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Synthesis of New Pyrrolo[3,4-*b*]- and [3,4-*c*]pyridin(on)es and Related 1,7-Naphthyridinones and 2,7-Naphthyridines *via* Intramolecular Diels-Alder Reactions of 2(1*H*)-Pyrazinones

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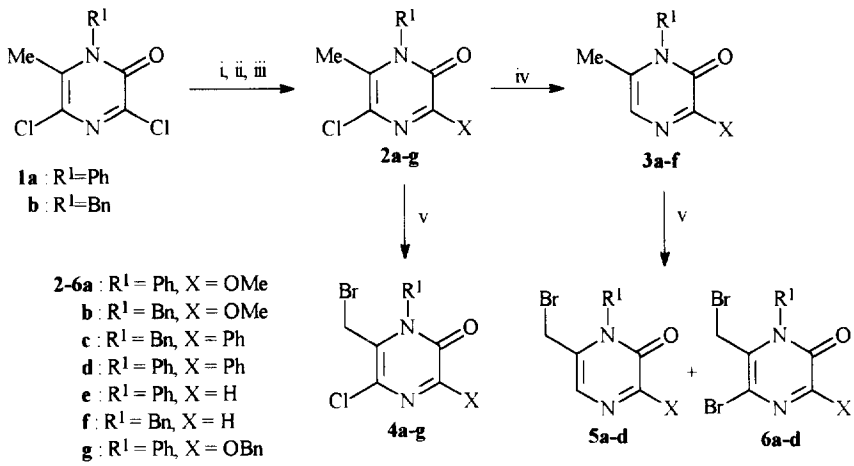
Abstract: 2(1*H*)-pyrazinones **7**, **10** or **12** with in 6-position a 2-propynylaminomethyl or 3-butynylaminomethyl side chain undergo intramolecular Diels-Alder reactions providing cycloadducts which can be isolated or functionalised in some cases. By further thermolysis of these compounds either pyrrolo-[3,4-*b*]pyridinones **15/16** and/or pyrrolo[3,4-*c*]pyridines **17/18** or 1,7-naphthyridinones **25** and/or 2,7-naphthyridines **26** can be generated. Loss of either cyanide or isocyanate from the respective adducts is shown to be dependent on their substitution pattern.

In a previous paper we described the intramolecular Diels-Alder reaction of 2(1*H*)-pyrazinones with an alkynyloxy- or alkynyloxyalkyl side chain in 3-position providing in this way a synthetic pathway to new furo/pyrano-pyridinones and pyridines.[1] Now, we report similar reactions of 2(1*H*)-pyrazinones with an alkynylaminomethyl side chain anchored in 6-position. To our knowledge, reactions of heterocyclic azadiene systems with this type of side chain have been investigated very rarely.[2] They could generate pyrrolopyridin(on)es and naphthyridin(on)es. While pyrrolo[3,4-*b*]/[3,4-*c*]pyridines with one or two carbonyl functionalities in the pyrrolo moiety are well documented and known to possess interesting biological activities,[3-6] the pyrrolopyridinone targets in our approach are scarcely described.[7] Only a few synthetic pathways[8,9] to the scarcely explored 1,7- and 2,7-naphthyridine derivatives are known in contrast with the various methods available for the synthesis of 2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridines. However the variability of their substitution pattern is rather limited.[10-12]

In this paper we describe the preparation of the required precursors, their thermolysis and the influence of the substitution pattern on the cycloaddition-elimination reaction. Also the isolation and further reaction of some intermediate cycloadducts will be considered.

Synthesis of the precursors

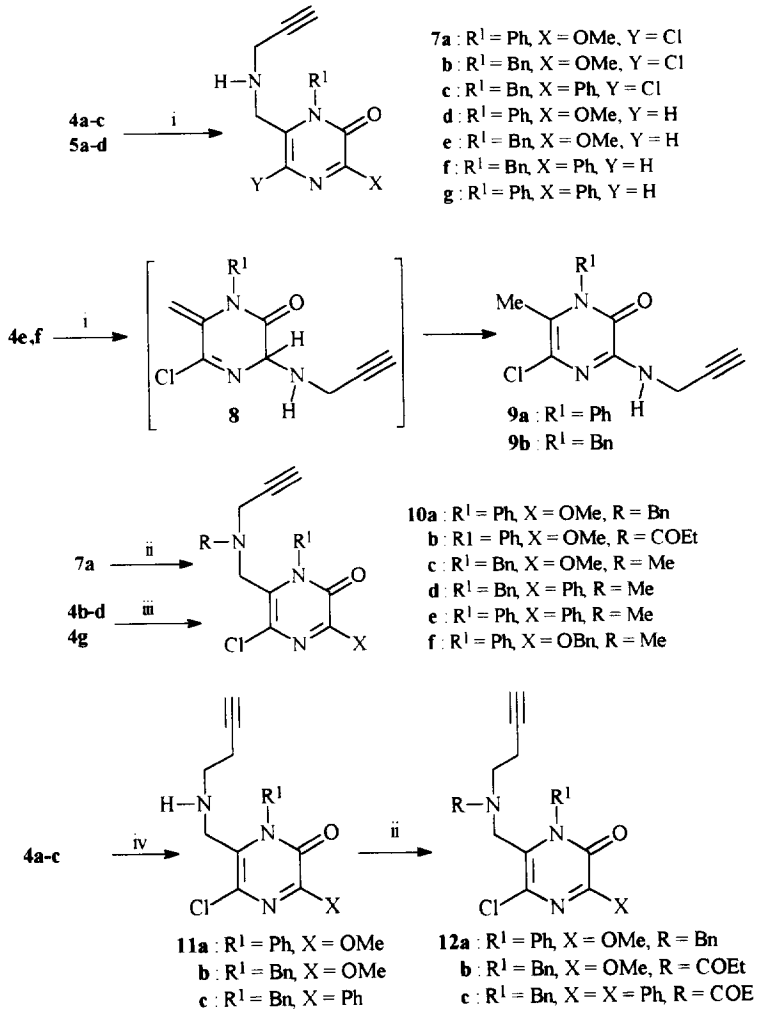
Firstly, the 6-methyl-3,5-dichloro-2(1*H*)-pyrazinones **1a,b** were reacted with sodium methoxide in methanol or with sodium benzyloxide in THF to provide 3-methoxy-2(1*H*)-pyrazinones **2a,b** (± 95 % yield) and the corresponding 3-benzyloxy derivative **2g** (87 % yield) (Scheme 1). Treatment of **1a,b** with tetraphenyltin and tetrakis(triphenylphosphine)palladium(0) (tetrakis) in toluene at 110 °C afforded the 3-phenyl-2(1*H*)-pyrazinones **2c** and **2d** (85-90 % yield).[13] Hydrogenolysis of the 3-position with sodium formate in the presence of tetrakis[14] at 100 °C in DMF provided **2e,f** (± 75 % yield). Reaction for a longer period under these conditions yielded compounds **3e,f**. Dehalogenation of 5-chloro-pyrazinones **2a-d** to afford compounds **3a-d** (90-95 %) could be done more efficiently by treatment with hydrogen gas (1 atm) and 10 % palladium on carbon in methanol.[15] In order to introduce an α-bromomethyl group into position 6, compounds **2a-g** and **3a-d** were reacted with *N*-bromosuccinimide (NBS) and benzoyl peroxide in dry refluxing CCl_4 to yield 6-bromomethyl-2(1*H*)-pyrazinones **4a-g** (80-90 %) and **5a-d** (60-70 %).[13] In the latter case (R^5 = H) the formation of the side products **6a-d** could not be avoided (± 20 %).



Scheme 1 *Reagents and Conditions*: i, NaH, MeOH, rt or NaH, BnOH, THF, rt: **2a-b, 2g**; ii, Ph_4Sn, $Pd(PPh_3)_4$, toluene,110 °C: **2c-d**; iii, HCOONa, $Pd(PPh_3)_4$, DMF, 110 °C: **2e-f**; iv, H_2, Pd/C, MeOH: **3a-d**; HCOONa, $Pd(PPh_3)_4$, DMF, 110 °C: **3e-f**; v, NBS, CCl_4, reflux

Further conversion of the 6-bromomethyl-2(1*H*)-pyrazinones **4** and **5** into the desired 6-(2-propynylaminomethyl)-2(1*H*)-pyrazinones **7** was attempted by reaction with 3 equiv propargylamine in THF (Scheme 2). This reaction was successful with compounds **4a-c** and **5a-d** affording **7a-g** in good yield. However with **4e** or **4f** the amine probably attacks the less sterically hindered 3-position affording intermediates of type **8** which undergo a 1,5-proton shift to give 3-(2-propynylamino)-2(1*H*)-pyrazinones **9a** and **9b**. *N*-benzylated and *N*-acylated derivatives **10a** and **10b** could be realised by reacting the precursor **7a** with benzyl bromide in refluxing THF (53 % yield) or with propionyl chloride in THF at

room temperature (82 %). The *N*-methylated derivatives **10c-f** were obtained from the reaction of the 6-bromomethyl-2(1*H*)-pyrazinones **4b-d** and **4g** with 3 equiv *N*-methyl propargylamine in THF (85-95 %). Compounds **4a-c** were also treated with the HCl-salt of 4-amino-1-butyne and triethylamine in THF yielding the 6-(3-butynylaminomethyl)-substituted analogues **11a-c** which were converted into **12a-c** by reaction with benzyl bromide and propionyl chloride, respectively.



Scheme 2 *Reagents and Conditions*: i, propargylamine, THF, rt; ii, BnBr, THF, reflux or propionyl chloride, THF, rt; iii, *N*-methyl propargylamine, THF, rt; iv, 4-amino-1-butyne.HCl, NEt_3, THF, rt

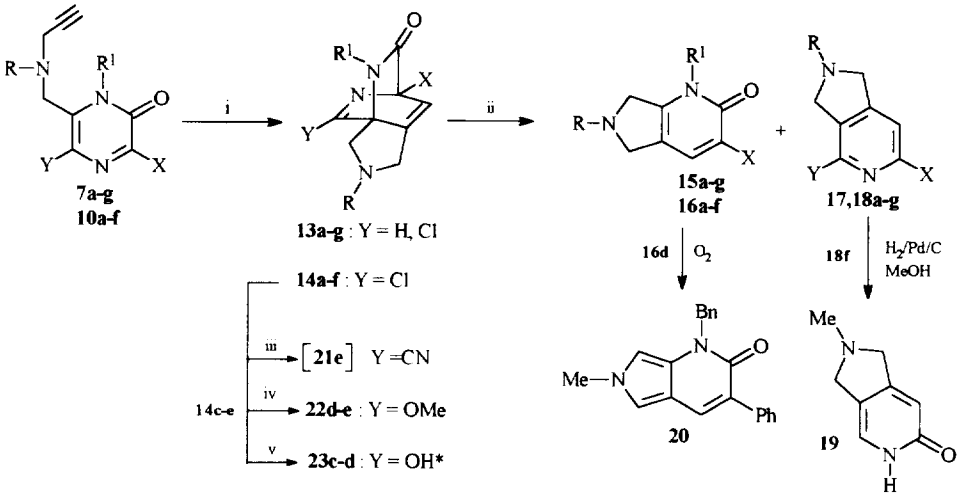
Thermolysis of the precursors

When the precursor **7b** or **7c** was refluxed in toluene for 5-20 minutes the formation of an intermediate, presumed to be cycloadduct **13b-c**, was observed (Scheme 3). Further reaction for 1-2 hours led to the formation of the 1-benzyl-6-cyano-1,5,6,7-tetrahydro-3-methoxy-2*H*-pyrrolo[3,4-*b*]pyridin-2-one **15b** and the corresponding 3-phenyl derivative **15c** respectively (50-55 % yield) (Table 1). Further reflux (1 h) of **13a**, obtained from **7a**, led to a complex reaction mixture: the 2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridines **17a** and **17a'** (32 % and 17 % yield respectively) were identified as the main products and also the formation of traces of pyridinone compounds could be observed. Probably, the secondary amine in the pyrrolopyridi(no)ne obtained after addition-elimination, reacts further with cyanogen chloride (ClCN) or phenyl isocyanate (PhNCO) evolved from the intermediate **13**.

