POTENTIAL ANTIDEPRESSANTS: 10-AMINO-2-CHLORO-10,11-DIHYDRODIBENZO[*b,f*]THIEPINS

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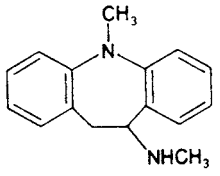
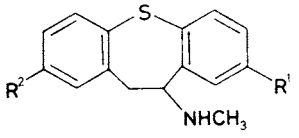
Reduction of N-(2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-yl)formamide with lithium aluminium hydride resulted in the methylamino compound *IV*. The dimethylamino compound *V* was obtained by methylation of 10-amino-2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin with formic acid and aqueous formaldehyde. Substitution reactions of 2,10-dichloro-10,11-dihydrodibenzo-[*b,f*]thiepin with a series of primary and secondary amines afforded the title compounds *VI* to *XXVIII*. The bases were transformed to salts and pharmacologically tested. Only the pyrrolidino compound *IX* (hydrogen succinate VÚFB-15 551) showed a clear phamacological profile of a potential antidepressant.

The 10-methylamino derivative of 5-methyl-10,11-dihydro-5*H*-dibenz[*b,f*]azepine (*I*) was synthesized by the Rhone-Poulenc chemists[1,2] and recognized in pharmacological tests as a potential antidepressant ("metapramine") (ref.[3]). Clinical trials[4,5] confirmed the preclinical results and *I* entered the market (Rodostene^R, Timaxel^R) as a drug for mental depression. In the similar 10,11-dihydrodibenzo[*b,f*]thiepin series, the nuclearly unsubstituted 10-methylamino compound *II* (ref.[6]) and its 8-chloro deriative *III* (ref.[7]) are known but their antidepressant potentiality was not mentioned. The 2-chloro-10-methylamino compound *IV* has been unknown until now and because of the rather easy accessibility of the 2-chloro-10-substituted 10,11-dihydrodibenzo[*b,f*]thiepins (cf. ref.[8]), the present communication is devoted to the synthesis of *IV* and various 10-amino-2-chloro-10,11-dihydrodibenzo[*b,f*]-



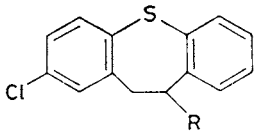
I



II, $R^1 = R^2 = H$
III, $R^1 = Cl$; $R^2 = H$
IV, $R^1 = H$; $R^2 = Cl$

thiepins. In addition to N-substituted 10-(1-piperazinyl) compounds[9-11] only the 10-amino and 10-(2-aminoethyl)amino compounds[12] were prepared within this series (in connection with the search after noncataleptic neuroleptic agents).

For preparing *IV*, the knownN-(2-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-yl)-formamide[12] was reduced with lithium aluminium hydride in boiling ether. The oily base *IV* was transformed to the hydrochloride and the released homogeneous base was used for recording the ^{1}H NMR spectrum. The next homologous *V* was prepared by methylation of 10-amino-2-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin[12] with formic acid and aqueous formaldehyde at 100°C (the Eschweiler–Clarke method[13]). The base *V* was crystalline; its ^{1}H NMR spectrum was measured, and it afforded a crystalline hydrogen maleate (its mass spectrum confirmed the composition $C_{16}H_{16}ClNS$ for the base *V*).



V, R = $N(CH_3)_2$
VI, R = $N(C_2H_5)_2$
VII, R = $NH(CH_2)_3CH_3$
VIII, R = NH–
IX, R = –N
X, R = –N
XI, R = –N
XII, R = –N O
XIII, R = $NHCH_2C_6H_5$
XIV, R = $NHCH_2CH_2C_6H_5$
XV, R = $NHCHCH_2C_6H_5$ (CH_3)
XVI, R = $NHCH_2CH_2OH$
XVII, R = $NH(CH_2)_3OH$
XVIII, R = $NHCH_2CH_2$–(2,3-OCH_3)

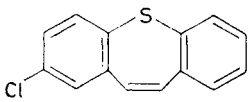
XIX, R = NCH_2CH_2–(2,3-OCH_3) (CH_3)
XX, R = $NHCH_2CH_2OC_6H_5$
XXI, R = –N (CH_2CH_2OH)
XXII, R = $NHCH_2CH_2N(CH_3)_2$
XXIII, R = $NH(CH_2)_3N$
XXIV, R = $NH(CH_2)_3N$
XXV, R = $NH(CH_2)_3N$ O
XXVI, R = $NHCH_2$–N (C_2H_5)
XXVII, R = NH–N (C_2H_5)
XXVIII, R = NH–N–CH_3
XXIX, R = –N O

A series of amines of formulae *V*–*XXVIII* was prepared by reactions of 2,10-dichloro-10,11-dihydrodibenzo[*b*,*f*]thiepin[14,15] with excessive diethylamine, 1-butylamine, cyclopentylamine, pyrrolidine, piperidine, hexamethyleneimine, morpholine, benzylamine, 2-phenylethylamine, 1-phenyl-2-propylamine[16], 2-aminoethanol, 3-

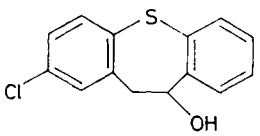
-aminopropanol, 2-(3,4-dimethoxyphenyl)ethylamine, N-methyl-2-(3,4-dimethoxyphenyl)ethylamine[17], 2-phenoxyethylamine[18], 2-(2-piperidinyl)ethanol[19], 2-(dimethylamino)ethylamine, 3-(1-pyrrolidinyl)propylamine[20,21] (it was prepared from 3-(1-pyrrolidinyl)propionitrile[20] by reduction with lithium aluminium hydride which is new for this compound), 3-(1-piperidinyl)propylamine[22], 3-(4-morpholinyl)propylamine[23], 1-ethyl-2-pyrrolidinylmethylamine[24], 3-amino-1-ethylpiperidine, and 4-amino-1-methylpiperidine[25,26] in boiling chloroform (general method). Two modifications of the general method were differentiated during the processing which was directed by the degree of lipophilicity (or hydrophilicity) of the starting amine as well as of the product. In the first modification (method *A*) the reaction mixture was washed with water and the base (oily or crystalline) was extracted with 2·5M-HCl. The released base was used for preparing the salts (hydrochloride, maleate, succinate, oxalate, fumarate). The crystalline base or the homogeneous oily base, released from the purified salt, was used for recording the ^{1}H NMR spectrum. In the second modification (method *B*), the extraction with 2·5M-HCl was not possible because the hydrochloride remained in the chloroform solution and was obtained by its evaporation. The rest of the procedure was the same. The amines *VI*–*XXVIII* are assembled in Table I with the usual experimental data. Preparation of *IX* and *XIV* is described in the Experimental as examples of methods *A* and *B*. Spectra of *VI*–*XXVIII* are assembled in Table II.

