Pergamon

Tetrahedron 54 (1998) 13211–13226

TETRAHEDRON

Synthesis of α-carbolines and β-carbolinones via Intramolecular Diels-Alder Reactions of 2(1*H*)-Pyrazinones

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Received 20 May 1998; revised 10 August 1998; accepted 19 August 1998

Abstract: 2(1*H*)-Pyrazinones bearing a X-(*o*-C_6H_4)-C≡C-R moiety (X=NH, NAc) are shown to undergo an intramolecular cycloaddition-elimination reaction on thermolysis in refluxing bromobenzene yielding α-carbolines or β-carbolinones. The product distribution depends strongly on the substitution pattern of the pyrazinone precursors and the solvent used for thermolysis. A high yield and selective formation of β-carbolinones is possible when heating in tetrahydronaphthalene at reflux. Use of acetic anhydride as solvent facilitated the reaction and made it possible to realise a carbolin(on)e unaccessible by thermolysis in the previously mentioned solvents.

Introduction

Intramolecular Diels-Alder reactions of an acetylenic side chain with the 2-azadiene system of 1,2,4-triazines,[1] pyrazines[2] and pyrimidines,[3] all leading to the formation of condensed pyridines, have been well documented during the last few years. Publications from our laboratory indicate that the 2-azadiene system of 2(1*H*)-pyrazinones also undergoes inter- and intramolecular [4+2] cycloaddition reactions with a wide variety of dienophiles.[4-6] Alkynyloxy- or alkynyloxyalkyl side chains in the 3-position provided in this way a synthetic pathway to new furo/pyrano-pyridinones and pyridines.[5] Thermolysis of pyrazinones with 2-propynylaminomethyl or 3-butynylaminomethyl side chain in 6-position yielded either pyrrolo[3,4-*b*]pyridines and/or pyrrolo[3,4-*c*]pyridines or 1,7-naphthyridines and/or 2,7-naphthyridines.[6] The 3-(3- or 4-alkynylamino)-2(1*H*)-pyrazinones undergo a rearrangement initiated by the electron lone pair of the N-atom resulting in C-fused pyridinones.[7] In continuation of these studies, we investigated an intramolecular reaction of pyrazinones bearing a X-(*o*-C_6H_4)-C≡C-R moiety (X=NH, NAc). We wish to report here some applications of this concept providing a convenient route to α-carbolines and especially β-carbolinones.

Results and discussion

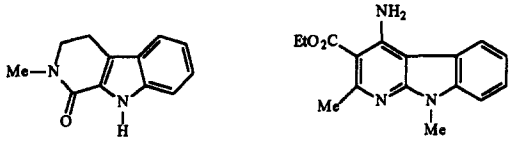
β-Carbolinones are of interest in medicine as many of them have been patented[8] and described as useful central nervous system depressants. A series of donor and acceptor substituted 1-oxo-β-carbolines, strychnocarpine I and the alkaloid from Alstonia venenata were tested on their Serotonin-Receptor-Binding activity (5-HT_1-Receptor).[9] Strychnocarpine is known as a weak muscle relaxant and serotonin receptor stimulator.[10]

0040-4020/98/$ - see front matter
PII: S0040-4020(98)00802-3

The α-carboline **II** is a $GABA_A$ modulator which showed[11] good potential for the treatment of anxiety diseases. However, further biological evaluation revealed that the ester acts shortly *in vivo* with a duration of one to two hours in the Geller-Seifter behavioural model of anxiety.[12]

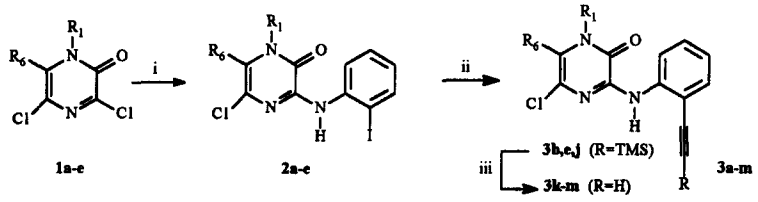
Existing synthetic routes to α-carbolines[3,13] suffer from several disadvantages: not easily available starting materials, low overall yields in many cases and limited scope for the introduction of variable substituents. In recent work Forbes and Johnson described the synthesis of substituted α-carbolines in 21% overall yield starting from substituted pyrrolo[2,3-*b*]pyridines.[14a] The same authors use an inverse electron demand Diels-Alder reaction to synthesise α-carbolines starting from substituted pyrimidines.[14b]

The described syntheses of β-carbolinones have 2-carboxyindole-3-acetic acid as the starting material[15a] or they are based on the Fischer reaction of 3-formyl-2-pyrrolidone derivatives with aryl-hydrazines.[15b]



I II

In our approach we used the 3-(2-ethynylamino)-2(1*H*)-pyrazinones **3a-m** as precursors. Therefore the 3,5-dichloro-2(1*H*)-pyrazinones **1a-e** were reacted with sodium hydride and 2-iodo-aniline in THF at reflux to provide 5-chloro-3-(2-iodophenylamino)-2(1*H*)-pyrazinones **2a-e** in good yield except for the 6-methyl derivative (40% only). The compounds **2a-e** were then reacted with terminal alkynes in the presence of a catalytic amount of bis (triphenylphosphine)-palladium dichloride and cuprous iodide in diethylamine to afford the corresponding pyrazinone derivatives **3a-j** in good yields[16] (table 1). The trimethylsilyl group in **3b,e,j** was removed by reaction with NaOH in methanol to yield **3k-m** (scheme 1).



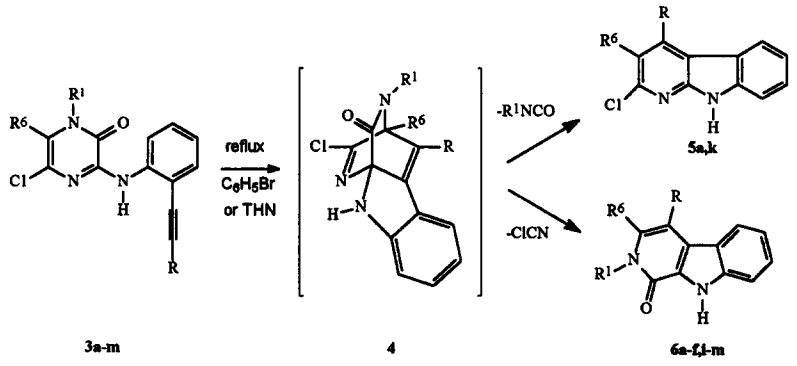
Scheme 1: Reagents and conditions: i) NaH, 2-iodoaniline, THF, reflux, 2h; ii) R–C≡CH, (Pd°), CuI, $NHEt_2$, 1-4 h, 40-45°C; iii) NaOH, MeOH, rt, 3 h.

Table 1: 3-(2-iodo/alkynylphenylamino)-2(1*H*)-pyrazinones.

	R^1	R^6	R	yield (%)		R^1	R^6	R	yield (%)
2a	Ph	Me	-	42	**3e**	Bn	H	TMS	89
2b	Bn	Me	-	40	**3f**	Bn	H	Ph	93
2c	Ph	H	-	80	**3g**	Bn	H	CH_2OH	95
2d	Bn	H	-	81	**3h**	Bn	Ph	CH_2OH	92
2e	Bn	Ph	-	78	**3i**	Bn	Ph	Ph	94
3a	Ph	Me	TMS	79	**3j**	Bn	Ph	TMS	94
3b	Bn	Me	TMS	79	**3k**	Bn	Ph	H	89
3c	Bn	Me	Ph	91	**3l**	Bn	H	H	93
3d	Ph	H	TMS	85	**3m**	Bn	Me	H	94

Thermolysis of the precursors:

As could be expected from analogous reactions of other azadienes having a -NH-(*o*-C_6H_4)-C≡C-R-side chain, relatively drastic reaction conditions (reflux in bromobenzene at 155°C) were required to react azadiene and dienophile. Starting from **3a**, 2-chloro-3-methyl-4-trimethylsilyl-9*H*-pyrido[2,3-*b*]indole **5a** was obtained in about 50% yield after 15 hours; some traces of the corresponding compound of type **6** were observed; pyrazinone **3k** gave **5k** and **6k** in a ratio 2/3 (scheme 2, table 2). Other precursors gave exclusively **6b-f,l-m** in moderate yields via the cycloadducts of type **4** whereas with **3g-j** no reaction could be observed after reflux for four days. However by heating compounds **3** at higher temperature (207°C) in tetrahydronaphthalene (THN) at reflux high selectivity and better yields of products of type **6** could be obtained except for **3g,h**. At this temperature removal of the trimethylsilyl group probably by interaction with the amine function has been observed.



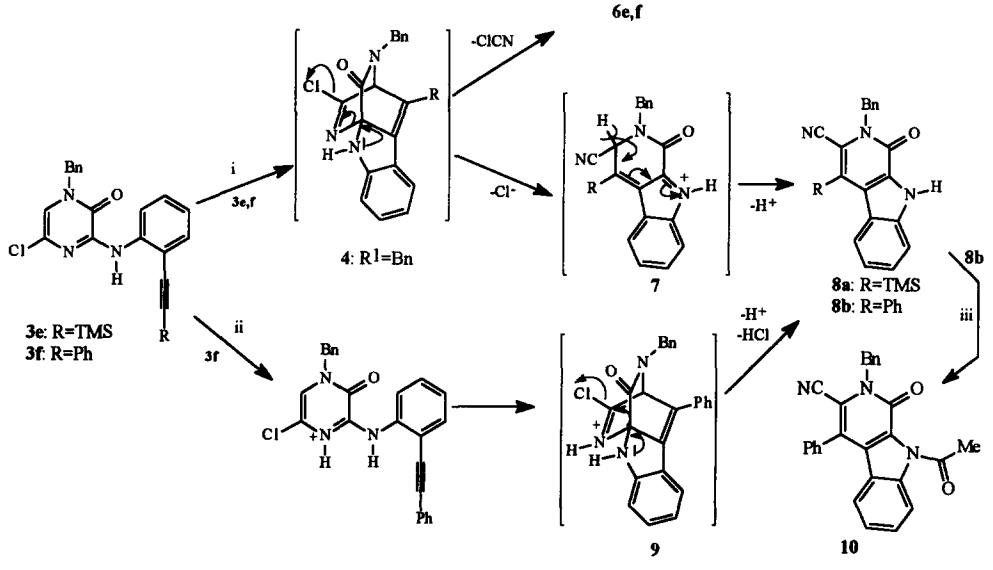
Scheme 2

Table 2: *THN: Tetrahydronaphthalene

starting compound	R^1	R^6	R	product	reaction time (h)		Yield (%)	
					C_6H_5Br	THN	C_6H_5Br	THN*
3a	Ph	Me	TMS	**5a**	15	4	48	50
3a	Ph	Me	TMS	**6a**	15	4	-	10
3b	Bn	Me	TMS	**6b**	22		30	
3b	Bn	Me	TMS	**6m**		12		80
3c	Bn	Me	Ph	**6c**	18	18	45	83
3d	Ph	H	TMS	**6d**	18		38	
3e	Bn	H	TMS	**6e**	20	2	41	81
3f	Bn	H	Ph	**6f**	16	4	43	90
3g	Bn	H	CH_2OH	**6g**	96	96	-	-
3h	Bn	Ph	CH_2OH	**6h**	96	96	-	-
3i	Bn	Ph	Ph	**6i**	96	60	-	84
3j	Bn	Ph	TMS	**6j**	96		-	
3j	Bn	Ph	TMS	**6k**		48		69
3k	Bn	Ph	H	**6k**	20	4	26	50
3k	Bn	Ph	H	**5k**	20	4	18	20
3l	Bn	H	H	**6l**	12		51	
3m	Bn	Me	H	**6m**	12	2	52	76

