Efficient Oxidative Synthesis of 2-Oxazolines

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Dedicated to Professor Dieter Hoppe on the occasion of his 65th birthday

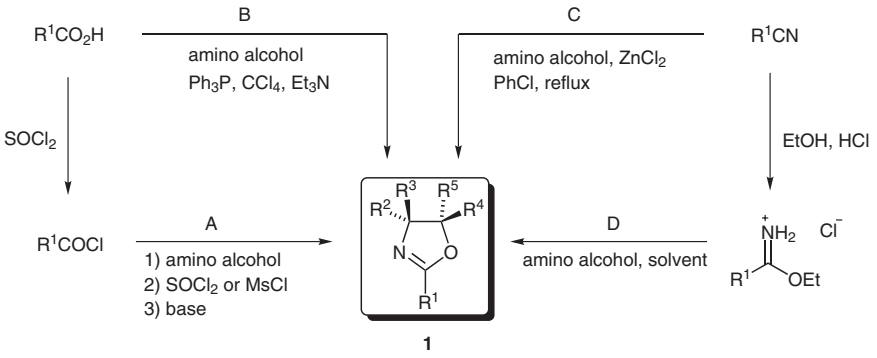
Abstract: New methodology for the synthesis of variously substituted 2-oxazolines and one dihydrooxazine using aldehydes, amino alcohols, and *N*-bromosuccinimide as an oxidizing agent is described. This one-pot synthesis is characterized by mild reaction conditions, broad scope, high yields, and its preparative simplicity.

Key words: amino alcohols, oxidative coupling, oxazolines, oxazolidines, *N*-bromosuccinimide

Since their first description in the 19th century[1] 2-oxazolines (**1**, IUPAC: 4,5-dihydrooxazoles)[2] have played an increasingly important role in many areas of chemistry. Oxazolines are used as carboxylate protection groups,[3] as an auxiliary to enable 'directed *ortho*-metalations',[4] or as monomers in polymerization reactions.[5] Moreover, chiral oxazolines are important fragments of many biologically active compounds,[6] chiral auxiliaries,[7] or as key elements in numerous ligands for asymmetric catalysis, like bisoxazolines or phosphinooxazolines.[8] As a result of this interest in oxazolines, many useful methods for the preparation of oxazolines have been developed.[2] In particular, the reaction of amino alcohols with acid chlorides (A), carboxylic acids (B), nitriles (C), and imidates (D) are commonly used (Scheme 1). The three-step method A generally results in good yields; following the formation of the amido alcohol, the hydroxy group is converted into a good leaving group and the molecule is cyclized under basic conditions.[2] A mild one-pot method uses carboxylic acids under Appel conditions (B),[9] however, this method often requires a tedious separation of the product from the byproducts. Another very efficient one-pot process is the Lewis acid catalyzed condensation of amino alcohols with nitriles at elevated temperatures (C).[10] Imidates and their salts, prepared by treatment of primary amides with Meerwein salt or by the reaction of nitriles with hydrogen chloride gas and ethanol, react smoothly with amino alcohols to give the desired oxazolines (D).[11] However, despite their success, some disadvantages of these methods must be mentioned: several steps must be used (A), a number of byproducts is formed requiring elaborate purification (B), the carboxylic acid derivative must be prepared (D), or rather forcing reaction conditions are necessary (A and C).

The nearly exclusive use of carboxylic acid derivatives as oxazoline precursors piqued our attention; complementary methods for the synthesis of oxazolines would be highly desirable. Oxidative methods for the formation of heterocycles are attractive and many methods can be found for the formation of benzoxazoles,[12] benzimidazoles,[12] and imidazolines[13] from aldehydes. However, oxidative oxazoline syntheses using aldehydes are rare. The few reported methods are not very practical: they require undesirable substrates, like 2-azidoethanol derivatives; they are unselective; or they have a very limited substrate scope.[14] In contrast, we report a versatile method for the highly practical oxidative synthesis of 2-oxazolines (Scheme 2).[15]

At the outset of this project we envisaged that the condensation of an aldehyde **2** with an amino alcohol **3** would



Scheme 1 Most common routes for the synthesis of 2-oxazolines.

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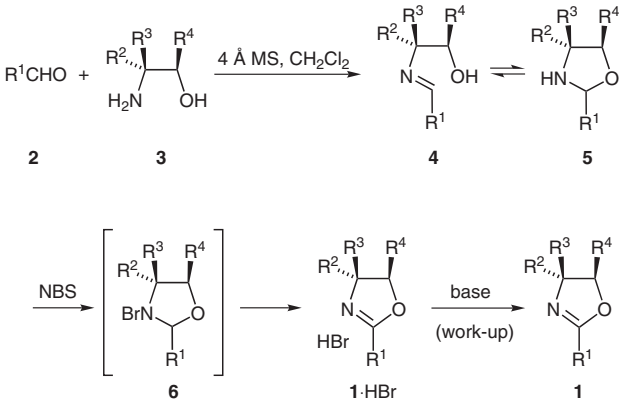
lead to an oxazolidine **5** and that subsequent oxidation would yield an oxazoline. The first step of this sequence is well described in the literature and the oxazolidine **5** can either be preformed and isolated or, alternatively, prepared in situ.[4] In solution, however, oxazolidines **5** exist in an equilibrium with their open-chain imine form **4**, rendering the analysis of these compounds difficult.[16] Several reaction conditions were compared using L-valinol and benzaldehyde as reactants for the initial oxazolidine formation. Stirring a dichloromethane solution of these reactants in the presence of 4 Å molecular sieves was found to be optimal, resulting in the complete formation of the corresponding oxazolidines. For reasons of convenience, the reactions were performed in a sealed flask under an atmosphere of air, not under an inert gas. In addition, dry or moist solvents were found to give comparably good results.

Comparison of several oxidizing agents in the subsequent oxidation step at ambient temperature indicated *N*-bromosuccinimide to be the oxidizing agent of choice. Whereas manganese dioxide and iron(III) chloride were not active, copper(II) chloride, copper(II) bromide, and *N*-chlorosuccinimide resulted in a rather unselective oxidation yielding mixtures of 2- and 3-oxazolines. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone gave partial overoxidation and the use of elemental halogens like bromine or iodine resulted in incomplete conversion and increased formation of byproducts. *N*-Bromosuccinimide was found to be optimal, no matter if one equivalent or a slight excess was used. Besides dichloromethane, other solvents like toluene, ethyl acetate, tetrahydrofuran, or ethanol also gave good results. Under optimized conditions, the in situ formation of the oxazolidines is followed by the addition of one equivalent *N*-bromosuccinimide, resulting in the formation of the oxazoline hydrobromide salts. In general, this salt was subsequently deprotonated using an aqueous basic workup. This also allowed rapid separation of the water-soluble succinimide byproduct. In many cases, the purity of the oxazolines was remarkably high after this simple purification step, in some cases obviating the need for an additional purification step.