In four cases the molecules of the products contain two centres of chirality (*XV*, *XXI*, *XXVI*, and *XXVII*). With the exception of *XXVI* (obtained only as a mixture of two racemates), their separation proceeded either by chromatography of the bases or by crystallization of salts. The cases with separation are explicitly described in the Experimental but analytical and spectral data of the individual racemates (A or B) are included in Tables I and II.

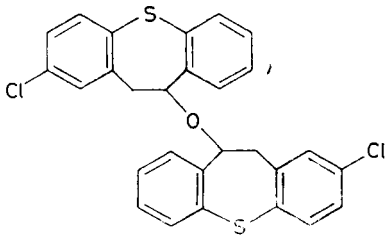
The extraction of the crude bases with 2·5M-HCl resulted in some cases in partial cleavage of the molecules. It was best apparent in the case of the benzylamino compound *XIII* where the chromatography of the „released base" afforded first *XXX* (cf.[14]) (product of elimination) and then *XXXI* (ref.[14]) (product of hydrolysis).



XXX



XXXI



XXXII

TABLE I

10-Amino-2-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepins

Compound[a]	Method (yield, %)	M.p., °C (solvent)	Formula (M.w.)	Calculated/Found				
				% C	% H	% Cl	% N	% S
VI	*A* (41)	61—62 (methanol)	$C_{18}H_{20}ClNS$ (317·9)	68·01 67·84	6·34 6·53	11·16 11·37	4·41 4·80	10·08 10·18
VI-HM		145·5—146·5 (ethanol–ether)	$C_{22}H_{24}ClNO_4S$ (434·0)	60·89 60·81	5·57 5·72	8·17 8·38	3·23 3·41	7·39 7·50
VII-HM	*A* (59)	163·5—164·5 (ethanol–ether)	$C_{22}H_{24}ClNO_4S$ (434·0)	60·89 60·94	5·57 5·53	8·17 8·40	3·23 3·36	7·39 7·33
VIII-HM	*A* (53)	156—159 (ethanol–ether)	$C_{23}H_{24}.ClNO_4S$ (446·0)	61·94 61·64	5·42 5·52	7·95 8·13	3·14 3·19	7·19 7·27
IX-HS	*A*[b] (63)	137—139 (acetone)	$C_{22}H_{24}ClNO_4S$ (434·0)	60·89 60·72	5·57 5·65	8·17 8·17	3·23 2·99	7·39 7·22
X	*A* (71)	117·5—119 (light petroleum)	$C_{19}H_{20}ClNS$ (329·9)	69·17 68·94	6·11 6·30	10·75 10·57	4·25 3·99	9·72 9·74
X-HCl		215—217 (2-propanol–ether)	$C_{19}H_{21}Cl_2NS$ (366·4)	62·29 62·36	5·78 5·93	19·36 19·05	3·82 3·44	8·75 8·70
XI	*A* (55)	98—99 (2-propanol)	$C_{20}H_{22}ClNS$ (343·9)	69·84 69·93	6·45 6·57	10·31 10·30	4·07 4·10	9·32 9·31
XI-HCl		186—188 (2-propanol)	$C_{20}H_{23}Cl_2NS$ (380·4)	63·15 62·96	6·10 6·19	18·64 18·41	3·68 3·82	8·43 8·48
XII	*A* (60)	139·5—141 (cyclohexane–hexane)	$C_{18}H_{18}ClNOS$ (331·9)	65·14 64·82	5·47 5·46	10·69 10·80	4·22 4·20	9·66 9·52

XII-HCl		196 – 199[c] (2-propanol)	$C_{18}H_{19}Cl_2NOS$ (368·3)	58·69 58·69	5·20 5·13	19·25 19·15	3·80 3·78	8·71 8·71
XIII-HCl	*B*[b] (24)	228–229 (ethanol–ether)	$C_{21}H_{19}Cl_2NS$ (388·4)	64·94 64·77	4·93 4·93	18·26 18·21	3·61 3·88	8·26 8·23
XIV-HCl	*B*[b] (53)	118–121 (ethanol–ether)	$C_{22}H_{21}Cl_2NS$ (402·4)	65·66 65·56	5·26 5·24	17·62 17·52	3·48 3·52	7·97 8·05
XV-A-HCl	[b] (27)	232–235 (aqueous ethanol)	$C_{23}H_{23}Cl_2NS$ (416·4)	66·34 66·56	5·57 5·55	17·03 17·14	3·36 3·37	7·70 7·80
XV-B-HCl	[b] (3)	265–268[c] (aqueous methanol)	$C_{23}H_{23}Cl_2NS$ (416·4)	66·34 65·99	5·57 5·48	17·03 16·82	3·36 3·06	7·70 7·74
XVI-HO	*A* (73)	190–192 (ethanol–ether)	$C_{18}H_{18}ClNO_5S$ (395·9)	54·61 54·77	4·58 4·73	8·96 9·17	3·54 3·57	8·10 8·19
XVII	*A* (72)	119–121 (ethanol)	$C_{17}H_{18}ClNOS$ (319·9)	63·83 63·79	5·67 5·76	11·09 10·96	4·38 4·37	10·03 10·08
XVII-HM		150–152 (ethanol)	$C_{21}H_{22}ClNO_5S$ (435·9)	57·86 57·58	5·09 5·15	8·13 8·19	3·21 3·33	7·36 7·66
XVIII-HCl	*B* (57)	220–222[c] (ethanol–ether)	$C_{24}H_{25}Cl_2NO_2S$ (462·4)	62·33 62·35	5·45 5·57	15·33 15·28	3·03 3·09	6·94 7·14
XIX-HCl	*B* (50)	182–184 (ethanol–ether)	$C_{25}H_{27}Cl_2NO_2S$ (476·5)	63·02 63·28	5·71 5·76	14·88 14·94	2·94 3·00	6·73 6·72
XX-HCl	*B* (11)	200–202·5 (ethanol)	$C_{22}H_{21}Cl_2NOS$ (418·4)	63·15 62·87	5·06 5·24	16·95 17·20	3·35 3·59	7·67 7·41
XXI-A	*A*[b] (21)	126·5–127·5 (cyclohexane)	$C_{21}H_{24}ClNOS$ (373·9)	67·44 67·37	6·47 6·63	9·48 9·57	3·75 3·94	8·58 8·68
XXI-A-HF		195–196 (ethanol-acetone–ether)	$C_{25}H_{28}ClNO_5S$ (490·0)	61·27 60·99	5·76 5·86	7·24 7·41	2·86 3·17	6·54 6·47

TABLE I
(*Continued*)

