SYNTHESIS OF 2-ACETYL AND 3-ACETYL DERIVATIVES OF 8-CHLORO-10-(4-METHYLPIPERAZINO)-10,11-DIHYDRODIBENZO[*b,f*]-THIEPIN; 2-ACYL-7-SUBSTITUTED THIOXANTHENES*

Karel ŠINDELÁŘ, Jiří O. JÍLEK, Josef POMYKÁČEK, Zdeněk ŠEDIVÝ and Miroslav PROTIVA

Research Institute for Pharmacy and Biochemistry, 130 00 Prague 3

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Reaction of 2-chlorodibenzo[*b,f*]thiepin with acetyl chloride and aluminium chloride proceeds under simultaneous acetylation of the nucleus and hydrogen chloride addition with contraction of the central ring resulting in 2-acetyl-7-chloro-9-chloromethylthioxanthene (*XXVII*). Substitution reaction with 1-methylpiperazine gives the amine *XXIX* together with the product of elimination, *i.e.* 2-acetyl-7-chloro-9-methylenethioxanthene (*XXXII*). This compound is oxidized with air oxygen to 2-acetyl-7-chlorothioxanthone (*XXXIV*), obtained also by cyclization of the acid *XXXVI*. In connection with this investigation, total syntheses of the 2-acetyl and 3-acetyl derivatives of the neuroleptic octoclothepin *II* and *XV* were undertaken. They started from the isomeric 2-(4-chlorophenylthio)-5(or 4)-nitrobenzoic acids (*IVa*, *XVIIa*), the first of which was transformed in 6 steps to the homologous amino acid *VIIIb*, cyclized to 2-amino-8-chlorodibenzo-[*b,f*]thiepin-10(11*H*)-one (*IX*). The acid *XVIIa* produced in three steps the homologous nitro acid *XXa*, cyclized to 8-chloro-3-nitrodibenzo[*b,f*]thiepin-10(11*H*)one (*XXIII*). The acetyl group was introduced in the stage of aminoalcohols *X* and *XXV* by reaction of the diazonium salts with acetaldehyde semicarbazone and by the following hydrolysis. The products *XI* and *XXVI* yielded by treatment with hydrogen chloride the chloro derivatives *I* and *XIV*, isomeric with the compound *XXVII*. Substitution reactions with 1-methylpiperazine gave compounds *II* and *XV* (isomeric with *XXIX*) together with products of elimination *III* and *XVI* (isomeric with *XXXII*). Whereas the thioxanthene derivative *XXIX*, when administered intravenously to mice, has a high central depressant activity, the 2-acetyl derivative of octoclothepin *II* has only mild activity; both substances in the test on rats are practically devoid of cataleptic activity.

In the synthesis of the neuroleptic agent octoclothepin, *i.e.* 8-chloro-10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b,f*]thiepin, the final step is a substitution reaction of 8,10-dichloro-10,11-dihydrodibenzo[*b,f*]thiepin with 1-methylpiperazine giving in addition to the desired base at least 20% of the elimination product, 2-chlorodibenzo[*b,f*]thiepin[1,2]. Efforts to find some chemical use for this by-product were quite obvious[3] and were also the motive of the investigation, described in the present paper.

Reaction of 2-chlorodibenzo[*b,f*]thiepin[1] with acetyl chloride and aluminium chloride in dichloromethane yielded 30% of a product $C_{16}H_{12}Cl_2OS$ (compound *A*), the composition of which

