NONCATALEPTIC NEUROLEPTICS: NEW APPROACHES TO THE SYNTHESIS OF 2-CHLORO-10-(4-METHYLPIPERAZINO) AND -10-[4-(2-HYDROXYETHYL)PIPERAZINO]--10,11-DIHYDRODIBENZO[*b*,*f*]THIEPIN*

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Addition of bromine to 2-chlorodibenzo[*b*,*f*]thiepin (*V*) gave rise to a mixture of stereoisomeric dibromides *VIII-A* and *VIII-B* which was treated with methanolic potassium hydroxide to a mixture of bromoolefins *VI* and *VII* where the 2-chloro-10-bromo derivative *VI* predominates, a by-product being the thioxanthene derivative X. Compound *VI* reacts with 1-methylpiperazine and 1-(2-hydroxyethyl)piperazine in the presence of potassium tert-butoxide, giving rise mainly to enamines *XIV* and *XVII*. Reduction of the enamine *XVII* with zinc in acetic acid and subsequent alkaline hydrolysis resulted in amino alcohol *II*. Bromination of 8-chlorodibenzo[*b*,*f*]thiepin--10(11*H*)-one (*XXI*) gave rise to bromoketone *XXII* which reacted with 1-methylpiperazine and 1-(2-hydroxyethyl)piperazine to unstable amino ketones. Reduction of these amino ketones with sodium borohydride or diborane resulted in *cis*- and *trans*-amino alcohols *XXV*—*XXVIII* which were separated and identified by their ^{1}H-NMR spectra. Attempts to remove selectively the oxygen function in position 11 from these amino alcohols were not successful. Enamine *XVII* shows practically the same central depressant activity as the dihydro derivative *II* but at higher doses it is clearly cataleptic.

In a previous communication of this series[1] we summarized the reasons for our attempting to find a neuroleptic with suppressed cataleptic activity; in further work[2,3] we described the way which led to selecting 2-chloro-10-[4-(2-hydroxyethyl)piperazino]-10,11-dihydrodibenzo[*b*,*f*]thiepin (VÚFB-10.032) (*II*) for detailed studies. This compound was preferred to the previously prepared[4] methylpiperazine derivative *I* (doclothepin) because of the more suitable ratio of toxicity to depressant activity. Compound *II* was compared with clozapine[5] in the principal pharmacological tests[6], by the electroencephalographic method[7] and with a view to the effect on the metabolism of brain dopamine[8]. We described further the synthesis of 8-hydroxy derivatives of *I* and *II* as their potential metabolites and, in that context, we reported[9] some modifications of the initial steps of the relatively complicated syntheses of *I*

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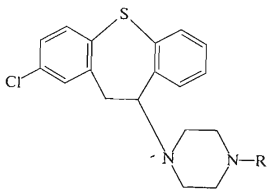
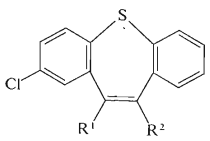
and *II*. It was the aim of the present work to find new approaches to noncataleptic 2-chloro-10-piperazino derivatives, especially to *II*, using compounds that occur in the synthesis of commercial 8-chloro-10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b*,*f*]thiepin[10,11] (octoclothepin) which is a position isomer of *I*.

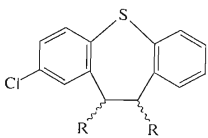


I, R = CH_3
II, R = CH_2CH_2OH

III, R = $CH_2CH_2OCOCH_3$
IV, R = CH_2CH_3



V, $R^1 = R^2 = H$
VI, $R^1 = H$, $R^2 = Br$
VII, $R^1 = Br$, $R^2 = H$



VIII, R = Br
IX, R = OCH_3

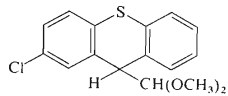
The first such starting compound was 2-chlorodibenzo[*b*,*f*]thiepin (*V*) which is a by-product of the final step of synthesis of octoclothepin: in the reaction of 8,10-dichloro-10,11-dihydrodibenzo[*b*,*f*]thiepin with 1-methylpiperazine[10,11] there arises some 80% of octoclothepin base plus 20% of the elimination product, *i.e. V*. It was our objective to add bromine to the olefinic double bond of *V* and to eliminate from the dibromide *VIII* formed a molecule of hydrogen bromide with the aid of a base. The expected products were the two isomeric bromoolefins *VI* and *VII*; compound *VI* offered the possibility of transformation to the desired *I* and *II*.

The bromination of the unsubstituted dibenzo[*b*,*f*]thiepin and subsequent dehydrobromination was studied first by this team[12]; only recently was the work taken up by Nógradi and coworkers[13] who had not seen the above paper[12] and who studied in some detail the stereochemistry of this bromine addition and the chemistry of the subsequent dehydrobromination. Dibenzo[*b*,*f*]-thiepin was brominated in a mixture of ether and chloroform and a high yield of a single crystalline dibromide[12] was obtained, the product being identical with *trans*-10,11-dibromo-10,11-di-

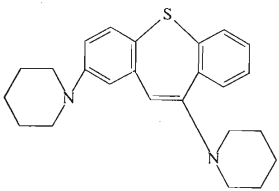
hydrodibenzo[*b,f*]thiepin, isolated by the above authors[13] as the main product; a minor product isolated and identified by these authors was the corresponding *cis*-dibromide. The dehydrobromination was done here[12] with 1-methylpiperazine or with 2,4,6-colidine; in both cases the sole resulting product was 10-bromodibenzo[*b,f*]thiepin. The same compound was the sole product during the dehydrobromination of the *trans*-bromide with the aid of potassium tert-butoxide in tert-butyl alcohol, carried out by Nógradi and coworkers[13]. During dehydrobromination with sodium methoxide in methanol[13] the 10-bromodibenzo[*b,f*]thiepin was the principal product but the reaction mixture contained relatively large amounts of the rearrangement product, identified as thioxanthene-9-carbaldehyde dimethyl acetal, and a small amount of the substitution product without rearrangement, identified as a mixture of *cis*- and *trans*-10,11-dimethoxy-10,11-dihydrodibenzo[*b,f*]thiepin. An attempt to react 10-bromodibenzo[*b,f*]thiepin with 1-methylpiperazine metallated with butyl lithium did not result in the desired 10-(4-methylpiperazino)-dibenzo[*b,f*]thiepin (the only isolated product was 1-butyl-4-methylpiperazine)[21].

In the series of chloro derivatives, *i.e.* in the case of 2-chlorodibenzo[*b,f*]thiepin (*V*), we carried out the bromine addition in acetic acid or in chloroform. The resulting mixtures of stereoisomeric dibromides *VIII* could not be separated on a preparative scale. Mechanical separation of the crystals yielded two substances, the crystallization of which resulted in pure dibromides *VIII-A* and *VIII-B*. The work carried out here did not permit to determine the configuration of these isomers or to decide which is the major and which the minor product. For further work, however, these problems are of no importance. In the reaction of a mixture of dibromides *VIIIAB* with excess methylpiperazine in a mixture of dichloromethane and ether at room temperature the product was not homogeneous and was separated mechanically and by crystallization into two pure isomeric substances, corresponding by their composition to bromoolefins *VI* and *VII*, the higher-melting product heavily predominating; after direct crystallization of the mixture it was the sole product. Even if the ^{1}H-NMR spectra could not decide about the identity of these products, the course of further work indicated that the higher-melting principal product is the desired 2-chloro-10-bromodibenzo[*b,f*]thiepin (*VI*) while the lower-melting minor isomer has the structure of *VII*. During dehydrobromination of a mixture of dibromides *VIIIAB* with boiling methanolic potassium hydroxide the situation was similar; the principal product was *VI*, the minor product isolated from the mother liquor being *VII*. When working with a larger batch there was a 3% yield of a bromine-free substance with formula $C_{16}H_{15}ClO_2S$, containing two methoxy groups in its molecule. According to Nógradi's work[13] it can be either *IX* or *X*. From the ^{1}H-NMR spectrum of the product and from its comparison with Nógradi's products our substance is seen to be 2-chlorothioxanthene-9-carbaldehyde dimethyl acetal (*X*). Its origin can be explained by the same mechanism as that proposed by Nógradi[13] in the dechloro series. In a reaction of a mixture of dibromides *VIIIAB* with potassium tert-butoxide in a mixture of tetrahydrofuran and tert-butyl alcohol in the presence of excess piperidine there was a fine yield of bromoolefin *VI* as the sole product. Attempts to transform this substance to 2-chlorodibenzo[*b,f*]thiepin-

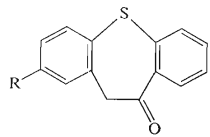
-10(11*H*)-one (*XIII*) by heating with sulfuric acid (130°C), with polyphosphoric acid (130°C), with boiling formic acid, boiling hydrochloric acid or fusion with potassium acetate (320°C) were not successful. Under the influence of acid agents most of the starting *VI* was recovered, in the reaction with potassium acetate there resulted polymeric products. Conversion of *VI* to ketone *XIII* was possible only in a reaction with piperidine in the presence of potassium tert-butoxide in a mixture of tetrahydrofuran and tert-butyl alcohol and subsequent hydrolysis of the unisolated enamine with hydrochloric acid. Crystallization of the crude product in which we assume the presence of a small amount of isomeric 8-chlorodibenzo[*b*,*f*]thiepin--10(11*H*)-one[10,11] (*XXI*), yielded 42% of ketone *XIII* (ref.[4,11,14]) which is applicable for the synthesis of *I* and *II* (ref.[3,4]). This result is now considered to be first evidence for compound *VI* being the main product of dehydrobromination of dibromides *VIIIAB*; it is assumed that the reaction does not proceed exclusively *via* the dehydrodibenzo[*b*,*f*]thiepin intermediate *XVIII* but that at least in part a direct nucleophilic substitution takes place with the result that most of the product carries the substituent in the same position as the starting substance.



