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Nucleophilic reactions of two 2,2'-bisbenzimidazole systems, namely the bis(2*H*-benzimidazole-2-ylidene) **2** and the dispiro[2*H*-benzimidazole-2,1'-cyclohexane-4',2"-2"*H*-benzimidazole] **3**, as well as the syntheses of new 2,2'-bisbenzimidazoles are reported and their conversion into other heterocycles is described.

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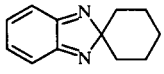
Introduction.

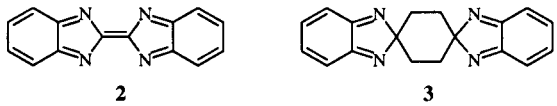
The results reported stem from our continuing interest in the convenient preparation of nucleophilically substituted heterocycles in acceptable yields. We have now used dimeric systems containing two 2*H*-benzimidazole moieties based on the 2*H*-benzimidazole-2-spirocyclohexane ("isobenzimidazole") **1**, which is a convenient starting material for such heterocycles [1-8].



1

Figure 1

Two such compounds have already been reported, namely the bis(2*H*-benzimidazol-2-ylidene) **2** made by Hill [9] and the dispiro[2*H*-benzimidazole-2,1'-cyclohexane-4',2"-2"*H*-benzimidazole] **3** prepared by Herbert [3]. While **3** is stabilized by a sp^3-hybridisized carbon as in **1**, compound **2** is of sp^2-hybridisation. Both compounds possess of an *o*-quinonediimine system wich makes it prone to nucleophilic attack.



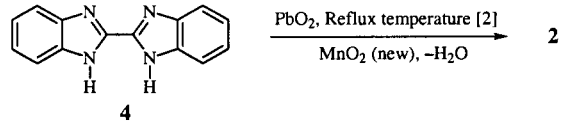
2 **3**

Figure 2

Synthesis and Reactions of Bis(2*H*-benzimidazol-2-ylidene) **2**.

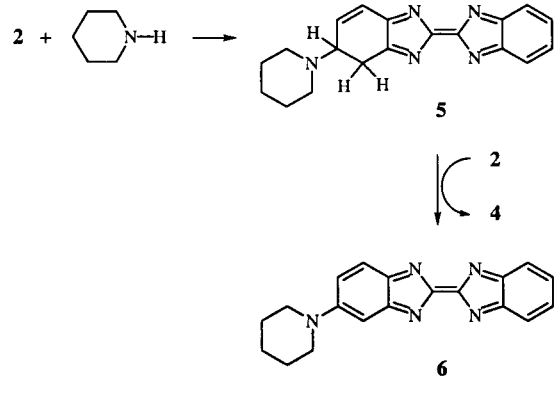
Hill [9] described the oxidation of **4**, carried out according to Lane [10] with lead oxide in benzene in 65% yield. However, we obtained only a maximum yield of 20%. On changing the oxidizing agent to activated manganese dioxide [11] in chloroform and using a bonding agent for the water liberated (molecular sieves 4 Å), we obtained a yield of 30% of **2** at room temperature.

Scheme 1



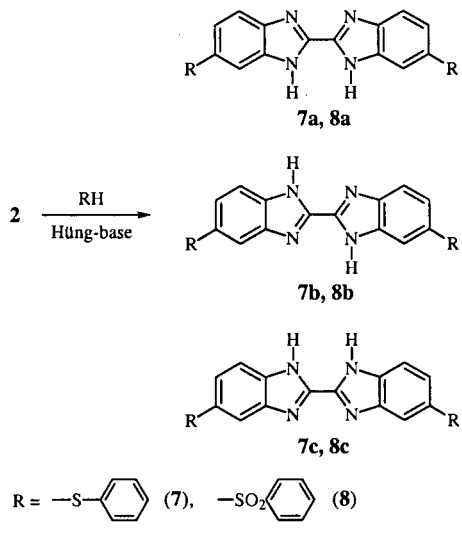
To bring about nucleophilic substitution we used piperidine and morpholine as *N*-nucleophiles and the *S*-nucleophiles thiophenol and benzene sulfinic acid. In the case of piperidine we found that addition of an equimolar quantity of *N*-ethyl diisopropylamine ("Hünig base") and 20-fold excess of manganese oxide give the highest yield (41%) of the 2-(2*H*-benzimidazol-2-ylidene)-5-piperidino-2*H*-benzimidazole **6** according to the following mechanism (Scheme 2).

Scheme 2



The large excess of the oxidizing agent regenerates the starting material **2** from its dihydrointermediate **4**, while the base is useful for generating a carbanion for the nucleophilic addition. Disubstitution in the case of piperidine and morpholine occurred only to a very small extent, as indicated by us. The conditions for the reactions with *S*-nucleophiles were similar, but without addition of manganese dioxide as these compounds are easily oxidisable; the results are shown in Scheme 3.

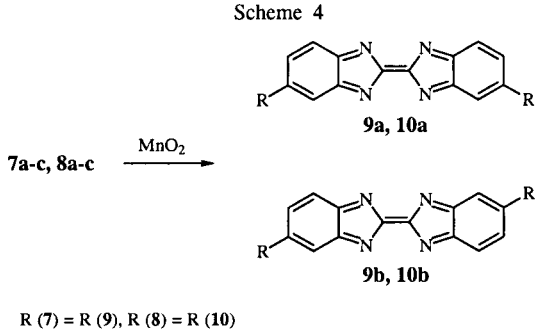
Scheme 3



As shown in Scheme 3 all possible tautomers of the disubstitution product were produced as indicated by signals in the ^1H and ^{13}C nmr spectra.

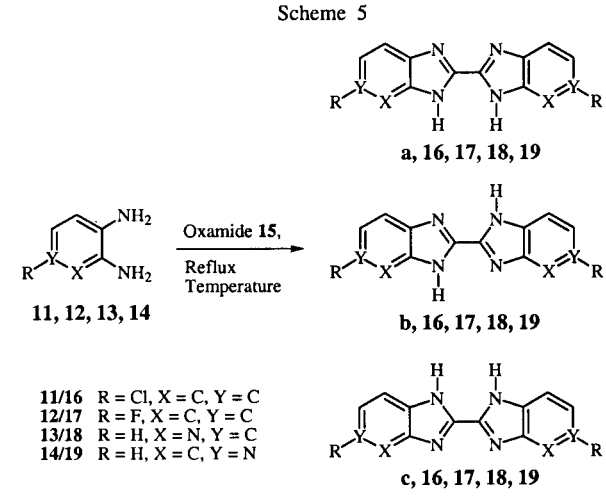
An indirect proof for the existence of all tautomeric forms is the oxidation of **7** and **8** to give **9** and **10**, *i.e.* the two isomeres *Z* and *E* (Scheme 4). The ^{13}C nmr provides evidence for all isolated products being mixtures of the isomeres **a** to **c** which, however, could not be separated by recrystallisation or chromatography.

Scheme 4



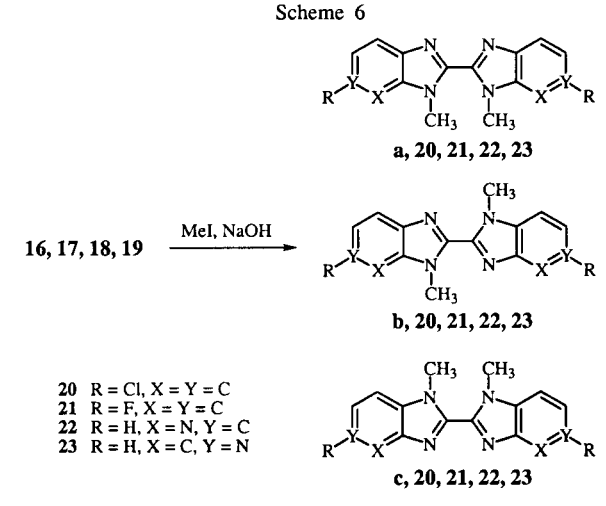
The preparative significance of the isobenzimidazoles lies in the ease of their reductive ring-opening by sodium dithionite to give the correspondending *o*-phenylenediamine [4], [7], [8]. However, the compounds mentioned above re-aromatised spontaneously when subjected to reduction. We also prepared bisbenzimidazoles with leaving groups like chlorine and fluorine or aza-analogues. These atoms are of special interest for the exact structural assignments in the nmr. Suitable starting materials are 4-chloro-*o*-phenylenediamine **11**, 4-fluoro-*o*-phenylenediamine **12**, 2,3-diaminopyridine **13** and 3,4-diaminopyridine **14**. By following Lane's method [10], *i.e.* condensation with oxamide **15**, we obtained new compounds in all tautomeric forms **16-19a-c**, which are potential starting materials for derivatives and analogues of **2**.

Scheme 5



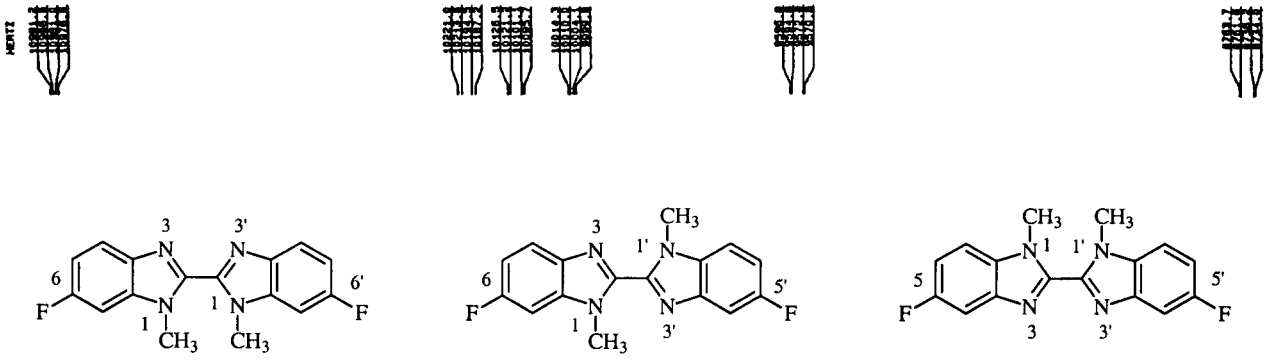
As it was not possible to separate the isomeric mixtures, we methylated the NH-groups to obtain compounds **20** to **23** of greater steric demand. These methylated isomers also defied separation. However, the presence of a fluorine substituent enabled us to assign the ^{13}C-nmr signals of each of the **20a** to **20c** isomers, owing to the characteristic ^{13}C-^{19}F-long range couplings and ^{13}C-chemical shifts.

Scheme 6



Thus the ^{13}C nmr spectrum of compound **21** showed three sets of signals, one for each isomer **a, b, c**. All signals exept for C-2, C-2' and CH_3 are split by ^{13}C-^{19}F-coupling. Thus the carbon atoms can be identified as directly bonded C-atoms ($^1J_{C-F}$ = 238.4 Hz) and as those which are separated by two ($^2J_{C-F}$ = 24.0...27.6 Hz) and three ($^3J_{C-F}$ = 10.2 Hz) bonds from the fluorine atom. The signals for the tertiary carbon atoms can be assigned on the reasonable assumption that the inductive effect of fluorine is similar to that in fluorobenzene [12] (upfield shift of the proton in the *o*-position ~ 13 ppm, small downfield shift of the proton in the *m*-position ~ 2 ppm) and that the electron donating effect of an sp^3-hybridized *N*-atom is larger than that of an sp^2-hybridized one. Moreover it appears that the relaxation times not only of the topologically corresponding carbon atoms in the different moieties of **21a** to **21c** (for instance C-7 in **21a** and **C-7** in **21b**) are of the same magnitude, but also the relaxation times of all tertiary carbon atoms seem to be of the same order of magnitude. With regard to the ^{13}C-nmr spectrum shown in Figure 3, we shall discuss the assignment of the tertiary carbon atoms of the fluoro compounds **21a-c.**

The spectrum shows two sets of three signals of large and medium intensities and one of small intensity containing six signals, which we assign to **21b** as it is the only asymmetric one (**21a** and **21c** are symmetric). The medium and the small doublets in the highest field (~96 ppm) derive from two chemically equivalent carbon atoms in **21a** (C-7, C-7') and one in **21b** (C-7). They show a typical coupling constant (27.6 Hz) and also a highfield shift due to the N-CH_3-group in neighbourhood and the C-F-group in the *o*-position. The C-5, C-5' in **21a** and the C-5 in **21b** are also in the *o*-position to the C-F-group, but do not show the highfield shift of the methyl group. Hence it is the correct assignment at 111.5 ppm. The signals at 121 ppm stem from two equivalent carbon atoms in **21c** (C-4, C-4') and one in **21b** (C-4'). They are in the *meta*-position to the C-F-group and are only slightly shifted downfield. C-7, C-7' in **21c** and C-7' in **21b** are easily assigned. They are characterized by being in the *meta*-position to the C-F-group and also by a small high field shift. Both the



