POTENTIAL NEUROTROPIC AND ANTIINFLAMMATORY AGENTS: 2-CHLORO-10,11-DIHYDRODIBENZO[*b*, *f*]THIEPIN-10-YL SULFIDES

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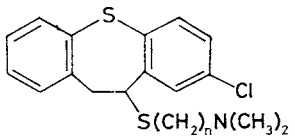
Received August 9, 1988
Accepted October 10, 1988

2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-thiol (*VII*) was synthesized from 2,10-dichloro--10,11-dihydrodibenzo[*b,f*]thiepin (*IV*) and was alkylated with a series of aminoalkyl chlorides which led to amino sulfides *IX*, *XII*, *XIII*, and *XVI*—*XX*. The primary amine *IXa* was transformed by treatment with ethyl chloroformate to the carbamate *Xa* which was reduced to the methylamino compound *XIa*. The carbamate *XX* was similarly reduced to compound *XXI*. Alkylation of *VII* with 2-bromoethanol gave the alcohol *XIVa* which was transformed to the crude tosylate *XVa*. Its reactions with the corresponding piperazines gave compounds *XXII* to *XXIV*. The alcohol *XXII* was esterified to the decanoate *XXV*. Reactions of the sodium salt of *VII* with ethyl chloroacetate, ethyl 2-chloropropionate and ethyl 4-chlorobutyrate gave the corresponding esters which were saponified to acids *XXVIb*—*XXVIIIb*. Their amides *XXVId* to *XXVIIId* and *XXVIe* were prepared either via the acid chlorides or via the esters. Out of the compounds prepared only *XIa* showed a clear profile of a potential antidepressant. The other compounds showed indications of thymoleptic, antiinflammatory and antimicrobial activities.

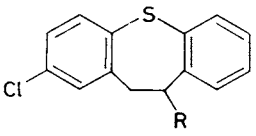
Some time ago our team[1] described the preparation of two 8-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-yl dimethylaminoalkyl sulfides *I* and *II* which showed various types of neurotropic activities. With the aim at preparing further neurotropic agents, we have now attacked the isomeric series of 2-chloro-10,11-dihydrodibenzo[*b,f*]-thiepin-10-yl dimethylaminoalkyl sulfides and several analogues which is being described in the present paper.



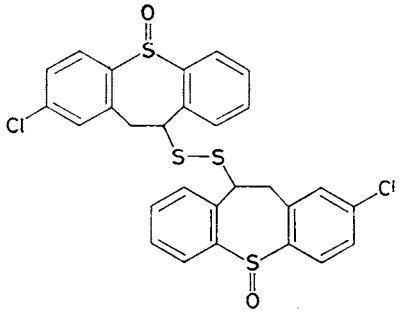
I, n = 2 *II*, n = 3

The substance of docloxythepin (*III*) (refs[2-4]), which was available in greater quantity, was used as the starting material for the present study. Its cleavage with ethyl chloroformate has already been mentioned[5] in connection with the effort to prepare docloxythepin monoethyl carbonate. Even when using only one equivalent

of ethyl chloroformate, the preferential reaction was the cleavage of the C(10)—N(1) bond and N(1)-acylation. 1-(Ethoxycarbonyl)-4-(2-ethoxycarbonyloxyethyl)piperazine was identified as the basic product of the cleavage (isolated as hydrogen maleate) and *IV* was assumed to be the neutral product which, however, was not isolated. Now, we needed *IV* and carried out the cleavage with more than 2 equivalents of ethyl chloroformate in boiling benzene: *IV* resulted as the neutral product in yields of about 85% (identical with *IV* prepared earlier differently[6]); the basic product was the mentioned 1-(ethoxycarbonyl)-4-(2-ethoxycarbonyloxyethyl)piperazine[5], isolated this time as hydrochloride and also as hydrogen maleate[5]. Heating of *IV* with ethanol resulted in *V*, formed by ethanolysis. Reaction of *IV* with thiourea in dimethylformamide at 80°C gave the hydrochloride of the S-substituted isothiourea *VI* which was obtained in two crystal modifications (*A*, m.p. 138–140°C; *B*, m.p. 185–186°C), both of them being characterized by the IR spectra. Both forms were cleaved by boiling with aqueous sodium hydroxide and acidification gave in both cases the same thiol *VII*. In the attempt at its transformation to the corresponding disulfide, *VII* was oxidized with hydrogen peroxide in acetic acid. The only crystalline product, isolated from the mixture formed, was characterized as the disulfide disulfoxide *VIII*. Its mass spectrum (EI) showed the peak of highest *m/z* (294) which corresponds to $C_{14}H_{10}ClOS_2$ which is the half of the molecule of *VIII*; this type of fragmentation of disulfides is quite common[7–9].



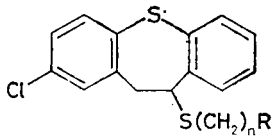
III, R = N⟨⟩NCH$_2$CH$_2$OH
IV, R = Cl
V, R = OC$_2$H$_5$
VI, R = SC(=NH)NH$_2$
VII, R = SH



VIII

The thiol *VII* reacted with 2-chloroethylamine hydrochloride[10] in boiling ethanol in the presence of sodium ethoxide and potassium carbonate and gave *IXa* which was transformed to the hydrochloride (crystallizing as hemihydrate). The homogeneous base *IXa* was obtained by decomposition of the purified hydrochloride with aqueous ammonia and was characterized by the ^{1}H NMR spectrum. Its reaction with ethyl chloroformate in boiling chloroform in the presence of sodium carbonate afforded the crystalline carbamate *Xa* which was reduced with lithium aluminium hydride in ether to the methylamino compound *XIa*. This was purified in the form of hydro-

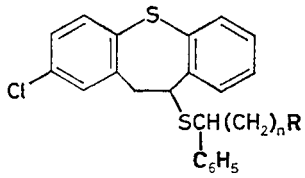
chloride and the released homogeneous base was used for recording the ^{1}H NMR spectrum. Similar alkylations of *VII* (like in the preparation of *IXa*) with 2-dimethylaminoethyl chloride, 2-diethylaminoethyl chloride and 3-dimethylaminopropyl chloride, used in the form of hydrochlorides, resulted in *XIIa*, *XIIIa*, and *XIIb*. These bases were oily, they gave crystalline salts (hydrogen maleates or oxalates), and the bases, released from these purified salts, were used for recording the ^{1}H NMR spectra. The sodium salt of *VII* was also alkylated with 2-bromoethanol in boiling ethanol. The crude *XIVa* was purified by chromatography and characterized by spectra. Its reaction with 4-toluenesulfonyl chloride (method[11]) in pyridine gave the semi-solid tosylate *XVa* which was further used in crude state.



IX, R = NH_2
X, R = $NHCOOC_2H_5$
XI, R = $NHCH_3$
XII, R = $N(CH_3)_2$
XIII, R = $N(C_2H_5)_2$
XIV, R = OH
XV, R = OSO_2-C$_6$H$_4$-CH_3

In formulae *IX*–*XV*: *a*, n = 2 *b*, n = 3

The sodium salt of the thiol *VII* was further alkylated with 3-(dimethylamino)-1--phenylpropyl chloride[12], 2-(cyclohexylamino)-1-phenylethyl chloride[13], and 3-(4--benzyl-1-piperazinyl)-1-phenylpropyl chloride[14], used again as hydrochlorides. All the three products *XVI*–*XVIII* contain in their molecules two centres of chirality and the crude products are thus mixtures of two racemates. The oily *XVI* was transformed to crystalline hydrogen oxalate, which however, was not separated by crystallization; the ^{1}H NMR spectrum of the released base proved stereochemical inhomogeneity. Compound *XVII* was also oily, gave the mixture of oxalates, from which the bases were released and separated by chromatography on silica gel. The major

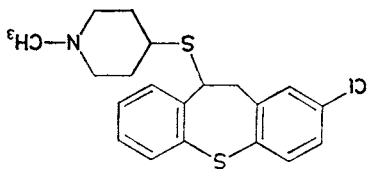


XVI, n = 2; R = $N(CH_3)_2$
XVII, n = 1; R = NH-C$_6$H$_{11}$
XVIII, n = 2; R = N(C$_4$H$_8$)N$CH_2C_6H_5$

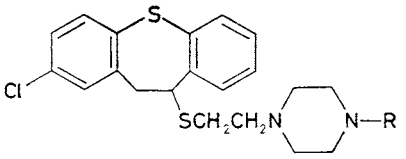
homogeneous base *A*, which was eluted first, afforded the higher melting oxalate *A* (m.p. 110·5–112°C), identified as monohydrate. It was followed by the base *XVII–B* giving the lower melting hydrogen oxalate (m.p. 99–102°C). Both racemic oxalates were characterized by the mass spectra showing the molecular ions of *m/z* 480 which correspond to elemental composition $C_{28}H_{30}ClNS_2$ of the bases. The ^{1}H NMR spectrum of the lower melting hydrogen oxalate (*XVII–B*) was also recorded. The inhomogeneous *XVIII* gave a crystalline bis(hydrogen oxalate) whose crystallization did not lead to separation of the diastereoisomers.

Alkylation of *VII* with 4-chloro-1-methylpiperidine[15] gave the crystalline *XIX*, characterized by the ^{1}H NMR spectrum and giving two dimorphic hydrochlorides: the higher melting obtained by slow crystallization from ethanol and the lower melting obtained by crystallization from a mixture of ethanol and ether; both forms were characterized by IR spectra which showed some differences.

