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161. A Novel Synthesis of 1-Aryl-9-alkyl-2,3,3a,4,9,9a-hexahydro-1H-pyrrolo[2,3-b] quinoxalines by Lithium Aluminium Hydride Reduction of N-Phenyl-1-benzimidazolyl-succinimides

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Herrn Dr. *Ch. E, Barrelet* zum 70. Geburtstag gewidmet

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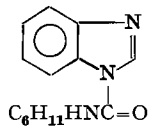
Summary. The N-substituted 1-benzimidazolyl-succinimides **6a–v** (Scheme 1, Table 1 and 2) have been prepared by the reaction of benzimidazole and its derivatives with maleimides. Reduction of the N-cyclohexyl and N-cyclo-octyl substituted 1-benzimidazolyl-succinimides **6i–k** with lithium aluminium hydride gives the normally expected substituted (N-alkyl-3-pyrrolidinyl)benzimidazoles **14i–k**. However by $LiAlH_4$-reduction of the N-phenyl substituted 1-benzimidazolyl-succinimides **6a–h** mainly the 1-aryl-9-alkyl-2,3,3a,4,9,9a-hexahydro-1*H*-pyrrolo[2,3-*b*]quinoxalines **7a–h** are obtained. The mechanism of this unusual reduction has been elucidated.

Reactions of benzimidazole and its derivatives with acrylonitrile [1] and acrylamide [2], acetylenedicarboxylic esters [3]–[6], ethyl and methyl propiolates [6], dimethyl azodicarboxylate [7], cyclohexyl isocyanate [8] and diphenylketene [9] have been reported. They give either compounds with new five-, six- or seven-membered rings or 1:1-addition products such as **1**, **2**, and **3** or both types together.

There seems to be no example for the reaction of benzimidazole and substituted benzimidazoles with N-aryl- and N-alkyl-maleimides, which prompted us to undertake such a study. Treatment of benzimidazoles **4** with 1 mol of maleimides **5** in boiling



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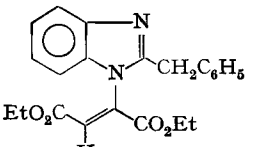

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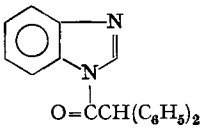
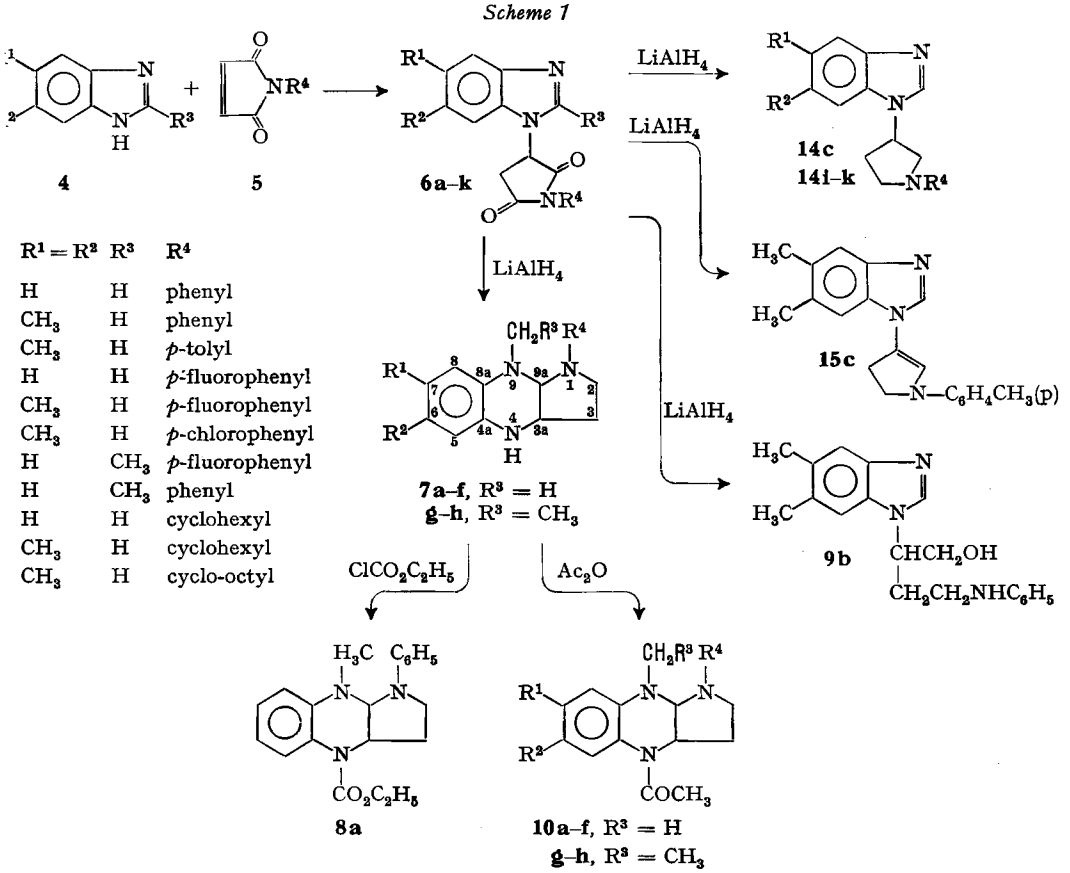


3

acetonitrile in the presence of hydroquinone readily afforded the N-substituted 1-benzimidazolyl-succinimides **6a–k** (Scheme 1) in good yields (60–80%). The absence of NH absorption in the IR. spectra shows that in these 1:1 addition products the NH-groups of benzimidazoles were involved. The structures of these compounds are in agreement with their elemental analyses, ^{1}H-NMR., and mass spectra.

