A Convenient Synthesis of 2-Oxazolines and 2-Benoxazoles with PPh_3-DDQ as the Dehydrating Reagent

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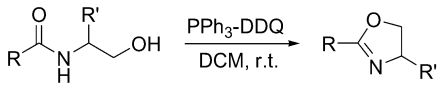
2-Oxazolines and 2-benoxazoles were synthesized in high yields from acylamino alcohols and acylaminophenols, respectively, with triphenylphosphine-2,3-dichloro-5,6-dicyanobenzoquinone (PPh_3-DDQ) as the dehydrating and activating reagent. The synthesis was accomplished under neutral conditions.

Keywords oxazoline, benzoxazole, synthesis, dehydrative cylization, 2,3-dichloro-5,6-dicyanobenzoquinone, triphenylphosphine

Introduction

2-Oxazoline is of great importance in synthetic organic chemistry, either as a functional group or as a protecting group to mask the reactive hydroxyl and amino groups in amino alcohols and carboxylic acids in organic reactions.[1] More importantly, 2-oxazoline derived from chiral amino alcohols has been used as auxiliary in asymmetric synthesis and as ligand in asymmetric catalysis in the last two decades.[2] It is also of pharmaceutical interests because this functional group was found in natural products and some drug-like compounds displaying anti-HIV, antimitotic, anti-cancer, and antibiotic activities.[3] Its hydrolytic property makes it a pro-drug of acid. In regarding to the wide applications of 2-oxazoline, it is not surprising that many synthetic methods have been reported for this kind of compounds. Most of the methods start from amino alcohols and carboxylic acids or acid derivatives like ester[4,5] and nitrile.[6] The intermediate, *N*-(2-hydroxyethyl) amide, is converted into 2-oxazoline via a dehydrative cyclization. In this transformation, it is necessary to transfer the poor leaving hydroxyl group into a good leaving one by the use of $SOCl_2$[7] or PPh_3/CCl_4,[8] or TsCl/Et_3N, followed by an S_N2 reaction under basic conditions.[9] Recently, dehydrating reagents including carbodiimide,[10] Et_2NSF_3[11a,11b] $(MeOCH_2CH_2)_2NSF_3$,[11b,11c] 2-chloro-4,6-dimeth-oxy-1,3,5-triazine,[3b] PPh_3-DEAD[12] were also used for this purpose. The exploration of new reagents for this transformation, for example, Loughlin's phosphonium anhydrides, is still an active research field.[3a] More recently, we have reported that the PPh_3-DDQ could be used for the synthesis of 2-oxazolines via a dehydrative cyclization of *N*-(2-hydroxyethyl) amides (Eq. 1).[13] PPh_3-DDQ has been extensively used as the dehydrating reagent in alcohol functional group transformation by Iranpoor.[14] Compared to Mistunobu reagent, PPh_3-DEAD,[15] the PPh_3-DDQ combination is cheaper, more stable, and usually yields cleaner product. In comparison to $SOCl_2$, DAST, or Deoxo-Fluor reagent, the PPh_3-DDQ combination system is neutral, and thus acid liable groups in substrates might be tolerated. Herein, we wish to report our results in detail and to show that the combination could be extended to the synthesis of benzoxazole.



(1)

Results and discussion

When *N*-(2-hydroxyethyl) benzamide (**1a**) was added to PPh_3-DDQ solution in dichloromethane, 2-phenyloxazoline was formed as judged by TLC, GC and NMR analyses by comparison with an authentic sample. Scan of solvents showed that nearly quantitative yields of oxazoline were obtained in dichloromethane, toluene, 1,4-dioxane or THF reaction system in 20 min, but no oxazoline or inferior yield of oxazoline was got in acetonitrile and ethyl acetate, respectively. In regarding to the reaction time and the yields, our current PPh_3-DDQ dehydrating reagent is more efficient than Linclau's isourea protocol,[10] which requires 24—48 h at THF refluxing temperature to get reasonable yields of 2-oxazolines. DDQ in the PPh_3-DDQ combination can be replaced by 7,7,8,8-tetracyanoquinodimethane (TCNQ) or 1,1,2,2-tetracyanoethene. In the case of PPh_3-TCNQ, clean and nearly quantitative conversion of **1b** to **2b** could be furnished in 1 h. However, difficulty in separation was encountered due to small difference of R_f val-

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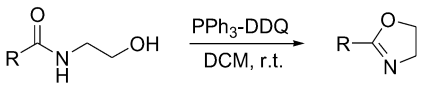
ues between the desired **2b** and other product. Using 1,1,2,2-tetracyanoethene, the reaction was relatively slow. A 45% yield of **2b** was obtained in 1 h.

