SYNTHESIS OF 6-SUBSTITUTED 2-PHENYLOXAZOLO-[4,5-*b*]PYRIDINES

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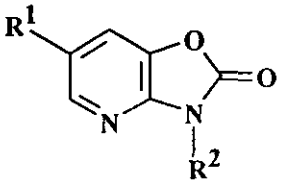
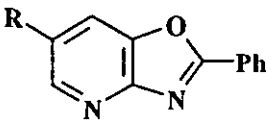
Abstract - The synthesis of 2-phenyloxazolo[4,5-*b*]pyridines substituted in position 6 by alkyl, aryl, benzyl, formyl, acetyl, benzoyl and nitrile group is described.

The main objective in current pain research is to develop improved non-opioid analgesics which are effective as an opioid but without their side effects.[1] Oxazolo[4,5-*b*]pyridin-2(3*H*)-one derivatives structure **A** constitute an important group of compounds due to their biological properties.[2] Their activities depend mainly on the nature of the substituents on the basic heterocyclic framework.



A

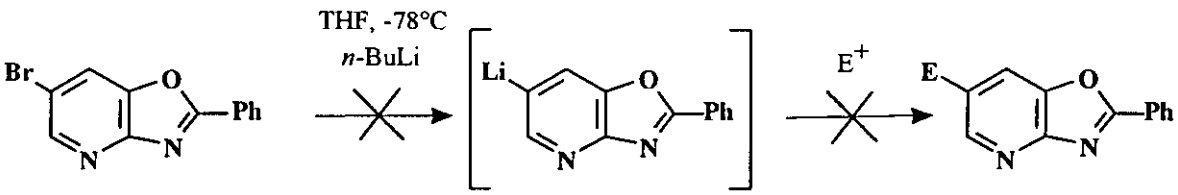


B

We report here the synthesis of derivatives (**B**) having a 2-phenyloxazolo[4,5-*b*]pyridine skeleton substituted at C-6 position by several groups as alkyl, formyl, acetyl, benzoyl, benzyl, aryl and nitrile groups, which should be potential intermediates in our project The fonctionalization at this position first had been tried *via* anionic reaction using *n*-butyllithium at -78°C according to Scheme 1. In fact, we didn't

use this methodology which lead to a rapid degradation of the substrat.

