-(4-methylphenyl)imidazoline was not formed at all. Based on these results, various aromatic aldehydes were treated with ethylenediamine and molecular iodine under the same conditions to provide the corresponding 2-substituted imidazolines in good yields, as shown in Table 2. Thus, aromatic aldehydes bearing electron-donating substituents and electron-withdrawing substituents can be successfully converted to the corresponding 2-arylimidazolines in good yields. Adamantanecarboxaldehyde can be also transformed to 2-adamantylimidazoline quantitatively (entry 10). However, cyclohexanecarboxaldehyde and 3-phenylpropionaldehyde, bearing the α-hydrogen atom, gave 2-cyclohexylimidazoline and 2-(2-phenylethyl)imidazoline in moderate yields, respectively, under the same conditions (entries 11 and 12). Treatment of 1-methyl-1,2-ethylenediamine under the same conditions gave the corresponding 2-aryl-4-methylimidazolines in good yields (entries 13 and 14). The same treatment of *p*-tolualdehyde with (*R*,*R*)-(+)-diphenylethylenediamine, instead of ethylenediamine, provided the corresponding (*R*,*R*)-2-(4-methylphenyl)-4,5-diphenylimidazoline in 92% yield as shown in Eq. 1.

Table 2. Preparation of 2-substituted imidazolines from aldehydes with ethylenediamine and iodine



Entry	R	R′	Yield (%)[a]
1		H	100
2		H	100
3		H	97
4		H	99
5		H	98
6		H	99
7		H	94
8		H	97
9		H	99
10		H	100
11		H	50
12		H	53
13		CH_3	98
14		CH_3	100

[a] Isolated yield.



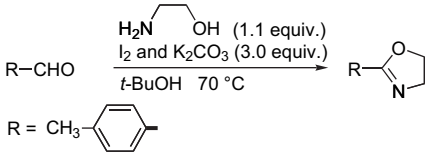
(1)

The addition of molecular iodine to a mixture of *p*-tolualdehyde and aminoethanol in the presence of K_2CO_3 provided the corresponding 2-(4-methylphenyl)oxazoline, and the use of 2.0 equiv of molecular iodine gave the product in the best yield as shown in Table 3 (entries 3 and 4). Based on these results, various aromatic aldehydes were treated with aminoethanol and molecular iodine under the same conditions to provide the corresponding 2-substituted oxazolines in good to moderate yields, as shown in Table 4. For *p*-nitrobenzaldehyde, *p*-cyanobenzaldehyde, 2-pyridinecarboxaldehyde, 1-naphthaldehyde, and 2-thiophenaldehyde, sodium carbonate and sodium hydrogen carbonate gave the corresponding 2-aryloxazolines in better yields than that of potassium carbonate (entries 4–8). Reactions of adamantanecarboxaldehyde and cyclohexanecarboxaldehyde under the same conditions gave 2-adamantyloxazoline and 2-cyclohexyloxazoline in 70% and 32% yields, respectively (entries 9 and 10). However, 3-phenylpropionaldehyde did not provide the corresponding oxazoline at all, and instead, a very complicated reaction mixture was formed (entry 11).

2.2. Preparation of 2-imidazolines and 2-oxazolines from alcohols

Then, direct one-pot oxidative conversion of primary alcohols to the corresponding 2-imidazolines and 2-oxazolines

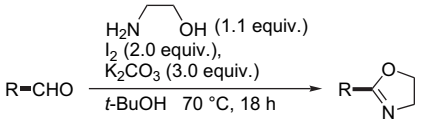
Table 3. Formation of 2-(4-methylphenyl)oxazoline from *p*-tolualdehyde with aminoethanol and iodine

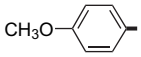
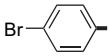
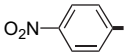
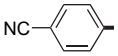
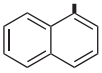
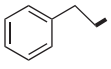


Entry	I_2 (equiv)	Time (h)	Yield (%)[a]
1	1.25	8	69
2	1.25	24	74
3	2.0	24	86
4	2.0	18	88
5	2.0[b]	18	12

[a] Isolated yield.
[b] Without K_2CO_3.

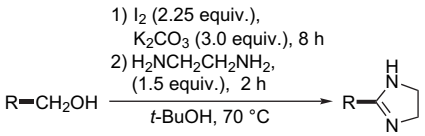
Table 4. Preparation of 2-oxazoline from aldehydes with aminoethanol and iodine

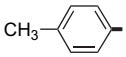
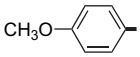
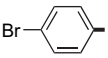
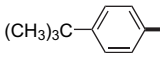
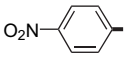
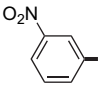
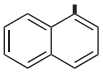


Entry	R-	Yield (%)[a]
1		75
2		83
3		75
4		55, 74,[b] 76[c]
5		55, 64,[b] 64[c]
6		41, 54,[b] 27[c]
7		54, 72,[b] 52[c]
8		17, 40,[b] 45[c]
9		70
10		32
11		0

[a] Isolated yield.
[b] Na_2CO_3 (3.0 equiv) was used, instead of K_2CO_3.
[c] $NaHCO_3$ (3.0 equiv) was used, instead of K_2CO_3.

