Synthesis and Structural Elucidation of Pyrimido-[1,2-*a*]benzimidazoles and Fused Derivatives. I. Dihydropyrimido[1,2-*a*]benzimidazoles [1,2]

Dalal Abou El Ella [3], Edith Gößnitzer and Winfried Wendelin*

Institut für Pharmazeutische Chemie der Karl-Franzens-Universität Graz, Schubertstraße 1, A-8010 Graz, Austria

Received July 25, 1995

The condensation of 2-benzimidazolamine (**4, BIA**) with α,β-unsaturated ketones **1** affords, according to Desenko, Orlov *et al.* [12,13], 1,4-dihydropyrimido[1,2-*a*]benzimidazoles (1,4-**DHPBI, 5I**). However, the described ring closure reactions could a priori also yield isomeric 1,2-**DHPBI 8I** or tautomers of **DHPBIs 5I** and **8I**. An unequivocal proof for the postulated structures **5I** was not presented. We prepared, as described [12,13], **BIA**-chalcone- and **BIA**-benzalacetone-condensate **X** and **Y**, **5a,e** or **8a,e**, and additionally, their hydrochlorides. One and two dimensional high resolution nmr analyses showed that only isomers **5a,e** and salts **5a,e**·HCl were generated. In DMSO-d_6 these isomers exclusively exist as 1,4-dihydro tautomers **5a,eI** and **5a,eI**·HCl. In trifluoroacetic acid 3,4-dihydro tautomers **5a,eIII**·CF_3COOH besides of tautomers **5a,eI**·CF_3COOH (≈1:4) were ascertained. Action of ethanolic hydrochloric acid on base **5eI** afforded, besides of **5eI**·HCl as main product, a small amount of 2-methyl-4-phenyltetrahydropyrimido[1,2-*a*]benzimidazol-2-ol hydrochloride **9e**·HCl. The reaction of **BIA 4** with α,β-unsaturated ketones **1b-d** and **f** yielded 1,4-**DHPBI 5b-dI** and **5fI** and their hydrochlorides, respectively. The stereochemistry of bases **5a,eI**, of salts **5a-eI**·HCl and **5a,eIII**·CF_3COOH, and of addition product **9e**·HCl was elucidated by nmr (stereoformulae in Figures 1-3 and Scheme 5). The accomplished nmr-analyses are documented in detail and discussed.

J. Heterocyclic Chem., **33**, 373 (1996).

Introduction.

In the course of investigations on dihydropyrimidines Wendelin and coworkers [4,5] synthetized, among others, 2-phenylaminodihydropyrimidines and fused derivatives **3**. Compounds **3** were prepared by reaction of arylguanidines **2** with α,β-unsaturated ketones **1** and by alternative methods [4,5]. Several pyrimidines **3** exhibited antifungal and other pharmacological activities [6,7].

These findings prompted us to design compounds with near structural relationship to arylaminopyrimidines **3** for further pharmacological tests. In this series we report on dihydropyrimido[1,2-*a*]benzimidazoles and fused derivatives **5**, which represent bridged and therefore rigid derivatives of arylaminopyrimidines **3** with direct connection between nitrogen atom of the pyrimidine ring and *o*-position of the aryl group. Compounds **5** should be synthetized from α,β-unsaturated ketones **1** and 2-benzimidazolamine (**4, BIA**) instead of arylguanidines **2** (Scheme 1).

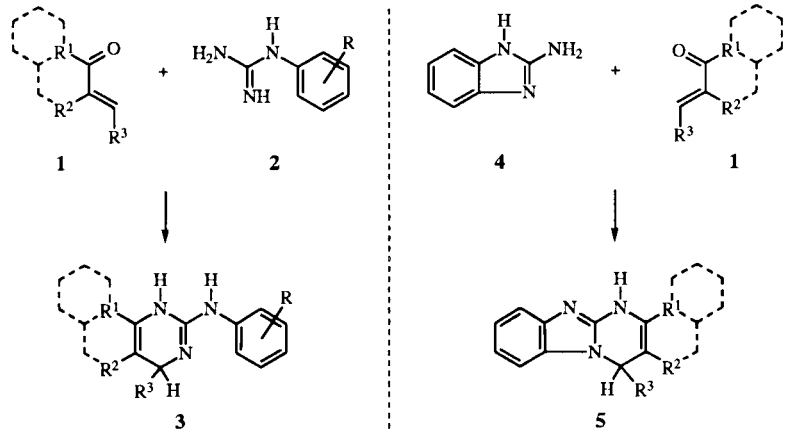
The first communication of the series deals with dihydropyrimido[1,2-*a*]benzimidazoles.

Short Review of the Literature on Pyrimido[1,2-*a*]benzimidazoles.

A literature search revealed a few reports on aromatic, dihydro- and tetrahydropyrimidobenzimidazoles **6**, **5** and **7**.

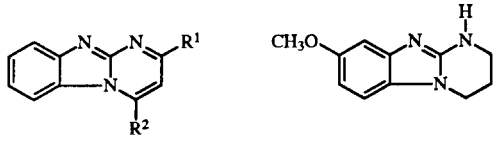
2,4-Disubstituted pyrimido[1,2-*a*]benzimidazoles **6** were synthetized from **BIA 4** and various β-diketones [8-10]. One compound **6** (R^1 = trifluoromethyl, R^2 = methyl) was tested and showed herbicidal activity [9].

Scheme 1



8-Methoxytetrahydropyrimidobenzimidazole **7** was prepared by reduction of 8-methoxy-3,4-dihydropyrimido[1,2-*a*]benzimidazol-2(1*H*)-one with lithium aluminum hydride [11]. Derivatisation of **7** yielded substituted tetrahydropyrimidobenzimidazoles. Some of these compounds, including **7**, showed moderate antidepressant effects.

Scheme 2



6 **7**

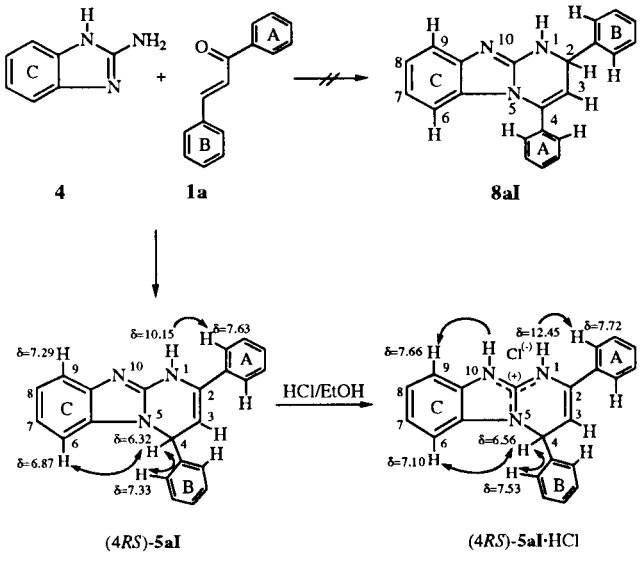
Several dihydropyrimido[1,2-*a*]benzimidazoles (**DHPBIs**) were synthetized from **BIA 4** and α,β-unsaturated ketones by Desenko, Orlov *et al.* [12,13]. The reactions afford, according to [12 and 13], 1,4-**DHPBIs 5**.

Results and Discussion. **BIA**-Chalcone-Condensate **X**.

A priori the described ring closure reaction, for example that one of **BIA 4** with chalcone **1a**, could not only yield 1,4-**DHPBIs 5I**, *e.g.* **5aI**, but also isomeric 1,2-**DHPBIs 8**, *e.g.* **8aI** (Scheme 3) or tautomers of **5I** and/or **8I**. The postulated structures **5I** were derived by Desenko, Orlov *et al.* [12,13] from the analogy of these reactions with similar ring closure reactions of 1,2,4-triazole-3-amine and 5-tetrazolamine with α,β-unsaturated ketones **1**, which were earlier accomplished by the same authors. An unequivocal proof for the formation of products **5I**, *e.g.* of chalkone-**BIA**-condensate **5aI**, was not presented.

We repeated the procedure of Desenko and Orlov [12] and were able to synthethize **BIA**-chalcone-condensate **X** (**5a** or **8a**) as described. The hydrochloride of base **X** (**X**·HCl) was also prepared. In order to find out the correct structures, we carried out proper nmr-experiments (^{1}H nmr, HH COSY, NOE difference spectra of base **X** and salt **X**·HCl, and additionally ^{13}C nmr, CH COSY and CH COLOC of **X**·HCl). The evaluation of the spectra showed that only one isomer had been generated and revealed the chemical shifts of all hydrogen atoms of base **X** and all hydrogen and carbon atoms of salt **X**·HCl (Table 1). In particular, ^{1}H nmr spectrum and HH COSY (Figure 1, for **5aI**·HCl) allowed to assign the chemical shifts of the aromatic protons of rings A, B and C including the sequence of protons H-6 to H-9. Methin proton H-4 and olefinic proton H-3 appear as doublets. A ^{4}J long range coupling of the methin proton H-4 with the *o*-protons of ring B (H-18,22), observed in the HH-COSY (Figure 1), shows the connection of ring B with the tertiary carbon atom (C-4 of **5a** or C-2 of **8a**).