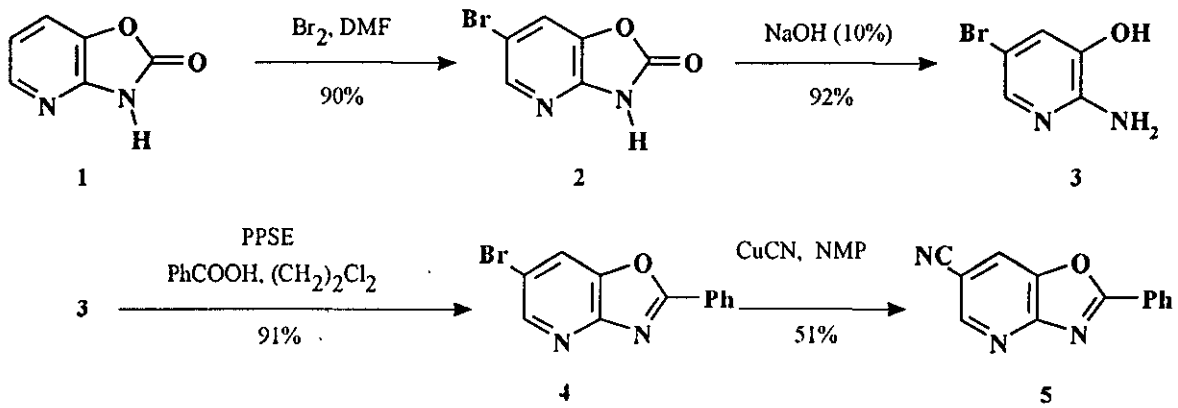
Scheme 1



4

All the trials of synthesis of **4** directly from 2-phenyloxazolo[4,5-*b*]pyridine *via* bromination reaction with bromine or *N*-bromosuccinimide were unsuccessfull. Consequently, the preparation of the appropriate substituted heteroaryl bromide (**4**) was considered from oxazolo[4,5-*b*]pyridin-2(3*H*)-one (**1**) in three steps : a bromination following successively by a basic hydrolysis of carbamate and cyclization. The first reaction involved **1** with bromine in *N,N*-dimethylformamide to afford **2** in 90% yield.[3] After ring opening of 6-bromooxazolo[4,5-*b*]pyridin-2(3*H*)-one (**2**) with a solution of NaOH (10%), the aminohydroxypyridine (**3**), obtained with a yield of 92%, was engaged to cyclisation using benzoic acid and trimethylsilylpolyphosphate ester (PPSE).[4] The reagent PPSE was easily accessible by treatment of hexamethyldisiloxane with phosphorus pentoxide (P_2O_5) in 1,2-dichloroethane. It differs from polyphosphoric acid in its aprotic character and its good solubility in organic solvents.[5] The desired compound (**4**) was obtained in 91% yield (Scheme 2).

Scheme 2



1 2 3

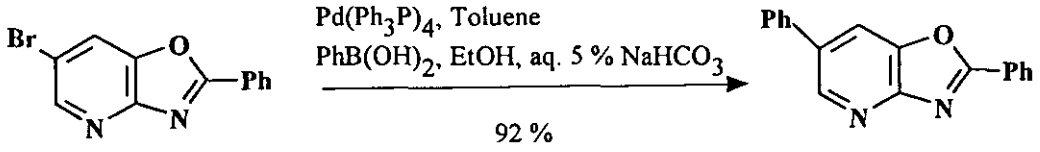
3 4 5

The cyano compound (**5**) was generated in 51% yield by direct substitution of **4** with copper (I) cyanide in 1-methyl-2-pyrrolidinone (NMP) at reflux (Scheme 2).

The Heck reaction has shown great versatility in the construction of carbon-aryl bond. Althrough generally utilized in the formation of cyclic or linear carbon-based systems, the Heck reaction has been effectively applied to heterocyclic ring systems.

We chose to investigate the palladium catalyzed cross coupling 6-bromo-2-phenyloxazolo[4,5-*b*]pyridine (**4**) with the commercially available boronic acid using Suzuki methodology.[6] Compound (**4**) was coupled directly with phenylboronic acid catalyzed with Pd(0) in toluene to give **6** in 92% yield (Scheme 3).

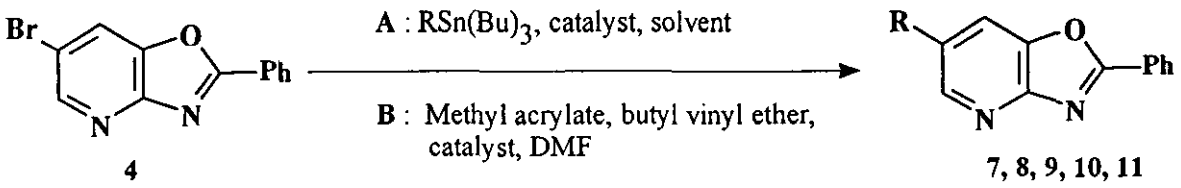
Scheme 3



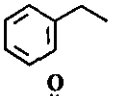
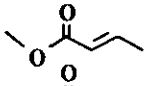
4 **6**

Synthesis of compounds (**7**, **8** and **9**) was performed according to Stille's reaction by using as key reaction palladium(0) and palladium(II) catalyzed coupling of aryl- or alkylstannane with 6-bromo-2-phenyloxazolo[4,5*b*]pyridine (**4**) (Scheme 4).[7]

