189. 2,3-Dihydrospiro[1*H*-4- and 5-azabenzimidazole-2,1′-cyclohexane] (= Spiro[cyclohexane-1,2′(3′*H*)-1′*H*-imidazo[4,5-*b*]pyridine] and Spiro[cyclohexane-1,2′(3′*H*)-1′*H*-imidazo[4,5-*c*]pyridine]): Reactions with Nucleophiles

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Dedicated to *Rolf Huisgen* on the occasion of his 75th birthday

(16.V.94)

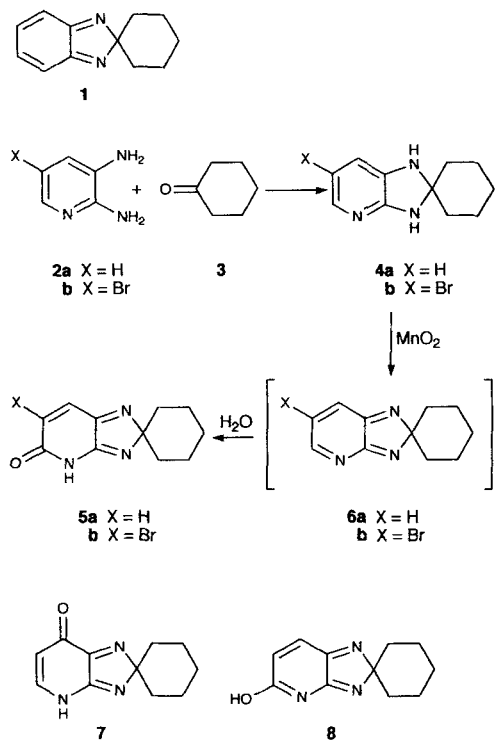
The readily available title compounds **4a** and **24** react with N-, O-, S-, and C-nucleophiles in presence of MnO_2 to give the corresponding mono- or disubstituted 2*H*-azabenzimidazoles (= azaisobenzimidazoles), *e.g.*, **11**–**18** and **26a**–**h**, respectively, or 2,3-dihydro-1*H*-azabenzimidazoles (= dihydro-azabenzimidazoles) such as **9** and **10** and **27** and **28**, respectively, by a 1,4- or 1,6-*Michael* addition (*Schemes 2* and *4*). The bromo-dihydro-1*H*-azabenzimidazole **4b** lost the Br-atom when treated with piperidine or morpholine yielding the corresponding disubstituted 2*H*-azabenzimidazole **21** (*Scheme 3*). Reductive ring opening of the substituted spiro compounds leads to mono- and disubstituted diaminopyridines which are intermediates for fused pyridine ring systems with substituents often not available by conventional routes and of potential pharmaceutical interest (see **32**–**37**). *E.g.*, starting from **4a**, a three-step synthesis of the analgesic flupirtine maleate (= ethyl {2-amino-6-[(4-fluorobenzyl)amino]pyridin-3-yl}carbamate maleate = *Katadolon*®; **39**) and of its non-fluorinated derivative *D-7195* is described. Its analogue **40** was similarly made from the spiro compound **24**.

Introduction. – Spiro[2*H*-benzimidazole-2,1′-cyclohexanes], *e.g.* **1**, were shown to be versatile synthons for introducing nucleophilic substituents into aromatic molecules [1] and for preparing new fused heterocycles after reductive hydrolysis [2] [3]. It was of obvious interest to apply this chemistry to the structurally related 2,3-dihydrospiro[1*H*-azabenzimidazole-2,1′-cyclohexanes] **4a** and **24**, available from the 2,3- and 3,4-diaminopyridines (**2a** and **22**), respectively. Moreover, new pyridine chemistry would be of potential interest to biochemistry and pharmaceutical chemistry.

Results. – *Reactions of 2,3-Diaminopyridine* (**2a**). Amine **2a** readily underwent condensation with cyclohexanone (**3**) under reflux to give the expected 2,3-dihydro-1*H*-4-azabenzimidazole **4a** (*Scheme 1*). Oxidation of **4a** with MnO_2 or other oxidizing agents in an inert solvent (THF) led invariably to the pyridinone **5a** and not to **6a** as expected. This is most likely due to the instability of the intermediate 2*H*-azabenzimidazole **6a** which, by a 1,4-*Michael* addition of adventitious H_2O followed by oxidation, led to formation of the stable **5a**.

The structural assignment of **5a** was made by $^{13}\{^1H\}$-NOE difference spectra (*cf. Fig.*). Selective irradiation of the protons *H*–C(6′) and *H*–C(7′) caused a clear NOE in each case excluding structure **7** and possible tautomeric forms. Irradiation of the exchangeable proton led to two NOE's of comparable intensity. This confirms structure **5a** with the exchangeable proton in a central position relative to C(3a′) and C(5′).

Scheme 1



A recent note on the preparation of 6-substituted 2,3-diaminopyridines [4] reports the formation of the pyridinol derivative **8**, when the spiro compound **4a** is treated with MnO_2 which we could not confirm. Following closely the literature procedure, we obtained a pure compound which was in all analytical details identical with our **5a**. Our conclusion is further supported by the absence of any by-products and of a tautomeric equilibrium on varying solvent and temperature. Attempts at producing the desired 2*H*-azabenzimidazole **6a** as an intermediate failed in spite of exploring different oxidizing agents (DDQ, PbO_2, HgO, $Ph_3C(BF_4)$, $KMnO_4$, tetracyanoethylene, $(COCl)_2$/DMSO, or **1**).

To achieve introduction of a nucleophile into **4a**, we had to employ a different strategy, namely to use a competition reaction between the reagent and MnO_2, *i.e.* to oxidize the dihydro compound **4a** in the presence of an excess of nucleophile. This method prevented pyridinone formation in favour of the required substitution products, *i.e.*, of the mono- and disubstituted 2,3-dihydro-1*H*-4-azabenzimidazoles **9** and **10** and 2*H*-4-azabenzimidazoles (= 4-azaisobenzimidazoles) **11**–**18** (*Scheme 2*, *Table 1*). The examples demonstrate the use of N-, S-, O-, and C-nucleophiles. With tetracyanoethylene (= ethylenetetracarbonitrile), the propanedinitrile **19** was formed without addition of MnO_2 as the reagent acted as oxidizing agent. The loss of $=C(CN)_2$ occurred by a sequence analogous to that reported by us for the reaction of 2*H*-benzimidazole **1** with this reagent [5]. It is noteworthy that the reactions proceeded at room temperature and heating lead to decomposition of the products. The phenylsulfonyl-substituted deriva-

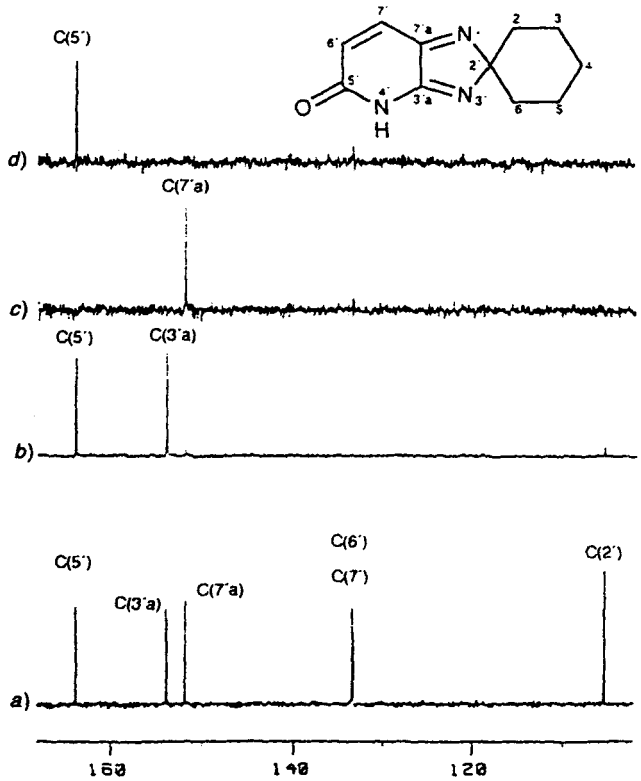
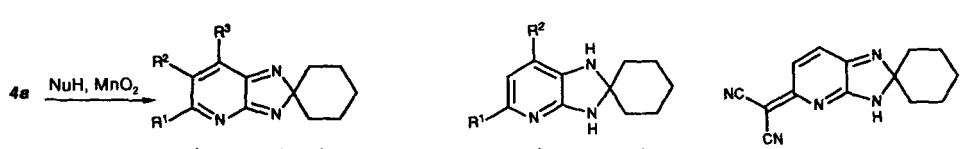


Figure. *^{13}C-NMR Spectra* (62.89 MHz; *Bruker WM 250*) *in* $CDCl_3$ *for compound* **5a**: *a*) *^{1}H-noise-decoupled spectrum*; b)c)d) *$^{13}C\{^1H\}$-NOE difference spectra obtained by selective irradiation of* H–*N(4')*, *of* H–*C(7')*, *and of* H–*C(6')*, *respectively*

tives **9** and **10** were obtained in the dihydro form owing to the reducing properties of the reagent. Intermediacy of **6a** in all these nucleophilic additions is supported by the fact that without MnO_2, no reaction between **4a** and the nucleophile occurred which is also valid for the formation of **10** from **9**.

Scheme 2



11 $R^1 = Et_2N$, $R^2 = R^3 = H$
12 $R^1 = PhCH_2NH$, $R^2 = R^3 = H$
13 $R^1 = 4\text{-}FC_6H_4CH_2NH$, $R^2 = R^3 = H$
14 $R^1 = EtS$, $R^2 = R^3 = H$
15 $R^1 = MeO$, $R^2 = R^3 = H$
16 $R^1 = R^3 =$ piperidino, $R^2 = H$
17 $R^1 = R^3 =$ morpholino, $R^2 = H$
18 $R^1 = R^2 =$ piperidino, $R^3 = H$

9 $R^1 = PhSO_2$; $R^2 = H$
10 $R^1 = R^2 = PhSO_2$

19

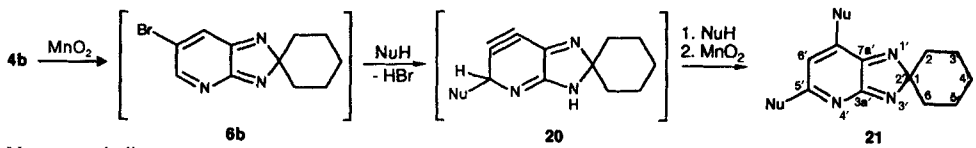
Table 1. *Reaction of* **4a** *with Nucleophiles at Room Temperature: Conditons and Products*

Nucleophile[a])	Solvent	Time	Product (yield [%])	M.p. [°]
Et_2NH	THF	140 h	**11** (16)	62
$PhCH_2NH_2$	THF	18 h	**12** (45)	198
$4\text{-}FC_6H_4CH_2NH_2$	THF	18 h	**13** (53)	189
EtSH	MeOH	4 h	**14** (28)	134
MeOH	–	70 h	**15** (25)	128
Piperidine	EtOH or THF[b])	6.5 h or 21 h[b])	**16** (5), **18** (10) or **16** (23)[b])	165 and 156, resp.
Morpholine[b])	THF	63 h	**17** (57)	226
NaOS(O)Ph[c])	$EtOH/H_2O$ 3:1	45 min	**9** (35), **10** (24)	86–88 and 146, resp.
$(CN)_2C{=}C(CN)_2$	THF	10 min	**19** (25)	258

[a]) Molar ratio nucleophile/**4a** 20:1.
[b]) Starting material **4b** instead of **4a**.
[c]) Reaction at 0°.

Reactions of 2,3-Diamino-5-bromopyridine (**2b**). It was of interest to use the bromo compound **2b** [6] to study the influence of the bulky Br-atom on the substitution pattern. Condensation with cyclohexanone (**3**) led to **4b** as expected (*Scheme 1*). A surprising result was obtained by reacting **4b** with N-nucleophiles (morpholine or piperidine) under conditions of the competition reaction (*cf.* above). The Br-atom was eliminated with formation of the disubstituted 2*H*-azabenzimidazole **21**. A plausible explanation to account for the loss of the Br-atom is the operation of a *cine*-mechanism [7] (*Scheme 3*): The unstable intermediate **6b** formed by oxidation adds the nucleophile by a 1,4-addition followed by loss of HBr to give the didehydro pyridine **20**. Addition of another molecule of nucleophile across the triple bond followed by oxidation leads to **21**.

Scheme 3



Nu = morpholino

The possibility of a direct attack on the Br-atom by the amine (protodebromination) [8] requires a polyhalogenated system and can, therefore, be discounted.

Reactions of 3,4-Diaminopyridine (**22**). Condensation of amine **22** with cyclohexanone (**3**) below 100° led to the *Schiff*'s base **23** which on reflux was converted into the required dihydro-1*H*-azabenzimidazole **24** (*Scheme 4*). This is in contrast to the direct formation of the isomeric **4a** even when the reaction was carried out under mild conditions. As oxidation of **24** (MnO_2) led to pyridinone **25**, we again used the strategy of a competition reaction for introducing nucleophiles. *Table 2* gives examples of N-, S-, and O-nucleophiles yielding mono-substituted 2*H*-5-azabenzimidazoles **26a–h** by *Michael* addition. Only sodium benzenesulfinate gave again the mono- and disubstituted products **27** and **28** in the dihydro form.