Compound[a]	Method (yield, %)	M.p., °C (solvent)	Formula (M.w.)	Calculated/Found				
				% C	% H	% Cl	% N	% S
XXI-B-HF	*A*[b]	155—157	$C_{23}H_{26}ClNO_3S$	63·94	6·07	8·21	3·24	7·43
	(36)	(ethanol–ether)	(431·9)	63·95	6·05	7·88	3·12	7·18
XXII-BHM	*A*	182·5	$C_{26}H_{29}ClN_2O_8S$	55·26	5·17	6·28	4·96	5·68
	(41)	(ethanol)	(565·0)	55·22	5·27	6·52	5·23	5·82
XXIII-BHM	*A*	171	$C_{29}H_{33}ClN_2O_8S$	57·56	5·50	5·86	4·63	5·30
	(66)	(ethanol)	(605·1)	57·28	5·63	6·08	4·74	5·20
XXIV-BHM	*A*	184—185	$C_{30}H_{35}ClN_2O_8S$	58·19	5·70	5·73	4·53	5·18
	(77)	(95% ethanol)	(619·1)	58·08	5·75	5·82	4·65	5·24
XXV-BHM	*A*	195·5	$C_{29}H_{33}ClN_2O_9S$	56·07	5·36	5·71	4·51	5·16
	(80)	(95% ethanol)	(621·1)	56·07	5·44	5·90	4·60	5·12
XXVI-BHO[d]	*A*	171—175[e]	$C_{25}H_{29}ClN_2O_8S$	53·43	5·38	6·31	4·98	5·70
	(78)	(ethanol)	+ 0·5 H_2O	53·30	5·49	6·30	4·98	5·62
XXVII-A-2 HCl	*A*[b]	165—168[f]	$C_{21}H_{27}Cl_3N_2S$	54·37	6·30	22·93	6·04	6·91
	(26)	(2-propanol–acetone)	+ H_2O	54·31	6·22	22·92	5·77	6·61
			(463·9)					
XXVII-B-2 HCl	*A*[b]	182—184	$C_{21}H_{27}Cl_3N_2S$	56·56	6·10	23·86	6·28	7·19
	(20)	(ethanol)	(445·9)	56·36	6·33	23·69	6·10	7·10
XXVIII-2 HCl	*A*	272—273	$C_{20}H_{25}Cl_3N_2S$	55·62	5·84	24·63	6·49	7·43
	(42)	(ethanol–ether)	(431·9)	55·45	5·84	25·01	6·59	7·69

[a] BHM bis(hydrogen maleate), BHO bis(hydrogen oxalate), HF hydrogen fumarate, HM hydrogen maleate, HO hydrogen oxalate, HS hydrogen succinate; [b] see Experimental; [c] with decomposition; [d] mixture of two racemates; [e] hemihydrate; [f] monohydrate.

Reaction of 2,10-dichloro-10,11-dihydrodibenzo[*b*,*f*]thiepin[14,15] with potassium phthalimide in refluxing dimethylformamide afforded *XXIX*; an attempt at its hydrazinolysis was not successful. An attempt to prepare 2-chloro-10-iodo-10,11-dihydrodibenzo[*b*,*f*]thiepin by treatment of 2,10-dichloro-10,11-dihydrodibenzo[*b*,*f*]thiepin[14,15] with sodium iodide in boiling acetone gave an oily product which, after hydrolysis, afforded a compound $C_{28}H_{20}Cl_2OS_2$ (mass spectrum and elemental analysis) which was identified as the ether *XXXII*.

Most of the compounds prepared were pharmacologically tested in a battery of tests for psychotropic activities or using the general screening programme. The compounds were administered orally (unless stated otherwise) in the form of salts, described in the Experimental and in Table I; the doses given were calculated per bases. The activities are expressed in the usual D_{50} doses or in effective doses ED (percent of positively responding animals) in mg/kg.

Acute toxicity in mice (LD_{50} in mg/kg): *VI*, 140 i.v.; *VII*, 35 i.v.; *IX*, 1 295; *XIV*, 1 000, *XXIII*, 40 i.v.; *XXIV*, 35 i.v. (>1 000 p.o.); *XXV*, 62·5 i.v.; *XXVIII*, 50 i. v. Doses i.v. (D in mg/kg) used in the screening: *VI*, 25; *VII*, 7; *XXIII*, 8; *XXIV*, 7; *XXV*, 12; *XXVIII*, 10.

Ataxic activity in the rotarod test in mice (ED_{50} or ED (%) in mg/kg): *IV*, 100 (60); *V*, >100; *VI*, 270; *VIII*, 500 (40); *IX*, >250; *X*, 1 000 (30); *XI*, 500 (20); *XII*, >1 000; *XIII*, 1 000 (20); *XV*, 2 500; *XVI*, 250 (70); *XVII*, 287; *XVIII*, 1 000 (20); *XIX*, 1 000 (40); *XXI*-A, 1 000 (40); *XXI*-B, 388; *XXII*, 53; *XXIII*, 250 (60); *XXIV*, 250 (90); *XXV*, 250 (50); *XXVI*, 100 (20); *XXVII*-A, 250 (50); *XXVIII*, 97.

Antireserpine activities: Inhibition of reserpine-induced ptosis in mice (ED, effective doses in mg/kg with statistically significant effect): *VI*, *X*, *XII*, *XV*, *XVII*, *XXII*, 300; *IX*, 100; *XI*, 1 000; *V*, >30; *XIV*, >25; *XVI*, *XXI*-B, *XXIII*–*XXV*, *XXVI*-A, *XXVII*-B, and *XXVIII*, >100; *VIII*, >300; *XIII*, *XVIII*, *XIX*, and *XXI*-A, >1 000. Antagonization of reserpine hypothermia in mice: the dose of 25 mg/kg of *IX* had significant effect. Antagonization of the ulcerogenic effect of reserpine in rats: the dose of 30 mg/kg of *IX* exhibited significant inhibition.

Potentiation of yohimbine toxicity in mice (ED_{50} or ED (%) in mg/kg): *IV*, 62·4; *V*, 51·4; *VI*, 145; *VIII*, 177; *IX*, 66·3; *X*, 431; *XI*, 612; *XII*, >1 000; *XIII*, 1 000; *XV*, 514; *XVI*, 90·7; *XVII*, 122; *XVIII*, 1 000 (40); *XIX*, 1 000 (30); *XXI*-A, 358; *XXI*-B, 287; *XXII*, 50 (60); *XXIII*, 81·3; *XXIV*, 100 (40); *XXV*, 100 (40); *XXVI*, 80; *XXVII*-A, 419; *XXVII*-B, >250; *XXVIII*, 120.