Scheme 4



4 **7, 8, 9, 10, 11**

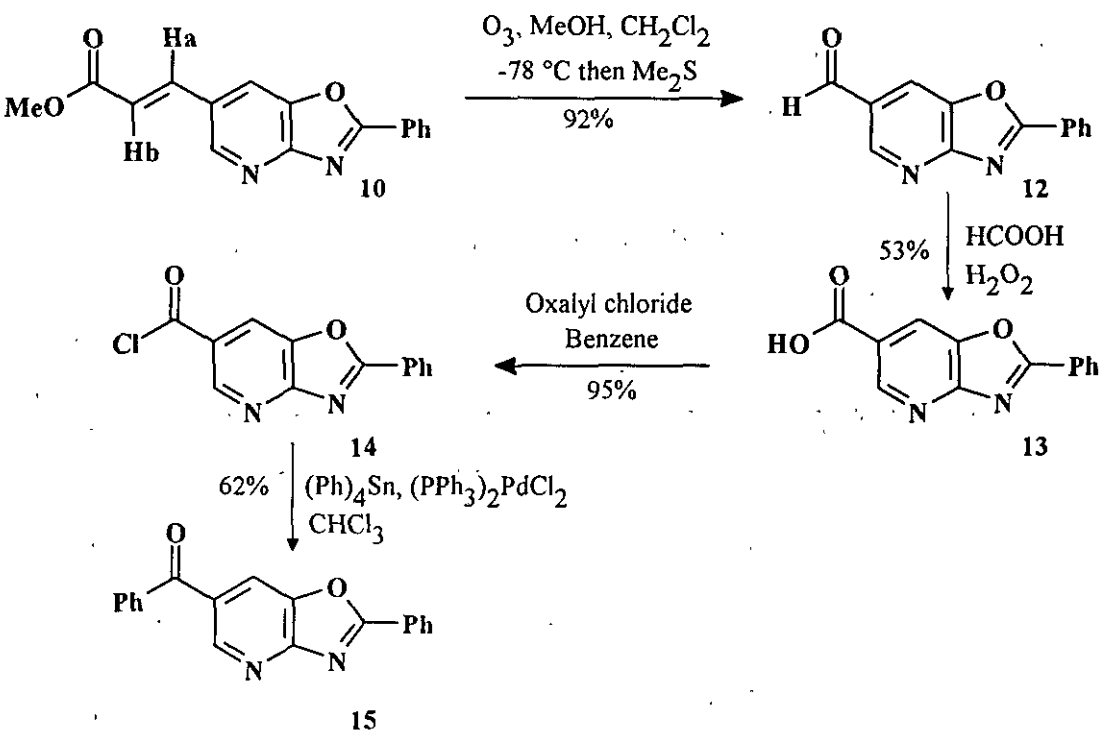
	Cpd	R	catalyst	solvent	yield %
A	7		$Pd(Ph_3)_4$, LiCl	Toluene	97
A	8		$Pd(Ph_3)_4$, LiCl	Toluene	81
A	9		$PdCl_2(PPh_3)_2$	HMPA	53
B	10		$Pd(OAc)_2$, P(*o*-tol)$_3$	DMF	94
B	11		$Pd(OAc)_2$, DPPE	DMF	82

Compounds (7) and (8) were prepared from commercially available alkyltin reagent (butyl and vinyl) when the compound (9) was obtained from benzyltributyltin which was prepared according a modified proceeding of litterature.[8-10]

Under a variety of normal Heck conditions[11] compounds (10) and (11) were obtained in good yields, respectively from methyl acrylate and butyl vinyl ether, in DMF as solvent with tri-*O*-tolylphosphine or 1,2-bis(diphenylphosphino)ethane as ligands. It should be noted that only the *E*-isomer was detected[12] for compound (10).

Ozonolysis of **10**, using the standard procedure, gave the aldehyde (12) which was oxidized to **13** with hydrogen peroxide in formic acid.[13] The acid chloride (14), prepared by treatment from **13**, was submitted *via* Stille's reaction[14] to the ketone (15), with tetraphenyltin, dichlorobis(triphenyl-phosphine)palladium and chloroform respectively as reagent, catalyst and solvent (Scheme 5). Some tries of direct formylation of **4** with carbon monoxide were unsuccessfull.[11]

Scheme 5



Using commercially or easily available reagents and catalysts, Heck or Stille or Suzuki reactions have been shown to be an efficient method for generating substituted 2-phenyloxazolo[4,5-*b*]pyridines. These compounds are interesting intermediates for the synthesis of potential analgesics. Indeed these derivatives can be modified, then substituted by the aryl piperazine unit.

