Reactions of 2,3-Dihydrospiro[1*H*-4- and 5-azabenzimidazole-2,1'-cyclohexane] with Nucleophiles: A Potential Route to some Substituted Aromatic Heterocycles

Ralf Reizner, Walter Kramer, and Richard Neidlein*

Pharmazeutisch-Chemisches Institut der Universität Heidelberg,
Im Neuenheimer Feld 364, D-69120 Heidelberg, Germany

Hans Suschitzky*

Division of Chemical Sciences, Science Research Institute, University of Salford, Salford M5 4WT, UK

Received April 22, 1997
Revised July 22, 1998

Dedicated to Professor Dr. Rolf Gleiter, Heidelberg, on the occasion of his 60th birthday

The readily available title compounds **2, 16** and **27** react with pseudohalogenes (cyanide, azide), carbon and heterocyclic *N*-nucleophiles in the presence of manganese dioxide to give the corresponding substituted azaisobenzimidazoles (= 2*H*-azabenzimidazoles) **4, 8, 23-26** and **29-33, 36** or dihydroazabenzimidazoles (= 2,3-dihydro-1*H*-azabenzimidazoles **7, 22, 34** and **35**. In **8** one of the two imidazolyl-substituents can be replaced by nucleophiles yielding the compounds **9-15**. Treatment of 6'-bromo-2,3-dihydro-4-azabenzimidazole **16** with morpholine or piperidine results in loss of the Br-atom presumably by an AE_a-mechanism. Reduction of the substituted azaisobenzimidazoles with sodium hydrosulfite followed by fission of the cyclohexane ring leads to substituted *o*-diaminopyridines. They were cyclised *in situ* with various condensing agents to give new heterocyclic systems. Equimolar mixtures of some azaisobenzimidazoles and dihydroazabenzimidazoles lead to the formation of coloured charge transfer complexes stable only in the solid state. Owing to poor electron-acceptor properties the complex dissociates in solution.

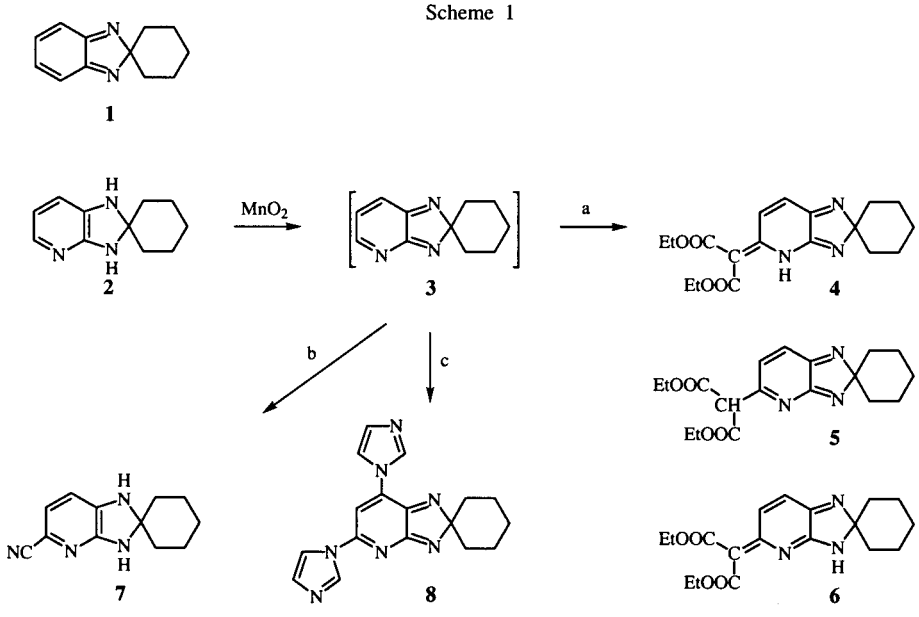
J. Heterocyclic Chem., **36**, 117 (1999).

Introduction.

2,3-Dihydro-1*H*-azabenzimidazoles **2, 16** and **27** readily obtained by condensation of the appropriate *o*-diaminopyridines with cyclohexanone [1] [2] show a structural relationship with spiro[2*H*-benzimidazole-2,1'-cyclohexane] **1**, a stable quinonediimine. Compound **1** displayed considerable synthetic potential for the introduction of nucleophiles by Michael addition [3] and for preparing new heterocycles of pharmaceutical interest by reductive hydrolysis followed by converting the generated *o*-diamines with condensating agents [4] [5] [6].

Using a competition reaction between the dihydro compound and manganese dioxide, the chemistry of the isobenzimidazole could be applied to the 2,3-dihydroazabenzimidazoles; the introduction of N, S and O-nucleophiles into the aza-compounds **2, 16** and **27** to give substituted azaisobenzimidazoles was shown to be feasible [1]. As a result of the biochemical and pharmaceutical importance of

Scheme 1



substituted pyridines there is obvious interest in extending the synthetic potential of the compounds **2, 16** and **27** by introducing further nucleophiles like pseudohalogenes as well as carbon and heterocyclic nucleophiles.

Moreover, the reaction of the bromo compound **16** with nucleophiles other than those reported [1] could give conclusive evidence about the mechanism leading to the loss of bromine reported previously [1].

Results.

Reactions of 2,3-Dihydrospiro[1*H*-4a-zabenzimidazole 2,1'-cyclohexane] **2**.

In a typical competition reaction compound **2** was allowed to react with diethyl malonate, trimethylsilyl cyanide and trimethylsilylimidazole in the presence of manganese dioxide at room temperature in tetrahydrofuran (products are shown in Scheme 1). The first step of the reaction is the oxidation of **2** to give the highly reactive, non-isolable 4-azaisobenzimidazole **3** which reacts immediately with the added nucleophiles.

Diethyl malonate led to formation of the stable methylidene compound **4** being inconsistent with a recent note on the synthesis of 6-substituted-2,3-diaminopyridines [2] reporting the production of **5**. Observing the literature conditions we could neither confirm the formation of **5** nor of **6**; the only product we were able to isolate was identical in all respects with our compound **4**.

In the ^{1}H-nmr-spectrum a broad singlet could be found at $\delta = 11.41$ which belongs to the N-H-proton so that **5** was excluded. The distinction between **4** and **6** was made by ^{13}C{H}-NOE difference spectrum (Figure 1). Selective irradiation of H-N(4') caused NOE's for both of the C=O-groups, C-3'a, C-5', C-7', C-6' and C-8'. The absence of an NOE for C-2 and the detected NOE's for C-3'a and C-5' confirm structure **4**.

The cyano-compound **7** was obtained only in its dihydro form. Dehydrogenation to a cyano-4-azaisobenzimidazole was unsuccessful even with strong oxidizing agents such as lead dioxide, manganese dioxide, potassium permanganate or mercuric oxide. We suggest that the strong electron withdrawing effect of the cyano substituent produces a positive charge in the molecule which can best be compensated by the dihydro form.

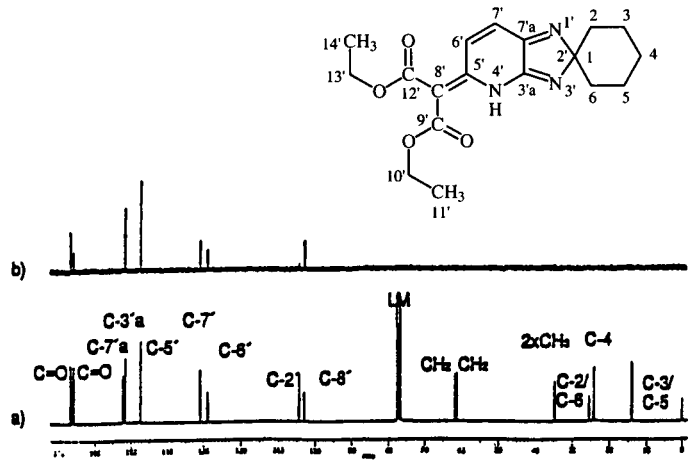
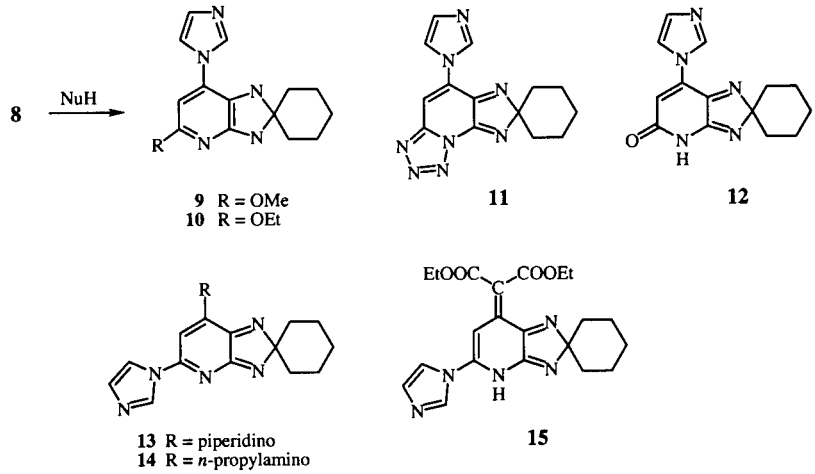


Figure 1. ^{13}C-nmr spectra (62.89 MHz, Bruker WM 250) in trichlorodeuteriomethane for compound **4**: a) ^{1}H-noise decoupled spectrum; b) ^{13}C{^{1}H}-NOE difference spectrum obtained by selective irradiation of H-N(4') respectively

When trimethylsilylimidazole was used as the nucleophile the disubstituted 4-azaisobenzimidazole **8** was formed. This compound is of pharmacological and synthetic interest. Imidazo functions are important structures in drugs [7] and are also convenient leaving groups particularly in the synthesis of peptides [8]. If one of the two imidazo-groups in **8** were replaceable, nucleophiles could be introduced by substituting one imidazo-group and thereby widening the synthetic potential of the azaisobenzimidazoles. Indeed it was found that replacement of one imidazo-group took place after addition of nucleophiles. For instance small nucleophiles, *e.g.* methanol reacted with **8** to give 7'-imidazo-5'-methoxy-4-azaisobenzimidazole **9**.

Scheme 2



Other small nucleophiles like ethanol, azide and water also attacked the 5-position of the molecule leading to products **10, 11** and **12** respectively. Bulky nucleophiles like piperidine, *n*-propylamine or diethyl malonate showed a different substitution pattern. Owing presumably to steric reasons *ipso*-substitution took place exclusively at the 7-position of the molecule to give compounds **13, 14** and **15**.

Reactions of 6'-Bromo-2,3-dihydro[1 *H*-4-azabenzimidazole-2,1'-cyclohexane] **16**.

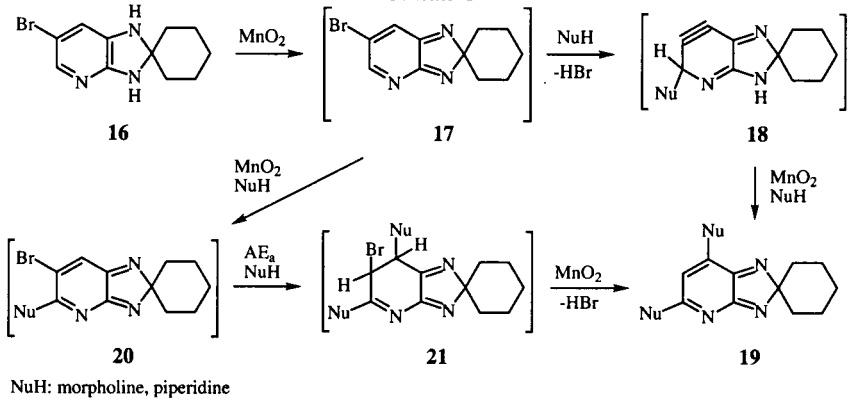
When **16** was allowed to react with piperidine or morpholine in a typical competition reaction an unexpected result was obtained. The bromo-atom was eliminated with formation of the disubstituted 4-azaisobenzimidazole **19**. This we previously interpreted as possibly being due to a pyridyne mechanism leading to a *cine* substitution as shown in Scheme 3 [1].