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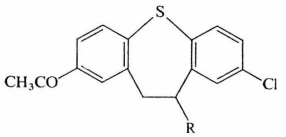
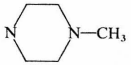
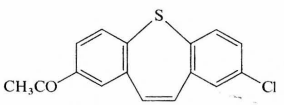
indicates that in addition to acetylation a hydrogen chloride addition took place. Since the only free *para*-position toward the sulfur atom (position 8) was considered the most reactive one, and becauce of the fact that the same product was obtained by a similar reaction from 8,10-dichloro-10,11-dihydrodibenzo[*b*,*f*]thiepin[1], it was assumed to have the structure of 2-acetyl-8,10--dichloro-10,11-dihydrodibenzo[*b*,*f*]thiepin (*I*). This formulation was not at variance with the UV and IR spectra ($\nu_{(ArCO)}$ 1 682 cm^{-1}) and was in agreement with the analysis of the semicarbazone. A similar reaction, in which propionyl chloride was used instead of acetyl chloride, led in a 21% yield to a compound $C_{17}H_{14}Cl_2OS$, assumed to be the 2-propionyl analogue of compound *I*. Both chloro derivatives were subjected to a reaction with 1-methylpiperazine and produced in addition to the expected bases (compound *B* of the assumed structure *II* and the corresponding 2-propionyl homologue) neutral products of elimination, the first of which (compound *C*) corresponded to the empirical composition $C_{16}H_{11}ClOS$. It was assumed to have structure *III*. Compound *B* was reduced with sodium borohydride to the corresponding secondary alcohol. Reaction of 10-chloro-8-fluoro-10,11-dihydrodibenzo[*b*,*f*]thiepin[1] with acetyl chloride and aluminium chloride in chloroform or dichloromethane produced a mixture which was chromatographed to give a compound $C_{16}H_{11}FOS$, assumed to be the 8-fluoro analogue of compound *III*. A similar reaction of 2-(methylthio)dibenzo[*b*,*f*]thiepin[4] gave also an inhomogeneous product, the chromatography of which separated in a low yield a substance having according to the analysis and the mass spectrum the empirical composition $C_{16}H_{12}O_2S_2$. Since the mentioned basic products showed in tests in mice central depressant effects, their method of synthesis was protected by a patent[5].



I, R = Cl

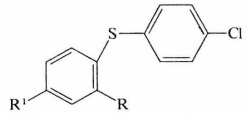
II, R = 



III

As evident from the foregoing paragraph, the structures of the whole group of the compounds prepared were not rigorously proven; especially the position of the acetyl group was considered uncertain. For clearing the situation, we proceeded to an unequivocal synthesis of compounds *I*–*III*, including the 2-acetyl derivative of octoclothepin *II*. A similar procedure was used as in our recent synthesis[6] of 2-acetyl-10--(4-methylpiperazino)-10,11-dihydrodibenzo[*b*,*f*]thiepin. 2-Chloro-5-nitrobenzoic acid[7] gave by reaction with 4-chlorothiophenol in the presence of potassium hydroxide and copper in boiling dimethylformamide 2-(4-chlorophenylthio)-5-nitrobenzoic acid (*IVa*) which was reduced with diborane to the nitro alcohol *Va*. The nitro group was reduced with stannous chloride and the product obtained was 5-amino-2-(4-chlorophenylthio)benzyl alcohol (*Vb*). Selective N-acetylation with isopropenyl acetate[8] resulted in the acetamido alcohol *Vc* which was treated with thionyl chloride in

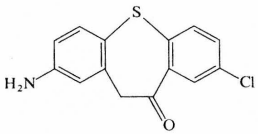
chloroform in the presence of pyridine yielding 5-acetamido-2-(4-chlorophenylthio)-benzyl chloride *VIc*. The nitrile *VIIc* was obtained by reaction with potassium cyanide



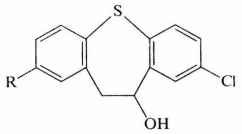
a, $R^1 = NO_2$
b, $R^1 = NH_2$
c, $R^1 = NHCOCH_3$