The β-carbolinones could be characterised by some typical spectral data. These solid compounds have a typical IR carbonyl band at about 1650 cm^{-1} (lactam) and a ^{13}C NMR signal at about δ 156 ppm. All products show correct mass spectral and combustion analytical data; their ^{1}H NMR spectra indicate the presence of the indole NH near δ 10-12 ppm. These results point out that the adducts **4** do not undergo a rearrangement reaction. Probably, the phenyl ring delocalises the nitrogen lone pair initiating the rearrangement. A normal retro-Diels-Alder reaction takes place with the product ratio depending on the pyrazinone substitution pattern: Ph-isocyanate is lost more easily than Bn-isocyanate; a sterically hindering group in 6-position probably hampers the loss of ClCN so that the combination of R^1=Ph and R^6=Me favours a pyridine derivative. Even with R^1=Bn and R^6=Ph (**3k**) a pyridine derivative is formed. In all the other cases and certainly at higher temperature in tetrahydronaphthalene a pyridinone derivative is obtained exclusively. Most of these results are in agreement with former intermolecular cycloaddition-elimination reactions with 2(1*H*)-pyrazinones.[4-6]

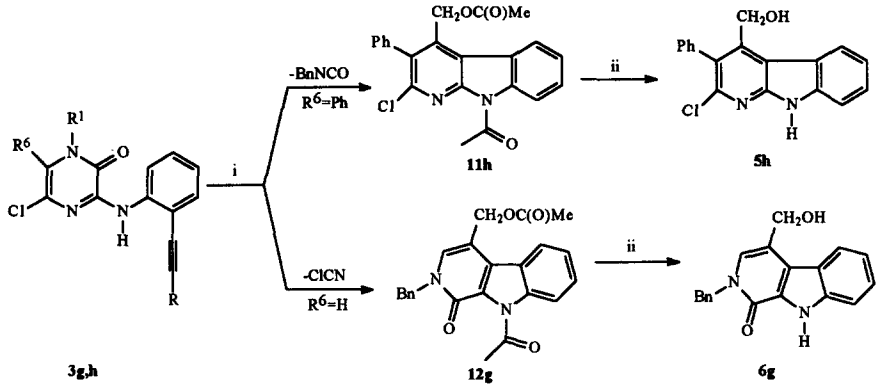
However the polarity of the solvent and catalysts may play an important role in the rearrangement reaction. When refluxing compounds **3e-f** in nitrobenzene, small quantities (10-15%) of the 2-benzyl-3-cyano-2,9-dihydro-1*H*-β-carbolin-1-one **8a-b** could be detected besides β-carbolinones **6e** and **6f**. Infrared spectra of these products **8a-b** show typical nitrile bands at 2220 cm^{-1} and carbonyl absorptions at 1640 cm^{-1}. ^{13}C NMR data are in agreement with the presence of the nitrile functionality. The nitrogen electron lone pair in the adduct **4** (scheme 3) initiates the reaction, resulting in a C–N cleavage and the expulsion of chloride ion. Probably, more polar solvents favour intermediates of type **7** which afford **8** after loss of a proton. Treatment of **3f** in acetic anhydride in the presence of a catalytic amount of concentrated sulphuric acid at 80°C for 10 h gave two products: 9-acetyl-2-benzyl-1-oxo-4-phenyl-2,9-dihydro-1*H*-β-carboline-3-carbonitrile **10** (43%) and the non-acylated product **8b** (11%). We assume that sulphuric acid protonates the 4-N-atom of the pyrazinone moiety, providing a more electron deficient diene undergoing Diels-Alder reaction more easily; it could also promote the expulsion of the chloride ion out of the intermediate adduct, during the rearrangement reaction. An easier cycloaddition process with protonated heterocyclic azadienes has also been observed by other groups.[17] In the conditions used the β-carbolinone **8b** can be acetylated easily giving **10**.



Scheme 3: Reagents and conditions i) $C_6H_5NO_2$, reflux, 15-20 h; ii) Ac_2O, H_2SO_4, 80°C, 10 h; iii) Ac_2O, reflux.

Study of the acetylation of 3-(2-alkynylamino)-2(1*H*)-pyrazinones:

We tried also to acetylate compounds of type **3** in order to speed up the cycloaddition step by a conformational effect; this acetylation could hinder rearrangement reactions and even facilitate cycloaddition elimination reactions not taking place with compounds **3g-h** in bromobenzene or in tetrahydronaphthalene. Indeed when the 3-(2-alkynylphenylamino)-2(1*H*)-pyrazinones **3g-h** were refluxed (140°C) in acetic anhydride, cycloaddition and the subsequent retro Diels-Alder reaction led to the α-carboline **11h** or β-carbolinone **12g** in good yield (Scheme 4, Table 3). The reaction rate seems to be influenced by the steric hindrance of R^6 and the acetylenic group probably in the first cycloaddition step. Hydrolysis of compounds **11-12** with KOH in methanol gave quantitative conversion into α-carboline **5h** and β-carbolinone **6g**. This means that this sequence could provide an excellent alternative for the approach via reflux in bromobenzene and also for some unsuccesful experiments in tetrahydronaphthalene.

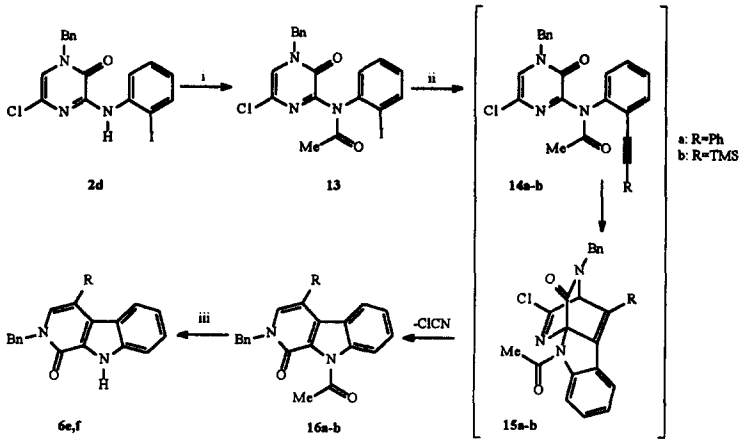


Scheme 4: Reagents and conditions: i) Ac_2O, reflux; ii) KOH, MeOH, r.t.

Table 3:

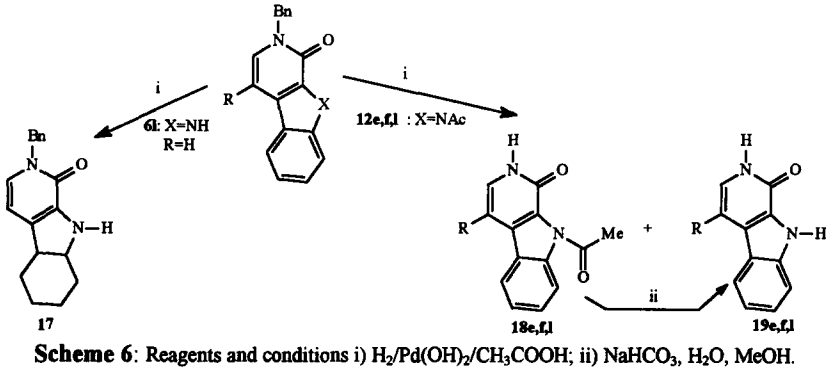
starting compound	R^1	R^6	R	reaction time (h)	yield (%) **11h**	**12g**	**5h**	**6g**
3h	Bn	Ph	CH_2OH	96	86		81	
3g	Bn	H	CH_2OH	48		88		70

It is not clear whether acetylation in the preceding series of experiments takes place before or after cycloaddition-elimination. Indeed, β-carbolinones and α-carbolines can be acetylated in refluxing acetic anhydride very easily. However acetylation of compounds of type **3** did not occur even at 100°C in acetic anhydride neither in pyridine with excess acetic anhydride and DMAP at 80°C. Some indication for acetylation taking place prior to cycloaddition is given by the results observed on alkynylation of compound **13**. From treatment of the 3-(2-iodophenylamino)-2(1*H*)-pyrazinone **2d** with an excess of acetic anhydride and DMAP in pyridine at 80°C the acylated product **13** could be obtained in good yield (scheme 5). On further reaction with Ph- or TMS-acetylene and $Pd(PPh_3)_2Cl_2$ CuI in diethylamine at 40-50°C compounds **14a-b** could not be isolated. Complete reaction took 2 days at 40°C or 12 hours at 70°C and afforded β-carbolinones **6e-f** in moderate yield (50-60%). The products are probably formed via the adducts **15a-b**, that loose ClCN providing **16a-b**, which hydrolyse easily to yield **6e-f**. Probably, the fact that cycloaddition takes place under very mild conditions can be explained by the electron withdrawing and conformational effect of the acyl group.



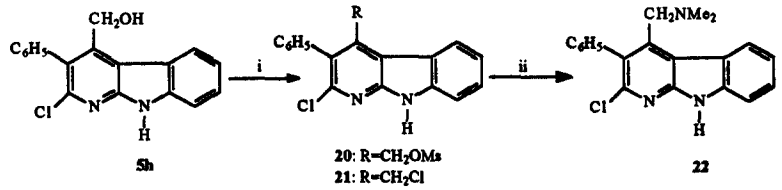
Scheme 5: Reagents and conditions: i) Ac_2O, DMAP, Pyridine, 80°C; ii) R–C≡CH, (Pd°), CuI, NEt_3, 40°C, 2d; iii) H_2O, CH_2Cl_2.

As biologically active monocyclic and fused pyridinones have a free lactam functionality, we tried to debenzylate the benzyl pyridinones obtained via intramolecular Diels-Alder reaction. In acetic acid under hydrogen atmosphere in the presence of $Pd(OH)_2$ compound **6l** did not give the desired product after stirring for three weeks. A complex mixture was obtained with the 5,6,7,8-tetrahydro derivative **17** as the main product. As we expected the secondary amine of the indole system to be the limiting factor, we treated derivatives **12e,f,l** with palladium hydroxide immediately after isolation from the reaction of **6e,f,l** with acetic anhydride. This led to the desired compounds **18e,f,l** together with the deacetylated products **19e,f,l**. The acetylated compounds **18e,f,l** are indeed very sensitive to hydrolysis and could be converted quantitatively to **19e,f,l** by stirring in methanol in the presence of aqueous sodium hydrogen carbonate.