X



XI

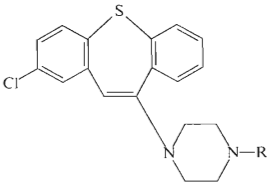


XII, R = N

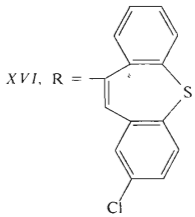
XIII, R = Cl

The reaction of bromoolefin *VI* with piperidine in the presence of excess sodium amide in boiling benzene results in compound $C_{24}H_{28}N_2S$ containing two piperidine residues per molecule. Its acid hydrolysis gives rise to the arylketone $C_{19}H_{19}NOS$ containing one piperidine residue. The products are expected to have structures

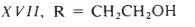
XI and *XII* although it is uncertain where the piperidine residues are located in the two molecules, their introduction apparently occurring *via* ynic intermediates[15–17]. The localization of the piperidine residue on the aromatic nucleus into the chlorine atom position in the starting compound is suggested by the analogy with a similar transformation of 2-chloro-10-methylphenothiazine to 2-morpholino-10-methylphenothiazine by a reaction with morpholine and sodium amide[18]. The spectra of *XI* and *XII* shown in the experimental section are in agreement with these structures.



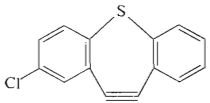
XIV, R = CH_3
XV, R = H



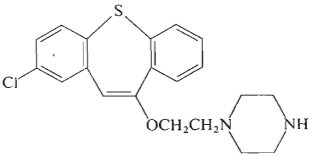
XVI, R =



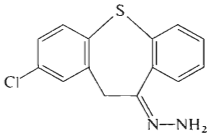
XVII, R = CH_2CH_2OH



XVIII



XIX



XX

Bromoolefin *VI* reacted then with excess 1-methylpiperazine in the presence of potassium tert-butoxide in a mixture of ether and tert-butyl alcohol. Isolation *via* the maleates yielded a mixture of bases which was separated chromatographically on alumina. The main product obtained was enamine[3] *XIV* (see also[19]) which is taken as evidence for the correctness of the structure *VI*. Even if one must assume in this case that the reaction proceeds at least partly through an elimination + addition mechanism, *i.e. via* the intermediate *XVIII* it has not been possible to detect as a product the isomeric 8-chloro-10-(4-methylpiperazino)dibenzo[*b*,*f*]thiepin[11,19–21]. On the

other hand, two further minor products were isolated during chromatography. The first of these is a high-melting base which is least polar of all the reaction mixture and, according to the mass spectrum, has an empirical formula of $C_{32}H_{24}Cl_2N_2S_2$. It has the structure of the double enamine *XVI* as indicated by its preparation through heating ketone *XIII* with piperazine monotosylate *in vacuo* at 190°C (for method see[11]). The second by-product is the most polar of the whole mixture and was isolated as maleate; its ^{1}H-NMR spectrum indicates structure *XV*. Its correctness was supported by an independent preparation of *XV* by the above reaction of ketone *XIII* with piperazine monotosylate when it is formed together with *XVI*. The formation of *XV* and *XVI* through the above reaction of *VI* with 1-methylpiperazine may be accounted for by the presence of 1–2% piperazine in the commercial preparation of 1-methylpiperazine and by a preferential reaction of this more reactive contaminant. Since the reduction of enamine *XIV* to doclothepin *I* is known[22] the attempt described here represents the attainment of another objective.

In analogy to the previous case, bromoolefin *VI* reacted with excess 1-(2-hydroxyethyl)piperazine in the presence of potassium tert-butoxide in a mixture of ether and tert-butyl alcohol. The main product isolated from the mixture of bases was enamine *XVII*, the identity of which was supported by spectra and transformation to *II*. Using chromatography, another more polar substance was isolated which was identified by analysis and ^{1}H-NMR spectrum as enol-ether *XIX* in mixture with the 8-chloro isomer[23] (about 55 : 45). The appearance of these products may be taken as evidence for the existence of dehydro-2-chlorodibenzo[*b*,*f*]thiepin (*XVIII*) as intermediate of the reactions; the formation of *XIX* and especially of its 8-chloro isomer can hardly be explained differently than by elimination + addition. The existence of dehydrodibenzo[*b*,*f*]thiepin intermediate was postulated by Tochtermann and coworkers[24]; in their case they were dealing with the corresponding 5,5-dioxide. Dehydrodibenzo[*b*,*f*]thiepin intermediates are mentioned in the patents of Richardson -Merrel[25] but no single experimental case is known that would support the existence of such intermediates. For comparison, enamine *XVII* was prepared directly from ketone *XIII* by a reaction with 1-(2-hydroxyethyl)piperazine and titanium tetrachloride in boiling benzene (method in[19,21,26]) and by heating with 1-(2-hydroxyethyl)piperazine monotosylate *in vacuo* at 190°C (method in[11]).

The enamine *XVII* was reduced to *II* by methods described for analogous cases. Most suitable appeared to be reduction with zinc in boiling acetic acid (method in[26–29]). At the same time, however, an O-acetylation took place so that the product obtained is a mixture of acetate *III* and amino alcohol *II* difficult to separate. Acetate *III* was prepared in a pure state by acetylation of *II* (ref.[3]) with acetic anhydride in boiling benzene. Alkaline hydrolysis of the crude product produced a fine yields of amino alcohol *II*. Much less suitable appeared to be the reduction of enamine *XVII* with diborane generated in the reaction of sodium borohydride with acetic acid in tetrahydrofuran (for method see[30]). The reduction is incomplete so that one

must separate the mixture of the starting enamine and the dihydro-product *II* formed; this was achieved by acid hydrolysis during which the enamine yields a readily separable ketone *XIII* and the water-soluble 1-(2-hydroethyl)piperazine. In attempts to reduce with gaseous diborane[31] or with diborane *in situ* generated in the reaction of sodium borohydride with boron trifluoride etherate in tetrahydrofuran[32] there was practically none of the desired reaction. In this context we characterized a new crystal modification of base *II*. Several other attempts to reduce enamine *XVII* to *II* were either unsuccessful or not suitable from the preparative point of view. Thus an attempt to reduce with sodium and 1-butanol results in a nonhomogeneous product which, according to TLC, consists of the starting compound and product *II*; using reduction with sodium and ethanol, reduction proceeds even to a lower degree. In an attempt to carry out reduction with boiling formic acid[21] the major product after subsequent hydrolysis with hydrochloric acid is ketone *XIII*; the presence of *II* was demonstrated only with the aid of TLC. Likewise, an attempt to reduce with iron in boiling acetic acid was unsuccessful. Introduction of mercury with mercuric acetate in tetrahydrofuran and subsequent demercurization with sodium borohydride reported to be a general method of transforming enamines to tertiary amines[33] was similarly unsuccessful. The last attempt was to use hydrazine in boiling ethanol with simultaneous introduction of air, *i.e.* in fact using the diimide[34–36]. This led to a fine yield of a crystalline product which was identified as hydrazone *XX*; the only reaction that has taken place was the hydrazinolysis of the starting enamine.

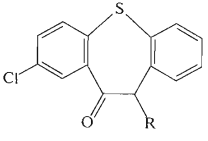
Attempts were made to resolve the racemic aminoalcohol *II* to the antipodes but with no success. Salts of base *II* with dibenzoyl-L(+)tartaric acid, dibenzoyl-D(−)-tartaric acid and 2,3; 4,6-di-O-iso-propylidene-2-oxo-L(−)-gulonic acid were not suitable for the purpose. The readily crystallizing neutral L(+)-tartrate does not change its melting point or optical rotation on repeated crystallization and after several crystallizations it yields by alkalification the optically inactive base *II*.

In the second part of the work the starting compound used was 8-chlorodibenzo-[*b*,*f*]thiepin-10(11*H*)-one (*XXI*, an intermediate of the synthesis of octoclothepin[10,11]). It was intended to convert this ketone by bromination to the bromo ketone *XXII*, then to carry out substitution with 1-methylpiperazine or with 1-(2-hydroxyethyl)piperazine and finally to remove selectively the oxygen function in position 11.

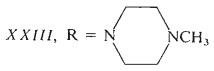
Bromination of the unsubstituted dibenzo[*b*,*f*]thiepin-10(11*H*)-one was described here[12] (using bromine in chloroform, see also[26]) and in patents of Geigy[37] (using bromine in carbon disulfide). It has been further reported that substitution reaction of the 11-bromodibenzo[*b*,*f*]-thiepin-10(11*H*)-one and analogous substituted in the ring with the above piperazine derivatives give rise to the corresponding piperazino ketones[12,26,37] which can be reduced with complex hydrides to the corresponding amino alcohols[12,26,38].