IV, R = COOH
V, R = CH_2OH
VI, R = CH_2Cl

VII, R = CH_2CN
VIII, R = CH_2COOH

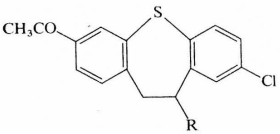


IX

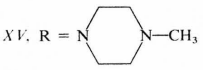


X, R = NH_2
XI, R = $COCH_3$

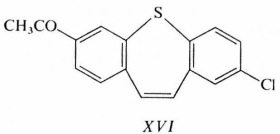
XII, R = Cl
XIII, R = H



XIV, R = Cl



XV, R =



XVI

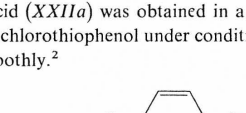
in dimethylformamide at 100°C; its hydrolysis with an aqueous–ethanolic solution of potassium hydroxide gave [5-amino-2-(4-chlorophenylthio)phenyl]acetic acid (*VIIIb*). Cyclization was effected by treatment with polyphosphoric acid at 125°C giving 2-amino-8-chlorodibenzo[*b*,*f*]thiepin-10(11*H*)-one (*IX*). Reduction with sodium borohydride in aqueous dioxane produced the amino alcohol *X* which was the starting material for the critical step of the synthesis, *i.e.* introduction of the acetyl group by the Beech method[9] (*cf.* also[6,10]). The amino alcohol *X* was diazotized, the diazonium salt solution was treated with acetaldehyde semicarbazone[11] under

the catalytic action of a mixture of solutions of cupric sulfate and sodium sulfite and the crude product was subjected to hydrolysis with a boiling solution of oxalic acid. The inhomogeneous product obtained was separated by chromatography on a column of silica gel. As first, two minor products were eluted: 2,8-dichloro-10,11--dihydrodibenzo[*b,f*]thiepin-10-ol (*XII*) (ref.[12]), formed by Sandmeyer reaction, and 8-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ol (*XIII*) (ref.[1]), resulting from a reductive elimination of the diazonium group. The mass spectrum of the latter compound shows a molecular ion corresponding to $C_{14}H_{11}ClOS$. In addition to compound *XIII*, the mass spectrum disclosed the presence of another compound with the molecular ion with *m/e* 303, corresponding to $C_{14}H_{10}ClN_3OS$. Most probably we are dealing here with the corresponding aryl azide $Ar-\overset{(+)}{N}=\overset{(-)}{N}=N$, as indicated by its fragmentation started with the cleavage of a nitrogen molecule and formation of a fragment with *m/e* 275 (*cf.*[13]). The presence of a nitrogen-containing component was indicated also by the analysis. 2-Acetyl-8-chloro-10,11-dihydrodibenzo[*b,f*]-thiepin-10-ol (*XI*) was eluted as the most polar component in a yield of c.30%. By treatment with hydrogen chloride it produces 2-acetyl-8,10-dichloro-10,11-dihydrodibenzo[*b,f*]thiepin (*I*) from which by substitution reaction with 1-methylpiperazine in boiling chloroform the base *II* was obtained. In a small amount, the product of elimination, *i.e.* 2-acetyl-8-chlorodibenzo[*b,f*]thiepin (*III*) was isolated. The identity of compounds *I*–*III* is in agreement with analyses, UV and IR spectra and was rigorously confirmed by the ^{1}H-NMR spectra. It was established that compound *I* is not identical with the product of reaction of 2-chlorodibenzo[*b,f*]-thiepin with acetyl chloride and aluminium chloride (*i.e.* with compound *A*) and that substances *II* and *III* are not identical with compounds *B* and *C*, mentioned in the first paragraph of this paper.