Scheme 6: Reagents and conditions i) $H_2/Pd(OH)_2/CH_3COOH$; ii) $NaHCO_3$, H_2O, MeOH.

This new synthetic method for α-carbolines and β-carbolinones offers the possibility for introducing new substituents in positions 2 and 3 and particularly in position 4. The group in position 4 corresponds with the acetylenic substituent in the precursor. A trimethylsilyl group may be transformed into nitro-, chloro- or acyl- functionality.[18,19] Also the hydroxymethyl group is of interest and conversion into aminomethyl group was tested. Treatment of the alcohol **5h** with methane sulfonyl chloride in pyridine gave a mixture of a desired mesyl derivative **20** and chloro compound **21** which were transformed into the amine compound **22** by treatment with sodium dimethylamide in THF at room temperature.



Scheme 7: Reagents and conditions i) $MeSO_2Cl$, DMAP, Pyridine, CH_2Cl_2; ii) Me_2NH, NaH, THF, rt.

Conclusion:

A efficient and selective approach is proposed for the synthesis of variable β-carbolinones **6** by heating 3-(2-ethynylphenylamino)-2(1*H*)-pyrazinones **3** in bromobenzene or tetrahydronaphthalene. The latter undergo an intramolecular cycloaddition reaction with concomitant loss of ClCN giving compounds **6**. By choosing appropriate substituents the intermediate adduct can loose isocyanate leading to a α-carboline **5**. Reaction in acetic anhydride followed by hydrolysis provides carbolin(on)es wihch are unaccessible by thermolysis in bromobenzene or tetrahydronaphthalene. Very mild thermolysis conditions can be realised by prior acetylation of compounds **2** and subsequent alkynylation. Under certain reaction conditions, an intermediate adduct can undergo a rearrangement reaction resulting in a β-carbolinone with a nitrile functionality in position 3.

Experimental section

General methods: Melting points were taken using a Reichert-jung Thermovar apparatus and an Electrothermal IA 9000 digital melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 297 grating IR spectrophotometer and a Perkin-Elmer 1720 Fourier transform spectrometer. ^1H NMR spectra were recorded on a Bruker WM 250 or on a Bruker AMX 400 instrument. They were taken using $CDCl_3$ as solvent unless stated otherwise and the ^1H and ^{13}C chemical shifts are reported in ppm relative to tetramethylsilane or the deuterated solvent as an internal reference. Mass spectra were run by using a Kratos MS50TC instrument and a DS90 data system. For the chromatography, analytical TLC plates (Alugram Sil G/UV_{254}) and 70-230 mesh silica gel 60 (E.M. Merck) were used. Microanalyses were performed by Janssen Pharmaceutica on a Carlo Erba elemental analyser type 1106.

The preparation and the analytical data of the 3,5-dichloro-2(1*H*)-pyrazinones **1a-e** were reported previously.[5,20]

Synthesis of 5-chloro-3-(2-iodophenylamino)-2(1*H*)-pyrazinones **2a-e**

A mixture of 30 mmol iodoaniline and 45 mmol NaH was stirred at room temperature in 300 ml dry THF during 30 min under nitrogen atmosphere. After addition of 30 mmol 2(1*H*)-pyrazinone the suspension was refluxed during 2-5 h. The resulting dark mixture was evaporated, 50 ml H_2O was added and the H_2O-layer extracted with 3x50 ml CH_2Cl_2. After evaporation the residue was subjected to column chromatography (SiO_2) using a 50% hexane/CH_2Cl_2 mixture as eluent.

5-Chloro-3-(2-iodophenylamino)-6-methyl-1-phenyl-2(1*H*)-pyrazinone (2a)

Yield: 42%; m.p. 193°C; IR (KBr) cm^{-1}: 3298 (NH); 1657 (CO), 1574 (C=N); ^1H NMR ($CDCl_3$): 8.80 (s(br), 1H, NH), 8.6 (dd, J = 7.6 and J = 1.4Hz, 1H, Ar-H), 7.78 (dd, J = 7.6 and J = 1.4Hz, 1H, Ar-H), 7.3-7.25 (m, 6H, Ar-H), 6.7 (dt, J = 7.6 and J = 1.4Hz, 1H, Ar-H), 2.00 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): 151.9 (CO), 145.0 (C_5), 138.9 (Ar-C-NH), 139.1-119.2 (Ar-C), 122.8 (C_6), 89.2 (Ar-C-I), 17.2 (CH_3); m/z (%): 437 ($M^{+\cdot}$, 7), 310 ($M^{+\cdot}$-I, 29), 77 ($C_6H_5^+$, 100); exact mass for $C_{17}H_{13}ClIN_3O$: 436.9791; found: 436.9783.

1-Benzyl-5-chloro-3-(2-iodophenylamino)-6-methyl-2(1*H*)-pyrazinone (2b)
Yield: 40%; m.p. 214°C; IR (KBr) cm^{-1}: 3288 (NH), 1646 (CO), 1576 (C=N); ^1H NMR ($CDCl_3$): 8.82 (s(br), 1H, NH), 8.59 (dd, J = 7.5 and J = 1.4Hz, 1H, Ar-H), 7.83 (dd, J = 7.5 and J = 1.4Hz, 1H, Ar-H), 7.35-7.25 (m, 6H, Ar-H), 6.69 (dt, J = 7.6 and J = 1.4Hz, 1H, Ar-H), 5.37 (s, 2H, CH_2Ph), 2.35 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): 152.1 (CO), 144.7 (C_5), 139.0 (Ar-C-NH), 139.1-119.3 (Ar-C), 122.8 (C_6), 89.2 (Ar-C-I), 48.9 (CH_2Ph), 15.9 (CH_3); m/z (%): 451 (M^+, 4), 324 (M^+-I, 3), 91 ($C_7H_7^+$, 100); exact mass for $C_{18}H_{15}ClIN_3O$: 450.9948; found: 450.9924.

5-Chloro-3-(2-iodophenylamino)-1-phenyl-2(1*H*)-pyrazinone (2c)
Yield: 80%; IR (KBr) cm^{-1}: 3295 (NH); 1657 (CO), 1573 (C=N); ^1H NMR ($CDCl_3$): 9.00 (s(br), 1H, NH), 8.69 (dd, J = 7.6 and J = 1.4Hz, 1H, Ar-H), 7.83 (dd, J = 7.6 and J = 1.4Hz, 1H, Ar-H), 7.4-7.25 (m, 6H, Ar-H), 6.79 (dt, J = 7.6 and J = 1.4Hz, 1H, Ar-H), 6.84 (s, 1H, H_6); ^{13}C NMR ($CDCl_3$): 150.5 (CO), 147.2 (C_5), 138.6 (Ar-C-NH), 139.0-120.0 (Ar-C), 114.8 (C_6), 89.7 (Ar-C-I); m/z (%): 423 (M^+, 37), 296 (M^+-I, 100), 77 ($C_6H_5^+$, 47); exact mass for $C_{16}H_{11}ClIN_3O$: 422.9635; found: 422.9647.

1-Benzyl-5-chloro-3-(2-iodophenylamino)-2(1*H*)-pyrazinone (2d)
Yield: 81%; m.p. 150-151°C; IR (KBr) cm^{-1}: 3294 (NH), 1651 (CO), 1573 (C=N); ^1H NMR ($CDCl_3$): 8.96 (s(br), 1H, NH), 8.62 (dd, J = 7.6 and J = 1.4Hz, 1H, Ar-H), 7.83 (dd, J = 7.6 and J = 1.4Hz, 1H, Ar-H), 7.4-7.25 (m, 6H, Ar-H), 6.8 (dt, J = 7.6 and J = 1.4Hz, 1H, Ar-H), 6.69 (s, 1H, H_6), 5.15 (s, 2H, CH_2); ^{13}C NMR ($CDCl_3$): 150.8 (CO), 147 (C_5), 139.3 (Ar-CH), 138.7 (Ar-C-NH), 134.7 (Ar-C), 129.4-129.3-128.8-128.6 (Ar-C), 125.9 (Ar-CH), 125.16 (Ar-C), 119.9 (Ar-CH), 114.9 (C_6), 89.7 (Ar-C-I), 52.52 (CH_2Ph); m/z (%): 437 (M^+, 19), 310 (M^+-I, 20), 219 (M^+-NH_2PhI, 11), 91 ($C_7H_7^+$, 100); exact mass for $C_{17}H_{13}ClIN_3O$: 436.9791; found: 436.9792.

1-Benzyl-5-chloro-3-(2-iodophenylamino)-6-phenyl-2(1*H*)-pyrazinone (2e)
Yield: 78%; m.p. 167-168°C; IR (KBr) cm^{-1}: 3298 (NH), 1649 (CO), 1574 (C=N); ^1H NMR ($CDCl_3$): 9 (s(br), 1H, NH), 8.7 (dd, J = 8 and J = 1.3Hz, 1H, Ar-H), 7.85 (dd, J = 8 and J = 1.3Hz, 1H, Ar-H), 7.5-7.3 (m, 4H, Ar-H), 7.25-7.1 (m, 4H, Ar-H), 6.85-6.75 (m, 4H, Ar-H), 5.1 (s, 2H, CH_2Ph); ^{13}C NMR ($CDCl_3$): 151.6 (CO), 145.9 (C_5), 139.2 (Ar-CH), 138.8 (Ar-C-NH), 135.5-131.4-130.6-129.5-128.3-128.6-128.4-127.6-127.2-126.7 (Ar-C), 125.4 (Ar-C), 124.8-119.7 (Ar-C), 89.5 (Ar-C-I), 49.9 (CH_2Ph); m/z (%): 513 (M^+, 54), 386 (M^+-I, 38), 295 (M^+-NH_2PhI, 69), 91 ($C_7H_7^+$, 100); exact mass for $C_{23}H_{17}ClIN_3O$: 513.0105; found: 513.0103.

II-1) Synthesis of 5-chloro-3-(2-alkynylphenylamino)-2(1*H*)-pyrazinones **3a-j**.
To a solution of 5 mmol **2** and 2 equiv. trimethylsilylacetylene/phenylacetylene/ propargyl alcohol in 40 ml diethylamine was added 75 mg (0.05 mmol) $PdCl_2(PPh_3)_2$ and 10 mg CuI. After the mixture was stirred for 1-4 h at 40-45°C the solvent was evaporated to give the crude compound **3**. Column chromatography (SiO_2) using 40% hexane/CH_2Cl_2 as eluent gave pure compound **3**. Which was recrystallised from hot CH_2Cl_2 followed by addition of cold hexane.

