Arch. Pharm. (Weinheim) *320*, 698–704 (1987)

Indoles, IV[1]

9-Substituted 4,9-Dihydropyrano[3,4-*b*]indol-1(3*H*)-ones – Synthesis and Conversion into 2,3,4,9-Tetrahydro-1*H*-pyrido-[3,4-*b*]indoles

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Pyrano[3,4-*b*]indolones **3a-d** are available from α-ethoxyalyllactones **1a, c** and disubstituted hydrazines **2a, b** without isolation of intermediates. In a two-phase system, however, the intermediate hydrazones **4a, c** can be isolated. Conversion of **3a–d** into β-carbolines was not possible by lactamisation but *via* the amides **8** and **9**.

Indole, 4. Mitt.: **9-Substituierte 4,9-Dihydropyrano[3,4-b]indol-1(3H)-one – Synthese und Umwandlung in 2,3,4,9-Tetrahydro-1H-pyrido[3,4-b]indole**

Die Pyrano[3,4-b]indolone **3a–d** erhält man ohne Isolierung von Zwischenprodukten aus den α-Ethoxalyllactonen **1a, c** und den disubstituierten Hydrazinen **2a, b**. Setzt man in einem Zweiphasensystem um, so können die intermediären Hydrazone **4a, c** aus der organischen Phase isoliert werden. Die Überführung von **3a–d** in β-Carboline gelingt nicht durch direkte Lactamisierung, wohl aber über die Amide **8** und **9**.

Cleavage and decarboxylation of α-ethoxalyllactones in mineral acid, followed by treatment with arylhydrazines yields α-hydrazonolactones, which produce pyrano [3,4-b]indoles under acidic conditions[2,3]. These pyranoindoles show interesting pharmacological properties and are valuable starting materials for the synthesis of β-carbolines[1,2].

Trying to extend this reaction sequence, we found, that the method described above[1], was not suitable for 1,1-disubstituted hydrazines, since the solubility of **2a, b** in hot mineral acid was not sufficient.

We therefore decomposed **1a, c** in hot mineral acid, extracted the resulting δ-hydroxy-α-ketoacid[2,3] together with its ester, lactone and other unidentified by-products and treated the residue of the organic layer with the hydrazine hydrochlorides **2a, b** in boiling EtOH. Surprisingly this procedure did not lead to the expected hydrazonolactones **4a–c**, but furthermore to the corresponding pyranoindolones **3a–d**. When, however, **2a** reacted, with decomposed **1a, c** in the two-phase system mineral acid/chloroform, the intermediate hydrazonolactones **4a, c** migrate into the organic layer, which obviously interrupts the reaction and enables their isolation.

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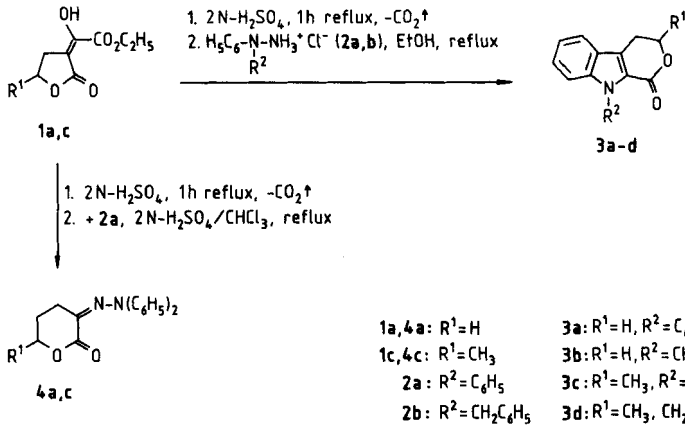
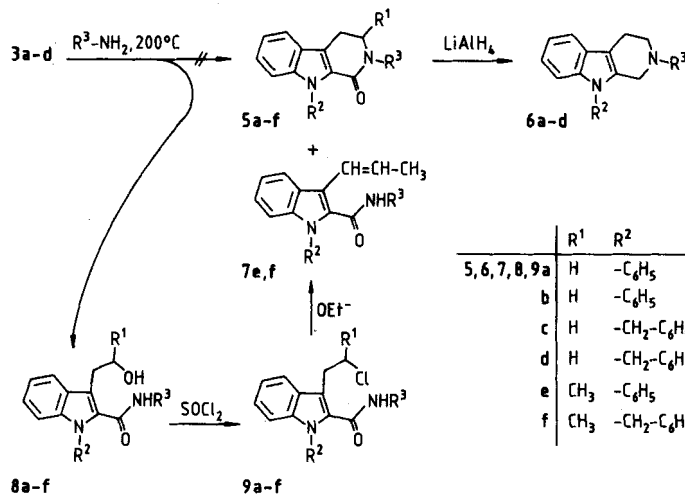