Comparison of the Reactivity of **2a** *and* **22**. Condensation with cyclohexanone (**3**) and subsequent oxidation led to analogous results, except for the isolable *Schiff*'s base **23** in

Scheme 4

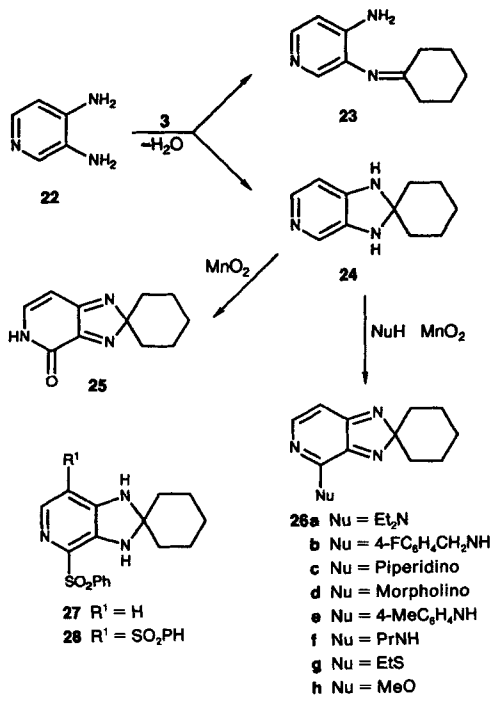


Table 2. *Reaction of* **24** *with Nucleophiles at Room Temperature: Conditions and Products*

Nucleophile[a])	Solvent	Time	Product (yield [%])	M.p. [°]
Et_2NH	THF	1 h	**26a** (29)	70
$4\text{-}FC_6H_4CH_2NH_2$	THF	1 h	**b** (53)	104
Piperidine	THF	1 h	**c** (60)	72
Morpholine	THF	1 h	**d** (65)	154
$4\text{-}MeC_6H_4NH_2$	THF	1 h	**e** (12)	148
$PrNH_2$	THF	1 h	**f** (50)	59–62
EtSH	THF	1 h	**g** (9)	97
MeOH	–	20 h	**h** (25)	86
NaOS(O)Ph	$EtOH/H_2O$ 6:1	2 h	**27** (31), **28** (14)	214 and 219–220, resp.

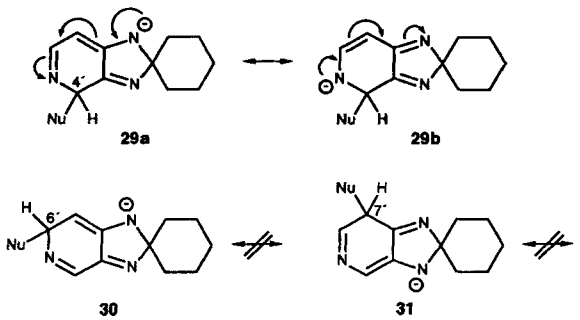
[a]) Molar ratio nucleophile/**24** 1:1.

the case of **22**. However, results in the competition reaction with N-nucleophiles differ: With **24** (derived from **22**), 1 equiv. of nucleophile led to the required product **26** within 1 h at room temperature (*Table 2*). With **4a** (derived from **2a**), variation of solvent and reaction time influenced the outcome: A 20:1 excess of nucleophile led to the optimum result avoiding pyridinone formation; depending on the nucleophile, mono- or disubstitution occurred (*Table 1*).

While disubstitution occurred readily in **4a** by 1,4- or 1,6-*Michael* additions, in the case of **24**, only monosubstitution to **26** by 1,6-addition was observed, except for the very

reactive S-nucleophile $PhSO_2Na$. The substitution pattern obtained from **24** is best accounted for by the extended conjugation in the transition state [N=C–C=C–N⁻] of the 1,6-addition (**29a**↔**29b**), in contrast to that of a 1,4(or 1,3)-addition (**30** or **31**; *Scheme 5*).

Scheme 5



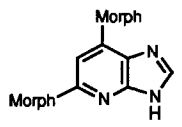
The O-nucleophile MeOH yielded the corresponding MeO-substituted 2*H*-azabenzimidazoles **15** (R^1 = MeO) or **26h** (Nu = MeO), while EtOH gave only the pyridinones **5a** or **25**.

It is of interest to compare the reactivity with nucleophiles of the 2*H*-benzimidazoles **1** [1] with that of the 2*H*-azabenzimidazoles derived from **4a** and **24**. The former can yield mono-, di-, or even polysubstituted derivatives [1] [9] depending on reaction conditions, while the aza analogues **4a** and **24** yield addition products (4-h refluxing and equimolar reagents **22** and **3**). It is striking that $(i\text{-}Pr)_2NH$ so far produced exclusively the pyridinones **5a** and **25** from the corresponding spiro derivatives **4a** and **24**, possibly because of its bulky character leading to lone-pair repulsion. By contrast it can be readily introduced into **1** [2].

*Synthetic Applications of 2,3-Dihydro-1*H*-4 and 5-azabenzimidazoles* **4a** *and* **24**, *Respectively*. The dimorpholino-substituted 2*H*-4-azabenzimidazole **17** ($R^1 = R^3$ = morpholino; obtained from **4a**) was ring-opened in an aqueous solution of sodium dithionite at room temperature yielding an unstable tetraamino-substituted pyridine which was cyclised *in situ* with formic acid or with SeO_2 to give the expected 3*H*-imidazo[4,5-*b*]-pyridine **32** or the selenadiazolo[3,4-*b*]pyridine **33**, respectively. The synthetic advantage of this procedure lies in the convenient preparation of fused pyridinoheterocycles with nucleophilic substituents, especially the imidazopyridines (*e.g.* **32**) being of current pharmaceutical interest [10]. Conventional methods for introducing nucleophiles into such systems make use of displacement reactions [11]. The imidazopyridine **32** exists only in the 3*H*-tautomeric form. The usual 1,3-tautomerism found in imidazoles [12] appears to be prevented, possibly owing to strong H-bonding between H–N(3) and the pyridine N-atom. The structure followed from $^{13}C\{^1H\}$-NOE difference spectra (irradiation of NH→clear NOE for C(3a), but not for C(3a) and C(7a) as expected in the case of tautomerism) and the IR spectrum (3150 and 3130 cm^{-1} (sharp, NH, intramolecular H-bond)).

Conversions of the monomorpholino-substituted 2*H*-5-azabenzimidazole **26d** (obtained from **24**) into fused heterocycles were carried out by a procedure analogous to the

one described above for **17**. The intermediate triamino-substituted pyridine was directly cyclised because of its instability to give the heterocycles **34–37**. Ring closure of this intermediate with SeO_2 occurred only under reflux yielding also the pyridinone **37** as a by-product, in contrast to the cyclisation to **33** which was effected at room temperature. In contrast to **32**, the imidazopyridine **34** exists in the 1*H*-tautomeric form. This follows from a homonuclear NOE experiment which established the position of the exchangeable NH as being central to H–C(2) and H–C(7) (irradiation of H–N(1)→NOE's for *H*–C(2) and *H*–C(7)). In the absence of an intramolecular H-bond in the 1*H*-form **34**, it is reasonable to assume that intermolecular association is responsible for holding the conformation, as supported by broad IR absorption at 3200–2580 cm^{-1} [13].



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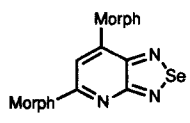

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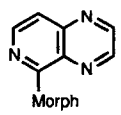

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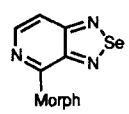

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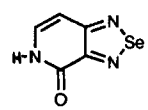

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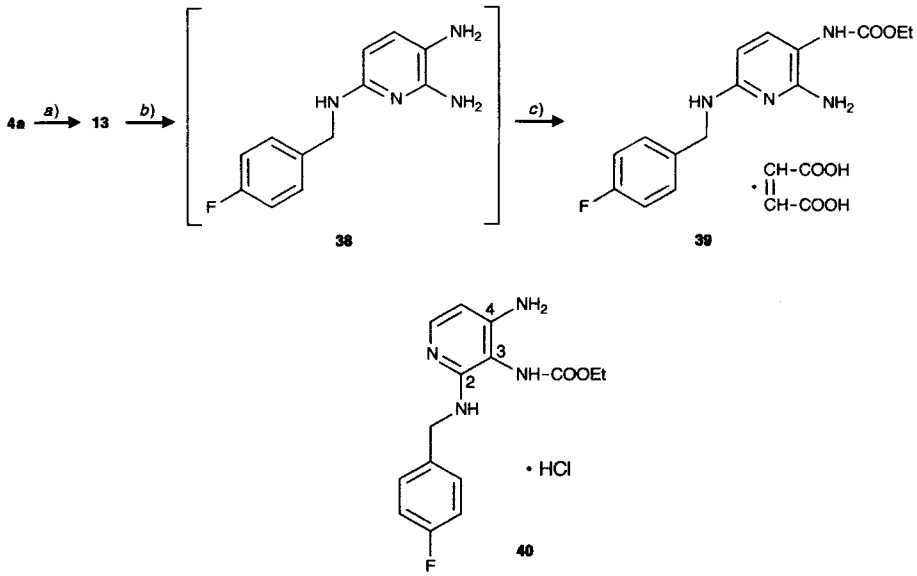
We also undertook a target synthesis of flupirtine maleate, *i.e.*, ethyl {2-amino-6-[(4-fluorobenzyl)amino]pyridin-3-yl}carbamate maleate (**39**), a novel analgesic developed by *Asta Medica AG*, Frankfurt/Main, and called *Katadolon*® [14–16]. The reported synthesis used 2,6-dichloro-3-nitropyridine as a starting material [14] [17] replacing the reactive Cl-atom at C(6) by (4-fluorobenzyl)amine or by benzylamine leading to **39** or *D-7175* (see **39**, H instead of F, HCl instead of $(CHCOOH)_2$; and anticonvulsant), respectively. As **39** is derived from a 2,3,6-triamino-substituted pyridine, an alternative synthesis based on our experience with 2,3-dihydro-1*H*-4-azabenzimidazole **4a** suggested itself (*Scheme 6*). Under moderate conditions of the above discussed competition reaction, the 2*H*-azabenzimidazole **13** was obtained. Reductive hydrolysis with $Na_2S_2O_4$ led to the unstable triamino-substituted pyridine **38**, and reaction with ethyl chloroformate and then with maleic acid gave the required crystalline maleate **39**. The yields were not optimized.

An advantage of the transformation of the type **4a** → **39** over the reported method [14] [18] is the simple reduction ($Na_2S_2O_4$) instead of catalytic hydrogenation and above all its better versatility. Indeed, the closely related anticonvulsant *D-7175* (see **39**, H instead of F) [18] was similarly prepared *via* **12** using benzylamine instead of (4-fluorobenzyl)amine in step *a* of *Scheme 6*.

We also used the 2,3-dihydro-1*H*-5-azabenzimidazole **24** (*Scheme 4*) as starting material to prepare the flupirtine analogue **40** (*Scheme 6*) *via* 2*H*-azabenzimidazole **26b**. Again the 3-NH_2 group of the intermediate 2,3,4-triamino-substituted pyridine reacted with ethyl chloroformate, as shown by a $^{13}C\{^1H\}$-NOE difference spectrum of **40** (irradiation of N*H*COOEt→NOE's at 154.4 (NH*C*OOEt) and 98.8 ppm (C(3); *i.e.*, signal at high field due to the *m*-position rel. to N(1)); ^{13}C-NMR: 154.7 (C(4)) and 149.9 ppm (C(2))).

Scheme 6



a) (4-Fluorobenzyl)amine, MnO_2. *b*) $Na_2S_2O_4$. *c*) ClCOOEt; NH_3; maleic acid.

Moreover, the ready formation of the *Schiff*'s base **23** from 3,4-diamine **22** and cyclohexanone (**3**; *Scheme 4*) confirms the preferential reactivity of the 3-NH_2 group in this diamine [19]. It is noteworthy that the flupirtine analogue **40**, unlike **39**, shows no fluorescence. Further structural elaboration of these compounds is of considerable interest in view of the parent system displaying pronounced pharmacological action.

We thank Mrs. *U. Hertle* for ^{1}H- and ^{13}C-NMR spectra, *H. Rudy* and *P. Weyrich* for MS and CHN analyses, Dr. *B. Kutscher* and Dr. *P. Emig* (*Asta Medica AG*) for useful discussions and gifts of chemicals as well as Dr. *E. F. V. Scriven* (*Reilly and Tar*, Indianapolis) for generous gifts of pyridines. Support of this work by *BASF AG*, *Bayer AG*, and *Hoechst AG* with generous gifts of chemicals is acknowledged. We are also grateful to *ICN Biomedicals GmbH* (Eschwege) for gifts of silica gel and to the *Verband der Chemischen Industrie – Fonds der Chemie*, and *Deutsche Forschungsgemeinschaft* for donation of chemicals.

Experimental Part

General. Activated MnO_2 was purchased from *Fluka* (CAS No. [1313-13-9]). Column chromatography (CC): silica gel *60* (*Merck*). M.p.: *Reichert* melting-point microscope, uncorrected. UV Spectra: *Carl-Zeiss-DMR-4* spectrometrer; λ (log ε) in nm. IR Spectra: *Perkin-Elmer-325* spectrometer. NMR Spectra: *Bruker WM 250* (250 MHz for ^{1}H and 62.89 MHz for ^{13}C) and *Varian XL-300* (300 MHz for ^{1}H and 75.43 MHz for ^{13}C); δ values relative to Me_4Si. MS: *Varian MAT-311-A* (80 eV).