Scheme 1



$R^1 = R^2$	R^3	R^4
H	H	phenyl
CH_3	H	phenyl
CH_3	H	*p*-tolyl
H	H	*p*-fluorophenyl
CH_3	H	*p*-fluorophenyl
CH_3	H	*p*-chlorophenyl
H	CH_3	*p*-fluorophenyl
H	CH_3	phenyl
H	H	cyclohexyl
CH_3	H	cyclohexyl
CH_3	H	cyclo-octyl

The $LiAlH_4$-reduction of N-(*n*-butyl)-1-benzimidazolyl-succinimide (**6p**) and its 5,6-dimethyl-derivative **6q** (Table 2) yielded a yellow oil which, in its IR.-spectrum, did not show any carbonyl bands. It was however not possible to isolate it as a pure product owing to its great susceptibility to oxidation. The N-cyclohexyl and cyclo-

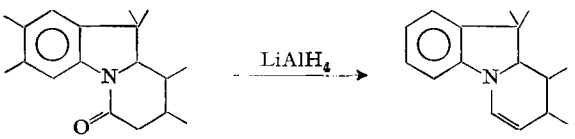
octyl succinimide derivatives **6i–k** on the other hand were readily reduced with $LiAlH_4$ to yield the expected stable pyrrolidine derivatives **14i–k**.

Surprisingly, the reduction of N-phenyl-1-benzimidazolyl-succinimide (**6a**) with lithium aluminium hydride gave with 40% yield a crystalline substance **7a** as the sole isolated product which contained, according to elemental analysis and mass spectroscopy, two hydrogen atoms more than the expected pyrrolidine derivative. The IR. spectrum indicated the presence of an NH group (3322 cm^{-1}), which was confirmed by the reaction with acetic anhydride and with ethyl chloroformate to give, with high yields, the N-acetyl derivate **10a** and the urethane **8a**, respectively.

The ^{1}H-NMR. spectrum of **7a** exhibited a $-NCH_3$ group. Since the ^{1}H-NMR. spectrum of the corresponding reduction product of N-phenyl-(2-methyl-1-benzimidazolyl)-succinimides (**6h**) revealed the presence of a $-NCH_2CH_3$ group, a break of the linkage between 1 and 2 positions of the benzimidazole ring seemed to be obvious. This, together with the other ^{1}H-NMR. data (given below), led to the formulation of **7a** = 1-phenyl-9-methyl-2,3,3a,4,9,9a-hexahydro-1*H*-pyrrolo[2,3-*b*]-quinoxaline as the structure of the $LiAlH_4$-reduction product of **6a** (see Scheme 1).

The ^{1}H-NMR. spectrum (100 MHz) of **7a** in $CDCl_3$ revealed the following data: Two aryl multiplets at δ 7.1–7.4 (2H) and 6.4–6.9 (7H), a methine proton doublet (J = 4.5 Hz) at 4.6 (1H, N-C*H*-N) a broadened NH singlet at 4.00 (1H), a second methine proton at 3.92 (1H, –N–C*H*–). This proton appeared as a broad signal due to its coupling with the NH proton and became sharp upon exchange with D_2O. Two multiplets of methylene protons at 3.1–3.7 and 1.9–2.4 (2H each, $-N-CH_2-$ and $-NCH_2CH_2-$ respectively), and a N-methyl singlet at 2.9 (3H). Decoupling experiments confirmed these assignments.

In view of this unusual rearrangement it seemed of interest to investigate the $LiAlH_4$-reduction of the other succinimide derivatives **6b–h**, which have in common N-phenyl or N-*p*-substituted phenyl groups. All these compounds afforded the quinoxalines **7b–h**, in yields ranging from 25–40% as the sole product, with two exceptions: **6c** gave, in addition to **7c**, the normal reduction product **14c**, together with its dehydrogenation product **15c**. This latter type of $LiAlH_4$-reduction product might be compared to the reaction



described in a paper on brucine [10].

6b yielded in addition to **7b** the amino alcohol **9b** (see Scheme 1). The structures of **9b** and **15c** are based on the IR., ^{1}H-NMR. and MS. analyses.