With regard to the fact that for substances *A*–*C* also the structures of the isomeric 3-acetyl derivatives *XIV*–*XVI* had to be considered, an unequivocal synthesis of these compounds was also undertaken. The synthetic procedure, used in the foregoing case, could only partly be used. 2-Bromo-4-nitrobenzoic acid[14,15] was transformed by heating with 4-chlorothiophenol, potassium carbonate and copper in hexamethylphosphoric triamide to 170°C to 2-(4-chlorophenylthio)-4-nitrobenzoic acid (*XVIIa*). Its reduction with diborane yielded the nitroalcohol *XVIIIa*. An attempt to reduce compound *XVIIIa* with stannous chloride and to effect the following reaction with isopropenyl acetate led only to a product of polymeric character. The nitro group in compound *XVIIIa* could then be reduced with hydrazine in the presence of palladium on carbon[16] but 2-(4-chlorophenylthio)-4-aminobenzyl alcohol (*XVIIIb*), obtained in this way, could not be transformed by treatment with isopropenyl acetate to the desired N-acetyl derivative. The nitro acid *XVIIa* was reduced with ferrous hydroxide to the amino acid *XVIIb*.

We attempted then to arrive at the homologous acids *XXa* and *XXb via* (2-bromo-

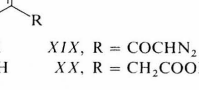
-4-nitrophenyl)acetic acid (*XXIa*) and (2-iodo-4-nitrophenyl)acetic acid (*XXIIa*). After unsuccessful attempts to prepare the acid *XXIa* from 2-bromo-4-nitrotoluene[14] by application of the oxalic ester method[17,18] and to obtain the acid *XXIIa* from (4-nitrophenyl)acetic acid[19,20] by reaction with thallic trifluoroacetate and potassium iodide (method[21]), we used for their preparation the reaction of diazonium salts with 1,1-dichloroethylene[22] and cupric chloride and the subsequent hydrolysis of the resulting 2,2,2-trichloroethyl derivatives with sulfuric acid[23]. In this manner, 2-bromo--4-nitroaniline[24] gave in a low yield the acid *XXIa*. It succeeded to reduce it with ferrous hydroxide to the amino acid *XXIb* but an attempt to effect a reaction of this acid with 4-chlorothiophenol under analogous conditions which were used in the synthesis of the acid *XVIIa*, was unsuccessful. This was the reason for our proceeding to the acid *XXIIa* having a more reactive halogen atom. Also in this case, the starting 2-iodo-4-nitroaniline[25] was diazotized and the diazonium salt subjected to the action of 1,1-dichloroethylene and then to hydrolysis with sulfuric acid; (2-iodo-4--nitrophenyl)acetic acid (*XXIIa*) was obtained in a poor yield. It was found that it does not react with 4-chlorothiophenol under conditions under which (2-iodophenyl)-acetic acid reacts smoothly.[2]



a, $R^1 = NO_2$
b, $R^1 = NH_2$

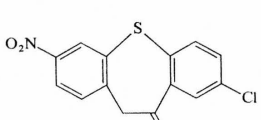
XVII, R = COOH
XVIII, R = CH_2OH

XIX, R = $COCHN_2$
XX, R = CH_2COOH

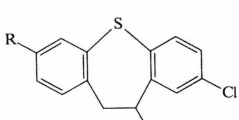


XXI, R = Br
XXII, R = I

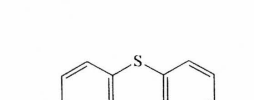
The difficulties were surmounted by applying the Arndt–Eistert synthesis[26] to the acid *XVIIa* as starting material. By treatment with thionyl chloride, this acid was transformed to the chloride which was treated in crude state with diazomethane to give the diazoketone *XIXa* (IR spectrum in the solid state indicates instead of the presence of a conjugated oxo group the enol form $Ar—C(OH)=C=\overset{(+)}{N}=\overset{(-)}{N}$). The Wolff rearrangement gave in a 50% yield [2-(4-chlorophenylthio)-4-nitrophenyl]-acetic acid (*XXa*). Cyclization with polyphosphoric acid in boiling toluene produced in a high yield 8-chloro-3-nitrodibenzo[*b*,*f*]thiepin-10(11*H*)-one (*XXIII*) which was