Contrary to 9-unsubstituted pyrano [3,4-b]indolones[1], fusion of **3a-d** with methylamine and benzylamine at 200–210° gave the hydroxyamides **8a–f** and not the corresponding lactams. This was easily concluded from the ^{1}H-NMR spectra with two exchangeable signals at δ = 5.25–5.60 and 8.64–9.85 ppm, ascribed to the OH- and NH-protons. All attempts to dehydrate these hydroxyamides led to the corresponding starting lactones **3** or decomposition products but not to the desired lactams **5**.

In order to activate **8a–f** for cyclisation we treated these compounds with $SOCl_2$ which produced the chloramides **9a–f**. The formation of iminolactone hydrochlorides, which we observed with analogous 1-unsubstituted indol-2-carboxamides[4] was excluded by spectral data.



	R1	R2	R3
5,6,7,8,9a	H	-C6H5	-CH3
b	H	-C6H5	-CH2-C6H5
c	H	-CH2-C6H5	-CH3
d	H	-CH2-C6H5	-CH2-C6H5
e	CH3	-C6H5	-CH2-C6H5
f	CH3	-CH2-C6H5	-CH2-C6H5

Refluxing **9a–f** with $NaOC_2H_5$ afforded the lactams **5a–f**, in the case of the 2-chlorpropyl derivatives **9e, f** together with the by-products **7e, f**.

Completing the transformation of pyrano[3,4-b]indolones to tetrahydro-β-carbolines, we reduced **5a–d** with $LiAlH_4$ to the 2,9-disubstituted 2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indoles **6a–d**, some of which have already been synthesized following other routes[5].

Experimental Part

MP: open capillaries (uncorr.), Gallencamp apparatus. – IR spectra: Beckman IR 33 (KBr). – ^{1}H-NMR specra: Varian EM 360 (60 MHz), DMSO-d^6, TMS as int. stand. – Elementary analyses: CHN-Autoanalyzer Chem. Inst. Univ. Bonn and Microanalytical Center, Cairo University.

4,9-Dihydropyrano[3,4-b]indol-1(3H)-ones **3a–d**

0.13 mol ethoxalylactone **1** in 60 ml 2 N H_2SO_4 was heated for 1 h at reflux temp. After cooling, the mixture was extracted with 2 × 150 ml ether. The ether extracts were dried with Na_2SO_4 and evaporated i. vac. – 0.1 mol disubstituted hydrazine hydrochloride **2** in 150 ml EtOH was added and the mixture was heated at reflux temp. for 2 h. The mixture was concentrated i. vac., treated with 200 ml water, the precipitated solid washed with ether and recrystallized from EtOH. Analytical data see tables 1 and 2.

5,6-Dihydro-3-(diphenylhydrazono)-4H-pyran-2-ones **4a, c**

0.013 mol **1a** or **1c** were treated with 2 N H_2SO_4, extracted with ether and evaporated as described above. 20 ml 2 N H_2SO_4, 40 ml $CHCl_3$ and 2.2 g (0.01 mol) N,N-diphenylhydrazine-HCl were added and the mixture refluxed for 0.5 h. The chloroform layer was separated, washed with water, dried with Na_2SO_4 and evaporated i. vac. The residue was treated with 30 ml ether and the resulting solid crystallized from EtOH. Analytical data see tables 1 and 2.