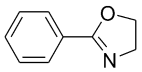
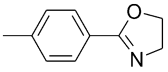
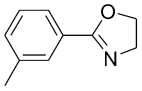
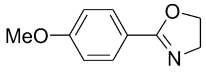
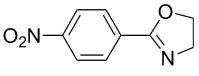
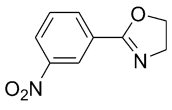
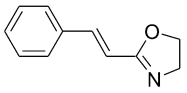
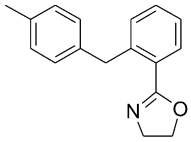
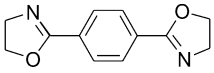
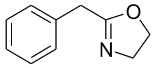
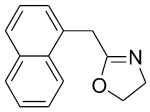
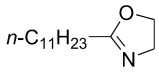
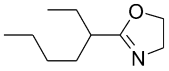
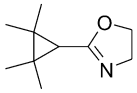
After successfully achieving the dehydrating cyclization above with PPh_3-DDQ, we began to employ the uses of other acylated aminoethanols as substrates. The results are summarized in Table 1. First, substituted phenyl ring substrates were tested, and yields above 80% were achieved in 20—120 min (Entries 2—4). Electron-withdrawing and electron-donating groups attached to phenyl do not influence the reaction too much. When nitro group exists, 60 min was needed for a complete conversion. The acyl can be extended to cinnamoyl. As shown in Entry 7, *N*-(2-hydroxyethyl) *trans*-cinnamamide produced the corresponding oxazoline in a high yield. This is in contrast to the method in literature in which the reaction could not be applied to cinnama aldehyde.[16] Our system is also effective to *ortho*-substituted benzamide (Entry 8), and in this case, 3 h reaction time was needed, furnishing the product in 90% yield. Bisoxazoline could be formed from biacylated amino alcohol (Entry 9).

When relative inactive alkylacylamino alcohols were used,[17] longer reaction time was necessary to ensure complete conversion. High yields of desired products were obtained in 24 h (Entries 10—14). Cyclopropyl was tolerated and the corresponding product could be formed smoothly.

Table 1 The synthesis of 2-aryl(alkyl)oxazolines[a]



1 **2**

Entry	Reaction time	Product	Yield[b]/%
1	20 min	 (**2a**)	96
2	20 min	 (**2b**)	99
3	2 h	 (**2c**)	99
4	20 min	 (**2d**)	97
5	60 min	 (**2e**)	92
6	60 min	 (**2f**)	82
7	60 min	 (**2g**)	98
8	3 h	 (**2h**)	90
9	24 h	 (**2i**)	97
10	24 h	 (**2j**)	70
11	24 h	 (**2k**)	90
12	24 h	 (**2l**)	93
13	24 h	 (**2m**)	97
14	24 h	 (**2n**)	91

[a] PPh_3/DDQ/acylamino alcohol = 1.5/1.5/1.0 (molar ratio), in dichloromethane, r.t.; [b] isolated yield.

Our effort was then devoted to the stereochemistry of the reaction. First, stereochemistry for acyl moiety was studied. Accordingly, amides derived from *trans* and *cis* substituted cyclopropanecarboxylic acid were chosen as the substrates. Except with *trans*-2-phenylcyclopropylcarboxamide, slight isomerization in cyclopropyl was observed. Using 2-phenylcyclopropylcarboxamide with a *cis*/*trans* molar ratio of 97.7%/2.3%, a product consisting of 96.0% *cis* and 4.0% *trans* was formed. The use of *trans*-2-[2,2-dimethyl-3-(2-methyl-propenyl)-cyclopropanecarboxylate (*trans*/*cis* = 97.7%/2.3%, molar ratio) yielded a product with a *trans*/*cis* ratio of 93.1%/6.9%,

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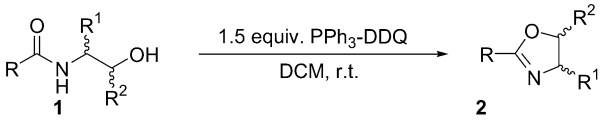
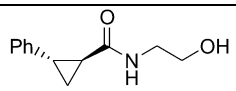
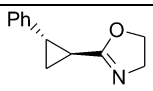
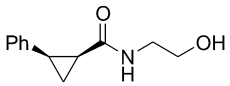
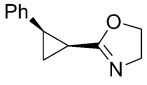
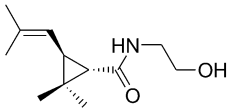
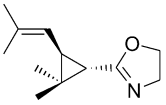
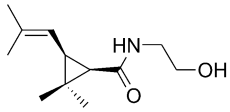
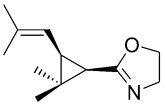
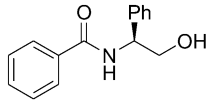
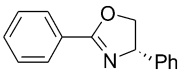
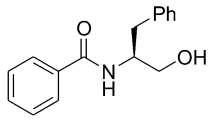
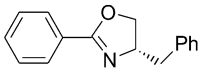
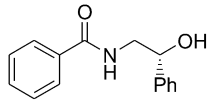
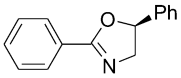
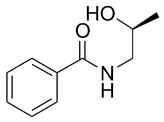
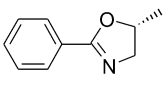
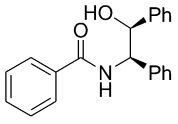
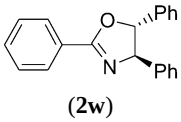
while using substrate consisting of 98.7% of *cis* and 1.3% of *trans*, the *cis*/*trans* ratio in the product was 86.0%/14.0%. The isomerization may be due to a deprotonation of α-H of acyl and a followed protonation.