XIX



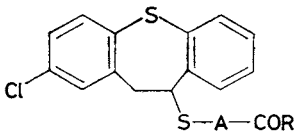
In the analogous ether series[16] we found in the subgroup of 4-substituted 1-(2-(2-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-yloxy)ethyl)piperazines some non-cataleptic or low-cataleptic neuroleptic agents. It was thus interesting to see the influence of the "oxa–thia" isosterism in this case on the activity; compounds *XX–XXV* were prepared to this end. Reaction of the sodium salt of *VII* with 1-(2-chloroethyl)-4-(ethoxycarbonyl)piperazine hydrochoride[17] in ethanol in the presence of sodium ethoxide gave *XX*, isolated as hydrochloride. The homogeneous oily base *XX*, which was released from the purified hydrochloride, was characterized by the ^{1}H NMR spectrum. *XX* was reduced with lithium aluminium hydride in a mixture of tetrahydrofuran and ether and afforded *XXI*. The oily base was transformed to the dihydrochloride, and the homogeneous base *XXI*, released from this salt, was used for recording the ^{1}H NMR spectrum. Reactions of the crude tosylate *XVa* with 2-(1-piperazinyl)ethanol, 3-(1-piperazinyl)propanol[18], and 3-(1-piperazinyl)-propionamide[19] in boiling dioxane in the presence of sodium carbonate afforded *XXII–XXIV* which were transformed to salts with aliphatic dicarboxylic acids. The released bases were mostly characterized by spectra. Reaction of *XXII* with decanoyl chloride in boiling chloroform gave the decanoate *XXV* which was purified in the form of bis(hydrogen maleate); the ^{1}H NMR spectrum of the released, homogeneous base was recorded.



XX, R = $COOC_2H_5$ *XXIII*, R = $(CH_2)_3OH$
XXI, R = CH_3 *XXIV*, R = $CH_2CH_2CONH_2$
XXII, R = CH_2CH_2OH *XXV*, R = $(CH_2)_2OCO(CH_2)_8CH_3$

In searching after new antiinflammatory and anticonvulsant agents (cf. ref.[20]) some (2-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-ylthio)alkanoic acids and their amides were synthesized. The sodium salt of *VII* was reacted with ethyl chloroacetate and ethyl 2-chloropropionate in boiling ethanol and the obtained crude esters *XXVIa* and *XXVIIa* (characterized only by the IR spectra) were hydrolyzed with sodium hydroxide in boiling aqueous ethanol to the acids *XXVIb* and *XXVIIb*. The first (*XXVIb*) was purified by crystallization and characterized by spectra. The second (*XXVIIb*) was inhomogeneous due to the presence of two chiral centres in its molecules. Fractional crystallization gave first the minor and higher melting (162–165°C) racemate *A* and processing of the mother liquors afforded the major lower melting (128–130°C) racemate *B*. Both racemates were characterized by IR and ^{1}H NMR spectra. The acids *XXVIb* and *XXVIIb* were transformed to acid chlorides by refluxing with thionyl chloride in benzene and the obtained crude *XXVIc* and *XXVIIc* were processed without characterization by treatment with a solution of ammonia in chloroform to give the amides *XXVId* and *XXVIId*. Whereas *XXVId* was easily obtained in homogeneous state, which was confirmed by spectra, *XXVIId* was again inhomogeneous. Crystallization gave first the minor racemate *XXVIId–A* (m.p. 203–204°C) corresponding evidently to the higher melting acid *XXVIIb–A*. Processing of the mother liquors gave the major lower melting racemate (m.p. 135–136·5°C) *XXVIIb–B*. Both racemates were characterized by the IR and ^{1}H NMR spectra. The crude ester *XXVIa* was subjected to treatment by excessive 2-diethylaminoethylamine in boiling toluene which resulted in the amide *XXVIa*. Because its salts (hydrochloride, maleate, fumarate, oxalate, salicylate) did not crystallize, the base *XXVIe* was purified by chromatography which led to its crystallization; its homogeneity was confirmed by spectra. For pharmacological testing the freshly prepared solution of methanesulfonate was used. Reaction of the sodium salt of *VII* with ethyl 4-chlorobutyrate gave the ester *XXVIIIa* which was purified by distillation and was characterized by spectra. Its alkaline hydrolysis afforded the acid *XXVIIIb* which could not be transformed to the amide *XXVIIId* via the chloride *XXVIIIc*; instead of *XXVIIId* a compound $C_{14}H_{10}Cl_2S$ was obtained which was identified as *IV* (analysis and comparison of melting point with

that of the authentic product[6]). Thionyl chloride effected evidently the cleavage of the C(10)—S bond of a similar type like the cleavage of *III* with ethyl chloroformate. For preparing the amide *XXVIIId* it was necessary to react the ester *XXVIIIa* with ammonia first in a mixture of chloroform and methanol at 40°C and finally in a boiling mixture with aqueous ammonia. The reaction proceeded very slowly and the yield was only 19% (most of *XXVIIIa* remained unchanged); its identity was confirmed by spectra.



XXVI, A = $-CH_2-$ *XXVIII*, A = $-(CH_2)_3-$
XXVII, A = $-CH(CH_3)-$

In formulae *XXVI*–*XXVIII*: *a*, R = OC_2H_5 *b*, R = OH *c*, R = Cl *d*, R = NH_2 *e*, R = $NH(CH_2)_2N(C_2H_5)_2$

Most of the compounds prepared were pharmacologically tested either within a general screening programme or in batteries of tests aimed specifically to antidepressant (*IXa*, *XIa*, *XIIb*, *XVI*–*XX*), neuroleptic (*XXI*–*XXIV*), antiinflammatory (*XXVIb*–*XXVIIIb*) or anticonvulsant activities (*XXVId*–*XXVIIId*, *XXVIe*). The compounds were administered orally (unless stated otherwise) in the form of salts, described in the Experimental; the doses given were calculated per bases.

Acute toxicity in mice (LD_{50} in mg/kg): *XIa*, 523; *XIIb*, 60 (i.v.); *XVI*, 1 500; *XVIII*, >2 500; *XX*, >2 500; *XXII*, 1 234; *XXVIb*, >1 000; *XXVIIb*–*AB*, >500; *XXVIIIb*, >500; *XXVId*, >500; *XXVIId*–*AB*, >500; *XXVIe*, 366. Doses (D in mg/kg) used in the general screening: *XIIb*, 12 (i.v.); *XVIII*, 300; *XX*, 300.

Ataxic activity in the rotarod test in mice (ED_{50} in mg/kg): *IXa*, 210; *XIa*, 401; *XIIa*, 126; *XIIb*, 145; *XIIIa*, 129; *XVI*, 204; *XVII*–*A*, 562; *XVII*–*B*, 500; *XVIII*, >1 000; *XIX*, 144; *XX*, >1 000; *XXI*, >250; *XXVIe*, >100. Inhibition of spontaneous locomotor activity in mice (Dews, D_{50} in mg/kg): *XVII*–*A*, >250; *XX*, 300 mildly increased the motility; *XXII*, 10 increased mildly the locomotor activity in 1 h after the administration.

Antireserpine activities: Antagonization of reserpine hypothermia in mice (dose with significant effect ED in mg/kg): *IXa*, 100; *XIa*, 25; *XIIa*, 25; *XIIIa*, >25. Inhibition of the reserpine ptosis in mice (dose with significant effect ED in mg/kg): *IXa*, >100; *XIa*, 100; *XIIa*, >30; *XIIb*, >30; *XIIIa*, >30; *XVI*, >100; *XVII*–*A*, >100; *XVII*–*B*, >100; *XVIII*, >300; *XIX*, >100; *XX*, 1 000; *XXI*, >100. Antagonization of the ulcerogenic effects of reserpine in rats: *XIa*, significant inhibition at 100 mg/kg; *XXVIe*, inactive at 60 mg/kg.

Potentiation of yohimbine toxicity in mice (ED_{50} in mg/kg): *IXa*, 123; *XIa*, 66·8; *XIIa*, 100 (ED_{10}); *XIIb*, 50 (ED_{40}); *XIIIa*, 100 (ED_{30}); *XVI*, 100 (ED_{40}); *XVII–A*, 250 (ED_{40}); *XVII–B*, inactive at 500; *XVIII*, inactive at 1 000; *XIX*, 86; *XX*, 500; *XXVIe*, 144.

Inhibition of binding of 4 nmol l^{-1} [^{3}H]imipramine in the hypothalamus of the rat brain (IC_{50} in nmol l^{-1}): *IXa*, >100; *XIa*, <100; *XIIa*, *XIIb*, *XIIIa*, *XVI*, *XVII–A*, *XVII–B*, *XVIII*, *XIX*, *XX*, *XXI*, >100; *XXIII*, 378; *XXIV*, >100, *XXVIe*, 6 364. Inhibition of binding of 4 nmol l^{-1} [^{3}H]desipramine in the rat hypothalamus (IC_{50} in nmol l^{-1}): *IXa*, >100; *XIa*, 1 528; *XIIa*, *XIIb*, *XIIIa*, *XVI*, *XVII–A*, *XVII–B*, *XVIII*, *XIX*, *XX*, *XXI*, >100; *XXIII*, 3 624; *XXIV*, >100; *XXVIe*, 559.

Antagonization of the toxicity of adrenaline in mice: *IXa*, ED_{40} = 250 mg/kg.