As cycloadducts lose hydrogen cyanide much more easily than cyanogen chloride[15] so that competitive loss of isocyanate could be avoided, the thermolysis (in toluene) was studied with precursors **7d-g** (Y = H). After reaction for 2-4 hours the 1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-ones **15d-g** (45-60 % yield) were isolated: we believe that the cycloaddition rate is slowed down because of the higher LUMO energy of the azadiene (no chloro atom in position 5).

Side reactions with ClCN or RNCO could also be avoided by using precursors **10**, with a trisubstituted amine in the side chain. These compounds underwent complete cycloaddition after 5 minutes (**10d,e**) or 20 minutes (X = OMe or OBn) reflux in toluene affording the corresponding adducts **14a-f**. In some cases, the formation of compounds **16/18** had already started. Further reflux of the adducts **14c** and **14d** (R^1 = Bn) provided predominantly annelated pyridinones **16**: **16c** starting from **14c** and **16d** together with traces of the 4-chloro-2-methyl-6-phenyl-2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridine **18d** starting from **14d**. Compounds **14a-b** and crude adducts **14e-f** (via **10e-f**) with R^1 = Ph yielded mixtures of 1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-ones **16a-b,e-f** and 2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridines **18a-b,d-f** in a ratio of approximately 1:4 (X = OMe or OBn) or 1:6 (X = Ph). The annelated pyridine **18f** could be further debenzylated in methanol using hydrogen gas and 10 % Pd/C affording the 1,2,3,5-tetrahydro-2-methyl-6*H*-pyrrolo[3,4-*c*]pyridin-6-one **19**.

6,7-Dihydro-5*H*-pyrrolo[3,4-*b*]pyridines are known to be unstable structures;[16] in our hands the related and undescribed 1,5,6,7-tetrahydro-2*H*-pyrrolopyridin-2-ones **15b-e** and **16a-c,f** were stable but the isolated analogues **15f-g** and **16d-e** with X = Ph and R = H or Me reacted slowly with oxygen resulting in complex reaction mixtures. In the case of, for example **16d**, the main product in the mixture was identified as the 1-benzyl-1,6-dihydro-6-methyl-3-phenyl-2*H*-pyrrolo[3,4-*b*]pyridin-2-one **20** (23 % yield). Also this compound was not stable in the presence of air oxygen.



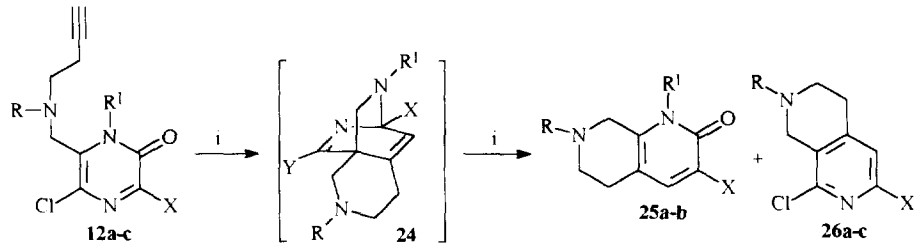
Scheme 3 *Reagents and Conditions*: i, reflux, toluene: 5-30min; ii, reflux, toluene: **13-14**: 1-4h; **22**: 5-24h or reflux, C_6H_5Br: **23**: 1-2h; iii, 14e: KCN, 18-crown-6, MeCN, 60 °C, 12h;iv, 14d,e: MeOH, NaH, rt: v, 14c-d: 1N NaOH/H_2O/dioxane, rt, *the compound appears under the lactam form

Table 1

starting compound	adduct	R^1	X	Y	R	**15** (% yield)	**17** (% yield)
7a	**13a**	Ph	OMe	Cl	H	-	**a** (R = PhNCO, 32) **a'** (R = CN, 17)
7b	**13b**	Bn	OMe	Cl	H	**b** (R = CN, 55)	-
7c	**13c**	Bn	Ph	Cl	H	**c** (R = CN, 51)	-
7d	[**13d**]	Ph	OMe	H	H	**d** (65)	-
7e	[**13e**]	Bn	OMe	H	H	**e** (59)	-
7f	[**13f**]	Bn	Ph	H	H	**f** (49)	-
7g	[**13g**]	Ph	Ph	H	H	**g** (43)	-
starting compound	**adduct**					**16** (% yield)	**18** (% yield)
10a	**14a**	Ph	OMe	Cl	Bn	**a** (14)	**a** (58)
10b	**14b**	Ph	OMe	Cl	COEt	**b** (10)	**b** (48)
10c	**14c**	Bn	OMe	Cl	Me	**c** (77)	-
10d	**14d**	Bn	Ph	Cl	Me	**d** (65)	**d** (8)
10e	**14e**	Ph	Ph	Cl	Me	**e** (10)	**d** (62)
10f	**14f**	Ph	OBn	Cl	Me	**f** (13)	**f** (55)
	[**21e**]	Ph	Ph	CN	Me	**e** (62)	-
	22d	Bn	Ph	OMe	Me	**d** (6)	**g** (62)
	22e	Ph	Ph	OMe	Me	-	**g** (42)
	23c	Bn	OMe	OH*	Me	**c** (51)	-
	23d	Bn	Ph	OH*	Me	**d** (44)	-

To test further the influence of the Y-substituent on the product distribution, the chlorimine function in the isolated cycloadducts **14c-e** was reacted with some nucleophiles. A cyano group was introduced by reaction of **14e** with potassium cyanide and a catalytic amount of 18-crown-6 in MeCN at 60 °C during 12 hours. The adduct **21e** could not be isolated under the required substitution conditions, but the immediate and selective formation of compound **16e** could be realised. The methoxy-substituted derivatives **22d-e**, obtained from **14d-e**, had to be refluxed in toluene for 24 hours and 5 hours respectively to yield nearly exclusively **18g** (and a small amount of the pyridinone **16d**). Conversion of compounds **23c-d** was possible by reaction with an aqueous 1N NaOH solution in dioxane. Reflux of compounds **23c-d** in bromobenzene (no reaction in toluene) afforded **16c** and **16d** without yield improvement in comparison with the thermolysis of **14c-d** (Scheme 3).

The cycloaddition of compounds of type **12** required higher reaction temperatures (reflux in bromobenzene) excluding the isolation of cycloadducts of type **24**; annelated pyridines **26** were obtained as the main products: 7-benzyl-1-chloro-3-methoxy-5,6,7,8-tetrahydro-2,7-naphthyridine **26a** was exclusively formed from **12a**; **12b** and **12c** gave a mixture of 1,7-naphthyridin-2(1*H*)-one : 2,7-naphthyridine in a ratio of approximately 5:1 (**25a**:**26b**) and 1:1 (**25b**:**26c**) respectively (Scheme 4, Table 2).



Scheme 4 *Reagents and Conditions*: i, bromobenzene, reflux

Table 2

	R^1	X	R	**25** (% yield)	**26** (% yield)
12a	Ph	OMe	Bn	-	**a** (78)
12b	Bn	OMe	COEt	**a** (63)	**b** (13)
12c	Bn	Ph	COEt	**b** (41)	**c** (48)

In conclusion, we can state that 2(1*H*)-pyrazinones anchored in 6-position with a 2-propynylaminomethyl or 3-butynylaminomethyl side chain can undergo intramolecular Diels-Alder reactions affording adducts which can be further converted. The formation and further thermolysis of these adducts is influenced by the substitution pattern. A methoxy group in 3-position or a hydrogen atom in 5-position seems to slow down the cycloaddition step. By an appropriate choice of the substituents R^1 and Y in the functionalised adducts from pyrazinones **7,10**, either pyrrolo[3,4-*b*]pyridinones **15-16** or pyrrolo[3,4-*c*]pyridines **18** can be generated. The nature of the Y-substituent influences the elimination of

the nitrile as in intermolecular reactions:[15] selective formation of pyridinone is observed if Y = CN, whereas pyridines are generated when Y = OMe. Cycloadducts of type **24** cannot be isolated nor functionalised. The ratio 1,7-naphthyridinone **25** : 2,7-naphthyridine **26** can only be influenced by the substituents in position 1 and 3 of the pyrazinone.

EXPERIMENTAL

Infrared spectra were recorded on a Perkin-Elmer 297 grating IR spectrophotometer and a Perkin-Elmer 1720 Fourier transform spectrometer. ^{1}H NMR spectra and ^{13}C 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 ^{1}H 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 MS5OTC 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. Melting points were taken using a Reichert-Jung Thermovar apparatus and an Electrothermal IA 9000 digital melting point apparatus and are uncorrected. Microanalyses were performed by Janssen Pharmaceutica on a Carlo Erba elemental analyser type 1106.

I. 3,5-Dichloro-2(1H)-pyrazinones ***1*** *and substituted derivatives* ***2-5****.*

The preparation and the analytical data of the 3,5-dichloro-2(1*H*)-pyrazinones **1a,b** were reported previously.[1,17]

The method for the introduction of an alkoxide, a phenyl group or a hydrogen atom in 3-position of the 3,5-dichloro-2(1*H*)-pyrazinones, the dehalogenation of the 5-position and the bromination of the methyl group in position 6 was described previously.[13,15] New compounds of type **2-4** and also 6-bromomethyl-2(1*H*)-pyrazinones **5** were prepared in comparable way.