The stereochemistry for the amino alcohol moiety was also investigated using chiral amino alcohols. Enantiopure, optical active oxazolines were obtained in these cases, as shown in Table 2. The configuration of

Table 2 The synthesis of oxazolines



1 **2**

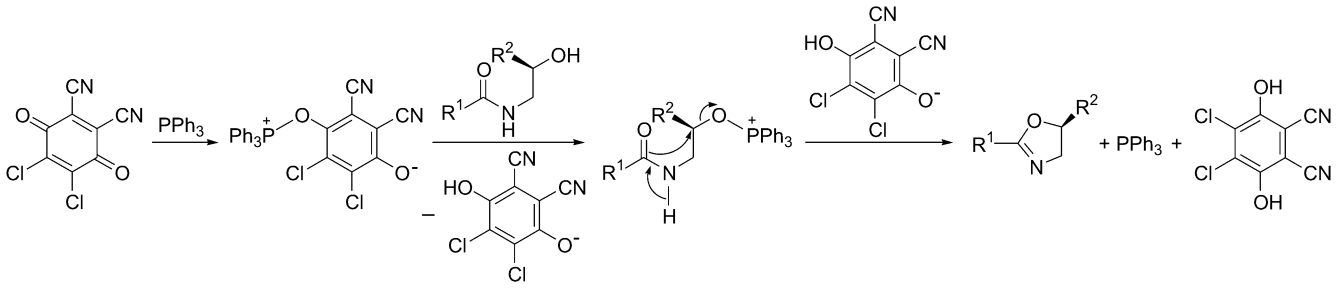
Entry	Substrate	Reaction time	Product	Yield[a]/%
1	 (**1o**)	12 h	 (**2o**)	80
2	 (**1p**)	24 h	 (**2p**)	73
3	 (**1q**)	24 h	 (**2q**)	48
4	 (**1r**)	24 h	 (**2r**)	44
5	 (**1s**)	1 h	 (**2s**)	93
6	 (**1t**)	1 h	 (**2t**)	97
7	 (**1u**)	41 h	 (**2u**)	68
8	**1u**	1 h	**2u**	88[b]
9	 (**1v**)	20 min	 (**2v**)	90
10	 (**1w**)	4 h	 (**2w**)	66[b]

[a] Unless noted, PPh_3/DDQ/acylamino alcohol = 1.5/1.5/1.0 (molar ratio), in dichloromethane, r.t.; [b] toluene as the solvent, reflux.

carbons attached to the hydroxyl inverted in this process, as demonstrated by the specific rotation value of the products and *J* value in ^{1}H NMR (Entries 5—9). For example, **1s**, prepared from (*R*)-2-phenylglycinol (Alfa, $[\alpha]_D^{20}$ −30°, *c* 0.75, 1 mol/L HCl), afforded **2s** with an $[\alpha]_D^{20}$ value as 199.5° (*c* 3.4, $CHCl_3$), which is even higher than the value reported in literature (162.3°, *c* 4.7, $CHCl_3$).[18] Substitution of hydroxyl group in alcohol with halide under the activation of PPh_3-DDQ combination has been reported,[19] and the configuration of the chiral carbon attached to the hydroxyl group inverts in the process. It has been reported that the mechanism is very similar to that of Mistunobu reaction, where PPh_3 combined with DDQ to generate a phosphonium intermediate which reacted with the alcohol oxygen, activating it as a leaving group. In the current system, an intramolecular substitution by the oxygen of the amide moiety yields the five-membered ring oxazoline and $OPPh_3$. The process is shown in Scheme 1. With (1*S*,2*R*)-2-benzoylamino-1,2-diphenylethanol as the substrate, the NMR data of the product can be assigned to a single oxazoline instead of a mixture of stereoisomers. It has been reported that in *trans* 2,4,5-triphenyloxazoline, the *J* value between H-4 and H-5 is 7.3 Hz, whereas it is 10.3 Hz in the *cis* isomer.[20] The *J* value in our sample between H-4 and H-5 is 7.6 Hz, indicating that the product is the *trans* one and its structure is (4*R*,5*R*)-2,4,5-triphenyloxazoline (**2w**) (Entry 10). This is further proved by the consistence of ^{1}H and ^{13}C NMR data with literature ones. Accordingly, there was no change of configuration for the stereocenter of carbon attached amino group.