Inhibition of binding of 4 nmol l^{-1} [^{3}H]imipramine in the hypothalamus of the rat brain, IC_{50} in nmol l^{-1}: *IX*, 4 629; the other compounds, >100. Inhibition of binding of 4 nmol l^{-1} [^{3}H]desipramine in the rat hypothalamus (IC_{50} in nmol l^{-1}): *V*, 263·6; *IX*, 755·9; *X*, 2 608; *XVIII*, 1 243; *VI*, *VII*, and *XIX*, significant affinity at 100 nmol l^{-1}; *IV*, *VIII*, *XI*, *XIII*–*XVII*, *XXI*, A, *XXI*-B, *XXII*–*XXVIII*, >100.

Inhibition of apomorphine-induced climbing behaviour in mice (ED (%) in mg/kg): *IV*, 100 (70); *V*, 100 (30); *VI*, 300 (40); *VIII*, 300 (20); *IX*, >1 000; *X*, >300; *XI*,

TABLE II

Spectra of compounds *VI*–*XXVIII*

Compound	Spectrum	Data
VI	^{1}H NMR	1·03 t, 6 H (2 CH_3 of ethyls, J = 7·0); 2·60 m, 4 H (CH_2NCH_2); 2·90–4·00 m, 3 H ($ArCH_2CHAr$); 6·90–7·80 m, 7 H (ArH)
VII	^{1}H NMR	0·90 def. t, 3 H (CH_3 of butyl); 1·40 m, 4 H (CH_2CH_2 in positions 2, 3 of butyl); 2·30 bs, 1 H (NH); 2·62 bt, 2 H (NCH_2); 3·30 m, 2 H ($ArCH_2$); 4·60 dd, 1 H (Ar–CH–N, J = 4·0; 8·0); 6·80–7·50 m, 7 H (ArH)
VIII	^{1}H NMR	1·20–2·10 m, 9 H (4 CH_2 of cyclopentyl and NH); c. 3·20 bm, 1 H (CH of cyclopentyl); 3·20 dd and 3·46 dd, 1 + 1 H ($ArCH_2$, J = 13·0; 8·0 and 13·0; 4·0); 4·65 dd, 1 H (Ar–CH–N, J = 8·0; 4·0); 6·90–8·50 m, 7 H (ArH)
IX	^{1}H NMR	1·80 m, 4 H (CH_2CH_2 in positions 3, 4 of pyrrolidine); 2·65 m, 4 H (CH_2NCH_2); 3·40 d, 2 H ($ArCH_2$, J = 7·5); 4·43 t, 1 H (Ar–CH–N, J = 7·5); 7·00–7·70 m, 7 H (ArH)
X	^{1}H NMR	1·50 bs, 6 H (3 CH_2 in positions 3, 4, 5 of piperidine); 2·60 bm, 4 H (CH_2NCH_2); 3·00–4·00 m, 3 H ($ArCH_2CHAr$); 6·90–7·80 m, 7 H (ArH)
XI	IR	750, 810, 866, 895 (4 and 2 adjacent and solitary Ar–H); 1 558, 1 576, 3 050 (Ar); 2 760 (N–CH_2)
	^{1}H NMR	1·55 bs, 8 H (4 CH_2 in positions 3, 4, 5, 6 of hexamethyleneimine); 2·70 bm, 4 H (CH_2NCH_2); 3·05 m, 1 H (Ar–CH–N); 3·98 m, 2 H ($ArCH_2$); 6·90–7·80 m, 7 H (ArH)
XII	IR	757, 824, 860, 870 (4 and 2 adjacent and solitary Ar–H); 1 110 (R–O–R); 1 560, 1 580, 3 010, 3 060 (Ar); 2 815 (N–CH_2)
	^{1}H NMR	2·65 m, 4 H (CH_2NCH_2); 3·70 m, 4 H (CH_2OCH_2); 3·00–4·00 m, 3 H ($ArCH_2CHAr$); 7·00–7·80 m, 7 H (ArH)
XIII	^{1}H NMR	1·75 bs, 1 H (NH); 3·35 m, 2 H ($ArCH_2$ in the cycle); 3·82 s, 2 H ($ArCH_2N$); 4·69 dd, 1 H (Ar–CH–N, J = 9·0; 4·0); 6·80–7·60 m, 12 H (ArH)
XIV	^{1}H NMR	1·80 bs, 1 H (NH); 2·80 m, 4 H ($ArCH_2CH_2N$); 3·25 m, 2 H ($ArCH_2$ in the cycle); 4·60 dd, 1 H (Ar–CH–N, J = 9·0; 4·0); 6·80–7·60 m, 12 H (ArH)
XIV·HCl	MS	365 (M^+, $C_{22}H_{20}ClNS$), 274 ($C_{15}H_{13}ClNS$), 245 ($C_{14}H_{10}ClS$), 210 ($C_{14}H_{10}S$)
XV-A	IR	700, 750, 811, 875 (5, 4, and 2 adjacent and solitary Ar–H); 1 030, 1 050, 1 110, 1 130 (C–N); 1 375, 1 430 (C–H); 1 465, 1 495, 1 554, 1 580, 1 602, 3 020, 3 060 (Ar); 2 845, 2 920, 2 960 (C–H); 3 320 (NH)
	^{1}H NMR	1·10 d, 3 H (CH_3, J = 5·0); 1·62 bs, 1 H (NH); 2·50–3·60 m, 5H ($ArCH_2$ in the cycle and $ArCH_2CH$); 4·85 dd, 1 H (Ar–CH–N, J = 9·0; 4·0); 6·80–7·50 m, 12 H (ArH)