3-(2-Hydroxyalkyl)-1H-indole-2-carboxamides **8a–f**

Reaction with benzylamine: 0.02 mol of the appropriate lactone **3** and 2.15 g (0.02 mol) benzylamine were heated in an oil bath at 200–210° (air condenser) for 3 h. After cooling, the sticky mass was crystallized from EtOH. Analytical data see tables 1 and 2.

Reaction with methylamine: A steel bomb containing 0.02 mol appropriate lactone **3** was cooled in acetone/dry ice. 10 ml condensed methylamine were added, the bomb was closed and heated in an oil-bath at 200° for 4 h. After cooling, the residue was taken up in EtOH, evaporated i. vac. and crystallized from EtOH. Analytical data see tables 1 and 2.

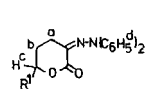
3-(2-Chlorethyl)-1H-indole-2-carboxamides **9a–f**

2.0 g **8a–f** in 50 ml $CHCl_3$ and 10 ml freshly distilled $SoCl_2$ were stirred for 0.5 h at room temp., then the solution was evaporated i. vac. to 1/10 volume, 40 ml $CHCl_3$ were added and evaporated again. The residue was treated with 20 ml petroleum ether 60/80, the solid separated and crystallized from EtOH. Analytical data see tables 1 and 2.

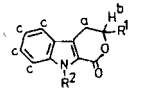
2,3,4,9-Tetrahydro-1H-pyrido[3,4-b]indol-1-ones **5a–d**

1.0 g **9** in 10 ml absol. EtOH and a solution of 0.2 g (8.7 mmol) Na in 10 ml absol. EtOH were refluxed together for 2 h. The solution was filtered, poured into 100 ml water and acidified to pH 6 with dil. HCl. The mixture was extracted with 30 ml $CHCl_3$, the organic layer washed with 30 ml water, dried with Na_2SO_4 and evaporated i. vac. The residue was crystallized from EtOH. Analytical data see tables 1 and 2.

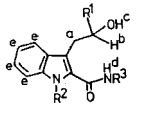
Tab. 1: Spectroscopic data of hydrazonolactones **4a, c** and indoles **3a–d, 8a–f, 9a–f, 5a–f, 7e, f 6a–d**, ^{1}H-NMR (TMS $\delta = 0$ ppm, in DMSO-d^6), IR (cm^{-1}, in KBr).