*Spiro[cyclohexane-1,2′(3′*H*)-1′*H*-imidazo[4,5-*b*]pyridine]* (**4a**). A soln. of 2,3-diaminopyridine (**2a**; 16.0 g, 147 mmol) and cyclohexanone (**3**; 14.4 g, 147 mmol) in i-PrOH (1 l) is heated under reflux for 71 h. After $^2/_3$ of the solvent is evaporated, recrystallisation of the solid residue from EtOH (99%) gives pure **4a** (11.45 g, 41.8%). Silvery platelets. M.p. 214° ([20]: 212–214°). UV (MeCN): 203 (3.964), 264 (3.122), 312 (3.344). IR (KBr): 3390, 3180 (NH); 3060 (Aryl-H); 2940, 2860 (C–H); 1620, 1600, 1500, 1450 (C=C, C=N); 1430. ^{1}H-NMR (250.13 MHz, $CDCl_3$): 7.35 (*dd*, ^3J = 5.5, ^4J = 1.5, H–C(5′)); 6.50 (*dd*, ^3J = 7.5, ^4J = 1.5, H–C(7′)); 6.37 (*dd*, ^3J = 7.5, 5.5,

H–C(6′)); 5.41 (*s*, NH); 3.95 (*s*, NH); 1.92–1.30 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, (D$_6$)DMSO): 154.6 (*s*, C(3′a)); 134.1 (*s*, C(5′)); 133.2 (*s*, C(7′a)); 112.2 (*s*, C(6′)); 107.2 (*s*, C(7′)); 7.77 (*s*, C(2′)); 39.5 (*s*, C(2), C(6)); 24.6 (*s*, C(4)); 21.9 (*s*, C(3), C(5)). MS: 189 (42, M^+), 146 (100, $[C_8H_8N_3]^+$). Anal. calc. for $C_{11}H_{15}N_3$ (189.26): C 69.80, H 7.99, N 22.21; found: C 70.04, H 8.09, N 22.17.

*6′-Bromospiro[cyclohexane-1,2′(3′*H*)-1′*H*-imidazo[4,5-*b*]pyridine]* (**4b**). As described for **4a**, from 2,3-diamino-5-bromopyridine [6] (**2b**; 5.6 g, 29.8 mmol), **3** (2.9 g, 30 mmol), and i-PrOH (350 ml; 24 h). Recrystallisation from $CHCl_3$ yields **4b** (3.75 g, 47%). Powder of an orange lustre. M.p. 194°. UV (MeCN): 208 (4.267), 274 (3.573), 330 (3.971). IR (KBr): 3340, 3195, 3160 (NH); 3075 (Aryl-H); 2920, 2860 (C–H); 1615, 1495, 1450 (C=C, C=N); 1370. ^{1}H-NMR (250.13 MHz, (D$_6$)DMSO): 7.31 (*s*, NH); 6.98 (*d*, ^4J = 1.98, H–C(5′)); 6.66 (*s*, NH); 6.18 (*d*, ^4J = 1.98, H–C(7′)); 1.87–1.17 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, (D$_6$)DMSO): 153.5 (*s*, C(3′a)); 135.3 (*s*, C(7′a)); 133.1 (*s*, C(5′)); 108.3 (*s*, C(7′)); 106.6 (*s*, C(6′)); 79.0 (*s*, C(2′)); 39.5 (*s*, C(2), C(6)); 24.5 (*s*, C(4)); 21.9 (*s*, C(3), C(5)). MS: 267 (26, M^+), 224 (100, $[C_8H_7BrN_3]^+$). Anal. calc. for $C_{11}H_{14}BrN_3$ (268.15): C 49.27, H 5.26, N 15.67; found: C 49.17, H 5.36, N 15.64.

*Spiro[cyclohexane-1,2′-2′*H*-imidazo[4,5-*b*]pyridine]-5′(4′*H*)-one* (**5a**). To a soln. of **4a** (1.0 g, 5.3 mmol) in dry THF (80 ml) MnO_2 (4.6 g, 53 mmol) is added and the mixture stirred at r.t. for 2 h. After filtration and evaporation, the crude residual is recrystallised from MeOH: **5a** (0.35 g, 32.5%). M.p. 184° ([21]: 184°). UV (MeCN): 255 (4.338), 425 (2.614). IR (KBr): 3300–2600 (band due to aggregation); 1740–1660 (C=O); 1605, 1445 (C=C, C=N); 1325. ^{1}H-NMR (250.13 MHz, $CDCl_3$): 8.35 (*s*, NH); 7.53 (*d*, ^3J = 9.75, H–C(7′)); 6.70 (*d*, ^3J = 9.75, H–C(6′)); 2.04–1.60 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, $CDCl_3$): 163.7 (*s*, C(5′)); 153.8 (*s*, C(3′a)); 151.9 (*s*, C(7′a)); 133.4 (*s*, C(6′), C(7′)); 105.5 (*s*, C(2′)); 34.4 (*s*, C(2), C(6)); 25.4 (*s*, C(4)); 24.0 (*s*, C(3), C(5)). MS: 203 (100, M^+). Anal. calc. for $C_{11}H_{13}N_3O$ (203.24): C 65.00, H 6.45, N 20.68; found: C 65.04, H 6.67, N 20.47.

*6′-Bromospiro[cyclohexane-1,2′-2′*H*-imidazo[4,5-*b*]pyridine]-5′(4′*H*)-one* (**5b**). As described for **5a**, from **4b** (0.3 g, 1.1 mmol) and MnO_2 (0.96 g, 11 mmol) in $CHCl_3$ (150 ml; 3 h): **5b** (0.1 g, 31.8%). Brown needles. M.p. 227° (dec.). UV (MeCN): 211 (3.898), 256 (3.942), 273 (3.942), 327 (3.491). IR (KBr): 3500–3350 (NH); 3030 (Aryl-H); 2940, 2860 (C–H); 1705 (C=O); 1620, 1595, 1505, 1455 (C=C, C=N); 1390. ^{1}H-NMR (250.13 MHz, (D$_6$)DMSO): 12.10 (*s*, NH); 8.29 (*s*, H–C(7′)); 1.93–1.27 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, (D$_6$)DMSO): 158.9 (*s*, C(5′)); 153.1 (*s*, C(3a′)); 151.8 (*s*, C(7′a)); 134.9 (*s*, C(7′)); 131.0 (*s*, C(6′)); 104.1 (*s*, C(2′)); 33.6 (*s*, C(2), C(6)); 25.0 (*s*, C(4)); 23.8 (*s*, C(3), C(5)). MS: 281 (100, M^+). Anal. calc. for $C_{11}H_{12}BrN_3O$ (282.14): C 46.83, H 4.29, N 14.89; found: C 46.80, H 4.36, N 14.78.

*5′-(Diethylamino)spiro[cyclohexane-1,2′-2′*H*-imidazo[4,5-*b*]pyridine]* (**11**). To **4a** (0.35 g, 1.85 mmol) in dry THF (60 ml), Et_2NH (2.7 g, 37 mmol) and MnO_2 (1.6 g, 18.5 mmol) are added and stirred at r.t. for 140 h. After filtration and evaporation, the residue oil is chromatographed twice (silica gel, 1. AcOEt/MeOH 5:2, 2. $CHCl_3$/MeOH 20:1). Recrystallisation from petroleum ether (40–60°) provides **11** (78.4 mg, 16.2%). Yellow crystals. M.p. 62°. UV (MeCN): 274 (4.054), 293 (4.030), 390 (3.733). IR (KBr): 3050 (Aryl-H); 2930, 2850 (C–H); 1630, 1600, 1505–1430 (C=C, C=N); 1355. ^{1}H-NMR (250.13 MHz, $CDCl_3$): 7.46 (*d*, ^3J = 10.26, H–C(7′)); 6.97 (*d*, ^3J = 10.26, H–C(6′)); 3.96–3.43 (br. 2 MeC*H*$_2$); 2.14–1.46 (*m*, C_6H_{10}); 1.27 (*t*, 2 *Me*CH$_2$). ^{13}C-NMR (62.89 MHz, $CDCl_3$): 161.7 (*s*, C(3′a)); 159.8 (*s*, C(5′)); 153.7 (*s*, C(7′a)); 133.1 (*s*, C(7′)); 123.6 (*s*, C(6′)); 102.4 (*s*, C(2′)); 43.7 (*s*, 2 Me*C*H$_2$); 34.2 (*s*, C(2), C(6)); 25.7 (*s*, C(4)); 24.5 (*s*, C(3), C(5)); 15.1 (*s*, *Me*CH$_2$); 13.0 (*s*, *Me*CH$_2$). MS: 258 (64, M^+), 79 (100). Anal. calc. for $C_{15}H_{22}N_4$ (258.35): C 69.73, H 8.58, N 21.69; found: C 69.18, H 8.65, N 21.28.

*5′-(Ethylthio)spiro[cyclohexane-1,2′-2′*H*-imidazo[4,5-*b*]pyridine]* (**14**). As described for **11**, from **4a** (1.0 g, 5.3 mmol) in MeOH (100 ml), EtSH (0.656 g, 10.58 mmol) MnO_2 (4.6 g, 52.9 mmol; 4 h). CC (silica gel, AcOEt) and recrystallisation from hexane yield **14** (362 mg, 27.8%). Yellow crystals. M.p. 134°. UV (MeCN): 301 (4.054), 350 (3.810). IR (KBr): 3065 (Aryl-H); 2940, 2860 (C–H); 1625, 1580, 1485, 1450, 1410 (C=C, C=N); 1265. ^{1}H-NMR (250.13 MHz, (D$_6$)DMSO): 7.60 (*d*, ^3J = 10.63, H–C(7′)); 7.03 (*d*, ^3J = 10.63, H–C(6′)); 3.22 (*q*, MeC*H*$_2$); 1.92–1.41 (*m*, C_6H_{10}); 1.35 (*t*, *Me*CH$_2$). ^{13}C-NMR (62.89 MHz, (D$_6$)DMSO): 174.9 (*s*, C(5′)); 159.4 (*s*, C(3′a)); 154.2 (*s*, C(7′a)); 131.3 (*s*, C(6′), C(7′)); 103.2 (*s*, C(2′)); 32.9 (*s*, C(2), C(6)); 25.1 (*s*, C(4)); 24.3 (*s*, MeC*H*$_2$); 24.0 (*s*, C(3), C(5)); 13.8 (*s*, *Me*CH$_2$). MS: 247 (32, M^+), 96 (100). Anal. calc. for $C_{13}H_{17}N_3S$ (247.35): C 63.12, H 6.93, N 16.99; found: C 63.18, H 6.93, N 16.92.

*5′-Methoxyspiro[cyclohexane-1,2′-2′*H*-imidazo[4,5-*b*]pyridine]* (**15**). As described for **11**, from **4a** (0.4 g, 2.12 mmol) in MeOH (40 ml) and MnO_2 (1.84 g, 21.2 mmol; 70 h). Recrystallisation from Et_2O provides pure **15** (115.2 mg, 25%). Brown-yellow crystals. M.p. 128°. UV (MeCN): 254 (4.050), 263 (4.016), 305 (3.283). IR (KBr): 3050, 3020 (Aryl-H); 2925, 2860 (C–H); 1630, 1605, 1525, 1445, 1405 (C=C, C=N); 1310 (C–O–C). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.53 (*d*, ^3J = 9.99, H–C(7′)); 6.72 (*d*, ^3J = 9.99, H–C(6′)); 4.17 (*s*, MeO); 2.25–1.40 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, $CDCl_3$): 169.4 (*s*, C(5′)); 160.4 (*s*, C(3′a)); 154.1 (*s*, C(7′a)); 134.5 (*s*, C(7′)); 127.4 (*s*, C(6′)); 104.6 (*s*, C(2′)); 55.2 (*s*, MeO); 33.4 (*s*, C(2), C(6)); 25.6 (*s*, C(4)); 24.4 (*s*, C(3), C(5)). MS: 217 (91, M^+), 80 (100). Anal. calc. for $C_{12}H_{15}N_3O$ (217.26): C 66.34, H 6.96, N 19.34; found: C 66.31, H 6.93, N 19.18.

5',7'-Di(piperidin-1-yl)spiro[cyclohexane-1,2'-2'H-imidazo[4,5-b]pyridine] (**16**). *Method A*: As described for **18**. The 2nd orange band provides pure compound. Rcrystallisation from Et_2O yields **16** (77 mg, 4.6%). Yellow-orange-crystals.

