REACTIVITY OF HETEROCYCLIC ENAMINONES : REGIOSELECTIVE SYNTHESIS OF SOME PYRIDOBENZODIAZEPINES AND IMIDAZO-PYRIDINES

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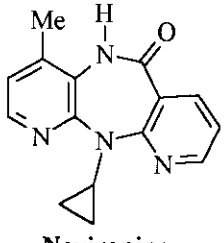
Abstract - Reactivity of enaminones derived from various diaminopyridines toward electrophilic carbons (imines, carbodiimides, isocyanates) is reported. The reactions leading to diazepinic or imidazolic ring systems are shown to be dependent of the electrophilic species as well as of the position of the nitrogen atom in the heterocyclic ring.

Introduction

Derivatives of diannelated 1,4-diazepines are known to exhibit a wide variety of biological activities such as antidepressive,[1] analgesic,[2] antipsychotic,[1-3] antihistaminic,[1,2,4] antimuscarinic,[1,2,5] and antiviral[6] activities. Of particular interest is nevirapine which represents a potent non-nucleoside HIV reverse transcriptase inhibitor.[7]

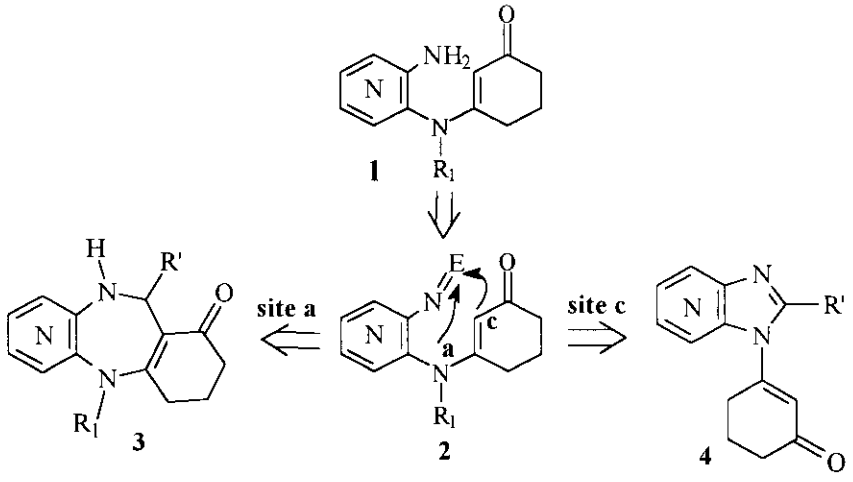


Nevirapine

As a part of our program concerning the synthesis of biologically active heterocycles, we were interested in the synthesis of partial hydrogenated pyridobenzodiazepines which could be further implicated in the elaboration of analogs of nevirapine.[8] Our strategy resides in the use of heterocyclic enaminones as synthetic intermediates. Particularity of this enaminone system (N^a-C^b=C^c-C^d=O^e) resides in both nucleophilic (sites a, c, e) and electrophilic properties (sites b, d). These multiplicity of sites implicates a wide variety of applications in heterocyclic chemistry.[9] While the chemistry of aromatic enaminones has been extensively studied,[10] the chemistry of heterocyclic ones is less described.[11] Presence of the heterocycle in such systems can modulate their reactivity and can induce high regiolectivities. This represents an interesting field for the development of new methodologies in heterocyclic synthesis. In this context, we have already described the synthesis of polyfused indolones from various pyridinic enaminones.[12] Regioselectivities of these reactions were found to be highly dependent of the nature of the heterocycles as well as of experimental conditions.[13]

In continuation of these investigations, we describe now the possibility to generate electrophilic species such as imines, isocyanates, and carbodiimides (compounds (**2**)) from heterocyclic enaminones derived from diaminopyridines (**1**) which can react either with the two nucleophilic sites (a,c) of the enaminone part to form diazepinic ring (**3**) or imidazolic ring (**4**). Considering both the position of the intracyclic nitrogen and the nature of the electrophilic species, the reactions are susceptible to evolve selectively to one or the other heterocyclic system.