1-benzyl-5-chloro-3-methoxy-6-methyl-2(1*H*)-pyrazinone 2b

Yield: 97 %; m.p.: 84-85 °C (EtOH); IR (KBr) cm^{-1}: 1669 (CO), 1592 (C=N); ^{1}H NMR: 7.35-7.08 (m, 5H, Ar-H), 5.30 (s, 2H, CH_2Ph), 3.97 (s, 3H, OCH_3), 2.27 (s, 3H, CH_3); m/z (%): 264 ($M^{+\cdot}$, 13), 173 ($M^{+\cdot}$-C_7H_7, 2), 91 ($C_7H_7^+$, 100); exact mass for $C_{13}H_{13}N_2O_2Cl$: 264.0666; found: 264.0665

1-benzyl-5-chloro-6-methyl-3-phenyl-2(1*H*)-pyrazinone 2c

Yield: 88 %; m.p.: 144 °C (EtOH); IR (KBr) cm^{-1}: 1656 (CO), 1557 (C=N); ^{1}H NMR: 8.45-7.10 (m, 10H, Ar-H), 5.35 (CH_2Ph), 2.33 (s, 3H, CH_3); m/z (%): 310 ($M^{+\cdot}$, 11), 219 ($M^{+\cdot}$-C_7H_7, 2), 91 ($C_7H_7^+$, 100); exact mass for $C_{18}H_{15}N_2OCl$: 310.0873; found: 310.0874

1-benzyl-5-chloro-6-methyl-2(1*H*)-pyrazinone 2f

Yield: 75 %; m.p.: 93-94 °C (EtOH); IR (KBr) cm^{-1}: 1657 (CO), 1558 (C=N); ^{1}H NMR: 7.95 (s, 1H, 3-H), 7.38-7.11 (m, 5H, Ar-H), 5.31 (s, 2H, CH_2Ph), 2.39 (s, 3H, CH_3), m/z (%): 234 ($M^{+\cdot}$, 24), 199 ($M^{+\cdot}$-Cl, 31), 91 ($C_7H_7^+$, 100); exact mass for $C_{12}H_{11}N_2OCl$: 234.0560; found: 234.0566

3-benzyloxy-5-chloro-6-methyl-1-phenyl-2(1*H*)-pyrazinone 2g

Yield: 87 %; m.p.: 158-159 °C (EtOH); IR (KBr) cm^{-1}: 1676 (CO), 1589 (C=N); ^{1}H NMR: 7.55-7.10 (m, 10H, Ar-H), 5.42 (s, 2H, OCH_2Ph), 1.95 (s, 3H, CH_3); m/z (%): 326 ($M^{+\cdot}$, 46), 207 ($M^{+\cdot}$-CO-C_7H_7, 9), 91 ($C_7H_7^+$, 100); exact mass for $C_{18}H_{15}N_2O_2Cl$: 326.0822; found: 326.0827

3-methoxy-6-methyl-1-phenyl-2(1*H*)-pyrazinone 3a

Yield: 93 %; m.p.: 171 °C (EtOH); IR (KBr) cm^{-1}: 1660 (CO), 1605 (C=N); ^1H NMR: 7.43-7.15 (m, 5H, Ar-H), 6.75 (q, 1H, 5-H), 3.98 (s, 3H, OCH_3), 1.84 (d, 3H, CH_3); m/z (%): 216 ($M^{+\cdot}$, 86), 188 ($M^{+\cdot}$-CO, 5), 77 ($C_6H_5^+$, 100); exact mass for $C_{12}H_{12}N_2O_2$: 216.0899; found: 216.0904

1-benzyl-3-methoxy-6-methyl-2(1*H*)-pyrazinone 3b

Yield: 96 %; m.p.: 69-70 °C (EtOH); IR (KBr) cm^{-1}: 1631 (CO), 1602 (C=N); ^1H NMR: 7.36-7.15 (m, 5H, Ar-H), 6.68 (s, 1H, 5-H), 5.30 (s, 2H, CH_2Ph), 3.97 (s, 3H, OCH_3), 2.15 (s, 3H, CH_3); m/z (%): 230 ($M^{+\cdot}$, 11), 139 ($M^{+\cdot}$-C_7H_7, 4), 91 ($C_7H_7^+$, 100); exact mass for $C_{13}H_{14}N_2O_2$: 230.1055; found: 230.1060

1-benzyl-6-methyl-3-phenyl-2(1*H*)-pyrazinone 3c

Yield: 92 %; m.p.: 146-147 °C (EtOH); IR (KBr) cm^{-1} : 1651 (CO), 1583 (C=N); ^1H NMR: 8.36-7.18 (m, 11H, Ar-H + 5-H), 5.40 (s, 2H, CH_2Ph), 2.35 (s, 3H, CH_3); m/z (%): 276 ($M^{+\cdot}$, 3), 185 ($M^{+\cdot}$-C_7H_7, 2), 91 ($C_7H_7^+$, 100); exact mass for $C_{18}H_{16}N_2O$: 276.1263; found: 276.1259

6-methyl-1-phenyl-2(1*H*)-pyrazinone 3e

Yield: 59 %; m.p.: 193-194 °C (EtOH); IR (KBr) cm^{-1}: 1661 (CO), 1598 (C=N); ^1H NMR: 8.12 (s, 1H, 3-H), 7.58-7.17 (m, 6H, Ar-H + 5-H), 1.96 (s, 3H, CH_3); m/z (%): 186 ($M^{+\cdot}$, 93), 158 ($M^{+\cdot}$-CO, 66), 77 ($C_6H_5^+$, 100); exact mass for $C_{11}H_{10}N_2O$: 186.0793; found: 186.0793

1-benzyl-6-methyl-2(1*H*)-pyrazinone 3f

Yield: 62 %; m.p.: 86-87 °C (EtOH); IR (KBr) cm^{-1}: 1625 (CO), 1592 (C=N); ^1H NMR: 8.09 (s, 1H, 3-H), 7.39-7.12 (m, 6H, Ar-H + 5-H), 5.24 (s, 2H, CH_2Ph), 2.22 (s, 3H, CH_3); m/z (%): 186 ($M^{+\cdot}$, 93), 158 ($M^{+\cdot}$-CO, 66), 77 ($C_6H_5^+$, 100); exact mass for $C_{11}H_{10}N_2O$: 186.0793; found: 186.0793

1-benzyl-6-bromomethyl-5-chloro-3-methoxy-2(1*H*)-pyrazinone 4b

Yield: 89 %; m.p.: 171 °C (EtOH); IR (KBr) cm^{-1}: 1680 (CO), 1590 (C=N); ^1H NMR : 7.60-7.10 (m, 5H, Ar-H), 5.55 (CH_2Ph), 4.43 (s, 2H, CH_2Br), 4.03 (s, 3H, OCH_3); m/z (%): 342 ($M^{+\cdot}$, 2), 263 ($M^{+\cdot}$-Br, 17), 91 ($C_7H_7^+$, 39); exact mass for $C_{13}H_{12}N_2O_2BrCl$: 341.9771; found: 341.9776

1-benzyl-6-bromomethyl-5-chloro-3-phenyl-2(1*H*)-pyrazinone 4c

Yield: 92 %; m.p. : 135-136 °C (EtOH); IR (KBr) cm^{-1}: 1651 (CO), 1552 (C=N); ^1H NMR: 8.45-7.15 (m, 10H, Ar-H), 5.55 (s, 2H, CH_2Ph), 4.45 (s, 2H, CH_2Br); m/z (%): 388 ($M^{+\cdot}$, 2), 309 ($M^{+\cdot}$-Br, 15), 91 ($C_7H_7^+$, 100); exact mass for $C_{18}H_{14}N_2OBrCl$: 387.9978; found: 387.9974

1-benzyl-6-bromomethyl-5-chloro-2(1*H*)-pyrazinone 4f

Yield: 94 %; IR (KBr) cm^{-1}: 1660 (CO), 1565 (C=N); ^1H NMR: 8.16 (s, 1H, 3-H), 7.75-7.10 (m, 5H, Ar-H), 5.50 (s, 2H, CH_2Ph), 4.45 (s, 2H, CH_2Br); m/z (%): 312 ($M^{+\cdot}$, 3), 233 ($M^{+\cdot}$-Br, 16), 91 ($C_7H_7^+$, 100); exact mass for $C_{11}H_8N_2OBrCl$: 311.9665; found: 311.9673

3-benzyloxy-6-bromomethyl-5-chloro-1-phenyl-2(1*H*)-pyrazinone 4g

Yield: 92 %; M.p. : 165-166 °C (EtOH); IR (KBr) cm^{-1}: 1680 (CO), 1589 (C=N); ^1H NMR: 7.60-7.25 (m, 10H, Ar-H), 5.45 (s, 2H, OCH_2Ph), 4.10 (s, 2H, CH_2Br); m/z (%): 404 ($M^{+\cdot}$, 1), 325 ($M^{+\cdot}$-Br, 6), 91 ($C_7H_7^+$, 39); exact mass for $C_{18}H_{14}N_2O_2BrCl$: 403.9927; found: 403.9936

6-bromomethyl-3-methoxy-1-phenyl-2(1*H*)-pyrazinone 5a

Yield: 72 %; m.p. : 184 °C (EtOH); IR (KBr) cm^{-1}: 1660 (CO), 1615 (C=N); ^1H NMR: 7.48-7.28 (m, 5H, Ar-H), 7.06 (s, 1H, 5-H), 4.02 (s, 5H, OCH_3, CH_2Br); m/z (%): 294 ($M^{+\cdot}$, 15), 215 ($M^{+\cdot}$-Br, 100), 77 ($C_6H_5^+$, 39); exact mass for $C_{12}H_{11}N_2O_2Br$: 294.0004; found: 294.0002

1-benzyl-6-bromomethyl-3-methoxy-2(1*H*)-pyrazinone 5b

Yield: 61 %; m.p.: 64-65 °C (EtOH); IR (KBr) cm^{-1}: 1666 (CO), 1624 (C=N); ^1H NMR: 7.38-7.13 (m, 5H, Ar-H), 6.98 (s, 1H, 5-H), 5.58 (s, 2H, CH_2Ph), 4.25 (s, 2H, CH_2Br), 4.06 (s, 3H, OCH_3); m/z (%): 308 ($M^{+\cdot}$, 2), 229 ($M^{+\cdot}$-Br, 9), 91 ($C_7H_7^+$, 100); exact mass for $C_{13}H_{13}N_2O_2Br$: 308.0160; found: 308.0153

1-benzyl-6-bromomethyl-3-phenyl-2(1*H*)-pyrazinone 5c

Yield: 59 %; m.p.: 150-151 °C; IR (KBr) cm^{-1}: 1652 (CO), 1583 (C=N); ^1H NMR: 8.39-7.21 (m, 11H, Ar-H + 5-H), 5.60 (s, 2H CH_2Ph), 4.26 (s, 2H, CH_2Br); m/z (%): 354 ($M^{+\cdot}$, 3), 275 ($M^{+\cdot}$-Br, 16), 91 ($C_7H_7^+$, 100); exact mass for $C_{18}H_{15}N_2OBr$: 354.0368; found: 354.0382

6-bromomethyl-1,3-diphenyl-2(1*H*)-pyrazinone 5d

Yield: 65 %; m.p.: 210 °C (EtOH); IR (KBr) cm^{-1}: 1660 (CO), 1575 (C=N); ^1H NMR : 8.39-7.38 (m, 10H, Ar-H), 7.66 (s, 1H, 5-H), 4.05 (s, 2H, CH_2Br); m/z (%): 340 ($M^{+\cdot}$, 25), 261 ($M^{+\cdot}$-Br, 100), 77 ($C_6H_5^+$, 59); exact mass for $C_{17}H_{13}N_2OBr$: 340.0211; found: 340.0211

II. 6-Alkynylaminomethyl-2(1H)-pyrazinones.

Synthesis of 6-alkynylaminomethyl-2(1*H*)-pyrazinones 7a-g,10a-f,11a-c,12a-c and of compounds **9.**

To a mixture of 10 mmol 6-bromomethyl-2(1*H*)-pyrazinone **4a-g,5a-d** in 80 ml dry THF was added 1.9 ml propargylamine (30 mmol) or 2.5 ml *N*-methyl propargylamine (30 mmol) or 210 mg 4-amino-3-butyne.HCl (20 mmol) and 4.25 ml triethylamine. After stirring for 1-3 hours at rt, the reaction mixture was subjected to flash chromatography (SiO_2, EtOAc). After evaporation of the eluent, the resulting product was purified using column chromatography (SiO_2,EtOAc/CH_2Cl_2). Treatment of **4e-f** under the above mentioned conditions afforded the undesired 2(1H)-pyrazinones **9a-b** instead of compounds of type **7**.