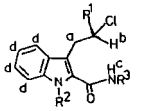
4a–c



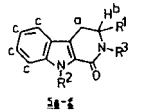
3a–d



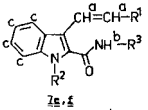
8a–f



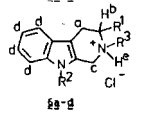
9a–f



5a–f



7e, f



6a–d

Compd.	R^1	R^2	R^3	H^a	H^b	H^c	H^d	H^e	H^f	H^g	H^h	
4a	H^c	-	-	1.65-2.00[1]	1.65-2.00[1]	4.15t	7.00-7.50[1]					1710
c	CH_3^e	-	-	1.55-2.00[1]	1.55-2.00[1]	4.2-4.7m	7.00-7.60[1]	1.25d				1710
3a	H^b	$C_6H_5^d$	-	3.15t	4.10t	7.10-7.70[1]	7.45s[1]					1710
b	H^b	CH_2^d-$C_6H_5^e$	-	3.12t	4.60t	7.00-7.80[1]	5.80s	7.15s				1685
c	CH_3^d	$C_6H_5^e$	-	3.28d	4.7-5.1m	7.00-7.80[1]	1.47d	7.44s				1710
d	CH_3^d	CH_2^e-$C_6H_5^f$	-	3.17d	4.6-5.1m	7.00-7.80[1]	1.55d	5.80s	7.20s			1690
8a	H^b	$C_6H_5^e$	CH_3^f	3.05t	3.55-3.84m[2]	5.34t[3]	8.46q[3]	7.00-7.70[1]	2.70d[4]			3360,3210 1630
b	H^b	$C_6H_5^e$	CH_2^f-$C_6H_5^g$	3.02t	3.55-3.85m[2]	5.25t[3]	9.17t[3]	7.05-7.70[1]	4.32d[4]			3320,3200 1625
c	H^b	CH_2^f-$C_6H_5^e$	CH_3^g	3.05t	3.62-3.90m[2]	5.46t[3]	8.90q[3]	7.00-7.72[1]	5.60s	2.80d[4]		3280,3200 1620
d	H^b	CH_2^f-$C_6H_5^e$	CH_2^g-$C_6H_5^e$	3.05t	3.50-3.90m[2]	5.40t[3]	9.45t[3]	7.00-7.72[1]	5.60s	4.40d[4]		3280,3210 1625
e	CH_3^f	$C_6H_5^e$	CH_2^g-$C_6H_5^e$	2.88-3.05m	3.95-4.20m	5.55s	9.22t[3]	7.00-7.65[1]	1.25d	4.35d[4]		3350,3230 1640
f	CH_3^f	CH_2^g-$C_6H_5^e$	CH_2^h-$C_6H_5^e$	2.88-3.05m	3.80-4.15m	5.55s	9.85t[3]	7.00-7.72[1]	1.20d	5.65s	4.51d[4]	3350,3230 1630
9a	H^b	$C_6H_5^d$	CH_3^e	3.34t	3.86t	8.20q[3]	7.10-7.87[1]	2.70d[4]				3280,1640