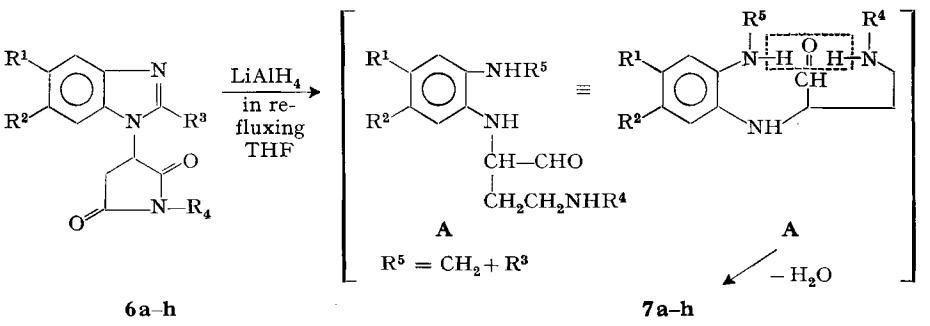
7b–h like **7a** readily afforded with acetic anhydride the acetyl derivatives (**10b–h**) in excellent yields (80–96%).

Lithium aluminium hydride reductions of a number of N-substituted succinimides have been reported. *Schreiber et al.* [11] found that N-benzhydryl-, N-(*t*-butyl)-, and N-phenyl-succinimide undergo ring opening to give the respective amine alcohols in addition to the normal reduction products. N-Tritylsuccinimide and benzyl-

succinimide afforded only N-trytyl-4-hydroxybutyramide and N-substituted pyrrolidine respectively. The open chain amino alcohol arises from the further reduction of the initially formed aldehyde during the process of reduction. The fact that an aldehyde intermediate can occur is suggested by the isolation of a number of aldehydes formed by lithium aluminium hydride reduction of tertiary amides [12–13]. Higher yields of aldehydes are obtained by reduction of amides derived from ethyleneimine, carbazole, N-methylaniline or imidazole [14].

It is known that reduction of the C,N double bond in benzimidazole in refluxing benzene/ether gives dihydrobenzimidazol [15]. Opening of the five-membered ring of 2,3-dihydro-5-phenyl-5*H*-imidazo[2,1-*a*]isoindole by lithium aluminium hydride in refluxing tetrahydrofuran to 2-benzylphenylimidazoline as the major product has also been documented [16]. Formation of the hexahydroquinoxalines **7a–h** might likewise be explained on the supposition that lithium aluminium hydride leads to the reduction of the C=N bond of benzimidazoles, opening of the five-membered ring by the hydride ion attack, with formation of intermediate amino aldehydes **A**, which then split off water with the formation of **7a–h** (Scheme 2).

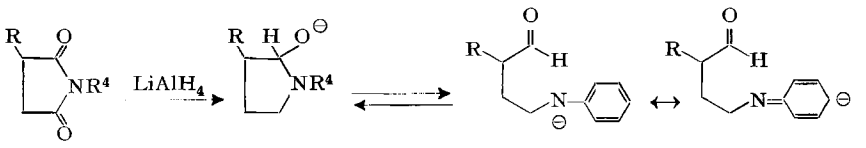
Scheme 2



The aminoalcohol **9b** (Scheme 1) is the reduction product of such an unstable aminoaldehyde **A**.

With dilute acids the compounds **7a–h** give dark brown solutions. Probably, by hydrolysis, the last step of Scheme 2 is reversed and the aminoaldehydes **A** in acid solution give dark colored polycondensation products.

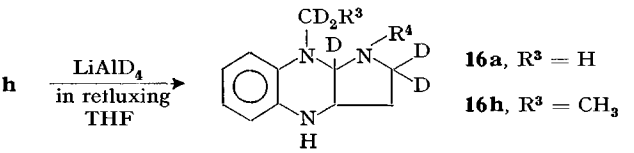
It might be assumed that the initial attack of the hydride ion on the succinimide derivative **6** gives rise to **11** as one of the possible anionic intermediates:



If the substituent R^4 is a phenyl group (eventually substituted in para position by F or Cl) an intermediate **12** will be formed which can stabilize by resonance *via* **13** and then gives rise to the hexahydro-1*H*-pyrrolo[2,3-*b*]quinoxaline derivatives **7**.

Electron donating alkyl groups (*e.g.*, cyclohexyl) on the other hand will destabilize an intermediate of the type **12** and therefore the normal reduction to the pyrrolidine derivatives **14i–k** takes place. The succinimide derivative **6c** has a phenyl group substituted in para position by the weak electron releasing methyl group. The formation of the quinoxaline **7c** in addition to the pyrrolidine **14c**, and **15c** by reduction of **6c** (in 40,5 and 2% yields, respectively), therefore seems plausible.

Experimental proof for the formulation given in Scheme 2 has been obtained by the reduction of **6a** and **6h** respectively with lithium aluminium deuteride ($LiAlD_4$):



The products of the reduction **16a** and **16h** should incorporate 5 deuterium atoms if the assumed mechanism is operativ. This indeed has been confirmed by ^{1}H-NMR. and MS. analyses of the deuterated compounds **16a** and **16h**. The former has a simple ^{1}H-NMR. spectrum which shows the proton of the deuteriomethyl group as a broad singlet at δ 2.8 (1H) and methylene protons as doublets (J = 9 Hz) at 2.15 (2H). A broad singlet at 3.8 (1H) and a broad triplet (J = 9 Hz) at 3.9 are attributable to NH and methine protons respectively, while two multiplets at 7.11–7.4 (2H) and 6.4–6.9 (7H) are due to the aromatic protons. The methine triplets became sharp on exchange of the NH proton with D_2O.

