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SYNTHESIS OF 4,5,6,7-TETRAHYDROISOXAZOLO[3,4-*c*]PYRIDINES AND THEIR ANTIFUNGAL ACTIVITIES

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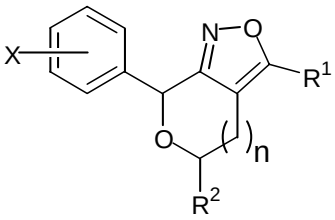
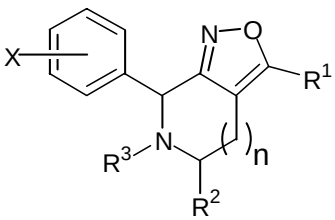
Abstract – 4,5,6,7-Terahydroisoxazolo[3,4-*c*]pyidine derivatives have been synthesized from the corresponding 4*H*,6*H*-pyrano[3,4-*c*]isoxazoles. They were found to display high antifungal activities against some plant pathogens.

It is well known that substituted isoxazole derivatives display a variety of biological activities in pharmaceutical and agricultural areas.[1] For instance, isoxazoylmethanols display antiinflammatory and analgesic activities,[2,3] haloisoxazolylureas display acaricidal and insecticidal activities,[4] and 3-hydroxy-5-methylisoxazole displays fungicidal activities.[5] In an effort to find a new lead compound to use as a plant fungicide, we have been interested in the synthesis of fused bicyclic isoxazole derivatives. Reports concerning the biologically active fused isoxazoles, however, are very rare. We have recently reported on the syntheses of some fused bicyclic isoxazole derivatives, such as 4*H*,6*H*-furo[3,4-*c*]isoxazoles (**I**),[6,7] 4*H*,6*H*-pyrano[3,4-*c*]isoxazoles (**II**)[8] and 4*H*,6*H*-pyrrolo[3,4-*c*]isoxazoles (**III**),[9] and found that they showed a broad spectrum of antifungal activities against some plant pathogens. Continuing our studies on new fused isoxazoles, we have designed 4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridines (**IV**), novel [5,6] fused ring system, which might display antifungal activities. To our best knowledge, a synthetic method for producing 4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine has not yet been reported. In this paper we describe a synthesis of 4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine derivatives and their antifungal activities.



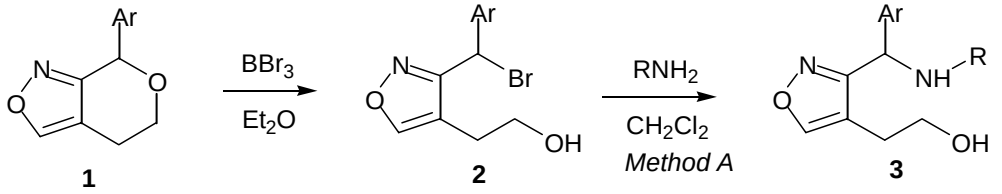
I n = 0
II n = 1



III n = 0
IV n = 1

R^1, R^2, R^3 = H, alkyl, aryl
X = H, alkyl, alkoxy, halo
n = 0 or 1

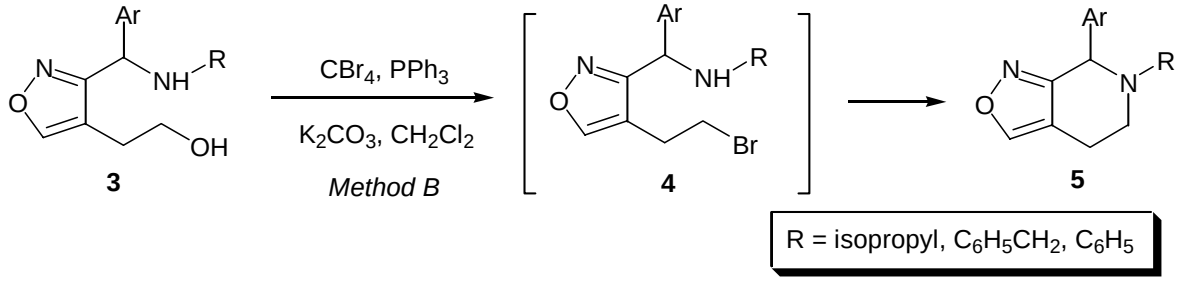
Our synthetic strategy is to prepare isoxazolo[3,4-*c*]pyridine (**5**) from the corresponding pyrano[3,4-*c*]isoxazole (**1**) through the regioselective cleavage of pyranoisoxazole (**1**) into **2**, the substitution reaction of **2** with primary amines and the subsequent recyclization reaction of **3**. The preparation of 4*H*,6*H*-pyrano[3,4-*c*]isoxazoles (**1**) and their selective cleavage into 3,4-disubstituted isoxazoles (**2**) has already been reported in our previous paper (**Scheme 1**).[10] Starting from the readily available 3,4-disubstituted isoxazoles (**2**), isoxazolo[3,4-*c*]pyridines (**5**) were then prepared in a two-step procedure.



Scheme 1

Initially most of the isoxazoles (**2**) were allowed to react with the primary amines (RNH_2) in the presence of an equimolar amount of potassium carbonate at room temperature to readily afford the corresponding amines (**3**) in excellent yields as shown in **Table 1**. When R is a substituted phenyl, as in the cases of **3e**, **3f**, **3k**, **3l**, **3q** and **3r**, the displacement was sluggish, though the process was completed at refluxing temperature, or when given a longer reaction time.

In order to transform the hydroxyl group of **3** into the labile bromo group as in **4**, we employed a neutral reaction condition, after considering the secondary amine group in **3**. When the alcohol (**3**) was treated with a mixture of carbon tetrabromide and triphenyl phosphine in methylene chloride, it is significant that isoxazolo[3,4-*c*]pyridine (**5**) was obtained without isolating the bromo compounds (**4**) when R was isopropyl, benzyl and phenyl (**Scheme 2**). In this reaction condition, however, the yield of **5** was unsatisfactory, though the addition of an equimolar amount of potassium carbonate or triethyl amine to the reaction mixture was very effective in completing the cyclization reaction of **3** into **5** as expected.



Scheme 2

In contrast, when R is a substituted phenyl, such as *o*-chlorophenyl, *p*-chlorophenyl or *o*-tolyl, the treatment of the amino alcohol (**3**) with a mixture of carbon tetrabromide and triphenyl phosphine never produced isoxazolo[3,4-*c*]pyridine (**5**)**,** even in the presence of potassium carbonate or triethylamine. Instead, the bromo compound (**4**) was isolated in good yields.