b	H^b	$C_6H_5^d$	CH_2^e-$C_6H_5^d$	3.35t	3.90t	8.90t[3]	6.90-7.90[1]	4.35d[4]				3280,1635
c	H^b	CH_2^e-$C_6H_5^d$	CH_3^f	3.28t	3.78t	8.35q[3]	7.00-7.73[1]	5.46s	2.75d[4]			3275,1630
d	H^b	CH_2^e-$C_6H_5^d$	CH_2^f-$C_6H_5^d$	3.28t	3.76t	8.86t[3]	6.90-7.84[1]	5.50s	4.44d[4]			3280,1630
e	CH_3^e	$C_6H_5^d$	CH_2^f-$C_6H_5^d$	3.42d	4.40-4.64m	6.05t[3]	6.85-7.80[1]	1.56d	4.35d[4]			3310,1630
f	CH_3^e	CH_2^f-$C_6H_5^d$	CH_2^f-$C_6H_5^d$	3.26d	4.35-4.67m	6.26t[3]	6.86-7.75[1]	1.56d	5.58s	4.53d[4]		3300,1630
5a	H^b	$C_6H_5^c$	CH_3^d	3.07t	3.71t	7.02-7.82[1]	2.92s					1630
b	H^b	$C_6H_5^c$	CH_2^d-$C_6H_5^c$	3.10t	3.75t	7.18-7.81[1]	4.64s					1640
c	H^b	CH_2^d-$C_6H_5^c$	CH_3^e	3.05t	3.64t	7.05-7.73[1]	5.87s	3.00s				1630
d	H^b	CH_2^d-$C_6H_5^c$	CH_2^e-$C_6H_5^c$	3.01t	3.62t	7.07-7.72[1]	5.90s	4.68s				1640
e	CH_3^d	$C_6H_5^c$	CH_2^e-$C_6H_5^c$	3.00d	4.30-4.85m	6.72-7.67[1]	1.54d	4.47s				1650
f	CH_3^d	CH_2^e-$C_6H_5^c$	CH_2^f-$C_6H_5^c$	3.00d	3.70-4.10m	7.00-7.70[1]	1.17d	5.91s	4.68s			1635
7e	CH_3^d	$C_6H_5^c$	CH_2^e-$C_6H_5^c$	6.10-6.58[1]	9.00t[3]	6.85-8.10[1]	1.91d	4.34d[4]				3280,1640 1620
f	CH_3^d	CH_2^e-$C_6H_5^c$	CH_2^f-$C_6H_5^c$	6.23-6.70[1]	9.03t[3]	7.00-8.00[1]	1.96d	6.78s	4.65d[4]			3290,1635 1600
6a	H^b	$C_6H_5^d$		3.12t	3.62t	4.34s	7.05-7.71[1]	11.64[3]	2.88s			2340-2700
b	H^b	CH_2^f-$C_6H_5^d$		3.05t	3.41t	4.46s	6.95-7.62[1]	11.62[3]	5.35s	2.90s		2200-2680
c	H^b	$C_6H_5^d$		3.12t	3.55t	4.31s	7.00-7.78[1]	12.05[3]	4.51s			2200-2700
d	H^b	CH_2^f-$C_6H_5^d$		3.16t	3.56t	4.52s	7.00-7.80[1]	12.05[3]	5.30s	4.52s		2200-2710