We were pleased to find that the substrate scope of this oxidative oxazoline formation is rather large. Variously substituted amino alcohols can successfully be reacted with benzaldehyde (Table 1). Unsubstituted (entry 2), mono- (entries 3–5), or disubstituted (entries 6–9) amino alcohols were successfully converted into variously substituted oxazolines **1** under standard conditions (Table 1).[17] It is important to note that, in contrast to a previous report,[14c] no substantial amounts of the regioisomeric 3-oxazolines could be detected in any of these reactions under optimized conditions (<1%). In addition, this method is not limited to the formation of five-membered oxazolines, but instead using a 1,3-amino alcohol allows the formation of six-membered dihydrooxazine heterocycle **7** in good yield (Table 1, entry 1).

In some cases, enantiomerically pure amino alcohols were employed (Table 1, entries 4–7; Table 2, entry 7; Table 3, entries 1–4). We believe that the enantiomeric purity of the substrates remains intact in this reaction sequence. First, the optical rotations of the purified 2-oxazolines were comparable to literature values for the optically pure compounds (Table 4). The deviations observed were ≤4%. Second, in cases where the oxazoline product bears two stereocenters, epimerization would lead to a mixture of diastereomers (**1e**,**f**,**o**,**s**,**t**). However, GC-MS and ^{1}H NMR analysis of these products revealed only a single diastereomer, indicating that no loss of enantiomeric purity has occurred.



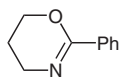
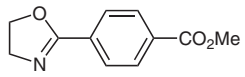
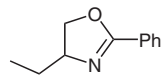
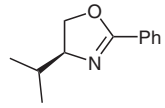
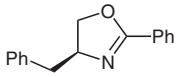
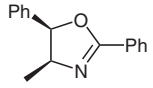
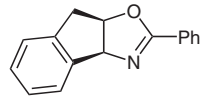
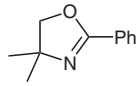
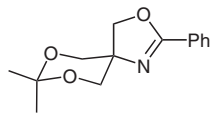
Scheme 2 Oxidative oxazoline formation.

In order to investigate the scope of the aldehyde that could be used, several benzaldehyde derivatives were employed in this reaction and mainly treated with (±)-2-aminobutan-1-ol (Table 2). Not only moderately electron-rich aromatic aldehydes (entries 1, 2) but also those substituted with an electron-withdrawing group (entries 3–4) or an electron-poor heteroaromatic system like pyridyl are well-suited substrates for this reaction (entries 6, 7). Consequently, the well-known pybox ligand can be synthesized from the corresponding dialdehyde in a single step (entry 7). The electron-poor aromatic substrates generally required slightly modified reaction conditions, because of an increased acid-sensitivity of the oxazoline products. Conducting these reactions in the presence of an added inorganic base (K_2CO_3, K_3PO_4) in toluene as a solvent resulted in the formation of the desired products in high yields. In contrast, electron-rich aromatic aldehydes like salicylaldehyde, 4-hydroxybenzaldehyde, or pyrrole-2-carbaldehyde were found not to be suitable substrates, since they undergo fast electrophilic aromatic bromination by the *N*-bromosuccinimide reagent.

Fortunately aliphatic aldehydes can also be successfully employed in this oxazoline synthesis. In this study, decanal and pivaldehyde were reacted with (*R*)-phenylglycinol, (*S*)-phenylalaninol, L-norephedrine, and 2-amino-2-methylpropan-1-ol providing the corresponding oxazolines in very good yields (Table 3).

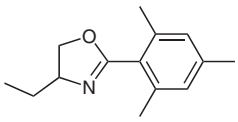
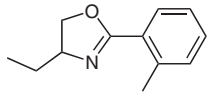
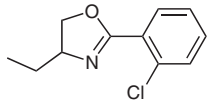
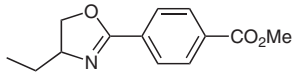
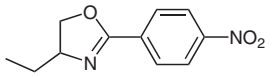
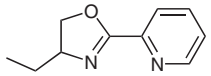
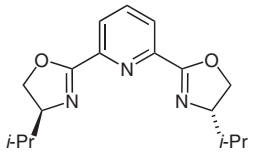
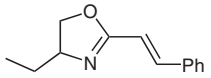
A number of observations shed light on the mechanism of the final oxidation step, rendering a radical based mechanism unlikely. *N*-Bromosuccinimide rather acts as a bro-

Table 1 Oxidative Oxazoline and Dihydrooxazine Formation Using Benzaldehyde[a]

Entry	Product		Yield (%)
1		**7**	90[b]
2		**1a**	88[c]
3		**1b**	91
4		**1c**	70
5		**1d**	80
6		**1e**	81
7		**1f**	65
8		**1g**	82
9		**1h**	88

[a] General reaction conditions: **3** (1 mmol), **2** (1 mmol), 4 Å MS (1.5 g), CH_2Cl_2 (6 mL), r.t., 14 h; NBS (1 mmol), r.t., 0.5 h.
[b] A 1,3-amino alcohol was used.
[c] Methyl 4-formylbenzoate was used instead of benzaldehyde.