The benzylation or acylation of the obtained 6-alkynylaminomethyl-2(1*H*)-pyrazinones **7a** or **11a-c** was performed by adding 0.62 ml (5.2 mmol) benzylbromide or 0.52 ml propionyl chloride (6 mmol) to a solution of the pyrazinone (4 mmol) in dry THF (40 ml). After refluxing for 3 hours (or stirring for 1 hour at rt), the reaction mixture was purified as described above.

5-chloro-3-methoxy-1-phenyl-6-(2-propynylaminomethyl)-2(1*H*)-pyrazinone 7a

Yield: 62 %; m.p.: 150-151 °C (EtOH); IR (KBr) cm^{-1}: 3240 (C≡CH), 2100 (C≡C), 1670 (CO), 1590 (C=N); ^1H NMR: 7.60-7.20 (m, 5H, Ar-H), 4.02 (s, 3H, OCH_3), 3.53 (s, 2H, CH_2NH), 3.19 (d, 2H, $NHCH_2$), 2.12 (t, 1H, C≡CH), 1.73 (s(br), 1H, NH); m/z (%): 303 ($M^{+\cdot}$, 70), 268 ($M^{+\cdot}$-Cl, 100); exact mass for $C_{15}H_{14}N_3O_2Cl$: 303.0775; found: 303.0776

1-benzyl-5-chloro-3-methoxy-6-(2-propynylaminomethyl)-2(1*H*)-pyrazinone 7b

Yield: 87 %; m.p.: 95-96 °C (EtOH); IR (KBr) cm^{-1}: 3309 (C≡CH), 2103 (C≡C), 1670 (CO), 1590 (C=N); ^1H NMR: 7.35-7.10 (m, 5H, Ar-H), 4.01 (s, 3H, OCH_3), 3.78 (s, 2H, CH_2NH), 3.44 (d, 2H, $NHCH_2$), 2.28 (t, 1H, C≡CH), 1.67 (s(br), 1H, NH); m/z (%): 317 ($M^{+\cdot}$, 17), 226 ($M^{+\cdot}$-C_7H_7, 22), 268 ($C_7H_7^+$, 100); exact mass for $C_{16}H_{16}N_3O_2Cl$: 317.0931; found: 317.0925

1-benzyl-5-chloro-3-phenyl-6-(2-propynylaminomethyl)-2(1*H*)-pyrazinone 7c

Yield: 78 %; m.p.: 90-91 °C (EtOH); IR (KBr) cm^{-1} : 3321 (C≡CH), 1650 (CO), 1552 (C=N); ^1H NMR: 8.50-7.00 (m, 10H, Ar-H), 5.67 (s, 2H, CH_2Ph), 3.90 (s, 2H, CH_2NH), 3.47 (d, 2H, $NHCH_2$), 2.30 (t, 1H, C≡CH), 1.73 (s(br), 1H, NH); m/z (%): 363 ($M^{+}\cdot$, 20), 272 ($M^{+}\cdot$-C_7H_7, 27), 91 ($C_7H_7^{+}$, 100); exact mass for $C_{21}H_{18}N_3OCl$: 363.11438; found: 363.11321

3-methoxy-1-phenyl-6-(2-propynylaminomethyl)-2(1*H*)-pyrazinone 7d

Yield: 95 %; m.p.: 123-124 °C (EtOH); IR (KBr) cm^{-1}: 3317 (C≡CH), 2103 (C≡C), 1664 (CO), 1613 (C=N); ^1H NMR: 7.55-7.25 (m, 5H, Ar-H), 6.91 (s, 1H, 5-H), 4.00 (s, 3H, OCH_3), 3.37 (s, 2H, CH_2NH), 3.21 (d, 2H, $NHCH_2$), 2.15 (t, 1H, C≡CH), 1.35 (s(br), 1H, NH); m/z (%): 269 ($M^{+}\cdot$, 17), 215 ($M^{+}\cdot$-C_3H_3NH, 26), 77 ($C_6H_5^{+}$, 100); exact mass for $C_{15}H_{15}N_3O_2$: 269.1164; found: 269.1163

1-benzyl-3-methoxy-6-(2-propynylaminomethyl)-2(1*H*)-pyrazinone 7e

Yield: 89 %; m.p.: 97-98 °C (EtOH); IR (KBr) cm^{-1}: 3318 (C≡CH), 2105 (C≡C), 1660 (CO), 1610 (C=N); ^1H NMR: 7.35-7.10 (m, 5H, Ar-H), 6.81 (s, 1H, 5-H), 5.61 (s, 2H, CH_2Ph), 4.01 (s, 3H, OCH_3), 3.64 (s, 2H, CH_2NH), 3.44 (d, 2H, $NHCH_2$), 2.29 (t, 1H, C≡CH), 1.45 (s(br), 1H, NH); m/z (%): 283 ($M^{+}\cdot$, 26), 228 ($M^{+}\cdot$-C_3H_3NH, 26), 91 ($C_7H_7^{+}$, 100); exact mass for $C_{16}H_{17}N_3O_2$: 283.1321; found: 283.1323

1-benzyl-3-phenyl-6-(2-propynylaminomethyl)-2(1*H*)-pyrazinone 7f

Yield: 91 %; m.p.: 85-86 °C (EtOH); IR (KBr) cm^{-1}: 3320 (C≡CH), 2147 (C≡C), 1700 (CO), 1594 (C=N); ^1H NMR: 8.35-7.15 (m, 11H, Ar-H + 5-H), 5.63 (s, 2H, CH_2Ph), 3.70 (s, 2H, CH_2NH), 3.41 (d, 2H, $NHCH_2$), 2.27 (t, 1H, C≡CH), 2.09 (s(br), 1H, NH); m/z (%): 329 ($M^{+}\cdot$, 2), 91 ($C_7H_7^{+}$, 100); exact mass for $C_{21}H_{19}N_3O$: 329.1528; found: 329.1510

1,3-diphenyl-6-(2-propynylaminomethyl)-2(1*H*)-pyrazinone 7g

Yield: 88 %; m.p.: 103-104 °C (EtOH); IR (KBr) cm^{-1}: 3297 (C≡CH), 1653 (CO), 1559 (C=N); ^1H NMR: 8.40-7.20 (m, 11H, Ar-H + 5-H), 3.77 (s, 2H, CH_2NH), 3.28 (d, 2H, $NHCH_2$), 2.15 (t, 1H, C≡CH), 2.05 (s(br), 1H, NH); m/z (%): 315 ($M^{+}\cdot$, 36), 77 ($C_6H_5^{+}$, 100); exact mass for $C_{20}H_{17}N_3O$: 315.1372; found: 315.1375

5-chloro-6-methyl-1-phenyl-3-(2-propynylamino)-2(1*H*)-pyrazinone 9a

Yield: 91 %; oil; IR (KBr) cm^{-1}: 3315 (m, C≡CH), 2122 (w, C≡C), 1650 (CO), 1581 (C=N); ^1H NMR: 7.60-7.10 (m, 5H, Ar-H), 6.39 ((br), 1H, NH), 4.24 ((br), 2H, CH_2), 2.25 (t, 1H, C≡CH), 1.95 (s, 3H, CH_3); m/z (%): 273 ($M^{+}\cdot$, 20), 196 ($M^{+}\cdot$-C_6H_5, 12), 77 ($C_6H_5^{+}$, 100)

1-benzyl-5-chloro-6-methyl-3-(2-propynylamino)-2(1*H*)-pyrazinone 9b

Yield: 92 %; m.p.: 178-179 °C (EtOH); IR (KBr) cm^{-1}: 3319 (C≡CH), 2122 (C≡C), 1645 (CO), 1578 (C=N); ^1H NMR: 7.40-7.10 (m, 5H, Ar-H), 6.37 ((br), 1H, NH), 5.28 (s, 2H, CH_2Ph), 4.24 ((br), 2H, CH_2), 2.27 (s, 3H, CH_3), 2.25 (t, 1H, C≡CH); m/z (%): 287 ($M^{+}\cdot$, 9), 196 ($M^{+}\cdot$-C_7H_7, 34), 91 ($C_7H_7^{+}$, 100); exact mass for $C_{15}H_{14}N_3OCl$: 287.0825; found: 287.0818

6-(*N*-benzyl-2-propynylaminomethyl)-5-chloro-3-methoxy-1-phenyl-2(1*H*)-pyrazinone 10a

Yield: 53 %; oil; IR (NaCl) cm^{-1}: 3211 (C≡CH), 2098 (C≡C), 1666 (CO), 1593 (C=N); ^1H NMR: 7.50-6.90 (m, 10H, Ar-H), 3.90 (s, 3H, OCH_3), 3.68 (s, 2H, CH_2Ph), 3.43 (s, 2H, CH_2N), 3.35 (d, 2H, NCH_2), 2.55 (t, 1H, C≡CH); m/z (%): 394 ($MH^{+}\cdot$, 7), 275 ($MH^{+}\cdot$-C_6H_5NCO, 22), 120 ($C_6H_6NCO^{+}$, 100); exact mass for $C_{22}H_{20}N_3O_2Cl$-C_6H_5NCO: 274.0873; found: 274.0855

5-chloro-3-methoxy-6-(*N*-(1-oxopropyl)-2-propynylaminomethyl)-1-phenyl-2(1*H*)-pyrazinone 10b

Yield: 82 %; m.p.: 130-131 °C (hexane/CH_2Cl_2); IR (KBr) cm^{-1}: 1667 (CO), 1590 (C=N); ^1H NMR: some peaks are broadened because of the amide function: 7.50-6.95 (m(br), 5H, Ar-H), 4.60, 4.10, 3.60 (3xm(br), 4H, CH_2NH + $NHCH_2$), 3.90 (s, 3H, OCH_3), 2.15 (t(br), 1H, C≡CH), 1.75 (m(br), 2H, CH_2), 1.00 (m(br), 3H, CH_3); m/z (%): 359 ($M^{+\cdot}$, 2), 298 ($M^{+\cdot}$-ClCN, 100), 240 ($M^{+\cdot}$-C_6H_5NCO, 42); exact mass for $C_{18}H_{18}N_3O_3Cl$: 359.1037; found: 359.1044

1-benzyl-5-chloro-3-methoxy-6-(*N*-methyl-2-propynylaminomethyl)-2(1*H*)-pyrazinone 10c

Yield: 93 %; m.p.: 118-119 °C (EtOH); IR (KBr) cm^{-1}: 3310 (C≡CH), 2100 (C≡C), 1670 (CO), 1590 (C=N); ^1H NMR: 7.40-7.00 (m, 5H, Ar-H), 5.63 (s, 2H, CH_2Ph), 4.00 (s, 3H, OCH_3), 3.50 (s, 2H, CH_2N), 3.30 (d, 2H, NCH_2), 2.33 (s, 3H, CH_3), 2.22 (t, 1H, C≡CH); m/z (%): 332 ($MH^{+\cdot}$, 100), 271 ($MH^{+\cdot}$-ClCN, 87); exact mass for $C_{17}H_{18}N_3O_2Cl$: 331.1088; found: 331.1084