Table 5. Direct oxidative conversion of alcohols to 2-imidazolines



Entry	R-	Yield (%)[a]
1		99
2		99
3		99
4		92 (4[b])
5		99
6		20 (26,[b] 6[c])
7		28 (21,[b] 8[c])
8		99
9		96[d]
10		99[e]
11		32 (7[b])

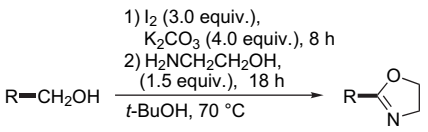
[a] Isolated yield.
[b] Yield of oxidatively condensed ester (RCO_2CH_2R).
[c] Recovery of starting substrate.
[d] Reaction time for the first step was 16 h.
[e] I_2 (2.5 equiv) was used.

through the formation of aldehydes, with ethylenediamine and aminoethanol, respectively, using molecular iodine and potassium carbonate was carried out. Thus, primary alcohols were initially treated with molecular iodine and potassium carbonate (70 °C, 8 h) to form the corresponding aldehydes, and then ethylenediamine was added to the mixture (70 °C, 2 h) to provide the corresponding 2-imidazolines. The results are shown in Table 5. Various *p*-substituted benzylic alcohols could be directly converted to the corresponding 2-arylimidazolines in good yields, except for nitrobenzyl alcohols. In nitrobenzyl alcohols, the formation of oxidatively condensed ester was observed, together with the starting nitrobenzylalcohols. In aliphatic primary alcohols, adamantanemethanol gave 2-adamantylimidazoline quantitatively (entry 10), while cyclohexanemethanol provided the corresponding 2-imidazoline in 32% yield (entry 11).

Then, under the same conditions, various *p*-substituted benzylic alcohols could be successfully converted to the corresponding 2-aryloxazoline in one-pot manner in good yields similarly, except for nitrobenzyl alcohols, by the reaction with molecular iodine, followed by treatment with aminoethanol as shown in Table 6. In aliphatic primary alcohols, adamantanemethanol gave the 2-adamantyloxazoline in good yield (entry 10), while cyclohexanemethanol provided 2-cyclohexyloxazoline in poor yield (entry 11).

Generally, the present oxidative conversion proceeded efficiently, except for benzylic alcohols bearing electron-withdrawing groups such as nitrobenzylalcohols, and cyclohexanemethanol containing the β-hydrogen atom (entries 6, 7 and 11 in Table 5 and entries 6, 7 and 11 in Table 6). In the former case, the formed aldehyde smoothly reacts with the starting primary alcohol to form the oxidatively condensed ester via oxidation of the formed hemiacetal,[12b] and in the latter case, the formed aldehyde may induce side reactions, such as aldol reaction or formation of enamine. Thus, benzylic alcohols bearing electron-donating substituents on the aromatic ring can be efficiently converted to the corresponding 2-arylimidazolines and 2-aryloxazolines in good yields. Neopentyl-type alcohols such as adamantanemethanol can also be effectively converted to the corresponding 2-alkylimidazolines and 2-alkyloxazolines.

Table 6. Direct oxidative conversion of alcohols to 2-oxazolines



Entry	R	Yield (%)[a]
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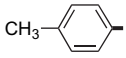
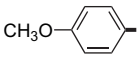
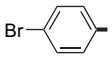
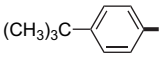
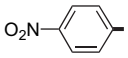
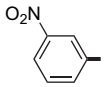
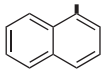
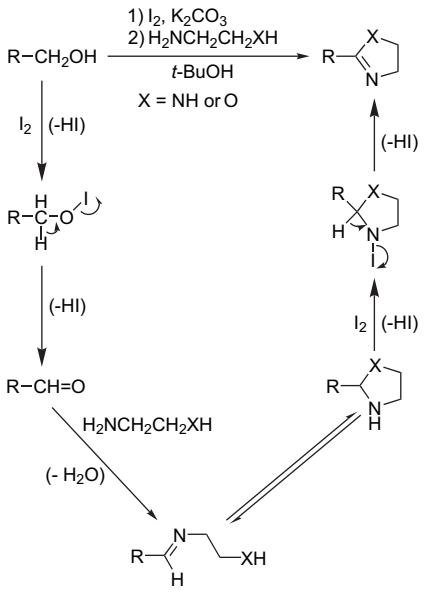
2		85
3		83
4		72 (3[b])
5		88
6		16 (14,[b] 15[c])
7		16 (14,[b] 9[c])
8		33
9		55
10		82
11		4

[a] Isolated yield.
[b] Yield of oxidatively condensed ester (RCO_2CH_2R).
[c] Recovery of starting substrate.



Scheme 1. Plausible reaction pathway.