Table 2 Oxidative Oxazoline Formation Using (±)-2-Aminobutan-1-ol[a]

Entry	Product		Yield (%)
1		**1i**	42[b]
2		**1j**	93
3		**1k**	76[b]
4		**1l**	83
5		**1m**	68[b]
6		**1n**	77[b]
7		**1o**	34[b,c]
8		**1p**	30[b]

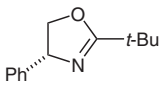
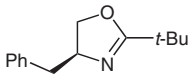
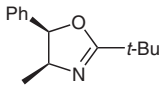
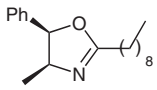
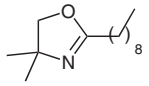
[a] General reaction conditions: **3** (1 mmol), **2** (1 mmol), 4 Å MS (1.5 g), CH_2Cl_2 (6 mL), r.t., 14 h; NBS (1 mmol), r.t., 0.5 h.
[b] Modified reaction conditions: **3** (1 mmol), **2** (1 mmol), 4 Å MS (1.5 g), toluene (6 mL), r.t., 14 h; NBS (1 mmol), K_3PO_4 (3 mmol), r.t., 1.5 h.
[c] (*S*)-Valinol was used instead of (±)-2-aminobutan-1-ol; not optimized.

monium source, since the reaction took place at ambient temperature and no radical initiator was necessary. Moreover, radical scavengers like cyclohexa-1,4-diene or 2,6-di-*tert*-butyl-4-methylphenol did not inhibit the reaction, although byproducts were formed and greatly reduced amounts of product were obtained.[18] Hence, the nucleophilic oxazolidine reacts with the *N*-bromosuccinimide to form an *N*-bromo-substituted oxazolidine **6**.[13a,19] This assumption is supported by a decrease in the rate of the reaction observed for the *N*-bromosuccinimide-mediated oxidation of sterically hindered oxazolidines. Whereas for unhindered aromatic aldehydes the oxidation using *N*-bromosuccinimide is generally complete within 10 minutes at ambient temperature, the oxidation of sterically hindered aromatic aldehyde substrates, like *ortho*-substituted aromatic aldehydes, requires much longer times. This decrease in reaction rate allowed the formation of two diastereomeric intermediates to be observed by ^1H NMR spectroscopy; these are thought to be the *N*-bromo-substituted oxazolidines. Elimination of hydrogen bromide leads to the oxazoline **1**, which forms a salt with the hydrogen bromide generated. Upon workup, these oxazolinium salts were smoothly deprotonated using aqueous base providing the oxazoline products **1**.

In summary, we have developed an efficient oxidative method for the synthesis of variously substituted 2-oxazolines in good yields making use of readily available aldehydes. The mild reaction conditions and preparative simplicity render this one-pot procedure especially attractive.

Chemicals were purchased in commercially available qualities puriss., p.a. or purum from Fluka, Aldrich, Acros, Lancaster, and Merck and were used without further purification. Toluene and CH_2Cl_2 were of technical quality and were distilled and dried over CaH_2. Solvents for extractions and column chromatography were of technical quality and were distilled prior to use. Molecular sieves (4 Å) were activated by microwave irradiation (3 × 3 min.) All re-

Table 3 Oxidative Oxazoline Formation Using Aliphatic Aldehydes[a]

Entry	Product		Yield (%)
1		**1q**	89
2		**1r**	85
3		**1s**	91
4		**1t**	94
5		**1u**	96

[a] General reaction conditions: **3** (1 mmol), **2** (1 mmol), 4 Å MS (1.5 g), CH_2Cl_2 (6 mL), r.t., 14 h; NBS (1 mmol), r.t., 0.5 h.

actions were carried out in closed vials (10 mL) under an atmosphere of air. Flash chromatography used Merck silica gel 60 (230–400 mesh), which was pretreated with a small amount of Et_3N prior to use in the cases where Et_3N was added to the eluent. NMR spectra were recorded on a ARX 300 or DRX 400 spectrometer (Bruker) in $CDCl_3$; chemical shifts (δ) are relative to TMS. IR were recorded on a Bruker IFS 88 spectrophotometer. EI-MS were recorded on a Varian CH7 (70 eV), and ESI-MS and HRMS were recorded on a Finnigan LTQ FT or TSQ 700.

Products **1a**,[14b] **1b**,[20] **1c**,[21] **1d**,[22–24] **1e**,[25] **1f**,[26] **1g**,[22] **1h**,[27] **1n**,[28] **1o**,[29] **1p**,[30] **1q**,[23,31] **1r**,[23,24] **1u**,[32] and **7**[14b,33] have previously been described in the literature. Characterization data for all new compounds and for compounds whose data is not completely available in the literature (oxazolines **1b**, **1h**, and **1u**) is given.

2-Oxazolines; General Procedure 1

The amino alcohol (1 mmol) was dissolved in CH_2Cl_2 (6 mL) and the aldehyde (1 mmol) was added. The mixture was stirred over 4 Å MS (1.5 g) for 14 h. NBS (1 mmol) was then added and the soln was stirred for an additional 30 min. The mixture was filtered and washed with sat. aq $NaHCO_3$ (40 mL) and H_2O (10 mL). The organic layer was dried ($MgSO_4$) and the solvent was evaporated. If required, the products were purified by column chromatography, Kugelrohr distillation or crystallization (**1o**).

2-Oxazolines under Basic Conditions; General Procedure 2

The amino alcohol (1 mmol) was dissolved in toluene (6 mL) and the aldehyde (1 mmol) was added. The mixture was stirred over 4 Å MS (1.5 g) for 14 h. K_3PO_4 was then added while stirring. After 5 min, NBS (1 mmol) was added and the soln was stirred for an additional 1.5 h. The mixture was filtered and washed with sat. aq $NaHCO_3$ (40 mL) and H_2O (10 mL). The organic layer was dried ($MgSO_4$) and the solvent was evaporated. If required, the products were purified by column chromatography.

4-Ethyl-2-phenyl-4,5-dihydrooxazole (1b)[20]

Oxazoline **1b** was prepared according to general procedure 1 using (±)-2-aminobutan-1-ol (89 mg, 1.0 mmol, 1.0 equiv), benzaldehyde (101 μL, 1.0 mmol, 1.0 equiv), and NBS (178 mg, 1.0 mmol, 1.0 equiv) in CH_2Cl_2. The crude product was purified by column chromatography (hexane–EtOAc, 90:10). The product was obtained as a colorless oil; yield: 159 mg (91%); R_f = 0.13 (hexane–EtOAc, 90:10).

IR (film): 3063, 2964, 2932, 2897, 2876, 1720, 1650, 1580, 1495, 1451, 1358, 1330, 1315, 1273, 1111, 1078, 1060, 1026, 951, 780, 696 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.98 (t, J = 7.4 Hz, 3 H, CH_2CH_3), 1.52–1.80 (m, 2 H, CH_2CH_3), 4.03 (dd, J = 7.8 Hz, J = 8.1 Hz, 1 H, OCH_2), 4.16–4.28 (m, 1 H, NCHEt), 4.45 (dd, J = 8.1 Hz, J = 9.4 Hz, 1 H, OCH_2), 7.35–7.48 (m, 3 H, ArH), 7.92–7.95 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.1 (CH_2CH_3), 28.8 (CH_2CH_3), 68.1 (NCHEt), 72.3 (OCH_2), 128.0 (C_{Ar}), 128.4 (C_{Ar}), 128.4 (C_{Ar}), 131.4 (C_{Ar}), 163.6 (OC=N).