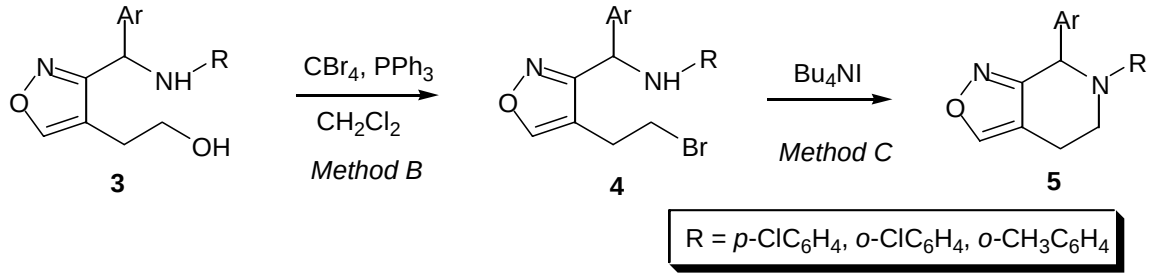
Table 1. **Yields of 3, 4 and 5**

No.	Ar	R	%Yield		
			3[a]	**4**	**5**
a	*o*-ClC_6H_4	isopropyl	92	-[b]	79[c]
b	*o*-ClC_6H_4	$C_6H_5CH_2$	92	-[b]	60[c]
c	*o*-ClC_6H_4	C_6H_5	82	-[b]	55[c]
d	*o*-ClC_6H_4	*p*-ClC_6H_4	95	76	85[d]
e	*o*-ClC_6H_4	*o*-ClC_6H_4	98	79	nr[e]
f	*o*-ClC_6H_4	*o*-$CH_3C_6H_4$	91	92	91[d]
g	*p*-ClC_6H_4	isopropyl	88	-[b]	62[c]
h	*p*-ClC_6H_4	$C_6H_5CH_2$	96	-[b]	60[c]
i	*p*-ClC_6H_4	C_6H_5	96	-[b]	95[c]
j	*p*-ClC_6H_4	*p*-ClC_6H_4	98	71	98[d]
k	*p*-ClC_6H_4	*o*-ClC_6H_4	93	95	nr[e]
l	*p*-ClC_6H_4	*o*-$CH_3C_6H_4$	97	74	97[d]
m	C_6H_5	isopropyl	98	-[b]	95[c]
n	C_6H_5	$C_6H_5CH_2$	90	-[b]	86[c]
o	C_6H_5	C_6H_5	88	-[b]	95[c]
p	C_6H_5	*p*-ClC_6H_4	92	-[b]	85[c]
q	C_6H_5	*o*-ClC_6H_4	83	82	nr[e]
r	C_6H_5	*o*-$CH_3C_6H_4$	92	94	83[d]

[a] The reaction was carried out according to the *Method A*.
[b] Desired product not isolated.
[c] The reaction was carried out according to the *Method B*.
[d] The reaction was carried out according to the *Method C*.
[e] No reaction.

In this last case, the nucleophilicity of the nitrogen nucleus in the compound (**4**) seems to be decreased by the presence of an electron-withdrawing substituent R, such as *o*- or *p*-chlorophenyl, or the sterically hindered *o*-tolyl group. However, only **3p** with *p*-chlorophenyl as the R substituent was directly converted into the isoxazolopyridine (**5p**) without isolating the intermediate (**4p**).

Finally, the cyclizaton reaction of **4** to **5** was accomplished by the addition of a catalytic amount of tetrabutylammonium iodide. For compounds (**4e**, **4k** and **4q**) with *o*-chlorophenyl as the R substituent, however, their cyclization reactions did not proceed even at reflux for 24 h.



Scheme 3

The antifungal activities of all new compounds were later examined against six representative plant pathogens, such as rice blast (RCB; *Pyricularia oryzae*), rice sheath blight (RSB; *Rhizoctonia solani*), cucumber gray mold (CGM; *Botrytis cinerea*), tomato late blight (TLB; *Phytophthora infestants*), wheat leaf rust (WLR; *Puccinia recondita*) and barley powdery mildew (BPM; *Erysiphe graminis*). The selected examples and their results are summarized in **Table 2**. Some of the compound (**3** and **5**) were found to possess relatively high antifungal activities, while compound (**4**) did not. Compounds (**3d**, **3e**, **3f**, **3i**, **3j**, **3k**, **3p** and **3r**) exhibited higher activities mainly against RCB with ~90% control. Selectively high activities on BPM was observed for isoxazolopyridines (**5g**, **5i**, **5l**, **5p** and **5r**).

In conclusion, in this work we extended our new synthetic methodology for fused bicyclic isoxazoles. Moreover, 3,4-functionalized isoxazoles (**3** and **4**) could be very useful precursors for synthesizing new isoxazoles by chemical transformation of the C-3 and/or C-4 funtionalities of the isoxazole ring. Finally, it should be noted that further structural derivatization of isoxazolo[3,4-*c*]pyridine is necessary in order to study its structure-activity relationship, and to eventually enhance its antifungal activity in the future.

EXPERIMENTAL

Melting points are uncorrected. IR spectra were recorded on a Shimadzu IR-435 spectrophotometer. ^{1}H-NMR and ^{13}C-NMR spectra were obtained with Varian UNITY-300 Plus spectrometer in $CDCl_3$ at 300 and 75.5 MHz, respectively. Chemical shifts were reported in ppm (δ) relative to tetramethylsilane. MS spectra were obtained with Jeol JMX-DX303 mass spectrometers using the electron impact mode at 70

Table 2. Antifungal activities of 3 and 5[a,b]

Comp.	RCB	RSB	CGM	TLB	WLR	BPM
3d	93	40	40	50	86	0
3e	99	30	0	64	0	16
3f	93	38	4	77	83	58
3j	86	35	40	75	6	33
3k	95	30	40	87	0	25
3p	93	55	0	61	86	16
3q	97	50	0	77	73	16
5g	0	20	40	87	40	93
5i	25	5	0	57	0	83
5l	50	30	0	35	6	86
5p	0	22	0	67	6	93
5r	80	66	0	74	66	93

[a] All activities were measured at 250 ppm according to the method reported in our previous paper.[7]

[b] Control value are calculated by the equation [1-(percentage of disease area in treatment)/(percentage of disease area in untreated area)]x100; 0 represents no activity and 100 means complete control of a disease.

eV. Column chromatography was performed using Merck Kieselgel 60 (70-230 mesh) as the stationary phase.

General Procedure for the Preparation of Compounds 3, 4 and 5.