XV-B	IR	700, 750, 810, 872 (5, 4, and 2 adjacent and solitary Ar–H); infl. 1 020, 1 030, 1 046, 1 110, 1 130, 1 265 (C–N); 1 375, 1 428 (C–H); 1 465, 1 495, 1 552, 1 582, 1 605, 3 020, 3 060 (Ar); 2 845, 2 920, 2 960 (C–H); 3 320 (NH)
	^{1}H NMR	1·10 d, 3 H (CH_3, J = 5·0); 1·62 bs, 1 H (NH); 2·50—3·60 m, 5 H ($ArCH_2$ in the cycle and $ArCH_2CH$); 4·85 dd, 1 H (Ar–CH–N, J = 9·0; 4·0); 6·80—7·50 m, 12 H (ArH)
XVI	^{1}H NMR	2·80 bs, 2 H (NH and OH); 2·60—3·70 m, 6 H ($ArCH_2$ and NCH_2CH_2O); 4·58 dd, 1 H (Ar–CH–N, J = 8·0; 4·0); 6·90—7·60 m, 7 H (ArH)
XVII	IR	750, 815, 898 (4 and 2 adjacent and solitary Ar–H); 1 069 (CH_2OH); 1 548, 1 575, 3 040 (Ar); 3 120, 3 255 (OH and NH)
	^{1}H NMR	1·65 m, 2 H (CH_2 in position 2 of propyl); 2·40 bs, 2 H (NH and OH); 2·80 t, 2 H (NCH_2, J = 6·0); 3·30 m, 2 H ($ArCH_2$); 3·70 t, 2 H (CH_2O, J = 6·0); 4·48 dd, 1 H (Ar–CH–N, J = 8·0; 4·0); 6·90—7·50 m, 7 H (ArH)
XVIII	^{1}H NMR	1·50 bs, 1 H (NH); 2·80 m, 4 H ($ArCH_2CH_2N$); 3·30 m, 2 H ($ArCH_2$ in the cycle); 3·78 s and 3·80 s, 6 H (2 OCH_3); 4·61 dd, 1 H (Ar–CH–N, J = 8·0; 4·0); c. 6·70 m, 3 H (3 ArH of dimethoxyphenyl); 6·80—7·50 m, 7 H (remaining ArH)
XIX	^{1}H NMR	2·25 t, 2 H (NCH_2); 2·34 s, 3 H (NCH_3); 2·74 bt, 2 H ($ArCH_2$ in phenylethyl); 3·78 s and 3·81 s, 6 H (2 OCH_3); 3·00—4·00 m, 3 H ($ArCH_2CHAr$); 6·50—7·50 m, 10 H (ArH)
XX	^{1}H NMR	1·95 bs, 1 H (NH); 3·02 t, 2 H (NCH_2, J = 7·0); 3·30 m, 2 H ($ArCH_2$); 4·10 t, 2 H (OCH_2, J = 7·0); 4·78 dd, 1 H (ArCH-N, J = 8·0; 4·0); 6·70—7·60 m, 12 H (ArH)
XX-HCl	IR	760, 780, 810, 875, 895 (5, 4, and 2 adjacent and solitary Ar–H); 1 088, 1 240 (Ar–O–R); 1 500, 1 558, 1 576, 1 595, 3 055 (Ar); 2 410, 2 600, 2 610 (NH_2^+)
XXI-A	IR	745, 815 870 (4 and 2 adjacent and solitary Ar–H); 1 084 (CH_2OH); 1 557, 1 576, 3 060 (Ar); 2 710, 2 790, 2 810 ($N–CH_2$); 3 100, 3 235 (OH)
	^{1}H NMR	1·00—2·30 m, 11 H ($(CH_2)_4CHCH_2$); 2·88 dd (J = 12·0; 4·0) and 3·92 t (J = 12·0), 2 H ($ArCH_2$); 3·80 t, 2 H (CH_2O, J = 7·0); 4·41 dd, 1 H (Ar–CH–N, J = 12·0; 4·0); 6·90—7·70 m, 7 H (ArH)
XXI-B	^{1}H NMR	1·10—2·20 and 2·80—4·00, 2 m, 15 H ($ArCH_2$ and $(CH_2)_4CHCH_2CH_2O$); 4·60 dd, 1 H (Ar–CH–N, J = 8·0; 4·0); 6·90—7·50 m, 7 H (ArH)
XXII	^{1}H NMR	2·00 bs, 1 H (NH); 2·18 s, 6 H ($N(CH_3)_2$); 2·40 t, 2 H (CH_2NMe_2); 2·68 t, 2 H (remaining CH_2N); 3·20 dd and 3·45 dd, 1 + 1 H ($ArCH_2$, J = 13·0; 8·0 and 13·0; 4·0); 4·70 dd, 1 H (Ar–CH–N, J = 8·0; 4·0); 6·90 to 7·60 m, 7 H (ArH)

TABLE II
(Continued)

Compound	Spectrum	Data
XXIII	^{1}H NMR	1·70 m, 7 H (CH_2CH_2 in positions 3, 4 of pyrrolidine, CH_2 in position 2 of propyl, and NH); 2·50 m, 6 H (CH_2NCH_2); 2·68 t, 2 H (remaining CH_2N, J = 7·0); 3·18 dd and 3·45 dd, 1 + 1 H (CH_2); ($ArCH_2$, J = 13·0; 8·0 and 13·0; 4·0); 4·62 dd, 1 H (Ar–CH–N, J = 8·0; 4·0); 6·90–7·60 m, 7 H (ArH)
XXIV	^{1}H NMR	1·40–2·00 m, 9 H (3 CH_2 in positions 3, 4, 5 of piperidine, CH_2 in position 2 of propyl, and NH); c. 2·30 bm, 6 H (CH_2NCH_2); 2·70 bt, 2 H (remaining CH_2N); 3·20 dd and 3·45 dd, 1 + 1 H (CH_2); ($ArCH_2$, J = 13·0; 8·0 and 13·0; 4·0); 4·62 dd, 1 H (Ar–CH–N, J = 8·0; 4·0); 6·90–7·60 m, 7 H (ArH)
XXVI	^{1}H NMR	1·08 bt, 3 H (CH_3 of ethyl); 1·40–3·60 m, 13 H ($NCH_2CH(CH_2)_3NCH_2$ and $ArCH_2$); 4·60 bm, 1 H (Ar–CH–N); 6·90–7·60 m, 7 H (ArH) (mixture of two racemates)
XXVII-A	^{1}H NMR	1·10 t, 3 H (CH_3 of ethyl); 1·40–2·20 and 2·50–3·00 2 m, 10 H ($NHCH(CH_2)_3N$); 2·40 q, 2 H (NCH_2 of N-ethyl, J = 7·0); 3·30 m, 2 H ($ArCH_2$); 4·88 dd, 1 H (Ar–CH–N, J = 8·0; 4·0); 6·90–7·60 m, 7 H (ArH)
XXVII-B	^{1}H NMR	1·10 t, 3 H (CH_3 of ethyl, J = 7·0); 1·40–2·20 and 2·50–3·00 2 m, 10 H ($NHCH(CH_2)_3N$); 2·40 q, 2 H (NCH_2 of N-ethyl, J = 7·0); c. 3·40 m, 2 H ($ArCH_2$); 4·79 dd, 1 H (Ar–CH–N, J = 8·0; 4·0); 6·90–7·60 m, 7 H (ArH)
XXVIII	^{1}H NMR	1·20–3·00 m, 10 H ($NHCHCH_2CH_2N$); 2·22 s, 3 H (NCH_3); 3·30 m, 2 H ($ArCH_2$); 4·88 dd, 1 H (Ar–CH–N, J = 8·0; 4·0); 6·90–7·60 m, 7 H (ArH)

1 000 (40); *XII* and *XV*, >1 000; *XVII*, 100 (50); *XVIII*, 1 000 (10); *XIX*, 1 000 (20); *XXII*, 100 (100); *XXIII*, 100 (40); *XXIV*, 100 (20); *XXV*, 100 (10); *XXVI*, 100 (40); *XXVII*-A, 250 (10).

Cataleptic activity in rats (ED (%) in mg/kg): *IV*, 100 (20); *V*, 100 (10); *IX*, 250 (30).