MS (EI): m/z (%) = 159 (9), 146 (35), 130 (4), 105 (25), 104 (8), 91 (15), 77 (11), 51 (3), 41 (8), 32 (21), 28 (100).

HRMS (EI): m/z $[M]^+$ calcd for $C_{11}H_{13}NO$: 175.0992; found: 175.0992.

2,2-Dimethyl-1,3-dioxane-5-spiro-4′-(2′-phenyl-4′,5′-dihydrooxazole) (1h)[27]

Oxazoline **1h** was prepared according to general procedure 1 using (5-amino-2,2-dimethyl-1,3-dioxan-5-yl)methanol (161 mg, 1.0 mmol, 1.0 equiv), benzaldehyde (101 μL, 1.0 mmol, 1.0 equiv), and NBS (178 mg, 1.0 mmol, 1.0 equiv) in CH_2Cl_2. The product was obtained as a white solid; yield: 217 mg (88%); R_f = 0.25 (pentane–MTBE–Et_3N, 90:10:1).

IR (KBr): 2994, 1638, 1474, 1449, 1372, 1354, 1327, 1253, 1203, 1082, 1063, 989, 967, 931, 835, 778, 751, 734, 688, 520 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.42 (s, 3 H, CH_3), 1.56 (s, 3 H, CH_3), 3.62–3.66 (m, 2 H, OCH_2), 4.20 (d, J = 11.5 Hz, 2 H, OCH_2), 4.56 (s, 2 H, OCH_2), 7.38–7.50 (m, 3 H, ArH), 7.91–7.94 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.6 (CH_3), 28.9 (CH_3), 67.7 (OCH_2), 67.9 (NC4′), 77.2 (OCH_2), 98.2 (OCO), 127.4, (C_{Ar}), 128.5 (C_{Ar}), 128.5 (C_{Ar}), 131.9 (C_{Ar}), 165.7 (OC=N).

MS (EI): m/z (%) = 247 $[M]^+$, 232 (4), 189 (3), 172 (6), 159 (3), 159 (100), 130 (16), 129 (3), 105 (14), 104 (23), 103 (15), 77 (16), 73 (11), 56 (2), 51 (4), 43 (23), 41 (3), 39 (2), 32 (2), 29 (2), 28 (25), 27 (2).

MS (ESI^+, MeOH): m/z = 270 $[M + Na]^+$.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{14}H_{17}NNaO_3$: 270.1101; found: 270.1096.

4-Ethyl-2-mesityl-4,5-dihydrooxazole (1i)

Oxazoline **1i** was prepared according to general procedure 2 using (±)-2-aminobutan-1-ol (89 mg, 1.0 mmol, 1.0 equiv), 2,4,6-trimethylbenzaldehyde (148 mg, 1.0 mmol, 1.0 equiv), K_3PO_4 (636 mg, 3.0 mmol, 3 equiv), and NBS (178 mg, 1.0 mmol, 1.0 equiv) in toluene. The crude product was purified by column chromatography (pentane–MTBE, 20:1). The product was obtained as a colorless oil; yield: 91 mg (42%); R_f = 0.05 (pentane–MTBE, 20:1).

IR (film): 2962, 2922, 1665, 1613, 1579, 1461, 1378, 1346, 1326, 1295, 1266, 1239, 1167, 1048, 958, 940, 890, 851 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.05 (t, J = 7.4 Hz, 3 H, CH_2CH_3), 1.57–1.85 (m, 2 H, CH_2CH_3), 2.27 (s, 3 H, Ar-p-CH_3), 2.29 (s, 6 H, Ar-o-CH_3), 4.02 (dd, J = 7.7 Hz, J = 7.8 Hz, 1 H, OCH_2), 4.21–4.31 (m, 1 H, NCHEt), 4.43 (dd, J = 8.1 Hz, J = 9.4 Hz, 1 H, OCH_2), 6.84 (s, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.4 (CH_2CH_3), 19.7 (Ar-*o*-CH_3), 21.3 (Ar-*p*-CH_3), 29.0 (CH_2CH_3), 68.5 (NCHEt), 71.8 (OCH_2), 126.4 (C_{Ar}), 128.8 (C_{Ar}), 136.9 (C_{Ar}), 139.1 (C_{Ar}), 164.0 (OC=N).

MS (EI$^+$): *m*/*z* (%) = 218 (15), 217 (3), 217 (100) [M]$^+$, 189 (4), 188 (84), 172 (20), 162 (9), 161 (31), 160 (80), 158 (3), 148 (5), 147 (86), 146 (63), 145 (17), 144 (6), 133 (41), 132 (6), 131 (10), 130 (21), 119 (11), 118 (7), 117 (18), 116 (5), 115 (13), 104 (3), 103 (10), 91 (40), 78 (3), 77 (17), 65 (8), 55 (4), 53 (3), 52 (2), 51 (5), 43 (7), 41 (50), 39 (40), 32 (5), 29 (28), 28 (52), 27 (57).

MS (ESI$^+$, MeOH): *m*/*z* = 218.2 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{20}NO$: 218.1539; found: 218.1539.

4-Ethyl-2-tolyl-4,5-dihydrooxazole (1j)

Oxazoline **1j** was prepared according to general procedure 1 using (±)-2-aminobutan-1-ol (89 mg, 1.0 mmol, 1.0 equiv), 2-methylbenzaldehyde (116 μL, 1.0 mmol, 1.0 equiv), and NBS (178 mg, 1.0 mmol, 1.0 equiv) in CH_2Cl_2. The crude product was purified by column chromatography (pentane–MTBE–Et_3N, 98:2:1). The product was obtained as a colorless oil; yield: 176 mg (93%); R_f = 0.31 (pentane–MTBE–Et_3N, 98:2:1).