Method B: As described for **11**, from **4b** (0.33 g, 1.24 mmol) in dry THF (66 ml) piperidine (2.11 g, 24.8 mmol), and MnO_2 (1.08 g, 12.4 mmol); 21 h; careful evaporation). CC (silica gel, $CHCl_3$/MeOH 8:1) and recrystallisation from Et_2O give **16** (101.5 mg, 23.4%). Yellow-orange crystals. M.p. 165°. UV (MeCN): 223 (4.373), 362 (4.108). IR (KBr): 2940, 2860 (C–H); 1620, 1575, 1495, 1440 (C=C, C=N); 1345. ^{1}H-NMR (250.13 MHz, $CDCl_3$): 5.73 (*s*, H–C(6')); 3.83–3.67 (*m*, 4 CH_2); 2.10–1.39 (*m*, 6 CH_2, C_6H_{10}). ^{13}C-NMR (62.89 MHz, $CDCl_3$): 163.6 (*s*, C(5') or C(3'a)); 163.5 (*s*, C(5') or C(3'a)); 153.0 (*s*, C(7'a)); 149.3 (*s*, C(7')); 100.8 (*s*, C(2')); 92.9 (*s*, C(6')); 49.1 (*s*, 2 CH_2); 46.8 (*s*, 2 CH_2); 34.7 (*s*, C(2), C(6)); 26.4 (*s*, 2 CH_2); 25.9 (*s*, C(4)); 25.3 (*s*, 2 CH_2); 24.8 (*s*, CH_2); 24.6 (*s*, C(3), C(5)); 24.5 (*s*, CH_2). MS: 353 (100, M^+). Anal. calc. for $C_{21}H_{31}N_5$ (353.51): 71.35, H 8.84, N 19.81; found: C 71.20, H 8.90, N 19.54.

5',7'-Di(morpholin-4-yl)spiro[cyclohexane-1,2'-2'H-imidazo[4,5-b]pyridine] (**17**). As described for **11**, from **4b** (6.0 g, 22.4 mmol) in dry THF (1200 ml), morpholine (39.2 g, 450 mmol), and MnO_2 (19.6 g, 225 mmol; 63 h). CC (silica gel, AcOEt/MeOH 5:2) and recrystallisation from Et_2O give **17** (4.55 g, 56.6%). Yellow-orange crystals. M.p. 226°. UV (MeCN): 216 (4.344), 350 (4.041). IR (KBr): 3020 (Aryl-H); 2940, 2850 (C–H); 1620, 1575, 1485, 1440 (C=C, C=N); 1350, 1120 (C–O–C). ^{1}H-NMR (250.13 MHz, $CDCl_3$): 5.66 (*s*, H–C(6')); 4.24–3.55 (*m*, 8 CH_2); 2.18–1.34 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, $CDCl_3$): 163.4 (*s*, C(5')); 162.6 (*s*, C(3'a)); 152.4 (*s*, C(7'a)); 149.2 (*s*, C(7')); 101.5 (*s*, C(2')); 92.5 (*s*, C(6')); 66.6 (*s*, 2 CH_2O); 66.1 (*s*, 2 CH_2OCH_2); 47.6 (*s*, 2 CH_2N); 45.6 (*s*, 2 CH_2N); 34.2 (*s*, C(2), C(6)); 25.6 (*s*, C(4')); 24.3 (*s*, C(3), C(5)). MS: 357 (83, M^+), 299 (100). Anal. calc. for $C_{19}H_{27}N_5O_2$ (357.44): C 63.84, H 7.62, N 19.59; found: C 63.60, H 7.81, N 19.32.

5',6'-Di(piperidin-1-yl)spiro[cyclohexane-1,2'-2'H-imidazo[4,5-b]pyridine] (**18**). As described for **11**, from **4a** (0.9 g, 4.76 mmol) in EtOH (240 ml), piperidine (8.28 g, 95.2 mmol), and MnO_2 (4.2 g, 47.6 mmol; 6.5 h). CC (silica gel, $CHCl_3$/MeOH 8:1) gives a 1st, yellow band which provides pure product. Recrystallisation from Et_2O yields **18** (0.17 g, 10.1%). Yellow crystals. M.p. 156°. UV (MeCN): 208 (4.226), 350 (4.085). IR (KBr): 2930, 2860 (C–H); 1535, 1495, 1445 (C=C, C=N); 1365. ^{1}H-NMR (250.13 MHz, $CDCl_3$): 6.64 (*s*, H–C(7')); 3.98–3.82 (*m*, 2 CH_2); 3.14–2.83 (*m*, 2 CH_2); 2.07–1.36 (*m*, 6 CH_2, C_6H_{10}). ^{13}C-NMR (62.89 MHz, $CDCl_3$): 162.0 (*s*, C(3'a) or C(5')); 159.7 (*s*, C(3'a) or C(5')); 155.4 (*s*, C(7'a) or C(6')); 149.2 (*s*, C(7'a) or C(6')); 111.7 (*s*, C(7')); 102.0 (*s*, C(2')); 51.2 (*s*, 2 CH_2); 49.4 (*s*, 2 CH_2); 34.1 (*s*, C(2), C(6)); 26.1 (*s*, 2 CH_2 or C(3), C(5)); 25.6 (*s*, CH_2 or C(4)); 25.4 (*s*, 2 CH_2 or C(3), C(5)); 24.5 (*s*, CH_2 or C(4)); 24.4 (*s*, 2 CH_2 or C(3), C(5)); 23.8 (*s*, CH_2 or C(4)). MS: 353 (100, M^+). Anal. calc. for $C_{21}H_{31}N_5$ (353.51): C 71.35, H 8.84, N 19.81; found: C 71.26, H 9.06, N 20.09.

5'-(Phenylsulfonyl)spiro[cyclohexane-1,2'(3'H)-1'H-imidazo[4,5-b]pyridine] (**9**). To a soln. of **4a** (0.7 g, 3.7 mmol) in EtOH (210 ml), a soln. of sodium benzenesulfinate (1.22 g, 7.4 mmol) in H_2O (70 ml), MnO_2 (3.2 g, 37 mmol), and AcOH (0.6 ml, 10.6 mmol) AcOH are added. The suspension is stirred at 0° for 45 min, the solid filtered off, and the filtrate evaporated. The solid is chromatographed twice (silica gel, 1. AcOEt, 2. $CHCl_3$/MeOH 20:1) and the more polar fraction (2nd band recrystallised from MeOH): colourless powder of **9** (426 mg, 35%). M.p. 86–88°. UV (MeCN): 216 (4.221), 335 (4.078). IR (KBr): 3370 (NH); 2940, 2870 (C–H); 1625, 1595, 1510, 1450 (C=C, C=N); 1300 (SO_2); 1150 (SO_2). ^{1}H-NMR (250.13 MHz, (D_6)DMSO): 7.98 (*s*, NH); 7.85–7.79 (*m*, 2 H, Ph); 7.68–7.54 (*m*, 3 H, Ph); 7.51 (*s*, NH); 7.13 (*d*, ^3J = 7.17, H–C(6')); 6.16 (*d*, ^3J = 7.17, H–C(7')); 1.69–1.28 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, (D_6)DMSO): 154.0 (*s*, C(3'a)); 141.2 (*s*, SO_2C); 140.1 (*s*, C(5')); 137.2 (*s*, C(7'a)); 132.7 (*s*, 1 C, Ph); 129.0 (*s*, 2 C, Ph); 127.4 (*s*, 2 C, Ph); 115.4 (*s*, C(6')); 102.4 (*s*, C(7')); 79.0 (*s*, C(2')); 39.7 (*s*, C(2), C(6)); 24.4 (*s*, C(4)); 21.7 (*s*, C(3), C(5)). MS: 329 (40, M^+), 286 (100, $[C_{14}H_{12}N_3O_2S]^+$). Anal. calc. for $C_{17}H_{19}N_3O_2S$ (329.40): C 61.98, H 5.81, N 12.76, S 9.73; found: C 62.00, H 5.76, N 12.91, S 9.79.

5',7'-Bis(phenylsulfonyl)spiro[cyclohexane-1,2'(3'H)-1'H-imidazo[4,5-b]pyridine] (**10**). As described for **9**, from **4a** (0.7 g, 3.7 mmol) in EtOH (210 ml), sodium benzenesulfinate (12.2 g, 74.2 mmol) in H_2O (70 ml), MnO_2 (3.2 g, 37 mmol), and AcOH (0.6 ml, 10.6 mmol). The 1st band of the CC leads, after recrystallisation from MeOH, to **10** (420 mg, 24.3%). Colourless powder. M.p. 146°. UV (MeCN): 220 (4.346), 328 (3.972), 355 (4.013). IR (KBr): 3360 (NH); 2950, 2870 (C–H); 1610, 1530, 1450 (C=C, C=N); 1305, 1150 (SO_2). ^{1}H-NMR (250.13 MHz, (D_6)DMSO): 9.20 (*s*, NH); 8.80 (*s*, NH); 8.14–7.95 (*m*, 2 H, Ph); 7.90–7.52 (*m*, 8 H, Ph); 7.24 (*s*, H–C(6')); 2.02–1.33 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, (D_6)DMSO): 155.5 (*s*, C(3'a)); 141.1 (*s*, SO_2C); 140.3 (*s*, C(5')); 139.9 (*s*, SO_2C); 135.2 (*s*, C(7'a)); 133.9 (*s*, 1 C, Ph); 133.3 (*s*, 1 C, Ph); 129.8 (*s*, 2 C, Ph); 129.3 (*s*, 2 C, Ph); 127.7 (*s*, 2 C, Ph); 126.4 (*s*, 2 C, Ph); 110.4 (*s*, C(7')); 109.6 (*s*, C(6')); 81.4 (*s*, C(2')); 38.5 (*s*, C(2), C(6)); 24.2 (*s*, C(4)); 21.6 (*s*, C(3), C(5)). MS: 469 (30, M^+), 426 (100, $[C_{20}H_{16}N_3O_4S_2]^+$). Anal. calc. for $C_{23}H_{23}N_3O_4S_2$ (469.56): C 58.83, H 4.94, N 8.95, S 13.65; found: C 58.75, H 4.80, N 8.64, S 13.47.

2-{Spiro[cyclohexane-1,2'(5'H)-3'H-imidazo[4,5-b]pyridine]-5'-ylidene}propanedinitrile (**19**). To **4a** (1.0 g, 5.3 mmol) in dry THF (167 ml) at 0°, a soln. of $(CN)_2C{=}C(CN)_2$ (0.68 g, 5.3 mmol) in THF (30 ml) is added and

stirred for 10 min. After evaporation, CC (silica gel, AcOEt) and recrystallisation from Et_2O give **19** (330.8 mg, 24.9%). Brown powder. M.p. 258°. UV (MeCN): 251 (3.903), 305 (3.891), 433 (4.184). IR (KBr): 3260–3080 (NH); 3030 (Aryl-H); 2940, 2860 (C–H); 2210 (CN); 1640, 1595, 1495 (C=C, C=N); 1440. ^{1}H-NMR (250.13 MHz, (D_6)DMSO): 12.30 (*s*, NH); 7.48 (*d*, ^3J = 10.47, H–C(7′)); 7.32 (*d*, ^3J = 10.47, H–C(6′)); 1.95–1.43 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, (D_6)DMSO): 168.5 (*s*, C(5′)); 157.2 (*s*, C(3′a)); 153.2 (*s*, C(7′a)); 130.8 (*s*, C(7′) or C(6′)); 129.1 (*s*, C(7′) or C(6′)); 115.4 (*s*, =C–*C*N); 115.0 (*s*, =C–*C*N); 93.5 (*s*, C(2′)); 66.9 (*s*, =*C*–CN); 34.5 (*s*, C(2), C(6)); 24.2 (*s*, C(4)); 22.5 (*s*, C(3), C(5)). MS: 251 (77, M^+), 61 (100). HR-MS (peak matching): 251.1172 ($[C_{14}H_{13}N_5]^+$, calc. 251.1171). Elemental analysis: unsatisfactory due to instability of **19**.

5′,7′-Dimorpholinospiro[cyclohexane-1,2′-2′H-imidazo[4,5-b]pyridine] (**21**). A soln. of **4b** (6 g, 22.4 mmol) in 1200 ml of dried THF, morpholin (39.2 g, 450 mmol) and MnO_2 (19.6 g, 225 mmol) is added and stirred 63 h at r.t. After filtration and careful evaporation of solvent, the residue is purified by SC (silica gel, AcOEt/MeOH 5:2). Its recrystallisation from Et_2O provides yellow-to-orange crystals of **21** (4.55 g, 56.6%). M.p. 226°. UV (MeCN): 216 (4.344), 350 (4.041). IR (KBr): 3020 (Aryl-H); 2940, 2850 (C–H); 1620, 1575, 1485, 1440 (C=C, C=N); 1350, 1260, 1230, 1120 (C–O–C); 1005, 905. ^{1}H-NMR (250.13 MHz): 5.66 (*s*, H–C(6′)); 4.24–3.55 (*m*, 2 morpholino-H, 8 CH_2); 2.18–1.34 (*m*, C_6H_{10}). MS: 358 (16, $[M+1]^+$); 357 (83, M^+), 328 (13, $[C_{17}H_{22}N_5O_2]^+$), 327 (57, $[C_{18}H_{25}N_5O]^+$), 326 (19, $[C_{18}H_{24}N_5O]^+$), 314 (8, $[C_{16}H_{20}N_5O_2]^+$), 312 (16, $[C_{17}H_{22}N_5O]^+$), 271 (9, $[C_{15}H_{19}N_4O]^+$). Anal. calc. for $C_{19}H_{27}N_5O_2$ (357.44): C 63.84, H 7.62, N 19.59; found: C 63.60, H 7.81, N 19.32.