EXPERIMENTAL

Melting points are uncorreted. ^{1}H Nmr (300 MHz) spectra was run on a Bruker AM 300 WB spectrometer. TMS served as an internal standard. Ir spectra of liquid films or KBr pellets were recorded on a Perkin-Elmer 297 instrument. Mass spectra were registered on a Nermag R-10-10-C apparatus. Analytical thin layer chromatography was performed on Merck $60F_{254}$ silica gel plate. Column chromatography was performed using silica gel 60 (0.063-0.0200 mm, E. Merck) and flash chromatography was conducted with silica gel (0.040-0.063 mm, E. Merck). All air- and moisture-sensitive reactions were conducted under a prepurified argon atmosphere in flame-dried glassware. Anhydrous solvents or reagents were transferred *via* syringe. Tetrakis(triphenylphosphine)palladium (0) was prepared by using the literature procedure.[15]

6-Bromooxazolo[4,5-*b*]pyridin-2(3*H*)-one (2). To a stirred solution of oxazolo[4,5-*b*]pyridin-2(3*H*)-one (**1**) (5 g, 23.25 mmol) in *N,N*-dimethylformamide (DMF) (100 ml) was added slowly bromine (1.28 ml, 25.6 mmol). The mixture was kept 2 h at room temperature Water (50 ml) was added to the mixture, the precipitate was filtered, dried over P_2O_5 to give 8.02 g (90%) of **2** as a crystalline product; mp 229-230 °C (lit.,[3] 230-232 °C).

2-Amino-5-bromo-3-hydroxypyridine (3). To a stirred solution of NaOH (10%) (300 ml) was added at room temperature compound (**3**) (3 g, 13 9 mmol). The mixture was kept under reflux for 8 h. A solution of HCl (10%) was added at room temperature until a precipitate appeared. After filtration 2.42 g (92%) of **3** was obtained as a crystalline product; mp > 250 °C (EtOH-H_2O); ir (KBr) 3400-3100 (OH), 3440 and 3340 (NH_2) cm^{-1}; ^{1}H nmr (DMSO-d_6 + D_2O) δ · 6.91 (d, $J_{4\,6}$ = 1 5 Hz, 1H, **H-4**), 7.45 (d ,$J_{6\,4}$=1.5 Hz, 1H,

H-6); ms : *m/z* 189 (M+1); *Anal.* Calcd for $C_5H_5N_2OBr$: C, 31.77; H, 2.67; N, 14 82; Br, 42.27. Found: C, 31.50; H, 2.50; N, 14 80; Br, 42 20.

6-Bromo-2-phenyloxazolo[4,5-*b*]pyridine (4). A solution of phosphorous pentoxide (3.5 g, 24.6 mmol) and hexamethyldisiloxane (8.5 ml, 40 mmol) in 1,2-dichloroethane (17 ml) was heated under reflux for 2 h. Then the solvent was removed under pressure, 2-amino-5-bromo-3-hydroxypyridine (**3**) (1.1 g, 5.8 mmol) and benzoic acid (1.1 g, 8.7 mmol) were added to the residue. The mixture was heated at 200 °C for 3 h. After cooling to room temperature the solution was poured in a mixture of ice and water, the pH was adjusted until 7-8 with saturated aqueous sodium hydrogen carbonate. The precipitate was filtered, washed several time with water to afford 4.6 g (91%) of **4** as crystalline compound; mp 187-189 °C (*i*PrOH-H_2O); ir (KBr) 1275 (C-O-C) cm^{-1}; ^1H nmr ($CDCl_3$) δ : 7.51-7.61 (m, 3H, $\mathbf{H}_{arom}$), 8.02 (d, $J_{7,5}$ = 2.2 Hz, **H-7**), 8 30 (d, J = 7.4 Hz, 2H, $\mathbf{H}_{arom}$), 8.63 (d, $J_{5,7}$ = 2.2 Hz, 1H, **H-5**); ms : *m/z* 275 (M+1). *Anal.* Calcd for $C_{12}H_7N_2OBr$: C, 52.39; H, 2.56; N, 10.18; Br, 29.04. Found: C, 52.30; H, 2.50; N, 10.15; Br, 29.00.