5-Chloro-6-methyl-1-phenyl-3-(2-trimethylsilylethynylphenylamino)-2(1*H*)-pyrazinone (3a)
Yield: 79%; m.p. 174-175°C; IR (KBr) cm^{-1}: 3297 (NH), 2152 (C≡C), 1662 (CO), 1575 (C=N); ^1H NMR ($CDCl_3$): 9.15 (s(br), 1H, NH), 8.76 (d, J = 8.3Hz, 1H, Ar-H), 7.6-7.2 (m, 7H, Ar-H), 7 (dt, J = 7.5 and J = 1Hz, 1H, Ar-H), 2 (s, 3H, CH_3), 0.26 (s, 9H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): 152 (CO), 147.1 (C_5), 139.8 (Ar-C-NH), 139.3-118.3 (Ar-C), 125.7 (Ar-C), 120.5 (C_6), 112.8 (Ar-C-C≡C), 102.5 (C≡CSi), 99.8 (C≡CSi), 17.2 (CH_3), -0.2 ($SiCH_3$); m/z (%): 407 (M^+, 100), 372 (M^+-Cl, 23), 77 ($C_6H_5^+$, 55); exact mass for $C_{22}H_{22}ClN_3OSi$: 407.1221; found: 407.1228.

1-Benzyl-5-chloro-6-methyl-3-(2-trimethylsilylethynylphenylamino)-2(1*H*)-pyrazinone (3b)
Yield: 79%; m.p. 159°C; IR (KBr) cm^{-1}: 3303 (NH), 2148 (C≡C), 1660 (CO), 1589 (C=N); ^1H NMR ($CDCl_3$): 9.3 (s(br), 1H, NH), 8.73 (d, J = 8.3Hz, 1H, Ar-H), 7.48-7.2 (m, 7H, Ar-H), 7 (dt, J = 7.5 and J = 1Hz, 1H, Ar-H), 5.37 (s, 2H, CH_2Ph), 2.32 (s, 3H, CH_3), 0.35 (s, 9H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): 152.2 (CO), 144.6 (C_5), 140.3 (Ar-C-NH), 135.4-117.7 (Ar-C), 124.5 (Ar-C), 122.5 (C_6), 112.3 (Ar-C-C≡C),

102.9 (C≡CSi), 100.2 (C≡CSi), 48.6 (CH_2Ph), 15.9 (CH_3), 0.1 ($SiCH_3$); m/z (%): 421 ($M^{+\cdot}$, 26), 386 ($M^{+\cdot}$-Cl, 4), 91 ($C_7H_7^+$, 100); exact mass for $C_{23}H_{24}ClN_3OSi$: 421.1377; found: 421.1371.

1-Benzyl-5-chloro-6-methyl-3-(2-phenylethynylphenylamino)-2(1*H*)-pyrazinone (3c)

Yield: 91%; m.p. 187-188°C; IR (KBr) cm^{-1}: 3324 (NH), 1640 (CO), 1574 (C=N); ^1H NMR ($CDCl_3$): 9.40 (s(br), 1H, NH), 8.78 (d, J = 8.3Hz, 1H, Ar-H), 7.76-7.19 (m, 12H, Ar-H), 7 (t, J = 7.5Hz, 1H, Ar-H), 5.39 (s, 2H, CH_2Ph), 2.3 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): 152.2 (CO), 144.5 (C_5), 139.7 (Ar-C-NH), 135.2-117.6 (Ar-C), 124.7 (Ar-C), 122.5 (C_6), 112.3 (Ar-C-C≡C), 97.3 (C≡C-Ph), 84.5 (C≡C-Ph), 48.7 (CH_2Ph), 15.9 (CH_3); m/z (%): 425 ($M^{+\cdot}$, 10), 390 ($M^{+\cdot}$-Cl, 4), 91 ($C_7H_7^+$, 100); exact mass for $C_{26}H_{20}ClN_3O$: 425.1295; found: 425.1304.

5-Chloro-1-phenyl-3-(2-trimethylsilylethynylphenylamino)-2(1*H*)-pyrazinone (3d)

Yield: 85%; m.p. 127-128°C; IR (KBr) cm^{-1}: 3308 (NH), 2150 (C≡C), 1666 (CO), 1574 (C=N); ^1H NMR ($CDCl_3$): 9.42 (s(br), 1H, NH), 8.78-6.98 (m, 9H, Ar-H), 6.83 (s, 1H, H_6), 0.30 (s, 9H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): 150.5 (CO), 147.1 (C_5), 139.8 (Ar-C-NH), 139.3-118.3 (Ar-C), 125.7 (Ar-C), 115.5 (C_6), 112.8 (Ar-C-C≡C), 103.1 (C≡CSi), 99.8 (C≡CSi), -0.2 ($SiCH_3$); m/z (%): 393 ($M^{+\cdot}$, 100), 358 ($M^{+\cdot}$-Cl, 77), 77 ($C_6H_5^+$, 32); exact mass for $C_{21}H_{20}ClN_3OSi$: 393.1064; found: 393.1068.

1-Benzyl-5-chloro-3-(2-trimethylsilylethynylphenylamino)-2(1*H*)-pyrazinone (3e)

Yield: 89%; m.p. 135-136°C; IR (KBr) cm^{-1}: 3330 (NH), 2150 (C≡C), 1650 (CO), 1570 (C=N); ^1H NMR ($CDCl_3$): 9.43 (s(br), 1H, NH), 8.69 (d, J = 8.4Hz, 1H, Ar-H), 7.48-7.27 (m, 7H, Ar-H), 7 (t, J = 7.6Hz, 1H, Ar-H), 6.65 (s, 1H, H_6), 5 (s, 2H, CH_2Ph), 0.36 (s, 9H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): 150.7 (CO), 148.8 (C_5), 139.8 (Ar-C-NH), 134.7 (Ar-C), 131.6(Ar-CH), 125.6 (Ar-C), 122.47 (Ar-CH), 118 (Ar-CH), 114.3 (C_6), 112.6 (Ar-C-C≡C), 103.4 (C≡CSi), 99.8 (C≡CSi), 52 (CH_2Ph), -0.2 ($SiCH_3$); m/z (%): 407 ($M^{+\cdot}$, 82), 372 ($M^{+\cdot}$-Cl, 40), 91 ($C_7H_7^+$, 100); exact mass for $C_{22}H_{22}ClN_3OSi$: 407.1220; found: 407.1225.

1-Benzyl-5-chloro-3-(2-phenylethynylphenylamino)-2(1*H*)-pyrazinone (3f)

Yield: 93%; m.p. 191°C; IR (KBr) cm^{-1}: 3310 (NH), 1650 (CO), 1574 (C=N); ^1H NMR ($CDCl_3$): 9.58 (s(br), 1H, NH), 8.73 (d J = 8.4Hz, 1H, Ar-H), 7.79-7.75 (m, 2H, Ar-H), 7.57 (dd, J = 1.3 and J = 7.7Hz, 1H, Ar-H), 7.4-7.3 (m, 9H, Ar-H), 7 (dt, J = 1.3 and J = 7.7Hz, 1H, Ar-H), 6.65 (s, 1H, H_6), 5.11 (s, 2H, CH_2Ph); ^{13}C NMR ($CDCl_3$): 150.8 (CO), 148.8 (C_5), 139.2 (Ar-C-NH), 134.7-128.37 (Ar-C), 125.8 (Ar-C), 122.7-112 (Ar-C), 114.4 (C_6), 97.5 (C≡CPh), 84.4 (C≡CPh), 52.1 (CH_2Ph); m/z (%): 411 ($M^{+\cdot}$, 71), 376 ($M^{+\cdot}$-Cl, 63), 278 ($M^{+\cdot}$-$PhCH_2NCO$, 35), 91 ($C_7H_7^+$, 100), 65 ($C_5H_5^+$, 21); exact mass for $C_{25}H_{18}ClN_3O$: 411.1138; found: 411.1155.

1-Benzyl-5-chloro-3-[2-(3-hydroxy-1-propynyl)phenylamino]-2(1*H*)-pyrazinone (3g)

Yield: 95%; m.p. 109-110°C; IR (KBr) cm^{-1}: 3455 (OH), 3322 (NH), 1640 (CO), 1576 (C=N); ^1H NMR ($CDCl_3$): 9.4 (s(br), 1H, NH), 8.6 (dd, J = 8.5 and J = 1Hz, 1H, Ar-H), 7.4-7.27 (m, 7H, Ar-H), 7 (dt, J = 7.6 and J = 1Hz, 1H, Ar-H), 6.6 (s, 1H, H_6), 5 (s, 2H, CH_2Ph), 4.63 (s, 2H, CH_2O), 3.3-3.2 (s(br), 1H, OH); ^{13}C NMR ($CDCl_3$): 150.8 (CO), 146.4 (C_5), 139.4 (Ar-C-NH), 134.5-128.4 (Ar-C), 126.5 (Ar-C), 122.7-112.4 (Ar-C), 114.4 (C_6), 96.48 (C≡CH), 81 (C≡CH), 52.5 (CH_2Ph), 51.5 (CH_2O); m/z (%): 365 ($M^{+\cdot}$, 87), 348 ($M^{+\cdot}$-OH, 9), 330 ($M^{+\cdot}$-Cl, 32), 274 ($M^{+\cdot}$-C_7H_7, 6), 91 ($C_7H_7^+$, 100), 65 ($C_5H_5^+$, 18). exact mass for $C_{20}H_{16}ClN_3O_2$: 365.0931; found: 365.0928.

1-Benzyl-5-chloro-6-phenyl-3-[2-(3-hydroxy-1-propynyl)phenylamino]-2(1*H*)-pyrazinone (3h)

Yield: 92%; m.p. 187-188°C; IR (KBr) cm^{-1}: 3450 (OH), 3320 (NH), 1638 (CO), 1574 (C=N); ^1H NMR ($CDCl_3$): 9.43 (s(br), 1H, NH), 8.72 (d, J = 8.5Hz, 1H, Ar-H), 7.44-6.81 (m, 13H, Ar-H), 5.1 (s, 2H, CH_2Ph), 4.59 (s, 2H, CH_2O), 3.3 (t, J = 5.45Hz, 1H, OH); ^{13}C NMR ($CDCl_3$): 152 (CO), 149.8 (C_5), 143.5 (Ar-C-NH), 137.5-126.5 (Ar-C), 125.9 (Ar-C), 122.4-111 (Ar-C), 97 (C≡CH), 79 (C≡CH), 50 (CH_2Ph), 48 (CH_2O); m/z (%): 441 ($M^{+\cdot}$, 100), 406 ($M^{+\cdot}$-Cl, 23), 350 ($M^{+\cdot}$-C_7H_7, 22), 91 ($C_7H_7^+$, 52), 65 ($C_5H_5^+$, 15); exact mass for: $C_{26}H_{20}ClN_3O_2$: 441.1244; found: 441.1247.

1-Benzyl-5-chloro-6-phenyl-3-(2-phenylethynylphenylamino)-2(1*H*)-pyrazinone (3i)

Yield: 94%; m.p. 176-177°C; IR (KBr) cm^{-1}: 3325 (NH), 2150 (C≡C), 1666 (CO), 1574 (C=N); ^1H NMR ($CDCl_3$): 9.56 (s(br), 1H, NH), 8.75 (d, J = 8.3Hz, 1H, Ar-H), 7.71-7.69 (m, 2H, Ar-H), 7.54-7.07 (m, 14H, Ar-H), 6.8-6.75.(m, 2H, Ar-H), 5.08 (s, 2H, CH_2Ph); ^{13}C NMR ($CDCl_3$): 151.5 (CO), 145.85 (C_5),

139.34 (Ar-C-NH), 135.5-117 (Ar-C), 126.2 (Ar-C), 125.2 (C_6), 112.56 (Ar-C-C≡C), 97.3 (C≡CSi), 84.35 (C≡CSi), 49.47 (CH_2Ph); m/z (%): 487 (M^+, 100), 452 (M^+-Cl, 72), 396 (M^+-C_7H_7, 25), 91 ($C_7H_7^+$, 44); exact mass for $C_{31}H_{22}ClN_3O$: 487.1451; found: 487.1449.