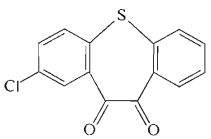
Bromination of ketone[10,11] *XXI* in chloroform yielded a satisfactory amount of bromo ketone *XXII*. This compound is mentioned in patents[37] but explicitly its

preparation has not been described and no physical constants have been reported. An attempt to remove the oxo group in *XXII* by ionic hydrogenation with triethylsilane[39] and trifluoroacetic acid[40–42] was not successful; it resulted in an oily product which reacted with 1-methylpiperazine in boiling chloroform to a minute amount of basic product free of chlorine and sulfur. Substitution reaction of bromoketone *XXII* with 1-methylpiperazine in boiling dichloromethane yielded as the main product aminoketone *XXIII* which is mentioned in patents[37]. A neutral by-product isolated here was 2-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10,11-dione (*XXIV*). This diketone is mentioned in patents[43] without any characterization; it should have been prepared by oxidation of the corresponding monoketone with selenium dioxide but it may be safely assumed that it has never been prepared. 10,11-Dihydrodibenzo-[*b*,*f*]thiepin-10,11-dione was prepared in a considerable amount in an earlier work[12] as a neutral by-product of the reaction of 11-bromodibenzo[*b*,*f*]thiepin-10(11*H*)-one with 1-methylpiperazine in benzene; its formation was explained as being due to a parallel disproportionation reaction of a type similar to that described in the reaction of α-bromodeoxybenzoin with water[44]. It was surprising, however, that the second postulated disproportionation product, *i.e.* dibenzo[*b*,*f*]thiepin-10(11*H*)-one, was detected in a rather small amount. The work carried out here indicates that an oxidative mechanism participates in the formation of diketone *XXIV* when



XXI, R = H
XXII, R = Br

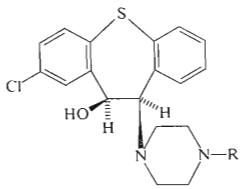




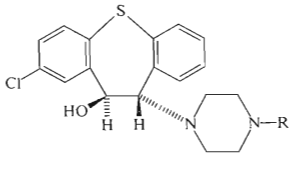
XXIV

atmospheric oxygen is involved. If the reaction of bromo ketone *XXII* with 1-methylpiperazine is carried out at room temperature and using a long reaction period (two weeks) which permitted the mixture to be in long contact with air the yield of the diketone *XXIV* was almost as high as that of base *XXIII*. Chromatography of the crude reaction product on alumina or on silica gel did not lead to isolation of ketone *XII*. Patents of Geigy[37] describing similar substitution reactions do not mention the formation of diketones. However, we are apparently dealing here with a general

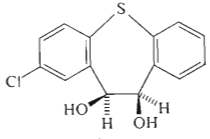
reaction type since a diketone was encountered in the reaction of 8-methoxy-11-bromodibenzo[*b*,*f*]thiepin-10(11*H*)-one with 1-methylpiperazine[45]. Amino ketone *XXIII* is apparently unstable; in an attempt to prepare its maleate it was split and the isolated salt was identified as bis(hydrogen maleate) of 1-methylpiperazine[46] (see also[45]). Two attempts were made to hydrogenolyze *XXIII* in order to obtain the deoxo base *I*. The first was a reaction with excess sodium dihydridobis(2-methoxyethoxy)-aluminate in boiling benzene (for hydrogenolysis of ketones using this agent see[47–51]), the second was a reductive silylation by combination of trichlorosilane with tertiary amine[52,53]. The tertiary amine used here was the methylpiperazine residue of the starting compound *XXIII*. Both attempts were unsuccessful.



XXV, R = CH_3
XXVI, R = CH_2CH_2OH



XXVII, R = CH_3
XXVIII, R = CH_2CH_2OH



XXIX

Reduction of the crude product of the reaction of bromo ketone *XXII* with 1-methylpiperazine in dioxane using sodium borohydride yielded a mixture which was separated into a basic and a neutral product. The base was purified by crystallization and using the ^{1}H-NMR spectrum it was identified as *cis*-amino alcohol *XXV* (two doublets at 5·22 and 4·13 ppm for single protons corresponding to 11-H and 10-H). The neutral product was identified as *cis*-diol *XXIX* (in the ^{1}H-NMR spectrum there were two doublets at 5·29 and 5·12 ppm for single protons corresponding to 10-H and 11-H). This diol is apparently the product of reduction during the substitution reaction of the diketone *XIV* formed here. Reduction of pure aminoketone *XXIII* with diborane, generated in the reaction of sodium borohydride with boron

trifluoride etherate in tetrahydrofuran resulted in a nonhomogeneous product from which a higher-melting amino alcohol was isolated (the identity was checked by IR and mass spectrum) which is ascribed without further evidence the structure of the *trans*-aminoalcohol *XXVII*. Patents of Geigy[38] describe the preparation of the amino alcohol by reduction of amino ketone *XXIII* with lithium aluminium hydride; the m.p. reported indicates that this must be a stereoisomeric mixture with predominating *cis*-isomer *XXV*. Unsuccessful attempts were made to remove the hydroxyl group from the molecule of *cis*-amino alcohol *XXV*. Reduction of non-characterized methanesulfone ester (prepared by reaction of *XXV* with methanesulfonyl chloride in pyridine) with lithium aluminium hydride in ether yielded a nonhomogeneous product with a low content of chlorine; together with removing the oxygen function there proceeds a hydrogenolysis of the aryl chloride. An attempt to carry out reduction with sodium in liquid ammonia leaves most of the starting compound *XXV* unreacted; to a small extent the molecule undergoes a more profound destruction as indicated by the thiophenol smell appearing after acidification of the residue. Unsuccessful attempts at dehydrating the similar 11-(4-methylpiperazin)-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-ol to the corresponding enamine using heating with *p*-toluenesulfonic acid[12] or with acetic anhydride[26] has been reported before.

A substitution reaction of bromo ketone *XXII* with 1-(2-hydroxyethyl)piperazine in dioxane was carried out and the amino ketone formed (see[37]) was reduced without isolation by sodium borohydride. The heavily predominating product (71%) was homogeneous amino alcohol which, according to the ^{1}H-NMR spectrum, has the structure of the *cis*-isomer *XXVI*. The *trans*-isomer *XXVIII* was isolated from the mother liquors in a 7% yield. Both isomers were converted to maleates. Several abortive attempts were undertaken to reduce the *cis*-amino alcohol *XXVI* to *II*: using zinc in acetic acid (nonhomogeneous product plus the starting compound and its acetates), using triethylsilane and trifluoroacetic acid[40,54], sodium borohydride in hexamethylphosphotriamide at 140°C, using a complex of pyridine–sulfuric oxide and finally by lithium aluminium hydride in tetrahydrofuran[55]. The new identified product was obtained by a sequence of reactions started with the reaction of *XXVI* with methanesulfonyl chloride in pyridine and terminated by reduction of the crude product with sodium borohydride in aqueous diethylene glycol dimethyl ether; both oxygens were then removed and the product was identified as the N-ethyl derivative *IV*.

Of the compounds prepared, the following were evaluated as potential noncataleptic neuroleptics: acetate *III* (as maleate VÚFB 12.391), enamine *XVII* (as maleate VÚFB 10.869) and *cis*-amino alcohol *XXVI* (as maleate VÚFB 10.702) (Dr A. Dlabač in the pharmacological department of this institute). These three compounds were applied in the tests *per os* in the form of the salts shown but the doses reported refer to the corresponding bases.

Compound *III* has acute toxicity LD_{50} for male mice of 94 mg/kg. Its mean effective dose ED_{50} bringing about ataxia in female mice in the rotating-rod test was 3·8 mg/kg (maximum effect 2–3·5 h after application). In a catalepsy test in female rats the compound is practically inactive; a dose of 10 mg/kg brings about catalepsy in 10% animals, a dose of 100 mg/kg in 30% animals. The compound is equally inactive in the antiapomorphine test using male rats: a dose of 50 mg/kg does not influence apomorphine-induced chewing and agitation. Enamine *XVII*: LD_{50} = c. 350 mg/kg; ED_{50} (rotating rod) = 1·17 mg/kg; ED_{50} (catalepsy) = = 42 mg/kg. Amino alcohol *XXVI*: LD_{50} is higher than 400 mg/kg (only 20% animals died after this dose); ED_{50} (rotating rod) = 60 mg/kg (maximum at 2 h after application); in the catalepsy test it is inactive up to 50 mg/kg.

In comparison with *II* (refs[2,3,6–8]), its acetate *III* is almost equally toxic, almost 5 times less effective in the rotating-rod test and similar in its inactivity in the catalepsy test. Enamine *XVII*, corresponding to *II*, is surprisingly less toxic, practically equally effective as central depressant and, in contrast with the 10,11-dihydro derivative *II* it is clearly cataleptic in higher doses. The 11-hydroxy derivative *XXVI* of *II* is 5 times less toxic, by two orders of magnitude less effective as central depressant (rotating rod) and it is completely ineffective cataleptically.

The compounds were further evaluated (as the salts shown) by Drs J. Turinová and A. Čapek (bacteriological department of this institute) using *in vitro* tests for antimicrobial activity towards a standard set of microorganisms (the minimum inhibitory concentrations are shown in μg/ml unless they exced 100 μg/ml): *Staphylococcus pyogenes aureus*, *III* 100; *Mycobacterium tuberculosis* H37Rv, *III* 12·5, *XVII* 25, *XXVI* 50; *Saccharomyces pasterianus*, *XVII* 50, *XXVI* 100; Trichophyton mentagrophytes, *III* 12·5, *XVII* 6·2, *XXVI* 50; *Candida albicans*, *XVII* 50, *XXVI* 100; *Aspergillus niger*, *XVII* 100. All the three compounds were inactive up to 100 μg/ml against the following microorganisms: *Streptococcus* β-*haemolyticus*, *Streptococcus faecalis*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Proteus vulgaris*. As occurs frequently in the series of 10-piperazinodibenzo[*b*,*f*]thiepin derivatives[56,57] there is here an antituberculosis activity and further an activity toward lower fungi (yeasts, molds). Remarkable is the activity of enamine *XVII* against *Trichophyton mentagrophytes*.