Alder product renders the participation of a pyridyne mechanism unlikely.

A more plausible explanation to account for the loss of the bromo-atom lies in the operation of an addition-elimination mechanism (AE_a) [13]. The unstable intermediate **17** formed by oxidation first adds the nucleophile by a 1,4-Michael addition followed by oxidation to give **20**. This is attacked by another molecule of nucleophile to give the intermediate **21**. Loss of hydrogen bromide leads to the observed compound **19** (Scheme 3).

To obtain more information about the reactivity of **16**, it was allowed to react with diethyl malonate, trimethylsilyl cyanide, methanol, trimethylsilylimidazole and trimethylsilyltriazole. Surprisingly we obtained the corresponding substituted 6'-bromo-4-azaisobenzimidazole, except for the cyano-compound which yielded the dihydro

Scheme 3



16 **17** **18** **20** **21** **19**

NuH: morpholine, piperidine

However a *cine*-mechanism of this type is usually observed only in the presence of strong bases [9]. Less doubt concerns the absence of another disubstitution product in Scheme 3. Usually a *cine* mechanism leads to the formation of two products which in our case would be the isolated **19** and a posssible 5',6'-disubstituted compound [10].

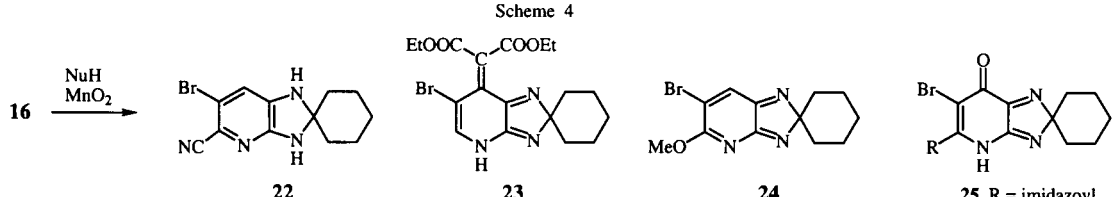
It was therefore of interest to try trapping the suggested pyridyne **18** as confirmation of a *cine* mechanism. Arynes [11] or pyridynes [12] can be trapped efficiently with furan in a Diels-Alder reaction to form endoxides. Following closely the literature procedure with morpholine as nucleophile [1] and using furan instead of tetrahydrofuran as solvent we obtained a pure compound which was in all analytical details identical with **19**. The absence of a Diels-

compound **22** without loss of the bromo-atom. Probably due to steric reasons diethyl malonate attacked the 7'-position of the molecule to give **23**. When methanol was used as the nucleophile compound **24** could be isolated. With trimethylsilylimidazole and trimethylsilyltriazole compounds **25** and **26** were formed by addition of one molecule water to the corresponding intermediates **20** followed by oxidation to give the pyridones.

Reactions of 2,3-Dihydrospiro[1*H*-5-azabenzimidazole 2,1'-cyclohexane] **27**.

We used again the strategy of a competition reaction, to generate the reactive intermediate **28** for introducing nucleophiles into the 2,3-dihydro-5-azabenzimidazole **27**.

Scheme 4



22 **23** **24**

25 R = imidazoyl
26 R = triazolyl

Only mono-substituted 2*H*-5-azabenzimidazoles **29-33** were produced. With trimethylsilylazide the *in situ* generated mono-substituted azido-aza-benzimidazole reacted in a further step to give the corresponding tetrazole **32**. The cyano- and triazolo-substituted derivatives **34** or **35** were obtained in the dihydro form again probably owing to the electron withdrawing effect of the substituents. When piperazine was used as the nucleophile two molecules of **28** reacted to give compound **36**.

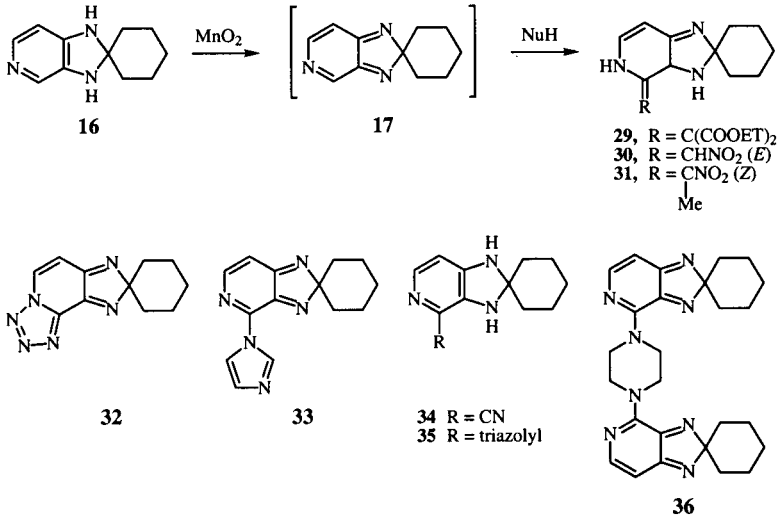
In contrast to the reaction of the isomer **2** a direct nucleophilic substitution occurred in **27** with trimethylsilylazide resulting in the formation of **32**. Using the less nucleophilic nitromethane and nitroethane **30** and **31** were isolated. Compound **30** existed in the *E*-form while nitroethane gave the *Z*-isomer **31** on account of the steric effect of the bulky methyl-group.

In contrast when the 4-aza-compound **2** was allowed to react with nitroalkanes no reaction occurred. Reactions of **27** with nucleophiles proceeded generally much faster than the corresponding substitutions with **2** indicating the greater reactivity of 2,3-dihydro[1*H*-5-azabenzimidazole-2,1'-cyclohexane] **27**.

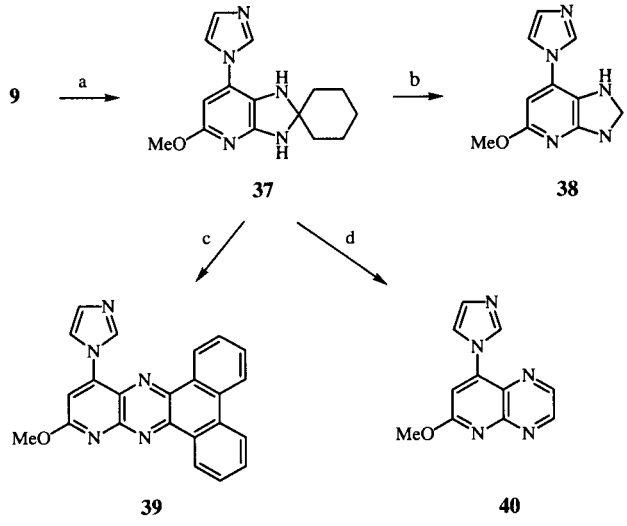
Heterocycles from Substituted 2*H*-4- and 5-azabenzimidazoles.

Substituted 2*H*-azabenzimidazoles can be regarded as protected *o*-diaminopyridines. The aromatic character could be readily restored by reductive fission with sodium dithionite leading first to dihydroazabenzimidazoles followed by ring-opening to give a diaminopyridine. Conventional cyclisation gave heterocycles of which particularly imidazopyridines are of current pharmaceutical

Scheme 5



Scheme 6

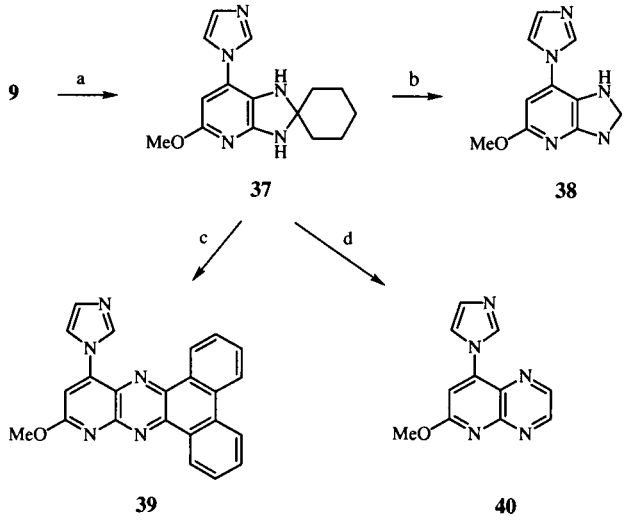


a) $Na_2S_2O_4$, b) HCOOH, c) 9,10-phenantrenequinone, d) CHO-CHO•$NaHSO_3$

interest [14] [15] [16].

Treatment of 7'-imidazo-5'-methoxy-4-azaisobenzimidazole **9** with sodium dithionite led to the dihydro compound **37**. Ring opening of **37** yielded an unstable *o*-diaminopyridine which was cyclised *in situ* with formic acid, 9,10-phenanthroquinone or glyoxal sodium bisulfite to give respectively the 1*H*-imidazo[4,5-*b*]pyridine **38**, the pyrido-[2,3-*b*]quinoxaline **39** and the pyrido[2,3-*b*]pyrazine **40**.

Scheme 6

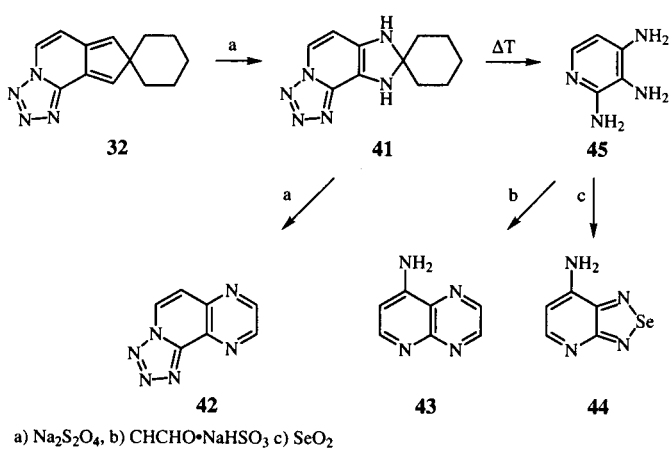


a) $Na_2S_2O_4$, b) HCOOH, c) 9,10-phenantrenequinone, d) CHO-CHO•$NaHSO_3$

Presumabely owing to strong H-bonding between H-N and the imidazolyl N-atoms the usual 1,3-tautomerism found in imidazoles [17] could not be detected in **38** which existed solely in the 1H-form.

The conversion of substituted 2*H*-5-azabenzimidazoles into heterocycles by reductive ring opening with sodium dithionite followed by cyclisation proved equally successful for the 2*H*-4-azabenzimidazoles. Thus treatment of the tetrazole **32** with aqueous sodium dithionite gave the stable dihydroform **41**. Hydrolysis of **41** followed by cyclisation with glyoxal sodium bisulfite led to the expected pyridopyrazine **42** and surprisingly to **43**. Cyclisation of **41** with selenium oxide led unexpectedly to give **44**.

Scheme 7



a) $Na_2S_2O_4$, b) CHCHO•$NaHSO_3$ c) SeO_2

The formation of **43** and **44** can be explained by an intermediate triaminopyridine **45** formed by decomposition of the tetrazole ring of **41** with loss of nitrogen after fission of the cyclohexane ring. Owing to the different reactivity of the amino-groups cyclisation took place exclusively involving the substituents in positions 2 and 3 to give the heterocycles **43** and **44** as shown in Scheme 7 for selenium dioxide.

Charge Transfer Complexes.