1-Benzyl-5-chloro-6-phenyl-3-(2-trimethylsilylethynylphenylamino)-2(1*H*)-pyrazinone (3j)

Yield: 94%; m.p. 112-113°C; IR (KBr) cm^{-1}: 3340 (NH), 2150 (C≡C), 1666 (CO), 1574 (C=N); ^1H NMR ($CDCl_3$): 9.47 (s(br), 1H, NH), 8.75 (d, J = 8.3Hz, 1H, Ar-H), 7.5-6.83 (m, 13H, Ar-H), 5.1 (s, 2H, CH_2Ph), 0.36 (s, 9H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): 151.7 (CO), 145.8 (C_5), 140.1 (Ar-C-NH), 135.8 (Ar-C), 131.6-117 (Ar-C), 126.3 (Ar-C), 125.2 (C_6), 112.6 (Ar-C-C≡C), 103 (C≡CSi), 100 (C≡CSi), 49.85 (CH_2Ph), -0.08 ($SiCH_3$); m/z (%): 483 (M^+, 100), 468 (M^+-CH_3, 4), 448 (M^+-Cl, 21), 392 (M^+-CH_2Ph, 34), 91 ($C_7H_7^+$, 54), 73 ($SiCH_3^+$, 70); exact mass for $C_{28}H_{26}ClN_3OSi$: 483.1533; found: 483.1531.

II-2) Synthesis of 5-chloro-3-(2-ethynylphenylamino)-2(1*H*)-pyrazinones **3k-m**

A solution of 2 mmol **3b,3e or 3j** in 15ml MeOH was stirred at room temperature for 3 h in the presence of NaOH 1N (5 equiv.). After completion the solvent was evaporated, H_2O added to the residue and the H_2O layer extracted with 3 x 20 ml CH_2Cl_2. The pure product was obtained after evaporation and recrystallisation from hot CH_2Cl_2 followed by addition of cold hexane.

1-Benzyl-5-chloro-6-phenyl-3-(2-ethynylphenylamino)-2(1*H*)-pyrazinone (3k)

Yield: 89%; m.p. 193-194°C; IR (KBr) cm^{-1}: 3330 (NH), 1652 (CO), 1570 (C=N); ^1H NMR ($CDCl_3$): 9.45 (s(br), 1H, NH), 8.85 (d, J = 8Hz, 1H, Ar-H), 7.8-6.75 (m, 13H, Ar-H), 5.15 (s, 2H, CH_2Ph), 3.65 (s, 1H, C≡CH); ^{13}C NMR ($CDCl_3$): 151.65 (CO), 145.75 (C_5), 140.18 (Ar-C-NH), 135.5 (Ar-C), 132.34-117.97 (Ar-C), 126.63 (Ar-C), 111.3 (Ar-C-C≡C), 85.15 (C≡CH), 79.12 (C≡CH), 49.9 (CH_2Ph); m/z (%): 411 (M^+, 100), 376 (M^+-Cl, 10), 320 (M^+-C_7H_7, 61), 91 ($C_7H_7^+$, 45), 77 ($C_6H_5^+$, 7); exact mass for $C_{25}H_{18}ClN_3O$: 411.1138; found: 411.1142.

1-Benzyl-5-chloro-3-(2-ethynylphenylamino)-2(1*H*)-pyrazinone (3l)

Yield: 93%; m.p. 182-183°C; IR (KBr) cm^{-1}: 3335 (NH), 1650 (CO), 1574 (C=N); ^1H NMR ($CDCl_3$): 9.39 (s(br), 1H, NH), 8.77 (d, J = 8.1Hz, 1H, Ar-H), 7.5-7.25 (m, 7H, Ar-H), 7.01 (t, J = 7.2Hz, 1H, Ar-H), 6.71 (s, 1H, H_6), 5.10 (s, 2H, CH_2Ph), 3.65 (s, 1H, C≡CH); ^{13}C NMR ($CDCl_3$): 150.8 (CO), 146.6 (C_5), 139.9 (Ar-C-NH), 134.6-118.1 (Ar-C), 126.0 (Ar-C), 114.6 (C_6), 111.4 (Ar-C-C≡CH), 85.0 (C≡CH), 79.0 (C≡CH), 52.4 (CH_2Ph); m/z (%): 335 (M^+, 19), 300 (M^+-Cl, 4), 91 ($C_7H_7^+$, 100); exact mass for $C_{19}H_{14}ClN_3O$: 335.0825; found: 335.0824.

1-Benzyl-5-chloro-3-(2-ethynylphenylamino)-6-methyl-2(1*H*)-pyrazinone (3m)

Yield: 94%; m.p. 217-218°C; IR (KBr) cm^{-1}: 3370 (NH), 3295 (C≡CH), 1647 (CO), 1574 (C=N); ^1H NMR ($CDCl_3$): 9.23 (s(br), 1H, NH), 8.74-6.96 (m, 9H, Ar-H), 5.36 (s, 2H, CH_2Ph), 3.60 (s, 1H, C≡CH), 2.34 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): 152.1 (CO), 144.5 (C_5), 140.4 (Ar-C-NH), 134.9-117.6 (Ar-C), 124.8 (Ar-C), 122.6 (C_6), 111.0 (Ar-C-I), 84.9 (C≡CH), 79.2 (C≡CH), 48.8 (CH_2Ph), 15.9 (CH_3); m/z (%): 349 (M^+, 88), 258 (M^+-C_7H_7, 58), 91 ($C_7H_7^+$, 100); exact mass for $C_{20}H_{16}ClN_3O$: 349.0982; found: 349.0990.

II-3) Synthesis of the 9*H*-pyrido[2,3-*b*]indoles **5** and β-carbolinones **6**

The 2(1*H*)-pyrazinones **3a-m** (3 mmol) were refluxed in bromobenzene (40 ml) for 12-22 h or in tetrahydronaphthalene (40 ml) for 2-96 h under nitrogen atmosphere. After evaporation the crude product was purified by column chromatography (SiO_2 or Al_2O_3) using 20-60% EtOAc/CH_2Cl_2 as eluent mixtures. The 2(1*H*)-pyrazinones **3g,h** (2 mmol) were refluxed in acetic anhydride (25 ml) during 40-96 h under nitrogen atmosphere. After evaporation the crude **11h** or **12g** was purified (see part IV) and subsequently hydrolysed. Therfore 5 equivalents of a 1M solution of KOH in methanol was added to a solution of 1 mmol of **11h** or **12g** in 15 ml of methanol. The mixture was stirred at room temperatur for 24 h and then neutralised with 1N HCl in water. Methanol was evaporated and the H_2O-layer extracted with AcOEt

(4x20 ml). After drying and evaporation the residue was recrystallised from MeOH to get white crystals of **5h** or **6g** (yield 70-80%).

2-Chloro-3-methyl-4-trimethylsilyl-9*H*-pyrido[2,3-*b*]indole (5a)
Yield: 48%; m.p. 231-232°C; IR (KBr) cm^{-1}: 1570, 1520 (pyridine); ^1H NMR ($CDCl_3$): 10.85 (s(br), 1H, NH), 8.12-7.20 (m, 4H, Ar-H), 2.68 (s, 3H, CH_3), 0.65 (s, 9H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): 149.1 (C_{9a}), 147.8 (C_2), 147.6 (C_4), 139.4 (C_{8a}), 126.8 (C_3), 126.3-111.8 (other Ar-C), 120.9 (C_{4b}), 120.3 (C_{4a}), 21.1 (CH_3), 2.3 ($SiCH_3$); m/z (%): 288 (M^+, 100), 273 (M^+-CH_3, 65), 180 (M^+-$Si(CH_3)_3$-Cl, 80); exact mass for $C_{15}H_{17}ClN_2Si$: 288.0849; found: 288.0843.

2-Chloro-4-(hydroxymethyl)-3-phenyl-9*H*-pyrido[2,3-*b*]indole (5h)
Yield: 81%; m.p. 262-263°C; IR (KBr) cm^{-1}: 3409 (OH), 3198 (NH), 1595 (pyridine); ^1H NMR (acetone-d_6): 11.05 (s(br), 1H, NH), 8.4 (d, J = 8Hz, 1H, Ar-H), 7.63 (d, J = 8Hz, 1H, Ar-H), 7.54-7.39 (m, 6H, Ar-H), 7.32 (dd, J = 8 and J = 7.2Hz, 1H, Ar-H), 4.85 (d, J = 5Hz, 2H, CH_2O), 4.41 (t, J = 5Hz, 1H, OH); ^1H NMR (DMSO-d_6): 12.1 (s(br), 1H, NH), 8.27 (d, J = 8Hz, 1H, H_8), 7.56-7.23 (m, 8H, Ar-H), 5.35 (t, J = 4.8Hz, 1H, OH), 4.64 (d, J = 4.8Hz, 2H, CH_2O); ^{13}C NMR (DMSO-d_6): 150.23 (C_{9a}), 145.6 (C_2), 144.35 (C_4), 139.18 (C_{8a}), 136.68-113.55 (other Ar-C), 119.93 (C_{4b}), 111.23 (C_8), 56.8 (CH_2O); m/z (%): 308 (M^+, 100), 273 (M^+-Cl, 15), 255 (M^+-Cl-H_2O, 28), 77 ($C_6H_5^+$, 8); exact mass for $C_{18}H_{13}N_2OCl$: 308.0716; found: 308.0715. Anal. Calcd for $C_{18}H_{13}ClN_2O$: C, 70.02, H, 4.24, N, 9.09. Found : C, 69.80, H, 4.29, N, 8.98.

2-Chloro-3-phenyl-9*H*-pyrido[2,3-*b*]indole (5k)
Yield: 20%; m.p. 264-265°C; IR (KBr) cm^{-1}: 3175 (NH), 1600-1560 (C=C), 1520 (pyridine); ^1H NMR (DMSO-d_6): 8.59 (s, 1H, NH), 8.2 (d, J = 7.7Hz, 1H, H_8), 7.55-7.27 (m, 8H, Ar-H), 7.24 (t, J = 6.6Hz, 1H, H_6); ^{13}C NMR (DMSO-d_6): 150.12 (C_{9a}), 144.42 (C_2), 139.29 (C_{8a}), 138.62-114 (other Ar-C), 132.09 (C_4), 128.18 (C_3), 121.61 (C_{4b}), 111.73 (C_8); m/z (%): 278 (M^+, 100), 242 (M^+-HCl, 27); exact mass for $C_{17}H_{11}ClN_2$: 278.0610; found: 278.0613. Anal. Calcd for $C_{17}H_{11}ClN_2$: C, 73.25, H, 3.98, N, 10.05. Found : C, 72.90, H, 3.84, N, 9.94.