On refluxing N-(*p*-methoxyphenyl)-maleimide (**5 1**; m.p. 149–150°) with 5,6-dimethylbenzimidazole in acetonitrile in the presence of hydroquinone, we obtained not only the expected N-(*p*-methoxyphenyl)-5,6-dimethyl-1-benzimidazolyl-succinimide (**6 1**), m.p. 224–226°, but also, in about 10% yield, a cyclic trimer of the imide **5 1**, 5,6-dimethylbenzimidazole obviously serving as a catalyst of this oligomerization [17]. In the reaction with benzimidazole the formation of trimerized N-(*p*-methoxyphenyl)-maleimide was even higher (ca. 25%).

Experimental Part

General remarks. All melting points were taken on a *Tottoli* melting point apparatus and are uncorrected. The maleimides used were prepared according to previously described procedures. N-Cyclohexylmaleimide contained 20% water (*Höchster Farbwerke AG*) und was used as obtained. Tetrahydrofuran (THF) was routinely dried by distilling over $LiAlH_4$. The IR. spectra were measured on a *Perkin-Elmer* Model 117 spectrometer. The NMR. spectra were recorded on either a *Varian* A-60A or HA-100 spectrometer using tetramethylsilane as an internal standard. Chemical shifts are reported in δ with the following abbreviations: *s* = singlet, *m* = multiplet, *t* = triplet, *q* = quartet. The MS. were determined with a *Hitachi Perkin-Elmer* RMU 6A.

The most important ion currents are reported as *m/e* values and relative intensities (% base peaks in parenthesis).

The elemental analyses were performed by the *Analytical Division, Siegfried AG.*

Reaction between Benzimidazole and N-Phenylmaleimide. A mixture of benzimidazole (9 g = 76 mmol), N-phenylmaleimide (13 g = 76 mmol), and hydroquinone (0.25 g) in 150 ml of acetonitrile was stirred under reflux for 24 h. Evaporation of the solvent at reduced pressure afforded a pink residue which was crystallized from methylene chloride to give 17 g (77%) of N-phenyl-1-benzimidazole-succinimide (**6a**) as white minute crystals, m.p. 196–198°.

^{1}H-NMR. [$(CD_3)_2SO$]: δ 3.1–3.9 (*m*, 2H) and 6.1 (*m*, 1H), representing *ABX*-system of the protons on the succinimide ring; 7.1–7.8 (*m*, 9H, aromatic); 8.5 (*s*, 1H, N=*CH*). MS.: M^+ 291 (87),

Table 1. *Derivatives of N-substituted 1-benzimidazolyl-succinimides listed in Scheme 1*

Nr.	M.p. (°)	Formula [a]	Mol.-Wt.	% C		% H		% N		% F	
				Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
6a	196–198	$C_{17}H_{13}N_3O_2$	291.3	70.09	70.00	4.50	4.62	14.42	14.37		
6b	199–200	$C_{19}H_{17}N_3O_2 \cdot 1^1/_2MeOH$	367.4	67.01	66.93	6.30	6.10	11.44	11.60		
6c	228	$C_{20}H_{19}N_3O_2$	333.4	72.05	71.70	5.74	5.66	12.60	12.66		
6d	176	$C_{17}H_{12}N_3O_2F$	309.3	–	–	–	–	–	–	6.14	6.10
6e	234	$C_{19}H_{16}N_3O_2F$	337.3	–	–	–	–	–	–	5.63	5.77
6f	230–232	$C_{19}H_{16}N_3O_2Cl$	353.8	64.50	64.45	4.56	5.08	11.88	12.8		
6g	184–187	$C_{18}H_{14}N_3O_2F \cdot 1^1/_2MeOH$	363.3	–	–	–	–	–	–	5.24	5.55
6h	199–200	$C_{18}H_{15}N_3O_2 \cdot 1MeOH$	337.4	67.64	67.37	5.68	5.65	12.45	12.57		
6i	187–188	$C_{17}H_{19}N_3O_2$	297.4	68.67	68.29	6.44	6.28	14.13	14.07		
6j	234–235	$C_{19}H_{23}N_3O_2 \cdot {}^1/_2MeOH$	333.4	69.33	69.25	7.25	7.23	12.60	12.54		
6k	239–241	$C_{29}H_{21}N_3O_2$	353.5	71.36	71.25	7.70	7.68	11.89	11.69		