Scheme 1

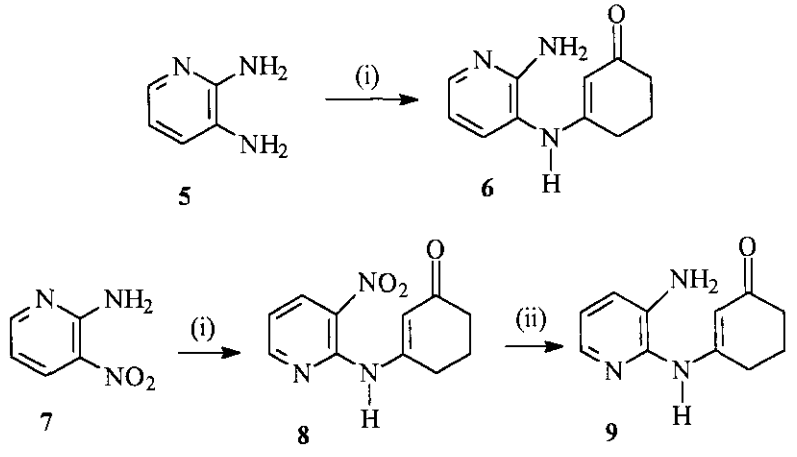


imines, isocyanates, carbodiimides

Results and discussion

The required starting material (compound (**6**)) was obtained regioselectively in one step from 2,3-diaminopyridine (**5**) and 1,3-cyclohexanedione in refluxing toluene (79%). Structural determination of this compound was made by ^{1}H and ^{13}C NMR which showed the characteristic signals of the enaminone system.[12] Determination of the regioselectivy on the 3-amino group to give **6** was clearly demonstrated by the synthesis of the regioisomer (**9**) which was obtained specifically in two steps from 2-amino-3-nitropyridine (**7**) using the same method to give the nitro derivative (**8**) in 41% yield, followed by catalytic hydrogenation to give **9** in a quantitative manner.[14] For this compound, ^{1}H and ^{13}C NMR spectra showed differences with those obtained for **6** confirming the unambigous assignement for structure (**6**).

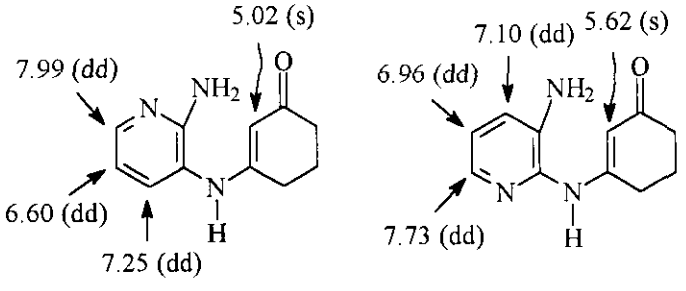
Scheme 2



(*i*) 1,3-cyclohexanedione, toluene, PTS, reflux
- 1 h for **6**, 79%
-3 h for **8**, 41%

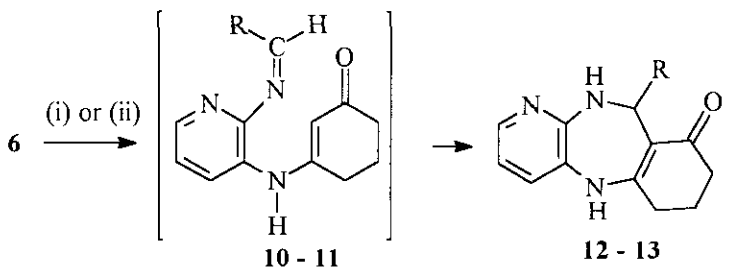
(ii) H_2, 5% Pd-C, MeOH

Characteristic ^{1}H chemical shifts (δ) for 6 and 9



Reactivity of enaminone (6) : Enaminone (**6**) treated with acetaldehyde and benzaldehyde using classical conditions [9] (ethanol, acidic media) led to the formation of the intermediary imines (**10**, **11**), which further cyclized into the pyridodiazepines (**12**, **13**). However, the compound (**6**) was poorly reactive in these conditions and the cyclized compounds were only obtained in 24 and 12 % after one week. In the case of benzaldehyde, the yield of the reaction, as well as the reactions times, were optimized by using a pyridinium salt (method b).[15]