Scheme 3 [14]



4 **1a** **8aI**

(4*RS*)-**5aI** (4*RS*)-**5aI**·HCl

Determination of Structure and Correct Tautomeric Forms of Base **X** and Salt **X**·HCl.

The question of the orientation of the ring closure reaction could be answered on the basis of the NOE-difference spectra of base **X** and salt **X**·HCl (Figure 1 and Scheme 3). Irradiation of the doublet at 6.32/6.56 ppm (methine proton, H-4 of **5a/5a**·HCl or H-2 of **8a/8a**·HCl) enhanced the doublet at 6.87/7.10 ppm (ring C, a priori H-6 of **5a/5a**·HCl or H-9 of **8a/8a**·HCl) and showed the spacial vicinity of these protons (Figure 1, trace 1, for **5aI**·HCl). The vice versa experiment was also successful (Figure 1, trace 2). Accordingly the methine proton is located in the 4- and the aromatic proton at 6.87/7.10 ppm of ring C in the 6-position. **BIA**-chalcone-condensate **X** and salt **X**·HCl are consequently 2,4-diphenyl-N,4-**DHPBI** (**5a**) and **5a**·HCl, and not 2,4-diphenyl-N,2-**DHPBI** (**8a**) and **8a**·HCl, respectively (Scheme 3).

Irradiation of the NH-protons of at 10.15 (**5a**) and 12.45 ppm (**5a**·HCl) gave strong NOEs of the *o*-protons of ring A (H-12,16) at 7.63 (**5aI**) and 7.72 ppm (**5aI**·HCl) and, in case of **5aI**·HCl, an additional moderate NOE of H-9 (ring C) at 7.66 ppm (Figure 1, trace 3, for **5aI**·HCl). These findings again and independently prove the structural formulae **5a** and **5a**·HCl. Additionally, they reveal the location of the NH-protons in 1-position of base **5a** and 1,10-position of salt **5a**·HCl. Consequently base **5a** exists in DMSO-d_6, in accordance with the so far not ascertained postulation of lit [12], as racemic 2,4-diphenyl-1,4-**DHPBI** [(4RS)-**5aI**]. The corresponding salt represents (4RS)-**5aI**·HCl (Schemes 3,4).

Stereochemistry of Base **5aI** and Salt **5aI**·HCl.

Irradiation of proton H-4 of **5aI/5aI**·HCl also causes a strong NOE of the *o*-protons of ring B (H-18,22) at 7.33/7.53 ppm (Figure 1, trace 1, for **5aI**·HCl). This finding again proves the connection of ring B with carbon

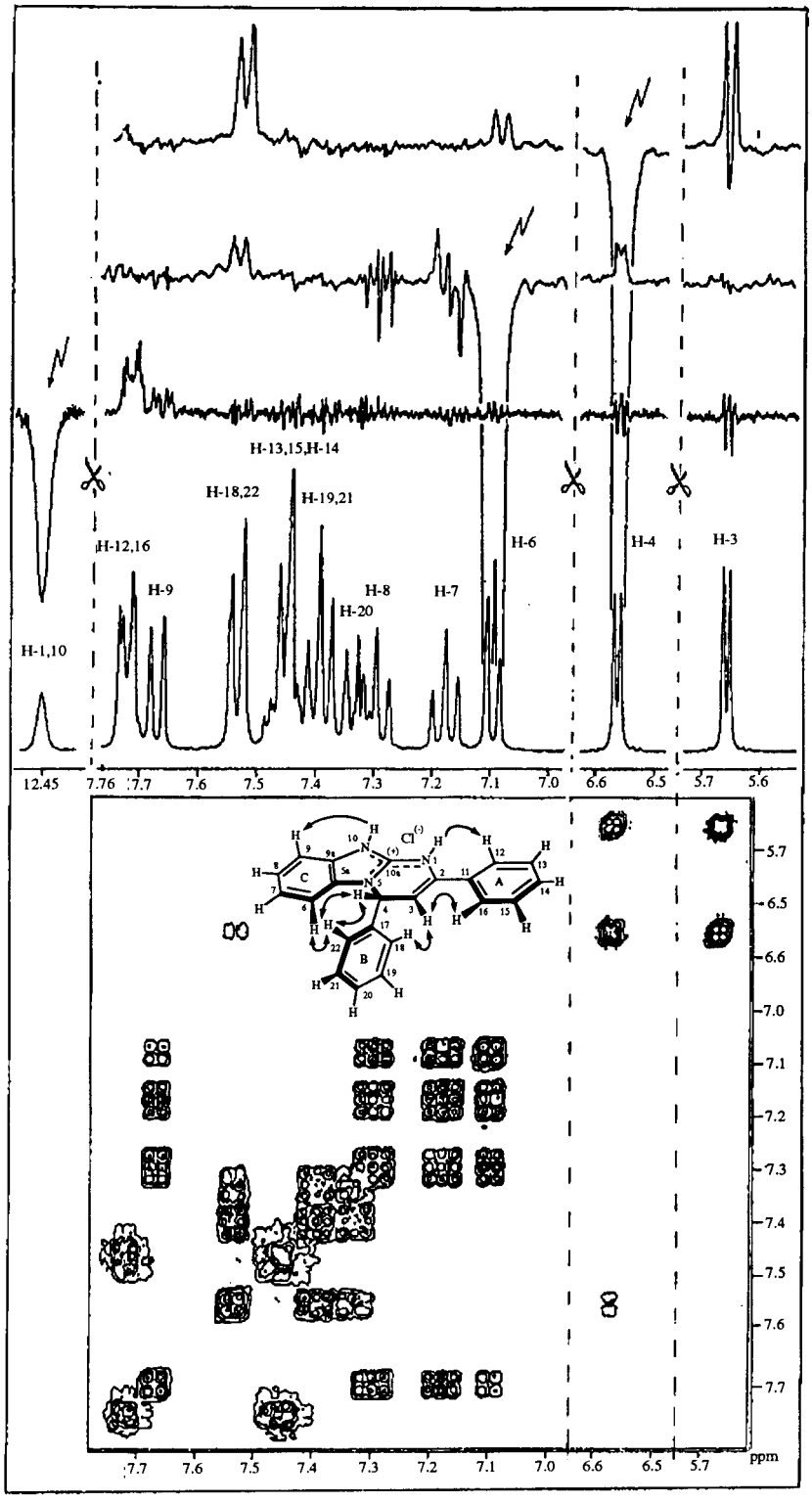


Figure 1. Stereoformula of (4*R*)-2,4-Diphenyl-1,4-**DHPBI** (**5aI**·HCl) [14]; 360 MHz ^{1}H NMR (Trace 4), NOE Difference Spectra (Traces 1-3) and HH COSY of (4*RS*)-**5aI**·HCl in DMSO-d_6, 300°K.

atom C-4. Additionally it points towards coplanarity of (C^{17}-C^4-H)-plane and ring B and towards an approximately perpendicular arrangement of ring B and pyrimidine ring, respectively, and allows to establish the stereo-

Table 1

NMR Data of (4*RS*)-2,4-Diphenyl-1,4-**DHPBI** Hydrochloride **5aI**·HCl [a]

Number	C-Atoms	H-Atoms, Correlating with C-Atoms over				
		1 bond		2 bonds	3 bonds	4 bonds
	δC (ppm)	δH (ppm) mult	J_{HH} (Hertz)			
2	131.8			H-3	H-12,16, H-4	
3	101.0	5.66 d	$^3J_{3,4} = 3.9$	H-4		
4	57.0	6.56 d	$^3J_{4,3} = 3.9$	H-3	H-18,22	
5a	128.1				H-7, H-9	
6	111.5	7.10 d	$^3J_{6,7} = 7.9$		H-8	
7	123.4	7.18 t	$^3J_{7,6} = {}^3J_{7,8} = 7.9$		H-9	
8	124.5	7.30 t	$^3J_{8,7} = {}^3J_{8,9} = 7.9$		H-6	
9	113.1	7.66 d	$^3J_{9,8} = 7.9$	(H-8)	H-7	
9a	129.8			H-6	H-8	(H-4,H-7)
10a	144.5				H-4	
11	139.5				H-13,15	
12,16	125.9	7.72 Dd	$^3J = 7.9$, $^4J = 1.8$		H-14	
13,15	128.7	7.46 m		H-12,16		
14	129.5	7.46 m			H-12,16	
17	132.3				H-19,21	(H-20)
18,22	127.1	7.53 db	$^3J = 7.2$	(H-19,21)	H-20	
19,21	129.1	7.39 tb	$^3J = 7.2$	H-18,22		
20	128.8	7.39 tm	$^3J = 7.2$	(H-19,21)	H-18,22	

[a] 360 MHz ^{1}H/90 MHz ^{13}C, DMSO-d_6, 300°K; H-atoms in brackets indicate weak correlations and cross-peaks, respectively.

formula of **5aI**·HCl shown in Figure 1. The mentioned coplanarity causes deshielding of H-4 and additional shielding of H-6 by ring B, which consequently appear at comparably deep (6.32/6.56 ppm) and rather high field (6.87/7.10 ppm), respectively.