Blood pressure of normotensive rats: *XIIb*, brief and deep drops after the dose D.

Spasmolytic effect on the isolated rat duodenum against acetylcholine contractions (concentrations in μg/ml reducing the contractions to 50%): *XIIb*, 1–10. Similar spasmolytic effect against barium chloride contractions: *XIIb*, 10. Antiarrhythmic effect against aconitine-induced arrhythmia in rats (ED in mg/kg): *XIIb*, 5–12 (i.v.).

Antitussive action in guinea-pigs (reduction of the cough attacks elicited by the aerosol of the citric acid solution in % of the control value (100%)): *XIIb*, 60 mg/kg, 23%; *XVIII*, D, 18%.

Anorectic effect in mice (dose in mg/kg reducing the food consumption to 50%): *XVI*, 50–100.

Inhibition of apomorphine-induced climbing behaviour in mice: *XXI*, inactive at 100 mg/kg.

Influence on the homovanillic acid (HVA) level in the rat brain striatum after the dose of 80 mg/kg in 3 h after adminstration: *XXI–XXIV*, slight drops of HVA levels indicating the complete lack of antidopaminergic activity. Catalepsy in rats: *XXII*, inactive at 50 mg/kg.

Antiinflammatory and antinociceptive actions (the compounds were administered in doses of 100 mg/kg and their activity was evaluated in two types of oedema in rats and the results are expressed as % of inhibition of the oedema ($^+$ means statistical significance)); the analgetic activity was assessed 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 pain): Carrageenan oedema: *XXVIb*, 23^+; *XXVIIb–AB*, 11; *XXVIIIb*, 23^+. Kaolin oedema: *XXVIIb–AB*, 7; *XXVIIIb*, 21. Antinociceptive action: *XXVIb*, 16 after 200 mg/kg; *XXVIIb–AB*, 30; *XXVIIIb*, 26. Ibuprofen used as the standard: carrageenan, 65^+; kaolin, 55^+; antinociceptive action, ED_{50} = 194 mg/kg.

Anticonvulsant activity. Electroshock in mice: *XXVId*, *XXVIId–AB* and *XXVIIId* in doses of 50 mg/kg protect neither against convulsions nor against the

lethal effect of the shock. Pentetrazole in mice: *XXVIId–AB*, 50 mg/kg do not protect from the convulsant effect; *XXVIIId*, 100 mg/kg do not protect from pentetrazole (75 mg/kg i.v.) convulsions; *XXVIe*, at 50 mg/kg inactive against pentetrazole.

In conclusion: Only *IXa* and *XIa* showed the pharmacological profile of potential antidepressnats, *XIa* (VUFB-16 555) being more interesting. Compounds *XXI* to *XXIV* lack completely the expected pharmacological profile of neuroleptics which is in striking contrast with their oxygen isosters (ethers) (ref.[16]). The acids *XXVIb* to *XXVIIIb* are significantly less active as antiinflammatory and analgetic agents than ibuprofen. The amides *XXVId–XXVIIId* and *XXVIe* are inactive as anticonvulsants.

The compounds prepared were also tested for antimicrobial activity in vitro (microorganisms and the minimum inhibitory concentrations in μg/ml are given unless they exceed 100 μg/ml): ***Streptococcus β-haemolyticus***, *IXa* 12·5, *XIa* 25, *XIIa* 50, *XIIb* 50, *XIIIa* 50, *XVI* 100, *XIX* 25, *XXI* 25, *XXII* 16, *XXIII* 16, *XXVIe* 12·5, *XXVIIb–AB* 50, *XXVIId–AB* 50, *XXVIIIb* 50, *XXVIIId* 128; *Streptococcus faecalis*, *IXa* 6·25, *XIa* 25, *XIIa* 25, *XIIb* 25, *XIIIa* 50, *XVI* 100, *XVIIb* 50, *XIX* 25, *XXI* 25, *XXII* 8, *XXIII* 8, *XXVIe* 50, *XXVIIId* 128; *Staphylococcus pyogenes aureus*, *IXa* 3·125, *XIa* 25, *XIIa* 3·1, *XIIb* 6·2, *XIIIa* 6·2, *XVI* 3·1, *XVII–B* 25, *XIX* 6·2, *XXI* 25, *XXII* 8, *XXIII* 128, *XXVIe* 50, *XXVIId–AB* 50, *XXVIIIb* 50, *XXVIIId* 128; *Pseudomonas aeruginosa*, *IXa* 50, *XIa* 100, *XIIb* 100, *XIIIa* 100, *XVI* 100, *XIX* 100, *XXII* 64, *XXVIIId* 128; *Escherichia coli*, *IXa* 12·5, *XIa* 25, *XIIa* 25, *XIIb* 50, *XIX* 50, *XXIII* 4, *XXVIIId* 128; *Proteus vulgaris*, *IXa* 12·5, *XIa* 6·2, *XIIa* 50, *XIIb* 100, *XIX* 50, *XXI* 100, *XXII* 64, *XXVIIId* 128; *Saccharomyces pasterianus*, *IXa* 125, *XIa* 50, *XIIa* 50, *XIIb* 50, *XIIIa* 50, *XVI* 25, *XXII* 25, *XXIII* 50; *Trichophyton mentagrophytes*, *IXa* 6·5, *XIa* 25, *XIIa* 25, *XIIb* 25, *XIIIa* 25, *XVI* 25, *XIX* 25, *XXI* 50, *XXII* 6·2, *XXIII* 12·5, *XXVIe* 50, *XXVIIb–AB* 50, *XXVIIIb* 12·5; *Candida albicans*, *IXa* 6·5, *XVI* 25, *XIX* 50; *Aspergillus niger*, *IXa* 50, *XVI* 50, *XIX* 50, *XXII* 50, *XXIII* 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 on 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 $CDCl_3$ unless stated otherwise, δ, J in Hz) with a Tesla BS 487C (80 MHz) spectrometer, and the mass spectra with MCH 1 320 and Varian MAT44S spectrometers (m/z and % 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 $MgSO_4$ of K_2CO_3 and evaporated under reduced pressure on a rotary evaporator.

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

A) A stirred mixture of 18·8 g *III* (ref.[3]) in 90 ml benzene was treated at 60°C over 1 h with a solution of 12·0 g ethyl chloroformate in 15 ml benzene and the mixture was refluxed under stirring for 2 h. Further 6·8 g of ethyl chloroformate were added and the stirring and refluxing was continued for 2·5 h. The mixture was allowed to stand overnight and the solid was filtered; 14·1 g (91%) of 1-(ethoxycarbonyl)-4-(2-ethoxycarbonyloxyethyl)piperazine hydrochloride, m.p. 166–168°C (dioxane). Mass spectrum: 274 (M^+, $C_{12}H_{22}N_2O_5$, 2), 229 ($C_{10}H_{17}N_2O_4$, 2·5), 184 ($C_9H_{16}N_2O_2$, 17), 171 ($C_8H_{15}N_2O_2$, 100), 143 ($C_6H_{11}N_2O_2$, 17), 97 (20), 89 (17), 70 (30) (cf. ref.[5]). For $C_{12}H_{23}ClN_2O_5$ (310·8) calculated: 46·37% C, 7·46% H, 11·41% Cl, 9·02% N; found: 46·29% C, 7·47% H, 11·76% Cl, 8·82% N.

Decomposition of a sample of this salt with 10% NH_4OH and extraction with chloroform gave the base which was transformed to the hydrogen maleate, m.p. 142–143°C (acetone). Ref.[5], m.p. 140–141°C.

The benzene filtrate was evaporated and the crude *IV* (13·8 g) was crystallized from hexane; 11·7 g (83%),m.p. 122–124·5°C. ^{1}H NMR spectrum: 3·60 dd and 3·95 dd, 1 + 1 H ($ArCH_2$, J = 8·0; 13·0 and 4·0; 13·0); 5·75 dd, 1 H (Ar–CH–Cl, J = 4·0; 8·0); 7·00–7·60 m, 7 H (ArH). Ref.[6], m.p. 124–124·5°C.

B) Compound *XXVIIIb* (9·8 g) in 50 ml benzene was treated with 6·7 g $SOCl_2$, the mixture was stirred for 1 h at room temperature and for 1·5 h at 78°C under reflux. The volatile components were evaporated in vacuo, the residue (10·4 g) was dissolved in 80 ml chloroform and the solution was saturated for 1 h with NH_3 at 60°C. After cooling the mixture was washed with water, dried, and evaporated. The residue (7·3 g, m.p. 118–122°C) was crystallized from a mixture of benzene and hexane and gavé homogeneous *IV*, m.p. 122·5–124°C, identical with the product obtained under *A*) (analysis in agreement with $C_{14}H_{10}Cl_2S$ and comparison by TLC).

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

Compound *IV* (2·81 g) was refluxed with 50 ml ethanol for 1 h, the solution was evaporated in vacuo, the residue was diluted with water, and extracted with chloroform. Processing gave 2·60 g (89%) of *V*, m.p. 89–90·5°C (cyclohexane–light petroleum). IR spectrum: 755, 820, 862 (4 and 2 adjacent and solitary Ar–H); 1 080, 1 110 (R–O–R'); 1 480, 1 550, 1 575, 3 040, 3 060 (Ar). ^{1}H NMR spectrum: 1·31 t, 3 H (CH_3 of ethyl, J = 7·0); 3·40 m, 2 H ($ArCH_2$); 3·68 q, 2 H (OCH_2, J = 7·0); 5·40 dd, 1 H (ArCH–O, J = 10·0; 4·0); 6·90–7·60, m (7 H, ArH). For $C_{16}H_{15}ClOS$ (290·8) calculated: 66·08% C, 5·20% H, 12·19% Cl, 11·03% S; found: 66·03% C, 5·22% H, 12·20% Cl, 11·20% S.