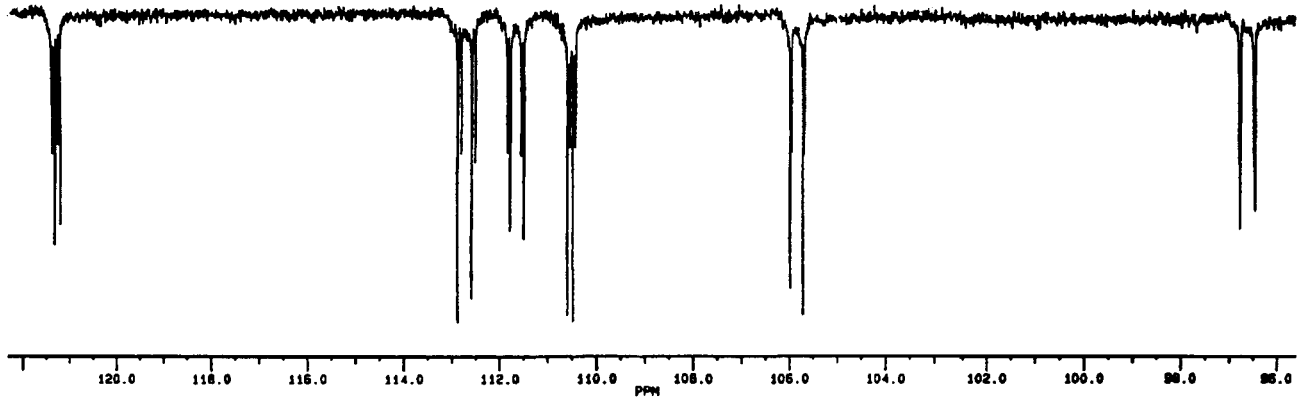


Figure 3

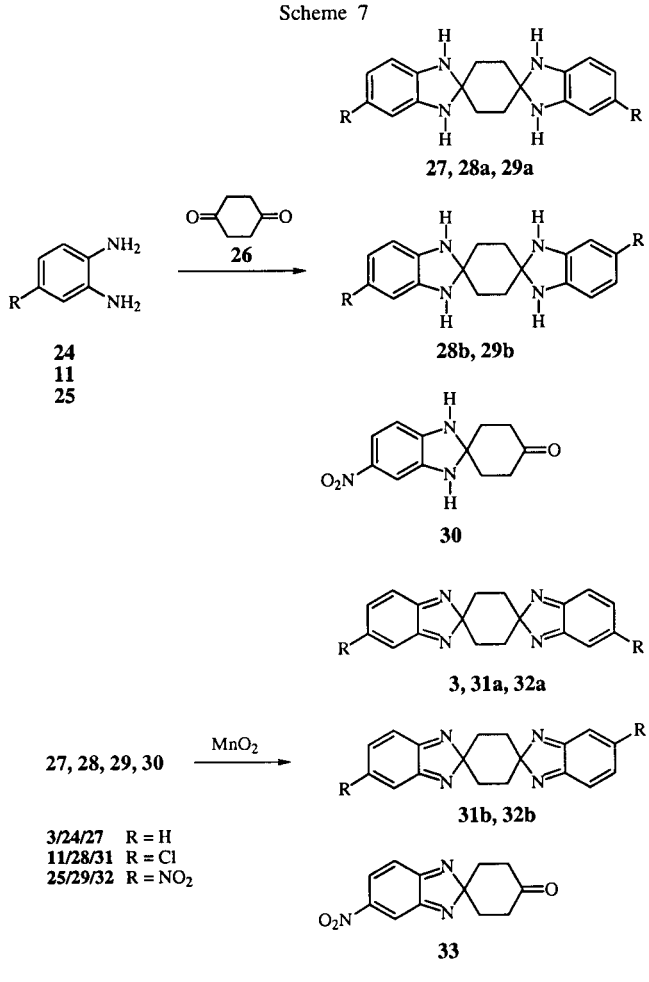
larger groups of signals with an *o*-coupling constant in **21c** (C-4, C-4') and C-4' in **21b** as well as the C-6, the C-6' in **21c** and the C-6' in **21b** are assignable by their different chemical shifts. A down-field shift larger than that of the C-6-set is shown by the C-4-set because of the C-4-being adjacent to the *N*-methyl group.

We have tried to oxidize compounds **16, 17, 18** and **19** with manganese dioxide, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone and chloranil. However, we did not obtain any analogues of **2**, probably owing to the stability of the aromatic system.

Synthesis and Reactions of Dispiro[2*H*-benzimidazole-2,1'-cyclohexane-4',2"-2"*H*-benzimidazole] **3**.

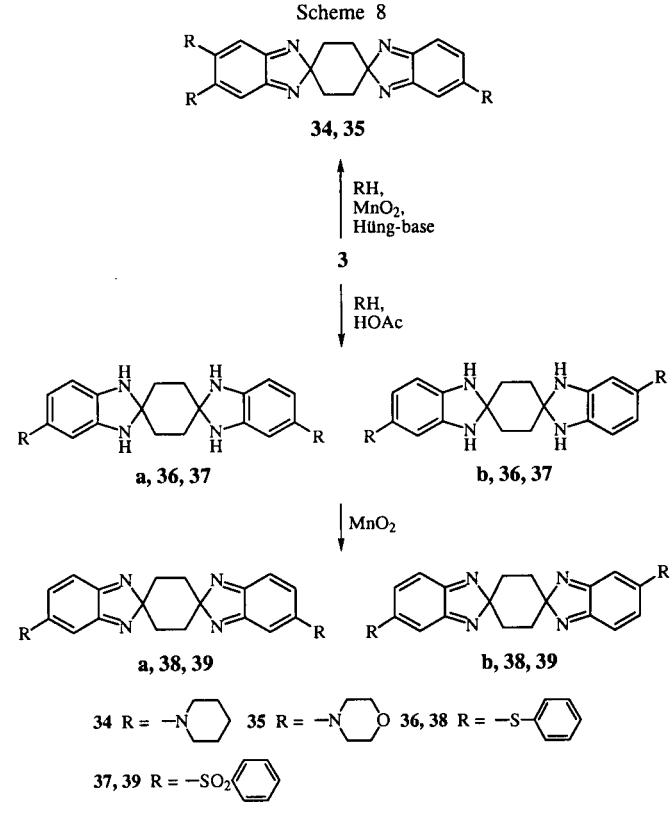
As described by Jefferson [3] it is possible to condense the cyclohexane-1,4-dione **26** with *o*-phenylenediamine **24** and oxidise the intermediate to give the dispirosystem **3**. We also used 4-chloro-*o*-phenylenediamine **11** (R = Cl) and 4-nitro-*o*-phenylenediamine **25** (R = NO_2) and obtained in each case both steric forms (*Z* and *E*) in equal yields. All attempts to separate them failed. Unexpectedly we obtained a stable mono addition product **30** in the reaction between **25** and **26** and its oxidised form **33**.

Scheme 7



Nucleophilic reactions with piperidine, morpholine, thiophenol and benzene-sulfinic acid were carried out with compounds **3** and **31a/b**. As compound **3** is much less reactive than isobenzimidazole, a ten times excess of the *N*-nucleophile and an equimolar amount of "Hünig base" were essential for the reaction to succeed. In the case of thiophenol only a single addition to each side of the molecule occurred unlike that in the case of isobenzimidazole. Results are shown in Scheme 8.

Scheme 8



The chlorine atom in compound **31a/b** is not replaced by the nucleophiles used, as can be seen in Scheme 9.

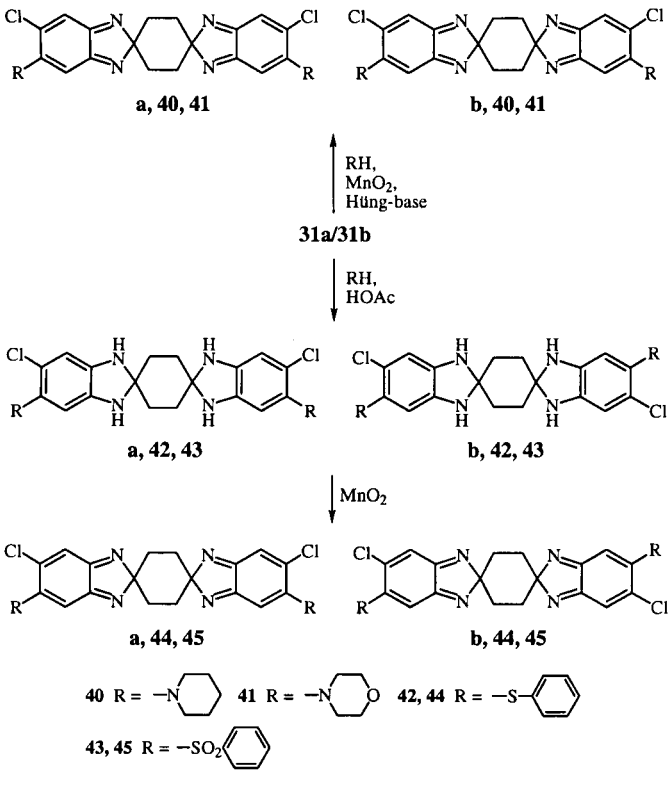
We found two methods for inserting the azido group into the bisbenzimidazole **3**. Suitable starting materials are compounds **39a/b** and **31a/b**, which react with trimethylsilyl azide to give a mixture of **46a** and **46b**.

In all cases of nucleophilic reactions in **3** and **31a/b** inseparable mixtures of *Z*- and *E*-isomeres were obtained. Compounds **40a/b** were ring-opened by sodium dithionite to give the 4-chloro-5-piperidino-*o*-phenylenediamine **47**, which on condensation with formic acid gave the benzimidazole derivative **48**.

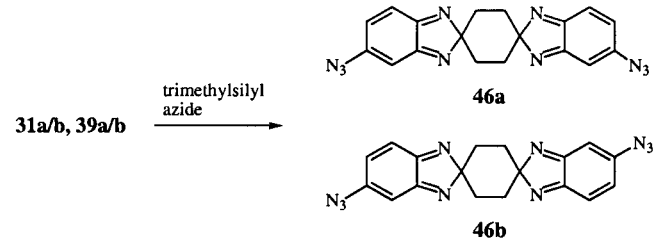
All derivates of **31a/b** are potential starting materials for preparing new heterocycles.

We also prepared the *N*-oxides **49-51** from the starting materials **2, 3** and **31a/b** as shown in Scheme 12 [13].

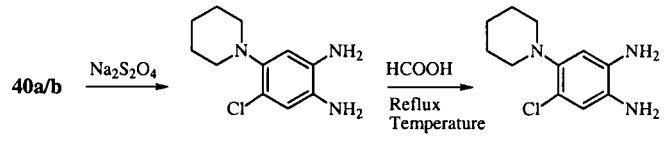
Scheme 9



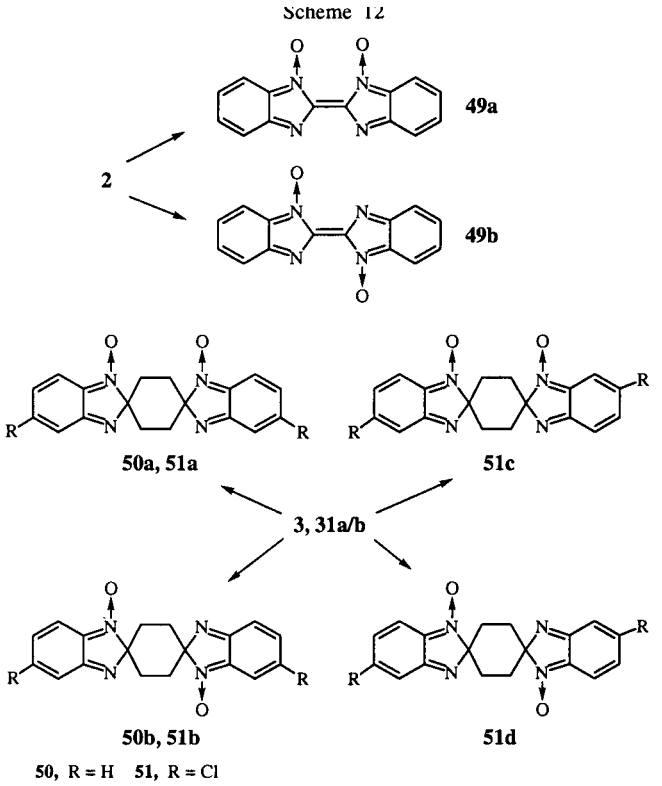
Scheme 10



Scheme 11



Scheme 12



EXPERIMENTAL

Melting points were determined on a Reichert hot stage microscope and are uncorrected. Inftared spectra were measured with a Perkin-Elmer spectrophotometer 283 using potassium bromide and are given as cm^{-1}. The ^1H and ^{13}C nmr spectra were recorded on either a Bruker WM-250 (^1H nmr: 250.13 MHz, ^{13}C nmr: 62.89 MHz) or a Varian XL 300 (^1H nmr: 299.95 MHz, ^{13}C nmr: 75.43 MHz) spectrometer. The chemical shifts are reported in parts per million (ppm) downfield from tetramethysilane and coupling constants J are given in Hz. Electron impact mass spectra were optained on a Varian MAT 311A instrument. Elemental analyses were performed on a Heraeus Vario EL CHNS apparatus.

2-(2*H*-Benzimidazole-2-ylidene)-5-piperidino-2*H*-benzimidazole (**6**).