Scheme 3



(i) RCHO, EtOH, $MeCO_2H$ (cat), 1 week

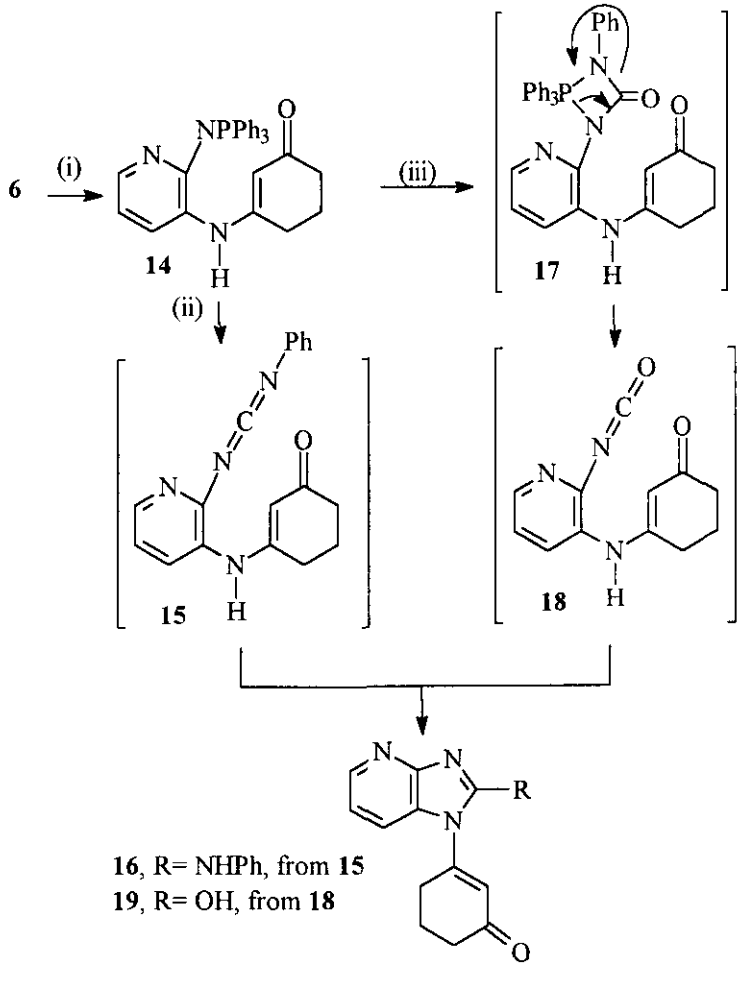
(ii) $SOCl_2$, RCHO, CH_2Cl_2, 0°C, 10 h

	12 R = Me	**13 R = Ph**
(i)	one week, 24%	one week, 12%
(ii)	--------	10 h, 63%

We then turned our interest to the reactivity of the carbodiimide (**15**) and the isocyanate (**18**) derived from **6** (Scheme 4). Iminophosphorane (**14**) was obtained by reaction of **6** with a mixture of carbon tetrachloride, triphenylphosphine, and triethylamine at room temperature. Subsequent aza-Wittig reaction of **14** with phenyl isocyanate at room temperature led to a carbodiimide (**15**) as a transient intermediate which spontaneously cyclised to give specifically the imidazo[2,3-*b*]pyridine (**16**). No evidence for the formation of the pyridobenzodiazepine nucleus was found. Structural determination of **16** was made on the basis of MS data with a molecular ion at *m/z* 304 and on NMR data. ^{1}H NMR spectra of **16** showed a singlet at δ 6.23 indicating the presence of the vinylic proton. Confirmation of this determination was made by examination of its DEPT spectra which indicated the presence of only six quaternary carbons (δ : 128.9, 138.7, 151.2, 154.4, 155.3, 199.5), instead of seven quaternary carbons for pyridobenzodiazepinic ring system. When the same aza-Wittig reaction was conducted in refluxing toluene, imidazopyridine (**19**) was

isolated as the sole reaction product. This compound was identified by MS ($M^{+\cdot}$ m/z 229) and by NMR. As in the case of **16**, its ^{1}H NMR spectra showed a singlet at δ 6.25 (vinylic proton), while the DEPT experiment indicated the presence of five quaternary carbons (δ : 122.9, 144.0, 152.3, 155.3, 199.0), instead of six for the pyridobenzodiazepine derivative. The hydroxy form of this compound was also demonstrated by NMR with δ_{OH} 11.8 as a broad singlet and absence of the lactam signal in ^{13}C NMR. Formation of **19** resulted from the cyclization of the intermediary isocyanate (**18**). This species was formed from the unstable species (**17**) which undergoes elimination of $RN{=}PPh_3$.[16]