A plausible reaction pathway is shown in Scheme 1. The rate-determining step is exactly the oxidation of alcohol to the aldehyde. Thus, it is required that ethylenediamine and aminoethanol should be added after the formation of aldehydes, to form the corresponding 2-substituted imidazoline and oxazoline effectively, since ethylenediamine and aminoethanol are smoothly oxidized by molecular iodine under the present reaction conditions.

3. Conclusion

In summary, 2-imidazolines and 2-oxazolines could be easily and efficiently obtained in good to moderate yields from the reaction of aldehydes and primary alcohols, with ethylenediamine and aminoethanol, respectively, using molecular iodine and potassium carbonate in *tert*-butyl alcohol. As is well known, the advantages of molecular iodine are operational simplicity, low cost, and low toxicity. Thus, the present method is useful for the preparation of 2-substituted imidazolines and oxazolines.

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were obtained with JEOL-JNM-LA-400, JEOL-JNM-LA-400s, JEOL-JNM-LA-500, spectrometers. Chemical shifts are expressed in parts per million downfield from tetramethylsilane (TMS) in δ units. IR spectra were measured with JASCO FT/IR-810 and FT/IR-4100 spectrometers. Mass spectra were recorded on JEOL-HX-110 and JEOL-JMS-ATII15 spectrometers. Melting points were determined on Yamato melting points apparatus Model MP-21. Silica gel 60 (Kanto Kagaku Co.) was used for column chromatography and Wakogel B-5F was used for preparative TLC.

4.2. Typical procedure for preparation of 2-imidazolines from aldehydes

To a solution of *p*-tolualdehyde (120.2 mg, 1 mmol) in *tert*-butyl alcohol (10 ml) was added ethylenediamine (66.1 mg, 1.1 mmol). The obtained mixture was stirred at room temperature under an argon atmosphere for 30 min, and then K_2CO_3 (414.6 mg, 3 mmol) and I_2 (317.3 mg, 1.25 mmol) were added to the mixture and stirred at 70 °C. After 3 h, the mixture was quenched with satd aq Na_2SO_3 until the iodine color almost disappeared, and was extracted with $CHCl_3$. The organic layer was washed with satd aq $NaHCO_3$ and brine, and dried over Na_2SO_4. After filtration, the mixture was evaporated in vacuo to provide 160.2 mg of 2-(4-methylphenyl)imidazoline in 100% yield in an almost pure state.

4.2.1. 2-(4-Methylphenyl)imidazoline. Mp 181–182 °C (lit.[15] mp 181 °C); IR (KBr): 3140, 2925, 1600, 1495, 985, 830 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ=2.38 (s, 3H), 3.77 (s, 4H), 7.21 (d, J=8.3 Hz, 2H), 7.67 (d, J=8.3 Hz, 2H).

4.2.2. 2-Phenylimidazoline. Mp 101.5–102 °C (lit.[15] mp 100–101 °C); IR (KBr): 3200, 2930, 1600, 1510, 1270, 985, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=3.90

(s, 4H), 7.46 (t, J=7.2 Hz, 2H), 7.57 (t, J=7.2 Hz, 1H), 7.95 (d, J=7.2 Hz, 2H).

4.2.3. 2-(4-Methoxyphenyl)imidazoline. Mp 136–138 °C (lit.[16] mp 137–139 °C); IR (KBr): 3120, 2830, 1605, 1490, 1255, 1035, 845 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=3.77 (s, 4H), 3.84 (s, 3H), 6.91 (d, J=8.9 Hz, 2H), 7.73 (d, J=8.9 Hz, 2H).

4.2.4. 2-(4-Bromophenyl)imidazoline. Mp 177–177.5 °C; IR (KBr): 3150, 2930, 1610, 1470, 1270, 1010, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=3.79 (s, 4H), 7.54 (d, J=8.7 Hz, 2H), 7.65 (d, J=8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=125.0, 128.5, 129.4, 131.6, 163.8; HRMS (FAB); obsd M+H=225.0021. Calcd for $C_9H_{10}N_2Br$ M+H=225.0027.

4.2.5. 2-(4-Nitrophenyl)imidazoline. Mp 235–237 °C (lit.[17] mp 231 °C); IR (KBr): 3180, 2935, 1580, 1520, 1335, 1105, 855 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=3.85 (s, 4H), 7.95 (d, J=8.9 Hz, 2H), 8.27 (d, J=8.9 Hz, 2H).

4.2.6. 2-(4-Cyanophenyl)imidazoline. Mp 195–196 °C; IR (KBr): 3160, 2230, 1595, 1490, 1275, 985, 850 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=3.83 (s, 4H), 7.70 (d, J=8.5 Hz, 2H), 7.88 (d, J=8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=114.2, 118.4, 127.7, 132.4, 134.7, 163.2; HRMS (FAB) obsd M+H=172.0883. Calcd for $C_{10}H_{10}N_3$ M+H=172.0875.