6-Phenyl-2-phenyloxazolo[4,5-*b*]pyridine (5). To a solution of **4** (100 mg, 0.364 mmol) in toluene (50 ml) was added successively tetrakis(triphenylphosphine)palladium (0) (13 mg, 0.011 mmol), phenylboronic acid (133 mg, 1 09 mmol) dissolved in ethanol (2 ml) and 2M aqueous solution of sodium carbonate (2.5 ml). The mixture was kept under reflux for 8 h. After cooling, the solvent was evaporated, the residue was partitioned between CH_2Cl_2 (20ml) and water (20 ml). The organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by chromatography (eluent : CH_2Cl_2) to give 91 mg (92%) of **5** as a crystalline product ; mp 149-150 °C (EtOH-H_2O) ; ir (KBr) 1275 (C-O-C-O-C) cm^{-1} ; ^1H nmr ($CDCl_3$) δ : 7.43-7.68 (m, 8H, $\mathbf{H}_{arom}$), 8.04 (d, $J_{7,5}$ = 2.1 Hz, 1H, **H-7**), 8.33-8.37 (m, 2H, $\mathbf{H}_{arom}$), 8 83 (d, $J_{5,7}$ = 2.1 Hz, 1H, **H-5**); ms . *m/z* 273 (M+1). *Anal.* Calcd for $C_{18}H_{12}N_2O$: C, 79.40, H, 4.44; N, 10.19 Found: C, 79.30, H, 4 40; N, 10.12.

6-Cyano-2-phenyloxazolo[4,5-*b*]pyridine (6). To a stirred solution of compound (**4**) (100 mg, 0.36 mmol) in 1-methyl-2-pyrrolidinone (2 ml) was added CuCN (202 mg, 2.26 mmol). The mixture was kept for 12 h under reflux. After cooling, an aqueous solution of NH_4OH (30%) (5 ml), was added, the mixture

was extracted with CH_2Cl_2 (10 ml) The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by chromatography (eluent: CH_2Cl_2) to give 4,9 mg (51%) of **6** as a crystalline compound ; mp 248-249 °C (EtOH-H_2O) ; ir (KBr) 2220 (C≡N) cm^{-1}, ^1H nmr ($CDCl_3$) δ : 7.49-7.61 (m, 3H, $\mathbf{H}_{arom}$), 8.06 (d, $J_{7,5}$ = 2.2 Hz, 1H, **H-7**), 8.26-8 30 (m, 2H, $\mathbf{H}_{arom}$), 8.79 (d, $J_{5,7}$ = 2.2 Hz, 1H, **H-5**); ms : *m/z* 222 (M+1). *Anal.* Calcd for $C_{13}H_7N_3O$: C, 70.58; H, 3 19; N, 18.99. Found: C, 70.40; H, 3.00; N, 18.90.

6-Vinyl-2-phenyloxazolo[4,5-*b*]pyridine (7). To a mixture of **4** (200 mg, 0.73 mmol) in toluene (7 ml) was added successively in that order vinyltributyltin (0.64 ml, 2.19 mmol), lithium chloride (90 mg, 2.12 mmol) and tetrakistriphenylphosphinepalladium (0) (17 mg, 0.028 mmol) The mixture was kept for 3 h under reflux. After cooling, the solvent was removed under pressure After addition of water (10 ml), the resulting mixture was extracted with CH_2Cl_2 (10 ml) The organic layer was dried over $MgSO_4$ and concentrated, the residue was purified by chromatography (eluent : CH_2Cl_2/AcOEt 95/5) to give 157 mg (97%) of **7** as a crystalline product ; mp 127-128 °C (*i*PrOH); ir (KBr) 1275 (C-O-C) cm^{-1}; ^1H nmr ($CDCl_3$) δ : 5.38 (d, J = 11.0 Hz, 1H, $\mathbf{H}_{vinyl}$), 5.81 (d, J = 17 7 Hz, 1H, $\mathbf{H}_{vinyl}$), 6.81 (dd, J = 11.0, 17.7 Hz, $\mathbf{H}_{vinyl}$), 7.46-7.54 (m, 3H, $\mathbf{H}_{arom}$), 7.86 (d, $J_{7,5}$ = 2.0 Hz, 1H, **H-7**), 8.23-8.28 (m, 2H, $\mathbf{H}_{arom}$), 8.54 (d , $J_{5,7}$ = 2.0 Hz, 1H, **H-5**); ms : *m/z* 223 (M+1) *Anal.* Calcd for $C_{14}H_{10}N_2O$: C, 75.66, H, 4.54; N, 12.60. Found: C, 75.60; H, 4.50; N, 12.50.