Charge transfer complexes between isobenzimidazoles and benzimidazoles in the solid state have been reported by us [18] [19]. Due to the structural similarity of our aza-systems we expected charge transfer complexes to be formed between azabenzimidazoles and their dihydro derivatives. On dissolving equimolar quantities of the yellow 4'-imidazolyl-5-aza-2*H*-benzimidazole **33** and the colourless 2'-triazolyl-2,3-dihydro-5-azabenzimidazole **35** in tetrahydrofuran a yellow solution resulted. A blue black complex was deposited on evaporating the solvent. The ^1H- and ^{13}C-nmr-spectra were the exact composite spectra of the constituent compounds **33** and **35**. A uv-spectrum (potassium bromide-disk) showed an absorption at λ_{max} = 584 nm ascribed to an electron transfer band indicative of a charge transfer complex [20] not present in either component. Since the complex dissociates on addition of solvent the charge transfer complex is apparently held together only by weak hydrogen bonds in the solid state. Owing to the poor electron acceptor properties and the absence of hydrogen bonding in solution the complex existed solely in the solid state.

Another electron transfer complex was obtained by dissolving 7'-imidazolyl-5'-methoxy-4-azabenzimidazole **37** and **9** in ethyl acetate. A mixture of the corresponding colourless compounds **9** and **37** in the proportion of 2:1 was formed leading to a wine-red complex after evaporation of the solvent. The complex showed a characteristic electron transfer band at λ_{max} = 469 nm in a uv-spectrum [20].

EXPERIMENTAL

General.

Activated manganese dioxide was purchased from Fluka (CAS No. [1313-13-9]). Column chromatography (CC): silica gel 60 (Merck); mp, Reichert. melting-point microscope, uncorrected uv spectra: Hewlett Packard-HP 8453-spectrometer; λ (logε) in nm; ir spectra: Perkin-Elmer-PE 1600 FT-spectrometer nmr spectra: Bruker WM 250 (250.13 MHz for ^1H and 62.89 MHz for ^{13}C) and Varian XL-300 (299.95 MHz for ^1H and 75.43 MHz for ^{13}C); δ values relative to tetramethylsilane; ms: Varian MAT-311-A (80eV).

5'-Diethoxycarbonylmethylenspiro[cyclohexane-1,2'(4'*H*)-2'*H*-imidazo[4,5-*b*]pyridine] (**4**).

To a solution of spiro[cyclohexane-1,2'(3'*H*)-1'*H*-imidazo[4,5-*b*]pyridine] **2** (500 mg, 2.65 mmoles) in tetrahydrofuran (100 ml), diethyl malonate (424 mg, 2.65 mmoles) and manganese dioxide (4.6 g, 52.9 mmoles) were added and stirred at rt for 23 hours. After filtration and evaporation, the residual oil was chromatographed (silica gel, ethyl acetate) followed by careful evaporation to provide light yellow crystals of pure **4** (505 mg, 55%), mp 104°; uv (acetonitrile): 287 (4.117), 298 (4.125), 385 (4.209); ir (potassium bromide): 3222 (N-H), 3046, 2930/2856 (C-H), 1720 (C=O), 1656/1606/1592/1443 (C=C, C=N), 1235, 1072, 1028. ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 11.41 (s, N-H), 7.17 (d, ^{3}J = 10.2, H-C(7-)), 7.07 (d, ^{3}J = 10.2, H-C(6')), 4.36-4.23 (m, H-C(10'), H-C(14')), 1.89-1.59 (m, C_6H_{10}), 1.37-1.27 (m, H-C(11'), H-C(14')). ^{13}C-nmr (62.89 MHz, trichlorodeuteriomethane): 166.9 (s, C=O), 166.1 (s, C=O), 152.3 (s, C(7'a)), 151.7 (s, C(3'a)), 147.4 (s, C(5')), 131.0 (s, C(7')), 128.8 (s, C(6')), 103.8 (s, C(2')), 103.0 (s, C(8')), 61.8 (s, CH_2), 61.3 (s, CH_2), 34.8 (s, C(2), C(6)), 25.5 (s, C(4)), 24.2 (s, C(3), C(5)), 14.1 (s, 2x CH_3). MS: 345 (35) [M+], 299 (100).

Anal. Calcd. for $C_{18}H_{23}N_3O_4$ (345.40): C, 62.59; H, 6.71; N, 12.17. Found: C, 62.32; H, 6.70; N, 12.00.

5'-Cyanospiro[cyclohexane-1,2'(3'*H*)-(1'*H*)-imidazo[4,5-*b*]-pyridine] (**7**).

Compound **7** was obtained from **2** (1.0 g, 5.3 mmoles) in tetrahydrofuran (200 ml), trimethylsilyl cyanide (10.4 g, 100.6 mmoles) and manganese dioxide (4.6 g, 52.9 mmoles, 7 hours) as previously described. Chromatography (silica gel, ethyl acetate) and recrystallisation from diethyl ether provided a light green powder of **7** (186 mg, 16.4%), mp 229°; uv (acetonitrile): 337 (4.172); ir (potassium bromide): 3346 (N-H), 3200, 3147, 3065 (Aryl-H), 2933/2860 (C-H), 2211 (CN), 1622/1606/1515/1412/ (C=C, C=N), 1259, 803; ^{1}H-nmr (250.13 MHz, dimethyl-d_6 sulfoxide): 7.79 (s, N-H), 7.53 (s, N-H), 6.79 (d,^{3}J = 6.25, H-C(6')), 6.10 (d, ^{3}J = 6.25, H-C(7')), 1.75-1.25 (m, C_6H_{10}); ^{13}C-nmr (62.89 MHz, dimethyl-d_6 sulfoxide): 154.2 (s, C(5'a)), 137.2 (s, C(7'a)), 121.9 (s, C(6')), 120.4 (s, CN), 113.9 (s, C(5')), 103.2 (s, C(7')), 78.7 (s, C(2')), 39.6 (s, C(2), C(6)), 24.4 (s, C(4)), 21.8 (s, C(3), C(5)); ms: 214 (28) [M+], 171 (100).

Anal. Calcd. for $C_{12}H_{14}N_4$ (214.27): C, 67.27; H, 6.58; N, 26.15. Found: C, 67.49; H, 6.49; N, 26.00.

5',7'-(Diimidazol-1-yl)spiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-*b*]pyridine].

Compound **8** was obtained from **2** (500 mg, 2.65 mmoles) in tetrahydrofuran (100 ml), trimethylsilylim idazole (1.4 g, 10.6 mmoles) and manganese dioxide (2.3 g, 26.4 mmoles, 24 hours) as previously described. Chromatographying (silica gel, ethylacetate/ethanole 5:2) and recrystallisation from diethyl ether provides a yellow powder of **8** (103 mg, 12%), mp 166°; uv (acetonitrile): 240 (4.276), 305 (4.057); ir (potassium bromide): 3129/3112 (Aryl-H), 2932/2847 (C-H), 1632/1603/1553/1523/1474/1424 (C=C, C=N), 1352, 1258, 1251, 1187, 1106, 996; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 9.02 (s, H-C(8')), 8.54 (s, H-C(11')), 7.89 (s, H-C(10')), 7.85 (s, H-C(13')), 7.32 (s, H-C(9')), 7.28 (s, H-C(12')), 7.24 (s, H-C(6')), 2.01-1.67 (m, C_6H_{10}); ^{13}C-nmr (62.89 MHz, trichlorodeuteriomethane): 160.3 (s, C(3'a)), 156.8 (s, C(5')), 150.2 (s, C(7'a)), 140.5 (s, C (7')), 13 8.4 (s, C (8')), 136.0 (s, C(11')), 132.2 (s, C(10')), 132.0 (s, C(13')), 116.8 (s, C(9')), 116.6 (s, C(12')), 107.3 (s, C(2')), 105.4 (s, C(6')), 33.4 (s, C(2), C(6)), 25.4 (s, C(4)), 24.4 (s, C(3), C(5)); ms: 319 (100) [M+]

Anal. Calcd. for $C_{17}H_{17}N_7$ (319.37): C, 63.93; H, 5.37; N, 30.70. Found: C, 64.07; H, 5.28; N, 30.50.

7'-(Imidazol-1-yl)-5'-methoxyspiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-*b*]pyridine] (**9**).

Compound **9** was obtained from **2** (500 mg, 2.65 mmoles) in tetrahydrofuran (100 ml), trimethylsilylimidazole (1.4 g, 10.6 mmoles) and manganese dioxide (2.3 g, 26.4 mmoles, 24 hours) as previously described. Chromatography (silica gel, ethyl acetate/methanol 5:2) and recrystallisation from diethyl ether yielded colourless crystals **9** (232 mg, 31%), mp 148-150°; uv (acetonitrile): 232 (3.955), 280 (3.961), 346 (3.603); ir (potassium bromide): 3037 (Aryl-H), 2935/2853 (C-H), 1634/1611/1565/1517/1482/1437 (C=C, C=N), l387, 1320, 1278, 1224, 948; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 8.90 (s, H-C(8')), 7.69 (s, H-C(10')), 7.24 (s, H-C(9')), 6.63 (s, H-C(6')), 4.12 (s, OCH_3), 1.98-1.62 (m, C_6H_{10}); ^{13}C-nmr (62.89 MHz, trichlorodeuteriomethane): 170.2 (s, C(5')), 160.4 (s, C(3'a)), 150.3 (s, C(7'a)), 138.5 (s, C(7')), 138.0 (s, C(8')), 131.3 (s, C(10')), 116.5 (s, C(9')), 109.3 (s, C(6')), 105.5 (s, C(2')), 55.6 (s, C(11')), 33.6 (s, C(2), C(6)), 25.5 (s, C(4)), 24.4 (s, C(3), C(5)); ms: 283 (100) [M+].

Anal. Calcd. for $C_{15}H_{17}N_5O$ (283,33): C, 63.59; H, 6.05; N, 24.71. Found: C, 63.46; H, 5.89; N, 24.56.

5'-Ethoxy-7'-(Imidazol-1-yl)spiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-*b*]pyridine] (**10**).

Compound **10** was obtained from **2** (500 mg, 2.65 mmoles) in tetrahydrofuran (100 ml), trimethylsilylimidazole (1.4 g, 10.6 mmoles) and manganese dioxide (2.3 g, 26.4 mmoles, 24 hours). Chromatography (aluminium oxide, ethyl acetate/ethanol 5:2) and recrystallisation from *n*-hexane gave colourless crystals **10** (213 mg, 27%), mp 90; uv (acetonitrile): 232 (3.979), 281 (3.989), 343 (3.621); ir (potassium bromide): 3056 (Aryl-H), 2930/2855 (C-H), 1635/1609/1516/1483/1412 (C=C, C=N), 1322, 1270, 1244, 1224, 1110; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 8.90 (s, H-C(8')), 7.6070 (s, H-C(10')), 7.25 (s, H- C(9')), 6.63 (s, H-C(6')), 4.45 (q, CH_2), 1.98-1.62 (m, C_6H_{10}), 1.44 (t, CH_3); ^{13}C-nmr (75.43 MHz, trichlorodeuteriomethane): 169.4 (s, C(5')), 160.3 (s, C(3'a)), 150.1 (s, C(7'a)), 138.1 (s, C(7')), 137.7 (s, C(8')), 131.0 (s, C(10')), 116.3 (s, C(9')), 109.5 (s, C(6')), 105.2 (s, C(2')), 64.4 (s, C(11')), 33.6 (s, C(2), C(6)), 25.5 (s, C(4)), 24.3 (s, C(3), C(5)), 14.2 (s, C(12')); ms: 297 (100) [M+].

Anal. Calcd. for $C_{16}H_{19}N_5O$ (297.36): C, 64.63; H, 6.44; N, 23.55. Found: C, 64.62; H, 6.74; N, 23.13.

7'-(Imidazol-1-yl)tetrazolo[5,1-*f*]spiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-*b*]pyridine] (**11**).