The similarity of PPh_3-DEAD and PPh_3-DDQ as activating and dehydrating reagent promoted us to extend PPh_3-DDQ to the synthesis of benzoxazole, an analogue of oxazoline, which also has found remarkable biological activities and significant applications.[21] After consulting the case with DEAD-PPh_3,[22] and the same key phosphonium intermediate with PPh_3-DEAD and PPh_3-DDQ as the dehydrating and activating reagent, a possible mechanism using PPh_3-DDQ in the synthesis of benzoxazole is proposed and shown in Scheme 2. The mechanism is different to that in the formation of oxazoline. In Scheme 2, the oxygen atom of the carbonyl instead of that of hydroxyl attached the phenyl is activated by the phosphonium intermediate derived from PPh_3-DDQ, and then a nucleophilic addition of phenol oxygen to carbonyl and a followed elimination of triphenylphosphine oxide yield the cyclized product, benzoxazole. Initially, we supposed that amide could be formed from carboxylic acid and 2-aminophenol via dehydration and a followed dehydration might produce benzoxazole in the presence of excess PPh_3-DDQ. However, almost no desired product was obtained in acetonitrile or dichloromethane at room temperature. The use of THF as the solvent generated a 5% yield of the product only, and change to toluene resulted in a 23% yield, which is still a very low yield (Table 3). We suspected that the low yields may be due to the slow or difficult formation of benzoylaminophenol under the reaction conditions. Accordingly, the amide was used as the substrate, and benzoxazole was formed in this case. However, high reaction temperature was needed for getting reasonable yield of the product. As shown in Table 4, good to excellent yields could be obtained for acyl benzoxazole and for alkyl one in 5—24 h in refluxing toluene except for **4d** (28% yield).

Scheme 1 Mechanism for the formation of oxazoline with PPh_3-DDQ



Scheme 2 A possible mechanism for the formation of benzoxazole using PPh_3-DDQ

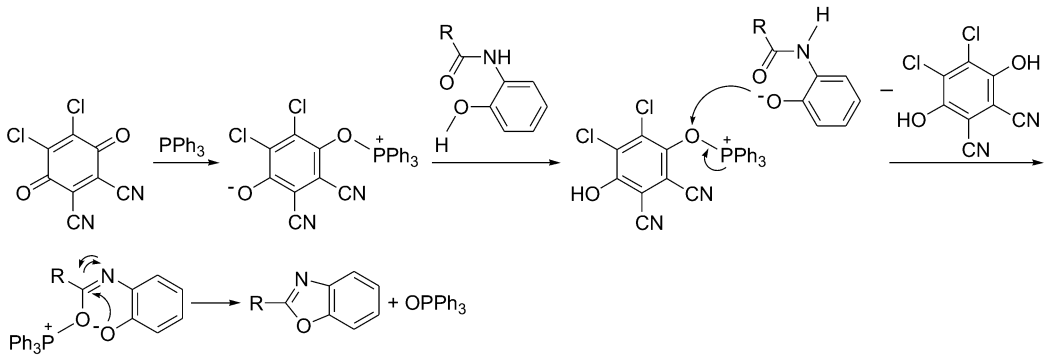
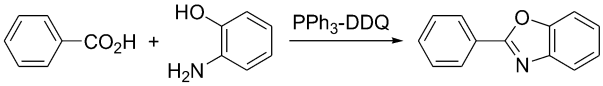


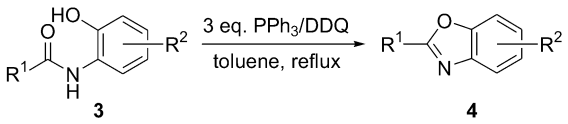
Table 3 One pot synthesis of benzoxazole from benzoic acid and 2-amino phenol



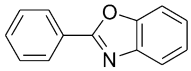
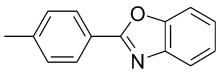
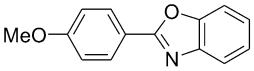
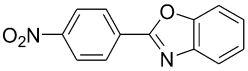
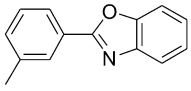
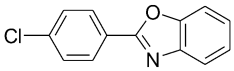
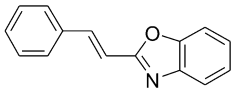
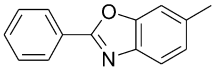
Entry	Solvent	Reaction time/h	acid∶aminophenol∶PPh_3∶DDQ (molar ratio)	Yield[a]/%
1	MeCN	24	1∶1∶4∶4	0
2	DCM	24	1∶1∶4∶4	trace
3	THF	24	1∶1∶4∶4	5
4	toluene	18	1∶1∶2.5∶2.5	10
5	toluene	23	1∶1∶4∶4	22
6	toluene	23	1∶3∶4∶4	24

[a] Isolated yield.