S-(2-Chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-yl)isothiuronium Chloride (*VI*)

A mixture of 4·2 g *IV*, 1·3 g thiourea and 10 ml dimethylformamide was stirred at 80°C for 3·5 h and the solvent was evaporated in vacuo. The residue was crystallized first from a mixture of 30 ml acetone and 30 ml ethanol and then from 2-propanol; 5·0 g (94%) modification *A* of *VI* m.p. 137–140°C. IR spectrum: 752, 817, 874, 900 (4 and 2 adjacent and solitary Ar–H); 1 640 (C=N); 2 715 (NH_3^+); 3 260, 3 410 (NH). For $C_{15}H_{14}Cl_2N_2S_2$ (357·3) calculated: 50·42% C, 3·95% H, 19·84% Cl, 7·84% N, 17·95% S; found: 50·07% C, 3·96% H, 19·80% Cl, 7·86% N, 17·81% S.

Recrystallization of the crude *VI* from a mixture of ethanol and ether gave modification *B* of *VI*, m.p. 183·5–184°C. IR spectrum: 752, 818, 824, 870, 890, 900 (4 and 2 adjacent and solitary Ar–H); 1 629, 1 642 (C=N); 2 715 (NH_3^+); 3 220, 3 410 (NH). For $C_{15}H_{14}Cl_2N_2S_2$ (357·3)

calculated: 50·42% C, 3·95% H, 19·84% Cl, 17·95% S; found: 50·05% C, 4·00% H, 19·70% Cl, 17·76% S.

2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-thiol (*VII*)

A) A mixture of 4·4 g *VI* (m.p. 137—140°C) and 6 ml 5M-NaOH was stirred and refluxed for 2 h in nitrogen atmosphere. The mixture was diluted with 15 ml water, acidified with 5M-H_2SO_4 (to pH 2) and the product was extracted with benzene. Processing of the extract gave 3·3 g (99%) of crude *VII*, m.p. 90—110°C. Crystallization from cyclohexane gave the pure product, m.p. 100—102°C. IR spectrum: 745, 828, 858, 898 (4 and 2 adjacent and solitary Ar–H); 1 559, 1 586, 1 603, 3 000, 3 048 (Ar); 2 570 (SH). ^{1}H NMR spectrum: 1·90 d, 1 H (SH, J = 8·0); 3·35 dd and 3·88 dd, 1 + 1 H ($ArCH_2$, J = 8·0; 13·0 and 4·0; 13·0); 4·74 dt, 1 H (Ar–CH–S, J = 8·0; 4·0); 6·90—7·80 m, 7 H (ArH). For $C_{14}H_{11}ClS_2$ (278·8) calculated: 60·30% C, 3·98% H, 12·72% Cl, 23·00% S; found: 60·31% C, 4·02% H, 13·00% Cl, 22·82% S.

B) Compound *VI* (m.p. 183—185·5°C) (3·5 g) was similarly hydrolyzed with 5 ml 5M-NaOH and gave 2·45 g (88%) of *VII*, m.p. 99—102°C, identical with the product obtained under *A*).

Bis(2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-yl)
Disulfide 5,5′-Dioxide (*VIII*)

Compound *VII* (0·56 g) was dissoved at 90—95°C in 5 ml acetic acid and the solution was treated under stirring with 0·35 ml 30% H_2O_2, the mixture was stirred for 10 min at 90—100°C and the solution formed was allowed to stand overnight at room temperature. The separated solid was filtered off and the filtrate was diluted with water. The inhomogeneous precipitate was filtered and crystallized from ethanol; 0·12 g (20%) of *VIII*, m.p. 224—225·5°C (benzene–light petroleum). MS spectrum (EI): 294 ($C_{14}H_{10}ClOS_2$), 277 ($C_{14}H_{10}ClS_2$), 261 ($C_{14}H_{10}ClOS$). For $C_{28}H_{20}Cl_2O_2S_4$ (587·6) calculated: 57·23% C, 3·43% H, 12·07% Cl, 21·83% S; found: 57·63% C, 3·43% H, 11·73% Cl, 21·24% S.

2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)ethylamine (*IXa*)

Compound *VII* (4·2 g) was dissolved in a stirred solution of sodium ethoxide (prepared from 0·35 g Na and 25 ml ethanol), the mixture was treated with 4·0 g K_2CO_3 and with a solution of 1·86 g 2-chloroethylamine hydrochloride[10] in 30 ml ethanol. The mixture was refluxed under stirring for 4·5 h, ethanol was evaporated and the residue was distributed between benzene and water. The benzene solution was shaken with 15 ml 2·5M-HCl, the precipitated hydrochloride of *IXa* was filtered, washed with a mixture of acetone and ether, and dried; 4·4 g (82%), m.p. 154—157°C. Crystallization from a mixture of 95% ethanol and ether gave the homogeneous hydrochloride hemihydrate, m.p. 158—162°C. For $C_{16}H_{17}Cl_2NS_2 + 0{\cdot}5\,H_2O$ (367·4) calculated: 52·30% C, 4·94% H, 19·30% Cl, 3·81% N, 17·46% S; found: 52·76% C, 4·86% H, 19·18% Cl, 4·18% N, 17·23% S.

Decomposition of a sample of this salt with NH_4OH and extraction with ether gave the homogeneous oily base *IXa* which was used for recording the ^{1}H NMR spectrum: 1·35 bs, 2 H (NH_2); 2·45 m, 2 H (SCH_2); 2·70 m, 2 H (CH_2N); 3·55 m, 2 H ($ArCH_2$); 4·68 dd, 1 H (Ar–CH–S, J = 9·0; 5·0); 6·80—7·60 m, 7 H (ArH).

Ethyl N-(2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)ethyl)carbamate (*Xa*)

A solution of 12·9 g *IXa* in 70 ml chloroform was treated with 14·8 g Na_2CO_3 and the stirred suspension was treated at 40—45°C with a solution of 6·3 g ethyl chloroformate in 30 ml chloro-

form. The mixture was refluxed for 3·5 h, treated with further 3·0 g ethyl chloroformate in 10 ml chloroform and refluxing was continued for 2 h. The mixture was then diluted with 60 ml chloroform, washed with water, 60 ml 1M-HCl, and with water, dried, and evaporated. The residue (17·2 g) was crystallized from a solution in 10 ml toluene by slow addition of 20 ml light petroleum; 13·4 g (85%) of *Xa*, m.p. 71–73°C (toluene–light petroleum). IR spectrum: 755, 783, 815, 875, 895 (4 and 2 adjacent and solitary Ar–H); 1 275, 1 550, 1 689 (RNHCOOR'); 1 580, 1 590, 3 050 (Ar); 3 230 (NH). For $C_{19}H_{20}ClNO_2S_2$ (394·0) calculated: 57·92% C, 5·12% H, 9·00% Cl, 3·56% N, 16·28% S; found: 57·88% C, 5·12% H, 9·15% Cl, 3·51% N, 16·50% S.

N-Methyl-2-(2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)ethylamine (*XIa*)

Compound *Xa* (5·5 g) was slowly added to a stirred solution of 3·5 g $LiAlH_4$ in 250 ml ether, the mixture was stirred and refluxed for 4·5 h and allowed to stand overnight. Under stirring the mixture was slowly decomposed by addition of 3·5 ml water, 3·5 ml 20% NaOH, 7 ml water, and 3·5 g K_2CO_3. After 30 min of stirring the solid was filtered off, washed with ether, and the filtrate was evaporated; 4·1 g (87%) of crude oily *XIa*. The solution of this base in 15 ml ethanol was treated under stirring with 4 ml ether, saturated with HCl, and the mixture was diluted with 15 ml ether, the precipitated hydrochloride was filtered and dried; 3·1 g, m.p. 206–207°C (95% ethanol). For $C_{17}H_{19}Cl_2NS_2$ (372·4) calculated: 54·83% C, 5·14% H, 19·04% Cl, 3·76% N, 17·22% S; found: 54·95% C, 5·17% H, 19·10% Cl, 3·77% N, 17·35% S.

A sample of the released, homogeneous base was used for recording the ^{1}H NMR spectrum: 1·30 s, 1 H (NH); 2·21 s, 3 H (NCH_3); 2·50 m, 4 H (SCH_2CH_2N); 3·50 m, 2 H ($ArCH_2$); 4·60 dd, 1 H (Ar–CH–S, J = 9·0; 5·0); 6·80–7·60 m, 7 H (ArH).