IR (KBr): 3027, 2963, 2925, 1645, 1603, 1575, 1492, 1456, 1383, 1350, 1328, 1305, 1265, 1241, 1137, 1043, 951, 898, 775, 729 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.56–1.83 (m, 2 H, CH_2CH_3), 2.58 (s, 3 H, CH_3), 4.02 (dd, *J* = 7.6 Hz, *J* = 7.9 Hz, 1 H, OCH_2), 4.22–4.32 (m, 1 H, NCHEt), 4.42 (dd, *J* = 7.9 Hz, *J* = 9.4 Hz, 1 H, OCH_2), 7.18–7.35 (m, 3 H, ArH), 7.75–7.78 (m, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.1 (CH_3), 21.7 ($ArCH_3$), 28.9 (CH_2CH_3), 68.4 (NCHEt), 71.6 (OCH_2), 125.6 (C_{Ar}), 127.6(C_{Ar}), 129.9 (C_{Ar}), 130.5 (C_{Ar}), 131.2 (C_{Ar}), 138.8 (C_{Ar}), 164.2 (OC=N).

MS (EI): *m*/*z* (%) = 190 (5), 189 (100) [M]$^+$, 161 (14), 161 (2), 166 (76), 144 (16), 134 (5), 133 (3), 132 (31), 130 (2), 119 (14), 118 (5), 117 (6), 116 (3), 106 (2), 105 (32), 104 (2), 103 (2), 91 (26), 90 (13), 89 (9), 77(3), 65 (12), 63 (2), 51 (2), 41 (8), 39 (13), 32 (5), 29 (4), 28 (42), 27 (9).

MS (ESI$^+$, MeOH): *m*/*z* = 190 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{16}NO$: 190.1226; found: 190.1228.

2-(2-Chlorophenyl)-4-ethyl-4,5-dihydrooxazole (1k)

Oxazoline **1k** was prepared according to general procedure 2 with (±)-2-aminobutan-1-ol (89 mg, 1.0 mmol, 1.0 equiv), 2-chlorobenzaldehyde (140 mg, 1.0 mmol, 1.0 equiv), K_3PO_4 (636 mg, 3.0 mmol, 3 equiv), and NBS (178 mg, 1.0 mmol, 1.0 equiv) in toluene. The crude product was purified by column chromatography (pentane–MTBE–Et_3N, 90:10:1). The product was obtained as a yellowish oil; yield: 146 mg (69%); R_f = 0.19 (pentane–MTBE–Et_3N, 90:10:1).

IR (film): 3070, 2974, 2932, 1652, 1594, 1570, 1479, 1436, 1355, 1329, 1305, 1240, 1129, 1094, 1035, 945, 900, 766, 735 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.59–1.86 (m, 2 H, CH_2CH_3), 4.09 (dd, *J* = 7.7 Hz, *J* = 7.8 Hz, 1 H, OCH_2), 4.26–4.35 (m, 1 H, NCHEt), 4.49 (dd, *J* = 8.0 Hz, *J* = 9.5 Hz, 1 H), 7.28–7.45 (m, 3 H, ArH), 7.72–7.75 (m, 1 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.0 (CH_3), 28.6 (CH_2CH_3), 68.4 (NCHR), 72.3 (OCHEt), 126.6 (C_{Ar}), 128.0 (C_{Ar}), 130.7 (C_{Ar}), 131.4 (C_{Ar}), 131.6 (C_{Ar}), 133.5 (C_{Ar}), 161.8 (OC=N).

MS (EI): *m*/*z* (%) = 211 (3) [M]$^+$, 209 (15) [M]$^+$, 183 (5), 182 (48), 181 (17), 180 (9), 180 (100), 179 (7), 166 (5), 164 (23), 154 (8), 153 (3), 152 (27), 151 (2), 141 (4), 140 (4), 139 (15), 138 (21), 137 (2), 127 (15), 126 (3), 125 (35), 117 (2), 113 (3), 111 (13), 103 (2), 102 (20), 89 (6), 76 (5), 75 (17), 51 (4), 50 (4), 43 (4), 41 (8), 39 (8), 29 (3), 28 (20), 27 (11).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{13}ClNO$: 210.0680; found: 210.0680.

Methyl 4-(4-Ethyl-4,5-dihydrooxazol-2-yl)benzoate (1l)

Oxazoline **1l** was prepared according to general procedure 1 using (±)-2-aminobutan-1-ol (89 mg, 1.0 mmol, 1.0 equiv), methyl 4-formylbenzoate (164 mg, 1.0 mmol, 1.0 equiv), and NBS (178 mg, 1.0 mmol, 1.0 equiv) in CH_2Cl_2. The crude product was purified by column chromatography (pentane–MTBE–Et_3N, 90:20:1) The product was obtained as a white solid; yield: 193 mg (83%); R_f = 0.27 (pentane–MTBE–Et_3N, 90:20:1).

IR (KBr): 2962, 2918, 1716, 1646, 1611, 1508, 1441, 1409, 1383, 1359, 1283, 1195, 1116, 1066, 1019, 967, 949, 871, 783, 710 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.60–1.85 (m, 2 H, CH_2CH_3), 3.94 (s, 3 H, OCH_3), 4.08 (t, *J* = 8.0 Hz, 1 H, OCH_2), 4.24–4.34 (m, 1 H, NCHEt), 4.53 (dd, *J* = 8.4 Hz, *J* = 9.2 Hz, 1 H), 8.00–8.10 (m, 4 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.1 (CH_3), 27.7 (CH_2CH_3), 51.4 (OCH_3), 67.3 (NCHR), 71.5 (OCHEt), 127.3 (C_{Ar}), 128.6 (C_{Ar}), 131.1 (C_{Ar}), 131.5 (C_{Ar}), 161.8, 164.2.

MS (EI): *m*/*z* (%) = 233 (7) [M]$^+$, 205 (11), 204 (2), 204 (100), 103 (2), 202 (4), 188 (5), 176 (5), 163 (5), 162 (7), 149 (2), 145 (2), 132 (3), 117 (5), 105 (5), 104 (2), 103 (6), 102 (2), 90 (3), 77 (2), 76 (5), 75 (4), 59 (19), 50 (3), 43 (4), 41 (4), 39 (3), 29 (4), 28 (14), 27 (10).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{15}NO_3$: 233.1046; found: 233.1055.

4-Ethyl-2-(4-nitrophenyl)-4,5-dihydrooxazole (1m)

Oxazoline **1m** was prepared according to general procedure 2 using (±)-2-aminobutan-1-ol (89 mg, 1.0 mmol, 1.0 equiv), 4-nitrobenzaldehyde (151 mg, 1.0 mmol, 1.0 equiv), K_3PO_4 (636 mg, 3.0 mmol, 3 equiv), and NBS (178 mg, 1.0 mmol, 1.0 equiv) in toluene. The crude product was purified by column chromatography (pentane–MTBE–Et_3N, 90:10:1). The product was obtained as a pale yellow solid; yield: 150 mg (68%); R_f = 0.21 (pentane–MTBE–Et_3N, 90:10:1).