Scheme 4

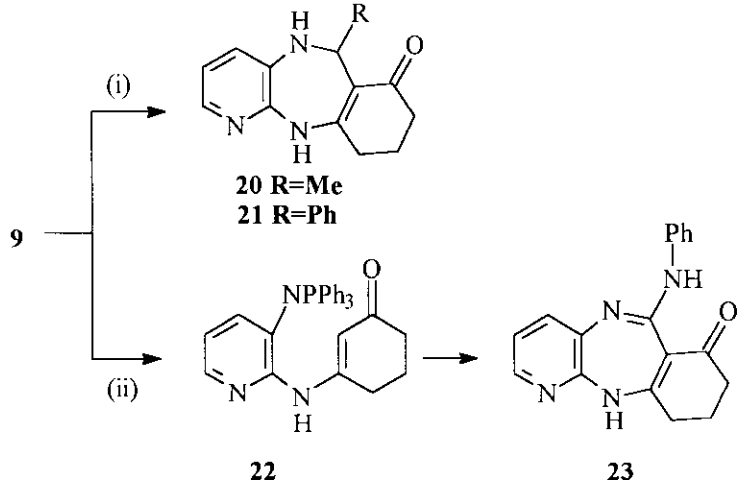


(i) PPh_3, Et_3N, MeCN, CCl_4 / rt /12 h
(ii) PhNCO, toluene, rt, 2 h
(iii) PhNCO, toluene, reflux, 2 h

Reactivity of enaminone (9) : In order to get some informations on the influence of the position of the intracyclic nitrogen on the reactivity of such enaminones, we have investigated the reactivity of the second

regioisomere (**9**). In this case, **9** reacted with acetaldehyde or benzaldehyde in ethanol (with a catalytic amount of acetic acid) to give the corresponding pyridobenzodiazepines (**20**) and (**21**) in only 1 hour and with 80% and 85% yields respectively. Formation of the iminophosphorane (**22**) was also more effective (only 45 minutes, 79%). Subsequent reaction of **22** under aza-Wittig reaction at room temperature led through the intermediary carbodiimide to the pyridobenzodiazepine (**23**). When the same reaction was conducted in refluxing toluene, no clear result was observed (compound (**23**) was only detected as a minor product by CCM from the crude reaction mixture). Structural determination of **23** was performed according to the same criteria described for **16**, **19**. ^{1}H NMR spectra showed the disparition of the vinylic proton in the field of 6.00-6.50 ppm, while the DEPT data indicated the presence of seven quaternary carbons (δ : 114.1, 136.6, 140.1, 148.6, 154.2, 172.8, 196.6) instead of only six for an imidazopyridinic ring system.

Scheme 5



(i) RCHO, EtOH, AcOH, 1 h
(ii) a: PPh_3, Et_3N, MeCN, CCl_4 / rt /12 h
b: PhNCO, toluene, rt, 2 h

These reactions showed great differences of reactivity between the two regioisomers. In each case, the C-2 position of the enaminone system (site c) can react with imine intermediates but with differents reaction times which probably are correlated to the facility of formation of imine (deactivated starting amino group for **6**). In the cases of the carbodiimide or isocyanate transient species, the reactivity of the enaminone system (sites a or c) is greatly related to the nature of the heterocycle which can deactivate the nucleophilic character of the nitrogen of the enaminone. In such case, the C-2 position of this system possesses a preferential reactivity toward the electrophiles leading to the formation of pyridobenzodiazepines

(**23**). When the nitrogen is not deactivated, the amino group reacts preferentially with the electrophiles leading to the formation of the imidazopyridines (**16**, **19**). Finally, in conclusion, we have described specific synthesis of pyridobenzodiazepines and imidazopyridines from heterocyclic enaminones as starting materials. In addition, the differences of reactivity observed in the different cases, give an addtional methodology to confirm the regioselectivity of the synthesis of enaminone (**6**) from starting 2,3-diaminopyridine.

EXPERIMENTAL

Melting points were determined on a Büchi capillary melting point apparatus and are not corrected. Elemental analysis was performed by the Microanalytical Center, ENSCM, Montpellier. Spectral measurements were taken using the following instruments: ^{1}H-NMR spectra were taken on a Brüker AC 100 instrument; ^{13}C NMR spectra were obtained at 26°C with proton noise decoupling at 25 MHz with a Brüker AC 100 instrument, an asterisk (*) indicates that the values can be inversed. All NMR chemical shifts are reported in δ (ppm) values relative to residual chloroforme. MS were recorded on a LKB 2091 spectrometer at 15 eV [θ (source)=180°C].