Compound **11** was obtained from **2** (500 mg, 2.65 mmoles) in tetrahydrofuran (100 ml), trimethylsilylimidazole (1.4 g, 10.6 mmoles) and manganese dioxide (2.3 g, 26.4 mmoles, 24 hours) as previously described. After filtration trimethylsilylazide (3.05 g, 26.5 mmoles) was added and the solution was stirred for 15 hours at rt. Chromatography (silica gel, ethyl acetate) and recrystallisation from diethyl ether provided a light yellow powder **11** (159 mg, 20% based upon **2**), mp 186-187°; uv (acetonitrile): 239 (4.097), 279 (3.834), 342 (3.734); ir (potassium bromide): 3050 (Aryl-H), 2937/2860 (C-H), 1663/1605/1570/1476/1444 (C=C, C=N), 1241,

945, 882; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 8.84 (s, H-C(8')), 7.73 (s, H-C(10')), 7.65 (s, H-C(6')), 7.31 (s, H-C(9')), 2.03-1.78 (m, C_6H_{10}); ^{13}C-nmr (75.43 MHz, trichlorodeuteriomethane): 151.1 (s, C(5')), 149.0 (s, C(7'a)), 144.5 (s, C(3'a)), 137.5 (s, C(8')), 134.0 (s, C(7')), 131.5 (s, C(10')), 116.9 (s, C(9')), 109.9 (s, C(2')), 106.3 (s, C(6')), 33.4 (s, C(2), C(6)), 25.1 (s, C(4)), 23.9 (s, C(3), C(5)); ms: 294 (36) [M+], 239 (100).

Anal. Calcd. for $C_{14}H_{14}N_8$ (294.32): C, 57.13; H, 4.79; N, 38.07. Found: C, 57.21; H, 4.63; N, 37.88.

7'-(Imidazol-1-yl)spiro[cyclohexane-1,2'-2'*H*-imidazo-[4,5-*b*]pyridin]-5'(4'*H*)-one (**12**).

Compound **12** was obtained from **2** (500 mg, 2.65 mmoles) in terahydrofuran (100 ml), trimethylsilylimidazole (1.4 g, 10.6 mmoles) and manganese dioxide (2.3 g, 26.4 mmoles, 24 hours) as previously described. After filtration *n*-tetrabutylammonium fluoride (4.17 g, 13.25 mmoles) was added and the solultion was stirred for 2 hours at rt. Chromatography (silica gel, ethyl acetate/methanol 10:1) and recrystallisation from ethyl acetate provided a colourless powder of **12** (240 mg, 34% based upon **2**), mp 277°; uv (acetonitrile): 234 (3.807), 281 (3.933); ir (potassium bromide): 3162 (N-H), 3072 (Aryl-H), 2940/2850 (C-H), 1688 (C=O), 1602/1580/14801441 (C=C, C=N), 1305, 1241, 1193, 1086; ^{1}H-nmr (299.95 MHz, dimethyl-d_6 sulfoxide): 11.84 (s, N-H), 8.82 (s, H-C(8')), 8.14 (s, H-C(10')), 7.19 (s, H-C(9')), 7.06 (s, H-C(6')), 1.92-1.53 (m, C_6H_{10}); ^{13}C-nmr (62.89 MHz, dimethyl-d_6 sulfoxide): 164.1 (s, C(5')), 152.8 (s, C(3'a)), 148.4 (s, C(7'a)), 137.3 (s, C(8')), 136.7 (s, C(7')), 130.1 (s, C(10')), 118.0 (s, C(9')), 116.2 (s, C(6')), 104.1 (s, C(2')), 33.7 (s, C(2), C(6)), 24.9 (s, C(4)), 23.8 (s, C(3), C(5)); ms: 269 (100) [M+].

Anal. Calcd. for $C_{14}H_{15}N_5O$ (269.31): C, 62.44; H, 5.61; N, 26.00. Found: C, 62.18; H, 5.68; N, 25.97.

5'-(Imidazol-1-yl)-7'-piperidinospiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-*b*]pyridine] (**13**).

Compound **13** was obtained from **2** (500 mg, 2.65 mmoles) in tetrahydrofuran (100 ml), trimethylsilylimidazole (1.4 g, 10.6 mmoles) and manganese dioxide (2.3 g, 26.4 mmoles, 24 hours) as previously described. After filtration piperidine (2.3 g, 26.5 mmoles) was added and the solution was stirred for 15 hours at rt. Chromatography (silica gel, ethyl acetate/methanol 5:1) and recrystallisation from diethyl ether provided crimson crystals **13** (28 mg, 3.1% based upon **2**), mp 179-181°; uv (acetonitrile): 246 (4.374), 325 (3.885); ir (potassium bromide): 2937 (C-H), 1617/1576/1550/1483/1457 (C=C, C=N), 1264, 1018; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 8.41 (s, H-C(8')), 7.75 (s, H-C(10')), 7.15 (s, H-C(9')), 5.92 (s, H-C(6')), 4.12-3.95 (m, 4H, 2x -CH_2), 1.98-1.45 (m, 16H, C_3H_6, C_6H_{10}); ^{13}C-nmr (75.43 MHz, trichlorodeuteriomethane): 161.8 (s, C(3'a)), 159.1 (s, C(5')), 152.9 (s, C(7'a)), 150.2 (s, C(7')), 135.6 (s, C(8')), 130.6 (s, C(10')), 116.6 (s, C(9')), 103.3 (s, C(2')), 89.7 (s, C(6')), 49.4 (s, C(11'), C(13')), 33.7 (s, C(2), C(6)), 25.7 (s, C(12'), C(14')), 25.6 (s, C(4)), 24.4 (s, C(3), C(5)), 24.1 (s, C(13')); ms: 336 (100) [M+]; hrms: (peak matching), Calcd. 336.2066. Found: 336.2064 ([$C_{19}H_{24}N_6$]+).

5'-(Imidazol-1-yl)-7'-*n*-propylaminospiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-*b*]pyridine] (**14**).

Compound **14** was obtained from **2** (500 mg, 2.65 mmoles) in tetrahydrofuran (100 ml), trimethylsilylimidazole (1.4 g, 10.6 mmoles) and manganese dioxide (2.3 g, 26.4 mmoles, 24 hours) as previously described. After filtration *n*-propylamine (1.56 g, 26.5 mmoles) was added and the solution was stirred for 15 hours at rt. Chromatography (silica gel, ethyl acetate/methanol 5:1) and recrystallisation from diethyl ether yielded orange needles **14** (30 mg, 3.6% based upon **2**), mp 177-178°; uv (acetonitrile): 244 (4.22), 315 (3.853), 431 (3.695); ir (potassium bromide): 3421 (N-H), 2939 (C-H), 1635/1617/1599/1476/1425 (C=C, C=N), 1273, 1218; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 8.44 (s, H-C(8')), 7.78 (s, H-C(10')), 7.17 (s, H-C(9')), 6.15 (s, N-H), 5.85 (s, H-C(6')), 3.31 (m, CH_2), 2.04-1.48 (m, 12H, CH_2, C_6H_{10}), 1.10 (t, CH_3); ^{13}C-nmr (62.89 MHz, trichlorodeuteriomethane): 161.1 (s, C(3'a)), 159.7 (s, C(5')), 151.9 (s, C(7'a)), 149.3 (s, C(7')), 135.9 (s, C(8')), 131.0 (s, C (10')), 116.8 (s, C (9')), 105.0 (s, C (2')), 86.6 (s, C(6')), 44.9 (s, C(11'),), 33.6 (s, C(2), C(6)), 25.4 (s, C(4)), 24.4 (s, C(3), C(5)), 21.8 (s, C(12')), 11.6 (s, C(13')); ms: 310 (41) [M+], 281 (100); hrms: (peak matching), Calcd: 310.1906. Found: 310.1906 ([$C_{17}H_{22}N_6$]+).

7'-Diethoxycarbonylmethylene-5'-(imidazol-1-yl)spiro[cyclohexane-1,2'(4'*H*)-2'*H*-imidazo[4,5-*b*]pyridine] (**15**).

Compound **15** was obtained from **2** (500 mg, 2.65 mmoles) in tetrahydrofuran (100 ml), trimethylsilylimidazole (1.4 g, 10.6 mmoles) and manganese dioxide (2.3 g, 26.4 mmoles, 24 hours) as previously described. After filtration diethyl malonate (14.24 g, 26.5 mmoles) and diisopropylethylamine (2.68 g, 26.5 mmoles) are added and the solution was stirred for 48 hours at rt. Chromatography (silica gel, ethyl acetate) and recrystallisation from diethyl ether yield yellow needles of **15** (120 mg, 11% based upon **2**), mp 117-118°; uv (acetonitrile): 287 (4.117), 298 (4.125), 385 (4.209); ir (potassium bromide): 3222 (N-H), 3046, 2930/2856 (CH), 1720 (C=O), 1656/1606/1592/1443 (C=C, C=N), 1235, 1072, 1028; ^{1}H-nmr (250.13 MHz, trichlorodeuteriomethane): 10.91 (s, N-H), 8.78 (s, H-C(8')), 7.60 (s, H-C(10')), 7.26 (s, H-C(6')), 7.23 (s, H-C(9')), 4.49 -4.24 (m, 2x CH_2), 1.96-1.63 (m, C_6H_{10}), 1.39-1.29 (m, 2x CH_3); ^{13}C-nmr (62.89 MHz, trichlorodeuteriomethane): 166.9 (s, C=O), 166.3 (s, C=O), 151.6 (s, C(3'a)), 148.1 (s, C(7'a)), 147.7 (s, C(5')), 137.3 (s, C(8')), 130.8 (s, C(10')), 116.6 (s, C(9')), 114.5 (s, C(6')), 105.2 (s, C(2')), 102.6 (s, C(11'),), 62.0 (s, CH_2), 61.5 (s, CH_2), 34.7 (s, C(2), C(6)), 25.2 (s, C(4)), 24.0 (s, C(3), C(5)), 14.1 (s, CH_3), 14.0 (s, CH_3); ms: 411 (71) [M+], 365 (100).

Anal. Calcd. for $C_{21}H_{25}N_5O_4$ (411.46): C, 61.30; H, 6.12; N, 17.02. Found: C, 61.08; H, 6.17; N, 16.83.

6'-Bromo-5'-cyanospiro[cyclohexane-1,2'(3'*H*)-1'*H*-imidazo[4,5-*b*]pyridine] (**22**).

To a solution of 6'-bromospiro[cyclohexane-1,2'(3'*H*)-1'*H*-imidazo[4,5-*b*]pyridine] **16** (800 mg, 2.96 mmoles) in tetrahydrofuran (100 ml), trimethylsilyl cyanide (5.94 g, 59.2 mmoles) and manganese dioxide (4.6 g, 52.9 mmoles) were added and stirred at rt for 72 hours. After filtration and evaporation, the residual oil was chromatographed (silica gel, ethyl acetate/n-hexane 1:1). Recrystallisation from diethyl ether provided a brown powder of pure **22** (58.4 mg, 6.7%), mp 208°; uv (acetonitrile): 234 (4.136), 258 (3.902), 292 (3.762); ir (potassium bromide): 3232 (N-H), 3050 (Aryl-H), 2942/2856 (CH), 2210 (CN), 1670/1634/1559/1507/1490 (C=C, C=N),1103, 1047, 855; ^{1}H-nmr (299.95 MHz, dimethyl-d_6 sulfoxide): 10.02 (s, NH), 7.84 (s, H-C(7')), 1.83-1.60 (m, C_6H_{10}); ^{13}C-nmr (75.43 MHz, dimethyl-d_6 sulfoxide): 155.7 (s, C(5')), 153.1 (s, C(3'a)), 149.1 (s, C(7'a)), 129.5 (s, C(7')), 126.3 (s, C(6')), 113.2 (s, C(8')), 35.9 (s, C(2), C(6)), 24.3 (s, C(4)), 22.3 (s, C(3), C(5)); ms: 292 (54) [M+], 291 (100); hrms: (peak matching), Calcd: ([$C_{12}H_{13}BrN_4$]+): 292.0324. Found: 292.0324

6'-Bromo-7'-diethoxycarbonylmethylenspiro[cyclohexane1,2'(4'*H*)-2'*H*-imidazo[4,5-*b*]pyridine] (**23**).