The CH COSY and COLOC (long range CH-correlation) revealed the positions of protonated and quaternary carbon atoms of **5aI**·HCl (Table 1). The COLOC also shows, among others, a ^4J long range coupling between C-9a and H-4 and thus provides an alternative and independent proof for structure **5a**·HCl.

Discussion of the Tautomerism of 2,4-Diphenyl-**DHPBI** **5a** and of Salts of **5a**.

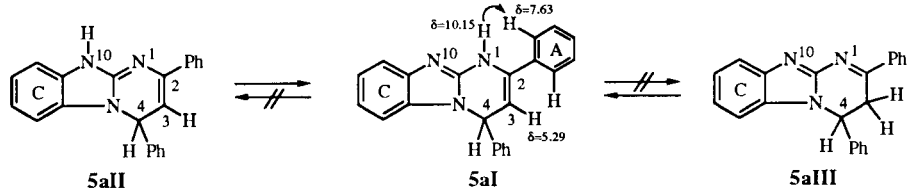
Migration of the NH-proton in 1-position to other basic positions of **DHPBI** **5aI** could afford also other tautomers, *e.g.* 4,10- and 3,4-**DHPBI** **5aII** and **5aIII**, respectively (Scheme 4). The above described nmr-data of **5a**-base and salt **5a**·HCl prove the exclusive existence of 1,4-dihydro tautomers **5aI** (Scheme 4) and **5aI**·HCl (Scheme 3, identical with **5aII**·HCl) in DMSO-d_6 solution, whereas tautomeric bases **5aII** and **5aIII** and tautomeric salt **5aIII**·HCl could not be traced.

In contrast, according to [12,13], 3,4-dihydro tautomers **5aIII**·CF_3COOH and **5aIII**·CF_3COOD are formed besides of the salts of 1,4-dihydro compound **5aI** in a (1:1)-ratio, if **5a**-base is dissolved in trifluoroacetic acid and deuterotrifluoroacetic acid, respectively.

The repetition of these experiments and additional detailed studies with a 360 MHz nmr spectrometer confirmed these findings and allowed to establish the stereoformula of **5aIII**·CF_3COOH. When the ^{1}H nmr spectra were recorded immediately after solution of base **5aI** in CF_3COOH and CF_3COOD, respectively, they showed only broad signals. After 40 minutes of waiting the signals had become well differentiated, but, in comparison with the spectrum of the hydrochloride **5aI**·HCl (Figure 1) the signals, especially in the aromatic region between H-8 and H-9, appeared in a smaller range.

The nmr signals of diagnostical value for 1,4-dihydro tautomer **5aI**·CF_3COOH are the doublets at 5.06 and 5.95 ppm for H-3 and H-4, whereas two double doublets at 3.46 and 3.66 ppm for the methylene protons a,b of C^3H_2 and a triplet at 5.62 ppm for methine proton H-4 (= x) with $J_{a,b} = 18.5$ Hz and $J_{a,x} = J_{b,x} = 8$ Hz, are characteris-

Scheme 4 [14]



tic of tautomer **5aIII**·CF_3COOH. In deuteriotrifluoroacetic acid the protons in 3-position are rapidly exchanged. Consequently, only (broad) singlets for the methine protons H-4 at 6.03 ppm (**5aI**·CF_3COOD) and 5.65 ppm (**5aIII**·CF_3COOD) were observed.

The ratios of the tautomers **5aI**·HX and **5aIII**·HX in our experiments were 3.5:1 in trifluoroacetic acid and 5:1 in deuteriotrifluoroacetic acid. When the solutions were diluted with water (**5a**·CF_3COOH) and DMSO-d_6 (**5a**·CF_3COOD), respectively, tautomers **5aIII**·HX disappeared and were transformed into tautomers **5aI**·HX, respectively. When the solution of **5a**·CF_3COOD was diluted with DMSO-d_6 (1:1;10:1), the signal for H-4 of **5aI**·CF_3COOD (6.03 ppm) shifted to 6.36 and finally 6.54 ppm and narrowed to a sharp singlet. Parallely all signals returned to the positions observed in the spectrum of **5aI**·HCl in DMSO-d_6.

Stereochemistry of the Trifluoroacetate of 3,4-**DHPBI 5aIII**.

The mentioned nmr signals indicate that protons a,b and x of the (C^3H_2-C^4H)-fragment of salt **5aIII**·CF_3COOH establish an ABX-system. The equality of the coupling constants $J_{a,x}$ and $J_{b,x}$ (2 x 8 Hz) points towards fast ring inversion (on the nmr time scale) and the existence of an equilibrium of conformers COEQ with pseudoequatorially directed ring B (Figure 2) and COAX with pseudoaxially orientated ring B, respectively.

Alternatively, as can be seen on hand of Dreiding models and by comparison with nmr studies in 1,3-cyclohexadienes and 3,4-dihydronaphthalenes [15], the observed coupling constants could also be consistent with fix dihedral angles between protons a and x as well as b and x of about 150° and 30°, or vice versa (but not 30° and 90°). In this case protons a and b (or vice versa) and x and phenyl group would be fixed each in pseudoaxial and pseudoequatorial position, respectively (the respective conformer corresponds to conformer COEQ shown in Figure 2).

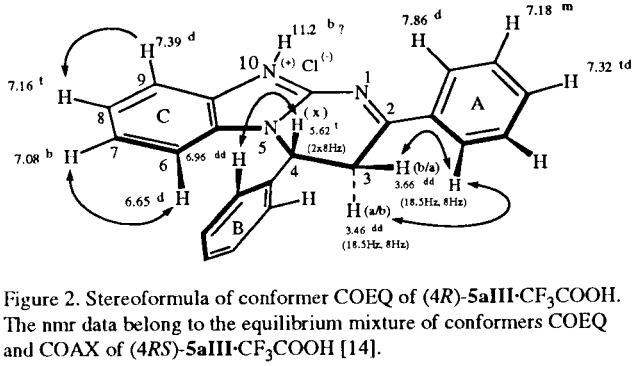


Figure 2. Stereoformula of conformer COEQ of (4*R*)-**5aIII**·CF_3COOH. The nmr data belong to the equilibrium mixture of conformers COEQ and COAX of (4*RS*)-**5aIII**·CF_3COOH [14].

The NOEs observed between the *o*-protons of ring A (δ = 7.86 ppm) and both, methylene protons a and b (or *vice versa*) at 3.46 and 3.66 ppm, argue for a rapid equilibrium between conformers COEQ and COAX. The dihydropyrimidine rings of conformers COEQ (Figure 2) and COAX exhibit a slightly twisted sofa-like conformation. The NOEs between methin protons (H-4) and *o*-protons of ring B (δ = 6.96 ppm) show that ring B is again arranged approximately perpendicular to the pyrimidine ring.

2,4-Disubstituted 1,4-Dihydropyrimido[1,2-*a*]benzimidazoles **5bI-5dI**.

The 1,4-**DHPBI 5b-5dI** were synthetized, in analogy to **5aI**, by condensation of **BIA 4** with 3,4-dichloro-3',4'-dimethoxychalcone (**1b**), 1-(4-fluorophenyl)-3-(2-thienyl)-2-propen-1-one (**1c**) and 1',2',3',4',5',6'-hexahydrochalcone (**1d**), respectively, in butanol or dimethylformamide as a solvent (Scheme 5). The crude base **5bI** could not sufficiently be purified. However trituration of bases **5b-5dI** with ethanolic hydrochloric acid yielded the corresponding hydrochlorides. The employed propenones **1b-d** were synthethized, as usual [16], by base catalyzed aldol condensation, see Experimental.

The structural elucidation of the salts **5b,c**·HCl was carried out *via* analogous nmr-experiments as in case of **5aI**·HCl. Consequently the salts are racemic hydrochlorides of 1,4-**DHPBI 5b,cI** with the stereoformulae shown in Scheme 5.

It may be remarkable that, in case of **5bI**·HCl, NOEs (arrows in Scheme 5) can at room temperature be observed between both chemically not equivalent *o*-protons of the 3,4-dimethoxyphenyl substituent in 2-position, H-12 and H-16, and both, protons H-1 and H-3 each. This finding points towards an oscillation of ring A between the two possible, approximately coplanar positions (the postulated coplanarity of ring A and partly positive pyrimidine ring can be derived from the downfield shift of H-12,16). Similarly the 3,4-dichlorophenyl radical in 4-position of **5bI**·HCl (NOEs between H-4 and not equivalent *o*-protons H-18 and H-22) seems to oscillate between the two possible approximately perpendicular positions.