4.2.7. 2-(2-Chlorophenyl)imidazoline. Mp 83 °C (lit.[18] mp 69–70 °C); IR (KBr): 3100, 2920, 1610, 1505, 1260, 985, 765 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=3.80 (s, 4H), 7.28–7.41 (m, 3H), 7.78 (dd, J=7.5 and 1.9 Hz, 1H).

4.2.8. 2-(2-Thienyl)imidazoline. Mp 175 °C (lit.[16] mp 175–177 °C); IR (KBr): 3150, 2935, 1595, 1495, 1270, 985, 710 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=3.78 (s, 4H), 7.06 (dd, J=4.9 and 3.7 Hz, 1H), 7.36 (dd, J=3.7 and 0.9 Hz, 1H), 7.40 (dd, J=4.9 and 0.9 Hz, 1H).

4.2.9. 2-(2-Pyridyl)imidazoline. Mp 95–96 °C; IR (KBr): 3270, 1595, 1505, 1280, 975, 805, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=3.85 (s, 4H), 7.36 (dd, J=4.8 and 1.2 Hz, 1H), 7.77 (td, J=7.7 and 1.7 Hz, 1H), 8.14 (d, J=8 Hz, 1H), 8.57 (dt, J=4.9 and 0.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=50.4, 122.2, 125.0, 136.5, 148.5, 148.6, 164.2; HRMS (FAB); obsd M+H=148.0876. Calcd for $C_8H_{10}N_3$ M+H=148.0875.

4.2.10. 2-(1-Naphthyl)imidazoline. Mp 131–133 °C (lit.[19] mp 134 °C); IR (KBr): 3140, 2860, 1570, 1515, 1270, 980, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=3.89 (s, 4H), 7.45–7.57 (m, 3H), 7.75 (dd, J=7.1 and 1.2 Hz, 1H), 7.85–7.91 (m, 2H), 8.68 (d, J=8.5 Hz, 1H).

4.2.11. 2-(1-Adamantyl)imidazoline. Mp 162.5–163.5 °C; IR (KBr): 3230, 3000, 1590, 1495, 1250, 1085, 980 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=1.69–1.77 (m, 6H), 1.86–1.87 (m, 6H), 2.03 (m, 3H), 3.56 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=28.1, 35.1, 36.5, 40.3, 49.4, 174.5; HRMS (FAB); obsd M+H=205.1703. Calcd for $C_{13}H_{21}N_2$ M+H=205.1705.

4.2.12. 2-Cyclohexylimidazoline. Mp 130.5–131 °C (lit.[15] mp 134 °C); IR (paraffin): 3085, 1600, 1510, 1275, 1060, 980 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=1.16–1.43 (m, 5H), 1.67–1.92 (m, 5H), 2.22 (tt, J=11.5 and 3.4 Hz, 1H), 3.56 (s, 4H).

4.2.13. 2-(2-Phenylethyl)imidazoline. Mp 101–103 °C; IR (KBr): 3160, 2925, 1605, 1500, 1285, 960, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=2.54 (t, J=8.0 Hz, 2H), 2.96 (t, J=8.0 Hz, 2H), 3.55 (br s, 4H), 7.21–7.36 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=31.3, 32.9, 126.3, 128.3, 128.6, 141.1, 167.2; HRMS (FAB); obsd M+H=175.1237. Calcd for $C_{11}H_{15}N_2$ M+H=175.1235.

4.2.14. 2-(4-Methylphenyl)-4-methylimidazoline. Mp 162–164 °C; IR (paraffin): 3400, 1590, 1540, 1330, 1015, 830, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=1.29 (d, J=6.3 Hz, 3H), 2.38 (s, 3H), 3.36 (br s, 1H), 3.91 (br s, 1H), 4.11 (br s, 1H), 7.20 (d, J=8.0 Hz, 2H), 7.66 (d, J=8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.3, 22.0, 51.2, 53.2, 118.3, 129.7, 130.0, 146.4, 164.1; HRMS (FAB); obsd M+H=175.1236. Calcd for $C_{11}H_{15}N_2$ M+H=175.1235.

4.2.15. 2-(4-Bromophenyl)-4-methylimidazoline. Mp 102 °C; IR (paraffin): 3140, 1610, 1270, 1130, 1015, 840, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=1.29 (d, J=5.8 Hz, 3H), 3.37 (br s, 1H), 3.92 (br s, 1H), 4.12 (br s, 1H), 7.53 (d, J=8.5 Hz, 2H), 7.64 (d, J=8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.8, 124.8, 128.5, 129.5, 131.5, 162.4; HRMS (FAB); obsd M+H=239.0170. Calcd for $C_{10}H_{12}BrN_2$ M+H=239.0184.

4.2.16. (4*R*,5*R*)-2-(4-Methylphenyl)-4,5-diphenylimidazoline. Mp 146.5 °C; IR (paraffin): 3150, 1600, 1130, 1020, 830, 765, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=2.43 (s, 3H), 4.75 (br, 1H), 5.07 (br, 1H), 5.33 (br, 1H), 7.26–7.37 (m, 12H), 7.84 (d, J=8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.4, 126.7, 127.3, 127.4, 128.6, 129.2, 143.6, 163.0; HRMS (FAB); obsd M+H=313.1676. Calcd for $C_{22}H_{21}N_2$ M+H=313.1705.