Antagonization of the toxicity of adrenaline in mice, ED (%) in mg/kg: *IV*, 100 (50); *V*, >100; *VI*, 500 (50); *VIII*, 500 (10); *IX*, 500 (20); *X*, 1 000 (30); *XI*, 1 000 (10); *XII*, 1 000 (20); *XIII*, 1 000 (10); *XV*, 1 000 (50); *XVI*, >100; *XVII*, 250 (10); *XVIII* and *XIX*, >1 000, *XXI*-A, 1 000 (20); *XXII*, 50 (60); *XXIII*–*XXV* and *XXVII*-A, >100; *XXVI*, 100 (10); *XXVIII*, 250 (20).

Blood pressure in normotensive rats: brief and deep drops after the doses D of *XXIV*, *XXV*, and *XXVIII*.

Spasmolytic effect on the isolated rat duodenum against acetylcholine contractions (concentration in mg/l reducing the contractions to 50%): *XXIII*, 1–10; *XXV*, 1–10; *XXVIII*, 1–10. Similar spasmolytic effect against barium chloride contractions: *XXIII*, *XXV*, and *XXVIII*, 1–10.

Antiarrhythmic effect against aconitine-induced arrhythmia in rats (ED in mg/kg: *XXIII*, 5–8 i.v.

Antitussive action in guinea-pigs (dose and reduction of the cough attacks elicited by the aerosol of the citric acid solution in % of the control value (100%)): *XXIII*, 20 mg/kg, 50%; *XXV*, 60 mg/kg, 46%; *XXVIII*, 10 mg/kg, 44%.

Compound *XXIV* was tested for antiinflammatory and antinociceptive actions. It was administered in oral doses of 100 mg/kg and the activity was evaluated (i) in the adjuvant oedema, (ii) in the carragheenan oedema, (iii) in the test of inhibition of the writhing syndrome in male mice using stimulation with intraperitoneal 0·7% acetic acid (results in % of inhibition of the oedema or pain, $^+$ means statistical significance): *XXIV*, (i) 26^+, (ii) 26^+, (iii) 200 mg/kg, 33%. Ibuprofen used as the standard: (i) 56^+, (ii) 45^+, (iii) ED_{50} = 194 mg/kg.

In conclusion: Only compound *IX* (VÚFB-15551) showed the pharmacological profile of potential antidepressants (effect in all the three tests for antireserpine activity, potentiates the toxicity of yohimbine, has some affinity to the desipramine binding sites in the hypothalamus).

The compounds prepared were also tested for antimicrobial activity in vitro (microorganism and the minimum inhibitory concentration in mg/l unless they exceed 100 mg/l): *Streptococcus β-haemolyticus*, *IV* 50, *VII* 25, *VIII* 50, *XVI* 100, *XVII* 100, *XXI*-B 50, *XXII* 50, *XXIII* 25, *XXIV* 50, *XXVI* 25, *XXVII*-A 25, *XXVII*-B 100, *XXVIII* 50; *Streptococcus faecalis*, *IV* 100, *VII* 50, *VIII* 100, *XVII* 100, *XXI*-B 25, *XXII* 25, *XXIII* 50, *XXIV* 100, *XXV* 100, *XXVI* 50, *XXVII*-A 50, *XXVII*-B 25, *XXVIII* 100; *Staphylococcus pyogenes aureus*, *IV* 12·5, *VII* 25, *VIII* 100, *XVI* 100, *XVII* 100, *XXI*-B 3·1, *XXII* 25, *XXIII* 25, *XXIV* 25, *XXV* 50, *XXVI* 25, *XXVII*-B 25, *XXVIII* 25; *Pseudomonas aeruginosa*, *IV* 50, *VIII* 50, *XI* 100, *XVII* 50, *XXI*-B 100, *XXII* 100, *XXIV* 50, *XXV* 50, *XXVI* 50, *XXVII*-B 100, *XXVIII* 100; *Escherichia*

coli, *IV* 50, *XXI*-B 50, *XXIII* 100, *XXVII*-B 25, *XXVIII* 100; *Proteus vulgaris*, *IV* 100, *XXI*-B 100, *XXII* 100, *XXVII*-B 100, *XXVIII* 50; *Saccharomyces pasterianus*, *IV* 50, *XXII* 50, *XXIII* 50, *XXIV* 50; *Trichophyton mentagrophytes*, *IV* 50, *V* 50, *VI* 50, *VII* 25, *VIII* 50, *IX* 50, *X* 50, *XII* 50, *XIII* 50, *XIV* 50, *XVIII* 50, *XIX* 50, *XXI*-A 50, *XXIII* 50, *XXIV* 50, *XXV* 50, *XXVI* 50, *XXVII*-A 50, *XXVII*-B 50, *XXVIII* 50.

EXPERIMENTAL

The melting points of analytical samples were determined in the Kofler block and were not corrected. The samples were dried in vacuo of about 60 Pa over P_2O_5 at room temperature or at a suitably elevated temperature. The UV spectrum was recorded at a Unicam SP 8 000 spectrophotometer, the IR spectra (mostly in Nujol, ν in cm^{-1}) were recorded with the Perkin–Elmer 298 spectrophotometer, ^1H NMR spectra (in $CDCl_3$, δ in ppm, J in Hz) with a Tesla BS 487C (80 MHz) spectrometer, and the mass spectra with MCH 1 320 and/or Varian MAT 44S (GC-MS) spectrometers (m/z, % and/or fragments given). The homogeneity of the substances and composition of the mixtures were checked by thin-layer chromatography (TLC) on silica gel (Silufol). The extracts were dried with $MgSO_4$, Na_2SO_4 or K_2CO_3 and evaporated under reduced pressure on a rotating evaporator.

3-(1-Pyrrolidinyl)propylamine

A solution of 58·0 g 3-(1-pyrrolidinyl)propionitrile[20] in 100 ml ether was added dropwise over 30 min to a stirred solution of 23·0 g $LiAlH_4$ in 500 ml ether and the mixture was refluxed for 5·5 h. After cooling, it was decomposed under stirring by slow addition of 23 ml water, 23 ml 20% NaOH, and 50 ml water, 23g K_2CO_3 were added and after stirring for 30 min the solid was filtered off. It was washed with ether, the filtrate was dried and distilled; 44·6 g (74%) of 3-(1-pyrrolidinyl)propylamine, b.p. 75—76°C/2·7 kPa. Refs[20,21], b.p. 86°C/2·3 kPa and 86—87°C/2·3 kPa, respectively.