To a solution of 2,2'-bisbenzimidazolylidene (**2**) (0.232 g, 0.001 mole) in dry tetrahydrofuran (100 ml) were added 0.258 g (0.002 mole) of *N*-ethyl diisopropylamine, 0.51 g (0.006 mole) piperidine and 1.74 g (0.02 mole) manganese dioxide and the mixture was stirred at room temperature for 5 days. The reaction mixture was filtered and the filtrate was evaporated to dryness. The residue was purified on a silica column with ethyl acetate and recrystallized from ethyl acetate as deep blue needles, 0.13 g (41%), mp 236°; ir: ν 2935 and 2853 (CH_2), 1618 (C=C), 1482 (C=N); ^1H nmr (deuteriochloroform): δ 8.33 (m, 1H, 6-H), 8.11 (d, $^3J_{6,7}$ = 9.6 Hz, 1H, 7-H), 7.84 (m, 4H, 4',5',6',7'-H), 7.25 (d, $^4J_{4,6}$ = 2.7 Hz, 1H, 4-H), 3.65 (m, 4H, 2",6"-H), 1.92 (m, 6H, 3",4",5"-H); ^{13}C nmr (deuteriochloroform): 152.8, 150.0, 147.0, 146.4, 145.4, 144.9, 143.0 (C-2,3a,7a,5,2',3'a, 7'a), 131.9, 131.4, 130.6, 130.2, 129.8 (C-7,4',5',6',7'), 127.6 (C-6), 103.3 (C-4), 49.1 (C-2",6"), 25.6, 24.3 (C-3",4",5"); ms: m/z 317 ($[M+2]^+$), 316 ($[M+1]^+$), 315 ($[M]^+$), 314 ($[M-1]^+$), 259 ($[M-C_3H_6N]^+$), 231 ($[M-C_5H_{10}N]^+$).

Anal. Calcd. for $C_{19}H_{17}N_5$: C, 72.36; H, 5.43; N, 22.21. Found: C, 71.97; H, 5.67; N, 21.76.

2,2'-Bis(6-phenylsulfanyl-1*H*-benzimidazole) (**7a**), 6-Phenylsulfanyl-2-(5-phenylsulfanyl-1*H*-benzimidazol-2-yl)-1*H*-benzimidazole and (**7b**), and 2,2'-Bis(5-phenylsulfanyl-1*H*-benzimidazole) (**7c**).

To a solution of 2,2'-bisbenzimidazolylidene (**2**) (0.232 g, 0.001 mole) in dry tetrahydrofuran (100 ml) were added 0.258 g

(0.002 mole) *N*-ethyldiisopropylamine and 0.22 g (0.002 mole) of thiophenol and the mixture was stirred at room temperature for 10 minutes turning yellow. The solution was evaporated to dryness and the yellow residue was purified on a silica column with a mixture of ethyl acetate/*n*-hexane (1:1) and recrystallized from *n*-hexane as a yellow powder to yield 0.2 g (44%), mp 242°; ir: ν 3409 (NH), 3056 (CH), 1617 (C=C), 1583 (C=N); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 10.1 (s, 6H, NH), 7.77 (m, 6H, 5,5'-H**a**/5,6'-H**b**/6,6'-H**c**), 7.58 (m, 6H, 4,4'-H**a**/4,7'-H**b**/7,7'-H**c**), 7.41 (m, 6H, 7,7'-H**a**/7,4'-H**b**/4,4'-H**c**), 7.24 (m, 12H, 2",6"-H**a/b/c**), 6.77 (m, 18H, 3",4",5"-H**a/b/c**); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 144.3, 143.8, 143.7, 143.4 (C-3a,7a,1"**a/b/c** und C-6,6'**a**/C-6,5'**b**/C-5,5'**c**), 134.7 (C-2,2' **a/b/c**), 129.5, 129.2, 123.5 (C-2"-6"**a/b/c**), 122.1 (C-4,4'**a**/C-4,7'**b**/C-7,7'**c**), 119.1 (C-5,5'**a**/C-5,6'**b**/C-6,6'**c**), 112.0 (C-7,7'**a**/C-7,4'**b**/C-4,4'**c**); ms: m/z 450 ([M]$^+$), 342 ([M-C_6H_4S]$^+$), 341 ([M-C_6H_5S]$^+$), 234 ([M-2 x C_6H_4S]$^+$), 232 ([M-2 x C_6H_5S]$^+$).

Anal. Calcd. for $C_{26}H_{18}N_4S_2$: C, 69.31; H, 4.03; N, 12.43; S, 14.23. Found: C, 69.52; H, 4.07; N, 12.13; S, 14.15.

2,2'-Bis(6-phenylsulfonyl-1*H*-benzimidazole) (**8a**), 6-Phenylsulfonyl-2-(5-phenylsulfonyl-1*H*-benzimidazol-2-yl)-1*H*-benzimidazole (**8b**), and 2,2'-Bis(5-phenylsulfonyl-1*H*-benzimidazole) (**8c**).

To a solution of 2,2'-bisbenzimidazolylidene (**2**) (0.232 g, 0.001 mole) in dry tetrahydrofuran (100 ml) were added 0.258 g (0.002 mmole) of *N*-ethyl diisopropylamine and a solution of 0.328 g (0.002 mole) sodium benzenesulfinate in 2.0 ml of water, containing 0.12 g of acetic acid. The mixture was stirred for 24 hours at room temperature. The residue was purified on a silica column with a mixture of ethyl acetate/*n*-hexane (1:1), to give a yellow powder with an intense green fluorescence to yield 0.150 g (29%); mp 224°; ir: ν 3335 (NH), 1617 (C=C), 1586 and 1539 (C=N); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 10.22 (s, 6H, NH **a/b/c**), 7.89 (m, 6H, 7,7'-H**a**/7,4'-H**b**/4,4'-H**c**), 7.65 (m, 12H, 6,6',4,4'-H**a** 4,6,6',7'-H b/6,6',7,7'-H**c**), 7.01 (m, 30H, 2",3",4",5",6"-H**a/b/c**); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 144.2, 143.7, 143.4, 142.9, 142.1, 141.8 (C- 3a,3'a,7a,7'a**a/b/c**), 137.8 (C-6,6'**a**/C-6,5'**b**/C-5,5'**c**), 136.8 (C-1'"**a/b/c**), 134.0 (C-2,2'**a/b/c**), 123.9, 123.7, 123.3, 122.5, 122.1, 119.9, 119.5, 119.1 (C-4,4',5',5**a**/C-4,5,6',7'**b**/C-6,6',7,7'**c** and C-2"'-6"' **a/b/c**) 112.4, 112.2, 111.7, 111.8 (C-7,7'**a**/C-7,4'**b**/C-4,4'**c**); ms: m/z 514 ([M]$^+$), 449 ([M-SO_2]$^+$), 374 ([M-$C_6H_5SO_2$]$^+$), 232 ([M-2 x $C_6H_5SO_2$]$^+$), 142 ([$C_6H_6SO_2$]$^+$).

Anal. Calcd. for $C_{26}H_{18}N_4O_4S_2$: C, 60.69; H, 3.53; N, 10.89; S, 12.46. Found: C, 60.97; H, 3.58; N, 10.63; S, 12.12.

Z-Bis(5-phenylsulfanyl-2*H*-benzimidazol-2-ylidene) (**9a**) and *E*-Bis(5-phenylsulfanyl-2*H*-benzimidazol-2-ylidene) (**9b**).

To a solution of 0.232 g (0.001 mole) of 2,2'-bisbenzimidazolylidene (**2**) in 50 ml of dry tetrahydrofuran were added 0.258 g (0.002 mole) of *N*-ethyldiisopropylamine and 0.22 g (0.002 mole) of thiophenol. After stirring for 10 minutes at room temperature, 1.74 g (20 mmole) of manganese dioxide was added. The mixture was stirred for 1 hour, filtered and evaporated to dryness. The residue was purified on a silica column with ethyl acetate to give a red powder, 0.1 g (22%), mp 217°; ir: ν 3057 (CH), 1607 (C=C), 1428 (C=N); ^{1}H nmr (deuteriochloroform): δ 8.35 (m, 4H, 6,6'-H**a/b**), 8.23 (m, 4H, 7,7'-H**a/b**), 7.93 (m, 4H, 4,4'-H**a/b**), 7.71 (m, 12H, 3",4",5"-H**a/b**), 7.56 (m, 8H, 2",6"-H**a/b**); ^{13}C nmr (deuteriochloroform): δ 148.1 (C-1"**a/b**), 147.6, 147.4, 147.0, 146.8 (C 3a,3'a, 7a, 7'a**a/b**), 142.5, 143.8 (C 5,5'**a/b**), 130.3 (C-2,2"**a/b**), 135.7, 135.2, 133.9, 132.9, 132.8, 132.4, 130.6, 130.32, 130.26, 122.8 (C-4,4',6,6',7,7',2",3",4",5",6"**a/b**); ms: m/z 448 ([M]$^+$), 340 ([M-C_6H_4S]$^+$), 308 ([M-$C_6H_4S_2$]$^+$), 109 ([C_6H_5S]$^+$), 77 ([C_6H_5]$^+$).

Anal. Calcd. for $C_{26}H_{16}N_4S_2$: C, 69.62; H, 3.59; N, 12.49; S, 14.30. Found: C, 69.68; H, 3.85; N, 12.73; S, 14.67.

Z-Bis(5-phenylsulfonyl-2*H*-benzimidazol-2-ylidene) (**10a**) and *E*-Bis(5-phenylsulfonyl-2*H*-benzimidazol-2-ylidene) (**10b**).

To a solution of 0.514 g (0.001mole) of **8a/b** in 100 ml dry of tetrahydrofuran was added 1.740 g (0.020 mole) manganese dioxide and the mixture was stirred at room temperature for 48 hours. After filtration and evaporation to dryness the residue was purified on a silica column with ethyl acetate to give reddish-brown needles, 0.32 g (62%), mp >230°; ir: ν 3058 (CH), 1606 (C=C), 1521 (C=N), 1151 and 1090 (SO_2); ^{1}H nmr (deuteriochloroform): δ 8.51 (m, 4H, 7,7'-H) **a/b**, 8.38 (m, 4H, 6,6'-H) **a/b**, 8.25 (m, 4H, 4,4'-H) **a/b**, 8.13 (m, 4H, 4"'-H) **a/b**, 8.05 (m, 8H, 3"',5"'-H) **a/b**, 7.61 (m, 8H, 2"',6"'-H) **a/b**, ^{13}C nmr (deuteriochloroform): δ 148.8, 148.6, 147.6, 147.4 (C-3a,3'a,7a,7'a) **a/b**, 145.8, 145.4 (C-1"') **a/b**, 144.4, 144.1 (C-5,5') **a/b**, 139.7 (C-2,2'), 134.3, 134.0, 133.8, 133.6, 133.0, 130.4, 132.4, 131.4, 130.6, 130.5, 130.0, 128.5 (C-4,4',6,6',7,7',2",3",4",5",6") **a/b**; ms: m/z 512 ([M]$^+$), 372 ([M-$C_6H_4SO_2$]$^+$), 247 ([$C_{12}H_{11}N_2SO_2$]$^+$), 230 ([M2 x $C_6H_5SO_2$]$^+$).

Anal. Calcd. for $C_{26}H_{16}N_4O_4S_2$: C, 60.93; H, 3.15; N, 10.93; S, 12.51. Found: C, 61.27; H, 3.23; N, 10.62; S, 12.23.

General Procedure for the Reaction of the *o*-Phenylenediamine Derivatives 4-Chloro-*o*-phenylenediamine (**11**) and 4-Fluoro-*o*-phenylenediamine (**12**) and Analogues 2,3-Diaminopyridine (**13**) and 3,4-Diaminopyridine (**14**) with Oxamide (**15**).

A suspension of **11** (0.1 mole), **12** (0.01 mole), **13** (0.05 mole) or **14** (0.05 mole) and a half equimolar quantity of oxamide (**15**) in of 10 ml of ethylene glycol was refluxed for 3 hours and immediately poured into 200 ml of water to give a precipitate identified as **16, 17, 18, 19**.

2,2'-Bis(6-chloro-1*H*-benzimidazole) (**16a**), 6-Chloro-2-(5-chloro-1*H*-benzimidazol-2-yl)-1*H*-benzimidazole (**16b**), and 2,2'-Bis(5-chloro-1*H*-benzimidazole) (**16c**).

The residue was purified on a silica column with a mixture of ethyl acetate/*n*-hexane 1:1, then recrystallized from ethyl acetate as yellow powder to yield 3.5 g (23%), mp >270°; ir: ν 3422 (NH), 1734, 1616 and 1580 (C=C, C=N); ^{1}H nmr (tetrahydrofuran-d_8): δ 12.73 (m, 2H, NH **a,b,c**), 7.60 (m, 4H, 5,5',4,4'-H**a**/4,5,6',7'-H**b**/6,7,6',7'-H**c**), 7.25 (m, 2H, 7,7'-H**a**/7,4'-H**b**/4,4'-H**c**); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 145.1 and 144.6 (C-3a,3'a, 7a, 7'a**a/b/c**), 143.8 and 143.3 (C-6,6',2,2'**a**/C-6,2,5',2'**b**/C-5,2,5',2'**c**), 123.6, 122.2, 119.2, 111.9 (C-4,4',5,5',7,7'**a**/C-4,5,7,4',6',7'**b**/C-4,6,7,4',6',7'**c**); ms: m/z 306 ([M+4]$^+$), 304 ([M+2]$^+$), 302 ([M]$^+$), 267 ([M-^{35}Cl]$^+$), 234 ([M-2^{35}Cl]$^+$), 152 ([$C_7H_5N_2Cl$]$^+$).

Anal. Calcd. for $C_{14}H_8Cl_2N_4$: C, 55.47; H, 2.66; N, 18.48. Found: C, 55.76; H, 2.87; N, 18.52.

2,2'-Bis(6-fluoro-1*H*-benzimidazole) (**17a**), 6-Fluoro-2-(5-fluoro-1*H*-benzimidazole-2-yl)-1*H*-benzimidazole (**17b**), and 2,2'-Bis-(5-fluoro-1*H*-benzimidazole) (**17c**).