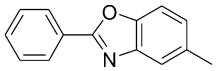
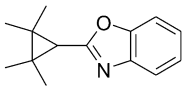
Table 4 The synthesis of benzoxazoles



3 **4**

Entry	Time/h	Product	Yield[a]/%
1	17	 (**4a**)	97
2	15	 (**4b**)	92
3	24	 (**4c**)	52
4	23	 (**4d**)	28
5	23	 (**4e**)	90
6	16	 (**4f**)	77
7	24	 (**4g**)	81
8	17	 (**4h**)	95

Continued

Entry	Time/h	Product	Yield[a]/%
9	17	 (**4i**)	99
10	16	 (**4j**)	76

[a] Isolated yield.

Conclusion

PPh_3-DDQ could be used as an efficient dehydrating reagent in the synthesis of 2-oxazolines and benzoxazoles from the corresponding 2-aryl or alkylacylamino alcohols or phenols. The reactions proceed under neutral conditions, and can produce 2-aryl as well as 2-alkyl oxazolines or benzoxazoles in high yields in most cases.

Experimental

Infrared spectra were recorded on a Nicolet 550 FT-IR spectrometer in nujol, from 4000 cm^{-1} to 400 cm^{-1}. NMR spectra were recorded in $CDCl_3$ on a Varian Mercury Plus 400 NMR spectrometer operating at 400 MHz, 100 MHz for ^1H NMR and ^{13}C NMR, respectively, or at a Bruker DRX500 spectrometer operating at 500 MHz, 125 MHz for ^1H NMR and ^{13}C NMR, respectively. Chemical shifts were referenced internally to tetramethylsilane (TMS) or $CDCl_3$. Spectral features are designated as: m＝multiplet, t＝triplet, d＝doublet, s＝singlet. Low resolution mass spectra (LRMS) were recorded on an HP 6890/5973 GC-MS mass spectrometer. High resolution mass (HRMS) for unreported compounds were recorded on a Micromass GTC Gas Chromatography/TOF Mass spectrometer or a UPLC/Q TOF Mass spectrometer, and spectral data were obtained for the molecular ion $[M]^+$, or $[M+H]^+$, respectively.

Typical procedure for the synthesis of 2-oxzoline

Under an argon atmosphere, PPh_3 (0.393 g, 1.50 mmol), DDQ (0.341 g, 1.50 mmol) and DCM (5.0 mL) were added to a dried Schlenk tube. After the mixture was stirred at room temperature for 3 min, *N*-(2-hydroxyethyl) benzamide (0.165 g, 1.00 mmol) was added. The color of the mixture turned into yellow and precipitation occurred. After 20 min, TLC showed the disappearance of the substrate, and the formation of a new spot. Then the mixture was washed with aqueous NaOH solution (5%, 40 mL), and the separated water layer was extracted with DCM (15 mL×4). The combined organic layer was washed with brine, and dried by anhydrous Na_2SO_4. Filtration and evaporation of the solvent followed by column chromatography separation (silica gel) using petroleum ether/ethyl acetate (4∶1, *V*/*V*) gave the corresponding 2-phenyl oxazoline (**2a**) as colorless liquid (0.156 g, 96%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.95 (d, J=7.2 Hz, 2H), 7.48—7.40 (m, 3H), 4.44 (t, J=9.6 Hz, 2H), 4.07 (t, J=9.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 164.5, 131.2, 128.2, 128.0, 127.6, 67.5, 54.8; IR (KBr) v: 2931, 1651, 1529, 1493, 1456, 1346, 1269, 1201, 1038, 967, 899, 712, 607 cm^{-1}. LRMS *m*/*z*: 148 (7, $[M+1]^+$), 147 (67, $[M]^+$), 117 (100).