Method A. To a stirred solution of the isoxazole (**2**) (3 mmol) dissolved in CH_2Cl_2 (15 mL) was added anhydrous K_2CO_3 (621 mg, 4.5 mmol) and RNH_2 (6 mmol). After being stirred for 2 h at rt, water (20 mL) was then added and the mixture was extracted with Et_2O (15 mL x 2). The extract was then dried ($MgSO_4$), concentrated and purified by column chromatography (hexane/EtOAc = 4:1) to afford **3**.

Method B. To a stirred mixture of **3** (2 mmol) and Ph_3P (786 mg, 3 mmol) dissolved in CH_2Cl_2 (15 mL) was slowly added CBr_4 (996 mg, 3 mmol) and Et_3N (404 mg, 4 mmol) at 0 ^oC, and the mixture was then stirred for 3 h at rt. Et_2O (20 mL) was then added and the mixture was filtered. Finally, the filtrate was

concentrated under reduced pressure and the crude product was then purified by column chromatography (hexane/EtOAc = 5:1).

Method C. The mixture of **4** (2 mmol), K_2CO_3 (304 mg, 2.2 mmol) and Bu_4NI (74 mg, 0.2 mmol) in THF (20 mL) was heated at reflux for 24 h. After cooling, water (20 mL) was added and the resulting mixture was then extracted with Et_2O (20 mL x 2). The extract was then dried ($MgSO_4$), concentrated and purified by column chromatography (hexane/EtOAc = 4:1) to afford **5**.

3-[(2-Chlorophenyl)(isopropylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3a): oil; ^{1}H NMR δ 1.09 (d, *J*=6.4 Hz, 3H), 1.12 (d, *J*=6.2 Hz, 3H), 2.61 (td, *J*=5.91, 1.5 Hz, 2H), 2.85 (m, 1H), 3.01 (br s, 2H, NH and OH), 3.58 (dtd, *J*=10.6, 6.2, 2.1 Hz, 1H), 3.75 (dtd, *J*=10.6, 5.4, 2.6 Hz), 5.59 (s, 1H), 7.23-7.49 (m, 4H), 8.29 (s, 1H); ^{13}C NMR δ 21.5, 23.2, 25.0, 45.86, 51.8, 62.1, 115.8, 127.2, 128.9, 128.9, 129.7, 133.6, 133.6, 156.4, 161.3; IR (neat) 3401 (NH), 3347 (OH), 2966, 1600, 1469, 1435 (isoxazole) cm^{-1}; HRMS calcd for $C_{15}H_{19}N_2O_2Cl$ (M^+) 294.1135, found 294.1140

3-[(2-Chlorophenyl)(benzylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3b): oil; ^{1}H NMR δ 2.52 (td, *J*=6.3, 0.8 Hz, 2H), 2.66 (br s, 2H, NH and OH), 3.57 (dt, *J*=10.7, 6.3 Hz , 1H), 3.66 (dt, *J*=10.7, 5.7 Hz, 1H), 3.78 (s, 2H), 5.50 (s, 1H), 7.25-7.57 (m, 9H), 8.21 (s, 1H); ^{13}C NMR δ 25.0, 51.5, 54.1, 62.1, 115.6, 127.2, 127.34, 128.4, 128.5, 128.9, 129.1, 129.8, 133.9, 136.4, 138.8, 156.5, 162.2; IR (neat) 3401 (NH), 3351 (OH), 1600, 1485, 1442 (isoxazole) cm^{-1}; HRMS calcd for $C_{19}H_{19}N_2O_2Cl$ (M^+) 342.1135, found 342.1138

3-[(2-Chlorophenyl)(phenylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3c): mp 87-91 ^{o}C (from hexane/EtOAc); ^{1}H NMR δ 2.65 (td, *J*=6.6, 0.9 Hz , 2H), 3.66 (dt, *J*=10.5, 6.3 Hz, 1H), 3.73 (dt, *J*=10.5, 6.3 Hz, 1H), 4.68 (br s, 2H), 6.11 (s, 1H), 7.11-7.56 (m, 9H), 8.28 (s, 1H); ^{13}C NMR δ 24.9, 51.1, 61.7, 113.5, 155.2, 118.6, 127.4, 128.9, 129.2, 129.3, 129.7, 133.2, 136.6, 145.9, 156.7, 162.2; IR (KBr) 3358 (NH), 3347 (OH), 1600, 1504 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{17}N_2O_2Cl$ (M^+) 328.0979, found 328.0983.

3-[(2-Chlorophenyl)(4-chlorophenylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3d): mp 83-87 ^{o}C (from hexane/EtOAc); ^{1}H NMR δ 2.31 (br s, 1H), 2.59 (td, *J*=6.0, 2.4 Hz, 2H), 3.62 (dt, *J*=10.5, 6.3 Hz, 1H), 3.69 (dt, *J*=10.5, 6.1 Hz, 1H), 6.06 (s, 1H), 7.04-7.49 (m, 8H), 8.26 (s, 1H); ^{13}C NMR δ 24.7, 51.2, 61.5, 114.6, 155.2, 123.2, 127.4, 128.8, 129.1, 129.4, 129.7, 133.1, 136.1, 144.5, 156.8, 161.9; IR (KBr) 3401 (NH), 3363 (OH), 1600, 1496 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{16}N_2O_2Cl_2$ (M^+) 362.0589, found 362.0592

3-[(2-Chlorophenyl)(2-chlorophenylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3e): oil; ^{1}H NMR δ 2.21 (br s, 1H), 2.68 (td, *J*=6.0, 0.6 Hz, 1H), 2.69 (td, *J*=6.0, 0.9 Hz, 1H), 3.72 (t, *J*=6.0 Hz, 1H), 3.76 (t, *J*=6.0 Hz, 1H), 5.37 (d, *J*=7.2 Hz, 1H), 6.17 (d, *J*=7.2 Hz, 1H), 6.55-7.54 (m, 8H), 8.33 (s, 1H); ^{13}C NMR δ 25.0, 50.8, 61.7, 112.2, 115.1, 118.6, 119.6, 127.6, 127.9, 128.7, 129.3, 129.4, 129.7, 133.1, 136.0, 141.7, 157.0, 161.7; IR (neat) 3412 (OH and NH), 1597, 1508, 1431 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{16}N_2O_2Cl_2$ (M^+) 362.0589, found 362.0588.