The residue was purified on a silica column with a mixture of ethyl acetate/*n*-hexane 1:1, then recrystallized from ethyl acetate to give a yellow powder with a yellow-green fluorescence to yield

1.0 g (72%), mp >270°; ir: ν 3432 (NH), 3047 (aryl-H), 1629 (C=C), 1594 (C=N), 1491 (NH); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 13.70 (m, 2H, NH), 7.66 (m, 2H, 7,7'- H**a**/7,4'-H**b**/4,4'H**c**), 7.44 (m, 2H, 4,4'-H**a**/4,7'-H**b**/7,7'-H**c**), 7.17 (m, 2H, 5,5'-H); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 160.5, 157.9 (C-6,6'**a**/C-6,5'**b**/C-5,5'**c**), 144.8 (C-3a, 3'a, 7a, 7'a), 133.4 (C-2,2') 111.5, 111.2 (C-4,4',5,5',7,7'**a**/C-4,5,7,4',6',7'**b**/C-4,6,7, 4',6',7'**c**); ms: m/z 271 ([M+1]$^+$), 270 ([M]$^+$), 252 ([M-^{18}F]$^+$), 135 ([$C_{12}H_8N_4F_2$]$^+$).

Anal. Calcd. for $C_{14}H_8N_4F_2$: C, 62.22; H, 2.98; N, 20.73. Found: C, 62.03; H, 3.32; N, 20.79.

The precipitate was digested in hot ethyl acetate to give **18a-c** and **19a-c** in 52 and 42% yield, respectively.

2,2'-Bis(3*H*-iinidazo[4,5-*b*]pyridine) (**18a**), 2-(3*H*-imidazo-[4,5-*b*]pyrid-2yl)-1*H*-imidazo[4,5-*b*]pyridine (**18b**), and 2,2'-Bis-(1*H*-imidazo[4,5-*b*]pyridine) (**18c**).

A yellow-green powder was obtained mp >270°; ir: ν 3447 (NH), 1700, 1608 (C=C), 1542 (C=N); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 12.09 (m, 2H, NH), 8.07 (m, 2H, 5,5'-H), 7.46 (m, 2H, 7,7'-H), 7.13 (m, 2H, 6,6'-H); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 155.6, 154.5 (C-3a, 3'a), 141.7 (C-5,5'), 138.9 (C-7a, 7'a); 122.0 (C-7,7'); 121.5 (C-2,2'); 118.5 (C-6,6'); ms: m/z 237 ([M+1]$^+$), 236 ([M]$^+$).

Anal. Calcd. for $C_{12}H_8N_6$: C, 61.01; H, 3.39; N, 35.57. Found: C, 61.43; H, 3.41; N, 35.25.

2,2'-Bis(3*H*-imidazo[4,5-*c*]pyridine) (**19a**), 2-(3*H*-Imidazo-[4,5-*c*]pyrid-2-yl)-1*H*-imidazo[4,5-*c*]pyridine (**19b**), and 2,2'-Bis-(1*H*-imidazo[4,5-*c*]pyridine) (**19c**).

A yellow powder was obtained mp >270°; ir: ν 3222 (NH), 3037 (CH), 1707 and 1618 (C=C), 1580, 1540 (C=N); ^{1}H nmr (deuteriotrifluoroacetic acid): δ 9.50 (s), 8.92 (s), 8.23 (s) (1H, 4,4'-H), 8.73 (d), 8.22 (d), 7.47 (d) ($^3J_{7,6/7',6}$ = 6.6 Hz, 1H, 7,7'-H), 8.37 (d), 7.89 (d), 7.37 (d) ($^3J_{6,7/6',7}$ = 6.6 Hz, 1H, 6,6'-H); ^{13}C nmr (deuteriotrifluoroacetic acid): δ 157.7, 157.0, 149.8, 147.8, 141.3, 140.5 (C-3a, 3'a,7a,7'a), 126.3 (C-2,2'), 139.4, 137.6, 137.3, 131.8, 115.4, 114.7 (C-4,4',6,6',7,7'); ms: m/z 237 ([M+1]$^+$), 236 ([M]$^+$), 235 (M-1]$^+$).

Anal. Calcd. for $C_{12}H_8N_6$: C, 61.10; H, 3.39; N, 35.57. Found: C, 61.39; H, 3.45; N, 35.27.

General Procedure for the Methylation of **16-19** to Give **20-22** or **23**.

To a suspension of 0.001 mole of **16, 17, 18** or **19** in 1.0 ml of ethanol was added 2.0 ml of 1*N* aqueous solution of sodium hydroxide and the mixture was stirred for 1 hour. Then 0.284 g (0.002 mole) of iodomethane was added and stirred for 48 hours at room temperature.

1,1'-Dimethyl-6,6'-dichloro-2,2'-bisbenzimidazole (**20a**), 1,1'-Dimethyl-6,5'-dichloro-2,2'-bisbenzimidazole (**20b**), and 1,1'-Dimethyl-5,5'-dichloro-2,2'-bisbenzimidazole (**20c**).

Recrystallisation from ethyl acetate yielded a light-yellow precipitate, 0.06 g (18%), mp 215°; ir: ν 2850 (N-CH_3), 1700 (C=N), 1607 (C=C); ^{1}H nmr (deuteriochloroform): δ 7.82 (m, 2H, 7,7'-H**a**/7,4'-H**b**/4,4'-H**c**), 7.39 (m, 4H, 5,5',4,4'-H**a**/4,5,6',7'-H**b**/6,7,6',7'-H**c**), 4.31 (m, 6H, CH_3); ^{13}C nmr (deuteriochloroform): δ 143.7, 143.4, 143.2, 141.1, 136.9, 134.9 (C-3a,3'a,7a,7'a**a/b/c**), 130.0 (C-6,6'**a**/C-6,5'**b**/ C-5,5'**c**), 128.7 (C-2,2'**a/b/c**), 124.2 (C-4,4'**c**), 123.7 (C-7,7'**a**), 123.8, 123.0 (C-7,4'**c**), 121.3 (C-5,5'**a**), 121.2, 120.5 (C-5,6'**b**), 120.1 (C-6,6'**c**), 111.3, 112.1 (C-4,7'**b**), 110.9 (C-7,7'**c**), 110.3 (C-4,4'**a**), 32.8 (*C*H_3); ms: m/z 334 ([M+4]$^+$), 332 ([M+2]$^+$), 330 ([M]$^+$), 315 ([M-CH_3]$^+$), 295 ([M-^{35}Cl]$^+$), 165 ([$C_8H_6N_2Cl$]$^+$).

Anal. Calcd. for $C_{16}H_{12}Cl_2N_4$: C, 58.02; H, 3.65; N, 16.92. Found C, 57.78; H, 3.88; N, 16.91.

1,1'-Dimethyl-6,6'-difluoro-2,2'-bisbenzimidazole (**21a**), 1,1'-Dimethyl-6,5'-difluoro-2,2'-bisbenzimidazole (**21b**), and 1,1'-Dimethyl-5,5'-difluoro-2,2'-bisbenzimidazole (**21c**).

Recrystallisation from ethyl acetate yielded light yellow needles, 0.18 g (60%), mp 197°; ir: ν 3058 (CH), 2949 (CH_3), 1685 and 1624 (C=C), 1597 (C=N); ^{1}H nmr (deuteriochloroform): δ 7.38 (m, 6H, 4,5,7,4',5',7'-H), 4.21 (m, 6H, CH_3); ^{13}C nmr (deuteriochloroform): δ 160.7 (d, $J_{C\text{-}F}$ = 238.4 Hz), 160.6 (d, $J_{C\text{-}F}$ = 238.4 Hz), 159.8 (d, $J_{C\text{-}F}$ = 238.4 Hz) - C-6,6'**a** C-6,5'**b** C-5,5'**c**, 144.2, 143.7, 142.9, 142.7 (C-3a,3'**aa**/C-3a,7'**ab**/C-7a,7'**ac**), 138.9, 136.6, 136.4 (C-7a,7'**aa**/C-7a,3'**ab**/C-3a, 3'**ac**), 132.8 (C-2,2'**a/b/c**), 121.3 (d, $J_{C\text{-}F}$ = 10.2 Hz, C-4**b**), 121.2 (d, $J_{C\text{-}F}$ = 10.2 Hz, C-4,4'**a**), 112.7 (d, $J_{C\text{-}F}$ = 26.6 Hz, C-6,6'**c**), 111.7 (d, $J_{C\text{-}F}$ = 25.4 Hz, C-5,5'**a**), 112.6 (d, $J_{C\text{-}F}$ = 26.6 Hz, C-6'**b**), 111.6 (d, $J_{C\text{-}F}$ = 25.4 Hz, C-5**b**), 110.6 (d, $J_{C\text{-}F}$ = 10.2 Hz, C-7,7'**c**), 110.5 (d, $J_{C\text{-}F}$ = 10.2 Hz, C-7'**b**), 105.6 (d, $J_{C\text{-}F}$ = 24 Hz, C-4,4'**c**), 105.3 (d, $J_{C\text{-}F}$ = 24 Hz, C-4'**b**), 96.5 (d, $J_{C\text{-}F}$ = 27.6 Hz, C-7**b**), 96.4 (d, $J_{C\text{-}F}$ = 27.6 Hz, C-7,7'**a**), 32.7, 32.5 (*C*H_3 **a/b/c**); ms: m/z 299 ([M+1]$^+$), 298 ([M]$^+$), 297 ([M-1]$^+$), 283 ([M- CH_3]$^+$), 149 [$C_8H_6N_2F$]$^+$).

Anal. Calcd. for $C_{16}H_{12}F_2N_4$: C, 64.42; H, 4.05; N, 18.78. Found: C, 64.16; H, 4.33; N, 18.79.

3,3'-Dimethylbis(imidazo[4,5-*b*]pyridine) (**22a**), 3,1'-Dimethylbis(imidazo[4,5-*b*]pyridine) (**22b**), and 1,1'-Dimethylbis-(imidazo[4,5-*b*]pyridine) (**22c**).

Recrystallization from ethyl acetate/ethanol yielded a reddish-brown precipitate, 0.07 g (13%), mp 243°; ir: ν 3075 (CH), 2800 (N-CH_3), 1672 (C-N), 1597 (C=C); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 8.26 (m, 2H, 5,5'-H), 7.88 (m, 2H, 7,7'-H), 7.32 (m, 2H, 6,6'-H), 3.57 (d, 6H, CH_3); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 154.7 (C-3a), 153.5 (C-3'a), 144.6 (C-7a), 141.6 (C-5,5'), 139.0 (C-7'a); 124.1 (C-2,2'), 122.6 (C-7,7'), 293 and 28.2 (*C*H_3); ms: m/z 265 ([M+1]$^+$), 264 ([M]$^+$), 263 ([M]$^+$), 250 ([M-CH_2]$^+$), 249 ([M-CH_3]$^+$), 134 ([$C_7H_6N_3$]$^+$).

Anal. Calcd. for $C_{14}H_{12}N_6$: C, 63.63; H, 4.58; N, 31.80. Found C, 63.45; H, 4.51; N 31.58.

3,3'-Dimethylbis(imidazo[4,5-*c*]pyridine) (**23a**), 3,1'-Dimethylbis(imidazo[4,5-*c*]pyridine) (**23b**), and 1,1'-Dimethylbis-(imidazo[4,5-*c*]pyridine) (**23c**).

Recrystallisation from ethyl acetate/ethanol gave a red precipitate, yield 0.4 g (75%), mp 234°; ir: ν 3018 (CH), 2803 (C-NH_3), 1636 (C=N), 1585 (C=C); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 9.65 (d, 1H, ^4J = 2.7 Hz, 4'-H**b**), 9.63 (d, 2H, ^4J = 2.7 Hz, 4,4'-H**c**), 9.31 (d, ^{1}H, ^4J = 2.7 Hz, 4-H**b**), 9.28 (d, 2H, ^4J = 2.6 Hz, 4,4'-H**a**), 8.75 (d, 1H, ^3J = 7.2 Hz, 7-H**b**), 8.4 (d, 2H, ^3J = 6.9 Hz, 7-H**c**), 8.24 (m, 6H, 6,7'-H**b**, 7,7'-H**a**, 6,6'-H**c**), 7.98 (m, 3H, 6'-H**b**, 6,6'-H**a**), 4.21 (m, 18H, CH_3**a/b/c**); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 160.5 (C-3a,3'**ac**, C-3'**ab**), 154.6, 153.7 (C-3a,3'**aa**, C-3**ab**), 144.7, 143.8, 142.9 (C-7a,7'**aa/b/c**), 139.2 (C-2,2'**a/b/c**), 138.5, 137.5, 136.4, 136.0, 135.5, 134.1, 132.7, 132.3 (C-6,6',7,7'**a/b/c**), 116.3, 114.2, 112.6, 109.3 (C-4,4'**a/b/c**), 34.2, 34.1, 34.0 (*C*H_3**a/b/c**); ms: m/z 265 ([M+1]$^+$), 264 ([M]$^+$), 263 ([M-1]), 250 (M-CH_2]$^+$), 249 ([M-CH_3]$^+$), 132 ([$C_7H_6N_3$]$^+$).

Anal. Calcd. for $C_{14}H_{12}N_6$: C, 63.63; H, 4.58; N, 31.80. Found C, 63.89; H, 4.56; N, 31.48.

General Procedure for the Reaction of 4-Chloro-*o*-phenylenediamine (**11**) and 4-nitro-*o*-phenylenediamine (**25**) with cyclohexane-1,4-dione **26** to give **28**, **29** and **30**.

To a solution of **11** (0.06 mole) or 25 (0.02 mole) in 100 ml ethanol a half-equimolar quantity of cyclohexanone (**26**) was added. The mixture was refluxed for 1 hour.