6-Butyl-2-phenyloxazolo[4,5-*b*]pyridine (8). Experimental conditions and also purification were the same as described for the preparation of compound (7) We had used tetrabutyltin instead of vinyl tributyltin. 81 % of **8** was obtained as a crystalline compound ; mp 69-71 °C (EtOH-H_2O) ; ir (KBr) 1275 (C-O-C) cm^{-1}; ^1H nmr ($CDCl_3$) δ : 0.88-0.98 (m, 3H, $\mathbf{CH_3}$), 1.25-1.48 (m, 2H, $\mathbf{CH_2}$), 1.61-1.74 (m, 2H, $\mathbf{CH_2}$), 2.78 (dd, J = 8 1, 7.9 Hz, 2H, $\mathbf{CH_2}$), 7.48-7.58 (m, 3H, $\mathbf{H}_{arom}$), 7.67 (d, $J_{7,5}$ = 1.5 Hz, 1H, **H-7**), 8.28-8.52 (m, 2H, $\mathbf{H}_{arom}$), 8.42 (d, $J_{5,7}$ = 1 5 Hz, 1H, **H-5**), ms : *m/z* 253 (M+1). *Anal.* Calcd for $C_{16}H_{16}N_2O$· C, 76.16; H, 6.39; N, 11.10. Found. C, 76.05; H, 6 30, N, 11.08.

6-Benzyl-2-phenyloxazolo[4,5-*b*]pyridine (9). To a stirred solution of **4** (100 mg, 0.36 mmol) in hexamethylphosphoramide (0.5 ml) was added benzyltributyltin[9] (144 mg, 0.37 mmol) and dichlorobis(triphenylphosphine)palladium .(II) (10 mg, 0.014 mmol) and the mixture heated to 65° C for 6 h. Upon cooling, the reaction was diluted with water (10 ml) and extracted with AcOEt (20 ml). The organic phase was dried over $MgSO_4$ and was concentrated, the crude product was purified by chromatography (eluent : CH_2Cl_2/AcOEt 95/5) to give 55 mg (53%) of **9** as a crystalline product ; mp 173°C (*i*PrOH-H_2O) ; ir (KBr) 1275 (C-O-C) cm^{-1}, ^1H nmr ($CDCl_3$) δ · 4.16 (s, 2H, $\mathbf{CH_2}$), 7.20-7.35 (m, 5H, $\mathbf{H_{arom}}$), 7.52-7.58 (m, 3H, $\mathbf{H_{arom}}$), 7.62 (d, $J_{7,5}$ = 1.7 Hz, 1H, **H-7**), 8.25-8.30 (m, 2H, $\mathbf{H_{arom}}$), 8.50 (d, $J_{5,7}$ = 1.7 Hz, 1H, **H-5**), ms : *m/z* 287 (M+1). *Anal.* Calcd for $C_{19}H_{14}N_2O$: C, 79 70; H, 4.93; N, 9.78. Found: C, 79.50; H, 4.90; N, 9.70.