4.2.17. 2-(4-*tert*-Butylphenyl)imidazoline. Mp 167–169 °C; IR (KBr): 3140, 2970, 1600, 1470, 1270, 985, 840 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=1.33 (s, 9H), 3.78 (s, 4H), 7.42 (d, J=8.5 Hz, 2H), 7.71 (d, J=8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=31.1, 34.8, 50.4, 125.3, 126.7, 127.6, 153.9, 164.6; HRMS (FAB); obsd M+H=203.1549. Calcd for $C_{13}H_{19}N_2$ M+H=203.1548.

4.2.18. 2-(3-Nitrophenyl)imidazoline. Mp 156–157 °C (lit.[18] 156–157 °C); IR (KBr): 3150, 2940, 1600, 1525, 1350, 980, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=3.63 (br s, 2H), 4.07 (br s, 2H), 4.87 (br s, 1H), 7.61 (t, J=7.9 Hz, 1H), 8.17 (d, J=7.9 Hz, 1H), 8.31 (d, J=7.9 Hz, 1H), 8.59 (s, 1H).

4.3. Typical procedure for preparation of 2-oxazolines from aldehydes

To a solution of *p*-tolualdehyde (120.2 mg, 1 mmol) in *tert*-butyl alcohol (10 ml) was added aminoethanol (67.2 mg, 1.1 mmol). The mixture was stirred at room temperature

under an argon atmosphere for 30 min, and K_2CO_3 (414.6 mg, 3 mmol) and I_2 (507.6 mg, 2 mmol) were added to the mixture and stirred at 70 °C. After 18 h, the mixture was quenched with satd aq Na_2SO_3 until the iodine color almost disappeared and was extracted with Et_2O. The organic layer was washed with brine and dried over Na_2SO_4. After filtration, the solvent was removed in vacuo. The residue was chromatographed on neutral silica gel (AcOEt) to give 141.9 mg of 2-(4-methylphenyl)oxazoline in 88% yield.

4.3.1. 2-(4-Methylphenyl)oxazoline. Mp 71–72 °C (lit.[3b] mp 69–71 °C); IR (KBr): 3040, 2940, 1650, 1355, 1260, 1070, 940 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=2.39 (s, 3H), 4.04 (t, J=9.4 Hz, 2H), 4.41 (t, J=9.4 Hz, 2H), 7.21 (d, J=8.1 Hz, 2H), 7.83 (d, J=8.1 Hz, 2H).

4.3.2. 2-Phenyloxazoline. Bp 80 °C/2 mmHg (lit.[20] bp 68–70 °C/0.5 mmHg); IR (Neat): 2975, 1650, 1360, 1260, 1065, 780, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=4.07 (t, J=9.5 Hz, 2H), 4.44 (t, J=9.5 Hz, 2H), 7.41 (t, J=7.0 Hz, 2H), 7.48 (t, J=7.0 Hz, 1H), 7.95 (d, J=7.0 Hz, 2H).

4.3.3. 2-(4-Methoxyphenyl)oxazoline. Mp 61.5–62 °C (lit.[16] mp 62.5–63.5 °C); IR (KBr): 2905, 1645, 1510, 1255, 1165, 1070, 940 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=3.85 (s, 3H), 4.04 (t, J=9.5 Hz, 2H), 4.41 (t, J=9.5 Hz, 2H), 6.92 (d, J=8.8 Hz, 2H), 7.89 (d, J=8.8 Hz, 2H).

4.3.4. 2-(4-Bromophenyl)oxazoline. Mp 95–97 °C; IR (KBr): 2910, 1645, 1395, 1260, 1075, 835, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=4.06 (t, J=9.6 Hz, 2H), 4.42 (t, J=9.6 Hz, 2H), 7.55 (d, J=8.5 Hz, 2H), 7.81 (d, J=8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=55.0, 67.7, 125.9, 126.7, 129.7, 131.6, 163.9; HRMS (FAB); obsd M+H=225.9859. Calcd for C_9H_9NOBr M+H= 225.9868.

4.3.5. 2-(4-Nitrophenyl)oxazoline. Mp 174 °C (lit.[21] mp 178–179 °C); IR (KBr): 2360, 1650, 1520, 1335, 1070, 940, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=4.13 (t, J=9.7 Hz, 2H), 4.51 (t, J=9.7 Hz, 2H), 8.12 (d, J=8.9 Hz, 2H), 8.28 (d, J=8.9 Hz, 2H).

4.3.6. 2-(4-Cyanophenyl)oxazoline. Mp 113–114 °C; IR (KBr): 2225, 1650, 1265, 1070, 940, 850, 670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=4.11 (t, J=9.7 Hz, 2H), 4.49 (t, J=9.7 Hz, 2H), 7.71 (d, J=8.5 Hz, 2H), 8.05 (d, J=8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=55.1, 68.0, 114.6, 118.2, 128.6, 131.8, 132.1, 163.0; HRMS (FAB) obsd M+H=173.0722. Calcd for $C_{10}H_9N_2O$ M+H=173.0715.