2-(4-Methylbenzoyl)phenyloxazoline (2h) Colorless solid, m.p. 113—115 ℃, R_f 0.22 (EtOAc∶petroleum ether=3∶7, volume ratio); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.95 (dd, J=6.6, 2.3 Hz, 1H), 7.64 (d, J=8.2 Hz, 2H), 7.60—7.50 (m, 2H), 7.43 (dd, J=7.0, 1.8 Hz, 1H), 7.22 (d, J=8.0 Hz, 2H), 4.03 (dd, J=14.4, 5.0 Hz, 2H), 3.77 (t, J=9.6 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 196.68, 163.64, 143.57, 140.34, 134.97, 130.97, 129.71, 129.46, 129.07, 128.08, 126.43, 67.83, 55.02, 21.73; IR (KBr) v: 2911, 2280, 1669, 1615, 1414, 1199, 1118, 1044, 950, 897, 736, 588, 507 cm^{-1}; LRMS *m*/*z*: 265 (3, $[M]^+$), 237 (18), 236 (100), 192 (10), 178 (3), 165 (6), 152 (3), 146 (1), 130 (4), 119 (2), 91 (9), 65 (5).

2-Benzyloxazoline (2j) Colorless liquid, R_f 0.33 (EtOAc∶petroleum ether=3∶7, volume ratio); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.31—7.24 (m, 5H), 4.22 (t, J=9.5 Hz, 2H), 3.82 (t, J=9.5 Hz, 2H), 3.60 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 167.0, 135.1, 129.3, 128.8, 126.9, 67.6, 54.3, 34.6; IR (KBr) v: 3052, 2979, 2932, 2864, 1642, 1582, 1488, 1354, 1091, 1071, 977, 722 cm^{-1}; LRMS *m*/*z*: 161 (51, $[M+1]^+$), 160 (100, $[M]^+$), 132 (24), 118 (9), 104 (14), 91 (89), 89 (9), 77(8), 65 (22), 51 (9), 39 (8); HRMS (EI) calcd for $C_{10}H_{11}NO$ 161.0841, found 161.0844 $[M]^+$.

2-*n*-Undecyloxazoline (2l) Colorless liquid, R_f 0.35 (EtOAc∶petroleum ether=3∶7, volume ratio); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.21 (t, J=9.4 Hz, 2H), 3.81 (t, J=9.4 Hz, 2H), 2.26 (t, J=7.6 Hz, 2H), 1.62 (pent, J=7.0 Hz, 2H), 1.30—1.26 (m, 16H), 0.88 (t, J=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ: 168.7, 67.1, 54.3, 31.9, 29.6 (2C), 29.4, 29.3, 29.23, 29.20, 27.9, 25.9, 22.6, 14.1; IR (KBr) v: 2925, 2858, 1683, 1468, 1374, 1233, 1166, 991, 964, 722 cm^{-1}; LRMS *m*/*z*: 224 (2, $[M-1]^+$), 196 (5), 182(6), 154 (6), 140 (11), 112 (7), 99 (7), 98(49), 85 (100), 55 (10), 41 (14); HRMS (EI) calcd for $C_{14}H_{27}NO$ 225.2093, found 225.2082 $[M]^+$.

2-(2,2,3,3-Tetramethylcyclopropyloxazoline (2n) Colorless liquid, R_f 0.28 (EtOAc∶petroleum ether=3∶7, volume ratio); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.15 (t, J=9.2 Hz, 2H), 3.83 (t, J=9.2 Hz, 2H), 1.20 (s, 6H), 1.18 (s, 6H), 1.13 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 167.3, 66.0, 54.5, 31.4 (2C), 27.0, 23.5 (2C), 17.7 (2C); IR (KBr) v: 2919, 1669, 1199, 1125, 1038, 951, 903, 751, 595, 501 cm^{-1}; LRMS *m*/*z*: 167 (2, $[M]^+$), 154 (8), 152 (100), 137 (6), 126 (30), 110 (12), 83 (45), 81 (17), 55 (14), 41 (14); HRMS (EI) calcd for $C_{14}H_{27}NO$ 225.2093, found 225.2082 $[M]^+$.

2-*trans*-(2-Phenylcyclopropyl)oxazoline (2o) Colorless liquid, R_f 0.14 (EtOAc∶petroleum ether=3∶7, volume ratio); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.27 (t, J=6.8 Hz, 2H), 7.19 (d, J=6.8 Hz, 1H), 7.11 (d, J=6.8 Hz, 2H), 4.25 (t, J=9.2 Hz, 2H), 3.84 (t, J=9.2 Hz, 2H), 2.49 (s, br, 1H), 1.94 (t, J=4.4 Hz, 1H), 1.56 (t, J=4.4 Hz, 1H), 1.32—1.30 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 168.1, 140.5, 128.4, 126.2, 126.1, 67.4, 54.3, 24.7, 19.6, 16.0; IR (KBr) v: 2972, 2925, 1656, 1602, 1501, 1407, 1367, 1260, 1172, 1071, 1038, 984, 917, 749 cm^{-1}; LRMS *m*/*z*: 188 (16, $[M+1]^+$), 187 (99, $[M]^+$), 172 (7), 158 (23), 144 (23), 132 (33), 116 (61), 115(97), 104 (39), 91 (35), 85 (47), 77 (28), 63 (18), 55 (100); HRMS (EI) calcd for $C_{12}H_{13}NO$ 187.0997, found 187.1006 $[M]^+$.