N,N-Dimethyl-2-(2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)ethylamine (*XIIa*)

Compound *VII* (4·2 g) was added to a sodium ethoxide solution (0·35 g Na and 30 ml ethanol) and the stirred solution was treated with 3·5 g K_2CO_3, 2·16 g 2-dimethylaminoethyl chloride hydrochloride, and 35 ml ethanol. The mixture was stirred for 1 h at 60°C and was refluxed for 1 h. Ethanol was evaporated and the residue was distributed between benzene and water. From the organic layer the base was extracted into 20 ml 2·5M-HCl, the aqueous solution was made alkaline with NH_4OH and the crude base *XIIa* was isolated by extradtion with benzene; 4·9 g (93%). Neutralization with 1·8 g maleic acid in 15 ml ethanol and addition of 30 ml ether resulted in 4·6 g hydrogen maleate, m.p. 108–110°C (ethanol), For $C_{22}H_{24}ClNO_4S_2$ (466·0) calculated: 56·70% C, 5·19% H, 7·61% Cl, 3·01% N, 13·76% S; found: 56·48% C, 5·19% H, 7·80% Cl, 3·01% N, 13·76% S.

^{1}H NMR spectrum of the released base: 2·13 s, 6 H ($N(CH_3)_2$); 2·35 m, 4 H (SCH_2CH_2N); 3·60 m, 2 H ($ArCH_2$); 4·70 dd, 1 H (Ar–CH–S, J = 9·0; 5·0); 6·90–7·70 m, 7 H (ArH).

N,N-Dimethyl-3-(2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)propylamine (*XIIb*)

Similar reaction of 4·2 g *VII*, sodium ethoxide (0·35 g Na and 30 ml ethanol), 3·5 g K_2CO_3, and 2·4 g 3-dimethylaminopropyl chloride hydrochloride in further 25 ml ethanol (refluxing for 3 h) gave 5·1 g (94%) of crude oily *XIIb*. Hydrogen maleate, m.p. 73·5–76°C (ethanol–ether). For $C_{23}H_{26}ClNO_4S_2$ (480·0) calculated: 57·54% C, 5·46% H, 7·39% Cl, 2·92% N, 13·36% S; found: 57·52% C, 5·61% H, 7·79% Cl, 2·99% N, 13·37% S.

^{1}H NMR spectrum of the released base: 1·65 m, 2 H (CH_2 in the middle of propyl); 2·13 s, 6 H ($N(CH_3)_2$); 2·21 t, 2 H (SCH_2, J = 7·0); 2·41 t, 2 H (CH_2N, J = 7·0); 3·60 m, 2 H ($ArCH_2$); 4·70 dd, 1 H (Ar–CH–S, J = 9·0; 5·0); 6·90–7·60 m, 7 H (ArH).

N,N-Diethyl-2-(2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)ethylamine (*XIIIa*)

A stirred solution of 4·2 g *VII* in 70 ml acetone was treated with 4·5 g K_2CO_3 and then 2·8 g 2-diethylaminoethyl chloride hydrochloride, acetone was evaporated and substituted with 10 ml dimethylformamide. The mixture was stirred for 2 h at 60°C and for 40 min at 100°C. It was diluted with 60 ml benzene, washed with water, and the base was extracted into 30 ml 2·5M-HCl. The solution of the hydrochloride was made alkaline with NH_4OH and the base was isolated by extraction with benzene; 4·6 g (81%) of crude oily *XIIIa*. Hydrogen oxalate, m.p. 162–165°C (90% aqueous ethanol). For $C_{22}H_{26}ClNO_4S_2$ (468·0) calculated: 56·45% C, 5·60% H, 7·58% Cl, 2·99% N, 13·70% S; found: 56·51% C, 5·54% H, 7·68% Cl, 2·69% N, 13·87% S.

^{1}H NMR spectrum of the released base: 0·91 t, 6 H (2 CH_3 of ethyls); 2·40 m, 8 H (SCH_2. .$CH_2N(CH_2)_2$); 3·50 m, 2 H ($ArCH_2$), 4·71 dd, 1 H (Ar–CH–S, J = 9·0; 5·0); 6·90–7·60 m, 7 H (ArH).

2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)ethanol (*XIVa*)

Compound *VII* (8·37 g) was added to a solution of sodium ethoxide (0·7 g Na and 20 ml ethanol), the solution was treated with 5·0 g 2-bromoethanol and the mixture was refluxed for 1·5 h. After cooling the precipitated NaBr was filtered off, the filtrate was evaporated and the residue was chromatographed on 100 g silica gel. Benzene eluted first 2·0 g of impurities which were followed by 7·2 g (74%) of homogeneous waxy *XIVa*. IR spectrum (KBr): 750, 812, 870 (4 and 2 adjacent and solitary Ar–H); 1 045, 1 060 (CH_2OH); 1 559, 1 578, 3 050 (Ar); 3 360 (OH). ^{1}H NMR spectrum: 2·08 bs, 1 H (OH); 2·60 bt, 2 H (SCH_2); 3·60 m, 4 H ($ArCH_2$ and CH_2O); 4·72 dd, 1 H (Ar–CH–S); 6·80–7·60 m, 7 H (ArH). For $C_{16}H_{15}ClOS_2$ (322·9) calculated: 10·98% Cl, 19·86% S; found: 10·91% Cl, 19·96% S.

A solution of 7·3 g *XIVa* in 5·4 g pyridine was stirred and slowly treated at 3–5°C with 4·5 g 4-toluenesulfonyl chloride, added in small portions. The mixture was stirred for 1 h at 0°C and 2 h at room temperature, it was decomposed by a slow addition of 35 ml water at –5°C, extracted with chloroform, the extract was washed with water, then with 100 ml 0·2M-tartaric acid and again with water, dried, and evaporated in vacuo; 10·8 g (theoretical) of crude tosylate *XVa* which was used in this state for further work.

N,N-Dimethyl-3-(2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-
-10-ylthio)-3-phenylpropylamine (*XVI*)

Compound *VII* (5·6 g) was added to a sodium ethoxide solution (0·92 g Na and 25 ml ethanol), the solution was treated with a warm solution of 4·7 g 3-(dimethylamino)-1-phenylpropyl chloride hydrochloride[12] in 50 ml ethanol, the mixture was refluxed for 4 h, and allowed to stand overnight. The precipitated NaCl was filtered off, washed with ethanol, and the filtrate was evaporated. The residue (8·8 g), consisting in the mixture of racemic bases *XVI*, was neutralized with 2·7 g oxalic acid dihydrate in 60 ml ethyl acetate at 70°C. Crystallization by standing at room temperature gave 7·6 g (72%) of hydrogen oxalate, m.p. 107–108°C (2-propanol–ethyl acetate). For $C_{27}H_{28}ClNO_4S_2$ (530·1) calculated: 61·17% C, 5·32% H, 6·69% Cl, 2·64% N, 12·10% S; found: 61·15% C, 5·46% H, 6·75% Cl, 2·77% N, 11·96% S.

The ^{1}H NMR spectrum of the released base confirmed the inhomogeneity, i.e. the presence of both racemates possible.

N-Cyclohexyl-2-(2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)--2-phenylethylamine (*XVII*)

Compound *VII* (4·5 g) was added to the sodium ethoxide solution (0·7 g Na and 20 ml ethanol), the solution was treated first with 0·6 g K_2CO_3 and then with a warm solution of 4·1 g 2-(cyclohexylamino)-1-phenylethyl chloride hydrochloride[13] in 20 ml ethanol, the stirred mixture was refluxed for 6 h and allowed to stand overnight. NaCl was filtered off, the filtrate was filtered with active carbon, and the filtrate was evaporated in vacuo. The residue was dissolved in 50 ml benzene, the solution was washed with water, dried, and evaporated. The remaining oily mixture of racemic bases *XVII* was neutralized with 1·9 g oxalic acid dihydrate in 55 ml ethyl acetate; 6·05 g (70%) mixture of hydrogen oxalates, m.p. 96–99°C. This was decomposed with NH_4OH, the bases were isolated by extraction with benzene and were chromatographed on 120 g silica gel. Elution with benzene and then chloroform gave 3·3 g of homogeneous base *XVII-A* which afforded a hydrogen oxalate, crystallizing from wet ethyl acetate as monohydrate, m.p. 110·5 to 112°C. Mass spectrum: 480 (M^+, $C_{28}H_{30}ClNS_2$, 0·1), 357 ($C_{21}H_{24}ClNS$, 0·9), 277 ($C_{14}H_{10}ClS_2$, 0·5), 245 ($C_{14}H_{10}ClS$, 3), 210 ($C_{14}H_{10}S$, 4·5), 112 ($C_7H_{14}N$, 100). For $C_{30}H_{32}ClNO_4S_2$ + H_2O (588·2) calculated: 61·25% C, 5·82% H, 6·03% Cl, 2·38% N, 10·91% S; found: 60·92% C, 5·43% H, 5·80% Cl, 2·38% N, 10·77% S.

Continued elution with chloroform containing 5% of ethanol gave 1·2 g homogeneous base *XVII-B*, different from the isomer *A* (TLC). This afforded the hydrogen oxalate crystallizing from a mixture of acetone and ether and melting at 99–102°C. Mass spectrum: 480 (M^+, $C_{28}H_{30}ClNS_2$, 0·1), 357 ($C_{21}H_{24}ClNS$, 1·5), 276 ($C_{14}H_{10}ClS_2$, 1·2), 245 ($C_{14}H_{10}ClS$, 7), 210 ($C_{14}H_{10}S$, 10), 188 ($C_{13}H_{18}N$, 17), 112 ($C_7H_{14}N$, 100). ^1H NMR spectrum (50°C): 0·90 to 2·00 m, 10 H (5 CH_2 of cyclohexyl); 2·50–3·50 m, 5 H ($ArCH_2$ and CH_2NCH); 4·40 m, 2 H (ArCHSCHAr); 6·80–7·40 m, 13 H (ArH). For $C_{30}H_{32}ClNO_4S_2$ (570·2) calculated: 63·19% C, 5·66% H, 6·22% Cl, 2·46% N, 11·25% S; found: 62·75% C, 5·35% H, 6·21% Cl, 2·71% N, 10·86% S.