4.3.7. 2-(2-Pyridyl)oxazoline. Bp 90 °C/2 mmHg; IR (Neat): 3400, 2940, 1640, 1370, 1100, 945, 800 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=4.13 (t, J=9.7 Hz, 2H), 4.54 (t, J=9.7 Hz, 2H), 7.39–7.42 (m, 1H), 7.79 (t, J=7.8 Hz, 1H), 8.05 (d, J=8.0 Hz, 1H), 8.71 (d, J=4.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=54.9, 68.0, 123.6, 125.3, 136.4, 146.5, 149.5, 163.6; HRMS (FAB) obsd M+H=149.0707. Calcd for $C_8H_9N_2O$ M+H=149.0715.

4.3.8. 2-(1-Naphthyl)oxazoline. Bp 150 °C/2 mmHg; IR (Neat): 2970, 1640, 1590, 1320, 1120, 1000, 780 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=4.17 (t, J=9.4 Hz, 2H), 4.39 (t, J=9.4 Hz, 2H), 7.44–7.51 (m, 2H), 7.56–7.61 (m, 1H), 7.84 (d, J=8.3 Hz, 1H), 7.92 (d, J=8.3 Hz, 1H), 8.08 (dd, J=7.3 and 0.2 Hz, 1H), 9.13 (d, J=8.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=55.6, 66.4, 124.4, 124.5, 126.0, 126.3, 127.2, 128.3, 128.5, 131.0, 131.8, 133.6, 164.3; HRMS (FAB) obsd M+H=198.0904. Calcd for $C_{13}H_{12}NO$ M+H 198.0919.

4.3.9. 2-(2-Thienyl)oxazoline. Mp 57–59 °C (lit.[16] mp 58–60 °C); IR (KBr): 3165, 2880, 1645, 1530, 1055, 1015, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=4.05 (t, J=9.4 Hz, 2H), 4.43 (t, J=9.4 Hz, 2H), 7.08 (dd, J=5 and 3.6 Hz, 1H), 7.45 (dd, J=5 and 1 Hz, 1H), 7.59 (dd, J=3.6 and 1 Hz, 1H).

4.3.10. 2-(1-Adamantyl)oxazoline. Mp 40–41 °C (lit.[20] mp 39–40 °C); IR (paraffin): 3320, 1660, 1345, 1225, 1060, 955 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=1.69–1.76 (m, 6H), 1.89–1.90 (m, 6H), 2.01 (m, 3H), 3.80 (t, J=9.4 Hz, 2H), 4.19 (t, J=9.4 Hz, 2H).

4.3.11. 2-Cyclohexyloxazoline. Bp 90 °C/2 mmHg (lit.[20] bp 120 °C/15 mmHg); IR (neat): 3050, 2980, 1560, 1120, 1000, 810, 780 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=1.20–1.47 (m, 3H), 1.63–1.95 (m, 6H), 2.30 (t, J=11.3 Hz, 2H), 3.82 (t, J=9.5 Hz, 2H), 4.21 (t, J=6.5 Hz, 2H).

4.3.12. 2-(4-*tert*-Butylphenyl)oxazoline. Mp 72–75 °C; IR (KBr): 2970, 1650, 1360, 1265, 1065, 940, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=1.33 (s, 9H), 4.05 (d, J=9.4 Hz, 2H), 4.42 (d, J=9.4 Hz, 2H), 7.43 (d, J=8.5 Hz, 2H), 7.87 (d, J=8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=31.2, 34.9, 54.9, 67.5, 124.9, 125.3, 127.9, 154.7, 164.7; HRMS (FAB); obsd M+H=204.1386. Calcd for $C_{13}H_{18}NO$ M+H=204.1388.

4.3.13. 2-(3-Nitrophenyl)oxazoline. Mp 120–121 °C (lit.[20] mp 117–118 °C); IR (paraffin): 3410, 1650, 1540, 1350, 1260, 1115, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=4.12 (t, J=9.6 Hz, 2H), 4.51 (t, J=9.6 Hz, 2H), 7.61 (t, J=8.0 Hz, 1H), 8.29 (d, J=8.0 Hz, 1H), 8.34 (d, J=8.0 Hz, 1H), 8.79 (s, 1H).

4.4. Typical procedure for preparation of 2-imidazolines from alcohols

To a solution of 4-methylbenzyl alcohol (122.2 mg, 1 mmol) in *tert*-butyl alcohol (8 ml) were added K_2CO_3 (414.6 mg, 3 mmol) and I_2 (584 mg, 2.3 mmol). The obtained mixture was stirred at 70 °C. After 8 h, ethylenediamine (90.2 mg, 1.5 mmol) in *tert*-butyl alcohol (2 ml) was added to the reaction mixture and stirred for another 2 h. The reaction mixture was quenched with satd aq Na_2SO_3 until the iodine color almost disappeared, and was extracted with $CHCl_3$. The organic layer was washed with aq NaOH, brine, and dried over Na_2SO_4. After filtration, the solvent was removed in vacuo to provide 158.6 mg of 2-(4-methylphenyl)imidazoline in 99% yield in an almost pure state. If necessary, the product was purified by flash column chromatography on neutral silica

gel ($CHCl_3/Et_3N$=10:1) to give pure 2-(4-methylphenyl) imidazoline.