2-Phenyl-3-methyl-2,9-dihydro-1*H*-β-carbolin-1-one (6a)
Yield: 10%; IR (KBr) cm^{-1}: 1640 (CO); ^1H NMR (DMSO-d_6): 11.86 (s(br), 1H, NH), 8.01 (d, J = 7.9 Hz, 1H, H_5), 7.6-7.12 (m, 8H, Ar-H), 7.03 (s, 1H, H_4), 2 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6): 155.9 (CO), 139.36 (C_{9a}), 135.3-119.4 (other Ar-C), 123.4 (C_{4b}), 112.4 (C_8), 99.6 (C_4), 21.72 (CH_3); m/z (%): 274 (M^+, 100); exact mass for $C_{18}H_{14}N_2O$: 274.1106; found: 274.1112.

2-Benzyl-3-methyl-4-trimethylsilyl-2,9-dihydro-1*H*-β-carbolin-1-one (6b)
Yield: 30%; m.p. 308-310°C; IR (KBr) cm^{-1}: 1642 (CO); ^1H NMR ($CDCl_3$): 10.51 (s(br), 1H, NH), 7.96-7.12 (m, 9H, Ar-H), 5.63 (s, 2H, CH_2Ph), 2.50 (s, 3H, CH_3), 0.18 (s, 9H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): 156.9 (CO), 139.8 (C_{9a}), 137.2-119.9 (other Ar-C), 135.7 (C_4), 126.4 (C_{4b}), 112.6 (C_8), 47.1 (CH_2Ph), 20.9 (CH_3), -0.4 ($SiCH_3$); m/z (%): 360 (M^+, 100), 269 (M^+-C_7H_7, 44), 91 ($C_7H_7^+$, 23); exact mass for $C_{22}H_{24}N_2OSi$: 360.1658; found: 360.1663.

2-Benzyl-3-methyl-4-phenyl-2,9-dihydro-1*H*-β-carbolin-1-one (6c)
Yield: 83%; m.p. 293°C; IR (KBr) cm^{-1}: 1644 (CO); ^1H NMR (DMSO-d_6): 12.06 (s(br), 1H, NH), 7.59-6.47 (m, 12H, Ar-H), 6.82 (dd, J = 8.2 and J = 7.3Hz, 1H, Ar-H), 6.5 (d, J = 8.2Hz, 1H, Ar-H), 5.56 (s, 2H, CH_2Ph), 2.1 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6): 155.6 (CO), 139.5 (C_{9a}), 137.86 (C_{8a}), 137.7-119.2 (other Ar-C), 122 (C_3), 115.4 (C_4), 112.6 (C_8), 46.4 (CH_2Ph), 16.5 (CH_3); m/z (%): 364 (M^+, 100), 273 (M^+-C_7H_7, 80), 91 ($C_7H_7^+$, 34); exact mass for $C_{25}H_{20}N_2O$: 364.1576; found: 364.1574.

2-Phenyl-4-trimethylsilyl-2,9-dihydro-1*H*-β-carbolin-1-one (6d)
Yield: 38%; m.p. 275-276°C; IR (KBr) cm^{-1}: 1648 (CO); ^1H NMR ($CDCl_3$): 11.27 (s(br), 1H, NH), 8.10-7.22 (m, 9H, Ar-H), 7.14 (s, 1H, H_3), 0.49 (s, 9H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): 155.8 (CO), 141.1 (C_{9a}), 140.1 (C_{8a}), 137.8 -119.9 (other Ar-C), 133.2 (C_3), 127.1 (C_{4a}), 123.0 (C_{4b}), 113.1 (C_8), 111.8 (C_4), -0.4 ($SiCH_3$); m/z (%): 332 (M^+, 100), 317 (M^+-CH_3, 96), 77 ($C_6H_5^+$, 9); exact mass for $C_{20}H_{20}N_2OSi$: 332.1345; found: 332.1345.

2-Benzyl-4-trimethylsilyl-2,9-dihydro-1*H*-β-carbolin-1-one (6e)
Yield: 81%; m.p. 252-253°C; IR (KBr) cm^{-1}: 1646 (CO); ^1H NMR ($CDCl_3$): 11.55 (s(br), 1H, NH), 8.07 (d, J = 8Hz, 1H, Ar-H), 7.45-7.22 (m, 8H, Ar-H), 7.12 (s, 1H, Ar-H), 5.49 (s, 2H, CH_2Ph), 0.47 (s, 9H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): 156.25 (CO), 140.06 (C_{8a}), 137.27 (C_{9a}), 132.65 (C_3), 128.87-119.7 (other Ar-C), 126.98 (C_{4b}), 112.99 (C_8), 111.9 (C_{4b}), 51.8 (CH_2Ph), -0.35 ($SiCH_3$); m/z (%): 346 (M^+, 100), 331 (M^+-CH_3, 51), 91 ($C_7H_7^+$, 49), 65 ($C_5H_5^+$, 11); exact mass for $C_{21}H_{22}N_2OSi$: 346.1501; found: 346.1498. Anal. Calcd for $C_{21}H_{22}N_2OSi$: C, 72.79, H, 6.40, N, 8.08. Found : C, 72.74, H, 6.53, N, 8.22.

2-Benzyl-4-phenyl-2,9-dihydro-1*H*-β-carbolin-1-one (6f)
Yield: 90%; m.p. 285-286°C; IR (KBr) cm^{-1}: 1649 (CO); ^1H NMR (DMSO-d_6): 11.17 (s(br), 1H, NH), 7.72-6.93 (m, 14H, Ar-H), 7.01 (s, 1H, H_3), 5.33 (s, 2H, CH_2Ph); ^{13}C NMR (DMSO-d_6): 154.3 (CO), 139.5 (C_{9a}), 137.9 (C_{8a}), 136.6-119.4 (other Ar-C), 127.6 (C_{4b}), 121.4 (C_4), 121.3 (C_{4a}), 117.2 (C_4), 112.7 (C_8), 50.4 (CH_2Ph); m/z (%): 350 (M^+, 100), 259 (M^+-C_7H_7, 36), 91 ($C_7H_7^+$, 53); exact mass for $C_{24}H_{18}N_2O$: 350.1419; found: 350.1426.

2-Benzyl-4-(hydroxymethyl)-2,9-dihydro-1*H*-β-carbolin-1-one (6g)
Yield: 70%; m.p. 268-269°C; IR (KBr) cm^{-1}: 3408 (OH), 3205 (NH), 1650 (CO); ^1H NMR (DMSO-d_6): 12.04 (s(br), 1H, NH), 8.07 (d, J = 8Hz, 1H, Ar-H), 7.53 (d, J = 8Hz, 1H, Ar-H), 7.42-7.24 (m, 8H, Ar-H), 5.28 (s, 2H, CH_2Ph), 5.24 (t, J = 4.5Hz, 1H, OH), 4.75 (d, J = 4.5Hz, 2H, CH_2O); ^{13}C NMR (DMSO-d_6): 154.64 (CO), 138.29 (C_{9a}), 136.09 (C_{8a}), 134.2-116.07 (other Ar-C), 127.47 (C_{4b}), 127.31 (C_4), 123.5 (C_{4a}), 116.07 (C_3), 112.33 (C_8), 59.61 (CH_2O), 50.21 (CH_2Ph); m/z (%): 304 (M^+, 89), 273 (M^+-CH_2OH, 11), 91 ($C_7H_7^+$, 100), 65 ($C_5H_5^+$, 28); exact mass for $C_{19}H_{16}N_2O_2$: 304.1211; found: 304.1214. Anal. Calcd for $C_{19}H_{16}N_2O_2$: C, 74.98, H, 5.30, N, 9.20. Found : C, 74.95, H, 5.35, N, 9.29.

2-Benzyl-3,4-diphenyl-2,9-dihydro-1*H*-β-carbolin-1-one (6i)
Yield: 84%; m.p. 363-364°C; IR (KBr) cm^{-1}: 1645 (CO); ^1H NMR (DMSO-d_6): 12.2 (s(br), 1H, NH), 7.53 (d, J = 8Hz, 1H, Ar-H), 7.34-6.8 (m, 11H, Ar-H), 6.48 (d, J = 8Hz, 1H, Ar-H), 5.16 (s, 2H, CH_2Ph); ^{13}C NMR (DMSO-d_6): 156.2 (CO), 137.69 (C_{9a}), 137.1-118.9 (other Ar-C), 112.5 (C_8), 49.3 (CH_2Ph); m/z (%): 426 (M^+, 100), 347 (M^+-C_6H_7, 11), 335 (M^+- C_7H_7, 39), 91 ($C_7H_7^+$, 24), 65 ($C_5H_5^+$, 7); exact mass for $C_{30}H_{22}N_2O$: 426.1732; found: 426.1740. Anal. Calcd for $C_{30}H_{22}N_2O$: C, 84.48, H, 5.20, N, 6.57. Found : C, 84.27, H, 5.25, N, 6.45.

2-Benzyl-3-phenyl-2,9-dihydro-1*H*-β-carbolin-1-one (6k)
Yield: 50% or 69%; m.p. 274-276°C; IR (KBr) cm^{-1}: 1646 (CO); ^1H NMR (DMSO-d_6): 12.03 (s(br), 1H, NH), 8.05 (d, J = 7.5Hz, 1H, Ar-H), 7.55 (d, J = 8.2Hz, 1H, Ar-H), 7.42-7.16 (m, 10H, Ar-H), 7.02 (s, 1H, H_4), 6.8-6.78 (m, 2H, Ar-H), 5.28 (s, 2H, CH_2Ph); ^{13}C NMR (DMSO-d_6): 155.43 (CO), 139.75 (C_{9a}), 139.52 (C_3), 137.96 (C_{8a}), 136.32-119.66 (other Ar-C), 126.5 (C_{4b}), 121.92(C_{4a}), 112.5 (C_8), 102.4 (C_4), 47.41 (CH_2Ph); m/z (%): 350 (M^+, 100), 273 (M^+-C_6H_5, 17), 259 (M^+-CH_2Ph, 41), 91 ($C_7H_7^+$, 41); $C_{24}H_{18}N_2O$: 350.1419; found: 350.1424.

2-Benzyl-2,9-dihydro-1*H*-β-carbolin-1-one (6l)
Yield: 51%; m.p. 297-298°C; IR (KBr) cm^{-1}: 1652 (CO); ^1H NMR (DMSO-d_6): 11.96 (s(br), 1H, NH), 8 (d, J = 7.9Hz, 1H, Ar-H), 7.54-7.31 (m, 8H, Ar-H), 7.2 (d, J = 7.1Hz, 1H, H_3), 7.06 (d, J = 7.1Hz, 1H, H_4), 5.3 (s, 2H, CH_2Ph); ^{13}C NMR (DMSO-d_6): 154.9 (CO), 139.3 (C_{9a}), 138.1(C_{8a}), 128.7-119.6 (other Ar-C), 127.7(C_{4b}), 123.4 (C_{4a}), 121.8 (C_3), 112.5 (C_8), 100.4 (C_4), 50.4 (CH_2Ph); m/z (%): 274 (M^+, 80), 183 (M^+-C_7H_7, 12), 91 ($C_7H_7^+$, 100), 65 ($C_5H_5^+$, 31); exact mass for $C_{18}H_{14}N_2O$: 274.1106; found: 274.1104. Anal. Calcd for $C_{18}H_{14}N_2O$: C, 78.81, H, 5.14, N, 10.21. Found : C, 79.03, H, 4.94, N, 10.01.