Compound **23** was obtained from **16** (500 mg, 1.85 mmoles) in tetrahydrofuran (100 ml), diethyl malonate (296 mg, 1.85 mmoles) and manganese dioxide (2.3 g, 26.4 mmoles; 5 hours) as previously described. Chromatography (silica gel, ethyl acetate/*n*-hexane 1:1) and recrystallisation from *n*-hexane yielded bright yellow crystals **23** (188 mg, 24%), mp 118°; uv (acetonitrile): 302 (4.142), 312 (4.162), 389 (4.053); ir (potassium bromide): 3252 (N-H), 3070 (Aryl-H), 2978/2855 (CH), 1740 (C=O), 1645/1592/1443 (C=C, C=N), 1294, 1221, 1066, 936; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 12.19 (s, N-H), 7.65 (s H-C(7')), 4.33-4.24 (m, H-C(10'), H-C(13')), 1.83-1.60 (m, C_6H_{10}), 1.38-1.27 (m, H-C (11'), H- C(14')); ^{13}C-nmr (62.89 MHz, trichlorodeuteriomethane): 166.9 (s, C=O), 165.2 (s, C=O), 151.6 (s, C(7'a)), 150.4 (s, C(7')), 143.7 (s, C(3'a)), 134.7 (s, C(5')), 123.8 (s, C(6')), 105.2 (s, C(2')), 104.9 (s, C(8')), 62.0 (s, CH_2), 61.9 (s, CH_2), 34.7 (s, C(2), C(6)), 25.4 (s, C(4)), 24.1 (s, C(3), C(5)), 13.9 (s, CH_3), 13.7 (s, CH_3); ms: 423 (22) [M$^+$], 270 (100).

Anal. Calcd. for $C_{18}H_{22}BrN_3O_4$ (424.29): C, 50.95; H, 5.23; N, 9.90; found: C, 50.69; H, 5.23; N, 9.79.

6'-Bromo-5'-methoxyspiro[cyclohexane-1,2'-2'*H*-imidazo-[4,5-*b*]pyridine] (**24**).

Compound **24** was obtained from **16** (500 mg, 1.85 mmoles) in methanol (100 ml) and manganese dioxide (2.3 g, 26.4 mmoles, 51 hours). Chromatography (silica gel, ethyl acetate) and recrystallisation from diethyl ether gave a beige powder **24** (267 mg, 49%), mp 144°; uv (acetonitrile): 302 (4.142), 312 (4.162), 389 (4.053); ir (potassium bromide): 3021 (Aryl-H), 2923/2858 (C-H), 1617/1588/1519/1436/1400 (C=C, C=N); 1320, 1281, 1010, 880; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 7.92 (s, H-C(7')), 4.14 (s, OCH_3), 2.04-1.45 (m, C_6H_{10}); ^{13}C-nmr (75.43 MHz, trichlorodeuteriomethane): 163.3 (s, C(5')), 158.8 (s, C(3'a)), 154.0 (s, C(7'a)), 136.3 (s, C(7')), 122.9 (s, C(6')), 105.3 (s, C(2')), 56.4 (s, C(8')), 33.2 (s, C(2), C(6)), 25.5 (s, C(4)), 24.3 (s, C(3), C(5)); ms: 295 (100) [M$^+$].

Anal. Calcd. for $C_{12}H_{14}BrN_3O$ (296.17): C, 48.66; H, 4.76; N, 14.19. Found: C, 48.33; H, 4.73; N, 13.96.

6'-Bromo-5'-(imidazol-1-yl)spiro[cyclohexane-1,2'-2'*H*-imdazo[4,5-*b*]pyridine]-7'(4'*H*)-one (**25**).

Compound **25** was obtained from **16** (500 mg, 1.85 mmoles) in tetrahydrofuran (100 ml), trimethylsilylimidazole (1.04 g, 7.4 mmoles) and manganese dioxide (2.3 g, 26.4 mmoles, 5 hours) as previously described. Chromatography (silica gel, ethyl acetate/methanol 10:1) and recrystallisation from ethyl acetate yield a beige powder of **25** (104 mg, 16.1%), mp >300°; uv (acetonitrile): 283 (4.227); ir (potassium bromide): 3500-3350 (N-H), 3114 (Aryl-H), 2938/2857 (C-H), 2794, 1698 (C=O), 1664/1576/1521/1491/1448 (C=C, C=N), 1321, 1212, 1080, 1002, 952, 910, 824; ^{1}H-nmr (299.95 MHz, dimethyl-d_6 sulfoxide): 12.38 (s, N-H), 8.02 (s, H-C(8')), 7.55 (s, H-C(10')), 7.18 (s, H-C(9')), 2.11-1.48 (m, C_6H_{10}); ^{13}C-nmr (62.89 MHz, dimethyl-d_6 sulfoxide): 158.9 (s, C(5')), 151.5 (s, C(3'a)), 148.9 (s, C(7'a)), 138.1 (s, C(7')), 137.8 (s, C(8')), 129.3 (s, C(10')), 122.6 (s, C(6')), 119.5 (s, C(9')), 106.1 (s, C(2')), 34.4 (s, C(2), C(6)), 25.2 (s, C(4)), 24.0 (s, C(3), C(5)); ms: 347 (89) [M$^+$], 320 (100).

Anal. Calcd. for $C_{13}H_{13}BrN_6O$ (348.20): C, 48.29; H, 4.05; N, 20.11. Found: C, 48.03; H, 3.94; N, 20.18.

6'-Bromo-5'-(1,2,4-triazol-1-yl)spiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-*b*]pyridin]-7'(4'*H*)-one (**26**).

Compound **26** was obtained froml6 (500 mg, 1.85 mmoles) in tetrahydrofuran (100 ml), trimethylsilyltriazole (1.04 g, 7.4 mmoles) and manganese dioxide (2.3 g, 26.4 mmoles, 51 hours) as previously described. Chromatography (silica gel, ethyl acetate/*n*-hexane 5:1) and recrystallisation from ethyl acetate provided a beige powder **26** (126 mg, 20%), mp 219°; uv (acetonitrile): 281 (4.206), 365 (3.194); ir (potassium bromide): 3500-3350 (N-H), 3132 (Aryl-H), 2941/2852 (C-H), 1698 (C=O); 1669/1576/1506/1450 (C=C, C=N), 1325, 1269, 1137, 987; ^{1}H-nmr (299.95 MHz, dimethyl-d_6 sulfoxide): 12.47 (s, NH), 8.93 (s, H-C(8')), 8.40 (s, H-C(9')), 2.00-1.42 (m, C_6H_{10}); ^{13}C-nmr (75.43 MHz, dimethyl-d_6 sulfoxide): 159.1 (s, C(5')), 152.0 (s, C(9')), 151.5 (s, C(3'a)), 149.1 (s, C(7'a)), 146.8 (s, C(8')), 137.7 (s, C(7')), 127.2 (s, C(6')), 103.9 (s, C(2')), 33.2 (s, C(2), C(6)), 24.7 (s, C(4)), 23.6 (s, C(3), C(5)); ms: 348 (100) [M$^+$].

Anal. Calcd. for $C_{13}H_{13}BrN_6O$(349.19): C, 44.71; H, 3.75; N, 24.07. Found: C, 44.96; H, 3.54; N, 23.79.

4'-Diethoxycarbonylmethylenespiro[cyclohexane-1,2'(5'*H*)-2'*H*-imidazo[4,5-*c*]pyridine] (**29**).

To a solution of spiro[cyclohexane-1,2'(3'*H*)-1'*H*-imidazo[4,5-*c*]pyridine] **27** (1.0 g, 5.3 mmoles) in tetrahydrofuran (200 ml), diethyl malonate (848 mg, 5.3 mmoles), diisopropylethylamine (682 mg, 5.3 mmoles) and manganese dioxide (4.6 g, 52.9 mmoles) are added and stirred at rt. for 2 hours. After filtration and evaporation, the residual oil was chromatographed (silica gel, ethyl acetate). Recrystallisation from *n*-hexane provided **29** (516 mg, 28%), orange needles, mp 130°; uv (acetonitrile): 241 (4.131), 303 (3.186), 443 (4.127); ir (potassium bromide): 3261 (N-H), 2944/2856 (C-H), 1729 (C=O), 1671/1611/1599 (C=C, C=N), 1328, 1280, 1200, 1084; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 10.76 (s, N-H), 6.89 (m, H-C(6')), 6.05 (d, ^{3}J = 9.0, H-C(7')), 4.36-4.23 (m, H- C(10'), H-C(14')), 1.94-1.51 (m, C_6H_{10}), 1.35-1.29 (m, H-C(11'), H-C(14')); ^{13}C-nmr (62.89 MHz, trichlorodeuteriomethane): 166.7 (s, C=O), 156.6 (s, C=O), 156.1 (s, C(7'a)), 154.7 (s, C(3'a)), 142.8 (s, C(4')), 135.8 (s, C(6')), 108.9 (s, C(2')), 101.8 (s, C(8')), 99.8 (s, C(7')), 61.9 (s, CH_2), 61.2 (s, CH_2), 34.0 (s, C(2), C(6)), 25.6 (s, C(4)), 24.4 (s, C(3), C(5)), 14.1 (s, CH_3), 13.8 (s, CH_3). ms: 345 (81) [M$^+$], 227 (100).

Anal. Calcd. for $C_{18}H_{23}N_3O_4$ (345.40): C, 62.59; H, 6.71; N, 12.17. Found: C, 62.67; H, 6.69; N, 11.96.

(E)-4'-Nitromethylenespiro[cyclohexane-1,2'(5'*H*)-2'*H*-imidazo[4,5-*c*]pyridine] (**30**).

Compound **30** was obtained from **27** (1.0 g, 5.3 mmoles) in tetrahydrofuran (200 ml), nitromethane (320 mg, 5.3 mmoles), diisopropylethylamine (683 mg, 5.3 mmoles), and manganese dioxide (4.6 g, 52.9 mmoles, 2 hours) as previously described. Chromatography (silica gel, ethyl acetate) and recrystallisation from *n*-hexane yielded crimson crystals **30** (136 mg, 10%), mp 81-83°; uv (acetonitrile): 233 (3.937), 292 (3.747), 463 (4.198); ir (potassium bromide): 3413 (N-H), 2936/2855 (C-H), 1652/1594/1423 (C=C, C=N), 1545/1355 (N=O), 1275, 1179; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 10.91 (s, N-H), 7.65 (s, H-C(8')), 7.04 (m, H-C(6')), 6.14 (d, ^{3}J = 7.8, H-C(7')), 1.99-1.61 (m, C_6H_{10}); ^{13}C-nmr (75.43 MHz, trichlorodeuteriomethane): 155.0 (s, C(7'a)), 153.5, (s, C(3'a)), 139.8 (s, C(4')), 134.2 (s, C(6')), 113.8 (s, C(8')), 110.9 (s, C(2')), 103.5 (s,

C(7')), 33.6 (s, C(2), C(6)), 25.4 (s, C(4)), 24.2 (s, C(3), C(5)); ms: 246 (64) [M+], 216 (100).

Anal. Calcd. for $C_{12}H_{14}N_4O_2$ (246.27): C, 58.53; H, 5.73; N, 22.75. Found: C, 58.26; H, 5.75; N, 22.75.

(Z)-4'-(1-Nitroethylidene)spiro[cyclohexane-1,2'(5'*H*)-2'*H*-imidazo[4,5-*c*]pyridine] (**31**).