(*E*)-3-(2-Phenyloxazolo[4,5-*b*]pyridin-6-yl)acrylic acid methyl ester (10). To a stirred solution of **4** (500 mg, 1.8 mmol) in *N,N*-dimethylformamide (15 ml) were added methyl acrylate (0.19 ml, 2.16 mmol), triethylamine (0.300 ml, 2.16 mml), palladium (II) acetate (5 mg, 0.02 mmol) and tri-*O*-tolylphosphine (26 mg, 0.08 mmol). The mixture was kept for 3 h under reflux. After concentration under pressure, the residue was partitioned between CH_2Cl_2 (30ml) and water (20 ml) The organic layer was dried over $MgSO_4$ and concentrated Purification by chromatography (eluent : CH_2Cl_2) furnished 469 mg (94%) of **10** as a crystalline compound ; mp 214-216 °C (EtOH-H_2O) , ir (KBr) 1715 (C=O) cm^{-1} ; ^1H nmr ($CDCl_3$) δ : 3.64 (s, 3H, $\mathbf{OCH_3}$), 6.55 (d, $J_{a,b}$ = 16.2 Hz, 1H, **H-a**), 7.51-7.65 (m, 3H, $\mathbf{H_{arom}}$), 7,86 (d, $J_{b,a}$ = 16.2 Hz, 1H, **H-b**), 8.04.(d, $J_{7,5}$ = 2.2 Hz, 1H, **H-7**), 8.36 (d, J = 8.1 Hz, 2H, $\mathbf{H_{arom}}$), 8.75 (d, $J_{5,7}$ = 2.2 Hz, 1H, **H-5**). ms : *m/z* 281 (M+1). *Anal.* Calcd for $C_{16}H_{12}N_2O_3$: C, 68.57; H, 4.32; N, 9.99. Found. C, 68.55; H, 4.30, N, 9.92.

(2-Phenyloxazolo[4,5-*b*]pyridin-6-yl)ethanone (11). Experimental conditions were the same as described for the preparation of **10** We used propyl vinyl ether instead of methyl acrylate and 1,2-bis(diphenylphosphino)ethane (DPPE) instead of tri-*O*-tolylphosphine. After 3 h under reflux, the conversion was complete and the reaction mixture was cooled to room temperature, HCl (5%,) was added

and after another 30 mn of stirring the mixture was poured into CH_2Cl_2. The organic layer was dried over $MgSO_4$ and concentrated purification by chromatography (eluent CH_2Cl_2/AcOEt 8/2) provided 82% of **11** as a crystalline compound, mp 192-194 °C (EtOH) ; ir (KBr) 1680 (C=O) cm^{-1}, ^1H nmr ($CDCl_3$) δ : 2.72 (s, 3H, CH_3), 7.54-7.66 (m, 3H, H_{arom}), 8.35 (d, J = 9.7 Hz, 2H, H_{arom}), 8.42 (d, $J_{7,5}$ = 1.7 Hz, 1H, H-7), 9.18 (d, $J_{5,7}$ = 1.7 Hz, 1H, H-5); ms: *m/z* 239 (M+1). *Anal.* Calcd for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.55; H, 4.20; N, 11.72.

(2-Phenyloxazolo[4,5-*b*]pyridin-6-yl)carboxaldehyde (12). Compound (**10**) (500 mg, 1.8 mmol) was dissolved in a solution of CH_2Cl_2 and MeOH (4/1) (10 ml) at -78 °C and placed in an ozonolysis apparatus. After 10 mn of reaction, the excess of ozone was removed by nitrogen stream and methyl sulfide (1 ml) was added to the solution, which was then allowed to warm up to room temperature. The solvents were evaporated. Chromatography (eluent . CH_2Cl_2/MeOH 98/2) of the residue gave 375 mg (92 %) of **11** as a crystalline compound , mp 207-209 °C (EtOH-H_2O) ; ir (KBr) 1680 (C=O) cm^{-1}; ^1H nmr ($CDCl_3$) δ : 7.56-7.66 (m, 3H, H_{arom}), 8.32-8.39 (m, 3H, H_{arom} + H-7), 9.07 (d, $J_{5,7}$ = 2.2 Hz, 1H, H-5), 10 21 (s, 1H, CHO) ; ms : *m/z* 225 (M+1). *Anal.* Calcd for $C_{13}H_8N_2O_2$. C, 69.64; H, 3.60; N, 12.49. Found: C, 69.60; H, 3.58, N, 12.40.