1-Benzyl-4-(3-(2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin--10-ylthio)-3-phenylpropyl)piperazine (*XVIII*)

Compound *VII* (4·2 g), sodium ethoxide (1·1 g Na, 25 ml ethanol), 6·0 g 3-(4-benzyl-1-piperazinyl)-1-phenylpropyl chloride hydrochloride[14], and 60 ml ethanol were processed similarly as in the synthesis of *XVI* (refluxing for 10·5 h). The inhomogeneous base was transformed to the bis(hydrogen oxalate) (9·5 g, 83%), m.p. 214–214·5°C (dimethylformamide–ethanol–acetone). For $C_{38}H_{39}ClN_2O_8S_2$ (751·3) calculated: 60·74% C, 5·23% H, 4·72% Cl, 3·73% N, 8·54% S; found: 60·32% C, 5·44% H, 4·85% Cl, 4·01% N, 8·30% S.

The released base was used for recording the spectra. IR spectrum: 700, 750, 815, 870 (4 and 2 adjacent and solitary Ar–H); 1 490, 1 560, 1 581, 1 600, 3 020, 3 060, 3 080 (Ar); 2 770, 2 810 (CH_2–N). The ^1H NMR spectrum indicated the inhomogeneity.

4-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)-1-methylpiperidine (*XIX*)

Compound *VII* (4·2 g) was dissolved in sodium ethoxide solution (0·35 g Na and 25 ml ethanol), ethanol was evaporated in vacuo, the residue was dissolved in 10 ml dimethylformamide at 50°C and 2·0 g 4-chloro-1-methylpiperidine[15] were added. The mixture was stirred at 90°C for 3·5 h, cooled, diluted with 50 ml benzene, the solution was washed with water and the base was extracted into 45 ml (3 × 15) 2·5M-HCl. The aqueous solution was made alkaline with NH_4OH and the base was isolated by extraction with benzene; 3·1 g (55%). The base *XIX* crystallized from

a mixture of cyclohexane, benzene, and light petroleum, m.p. 174–177°C. ^{1}H NMR spectrum: 1·30–3·00 m, 12 H (4 CH_2 and CH of piperidine, $ArCH_2CHAr$); 2·18 s, 3 H (NCH_3); 6·90 to 8·00 m, 7 H (ArH). For $C_{20}H_{22}ClNS_2$ (376·0) calculated: 63·88% C, 5·90% H, 9·43% Cl, 3·73% N, 17·06% S; found: 63·79% C, 5·46% H, 9·65% Cl, 3·82% N, 16·82% S.

The hydrochloride, which was obtained by slow crystallization from ethanol, melted at 240 to 245°C (form *A*). IR spectrum: 751, 812, 880 (4 and 2 adjacent and solitary Ar–H); 1 542, 1 569, 1 571, 1 580, 1 595, 3 000, 3 040, 3 055 (Ar); 2 420, 2 465, 2 530, 2 585, 2 625, 2 650 (NH^+). For $C_{20}H_{23}Cl_2NS_2$ (412·4) calculated: 58·24% C, 5·62% H, 17·19% Cl, 3·40% N, 15·55% S; found: 58·15% C, 5·30% H, 16·98% Cl, 3·60% N, 15·57% S.

The hydrochloride which was obtained by repeated precipitation from a solution in a mixture of ethanol and acetone by addition of ether, melted constantly at 208–212°C (form *B*). IR spectrum: 750, 837, 885 (4 and 2 adjacent and solitary Ar–H); 1 545, 1 560, 1 580, 1 590, 3 060 (Ar); 2 400, 2 490, 2 540 (NH^+). For $C_{20}H_{23}Cl_2NS_2$ (412·4) calculated: 58·24% C, 5·62% H, 17·19% Cl, 3·40% N, 15·55% S; found: 57·84% C, 5·39% H, 17·05% Cl, 3·67% N, 15·42% S.

1-(2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)ethyl)-4-(ethoxycarbonyl)piperazine (*XX*)

Compound *VII* (5·6 g) was added to a sodium ethoxide solution (0·95 g Na and 40 ml ethanol), the solution was treated with a warm solution of 5·14 g 1-(2-chloroethyl)-4-(ethoxycarbonyl)-piperazine hydrochloride[17] in 40 ml ethanol, and the mixture was stirred and refluxed for 3·5 h. Ethanol was evaporated, the residue was diluted with water and extracted with benzene. Processing of the extract gave 9·26 g of crude oily base *XX* which was transformed to hydrochloride in a mixture of ethanol, acetone and ether; 8·3 g (83%), m.p. 202–203·5°C (95% ethanol). For $C_{23}H_{28}Cl_2N_2O_2S_2$ (499·5) calculated: 55·30% C, 5·65% H, 14·20% Cl, 5·61% N 12·84 S; found: 55·29% C, 5·60% H, 14·03% Cl, 5·75% N, 13·10% S.

The released base (homogeneous oil) was used for recording the spectra. IR spectrum: 758, 820, 878 (4 and 2 adjacent and solitary Ar–H); 1 243, 1 700 (NCOOR); 1 565, 1 585, 3 060 (Ar); 2 770, 2 815 (CH_2–N). ^{1}H NMR spectrum: 1·21 t, 3 H (CH_3 of ethyl, J = 7·0); 2·20 t, 4 H ($CH_2N^1CH_2$ of piperazine); 2·40 s, 4 H (SCH_2CH_2N); 3·40 t, 4 H ($CH_2N^4CH_2$ of piperazine); 3·60 m, 2 H ($ArCH_2$); 4·10 q, 2 H (OCH_2, J = 7·0); 4·71 dd, 1 H (Ar–CH–S, J = 4·0; 8·0); 6·90–7·60 m, 7 H (ArH).

1-(2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)ethyl)-4-methylpiperazine (*XXI*)

A solution of 7·0 g *XX* in 30 ml tetrahydrofuran was slowly added to a stirred and refluxing solution of 2·3 g $LiAlH_4$ in 100 ml ether and the mixture was refluxed for 4·5 h. After cooling it was decomposed by slow addition of 2·3 ml water, 2·3 ml 5M-NaOH, and 4·6 ml water, 2·3 g K_2CO_3 were added and after 30 min standing the solid was filtered off. The filtrate was evaporated; 5·3 g (87%) crude *XXI* which was chromatographed on 150 g neutral Al_2O_3 (activity II). The first fractions, obtained by elution with benzene, represented the homogeneous base *XXI*. ^{1}H NMR spectrum: 2·20 s, 3 H (NCH_3); 2·31, S, 8 H (4 NCH_2 of piperazine); 2·40 s, 4 H (SCH_2CH_2N); 3·50 m, 2 H ($ArCH_2$); 4·70 dd, 1 H (Ar–CH–S, J = 4·0; 8·0); 6·90–7·60 m, 7 H (ArH).

Dihydrochloride, m.p. 221–223°C (aqueous ethanol). For $C_{21}H_{27}Cl_3N_2S_2$ (478·0) calculated: 52·77% C, 5·69% H, 22·26% Cl, 5·86% N, 13·42% S; found: 52·27% C, 5·84% H, 21·82% Cl, 5·76% N, 13·47% S.

2-(4-(2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)ethyl)-1-piperazinyl)ethanol (*XXII*)

A mixture of 7·5 g crude *XVa*, 3·0 g 2-(1-piperazinyl)ethanol, 3·3 g Na_2CO_3, and 10 ml dioxane was stirred and refluxed for 4 h. After cooling it was diluted with 50 ml chloroform, washed with water, 10% $NaHCO_3$ and water, filtered with active carbon, and evaporated; 6·0 g (88%) of crude *XXII*. Succinate monohydrate, m.p. 134·5–137°C (ethanol). Mass spectrum: 434 (M^+, $C_{22}H_{27}ClN_2OS_2$, 0·4), 416 (0·1), 403 (0·1), 277 (1·5), 245 (6), 210 (8), 157 (30), 143 (100). IR spectrum: 752, 815, 890 (4 and 2 adjacent and solitary Ar–H); 1 175, 1 710 (COOH); 1 585, 2 460 (COO^-); 3 190 (OH). For $C_{26}H_{33}ClN_2O_5S_2 + H_2O$ (571·2) calculated: 54·67% C, 6·17% H, 6·21% Cl, 4·91% N, 11·23% S; found: 54·67% C, 6·12% H, 6·29% Cl, 4·93% N, 11·23% S.

The homogeneous base *XXII*, released from the salt with NH_4OH and isolated by extraction with ether, was used for recording the ^1H NMR spectrum: 2·35 bm, 14 H (SCH_2 and 6 NCH_2); 2·75 bs, 1 H (OH); 3·50 m, 4 H ($ArCH_2$ and CH_2O); 4·70 dd, 1 H (Ar–CH–S, $J = 4·0$; 8·0); 6·90–7·60 m, 7 H (ArH).