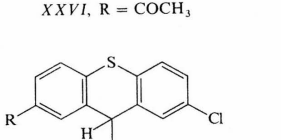
XXIII



XXIV, R = NO_2
XXV, R = NH_2
XXVI, R = $COCH_3$

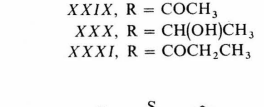


XXVII, R = CH_3
XXVIII, R = CH_2CH_3



XXIX, R = $COCH_3$
XXX, R = $CH(OH)CH_3$
XXXI, R = $COCH_2CH_3$

XXXII, R = Cl
XXXIII, R = F



XXXIV, R = Cl
XXXV, R = SCH_3

XXXVI

reduced with sodium borohydride in aqueous dioxane to the nitro alcohol *XXIV*. The nitro group was reduced with hydrazine under catalysis with ferric chloride on carbon (method[27,28]) whereby the amino alcohol *XXV* was formed. This was used as the starting product of the preparation of the acetyl derivative *XXVI* by Beech method[9]

similarly as in the preceding series. Again it was necessary to separate the product by chromatography; the less polar component proved again to be 8-chloro-10,11--dihydrodibenzo[*b*,*f*]thiepin-10-ol (*XIII*), *i.e.* product of the reductive elimination of the diazonium group. The ketone *XXVI* was obtained in a lower yield than in the preceding case. It was transformed by treatment with boiling thionyl chloride to 3-acetyl-8,10-dichloro-10,11-dihydrodibenzo[*b*,*f*]thiepin (*XIV*) giving by reaction with 1-methylpiperazine in boiling chloroform the base *XV* and 7-acetyl-2-chlorodibenzo[*b*,*f*]thiepin (*XVI*). Structures of compounds *XIV*–*XVI* were confirmed by analyses and spectra. A comparison of these substances with the products of the Friedel–Crafts reaction of 2-chlorodibenzo[*b*,*f*]thiepin with acetyl chloride (compound *A*) and its transformation products (*B* and *C*) proved even in this case that the compounds compared are not identical.

Only at this stage of work we proceeded to a more detailed investigation of spectra of the isomers compared, especially the ^{1}H-NMR spectra. It was clear that of diagnostic value could especially by the chemical shifts and spin–spin interactions corresponding to protons on the two-carbon bridge between the aromatic nuclei. In this line, important differences between the dibenzo[*b*,*f*]thiepin derivatives *I*–*III* and *XIV*–*XVI* on the one hand, and their isomers *A*, *B* nad *C* on the other were established. So, in the case of the chloro compound *I*, the proton in position 10 appears as a dd at 5·76 ppm (J = 8·0; 4·0 Hz) and protons of the CH_2 group in position 11 appear as two dd at 3·98 and 3·65 ppm (J = 14·0; 4·0 and 14·0; 8·0 Hz). Almost the same shifts and interactions were found for the isomer *XIV*: the proton in position 10 appears as a dd at 5·80 ppm (J = 8·0; 4·0 Hz) and protons of the 11-CH_2 group appear as two dd at 4·05 and 3·68 ppm (J = 14·0; 4·0 and 14·0; 8·0 Hz). On the contrary, the situation is completely different with the isomeric chloride *A*: we meet here with a triplet at 4·30 ppm (J = 7·5 Hz), corresponding to one proton, and further with a doublet at 3·62 ppm (J = 7·5 Hz), corresponding to two protons. In this case, the chemical equivalence of the methylene group protons indicates its free rotation and excludes its presence in the cycle. Similarly important are the differences in chemical shifts and interactions of the same protons in the spectra of the methylpiperazine derivatives. Whereas for the dibenzo[*b*,*f*]thiepin derivatives *II* and *XV*, the protons of the bridge Ar—CH_2CH(—N)—Ar appear as an indistinguishable multiplet at 3·00–4·00 ppm (confirmed in many cases, *cf.*[2,3,6,10]), compound *B* shows a triplet at 4·12 ppm (J = 8·0 Hz), corresponding to one proton and being very similar to the triplet shown by the compound *A*, and further a doublet at 2·55 ppm (J = = 8·0 Hz), corresponding to a CH_2 group. These comparisons led to proposal of structure *XXVII* for compound *A* and *XXIX* for compound *B*; the consequence was the proposal of structure *XXXII* for compound *C*. There was, however, still unsufficient evidence for the position of the acetyl group in the nucleus.