Compound **31** was obtained from **27** (1.0 g, 5.3 mmoles) in tetrahydrofuran (200 ml), nitroethane (398 mg, 5.3 mmoles), diisopropylethylamine (683 mg, 5.3 mmoles), and manganese dioxide (4.6 g, 52.9 mmoles, 2 hours) as previously described. Chromatography (silica gel, ethyl acetate) and recrystallisation from *n*-hexane provided crimson crystals of **31** (39 mg, 2.8%), mp 133-134°; uv (acetonitrile): 283 (3.876), 304 (3.876), 488 (4.222); ir (potassium bromide): 3428 (N-H), 2930/2853 (C-H), 1641/1598 (C=C, C=N), 1584 (N=O), 1407, 1390, 1196, 1131; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 11.96 (s, N-H), 6.99 (m, H-C(6')), 6.27 (d, ^{3}J = 8.7, H-C (7')), 2.85 (s, H-C (9')), 1.98-1.53 (m, C_6H_{10}); ^{13}C-nmr (62.89 MHz, trichlorodeuteriomethane): 156.1 (s, C(7'a)), 155.1 (s, C(3'a)), 137.6 (s, C(4')), 134.9 (s, C(6')), 128.7 (s, C(8')), 109.1 (s, C(2')), 102.7 (s, C(7')), 34.1 (s, C(2), C(6)), 25.5 (s, C(4)), 24.2 (s, C(3), C(5)), 15.4 (s, C(9')); ms: 260 (37) [M+], 212 (100).

Anal. Calcd. for $C_{13}H_{16}N_4O_2$ (260.29): C, 59.99; H, 6.19; N, 21.52. Found: C, 59.91; H, 6.14; N, 21.24.

Tetrazolo[1,5-*a*]spiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-*c*]pyridine] (**32**).

Compound **32** was obtained from **27** (1.0 g, 5.3 mmoles) in tetrahydrofuran (200 ml), trimethylsilyl azide (900 mg, 7.8 mmoles), and manganese dioxide (4.6 g, 52.9 mmoles, 2 hours) as previously described. After chromatography (silica gel, ethyl acetate) careful evaporation of the solvent provided brown crystals of pure **32** (552 mg, 46%), mp 142°; uv (acetonitrile): 272 (3.764), 488 (2.015); ir (potassium bromide): 3052 (Aryl-H), 2935/2848 (C-H), 1653/1570/1430/1412 (C=C, C=N), 1110, 938, 823; ^{1}H-NMR (299.95 MHz, deuteriochloroform): 8.29 (d, ^{3}J = 7.5, H-C(6')), 7.08 (d, ^{3}J = 7.5, H-C(7')), 2.58-1.19 (m, C_6H_{10}); ^{13}C-nmr (75.43 MHz, deuteriochloroform): 156.0 (s, C(7'a)), 147.0 (s, C(4')), 146.4 (s, C(3'a)), 129.6 (s, C(6')), 113.2 (s, C(2')), 112.8 (s, C(7')), 33.0 (s, C(2), C(6)), 25.3 (s, C(4)), 24,1 (s, C(3), C(5)); ms: 228 (2) [M+], 41 (100).

Anal. Calcd. for $C_{11}H_{12}N_6$ (228.26): C, 57.88; H, 5.30; N, 36.82; found: C, 58.13; H, 5.19; N, 36.57.

4'-(Imidazol-1-yl)spiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-*c*]-pyridine] (**33**).

Compound **33** was obtained from **27** (1.0 g, 5.3 mmoles) in tetrahydrofuran (200 ml), trimethylsilylimidazole (740 mg, 5.3 mmoles), and manganese dioxide (4.6 g, 52.9 mmoles, 2 hours) as previously described. Chromatography (silica gel, ethyl acetate) and recrystallisation from diethyl ether gave yellow needles **33** (590 mg, 44%), mp 139°; uv (acetonitrile): 237 (4.009), 392 (3.700); ir (potassium bromide): 3102 (Aryl-H), 2934/2910/2848 (CH), 1630/1559/1536/1499/1474 (C=C, C=N), 1298, 1180, 1034, 844; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 9.15 (s, H-C(8')), 8.17 (s, H-C(10')), 7.79 (d, ^{3}J = 7.2, H-C(6')), 7.19 (s, H-C(9')), 7.00 (d, ^{3}J = 6.9, H-C(7')), 2.27-1.58 (m, C_6H_{10}); ^{13}C-nmr (75.43 MHz, trichlorodeuteriomethane): 157.8 (s, C(7'a)), 150.7 (s, C(4')), 147.6 (s, C(3'a)), 145.2 (s, C(6')), 138.1 (s, C(8')), 130.5 (s, C(10')), 116.7 (s, C(9')), 115.4 (s, C(7')), 110.4 (s, C(2')), 32.7 (s, C(2), C(6)), 25.4 (s, C(4)), 24.6 (s, C(3), C(5)); ms: 253 (82) [M+], 227 (100).

Anal. Calcd. for $C_{14}H_{15}N_5$ (253.31): C, 66.38; H, 5.97; N, 27.65. Found: C, 66.65; H, 5.83; N, 27.81.

4'-Cyanospiro[cyclohexane-1,2'(3'*H*)-(1'*H*)-imidazo[4,5-*c*]pyridine] (**34**).

Compound **34** was obtained from **27** (10 g, 5.3 mmoles) in tetrahydrofuran (200 ml), trimethylsilylcyanide (900 mg, 7.8 mmoles) and manganese dioxide (4.6 g, 52.9 mmoles, 2 hours) as previously described. Chromatography (silica gel, ethyl acetate) and careful evaporation of the solvent provided brown crystals of pure **34** (254 mg, 22%), mp 222-224°; uv (acetonitrile): 242 (4.081), 286 (3,148), 342 (3,883); ir (potassium bromide): 3341 (N-H), 3048 (Aryl-H), 2920/2851 (C-H), 2212 (CN), 1604/1508/1449/1424 (C=C, C=N); 1209, 1073, 827; ^{1}H-nmr (299.95 MHz, dimethyl-d_6 sulfoxide): 7.71 (s, H-N(3')), 7.56 (s, H-N(1')), 7.47 (d, ^{3}J = 4.5, H-C(6')), 6.14(d, ^{3}J = 5.1, H-C(7')), 2.16-1.24 (m, C_6H_{10}); ^{13}C-nmr (62.89 MHz, dimethyl-d_6 sulfoxide): 146.6 (s, C(7'a)), 142.4 (s, C(3'a)), 142.9 (s, (C-6')), 118.1 (s, C(8')), 103.3 (s, C(4')), 99.7 (s, C(7')), 81.7 (s, C(2')), 39.2 (s, C(2), C-6)), 24.3 (s, C(4)), 21.8 (s, C(3), C(5)); ms: 214 (23) [M+], 171 (100).

Anal. Calcd. for $C_{12}H_{14}N_4$ (214.27): C, 67.27; H, 6.58; N, 26.15. Found: C, 67.50; H, 6.41; N, 26.02.

4'-[(1,2,4)-(Triazol-1-yl)]spiro[cyclohexane-1,2'(3'*H*)-(1'*H*)-imidazo[4,5-*c*]pyridine] (**35**).

Compound **35** was obtained from **27** (500 mg, 2.65 mmoles) in tetrahydrofuran (100 ml), trimethylsilyltriazole (370 mg, 2.65 mmoles), and manganese dioxide (2.3 g, 26.4 mmoles, 2 hours) as previously described. Chromatography (silica gel, ethyl acetate) and recrystallisation from diethyl ether provided colourless crystals **35** (174 mg, 26%), mp 145°; uv (acetonitrile): 3301 (4.054), 350 (3.810); ir (potassium bromide): 330/3250 (NH), 3124 (Aryl-H), 2924/2855 (C-H), 1617/1506/1495/1451 (C=C, C=N); 1272, 1027, 928, 807; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 9.06 (s, H-C(9')), 8.09 (s, H-C(8')), 7.62 (d, ^{3}J = 6.0, H- C(6')), 6.32 (d, ^{3}J = 4.8, H-C(7')), 5.75 (s, N-H), 4.86 (s, N-H), 1.90-1.44 (m, C_6H_{10}); ^{13}C-nmr (75.43 MHz, trichlorodeuteriomethane): 151.6 (s, C(8')), 148.8 (s, C(7'a)), 140.6 (s, C(9')), 139.9 (s, C(6')), 130.2 (s, C(3'a)), 125.1 (s, C(4')), 101.7 (s, C(7')), 81.9 (s, C(2')), 39.5 (s, C(2), C(6)), 24.7 (s, C(4)), 23.9 (s, C(3), C(5)); ms: 256 (25) [M+], 213 (100).

Anal. Calcd. for $C_{13}H_{16}N_6$ (256.31): C, 60.92; H, 6.29; N, 32.79. Found: C, 61.15; H; 6.47; N, 32.96.

4',4'''-Piperazin-(1,4)-yldispiro[cyclohexane-1,2'-*H*-imidazo-[4,5-*c*]pyridine (**36**).

Compound **36** was obtained from **27** (1.0 g, 5.3 mmoles) in tetrahydrofuran (300 ml), piperazine (230 mg, 2.65 mmoles), and manganese dioxide (4.6 g, 52.9 mmoles 2 hours) as previously described. Chromatography (silica gel, ethyl acetate) and recrystallisation from *n*-hexane yielded crimson needles **36** (221 mg, 18%), mp 195°; uv (acetonitrile): 234 (4.443), 474 (3.992); ir (potassium bromide): 3015 (Aryl-H), 2922/2856 (CH), 1653/1620/1534/1506/1444 (C=C, C=N), 1251; ^{1}H-nmr (250.13 MHz, trichlorodeuteriomethane): 7.50 (d, ^{3}J = 6.75, H-C(6'), H-C(6''')), 7.50 (d, ^{3}J = 6.75, H-C(7'), H-C(7''')), 4.35 (s, H-C(8'), H-C(9'), H-C(10'), H-C(11)), 2.27-1.58 (m, 2x-C_6H_{10}); ^{13}C-nmr (75.43 MHz, trichlorodeuteriomethane): 159,3 (s, C(7'a), C(7'''a)), 154.0 (s, C(4'), C(4''')), 153.2 (s, C(3'a), C(3'''a)), 148.4

(s, C(6'), C(6'")), 107.2 (s, C(2'), C(2'")), 105.6 (s, C(7'), C(7'")), 33,2 (s, C(8)', (C9'), (C10'), (C11')), 32.7 (s, C(2), C(6), C(2"), C(6")), 25.4 (s, C(4), C(4")), 24.6 (s, C(3), C(5), C(3"), C(5")); ms: 456 (65) [M+], 413 (100).

Anal. Calcd. for $C_{26}H_{32}N_8$ (456.59): C, 68.39; H, 7.06; N, 24.55. Found: C, 68.15; H, 6.96, N; 24.44.

7'-(Imidazol-1-yl)-5'-methoxyspiro[cyclohexane1,2-(3'*H*)-(1'*H*)imidazo[4,5-*b*]pyridine] (**37**).

To a solution of **9** (283 mg, 1.0 mmoles) in tetrahydrofuran/water 4:3 (135 ml) sodium dithionite (1.47 g, 8.4 mmoles) was added. The mixture is stirred at rt for 50 minutes and then made alkaline with potassium carbonate. Extraction with ethyl acetate, followed by evaporation and column chromatography (ethyl acetate/methanol 5:1) provided a beige powder **37** (2.8 mg , 1.0%), mp 153°; uv (acetonitrile): 231 (3.951), 282 (3.945), ir (potassium bromide): 3150/3114 (N-H), 3030 (Aryl-H), 2922/2849 (C-H), 1617/1506/1496/1452 (C=C, C=N), 1390, 1227, 1047; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 8.06 (s, H-C(8')), 7.42 (s, H-C(10')), 7.19 (s, H-C(9')), 5.88 (s, H-C(6')), 5.11 (s, N-H), 3.91 (s, OCH_3), 3.47 (s, N-H), 1.85-1.45 (m, C_6H_{10}); ^{13}Cnmr (62.89 MHz, trichlorodeuteriomethane): 160.4 (s, C(5')), 155.9 (s, C(3'a)), 136.0 (s, C(8')), 130.0 (s, C(10')), 128.3 (s, C(7'a)), 117.5 (s, C(9')), 116.5 (s, C(7')), 88.7 (s, C(6')), 79.5 (s, C(2')), 54.1 (s, C(11')), 39.4 (s, C(2), C(6)), 24.7 (s, C(4)), 22.9 (s, C(3), C(5)); ms: 285 (42) [M+], 242 (100); hrms: (peak matching): Calcd: 285.1588. Found: 285.1589 ($[C_{15}H_{19}N_5O]^+$).