2-*cis*-(2-Phenylcyclopropyl)oxazoline (2p) Colorless liquid, R_f 0.14 (EtOAc∶petroleum ether=3∶7, volume ratio); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.36—7.20 (m, 4H), 7.21—7.14 (m, 1H), 4.17—4.07 (m, 1H), 3.98—3.89 (m, 1H), 3.74 (td, J=9.7, 7.8 Hz, 1H), 3.67—3.60 (m, 1H), 3.55—3.43 (m, 1H), 2.54—2.43 (m, 1H), 2.14—2.06 (m, 1H), 1.66 (dt, J=6.9, 5.6 Hz, 1H), 1.34 (td, J=8.4, 5.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 165.9, 136.9, 128.6, 127.4, 126.0, 66.8, 53.7, 23.6, 16.7, 10.0; IR (KBr) v: 2919, 1669, 1602, 1508, 1454, 1407, 1179, 1119, 984, 923, 776, 702 cm^{-1}; LRMS *m*/*z*: 188 (15, $[M+1]^+$), 187 (90, $[M]^+$), 186 (61), 172 (8), 158 (23), 144 (18), 132 (31), 116 (56), 115(92), 104 (37), 91 (33), 85 (42), 77 (31), 63 (21), 55 (100); HRMS (EI) calcd for $C_{12}H_{13}NO$ 187.0997, found 187.1001 $[M]^+$.

2-*trans*-[2,2-Dimethyl-3-(2-methyl-propenyl)cyclopropyl]oxazoline (2q) Colorless liquid, R_f 0.32 (EtOAc∶petroleum ether=3∶7, volume ratio); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.89 (d, J=7.5 Hz, 1H), 4.35—4.12 (m, 2H), 3.92—3.75 (m, 2H), 2.06—1.93 (m, 1H), 1.71 (s, 6H), 1.36 (d, J=5.3 Hz, 1H), 1.22 (s, 3H), 1.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 167.87, 135.06, 121.79, 77.48, 77.16, 76.84, 67.22, 54.44, 30.75, 30.15, 26.85, 25.66, 22.15, 21.09, 18.61; IR (KBr) v: 2979, 2932, 2878, 1656, 1454, 1407, 1380, 1253, 1193, 1172, 1125, 1024, 984, 917, 843 cm^{-1}; LRMS *m*/*z*: 193 (35, $[M]^+$), 178 (100), 163 (13), 152 (20), 151 (18), 136, (14) 109 (39), 108 (23), 98 (7), 91 (23), 83 (34), 82 (9),

81 (26), 67 (14), 53 (14), 41 (23), 39 (15).

2-*cis*-[2,2-Dimethyl-3-(2-methyl-propenyl)cyclopropyl]oxazoline (2r) Colorless liquid, R_f 0.38 (EtOAc∶petroleum ether＝3∶7, volume ratio); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.30 (d, J＝8.5 Hz, 1H), 4.17 (t, J＝9.1 Hz, 2H), 3.84 (t, J＝9.4 Hz, 2H), 1.80 (t, J＝8.8 Hz, 1H), 1.75 (s, 3H), 1.70 (s, 3H), 1.64 (d, J＝8.9 Hz, 1H), 1.20 (s, 3H), 1.19 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 166.45, 134.03, 119.17, 66.24, 54.53, 30.12, 28.77, 26.79, 25.92, 24.33, 18.26, 15.81; IR (KBr) v: 3409, 2938, 2876, 1656, 1416, 1420, 1380, 1253, 1185, 1158, 1125, 1071, 1044, 1024, 997, 924, 850 cm^{-1}; LRMS m/z: 193 (17, $[M]^+$), 178 (100), 163 (12), 150 (12), 136 (12), 109 (22), 107 (13), 91 (12), 83 (22), 77 (8), 67 (7), 55 (8).