The final solution was attained by further synthetic work. We attempted to transform the chloro derivative *A* (*i.e.* having the proposed structure *XXVII*) to the corres-

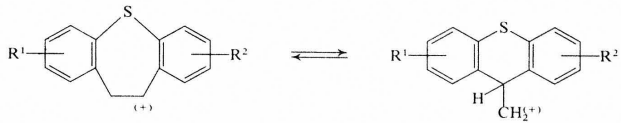
ponding tosyloxy derivative and rearrange this using the Wagner–Meerwein reaction (ref.[29–31]) to one of the dibenzo[*b,f*]thiepins *III* or *XVI*. To this end, compound *A* was treated with silver *p*-toluenesulfonate first in boiling acetonitrile (analogy[32]) and finally in triethylene glycol at 160°C. A mixture was obtained from which by chromatography on silica gel a yellow substance was isolated, the analysis and mass spectrum of which indicate the empirical formula $C_{15}H_9ClO_2S$; UV and IR spectra establish the structure of the thioxanthone *XXXIV* or of its 6-acetyl isomer. The structure of this compound was corroborated by an independent synthesis of 2-acetyl-7-chlorothioxanthone (*XXXIV*). 5-Chloroanthranilic acid[33] was transformed into 5,5'-dichlorodithiosalicylic acid (analogy of the known synthesis of dithiosalicylic acid[34]) which was reduced according to the literature[35] to 5-chlorothiosalicylic acid. Reaction of this compound with 4-bromoacetophenone[36] in boiling dimethylformamide in the presence of sodium carbonate and copper resulted in the acid *XXXVI*, which was cyclized with polyphosphoric acid at 55°C, similarly as described for the deschloro analogue[37]. 2-Acetyl-7-chlorothioxanthone (*XXXIV*) was obtained and found to be identical with the product prepared from compound *A*. A little discrepancy in the IR spectra of the products, obtained by different ways, was explained by dimorphism; compound *XXXIV* crystallizes on the one hand in the form of needles melting at 210–212°C, on the other in the form of leaves melting at 206–208°C. The IR spectra of both modification in solid state (in KBr) show small differences. On the contrary, spectra of both modifications in solution (in CS_2) are completely identical and the identity of both samples, obtained by different routes, is without any doubt. Structures *XXVII*, *XXIX* and *XXXII* are thus confirmed for compounds *A*, *B* and *C*. The formation of the thioxanthone *XXXIV* from the derivative *XXVII* is to be explained by primary elimination to the 9-methylenethioxanthene *XXXII* which easily undergoes oxidation to the thioxanthone *XXXIV*. The easy oxidation of 9-methylenethioxanthenes with air oxygen was mentioned in one of our preceding papers[2].

The reaction of 2-chlorodibenzo[*b,f*]thiepin[1] with acetyl chloride and aluminium chloride in dichloromethane under conditions of the Friedel–Crafts reaction proceeds thus with acetylation into the assumed position of the aromatic nucleus; addition of hydrogen chloride takes simultaneously place and under rearrangement of the skeleton and contraction of the central ring, the thioxanthene derivative *XXVII* is formed, giving a semicarbazone in the usual way. The compound *XXVII* easily eliminates hydrogen chloride, *e.g.* during chromatography on alumina, giving rise to the 9-methylenethioxanthene derivative *XXXII*. When the mentioned Friedel–Crafts reaction was carried out in carbon disulfide, a product was formed from which only after chromatography a small amount of compound *XXVII* could be isolated; the oily residue was used to prepare a semicarbazone which is not identical with the semicarbazone of compound *XXVII* but which corresponds by its analysis and spectra to the semicarbazone of compound *XXXII*. The chloromethyl derivative *XXVII*