3-(Cyclohexylideneamino)pyridine-4-amine (**23**). A soln. of 3,4-diaminopyridine (0.5 g, 4.59 mmol; **22**) and **3** (0.9 g, 9.17 mmol) in MeOH (10 ml) is heated under reflux for 26 h and then carefully evaporated. After dissolving the residue in pentane, a crude solid is obtained on cooling at −20°. Its recystallisation from Et_2O provides **23** (118.0 mg, 13.5%). Salmon-coloured crystals which become discoloured rapidly when exposed to air. M.p. 143°. UV (MeCN): 211 (4.375), 280 (3.398). IR (KBr): 3340, 3180 (NH_2); 2940, 2860 (C–H); 1655, 1585, 1500 (C=C, C=N); 1270. ^{1}H-NMR (250.13 MHz, $CDCl_3$): 7.98 (*d*, ^3J = 5.90, H–C(6)); 7.67 (*s*, H–C(2)); 6.57 (*d*, ^3J = 5.90, H–C(5)); 4.26 (*s*, NH_2); 2.52 (*t*, 2 H–C(6′)); 2.28 (*t*, 2 H–C(2′)); 1.95–1.59 (*m*, 2 H–C(3′), 2 H–C(4′), 2 H–C(5′)). ^{13}C-NMR (62.89 MHz, $CDCl_3$): 179.1 (*s*, C(1′)); 145.8 (*s*, C(6)); 144.9 (*s*, C(4)); 139.7 (*s*, C(2)); 132.3 (*s*, C(3)); 109.1 (*s*, C(5)); 39.6 (*s*, C(6′)); 31.2 (*s*, C(2′)); 28.0 (*s*, C(3′) or C(5′)); 27.7 (*s*, C(3′) or C(5′)); 25.6 (*s*, C(4′)). MS: 189 (38, M^+), 146 (100, $[C_8H_8N_3]^+$). Anal. calc. for $C_{11}H_{15}N_3$ (189.26): C 89.80, H 7.99, N 22.21; found: C 69.25, H 8.12, N 22.43.

Spiro[cyclohexane-1,2′(3′H)-1′H-imidazo[4,5-c]pyridine] (**24**). A soln. of **22** (4.0 g, 36.7 mmol) in **3** (36.0 g, 367 mmol) is heated under reflux for 4 h and then allowed to cool. On addition of Et_2O (70 ml), crude **24** is precipitated which crystallises from toluene as colourless needles (3.25 g, 46.9%). M.p. 186°. UV (MeCN): 216 (4.262), 300 (3.465). IR (KBr): 3400, 3240, 3200 (NH); 3040 (Aryl-H); 2920, 2860 (C–H); 1670, 1605, 1500, 1475, 1460, 1430 (C=C, C=N). ^{1}H-NMR (250.13 MHz, (D_6)DMSO): 7.51 (*d*, ^3J = 5.60, H–C(6′)); 7.33 (*s*, H–C(4′)); 6.80 (*s*, H–N(1′)); 6.16 (*d*, ^3J = 5.60, H–C(7′)); 5.87 (*s*, H–N(3′)); 1.66–1.23 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, (D_6)DMSO): 147.0 (*s*, C(7′a)); 141.2 (*s*, C(6′)); 137.2 (*s*, C(3′a)); 125.6 (*s*, C(4′)); 101.3 (*s*, C(7′)); 81.3 (*s*, C(2′)); 39.6 (*s*, C(2), C(6)); 25.1 (*s*, C(4)); 22.8 (*s*, C(3), C(5)). MS: 189 (37, M^+), 146 (100, $[C_8H_8N_3]^+$). Anal. calc. for $C_{11}H_{15}N_3$ (189.26): C 69.80, H 7.99, N 22.21; found: C 69.67, H 7.99, N 22.21.

Spiro[cyclohexane-1,2′-2′H-imidazo[4,5-c]pyridine]-4′(5′H)-one (**25**). *Method A*: As described for **5a**, from **24** (1.2 g, 6.34 mmol), dry THF (200 ml), and MnO_2 (8.8 g, 101 mmol; 17 h). CC (silica gel, MeOH/AcOH 500:1) provides a 1st band of pure product which is recrystallised from benzene/hexane 1:1: lemon-coloured powder (250 mg, 19.4%).

Method B: To a soln. of **24** (0.35 g, 1.85 mmol) in EtOH (20 ml), a soln. of Na (01 g, 4.35 mmol) in dry EtOH (40 ml) is added and the mixture stirred at r.t. for 2 h. After evaporation, CC (silica gel, AcOEt/MeOH 5:2) and recrystallisation from benzene/hexane 1:1 yield **25** (184 mg, 49%). Lemon-coloured powder. M.p. 226°. UV (MeCN): 262 (2.914). IR (KBr): 3600–3030 (band due to aggregation); 2940, 2860 (C–H); 1710 (C=O); 1655–1525, 1410 (C=C, C=N); 1260. ^{1}H-NMR (250.13 MHz, (D_6)DMSO): 7.62 (*s*, NH); 7.10 (*m*, H,D-exchange→*d*, ^3J = 7.25, H–C(6′)); 6.17 (*d*, ^3J = 7.25, H–C(7′)); 1.89–1.43 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, (D_6)DMSO): 159.53 (*s*, C(7′a) or C(4′)); 159.45 (*s*, C(7′a) or C(4′)); 155.7 (*s*, C(3′a)); 137.8 (*s*, C(6′)); 107.7 (*s*, C(2′)); 100.4 (*s*, C(7′)); 32.8 (*s*, C(2), C(6)); 25.0 (*s*, C(4)); 23.9 (*s*, C(3), C(5)). MS: 203 (100, M^+). Anal. calc. for $C_{11}H_{13}N_3O$ (203.24): C 65.00, H 6.45, N 20.68; found: C 65.22, H 6.53, N 20.61.

4′-(Diethylamino)spiro[cyclohexane-1,2′-2′H-imidazo[4,5-c]pyridine] (**26a**). As described for **11**, from **24** (0.7 g, 3.7 mmol) in dry THF (245 ml), Et_2NH (0.275 g, 3.7 mmol), and MnO_2 (5.2 g, 59.2 mmol; 1 h). CC (silica gel, AcOEt) and recrystallisation from hexane give **26a** (276 mg, 29%). Red platelets. M.p. 70°. UV (MeCN): 234 (4.303), 466 (3.783). IR (KBr): 2940, 2860 (C–H); 1620, 1540, 1520, 1440 (C=C, C=N); 1360. ^{1}H-NMR (250.13 MHz, $CDCl_3$): 7.50 (*d*, ^3J = 5.79, H–C(6′)); 6.28 (*d*, ^3J = 5.79, H–C(7′)); 4.38–3.52 (br., 2 MeCH_2); 2.10–1.40 (*m*, C_6H_{10}); 1.28 (*t*, 2 *Me*CH_2). ^{13}C-NMR (62.89 MHz, $CDCl_3$): 159.7 (*s*, C(7′a)); 154.1 (*s*, C(4′)); 153.5 (*s*, C(3′a));

149.8 (*s*, C(6′)); 106.7 (*s*, C(2′)); 103.7 (*s*, C(7′)); 44.6 (*s*, 2 Me*C*H_2); 33.4 (*s*, C(2), C(6)); 25.7 (*s*, C(4)); 24.7 (*s*, C(3), C(5)); signal for 2 *Me*CH_2 not distinguishable because of extreme broadening. MS: 258 (32, M^+), 229 (100, $[C_{13}H_{17}N_4]^+$). Anal. calc. for $C_{15}H_{22}N_4$ (258.35): C 69.73, H 8.58, N 21.69; found: C 69.57, H 8.59, N 21.55.

*4′-(Piperidin-1-yl)spiro[cyclohexane-1,2′-2′*H*-imidazo[4,5-c]pyridine]* (**26c**). As described for **11**, from **24** (0.3 g, 1.59 mmol) in dry THF (55 ml), piperidine (0.135 g, 1.59 mmol), and MnO_2 (2.2 g, 25.3 mmol; 1 h). CC (silica gel, AcOEt) and recrystallisation from MeOH provides **26c** (256.5 mg, 60%). Red platelets. M.p. 72°. UV (MeCN): 231 (4.283), 467 (3.763). IR (KBr): 3040, 3020 (Aryl-H); 2940, 2860 (C–H); 1620, 1540, 1510, 1430 (C=C, C=N); 1370. ^{1}H-NMR (250.13 MHz, $CDCl_3$): 7.48 (*d*, ^3J = 6.77, H–C(6′)); 6.30 (*d*, ^3J = 6.77, H–C(7′)); 4.56–4.00 (*m*, 2 CH_2); 2.10–1.43 (*m*, 3 $CH_2C_6H_{10}$). ^{13}C-NMR (62.89 MHz, $CDCl_3$, 300 K): 159.8 (*s*, C(7′a)); 154.2 (*s*, C(4′)); 153.9 (*s*, C(3′a)); 149.4 (*s*, C(6′)); 106.5 (*s*, C(2′)); 104.2 (*s*, C(7′)); 32.7 (*s*, C(2), C(6)); 26.3 (only pip. signal); 25.2 (*s*, C(4)); 24.4 (*s*, C(3), C(5)). ^{13}C-NMR (233 K): single pip. signals at 48.5 (*s*, CH_2N); 46.1 (*s*, CH_2N); 26.7 (*s*, CH_2); 25.6 (*s*, CH_2); 24.3 (*s*, CH_2). MS: 270 (88, M^+), 227 (100, $[C_{13}H_{15}N_4]^+$). Anal. calc. for $C_{16}H_{22}N_4$ (270.39): C 71.08, H 8.20, N 20.72; found: C 71.19, H 8.20, N 20.61.

*4′-(Morpholin-4-yl)spiro[cyclohexane-1,2′-2′*H*-imidazo[4,5-c]pyridine]* (**26d**). As described for **11**, from **24** (4.26 g, 22.5 mmol) in dry THF (1490 ml), morpholine (1.96 g, 22.5 mmol), and MnO_2 (31.4 g, 361 mmol; 1 h). CC (silica gel, AcOEt) and recrystallisation from MeOH yield red needles of **26d** (3.98 g, 65%). M.p. 154°. UV (MeCN): 234 (4.004), 460 (3.501). IR (KBr): 3030 (Aryl-H); 2940, 2860 (C–H); 1625, 1535, 1505, 1440 (C=C, C=N); 1120 (C–O–C). ^{1}H-NMR (250.13 MHz, $CDCl_3$): 7.47 (*d*, ^3J = 7.04, H–C(6′)); 6.37 (*d*, ^3J = 7.04, H–C(7′)); 4.72–4.00 (*m*, 2 CH_2O); 4.00–3.58 (*m*, 2 CH_2N); 2.10–1.34 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, $CDCl_3$, 300 K): 159.4 (*s*, C(7′a)); 154.0 (*s*, C(4′)); 153.4 (*s*, C(3′a)); 148.7 (*s*, C(6′)); 107.2 (*s*, C(2′)); 105.6 (*s*, C(7′)); 67.0 (*s*, 2 CH_2O); 47.7 (*s*, (at 233 K), CH_2N); 44.2 (*s*, (at 233 K), CH_2N); 33.2 (*s*, C(2), C(6)); 25.6 (*s*, C(4)); 24.6 (*s*, C(3), C(5)). MS: 272 (54, M^+), 241 (100, $[C_{14}H_{17}N_4]^+$). Anal. calc. for $C_{15}H_{20}N_4O$ (272.34): C 66.15, H 7.40, N 20.57; found: C 66.21, H 7.27, N 20.43.

*4′-[(4-Methylphenyl)amino]spiro[cyclohexane-1,2′-2′*H*-imidazo[4,5-c]pyridine]* (**26e**). As described for **11**, from **24** (0.242 g, 1.28 mmol) in dry THF (105 ml), 4-methylbenzenamine (0.137 g, 1.28 mmol), and MnO_2 (2.22 g, 25.52 mmol; 1 h). The oil is chromatographed twice (silica gel, 1. AcOEt, 2. AcOEt/petroleum ether (40–60°) 4:1): **26e** (45 mg, 12%). Dark red crystals. M.p. 148°. UV (MeCN): 228 (4.218), 420 (3.836). IR (KBr): 3280 (NH); 3020 (Aryl-H); 2940, 2860 (C–H); 1650, 1625, 1600, 1550, 1505 (C=C, C=N). ^{1}H-NMR (300 MHz, $CDCl_3$): 8.02 (*s*, NH); 7.73 (*d*, ^3J = 7.76, 2 H, Ph); 7.59 (*d*, ^3J = 7.06, H–C(6′)); 7.18 (*d*, ^3J = 7.76, 2 H, Ph); 6.48 (*d*, ^3J = 7.06, H–C(7′)); 2.35 (*s*, Me); 2.10–1.40 (*m*, C_6H_{10}). ^{13}C-NMR (75.43 MHz, $CDCl_3$): 158.1 (*s*, C(7′a)); 152.6 (*s*, C(4′)); 151.6 (*s*, C(3′a)); 149.2 (*s*, C(6′)); 135.6 (*s*, 1 C, Ph); 133.8 (*s*, 1 C, Ph); 129.4 (*s*, 2 C, Ph); 120.3 (*s*, 2 C, Ph); 108.3 (*s*, C(2′)); 107.2 (*s*, C(7′)); 33.1 (*s*, C(2), C(6)); 25.6 (*s*, C(4)); 24.7 (*s*, C(3), C(5)); 20.9 (*s*, Me). MS: 292 (78, M^+), 291 (100, $[M-1]^+$). Anal. calc. for $C_{18}H_{20}N_4$ (292.37): C 73.94, H 6.90, N 19.16; found: C 73.88, H 6.95, N 18.64.