2-Benzyl-3-methyl-2,9-dihydro-1*H*-β-carbolin-1-one (6m)
Yield: 76% or 80%; m.p. 284°C; IR (KBr) cm^{-1}: 1657 (CO); ^1H NMR (DMSO-d_6): 11.90 (s(br), 1H, NH), 8.34-7.10 (m, 9H, Ar-H), 6.97 (s, 1H, H-C_4), 5.50 (s, 2H, CH_2Ph), 2.38 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6): 155.9 (CO), 139.4 (C_{9a}), 137.8-119.4 (other Ar-C), 135.8 (C_3), 123.2 (C_{4a}), 121.6 (C_{4b}), 112.4 (C_8), 100.2 (C_4), 45.9 (CH_2Ph); m/z (%): 288 (M^+, 100), 197 (M^+-C_7H_7, 72), 91 ($C_7H_7^+$, 54); exact mass for $C_{19}H_{16}N_2O$: 288.1263; found: 288.1258.

III- Synthesis of β-carbolinones **8a-b** and **10**

Method A: The 2(1*H*)-pyrazinones **3e-f** (2 mmol) were refluxed in nitrobenzene (25 ml) for 15-20 h under nitrogen atmosphere. After evaporation the crude product was purified chromatographically using silica with EtOAc/CH_2Cl_2 as eluent mixtures. This yielded β-carbolinones **6e** (44%) and **6f** (51%) together with **8a** and **8b** respectively.

Method B: A solution of 2(1*H*)-pyrazinone **3f** (1mmol) in 20 ml acetic anhydride and one drop concentrated H_2SO_4 was heated at 80°C for 10 h. The reaction mixture was poured into water (50 ml) and extracted with CH_2Cl_2 (3x30 ml). The combined CH_2Cl_2 layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over a silica column using EtOAc/CH_2Cl_2 as eluent. Compound **8b** (11%) and the acetylated derivative **10** were isolated. The latter compound was obtained when refluxing **8b** in acetic anhydride for 10 hours under nitrogen atmosphere. After evaporation the crude compound **10** was purified by column chromatography (Al_2O_3) using 20% CH_2Cl_2/hexane as eluent.

2-Benzyl-3-cyano-4-trimethylsilyl-2,9-dihydro-1*H*-β-carbolin-1-one (8a)

Yield: 10%; m.p. 240°C; IR (KBr) cm^{-1}: 2217 (C≡N), 1651 (CO); ^1H NMR ($CDCl_3$): 11.05 (s(br), 1H, NH), 7.5-7 (m, 9H, Ar-H), 5.12 (s, 2H, CH_2Ph), 1.17 (s, 9H, $SiCH_3$); ^{13}C NMR ($CDCl_3$): 154.9 (CO), 140.1 (C_{9a}), 135.8 (C_4), 134.2-121.5 (other Ar-C), 130.2 (C_{8a}), 129 (C_{4b}), 122 (C_{4a}), 113.3 (C≡N), 113.1 (C_8), 109.7 (C_3), 50.4 (CH_2Ph), -0.3 ($SiCH_3$); m/z (%): 371 (M^+, 39), 356 (M^+-CH_3, 15), 91 ($C_7H_7^+$, 100); exact mass for $C_{22}H_{21}N_3OSi$: 371.1454; found: 371.1453.

2-Benzyl-3-cyano-4-phenyl-2,9-dihydro-1*H*-β-carbolin-1-one (8b)

Yield: 14%; m.p. 283-284°C; IR (KBr) cm^{-1}: 2211 (C≡N), 1640 (CO); ^1H NMR ($CDCl_3$): 10.02 (s(br), 1H, NH), 7.62-6.99 (m, 14H, Ar-H), 5.8 (s, 2H, CH_2Ph); m/z (%):^{13}C NMR ($CDCl_3$): 155 (CO), 140.2 (C_{9a}), 136 (C_{8a}), 134.5-121.5 (other Ar-C), 131 (C_4), 130 (C_{4b}), 122.4 (C_{4a}), 114.3 (C≡N), 113.1 (C_8), 109.7 (C_3), 50.4 (CH_2Ph); m/z (%): 375 (M^+, 35), 284 (M^+-C_7H_7, 3), 91 ($C_7H_7^+$, 100); exact mass for $C_{25}H_{17}N_3O$: 375.1372; found: 375.1369.

9-Acetyl-2-benzyl-3-cyano-4-phenyl-2,9-dihydro-1*H*-β-carbolin-1-one (10)

Yield: 43%; m.p. 190-191°C; IR (KBr) cm^{-1}: 2210 (C≡N), 1723, 1640 (CO); ^1H NMR ($CDCl_3$): 8.18-6.78 (m, 14H, Ar-H), 5.65 (s, 2H, CH_2Ph), 2.87 (s, 3H, $COCH_3$); ^{13}C NMR ($CDCl_3$): 170.8 (C(O)N), 154 (CO), 140.1 (C_{9a}), 135.7 (C_{8a}) 133.5-122.4 (other Ar-C), 128.5 (C_4), 128.2(C_{4b}), 122.5 (C_{4a}), 114.8 (C_8), 114.3 (C≡N), 113.3 (C_3), 50.7 (CH_2Ph), 28.7 (CH_3); m/z (%): 417 (M^+, 6), 375 (M^+-$COCH_2$, 85), 91 ($C_7H_7^+$, 100); exact mass for $C_{27}H_{19}N_3O_2$: 417.1477; found: 417.1479.

IV-1) Synthesis of the α-carboline **11h** and the β-carbolinone **12g**

The 2(1*H*)-pyrazinones **3g,h** (2 mmol) were refluxed in acetic anhydride (25 ml) during 2-4 days under nitrogen atmosphere. After evaporation the crude compound **11h** or **12g** was purified by column chromatography (SiO_2) using 20-60% CH_2Cl_2/hexane as eluent. The resulting products were recrystallised from CH_2Cl_2/hexane.

9-Acetyl-4-acetoxymethyl-2-chloro-3-phenyl-9*H*-pyrido[2,3-*b*]indole (11h)

Yield: 86%; m.p. 169-170°C; IR (KBr) cm^{-1}: 1738-1704 (CO), 1640-1562-1458 (C=C); ^1H NMR ($CDCl_3$): 8.79 (d, J = 8.4Hz, 1H, Ar-H), 7.9 (d, J = 8Hz, 1H, Ar-H), 7.59 (dd, J = 1.4 and J = 7.4Hz, 1H, Ar-H), 7.55-7.27 (m, 6H, Ar-H), 5.28 (s, 2H, CH_2O), 3.15 (s, 3H, CH_3CON), 2.03 (s, 3H, CH_3COO); ^{13}C NMR ($CDCl_3$): 170.9 (C(O)O), 170.3 (C(O)N), 149.28 (C_{8a}), 146.97 (C_4), 138.9 (C_2), 138.7 (C_{9a}), 135.48-122.21 (other Ar-C), 132.8 (C_3), 121.8 (C_{4b}), 117.8 (C_{4a}), 116.9 (C_8), 61.3 (CH_2O), 28.09 (CH_3CON), 20.54 (CH_3COO); m/z (%): 392 (M^+, 20), 350 (M^+-CH_2CO, 100), 307 (M^+-2(CH_2CO), 9), 43 (CH_3CO^+, 27); exact mass for $C_{22}H_{17}ClN_2O_3$: 392.0927; found: 392.0934.

9-Acetyl-4-acetoxymethyl-2-benzyl-2,9-dihydro-1*H*-β-carbolin-1-one (12g)

Yield: 88%; m.p. 185-186°C; IR (KBr) cm^{-1}: 1720-1708-1662 (CO); ^1H NMR ($CDCl_3$): 8.3 (d, J = 8.5Hz, 1H, Ar-H), 7.98 (d, J = 8Hz, 1H, Ar-H), 7.58 (dt, J = 1.3 and J = 6Hz, 1H, Ar-H), 7.43-7.21 (m, 7H, Ar-H), 5.42 (s, 2H, CH_2Ph), 5.3 (s, 2H, CH_2O), 2.81 (s, 3H, CH_3CON), 2.43 (s, 3H, CH_3COO); ^{13}C NMR

($CDCl_3$): 172.4 (C(O)N), 170.8 (C(O)O), 155.1 (CO), 140.27 (C_{8a}), 136.38 (C_{9a}), 133.53-122.46 (other Ar-C), 127.8 (C_{4b}), 122.73 (C_{4a}), 115.32 (C_8), 109.6 (C_4), 62.16 (CH_2O), 52.15 (CH_2Ph), 28.47 (CH_3CON), 20.99 (CH_3COO); m/z (%): 388 (M^+, 12), 346 (M^+-CH_2CO, 100), 287 (M^+- CH_2CO-CH_3CO, 49), 91 ($C_7H_7^+$, 96), 65 ($C_5H_5^+$, 20), 43 (CH_3CO^+, 94); exact mass for $C_{23}H_{20}N_2O_4$: 388.1423; found: 388.1427.

V) Synthesis of β-carbolinones **6e,f** via acetylation of compound **2d** followed by cycloaddition elimination reaction with phenyl or trimethylsilylacetylene.

To a solution of 1-benzyl-5-chloro-3-(2-iodophenylamino)-2(1*H*)-pyrazinone **2d** (1.3 g, 3 mmol) in pyridine (30 ml) acetic anhydride (3 ml) and DMAP (10%) were added. The mixture was heated under nitrogen atmosphere at 80°C for 48 h. After evaporation the crude **13** was purified using column chromatography Al_2O_3 and $EtOAc/CH_2Cl_2$ as eluent mixtures.

N-(4-Benzyl-6-chloro-3-oxo-3,4-dihydro-2-pyrazinyl)-N-(2-iodophenyl)acetamide (13)

Yield: 73%; m.p. 65°C; IR (KBr) cm^{-1}: 1694, 1660 (CO), 1587 (C=N); ^1H NMR ($CDCl_3$): 8.1-7.2 (m, 9H, Ar-H), 7.1 (s, 1H, H_6), 5.05 (s, 2H, CH_2Ph), 2.07 (s, 3H, CH_3CO); m/z (%): 480 (MH^+, 31), 438 (MH^+-CH_2CO, 100), 91 ($C_7H_7^+$, 18); exact mass for $C_{19}H_{15}ClIN_3O_2$: 478.9898; found: 478.9886.

To a solution of 2 mmol **13** and 2 equiv. trimethylsilylacetylene or phenylacetylene in 40 ml diethylamine was added 21 mg $PdCl_2(PPh_3)_2$ and 3 mg CuI. After the mixture had been stirred for 48 h at 40°C or for 12 h at 70°C, the solvent was evaporated and water (40 ml) was added. The aqueous phase was extracted with CH_2Cl_2 (3 x 30 ml), whereupon the combined oraganic layers were washed with brine and dried over $MgSO_4$. After evaporation, the crude products were purified by column chromatography (SiO_2 using 40% hexane/CH_2Cl_2) as eluent yielding pure compound **6e** (50%) or **6f** (60%).