3-[(2-Chlorophenyl)(2-methylphenylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3f): oil; ^{1}H NMR δ 2.22 (s, 3H), 2.67 (t, *J*=6 Hz, 2H), 3.70 (t, *J*=6 Hz, 2H), 3.72 (br, 1H, OH), 4.57 (d, *J*=6.3 Hz, 1H, NH), 6.16 (d, *J*=6.3 Hz, 1H), 6.99-7.52 (m, 8H), 8.30 (s, 1H); ^{13}C NMR δ 17.6, 25.0, 50.9, 61.6, 110.8, 115.2, 118.2, 122.5, 127.1, 127.5, 128.7, 129.2, 129.7, 130.3, 133.1, 136.5, 143.7, 156.8, 162.3; IR (neat) 3426 (OH and NH), 1597, 1526, 1441 (isoxazole) cm^{-1}; HRMS calcd for $C_{19}H_{19}N_2O_2Cl$ (M^+) 342.1135, found 342.1134.

3-[(4-Chlorophenyl)(isopropylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3g): oil; ^{1}H NMR δ 1.10 (d, *J*=6.0 Hz, 6H), 2.52 (m, 2H), 2.76 (m, 1H), 3.65 (m, 2H), 5.14 (s, 1H), 7.34 (m, 4H), 8.20 (s, 1H); ^{13}C NMR δ 21.8, 22.9, 25.2, 45.9, 55.2, 62.3, 115.6, 128.8, 128.9, 133.6, 137.7, 156.8, 162.8; IR (neat) 3405 (OH and NH), 1598, 1530, 1471 (isoxazole) cm^{-1}; HRMS calcd for $C_{15}H_{19}N_2O_2Cl$ (M^+) 294.1135, found 294.1135.

3-[(4-Chlorophenyl)(benzylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3h): oil; ^{1}H NMR δ 2.45 (br, 2H, NH and OH), 2.46 (t, *J*=6 Hz, 2H), 3.60 (t, *J*=6 Hz, 2H), 3.75 (s, 2H), 5.05 (s, 1H), 7.26-7.35 (m, 9H), 8.22 (s, 1H); ^{13}C NMR δ 25.1, 51.4, 57.2, 62.11, 115.4, 127.4, 128.4, 128.5, 128.8, 129.0, 133.7, 137.6, 138.8, 156.9, 162.5; IR (neat) 3400 (NH), 3325 (OH), 1600, 1490, 1410 (isoxazole) cm^{-1}; HRMS calcd for $C_{19}H_{19}N_2O_2Cl$ (M^+) 342.1135, found 342.1138.

3-[(4-Chlorophenyl)(phenylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3i): oil; ^{1}H NMR δ 2.53 (t, *J*=6 Hz, 2H), 3.67 (t, *J*=6 Hz, 2H), 5.76 (s, 1H), 6.60-7.38 (m, 9H), 8.25 (s, 1H); ^{13}C NMR δ 24.8, 54.1, 61.9, 113.6, 114.8, 118.5, 128.6, 129.0, 129.3, 133.8, 138.0, 146.2, 157.0, 162.4; IR (neat) 3400 (NH), 3340 (OH), 1600, 1500, 1410 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{17}N_2O_2Cl$ (M^+) 328.0979, found 328.0977.

3-[(4-Chlorophenyl)(4-chlorophenylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3j): oil; ^{1}H NMR δ 2.00 (br, 1H, NH), 2.50 (t, *J*=6 Hz, 2H), 3.67 (t, *J*=6 Hz, 2H), 5.12 (br, 1H, OH), 5.71 (s, 1H), 7.7.05-7.35 (m, 8H), 8.24 (s, 1H); ^{13}C NMR δ 24.7, 54.2, 62.0, 114.7, 114.9, 123.0, 128.6, 129.0, 129.1, 133.9, 137.5, 144.8, 157.1, 162.2; IR (neat) 3402 (NH), 3365 (OH), 1605, 1498, 1430 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{16}N_2O_2Cl_2$ (M^+) 362.0589, found 362.0588.

3-[(4-Chlorophenyl)(2-chlorophenylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3k): oil; ^{1}H NMR δ 1.83 (br s, 1H, OH), 2.53 (t, *J*=6.3 Hz, 2H), 3.66 (t, *J*=6.3 Hz, 2H), 5.40 (br s, 1H, NH), 5.83 (s, 1H), 6.59-7.38 (m, 8H), 8.28 (s, 1H); ^{13}C NMR δ 24.9, 53.8, 61.6, 112.3, 114.7, 118.6, 119.7, 127.7, 128.5, 129.1, 129.3, 134.0, 137.2, 142.0, 157.2, 161.9; IR (neat) 3400 (OH and NH), 1600, 1500, 1430 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{16}N_2O_2Cl_2$ (M^+) 362.0589, found 362.0585.

3-[(4-Chlorophenyl)(2-methylphenylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3l): oil; ^{1}H NMR δ 2.12 (s, 3H), 2.57 (t, *J*=6.0 Hz, 2H), 3.67 (t, *J*=6.0 Hz, 2H), 5.84 (s, 1H), 6.57-7.50 (m, 8H), 8.28 (s, 1H); ^{13}C NMR δ 17.6, 24.9, 54.6, 61.7, 112.1, 114.9, 119.1, 123.5, 127.0, 129.0, 129.0, 130.4, 134.0, 137.1, 143.0, 157.1, 162.1; IR (neat) 3427 (OH and NH), 1597, 1506, 1444 (isoxazole) cm^{-1}; HRMS calcd for $C_{19}H_{19}N_2O_2Cl$ (M^+) 342.1135, found 342.1130.

3-[(Phenyl)(isopropylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3m): mp 74-76 ^{o}C (from hexane/EtOAc); ^{1}H NMR δ 1.11 (d, *J*=6.3 Hz, 6H), 2.48 (dt, *J*=14.5, 5.4 Hz, 1H), 2.55 (dt, *J*=14.5, 5.1 Hz,

1H), 2.71 (m, 1H), 3.21 (br s, 2H, NH and OH), 3.62 (m, 2H), 5.17 (s, 1H), 7.26-7.42 (m, 5H), 8.18 (s, 1H); ^{13}C NMR δ 21.8, 22.9, 25.2, 45.8, 55.7, 62.4, 115.8, 127.4, 127.8, 128.6, 139.0, 156.6, 163.1; IR (KBr) 3320 (NH), 3260 (OH), 2961, 1597, 1451 (isoxazole) cm^{-1}; HRMS calcd for $C_{15}H_{20}N_2O_2$ (M^+) 260.1525, found 260.1520.