Z-Dispiro(5-chlorodihydrobenzimidazole-2,1'-cyclohexane-4',2"-5"chlorodihydrobenzimidazole) (**28a**), and *E*-Dispiro(5-chlorodihydrobenzimidazole-2,1'-cyclohexane-4',2"-5"-chlorodihydrobenzimidazole) (**28b**).

After cooling to room temperature a precipitate was observed which was purified on a silica column with a mixture of ethyl acetate/*n*-hexane 1:1; recrystallisation from ethyl acetate gave a white powder to yield 8.95 g (66%), mp 210°; ir: ν 3356 and 3277 (N-H), 2938 and 2852 (CH_2), 1696, 1685 and 1607 (C=C, C-N); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 6.32 (m, 2H, 4,4"-H), 6.21 (m, 4H, 6,6",7,7"-H), 6.05 (m, 2H, NH), 5.85 (m, 2H, NH), 1.71 (m, 8H, cyclohexyl-H); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 142.1 (C-7a,7"a), 139.3 (C-3a,3"a), 120.98 (*C*-Cl), 116.2 (C-4,4"), 106.8 (C6,6"), 106.1 (C-7,7"), 79.7 (C- 2,2"), 35.1 (*C*H_2); ms: m/z 364 ([M+4]$^+$), 362 ([M+2]$^+$), 360 ([M]$^+$), 166 (100%, [$C_8H_7N_2Cl$]$^+$).

Anal. Calcd. for: $C_{18}H_{18}Cl_2N_4$: C, 59.82; H, 5.02; N, 15.52. Found: C, 59.58; H, 5.14; N, 15.26.

Z-Dispiro(5-nitro-2,3-dihydro-1*H*-benzimidazole-2,1'-cyclohexane-4',2"5"-nitro-2",3"-dihydro-1"*H*-benzimidazole) (**29a**), and *E*-Dispiro(5-nitro-2,3-dihydro-1*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-nitro-2",3"-dihydro-1*H*-benzimidazole) (**29b**).

Cooling overnight gave a black-red precipitate, which was washed several times with ethyl acetate to yield 0.6 g (15%), mp 258°; ir: ν 3334 (NH), 2932 (CH_2), 1607 (C=C), 1512 and 1320 (NO_2), 1441 (N-H); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 7.87 (s, 1H, NH), 7.80 (s, 1H, NH), 7.52-7.50 (m, 2H, 6,6"-H), 6.85-7.00 (m, 2H, 4,4"-H), 6.65 (s, 1H, NH), 6.57 (s, 1H, NH), 6.23-6.26 (m, 2H, 7,7"-H), 1.70-2.10 (m, 8H, cyclohexyl-*H*); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 147.5 (C-5,5"), 140.0 (C-3a, 3"a), 137.6, 137.6 (C-7a,7"a), 118.9, 118.8 (C-7,7 102.1, 102.0 (C-6,6"), 99.2, 98.9 (C-4, 4"), 80.7 (C-2,2"), 35.2 (*C*H_2), ms: m/z 382 ([M]$^+$), 381 ([M-1]$^+$), 352 (15%, [M-^{30}NO]$^+$), 336 (7%, [M-$^{46}NO_2$]$^+$), 191 (100%, [$C_9H_9N_3O_2$]$^+$)

Anal. Calcd. for $C_{18}H_{18}N_6O_4$: C, 56.54; H, 4.75; N, 21.98. Found: C, 55.99; H, 4.86; N, 21.79.

Spiro(5-nitro-2,3-dihydro-1*H*-benzimidazole-2,1'-cyclohexan-4'-one) (**30**).

The filtrate after separation of **29** was evaporated to dryness and the residue was purified on a silica column with a mixture of ethyl acetate/*n*-hexane 1:1. Recrystallization from ethyl acetate gave red needles, yield 0.7 g (28%), mp 238°; ir: ν 3288 (NH), 2951 (CH_2),1855, 1701 (C=O), 1598 (NO_2, C=C), 1500 (N-H); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 7.96 (s, 1H, NH), 7.54 (dd, $^3J_{6,7}$ = 8.4 Hz, $^4J_{6,4}$ = 2.4 Hz, 1H, 6-H), 6.94 (d, $^4J_{4,6}$ = 2 Hz, 1H, 4-H), 6.88 (s, 1H, NH), 6.26 (d, $^3J_{7,6}$ = 7.5 Hz, 1H, 7-H), 2.44-2.50 (t, $^2J_{3'/5',2'/6'}$ = 7 Hz, 4H, 3',5'-H), 2.06 (t, $^2J_{2'/6',3'/5'}$ = 7 Hz, 4H, 2',6'-H); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 208.8 (C-4'), 147.0 (C-5), 139.8 (C-3a), 137.8 (C-7a), 118.7 (C-7), 102.1 (C-6), 98.9 (C-4), 80.8 (C-2), 37.6, 36.7, 36.1, 35.3 (*C*H_2); ms: m/z 247 ([M]$^+$), 191, 190, 145, 144.

Anal. Calcd. for $C_{12}H_{13}N_3O_3$: C, 58.29; H, 5.30; N, 16.99. Found: C, 58.44; H, 5.42; N, 16.57.

General Procedure for the Oxidation of **28, 29** and **30** to give **31, 32** and **33**.

To a solution of **28**, **29** or **30** in dichloromethane was added 20 times excess of manganese dioxide and the mixture was stirred for 12 hours. After filtration of the reaction mixture and evaporation to dryness the following crude residues were obtained:

Z-Dispiro(5-chloro-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5-chloro-2"*H*-benzimidazole) (**31a**), and *E*-Dispiro(5-chloro-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-6"-chloro- 2"*H*-benzimidazole) (**31b**).

After purification on a silica column with ethyl acetate the residue was recrystallized from ethyl acetate as a white powder to yield 5.2 g (73%), mp 186°; ir: ν 3034 (C-H), 2914 (CH_3), 1628 (C=C), 1560, 1525 and 1507 (C=N); ^{1}H nmr (deuteriochloroform): δ 7.28 (m, 4H, 6,6",7,7"-H), 6.96 (m, 2H, 4,4"- H), 2.20 (m, 8H, cyclohexyl-H); ^{13}C nmr (deuteriochloroform): δ 159.1 (C-3a, 3"a), 158.2 (C-7a, 7"a), 141.0 (C-5,5"), 137.0 (C-4,4"), 126.9 (C-6,6"), 123.8 (C-7,7"), 107.9 (C-2,2"), 31.5 (CH_2); ms: m/z 360 ([M+4]$^+$), 358 ([M+2]$^+$), 356 ([M]$^+$), 178 (32%, [$C_9H_7N_2Cl$]$^+$).

Anal. Calcd. for $C_{18}H_{14}Cl_2N_4$: C, 60.52; H, 3.95; N, 15.68. Found C, 60.48; H, 4.20; N, 15.62.

Z-Dispiro-(5-nitro-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5-nitro-2"*H*-benzimidazole) (**32a**), and *E*-Dispiro-(5-nitro-2*H*-benzimidazole-2,1-cyclohexane-4',2"-5"-nitro-2"*H*-benzimidazole) (**32b**).

After purification on a silica column with a mixture of ethyl acetate/*n*-hexane 5:1 the residue was recrystallized from ethyl acetate/*n*-hexane as a brown powder to yield 0.21 g (55%), mp >270°; ir: ν 3082 (CH), 2928 (CH_2), 1734 and 1635 (C=C), 1577, 1549 and 1521 (C=N, C-NO_2); ^{1}H nmr (deuteriochloroform): δ 8.35 (m, 2H, 4,4"-H), 7.85 (m, 2H, 6,6"-H), 7.39 (m, 2H, 7,7"-H), 2.25 (m, 8H, cyclohexyl-H); ^{13}C nmr (deuteriochloroform): δ 159.2, 158.4 (C-3a,3"a,7a,7"a), 152.8 (C-5,5"), 127.9 (C-4,4"), 124.2 (C-6, 6",7,7"), 110.3 (C-2,2"), 31.2 (C-2',3',5',6'); ms: m/z 379 ([M+1]$^+$), 378 ([M]$^+$), 350 ([M-C_2H_4]$^+$), 332 ([M-NO_2]$^+$), 189 ([$C_9H_7N_3O_2$]$^+$).

Anal. Calcd. for $C_{18}H_{14}N_6O_4$: C, 57.14; H, 3.73; N, 22.21. Found: C, 57.13; H, 4.03; N, 22.13.

Spiro-(5-nitro-2*H*-benzimidazole-2,1'-cyclohexan-4'-one) (**33**).

After purification on a silica column with a mixture of ethyl acetate/*n*-hexane 5:1 the residue was recrystallized from ethyl acetate/*n*-hexane as a brown powder to yield 0.15 g (61%), mp 125°; ir: ν 3039 (CH), 2936 (CH_2), 1722 (C=O), 1632 (C=C), 1577, 1551 and 1524 (C=N, C-NO_2); ^{1}H nmr (deuteriochloroform): δ 8.28 (dd, $^5J_{4,7}$ = 0.95 Hz, $^4J_{4,6}$ = 2 Hz, 1H, 4-H), 7.82 (dd, $^3J_{6,7}$ = 10 Hz, $^4J_{6,4}$ = 2 Hz, 1H, 6-H), 7.47 (dd, $^3J_{7,6}$ = 10 Hz, $^5J_{7,4}$ = 1 Hz, 1H, 7-H), 2.86 (t, $^2J_{2'/6',3'/5'/7}$ Hz, 4H, 2',6'-H), 2.11 (t, $^2J_{3'/5',2'/6'}$ = 7 Hz, 4H, 3',5'-H); ^{13}C nmr (deuteriochloroform): δ 209.0 (*C*=O), 159.5, 158.8 (C-3a,7a), 153.0 (C-5), 128.3, 127.8 (C-6,7), 123.9 (C-4), 109.1 (C-2), 39.9 (C-2',6'), 32.0 (C-3',5'); ms: m/z 245 ([M]$^+$), 218 ([M-HNO_2]$^+$)

Anal. Calcd. for $C_{12}H_{11}N_3O_3$: C, 58.77; H, 4.52; N, 17.13. Found: C, 58.67; H, 4.66; N, 17.41.

General Procedure for the Reaction of **3** with the *N*-Nucleophiles Piperidine and Morpholine to Give (**34**) and (**35**).

To a solution of 3 g (0.01 mole) of dispiro(2*H*-benzimidazole-2,1'-cyclohexane-4',2"-2"*H*-benzimidazole) (**3**) in 20 ml of

chloroform were added 1.8 g (0.007 mmole) *N*-ethyl diisopropylamine, 0.2 mmole *N*-nucleophile and 15 g (172 mmole) manganese dioxide and the mixture was stirred for 7 days at room temperature. After adding 200 ml of chloroforme, the mixture was filtered and evaporated to dryness to give the crude products.

Dispiro-(5,6-dipiperidino-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5'-piperidino-2"*H*-benzimidazole) **34**.

After purification on a neutral Alox column with ethyl acetate the residue was recrystallized from ethyl acetate as orange powder to yield 1.9 g (34%), mp >270°; ir: ν 3040 (CH), 2930 and 2852 (CH_3), 1627 (C=C), 1575 (C=N); ^{1}H nmr (deuteriochloroform): δ 7.14 (m, 3H, 4",6",7"-H), 6.51, 6.24 (every s, every 1H, 4,7-H), 3.35 (m, 12H, 2"',6"'-H), 1.95 (m, 26H, 2",3",5",6", 3"',4"',5"'-H); ^{13}C nmr (deuteriochloroform): δ 160.6, 159.5, 158.6, 156.9, 156.54, 156.51, 153.7 (C-3a,5,6,7a,3"a,5",7"a), 132.4 (C-4,6), 125.6 (C-4"), 107.0 (C-6"), 106.96, 106.1 (C-2,2"), 98.2 (C-7"), 52.3, 49.6 (C-2"', 6"'), 26.1, 25.5, 24.6 (C-3"',4"',5"'), 32.4 (CH_2-cyclohexyl rest); ms: m/z 538 ([M+1]$^+$), 537 ([M]$^+$), 511 ([M-C_2H_4]$^+$), 454 ([M-C_5H_9N]$^+$).

Anal. Calcd. for $C_{33}H_{43}N_7$: C, 73.71; H, 8.06; N, 18.23. Found C, 73.53; H, 7.87; N, 18.39.

Dispiro(5,6-dimorpholino-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5'-morpholino-2"'*H*-benzimidazole) (**35**).

After purification on a neutral Alox column by ethyl acetate the residue was recrystallized from ethyl acetate as an orange powder to yield 0.82 g (43%), mp 168°; ir: ν 2962 and 2850 (CH_2), 1630 (C=C), 1577 (C=N); ^{1}H nmr (deuteriochloroform): δ 7.26 (m, 2H, 4",7"-H), 7.05 (m, 1H, 6"-H), 6.57 (s, 1H, 7-H), 6.28 (s, 1H, 4-H), 3.60 (m, 12H, 3"',5"'-H), 3.25 (m, 12H, 2"',6"'-H), 2.15 (m, 8H, cyclohexyl-*H*). ^{13}C nmr (deuteriochloroform): δ 160.3, 159.0, 158.6 (C-5,6,5"), 154.3, 153.7 (C-3a,3"a,7a,7"a), 134.3 (C-7"), 131.5 (C-6"), 126.1 (C-4"), 108.1 (C-7"), 106.2 (C-2,2"), 99.4 (C4"), 51.4 (C-3"',5"'), 48.4 (C-2"',6"'), 32.2 (C-2',3',5',6'); ms: M/z 544 ([M+1]$^+$), 543 ([M]$^+$), 458 ([M-C_4H_7NO]$^+$), 373 ([M-2 x C_4H_7NO]$^+$), 288 ([$C_{18}H_{16}N_4$]$^+$), 216 ([$C_{13}H_{10}N_4$]$^+$), 145 ([$C_9H_9N_2$]$^+$), 86 ([C_4H_8NO]$^+$).