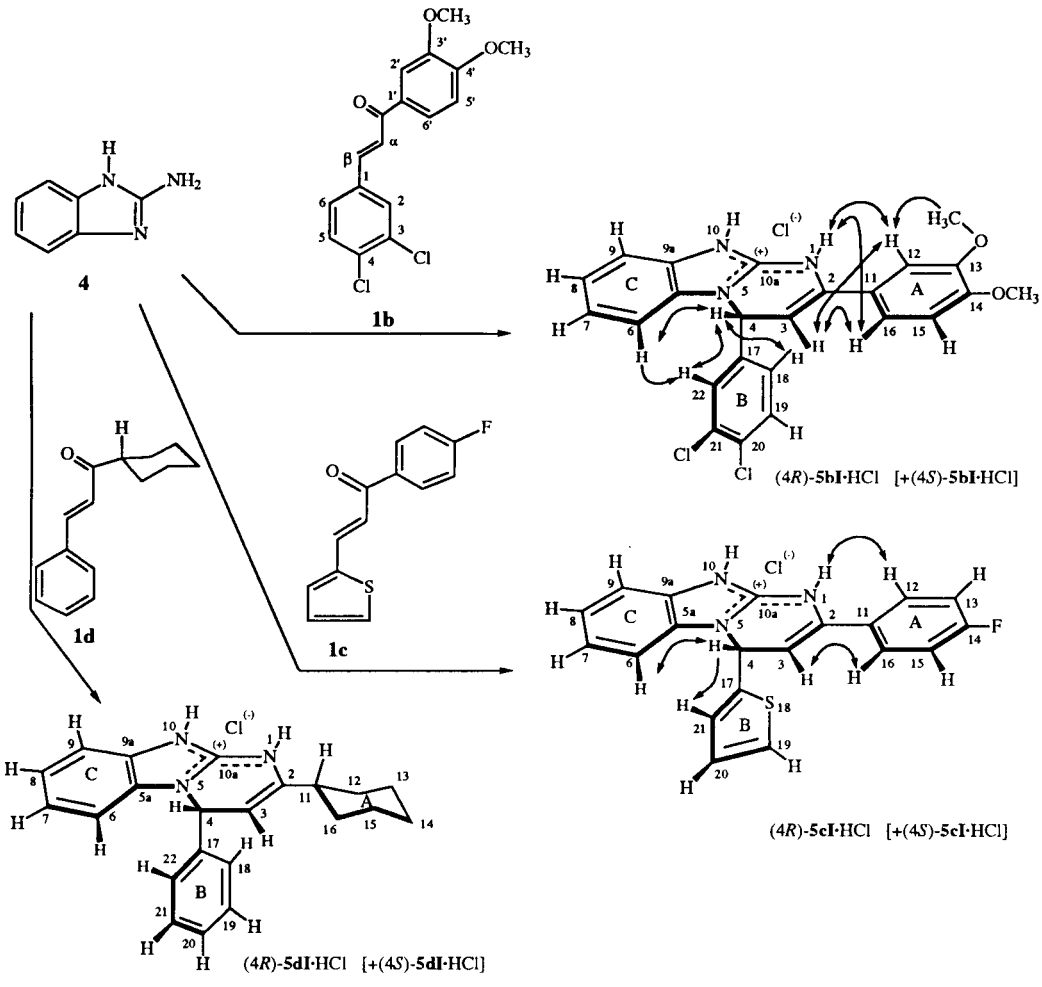
In case of the 2-(4-fluorophenyl)-4-(2-thienyl) compound (4*RS*)-**5cI**·HCl an NOE was observed, among others, between H-4 and H-21 of the thienyl substituent (ring B), which supports the proposed stereoformula of **5cI**·HCl in Scheme 5.

The ^{1}H-nmr spectrum of the hydrochloride of the **BIA**-hexahydrochalcone-condensate shows that the compound is racemic 2-cyclohexyl-4-phenyl-1,4-**DHPBI** hydrochloride [(4*RS*)-**5dI**·HCl]. The cyclohexyl residue in 2-position probably exists in a chair form (characteristic triplet of a triplet for H-11 at 2.27 ppm, see Experimental). A possible stereoformula is shown in Scheme 5.

2-Methyl-4-phenyl-1,4-**DHPBI** (**5eI**) and Salts of **5e**.

Desenko, Orlov *et al.* [13] also synthethized a **BIA**-benzylideneacetone-condensate **Y** (**5e** or **8e**) and postulated

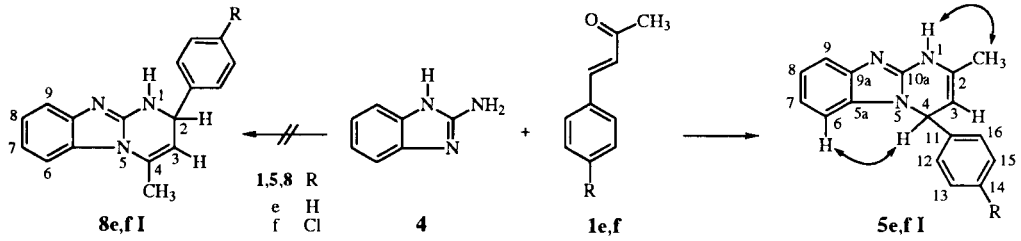
Scheme 5 [14]
[Only the (4*R*)-enantiomers of the generated (4*RS*)-**DHPBIs 5b-dI** are shown]



for the prepared base **Y** (again without unequivocal proof) the structural formula **5eI** (Scheme 6). We repeated the experiment [13] and were able to prove with the above mentioned nmr-methods (see Experimental) that the generated product indeed represents homogenous racemic 2-methyl-4-phenyl-1,4-**DHPBI** (**5eI**) in DMSO-d_6. The stereoformula could also be established (Figure 3).

Action of ethanolic hydrochloric acid on base **5eI** (molecular formula: $C_{17}H_{15}N_3$) yielded, besides of the expected hydrochloride **5eI**·HCl, a small amount of a compound with the molecular formula $C_{17}H_{17}N_3O$·HCl. Correspondingly, the product was generated by addition of water to 1,4-**DHPBI** (**5eI**). The elucidation of structure and stereochemistry of this by-product with the above described nmr-methods (see Experimental) firstly revealed, that it consists of 1,2,3,4-tetrahydropyrimido[1,2-*a*]benzimidazol-2-ol hydrochloride (**9e**·HCl). Additionally, the observed signal pattern for the hydrogen atoms in 4-position (double doublet with $J_{4,3ax}$ = 12.2 Hz and $J_{4,3eq}$ = 4.7 Hz) and for the the methylene protons in

Scheme 6 [14, NOEs shown for **5eI**]



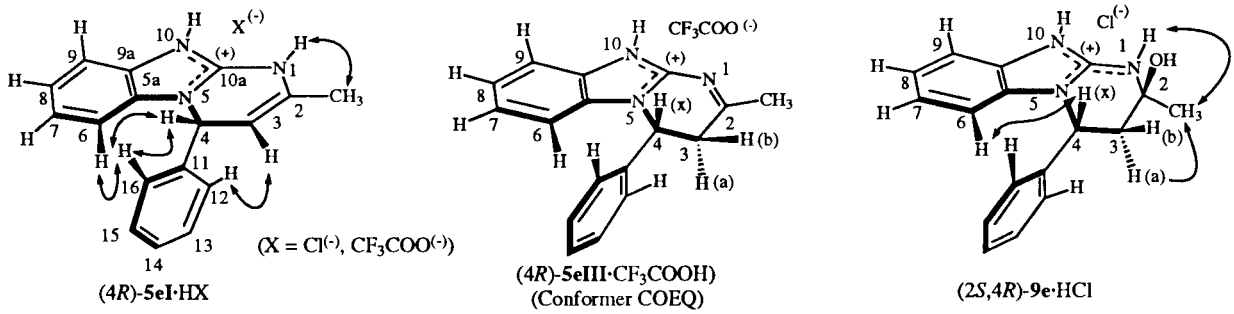


Figure 3. Stereoformula of (4*R*)-**5eI**·HX, conformer COEQ of (4*R*)-**5eIII**·CF_3COOH and (2*S*,4*R*)-**9e**·HCl [14].