3-[(Phenyl)(benzylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3n): oil; ^{1}H NMR δ 2.43 (dt, *J*=14.7, 5.4 Hz, 1H), 2.50 (dt, *J*=14.7, 5.1 Hz) 2.82 (br, 2H, NH and OH), 3.58 (m, 2H), 3.77 (s, 2H), 5.09 (s, 1H), 7.26-7.43 (m, 10H), 8.20 (s, 1H); ^{13}C NMR δ 25.9, 51.4, 57.7, 62.2, 115.5, 127.3, 127.5, 127.9, 128.5, 128.5, 128.7, 138.8, 138.9, 156.8, 162.7; IR (neat) 3399 (OH and NH), 1601, 1487, 1450 (isoxazole) cm^{-1}; HRMS calcd for $C_{19}H_{20}N_2O_2$ (M^+) 308.1525, found 308.1525.

3-[(Phenyl)(phenylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3o): mp 87-91 ^{o}C (from hexane/EtOAc); ^{1}H NMR δ 2.54 (td, *J*=6.0, 0.9 Hz, 2H), 3.63 (t, *J*=6.0 Hz, 2H), 5.80 (s, 1H), 6.66-7.44 (m, 10H), 8.25 (s, 1H); ^{13}C NMR δ 24.9, 55.1, 61.8, 114.0, 114.7, 118.7, 127.4, 128.1, 128.9, 129.2, 129.6, 139.0, 156.9, 162.5; IR (KBr) 3404 (OH and NH), 1601, 1502, 1417 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{18}N_2O_2$ (M^+) 294.1368, found 294.1367.

3-[(Phenyl)(4-chlorophenylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3p): oil; ^{1}H NMR δ 2.51 (td, *J*=6.0, 3.0 Hz, 2H), 3.12 (br s, 2H, NH and OH), 3.63 (t, *J*=6.0 Hz, 2H), 5.70 (s, 1H), 6.55-7.42 (m, 9H), 8.24 (s, 1H); ^{13}C NMR δ 24.8, 54.9, 61.9, 114.7, 122.9, 127.3, 128.1, 128.9, 129.0, 129.1, 138.8, 144.9, 157.0, 162.3; IR (neat) 3408 (OH and NH), 1599, 1500, 1452 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{17}N_2O_2Cl$ (M^+) 328.0979, found 328.0979.

3-[(Phenyl)(2-chlorophenylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3q): oil; ^{1}H NMR δ 2.50 (t, *J*=6.3 Hz, 2H), 3.57 (t, *J*=6.3 Hz, 2H), 5.29 (br, 2H, NH and OH), 5.84 (s, 1H), 6.59-7.52 (m, 9H), 8.24 (s, 1H); ^{13}C NMR δ 24.9, 54.4, 61.4, 112.3, 114.6, 118.2, 119.6, 127.1, 127.7, 128.1, 128.9, 129.1, 138.5, 142.2, 157.1, 162.1; IR (neat) 3412 (OH and NH), 1595, 1506, 1446 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{17}N_2O_2Cl$ (M^+) 328.0979, found 328.0981.

3-[(Phenyl)(2-methylphenylamino)methyl]-4-(2-hydroxyethyl)isoxazole (3r): oil; ^{1}H NMR δ 2.21 (s, 3H,), 2.50 (m, 2H), 3.55 (t, *J*=5.7 Hz, 2H), 5.80 (s, 1H), 6.98-7.44 (m, 9H), 8.20 (s, 1H); ^{13}C NMR δ 17.5, 24.9, 54.7, 61.4, 110.8, 114.7, 117.8, 122.5, 126.9, 127.2, 127.9, 128.8, 130.1, 139.4, 144.3, 156.8, 162.7; IR (neat) 3427 (OH and NH), 1597, 1510, 1446 (isoxazole) cm^{-1}; HRMS calcd for $C_{19}H_{20}N_2O_2$ (M^+) 308.1525, found 308.1527.

3-[(2-Chlorophenyl)(4-chlorophenylamino)methyl]-4-(2-bromoethyl)isoxazole (4d): mp 114-145 ^{o}C (from hexane/EtOAc); ^{1}H NMR δ 2.93 (tdd, *J*=6.8, 2.5, 0.67 Hz, 2H), 3.28 (dt, *J*=10.5, 6.6 Hz, 1H), 3.35 (dt, *J*=10.5, 6.8 Hz, 1H), 6.05 (s, 1H), 7.05-7.52 (m, 8H), 8.32 (s, 1H); ^{13}C NMR δ 25.1, 30.9, 51.6, 115.1, 115.1, 123.8, 127.6, 129.0, 129.1, 129.7, 129.8, 133.1, 135.6, 143.8, 157.0, 161.2; IR (KBr) 3410 (NH), 1599, 1500, 1435 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{15}N_2OBrCl_2$ (M^+) 423.9745, found 423.9742.

3-[(2-Chlorophenyl)(2-chlorophenylamino)methyl]-4-(2-bromoethyl)isoxazole (4e): mp 62-65 ^{o}C (from hexane/EtOAc); ^{1}H NMR δ 3.02 (td, *J*=6.3, 0.9 Hz, 1H), 3.03 (td, *J*=6.6, 0.9 Hz, 1H), 3.38 (dt, *J*=10.5, 6.6 Hz, 1H), 3.40 (dt, *J*=10.5, 6.3 Hz, 1H), 5.31 (d, *J*=7.2 Hz, 1H, NH), 6.14 (d, *J*=7.2 Hz, 1H), 6.56-7.54 (m, 8H), 8.38 (s, 1H); ^{13}C NMR δ 25.4, 30.9, 50.9, 112.1, 115.3, 118.7, 119.8, 127.7, 127.9,

128.8, 129.4, 129.7, 129.8, 133.1, 135.8, 141.7, 157.1, 161.4; IR (KBr) 3409 (NH), 1596, 1504, 1434 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{15}N_2OBrCl_2$ (M^+) 423.9745, found 423.9744.

3-[(2-Chlorophenyl)(2-methylphenylamino)methyl]-4-(2-bromoethyl)isoxazole (4f): mp 75-77 ^oC (from hexane/EtOAc); ^1H NMR δ 2.23 (s, 3H), 3.02 (td, *J*=6.6, 0.9 Hz, 1H), 3.03 (td, *J*=6.3, 0.9 Hz, 1H), 3.38 (t, *J*=6.6 Hz, 1H), 3.39 (t, *J*=6.3 Hz, 1H), 4.53 (d, *J*=6.6 Hz, 1H, NH), 6.12 (d, *J*=6.6 Hz, 1H), 6.47-7.52 (m, 8H), 8.36 (s, 1H); ^{13}C NMR δ 17.6, 25.3, 31.1, 51.0, 110.7, 115.3, 118.3, 122.6, 127.1, 127.6, 128.7, 129.4, 129.8, 130.3, 133.1, 136.4, 143.7, 156.9, 161.9; IR (KBr) 3427 (NH), 1597, 1510, 1441(isoxazole) cm^{-1}; HRMS calcd for $C_{19}H_{18}N_2OBrCl$ (M^+) 404.0291, found 404.0287.