7-(Imidazol-1-yl)-5-methoxy-3*H*-imidazo[4,5-*b*]pyridine (**38**).

As described for **37**, compound **9** (283 mg, 1.0 mmoles) in tetrahydrofuran/water 4:3 (135 ml) was reduced with sodium dithionite (1.47 g, 8.4 mmoles). The combined organic phase is carefully evaporated and dissolved in concentrated hydrochloric acid/water 2:3 (10 ml) and after addition of formic acid (10 ml) heated on an oil bath for 3 hours. After addition of potassium carbonate the alkaline solution was extracted with ethyl acetate. Recrystallisation from ethyl acetate yields **38** (107 mg, 50% based upon **9**) as a coloureless powder, mp 256°; uv (acetonitrile): 262 (4.006), 298 (3.891); ir (potassium bromide): 3148 (N-H), 3010 (Aryl-H), 2934/2804 (C-H), 1619/1597/1524/1480 (C=C, C=N), 1392, 1251, 1057; ^{1}H-nmr (299.95 MHz, dimethyl-d_6 sulfoxide): 13.27 (s, N-H), 9.06 (s, H-C(8)), 8.37 (s, H-C(10)), 8.32 (s, H-C(2)), 7.19 (s, H-C(9)), 7.14 (s, H-C(6)), 3.95 (s, OCH_3); ^{13}C-nmr (62.89 MHz, dimethyl-d_6 sulfoxide): 161.8 (s, C(5)), 146.2 (s, C(3a)), 140.7 (s, C(2)), 137.2 (s, C(8)), 135.6 (s, C(7)), 129.7 (s, C(10)), 120.9 (s, C(7a)), 118.2 (s, C(9)), 93.8 (s, C(8)), 53.7 (s, C(11)); ms: 215 (100) [M+].

Anal. Calcd. for $C_{10}H_9N_5O$ (215.21): C, 55.81; H, 4.21; N, 32.54. Found: C, 55.83; H, 4.33; N, 32.36.

13-(Imidazol-1-yl)-11-methoxydibenzo[*f,h*]pyrido[2,3-*b*]-quinoxaline (**39**).

As described for **37**, compound **9** (283 mg, 1.0 mmoles) in tetrahydrofuran/water 4:3 (135 ml) was reduced with sodium dithionite (1.47 g, 8.4 mmoles). The combined organic phase were carefully evaporated and dissolved in ethanol (10 ml) to which a sololution of 9,10-phenanthrenequinone (208 mg, 1.0 mmole) in hot acetic acid (10 ml) was added. The mixture is refluxed for 1 hour. The residue was filtered and subjected to column chromatography (silica gel, ethyl acetate/methanol 10:1). Recrystallisation from dichloromethane gave **39** (217 mg, 58% based upon **9**) as lemon-coloured crystals, mp 262°; uv (acetonitrile): 253 (4.668), 261 (4.683), 410 (4.241); ir (potassium bromide): 3010 (Aryl-H), 1617/1606/1553/1473 (C=C, C=N), 1398, 1359, 1260; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 9.37 (d, ^{3}J = 0.9, H-C(8)), 8.97 (d, ^{3}J = 1.2, H-C(1)), 8.72 (s, H-C(15)), 8.50 (m, H-C(4), H-C(5)), 7.78 (m, H-C(2), H-C(3), H-C(6), H-C(7), H-C(17)), 7.40 (s, H-C(17)), 7.17 (s, H-C(12)), 4.29 (s, OCH_3); ^{13}C-nmr (62.89 MHz, trichlorodeuteriomethane): 165.4 (s, C(11)), 144.5 (s, C(9a)), 143.2 (s, C(13a)), 140.3 (s, C(13)), 132,6 (s, C(8b)), 131.7 (s, C(14a)), 131.2 (s, C(17)), 130.4 (s, C(8)), 130.3 (s, C(1)), 129.3 (s, C(14b), C(8a)), 129.1 (s, C(4a) C(4b)), 128.3 (s, C(4)), 127.9 (s, C(5)), 127.3 (s, C(7)), 126.1 (s, C(2)),123.0 (s, C(3)), 122.9 (s, C(6)), 119.8 (s, C(l 6)), 108.8 (s, C(12)), 55.0 (s, C(18)); ms: 377 (100) [M+]; hrms: (peak matching): Calcd. 373.1275. Found: 373.1276 ($[C_{23}H_{15}N_5O]^+$)

8-(Imidazol-1-yl)-6-methoxypyrido[2,3-*b*]pyrazine (**40**).

As described for **37**, compound **9** (283 mg, 1.0 mmole) in tetrahydrofuran/water 4:3 (135 ml) was reduced with sodium dithionite (1.47 g, 8.4 mmoles). The combined organic phases were carefully evaporated and dissolved in tetrahydrofuran (20 ml) to which a solution of glyoxal sodium bisulfite (700 mg, 2.46 mmoles) in water (20 ml) was added. The mixture was stirred at 50-60° for 20 hours. After addition of ptassium carbonate the alkaline solution was extracted with ethyl acetate.

The organic phases were evaporated and the residual oil subjected to column chromatography (silica gel, ethyl acetate/methanol 5:2). Recrystallisation from ethyl acetate provided **40** (81 mg, 36% based upon **9**) as colourless needles, mp 212°; uv (acetonitrile): 319 (3.998), 329 (4.004); ir (potassium bromide): 3057 (Aryl-H), 2970/2860 (C-H), 1615/1548/1488 (C=C, C=N), 1387, 1326, 1277, 1112, 967, 869; ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 8.99 (d, ^{3}J = 1.8, H-C(3)), 8.82 (d, ^{3}J = 1.8, H-C(2)), 8.48 (s, H-C(9)), 7.65 (s, H-C(11)), 7.30 (s, H-C(10)), 7.19 (s, H-C(7)), 4.16 (s, OCH_3); ^{13}C-nmr (62.89 MHz, trichlorodeuteriomethane): 164.9 (s, C(6)), 151.5 (s, C(4a)), 147.3 (s, C(3)), 143.3 (s, C(8a)), 142.1 (s, C(2)), 138.8 (s, C(9)), 130.3 (s, C(7)), 130.2 (s, (10)), 119.5 (s, C(11)), 108.5 (s, C(6)), 54.9 (s, C(12)); ms: 227 (100) [M+].

Anal. Calcd. for $C_{11}H_9N_5O$ (227.23): C, 58.14; H, 3.99; N, 30.82. Found: C, 57.94; H, 3.92; N, 30.76.

Tetrazolo[1,5-*a*]spiro[cyclohexane-1,2'(3'*H*)-(1'*H*)-imidazo-[4,5-*c*]pyridine] (**41**).

To a solution of **32** (600 mg, 2.63 moles) in tetrahydrofuran/water 4:3 (320 ml) sodium dithionite (3.66 g, 21.03 mmoles) was added. The mixture was stirred at rt for 20 minutes and then made alkaline with potassium carbonate. Extraction with ethyl acetate, followed by evaporation and recrystallisation from methanol provided a light brown powder of **41** (414 mg 68%), mp 181°; uv (acetonitrile): 323 (3.909); ir (potassium bromide): 3260 (N-H), 2937/2854 (C-H), 1644/1570/1539/1440/1382 (C=C, C=N), 1240, 1115; ^{1}H-nmr (250.13 MHz, dimethyl-d_6 sulfoxide): 8.45 (d, ^{3}J = 6.8, H-C(6')), 6.80 (s, N-H), 6.70 (d, ^{3}J = 6.8, H-C(7')), 6.65 (s, N-H), 1.71-1.39 (m, C_6H_{10}); ^{13}C-nmr (62.89 MHz, dimethyl-d_6 sulfoxide): 139.7 (s, C(7'a)), 138.7 (s, C(3'a)), 120.6 (s, C(4')), 116.1 (s, C(6')), 102.9 (s, C(7')), 83.7 (s, C(2')), 38.8 (s, C(2), C(6)), 24.5 (s, C(4)), 21.8 (s, C(3), C(5)); ms: 230 (61) [M+], 159 (100).

Anal. Calcd. for $C_{11}H_{14}N_6$ (230.27): C, 57.37; H, 6.13; N, 36.50. Found: C, 57.29; H, 5.99; N, 36.21.

Tetrazolo[1,5-*a*]pyrido[2,3-*b*]pyrazine (**42**).

As described for **41**, compound **32** (1.0 g, 4.39 mmoles) in tetrahydrofuran/water 4:3 (410 ml) was reduced with sodium dithionite (14.7 g, 84,48 mmoles). The combined organic phase was carefully evaporated and dissolved in tetrahydrofuran (80 ml) to which a solution of glyoxal sodium bisulfite (2.8 g, 9.84 mmoles) in water (20 ml) was added. The mixture was stirred at 50-60° for 20 hours; After addition of potassium carbonate the alkaline solution was extracted with ethyl acetate, the organic phase evaporated and the residual oil subjected to column chromatography (silica gel, ethyl acetate/methanol 5:2). The first band was recrystallised from ethyl acetate; light brown powder **42** (495 mg, 66% based upon **32**), mp 257-258°; uv (acetonitrile): 316 (3.834), 238 (3.969); ir (potassium bromide): 3062, 1628/1543/1511/1477 (C=C, C=N), 1368, 1213, 1160, 1114; ^{1}H-nmr (299.95 MHz, dimethyl-d_6 sulfoxide): 9.43 (d, ^{3}J = 7.5, H-C(7)), 9.27 (d, ^{3}J = 2.1, H-C(2)), 9.21 (d, ^{3}J = 2.1, H-C(3)), 7.87 (d, ^{3}J = 7.5, H-C(8)); ^{13}C-nmr (75.43 MHz, dimethyl-d_6 sulfoxide): 148.7 (s, C(7)), 147.7 (s, C(4a)), 146.1 (s, C(3)), 143.9 (s, C(5)), 132.7 (s, C(8a)), 126.6 (s, C(2)), 117.6 (s, C(8)); ms: 172 (17) [M$^+$], 143 (100).

Anal. Calcd. for $C_7H_4N_6$ (172.15): C, 48.84; H, 2.34; N, 48.82. Found: C, 48.56; H, 2.12; N, 48.70.

8-Aminopyrido[2,3-*b*]pyrazine (**43**).

As described for **42**, compund **32** (1.0 g, 4.39 mmoles) in tetrahydrofuran/water 4:3 (410 ml) was reduced with sodium dithionite (14.7 g, 84.48 mmoles). The combined organic phasee were carefully evaporated and dissolved in tetrahydrofuran (80 ml) to which a solution of glyoxal sodium bisulfite (2.8 g, 9.84 mmoles) in water (20 ml) was added. The second band of the column chromatography (silica gel, ethyl acetate/methanol 5:2) yielded, after recrystallisation from ethyl acetate **43** (70 mg, 11% based upon **32**) as a lemon coloured powder, mp 222-224°; uv (acetonitrile): 234 (3.944), 255 (4.344), 354 (3.542); ir (potassium bromide): 3323/3185 (NH_2), 1660/1593/1550/1516 (C=C, C=N), 1344, 1200, 1140; ^{1}H-nmr (299.95 MHz, dimethyl-d_6 sulfoxide): 8.99 (d, ^{3}J = 1.8, H-C(2)), 8.99 (d, ^{3}J = 1.8, H-C(3)), 8.99 (d, ^{3}J = 5.4, H-C(6)), 7.23 (s, NH_2), 6.80 (d, ^{3}J = 5.4, H-C(7)); ^{13}C-nmr (75.43 MHz, dimethyl-d_6 sulfoxide): 153.4 (s, C(6)), 152.7 (s, C(8)), 151.2 (s, C(4a)), 147.7 (s, C(3)), 141.5 (s, C(2)), 128.7 (s, C(8a)), 104.2 (s, C(7)); ms: 146 (100) [M$^+$].