3-position (see Experimental) indicated the axial position of H-4 and pointed towards a sofa conformation of the tetrahydropyrimidinol ring. The question of the position of the methyl group at carbon atom 2 was clarified by NOE. Irradiation of the methyl protons gave an enhancement of the axially arranged protons at carbon atom 3, which proves the equatorial position of the methyl group. Together these findings revealed that the product consists of racemic (2*RS*,4*SR*)-2-methyl-4-phenyl-1,2,3,4-tetrahydropyrimido[1,2-*a*]benzimidazol-2-ol hydrochloride [(2*RS*,4*SR*)-**9e**·HCl], that is of only one of two possible pairs of enantiomers, and that the generated enantiomers exhibit a sofa conformation with equatorially directed phenyl and methyl group, see stereoformula of (2*S*,4*R*)-**9e**·HCl, Figure 3.

If base **5e** is dissolved in trifluoroacetic acid one can observe *via* nmr the formation of a (4:1)-mixture of 1,4-dihydro- and 3,4-dihydro tautomer **5eI**·CF_3COOH and **5eIII**·CF_3COOH. The nmr-analyses (see Experimental) showed, that the 3,4-dihydropyrimidine ring of **5eIII**·CF_3COOH with two sp^3-carbon atoms could be flexible (equilibrium of conformers COEQ, see Figure 3, and COAX, with equatorially and axially arranged phenyl groups, respectively, as in case of **5aIII**·CF_3COOH). On the other hand the nmr data of **5aIII**·CF_3COOH are also consistent with the existence of a stable conformer COEQ. This conformer exhibits a slightly twisted sofa conformation which only slightly differs from the above described sofa conformation of the tetrahydropyrimidinol ring of addition product **9e**·HCl with three sp^3-carbon atoms (Figure 3).

It should be mentioned, that separate signals for both NH-protons of salts were only observed in the ^{1}H-nmr spectrum of **5eI**·CF_3COOH. In the spectrum of salt **5eI**·HCl only the signal for H-1 could be recognized. The resonance of the NH-protons of **5eIII**·CF_3COOH (which are probably situated, for reasons of a good resonance stabilization, in 10-position) seems to coincide with the intense signal for protons of trifluoroacetic acid at 11.82 ppm.

The recorded ^{1}H-nmr spectra of the of the **BIA**-*p*-chlorobenzylidenacetone condensate and its hydrochloride (Experimental) reveal that these compounds, in analogy to **5eI** and **5eI**·HCl, are racemic 2-methyl-4-(*p*-chlorophenyl)-1,4-**DHPBI** [(4*RS*)-**5fI**] and corresponding salt (4*RS*)-**5fI**·HCl.

EXPERIMENTAL

Melting points were determined on a Kofler melting point apparatus. Thin-layer chromatograms (tlc) were run on tlc plastic sheets silica gel 60 F_{254} (E. Merck, Darmstadt). Elution solvent I (e.s. I), toluene-methanol 90:40; e.s. II, toluene-methanol 90:20; e.s. III, toluene-methanol-glacial acetic acid 90:20:5. The developed spots were detected by visual examination under uv light. Infrared spectra were recorded with Perkin-Elmer 881 and 2000 FTIR spectrophotometers. Nuclear magnetic resonance spectra were taken with 360 MHz-BRUKER Aspect 3000 and 200 MHz Gemini Varian spectrometers. Chemical shifts are reported as δ units (ppm) with trimethylsilane as an internal standard. Mass spectra were taken with a Finigan Mat 212 Spectrometer (ei 120 ev, R 1000). Elemental analyses were performed by J. Theiner, Institute of Physical Chemistry, University of Vienna.

2-Benzimidazolamine (**BIA**, **4**) compare lit [17].

Compound **BIA 4** was prepared according to the literature [17] from 35.25 g (0.326 mole) of *o*-phenylendiamine in 200 ml of ice-water and 34.24 g (0.325 mole) of cyanogen bromide. As the solid cyanogen bromide could not be added dropwise as indicated, it was dissolved in a mixture of 100 ml of ice-water and 50 ml of THF. After completion of the reaction the THF was removed. Addition of alkali as indicated yielded 34 g (79%) of **4**, pale beige plates, mp 229-232° (lit [17], no yield given, mp 229-230°); tlc (e.s.I), Rf = 0.32.

(*E*)-3,4-Dichloro-3',4'-dimethoxychalcone (**1b**).

A solution of 10 g (0.0555 mole) of 3,4-dimethoxyacetophenone in 50 ml of ethanol was mixed with a solution of 2.8 g (0.07 mole) of sodium hydroxide in 25 ml of water. Then, under ice cooling (0-5°) and stirring, a solution of 9.7 g (0.0555 mole) of 3,4-dichlorobenzaldehyde in 60 ml of ethanol was added dropwise to the previous mixture. After further stirring at room temperature (1 hour) the precipitated crystals were filtered, yield 11 g (59%) of **1b**, colorless plates, mp 125-128° (from ethanol); tlc (e.s.II), Rf = 0.7; ir: ν 3060, 2970/2940, 1650 (C=O), 1600/1575, 1510, 1470, 1420, 1310, 1258, 1160, 1148 cm^{-1};

200 MHz ^{1}H nmr, (DMSO-d_6): δ 3.85 and 3.87 (2 x s, 2 x 3H, CH_3O-C$^{3'}$ and CH_3O-C$^{4'}$, or *vice versa*), 7.09, 7.59 and 7.94 (d, d, dd, 3 x 1H, H-5', H-2, and H-6', $J_{5',6'}$ = 8.6 Hz, $J_{2',6'}$ = 2 Hz), 7.66 and 8.03 (2 x d, 2 x 1H, H-α and H-β $J_{\alpha,\beta}$ = 15.6 Hz), 7.70, 7.86 and 8.24 (d, dd, d, 3 x 1H, H-5, H-6 and H-2, $J_{5,6}$ = 8.2 Hz, $J_{2,6}$ = 2 Hz)

Anal. Calcd. for $C_{17}H_{14}Cl_2O_3$: C, 60.55; H, 4.19; Cl, 21.03. Found: C, 60.73; H, 4.33; Cl, 20.75.

1-(4-Fluorophenyl)-3-(2-thienyl)-2-propen-1-one (**1c**) and 1',2',3',4',5',6'-hexahydrohydrochalcone (**1d**), compounds, which were already mentioned in the literature [18] (**1c**), [19] and [20] (**1d**), were prepared in analogy to **1b**, mp 87°(**1c**) and 54°(**1d**).

General Procedure for the Preparation of Pyrimido[1,2-*a*]benzimidazoles **5a-fI** and of Salts **5a-fI**·HCl.

Preparation of bases **5a-fI**.

2-Benzimidazolamine (**BIA 4**, 0.015 mole) and α,β-unsaturated ketone **1a-f** (0.015 mole) were dissolved in 40 ml of butanol (in the case of **1a** and **c**, dimethylformamide). The mixture was heated to reflux for the indicated time t. After cooling, the precipitated bases (**5aI**, **5d-fI**) were filtered and washed with butanol and ether. If the base did not precipitate (**5b** and **cI**), the reaction mixture was evaporated to dryness and the residue triturated with the solvent indicated.

Preparation of salts **5a-fI**·HCl.

Analytical samples (0.3 g) of bases **5a-fI** were suspended in 3 ml of ethanol. Then 2*M* ethanolic hydrochloric acid was added to *p*H 3. Compound **5bI**·HCl immediately precipitated and was filtered and recrystallized from ethanol. The resulting solutions of **5aI**·HCl and **5c-fI**·HCl were filtered and evaporated to dryness. The residues were recrystallized from the indicated solvents, yields 50-70%.

(4*RS*)-2,4-Diphenyl-1,4-dihydropyrimido[1,2-*a*]benzimidazole [(4*RS*)-**5aI**].

Base **5aI** was prepared from **BIA 4** and chalcone **1a** (solvent, 15 ml of dimethylformamide, t = 10 minutes), yield 3 g (62%), colorless needles, mp 250-252° (lit [12], yield 62%, mp 249°); tlc (e.s.II), Rf = 0.55; ir: ν 3442 (NH), 3145, 3051/3019, 2918, 2828, 1667 (C=C-N), 1626, 1572, 1455, 1337, 740, 696 cm^{-1}; 360 MHz ^{1}H nmr (DMSO-d_6, locants see Scheme 3): δ 5.26 and 6.32 (2 x d, 2 x 1H, H-3 and H-4, $J_{3,4}$ = 4 Hz), 6.84, 6.87, 7.0 and 7.29 (td, dd, td, d, 4 x 1H, H-7, H-6, H-8 and H-9, $J_{6,7} \cong J_{7,8} \cong J_{8,9} \cong$ 8 Hz, $J_{6,8}$ = 2 Hz, $J_{7,9}$ = 0.9 Hz), 7.25 and 7.33 (m, m, 1H and 4H, H-20 and H-18,19,21,22), 7.41 and 7.63 (m, dm, 3H and 2H, H-13,14,15 and H-12,16, $J_{12,13}$ = 7.2 Hz), 10.15 (s, 1H, H-1). For significant NOEs see Scheme 3.

Anal. Calcd. for $C_{22}H_{17}N_3$: C, 81.70; H, 5.30; N, 13.00. Found: C, 81.48; H, 5.46; N, 12.77 (lit [12], elemental analyses only reported for N).