3-(4-(2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)ethyl)-1-piperazinyl)propanol (*XXIII*)

A similar reaction of 13·5 g crude *XVa*, 4·9 g 3-(1-piperazinyl)propanol[18], 20 ml dioxane, and 5·3 g Na_2CO_3 gave 10·2 g of crude oily *XXIII* which was transformed to the bis(hydrogen maleate) (8·3 g, 54%), m.p. 149–150°C (acetone–ethanol). For $C_{31}H_{37}ClN_2O_9S_2$ calculated: 54·65% C, 5·47% H, 5·20% Cl, 4·11% N, 9·42% S; found: 54·78% C, 5·49% H, 5·35% Cl, 3·91% N, 9·40% S.

The released homogeneous base was used for recording the spectra. IR spectrum (film): 753, 819, 871, 900 (4 and 2 adjacent and solitary Ar–H); 1 070 (CH_2OH); 1 560, 1 579, 3 020, 3 050 (Ar); 3 260 (OH). ^1H NMR spectrum: 1·65 m 2 H (CH_2 in the middle of propyl); 2·40 bm, 14 H (SCH_2 and 6 NCH_2); 3·50 m, 2 H ($ArCH_2$); 3·70 t, 2 H (CH_2O); 4·20 bs, 1 H (OH); 4·68 dd, 1 H (Ar–CH–S, $J = 8·0$; 4·0); 6·90–7·60 m, 7 H (ArH).

3-(4-(2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)ethyl)-1-piperazinyl)propionamide (*XXIV*)

A similar reaction of 13·3 g crude *XVa*, 6·2 g 3-(1-piperazinyl)propionamide[19], 5·5 g Na_2CO_3, and 25 ml dioxane gave 9·2 g (77%) of the crude oily *XXIV* which was transformed to the succinate, m.p. 132–135·5°C (acetone). For $C_{27}H_{34}ClN_3O_5S_2$ (580·2) calculated: 55·89% C, 5·90% H, 6·11% Cl, 7·24% N, 11·06% S; found: 55·69% C, 5·93% H, 6·42% Cl, 7·05% N, 11·47% S.

2-(4-(2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)-ethyl)-1-piperazinyl)ethyl Decanoate (*XXV*)

A stirred solution of 3·9 g *XXII* in 30 ml chloroform was treated with a solution of 3·4 g decanoyl chloride in 10 ml chloroform, added dropwise. The mixture was stirred for 2 h at 50°C and refluxed for 7 h. After cooling it was diluted with 50 ml chloroform, washed with 5% $NaHCO_3$ and water, 1·0 g active carbon and 2·0 g Na_2SO_4 were added, the mixture was filtered after 30 min stirring, and the filtrate was evaporated; 5·2 g (98%) of crude oily *XXV*.

Bis(hydrogen maleate), m.p. 162–165°C (acetone). For $C_{40}H_{53}ClN_2O_{10}S_2$ (821·4) calculated: 58·48% C, 6·50% H, 4·32% Cl, 3·41% N, 7·80% S; found: 58·26% C, 6·52% H, 4·66% Cl, 3·27% N, 7·77% S.

The base was released by a 10% solution of $NaHCO_3$ and isolated by extraction with ether; oil. ^{1}H NMR spectrum: 0·85 def. t, 3 H (terminal CH_3 of decanoyl); 1·25 bs, 12 H (6 CH_2 in positions 3—8 of decanoyl); 1·60 bm, 2 H (CH_2-9 of decanoyl); 2·10—2·80 m, 16 H (SCH_2, 6 NCH_2 and $COCH_2$); 3·60 m, 2 H ($ArCH_2$); 4·20 t, 2 H (CH_2O, J = 6·0); 4·78 dd, 1 H (Ar–CH–S, J = 4·0; 8·0); 7·00—7·70 m, 7 H (ArH).

2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)acetic Acid (*XXVIb*)

Compound *VII* (14·0 g) was added to a solution of sodium ethoxide (1·25 g Na and 50 ml ethanol) and the solution was treated with a solution of 9·5 g ethyl chloroacetate in 10 ml ethanol and the mixture was stirred and refluxed for 6 h. Ethanol was evaporated, the residue was diluted with water and extracted with benzene. Processing of the extract gave 18·2 g (99%) of crude *XXVIa*. IR spectrum (film): 752, 817, 871 (4 and 2 adjacent and solitary Ar–H); 1 130, 1 270, 1 730 (RCOOR'); 1 560, 1 580, 3 055 (Ar).

A solution of 17·8 g crude *XXVIa* in 50 ml ethanol was treated with a solution of 7·0 g NaOH in 30 ml water and the mixture was stirred and refluxed for 2 h. Ethanol was evaporated, the residue was diluted with 175 ml water, the solution was filtered with active carbon, and the filtrate was acidified with hydrochloric acid at 50°C (to pH 1). The product was extracted with chloroform; processing of the extract gave 10·7 g (64%) of *XXVIb*, m.p. 120—125°C. Analytical sample, m.p. 128—129°C (benzene–hexane). IR spectrum: 760, 780, 820, 875, 887 (4 and 2 adjacent and solitary Ar–H); 915, 1 210, 1 715, 2 590, 2 670, 2 690, infl. 3 100 (COOH); 1 565, 1 581 (Ar). ^{1}H NMR spectrum: 3·18 s, 2 H (SCH_2); 3·60 m, 2 H ($ArCH_2$); 4·80 dd, 1 H (Ar–CH–S, J = 4·0; 8·0); 7·00—7·50 m, 7 H (ArH); 11·20 bs, 1 H (COOH). For $C_{16}H_{13}ClO_2S_2$ (336·9) calculated: 57·04% C, 3·89% H, 10·52% Cl, 19·04% S; found: 56·96% C, 3·92% H, 10·23% Cl, 18·87% S.

2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)propionic Acid (*XXVIIb*)

Similarly like in the preceding case, 14·0 g *VII* was trasformed to a solution of the sodium salt (1·25 g Na, 50 ml ethanol) and was reacted with a solution of 8·2 g ethyl 2-chloropropionate in 10 ml ethanol (refluxing for 4 h). Similar processing gave 18·7 g (99%) of crude oily *XXVIIa*. IR spectrum: 1 730 (RCOOR').

Hydrolysis of 3·5 g of crude *XXVIIa* by 1·4 g NaOH in a mixture of 10 ml ethanol and 5 ml water (2 h refluxing) gave similarly 3·2 g (theoretical) of the oily mixture of two racemic *XXVIIb*. It crystallized from a mixture of 2 ml benzene and 10 ml hexane; 2·6 g (81%), m.p. unsharp 126—165°C. Three crystallizations from a 1 : 1 mixture of benzene and hexane gave the homogeneous minor racemate *A*, m.p. 162—165°C. IR spectrum: 767, 813, 883 (4 and 2 adjacent and solitary Ar–H); 941, 1 062, 1 243, 1 696, 2 559, 2 630, 2 720 (COOH); 1 550, 1 578 (Ar). ^{1}H NMR spectrum (CD_3SOCD_3): 1·30 d, 3 H (CH_3, J = 7·0); 3·50 m, 3 H ($ArCH_2$ and SCH); 4·90 dd, 1 H (Ar–CH–S); 7·10—7·60 m, 7 H (ArH). For $C_{17}H_{15}ClO_2S_2$ (350·9) calculated: 58·18% C, 4·31% H, 10·11% Cl, 18·28% S; found: 57·76% C, 4·36% H, 10·09% Cl, 17·97% S.

Processing of the mother liquors gave the major racemate *B* of *XXVIIb*, m.p. 128—130°C (benzene–light petroleum). IR spectrum: 755, 769, 817, 870 (4 and 2 adjacent and solitary Ar–H); 943, 1 063, 1 240, 1 700, 2 550, 2 625, 2 720 (COOH); 1 550, 1 588, 3 050 (Ar). ^{1}H NMR spectrum (CD_3SOCD_3): 1·30 d and 1·32 d, $\sum$ 3 H (CH_3, J = 0·7); 3·60 m, 3 H ($ArCH_2$, SCH); 4·90 bm, 1 H (Ar–CH–S); 7·00—7·60 m, 7 H (ArH). For $C_{17}H_{15}ClO_2S_2$ (350·9) calculated: 58·18% C, 4·31% H, 10·11% Cl, 18·28% S; found: 58·06% C, 4·35% H, 10·02% Cl, 18·37% S.

2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)acetamide (*XXVId*)

A mixture of 4·1 g *XXVIb*, 10 ml benzene and 5·0 g $SOCl_2$ was stirred and refluxed for 5 h. Evaporation in vacuo gave 4·5 g crude *XXVIc*. It was dissolved in 50 ml chloroform and the

solution was stirred and saturated with NH_3 at room temperature for 5 h. It was then diluted with 50 ml chloroform, the solution was washed with 10% $NaHCO_3$ and water, dried, and evaporated; 2·8 g (70%) of crude *XXVId*, m.p. 98—110°C. Analytical sample, m.p. 110—112°C (benzene–hexane). IR spectrum: 749, 810, 899 (4 and 2 adjacent and solitary Ar–H); 1 610, 3 040 (Ar); 1 659, 1 685 ($CONH_2$); 3 190, 3 280, 3 405 (NH_2). ^{1}H NMR spectrum: 3·13 s, 2 H (SCH_2); 3·60 bm, 2 H ($ArCH_2$); 4·65 bm, 1 H (Ar–CH–S); 6·15 bs and 6·35 bs, $\sum$ 2 H ($CONH_2$); 7·00 to 7·50 m, 7 H (ArH). For $C_{16}H_{14}ClNOS_2$ (335·9) calculated: 57·21% C, 4·20% H, 10·56% Cl, 4·17% N, 19·09% S; found: 57·14% C, 4·24% H, 10·63% Cl, 4·17% N, 19·01% S.