Anal. Calcd. for $C_{30}H_{37}N_7O_3$: C, 66.28; H, 6.28; N, 18.03. Found: C, 66.24; H, 6.54; N, 17.88.

Z-Dispiro(5-chloro-6-piperidino-2*H*-benzimidazole-2,1'-cyclohexane 4',2"-5"-chloro-6"-piperidino-2"*H*-benzimidazole) (**40a**), and *E*-Dispiro(5-chloro-6-piperidino-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-6"-piperidino-2"*H*-benzimidazole) (**40b**).

To a solution of 3 g (0.01 mole) of *Z/E*-dispiro(5-chloro-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-2"*H*-benzimidazole) (**31**) in 20 ml chloroform were added 0.2 mole piperidine and 15 g (172 mmoles) manganese dioxide and the mixture was stirred for 7 days at room temperature. After adding 200 ml of chloroform, the mixture was filtered and evaporated to dryness. The crude products were purified on a silica column with a mixture of ethyl acetate/*n*-hexane 5:1 as a dark red powder to yield 1.25 g (28%), mp 208°; ir: ν 2933, 2852 and 2820 (CH_2), 1616 (C=C); ^{1}H nmr (deuteriochloroform): δ 6.70 (s, 2H, 4,4"-H), 5.80 (s, 2H, 7,7"-H), 3.65 (m, 8H, 2"',6"'-H), 2.71 (m, 4H, 4"'-H), 1.67 (m, 16H, 3"',5"'-H + cyclohexyl-H); ^{13}C nmr (deuteriochloroform): δ 160.2, 156.5 (C-3a,3"a, 7a,7"a), 145.3. (C-6,6"), 144.6 (C-5,5"), 111.5 (C-4,4"), 109.5 (C-7,7"), 105.9 (C-2,2"), 50.0, 25.5, 24.4 (*C*H_2 piperidyl rest), 32.2 (*C*H_2 cyclohexyl); ms: m/z 526 ([M+4]$^+$), 524 ([M+2]$^+$), 522 ([M]$^+$), 496 ([M-C_2H_2]$^+$), 494 ([M-C_2H_4]$^+$), 438 ([M-$C_5H_{10}N$]$^+$), 261 ([$C_{14}H_{16}N_3Cl$]$^+$), 84 ([$C_5H_{10}N$]$^+$).

Anal. Calcd. for $C_{28}H_{32}Cl_2N_6$: C, 64.24; H, 6.16; N, 16.05. Found: C, 64.06; H, 6.14; N, 15.64.

Z-Dispiro(5-chloro-6-morpholino-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-6"-morpholino-2"*H*-benzimidazole) (**41a**), and *E*-Dispiro-(5-chloro-6-morpliolino-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-6"-morpholino-2"*H*-benzimidazole) (**41b**).

To a solution of 1.25 g (0.0035 mole) of *Z/E*-dispiro(5-chloro-2*H*-benzimidazole-2,1'-cyclohexane- 4',2"-5"-chloro-2"*H*-benzimidazole) (**31a/b**) in 50 ml of dichloromethane were added 0.07 mole morpholine and 6.09 g (0.07 mole) of manganese dioxide and the mixture was stirred for 14 days at room temperature. After adding 200 ml of dichloromethane, the mixture was filtered and evaporated to dryness. The crude products were purified on silica column with a mixture of ethyl acetate/methanol 10:1, which was recrystallized from ethyl acetate as red needles to yield 0.16 g (8%), mp >230°; ir: ν 2966 and 2850 (CH_2), 1616 (C=C), 1558 and 1537 (C=N); ^{1}H nmr (deuteriochloroform): δ 7.45 (s, 1H), 7.41 (s, 1H), 4,4"-H**b**, 6.83 (s, 2H, 4,4"-H) **a**, 6.64 (s, 1H), 6.58 (s, 1H), 7,7"-H**b**, 5.84 (s, 2H, 7,7"-H) **a**, 3.67 (m, 16H, 3"',5"'-H) **a/b**, 3.12 (m, 16H, 2"',6"'-H) **a/b**, 211 (m, 16H, cyclohexyl-*H*) **a/b**; ^{13}C nmr (deuteriochloroform): δ 160.0 (C-3a,3"a) **a**, 159.1, 159.0 (C-3a,3"a) **b**, 157.82, 157.78 (C-7a,7"a) **b**, 156.0 (C-7a,7"a) **a**, 154.2, 154.0 (C-6,6") **b**, 144.8 (C-6,6") **a**, 143.6 (C-5,5") **a**, 141.4, 141.0 (C-5,5") **b**, 126.2, 125.8 (C-7,7") **b**, 113.5 (C-7,7") **a**, 110.8 (C-4,4") **a**, 109.0, 108.6 (C-4,4") **b**, 107.3, 107.2 (C-2,2") **b**, 106.4 (C-2,2") **a**, 66.4 (C-3"',5"') **a/b**, 52.0, 51.9 (C-2"',6"') **b**, 48.8 (C-2"',6"') **a**, 31.8 (*C*H_2) **a/b**, ms: m/z 528 ([M+2]$^+$), 526 ([M]$^+$), 85 ([C_4H_7NO]$^+$).

Anal. Calcd. for $C_{26}H_{28}Cl_2N_6O_2$: C, 59.21; H, 5.35; N, 15.93. Found: C, 59.49; H, 5.47; N, 15.72.

General Procedure for the Reaction of **3** and **31a/b** with Thiophenol.

To a solution of 0.0018 mole of dispiro(2*H*-benzimidazole-2,1'-cyclohexane-4',2"-2"*H*-benzimidazole) (**3**) or *Z/E*-dispiro(5-chloro-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-2"*H*-benzimidazole) (**31a/b**) dissolved in 50 ml of dichloromethane were added 0.1 ml of acetic acid, 0.396 g (0.0036 mole) of thiophenol and stirred at room temperature. The development of a red colour was observed after 10 minutes.

Z-Dispiro(5-phenylsulfanyl-2,3-dihydro-1*H*-benzimidazol-2,1'-cyclohexane-4',2"-5"-phenylsulfanyl-2",3"-dihydro-1"*H*-benzimidazole) (**36a**), and *E*-Dispiro(5-phenylsulfanyl-2,3-dihydro-1*H*-benzimidazole-2,1'-cyclohexane-4',2-5"-phenylsulfanyl-2",3"-dihydro-1"*H*-benzimidazole) (**36b**).

Purification on a silica column with a mixture of ethyl acetate/*n*-hexane 1:3 gave the residue, which was recrystallized from diethyl ether as a yellow powder to yield 0.15 g (16%), mp 90°; ir: ν 3378 (NH), 3055 (CH), 2982 (CH_2), 1581 (C=C); ^{1}H nmr (deuteriochloroform): δ 7.17 (m, 20H, 2"'-6"'-H), 6.81 (m, 4H, 4,4"-H), 6.53 (m, 8H, 6,6",7,7"-H), 3.91 (m, 8H, NH), 1.73 (m, 16H, cyclohexyl-H); ^{13}C nmr (deuteriochloroform): δ 143.5, 142.6, 142.5, 139.3, 135.5 (C-1"',5,5",3a,3"a,7a,7"a), 129.9, 128.8, 127.1, 126.9, 126.4, 126.3, 125.8, 125.6 (C-2"'-6"',6,6",7,7"), 120.0, 119.9, 110.1, 109.6 (C-4,4"), 79.5 (C-2,2"), 35.3 (*C*H_2); ms: m/z 508 ([M]$^+$), 479 ([M-C_2H_5]$^+$), 254 ([$C_{15}H_{14}N_2S$]$^+$), 240 ([$C_{15}H_{14}NS$]$^+$), 109 ([C_6H_5S]$^+$).

Anal. Calcd. for $C_{30}H_{28}N_4S_2$: C, 70.83; H, 5.55; N, 11.01; S, 12.61. Found: C, 70.33; H, 5.50; N, 10.84; S, 12.06.

Z-Dispiro(5-chloro-6-phenylsulfanyl-2,3-dihydro-1*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-6"-phenylsulfanyl-2",3"-dihydro-1"*H*-benzimidazole) (**42a**), and *E*-Dispiro(5-chloro-6-phenylsulfanyl-2,3-dihydro-1*H*--benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-6"-phenylsulfanyl-2",3"-dihydro-1"*H*-benzimidazole) (**42b**).

Purification on a silica column with a mixture of ethyl acetate/*n*-hexane 3:1 gives the crude product, which was recrystallized from diethyl ether as yellow-brown powder to yield 0.18 g (17%), mp 112°; ir: ν 3389 (NH), 3056 (CH), 1581 (C=C); ^{1}H nmr (deuteriochloroform): δ 7.19 (m, 20H, 2"'-6"'- H), 6.7 (br s, 4H, 7,7"-H), 6.4 (br s, 4H, 4,4"-H), 3.95 (br s, 8H, NH), 1.65 (m, 16H, cyclohexyl-H); ^{13}C nmr (deuteriochloroform): δ 145.2, 145.1, 140.8, 140.1, 138.7, 137.3, 137.2 (C-1"',5,5",6,6",3a,3"a,7a,7"a), 135.4, 132.9, 132.8, 129.4, 129.3, 128.8, 127.0, 126.5, 125.7, 125.0 (C-2,"6"',7,7"), 119.5, 118.4, 117.5 (C-6,6"), 110.4, 110.2, 109.8 (C-4,4"); ms: m/z 578 ([M+2]$^+$), 576 ([M]$^+$), 506 ([M-2 x ^{35}Cl]$^+$), 470 ([M-C_6H_5S]$^+$), 360 ([M-2 x C_6H_5S]$^+$).

Anal. Calcd. for $C_{30}H_{26}Cl_2N_4S_2$: C, 62.38; H, 4.54; N, 9.70; S, 11.10. Found: C, 62.28; H, 4.43; N, 9.87; S, 11.15.

General Procedure for the Reaction of **3** and **31a/b** with Benzenesulfenic Acid.

To a solution of (0.0035 mole) of dispiro(2*H*-benzimidazole-2,1'-cyclohexane-4',2"-2"*H*-benzimidazole) (**3**) or *Z/E*-dispiro(5-chloro-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-2"*H*-benzimidazole) (**31a/b**) dissolved in 50 ml of dichloromethane were added 0.420 g (0.007 mole) acetic acid and a solution of 1.148 g (0.007 mole) sodium benzenesulfinate in 2.0 ml of water. The mixture was stirred for 3 hours at room temperature.

Z-Dispiro(5-phenylsulfonyl-2,3-dihydro-1*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-phenylsulfonyl-2",3"-dihydro-1"*H*-benzimidazole) and (**37a**), and *E*-Dispiro(5-phenylsulfonyl-2,3-dihydro-1*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-phenylsulfonyl-2",3"-dihydro-1"*H*-benzimidazole) (**37b**).

A white precipitate was produced by adding 50 ml of *n*-hexane; recrystallisation from ethyl acetate/*n*-hexane gave a beige powder to yield 1.75 g (87%), mp 186°; ir: ν 3377 (NH), 2934 (CH_2), 1700 and 1602 (C=C); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 7.81 (m, 4H, 2"',6"'-H), 7.56 (m, 6H, 3"',4"',5"'-H), 7.04 (m, 4H, 4,4"-H and NH), 6.54 (m, 2H, 6,6"-H), 6.29 (m, 4H, 7,7"-H and NH), 1.75 (m, 8H, cyclohexyl-*H*); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 145.2 (C-3a,3"a), 143.4 (C-7a,7"a), 140.4 (C-5,5"), 132.3 (C-4,4"), 129.2 (C-6,6"), 127.2 (C-1"'), 126.3 (C-7,7"), 120.3, 103.4, 102.7 (C-2"',3"', 4"',5"',6"'), 80.0 (C-2,2"), 35.2 (*C*H$_3$); ms: m/z 324 ([$C_{17}H_{18}N_2SO_2$]$^+$), 322 ([$C_{17}H_{16}N_2SO_2$]$^+$), 286 ([$C_{18}H_{14}N_4$]$^+$), 248 ([$C_{12}H_{12}N_2SO_2$]$^+$), 142 ([$C_6H_6SO_2$]$^+$).

Anal. Calcd. for $C_{30}H_{28}N_4O_4S_4$: C, 62.92; H, 4.93; N, 9.78; S, 11.20. Found C, 63.07; H, 5.19; N, 9.62; S, 11.49.

Z-Dispiro(5-chloro-6-phenylsulfonyl-2,3-dihydro-1*H*-benzimidazole-2,1-cyclohexane-4',2"-5-chloro-6"-phenylsulfonyl-2",3"-dihydro-1"*H*-benzimidazole) (**43a**), and *E*-Dispiro(5-chloro-6-phenylsulfonyl-2,3-dihydro-1*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-6"-phenylsulfonyl-2",3"-dihydro-1"*H*-benzimidazole) (**43b**).