Hydrochloride of (4*RS*)-**5aI**.

Colourless plates were obtained, mp 193-195° (from tetrahydrofuran-ethanol); tlc (e.s.III), Rf = 0.58; ir: ν 3432 (NH), 3059/3035, 2923, 2864, 2808, 1671 (C=C-N), 1623, 1563, 1471, 1296, 747, 661. For 360 MHz ^{1}H nmr, 90 MHz ^{13}C nmr and two dimensional spectra see Results and Discussion, Figure 1 and Table 1. The salt **5aI**·HCl crystallized with 0.2 mole of tetrahydrofuran and 0.2 mole of ethanol, which could not be removed by drying *in vacuo* without decomposition. The solvents of crystallization were also found in the nmr spectrum. In any case, the molecular formula is proved by ms: m/z 323 [M$^+$ (**5a**), 48], 322 (M$^+$-1, 13), 321 (M$^+$-2, 11), 246 (M$^+$-77, 100), 77 (14), 72 (THF$^+$, 12), 71 (THF$^+$-1, 18), 46 (EtOH$^+$, 12), 45 (EtOH$^+$-1, 32), 38 ($H^{37}Cl^+$ and other ions, 2.5), 36 ($H^{35}Cl^+$, 4), 31 (EtOH$^+$-15, 27).

Anal. Calcd. for $C_{22}H_{18}ClN_3 \cdot 0.2C_4H_8O$ (THF)·0.2 C_2H_5OH: C, 72.66; H, 5.46; Cl, 9.24; N, 10.96. Found: C, 72.17; H, 5.43; Cl, 9.11; N, 10.76.

For 360 MHz ^{1}H nmr of salts **5aI**·CF_3COOH, **5aI**·CF_3COOD, **5aIII**·CF_3COOH and **5aIII**·CF_3COOD see Results and Discussion, and Figure 2.

(4*RS*)-4-(3,4-Dichlorophenyl)-2-(3,4-dimethoxyphenyl)-1,4-dihydropyrimido[1,2-*a*]benzimidazole[(4*RS*)-**5bI**, crude base] and (4*RS*)-**5bI**·HCl.

Crude **5b**-base was prepared from **BIA 4** and chalcone **1b** (t = 2 hours). The residue was triturated with ether, yield 4 g of crude **5b**, yellow needles, mp 157-160° (from ethanol), which could not be sufficiently purified. Elemental analyses gave no sufficient correspondence of calculated and found values.

Hydrochloride of (4*RS*)-**5b**.

Trituration of the crude base **5b** (4 g) with ethanolic hydrochloric acid yielded 3.6 g of **5b**·HCl (49%, based on **4**), yellow cubes, mp 220-222° (from ethanol); tlc (e.s.III), Rf = 0.53; ir: ν 3400 (NH), 3040, 2920, 2820, 1665 (C=C-N), 1625, 1465, 1263, 1220, 1145, 1023, 738 cm^{-1}; 360 MHz ^{1}H nmr (DMSO-d_6, locants see Scheme 5): δ 3.78 and 3.84 (2 x s, 2 x 3H, CH_3O-C^{14} and CH_3O-C^{13}), 5.62 and 6.57 (2 x d, 2 x 1H, H-3 and H-4, $J_{3,4}$ = 3.7 Hz), 7.03, 7.28 and 7.32 (d, dd, d, 3 x 1H, H-15, H-16 and H-12, $J_{15,16}$ = 8.5 Hz, $J_{12,16}$ = 2.2), 7.06, 7.20, 7.32 and 7.67 (d, td, t, d, 4 x 1H, H-6, H-7, H-8 and H-9, $J_{6,7} \cong J_{7,8} \cong J_{8,9} \cong$ 8 Hz, $J_{7,9}$ = 0.9 Hz), 7.51, 7.65 and 7.97 (dd, d, d, 3 x 1H, H-22, H-21 and H-18, $J_{21,22}$ = 8.3 Hz, $J_{18,22}$ = 2.1 Hz), 12.4 (sb, NH). For significant NOEs see Scheme 5; 90 MHz ^{13}C nmr (DMSO-d_6): δ 55.7 (CH_3O-C^{13}), 55.6 (CH_3O-C^{14}), 56.0 (C-4), 98.5 (C-3), 109.6 (C-12), 111.3 (C-6), 111.5 (C-15), 113.2 (C-9), 118.4 (C-16), 123.4 (C-7), 124.5 (C-8), 124.2 (C-11), 127.4 (C-22), 128.1 (C-5a), 129.3 (C-18), 130.0 (C-9a), 131.4 (C-21), 131.7 (low intensity, C-20, eventually together with C-17 or C-19), 131.9 (C-2), 140.6 (high intensity, C-17 and/or C-19), 144.7 (C-10a), 148.6 (C-13), 149.9 (C-14). COLOCs of diagnostic value for the assignment of the quaternary carbon atoms: C-2 → H-3, H-4, H-12,16; C-5a → H-7 and H-9; C-9a → H-6 and H-8; C-10a → H-4; C-11 → H-3, H-15; C-13 → H-15, CH_3O-C^{13}; C-14 → H-12, H-16, CH_3O-C^{14}.

Anal. Calcd. for $C_{24}H_{20}Cl_3N_3O_2$: C, 58.97; H, 4.12; Cl, 21.76; N, 8.60. Found: C, 59.01; H, 4.13; Cl, 21.48; N, 8.32.

(4*RS*)-2-(4-Fluorophenyl)-4-(2-thienyl)-1,4-dihydropyrimido[1,2-*a*]benzimidazole[(4*RS*)-**5cI**].

Base **5c** was prepared from **BIA 4** and 1-fluorophenyl-3-thienyl-2-propene-1-one **1c** (solvent, 30 ml of dimethylformamide, t = 9 hours). The residue was triturated with ethanol, yielding 2 g (39%) of **5c**, colorless needles, mp 235-237° (from ethanol); tlc (e.s.II), Rf = 0.5; ir: ν 3400 (NH), 3040, 2900/2860, 1658 (C=C-N), 1620/1593/1570, 1507, 1453, 1225/1217, 830, 733, 698 cm^{-1}.

Anal. Calcd. for $C_{20}H_{14}FN_3S$: C, 69.14; H, 4.06; F, 5.47; N, 12.10; S, 9.23. Found: C, 69.09; H, 4.35; F, 5.61; N, 11.97; S, 9.27.

Hydrochloride of (4*RS*)-**5c**.

Pale yellow plates were obtained, mp 177-180° (from ethanol); tlc (e.s.III), Rf = 0.56; ir: ν 3380 (NH), 3040, 2860/2800, 1668 (C=C-N), 1625/1598, 1560, 1500, 1220, 735, 690 cm^{-1}; 360 MHz ^1H nmr (DMSO-d_6, locants see Scheme 5): δ 5.77 and 6.99 (2 x d, 2 x 1H, H-3 and H-4, $J_{3,4}$ = 4.3 Hz), 7.04, 7.53 and 7.56 (dd, d, d, 3 x 1H, H-20, H-21 and H-19, $J_{19,20}$ = 5.1 Hz, $J_{20,21}$ = 3.5 Hz), 7.27, 7.33, 7.54 and 7.64 (td, td, d, d, 4 x 1H, H-7, H-8, H-6 and H-9, $J_{6,7} \cong J_{7,8} \cong J_{8,9} \cong$ 7.6 Hz, $J_{7,9} \cong J_{8,6} \cong$ 1.2 Hz), 7.34 and 7.8 (t, dd, 2 x 2H, H-13,15 and H-12,16, $J_{12,13} = J_{13,F}$ = 8.9 Hz, $J_{12,F}$ = 5.3 Hz), 12.52 (sb, NH). For significant NOEs see Scheme 5; 90 MHz ^{13}C nmr (DMSO-d_6): δ 51.7 (C-4), 100.5 (C-3), 111.7 (C-6), 113.2 (C-9), 115.7 (d, 2C, C-13,15, $^2J_{13,F}$ = 21.7 Hz), 123.5 (C-7), 124.7 (C-8), 127.2 (C-20), 127.8 (C-21), 127.93 (C-19), 127.94 (C-5a), 128.6 (d, 2C, C-12,16, $^3J_{12,F}$ = 8.3 Hz), 128.8 (d, 1C, C-11 , $^4J_{11,F}$ = 3.4 Hz), 130.0 (C-9a), 131.7 (C-2), 142.8 (C-17), 143.8 (C-10a), 162.8 (d, C-14, $^1J_{14,F}$ = 245.6 Hz); COLOCs of diagnostic value for the assignment of the quaternary carbon atoms: C-2 → H-4, H-12,16; C-5a → H-7, H-9; C-9a → H-6, H-8; C-10a → H-4; C-11 → H-3, H-13,15; C-14 → H-12,16 and H-13,15; C-17 → H-19,20. The salt **5c**·HCl crystallized with 0.5 moles ethanol, which could not be removed *in vacuo* without decomposition. The solvent of crystallization was also found in the nmr and ms. The molecular formula is also proved by ms: m/z 347 (M^+, 100), 346 (M^+-1, 36), 264 (M^+-83 [thienyl], 58), 215 (M^+-132 [**BIA**-1], 16), 133 (**BIA**$^+$, 8), 45 ($EtOH^+$-1 , 11), 38 ($H^{37}Cl^+$ and other ions, 9), 36 ($H^{35}Cl^+$, 18).