3-[(4-Chlorophenyl)(4-chlorophenylamino)methyl]-4-(2-bromoethyl)isoxazole (4j): oil; ^1H NMR δ 2.86 (t, *J*=6.9 Hz, 2H), 3.28 (t, *J*=6.9 Hz, 2H), 5.66 (s, 1H), 7.11 (m, 8H), 8.33 (s, 1H); ^{13}C NMR δ 25.4, 30.7, 54.7, 114.9, 115.0, 128.7, 128.8, 129.2, 129.3, 134.4, 137.1, 153.8, 157.2, 161.5; IR (neat) 3410 (NH), 1595, 1495, 1400 (isoxazole) cm^{-1} ; HRMS calcd for $C_{18}H_{15}N_2OBrCl_2$ (M^+) 423.9745, found 423.9740.

3-[(4-Chlorophenyl)(2-chlorophenylamino)methyl]-4-(2-bromoethyl)isoxazole (4k): oil; ^1H NMR δ 2.88 (t, *J*=6.9 Hz, 2H), 3.29 (t, *J*=6.9 Hz, 2H), 5.23 (br s, 1H, NH), 5.78 (s, 1H), 7.12(m, 8H), 8.29 (s, 1H); ^{13}C NMR δ 25.4, 30.6, 54.0, 112.4, 114.9, 118.8, 119.9, 127.8, 128.5, 129.3, 129.3, 134.2, 137.0, 141.9, 157.3, 161.4; IR (neat) 3400 (NH), 1595, 1500, 1450 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{15}N_2OBrCl_2$ (M^+) 423.9745, found 423.9749.

3-[(4-Chlorophenyl)(2-methylphenylamino)methyl]-4-(2-bromoethyl)isoxazole (4l): oil; ^1H NMR δ 2.23 (s, 3H), 2.89 (tdd, *J*=6.9, 3.0, 0.6 Hz, 2H), 3.29 (t, *J*=6.9 Hz, 2H), 4.56 (br s, 1H), 5.75 (s, 1H), 6.50-7.39 (m, 8H), 8.33 (s, 1H); ^{13}C NMR δ 17.6, 25.5, 30.8, 54.3, 111.0, 114.9, 118.4, 122.8, 127.0, 128.6, 129.2, 130.4, 134.0, 137.7, 143.0, 157.2, 162.1; IR (neat) 3427 (NH), 1597, 1509, 1442 (isoxazole) cm^{-1}; HRMS calcd for $C_{19}H_{18}N_2OBrCl$ (M^+) 404.0291, found 404.0288.

3-[(Phenyl)(2-chlorophenylamino)methyl]-4-(2-bromoethyl)isoxazole (4q): oil; ^1H NMR δ 2.88 (td, *J*=6.6, 0.9 Hz, 2H), 3.19 (t, *J*=6.6 Hz, 2H), 5.30 (d, *J*=5.7 Hz, 1H, NH), 5.81 (d, *J*=5.7 Hz, 1H), 6.65-7.44 (m, 9H), 8.33 (s, 1H); ^{13}C NMR δ 25.5, 30.7, 54.7, 112.4, 114.8, 118.5, 119.7, 127.1, 127.7, 128.4, 129.1, 129.2, 138.4, 142.1, 157.3, 161.7; IR (neat) 3408 (NH), 1595, 1506, 1431 (isoxazole) cm^{-1}; HRMS calcd for $C_{18}H_{16}N_2OBrCl$ (M^+) 390.0135, found 390.390.0129.

3-[(Phenyl)(2-methylphenylamino)methyl]-4-(2-bromoethyl)isoxazole (4r): mp 71-73 ^oC (from hexane/EtOAc); ^1H NMR δ 2.23 (s, 3H), 2.87 (tdd, *J*=6.9, 2.7, 0.6 Hz, 2H), 3.18 (t, *J*=6.9 Hz, 2H), 4.56 (s, 1H, NH), 5.78 (s, 1H), 6.57-7.44 (m, 9H), 8.30 (s, 1H); ^{13}C NMR δ 17.6, 25.5, 30.7, 55.0, 111.0, 114.9, 118.1, 122.6, 127.0, 127.3, 128.2, 129.0, 130.2, 139.2, 144.3, 157.1, 162.3; IR (KBr) 3427 (NH), 2922, 1597, 1508, 1444 (isoxazole) cm^{-1}; HRMS calcd for $C_{19}H_{19}N_2OBr$ (M^+) 370.0681, found 370.0677.

7-(2-Chlorophenyl)-6-isopropyl-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5a): mp 115-117 ^oC (from hexane/EtOAc); ^1H NMR δ 0.99 (d, *J*=6.6 Hz, 3H), 1.05 (d, *J*=6.7 Hz, 3H), 2.53 (ddd, *J*=12.0, 8.1, 6.8 Hz, 1H), 2.72 (m, 2H), 2.82 (m, 1H), 3.14 (dt, *J*=12.0, 3.9 Hz, 1H), 5.43 (s, 1H), 7.16-7.42 (m, 4H), 8.11 (t, *J*=1.1 Hz, 1H); ^{13}C NMR δ 13.9, 19.8, 21.6, 41.1, 48.5, 57.2, 113.7, 127.1, 128.7, 129.6, 130.0, 124.3, 139.0, 152.7, 162.7; IR (KBr) 2968, 1612, 1468, 1444 (isoxazole) cm^{-1}. Anal. Calcd for $C_{15}H_{17}N_2OCl$: C,

65.10; H, 6.19; N, 10.12. Found: C, 65.52; H, 6.30; N, 9.95.

7-(2-Chlorophenyl)-6-benzyl-4,5,6,7-tetrahydroisoxazolo[3,4-c]pyridine (5b): mp 117-119 ^{o}C (from hexane/EtOAc); ^{1}H NMR δ 2.47 (ddd, *J*=12.1, 9.4, 5.2 Hz, 1H), 2.68 (m, 2H), 3.09 (dt, *J*=12.1, 4.11 Hz, 1H), 3.31 (d, *J*=13.6 Hz, 1H), 3.87 (d, *J*=13.6 Hz, 1H), 5.25 (s, 1H), 7.36 (m, 4H), 8.16 (t, *J*=1.2 Hz, 1H); ^{13}C NMR δ 18.6, 47.2, 57.7, 60.3, 113.4, 127.1, 127.2, 128.3, 128.6, 129.0, 129.8, 130.1, 134.7, 138.3, 138.7, 153.1, 161.6; IR (KBr) 1595, 1442 (isoxazole) cm^{-1}. Anal. Calcd for $C_{19}H_{17}N_2OCl$: C, 70.26; H, 5.28; N, 8.62. Found: C, 70.30; H, 5.10; N, 8.51.