4.5. Typical procedure for preparation of 2-oxazolines from alcohols

To a solution of 4-methylbenzyl alcohol (122.2 mg, 1 mmol) in *tert*-butyl alcohol (8 ml) were added K_2CO_3 (552.8 mg, 4 mmol) and I_2 (761.4 mg, 3 mmol). The obtained mixture was stirred at 70 °C. After 8 h, aminoethanol (91.6 mg, 1.5 mmol) in *tert*-butyl alcohol (2 ml) was added to the reaction mixture and stirred for another 18 h. The reaction mixture was quenched with satd aq Na_2SO_3 until the iodine color almost disappeared, and was extracted with Et_2O. The organic layer was washed with aq $NaHCO_3$, brine, and dried over Na_2SO_4. After filtration, the solvent was removed in vacuo. The residue was chromatographed on neutral silica gel (AcOEt) to give 137.0 mg of the pure 2-(4-methylphenyl)-oxazoline in 85% yield.

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References and notes

1. (a) Grimmett, M. R. *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 5, pp 345–498; (b) Grimmett, M. R. *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scvien, E. F. V., Eds.; Elsevier Science: Oxford, 1996; Vol. 3, pp 77–220 and pp 261–318; (c) Gilman, A. G.; Goodman, L. S. *The Pharmacological Basic of Therapeutics*, 10th ed.; Macmillan: New York, NY, 2001; (d) Genet, J. P.; Thorimbert, S.; Touzin, A. M. *Tetrahedron Lett.* **1993**, *34*, 1159; (e) Wipf, P.; Venkatraman, S. *Synlett* **1997**, 1; (f) Rodriguez, A. D.; Ramirez, C.; Rodriguez, I. I.; Gonzalez, E. *Org. Lett.* **1999**, *1*, 527; (g) Li, Q.; Woods, K. W.; Claiborne, A.; Gwaltney, S. L. H.; Barr, K. J.; Liu, G.; Gehrke, L.; Credo, R. B.; Hua-Hui, Y.; Lee, L.; Warner, R. B.; Kovar, P.; Nukkala, M. A.; Zielinski, N. A.; Tahir, S. K.; Fitzgerald, M.; Kim, K. H.; Marsh, K.; Frost, D.; Ng, S. C.; Rosenberg, S.; Fattorusso, C.; Catalanotti, B.; Ramunno, A.; Nacci, V.; Novellino, E.; Grewer, C.; Ionescu, D.; Rauen, T.; Griffiths, R.; Sinclair, C.; Fumagalli, E.; Mennini, T. *J. Med. Chem.* **2001**, *44*, 2507; (h) Prisinzano, T.; Law, H.; Dukat, M.; Slassi, A.; MaClean, N.; Demchyshyn, L.; Glennon, R. A. *Bioorg. Med. Chem.* **2001**, *9*, 613; (i) Testard, A.; Picot, L.; Eruitier-Arnaudin, I.; Piot, J. M.; Chabane, H.; Domon, L.; Thiery, V.; Besson, T. *J. Enzyme Inhib. Med. Chem.* **2004**, *19*, 467; (j) Brage, A. L.; Lüdtke, D. S.; Vargas, F.; Braga, R. C. *Synlett* **2006**, 1453.
2. For examples, see: (a) Jones, R. C. F.; Nichols, J. R. *Tetrahedron Lett.* **1990**, *31*, 1771; (b) Langlois, Y.; Dalko, P. I. *J. Org. Chem.* **1998**, *63*, 8107; (c) Menges, F.; Neuburger, M.; Pfaltz, A. *Org. Lett.* **2002**, *4*, 4713; (d) Meiere, S. H.; Valahovic, M. T.; Harman, W. D. *J. Am. Chem. Soc.* **2002**, *124*, 15099; (e) Evans, D. A.; Downey, C. W.; Hubbs, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 8706; (f) Bhor, S.; Anilkumar, G.; Tse, M. K.; Klawonn, M.; Döbler, C.; Bitterlich, B.; Grotevendt, A.; Beller, M. *Org. Lett.* **2005**, *7*, 3393; (g) Du, H.; He, Y.; Sivappa, R.; Lovely, C. J. *Synlett* **2006**, 965.