EXPERIMENTAL

The melting points of analytical preparations were determined in Kofler's block and are not corrected; the samples were dried *in vacuo* at 0·5 Torr over P_2O_5 at room temperature or at 77°C. The UV spectra (in methanol) were recorded in a Unicam SP 8000 spectrophotometer, the IR spectra (in Nujol unless stated otherwise) in a Unicam SP 200G spectrophotometer. The ^{1}H-NMR spectra (in $CDCl_3$ unless stated otherwise) in a Tesla BC 487 spectrometer (80 MHz) and mass spectra in a MS 902 AEI spectrometer. The homogeneity of the substances was checked by thin-layer chromatography on silica gel.

10,11-Dibromo-2-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin (*VIII*)

A. A solution of 9·3 g V (ref.[10]) was prepared at 50°C in 100 ml acetic acid and, after cooling, 6·4 g bromine in 20 ml acetic acid was added dropwise over a period of 5 min at 25°C. The mixture

was stirred for 30 min, cooled to 5°C and the precipitated product (a mixture of stereoisomeric dibromides *VIII*) was filtered; 13·15 g (86%), m.p. 105—147°C. Crystallization of the mixture from benzene and light petroleum does not separate the isomers. The mixture consists of two types of crystals: flakes and prisms. The sample was separated mechanically. From 10·0 g of the mixture a total of 3·2 g lighter flakes were separated; m.p. 111—112·5°C; after repeared crystallization from a mixture of benzene and light petroleum, m.p. 113—114°C. The substance is dibromide *VIII-A*. IR spectrum: 760, 816, 870 (4 and 2 adjacent and solitary Ar-H), 1 590 cm^{-1} (Ar). ^{1}H-NMR spectrum: δ 7·00—7·50 (m, 7 H, Ar—H), 5·80 (s, 2 H, Ar—CHBr—CHBr—Ar). For $C_{14}H_9Br_2ClS$ (404·6) calculated: 41·56% C, 2·24% H, 8·76% Cl, 7·93% S; found: 42·06% C, 2·26% H, 8·44% Cl, 7·82% S.

Further separated were 1·5 g darker prisms melting at 155—160°C (5·3 g of an unresolved mixture remained). After several crystallizations from a mixture of benzene and light petroleum this product was homogeneous; m.p. 168—170°C. It is dibromide *VIII-B*. IR spectrum: 740, 775, 812, 870, 888 (4 and 2 adjacent and solitary Ar—H), 1 575 cm^{-1} (Ar). For $C_{14}H_9Br_2ClS$ (404·6) calculated: 41·56% C, 2·24% H, 39·51% Br, 8·76% Cl, 7·93% S; found: 41·64% C, 2·19% H, 39·37% Br, 8·73% Cl, 8·18% S.

B. Powdery $CaCO_3$ (5·0 g) was suspended in a solution of 13·8 g *V* (ref.[10]) in 80 ml chloroform and a solution of 9·0 g bromine in 20 ml chloroform was added at 0°C under stirring. The mixture was stirred for 3 h, the inorganic fraction was filtered, the filtrate was washed with a solution of $NaHSO_3$, dried with $MgSO_4$, evaporated, and the residue was recrystallized from 40 ml benzene; 16·6 g (73%) of a mixture of dibromides *VIII-A* and *VIII-B*; m.p. 107—145°C.

10-Bromo-2-chlorodibenzo[*b*,*f*]thiepin (*VI*)

A. A solution obtained by dissolving 8·1 g of a mixture of dibromides *VIIIAB* in a solution of 10 ml 1-methylpiperazine in 80 ml dichloromethane and 30 ml ether was left to stand for 10 days at room temperature. The precipitated 1-methylpiperazine hydrobromide (2·1 g) was then filtered, the filtrate was washed with water, 5% hydrochloric acid, it was dried with $MgSO_4$ and evaporated. A total of 6·5 g (100%) of a mixture of bromo derivatives *VI* and *VII* was obtained and crystallized from ethanol. From the crystalline mixture it was possible to separate mechanically first 4·5 g (69%) of product *VI*, melting at 112—115°C (prisms). Further crystallization from ethanol yielded the pure product, melting at 115—116°C. UV spectrum: λ_{max} 261 nm (log ε 4·28), 295 nm (3·87). IR spectrum: 748, 818, 880 (4 and 2 adjacent and solitary Ar—H), 1 542, 1 572, 1 608 cm^{-1} (Ar). ^{1}H-NMR spectrum: δ 7·73 (s, 2 H, 1,11-H_2), 7·00—7·50 (m, 6 H, remaining Ar—H). For $C_{14}H_8BrClS$ (323·7) calculated: 51·95% C, 2·49% H, 24·69% Br, 10·95% Cl, 9·91% S; found: 52·04% C, 2·47% H, 24·37% Br, 10·81% Cl, 9·85% S.

Further separated from the mixture were needles (0·1 g) which change their modification at 103—105°C and melt again at 107—109°C. After recrystallization from ethanol the higher-melting modification melts at 109—110°C. The substance is homogeneous and is postulated to have the structure of 10-bromo-8-chlorodibenzo[*b*,*f*]thiepin (*VII*). For $C_{14}H_8BrClS$ (323·7) calculated: 51·95% C, 2·49% H, 24·69% Br, 10·93% Cl, 9·91% S; found: 52·05% C, 2·53% H, 24·72% Br, 10·97% Cl, 10·08% S.

B. A mixture of 14·9 g dibromide *VIIIAB*, 15 g KOH and 300 ml methanol was refluxed for 6 h. On standing overnight, 9·6 g (81%) crude *VI* crystallized, m.p. 111—114°C. After a single crystallization from ethanol the m.p. was 115—116°C and the product was identical with that obtained under *A*. The methanolic filtrate was evaporated, the solution was washed with water and, after drying, evaporated again. The residue (2·6 g oil) crystallized from ethanol to 1·5 g

(13%) compound *VII* melting at 104–106°C, after further crystallization from ethanol at 107 to 109°C; it is identical with the product obtained under *A*.

C. A solution of 16 g bromine in 10 ml chloroform was added dropwise under stirring to a solution of 24·5 g *V* (ref.[10]) in 100 ml chloroform over a period of 30 min. The mixture was stirred for 3 h and chloroform was evaporated. The residue was dissolved in 100 ml tetrahydrofuran, 25 g piperidine was added, followed with 20 g potassium tert-butoxide in 200 ml tert-butyl alcohol. The mixture was refluxed under stirring for 18 h. After cooling, it was decomposed with 80 ml water and 80 ml concentrated hydrochloric acid, after 1 h of stirring it was shaken with water and extracted with benzene. Processing of the extract yielded a residue which was crystallized from a mixture of ethanol and benzene; 22·8 g (71%) compound *VI*, m.p. 114–115°C.

2-Chlorothioxanthene-9-carbaldehyde Dimethyl Acetal (*X*)

Like in the preceding case under *C*, 209·3 g *V* (ref.[10]) was brominated with 137 g bromine in 1·1 litre chloroform over 60 min. After 3 h of stirring, the chloroform was evaporated, the residue was briefly boiled with 1·5 litre methanol, 200 g KOH was added in parts and the mixture was refluxed for 6 h under stirring. After standing overnight the crude *VI* was filtered and recrystallized from a mixture of ethanol and benzene; 152·6 g (55%), m.p. 114–116°C. The methanolic mother liquor was partly evaporated, the residue was diluted with water and extracted with benzene. The extract was washed with dilute hydrochloric acid and water, dried and evaporated. The residue crystallized from ethanol to 7·2 g (3%) of substance *X*; analytical sample, m.p. 128 to 129°C (ethanol). UV spectrum: λ_{max} 270 nm (log ε 3·61), infl. 255 nm (3·92). IR spectrum: 738, 819, 850 (4 and 2 adjacent and solitary Ar—H), 1079, 1102 (C—O—C—O—C), 1448, 1460, 1570, 1590 (Ar), 2820 cm^{-1} (OCH_3). ^{1}H-NMR spectrum: δ 7·00–7·40 (m, 7 H, Ar—H), 4·46 (d, J = 8·0 Hz, 1 H, 9-H), 4·10 (d, J = 8·0 Hz, 1 H, O—CH—O), 3·11 and 3·06 (2 s, 6 H, 2 OCH_3). For $C_{16}H_{15}ClO_2S$ (306·8) calculated 62·63% C, 4·93% H, 11·56% Cl, 10·45% S; found: 62·51% C, 4·99% H, 11·29% Cl, 10·50% S.

2-Chlorodibenzo[*b,f*]thiepin-10(11*H*)-one (*XIII*)

A solution of 90 g potassium tert-butoxide in 1 litre tert-butyl alcohol was added to a solution of 133 g *VI* in a mixture of 76 g piperidine in 1 litre tetrahydrofuran and the mixture was refluxed for 17 h. It was decomposed while hot by a slow addition of 800 ml 20% hydrochloric acid and extracted with dichloromethane. Ketone *XIII* predominates in the residue after evaporation of the extract. After two crystallization from a mixture of ethanol and benzene the yield was 44·3 g (42%) pure ketone *XIII* melting at 142–144°C. For the same product obtained in a different way we reported before[4] a m.p. of 142·5–143°C.