3-[(2-Amino-3-pyridinyl)amino]cyclohex-2-en-1-one (6). A solution of 2,3-diaminopyridine (**5**) (1 g, 9.1 mmol), 1,3-cyclohexanedione (1.2 g, 9.1 mmol), and *p*-toluenesulfonic acid monohydrate (70 mg, 0.39 mmol) in 265 mL of anhydrous toluene was refluxed with a Dean-Stark for 3 h. After beeing cooled, the solution was basified with $NaHCO_3$ (10% in water) and extracted with dichloromethane. Organic layers were dried over sodium sulfate and evaporated in vacuo. Chrmatography on silica gel eluted with CH_2Cl_2/MeOH (95/5) gave 1.46 g of **6**; yield 79%; brown oil; ^{1}H-NMR ($CDCl_3$, 100 MHz); δ 1.93 (m, 2H, H-5), 2.27 (m, 2H, H-6*), 2.48 (m, 2H, H-4*), 4.95 (br s, NH_2), 5.02 (s, 1H, H-2), 6.61 (dd, J = 7.6 and 4.9 Hz, 1H, H-12), 7.26 (dd, J = 7.6 and 1.6 Hz, 1H, H-13), 7.38 (br s, NH), 7.92 (dd, J = 4.9 and 1.6 Hz, 1H, H-11); ^{13}H-NMR ($CDCl_3$, 25 MHz); δ 21.5, 28.3, 36.0, 98.3, 113.4, 118.5, 135.4, 145.8, 154.7, 165.4, 198.3); Anal. Calcd for $C_{11}H_{13}N_3O$: C, 65.01; H, 6.45; N, 20.67. Found : C, 65.11; H, 6.39; N, 20.56

3-[(3-Nitro-2-pyridinyl)amino]cyclohex-2-en-1-one (8). This compound was obtained in 41% yield according the procedure employed for the synthesis of **6**, using 2-amino-3-nitropyridine (**7**) as starting material; yellow oil; ^{1}H-NMR ($CDCl_3$, 100 MHz); δ : 2.14 (m, 2H, H-5), 2.45 (t, J = 5.6 Hz, H-6*), 2.67 (t, J = 5.9 Hz, H-4*), 7.06 (dd, J = 8.1 and 4.7 Hz, 1H, H-11), 7.31 (s, 1H, H-2), 8.56 (m, 2H, H-10, H-12), 9,81 (br s, NH); ^{13}H-NMR ($CDCl_3$, 25 MHz) δ :21.5, 30.3, 36.4, 111.6, 116.5, 130.5, 135.0, 148.0, 154.1, 154.4, 199.6; Anal. Calcd for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.75; N, 18.02. Found : C, 56.49; H, 5.51;

N, 18.14.

3-[(3-Amino-2-pyridinyl)amino]cyclohex-2-en-1-one (9). A solution of **8** (1 g, 4.29 mmol) in absolute ethanol (50 mL) was hydrogenated on a Palladium support (Pd/C 5%, 100 mg) at atmospheric pressure. After the absortion of hydrogen was complete, the solution was filtred, and the filtrate evaporated *in vacuo* to give 0.84 g of **9**. The crude product was used without further purification. An analytical sample was obtained by recrystallization from ether; total yield 96%; mp 174-176°C; ^{1}H-NMR ($CDCl_3$, 100 MHz); δ 1.87 (m, 2H, H-5), 2.22, (t, J = 5.6 Hz, 2H, H-6*), 2.47 (t, J = 6.0 Hz, 2H, H-4*), 4.15 (br s, 2H, NH_2), 5.47 (s, 1H, H-2), 6.85 (dd, J = 7.9 and 4.4 Hz, 1H, H-11), 7.00 (dd, J = 7.9 and 2.0 Hz, 1H, H-12), 7.67 (dd, J = 4.4 and 2.0 Hz 1H, H-10), 8.14, (br s, NH); ^{13}C-NMR ($CDCl_3$, 25 MHz); δ 21.8, 28.7, 36.3, 101.8, 121.8, 124.0, 136.2, 137.4, 138.8, 162.6, 199.3. Anal. Calcd for : $C_{11}H_{13}N_3O$: C, 65.01; H, 6.45; N, 20.67. Found : C, 64.89; H, 6.33; N, 20.71