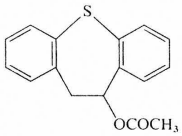
does not react with boiling formic acid (attempt to transform it to the olefin *III* in analogy to ref.[29]), with silver *p*-toluenesulfonate in boiling xylene or with silver nitrate in boiling aqueous 2-methoxyethanol (attempt to transform it to the corresponding hydroxymethyl derivative; for analogy see ref.[38]). Reaction with potassium acetate in dimethylformamide leads to a mixture of products, from which by crystallization and chromatography the olefin *XXXII* and the thioxanthone *XXXIV* were obtained. As already mentioned, compound *XXVII* undergoes a substitution reaction with 1-methylpiperazine under formation of the amine *XXIX*. For effecting this reaction, more severe conditions are necessary than those usual in reactions of substituted 10-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepins[6,10]. It does not proceed in boiling chloroform but the heating of both reaction components to 120–125°C is necessary. This observation suggests a substantially lower reactivity of the chlorine atom in compound *XXVII* in comparison with the atom of chlorine in compound *I*, in agreement with the expectation. As a by-product of this substitution reaction, an inhomogeneous neutral substance was obtained which was easily separated by chromatography on alumina. The olefin *XXXII* was obtained as the less polar product and the thioxanthone *XXXIV* as the more polar one, resulting from the oxidation of the olefin *XXXII* with air oxygen. This olefin was obtained in a high yield by heating compound *XXVII* with 2,4,6-collidine. Reduction of the aminoketone *XXIX* with sodium borohydride in aqueous methanol gave rise to the aminoalcohol *XXX*, primarily obtained as a mixture of two racemates; repeated crystallization led to the prevailing racemate in pure form. The structure was supported again by the ^{1}H-NMR spectrum. Reaction of 2-chlorodibenzo[*b*,*f*]thiepin[1] with propionyl chloride under conditions, similar to those used in the preparation of compound *XXVII*, resulted in the homologue $C_{17}H_{14}Cl_2OS$ to which structure *XXVIII* was ascribed *per analogiam*. Its substitution reaction with 1-methylpiperazine gave the amine *XXXI*, isolated only in the form of bis(hydrogen maleate). Compound $C_{16}H_{11}FOS$, obtained from 10-chloro-8-fluoro-10,11-dihydrodibenzo[*b*,*f*]thiepin[1] and mentioned in the first paragraph of this paper, has evidently the structure of 2-acetyl-7-fluoro-9-methylenethioxanthene (*XXXIII*) which was confirmed by the ^{1}H-NMR spectrum. In this case, the product of elimination was thus isolated instead of the primary product, *i.e.* the 9-chloromethyl derivative. Compound $C_{16}H_{12}O_2S_2$, obtained from 2-(methylthio)-dibenzo[*b*,*f*]thiepin[4] and also mentioned at the beginning of this paper, could now be identified as 2-acetyl-7-(methylthio)thioxanthone (*XXXV*). Out of the easily proceeding sequence 9-chloromethyl → 9-methylene → 9-oxo, the final member was thus isolated as a minor but the only crystalline product. The same product resulted from the acetylation of 10-chloro-8-(methylthio)-10,11-dihydrodibenzo[*b*,*f*]-thiepin[4]. In agreement with the present disclosures, it is necessary to correct the formulae of products described in the mentioned patent[5].