Table 2. *Further derivatives of N-substituted 1-benzimidazolyl-succinimides*

Nr.	R^1=R^2	R^3	R^4	m.p. (°)	Formula	Mol.-wt.
6l	CH_3	H	*p*-methoxyphenyl	349	$C_{20}H_{19}N_3O_3$	349.4
6m	H	H	ethyl	207	$C_{13}H_{13}N_3O_2$	243.3
6n	CH_3	H	ethyl	205	$C_{15}H_{17}N_3O_2$	271.3
6o	H	CH_3	ethyl	165	$C_{14}H_{15}N_3O_2 \cdot HCl \cdot {}^1/_2H_2O$	302.7
6p	H	H	*n*-butyl	191–193	$C_{15}H_{17}N_3O_2 \cdot HCl$	307.7
6q	CH_3	H	*n*-butyl	118–120	$C_{17}H_{21}N_3O_2$	299.4
6r	H	CH_3	*n*-butyl	223–225	$C_{16}H_{19}N_3O_2 \cdot HCl$	321.7
6s	H	CH_3	cyclohexyl	172	$C_{18}H_{21}N_3O_2$	311.4
6t	H	H	*p*-dimethylaminophenyl	251	$C_{19}H_{18}N_4O_2$	334.4
6u	CH_3	H	*p*-dimethylaminophenyl	266	$C_{21}H_{22}N_4O_2$	362.4
6v	H	CH_3	*p*-dimethylaminophenyl	240	$C_{20}H_{20}N_4O_2$	348.4
6w	H	H	*p*-nitrophenyl	181–182	$C_{17}H_{12}N_2O_4$	336.3
6x	R^2=H, R^1=NO_2	H	phenyl	240 (dec.)	$C_{17}H_{12}N_4O_4$	336.3
6y [a]	R^2=H, R^1=$NHCOCH_3$	H	phenyl	212	$C_{19}H_{16}N_4O_3 \cdot CH_3OH$	380.4

[a] Prepared by catalytic hydrogenation (H_2, Pd/C) of **6x** in acetic acid, followed by immediate reaction with acetic anhydride.

129 (21), 117 (28), 103 (14), 91 (48), 90 (18). The most important fragment peaks were observed at *m/e* 173 (85, N-phenylmaleimide), *m/e* 144 (93, N-vinylbenzimidazole), and *m/e* 118 (100, benzimidazole). For the calculated mol.-weight and the elemental analysis see Table 1.

The compounds **6a** and **6i–k** were soluble in dilute acids.

Besides the compounds of Scheme 1 mentioned in Table 1, the 1:1 adducts **6l–y** of benzimidazoles and maleimides listed in Table 2 were also prepared in the usual way. The N-Alkyl and N-Aryl 1-benzimidazolyl-succinimides 6**m–v** are soluble in acids; a few of them were isolated as crystalline water soluble hydrochlorides. Satisfactory microanalytical N or C, H data were obtained for these compounds.

From the mother liquor of **6a** a trimer of **5a**, $C_{30}H_{21}N_3O_6$, m.p. 307–308° was obtained in 1% yield. For the structure of this trimer see [17].

Reaction between 5,6-Dimethylbenzimidazole and N-Cyclohexylmaleimide. A mixture of 5,6-dimethylbenzimidazole (3 g = 20 mmol), N-cyclohexylmaleimide (4,5 g = 20 mmol), and hydroquinone (0,5 g) in 50 ml of acetonitrile was refluxed with stirring for 7 h. The solvent was removed under reduced pressure and the crystalline residue was filtered and washed with ether. Crystallization from methanol afforded 6,2 g (82,6%) of N-cyclohexyl-5,6-dimethyl-1-benzimidazolylsuccinimide (**6j**), m.p. 234–235°.

In Table 1 other examples of this series are listed.

Lithium Aluminum Hydride Reduction of **6a** *to* **7a**. A solution of **6a** (10 g = 35 mmol) in 500 ml of dry tetrahydrofuran (THF) was added to a stirred slurry of lithium aluminum hydride (5,3 g = 140 mmol) in 1000 ml of dry THF over a period of 10 min. The reaction mixture was refluxed for 2 h., cooled in an ice-water bath, and the excess of lithium aluminum hydride was decomposed successively with 5 ml of water, 5 ml of 10% sodium hydroxide solution, and 5 ml of water. The organic layer was filtered, and the solids were washed with THF. The filtrate was dried ($MgSO_4$) and the solvent was removed under reduced pressure to give a brown gum. The gum was dissolved in 25 ml of benzene and chromatographed over alumina (75 g) using benzene as the eluant. The yellow benzene fractions on evaporation gave a thick oil which on trituration with a little methanol solidified. Crystallization from dichloromethane/methanol gave 3,7 g (40%) of white flakes of 1-phenyl-9-methyl-2,3,3a,4,9,9a-hexahydro-1*H*-pyrrolo[2,3-*b*]quinoxaline (**7a**), m.p. 140–142°. MS.: M^+ 265 (84), 172 (27), 171 (29), 159 (100), 145 (59), 144 (18), 131 (10), 120 (18), 106 (8), 104 (8), 93 (47). 1H-NMR.: see page 1648.

A similar reduction of **6h** with lithium aluminum hydride furnished 1-phenyl-9-ethyl-2,3,3a,4,9,9a-hexahydro-1*H*-pyrrolo[2,3-*b*]quinoxaline (**7h**), m.p. 129–131°. MS.: M^+ 279 (30), 173 (83), 159 (40), 145 (100), 144 (37), 131 (33), 120 (48), 119 (20), 106 (33), 104 (37), 93 (62), 77 (63). Degradation of the N-phenylpyrrolidine residue produces a spectrum similar to **9b** after formaldehyde elimination. Additional fragments (*m/e* 145, 131) are formed by ethylene elimination.