5,6,7,8,10,11-Hexahydro-10-methylpyrido[3,2-*b*][1,4]benzodiazepin-9-one (12) : A solution of **6** (1 g, 4,92 mmol) in absolute ethanol (30 mL) is slowly added to a stirred solution of acetaldehyde (216 mg, 4,92 mmol) and a catalytic amount of acetic acid in absolute ethanol (15 mL). This solution was stirred at rt. After one week, the solvents were evaporated, and the residual oil was chromatographed on silica gel eluted with a CH_2Cl_2/MeOH (95/5) mixture to give 0.27 g of **12**; yield 24%; mp > 260 °C (chloroform); ^{1}H-NMR (CD_3OD, 100 MHz); δ 0.95 (d, J = 8.8 Hz, 3H, CH_3), 1.83 (m, 2H, H-7), 2.18 (t, J = 6.5 Hz, 2H, H-6*), 2.48 (t, J = 6.3 Hz, 2H, H-8*), 4.87 (m, 1H, H-10), 6.64 (dd, J = 8.0 and 4.8 Hz, 1H, H-3), 7.17(dd, J = 8.0 and 1.4 Hz, 1H, H-4), 7,58 (dd, J = 4.8 and 1.4 Hz, 1H, H-2); ^{13}C-NMR (CD_3OD, 25 MHz); δ 20.9, 21.8, 30.4, 35.4, 46.3, 114.4, 115.7, 125.9, 126.9, 140.8, 149.5, 156.7, 194.8. Anal. Calcd for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33. Found : C, 68.02; H, 6.45; N, 18.16.

5,6,7,8,10,11-Hexahydro-10-phenylpyrido[3,2-*b*][1,4]benzodiazepin-9-one (13) : This compound was obtained following the method employed for **12** using benzaldehyde as starting material with 12 % yield.
Method b: a solution of pyridine (1 mL, 12 mmol) in dichloromethane (5 mL) was added dropwise to a solution of thionyl chloride (1 mL, 14,7 mmol) in dichloromethane (11 mL) maintained at 0°C. Then benzaldehyde (1.25 mL, 12.3 mmol) was introduced in the solution. This mixture was allowed to warm up to rt for 1h. The enaminone (**6**) (5 g, 24.6 mmol) was then slowly added and stirring at rt was maintened overnight. The solvent was evaporated under reduced pressure and the crude product chromatographed on silica gel using a CH_2Cl_2/MeOH (95/5) mixture as eluent to give 2.2 g of **13**; yield 63 %; brown oil; ^{1}H-NMR (DMSO-D_6, 100 MHz); δ 1.96 (m, 2H, H-7), 2.27 (m, 2H, H-6*), 2.69 (m, 2H, H-8*), 5.82 (d, J = 6.3, 1H, H-10), 6.58 (dd, J = 7.7 and 4.7 Hz, 1H, H-3), 6.88 (d, J = 6.3 Hz, 1H, H-11 (NH)), 7.05-7.25 (m, 6H, Hphenyl and H-4), 7.59 (dd, J = 4.7 and 1.3 Hz, 1H, H-2), 8.84 (br s, 1H, H-5 (NH); ^{13}C-NMR

(DMSO-D_6, 25 MHz); δ 21.3, 30.5, 36.0, 53.1, 111.8, 115.0, 125.7, 126.0, 126.3, 127.2 (2C), 127.8 (2C), 141.1, 144.2, 150.5, 156.7, 192.7. Anal. Calcd for $C_{18}H_{17}N_3O$: C, 74.20; H, 5.88; N, 14.42. Found : C, 74.31; H, 6.01; N, 14.35.

3-[(2-Triphenylphosphoranylidene)amino-3-pyridinyl)amino]cyclohex-2-en-1-one (14). To a solution of 0.5 g (2.46 mmol) of enaminone (**6**) in 6.3 mL of acetonitrile, were added triphenylphosphine (1.g, 5 mmol), 3.7 mL of triethylamine, and 2.5 mL of CCl_4. The resultant mixture was then stirred at rt overnight. Triethylammonium chloride was separated by filtration, and the filtrate concentrated to dryness. The crude product was chromatographed on silica gel eluted with a mixture AcOEt/MeOH 95/5 to give 0.46 g of **14** in 41% yield; red oil ; MS (m/z, relative intensity) 463 (M^+, 100), 407 (10), 277 (15), 262 (80), 183 (31); ^{1}H-NMR ($CDCl_3$, 100 MHz); δ 2.09 (m, 2H, H-5), 2.47 (t, J = 6.0 Hz, 2H, H-4*), 2.68 (t, J = 5.6 Hz, 2H, H-6*), 6.02 (s, H-2), 6.51 (dd, J = 7.9 and 4.8 Hz, H-12), 7.44 -7.60 (m, 10H), 7.7.-7.97 (m, 7H), 8.04 (br s, NH); ^{13}C-NMR ($CDCl_3$, 25 MHz); δ 21.7, 30.7, 36.4, 100.6, 112.3, 123.4, 128.3 (6C, J^2PC = 12.1 Hz), 129.4 (3C, J^1PC = 100.3 Hz), 131.8 (3C), 131.9 (J^3PC = 9.3 Hz), 132.8 (6C, J^3PC = 9.7 Hz), 140.8, 153.0 (J^2PC = 7.0 Hz), 159.6, 198.2. Anal. Calcd for $C_{29}H_{26}N_3OP$: C, 75.15; H, 5.65; N, 9.07. Found : C, 75.00; H, 5.74; N, 9.21.