After evaporation to dryness the residue was purified on a silica column with a mixture of ethyl acetate/*n*-hexane 5:1 to give an oil, which crystallized on addition of ethyl acetate and 20 ml of *n*-hexane as a beige powder to yield 0.96 g (42%), mp 177°; ir: ν 3375 (NH), 3066 (CH), 2928 (CH_2), 1604 (C=C), 1502 (N-H), 1089 (SO_2); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 7.79 (m, 4H, 2"',6"'-H), 7.61 (m, 7H, 3"',4"',5"'-H + NH), 7.33 (m, 1H, NH), 6.68 (m, 6H, 2 x NH, 4,4",7,7"-H), 1.81 (m, 8H, cyclohexyl-H); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 146.1, 141.8 (C-3a,3"a,7a,7"a), 139.0 (C-1"'), 123.3, 122.2 (C-5,5", 6,6"), 80.7 (C-2,2"), 132.7, 129.0, 126.4 (C-2"',3"',4"',5"', 6"'), 105.7, 103.4 (C-4,4",7,7"), 36.6 (CH_2); ms: m/z 640 ([M]$^+$), 576 ([M-SO_2]$^+$), 360 ([$C_{18}H_{18}N_4Cl_2$]$^+$), 320 ([$C_{15}H_{13}N_2SO_2Cl$]$^+$), 285 ([$C_{15}H_{13}N_2SO_2$]$^+$).

Anal. Calcd. for $C_{30}H_{26}Cl_2N_4O_4S_2$: C, 56.16; H, 4.08; N, 8.73; S, 9.99. Found: C, 56.35; H, 4.43; N, 8.42; S, 9.73.

General Procedure for the Oxidation of **36, 37, 42** and **43** to give **38, 39, 44, 45**.

To a solution of (0.001 mole) *Z/E*-dispiro(5-phenylsulfanyl-2,3-dihydro-1*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-phenylsulfanyl-2",3"-dihydro-1"*H*-benzimidazole) (**36a/b**), *Z/E*-dispiro(5-phenylsulfonyl-2,3-dihydro-1*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-phenylsulfonyl-2",3"-1"*H*-benzimidazole) (**37a/b**), *Z/E*-dispiro(5-chloro-6-phenylsulfanyl-2,3-dihydro-1*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-6"-phenylsulfanyl-2",3"-dihydro-1"*H*-benzimidazole) (**42a/b**) or *Z/E*-dispiro(5-chloro-6-phenylsulfonyl-2,3-dihydro-1*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-6"-phenylsulfonyl-2",3"-dihydro-1"*H*-benzimidazole) (**43a/b**) dissolved in 50 ml of dichloromethane was added 1.74 g (0.020 mole) of manganese dioxide and the mixture was stirred for 1 hour at room temperature. The mixture was filtered and evaporated to dryness to give the crude products.

Z-Dispiro(5-phenylsulfanyl-2*H*-benzimidazole-2,1'-cyclohexane -4',2"-5"-phenylsulfanyl-2"*H*-benzimidazole) (**38a**), and *E*-Dispiro(5-phenylsulfanyl-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-phenylsulfanyl-2"*H*-benzimidazole) (**38b**).

Purification on a silica column with a mixture of ethyl acetate/*n*-hexane 1:1 gave a residue, which was recrystallized from diethyl ether as orange needles to yield 0.310 g (61%), mp 235°; ir: ν 3050 (CH), 2934 (CH_2), 1617 (C=C), 1522 (C=N); ^{1}H nmr (deuteriochloroform): δ 7.67 (m, 4H, 2"',6"'-H), 7.45 (m, 6H, 3"',4"',5"'-H), 7.01 (d, $^3J_{6,7/6",7"}$ = 7.5 Hz, 2H, 7,7"-H), 6.83 (m, 2H, 6,6"-H), 6.22 (d, $^4J_{6,4/6",4"}$ = 2.9 Hz, 2H, 4,4"-H), 2.25 (m, 8H, cyclohexyl-H); ^{13}C nmr (deuteriochloroform): δ 160.0, 158.3 (C-3a,3"a,7a,7"a), 137.9 (C-5,5"), 129.5 (C-1"'), 106.9 (C-2,2"), 135.4, 134.8, 129.8, 129.5, 126.2, 121.3 (C-4,6,7,4",6",7",2"',3"',4"',5"',6"'), 31.6 (*C*H$_2$); ms: m/z 504 ([M]$^+$), 478 ([M-C_2H_2]$^+$), 252 (41%, [$C_{15}H_{12}N_2S$]$^+$).

Anal. Calcd. for $C_{30}H_{24}N_4S_2$: C, 71.40; H, 4.79; N, 11.10; S, 12.71. Found: C, 71.53; H, 4.83; N, 11.34; S, 12.64.

Z-Dispiro(5-phenylsulfonyl-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-phenylsulfonyl-2"*H*-benzimidazole) (**39a**), and *E*-Dispiro-(5-phenylsulfonyl-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-phenylsulfonyl-2"*H*-benzimidazole) (**39b**).

Recrystallisation from ethyl acetate/*n*-hexane gave a white powder, 0.38 g (66%), mp 211°; ir: ν 3056 (CH), 2930 (CH_2), 1628 (C=C), 1526 and 1446 (C=N), 1.314 and 1153 (SO_2); ^{1}H nmr (deuteriochloroform): δ 8.05 (m, 6H, 4,4'-H and 2"',6"'-H), 7.69 (m, 6H, 3"',4"',5"'-H), 7.39 (m, 2H, 6,6'-H), 7.30 (m, 2H, 7,7'-H), 2.01 (m, 8H, cyclohexyl-*H*); ^{13}C nmr (deuteriochloroform): δ 159.1, 158.5 (C-3a,3"a, 7a,7"a), 147.9 (C-5,5"), 138.7 (C-1"'), 134.4 (C-4,4"), 129.9, 129.8, 128.5, 128.4, 128.2

(C-6,6",7,7",2"',3"',4"',5"',6"'), 109.2 (C- 2,2"), 31.1 (CH_2); ms: m/z 570 ([M+2]$^+$), 56:9 ([M]$^+$), 542 ([M-C_2H_4]$^+$), 286 ([$C_{18}H_{14}N_4$]$^+$), 142 ([$C_6H_6SO_2$]$^+$), 78 ([C_6H_6]$^+$)

Anal. Calcd. for $C_{30}H_{24}N_4O_4S_2$: C, 63.36; H, 4.25; N, 9.85; S, 11.28. Found C, 62.72; H, 433; N, 9.91; S, 11.06.

Z-Dispiro(5-chloro-6-phenylsulfanyl-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-6"-phenylsulfanyl-2"*H*-benzimidazole) (**44a**), and *E*-Dispiro(5-chloro-6-phenylsulfanyl-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-6"-phenylsulfanyl-2"*H*-benzimidazole) (**44b**).

Purification on a silica column with a mixture of ethyl acetate/*n*-hexane 1:1 gave a residue, which was recrystallized from diethyl ether as orange powder to yield 0.430 g (75%), mp 205°; ir: ν 3056 (CH), 2923 (CH_2), 1606 (C=C), 1581 (C=N); ^{1}H nmr (deuteriochloroform): δ 7.60 (m, 10H, 2"',3"', 4"',5"',6"'-H); 7.09 (s, 2H, 7,7"-H); 6.0 (s, 2H, 4,4"-H), 2.15 (cyclohexyl-H); ^{13}C nmr (deuteriochloroform): δ 159.0, 156.7 (C-3a,7a,3"a,7"a'), 141.9 (C-5,5"), 140.1 (C-6,6"), 135.6 (C- 4,4"), 130.2 (C-7,7"), 129.5 (C-4"'), 127.1 (C-3"',5"'), 118.7 (C-2"',6"'), 128.1 (C-1"'), 108.0 (C-2,2"), 31.6 (CH_2); ms: m/z 576 ([M+4]$^+$), 574 ([M+2]$^+$), 572 ([M]$^+$), 546 ([M-C_2H_4]$^+$), 545 ([M-C_2H_5]$^+$), 286 ([$C_{15}H_{11}N_2SCl$]$^+$), 285 ([$C_{15}H_{10}N_2SCl$]$^+$), 109 ([C_6H_5S]$^+$).

Anal. Calcd. for $C_{30}H_{22}Cl_2N_4S_2$: C, 62.82; H, 3.87; N, 9.77; S 11.18. Found C, 62.43; H, 3.95; N, 10.07; S, 11.21.

Z-Dispiro(5-chloro-6-phenylsulfonyl-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-6"-phenylsulfonyl-2"*H*-benzimidazole) (**45a**), and *E*-Dispiro(5-chloro-6-phenylsulfonyl-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-chloro-6"-phenylsulfonyl-2"*H*-benzimidazole) (**45b**).

Purification on a silica column with a mixture of ethyl acetate/*n*-hexane 5:1 gave the product, which was recrystallized from ethyl acetate and 20 ml of *n*-hexane as a white powder to yield 0.50 g (78%), mp 217°; ir: ν 3068 (CH), 2928 (CH_2), 1623 (C=C), 1521 (C=N), 1156 (SO_2); ^{1}H nmr (deuteriochloroform): δ 8.5 (s, 2H, 7,7"), 8.01 (m, 4H, 2"',6"'-H), 7.65 (m, 6H, 3"',4"',5"'-H), 7.45 (s, 2H, 4,4"-H), 2.13 (m, 8H, cyclohexyl-H); ^{13}C nmr (deuteriochloroform): δ 158.6, 157.4 (C-3a,3"a,7a,7"a), 145.8 (C-5,5"), 138.8 (C-1"'), 135.6 (C-6,6"), 135.6 (C-7,7"), 134.3 (C-4,4"), 129.9, 129.8, 129.4, 128.5, 127.8 (C-2"', 3"',4"',5"',6"'), 31.2 (CH_3); ms: m/z 640 ([M+4]$^+$), 638 ([M+2]$^+$), 636 ([M]$^+$), 320 ([$C_{15}H_{13}N_2ClSO_2$]$^+$), 318 ([$C_{15}H_{11}N_2ClSO_2$]$^+$), 142 ([$C_6H_6SO_2$]$^+$), 125 ([C_6H_5SO]$^+$), 110 ([C_6H_5S]$^+$), 78 ([C_6H_6]$^+$).

Anal. Calcd. for $C_{30}H_{22}Cl_2N_4O_4S_2$: C, 56.52; H, 3.48; N, 8.79; S, 10.06. Found C, 56.90; H, 3.14; N, 9.09; S, 10.04.

Z-Dispiro(5-azido-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-azido-2"*H*-benzimidazole) (**46a**), and *E*-Dispiro(5-azido-2*H*-benzimidazole-2,1'-cyclohexane-4',2"-5"-azido-2"*H*-benzimidazole) (**46b**).

Method A.

To a solution of 1.25 g (0.0035 mole) *Z/E*-dispiro(5-chloro-2*H*-benzimidazole-2,1'-cyclohexane-5"-chloro-2"*H*-benzimidazole) (**31a/b**) in 50 ml of dry tetrahydrofuran was added 1.1 g (0.00954 mole) of trimethylsilyl azide. It was stirred for 24 hours at room temperature. The residue was purified on a silica column with a mixture of ethyl acetate/methanol 5:2 and recrystallized from ethyl acetate as an orange powder to yield 0.30 g (23%), mp 200° dec; ir: ν 3034 (CH), 2915 and 2850 (CH_2), 2113 (N_3), 1628 (C=C), 1560 (C=N); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 7.24 (m, 4H, 6,6",7,7"-H), 6.15 (m, 2H, 4,4"-H), 1.95 (m, 8H, cyclohexyl-*H*); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 158.8, 158.2 (C-5,5"), 146.9, 146.0, 140.3 (C-3a,3"a,7a,7"a), 137.2, 133.9, 132.3, 128.0, 127.1, 124.7 (C-6,6",7,7"), 109.5 (C-4,4"), 106.9, 106.4 (C-2,2"), 32.9, 32.1, 30.9 (CH_2); ms: (FAB, glycerine) 370 (M$^+$), 185 ($^1/_2$M$^+$).

Anal. Calcd. $C_{18}H_{14}N_{10}$: C, 58.37; H, 3.81; N, 37.82. Found C, 58.46; H, 3.78; N, 37.39.

Method B.

To a solution of 1.136 g (0.002 mole) *Z/E*-dispiro(5-phenylsulfonylphenylsulfonyl-2"*H*-benzimidazole) (**39a/b**) in 50 ml of dry tetrahydrofuran was added 0.63 g (0.00548 mole) of trimethylsilyl azide and it was stirred for 24 hours at room temperature. The residue was purified on a silica column with a mixture of ethyl acetate/methanol 5:2, and recrystallized from ethyl acetate as an orange powder to yield 0.110 g (14%).

4-Chloro-5-piperidino-*o*-phenylenediainine (**47**).

To a solution of 0.522 g (0.001 mole) of *Z/E*-dispiro(5-chloro-6-piperidyl-2*H*-benzimidazole-2,1'-cyclohexane-5"-chloro-6"-piperidyl-4',2"-2"*H*-benzimidazole) (**40a/b**) in 25 ml of dry tetrahydrofuran was added 25 ml of water and 4.35 g (0.025 mole) of sodium dithionite. The mixture was stirred for 45 minutes at room temperature and then adjusted by addition of sodium hydrogen carbonate to *p*H 10. The organic product was isolated by extraction with ethyl acetate, the residue was dried over magnesium sulfate, evaporated to dryness and purified on a silica column with ethyl acetate/*n*-hexane to give a dark-red compound, 0.260 g (57%), mp 112°; ir: ν 3421 (NH_2), 2932 and 2853 (CH_2), 1616 (C=C); ^{1}H nmr (deuteriochloroform): δ 6.72 (s, 1H, 3-H), 6.45 (s, 1H, 641), 3.15 (m, 8H, 1,2-NH_2, 2',6'-H), 1.65 (m, 6H, 3',4',5'-H); ^{13}C nmr (deuteriochloroform): δ 138.5 (C-4), 134.4 (C-5), 118.8 (C-3), 109.1 (C-6), 108.0, 107.3 (C-1,2); ms: m/z 227 ([M+2]$^+$), 225 ([M]$^+$), 224 ([M-1]$^+$), 196 ([M-C_2H_5]$^+$), 19, ([M-^{15}Cl]$^+$), 168 ([$C_7H_7N_3Cl$]$^+$), 142 ([$C_7H_5N_2Cl$]$^+$), 84 (100%, [$C_5H_{10}N$]$^+$).