1-benzyl-5-chloro-6-(*N*-methyl-2-propynylaminomethyl)-3-phenyl-2(1*H*)-pyrazinone 10d

Yield: 90 %; unstable, solid; IR (KBr) cm^{-1}: 3277 (C≡CH), 1648 (CO), 1555 (C=N); ^1H NMR: 8.60-7.00 (m, 10H, Ar-H), 5.77 (s, 2H, CH_2Ph), 3.67 (s, 2H, CH_2N), 3.38 (d, 2H, NCH_2), 2.37 (s, 3H, CH_3), 2.23 (t, 1H, C≡CH); m/z (%): 378 ($MH^{+\cdot}$, 11), 317 ($MH^{+\cdot}$-ClCN, 100)

5-chloro-6-(*N*-methyl-2-propynylaminomethyl)-1,3-diphenyl-2(1*H*)-pyrazinone 10e

Yield: 91 %; unstable, solid; IR (KBr) cm^{-1}: 3303 (C≡CH), 2100 (C≡C), 1664 (CO), 1604 (C=N); ^1H NMR : 8.00-7.00 (m, 10H, Ar-H), 3.37 (s, 2H, CH_2N), 2.90 (d, 2H, NCH_2), 2.17 (t, 1H, C≡CH), 2.10 (s, 3H, CH_3); m/z (%): 364 ($MH^{+\cdot}$, 6), 245 ($MH^{+\cdot}$-C_6H_5NCO, 52), 120 ($C_6H_6NCO^+$, 100)

3-benzyloxy-5-chloro-6-(*N*-methyl-2-propynylaminomethyl)-1-phenyl-2(1*H*)-pyrazinone 10f

Yield: 86 %; m.p.: 141-142 °C (EtOH); IR (KBr) cm^{-1}: 3240 (C≡CH), 2101 (C≡C), 1687 (CO), 1588 (C=N); ^1H NMR: 7.65-7.00 (m, 10H, Ar-H), 5.43 (s, 2H, OCH_2Ph), 3.23 (s, 2H, CH_2N), 3.83 (d, 2H, NCH_2), 2.10 (t, 1H, C≡CH), 2.00 (s, 3H, CH_3); m/z (%): 393 ($M^{+\cdot}$, 1), 274 ($M^{+\cdot}$-C_6H_5NCO, 3), 91 ($C_7H_7^+$, 100); exact mass for $C_{22}H_{20}N_3O_2Cl$: 393.1245; found: 393.1244

6-(3-butynylaminomethyl)-5-chloro-3-methoxy-1-phenyl-2(1*H*)-pyrazinone 11a

Yield: 57 %; oil; IR (NaCl) cm^{-1}: 3298 (C≡CH), 2085 (C≡C), 1682 (CO), 1588 (C=N); ^1H NMR: 7.52-7.27 (m, 5H, Ar-H), 4.01 (s, 3H, OCH_3), 3.47 (s, 2H, CH_2NH), 2.51 (t, 2H, $NHCH_2$), 2.18 (txd, 2H, CH_2), 1.97 (t, 1H, C≡CH), 1.35 (s(br), 1H, NH); m/z (%): 317 ($M^{+\cdot}$, 13), 249 ($M^{+\cdot}$-C_4H_6N, 100); exact mass for $C_{16}H_{16}N_3O_2Cl$: 317.0931; found: 317.0933

1-benzyl-6-(3-butynylaminomethyl)-5-chloro-3-methoxy-2(1*H*)-pyrazinone 11b

Yield: 66 %; oil; IR (NaCl) cm^{-1} : 3300 (C≡CH), 2115 (C≡C), 1666 (CO), 1589 (C=N); ^1H NMR: 7.50-7.00 (m, 5H, Ar-H), 5.63 (s, 2H, CH_2Ph), 4.00 (s, 3H, OCH_3), 3.73 (s, 2H, CH_2NH), 2.78 (t, 2H, $NHCH_2$), 2.37 (txd, 2H, CH_2), 1.98 (t, 1H, C≡CH), 1.55 (s(br), 1H, NH); m/z (%): 331 ($M^{+\cdot}$, 13), 263 ($M^{+\cdot}$-C_4H_6N, 68), 91 ($C_7H_7^{+\cdot}$, 100); exact mass for $C_{17}H_{18}N_3O_2Cl$: 331.1088; found: 331.1086

1-benzyl-6-(3-butynylaminomethyl)-5-chloro-3-phenyl-2(1*H*)-pyrazinone 11c

Yield: 56 %; oil; IR (NaCl) cm^{-1}: 3300 (C≡CH), 2085 (C≡C), 1651 (CO), 1557 (C=N); ^1H NMR: 8.60-7.10 (m, 10, Ar-H), 5.70 (s, 2H, CH_2Ph), 3.85 (s, 2H, CH_2NH), 2.80 (t, 2H, $NHCH_2$), 2.40 (txd, 2H, CH_2), 2.00 (t, 1H, C≡CH); m/z (%): 377 ($M^{+\cdot}$, 8), 309 ($M^{+\cdot}$-C_4H_6N, 44), 91 ($C_7H_7^{+\cdot}$, 100); exact mass for $C_{22}H_{20}N_3OCl$: 377.1295; found: 377.1286

6-(*N*-benzyl-3-butynylaminomethyl)-5-chloro-3-methoxy-1-phenyl-2(1*H*)-pyrazinone 12a

Yield: 51 %; oil; IR (NaCl) cm^{-1}: 3298 (C≡CH), 2100 (C≡C), 1682 (CO), 1588 (C=N); ^1H NMR: 7.55-7.05 (m, 10H, Ar-H), 4.01 (s, 3H, OCH_3), 3.50 (s, 2H, CH_2N of CH_2Ph), 3.42 (s, 2H, CH_2N of CH_2Ph), 2.33 (t, 2H, NCH_2), 1.86 (t, 1H, C≡CH), 1.81 (txd, 2H, CH_2); m/z (%): 407 ($M^{+\cdot}$, 1), 91 ($C_7H_7^{+\cdot}$, 100); exact mass for $C_{23}H_{22}N_3O_2Cl$: 407.1401; found: 407.1378

1-benzyl-5-chloro-3-methoxy-6-(*N*-(1-oxopropyl)-3-butynylaminomethyl)-2(1*H*)-pyrazinone 12b

Yield: 83 %; m.p.: 151 °C (hexane/CH_2Cl_2); IR (KBr) cm^{-1}: 3278 (C≡CH), 1685, 1643 (CO), 1588 (C=N); ^1H NMR: 7.50-6.80 (m, 5H, Ar-H), 5.30 (s, 2H, CH_2Ph), 4.83 (s, 2H, CH_2N), 4.03 (s, 3H, OCH_3), 3.13 (t, 2H, NCH_2), 2.43 (txd, 2H, CH_2), 2.00 (t, 1H, C≡CH), 1.83 (q, 2H, CH_2), 0.95 (t, ,3H, CH_3); m/z (%): 387 ($M^{+\cdot}$, 7), 352 ($M^{+\cdot}$-Cl, 74), 91 ($C_7H_7^{+\cdot}$, 100); exact mass for $C_{20}H_{22}N_3O_3Cl$: 387.1350; found: 387.1352

1-benzyl-5-chloro-6-(*N*-(1-oxopropyl)-3-butynylaminomethyl)-3-phenyl-2(1*H*)-pyrazinone 12c

Yield: 87 %; M.p.: 157-158 °C (hexane/CH_2Cl_2); IR (KBr) cm^{-1}: 3277 (C≡CH), 1645, 1640 (CO), 1550 (C=N); ^1H NMR: 8.60-6.85 (m, 10H, Ar-H), 5.37 (s, 2H, CH_2Ph), 4.90 (s, 2H, CH_2N), 3.20 (t, 2H, NCH_2), 2.47 (txd, 2H, CH_2), 2.00 (t, 1H, C≡CH), 1.83 (q, 2H, CH_2), 0.90 (t, 3H, CH_3); m/z (%): 433 ($M^{+\cdot}$, 6), 398 ($M^{+\cdot}$-Cl, 20), 91 ($C_7H_7^{+\cdot}$, 100); exact mass for $C_{25}H_{24}N_3O_2Cl$: 433.1557; found: 433.1555

*III. 2H-pyrrolo[3,4-b]pyridin-2-ones **15-16**, 1H-pyrrolo[3,4-c]pyridines **17-18** and some intermediate cycloadducts **14**.*

A solution of precursors **7a-g** or **10a-f** (3 mmol) in 40 ml toluene was refluxed for 1-4 hours. After evaporation of the solvent, the reaction mixture was subjected to column chromatography (SiO_2, EtOAc/CH_2Cl_2) and the resulting products crystallised from hexane/CH_2Cl_2.

In the case of precursors **10c-e**, the reaction was stopped after 5-30 minutes; after evaporation of the solvent and purification on a silica gel column (SiO_2, EtOAc/CH_2Cl_2), the cycloadducts **14c-e** were isolated.

Intermediate cycloadducts 14.

3-benzyl-5-chloro-1-methoxy-10-methyl-4,8-(methanaminomethano)-3,6-diazabicyclo[2.2.2]octa-5,7-dien-2-one 14c

Yield: 91 %; m.p.: 75 °C; IR (KBr) cm^{-1}: 1707 (CO), 1604 (C=N); ^1H NMR : 7.25-6.80 (m, 5H, Ar-H), 6.30 (t, ^4J = 1.5Hz, 1H, 7-H), 4.85/4.04 (2xd, 2H, CH_2Ph), 3.78 (s, 3H, OCH_3), 3.18/3.02 (2xdxd, 2H, 9-CH_2), 3.15/2.87 (2xd, 2H, 11-CH_2), 2.31 (s, 3H, CH_3); ^{13}C NMR: 167.9 (CO), 163.4 (C-5), 148.0 (C-8), 136.0-127.0 (Ar-C), 125.4 (C-7), 100.1 (C-1), 72.9 (C-4), 56.2, 54.6, 53.5 (C-9 + C-11 + OCH_3), 45.6 (CH_2Ph), 41.1 (CH_3); m/z (%)(CI): 332 (MH^+, 19), 271 (MH^+-ClCN, 100);

3-benzyl-5-chloro-10-methyl-1-phenyl-4,8-(methanaminomethano)-3,6-diazabicyclo[2.2.2]octa-5,7-dien-2-one 14d

Yield: 95 %; m.p.: 140-141 °C; IR (KBr) cm^{-1}: 1695 (CO), 1607 (C=N); ^1H NMR: 7.90-6.95 (m, 10H, Ar-H), 6.45 (t, 1H, 7-H), 4.91/4.13 (2xd, 2H, CH_2Ph), 3.29/3.10 (2xdxd, 2H, 9-CH_2), 3.32/2.97 (2xd, 2H, 11-CH_2), 2.38 (s, 3H, CH_3); ^{13}C NMR: 169.8 (CO), 166.8 (C-5), 149.7 (C-8), 136.6-127.3 (Ar-C), 128.0 (C-7), 81.3 (C-1), 73.7 (C-4), 56.6, 54.9 (C-9 + C-11), 46.4 (CH_2Ph), 41.3 (CH_3); m/z (%)(CI) : 378 (MH^+,

7), 317 (MH^+-ClCN, 40), 62 ($ClCNH^+$, 100); exact mass for $C_{22}H_{20}N_3OCl$-ClCN: 316.1576; found: 316.1558

5-chloro-10-methyl-1,3-diphenyl-4,8-(methanaminomethano)-3,6-diazabicyclo[2.2.2]octa-5,7-dien-2-one 14e

Yield: 92 %; m.p.: 108-109 °C; IR (KBr) cm^{-1}: 1709 (CO), 1604 (C=N); ^1H NMR: 7.90-6.95 (m, 10H, Ar-H), 6.63 (t, 1H, 7-H), 3.56/3.18 (2xdxd, 2H, 9-CH_2), 3.62/2.58 (2xd, 2H, 11-CH_2), 2.40 (s, 3H, CH_3); ^{13}C NMR: 169.0 (CO), 166.6 (C-5), 149.9 (C-8), 136.8-126.5 (Ar-C), 128.4 (C-7), 82.0 (C-1), 74.9 (C-4), 58.4, 55.5 (C-9 + C-11), 41.5 (CH_3); m/z (%)(CI): 364 (MH^+, 10), 245 (MH^+-C_6H_5NCO, 35), 120 ($C_6H_6NCO^+$, 100);

2H-pyrrolo[3,4-b]pyridin-2-ones 15-16.