^{1}H-NMR. (in CD_3Cl): 7.1–7.4/*m* (2H) and 6.4–6.9/*m* (7H): aromatic protons; 4.9/*d*, *J* = 5 Hz (1H): methine with two nitrogen neighbours; 3.0–4.1/*m* (6H): protons bonded to carbons with one nitrogen in α-position and NH; 1.8–2.4/*m* (2H): methylene β to nitrogen; 1.1/*t* (3H): methyl.

Other examples of this series are given in Table 3.

Deuterated **16a** *and* **16h** were prepared by reducing **6a** and **6h** respectively with lithium aluminum deuteride in THF in exactly the same way as described above. The following deuterium analysis was obtained from the mass spectrum of **16a**: 2% d_4, 91% d_5, 7% d_6. This d_6 content is ascribed to partial exchange of the NH proton. The deuterium content of the fragments listed taking the unlabeled **7a** as the reference compound are essentially as follows: M^+ 265 d_5, 172, 171 d_5, d_4, 159 d_3, 145 d_3, 144 d_3, d_2, 131 d_1, 120 d_3, 106 d_2, 104 d_1, 93 d_0.

The ^{1}H-NMR. spectrum of **16h** in $CDCl_3$ revealed the following data: 1.1 (broad *s*, 3H, N–CD_2CH_3); 2.1 (*d*, 2H, *J* = 9 Hz, –CD_2–CH_2–); 3.7 (broad, 1H, NH); 3.9 (*t*, 1H, *J* = 9 Hz, –N–CH–); 6.4–6.9 (*m*, 7H aromatic); 7.1–7.4 (*m*, 2H, aromatic). The methine proton appears broad because of coupling with NH, which becomes sharp after exchanging the NH proton with D_2O. The deuterium analysis obtained from the mass spectrum of **16h** is as follows: 1% d_4, 93% d_5, 6% d_6. The contribution of hexadeuterated species is attributed to partial exchange of the proton of nitrogen. The fragments specified for the unlabeled reference compound **7h** have the following deuterium content: M^+ 279 d_5, 173 d_3, 159 d_3, 145, 144 mainly d_1 besides d_2, d_3, 131 d_1, 120 d_3, 106 d_2, 93, 77 d_0.

Lithium Aluminum Hydride Reduction of **6b**. A solution of **6b** (12.0 g = 0.32 mmol) in 400 ml of dry THF was added to a suspension of lithium aluminum hydride (7.4 g = 196 mmol) in 800 ml of dry THF over a period of 10 min. The reaction mixture was stirred under reflux for 2 h. The usual work-up gave a gum which was chromatographed over alumina (90 g). Elution with benzene gave a residue which was crystallised from dichloromethane/methanol to yield 0.5 g (5%) of 1-phenyl-9-methyl-2,3,3a,4,9,9a-hexahydro-1*H*-pyrrolo[2,3-*b*]quinoxaline (**7b**) as needles, m.p. 142–143°. Further elution with acetone gave a gum which solidified on trituration with methanol/ether. Crystallisation from a mixture of dichloromethane/methanol/ether gave 4.5 g (45.5%) of the amino-alkohol **9b** as white flakes, m.p. 135–136°. ^{1}H-NMR. (pyridine-d_5): 2.25 (broad *s*, 6H, $-CH_3$ groups); 2.55 (*t*, 2H, J = 6.5 Hz, $-CH_2-CH_2-NH-$); 3.25 (*q*, 2H, J = 6.5 Hz, $-CH_2NH-$, collapses to a triplet on exchange with D_2O); 4.25 (broad *d*, 2H, $-CH_2OH$); 4.95 (*m*, 1H, $-\underset{|}{C}H-CH_2OH$); 5.7 (broad *t*, 1H, J = 6.5 Hz, NH); 6.7–6.9 (*m*, 4H aromatic protons and of OH); 7.1–7.4 (*m*, 2H, aromatic); 7.45 and 7.8 (each broad *s*, each 1H, aromatic protons of benzimidazole moeity); 8.4 (*s*, 1H, –N=CH). MS.: M^+ 309 (100), 279 (5), 173 (82), 159 (34), 147 (20), 146 (35), 120 (47), 106 (47). The bulk of the spectrum is formed by elimination of formaldehyde from the hydroxymethyl group (weak *m/e* 279) and subsequent cleavage of the alkylaniline residue (*m/e* 173, 159, 120, 106).