IR (film): 2971, 2894, 1647, 1597, 1520, 1471, 1410, 1345, 1287, 1263, 1104, 1070, 1010, 969, 956, 897, 862, 851, 704, 654 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.57–1.85 (m, 2 H, CH_2CH_3), 4.11 (dd, *J* = 8.0 Hz, *J* = 8.0 Hz, 1 H, OCH_2), 4.25–4.35 (m, 1 H, NCHEt), 4.54 (dd, *J* = 8.2 Hz, *J* = 9.5 Hz, 1 H), 8.09–8.14 (m, 2 H, ArH), 8.24–8.28 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.1 (CH_3), 28.7 (CH_2CH_3), 68.6 (NCHR), 72.0 (OCHEt), 123.6 (C_{Ar}), 129.4 (C_{Ar}), 133.9 (C_{Ar}), 149.6 ($C_{Ar}NO_2$), 161.8 (OC=N).

MS (EI): *m*/*z* (%) = 220 (5) [M]$^+$, 192 (12), 192 (2), 191 (100), 175 (5), 163 (11), 117 (13), 104 (2), 103 (5), 90 (6), 76 (8), 75 (2), 43 (4), 41 (3), 39 (2), 32 (4), 28 (46), 27 (3).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{11}H_{12}N_2O_3$: 220.0842; found: 220.0844.

(4*S*,5*R*)-2-*tert*-Butyl-4-methyl-5-phenyl-4,5-dihydrooxazole (1s)

Oxazoline **1s** was prepared according to general procedure 1 using L-norephedrine (151 mg, 1.0 mmol, 1.0 equiv), pivalaldehyde (110 μL, 1.0 mmol, 1.0 equiv), and NBS (178 mg, 1.0 mmol, 1.0 equiv) in CH_2Cl_2. The product was obtained as a colorless oil; yield: 197 mg (91%); $[\alpha]_D^{21}$ –214 (*c* 1.01, $CHCl_3$); R_f = 0.50 (pentane–MTBE–Et_3N, 90:10:1).

IR (film): 3442, 3033, 2974, 2931, 2871, 1661, 1497, 1480, 1456, 1394, 1363, 1339, 1317, 1140, 1027, 980, 942, 918, 748, 700 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.75 (d, *J* = 7.0 Hz, 3 H, CH_3), 1.32 [s, 9 H, $C(CH_3)_3$], 4.37 –4.48 (m, 1 H, NCHMe), 5.55 (d, *J* = 9.9 Hz, 1 H, OCHPh), 7.16–7.38 (m, 5 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.1 (CH_3), 28.0 [$C(CH_3)_3$], 33.4 [$C(CH_3)_3$], 65.1 (NCHMe), 83.8 (OCHPh), 126.2 (C_{Ar}), 127.8 (C_{Ar}), 128.4 (C_{Ar}), 137.7 (C_{Ar}), 173.2 (OC=N).

MS (EI): *m/z* (%) = 216 (<1), 132 (3), 112 (2), 111 (25), 107 (3), 106 (3), 105 (46), 96 (2), 91 (2), 84 (9), 77 (14), 57 (24), 55 (33), 51 (2), 44 (15), 43 (100), 42 (2), 41 (23), 39 (4), 29 (11), 28 (30), 27 (5).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{14}H_{19}NO$: 217.1461; found: 217.1468.

(4*S*,5*R*)-4-Methyl-2-nonyl-5-phenyl-4,5-dihydrooxazole (1t)

Oxazoline **1t** was prepared according to general procedure 1 using L-norephedrine (151 mg, 1.0 mmol, 1.0 equiv), decanal (156 mg, 1.0 mmol, 1.0 equiv), and NBS (178 mg, 1.0 mmol, 1.0 equiv) in CH_2Cl_2. The product was obtained as a yellowish oil; yield: 270 mg (94%); $[\alpha]_D^{20}$ –110 (*c* 1.01 $CHCl_3$); R_f = 0.75 (pentane–MTBE–Et_3N, 90:10:1).

IR (film): 3031, 2926, 2855, 1743, 1669, 1495, 1455, 1377, 1234, 1168, 1087, 981, 916, 746, 700, 536 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.76 (d, *J* = 7.0 Hz, 3 H, CH_3), 0.83–0.93 [m, 3 H, $CH_3(CH_2)_8$], 1.17–1.46 [m, 12 H, $(CH_2)_6$], 1.68–1.78 (m, 2 H, CH_2CH_3), 2.36–2.42 [m, 2 H, $CH_2C(O)=N$], 4.36–4.48 (m, 1 H, NCHMe), 5.56 (d, *J* = 9.8 Hz, 1 H, OCHPh), 7.17–7.21 (m, 2 H, ArH), 7.27–7.40 (m, 3 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 18.1 (CH_3), 22.8 (CH_2), 26.2 (CH_2), 28.4 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 32.0 (CH_2), 65.0 (NCHMe), 83.9 (OCHPh), 126.2 (C_{Ar}), 127.9 (C_{Ar}), 128.4 (C_{Ar}), 137.4 (C_{Ar}), 167.4 (OC=N).

MS (EI): *m/z* (%) = 287 (<1) $[M]^+$, 188 (7), 181 (7), 180 (11), 176 (4), 175 (61), 167 (2), 166 (74), 152 (43), 139 (8), 138 (54), 134 (13), 133 (6), 132 (13), 125 (5), 124 (38), 117 (4), 111 (20), 110 (19), 105 (6), 97 (10), 96 (25), 95 (2), 91 (6), 84 (10), 83 (11), 82 (32), 81 (20), 80 (2), 79 (4), 77 (7), 71 (5) 70 (13), 69 (50), 68 (19), 67 (11), 58 (3), 57 (14), 56 (5), 55 (35), 54 (17), 44 (100), 43 (33), 42 (25), 41 (62), 39 (3), 32 (3); 29 (23), 28 (46), 27 (9).

MS (ESI^+, MeOH): *m/z* = 288.3 $[M + H]^+$.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{30}NO$: 288.2322; found: 288.2323.

4,4-Dimethyl-2-nonyl-4,5-dihydrooxazole (1u)[32]

Oxazoline **1u** was prepared according to general procedure 1 using 2-amino-2-methylpropan-1-ol (89 mg, 1.0 mmol, 1.0 equiv), decanal (156 mg, 1.0 mmol, 1.0 equiv), and NBS (178 mg, 1.0 mmol, 1.0 equiv) in CH_2Cl_2. The product was obtained as a colorless oil; yield: 217 mg (96%).