*4′-(Propylamino)spiro[cyclohexane-1,2′-2′*H*-imidazo[4,5-c]pyridine]* (**26f**). As described for **11**, from **24** (0.7 g, 3.7 mmol) in dry THF (245 ml), $PrNH_2$ (0.22 g, 3.7 mmol), and MnO_2 (5.2 g, 59.2 mmol; 1 h). CC (silica gel, AcOEt) and recrystallisation from hexane lead to **26f** (450 mg, 49.7%). Orange-red crystals. M.p. 59–62°. UV (MeCN): 223 (4.231), 434 (3.670). IR (KBr): 3340–3200 (NH); 3080 (Aryl-H); 2940, 2860 (C–H); 1635, 1570, 1500 (C=C, C=N). ^{1}H-NMR (250.13 MHz, $CDCl_3$): 7.50 (*d*, ^3J = 7.17, H–C(6′)); 6.37–6.23 (br., NH); 6.34 (*d*, ^3J = 7.17, H–C(7′)); 3.63–3.40 (*m*, $MeCH_2CH_2$N); 2.18–1.46 (*m*, $MeCH_2CH_2$N, C_6H_{10}); 1.04 (*t*, *Me*CH_2CH_2N). ^{13}C-NMR (62.89 MHz, $CDCl_3$): 158.6 (*s*, C(7′a)); 154.9 (*s*, C(4′)); 152.5 (*s*, C(3′a)); 150.0 (*s*, C(6′)); 108.1 (*s*, C(2′)); 105.2 (*s*, C(7′)); 42.8 (*s*, $MeCH_2CH_2$N); 33.0 (*s*, C(2), C(6)); 25.5 (*s*, C(4)); 24.5 (*s*, C(3), C(5)); 22.3 (*s*, Me*C*H_2CH_2N); 11.5 (*s*, *Me*CH_2CH_2N). MS: 244 (22, M^+), 215 (100, $[C_{12}H_{15}N_4]^+$). Anal. calc. for $C_{14}H_{20}N_4$ (244.33): C 68.82, H 8.25, N 22.93; found: C 68.59, H 8.22, N 22.79.

*4′-(Ethylthio)spiro[cyclohexane-1,2′-2′*H*-imidazo[4,5-c]pyridine]* (**26g**). As described for **11**, from **24** (0.3 g, 1.59 mmol) in dry THF (105 ml), EtSH (0.099 g, 1.59 mmol), and MnO_2 (2.22 g, 25.52 mmol; 1 h). CC (25 cm, silica gel, AcOEt) followed by careful evaporation provide orange crystals of pure **26g** (36.2 mg, 9.2%). M.p. 97°. UV (MeCN): 408 (3.558). IR (KBr): 2920, 2850 (C–H); 1705, 1620, 1460 (C=C, C=N). ^{1}H-NMR (250.13 MHz, $CDCl_3$): 7.72 (*d*, ^3J = 6.45, H–C(6′)); 6.77 (*d*, ^3J = 6.45, H–C(7′)); 3.25 (*q*, Me*C*H_2); 2.10–1.60 (*m*, C_6H_{10}); 1.44 (*t*, *Me*CH_2). ^{13}C-NMR (62.89 MHz, $CDCl_3$): 166.6 (*s*, C(4′)); 157.7 (*s*, C(7′a)); 154.1 (*s*, C(3′a)); 146.2 (*s*, C(6′)); 111.8 (*s*, C(7′)); 108.9 (*s*, C(2′)); 32.5 (*s*, C(2), C(6)); 25.5 (*s*, C(4)); 24.5 (*s*, C(3), C(5)); 23.8 (*s*, Me*C*H_2); 13.8 (*s*, *Me*CH_2). MS: 247 (45, M^+), 214 (100, $[C_{13}H_{16}N_3]^+$). Anal. calc. for $C_{13}H_{17}N_3S$ (247.35): C 63.12, H 6.93, N 16.99; found: C 62.96, H 6.89, N 16.75.

*4′-Methoxyspiro[cyclohexane-1,2′-2′*H*-imidazo[4,5-c]pyridine]* (**26h**). A mixture of **24** (0.4 g, 2.12 mmol) and MnO_2 (1.84 g, 21.2 mmol) in MeOH (40 ml) is stirred at r.t. for 20 h. After filtration and evaporation, recrystallisation from Et_2O provides **26h** (115 mg, 25%). Ochreous crystals. M.p. 86°. UV (MeCN): 362 (3.479). IR (KBr): 3030 (Aryl-H); 2960, 2840 (C–H); 1630, 1530, 1455 (C=C, C=N); 1310 (C–O–C). ^{1}H-NMR (300 MHz, $CDCl_3$):

7.53 (*d*, ^3J = 7.71 H–C(6′)); 6.73 (*d*, ^3J = 7.71, H–C(7′)); 4.10 (*s*, MeO); 2.25–1.50 (*m*, C_6H_{10}). ^{13}C-NMR (75.43 MHz, $CDCl_3$): 160.6 (*s*, C(4′) or C(7′a)); 159.0 (*s*, C(4′) or C(7′a)); 151.3 (*s*, C(3′a)); 146.0 (*s*, C(6′)); 111.6 (*s*, C(7′)); 109.5 (*s*, C(2′)); 54.6 (*s*, MeO); 32.6 (*s*, C(2), C(6)); 25.4 (*s*, C(4)); 24.4 (*s*, C(3), C(5)). MS: 217 (60, M^+), 216 (100, $M-1]^+$). Anal. calc. for $C_{12}H_{15}N_3O$ (217.26): C 66.34, H 6.96, N 19.34; found: C 66.28, H 6.87, N 19.08.

*4′-(Phenylsulfonyl)spiro[cyclohexane-1,2′(3′*H*)-1′*H*-imidazo[4,5-*c*]pyridine]* (**27**). As described for **9**, from **24** (0.6 g, 3.17 mmol), EtOH (180 ml), sodium benzenesulfinate (10.48 g, 63.2 mmol), H_2O (30 ml), MnO_2 (2.76 g, 31.7 mmol), and AcOH (0.4 ml, 6.93 mmol, 2 h r.t.). The residue is suspended in H_2O, the aq. layer extracted with $CHCl_3$, the combined org. phase evaporated and the residue chromatographed (silica gel, AcOEt/petroleum ether (40–60°) 20:1). The 2nd, yellow-fluorescent band furnishes, after recrystallisation from MeOH, **27** (325 mg, 31.2%). Colourless needles. M.p. 214°. UV (MeCN): 223 (4.417), 247 (4.104), 345 (3.933). IR (KBr): 3440, 3360 (NH); 3060 (Aryl-H); 2940, 2860 (C–H); 1615, 1505, 1455 (C=C, C=H); 1310, 1300, 1275 (SO_2); 1140 (SO_2). ^{1}H-NMR (250.13 MHz, (D_6)DMSO): 8.04–7.93 (*m*, 2 H, Ph); 7.87 (*s*, NH); 7.78–7.55 (*m*, 3 H, Ph); 7.45 (*d*, ^3J = 5.26, H–C(6′)); 6.96 (*s*, NH); 6.13 (*d*, ^3J = 5.26, H–C(7′)); 1.96–1.34 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, (D_6)DMSO): 148.4 (*s*, C(7′a)); 141.3 (*s*, SO_2C); 140.6 (*s*, C(6′)); 136.5 (*s*, C(3′a)); 133.1 (*s*, 1 C, Ph); 129.1 (*s*, 2 C, Ph); 127.8 (*s*, C(4′)); 127.0 (*s*, 2 C, Ph); 100.0 (*s*, C(7′)); 81.9 (*s*, C(2′)); 38.9 (*s*, C(2), C(6)); 24.3 (*s*, C(4)); 22.1 (*s*, C(3), C(5)). MS: 329 (32, M^+), 286 (100, $[C_{14}H_{12}N_3O_2S]^+$). Anal. calc. for $C_{17}H_{19}N_3O_2S$ (329.40): C 61.98, H 5.81, N 12.76; found: C 62.13, H 5.93, N 12.62.

*4′,7′-Bis(phenylsulfonyl)spiro[cyclohexane-1,2′(3′*H*)-1′*H*-imidazo[4,5-*c*]pyridine]* (**28**). As described for **9**, from **24** (0.6 g, 3.17 mmol), EtOH (180 ml), sodium benzenesulfinate (10.48 g, 63.2 mmol), H_2O (30 ml), MnO_2 (2.76 g, 31.7 mmol), and AcOH (0.4 ml, 6.93 mmol; 2 h r.t). Workup as described for **27**. The 1st band gives, after recrystallisation from MeOH, pure **28** (0.2 g, 13.6%). Pale yellow powder. M.p. 219–220°. UV (MeCN): 217 (4.391), 254 (4.158), 353 (3.819). IR (KBr): 3380 (NH); 2930, 2860 (C–H); 1605, 1510, 1450 (C=C, C=N); 1305, 1145 (SO_2). ^{1}H-NMR (250.13 MHz, (D_6)DMSO): 8.54 (*s*, H–N(1′)); 8.08–7.99 (*m*, 2 H, Ph); 7.96–7.84 (*m*, 2 H, Ph); 7.73 (*s*, H–C(6′)); 7.71–7.53 (*m*, 6 H, Ph); 7.32 (*s*, H–N(3′)); 1.93–1.24 (*m*, C_6H_{10}). ^{13}C-NMR (62.89 MHz, (D_6)DMSO): 146.0 (*s*, C(7′a)); 141.3 (*s*, SO_2C); 140.0 (*s*, SO_2C); 137.5 (*s*, C(6′)); 137.0 (*s*, C(3′a)); 133.7 (*s*, 1 C, Ph); 133.5 (*s*, 1 C, Ph); 129.5 (*s*, 2 C, Ph); 129.2 (*s*, 2 C, Ph); 128.3 (*s*, C(4′)); 127.2 (*s*, 2 C, Ph); 126.4 (*s*, 2 C, Ph); 110.6 (*s*, C(7′)); 84.4 (*s*, C(2′)); 38.2 (*s*, C(2), C(6)); 24.0 (*s*, C(4)); 21.7 (*s*, C(3), C(5)). MS: 469 (36, M^+), 426 (100, $[C_{20}H_{16}N_3O_4S_2]^+$). Anal. calc. for $C_{23}H_{23}N_3O_4S_2$ (469.56): C 58.83, H 4.94, N 8.95; found: C 58.58, H 4.92, N 8.75.

*5,7-Di(morpholin-4-yl)-3*H*-imidazo[4,5-*b*]pyridine* (**32**). To a soln. of **17** (1.0 g, 2.8 mmol) in THF/H_2O 4:3 (350 ml), $Na_2S_2O_4$ (3.9 g, 22.4 mmol) is added (immediately orange→yellow). The mixture is stirred at r.t. for 1 h and then made alkaline with K_2CO_3 (pH 10). The unstable tetraaminopyridine is extracted with AcOEt, the combined org. phase carefully evaporated, and the residual oil immediately dissolved in aq. conc. HCl soln./H_2O 2:3 (20 ml). After addition of HCOOH (20 ml), the soln. is heated at 100° (oil bath) for 3 h and then allowed to cool. The diluted (40 ml of H_2O) and alkaline soln. (Na_2CO_3, pH 9–10) is again extracted with AcOEt followed by evaporation. Recrystallisation from AcOEt provides a light grey powder of **32** (37.4 mg, 4.6% rel. to **17**), which is finally washed with hexane. M.p. 227°. UV (MeCN): 212 (4.550), 242 (4.570), 267 (4.373). IR (KBr): 3150, 3130 (NH); 3010 (Aryl-H); 2960, 2860 (C–H); 1615, 1580, 1445 (C=C, C=N); 1120 (C–O–C). ^{1}H-NMR (300 MHz, (D_6)DMSO): 12.35 (*s*, H–N(3)); 7.80 (*s*, H–C(2)); 5.93 (*s*, H–C(6)); 4.05–3.23 (*m*, 8 CH_2). ^{13}C-NMR (75.43 MHz, (D_6)DMSO): 157.8 (*s*, C(5)); 148.7 (*s*, C(7)); 147.2 (*s*, C(3a)); 135.5 (*s*, C(2)); 118.8 (*s*, C(7a)); 85.9 (*s*, C(6)); 66.1 (*s*, 2 CH_2O); 66.0 (*s*, 2 CH_2O); 47.7 (*s*, 2 CH_2N); 46.4 (*s*, 2 CH_2N). MS: 289 (100, M^+). Anal. calc. for $C_{14}H_{19}N_5O_2$ (289.32): C 58.12, H 6.62, N 24.20; found: C 58.21, H 6.60, N 24.01.

*5,7-Di(morpholin-4-yl)-2,1,3-selenadiazolo[3,4-*b*]pyridine* (**33**). As described for **32**, **17** (1.0 g, 2.8 mmol) in THF/H_2O 4:3 (350 ml) is reduced with $Na_2S_2O_4$ (3.9 g, 22.4 mmol). The combined org. phase is carefully evaporated and the unstable tetraaminopyridine dissolved in EtOH (10 ml) to which a freshly prepared and filtered soln. of SeO_2 (310.8 mg, 2.8 mmol) in H_2O (3 ml) is added (brown→red). After 1 h stirring at r.t., the mixture is diluted with H_2O (40 ml) and basified (K_2CO_3, pH 10), the aq. layer extracted with AcOEt and the org. phase evaporated: lemon yellow needles of **33** (167.7 mg, 16.9% rel. to **17**) which are recrystallised from MeOH. M.p. 259–261°. UV (MeCN): 236 (4.413), 284 (3.448), 377 (4.177). IR (KBr): 3000 (Aryl-H); 2960, 2860 (C–H); 1585, 1500, 1445 (C=C, C=N); 1110 (C–O–C). ^{1}H-NMR (250.13 MHz, (D_6)DMSO): 6.28 (*s*, H–C(6)); 3.95–3.60 (*m*, 8 CH_2). ^{13}C-NMR (75.43 MHz, (D_6)DMSO): 165.1 (*s*, C(5)); 160.7 (*s*, C(3a)); 149.5 (*s*, C(7a)); 146.6 (*s*, C(7)); 93.1 (*s*, C(6)); 65.9 (*s*, 2 CH_2O); 65.7 (*s*, 2 CH_2O); 48.7 (*s*, 2 CH_2N); 45.2 (*s*, 2 CH_2N). MS: 355 (100, $M^+(^{80}Se)$). Anal. calc. for $C_{13}H_{17}N_5O_2Se$ (354.26): C 44.07, H 4.84, N 19.77; found: C 44.26, H 5.00, N 19.55.