1-[3-Oxo-1-cyclohexenyl]-2-aminophenylimidazo[2,3-*b*]pyridine (16). To a stirred solution of iminophosphorane **14** (0.5 g, 1.08 mmol) in dry toluene (20 mL), was added 0.12 mL (1.08 mmol) of phenyl isocyanate. The resulting mixture was stirred for 3 hours at rt. After evaporation of the solvent, the residue was purified be chromatography on silica gel eluted with CH_2Cl_2 to give 0.1 g of **16**; yield 31%; mp 232-234 °C (ether) ; MS (m/z, relative intensity) 304 (74), 276 (39), 248 (100), 209 (31), 171 (24); ^{1}H-NMR (CD_3OD, 100 MHz); δ 2.13 (m, 2H, H-5'), 2.51 (t, J = 6.9 Hz, 2H, H-4'*), 2.78 (t, J = 5.4 Hz, 2H, H-6'*), 6.23 (s, H-2'), 7.00-7.50 (m, 7H), 8.20 (d, J = 5.0 Hz, H-2); ^{13}C-NMR (CD_3OD, 25 MHz); δ 21.5, 28.1, 36.7, 116.2, 116.3, 119.7 (2C), 123.4, 126.0, 128.8 (2C), 128.9, 138.7, 142.8, 151.2, 154.4, 155.3, 199.5. Anal. Calcd for $C_{18}H_{16}N_4O$: C, 71.04; H, 5.30; N, 18.41. Found : C, 70.89; H, 5.32; N, 18.52.

1-[3-Oxo-1-cyclohexenyl]-2-hydroxyimidazo[2,3-*b*]pyridine (19). To a stirred solution of iminophosphorane (**14**) (0.5 g, 1.08 mmol) in dry toluene (20 mL), was added 0.12 mL (1.08 mmol) of phenyl socyanate. The resulting mixture was refluxed for 2 h. After evaporation of the solvent, the residue was purified be chromatography on silica gel eluted with CH_2Cl_2 to give 72 mg of **19**; yield 29%; mp 188-190 °C (methanol); MS (m/z, relative intensity) 229 (100), 187 (15), 173 (46), 135

(46); ^{1}H-NMR ($CDCl_3$, 100 MHz); δ 2.19 (m, 2H, H-5'), 2.56 (t, J = 6.3 Hz, 2H, H-4'*), 3.13 (t, J = 5.8 Hz, 2H, H-6'*), 6.25 (s, H-2'), 7.11 (dd, J = 7.9 and 5.3 Hz, H-3), 7.51 (dd, J = 7.9 and 1.1 Hz, H-4), 8.14 (dd, J = 5.3 and 1.1 Hz, H-2), 11.80 (br s, OH); ^{13}C-NMR ($CDCl_3$, 25 MHz); δ 22.14, 27.6, 37.0, 117.4, 117.5, 120.5, 122.9, 141.6, 144.0, 152.2, 155.3, 199.4. Anal. Calcd for $C_{12}H_{11}N_3O_2$: C, 62.87; H, 4.84; N, 18.33. Found : C, 62.77; H, 4.92; N, 18.49.

5,6,8,9,10,11-Hexahydro-6-methylpyrido[2,3-*b*][1,4]benzodiazepin-7-one (20). This compound was obtained in 80 % yield using the same method employed for the synthesis of **12** using **9** as starting material (reaction time : 1 hour). mp: 108-110 °C (methanol); MS (m/z, rel. intensity) 229 (40), 214 (100), 200 (12); ^{1}H-NMR ($CDCl_3$, 100 MHz); δ 1.99 (m, 2H, H-9), 2.34 (t, J = 5.5 Hz, 2H, H-8*), 2.47 (t, J = 5.3 Hz, 2H, H-10*), 4.00 (brs, NH), 4.89 (m, H-6), 6.75 (dd, J = 7.47 and 4.44 Hz, H-3), 7.01 (d, J = 7.47 Hz, H-4), 7.73 (d, J = 4.44 Hz, H-2), 7.94 (br s, NH); ^{13}C-NMR ($CDCl_3$, 25 MHz); δ 21.5, 22.7, 31.9, 36.1, 48.0, 117.2, 118.7, 127.6, 132.6, 139.5, 143.6, 152.9, 194.6. Anal. Calcd for $C_{13}H_{15}N_3O$: C, 68.10; H, 6.59; N, 18.33. Found : C, 68.21; H, 6.51; N, 18.26.