Anal. Calcd. for $C_7H_6N_4$ (146.15): C, 57.53; H, 4.14; N, 38.33. Found: C, 57.46 H; 4.12; N, 38.50.

7-Amino-2,1,3-selenadiazolo[3,4-*b*]pyridine (**44**).

As described for **41**, compound **32** (1.0 g, 4.39 mmoles) in tetrahydrofuran/water 4:3 (410 ml) was reduced with sodium dithionite (14.7 g, 84.48 mmoles). The combined organic phase was carefully evaporated, the residue was dissolved in ethanol (60 ml) to which a solution of selenium oxide (450 mg, 4.05 mmoles) in water (4.5 ml) was added. The mixture was refluxed for 3 hours. After addition of potassium carbonate the alkaline solution was extracted with ethyl acetate, the organic phases evaporated and the residual oil subjected to column chromatography (silica gel, ethyl acetate/methanol 5:2). Recrystallisation from ethyl acetate gave **44** (65 mg, 8.9% based upon **32**) as a yellow powder, mp 225°; uv (acetonitrile): 238 (4.458), 329 (4.136); ir (potassium bromide): 3412/3302 (NH_2), 3187 (CH), 1684/1631/1581/1537/1491 (C=C, C=N), 1347,1297, 1135, 879; ^{1}H-nmr (250.13 MHz, dimethyl-d_6 sulfoxide): 8.43 (d, ^{3}J = 5.1, H-C(5)), 7.19 (s, NH_2), 6.29 (d, ^{3}J = 5.0, H-C(3)); ^{13}C-nmr (62.89 MHz, (dimethyl-d_6 sulfoxide): 165.4 (s, C(3a)), 157.6 (s, C(5)), 148.6 (s, C(7)), 148.0 (s, C(7a)), 98.5 (s, C(6)); ms: 200 (100) [M$^+$, 80_{Se}].

Anal. Calcd. for $C_5H_4N_4Se$ (199.07): C, 30.17; H, 2.02; N, 28.14. Found: C, 30.09; H, 1.54; N, 27.94.

Charge Transfer Complex between 7'-(Imidazol-1-yl)-5'-methoxyspiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-*b*]pyridine] (**9**) and 7'-(Imidazol-1-yl)-5'-methoxyspiro[cyclohexane-1,2'(3'*H*)-(1'*H*)-imidazo[4,5-*b*]pyridine] (**37**) (2:1).

To a solution of **9** (283 mg, 1.0 mmoles) in tetrahydrofuran/water 4:3 (135 ml) sodium dithionite (1.47 g, 8.4 mmoles) was added. The mixture was stirred at rt for 50 minutes and then made alkaline with potassium carbonate. Extraction with ethyl acetate was followed by evaporation and column chromatography (ethyl acetate/methanol 5:1). The second band leads to a wine-red complex between **9** and **37** (183 mg , 64%), mp 139°; uv (acetonitrile): 231, 282, 469; ir (potassium bromide): 3358/3114 (N-H), 2935/2855 (C-H), 1636/1612/1566/1528/1517/1483/1455 (C=C, C=N), 1390, 1278, 1226; compound **9** exhibited ^{1}H-nmr (299.95 MHz, trichlorodeuteriomethane): 8.90 (s, H-C(8')), 7.69 (s, H-C(10')), 7.24 (s, H-C(9')), 6.63 (s, H-C(6')), 4.12 (s, OCH_3), 1.98-1.62 (m, C_6H_{10}); compound **37** exhibited 8.06 (s, H-C(8')), 7.42 (s, H-C(10')), 7.19 (s, H-C(9')), 5.88 (s, H-C(6')), 5.11 (s, N-H), 3.91 (s, OCH_3), 3.47 (s, N-H), 1.85-1.45 (m, C_6H_{10}); compound **9** exhibited ^{13}C-nmr (62.89 MHz, trichlorodeuteriomethane): 170.2 (s, C(5')), 160.4 (s, C(3'a)), 150.3 (s, C(7'a)), 138.5 (s, C(7')), 138.0 (s, C(8')), 131.3 (s, C(10')), 116.5 (s, C(9')), 109.3 (s, C(6')), 105.5 (s, C(2')), 55.6 (s, C(11')), 33.6 (s, C(2), C(6)), 25.5 (s, C(4)), 24.4 (s, C(3), C(5)); compound **37** exhibited 160.4 (s, C(5')), 155.9 (s, C(3'a)), 136.0 (s, C(8')), 130.0 (s, C(10')), 128.3 (s, C(7'a)), 117.5 (s, C(9')), 116.5 (s, C(7')), 88.7 (s, C(6')), 79.5 (s, C(2')), 54.1 (s, C(11')), 39.4 (s, C(2), C(6)), 24.7 (s, C(4)), 22.9 (s, C(3), C(5)); ms: 285 (48) [M$^+$ (37)], 283 (45) [M+ (8)], 242 (100).

Anal. Calcd. for $C_{45}H_{53}N_{15}O_3$ (852.01): C, 63.44; H, 6.27; N, 24.66. Found: C, 63.67; H, 5.99; N, 24.75.

4'-(Imidazol-1-yl)spiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-*c*]-pyridine] (**33**) and 4'-[(1,2,4)-(Triazol-1-yl)]spiro[cyclohexane-1,2'(3'*H*)-(1'*H*)-imidazo [4,5-*c*]pyridine] (**35**) (1:1).

4'-(Imidazol-1-yl)spiro[cyclohexane-1,2'-2'*H*-imidazo[4,5-*c*]-pyridinel **33** (29.6 mg, 0.12 mmole) and 4'-[(1,2,4)(Triazol-1-yl)]spiro[cyclohexane-1,2'(3'*H*)-(1'*H*)-imidazo[4,5-*c*]pyridin] **35** (30.0 mg, 0.12 mmoles) were dissolved in tetrahydrofuran (20 ml). Careful evaporation of the solvent led to a blue-black complex of **33** and **35** (59.6 mg, 100%), mp 114°; uv (acetonitrile): 237, 392, 584; ir (potassium bromide): 3419/3226 (N-H), 3189 (Aryl-H), 2925/2855(CH), 1627/1608/1521/1500/1472/1457/1448/1429 (C=C, C=N); 1308, 1276; ^{1}H-nmr (299,95 MHz, trichlorodeuteriomethane): compound **33** exhibited 9.15 (s, H-C(8')), 8.17 (s, H-C(10')), 7.79 (d, ^{3}J= 7.2, H-C(6')), 7.19 (s, H-C(9')), 7.00 (d, ^{3}J = 6.9, H-C(7')), 2.27-1.58 (m, C_6H_{10}); 9.06 (s, H-C(9')), 8.09 (s, H-C(8')), 7.62 (d, ^{3}J= 6.0, H-C(6')), 6.32 (d, ^{3}J = 4.8, H-C(7')), 5.75 (s, N-H), 4.86 (s, N-H), 1.90-1.44 (m, C_6H_{10}); ^{13}C-nmr (75,43 MHz, trichlorodeuteriomethane): compound **33** exhibited 157.8 (s, C(7'a)), 150.7 (s, C(4')), 147.6 (s, C(3'a)), 145.2 (s, C(6')), 138.1 (s, C (8')), 130.5 (s, C (10')), 116.7 (s, C (9')), 115.4 (s, C(7')), 110.4 (s, C(2')), 32.7 (s, C(2),. C(6)), 25.4 (s, C(4)), 24.6 (s, C(3), C(5)). (35): 151.6 (s, C(8')), 148.8 (s, C(7'a)), 140.6 (s, C(9')), 139.9 (s, C(6')), 130.2 (s, C(3'a)), 125.1 (s, C(4')), 101.7 (s, C(7)),

81.9 (s, C(2')), 39.5 (s, C(2), C(6)), 24.7 (s, C(4)), 23.9 (s, C(3), C(5)); ms: 256 (27) [M^+ (35)], 253 (37) [M^+ (33)], 213 (100).

Anal. Calcd. for $C_{27}H_{31}N_{11}$ (509.62): C, 63.63; H, 6.13; N, 30.23. Found: C, 63.36; H, 5.86; N, 30.07.

Acknowledgement.

We thank Mrs. U. Hertle for ^1H- and ^{13}C-nmr spectra, H. Rudy and P. Weyfich for ms- and CHN-analyses and Dr. E. F. V. Scriven (Reilly and Tar, Indianapolis) for generous gifts of *o*-diaminopyridines. Support. of this work by BASF AG, Bayer AG and Hoechst AG with gifts of solvents 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.

REFERENCES AND NOTES

[1] S. Schwoch, W. Kramer, R. Neidlein, and H. Suschitzky, *Helv. Chim. Acta,* **77**, 2175 (1994).

[2] D. L. Bussolotti, J. L. La Mattina, and K. James, *Tetrahedron Letters,* **32**, 6503 (1991).

[3] K. E. Davies, G. E. Domany, M. Farhat, J. A. L. Herbert, A. M. Jefferson, M. de Los A. G. Martin, and H. Suschitzky, *J. Chem. Soc. Perkin Trans. 1,* 2465 (1984); H. Suschitzky, Croat *Chem. Acta,* **59**, 57 (1986).

[4] H. Suschitzky, W. Kramer, R. Neidlein, and H. Uhl, *J. Chem. Soc., Perkin Trans. 1,* 983 (1988).

[5] A. Cada, W. Kramer, R. Neidlein, and H. Suschitzky, *Helv. Chim. Acta,* **73**, 902 (1990).

[6] B. Iddon, P. Kutschy, A. G. Robinson, H. Suschitzky, W. Kramer, and F. A. Neugebauer, *J. Chem. Soc., Perkin Trans 1,* 3129 (1992).

[7] E. Mutschler, Arzneimittelwirkunaen, 6 th Ed, Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, 1991, p 479; H. J. Roth, and H. Fenner, Arzneistoffe, 1st, Ed, G. Thierne Verlag, Stuttgart, 1985, p 115.

[8] H. A. Staab and P. Rohr, Prep. *Org. Chem.,* **5**, 61 (1968); R. C. Morton, D. Mangroo, and G. E. Gerber, *Can. J. Chem.,* **66**,1701 (1988).

[9] J. March, Advanced Organic Chemistry, 4th, Ed, Interscience Publicaton, J. Wiley & Sons, New York, 1992, p 646.

[10] T. Kauffmann, and F. P. Boettcher, *Chem. Ber.* **95**, 1528 (1962).

[11] G. Wittig and R. Ludwig, *Angew. Chem.,* **68**, 40 (1956).

[12] R. J. Mortens and H. J. den Hertog, *Tetrahedron Letters,* 643 (1962); H. M. N. v. d. Lans, and H. J. den Hertog, *Recl. Trav. Chim. Pays-Bas,* **87**, 549 (1968); T. Kauffmann and F. P. Boettcher, *Angew. Chem.,* **73**, 65 (1961).

[13] T. Kauffmann, A. Risberg, J. Schulz, and R. Weber, *Tetrahedron Letters,* 3563 (1964).

[14] G. Allan, D. Cambridge, M. J. Follenfant, D. Stone, and M. V. Whiting, *Br. J. Pharmacol,* **93**, 387 (1988).

[15] P. Barraclough, S. Smith, J. M. Gillam, D. Kettle, and M. S. Nobbs, *J. Chem. Res. (S),* 426 (1994).

[16] D. A. Roberts, S. T. Russell, A. H. Ratcliffe, K. H. Gibson, and R. Wood, European Patent Application EP 0399731, May 5, 1990 to ICI.

[17] P. J. Black and L. J. Heffernan, *Aust. J. Chem.,* **15**, 862 (1962).

[18] J. A. L. Herbert and H. Suschitzky, *Chem. Ind.,* 482(1973).

[19] J. C. Barnes and A. Hetherington, *Acta Oystallogr.,* **34**, 2146 (1978).

[20] J. N. Murrell, *J. Chem. Soc.,* 191 (1961).