N-(2-Diethylaminoethyl)-2-(2-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)acetamide (*XXVIe*)

A mixture of 3·6 g crude *XXVIa*, 10 ml toluene and 5·8 g 2-diethylaminoethylamine was refluxed for 6 h, diluted with 50 ml toluene, washed with water, and evaporated. The residue was chromatographed on 100 g neutral Al_2O_3 (activity II) and the fraction, obtained by elution with a 1 : 1 mixture of benzene and chloroform crystallized from a mixture of benzene and hexane; 1·3 g (28%) of *XXVIe*, m.p. 74—76°C (benzene–hexane). UV spectrum (methanol): λ_{max} 255 nm (log ε 3·86), 272 nm (3·85). IR spectrum: 711, 759, 823, 898 (4 and 2 adjacent and solitaryAr–H); 1 570 (RCONHR'); 2 835 (CH_2–N); 3 065, 3 100 (Ar); 3 275 (NH). ^{1}H NMR spectrum: 1·00 t, 6 H (2 CH_3 of ethyls, J = 7·0); 2·52 q, 4 H (CH_2NCH_2 of diethylamino, J = 7·0); 2·55 t, 2 H (CH_2-2 of aminoethyl, J = 7·0); 3·00—3·70 m, 6 H ($ArCH_2$, SCH_2CONCH_2); 4·65 m, 1 H (Ar–CH–S); 7·00—7·50 m, 8 H (7 ArH and CONH). For $C_{22}H_{27}ClN_2OS_2$ (435·1) calculated: 60·73% C, 6·26% H, 8·15% Cl, 6·44% N, 14·74% S; found: 60·72% C, 6·56% H, 8·45% Cl, 6·49% N, 14·87% S.

2-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)propionamide (*XXVIId*)

Similarly like in the synthesis of *XXVId*, 1·7 g inhomogeneous *XXVIIb* was transformed by treatment with $SOCl_2$ (2·0 g) in 5 ml benzene to 1·9 g crude *XXVIIc*. This was dissolved in 45 ml chloroform and the solution was saturated with NH_3. Processing gave 1·6 g (91%) of stereoisomeric mixture of *XXVIId*. Repeated crystallization from a mixture of benzene and ethanol gave 0·6 g (35%) of homogeneous racemate *A* of *XXVIId*, m.p. 203—204°C. IR spectrum (KBr): 756, 817, 890 (4 and 2 adjacent and solitary Ar–H); 1 560, 1 580, 3 045 (Ar); 1 638, 1 663 ($CONH_2$); 3 175, 3 380 (NH_2). ^{1}H NMR spectrum (CD_3SOCD_3): 1·28 d, 3 H (CH_3, J = 6·0); 3·60 m, 3 H ($ArCH_2$ and SCH); 4·70 dd, 1 H (Ar–CH–S); 7·00—7·60 m, 7 H (ArH). For $C_{17}H_{16}ClNOS_2$ (349·9) calculated: 10·13% Cl, 4·00% N; found: 10·47% Cl, 3·78% N.

Processing of the mother liquors gave 1·0 g (56%) of crude racemate *B* of *XXVIId*, m.p. 130 to 135°C which was purified by three crystallizations from benzene; m.p. 135—136·5°C. IR spectrum: 747, 811, 891 (4 and 2 adjacent and solitary Ar–H); 1 562, 3 050 (Ar); 1 649 ($CONH_2$); 3 165, 3 340 (NH_2). ^{1}H NMR spectrum (CD_3SOCD_3): 1·27 d and 1·30 d, $\sum$ 3 H (CH_3, J = = 6·0 Hz); 3·50 m, 3 H ($ArCH_2$ and SCH); 4·78 bm, 1 H (Ar–CH–S); 7·00—7·70 m, 7 H (ArH). For $C_{17}H_{16}ClNOS_2$ (349·9) calculated: 58·35% C, 4·61% H, 10·13% Cl, 4·00% N, 18·33% S; found: 57·96% C, 4·65% H, 10·28% Cl, 4·18% N, 18·30% S.

Ethyl 4-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)butyrate (*XXVIIIa*)

Compound *VII* (14·0 g) was added to a solution of sodium ethoxide (1·25 g Na and 50 ml ethanol), a solution of 9·04 g ethyl 4-chlorobutyrate in 10 ml ethanol was added and the mixture was refluxed for 6 h. Ethanol was evaporated, the residue was diluted with water and extracted with benzene. Processing of the extract gave 19·5 g (99%) of crude *XXVIIIa* which was distilled;

b.p. 230—235°C/47 Pa. IR spectrum: 1 725 (RCOOR'). ^{1}H NMR spectrum: 1·20 t, 3 H (CH_3 of ethyl, J = 7·0); 1·80 m, 2 H (CH_2 in position 3 of butyrate); 2·25 and 2·39 2 t, 2 + 2 H (SCH_2 and CH_2CO); 3·50 m, 2 H ($ArCH_2$); 4·05 q, 2 H (OCH_2, J = 7·0); 4·65 dd, 1 H (Ar–CH–S, J = 5·0; 8·0); 6·80—7·50 m, 7 H (ArH). For $C_{20}H_{21}ClO_2S_2$ (393·0) calculated: 61·12% C, 5·39% H, 9·02% Cl, 16·32% S; found: 61·09% C, 5·46% H, 8·88% Cl, 16·44% S.

4-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)butyric Acid (*XXVIIIb*)

A solution of 7·1 g *XXVIIIa* in 10 ml ethanol was treated with a solution of 3·0 g NaOH in 10 ml water and the mixture was refluxed for 2 h. Ethanol was evaporated, the residue was diluted with water, acidified with 25 ml 2·5M-HCl, and the product was extracted with chloroform. Processing of the extract gave 6·6 g oily product which crystallized after trituration with 2 ml light petroleum; 5·9 g (90%) of *XXVIIIb*, m.p. 107—108·5°C (benzene–light petroleum). IR spectrum: 688, 749, 817, 900 (4 and 2 adjacent and solitary Ar–H); 956, 1 693, 2 680 (COOH); 1 580, 3 065 (Ar). ^{1}H NMR spectrum: 1·80 m, 2 H (CH_2 in position 3 of butyric residue); 2·38 t, 2 H (SCH_2, J = 7·0); 2·42 t, 2 H (CH_2CO, J = 7·0); 3·55 m, 2 H ($ArCH_2$); 4·68 m, 1 H (Ar–CH–S); 6·80—7·60 m, 7 H (ArH); 9·90 bs, 1 H (COOH). For $C_{18}H_{17}ClO_2S_2$ (364·9) calculated: 59·24% C, 4·70% H, 9·72% Cl, 17·58% S; found: 59·22% C, 4·72% H, 9·40% Cl, 17·34% S.

4-(2-Chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ylthio)butyramide (*XXVIIId*)

A solution of 5·8 g *XXVIIIa* in 8 ml chloroform and 20 ml methanol was treated with 50 ml methanol, saturated with NH_3. The mixture was stirred and saturated for 5 h with NH_3 at 40°C, 50 ml NH_4OH were added and the mixture was refluxed for 5 h. It was evaporated in vacuo, the residue was dissolved in 50 ml chloroform, the solution was washed with water, dried, and evaporated. The residue was chromatographed on 200 g neutral Al_2O_3 (activity II). Benzene elution removed the starting *XXVIIIa* and chloroform eluted 1·05 g (19%) of the desired *XXVIIId*, m.p. 118—119·5°C (tolune). IR spectrum: 753, 820, 873 (4 and 2 adjacent and solitary Ar–H); 1 562, 3 000, 3 045 (Ar); 1 643 ($CONH_2$), 3 200, 3 410 (NH_2). ^{1}H NMR spectrum: 1·88 m, 2 H (CH_2 in position 3 of butyramide); 2·20 t, 2 H (SCH_2, J = 6·0); 2·47 t, 2 H (CH_2CO, J = 6·0); 3·58 m, 2 H ($ArCH_2$); 4·70 dd, 1 H (Ar–CH–S, J = 5·0; 8·00); 5·54 bs and 5·94 bs, 1 + 1 H ($CONH_2$); 7·00—7·60 m, 7 H (ArH). For $C_{18}H_{18}ClNOS_2$ (363·9) calculated: 59·40% C, 4·98% H, 9·74% Cl, 3·85% N, 17·62% S; found: 58·76% C, 5·07% H, 10·02% Cl, 4·02% N, 17·48% S.

The authors wish to thank their colleagues at the Research Institute for Pharmacy and Biochemistry for their contributions to the present study: Drs J. Holubek, E. Svátek, B. Schneider, M. Ryska, I. Koruna, J. Schlanger, O. Matoušová, Mrs A. Hrádková and Mrs Z. Janová (spectral data); Mrs J. Komancová, Mrs V. Šmídová and Mrs A. Svatošová (elemental analyses); Drs J. Metyš, J. Metyšová, M. Valchář, N. Dlohožková, J. Grimová, E. Maturová, S. Wildt, Mrs J. Ezrová, Miss A. Vykulilová. Mrs A. Kargerová, Mrs S. Schubertová, Mrs M. Jandová, Mrs J. Horáková, and Mrs E. Šulcová (pharmacology, biochemical pharmacology and pharmacological screening); Dr V. Holá (microbiological screening).

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Translated by the author (M.P.).