[1] overlaped signals [2] triplet after D_2O exchange [3] no signal after exchange with D_2O [4] singlet after D_2O exchange

Reaction of 3-(2-chlorpropyl)-1H-indole-2-carboxamides **9e, f** *with sodium ethoxide:*

1.0 g **9e, f** were treated with $NaOC_2H_5$ solution as described above. After evaporation of $CHCl_3$, the residue was chromatographed on a silica gel column (silica gel 60, 230 mesh ASTM, Merck) with ether/petroleum ether 60/80. First fractions yielded pure **5e** resp. **5f**. Second fractions gave **7e**, respectively **7f**, which were crystallized from ether/petroleum ether 60/80. Yields and analytical data see tables 1 and 2.

Tab. 2: Analytical data of hydrazonolactones **4a, c** and indoles **3a–d, 8a–f, 9a–f, 5a–f, 7e, f, 6a–d.**

Compound	Yield (%)	M.p. (°C)	Mol.form. (Mol.mass)	Calcd. / Found	C	H	N
5,6-Dihydro-3-(diphenylhydrazono)-4H-pyran-2-one(4a)	43	192-193	$C_{17}H_{16}N_2O_2$ (280.4)	Calcd.	72.8	5.76	10.0
				Found	72.9	5.89	10.0
5,6-Dihydro-6-methyl-3-(diphenylhydrazono)-4H-pyran-2-one(4c)	46	162-163	$C_{18}H_{18}N_2O_2$ (294.4)	Calcd.	73.4	6.18	9.5
				Found	73.3	6.22	9.6
9-Phenyl-4,9-dihydropyrano[3,4-b]-indol-1(3H)-one(3a)	81	123-124	$C_{17}H_{13}NO_2$ (263.3)	Calcd.	77.5	4.99	5.3
				Found	77.1	4.99	5.2
9-(Phenylmethyl)-4,9-dihydropyrano-[3,4-b]indol-1(3H)-one(3b)	67	108 (Lit.[6] 109-109.5)					
3-Methyl-9-phenyl-4,9-dihydropyrano-[3,4-b]indol-1(3H)-one(3c)	63	109-110	$C_{18}H_{15}NO_2$ (277.3)	Calcd.	77.9	5.46	5.1
				Found	77.7	5.54	5.0
3-Methyl-9-(phenylmethyl)-4,9-dihydro-pyrano[3,4-b]indol-1(3H)-one(3d)	72	98-99	$C_{19}H_{17}NO_2$ (291.4)	Calcd.	78.2	5.89	4.8
				Found	78.6	5.81	4.9
3-(2-Hydroxyethyl)-N-methyl-1-phenyl--1H-indole-2-carboxamide(8a)	73	170-171	$C_{18}H_{18}N_2O_2$ (294.4)	Calcd.	73.4	6.18	9.5
				Found	73.6	6.25	9.5
3-(2-Hydroxyethyl)-1-phenyl-N-(phenyl-methyl)-1H-indole-2-carboxamide(8b)	75	169	$C_{24}H_{22}N_2O_2$ (370.5)	Calcd.	77.8	6.00	7.6
				Found	77.7	6.18	7.4
3-(2-Hydroxyethyl)-N-methyl-1-(phenyl-methyl)-1H-indole-2-carboxamide(8c)	75	184-185	$C_{19}H_{20}N_2O_2$ (308.4)	Calcd.	74.0	6.55	9.1
				Found	74.1	6.54	9.0
3-(2-Hydroxyethyl)-1,N-bis-(phenyl-methyl)-1H-indole-2-carboxamide(8d)	66	179-180	$C_{25}H_{24}N_2O_2$ (384.5)	Calcd.	78.1	6.30	7.3
				Found	78.2	6.17	7.4
3-(2-Hydroxypropyl)-1-phenyl-N-(phenyl-methyl)-1H-indole-2-carboxamide(8e)	72	129-130	$C_{25}H_{24}N_2O_4$ (384.5)	Calcd.	78.1	6.30	7.3
				Found	77.9	6.35	7.2
3-(2-Hydroxypropyl)-1,N-bis-(phenyl-methyl)-1H-indole-2-carboxamide(8f)	55	126-127	$C_{26}H_{26}N_2O_2$ (398.5)	Calcd.	78.3	6.59	7.0
				Found	78.1	6.68	7.0
3-(2-Chlorethyl)-N-methyl-1-phenyl--1H-indole-2-carboxamide(9a)	93	152-153	$C_{18}H_{17}ClN_2O$ (312.8)	Calcd.	69.1	5.49	9.0
				Found	69.3	5.55	8.9
3-(2-Chlorethyl)-1-phenyl-N-(phenyl-methyl)-1H-indole-2-carboxamide(9b)	91	136-137	$C_{24}H_{21}ClN_2O$ (388.9)	Calcd.	74.1	5.45	7.2
				Found	73.7	5.41	7.2
3-(2-Chlorethyl)-N-methyl-1-(phenyl-methyl)-1H-indole-2-carboxamide(9c)	89	178-179	$C_{19}H_{19}ClN_2O$ (326.9)	Calcd.	69.8	5.87	8.6
				Found	69.9	5.80	8.5
3-(2-Chlorethyl)-1,N-bis-(phenyl-methyl)-1H-indole-2-carboxamide(9d)	83	164-165	$C_{25}H_{23}ClN_2O$ (402.9)	Calcd.	74.5	5,76	7.0
				Found	74.3	5.64	6.9
3-(2-Chlorpropyl)-1-phenyl-N-(phenyl-methyl)-1H-indole-2-carboxamide(9e)	86	144-145	$C_{25}H_{23}ClN_2O$ (402.9)	Calcd.	74.5	5.76	7.0
				Found	74.4	6.09	6.9
3-(2-Chlorpropyl)-1,N-bis-(phenyl-methyl)-1H-indole-2-carboxamide(9f)	86	166-167	$C_{26}H_{25}ClN_2O$ (417.0)	Calcd.	74.9	6.06	6.7
				Found	74.7	6.16	6.7