1-benzyl-6-cyano-1,5,6,7-tetrahydro-3-methoxy-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 15b

Yield: 55 %; m.p.: 181-182 °C; IR (KBr) cm^{-1}: 2215 (C≡N), 1662 (s, C=O); ^1H NMR: 7.35-7.20 (m, 5H, Ar-H), 6.52 (s, 1H, 4-H), 5.16 (s, 2H, CH_2Ph), 4.57, 4.53 (2xs(br), 4H, NCH_2), 3.84 (s, 3H, OCH_3); ^{13}C NMR: 158.0 (CO), 150.0 (C-3), 135.1-127.2 (Ar-C), 130.3 (C-7a), 115.7 (C≡N), 109.9 (C-4a), 106.8 (C-4), 56.1 (OCH_3), 55.7, 53.9 (C-5 + C-7), 48.9 (CH_2Ph); m/z (%): 281 ($M^+\cdot$, 12), 190 ($M^+\cdot$-C_7H_7, 4), 91 ($C_7H_7^+$, 100); exact mass for $C_{16}H_{15}N_3O_2$: 281.1164; found: 281.1166

1-benzyl-6-cyano-3-phenyl-1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 15c

Yield: 51 %; m.p.: 193-194 °C; IR (KBr) cm^{-1}: 2216 (C≡N), 1657 (s, C=O); ^1H NMR: 7.70-7.10 (m, 11H, Ar-H + 4-H), 5.18 (s, 2H, CH_2Ph), 4.61 (s, 4H, NCH_2); ^{13}C NMR: 161.5 (CO), 140.2 (C-7a), 136.4-127.2 (Ar-C), 131.7 (C-4), 128.3 (C-3), 115.6 (C≡N), 111.3 (C-4a), 55.4, 54.2 (C-5 + C-7), 49.1 (CH_2Ph); m/z (%): 327 ($M^+\cdot$, 9), 236 ($M^+\cdot$-C_7H_7, 4), 91 ($C_7H_7^+$, 100); exact mass for $C_{21}H_{17}N_3O$: 327.1372; found: 327.1367

3-methoxy-1-phenyl-1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 15d

Yield: 65 %; m.p.: 176-177 °C; IR (KBr) cm^{-1}: 1663 (CO); ^1H NMR: 7.55-7.20 (m, 5H, Ar-H), 6.67 (s, 1H, 4-H), 4.15 (s(br), 2H, NCH_2), 3.83 (s, 3H, OCH_3), 3.75 (s(br), 2H, NCH_2), 2.63 (s(br), 1H, NH); ^{13}C NMR: 158.2 (CO), 149.1 (C-3), 138.0-126.9 (Ar-C), 136.3 (C-7a), 114.4 (C-4a), 109.0 (C-4), 56.0 (OCH_3), 52.4, 51.9 (C-5 + C-7); m/z (%): 242 ($M^+\cdot$, 93), 241 ($M^+\cdot$-H, 100), 77 ($C_6H_5^+$, 51); exact mass for $C_{14}H_{14}N_2O_2$: 242.1055; found: 242.1052; anal calcd for: C 69.40, H 5.82, N 11.56; found : C 69.05, H 5.70, N 11.46

1-benzyl-3-methoxy-1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 15e

Yield: 59 %; m.p.: 294-295 °C; IR (KBr) cm^{-1}: 1601 (CO); ^1H NMR: 7.35-7.15 (m, 5H, Ar-H), 6.60 (s, 1H, 4-H), 5.20 (s, 2H, CH_2Ph), 4.10 (s, 4H, NCH_2), 3.85 (s, 3H, OCH_3), 1.94 (s(br), 1H, NH); ^{13}C NMR: 158.4 (CO), 149.0 (C-3), 136.6-127.4 (Ar-C), 136.2 (C-7a), 114.9 (C-4a), 108.6 (C-4), 56.0 (OCH_3), 52.3, 51.4 (C-5 + C-7), 49.0 (CH_2Ph); m/z (%): 256 ($M^+\cdot$, 6), 165 ($M^+\cdot$-C_7H_7, 12), 91 ($C_7H_7^+$, 100); exact mass for $C_{15}H_{16}N_2O_2$: 256.1212; found: 256.1205

1-benzyl-3-phenyl-1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 15f

Yield: 49 %; m.p.: 117-118 °C, unstable; IR (KBr) cm^{-1}: 1651 (CO); ^1H NMR: 7.75-7.20 (m, 11H, Ar-H + 4-H), 5.23 (s, 2H, CH_2Ph), 4.19, 4.15 (2xs(br), 4H, NCH_2), 1.90 (s(br), 1H, NH); ^{13}C NMR: 162.1 (CO), 147.1 (C-7a), 137.4-127.5 (Ar-C), 133.3 (C-4), 129.5 (C-3), 116.7 (C-4a), 51.9, 51.8 (C-5 + C-7), 49.3

(CH_2Ph); m/z (%): 302 ($M^{+\cdot}$, 17), 211 ($M^{+\cdot}$-C_7H_7, 31), 91 ($C_7H_7^+$, 100); exact mass for $C_{20}H_{18}N_2O$: 302.1419; found: 302.1408

1,3-diphenyl-1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 15g

Yield: 43 %; solid, unstable; IR (KBr) cm^{-1}: 1652 (CO); ^1H NMR: 7.75-7.20 (m, 11H, Ar-H + 4-H), 4.17, 3.80 (2xs(br), 4H, NCH_2), 2.47 (s(br), 1H, NH); ^{13}C NMR: 162.0 (CO), 146.7 (C-7a), 138.5-127.0 (Ar-C), 133.7 (C-4), 129.8 (C-3), 116.3 (C-4a), 52.4, 52.1 (C-5 + C-7); m/z (%): 288 ($M^{+\cdot}$, 64), 77 ($C_6H_5^+$, 100); exact mass for $C_{19}H_{16}N_2O$: 288.1263; found: 288.1269

6-benzyl-3-methoxy-1-phenyl-1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 16a

Yield: 14 %; m.p.: 126-127 °C; IR (KBr) cm^{-1}: 1669 (CO); ^1H NMR: 7.50-7.15 (m, 10H, Ar-H), 6.59 (s, 1H, 4-H), 3.89 (s(br), 2H, NCH_2), 3.84 (s, 2H, CH_2Ph), 3.81 (s, 3H, OCH_3), 3.59 (s(br), 2H, NCH_2); ^{13}C NMR: 158.1 (CO), 149.5 (C-3), 137.9-127.0 (Ar-C), 132.4 (C-7a), 113.2 (C-4a), 109.0 (C-4), 59.9, 58.0, 57.7 (C-5 + C-7 + CH_2Ph), 56.0 (OCH_3); m/z (%): 332 ($M^{+\cdot}$, 29), 241 ($M^{+\cdot}$-C_7H_7, 21), 91 ($C_7H_7^+$, 100); exact mass for $C_{21}H_{20}N_2O_2$: 332.1525; found: 332.1520

3-methoxy-6-(1-oxopropyl)-1-phenyl-1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 16b

Yield: 10 %; m.p.: decomposes at 200 °C; IR (KBr) cm^{-1}: 1716, 1677 (CO); in the NMR spectra, some peaks are broadened or duoble because of the amide function; ^1H NMR: 7.55-7.00 (m, 5H, Ar-H), 6.69, 6.63 (s, 1H, 4-H), 4.65, 4.25 (2xs(br) 4H, NCH_2), 3.88, 3.74 (s, 3H, OCH_3), 2.32, 2.17 (m, 2H, $COCH_2$), 1.03 (m, 3H, CH_3); ^{13}C NMR: 172.4, 172.3 (CO), 158.0 (CO), 150.1 (C-3), 137.3-126.9 (Ar-C), 132.4 (C-7a), 111.0, 110.0 (C-4a), 108.3, 108.1 (C-4), 56.1 (OCH_3), 51.8, 51.5, 50.9 (C-5 + C-7), 27.1, 26.8 (CH_2), 8.9, 8.7 (CH_3); m/z (%): 298 ($M^{+\cdot}$, 100), 269 ($M^{+\cdot}$-C_2H_5, 49); exact mass for $C_{17}H_{18}N_2O_3$: 298.1317; found: 298.1321

1-benzyl-3-methoxy-6-methyl-1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 16c

Yield : 77 % (from **14c**), 51 % (from **23c**); m.p.: 285-286 °C; IR (KBr) cm^{-1}: 1601 (CO); ^1H NMR: 7.55-7.10 (m, 5H, Ar-H), 6.55 (s, 1H, 4-H), 5.10 (s, 2H, CH_2Ph), 3.75 (s, 7H, OCH_3 + NCH_2), 2.60 (s, 3H, CH_3); m/z (%): 270 ($M^{+\cdot}$, 55), 179 ($M^{+\cdot}$-C_7H_7, 40), 91 ($C_7H_7^+$, 100); exact mass for $C_{16}H_{18}N_2O_2$: 270.1368; found: 270.1352

1-benzyl-6-methyl-3-phenyl-1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 16d

Yield: 65 % (from **14d**), 44 % (from **23d**); unstable oil; IR (KBr) cm^{-1}: 1652 (CO); ^1H NMR: 7.80-7.10 (m, 11H, Ar-H + 4-H), 5.15 (s, 2H, CH_2Ph), 3.85 (s(br), 4H, NCH_2), 2.50 (s, 3H, CH_3); m/z (%): 316 ($M^{+\cdot}$, 83), 225 ($M^{+\cdot}$-C_7H_7, 98), 91 ($C_7H_7^+$, 100); exact mass for $C_{21}H_{20}N_2O$: 316.1576; found: 316.1572

6-methyl-1,3-diphenyl-1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 16e

Yield: 10 % (from **14e**), 62 % (from **21e**); unstable oil; IR (NaCl) cm^{-1}: 1660 (CO); ^1H NMR: 7.80-7.20 (m, 11H, Ar-H + 4-H), 3.90, 3.60 (2xs(br), 2H, NCH_2), 2.50 (s, 3H, CH_3); m/z (%): 302 ($M^{+\cdot}$, 76), ($M^{+\cdot}$-H, 100); exact mass for $C_{20}H_{18}N_2O$: 302.1419; found: 302.1408

3-benzyloxy-6-methyl-1-phenyl-1,5,6,7-tetrahydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 16f

Yield: 13 %; m.p.: 164-165 °C; IR (KBr) cm^{-1}: 1673 (CO); ^1H NMR: 7.55-7.20 (m, 10H, Ar-H), 6.69 (s, 1H, 4-H), 5.12 (s, 2H, OCH_2Ph), 3.80, 3.49 (2xs(br), 4H, NCH_2) 2.45 (s, 3H CH_3); ^{13}C NMR: 158.2 (CO), 147.8 (C-3), 137.8-126.9 (Ar-C), 136.0 (C-7a), 113.3 (C-4), 113.2 (C-4a), 70.9 (OCH_2Ph), 59.8, 58.4 (C-5 + C-7), 42.0 (CH_3); m/z (%): 332 ($M^{+\cdot}$, 17), 241 ($M^{+\cdot}$-C_7H_7, 41), 91 ($C_7H_7^+$, 100); exact mass for $C_{21}H_{20}N_2O_2$: 332.1525; found: 332.1523

1H-pyrrolo[3,4-c]pyridines 17-18.