2,10-Bis(piperidino)dibenzo[*b,f*]thiepin (*XI*)

Piperidine (30 ml) was added to a suspension of 7·5 g triturated 70% $NaNH_2$ in some benzene and this was followed after 30 min of refluxing by 9·5 g *VI*. The mixture was refluxed under stirring for 6 h, left to stand overnight and decomposed first by adding dropwise 6 ml ethanol and then water. The product was extracted with benzene, the benzene extract was washed with 10% hydrochloric acid, the precipitate was filtered and combined with the acid aqueous phase of the filtrate. Alkalification and further processing produced no characterized substance from this fraction. The original benzene solution was evaporated and the oil obtained (8·0 g) was chromatographed on a column of 200 g silica gel. A mixture of benzene and light petroleum was applied to elute 0·28 g of the starting *VI*. This was followed by 2·38 g (21%) *XI* which crystallizes from

a mixture of cyclohexane and light petroleum and melts at 182—183°C. UV spectrum: infl. 233 nm (log ε 4·31), λ_{max} 273 nm (4·07), 330 nm (3·91). IR spectrum (KBr): 729, 752, 762, 788, 856 (4 and 2 adjacent and solitary Ar—H), 1 209, 1 219, 1 230, 1 339 (C—N), 1 551, 1 573, 1 605 (Ar), 2 800, 2 825 cm^{-1} (CH_2N). ^{1}H-NMR spectrum: δ 6·70—7·80 (m, 7 H, Ar—H), 638 (s, 1 H, 11-H), 2·30—3·30 (m, 8 H, 4 NCH_2), 1·60 (m, 12 H, remaining 6 CH_2). For $C_{24}H_{28}N_2S$ (376·6) calculated: 76·55% C, 7·49% H, 7·44% N, 8·52% S; found: 76·82% C, 7·52% H, 7·31% N, 8·13% S.

Chromatography was continued by elution with benzene and chloroform. After a nonhomogeneous intermediate fraction there was eluted 2·0 g (22%) oily 2-piperidinodibenzo[*b,f*]thiepin-10(11*H*)-one (*XII*). Neutralization with an ether solution of hydrogen chloride yields a hydrochloride which crystallizes from a mixture of acetone, ethanol and ether and which melts at 165 to 170°C. UV spectrum: λ_{max} 238 nm (log ε 4·31), 257·5 nm (4·32), 343 nm (3·95). IR spectrum (KBr): 759, 819, 853 (4 and 2 adjacent and solitary Ar—H), 1 481, 1 583 (Ar), 1 679 (Ar—CO), 2 448 cm^{-1} (NH^+). ^{1}H-NMR spectrum (CD_3SOCD_3): δ 7·00—8·00 (m, 7 H, Ar—H), 4·25 (s, 2 H, $ArCH_2CO$), c. 3·30 (m, 4 H, CH_2NCH_2), 1·30—2·00 (m, 6 H, remaining 3 CH_2). For $C_{19}H_{20}ClNOS$ (345·9) calculated: 65·97% C, 5·83% H, 10·25% Cl, 4·05% N, 9·27% S; found: 65·50% C, 5·89% H, 10·32% Cl, 4·06% N, 9·37% S.

2-Chloro-10-(4-methylpiperazino)dibenzo[*b,f*]thiepin (*XIV*)

A solution of 7·5 g potassium tert-butoxide in 150 ml tert-butyl alcohol was added to a solution of 20·0 g *VI* in 300 ml ether and 50 ml 1-methylpiperazine and the mixture was refluxed for 13 h. After cooling, it was washed with water, dried with K_2CO_3 and evaporated. The remaining oil (25 g) was dissolved in ethanol and, by neutralization with 6·9 g maleic acid, it was converted to 24·8 g nonhomogeneous maleate, melting at 216—218°C (for maleate of the pure *XIV*, patent[19] gives a m.p. of 239°C under decomposition). The total amount of maleate was decomposed with NH_4OH, the base was isolated by extraction with benzene and chromatographed on a column of 600 g alumina (activity II). The least polar fraction eluted with benzene was 1·5 g compound crystallizing from a mixture of ethanol and benzene and melting at 298—302°C. Analysis and mass spectrum (molecular ion *m/e* 570; principal fragment *m/e* 298) indicate the formula $C_{23}H_{24}$. $Cl_2N_2S_2$. Comparison with an authentic product identifies the compound as 1,4-bis(2-chlorodibenzo[*b,f*]thiepin-10-yl)piperazine (*XVI*). UV spectrum: infl. 240 nm (log ε 4·03), λ_{max} 266 nm (3·83), 313 nm (3·73). IR spectrum (KBr): 754, 763, 807, 880 (4 and 2 adjacent and solitary Ar—H), 1 009 (C=C—H), 1 091, 1 201, 1 215 (C—N), 1 543, 1 571, 1 601 (Ar), 2 825 cm^{-1} (CH_2—N). For $C_{32}H_{24}Cl_2N_2S_2$ (571·6) calculated: 67·24% C, 4·24% H, 12·41% Cl, 4·90% N, 11·22% S; found: 68·01% C, 4·34% H, 12·26% Cl, 4·50% N, 11·24% S.

On continuing the chromatography a mixture of benzene and chloroform and then chloroform alone eluted a total of 13·5 g (64%) *XIV* which crystallizes from ethanol and melts at 147 to 148°C (in agreement with an earlier report[3]). IR spectrum: 772, 759, 819, 878 (4 and 2 adjacent and solitary Ar—H), 1 545, 1 574 (Ar), 1 607 (Ar—C=C), 2 800 cm^{-1} (CH_2—N). For $C_{19}H_{19}Cl$. N_2S (342·9) calculated: 66·55% C, 5·59% H, 8·17% N; found: 66·79% C, 5·68% H, 8·14% N.

The most polar fraction was eluted with ethanol: 1·6 g oily base which was neutralized with maleic acid in a mixture of ethanol and ether to yield 1·2 g maleate melting at 202—203°C. As follows from the analysis, the ^{1}H-NMR spectrum and comparison with an authentic product, this is maleate of base *XV*. The oily base set free from the maleate was used for measuring the ^{1}H-NMR spectrum which indicates a contamination with the 8-chloro-10-piperazino isomer: δ 6·90—7·70 (m, 7 H, Ar—H), 6·12 and 6·28 (2 s, together 1 H, ArCH=), 2·90 (bs, 8 H, 4 NCH_2 of piperazine), 1·90 (s, 1 H, disappears after D_2O, NH).

2-Chloro-10-piperazinodibenzo[*b,f*]thiepin (*XV*)

A mixture of 5·2 g *XIII* (ref.[4]), 38·8 g piperazine hexahydrate and 36 g mononhydrate of *p*-toluenesulfonic acid was heated for 1 h in an open flask on a 160—170°C bath and then for 2 h *in vacuo* at 190°C. After decomposition with dilute NH_4OH it was extracted with benzene. Filtration produced 1·5 g insoluble substance which crystallizes from a mixture of toluene and 1-propanol and which melts at 305—308°C under decomposition It is 1,4-bis-(2-chlorodibenzo[*b,f*]thiepin--10-yl)piperazine (*XVI*) which is identical with the low-polar by-product of preparation of *XIV* (mixed melting point and TLC). Evaporation of the benzene extract yielded 4·7 g (71%) oily base *XV* which was neutralized with maleic acid in ethanol to yield 6·0 g maleate, melting at 202 to 203°C (ethanol). For $C_{22}H_{21}ClN_2O_4S$ (445·0) calculated: 59·39% C, 4·76% H, 7·97% Cl, 6·29% N, 7·21% S; found: 59·17% C, 4·66% H, 8·16% Cl, 6·42% N, 7·20% S.

2-Chloro-10-[4-(2-hydroxyethyl)piperazino]dibenzo[*b,f*]thiepin (*XVII*)

A. A solution of 22·5 g potassium tert-butoxide in 450 ml tert-butyl alcohol was added to a solution of 60 g *VI* in 900 ml ether and 150 ml 1-(2-hydroxyethyl)piperazine and the mixture was refluxed for 15 h. After cooling, it was washed with water, dried with K_2CO_3 and partly evaporated. On standing, 18·3 g nearly pure enamine *XVII* precipitated; m.p. 166—169°C; the analytical product, m.p. 169—170°C (ethanol–benzene). UV spectrum: infl. 240 nm (log ε 4·28), 267 nm (4·06), λ_{max} 307 nm (3·98). IR spectrum: 754, 769, 809, 876 (4 and 2 adjacent and solitary Ar—H), 1045, 1090 (CH_2OH), 1219 (C—N), 1380 (C—OH), 1545, 1571 (Ar), 1603 (Ar—C=C), 3170, 3420 cm^{-1} (OH). ^{1}H-NMR spectrum: δ 6·90—7·70 (m, 7 H, Ar—H), 6·18 (s, 1 H, ArCH=), 3·62 (t, J = 6·0 Hz, 2 H, CH_2O), 3·00 (def. t, 4 H, $CH_2N^1CH_2$ of piperazine), 2·80 (s 1 H, OH), 2·60 (def. t, 6 H, remaining NCH_2). For $C_{20}H_{21}ClN_2OS$ (372·9) calculated: 64·41% C, 5·68%H, 9·51% Cl, 7·51% N, 8·60% S; found: 64·46% C, 5·83% H, 9·46% Cl, 7·27% N, 8·84% S.

Maleate, m.p. 205—206°C (ethanol–ether). For $C_{24}H_{25}ClN_2O_5S$ (489·0) calculated: 58·95% C, 5·15% H, 7·25% Cl, 5·73% N, 6·56% S; found: 58·48% C, 5·24% H, 7·38% Cl, 5·53% N, 6·82%S.