Compound	Yield (%)	M.p. (°C)	Mol.form. Calcd. (Mol.mass) Found	C	H	N
2,3,4,9-Tetrahydro-2-methyl-9-phenyl--1H-pyrido[3,4-b]indol-1-one(5a)	90	158-160	(Lit.[7] 160)			
2,3,4,9-Tetrahydro-9-phenyl-2-(phenylmethyl)-1H-pyrido[3,4-b]indol-1-one(5b)	88	125-126	$C_{24}H_{20}N_2O$ (352.4)	81.8 81.4	5.72 5.85	7.9 7.9
2,3,4,9-Tetrahydro-2-methyl-9-(phenylmethyl)-1H-pyrido[3,4-b]indol-1-one(5c)	81	147-148	(Lit.[7] 149)			
2,3,4,9-Tetrahydro-2,9-bis-(phenylmethyl)-1H-pyrido[3,4-b]indol-1-one(5d)	71	107	$C_{25}H_{22}N_2O$ (366.5)	81.9 81.5	6.05 6.15	7.6 7.5
2,3,4,9-Tetrahydro-3-methyl-9-phenyl-2--(phenylmethyl)-1H-pyrido[3,4-b]indol-1-one(5e)	53	118	$C_{25}H_{22}N_2O$ (366.5)	81.9 81.5	6.05 6.18	7.6 7.5
2,3,4,9-Tetrahydro-3-methyl-2,9-bis-(phenylmethyl)-1H-pyrido[3,4-b]indol-1-one(5f)	44	132	$C_{26}H_{24}N_2O$ (380.5)	82.1 81.9	6.36 6.69	7.4 7.2
1-Phenyl-N-(phenylmethyl)-3-(1-propenyl)--1H-indole-2-carboxamide(7e)	27	132-134	$C_{25}H_{22}N_2O$ (366.5)	81.9 81.7	6.05 6.11	7.6 7.6
1,N-Bis-(phenylmethyl)-3-(1-propenyl)--1H-indole-2-carboxamide(7f)	32	155-156	$C_{26}H_{24}N_2O$ (380.5)	82.1 81.9	6.36 6.61	7.4 7.3
2,3,4,9-Tetrahydro-2-methyl-9-phenyl-1H--pyrido[3,4-b]indole hydrochloride(6a)	82	219-221	(Lit.[5] 221-222)			
2,3,4,9-Tetrahydro-2-methyl-9-(phenylmethyl)-1H-pyrido[3,4-b]indole hydrochloride(6c)	80	225-226	(Lit.[5] 225-227)			
2,3,4,9-Tetrahydro-2-(phenylmethyl)-9-phenyl--1H-pyrido[3,4-b]indole hydrochloride(6b)	90	226-227	$C_{24}H_{23}ClN_2$ (374.9)	76.9 76.5	6.18 6.43	7.5 7.3
2.3.4.9-Tetrahydro-2,9-bis-(phenylmethyl)--1H-pyrido[3,4-b]indole hydrochloride(6d)	81	208-209	$C_{25}H_{25}ClN_2$ (388.9)	77.2 77.1	6.48 6.71	7.2 7.0

2,3,4,9-Tetrahydro-1H-pyrido[3,4-b]indole hydrochlorides **6a–d**

4 mmol appropriate indolone **5** were added in small amounts to well stirred 0.3 g (8 mmol) $LiAlH_4$ in 75 ml dry ether, kept at room temp. for 1 h and then refluxed for 3 h. After cooling, the mixture was decomposed by dropwise addition of 3 ml water, stirred vigorously for 0.5 h, filtered and the granular precipitate was washed twice with 30 ml ether. The etheral solutions were dried with Na_2SO_4, concentrated i. vac. and dry HCl gas passed in. After cooling, the white crystals were collected and crystallized from EtOH/ether. Analytical data see tables 1 and 2.

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Pyrido[4,3-e]-1,4-diazepines and Pyrido[4,3-b]-1,5-benzodiazepines: Synthesis and Affinity to Brain Benzodiazepine Receptors

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Pyrido[4,3-*e*]-1,4-diazepines and fused tricyclic analogs thereof have been synthesized and tested for inhibition of benzodiazepine binding to receptors in various rat brain structures in comparison with standard drugs. Structure-affinity relationships are discussed.

Pyrido[4,3-e]-1,4-diazepine und Pyrido[4,3-b]-1,5-benzodiazepine: Synthese und Affinität zu Benzodiazepinrezeptoren im Gehirn.

Pyrido[4,3-e]-1,4-diazepine und ihre anellierten tricyclischen Analoga wurden synthetisiert und auf Affinität zu Benzodiazepinrezeptoren in verschiedenen Gehirnstrukturen von Ratten im Vergleich zu Standardarzneimitteln getestet. Struktur-Affinitäts-Beziehungen werden diskutiert.

We have recently reported on the synthesis of 4-chloro- and 4-amino-3-aroylpyridines via o-lithiation of 4-chloropyridine in the key step.[1] We describe now the application of the chloroketones **1a, b, c** for the synthesis of heterocycles with the pyrido[4,3-e]-1,4-diazepine ring system.

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