Anal. Calcd. for $C_{20}H_{15}ClFN_3S \cdot 0.5C_2H_5OH$: C, 61.99; H, 4.45; Cl, 8.71; F, 4.67; N, 10.32; S, 7.88. Found: C, 61.68; H, 4.44; Cl, 8.74; F, 4.90; N, 10.16; S, 8.14.

(4*RS*)-2-Cyclohexyl-4-phenyl-1,4-dihydropyrimido[1,2-*a*]benzimidazole[(4*RS*)-**5dI**].

Base **5d** was prepared from **BIA 4** and hexahydrochalcone **1d** (t = 3 hours), yield 3.6 g (73%), colorless needles, mp 230-232° (from ethanol-DMF); tlc (e.s.II), Rf = 0.52; ir: ν 3400 (NH), 3040/3000, 2920/2840, 1670 (C=C-N), 1624/1595/1568, 1505, 1455, 1272, 730 cm^{-1}.

Anal. Calcd. for $C_{22}H_{23}N_3$: C, 80.21; H, 7.04; N, 12.76. Found: C, 80.18; H, 7.00; N, 12.77.

Hydrochloride of (4*RS*)-**5d**.

Pale yellow crystals were obtained, mp 175-177° (from ethyl acetate-ethanol); tlc (e.s.III), Rf = 0.54; ir: ν 3426 (NH), 3032, 2927, 2853, 1689 (C=C-N), 1633, 1561, 1473, 1450, 1291, 747, 701 cm^{-1}; 200 MHz ^1H nmr (deuteriochloroform, locants see Scheme 5): δ 1.2-1.46 (overlapping signals, 5H, H-12ax, 16ax, H-13ax, 15ax, H-14ax), 1.52-1.82 (overlapping signals, 4H, H-12eq,16eq, H-13eq,15eq), 1.95 (dm, 1 H, H-14eq, $2J_{ax,eq} \cong$ 11 Hz), 2.27 (tt, 1H, H-11 , $J_{11,12ax} = J_{11,16ax} \cong$ 12 Hz and $J_{11,12eq} = J_{11,16eq} \cong$ 4 Hz), 4.76 and 6.02 (2 x dm, 2 x 1H, H-3 and H-4, $J_{3,4}$ = 3.4 Hz, suggested long-range-couplings of H-3 and H-4 with H-11), 6.82, 7.03, 7.18 and 7.47 (d, td, td, dm, 4 x 1H, H-6, H-7, H-8 and H-9, $J_{6,7} \cong J_{7,8} \cong J_{8,9} \cong$ 8 Hz, $J_{7,9} \cong J_{8,6} \cong$ 1.2 Hz), 7.24-7.40 (overlapping signals, 5H, C_6H_5). The salt **5d**·HCl crystallized with 0.5 mole of ethyl acetate, which could not be removed *in vacuo* without decomposition. The solvent of crystallization was also found in the nmr spectrum. The molecular formula is also proved by ms: m/z 329 (M^+, 100), 328 (M^+-1, 13), 252 (M^+-77, 73), 246 (M^+-83 [C_6H_{11}], 17), 196 (M^+- 133 [**BIA**], 20), 38 ($H^{37}Cl^+$ and other ions, 3), 36 ($H^{35}Cl^+$, 4).

Anal. Calcd. for $C_{22}H_{24}ClN_3 \cdot 0.45CH_3CO_2C_2H_5$: C, 70.49; H, 6.86; Cl, 8.74; N, 10.36. Found: C, 70.87; H, 7.15; Cl, 8.81; N, 10.34.

(4*RS*)-2-Methyl-4-phenyl-1,4-dihydropyrimido[1,2-*a*]benzimidazole [(4*RS*)-**5eI**].

Base **5eI** was prepared from **BIA 4** and benzylidenacetone **1e** (t = 8 hours), yield 3.15 g (80%), colorless needles, mp 264-268° (from ethanol) (lit [13], mp 260-262°); tlc (e.s.II), Rf = 0.45; ir: ν 3440 (NH), 3218, 3162, 3065, 3020, 2875, 1688, 1638, 1578, 1508, 1452, 740 cm^{-1}; ^1H nmr, 360 MHz (DMSO-d_6, locants see Scheme 6): δ 1.88 (s, 3H, CH_3); 4.63 and 6.09 (2 x dm, 2 x 1H, H-3 and H-4, $J_{3,4}$ = 3.6 Hz, suggested long-range-couplings of H-3 and H-4 with CH_3), 6.77, 6.79, 6.96 and 7.25 (d, td, td, d, 4 x 1H, H-6, H-7, H-8 and H-9, $J_{6,7} \cong J_{7,8} \cong J_{8,9} \cong$ 7.9 Hz, $J_{7,9}$ = 0.9 Hz, $J_{8,6} \cong$ 2 Hz), 7.21, 7.24 and 7.30 (m, d, tm, 1H and 2 x 2H, H-14, H-12,16 and H-13,15, $J_{12,13} = J_{13,14}$ = 7.3 Hz), 9.63 (s, NH). For significant NOEs see Scheme 6.

(4:1) Mixture of (4*RS*)-2-Methyl-4-phenyl-1,4-dihydropyrimido[1,2-*a*]benzimidazole Hydrochloride (**5eI**·HCl) and [(2*RS*,4*SR*]-2-Methyl-4-phenyl-1,2,3,4-tetrahydropyrimido-[1,2-*a*]benzimidazole-2-ol Hydrochloride (**9e**·HCl).

An analytical sample of the (4:1)-mixture of salts **5eI**·HCl and **9e**·HCl was prepared according to the general procedure by trituration of 0.3 g of base **5eI** with ethanolic hydrogen chloride, pale yellow crystals, mp 165° (from benzene); tlc (e.s.III), Rf = 0.51 (only one spot visible); ir: ν 3420 (NH), 3060/3020, 2930, 2840, 1700, 1638, 1425/1415, 750, 695 cm^{-1}; 360 MHz ^1H nmr (DMSO-d_6, locants see Figure 3), signals of **DHPBI 5eI**·HCl, δ 1.98 (s, 3H, CH_3), 4.97 and 6.33 (dm, dm, 2 x 1H, H-3 and H-4, $J_{3,4} \cong$ 3.4 Hz, suggested long-range-couplings of H-3 and H-4 with CH_3), 6.99, 7.13, 7.26 and 7.53 (d, td, td, d, 4 x 1H, H-6, H-7, H-8 and H-9, $J_{6,7} \cong J_{7,8} \cong J_{8,9} \cong$ 8.1 Hz, $J_{7,9} \cong J_{8,6} \cong$ 0.9 Hz), 7.29, 7.36 and 7.43 (tm, tm, dm, 1H and 2 x 2H, H-14, H-13,15 and H-12,16, $J_{12,13} = J_{13,14}$ = 7 Hz), 12.03 (s, NH). For significant NOEs see Figure 3; 90 MHz ^{13}C nmr (DMSO-d_6): δ 17.9 (CH_3), 56.8 (C-4), 99.9 (C-3), 111.4 (C-6), 112.5 (C-9), 123.3 (C-7), 124.4 (C-8), 126.8 (C-12,16), 128.3 (C-5a), 128.6 (C-14), 129.0 (C-2), 129.1 (C-13,15), 129.6 (C-9a), 140.0 (C-11), 143.7 (C-10a); COLOCs of diagnostic value for the assignment of the quaternary carbon atoms: C-2 → H-4; C-5a → H-7, H-9; C-9a → H-6, H-8; C-10a → H-4; C-11 → H4, H-13,15.

The nmr data of addition product **9e**·HCl are as follows: 360 MHz ^1H nmr (DMSO-d_6, locants see Figure 3), δ 1.61 (s, 3H, CH_3), 2.23, 2.38 and 5.50 (t, dd, dd, 3 x 1H, H-3ax, H-3eq, H-4ax, $J_{3ax,eq} = J_{3ax,4ax}$ = 12.2 Hz, $J_{3eq,4ax}$ = 4.7 Hz), 6.0, 6.89, 7.14 and 7.49 (d, td, t, d, 4 x 1H, H-6, H-7, H-8 and H-9, $J_{6,7} \cong J_{7,8} \cong J_{8,9} \cong$ 8.0 Hz, $J_{7,9}$ = 0.9 Hz), 7.4-7.5 (covered, 5H, H-12,16, H-13,15 and H-14); for significant NOEs see Figure 3; 90 MHz ^{13}C nmr (DMSO-d_6): δ 27.3 (CH_3), 43.5 (C-3), 54.7 (C-4), 77.9 (C-2), 111.7 (C-6), 112.0 (C-9), 122.3 (C-7), 123.3 (C-8), 127.8 (C-12, 16 and/or C-13,15 and/or C-14), 129.2 (C-5a), 129.3 (C-9a ?), 137.4 (C-11), 147.6 (C-10a ?).