2-(Morpholin-4-yl)-pyridine-3,4-diamine. To a soln. of **26d** (0.5 g, 1.85 mmol) in MeOH/H_2O 5:1 (150 ml), $Na_2S_2O_4$ (8.0 g, 46.25 mmol) is added (→colourless) and stirred at r.t. for 30 min. After addition of a sat. aq. soln. of $NaHSO_3$ (5.0 g, 48.1 mmol), stirring is continued for another 2 h. The residue obtained on evaporation is suspended in $CHCl_3$ (70 ml), the product extracted into $CHCl_3$ under reflux, the mixture filtered, the filtrate

concentrated to 1/3, and hexane (40 ml) added. The white precipitate is isolated and washed with hexane yielding colourless crystals (98 mg, 27.3%) which quickly darken on exposure to air. M.p. 183°. UV (MeCN): 226 (4.374), 290 (3.744). IR (KBr): 3420, 3360, 3230 (NH_2); 2850 (C–H); 1655, 1595, 1500, 1450 (C=C, C=N); 1115, 1110 (C–O–C). ^{1}H-NMR (250.13 MHz, (D_6)DMSO): 7.32 (*d*, ^3J = 5.25, H–C(6)); 6.30 (*d*, ^3J = 5.25, H–C(5)); 5.29 (*s*, NH_2); 4.09 (*s*, NH_2); 3.80–3.67 (*m*, 2 CH_2O); 2.95–2.82 (*m*, 2 CH_2N). ^{13}C-NMR (62.89 MHz, (D_6)DMSO): 149.3 (*s*, C(2)); 141.7 (*s*, C(4)); 136.5 (*s*, C(6)); 121.1 (*s*, C(3)); 106.7 (*s*, C(5)); 66.5 (*s*, CH_2O); 49.3 (*s*, 2 CH_2N). MS: 194 (81, M^+), 135 (100). HR-MS (peak matching): 194.1164 ($[C_9H_{14}N_4O]^+$, calc. 194.1168). Elemental analysis: unsatisfactory due to instability of product.

*4-(Morpholin-4-yl)-1*H*-imidazo[4,5-c]pyridine* (**34**). A soln. of **26d** (0.275 g, 1.01 mmol) in MeOH/H_2O 5:1 (84 ml) undergoes hydrolysis on addition of $Na_2S_2O_4$ (4.4 g, 25.29 mmol). The crude triaminopyridine is dissolved in conc. HCl soln./H_2O 2:3 (10 ml) and, after addition of HCOOH (10 ml), heated on the oil bath (100°) for 3 h and finally allowed to cool. The diluted (30 ml of H_2O) and basified soln. (Na_2CO_3, pH 10) is extracted with $CHCl_3$, the extract evaporated, and the residue recrystallised: **34** (62 mg, 29.7% rel. to **26d**). Brown crystals. M.p. 209°. UV (MeCN): 208 (4.290), 275 (4.180). IR (KBr): 3200–2580 (band due to aggregation); 1600, 1485, 1460 (C=C, C=N); 1120, 1110 (C–O–C). ^{1}H-NMR (250.13 MHz, (D_6)DMSO): 13.00–12.27 (br., H–N(1)); 8.12 (*s*, H–C(2)); 7.82 (*d*, ^3J = 5.56, H–C(6)); 6.92 (*d*, ^3J = 5.56, H–C(7)); 4.18–3.84 (*m*, 2 CH_2O); 3.84–3.60 (*m*, 2 CH_2N). ^{13}C-NMR (62.89 MHz, (D_6)DMSO): 151.1 (*s*, C(4)); 139.4 (*s*, C(6)); 139.1 (*s*, C(7a)); 138.9 (*s*, C(2)); 127.7 (*s*, C(3a)); 99.3 (*s*, C(7)); 66.3 (*s*, 2 CH_2O); 46.5 (*s*, 2 CH_2N). MS: 204 (56, M^+), 119 (100, $[C_6H_5N_3]^+$). Anal. calc. for $C_{10}H_{12}N_4O$ (204.23): C 58.81, H 5.93, N 27.43; found: C 58.82, H 6.00, N 27.38.

5-(Morpholin-4-yl)pyrido[3,4-b]pyrazine (**35**). As described for **32**, **26d** (0.3 g, 1.1 mmol) in THF/H_2O 8:7 (150 ml) is reduced by $Na_2S_2O_4$ (1.84 g, 10.56 mmol). The residue of the evaporated org. layer is dissolved in THF/H_2O 2:1 (30 ml) and the resulting mixture treated with CHO–CHO · $NaHSO_3$ (0.7 g, 2.46 mmol) in H_2O (20 ml). The mixture is stirred at 50–60° (H_2O bath) for 20 h and then allowed to cool. The alkaline soln. (K_2CO_3, pH 9–10) is extracted with AcOEt, the org. phase dried ($MgSO_4$) and evaporated, and the residual oil subjected to CC (50 cm, silica gel, AcOEt). Recrystallisation from Et_2O yields **35** (44 mg, 18.5% rel. to **26d**). Lemon-coloured, long needles. M.p. 121°. UV (MeCN): 252 (4.233), 387 (3.670). IR (KBr): 3030 (Aryl-H); 2970, 2860 (C–H); 1570, 1455 (C=C, C=N); 1120 (C–O–C). ^{1}H-NMR (250.13 MHz, $CDCl_3$): 8.88 (*d*, ^3J = 1.53, H–C(2) or H–C(3)); 8.72 (*d*, ^3J = 1.53, H–C(2) or H–C(3)); 8.30 (*d*, ^3J = 5.76, H–C(7)); 7.32 (*d*, ^3J = 5.76, H–C(8)); 4.24–4.00 (*m*, 2 CH_2O); 4.00–3.78 (*m*, 2 CH_2N). ^{13}C-NMR (62.89 MHz, $CDCl_3$): 158.5 (*s*, C(5)); 148.2 (*s*, C(8a)); 147.7 (*s*, C(2) or C(3)); 145.6 (*s*, C(2) or C(3)); 141.4 (*s*, C(7)); 131.7 (*s*, C(4a)); 113.6 (*s*, C(8)); 67.1 (*s*, 2 CH_2O); 49.7 (*s*, 2 CH_2N). MS: 216 (100, M^+). Anal. calc. for $C_{11}H_{12}N_4O$ (216.23): C 61.10, H 5.59, N 25.91; found: C 61.21, H 5.71, N 25.65.

4-(Morpholin-4-yl)-2,1,3-selenadiazolo[3,4-c]pyridine (**36**). As described for **32**, **26d** (1.0 g, 3.68 mmol) in THF/H_2O 13:10 (460 ml) is reduced by $Na_2S_2O_4$ (5.14 g, 29.44 mmol). The combined org. phase is evaporated, the residue dissolved in EtOH (50 ml) and a freshly prepared and filtered soln. of SeO_2 (0.409 g, 3.68 mmol) in H_2O (4 ml) added. The mixture is refluxed for 2 h, allowed to cool, and, after addition of H_2O/AcOEt 1:1 (240 ml), made alkaline (K_2CO_3, pH 10). Extraction with AcOEt, evaporation of the org. layer, and recrystallisation of the residue from MeOH gives pure **36** (320 mg, 32.3% rel. to **26d**). Orange platelets. M.p. 126°. UV (MeCN): 250 (4.094), 310 (3.813), 443 (3.699). IR (KBr): 2980, 2860 (C–H); 1565, 1520, 1485, 1445 (C=C, C=N); 1110 (C–O–C). ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.82 (*d*, ^3J = 6.35, H–C(6)); 7.00 (*d*, ^3J = 6.35, H–C(7)); 4.43–4.05 (*m*, 2 CH_2O); 3.97–3.66 (*m*, 2 CH_2N). ^{13}C-NMR (75.43 MHz, (D_6)DMSO): 162.6 (*s*, C(7a)); 152.4 (*s*, C(4)); 149.4 (*s*, C(3a)); 143.5 (*s*, C(6)); 107.4 (*s*, C(7)); 66.1 (*s*, 2 CH_2O); 47.2 (*s*, 2 CH_2N). MS: 270 (100, M^+(^{80}Se)). Anal. calc. for $C_9H_{10}N_4OSe$ (269.16): C 40.16, H 3.74, N 20.82; found: C 40.34, H 4.07, N 20.71.

*2,1,3-Selenadiazolo[3,4-c]pyridine-4(5*H*)-one* (**37**). As described for **36**, from **26d** (1.0 g) in THF/H_2O 13:10 $Na_2S_2O_4$, and SeO_2. The evaporated org. layer is chromatographed (50 cm, silica gel, AcOEt). The 1st orange band containing the main product **36** is rejected; the residue of the 2nd, weakly fluorescent band is recrystallised from MeOH to provide ochreous crystals of **37** (40 mg, 5.4% based on **26d**). M.p. 279–281°. UV (MeCN): 244 (3.853), 282 (3.411), 363 (3.609). IR (KBr): 3520–3360 (NH); 3190; 3070 (Aryl-H); 2950 (C–H); 1730 (C=O); 1650; 1330. ^{1}H-NMR (250.13 MHz, (D_6)DMSO): 11.30 (*s*, H–N(5)); 7.30 (*d*, ^3J = 7.94, H–C(6)); 6.60 (*d*, ^3J = 7.94, H–C(7)). ^{13}C-NMR (62.89 MHz, (D_6)DMSO): 162.4 (*s*, C(7a) or C(4) or C(3a)); 157.6 (*s*, C(7a) or C(4) or C(3a)); 154.2 (*s*, C(7a) or C(4) or C(3a)); 132.5 (*s*, C(6)); 102.0 (*s*, C(7)). MS: 201 (100, M^+(^{80}Se)). HR-MS (peak matching): 200.9442 ($[C_5H_3N_3OSe]^+$, calc. 200.9441). Elemental analysis: unsatisfactory due to instability of **37**.

*5'-[(4-Fluorobenzyl)amino]spiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-b]pyridine]* (**13**). As described for **11**, from **4a** (1.31 g, 6.9 mmol) in dry THF (260 ml), 4-fluorobenzylamine (17.47 g, 139.8 mmol), and MnO_2 (6.03 g, 69 mmol; 18 h r.t.). CC (silica gel, AcOEt/MeOH 5:2) and recrystallisation from AcOEt give ochreous crystals of **13** (1.13 g, 52.8%) which are finally washed with hexane. M.p. 189°. UV (MeCN): 202 (4.409), 266 (4.166), 274 (4.143), 353 (3.663). IR (KBr): 3220 (NH); 3050 (Aryl-H); 2930, 2850 (C–H); 1630, 1610, 1510 (C=C, C=N); 1430,

1220 (C–F). ^{1}H-NMR (250.13 MHz, (D$_6$)DMSO): 8.79 (*t*, NH); 7.48 (*d*, ^3J = 10.00, H–C(7′)); 7.47–7.35 (*m*, 2 H, FC$_6$*H*$_4$CH$_2$); 7.28–7.14 (*m*, 2 H, FC$_6$*H*$_4$CH$_2$); 6.88 (*d*, ^3J = 10.00, H–C(6′)); 4.62 (*d*, ^3J = 5.31, 2 H, FC$_6$H$_4$C*H*$_2$); 1.90–1.30 (*m*, C$_6$H$_{10}$). ^{13}C-NMR (62.89 MHz, (D$_6$)DMSO): 161.3 (*d*, ^1J = 243.1, C$_p$ of FC$_6$H$_4$CH$_2$); 161.1 (*s*, C(3′a)); 160.6 (*s*, C(5′)); 154.0 (*s*, C(7′a)); 134.5 (*d*, ^4J = 3.1, C$_{ipso}$ of FC$_6$H$_4$CH$_2$); 131.9 (*s*, C(7′)); 129.7 (*d*, ^3J = 8.6, 2 C$_o$ of FC$_6$H$_4$CH$_2$); 128.8 (*s*, C(6′)); 115.1 (*d*, ^2J = 21.1, 2 C$_m$ of FC$_6$H$_4$CH$_2$); 101.4 (*s*, C(2′)); 43.3 (*s*, FC$_6$H$_4$*C*H$_2$); 34.0 (*s*, C(2), C(6)); 25.3 (*s*, C(4)); 24.0 (*s*, C(3), C(5)). MS: 310 (100, M^+). Anal. calc. for C$_{18}$H$_{19}$FN$_4$ (310.36): C 69.66, H 6.17, N 18.05; found: C 69.53, H 6.26, N 18.05.