The mother liquor after base *XVII* was evaporated and the residue (37·2 g) was chromatographed on a column of 500 g alumina (activity II). Benzene eluted 22·0 g of the starting *VI* (m.p. 113—115°C). Chloroform was then applied to elute further 13·8 g pure base *XVII* so that the total yield is 32·1 g (73% *per conversion*). Finally, ethanol was used to elute 1·95 g 2-chloro--10-(2-piperazinoethoxy)dibenzo[*b,f*]thiepin (*XIX*) in mixture with the 8-chloro isomer (according to the ^{1}H-NMR spectrum in a ratio of about 55 : 45). Neutralization with maleic acid yields di(hydrogen maleate) which crystallizes from 95% ethanol as hemihydrate and melts at 144—145°C. UV spectrum: λ_{max} 264 nm (log ε 4·36), infl. 300 nm (3·95). For $C_{28}H_{29}ClN_2O_9S$ + 0·5 H_2O (614·1) calculated: 54·77% C, 4·92% H, 5·77% Cl, 4·56% N, 5·22% S; found: 54·96% C, 4·91% H, 5·74% Cl, 4·51% N, 5·30% S. For maleate of a differently prepared 8-chloro-10-(2--piperazinoethoxy)dibenzo[*b,f*]thiepin patent[23] shows a m.p. of 153—156°C under decomposition. The oily base released from our maleate was used for obtaining the ^{1}H-NMR spectrum: δ 7·10—7·40 (m, 7 H, Ar—H), 6·39 and 6·23 (2 s, together 1 H, ArCH=), 4·16 (t, J = 6·0 Hz, 2 H, OCH_2), 2·98 (def. t, 4 H, $CH_2N^4CH_2$ of piperazine), 2·94 (s, 1 H, NH), 2·85 (t, J = 6·0 Hz, 2 H, CH_2N in a chain), 2·59 (def. t, 4 H, $CH_2N^1CH_2$ of piperazine).

B. A solution of 4·0 g $TiCl_4$ in 20 ml benzene was added to a mixture of 5·2 g *XIII* (ref.[4]), 50 ml benzene and 13 g 1-(2-hydroxyethyl)piperazine and the mixture was refluxed for 24 h, decomposed with water, the insoluble fraction was filtered, washed with water and the benzene layer of the filtrate was evaporated after separation. Crystallization of the residue (5·7 g) from ethanol recovered 4·0 g of the starting *XIII* melting at 143—144°C. The mother liquor yielded 0·5 g (29% *per conversion*) crystalline enamine *XVII*, melting at 168—170°C.

C. A mixture of 5·2 g *XIII* (ref.[4]), 9·1 g 1-(2-hydroxyethyl)piperazine and 13·3 g monohydrate of *p*-toluenesulfonic acid was heated for 1 h in a 160—170/°C bath and then for 2 h *in vacuo* at 190°C. After decomposition with dilute NH_4OH it was extracted with benzene, the extract was dried with K_2CO_3 and evaporated. The residue crystallized from ethanol to 5·1 g (68%) enamine *XVII* which melts at 167—169°C and then, after a change of crystal modification, melts again at 172—173°C. The identity of the products obtaind according to *A*, *B*, and *C* was checked by mixed melting points and with the aid of TLC.

10-[4-(2-Acetoxyethyl)piperazino]-2-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin (*III*)

A. *XVII* (21·5 g) was added under stirring to a boiling mixture of 180 ml acetic acid and 40 g Zn, the mixture was refluxed for 20 min, filtered, the filtrate was evaporated *in vacuo* and the residue was divided between benzene and excess dilute hydrochloric acid. The acid aqueous phase was combined with the salted-out oily hydrochloride, alkalified with NH_4OH and the base was isolated by extraction with benzene; 15·3 g oily compound. According to TLC this is a mixture of *II* with the less polar base *III*. The mixture was dissolved in ether and, by adding a solution of 4·6 g succinic acid in acetone, an oily succinate was precipitated, corresponding mainly to base *II*. After shaking with water, the aqueous phase was separated, alkalified with NH_4OH and the base was isolated by extraction with benzene; 11·3 g (according to TLC mainly *II*). Neutralization with succinic acid in acetone yielded a crude succinate of base *II*, melting at 152—165°C; the base *II* released from the succinate melted at 98—102°C. Evaporation of the ether layer yielded 4·0 g of another base where acetate *III* predominates according to TLC. This base was converted to bis(hydrogen maleate) which was repeatedly crystallized from acetone to melt at 151—152°C. An analysis indicated contamination with maleate of base *II*. For $C_{30}H_{33}ClN_2O_{10}S$ (649·1) calculated: 55·51% C, 5·12% H, 5·46% Cl, 4·32% N, 4·94% S; found: 56·39% C, 5·34% H, 5·86% Cl, 4·52% N, 5·32% S.

The crude base was used to prepare the dihydrochloride which is also contaminated with the dihydrochloride of *II*, m.p. 203—204°C (ethanol). IR spectrum: 754, 831, 881 (4 and 2 adjacent and solitary Ar—H), 1015, 1091 (C—O), 1046 (CH_2OH), 1230, 1250 (CH_3COOR), 1560, 1580 (Ar), 1742 (COOR), 2440, 2540 (NH^+), 3260, 3340 cm^{-1} (OH). For $C_{22}H_{27}Cl_3N_2O_2S$ (389·9) calculated: 53·93% C, 5·56% H, 21·71% Cl, 5·72% N, 6·54% S; found: 53·09% C, 5·75% H, 22·17% Cl, 5·95% N, 6·80% S.

B. A mixture of 5·54 g *II* (ref.[3]), 30 ml benzene and 5 ml acetic anhydride was refluxed for 8 h, diluted with benzene, washed with 5% NaOH and water, dried with $MgSO_4$ and evaporated. According to TLC, the residue is homogeneous base *III*. In an acetone solution, it was neutralized with 3·5 g maleic acid; 7·4 g (93%) monomaleate, m.p. 202—204°C (acetone–methanol). IR spectrum (KBr): 754, 811, 871 (4 and 2 adjacent and solitary Ar—H), 989, 1050, 1097 (C—O), 1230 (CH_3COOR), 1355 (OH), 1582 (Ar), 1742 (COOR), 2460, 2580 (NH^+), 3033, 3058 cm^{-1} (Ar). ^{1}H-NMR spectrum (CD_3SOCD_3): δ 7·00—7·50 (m, 7 H, Ar—H), 5·98 (s, 2 H, CH=CH of maleic acid), 4·20 (def. t, 2 H, CH_2O), 3·40—4·20 (m, 3 H, $ArCH_2CHAr$), c. 3·10 (2 H, NCH_2 in a chain), 2·50—3·35 (m, 8 H, 4 NCH_2 of piperazine), 1·97 (s, 3 H, $COCH_3$). For $C_{26}H_{29}$·ClN_2O_6S (533·1) calculated: 58·58% C, 5·48% H, 6·65% Cl, 5·26% N, 6·02% S; found: 59·00% C, 5·82% H, 6·86% Cl, 5·29% N, 5·99% S.

2-Chloro-10-[4-(2-hydroxyethyl)piperazino]-10,11-dihydrodibenzo[*b*,*f*]thiepin (*II*)

A. A mixture of 32·9 g *XVII*, 60 g Zn and 300 ml acetic acid was refluxed under stirring for 20 min, filtered and the filtrate was evaporated *in vacuo*. The residue was combined with 400 ml ethanol and 50 ml 20% NaOH and the mixture was refluxed for 6 h. Ethanol was evaporated at reduced

pressure, the residue was diluted with water and extracted with benzene. The extract was shaken with excess 5% hydrochloric acid, the acid aqueous solution was separated, alkalified with NH_4OH and the base was isolated by extraction with benzene; 23·0 g (70%). Neutralization with 7·0 g succinic acid in acetone yielded 24·5 g crude succinate, melting at 158—161°C which crystallized from a mixture of ethanol, acetone and ether to yield 20·5 g pure succinate, melting at 165·5 to 167°C (our earlier value for a product prepared differently was 167—168°C) (ref.[3]). Treatment with NH_4OH released the base which was isolated by extraction with benzene; m.p. 98—102°C(acetone) (our earlier value[3] 102—103°C). This was used for measuring the hitherto undescribed spectra. UV spectrum: λ_{max} 245 nm (log ε 4·03), 275 nm (3·83). IR spectrum: 750, 810, 870, 895 (4 and 2 adjacent and solitary Ar—H), 1038, 1090 (CH_2OH), 1558, 1580 (Ar), 2800 (NCH_2), 3165 cm^{-1} (OH···N). ^{1}H-NMR spectrum: δ 6·90—7·70 (m, 7 H, Ar—H), 3·00—4·00 (m, 3 H, $ArCH_2CHAr$), 3·60 (t, J = 6·0 Hz, 2 H, CH_2O), 2·40—3·00 (m, 11 H, NCH_2 and OH).

L(+)-*Tartrate* (diastereoisomeric mixture), m.p. 103—107°C (aqueous ethanol), $[\alpha]_D^{20}$ +9·5° (1% solution in methanol). For $C_{24}H_{29}ClN_2O_7S$ (525·0) calculated: 54·90% C, 5·57% H, 6·75% Cl, 5·34% N, 6·11% S; found: 54·77% C, 5·48% H, 6·98% Cl, 5·25% N, 6·19% S.