7-(2-Chlorophenyl)-6-phenyl-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5c): mp 194-197 ^{o}C (from hexane/EtOAc); ^{1}H NMR δ 2.75 (m, 2H), 3.43 (ddd, *J*=14.0, 9.2, 5.0 Hz, 1H), 3.68 (dt, *J*=14.0, 4.4 Hz, 1H), 6.37 (s, 1H), 6.98-7.27 (m, 9H), 8.24 (t, *J*=1.1 Hz, 1H); ^{13}C NMR δ 17.3, 44.6, 54.9, 113.8, 118.3, 120.7, 126.5, 129.04, 129.2, 129.6, 130.1, 134.5, 138.0, 1489.0, 153.8, 159.6; IR (KBr) 1597, 1495, 1441 (isoxazole) cm^{-1}. Anal. Calcd for $C_{18}H_{15}N_2OCl$: C, 69.57; H, 4.86; N, 9.01. Found: C, 69.72; H, 4.55; N, 8.89.

7-(2-Chlorophenyl)-6-(4-chlorophenyl)-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5d): mp 155-157 ^{o}C (from hexane/EtOAc); ^{1}H NMR δ 2.75 (m, 2H), 3.40 (ddd, *J*=14.2, 9.0, 5.4 Hz, 1H), 3.62 (dt, *J*=14.2, 4.8 Hz, 1H), 6.30 (s, 1H), 7.18 (m, 8H), 8.26 (br s, 1H); ^{13}C NMR δ 17.3, 44.8, 55.0, 113.5, 119.6, 125.9, 126.6, 129.1, 129.2, 129.5, 130.1, 134.5, 137.6, 147.6, 153.9, 159.3; IR (KBr) 1596, 1491, 1439 (isoxazole) cm^{-1}. Anal. Calcd for $C_{18}H_{14}N_2OCl_2$: C, 62.62; H, 4.09; N, 8.11. Found: C, 62.76; H, 3.87; N 8.03.

7-(2-Chlorophenyl)-6-(2-methylphenyl)-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5f): mp 140-144 ^{o}C (from hexane/EtOAc); ^{1}H NMR δ 2.36 (s, 3H), 2.70 (dt, *J*=15.3, 4.5 Hz, 1H), 2.90 (dddd, *J*=13.2, 8.4, 5.4, 0.9 Hz, 1H), 3.07 (ddd, *J*=15.3, 8.4, 4.2 Hz, 1H), 3.26 (dt, *J*=13.2, 5.4 Hz, 1H), 6.08 (s, 1H), 7.10 (m, 8H), 8.26 (br s, 1H); ^{13}C NMR δ 178.0, 18.9, 49.2, 57.1, 113.7, 121.8, 124.3, 126.3, 126.6, 128.7, 129.3, 129.6, 131.0, 134.1, 134.3, 137.8, 148.5, 153.4, 161.3; IR (KBr) 1610, 1485, 1442 (isoxazole) cm^{-1}. Anal. Calcd for $C_{19}H_{17}N_2OCl$: C, 70.26; H, 5.28; N, 8.62. Found: C, 70.40; H, 5.03; N, 8.42.

7-(4-Chlorophenyl)-6-isopropyl-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5g): oil; ^{1}H NMR δ 2.57 (m, 1H), 2.70 (m, 2H), 2.88 (m, 1H), 3.09 (m, 1H), 4.86 (s, 1H), 7.33 (m, 4H), 8.12 (s, 1H); ^{13}C NMR δ 14.3, 19.3, 21.7, 41.0, 48.4, 59.9, 113.5, 128.7, 129.6, 133.3, 139.8, 152.9, 162.4; IR (neat) 1590, 1485, 1450 (isoxazole) cm^{-1}. Anal. Calcd for $C_{15}H_{17}N_2OCl$: C, 65.10; H, 6.19; N, 10.12. Found: C, 65.19; H, 5.84; N, 10.03.

7-(4-Chlorophenyl)-6-benzyl-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]-pyridine(5h): oil; ^{1}H NMR δ 2.66 (br s, 1H), 2.74 (br s, 1H), 3.14 (br s, 1H), 3.49 (br s, 1H), 3.88 (br s, 1H), 4.82 (br s, 1H), 7.29 (m, 9H), 8.21 (br s, 1H) ; ^{13}C NMR δ 17.6, 46.7, 57.3, 61.9, 127.7, 128.5, 128.9, 129.5, 130.1, 130.37, 131.1, 153.7, 157.4; IR (neat) 1610, 1495 (isoxazole) cm^{-1}. Anal. Calcd for $C_{19}H_{17}N_2OCl$: C, 70.26; H, 5.28; N, 8.62. Found: C, 70.37; H, 5.08; N, 8.50.

7-(4-Chlorophenyl)-6-phenyl-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5i): oil; ^{1}H NMR δ 2.60 (dt, *J*=15.9, 3.0 Hz, 1H), 2.87 (dddd, *J*=15.9, 11.4, 5.4, 1.2 Hz, 1H), 3.30 (ddd, *J*=14.4, 11.4, 4.2 Hz, 1H), 3.86 (dddd, *J*=14.4, 5.4, 4.0, 1.2 Hz, 1H), 6.09 (s, 1H), 7.13 (m, 9H), 8.21 (br s, 1H); ^{13}C NMR δ 17.4,

42.1, 56.8, 113.2, 115.7, 119.6, 128.7, 129.5, 133.6, 137.2, 153.6, 159.4; IR (neat) 1610, 1505, 1400 (isoxazole) cm^{-1}. Anal. Calcd for $C_{18}H_{15}N_2OCl$: C, 69.57; H, 4.86; N, 9.01. Found: C, 69.43; H, 4.80; N, 8.79.