The high resolution ms of the (4:1)-mixture of **5eI**·HCl and **9e**·HCl exhibits the following peaks: m/z 261.1272 (M^+ [**5eI**$^+$], 58), 260 (M^+-1 , 17), 259 (M^+-2, 12), 184 (M^+-77, 100), 133.0640 (**BIA**$^+$[probably fragment of **9e**], 52), 131 (cinnamoyl$^+$ [fragment of benzylideneacetone **1e** and **9e**, respectively?], 8), 103 (styryl$^+$[fragment of benzylideneacetone **1e** and **9e**, respectively?], 10), 90 (27), 77 (20).

Anal. Calcd. for 0.8 $C_{17}H_{16}ClN_3$ (**5eI**·HCl)·0.2$C_{17}H_{18}ClN_3O$ (**9e**·HCl): C, 67.79; H, 5.35; Cl, 11.77; N, 13.95. Found: C, 67.93; H, 5.43; Cl, 11.37; N, 13.82.

Data (^{1}H-NMR) for the free base **5e** in trifluoroacetic acid (360 MHz)[4:1-Mixture of **5eI**·CF_3COOH and Tautomeric 2-Methyl-4-Phenyl-3,4-dihydropyrmido[1,2-*a*]benzimidazole (**5eIII**·CF_3COOH).

Signals for **5eI**·CF_3COOH are: δ 2.07 (s, 3H, CH_3), 5.02 and 6.12 (2 x dm, 2 x 1H, H-3 and H-4, $J_{3,4} \cong 3$ Hz, suggested longe-rang-couplings of H-3 and H-4 with CH_3), 7.01 and 7.19 (d and t, 2 x 1H, H-6 and H-7, $J_{6,7} \cong 8$ Hz), 7.25-7.48 (7H, H-8 and H-9; H-12,16, H-13,15 and H-14), 8.53 (s, 1H, H-1), 10.61 (s, 1H, H-10). Signals for **5eIII**·CF_3COOH are: δ 2.61 (s, 3H, CH_3), 3.4, 3.7 and 5.88 (dd, dd, t, 3 x 1H, H-3ax, H3eq, H-4ax, $J_{3ax,eq} = 19$ Hz, $J_{3ax,4ax} = J_{3eq,4ax} = 8$ Hz), 6.9, 7.1 and 7.79 (d, t, d, 3 x 1H, H-6, H-8 and H-9, $J_{6,7} \cong J_{8,7} \cong J_{8,9} \cong 8.2$ Hz), 7.25-7.48 (6H, H-7 and H-12,16, H-13,15 and H-14).

(4*RS*)-2-Methyl-4-(*p*-chlorphenyl)-1,4-dihydropyrimido[1,2-*a*]-benzimidazole (**5f**).

Compound **5f** was prepared from **BIA 4** and **1f** (t = 6 hours), yield 3.3 g (75%), colorless needles, mp 265-267° (from DMF); tlc (e.s.II), Rf = 0.51; ir: ν 3440 (NH), 3205, 3155, 3060, 2920/2880, 1692, 1635, 1600, 1580, 1505, 1488, 1460, 1445, 1248, 732 cm^{-1}; 60 MHz ^{1}H nmr ($CDCl_3$ + CF_3COOD, locants see Scheme 6): δ 2.08 (sb, 3H, CH_3), 4.85 and 6.05 (2 x dm, 2 x 1H, H-3 and H-4, $J_{3,4} \cong 3.5$ Hz, suggested long-range-couplings of H-3 and H-4 with CH_3), 6.78-7.25 (3H, H-6, H-7 and H-8), 7.3 (b, 4H, *p*-ClC_6H_4); 7.6 (m, 1H, H-9).

Anal. Calcd. for $C_{17}H_{14}ClN_3$: C, 69.03; H, 4.77; N, 14.21; Cl, 11.99. Found: C, 68.92; H, 4.60; N , 14.18; Cl, 11.93.

Hydrochloride of (4*RS*)-**5f**.

This salt was obtained as a pale yellow plates, mp 190-193° (from benzene); tlc (e.s.III), Rf = 0.53; ir: ν 3400 (NH), 3040/3020, 2920/2820, 1735/1700, 1635, 1490, 1473, 1235/1215, 1085, 748 cm^{-1}; 200 MHz ^{1}H nmr (DMSO-d_6, locants see Scheme 6): δ 1.97 (s, 3H, CH_3), 4.96 and 6.35 (2 x d, 2 x 1H, H-3 and H-4, $J_{3,4} = 3.7$ Hz), 6.99, 7.16, 7.28 and 7.51 (d, t, t, d, 4 x 1H, H-6, H-7, H-8 and H-9, $J_{6,7} \cong J_{7,8} \cong J_{8,9} \cong 8.0$ Hz), 7.44 and 7.49 (2 x d, 2 x 2H, H-12,16 and H-13,15, $J_{12,13} = J_{15,16} = 8.6$ Hz).

Anal. Calcd. for $C_{17}H_{15}Cl_2N_3$·0.3H_2O: C, 60.83; H, 4.59; N, 12.52. Found: C, 60.65; H, 4.46; N, 12.34.

REFERENCES AND NOTES

[1] Dedicated to Professor Dr. Gustav Zigeuner with the best wishes on the occasion of his 75th birthday.

[2] Presented in part at the Fifteenth International Congress of Heterocyclic Chemistry, Taipei, Taiwan, August 6-11, 1995.

[3] Dr. Dalal Abou El Ella, lecturer at the Pharmaceutical Chemistry Department, Faculty of Pharmacy, Cairo University, Egypt, has accomplished part of this research on the occasion of a research stay in Graz, Austria, during November 1992-July 1995.

[4] W. Wendelin, K. Schermanz, A. Fuchsgruber and A. Harler, *Monatsh. Chem.*, **111**, 1399 (1980).

[5] W. Wendelin and K. Schermanz, *J. Heterocyclic Chem.*, **21**, 65 (1990).

[6] W. Wendelin, A. Exner, P. Egger and A. W. Frahm, *Sci. Pharm.*, **57**, 232 (1989).

[7] W. Wendelin *et al.*, unpublished results.

[8] A. Kreutzberger and M. Egger, *Chem.-Ztg.*, **107**, 127 (1983).

[9] A. Kreutzberger and M. Egger, *Arch. Pharm.*, **315**, 438 (1982).

[10] A. Kreutzberger and M. Egger, *J. Heterocyclic Chem.*, **18**, 1587 (1981).

[11] E. Szarvasi, D. Festal, M. Grand, J. C. Depin and T. N. Luong, *Eur. J. Med. Chem.-Chim. Ther.*, **16**, 327 (1981).

[12] S. M. Desenko, V. D. Orlov, *Khim. Geterotsikl. Soedin.*, **8**, 1071 (1989).

[13] S. M. Desenko, V. D. Orlov, V. V. Lipson and Kh. Estrada, *Khim. Geterotsikl. Soedin.*, **9**, 1215 (1991).

[14] In order to simplify the description of the nmr-data, the carbon atoms of the substituents in 2,4-position of the **DHPBIs 5** are continuously enumerated (and not, according to the rules of nomenclature, systematically). Arrows show observed NOE-effects.

[15] P. W. Rabideau, Conformational Analysis of Cyclohexenes, Cyclohexadienes, and Related Hydroaromatic Compounds, Chapter **3**, Conformational Analysis of 1,3-Cyclohexadienes and Related Hydroaromatics, P. W. Rabideau and A. Sygula, eds, VCH Publishers, Inc., New York, NY, 1989, pp 73 and 77-79.

[16] E. P. Kohler and H. M. Chadwell in *Org. Synth., Coll Vol I*, John Wiley & Sons, New York, NY, 1967, p 78.

[17] P. Biddle, E. S. Lane and J. L. Willans, *J. Chem. Soc.*, 2369 (1960).

[18] Chen, Fa-Ching, Chen, Lin-Sheng, Chen, and Yu-Hsun, *Tai-Wan K'o Hsuch*, **26**, 97 (1972); *Chem. Abstr.*, **78**, 147718 (1973).

[19] R. P. Mariella and R. R. Raube, *J. Am. Chem. Soc.*, **74**, 518 (1952).

[20] K. Kohler and P. Burnley, *Am. J. Chem.*, **43**, 416 (1910).