Ethyl {2-Amino-6-[(4-fluorobenzyl)amino]pyridin-3-yl}carbamate Maleate (**39**). As described for **32**, **13** (0.5 g, 1.61 mmol) in THF/H$_2$O 4:3 (175 ml) is reductively hydrolysed by Na$_2$S$_2$O$_4$ (2.4 g, 13.68 mmol). The combined org. phase is carefully concentrated to 5 ml and the unstable intermediate directly chromatographed (25 cm, silica gel, AcOEt/MeOH 5:2). The main fraction is dried (MgSO$_4$), again concentrated to 5 ml, and immediately dissolved in dry THF (10 ml). Slowly a soln. of ClCOOEt (216 mg, 2 mmol) in dry THF (5 ml) is added at r.t. (→turquoise soln. and precipitate). After evaporation, the residue is dissolved in MeOH (5 ml) and 25% aq. NH$_3$ soln. (20 ml) added. The aq. soln. is extracted with AcOEt and to the extract a soln. of maleic acid (0.175 g, 1.5 mmol) in AcOEt/MeOH 7:2 (9 ml) added (deep violet→turquoise). At –20°, a fine, sandy, light blue precipitate is formed which is recrystallised from i-PrOH: pure **39** (216 mg, 31.7% rel. to **13**). Colourless crystals. M.p. 170 and 177° (2 modifications). UV (MeCN): 248 (4.046), 319 (3.864), 343 (3.826). IR (KBr): 3450, 3330, 3250 (NH, NH$_2$); 2980 (C–H); 1730–1710 (C=O); 1655, 1620, 1575, 1510 (C=C, C=N); 1360, 1250 (C–O–C); 1230 (C–F). ^{1}H-NMR (300 MHz, (D$_6$)DMSO): 8.35 (*s*, N*H*COOEt); 7.54–7.00 (*m*, FC$_6$*H*$_4$CH$_2$, H–C(4)); 6.15 (*s*, HC=CH); 5.79 (*d*, ^3J = 8.25, H–C(5)); 4.39 (*s*, 2 H, FC$_6$C*H*$_2$); 4.03 (*q*, MeCH$_2$); 1.21 (*t*, *Me*CH$_2$); signals for 5 exchangeable H's not distinguishable because of extreme broadening. ^{13}C-NMR (62.89 MHz, (D$_6$)DMSO): 166.8 (*s*, 2 COOH); 161.1 (*d*, ^1J = 242.4, C$_p$ of FC$_6$H$_4$CH$_2$); 155.0 (*s*, C(2)); 152.5 (*s*, C(6) or NH*C*OOEt); 151.0 (*s*, C(6) or NH*C*OOEt); 139.1 (*s*, C(4)); 135.4 (*s*, C$_{ipso}$ of FC$_6$H$_4$CH$_2$); 132.8 (*s*, HC=CH); 129.1 (*d*, ^3J = 7.4, 2 C$_o$ of FC$_6$H$_4$CH$_2$); 115.0 (*d*, ^2J = 21.0, 2 C$_m$ of FC$_6$H$_4$CH$_2$); 106.8 (*s*, C(3)); 94.1 (*s*, C(5)); 60.1 (*s*, MeC*H*$_2$); 44.0 (*s*, FC$_6$H$_4$*C*H$_2$); 14.4 (*s*, *Me*CH$_2$). MS: 304 (78, [C$_{15}$H$_{17}$FN$_4$O$_2$]$^+$), 109 (100, [C$_7$H$_6$F]$^+$). Anal. calc. for C$_{15}$H$_{17}$FN$_4$O$_2$·C$_4$H$_4$O$_4$ (420.39): C 54.28, H 5.03, N 13.33; found: C 54.29, H 5.07, N 13.24.

*5′-(Benzylamino)spiro[cyclohexane-1,2′-2*H*-imidazo[4,5-*b*]pyridine]* (**12**). As described for **11**, from **4a** (1.31 g, 6.9 mmol) in dry THF (260 ml), PhCH$_2$NH$_2$ (14.85 g, 138 mmol), and MnO$_2$ (6.03 g, 69 mmol; 18 h r.t.). Recrystallisation from AcOEt gives yellow crystals of **12** (0.9 g, 44.6%). M.p. 198°. UV (MeCN): 266 (4.186), 275 (4.164), 352 (3.690). IR (KBr): 3230 (NH); 3030 (Aryl-H); 2930, 2860 (C–H); 1640, 1615, 1530–1480 (C=C, C=N); 1455. ^{1}H-NMR (250.13 MHz, (D$_6$)DMSO): 8.78 (br., NH); 7.47 (*d*, ^3J = 9.32, H–C(7′)); 7.43–7.20 (*m*, *Ph*CH$_2$); 6.88 (*d*, ^3J = 9.32, H–C(6′)); 4.63 (*d*, ^3J = 4.97, PhC*H*$_2$); 1.90–1.32 (*m*, C$_6$H$_{10}$). ^{13}C-NMR (62.89 MHz, CDCl$_3$): 161.7 (*s*, C(3′a)); 160.8 (*s*, C(5′)); 154.1 (*s*, C(7′a)); 137.4 (*s*, 1 C, Ph); 132.1 (*s*, C(7′)); 128.7 (*s*, C(6′)); 128.6 (*s*, 2 C, Ph); 128.1 (*s*, 2 C, Ph); 127.6 (*s*, 1 C, Ph); 102.4 (*s*, C(2′)); 45.5 (*s*, PhC*H*$_2$); 34.1 (*s*, C(2), C(6)); 25.5 (*s*, C(4)); 24.3 (*s*, C(3), C(5)). MS: 292 (100, M^+). Anal. calc. for C$_{18}$H$_{20}$N$_4$ (292.37): C 73.94, H 6.90, N 19.16; found: C 73.52, H 6.95, N 18.95.

Ethyl [2-Amino-6-(benzylamino)pyridin-3-yl]carbamate Hydrochloride (*D-7175*; see **39**, H instead of F, HCl instead of (CHCOOH)$_2$). As described for **39**, from **12** (0.44 g, 1.5 mmol) in THF/H$_2$O 4:3 (175 ml), Na$_2$S$_2$O$_4$ (2.1 g, 12.04 mmol), and ClCOOEt (216 mg, 2 mmol). After evaporation of the THF, recrystallisation from i-PrOH yields *D-7175* (62.9 mg, 13% rel. to **12**). Light-brown crystals. M.p. 195°. UV (MeCN): 242 (3.642), 338 (3.678). IR (KBr): 3320, 3170 (NH, NH$_2$); 2990, 2930 (C–H); 1695 (C=O); 1660, 1640, 1610, 1525 (C=C, C=N); 1260 (C–O–C). ^{1}H-NMR (300 MHz, (D$_6$)DMSO): 13.40 (*s*, NH$^+$(pyr.)); 8.28 (*s*, N*H*COOEt); 8.18 (br., PhCH$_2$N*H*); 7.80–7.20 (*m*, *Ph*$_2$CH$_2$, H–C(4), NH$_2$); 5.95 (*d*, ^3J not measurable, H–C(5)); 4.60 (*d*, ^3J not measurable, PhC*H*$_2$); 4.07 (*q*, MeC*H*$_2$); 1.20 (*t*, *Me*CH$_2$). ^{13}C-NMR (62.89 MHz, (D$_6$)DMSO): 154.9 (*s*, C(2)); 149.1 (*s*, C(6) or NH*C*OOEt); 149.0 (*s*, C(6) or NH*C*OOEt); 142.7 (*s*, C(4)); 137.4 (*s*, 1 C, Ph); 128.4 (*s*, 2 C, Ph); 127.4 (*s*, 2 C, Ph); 127.3 (*s*, 1 C, Ph); 106.3 (*s*, C(3)); 93.7 (*s*, C(5)); 60.4 (*s*, MeC*H*$_2$); 45.2 (*s*, PhC*H*$_2$); 14.4 (*s*, *Me*CH$_2$). MS: 286 (83, [C$_{15}$H$_{18}$N$_4$O$_2$]$^+$), 91 (100, [C$_7$H$_7$]$^+$). Anal. calc. for C$_{15}$H$_{18}$N$_4$O$_2$·HCl (322.79): C 55.81, H 5.93, N 17.35; found: C 55.64, H 5.87, N 17.25.

*4′-[(4-Fluorobenzyl)amino]spiro[cyclohexane-1,2′-2′*H*-imidazo[4,5-*c*]pyridine]* (**26b**). As described for **11**, from **24** (1.31 g, 6.9 mmol) in dry THF (400 ml), (4-fluorobenzyl)amine (0.868 g, 6.9 mmol), and MnO$_2$ (12 g, 137.9 mmol; 1 h). CC (silica gel, AcOEt) and recrystallisation from hexane give **26b** (1.13 g, 52.8%). Orange crystals. M.p. 104°. UV (MeCN): 218 (4.219), 423 (3.657). IR (KBr): 3290 (NH); 3070 (Aryl-H); 2930, 2860 (C–H); 1640, 1580, 1570, 1505 (C=C, C=N); 1290; 1220 (C–F). ^{1}H-NMR (250.13 MHz, CDCl$_3$): 7.53 (*d*, ^3J = 6.25, H–C(6′)); 7.47–7.32 (*m*, 2 H, FC$_6$*H*$_4$CH$_2$); 7.17–7.00 (*m*, 2 H, FC$_6$*H*$_4$CH$_2$); 6.64–6.36 (br., NH); 6.41 (*d*, ^3J = 6.25, H–C(7′)); 4.72 (*s*, 2 H, FC$_6$H$_4$C*H*$_2$); 2.06–1.50 (*m*, C$_6$H$_{10}$). ^{13}C-NMR (62.89 MHz, CDCl$_3$): 162.4 (*d*, ^1J = 247.0, C$_p$ of FC$_6$H$_4$CH$_2$); 158.5 (*s*, C(7′a)); 154.6 (*s*, C(4′)); 152.3 (*s*, C(3′a)); 149.6 (*s*, C(6′)); 133.3 (*d*, ^4J = 3.1, C$_{ipso}$ of

$FC_6H_4CH_2$); 129.9 (*d*, ^3J = 8.4, 2 C_o of $FC_6H_4CH_2$); 115.7 (*d*, ^2J = 21.7, 2 C_m of $FC_6H_4CH_2$); 108.5 (*s*, C(2')); 106.1 (*s*, C(7')); 44.4 (*s*, $FC_6H_4CH_2$); 33.1 (*s*, C(2), C(6)); 25.5 (*s*, C(4)); 24.6 (*s*, C(3), C(5)). MS: 310 (97, M^+), 187 (100, $[C_{11}H_{13}N_3]^+$). Anal. calc. for $C_{18}H_{19}FN_4$ (310.36): C 69.66, H 6.17, N 18.05; found: C 69.53, H 6.37, N 18.02.

Ethyl {4-Amino-2-[(4-fluorobenzyl)amino]pyridin-3-yl}carbamate Hydrochloride (**40**). As described for **32**, **26b** (0.462 g, 1.49 mmol) in THF/H_2O 108:78 (186 ml) is reductively hydrolysed with $Na_2S_2O_4$ (2.08 g, 11.93 mmol). The extract is concentrated and chromatographed (25 cm, silica gel, AcOEt/MeOH 5:2) and the solid thus obtained dissolved in dry THF (5 ml). A soln. of ClCOOEt (216 mg, 2 mmol) in dry THF (5 ml) is slowly added (→cloudy, then brown and viscous precipitate). Evaporation and recrystallisation of the residue from i-PrOH give **40** (92 mg, 18.2% rel. to **26b**). Colourless crystals. M.p. 155°. UV (MeCN): 276 (3.904). IR (KBr): 3480–2920 (band due to aggregation); 1715 (C=O); 1660, 2615, 1450 (C=C, C=N); 1380; 1250 (C–O–C); 1225 (C–F). ^{1}H-NMR (300 MHz, (D_6)DMSO): 12.54 (*s*, NH^+(pyr.)); 8.27 (*s*, NHCOOEt); 7.95 (br., $FC_6H_4CH_2NH$); 7.61–6.91 (*m*, $FC_6H_4CH_2$, H–C(6), NH_2); 6.34 (*d*, ^3J = 7.00, H–C(5)); 4.68 (*d*, ^3J = 5.92, $FC_6H_4CH_2$); 4.10 (*q*, $MeCH_2$); 1.28 (*t*, $MeCH_2$). ^{13}C-NMR (75.43 MHz, (D_6)DMSO): 161.0 (*d*, ^1J = 242.3, C_p of $FC_6H_4CH_2$); 154.7 (*s*, C(4) or C(2)); 154.4 (*s*, NHCOOEt); 149.9 (*s*, C(4) or C(2)); 133.8 (*s*, C_{ipso} of $FC_6H_4CH_2$); 133.4 (*s*, C(6)); 128.7 (*d*, ^3J = 7.9, 2 C_o of $FC_6H_4CH_2$); 114.7 (*d*, ^2J = 21.4, 2 C_m of $FC_6H_4CH_2$); 102.9 (*s*, C(5)); 98.9 (*s*, C(3)); 60.5 (*s*, $MeCH_2$); 43.2 (*s*, $FC_6H_4CH_2$); 14.3 (*s*, $MeCH_2$). MS: 304 (76, $[C_{15}H_{17}FN_4O_2]^+$), 109 (100, $[C_7H_6F]^+$). HR-MS (peak matching): 304.1337 ($[C_{15}H_{17}FN_4O_2 \cdot HCl]^+$, calc. 304.1336). Elemental analysis: unsatisfactory due to instability of **40**.

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