B. Sodium borohydride (1·40 g) was added to a solution of 4·28 g *XVII* in 30 ml tetrahydrofuran and then a solution of 3·5 ml acetic acid in 10 ml tetrahydrofuran was added dropwise under nitrogen over a period of 1·5 h. The mixture was stirred for 30 min, refluxed for 3 h, left to stand overnight, decomposed by adding dropwise 10 ml 20% hydrochloric acid, the mixture was stirred for 30 min, alkalified with NH_4OH and extracted with benzene. The benzene extract was shaken with excess 10% hydrochloric acid, the precipitate was filtered and combined with the acid aqueous phase of the filtrate, treated with NH_4OH and re-extracted with benzene; 1·56 g crude base containing still the starting enamine *XVII* and ketone *XIII*. For this reason the product dissolved in ether was subjected to the action of concentratioed hydrochloric acid. Alkalification of the acid layer and isolation by extraction with benzene yielded only 0·26 g base *II* which was neutralized with succinic acid in acetone to yield 0·26 g pure succinate, melting at 166·5—167°C (see product under *A*). The benzene and ether solutions were evaporated to yield 2·91 g ketone *XIII*, m.p. 141—143°C. The base released from the succinate was crystallized from a mixture of cyclohexane and acetone to yield a new crystal modification of base *II*, melting at 122—124°C. While the IR spectrum (crystals in Nujol) is somewhat different from that obtained for the modification melting at 102°C (under *A*), the ^{1}H-NMR spectrum was more sharply differentiated. IR spectrum: 755, 766, 810, 832, 886 (4 and 2 adjacent and solitary Ar—H), 1004, 1054 (CH_2OH), 1146, 1301, 1378, 1551, 1581 (Ar), 3170 cm^{-1}. (OH). ^{1}H-NMR spectrum: δ 7·60 (mcs, J = 3·0 Hz, 1 H, 1-H), 6·90—7·50 (m, 6 H, remaining Ar—H), 3·00—4·00 (m, 3 H, $ArCH_2CHAr$), 3·55 (t, J = 6·0 Hz, 2 H, CH_2O), c. 2·50 (m, 10 H, 5 NCH_2), 2·98 (s, 1 H, OH). For $C_{20}H_{23}ClN_2OS$ (374·9) calculated: 64·07% C, 6·18% H, 9·45% Cl, 7·47% N, 8·55% S; found: 63·60% C, 6·12% H, 9·90% Cl, 7·24% N, 8·84% S.

2-Chlorodibenzo[*b*,*f*]thiepin-10(11*H*)-one Hydrazone (*XX*)

A mixture of 3·0 g *XVII*, 3·0 g 100% hydrazine hydrate, 40 ml ethanol and 1 ml acetic acid was stirred for 2·5 h at 50°C while introducing air and adding ethanol to replace its loss by volatilization. This was followed by an addition of further 3·0 g hydrazine hydrate and the mixture was refluxed for 9 h in a 80°C bath. After this, the starting *XVII* was no more detected in the sample by TLC. The solution formed was left to stand in the cold whereupon 1·9 g (86%) product precipitated; m.p. 150—152°C. Crystallization from ethanol did not raise this m.p. further. UV spectrum: infl. 255 nm (log ε 4·21), absorption up to 325 nm. IR spectrum: 745, 823, 869 (4 and 2 adjacent and solitary Ar—H), 1597, 3055 (Ar), 3385 cm^{-1} (NH). ^{1}H-NMR spectrum:

δ 7·75 (m, 1 H, 9-H), 7·48 (d, J = 8·0 Hz, 1 H, 4-H), 7·10—7·45 (m, 4 H, 1,6,7,8-H_4), 7·08 (mcd, J = 8·0; 2·0 Hz, 1 H, 3-H), 5·40 (bs, 2 H, NH_2), 4·00 (s, 2 H, $ArCH_2$). For $C_{14}H_{11}ClN_2S$ (274·8) calculated: 61·19% C, 4·04% H, 12·90% Cl, 10·20% N, 11·67% S; found: 61·67% C, 4·13% H, 13·05% Cl, 10·24% N, 11·88% S.

11-Bromo-8-chlorodibenzo[*b*,*f*]thiepin-10(11*H*)-one (*XXII*)

A solution of 31·2 g bromine in 80 ml chloroform was added dropwise over 90 min to a solution of 51 g *XXI* (ref.[10,11]) in 240 ml chloroform and the solution obtained was washed with water, dried and evaporated. The crystalline residue was filtered after adding a little benzene; 62 g (93%), m.p. 165—167°C; analytical sample, m.p. 167—169°C (benzene). UV spectrum: λ_{max} 241·5 nm (log ε 4·31), infl. 262 nm (4·13), 337·5 nm (3·54). IR spectrum: 744, 760, 829, 856 (4 and 2 adjacent and solitary Ar—H), 1574 (Ar), 1684 cm^{-1} (Ar—CO). ^{1}H-NMR spectrum: δ 8·18 (mcs, J = = 2·0 Hz, 1 H, 9-H), 7·80 (mcd, 1 H, 1-H), 7·62 (mcd, 1 H, 4-H), 7·10—7·60 (m, 4 H, remaining Ar—H), 6·70 (s, 1 H, Ar—CH—Br). For $C_{14}H_8BrClOS$ (339·7) calculated: 49·51% C, 2·37% H, 23·53% Br, 10·44% Cl, 9·44% S; found: 49·77% C, 2·41% H, 23·25% Br, 10·32% Cl, 9·29% S.

8-Chloro-11-(4-methylpiperazino)dibenzo[*b*,*f*]thiepin-10(11*H*)-one (*XXIII*)

A. A mixture of 6·8 g *XXII*, 15 ml 1-methylpiperazine and 15 ml dichloromethane was refluxed for 10 h, cooled, diluted with benzene, washed with water and shaken with excess 5% hydrochloric acid. The precipitate was filtered, combined with the acid aqueous phase of the filtrate, alkalified with NH_4OH and the base was isolated by extraction with dichloromethane. The extract was dried with K_2CO_3 and evaporated; 5·6 g, m.p. 123—128°C. An analytical sample was obtained by recrystallization from ethanol, m.p. 135—138°C. UV spectrum: λ_{max} 243·5 nm (log ε 4·33), infl. 265 nm (4·09), 345 nm (3·63). IR spectrum: 759, 826, 881 (4 and 2 adjacent and solitary Ar—H), 1178 (C—O), 1576 (Ar), 1680 (Ar—CO), 2790 cm^{-1} (CH_2—N). ^{1}H-NMR spectrum: δ 8·00 (mcs, J = 2·0 Hz, 1 H, 9-H), 7·00—7·80 (m, 6 H, remaining Ar—H), 4·89 (s, 1 H, Ar—CH—N), 2·52 (s, 8 H, 4 NCH_2 of piperazine), 2·28 (s, 3 H, NCH_3). For $C_{19}H_{19}ClN_2OS$ (358·9) calculated: 63·58% C, 5·34% H, 9·88% Cl, 7·81% N, 8·93% S; found: 63·58% C, 5·46% H, 10·03% Cl, 7·48% N, 9·20% S. In patents[37] a m.p. of 153—157°C is given. By neutralization of the ethanolic mother liquor with maleic acid to maleate a total of 1·3 g bis(hydrogen maleate) of 1-methylpiperazine was obtained[46] (m.p. 173—174°C). Evaporation of the benzene layer (after shaking with hydrochloric acid) yielded 0·30 g diketone *XXIV*, m.p. 161—168°C (benzene–light petroleum) (see under *B*).

B. A mixture of 11·8 g *XXII*, 20 ml 1-methylpiperazine, 200 ml dichloromethane and 20 ml ether was left to stand for 12 days at room temperature, was then washed with water and shaken with excess 1 : 1 hydrochloric acid. Drying and evaporation of the organic layer yielded 4·0 g of yellow 2-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10,11-dione (*XXIV*), m.p. 169—171°C (benzene). UV spectrum: λ_{max} 244 nm (log ε 4·29), infl. 276 nm (4·01), 296 nm (3·87), 355 nm (3·63). IR spectrum: 749, 768, 790, 839, 898 (4 and 2 adjacent and solitary Ar-H), 1219 (CO), 1559, 1568, 1589, 3073, 3100 (Ar), 1694 cm^{-1} (ArCOCOAr). The mass spectrum has a molecular ion at *m/e* 274, corresponding to $C_{14}H_7ClO_2S$; fragments at 246, 239 and 218 indicate the splitting of one and two molecules of CO, as well as of a chlorine radical. For $C_{14}H_7ClO_2S$ (274·7) calculated: 61·20% C, 2·57% H, 12·91% Cl, 11·67% S; found: 61·32% C, 2·67% H, 12·94% Cl, 11·57% S.

Alkalification of the acid aqueous layer with NH_4OH and extraction with benzene yielded 6·6 g (53%) crude base *XXIII* which was recrystallized from a mixture of benzene and light petroleum

to melt at 136—138°C. The mother liquors after crystallization of this base yielded 1·6 g bis (hydrogen maleate) of 1-methylpiperazine[46], melting at 171—173°C. The mother liquor after this compound was evaporated and crystallized from benzene to obtain further 1·8 g diketone *XXIV*.

cis-8-Chloro-11-(4-methylpiperazino)-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-ol (*XXV*)

A mixture of 6·8 g *XXII*, 10 ml 1-methylpiperazine and 30 ml dioxane was stirred for 3 h at room temperature and then refluxed for 1 h. After cooling, the separated hydrobromide of 1-methylpiperazine was filtered and washed with dioxane, the filtrate was combined with a solution of 1·3 g $NaBH_4$ in 5 ml water with a drop of 20% NaOH and the mixture was refluxed for 1·5 h. After standing overnight the dioxane was evaporated, the residue was mixed with water and extracted with benzene. The benzene layer was shaken with 100 ml 10% hydrochloric acid. The precipitated hydrochloride was filtered, added to the acid aqueous layer of the filtrate, the suspension was alkalified with NH_4OH and the base was extracted with benzene; 6·7 g of a compound which was crystallized from a mixture of ethanol and benzene to obtain 5·5 g (76%) homogeneous base, melting at 181—183°C. IR spectrum (KBr): 779, 809, 789 (4 and 2 adjacent and solitary Ar—H), 1102 (CHOH), 1460, 1579 (Ar), 2720 (OH···N), 3200 cm^{-1} (OH). ^{1}H-NMR spectrum (CD_3SOCD_3): δ 7·68 (mcs, J = 3·0 Hz, 1 H, 9-H), 7·00—7·40 (m, 6 H, remaining Ar—H), 5·70 (d, J = 4·5 Hz, disappears after D_2O, 1 H, OH), 5·22 (bd, J = 4·5 Hz, after D_2O d, J = 1·2 Hz, 1 H, 10-H), 4·13 (d, J = 1·2 Hz, 1 H, 11-H), 1·60—2·30 (m, 8 H, 4 NCH_2 of piperazine), 1·92 (s, 3 H, NCH_3). For $C_{19}H_{21}ClN_2OS$ (360·9) calculated: 63·23% C, 5·87% H, 9·82% Cl, 7·76% N, 8·88% S; found: 63·26% C, 5·95% H, 9·56% Cl, 7·67% N, 8·97% S. Patent[38] reports a m.p. of 175—177°C for a compound of undefined configuration.