2-benzyl-4-chloro-6-methoxy-2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridine 18a

Yield: 58 %; m.p.: 76-77 °C; IR (KBr) cm^{-1}: 1636, 1554 (pyridine); ^1H NMR: 7.40-7.20 (m, 5H, Ar-H), 6.46 (s, 1H, 7-H), 3.90 (s, 3H, OCH_3), 3.86 (s, 6H, CH_2Ph + NCH_2); ^{13}C NMR: 163.2 (C-6), 155.1 (C-7a), 141.2 (C-4), 138.7-120.2 (Ar-C), 127.5 (C-3a), 103.3 (C-7), 59.8 (CH_2Ph), 58.7, 56.1 (C-1 + C-3), 54.1 (OCH_3); m/z (%): 274 ($M^{+\cdot}$, 61), 273 ($M^{+\cdot}$-H, 84), 183 ($M^{+\cdot}$-C_7H_7, 93), 91 ($C_7H_7^+$, 100); exact mass for $C_{15}H_{15}N_2OCl$: 274.0873; found: 274.0855

4-chloro-2,3-dihydro-6-methoxy-2-(1-oxopropyl)-1*H*-pyrrolo[3,4-*c*]pyridine 18b

Yield: 48 %; m.p.: 174 °C; IR (KBr) cm^{-1}: 1652 (CO), 1625, 1562 (pyridine); in the NMR spectra some peaks are broadened or double because of the amide function; ^1H NMR: 6.60, 6.56 (s, 1H, 7-H), 4.79, 4.70 (2xs, 4H, NCH_2), 3.94 (s, 3H, OCH_3), 2.43, 2.37 (q, 2H, $COCH_2$), 1.23, 1.22 (t, 3H, CH_3); ^{13}C NMR: 172.9 (CO), 164.0, 163.7 (C-6), 151.4, 151.0 (C-7a), 142.6, 142.0 (C-4), 124.3, 124.1 (C-3a), 103.7, 103.3 (C-7), 54.4 (OCH_3), 52.4, 52.3, 50.2, 50.0 (C-1 + C-3), 27.6, 27.5 (CH_2), 8.8 (CH_3); m/z (%): 240 ($M^{+\cdot}$, 100), 183 ($M^{+\cdot}$-C_2H_5CO, 77); exact mass for $C_{11}H_{13}N_2O_2Cl$: 240.0666; found: 240.0667; anal calcd for: C 54.89, H 5.44, N 11.64; found: C 54.76, H 5.38, N 11.55

4-chloro-2-methyl-6-phenyl-2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridine 18d

Yield: 62 % (from **14e**), 8 % (from **14d**); m.p.: 73-74 °C; IR (KBr) cm^{-1}: 1640 (pyridine); ^1H NMR: 8.00-7.35 (m, 5H, Ar-H), 7.48 (s, 1H, 7-H), 4.00, 3.98 (2xs, 4H, NCH_2), 2.69 (s, 3H, CH_3); ^{13}C NMR: 157.1 (C-6), 153.9 (C-7a), 145.0 (C-4), 138.0-126.9 (Ar-C), 134.0 (C-3a), 113.3 (C-7), 61.1, 58.7 (C-1 + C-3), 42.0 (CH_3); m/z (%): 244 ($M^{+\cdot}$, 81), 243 ($M^{+\cdot}$-H, 100); exact mass for $C_{14}H_{13}N_2Cl$: 244.0767; found: 244.0750

6-benzyloxy-4-chloro-2-methyl-2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridine 18f

Yield: 55 %; m.p.: 142-143 °C; IR (KBr) cm^{-1}: 1632, 1562 (pyridine); ^1H NMR: 7.50-7.20 (m, 5H, Ar-H), 6.55 (s, 1H, 7-H), 5.33 (s, 2H, CH_2Ph), 3.88, 3.86 (2xs, 4H, NCH_2), 2.56 (s, 3H, CH_3); ^{13}C NMR: 162.5 (C-6), 155.6 (C-7a), 140.4 (C-4), 136.7-127.8 (Ar-C), 128.0 (C-3a), 103.6 (C-7), 68.5 (CH_2Ph), 60.7, 58.1 (C-1 + C-3), 42.0 (CH_3); m/z (%): 274 ($M^{+\cdot}$, 61), 273 ($M^{+\cdot}$-H, 84), 183 ($M^{+\cdot}$-C_7H_7, 93), 91 ($C_7H_7^+$, 100); exact mass for $C_{15}H_{15}N_2OCl$: 274.0873; found: 274.0867

4-methoxy-2-methyl-6-phenyl-2,3-dihydro-1*H*-pyrrolo[3,4-*c*]pyridine 18g

Yield: 62 % (from **22d**), 42 % (uit **22e**); unstable oil; IR (NaCl) cm^{-1}: 1610, 1574 (pyridine); ^1H NMR: 8.05-7.95 (m, 5H, Ar-H), 7.24 (s, 1H, 7-H), 4.08 (s, 3H, OCH_3), 4.00, 3.95 (2xs(br), 4H, NCH_2), 2.64 (s, 3H, CH_3); ^{13}C NMR: 158.4 (C-4), 154.1, 152.9 (C-6 + C-7a), 139.2-126.7 (Ar-C), 120.5 (C-3a), 107.7 (C-7), 61.0, 57.4 (C-1 + C-3), 53.1 (OCH_3), 42.4 (CH_3); m/z (%): 240 ($M^{+\cdot}$, 28), 239 ($M^{+\cdot}$-H, 100); exact mass for $C_{15}H_{16}N_2O$: 240.1263; found : 240.1234

IV. 1,2,3,5-Tetrahydro-2-methyl-6H-pyrrolo[3,4-c]pyridin-6-one ***19*** *and 1,6-dihydro-2H-pyrrolo[3,4-b]pyridin-2-one* ***20.***

1,2,3,5-tetrahydro-2-methyl-6*H*-pyrrolo[3,4-*c*]pyridin-6-one 19

To a solution of 550 mg (2 mmol) pyrrolo[3,4-*c*]pyridine **18f** in 20 ml methanol was added 50 mg Pd (10 %/C). After stirring for 1 hour under H_2-atmosphere, the catalyst was filtered off and the solvent evaporated. Purification of product **19** was performed on alumina preparative plates (MeOH/CH_2Cl_2).

Yield: 81 %; m.p.: 214-215 °C (*i*-PrOH); IR (KBr) cm^{-1}: 1673, 1627 (CO, C=N); ^{1}H-NMR (DMSO-d_6): 11.00 (s(br), 1H, NH), 7.19 (s, 1H, 4-H), 6.17 (s, 1H, 7-H), 3.60 (s, 2H, NCH_2), 3.52 (s, 2H, NCH_2), 2.40 (s, 3H, CH_3); ^{13}C-NMR (DMSO-d_6): 162.3 (C-6), 156.5 (C-7a), 126.9 (C-4), 118.6 (C-3a), 111.4 (C-7), 59.1, 56.3 (C-1 + C-3), 41.4 (CH_3); m/z (%): 150 (M^+·, 35), 149 (M^+·-H, 100); exact mass for $C_8H_{10}N_2Cl$: 150.0793; found: 150.0780; anal calcd for: C 63.98, H 6.71, N 18.65; found: C 63.95, H 6.65, N 18.53

1-benzyl-6-methyl-3-phenyl-1,6-dihydro-2*H*-pyrrolo[3,4-*b*]pyridin-2-one 20 (air oxidised 16d)

Yield: 23 %; m.p.: 164 °C, unstable; IR (KBr) cm^{-1}: 1628 (CO); ^{1}H NMR: 7.65-7.20 (m, 10H, Ar-H + 4-H), 6.79 (d, ^4J = 2Hz, 1H, 5-H), 6.28 (d, ^4J = 2Hz, 1H, 7-H), 5.24 (s, 2H, CH_2Ph), 3.71 (s, 3H CH_3); ^{13}C NMR: 161.6 (CO), 136.4-127.0 (Ar-C), 131.0 (C-4), 129.6 (C-7a), 116.1 (C-5), 114.5 (C-4a), 111.0 (C-3), 102.9 (C-7), 48.0 (CH_2Ph), 37.2 (CH_3); m/z (%): 314 (M^+·, 15), 223 (M^+·-C_7H_7, 18), 91 ($C_7H_7^+$, 100); exact mass for $C_{21}H_{28}N_2O$: 314.1419; found: 314.1426

V. Substituted cycloadducts 22d-e and 23c-d.

For the chloride substitution by cyanide or methoxide, the adducts **14d-e** (2 mmol) were stirred with KCN (6 mmol) and a catalytic amount of 18-crown-6 in 10 ml MeCN at 60 °C (12 h) or with sodium methoxide (2.6 mmol) in 10 ml THF at rt (2 h). After evaporation of the solvent the residue was dissolved in 15 ml CH_2Cl_2 and washed with 3x 10 ml H_2O. Drying of the organic layer over $MgSO_4$ and evaporation of the solvent afforded compounds **16e** (the cyano substituted adduct **21e** could not be isolated) and **22d-e**.

For substitution of **14c-d** by hydroxide, 10 ml of a 3M aqueous NaOH-solution was added. After stirring for 12 hours at rt, the mixture was concentrated and 10 ml H_2O was added. Then the water layer was extracted with 3 x 10 ml CH_2Cl_2 and the combined extracts were dried over $MgSO_4$. After evaporation, the crude mixture was crystallised from hexane/CH_2Cl_2.