$C_{19}H_{23}N_3O$ (309.4) Calc. C 73.76 H 7.49 N 13.58% Found C 73.58 H 7.50 N 13.37%

Lithium Aluminum Hydride Reduction of **6c**. To a stirred slurry of lithium aluminum hydride (4.6 g = 240 mmol) in 500 ml of dry THF was added portionswise a suspension of **6c** (10 g = 60 mmol) in 400 ml of dry THF over a period of 15 min. The reaction mixture was refluxed for 2 h. and after the usual work-up the residue was chromatographed over 150 g of alumina. Elution with benzene afforded 4.0 g of product. Crystallization from ether/*n*-pentane gave 3.6 g (40%) of **7c**, m.p. 123–125°. Elution with methanol yielded 1.5 g of a brown gum which solidified on treatment with ether. It was thrice crystallized from dichloromethane/ether to give 0.45 g (5%) of 5,6-dimethyl-1-(1-*p*-tolyl-3-pyrrolodinyl)-benzimidazole (**14c**) as shiny rectangles, m.p. 157–158°. ^{1}H-NMR. ($CDCl_3$): 2.3 (*s*, 3H, methyl of *p*-tolyl); 2.4 (*s*, 6H, methyl groups); 2.3–2.6 (*m*, 2H, N–CH_2–CH_2); 3.2–3.9 (*m*, 4H, $-CH_2-N-CH_2-$); 5.0 (*m*, 1H, N–CH_2–CH–); 6.6–7.1 (each *m*, each 2H, aromatic protons of *p*-tolyl moeity); 7.25 and 7.6 (each broad *s*, each 1H, aromatic). MS.: M^+ 305 (100), 159 (68), 133 (33), 118 (11), 105 (54), 91 (14), 77 (6), 65 (4). As might be expected from the structure, N-*p*-tolylpyrroline (*m/e* 159) was the major fragmentation product.

$C_{20}H_{23}N_3$ (305.4) Calc. C 78.65 H 7.59 N 13.76% Found C 78.52 H 7.44 N 14.04%

The column on further elution with methanol gave a red gum which solidified on addition of *n*-hexane/ether. The substance was four times crystallized from dichloromethane/benzene to afford 0.2 g (2.2%) of **15c** as glistening white needles, m.p. 167–169°. ^{1}H–NMR. ($CDCl_3$): 2.3 (*s*, 3H, methyl of *p*-tolyl); 2.4 (*s*, 6H, methyl groups); 3.2 (*m*, 2H, N–CH_2–CH_2–C=); 4.0 (*m*, 2H, N–CH_2); 6.4–7.6 (*m*, 7H, aromatic and olefinic); 7.8 (*s*, 1H, N=CH). Ms.: M^+ 303 (100), 302 (58), 186 (6.6), 185 (10), 144 (4.8), 143 (5.7), 118 (14), 105 (7.3), 103 (7.6), 91 (40), 77 (10.2), 65 (20), 51 (6.2), 41 (5.6), 39 (11).

$C_{20}H_{21}N_3$ (303.4) Calc. C 79.17 H 6.98 N 13.85% Found C 79.33 H 7.03 N 13.64%

Lithium Aluminum Hydride Reduction of **6j** *to* **14j**. A slurry of lithium aluminum hydride (0.9 g = 240 mmol) in 100 ml of dry THF was treated with a suspension of **6j** (2.0 g = 6 mmol) in 100 ml of dry THF in small portions over a period of 3 min. The mixture was refluxed for 2 h, cooled, and the excess lithium aluminum hydride was decomposed as described before. After removal of the solvent the reaction mixture was dissolved in benzene and worked up by column chromatography (alumina: 15 g) which afforded 1 g of crystalline residue. Recrystallization from ether/*n*-pentane yielded 0.8 g (45%) of 5,6-dimethyl-1-(1-cyclohexyl-3-pyrrolidinyl)-benzimidazole (**14j**) as colorless needles, m.p. 93–94°. ^{1}H–NMR. ($CDCl_3$): 1.0–2.3 (*m*, 12H, CH_2's of cyclohexyl and pyrrolidine $-N-CH_2-CH_2$); 2.3 (*s*, 6H, methyl groups); 2.3–3.4 (*m*, 5H, $-CH_2-N\langle^{CH_2-}_{CH\langle}$); 4.8 (*m*, $-N-\underset{|}{C}H-CH_2-N$); 7.35 and 7.55 (each broad *s*, each 1H, aromatic protons); 8.0 (*s*, 1H,

Table 3. *Hexahydro-2*H-*pyrrolo*[*2,3*-b]*quinoxaline derivatives* (**7a–7h**)

Nr.	M.p. (°)	Formula	Mol.-wt.	% C		% H		% N		% F	
				Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
7a	140–142	$C_{17}H_{19}N_3$	265.4	76.95	76.97	7.22	7.22	15.84	15.80		
7b	142–143	$C_{19}H_{23}N_3$	293.4	77.78	77.91	7.90	7.89	14.32	14.20		
7c	123–125	$C_{20}H_{25}N_3$	307.4	–	–	–	–	13.67	13.56		
7d	150–151	$C_{17}H_{18}N_3F$	283.3	72.02	72.23	6.40	6.41	14.83	14.80	6.70	6.56
7e	142–143	$C_{19}H_{22}N_3F$	311.4	73.28	73.32	7.12	7.20	13.49	13.38	6.10	6.12
7f	160	$C_{19}H_{22}N_3Cl$	327.8	69.40	69.98	6.74	7.01	12.77	12.54		
7g	128–130	$C_{18}H_{18}N_3F$	297.3	72.69	72.73	6.78	6.88	14.14	13.93	6.39	6.46
7h	129–131	$C_{18}H_{21}N_3$	279.4	77.38	77.17	7.58	7.97	15.04	14.85		