Anal. Calcd. for $C_{11}H_{16}ClN_3$: C, 58.53; H, 7.14; N, 18.62. Found C, 58.78; H, 7.3 9; N, 18.91.

5-Chloro-6-piperidino-1*H*-benzimidazole (**48**).

The impure but dried ethyl acetate solution of **47** was evaporated and dissolved in a mixture of 4 ml of concentrated hydrochloric acid and 6 ml of water. After adding 10 ml of formic acid the mixture was refluxed for 3 hours. After cooling were added 30 ml of water and the mixture adjusted to *p*H 9 with potassium carbonate. The organic product was isolated by extraction with ethyl acetate, dried over magnesium sulfate, evaporated to dryness and purified on a silica column with ethyl acetate; recrystallization from ethyl acetate yielded light pink needles, 0.260 g (55%), mp 181°; ir: ν 3487 (NH), 3087 (CH), 2938 and 2807 (CH_2), 1734, 1718 and 1700 (C-N), 1607 (C=C), 1584 (C=N), 1506 (NH); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 12.39 (s, 1H, NH), 8.06 (s, 1H, 2-H), 7.00 (d, ^{5}J = 1.6 Hz, 1H, 4-H), 6.43 (d, ^{5}J = 1.45 Hz, 1H, 7-H), 3.39 (s, 2H, 4'-H), 2.71 (m, 4H, 2',6'-H), 1.65 (m, 4H, 3',5'-H); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 144.2 (C-3a), 139.2 (C-2), 134.7 (C-7a), 132.9 (C-5), 127.5 (C-6), 106.2 (C-7), 102.4 (C-6), 49.8 (C-2',6'), 25.3 (C-3',5'), 24.0 (C-4'); ms: m/z 237 ([M+2]$^+$), 236 ([M+1]), 235 ([M]$^+$), 234 ([M-1]$^+$), 206 ([M-C_2H_5]$^+$), 200 ([M^{35}Cl]$^+$), 152 ([M-C_5H_9N]$^+$), 117 ([M-C_5H_9N-^{35}Cl]$^+$), 84 ([$C_5H_{10}N$]$^+$).

Anal. Calcd. for $C_{12}H_{14}ClN_3$: C, 61.15; H, 5.99; N, 17.83. Found C, 61.07; H, 6.03; N, 17.57.

General Procedure for Preparing *N*-Oxides from **2, 3** and **31a/b**.

To a solution of 0.001 mole of **2, 3** or (**31a/b**) in 30 ml of chloroform was added a solution of 0.340 g (0.002 mole) of *m*-chloroperoxybenzoic acid in 3 ml of chloroform and the mixture stirred for 48 hours at room temperature.

Z-Bis(2*H*-benzimidazol-2-ylidene 1-*N*-Oxide) (**49a**), and *E*-Bis(2*H*-benzimidazol-2-ylidene 1-*N*-Oxide) (**49b**).

After evaporation to dryness the residue was purified on a silica column with ethyl acetate to give red needles, 0.050 g (20%), mp >250°; ir: ν 1734, 1616 (C=C), 1576 (C=N), 1299 (*N*-oxide); ^{1}H nmr (deuteriochloroform): δ 8.74 (d, ^{3}J = 9.1 Hz, 2H, 7,7'-H**a**); 8.43 (m, 6H, 7,7'-H**b**, 5,5',6,6'-H**a**), 7.98 (m, 6H, 5,5',6,6'-H**b**, 4,4'-H**a**); 7.81 (d, ^{3}J = 9.1 Hz, 2H, 4,4'-H**b**); ^{13}C nmr (deuteriochloroform): δ 148.8, 147.8, 147.7, 145.6, 144.1 (C-3a,3"a,7a, 7'a**a/b**); 139.1, 137.7 (C-2,2'**a/b**); 133.7, 133.6, 133.3, 133.0, 131.4, 131.1, 130.4, 130.2, 130.0, 128.0, 119.6 (C4,5,6,7,4',5',6',7'**a/b**); ms: m/z 264 ([M]$^+$), 248 ([M-^{16}O]$^+$), 232 ([M-2 x ^{16}O]$^+$).

Anal. Calcd. for $C_{14}H_8N_4O_2$: C, 63.64; H, 3.05; N, 21.20. Found C, 63.53; H, 3.03; N, 20.84.

E-Dispiro(2*H*-benzimidazole 1-*N*-Oxide-2,1'-cyclohexane-4',2"-2"*H*-benzimidazole 1-*N*-Oxide) (**50b**).

The above solution was evaporated to dryness and purified on a silica column; the first fraction was crystallized from ethyl acetate as a red powder to yield 0.10 g (31%), mp >230°; ir: ν 2971 and 2923 (CH_3), 1612 (C=C), 1558 and 1526 (C=N), 1264 (*N*-oxide); ^{1}H nmr (deuteriochloroform): δ 7.33 (m, 1H, 7-H), 7.28 (m, 2H, 5,6-H), 7.22 (m, 1H, 7"-H), 7.15 (m, 1H, 4-H), 7.05 (m, 2H, 5",6"-H), 6.82 (m, 1H, 4"-H), 3.09 (m, 2H, 2'-H), 2.87 (m, 2H, 5'-H), 1.49 (m, 2H, 3'-H), 1.16 (m, 2H, 6'-H); ^{13}C nmr (deuteriochloroform): δ 163.0 (C-7a, 7"a), 160.1 (C-3a,3"a), 135.4 134.6, 134.5 (C-4", 5", 6"),128.4 (C-7"), 126.1, 126.0, 125.7 (C-4,5,6), 117.0 (C-7), 105.5, 104.3 (C-2,2"), 33.9 (C-2',5'), 30.2 (C-3',6'); ms: m/z 320 ([M]$^+$), 304 ([M-^{16}O]$^+$), 288 ([M-2 x ^{16}O]$^+$).

Anal. Calcd. for $C_{18}H_{16}N_4O_2$: C, 67.49; H, 5.03; N, 17.49. Found C, 67.59; H, 5.28; N, 1718.

Z-Dispiro(2*H*-benzimdazole 1-*N*-Oxide-2,1'-cyclohexane-4',2"-2"*H*-benzimidazole 1-*N*-Oxide) (**50a**).

The second fraction after purification was recrystallized from ethyl acetate as yellow-orange needles to yield 0.090 g (28%), mp >230°; ir: ν 2933 (CH_2), 1611 (C=C), 1556 (C=N), 1093 (*N*-oxide); ^{1}H nmr (deuteriochloroform): δ 7.03 (m, 8H, 4, 5, 6, 7, 4", 5",6",7"-H), 2.13 (m, 8H, cyclohexyl-H); ^{13}C nmr (deuteriochloroform): δ 163.0 (C-7a, 7"a), 106.1 (C-3a,3"a), 136.8 (C-7,7"), 128.5 (C-6,6"), 125.7 (C-5,5"), 117.0 (C-4,4"), 105.5 (C-2,2"), 30.8 (*C*H$_2$); ms: m/z 320 ([M]$^+$), 304 ([M-^{16}O]$^+$), 288 ([M-2 x ^{16}O]$^+$).

Anal. Calcd. for $C_{18}H_{16}N_4O_2$: C, 67.49; H, 5.03; N, 17.49. Found C, 67.63; H, 5.17; N, 17.34.

Z-Dispiro(5-chloro-2*H*-benzimidazole 1-*N*-Oxide-2,1'-cyclohexane-4',2 5"-chloro-2"*H*-benzimidazole 1"-*N*-Oxide) (**51a**).

The solution was evaporated to dryness and purified on a silica column with a mixture of ethyl acetate/methanol 10:1; the second fraction was recrystallized from ethyl acetate as orange-red needles to yield 0.010 g (25%), mp >230°; ir: ν 3033 (CH), 2915 (CH_2), 1627 (C=C), 1559 (C=N), 1258 (*N*-oxide); ^{1}H nmr (deuteriochloroform): δ 7.35 (dd, ^{4}J = 1.84 Hz, ^{5}J = 0.94 Hz, 2H, 4,4"-H), 7.29 (dd, ^{3}J = 9.8 Hz, ^{5}J = 0.98 Hz, 2H, 7,7"-H), 6.98 (dd, ^{3}J = 9.8 Hz, ^{4}J = 1.94 Hz, 2H, 6,6"-H), 2.01 (m, 8H, cyclohexyl-*H*); ^{13}C nmr (deuteriochloroform): δ 169.2, 165.1 (C-3a, 3"a,7a,7"a), 141.1 (C-5,5"), 137.8 (C-4,4"), 126.6 (C-7,7"), 115.4 (C-6,6"), 105.8 (C-2,2"), 33.9, 30.2 (*C*H$_2$); ms: m/z 390 ([M+2]$^+$), 388 ([M]$^+$), 371 ([M-^{17}OH]$^+$), 356 ([M-^{32}O$_2$]), 353 ([M-^{35}Cl]$^+$), 194 ([^{1}/$_2$M]$^+$).

Anal. Calcd. for $C_{18}H_{14}Cl_2N_4O_2$: C, 55.55; H, 3.62; N, 14.40. Found C, 55.86; H, 3.69; N, 14.13.

E-Dispiro(5-chloro-2*H*-benzimidazole 1-*N*-Oxide-2,1'-cyclohexane-4',2"-5"-chloro-2"*H*-benzimidazole 1"-*N*-Oxide) (**51b**), *E*-Dispiro(5-chloro-2*H*-benzimidazole 1-*N*-Oxide-2,1'-cyclohexane-4',2"-6"-chloro-2"*H*-benzimidazole 1"-*N*-Oxide) (**51c**), *Z*-Dispiro(5-chloro-2*H*-benzimidazole 1-*N*-Oxide-2,1'-cyclohexane-4',2"-6"-chloro-2"*H*-benzimidazole 1"-*N*-Oxide) (**51d**).

The third fraction after purification on a silica column was recrystallized from ethyl acetate as a red-orange powder to yield 0.110 mg (28%), mp >230°; ir: ν 3035 (CH), 2965 (CH_2), 1628 (C=C), 1526 (C=N), 1260 (*N*-oxide); ^{1}H nmr (deuteriochloroform): δ 6.8-8.4 (m, 18H, 4,6,7,4", 6",7"-H), 0.8-3.1 (m, 24H, cyclohexyl-*H*); ^{13}C nmr (deuteriochloroform): δ 162.2, 161.6, 159.7, 159.1, 158.9, 158.2 (C-7a,7"a), 142.6, 141.8, 141.5 (C-5,5"), 135.8, 135.0, 134.6, 134.1, 131.8 (C-3a,3"a), 138.0, 137.5, 137.4, 133.3 (C-7,7"), 130.6, 130.2, 129.7, 128.2, 126.7, 126.5, 123.7, 123.4, 117.7, 115.2 (C-4,6,4",6"), 106.5, 105.1, 104.1, 104.0 (C-2,2"), 33.8, 33.8, 32.6, 32.6, 31.4, 31.3, 30.1, 28.5, 28.3 (*C*H$_2$); ms: m/z 392 ([M+4]$^+$), 390 ([M+2]$^+$), 388 ([M]$^+$), 371 ([M-^{17}OH]$^+$), 356 ([M-^{32}O$_2$]), 353 ([M-^{35}Cl]$^+$), 194 ([^{1}/$_2$M]$^+$).

Anal. Calcd. for $C_{18}H_{14}Cl_2N_4O_2$: C, 55.55; H, 3.62; N, 14.40. Found C, 55.78; H, 3.71; N, 14.24.

REFERENCES AND NOTES

[1] H. A. Staab and F. Vögtle, *Chem. Ber.*, **98**, 2861 (1965).

[2] G. V. Garner, R. Garner, and H. Suschitzky, *J. Chem. Soc.*, 825 (1970).

[3] K. E. Davies, G. E. Dornany, 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).

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

[5] J. A. L. Herbert, B. Iddon, A. G. Robinson, and H. Suschitzky, *J. Chem. Soc. Perkin. Trans.1*, 991 (1988).

[6] B. Iddon, A. G. Robinson, H. Suschitzky, *Synthesis*, 871 (1988).

[7] J. C. Hazelton, B. Iddon, H. Suschitzky, and L. H. Woolley, *J. Chem. Soc. Perkin. Trans.1*, 685 (1992).

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

[9] J. H. M. Hill, *J. Org. Chem.*, **28**, 1931 (1963).

[10] T. S. Lane, *J. Chem.* Soc., 2238 (1953).

[11] A. J. Fatiadi, *Synthesis*, **65** (1976).

[12] M. Hesse, H. Meier, and B. Zeeh, Spektroskopische Methoden in der organischen Chemie, 5. Aufl., Georg Thieme Verlag Stuttgart/New York 1995, p 158.

[13] R. Mc Donald, R. Steppe, J. Dorsey, *Org. Synth. Coll., Vol,* **VI**, New York 1967, p 276.