7-(4-Chlorophenyl)-6-(4-chlorophenyl)-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5j): oil; ^1H NMR δ 2.62 (dddd, *J*=15.6, 4.8, 2.7. 1.2 Hz, 1H), 2.84 (dddd, *J*=15.6, 11.1, 5.1, 1.2 Hz, 1H), 3.30 (ddd, *J*=14.4, 11.1, 5.1 Hz, 1H), 3.79 (dddd, *J*=14.4, 4.8, 2.7, 0.9 Hz, 1H), 6.01 (s, 1H), 7.17 (m, 8H), 8.22 (br s, 1H); ^{13}C NMR δ 17.4, 42.4, 56.9, 112.9, 117.0, 124.4, 128.6, 128.7, 129.3, 133.6, 136.7, 147.58, 153.8, 159.2; IR (neat) 1597, 1496 (isoxazole) cm^{-1}. Anal. Calcd for $C_{18}H_{14}N_2OCl_2$: C, 62.62; H, 4.09; N, 8.11. Found: C, 62.68; H, 4.23; N, 8.30.

7-(4-Chlorophenyl)-6-(2-methylphenyl)-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5l): oil; ^1H NMR δ 2.38 (s, 3H), 2.68 (dtd, *J*=15.6, 5.7, 0.9 Hz, 1H), 2.79 (dtd, *J*=15.6, 5.4, 0.9 Hz, 1H), 3.13 (dt, *J*=13.5, 5.4 Hz, 1H), 3.20 (ddd, *J*=13.5, 6.9, 5.1 Hz, 1H), 5.59 (s, 1H), 7.20 (m, 8H), 8.26 (br s, 1H); ^{13}C NMR δ 18.2, 18.5, 47.3, 59.6, 113.5, 122.5, 124.3, 126.3, 128.3, 129.5, 131.2, 133.2, 133.9, 137.8, 148.4, 153.6, 161.1; IR (neat) 1599, 1491, 1444 (isoxazole) cm^{-1}. Anal. Calcd for $C_{19}H_{17}N_2OCl$: C, 70.26; H, 5.28; N, 8.62. Found: C, 70.39; H, 5.05; N, 8.55.

7-Phenyl-6-isopropyl-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5m): oil; ^1H NMR δ 0.98 (d, *J*=6.9 Hz, 3H), 1.07 (d, *J*=6.9 Hz, 3H), 2.56 (ddd, *J*=12.0, 9.0, 4.8 Hz, 1H), 2.70 (m, 2H), 2.92 (m, 1H), 3.11 (dt, *J*=11.7, 5.4 Hz, 1H), 4.88 (s, 1H), 7.34 (m, 5H), 8.12(br s, 1H); ^{13}C NMR δ 14.3, 19.4, 21.7, 41.0, 48.2, 60.6, 113.5, 127.7, 128.3, 128.8, 141.1, 152.8, 162.8; IR (neat) 2968, 1594, 1495, 1434 (isoxazole) cm^{-1}. Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.31; H, 7.40; N, 11.38.

7-Phenyl-6-benzyl-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5n): mp 122-125 ^oC (from hexane/EtOAc); ^1H NMR δ 2.53 (dtd, *J*=11.4, 6.9, 1.2 Hz, 1H), 2.67 (m, 2H), 3.08 (dt, *J*=12.3, 6.9 Hz, 2H), 3.35 (d, *J*=13.5 Hz, 1H), 3.86 (d, *J*=13.5 Hz, 1H), 4.72 (s, 1H), 7.33 (m, 10H), 8.17 (t, *J*=1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 18.2, 46.6, 57.6, 62.8, 1123.0, 127.1, 127.8, 128.3, 128.4, 128.5, 128.6, 138.78, 140.1, 153.1, 161.7; IR (KBr) 2802, 1604, 1491, 1446 (isoxazole) cm^{-1}. Anal. Calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.71; H, 6.31; N, 9.52.

7-Phenyl-6-phenyl-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5o): mp 103-107 ^oC (from hexane/EtOAc); ^1H NMR δ 2.59 (dddd, *J*=15.6, 4.5, 2.4, 1.2Hz, 1H), 2.88 (dddd, *J*=15.6, 11.7, 4.8, 1.5Hz, 1H), 3.35 (ddd, *J*=14.1, 11.7, 4.8Hz, 1H), 3.87 (dddd, *J*=14.1, 4.5, 2.4, 1.5Hz, 1H), 6.16s, 1H), 7.23 (m, 10H), 8.19 (br s, 1H); ^{13}C NMR δ 17.4, 41.7, 57.1, 113.2, 115.3, 119.0, 127.2, 127.6, 128.5, 129.5, 138.5, 149.1, 153.5, 159.6; IR (KBr) 1597, 1498, 1446 (isoxazole) cm^{-1}. Anal. Calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84; N, 10.14. Found: C, 78.38; H, 5.75; N 9.98.

7-Phenyl-6-(4-chlorophenyl)-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5p): oil; ^1H NMR δ 2.61 (dddd, *J*=15.6, 5.1, 2.4. 1.2 Hz, 1H), 2.85 (dddd, *J*=15.6, 11.4, 5.1, 1.5 Hz, 1H), 3.36 (ddd, *J*=13.6, 11.4, 5.1 Hz, 1H), 3.85 (dddd, *J*=13.6, 5.1, 2.4, 1.5 Hz, 1H), 6.08 (s, 1H), 7.19(m, 9H), 8.21 (br s, 1H); ^{13}C NMR δ 17.4, 42.1, 57.3, 113.1, 116.7, 123.9, 127.1, 127.7, 128.6, 129.3, 138.1, 147.8, 153.6, 159.5 ; IR (neat) 2968, 1595, 1496, 1446 (isoxazole) cm^{-1}. Anal. Calcd for $C_{18}H_{15}N_2OCl$: C, 69.57; H, 4.86; N, 9.01. Found: C, 69.50; H, 4.91; N 8.87.

7-Phenyl-6-(2-methylphenyl)-4,5,6,7-tetrahydroisoxazolo[3,4-*c*]pyridine (5r): mp 111-116 ^{o}C (from hexane/EtOAc); ^{1}H NMR δ 2.40 (s, 3H), 2.68 (dddd, *J*=15.3, 6.3, 5.1, 1.2 Hz, 1H), 2.73 (dt, *J*=15.3, 5.4 Hz, 1H), 3.14 (dt, *J*=13.5, 5.4 Hz, 1H), 3.24 (ddd, *J*=13.5, 7.8, 5.1 Hz, 1H), 5.63 (s, 1H), 7.17 (m, 9H), 8.26 (br s, 1H); ^{13}C NMR δ 18.2, 18.4, 46.6, 60.1, 113.6, 122.6, 124.9, 126.2, 127.3, 127.5, 128.1, 128.1, 131.1, 139.2, 148.8, 153.4, 161.3; IR (KBr) 1601, 1495, 1446 (isoxazole) cm^{-1}. Anal. Calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.64; H, 6.15; N, 9.39

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