(2-Phenyloxazolo[4,5-*b*]pyridin-6-yl)methanoic acid (13). To a stirred solution of **12** (182 mg, 1 mmol) dissolved in formic acid (1 ml), was added at 0 °C hydrogen peroxide (0.3 ml, 3 mmol) The mixture was kept for 8 h at 5 °C. The precipitate was filtrated, washed with water and dried to give 104 mg (53%) of **13** as a crystalline compound; mp >250 °C (EtOH) ; ir (KBr) 3600-3200 (OH); 1720 (C=O) cm^{-1}; ^1H nmr (DMSO-d_6 + D_2O) δ : 7.63-7.75 (m, 3H, H_{arom}), 8.28 (m, J = 7.4 Hz, 1H, H_{arom}), 8.62 (d, $J_{7,5}$ = 2.2 Hz, 1H, H-7), 9.07 (d, $J_{5,7}$ = 2.2 Hz, 1H, H-5). *Anal.* Calcd for $C_{13}H_8N_2O_3$: C, 65.00; H, 3.35; N, 11.66. Found. C, 65.04; H, 3.40; N, 11.70

(2-Phenyloxazolo[4,5-*b*]pyridin-6-yl)methanoyl chloride (14). Compound (**13**) (200 mg, 1.1 mmol) was dissolved in benzene (5 ml), then was added oxalyl chloride (0.12 ml, 1.1 mmol). The reaction was kept for 8 h under reflux After cooling, the mixture was concentrated under reduced pressure. After addition of

water (10 ml), the resulting mixture was extracted with CH_2Cl_2 (20 ml), the organic layers were dried over $MgSO_4$ and concentrated. Purification was not neccessary and **14** was obtained with a yield of 95% as a crystalline compound. This product was used in the next step whithout purification; mp 160-162 °C;. ir (KBr) 1750 (C=O) cm^{-1}; ^1H nmr ($CDCl_3$) δ :7.58-7.72 (m, 4H, $\mathbf{H}_{arom}$), 8.37-8.42 (m, 2H, **H-7** + $\mathbf{H}_{arom}$), 8.57 (d, $J_{5,7}$ = 1.5 Hz, 1H, **H-5**).

(2-Phenyloxazolo[4,5-*b*]pyridin-6-yl)phenone (15). This compound was prepared according to the same methodology as described for **9**. Hexamethylphosphoramide and benzyltributyltin was replaced respectively by chloroform and tetraphenyltin, catalyst was the same. After 18 h of reaction under reflux, then cooling, the crude mixture was diluted with water (10 ml) and extracted with AcOEt. The organic layer was dired over $MgSO_4$, then evaporated. The ketone (**15**), after purification by chromatography (eluent : CH_2Cl_2), was obtained with a yield of 62 % as a crystalline compound; mp 189-191 °C (EtOH-H_2O) ; ir (KBr) 1650 (C=O) cm^{-1}; ^1H nmr ($CDCl_3$) δ : 7 46-7.63 (m, 6H, $\mathbf{H}_{arom}$), 7.77-7.82 (m, 2H, $\mathbf{H}_{arom}$), 8.29-8.33 (m, 3H, **H-7** + $\mathbf{H}_{arom}$), 8.95 (d, $J_{5\,7}$ = 1.5 Hz, 1H, **H-5**); ms: *m/z* 301 (M+1). *Anal.* Calcd for $C_{19}H_{12}N_2O_2$: C, 76.07; H, 4.03; N, 9.34. Found: C, 76.04; H, 4 00, N, 9.30.

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10. Tributyltin hydride (2 g, 6.87 mmol) was added to a solution of THF (56 ml) at -20 °C then was added lithium diisopropylamide (1.6 M in THF) (3.44 ml) After 30 min at -20 °C, this solution was transferred under argon to benzyl chloride (0.8 ml, 6.9 mmol). The reaction was kept for 1 h at -20 °C then to room temperature. Evaporation following by chromatography (eluent. petroleum ether) furnished benzyltributyltin with a yield of 50%.

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