Table 4. *Acyl derivatives of hexahydro-2*H-*pyrrolo*[*2,3*-b]*quinoxalines* (**10a–h**)

Nr.	M.p. (°)	Formula	Mol.-wt.	% C		% H		% N		% F	
				Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
10a	180–182	$C_{19}H_{21}N_3O$	307.4	74.24	74.74	6.98	6.56	13.67	13.94		
10b	177	$C_{21}H_{25}N_3O$	335.5	75.19	74.93	7.51	7.39	12.53	12.70		
10c	190	$C_{22}H_{27}N_3O$	349.5	75.61	75.55	7.79	7.70	12.02	12.04		
10d	173–175	$C_{19}H_{20}N_3OF$	325.3	–	–	–	–	–	–	5.84	6.04
10e	181–183	$C_{21}H_{24}N_3OF$	353.4	–	–	–	–	–	–	5.37	5.53
10f	158–159	$C_{21}H_{24}N_3OCl$	369.8	68.21	67.90	6.54	6.48	11.36	11.12		
10g	165–166	$C_{20}H_{22}N_3OF$	339.4							5.59	5.77
10h	173–175	$C_{20}H_{23}N_3O$	305.4	74.74	77.75	7.21	7.05	13.07	13.25		

—N=C*H*—). MS.: M^+ 279 (50), 254 (100), 200 (13), 151 (63), 147 (10), 109 (10), 108 (18), 96 (13), 82 (30).

$C_{19}H_{27}N_3$ (297.4) Calc. C 76.72 H 9.15 N 14.13% Found C 76.75 H 9.15 N 14.10%

In a similar manner **14i** (m.p. 78–81°) and **14k** (m.p. 93–95°) were prepared. They gave the right C, H and N analysis for $C_{17}H_{23}N_3$ and $C_{21}H_{31}N_3$, respectively.

*1-Phenyl-4-acetyl-9-methyl-2,3,3a,4,9,9a-hexahydro-1*H*-pyrrolo[2,3-*b*]quinoxaline* (**10a**). A mixture of 1.8 g of **7a** in 3 ml of dry pyridine and 3 ml of acetic anhydride was heated to 60–70° on a water bath for 10 min. The reaction mixture was then allowed to stand at room temperature for 0.5 h and was scratched with a glass rod. After filtration the substance was washed with ether and recrystallized from dichloromethane/methanol to yield 2 g (96%) of **10a** as colorless needles. ^{1}H—NMR. (CF_3COOH): 2.5 (broad *m*, 2H, N—CH_2—CH_2—); 2.6 (*s*, 3H, $COCH_3$); 3.9 (broad *t*, 2H, —N—CH_2—); 4.4 (broad *s*, 3H, N—CH_3); 6.5 (broad *m*, 1H, N—$\underset{\displaystyle COCH_3}{\overset{|}{C}}H$—); 7.2–8.1 (*m*, 11H, aromatic and of protonated N's); 9.1 (broad *d*, 1H, N—C*H*—N). MS.: M^+ 307 (40), 264 (19), 201 (97), 173 (37), 159 (100), 145 (51), 144 (33), 121 (30). For other members of this series see Table 4.

*1-Phenyl-4-carbethoxy-9-methyl-2,3,3a,4,9,9a-hexahydro-1*H*-pyrrolo[2,3-*b*]quinoxaline* (**8a**). To a solution of **6a** (1 g = 4 mmol), 0.5 g of dry triethylamine (over KOH), and 15 ml of dry dichloromethane (over $CaCl_2$) there was added cautiously with stirring a solution of ethyl chloroformate (1 g = 9 mmol) in 5 ml of dichloromethane over a period of 5 min. The initial vigorous reaction was controlled by placing the reaction flask in cold water. The water bath was then removed and the reaction mixture was stirred at room temperature for 5 h. Removal of the solvent at reduced pressure gave a thick gum which was then treated with 20 ml of water. The precipitates were filtered, washed with water and dried. Crystallization of the residue from dichloromethane/methanol yielded 1 g (75%) of **8a** as white needles, m.p. 180–181°. NMR. ($CDCl_3$): 1.3 (*t*, 3H, —CH_2—CH_3); 2.2 (*m*, 2H, —NCH_2—CH_2—); 2.8 (*s*, 3H, N—CH_3); 3.3 (*m*, 2H, —N—CH_2—); 4.25 (*m*, 2H, *AB*-part of the ABX_3-system, diastereotopic methylene protons of the ethoxy group); 4.8–5.5 (*m*, 2H, methine protons); 6.5–7.7 (*m*, 9H, aromatic). MS.: M^+ 337 (100), 292 (2), 291 (3), 290 (6), 264 (5), 231 (5), 159 (28), 145 (17), 144 (12).

$C_{20}H_{23}N_3O_2$ (337.4) Calc. C 71.19 H 6.87 N 12.45 O 9.48%
Found ,, 71.14 ,, 6.87 ,, 12.60 ,, 9.41%

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