IR (film): 2926, 2855, 2061, 1746, 1720, 1668, 1464, 1364, 1277, 1248, 1192, 1152, 1115, 997, 925, 818, 723, 593 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.80–0.90 [m, 3 H, $CH_3(CH_2)_8$], 1.18–1.36 [m, 18 H, $CH_3CH_2(CH_2)_6$, 2 × CH_3], 1.54–1.65 (m, 2 H, CH_2CH_3), 2.19–2.24 [m, 2 H, $CH_2C(O)=N$], 3.88 (s, 2 H, OCH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2 (CH_3), 22.8 (CH_3), 26.2 (CH_2), 28.3 (CH_2), 28.6 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 32.0 (CH_2), 67.0 ($NCMe_2$), 79.0 (OCH_2), 166.3 (OC=N).

MS (EI): *m/z* (%) = 224 (10), 193 (3), 126 (3), 113 (35), 72 (10), 69 (7), 58 (67), 57 (10), 56 (2), 55 (17), 54 (11), 43 (16), 42 (23), 41 (100), 39 (19), 32 (11), 29 (75), 28 (65), 27 (10).

MS (ESI^+, MeOH): *m/z* = 226.3 $[M + H]^+$.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{28}NO$: 226.2165; found: 226.2165.

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Table 4 Comparison of the Optical Rotations with the Literature Values

Entry	Product	Measured			Literature		
		$[\alpha]_D$	*c* [10·g L^{-1}]	Solvent	$[\alpha]_D$	*c* [10 g·L^{-1}]	Ref.
1	**1c**	$[\alpha]_D^{22}$ –83	0.63	$CHCl_3$	$[\alpha]_D^{23}$ –85.2	1.09	21a
2	**1c**			$CHCl_3$	$[\alpha]_D^{23}$ –83.2	0.56	21b
3	**1c**			$CHCl_3$	$[\alpha]_D^{25}$ –72	6.5	21c
4	**1d**	$[\alpha]_D^{21}$ +22	1.25	MeOH	$[\alpha]_D^{20}$ +22.9	1.23	23
5	**1e**	$[\alpha]_D^{17}$ –369	3.24	$CHCl_3$	$[\alpha]_D^{24}$ –355	3.23	25
6	**1f**	$[\alpha]_D^{20}$ –169	0.99	MeOH	$[\alpha]_D^{20}$ –177.1	0.99	26
7	**1o**	$[\alpha]_D^{20}$ –106	0.70	CH_2Cl_2	$[\alpha]_D^{20}$ –110	0.70	29
8	**1q**	$[\alpha]_D^{20}$ +86	1.55	MeOH	$[\alpha]_D^{23}$ +89.2	4.54	31
9	**1r**	$[\alpha]_D^{20}$ –36	1.34	$CHCl_3$	$[\alpha]_D^{23}$ –38.2	1.31	24
10	**1s**	$[\alpha]_D^{21}$ –214	1.01	$CHCl_3$	–	–	–
11	**1t**	$[\alpha]_D^{20}$ –110	1.01	$CHCl_3$	–	–	–

Note added in proof

After the submission of this manuscript, a related report has appeared: *A Convenient Synthesis of Oxazolines and Imidazolines from Aromatic Aldehydes with Pyridinium Hydrobromide Perbromide in Water*, Sayama, S. *Synlett* **2006**, 1479.