The benzene layer was shaken with hydrochloric acid and evaporated to obtain 0·3 g of a compound which was recrystallized from a mixture of ethanol and benzene to melt at 210—212°C. It was identified as *cis*-2-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10,11-diol (*XXIX*). IR spectrum: 749, 785, 815 (Ar—H), 1065, 1076, 1092 (CHOH), 1582 (Ar), 3230, 3390 cm^{-1} (OH). ^{1}H-NMR spectrum (CD_3SOCD_3): δ 7·00—7·60 (m, 7 H, Ar—H), 5·75 and 5·58 (2 d, J = 5·0 Hz, disappears after D_2O, 2 H, 2 OH), 5·29 and 5·12 (2 bd, J = 5·0 Hz, after D_2O bs, J = c. 1·0 Hz, 2 H, 10,11-H_2). For $C_{14}H_{11}ClO_2S$ (278·8) calculated: 60·32% C, 3·98% H, 12·72% Cl, 11·50% S; found: 60·50% C, 4·05% H, 12·99% Cl, 11·88% S.

trans-8-Chloro-11-(4-methylpiperazino)-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-ol (*XXVII*)

Sodium borohydride (0·43 g) was added to a solution of 2·03 g *XXIII* in 20 ml tetrahydrofuran and this was followed by a dropwise addition under nitrogen and with stirring of 2·13 g boron trifluoride etherate (over a period of 15 min). The mixture was stirred for 4 h at room temperature, left to stand overnight, decomposed with 10 ml 5% hydrochloric acid, alkalified with NH_4OH and extracted with benzene. A total of 2·0 g nonhomogeneous product was obtained which crystallized from ethanol to yield 0·70 g (34%) amino alcohol melting at 232—234°C (ethanol–benzene). Mass spectrum with a molecular ion at m/e 360 supports the composition $C_{19}H_{21}ClN_2OS$; the fragment at *m/e* 342 (M—18) indicates the presence of a hydroxyl, intense fragments at *m/e* 260 and 231 then correspond to the splitting of a piperazine moiety of the molecule. UV spectrum: λ_{max} 250 nm (log ε 3·67). IR spectrum (KBr): 741, 780, 816, 855 (4 and 2 adjacent and solitary Ar—H), 1000, 1041, 1071, 1084, 1141 (C—O, CHOH) 1450, 1561, 1579, 1632 (Ar), 2812 and 3065 cm^{-1} (OH..N). For $C_{19}H_{21}ClN_2OS$ (360·9) calculated: 63·23% C, 5·87% H, 9·82% Cl, 7·76% N, 8·88% S; found: 63·63% C, 5·89% H, 9·92% Cl, 7·81% N, 8·78% S.

cis- and *trans*-8-Chloro-11-[4-(2-hydroxyethyl)piperazino]-10,11-dihydrodibenzo[*b,f*]thiepin--10-ol (*XXVI* and *XXVIII*)

A solution of 68 g *XXII* and 130 g 1-(2-hydroxyethyl)piperazine in 300 ml dioxane was stirred for 3 h at room temperature and refluxed for 1·5 h. After standing overnight the precipitated substance was filtered, the filtrate was combined with a solution of 7·6 g $NaBH_4$ in 30 ml water with 4 drops of 20% NaOH and the mixture was refluxed for 2 h under stirring. The dioxane was then evaporated at reduced pressure, the residue was decomposed with water and extracted with benzene. After partial evaporation of the extract, 52·1 g crude *cis*-amino alcohol *XXVI* precipitated; m.p. 168—174°C; the analytical product melted at 174—176°C (benzene–ethanol). ^{1}H-NMR spectrum (CD_3SOCD_3): δ 7·55 (mcs, J = 2·0 Hz, 1 H, 9-H), 8·27 (d, J = 8·0 Hz, 1 H, 6-H), 7·10 (m, 5 H, remaining Ar—H), 5·62 (d, J = 5·0 Hz, disappears after D_2O, 1 H, 10-OH), 5·20 (d, J = 5·0 Hz, after D_2O s, 1 H, 10-H). 4·10 (bs, disappears after D_2O, 1 H, OH in the side-chain), 4·10 (s, 1 H, 11-H), 3·25 (t, J = 6·0 Hz, 2 H, CH_2O), 2·18 (t, J = 6·0 Hz, 2 H, NCH_2 in a chain), c. 2·00 (m, 8 H, 4 NCH_2 of piperazine). For $C_{20}H_{23}ClN_2O_2S$ (390·9) calculated: 61·44% C, 5·93% H, 9·07% Cl, 7·17% N, 8·20% S; found: 61·56% C, 6·00% H, 9·15% Cl, 7·13% N, 8·40% S.

Maleate, m.p. 148—150°C (ethanol–ether). For $C_{24}H_{27}ClN_2O_6S$ (507·0) calculated: 56·85% C, 5·37% H, 6·99% Cl, 5·53% N, 6·32% S; found: 56·62% C, 5·50% H, 6·79% Cl, 5·46% N, 6·23% S.

The benzene mother liquor after base *XXVI* was shaken with 300 ml 10% hydrochloric acid, the aqueous layer from which the hydrochloride crystallizes was alkalified with NH_4OH and the base was extracted with dichloromethane. Evaporation yielded 20 g oil which was crystallized from a mixture of benzene–ethanol to yield further 3·7 g *cis*-base *XXVI* melting at 168—174°C. The total yield of this substance was thus 55·8 g (71%). Evaporation of the mother liquor produced 15·6 g oil which crystallized from ethanol to 5·2 g (7%) *trans*-isomer *XXVIII*, m.p. 188—191°C; analytical sample, m.p. 192·5—194°C (ethanol). ^{1}H-NMR spectrum (CD_3SOCD_3): δ 7·50 (mcs, J = 2·0 Hz, 1 H, 9-H), 7·38 (d, J = 8·0 Hz, 1 H, 6-H), 7·00 (m, 5 H, remaining Ar—H), c. 5·60 (m, 2 H, after D_2O d, J = 8·0 Hz, 1 H, 10-OH and 10-H), 4·20 (bs disappears after D_2O, 1 H, OH in a chain) 3·60 (d, J = 8·0 Hz, 1 H, 11-H), 3·30 (t, J = 6·0 Hz, 2 H, CH_2O), c. 2·30 (m, 10 H, 5 NCH_2). For $C_{20}H_{23}ClN_2O_2S$ (390·9) calculated: 61·44% C, 5·93% H, 9·07% Cl, 7·17% N, 8·20% S; found: 61·64% C, 5·90% H, 9·23% Cl, 7·14% N, 8·15% S.

The maleate crystallizes from a mixture of 95% ethanol and ether as monohydrate, m.p. 116—119°C (remainder only at 130°C). For $C_{24}H_{27}ClN_2O_6S + H_2O$ (525·0) calculated: 54·90% C, 5·57% H, 6·75% Cl, 5·34% N, 6·11% S; found: 55·24% C, 5·48% H, 6·47% Cl, 5·02% N, 5·84% S.

2-Chloro-10-(4-ethylpiperazino)-10,11-dihydrodibenzo[*b,f*]thiepin (*IV*)

A solution of 6·3 g methanesulfonyl chloride in 10 ml pyridine was added to a suspension of 5·3 g *XXVII* in 35 ml pyridine cooled with water. The mixture was stirred for 4 h, left to stand for 48 h, decomposed with water and extracted with benzene. Drying and evaporation of the extract yielded 5·1 g oil (according to TLC it contains no starting *XXVII*) which was combined with 20 ml diethylene glycol dimethyl ether and added to a solution of 3·0 g $NaBH_4$ and 1·0 g NaOH in 7 ml water. The mixture was stirred for 6·5 h at 50°C, diluted with water and extracted with benzene. The residue obtained on drying and evaporating the extract was dissolved in ether and extracted with hydrogen chloride in ether to precipitate an amorphous hydrochloride (4·0 g). The base was again released by alkalification, the product was purified once more *via* the succinate (m.p. 110—112°C) and finally converted to bis(hydrogen maleate) (1·6 g, 20%), m.p.

189—191°C (aqueous ethanol). For $C_{28}H_{31}ClN_2O_8S$ (591·1) calculated: 56·90% C, 5·29% H, 6·00% Cl, 4·74% N, 5·43% S; found: 57·37% C, 4·72% H, 6·01% Cl, 4·89% N, 6·57% S. The released oily base was used for obtaining the ^{1}H-NMR spectrum: δ 7·00—7·40 (m, 7 H, Ar—H), 4·10 (t, 1 H, Ar—CH—N), 1·10 (t, 3 H, C—CH_3), 2·40—2·70 (m, 13 H, ArCH_2CHAr and 5 NCH_2).

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