3-benzyl-5-methoxy-10-methyl-1-phenyl-4,8-(methanaminomethano)-3,6-diazabicyclo[2.2.2]octa-5,7-dien-2-one 22d

Yield: 91 %; m.p.: 90-91 °C; IR (KBr) cm^{-1}: 1696 (CO), 1633 (C=N); ^{1}H NMR: 8.00-7.00 (m, 10H, Ar-H), 6.53 (t, 1H, 7-H), 4.90/4.20 (2xd, 2H, CH_2Ph), 3.73 (s, 3H, OCH_3), 3.30 (m, 2H, 9-CH_2), 3.40/2.93 (2xd, 2H, 11-CH_2), 2.40 (s, 3H, CH_3); m/z (%)(CI): 374 (MH^+, 100), 241 (MH^+-C_7H_7NCO, 35); exact mass for $C_{23}H_{23}N_3O_2Cl$: 373.1790; found: 373.1788

5-methoxy-10-methyl-1,3-diphenyl-4,8-(methanaminomethano)-3,6-diazabicyclo[2.2.2]octa-5,7-dien-2-one 22e

Yield: 88 %; m.p.: 189 °C; IR (KBr) cm^{-1}: 1704 (CO), 1630 (C=N); ^{1}H NMR: 8.00-6.90 (m, 10H, Ar-H), 6.68 (t, ^4J = 1.5Hz, 1H, 7-H), 4.03 (s, 3H, OCH_3), 3.67/3.17 (2xdxd, ^2J = 14Hz, ^4J = 1.5Hz, 2H, 9-CH_2), 3.60/2.43 (2xd, ^2J = 12Hz, 2H, 11-CH_2), 2.40 (s, 3H, CH_3); m/z (%)(CI): 360 (MH^+, 54), 241 (MH^+-C_6H_5NCO, 100), 120 ($C_6H_6NCO^+$, 85); exact mass for $C_{22}H_{21}N_3O_2$-C_6H_5NCO: 240.1263; found: 240.1250

3-benzyl-1-methoxy-10-methyl-4,8-(methanaminomethano)-3,6-diazabicyclo[2.2.2]oct-7-ene-2,5-dione 23c

Yield: 78 %; m.p. : 180 °C; IR (KBr) cm^{-1}: 1695 (CO); ^{1}H NMR : 8.19 (s(br), 1H, NH), 7.35-7.00 (m, 5H, Ar-H), 6.41 (t, ^4J = 1.5Hz, 1H, 7-H), 4.84/4.38 (2xd, ^2J = 16Hz, 2H, CH_2Ph), 3.75 (s, 3H, OCH_3), 3.23 (m, 2H, 9-CH_2), 3.35/2.87 (2xd, ^2J = 13Hz, 2H, 11-CH_2), 2.39 (s, 3H, CH_3); ^{13}C NMR: 170.6 (CO), 169.8

(CO), 152.0 (C-8), 136.8-126.7 (Ar-C), 124.2 (C-7), 88.6 (C-1), 72.1 (C-4), 55.5, 53.9, 53.7 (C-9 + C-11 + OCH_3), 45.6 (CH_2Ph), 41.6 (CH_3); m/z (%): 313 ($M^{+\cdot}$, 1), 270 ($M^{+\cdot}$-HNCO, 57), 179 ($M^{+\cdot}$-HNCO-C_7H_7, 100); exact mass for $C_{17}H_{19}N_3O_3$: 313.1426; found: 313.1418; anal calcd for: C 65.16, H 6.11, N 13.41; found: C 65.01, H 5.84, N 13.31

3-benzyl-10-methyl-1-phenyl-4,8-(methanaminomethano)-3,6-diazabicyclo[2.2.2]octa-7-ene-2,5-dione 23d

Yield: 82 %; m.p.: 108-109 °C; IR (KBr) cm^{-1}: 1697 (CO); ^1H NMR: 7.80 (s(br), 1H, NH), 7.55-7.10 (m, 10H, Ar-H), 6.62 (t, ^4J = 2Hz, 1H, 7-H), 4.85/4.39 (2xd, ^2J = 15Hz, 2H, CH_2Ph), 3.29/3.23 (2xdxd, ^2J = 14Hz, ^4J = 2Hz, 2H, 9-CH_2), 3.40/2.94 (2xd, ^2J = 11Hz, 2H, 11-CH_2), 2.38 (s, 3H, CH_3); ^{13}C NMR: 172.2 (CO), 171.4 (CO), 153.7 (C-8), 137.0-126.8 (Ar-C), 126.1 (C-7), 72.4 (C-4), 67.3 (C-1), 55.7, 54.0 (C-9 + C-11), 46.2 (CH_2Ph), 41.7 (CH_3); m/z (%)(CI) : 360 (MH^+, 100), 317 (MH^+-HNCO, 65); exact mass for $C_{22}H_{21}N_3O_2$: 359.1634; found: 359.1627; anal calcd for: C 73.52, H 5.89, N 11.69; found: C 73.54, H 5.89, N 11.73

For the further conversion of adducts **22d and 22e** by thermolysis, 1 day **(22d)** or 5 hours **(22e)** reflux in toluene was required; the hydrolysed adducts **23c-d** had to be refluxed in bromobenzene during 2-4 hours.

*VI. 1,7-Naphthyridin-2(1H)-ones **25** and 2,7-naphthyridines **26**.*

A solution of the precursor **12a-c** (2.5 mmol) in 30 ml bromobenzene was refluxed during 1-2 hours. After evaporation of the solvent the residue was purified using colomn chromatography (SiO_2, EtOAc/CH_2Cl_2) and the the obtained products were recrystallised from hexane/CH_2Cl_2.

In the NMR spectra of **25a-b** and **26b-c** some of the peaks are broadened or doubled due to the amide function.

1-benzyl-3-methoxy-7-(1-oxopropyl)-5,6,7,8-tetrahydro-1,7-naphthyridin-2(1*H*)-one 25a

Yield: 63 %; m.p.: 88-89 °C; IR (KBr) cm^{-1}: 1650 (CO); ^1H NMR: 7.40-7.10 (m, 5H, Ar-H), 6.44, 6.42 (s, 1H, 4-H), 5.36 (s, 2H, CH_2Ph), 4.52, 4.33 (s, 2H, NCH_2), 3.85, 3.83 (s, 3H, OCH_3), 3.72, 3.56 (t, 2H, NCH_2), 2.62, 2.56 (t, 2H, CH_2), 2.37, 1.87 (q, 2H, $COCH_2$), 1.43, 0.89 (t, 3H, CH_3); ^{13}C NMR: 172.5 (CO), 159.3 (CO), 148.0 (C-3), 136.0-126.3 (Ar-C), 130.0 (C-8a), 114.0, 113.7 (C-4), 110.2 (C-4a), 55.8 (OCH_3), 46.4, 46.3 (CH_2Ph), 44.1, 41.9, 41.1, 39.5 (C-6 + C-8), 27.7, 26.6, 26.4, 26.3 (C-5 + $COCH_2$), 9.2, 9.0 (CH_3); m/z (%): 326 ($M^{+\cdot}$, 33), 179 ($M^{+\cdot}$-C_7H_7-C_2H_4CO, 100), 91 ($C_7H_7^+$, 92); exact mass for $C_{19}H_{22}N_2O_3$: 326.1630; found: 326.1632

1-benzyl-7-(1-oxopropyl)-3-phenyl-5,6,7,8-tetrahydro-1,7-naphthyridin-2(1*H*)-one 25b

Yield: 41 %; m.p.: 88-89 °C; IR (KBr) cm^{-1}: 1650 (CO); ^1H NMR: 7.80-6.95 (m, 11H, Ar-H + 4-H), 5.25 (s, 2H, CH_2Ph), 4.61, 4.38 (s, 2H, NCH_2), 3.72, 3.55 (t, 2H, NCH_2), 2.65, 2.58 (t, 2H, CH_2), 2.35, 1.88 (q, 2H, $COCH_2$), 1.15, 0.90 (t, 3H, CH_3); ^{13}C NMR: 172.5 (CO), 161.5 (CO), 139.1 (C-8a), 138.6 (C-4), 136.6-126.3 (Ar-C), 112.9, 111.5 (C-4a), 46.5 (CH_2Ph), 44.6, 44.0, 41.9, 41.6 (C-6 + C-8), 27.2, 26.5, 26.3, 25.8 (C-5 + $COCH_2$), 9.1 (CH_3); m/z (%): 372 ($M^{+\cdot}$, 24), 235 ($M^{+\cdot}$-C_7H_7-C_2H_4CO, 100), 91 ($C_7H_7^+$, 74); exact mass for $C_{24}H_{24}N_2O_2$: 372.1838; found: 372.1836

7-benzyl-1-chloro-3-methoxy-5,6,7,8-tetrahydro-2,7-naphthyridine 26a

Yield: 78 %; m.p.: 79-80 °C; IR (KBr) cm^{-1}: 1607 (pyridine); ^1H NMR: 7.40-7.15 (m, 5H, Ar-H), 6.40 (s, 1H, 4-H), 3.86 (s, 3H, OCH_3), 3.68 (s, 2H, CH_2Ph or NCH_2), 3.58 (s, 2H, CH_2Ph or NCH_2), 2.76 (t, 2H,

NCH_2), 2.61 (t, 2H, CH_2); ^{13}C NMR: 161.6 (C-3), 149.6 (C-4a), 145.5 (C-1), 137.8-127.2 (Ar-C), 121.9 (C-8a), 108.2 (C-4), 62.4 (CH_2Ph), 53.7 (OCH_3), 53.0 (C-8), 48.6 (C-6), 29.3 (C-5); m/z (%): 288 ($M^{+\cdot}$, 26), 287 ($M^{+\cdot}$-H, 47), 197 ($M^{+\cdot}$-C_7H_7, 42), 91 ($C_7H_7^+$, 100); exact mass for $C_{16}H_{17}N_2OCl$: 288.1029; found: 288.1038

1-chloro-3-methoxy-7-(1-oxopropyl)-5,6,7,8-tetrahydro-2,7-naphthyridine 26b

Yield: 13 %; oil; IR (NaCl) cm^{-1}: 1650 (CO), 1607 (pyridine); ^1H NMR: 6.55 (s, 1H, 4-H), 4.70, 4.55 (s, 2H, NCH_2), 3.90 (s, 3H, OCH_3), 3.75 (m, 2H, NCH_2), 2.85 (m, 2H, CH_2), 2.50 (q, 2H, $COCH_2$), 1.25 (t, 3H, CH_3); m/z (%): 254 ($M^{+\cdot}$, 100), 197 ($M^{+\cdot}$-C_2H_5CO, 61); exact mass for $C_{12}H_{15}N_2O_2Cl$: 254.0822; found: 254.0822

1-chloro-7-(1-oxopropyl)-3-phenyl-5,6,7,8-tetrahydro-2,7-naphthyridine 26c

Yield: 48 %; m.p.: 119-120 °C; IR (KBr) cm^{-1}: 1647 (CO), 1594 (pyridine); ^1H NMR: 8.00-7.10 (m, 11H, Ar-H + 4-H), 4.72, 4.58 (s, 2H, NCH_2), 3.85, 3.67 (t, 2H, NCH_2), 2.87 (m, 2H, CH_2), 2.45 (m, 2H, $COCH_2$), 1.20 (t, 3H, CH_3); ^{13}C NMR: 172.6 (CO), 155.5, 155.0 (C-3), 149.4, 148.7 (C-1), 148.1, 146.6 (C-4a), 137.3-126.7 (Ar-C), 125.6 (C-8a), 119.4, 118.9 (C-4), 44.9, 42.0 (C-8), 41.8, 38.1 (C-6), 29.5, 28.5 (CH_2), 9.2 (CH_3); m/z (%): 300 ($M^{+\cdot}$, 100), 243 ($M^{+\cdot}$-C_2H_5CO, 57); exact mass for $C_{17}H_{17}N_2OCl$: 300.1029; found: 300.1031

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