(*S*)-2,4-Diphenyloxazoline (2s) Colorless liquid, $[\alpha]_D^{20}$ －12.3 (c 1.24, $CHCl_3$), R_f 0.70 (EtOAc∶petroleum ether＝1∶4, volume ratio); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.05 (d, J＝7.6 Hz, 2H), 7.53—7.42 (m, 3H), 7.38—7.26 (m, 5H), 5.39 (t, J＝8.4 Hz, 1H), 4.81 (t, J＝8.4 Hz, 1H), 4.28 (t, J＝8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 165.7, 142.3, 131.5, 128.7, 128.4, 128.3, 127.5, 126.7, 74.8, 70.0; IR (KBr) v: 3069, 3025, 1660, 1614, 1582, 1497, 1480, 1452, 1363, 1314, 1249, 1184, 1131, 1102, 1094, 1029, 981, 965, 899, 765, 705, 546 cm^{-1}; LRMS m/z: 223 (4, $[M]^+$), 222 (18, $[M-1]^+$), 221 (100), 194 (11), 193 (78), 192 (27), 165 (21), 88 (26), 77 (5), 63 (10), 51 (5). HRMS (EI) calcd for $C_{15}H_{13}NO$ 223.0997, found 223.1006 $[M]^+$.

(*R*)-5-Methyl-2-phenyloxazoline (2v) Colorless liquid, $[\alpha]_D^{20}$ －19.8 (c 3.98, $CHCl_3$). R_f 0.59 (EtOAc∶petroleum ether＝1∶1, volume ratio). ^{1}H NMR δ: 7.95 (d, J＝7.6 Hz, 2H), 7.47 (t, J＝7.2 Hz, 1H), 7.41 (t, J＝7.6 Hz, 2H), 4.86 (m, 1H) 4.63—4.55 (m, 1H), 4.15 (dd, J＝9.6, 14.4 Hz, 1H), 3.62 (dd, J＝7.2, 14.4 Hz, 1H), 1.43 (d, J＝6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 163.8, 131.2, 128.3, 128.1, 128.0, 76.2, 61.6, 21.1; IR (KBr) v: 3052, 2979, 2932, 2864, 1642, 1582, 1488, 1354, 1091, 1071 cm^{-1}. HRMS (EI) calcd for $C_{10}H_{11}NO$ 164.0841, found 161.0844 $[M]^+$.

Typical procedure for the synthesis of benzoxazole 4a

PPh_3 (157 mg, 0.6 mmol), DDQ (137 mg, 0.6 mmol), and toluene (4.0 mL) were added to a flask, and the mixture was stirred for 3 min, then *N*-2-benzoaminophenenol **3a** (44 mg, 0.2 mmol) was added. The mixture was refluxed for 17 h. after TLC indicted the completion of the reaction, the mixture was worked-up and separated as that for oxazoline, yielding **4a** as colorless solid, 39 mg (97%), m.p. 102—103 ℃ (Lit.[23] 101—103 ℃; lit.[24] 102 ℃). R_f 0.64 (EtOAc∶petroleum ether＝1∶4, volume ratio); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.27 (dd, J＝6.6, 3.1 Hz, 2H), 7.82—7.75 (m, 1H), 7.63—7.56 (m, 1H), 7.56—7.50 (m, 3H), 7.40—7.32 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 163.08, 150.75, 142.05, 131.63, 128.99, 127.66, 127.12, 125.20, 124.66, 120.04, 110.68; IR (KBr) v: 3395, 2952, 2851, 1742, 1609, 1555, 1441, 1374, 1239, 1152, 1058, 1024, 735 cm^{-1}; LRMS m/z: 196 (14), 195 (100, $[M]^+$), 168 (16), 167 (79), 166 (41), 140 (15), 139 (18), 92 (31), 77 (40), 64 (49), 63 (62), 51 (18).

2-(2,2,3,3-Tetramethylcyclopropyl)benzoxazole (4j) Colorless solid, m.p. 63—64 ℃, R_f 0.18 (EtOAc∶petroleum ether＝3∶97, volume ratio); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.64 (dd, J＝6.7, 2.2 Hz, 1H), 7.43 (dd, J＝6.8, 2.1 Hz, 1H), 7.32—7.19 (m, 2H), 1.73 (s, 1H), 1.32 (s, 6H), 1.30 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 166.36, 150.38, 141.89, 123.81, 123.79, 119.26, 109.83, 77.35, 77.10, 76.85, 32.38, 29.05, 23.52, 17.82; IR (KBr) v: 2901, 1642, 1542, 1421, 1199, 1038, 970, 890, 742 cm^{-1}; LRMS m/z: 216 (18), 215 (80, $[M]^+$), 200 (100), 184 (38), 174 (68), 158 (71), 146 (14), 133 (47), 120 (12), 108 (8), 93 (12), 91 (11), 81 (16), 77 (22), 55 (14), 41 (23).

Supporting Information

Supporting information features: copies of some of oxazolines and benzoxazoles.

Title: NMR spectra of compounds **2c**, **2h**, **2k**, **2m**, **2q**, **2r**, **2u**, **2w**, **4a**—**4c**, and **4e**—**4j**.

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