VI) Generation of the debenzylated β-carbolinones **17** and **19e,f,l**

The β-carbolinones **6e,f** or **l** (2 mmol) were refluxed in acetic anhydride (25 ml) for 10 h under nitrogen atmosphere. After evaporation the crude compound **12e,f** or **l** was purified by column chromatography (Al_2O_3) using 20% CH_2Cl_2/hexane as eluent.

A mixture of 1 mmol **12e,f** or **l** and 20 % $Pd(OH)_2$ (50 mg) on carbon in acetic acid (10 ml) was stirred under H_2 atmosphere (1 atm) during 5 h (or 3 weeks for **6l**). After completion, the catalyst was filtered off and the solvent evaporated. The crude product was purified on a silica using 5% $MeOH/CH_2Cl_2$ as eluent.

2-Benzyl-2,4b,5,6,7,8,8a,9-octahydro-1*H*-β-carbolin-1-one (17)

Yield: 47%; IR (KBr) cm^{-1}: 1648 (CO); ^1H NMR ($CDCl_3$): 11.19 (s(br), 1H, NH), 7.3-7. (m, 9H, Ar-H), 6.9 (d, J = 7Hz, 1H, H_3), 6.43 (d, J = 7Hz, 1H, H_4), 5.3 (s, 2H, CH_2Ph), 2.57 (m, 4H, CH_2), 1.77 (m, 4H, CH_2); ^{13}C NMR ($CDCl_3$): 154.2 (CO), 136.1-126.2 (other Ar-C), 134.8 (C_{9a}), 130.1 (C_{4a}), 122.3 (C_3), 109 (C_4), 50.7 (CH_2Ph), 48.2-20.3 (CH_2); m/z (%): 280 (M^+, 100), 250 (M^+-CO, 18), 91 ($C_7H_7^+$, 88); exact mass for $C_{18}H_{20}N_2O$: 280.1575; found: 280.1571.

4-Trimethylsilyl-2,9-dihydro-1*H*-β-carbolin-1-one (19e)

Yield: 81%; m.p. 260-261°C; IR (KBr) cm^{-1}: 1653 (CO); ^1H NMR (DMSO-d_6): 12.08 (s(br), 1H, NH), 11.56 (s(br), 1H, NH), 8.01-7.2 (m, 4H, Ar-H), 6.93 (d, J = 4Hz, 1H, H_3), 0.41 (s, 9H, $SiCH_3$); ^{13}C NMR (DMSO-d_6): 155.7 (CO), 139.1 (C_{9a}), 129.7 (C_3), 128 (C_{8a}), 126.1 (C_{4b}), 125.7-119.5 (other Ar-C), 122.4 (C_4), 112.8 (C_8), 108.2 (C_{4a}), -0.33 ($SiCH_3$); m/z (%): 256 (M^+, 94), 241 (M^+-CH_3, 100); exact mass for $C_{14}H_{16}N_2OSi$: 256.1032; found: 256.1034.

4-Phenyl-2,9-dihydro-1*H*-β-carbolin-1-one (19f)

Yield: 43%; m.p. 285-286°C; IR (KBr) cm^{-1}: 1652 (CO); ^1H NMR (DMSO-d_6): 12.12 (s(br), 1H, NH), 11.59 (s(br), 1H, NH), 7.6-6.8 (m, 9H, Ar-H), 6.91 (d, J = 4Hz, 1H, H_3); ^{13}C NMR (DMSO-d_6): 155 (CO), 139.2 (C_{9a}), 136.9-119.1 (other Ar-C), 127.9 (C_{8a}), 125.8 (C_4), 122 (C_{4b}), 121.5 (C_{4a}), 116.6 (C_3), 112.8 (C_8); m/z (%): 260 (M^+, 100), 183 (M^+- C_6H_5, 30); exact mass for $C_{17}H_{12}N_2O$: 260.0950; found: 260.0957.

2,9-Dihydro-1*H*-β-carbolin-1-one (19l)
Yield: 86%; m.p. 252-256°C; IR (KBr) cm^{-1}: 1640 (CO); ^1H NMR (DMSO-d_6): 11.98 (s(br), 1H, NH), 11.5 (s(br), 1H, NH), 8.03 (br. d, J = 7.9 Hz, 1H, Ar-H), 7.6-6.8 (m, 4H, Ar-H), 6.91 (d, J = 7Hz, 1H, H_3 or H_4); ^{13}C NMR (DMSO-d_6): 155 (CO), 138.9 (C_{9a}), 136.9-119.1 (other Ar-C), 127.9 (C_{8a}), 124 (C_{4b}), 121.5 (C_{4a}), 116.6 (C_3), 112.8 (C_8), 99.7 (C_4),; m/z (%): 184 ($M^{+\cdot}$, 100), 166 ($M^{+\cdot}$- H_2O, 9); exact mass for $C_{11}H_8N_2O$: 184.1943; found: 184.1947.

VII-1) Synthesis of α-carbolines **20** and **21**
A mixture of alcohol **5h** (1.84 mmol, 570 mg), methanesulfonyl chloride (2.03 mmol, 294 mg, 1.1 eq), DMAP (0.2 mmol, 23 mg, 0.1 eq) and pyridine (9.2 mmol, 727 mg) in dry CH_2Cl_2 (30 ml) was stirred for 20 h under nitrogen atmosphere at rt. Water was added and the mixture was neutralised with 3% HCl, extracted with CH_2Cl_2 (5 x 30 ml), dried with $MgSO_4$. Filtration, concentration in vacuo and column chromatography over silica gel using (hexane/CH_2Cl_2 and CH_2Cl_2/EtOAc) gave compounds **20** (427 mg, 60%) and **21** (108 mg, 18%).

2-Chloro-4-[(methylsulfonyl)oxymethyl]-3-phenyl-9*H*-pyrido[2,3-*b*]indole (20)
Yield: 60%; m.p. 231-232°C; IR (KBr) cm^{-1}: 3168 (NH); ^1H NMR ($CDCl_3$): 11.2 (s(br), 1H, NH), 8.41 (d, J = 8.5Hz, 1H, Ar-H), 8.17 (d, J = 7.8Hz, 1H, Ar-H), 7.67-7.27 (m, 7H, Ar-H), 5.4 (s, 2H, CH_2O), 3.73 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): 151.2 (C_{9a}), 147.2 (C_3), 142.6 (C_2), 139.2 (C_{8a}), 137-121.8 (other Ar-C), 121.6 (C_{4b}), 115.9 (C_{4a}), 113.7 (C_8), 64.7 (CH_2O), 36 (CH_3); m/z (%): 386 ($M^{+\cdot}$, 100), 291 ($M^{+\cdot}$-SO_3Me, 17), 256 ($M^{+\cdot}$-$ClSO_3Me$, 54), 79 (SO_2Me^+, 20); exact mass for $C_{19}H_{15}ClN_2O_3S$: 386.0491; found: 386.0489.

2-Chloro-4-(chloromethyl)-3-phenyl-9*H*-pyrido[2,3-*b*]indole (21)
Yield: 18%; m.p. 241-242°C; IR (KBr) cm^{-1}: 3170 (NH); ^1H NMR ($CDCl_3$): 11.37 (s(br), 1H, NH), 8.2 (d, J = 8Hz, 1H, Ar-H), 7.77 (d, J = 8Hz, 1H, Ar-H), 7.59-7.44 (m, 6H, Ar-H), 7.34 (dd, J = 7.2Hz, J = 8Hz, 1H, Ar-H), 4.8 (s, 2H, CH_2Cl); ^{13}C NMR ($CDCl_3$): 150.85 (C_{9a}), 146.59 (C_4), 140.64 (C_2), 139.49 (C_{8a}), 135.69-112.1 (other Ar-C), 120.62 (C_{4b}), 116.99 (C_{4a}), 113.96 (C_8), 40.64 (CH_2Cl); m/z (%): 326 ($M^{+\cdot}$,100), 291 ($M^{+\cdot}$-Cl, 13), 256 ($M^{+\cdot}$-Cl_2, 75); exact mass for $C_{18}H_{12}Cl_2N_2$: 326.0377; found: 326.0381.

VII-2) Synthesis of α-carboline **22**
A mixture of N,N-dimethylamine (1.15 mmol, 0.58 ml) and powdered 80% NaH (1.26 mmol, 38 mg) in dry THF (10 ml) under nitrogen atmosphere was stirred at rt for 1 h. A solution of **20** (0.23 mmol, 90 mg) or **21** (0.23 mmol, 75 mg) in dry THF (5 ml) was added dropwise. After 5 h (for **20**), or 10 days (for **21**) water (50 ml) was added and the mixture was extracted with EtOAc (4 x 10 ml). Drying with $MgSO_4$, filtration, concentration in vacuo and recrystallisation from MeOH gave compound **22** (62 mg, 82%).

2-Chloro-4-(N,N-dimethylaminomethyl)-3-phenyl-9*H*-pyrido[2,3-*b*]indole (22)
Yield: 82%; m.p. 273-274°C; IR (KBr) cm^{-1}: 3205 (NH), 2816-2769 ($N(CH_3)_2$), 1590 (pyridine); ^1H NMR ($CDCl_3$): 10.62 (s(br), 1H, NH), 8.23 (d, J = 8Hz, 1H, Ar-H), 7.7 (d, J = 8Hz, 1H, Ar-H), 7.52-7.47 (m, 4H, Ar-H), 7.35-7.27 (m, 3H, Ar-H), 3.73 (s, 2H, CH_2N), 2.19 (s, 6H, $N(CH_3)_2$); ^{13}C NMR ($CDCl_3$): 150.65 (C_{9a}), 146.8 (C_3), 144.17 (C_2), 139.24 (C_4), 137.5-120.5 (other Ar-C), 121.05 (C_{4a}), 115.1 (C_{4b}), 111.48 (C_8), 58.39 (CH_2N), 45.44 (CH_3); m/z (%): 335 ($M^{+\cdot}$, 33), 320 ($M^{+\cdot}$-CH_3, 7), 292 ($M^{+\cdot}$-CH_2NCH_3, 66), 255 ($M^{+\cdot}$-$HClN(CH_3)_2$, 34), 58 ($CH_2N(CH_3)_2^+$, 100); exact mass for $C_{20}H_{18}ClN_3$: 335.1189; found: 335.1193. Anal. Calcd for $C_{20}H_{18}ClN_3$: C, 71.53, H, 5.40, N, 12.51. Found : C, 71.25, H, 5.27, N, 12.24.

ACKNOWLEDGEMENTS The authors wish to thank the F.K.F.O. and the Ministerie voor Wetenschapsbeleid, I.U.A.P. for financial support. They are also grateful to R. De Boer for mass spectral analysis and to the Janssen Pharmaceutica company for element analysis. A.T., K.B. and D.M.V. thank the K.U. Leuven for the fellowships received.

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