5,6,8,9,10,11-Hexahydro-6-phenylpyrido[2,3-*b*][1,4]benzodiazepin-7-one (21). This compound was obtained in 85 % yield using the same method employed for the synthesis of **12** using **9** as starting material (reaction time : 1 h). In this case, componud **21** precipitated as a yellow powder. After filtration of the solvent , the precipitate was washed with ether. An analytical sample was obtained by recrystallization from ethanol. mp >260°C; ^{1}H-NMR (CD_3OD, 100 MHz); δ 2.30 (m, H-9), 2.60 (t, J = 5.9 Hz, H-8*), 2.97 (t, J = 6.0 Hz, H-10*), 6.06 (s, H-6), 6.86 (dd, J = 7.3 and 4.7 Hz, H-3), 7.07 (d, J = 7.3 Hz, H-4), 7.24 (m, 5H, H_{phenyl}), 7.83 (d, J= 4.7 Hz, H-2); ^{13}C-NMR (CD_3OD, 25 MHz); δ 21.1, 31.1, 35.6, 56.1, 113.1, 118.7, 126.2, 126.6 (2C), 127.8 (2C), 128.2, 133.4, 139.1, 142.3, 143.7, 156.4, 195.5. Anal. Calcd for $C_{18}H_{17}N_3O$: C, 74.20; H, 5.88; N, 14.42. Found : C, 74.07; H, 5.99; N, 14.36.

3-[(3-Triphenylphosphoranylidene)amino-2-pyridinyl)amino]cyclohex-2-en-1-one (22). This compound was obtained using the same method employed for the synthesis of **14** using **9** as starting material (reaction time : 45 min); yield 79%; red oil; MS (m/z, rel. intensity) 463 (5), 407 (13), 277 (100), 262 (20); ^{1}H-NMR ($CDCl_3$, 100 MHz); δ 2.08 (m, 2H, H-5), 2.42 (t, J = 6.1 Hz, 2H, H-6*), 2.72 (t, J = 6.2 Hz, 2H, H-4*), 6.48 (s, H-2), 7.40-7.80 (m, 18H), 8.72 (br s, NH); ^{13}C-NMR ($CDCl_3$, 25 MHz); δ 22.0, 30.2, 36.6, 105.1, 117.1, 123.5 (J^3PC = 9.3 Hz), 128.8 (6C, J^2PC = 12.0 Hz), 129.2 (3C, J^1PC = 99.7 Hz), 132.0-132.2 (7C), 135.2, 135.5, 149.1, J^3PC = 20.7 Hz), 157.6, 199.3. Anal. Calcd for $C_{29}H_{26}N_3OP$: C, 75.15; H, 5.65; N, 9.07. Found : C, 75.31; H, 5.51; N, 9.19.

8,9,10,11-Tetrahydro-6-aminophenylpyrido[2,3-*b*][1,4]benzodiazepin-7-one (23). This compound was obtained using the same method employed for the synthesis of **16** using **21** as starting material. yield 69%; mp 184-186 °C (cyclohexane); ^{1}H-NMR ($CDCl_3$, 100 MHz); δ 1.88, (m, 2H, H-9), 2.36-2.65 (m, 4H, H-8, H-10), 6.67-7.08 (m, 3H), 7.20-7.37 (m, 3H), 7.59-7.75 (m, 3H), 8.94 (br s, 1H, NH); ^{13}C-NMR ($CDCl_3$, 25 MHz); δ 18.5, 33.0, 37.7, 114.1, 121.1, 121.9, 122.8, 128.6, 135.6, 136.6, 140.1, 140.5, 148.6, 154.2, 172.8, 196.6. Anal. Calcd for $C_{18}H_{16}N_4O$: C, 71.04; H, 5.30; N, 18.41. Found : C, 70.89; H, 5.44; N, 18.44.

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