3. (a) Ferm, R. J.; Riebsomer, J. L. *Chem. Rev.* **1954**, *54*, 593; (b) Mohammadpoor-Baltork, I.; Khosropour, A. R.; Hojati, S. F. *Synlett* **2005**, 2747; (c) Mirkhani, V.; Moghadam, M.; Tangestaninejad, S.; Kargar, H. *Tetrahedron Lett.* **2006**, *47*, 2129; (d) De la Hoz, A.; Diaz-Ortiz, A.; Mateo, M. D. C.; Moral, M.; Moreno, A.; Elguero, J.; Foces-Foces, C.; Rodriguez, M. L.; Sanchez-Migallon, A. *Tetrahedron* **2006**, *62*, 5868; (e) Wu, J.; Sun, X.; Xia, H. *Tetrahedron Lett.* **2006**, *47*, 1509; (f) Anastassiadou, M.; Baziard-Mouysset, G.; Payard, M. *Synthesis* **2000**, 1814.
4. For examples, see: (a) Hughey, J. L., IV; Knapp, S.; Schugar, H. *Synthesis* **1980**, 489; (b) Quaglia, W.; Bousquet, P.; Pigini, M.; Carotti, A.; Carrieri, A.; Dontenwill, M.; Gentili, F.; Giannella, M.; Maranca, F.; Piergentili, A.; Brasili, L. *J. Med. Chem.* **1999**, *42*, 2737; (c) Neef, G.; Eder, U.; Sauer, G. *J. Org. Chem.* **1981**, *46*, 2824; (d) Mitchell, J. M.; Finney, N. S. *Tetrahedron Lett.* **2000**, *41*, 8431; (e) You, S.; Kelly, J. W. *Org. Lett.* **2004**, *6*, 1681; (f) Aidouni, A.; Demonceau, A.; Delaude, L. *Synlett* **2006**, 493.
5. (a) Vorbrüggen, H.; Krolikiewicz, K. *Tetrahedron* **1993**, *49*, 9353; (b) Cwik, A.; Hell, Z.; Hegedüs, A.; Finta, Z.; Horvath, Z. *Tetrahedron Lett.* **2002**, *43*, 3985; (c) Bandgar, B. P.; Pandit, S. S. *Tetrahedron Lett.* **2003**, *44*, 2331; (d) Whelligan, D. K.; Bolm, C. *J. Org. Chem.* **2006**, *71*, 4609; (e) Kangani, C. O.; Kelley, D. E.; Day, B. N. *Tetrahedron Lett.* **2006**, *47*, 6497.
6. Katritzky, A. R.; Cai, C.; Suzuki, K.; Singh, S. K. *J. Org. Chem.* **2004**, *69*, 811.
7. Badiang, J. G.; Aubé, J. *J. Org. Chem.* **1996**, *61*, 2484.
8. Huh, D. H.; Ryu, H.; Kim, Y. G. *Tetrahedron* **2004**, *60*, 9857.
9. Fujioka, H.; Murai, K.; Ohba, Y.; Hiramatsu, A.; Kita, Y. *Tetrahedron Lett.* **2005**, *46*, 2197.
10. Sayama, S. *Synlett* **2006**, 1479.
11. (a) Martin, P. K.; Matthews, H. R.; Rapoport, H.; Thyagarajan, G. *J. Org. Chem.* **1968**, *33*, 3758; (b) Evans, D. L.; Minster, D. K.; Jordis, U.; Hecht, S. M.; Mazzu, A. L., Jr.; Meyers, A. I. *J. Org. Chem.* **1979**, *44*, 497; (c) Amemiya, Y.; Miller, D. D.; Hsu, F. L. *Synth. Commun.* **1990**, *20*, 2483; (d) Mohammadpoor-Baltork, I.; Zolfigol, M. A.; Abdollahi-Alibeik, M. *Tetrahedron Lett.* **2004**, *45*, 8687 and references cited therein; (e) Mohammadpoor-Baltork, I.; Zolfigol, M. A.; Abdollahi-Alibeik, M. *Synlett* **2004**, 2803; (f) Nicolaou, K. C.; Mathison, C. J. N.; Montagnon, T. *Angew. Chem., Int. Ed.* **2003**, *42*, 4077.
12. (a) Mori, N.; Togo, H. *Synlett* **2004**, 880; (b) Mori, N.; Togo, H. *Tetrahedron* **2005**, *61*, 5915.
13. Mori, N.; Togo, H. *Synlett* **2005**, 1456.
14. Ishihara, M.; Togo, H. *Synlett* **2006**, 227.
15. Levesque, G.; Gressier, J. C.; Proust, M. *Synthesis* **1981**, 963.
16. George, B.; Papadopoulos, E. P. *J. Org. Chem.* **1977**, *42*, 441.
17. Gogoi, P.; Konwar, D. *Tetrahedron Lett.* **2006**, *47*, 79.
18. Piskov, V. B.; Kasperovich, V. P.; Yakovleva, L. M. *Khim. Geterotsikl. Soedin.* **1976**, *8*, 1112.
19. Dash, P.; Kudav, D. P.; Parihar, J. A. *J. Chem. Res.* **2004**, *7*, 490.
20. Poindexter, G. S. *J. Heterocycl. Chem.* **1983**, *20*, 1431.
21. Roush, D. M. *Synth. Commun.* **1985**, *15*, 675.