References

(1) Andreasch, R. *Monatsh. Chem.* **1884**, *5*, 33.
(2) (a) Gant, T. G.; Meyers, A. I. *Tetrahedron* **1994**, *50*, 2297; and references cited therein. (b) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835.
(3) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, **1999**.
(4) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.
(5) (a) Huang, H.; Hoogenboom, R.; Leenen, M. A. M.; Guillet, P.; Jonas, A. M.; Schubert, U. S.; Gohy, J.-F. *J. Am. Chem. Soc.* **2006**, *128*, 3784. (b) Kobayashi, S.; Fujikawa, S.-i.; Ohmae, M. *J. Am. Chem. Soc.* **2003**, *125*, 14357.
(6) (a) Nicolaou, K. C.; Lizos, D. E.; Kim, D. W.; Schlawe, D.; de Noronha, R. G.; Longbottom, D. A.; Rodriguez, M.; Bucci, M.; Cirino, G. *J. Am. Chem. Soc.* **2006**, *128*, 4460. (b) Pirrung, M. C.; Tumey, L. N.; McClerren, A. L.; Raetz, C. R. H. *J. Am. Chem. Soc.* **2003**, *125*, 1575. (c) Bode, H. B.; Irschik, H.; Wenzel, S. C.; Reichenbach, H.; Müller, R.; Höfle, G. *J. Nat. Prod.* **2003**, *66*, 1203. (d) Kline, T.; Andersen, N. H.; Harwood, E. A.; Bowman, J.; Malanda, A.; Endsley, S.; Erwin, A. L.; Doyle, M.; Fong, S.; Harris, A. L.; Mendelsohn, B.; Mdluli, K.; Raetz, C. R. H.; Stover, C. K.; Witte, P. R.; Yabannavar, A.; Zhu, S. *J. Med. Chem.* **2002**, *45*, 3112. (e) Bergeron, R. J.; Xin, M. G.; Weimar, W. R.; Smith, R. E.; Wiegand, J. *J. Med. Chem.* **2001**, *44*, 2469.
(7) (a) Meyers, A. I.; Shipman, M. *J. Org. Chem.* **1991**, *56*, 7098. (b) Gnas, Y.; Glorius, F. *Synthesis* **2006**, 1899.
(8) (a) Ghosh, A. K.; Mathivanan, P.; Cappiello, J. *Tetrahedron: Asymmetry* **1998**, *9*, 1. (b) Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339. (c) Helmchen, G.; Pfaltz, A. *Acc. Chem. Res.* **2000**, *33*, 336.
(9) (a) Vorbrüggen, H.; Krolikiewicz, K. *Tetrahedron* **1993**, *49*, 9353. (b) Appel, R. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 801.
(10) Witte, H.; Seeliger, W. *Justus Liebigs Ann. Chem.* **1974**, 996.
(11) (a) Neilson, D. G. In *The Chemistry of Amidines and Imidates*; Patai, S., Ed.; Wiley: London, **1975**, 389. (b) For an alternative method, see: Hoppe, D.; Schöllkopf, U. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 300.
(12) (a) Kawashita, Y.; Nakamichi, N.; Kawabata, H.; Hayashi, M. *Org. Lett.* **2003**, *5*, 3713. (b) Chang, J.; Zhao, K.; Pan, S. *Tetrahedron Lett.* **2002**, *43*, 951. (c) Varma, R. S.; Kumar, D. *J. Heterocycl. Chem.* **1998**, *35*, 1539. (d) Varma, R. S.; Saini, R. K.; Prakash, O. *Tetrahedron Lett.* **1997**, *38*, 2621. (e) Park, K. H.; Jun, K.; Shin, S. R.; Oh, S. W. *Tetrahedron Lett.* **1996**, *37*, 8869.
(13) Very recently, the first oxidative synthesis of imidazolines has been reported: (a) Fujioka, H.; Murai, K.; Ohba, Y.; Hiramatsu, A.; Kita, Y. *Tetrahedron Lett.* **2005**, *46*, 2197. See also these related oxidation reactions: (b) Fujioka, H.; Murai, K.; Ohba, Y.; Hirose, H.; Kita, Y. *Chem. Commun.* **2006**, 832. (c) Ishihara, M.; Togo, H. *Synlett* **2006**, 227. (d) Gogoi, P.; Konwar, D. *Tetrahedron Lett.* **2006**, *47*, 79.
(14) (a) Intramolecular redox reaction of 2-formylbenzaldehyde, see: Shipchandler, M. T. *J. Heterocycl. Chem.* **1977**, *14*, 305. (b) Reaction of aldehydes with 1,2-hydroxy azides, see: Badiang, J. G.; Aubé, J. *J. Org. Chem.* **1996**, *61*, 2484. (c) Synthesis of 3-oxazolines (with the formation of 2-oxazoline as minor byproducts), see: Favreau, S.; Lizzani-Cuvelier, L.; Loiseau, M.; Duñach, E.; Fellous, R. *Tetrahedron Lett.* **2000**, *41*, 9787.
(15) This work was first presented on the BASF Catalysis Award Symposium, in Heidelberg, Germany, July 8 2005.
(16) (a) Martinek, T.; Lazar, L.; Fülöp, F.; Riddell, F. G. *Tetrahedron* **1998**, *54*, 12887. (b) Agami, C.; Comesse, S.; Kadouri-Puchot, C. *J. Org. Chem.* **2002**, *67*, 1496.
(17) More highly substituted amino alcohols have not been tested.
(18) Related oxidations are known: (a) Convenient one-pot conversion of alcohols into esters via hemiacetal intermediates using Br_2, see: Lichtenthaler, F. W.; Jarglis, P.; Lorenz, K. *Synthesis* **1988**, 790. (b) Oxidation of isolated oxazolidines to oxazoles with NBS/$(BzO)_2$ in refluxing CCl_4, see: Badr, M. Z. A.; Aly, M. M.; Fahmy, A. M.; Mansour, M. E. Y. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1844. (c) The oxidation of aldehydes to acid bromides requires more forcing conditions, see: Cheung, Y.-F. *Tetrahedron Lett.* **1979**, *20*, 3809.
(19) (a) Scully, F. E. J. *J. Org. Chem.* **1980**, *45*, 1515. (b) Bachmann, W. E.; Cava, M. P.; Dreiding, A. S. *J. Am. Chem. Soc.* **1954**, *76*, 5554. (c) Abou-Gharbia, M.; Ketcha, D. M.; Zacharias, D. E.; Swern, D. *J. Org. Chem.* **1985**, *50*, 2224.
(20) (a) Mugesh, G.; Singh, H. B.; Butcher, R. J. *Tetrahedron: Asymmetry* **1999**, *10*, 237. (b) Cwik, A.; Hell, Z.; Hegedüs, A.; Finta, Z.; Horváth, Z. *Tetrahedron Lett.* **2002**, *43*, 3985.
(21) (a) Koch, G.; Lloyd-Jones, G. C.; Loiseleur, O.; Pfaltz, A.; Prétôt, R.; Schaffner, S.; Schnider, P.; von Matt, P. *Recl. Trav. Chim. Pays-Bas* **1995**, *114*, 206. (b) Ikeda, S.; Kondo, H.; Arii, T.; Odashima, K. *Chem. Commun.* **2002**, 2422. (c) Bower, J. F.; Martin, C. J.; Rawson, D. J.; Slawin, A. M. Z.; Williams, J. M. J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 333.
(22) Katritzky, A. R.; Cai, C.; Suzuki, K.; Singh, S. K. *J. Org. Chem.* **2004**, *69*, 811.
(23) Lafargue, P.; Guenot, P.; Lellouche, J.-P. *Heterocycles* **1995**, *41*, 947.
(24) Bates, G. S.; Varelas, M. A. *Can. J. Chem.* **1980**, *58*, 2562.
(25) Kamata, K.; Agata, I.; Meyers, A. I. *J. Org. Chem.* **1998**, *63*, 3113.
(26) Lehr, P.; Billich, A.; Charpiot, B.; Ettmayer, P.; Scholz, D.; Rosenwirth, B.; Gstach, H. *J. Med. Chem.* **1996**, *39*, 2060.
(27) Jones, R. A. Y.; Katritzky, A. R.; Record, K. A. F.; Scattergood, R.; Sullivan, J. M. *J. Chem. Soc., Perkin Trans. 2* **1974**, 402.
(28) Brunner, H.; Obermann, U. *Chem. Ber.* **1989**, *122*, 499.
(29) Totleben, M. J.; Prasad, J. S.; Simpson, J. H.; Chan, S. H.; Vanyo, D. J.; Kuehner, D. E.; Deshpande, R.; Kodersha, G. A. *J. Org. Chem.* **2001**, *66*, 1057.
(30) Elliott, M. C.; Kruiswijk, E. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3157.
(31) Yamauchi, M.; Itai, K.; Honda, Y. *Chem. Pharm. Bull.* **2002**, *50*, 1255.
(32) (a) Bandgar, B. P.; Pandit, S. S. *Tetrahedron Lett.* **2003**, *44*, 2331. (b) Serota, S.; Simon, J. R.; Murray, E. B.; Linfield, W. M. *J. Org. Chem.* **1981**, *46*, 4147.
(33) Wipf, P.; Hayes, G. B. *Tetrahedron* **1998**, *54*, 6987.