2-Chloro-10-(methylamino)-10,11-dihydrodibenzo[*b*,*f*]thiepin (*IV*)

A stirred solution of 1·5 g $LiAlH_4$ in 100 ml ether was slowly treated with 6·0 g N-(2-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-yl)formamide[12] and the suspension was refluxed with stirring for 5 h. After cooling, the mixture was decomposed by slow addition of 1·5 ml water, 1·5 ml 20% NaOH, and 3 ml water. After the addition of 1·5 g K_2CO_3 the mixture was stirred for 1 h, the solid was filtered off and the filtrate was evaporated; 4·9 g (84%) of crude, oily *IV*. It was dissolved in 25 ml ethanol, an excess of HCl in 7·5 ml ether was added under stirring, the mixture was diluted with 50 ml ether and allowed to crystallize. The product was filtered after 24 h; 4·5 g of hydrochloride, m.p. 217·5—218·5°C (ethanol–ether). For $C_{15}H_{15}Cl_2NS$ (312·3) calculated: 57·69% C, 4·84% H, 22·71% Cl, 4·49% N, 10·27% S; found: 57·67% C, 4·77% H, 22·68% Cl, 4·78% N, 10·16% S.

A sample of the purified hydrochloride was decomposed with NH_4OH and the homogeneous (TLC) oily base was isolated by extraction with ether. ^1H NMR spectrum: 2·45 s, 3 H (NCH_3); c. 3·20 m, 2 H ($ArCH_2$); 4·48 dd, 1 H (ArCHN, J = 8·0; 4·0); 6·90—7·50 m, 7 H (ArH).

2-Chloro-10-(dimethylamino)-10,11-dihydrodibenzo[*b,f*]thiepin (*V*)

A mixture of 5·0 g 10-amino-2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin[12], 6·5 g 100% formic acid, 9 ml 30% formaldehyde, and 9 ml water was stirred and heated under reflux for 12 h to 105°C (bath temperature). After cooling the mixture was diluted with 60 ml chloroform, under stirring and cooling to 5—8°C it was treated with 40 ml 5M-NaOH, the separated organic layer was washed with water, evaporated under reduced pressure and the residue was crystallized from 20 ml ethanol; 3·6 g (74%) of *V*, m.p. 98·5—102°C (methanol–acetone). ^{1}H NMR spectrum: 2·38 s, 6 H ($N(CH_3)_2$); 3·00—4·00 m, 3 H ($ArCH_2CHAr$); 7·00—7·60 m, 7 H (ArH). For $C_{16}H_{16}ClNS$ (289·8) calculated: 66·30% C, 5·57% H, 12·23% Cl, 4·83% N, 11·07% S; found: 66·38% C, 5·64% H, 12·21% Cl, 4·93% N, 11·00% S.

Hydrog n maleate, m.p. 185·5—186·5°C (ethanol-ether), Mass spectrum: 289 (M^+, $C_{16}H_{16}ClNS$, 37); 288 (30), 274 ($C_{15}H_{13}ClNS$, 17), 244 ($C_{14}H_9ClS$, 86), 211 ($C_{14}H_{11}S$, 32), 209 ($C_{14}H_9S$, 34), 178 ($C_{14}H_{10}$, 72), 155 ($C_{13}H_9$, 36), 132 ($C_9H_{10}N$, 56), 91 (47), 72 (80), 45 (85), 44 (62), 42 (100). For $C_{20}H_{20}ClNO_4S$ (405·9) calculated: 59·18% C, 4·97% H, 8·77% Cl, 3·45% N, 7·90% S; found: 59·15% C, 5·24% H, 8·94% Cl, 3·12% N, 7·66% S.

2-Chloro-10-(1-pyrrolidinyl)-10,11-dihydrodibenzo[*b,f*]thiepin (*IX*) (Method *A*)

A mixture of 14·6 g 2,10-dichloro-10,11-dihydrodibenzo[*b,f*]thiepin[14,15], 45 ml chloroform, and 14·6 g pyrrolidine was stirred and refluxed for 5 h. After standing overnight, chloroform was evaporated, the residue was dissolved in 200 ml toluene, the solution was washed with water, and the basic product was extracted into excessive 2·5M-HCl. The aqueous solution was separated, made alkaline with NH_4OH, and the released base was isolated by extraction with toluene; 11·7 g (71%) of oily *IX*. It was dissolved in 45 ml acetone and the boiling solution was neutralized with 4·4 g succinic acid; 12·2 g of hydrogen succinate, m.p. 137—139°C (acetone). A sample of the purified succinate was decomposed with NH_4OH and the homogeneous oily base was isolated by extraction with ether and used for recording the ^{1}H NMR spectrum. For the analysis of the succinate and the ^{1}H NMR spectrum of the base, cf. Tables I and II.

2-Chloro-10-(benzylamino)-10,11-dihydrodibenzo[*b,f*]thiepin (*XIII*)

A mixture of 9·84 g 2,10-dichloro-10,11-dihydrodibenzo[*b,f*]thiepin[14,15], 20 ml chloroform, and 7·85 g benzylamine was stirred and refluxed for 5·5 h. After cooling it was diluted with 60 ml chloroform, washed with water, and shaken with excessive 2·5M-HCl. The separated solid (2·5 g, m.p. 255—260°C) was identified as benzylamine hydrochloride. The chloroform solution, containing a mixture of compounds including *XIII* hydrochloride, was filtered with active carbon, the filtrate was evaporated, the residue was treated with NH_4OH and extracted with chloroform. The extract was evaporated and the residue was chromatographed on 240 g silica gel (Silpearl). The first to be eluted with benzene (0·5 g, m.p. 78—80°C) was identified as 2-chlorodibenzo[*b,f*]-thiepin (*XXX*) (ref.[14], m.p. 78—79°C). It was followed by 1·0 g of 2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ol (*XXXI*), m.p. 105—107°C (cyclohexane); ref.[14], m.p. 106·5—107·5°C. The last to be eluted was the oily *XIII* (3·0 g, 24%) which was transformed to hydrochloride, m.p. 228—229°C (96% ethanol–ether). For recording the spectra, the homogeneous base *XIII* was released from the hydrochloride similarly like in the preceding case. For analysis and spectrum, cf. Tables I and II.

2-Chloro-10-(2-phenylethyl)amino-10,11-dihydrodibenzo[*b,f*]thiepin (*XIV*) (Method *B*)

A mixture of 5·6 g 2,10-dichloro-10,11-dihydrodibenzo[*b,f*]thiepin[14,15], 10 ml chloroform, and 5·6 g 2-phenylethylamine was stirred and refluxed for 7 h, it was diluted with 40 ml chloroform,

washed with water, and then shaken with excessive 2·5M-HCl. The chloroform layer (containing *XIV* hydrochloride) was evaporated under reduced pressure, the semisolid residue was treated with NH_4OH, the oily base was isolated by extraction with ether and transformed to the hydrochloride; 4·2 g (53%) of *XIV* hydrochloride, m.p. 118—121°C (ethanol–ether). The released base was used for recording the ^1H NMR spectrum. For analysis and spectra, cf. Tables I and II.

2-Chloro-10-(1-phenyl-2-propyl)amino-10,11-dihydrodibenzo[*b,f*]thiepin (*XV*-A and *XV*-B)

A mixture of 8·4 g 2,10-dichloro-10,11-dihydrodibenzo[*b,f*]thiepin[14,15], 15 ml chloroform, and 8·1 g 1-phenyl-2-propylamine[16] was stirred and refluxed for 9 h. It was diluted with 10 ml chloroform, washed with water, and evaporated in vacuo. The residue was chromatographed on 200 g silica gel. Benzene eluted 0·8 g of *XXX* (m.p. 75—80°C, cf. ref.[14]). Benzene, containing 10% of chloroform, eluted then 3·1 g of *XXXI* (m.p. 105—107°C, cf. ref.[14]). A mixture of 1 : 1 benzene and chloroform eluted 3·1 g (27%) of homogeneous oily base *XV*, representing the racemate A. It was transformed to the hydrochloride melting at 232—235°C (aqueous ethanol). The base was released for recording the spectra. The last component, which was eluted with a mixture 1 : 1 of chloroform and methanol, was directly the hydrochloride of the racemate *XV*-B (0·4 g, 3%), m.p. 265—268°C with decomposition (aqueous methanol). The oily base *XV*-B, obtained by decomposition of this salt with NH_4OH, was also used for recording the spectra. Analyses and spectra are included in Tables I and II.

2-(1-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-yl)piperidine-2-yl)ethanol (*XXI*-A and *XXI*-B)

A mixture of 8·03 g 2,10-dichloro-10,11-dihydrodibenzo[*b,f*]thiepin[14,15], 15 ml chloroform, and 8·6 g 2-(2-piperidinyl)ethanol[19] was processed by method *A* and the crude base (6·7 g, 62%) was chromatographed on 200 g neutral Al_2O_3 (activity II). Benzene eluted 2·2 g (21%) of the less polar oily base *XXI*-A which was transformed to the hydrogen fumarate, m.p. 195—196°C (ethanol–acetone–ether). Continued elution with benzene gave 1·6 g of a mixture of bases A and B (TLC). Elution with benzene containing 1% of methanol resulted in 3·7 g (36%) of the more polar racemate *XXI*-B; neutral fumarate, m.p. 155—157°C (ethanol–ether). Both fumarates were transformed to homogeneous oily bases. Analyses of the fumarates and spectra of the bases are included in Tables I and II.

2-Chloro-10-(1-ethyl-3-piperidinyl)amino-10,11-dihydrodibenzo[*b,f*]thiepin (*XXVII*-A and *XXVII*-B)

A mixture of 9·3 g 2,10-dichloro-10,11-dihydrodibenzo[*b,f*]thiepin[14,15], 20 ml chloroform, and 8·5 g 3-amino-1-ethylpiperidine (Janssen) was processed by method *A*. The obtained oily mixture of bases (7·5 g, 67%) was transformed to the mixture of dihydrochlorides which was repeatedly crystallized from a mixture 1 : 1 2-propanol and acetone resulting in 3·5 g (26%) of the constantly melting dihydrochloride of racemate *XXVII*-A which appeared to be the monohydrate, m.p. 165—168°C (2-propanol–acetone). Processing of the mother liquors resulted in 3·0 g (20%) of dihydrochloride of the racemate *XXVII*-B, m.p. 182—184°C (ehanol). The oily bases were released from both salts and were used for recording the spectra. Analyses and spectra are included in Tables I and II.

N-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-yl)phthalimide (*XXIX*)

A mixture of 4·2 g 2,10-dichloro-10,11-dihydrodibenzo[*b,f*]thiepin[14,15], 30 ml dimethylformamide, and 4·2 g potassium phthalimide was stirred and refluxed (155°C) for 2 h. After cooling

the mixture was diluted with 150 ml chloroform, the solution was washed with water, 0·5M-NaOH, and water, dried, and evaporated in vacuo. The oily residue crystallized from a mixture of 25 ml cyclohexane and 2·5 ml benzene; 0·75 g (12%) of *XXIX*, m.p. 187–188·5°C (benzene–cyclohexane). UV spectrum (methanol): λ_{max} 221 nm (log ε 4·73), 271 nm (3·85), infl. 286 nm (3·70). IR spectrum: 720, 750, 765, 876, 900 (4 and 2 adjacent and solitary Ar—H); 1 480, 1 565, 1 585, 1 610, 3 060 (Ar); 1 708, 1 770 (ArCONCOAr). ^{1}H NMR spectrum: 3·19 dd (J = 12·0; 4·0) and 4·60 t (J = 12·0), 1 + 1 H ($ArCH_2$); 5·85 dd, 1 H (Ar—CH—N, J = 12·0; 4·0); 7·00–8·00 m, 11 H (ArH). For $C_{22}H_{14}ClNO_2S$ (391·9) calculated: 67·42% C, 3·60% H, 9·05% Cl, 3·58% N, 8·18% S; found: 67·19% C, 3·50% H, 8·88% Cl, 3·70% N, 8·04% S.

Processing of the mother liquors after crystallization of *XXIX* gave 2·1 g (57%) of *XXX*, m.p. 75–78°C (cf. ref.[14]).

Bis(2-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-yl) Ether (*XXXII*)

A solution of 8·5 g 2,10-dichloro-10,11-dihydrodibenzo[*b*,*f*]thiepin[14,15] in 100 ml acetone was treated at 40°C with 5·0 g NaI and the mixture was stirred and refluxed for 3·5 h. Acetone was evaporated, the residue was distributed between 100 ml water and 100 ml chloroform, the organic layer was washed with water, dried, and evaporated. The dark oily residue (10·2 g) was dissolved in dichloromethane and the solution was filtered through a column of 25 g silica gel. The column was washed with dichloromethane, the filtrate was evaporated, and the residue (8·2 g) gave by crystallization from cyclohexane 1·8 g (24%) of *XXXII*, m.p. 158–160°C (benzene). Mass spectrum: 506 (M^+, $C_{28}H_{20}Cl_2OS_2$, 6), 261 ($C_{14}H_{10}ClOS$, 14), 245 ($C_{14}H_{10}ClS$, 100), 210 (42), 165 (22). IR spectrum: 752, 808, 822, 860 (4 and 2 adjacent and solitary Ar—H); 1 096 (R—O—R); 1 589, 3 050, 3 080 (Ar). ^{1}H NMR spectrum: 3·00–3·70 bm, 4 H (2 $ArCH_2$); 5·60 bm, 2 H (Ar—CH—O—CH—Ar); 6·80–7·20 bm, 14 H (ArH). For $C_{28}H_{20}Cl_2OS_2$ (507·5) calculated: 66·26% C, 3·97% H, 13·97% Cl, 12·59% S; found: 66·22% C, 3·97% H, 13·90% Cl, 12·59% S.

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