In considering the mechanism of formation of the thioxanthene derivative *XXVII* in the Friedel–Crafts acetylation of 2-chlorodibenzo[*b*,*f*]thiepin, we cannot avoid

the idea that the crucial step is the rearrangement of the carbonium cation *XXXVII* to the cation *XXXVIII*. This idea is unusual because just the opposite process, *i.e.* rearrangement of *XXXVIII* to *XXXVII*, is well known and forms the basis of mechanism of formation of dibenzo[*b*,*f*]thiepin derivatives from 9-(hydroxymethyl)-thioxanthenes and their tosylates by the Wagner–Meerwein rearrangement[29–31], as well as of formation of dibenzo[*b*,*f*]thiepin by reaction of thioxanthylium perchlorate with diazomethane[39,40]. The assumed higher stability[41] of the cation *XXXVII* in comparison with the stability of cation *XXXVIII* has evidently not a general validity and it is necessary to consider interconversions of species *XXXVII* and *XXXVIII*. The case described in this paper is not the only evidence of this conception. Conversion of *XXXVII* to *XXXVIII* played evidently role in the formation of 9-methylthioxanthene by reduction of dibenzo[*b*,*f*]thiepin with hydroiodic acid[42] and further in the formation of 9-(chloromethyl)-2,3-dimethoxythioxanthene by reaction of 2,3-dimethoxy-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-ol with hydrogen chloride[43] (for a close analogy in the dibenz[*b*,*f*]oxepin series[48]). The question was, whether the transformation of 2-chlorodibenzo[*b*,*f*]thiepin to 2-chloro-9-(chloromethyl)thioxanthene could be achieved only by the action of hydrogen chloride and aluminium chloride. The reaction was carried out in boiling dichloromethane and gave a mixture of products in which the starting compound predominated. Chromatography on alumina did not separate any crystalline component of the mixture but in one fraction there was a compound showing precisely the same chromatographic behaviour (thin layer of silica gel) as 2-chlorothioxanthone. The contraction of the ring takes thus place at least in a small extent and instead of the primary product, only the final member of the sequence 9-chloromethyl → 9-methylene → 9-oxo could be detected. The mentioned acylation of 8,10-dichloro-10,11-dihydrodibenzo[*b*,*f*]thiepin[1] to compound *XXVII* had also to proceed *via* a cation of type *XXXVII*. An attempt to acetylate 10-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin[44] with acetyl chloride in chloroform in the presence of aluminium chloride led to a mixture of at least seven substances from which not a single crystalline compound was obtained by chromatography. Only the fluorescence of some fractions on Silufol in the UV suggested the formation of small quantities of Ar-acetyl derivatives or thioxanthones. An attempt to acetylate the same starting compound with a mixture of acetic acid and trifluoroacetic anhydride (for method *cf.*[45,46]) was also unsuccessful. Attempt to acylate 2-chlorodibenzo[*b*,*f*]thiepin-10(11*H*)-one[12] with chloroacetyl chloride in dichloromethane in the presence of aluminium chloride resulted in quantitative recovery of the starting ketone. In connection with these acylation experiments, the new acetoxy derivative *XXXIX* was prepared by treatment of 10,11-dihydrodibenzo[*b*,*f*]thiepin-10-ol[44] with acetic anhydride in pyridine. In general, it has to be concluded that after negative results of attempts to achieve Ar-nitration of dibenzo[*b*,*f*]thiepin derivatives[6], Ar-acylation too appears to be of no preparative usefulness.



XXXVII *XXXVIII*



XXXIX

The 2-acetyl derivative of octoclothepin *II* (VÚFB-10.651), the amino ketone *XXIX* (VÚFB--8762), the amino alcohol *XXX* (VÚFB-8806) and the amino ketone *XXXI* (VÚFB-9477) were evaluated as potential neuroleptics (Dr J. Metyšová, pharmacological department of this institute). These substances were administered parenterally in the form of the bis(hydrogen maleates) but the doses given were calculated for the bases.

Compound *II* has acute toxicity in mice, LD_{50} 81 mg/kg *i.v.* Its mean effective dose bringing about ataxia in mice in the test of rotating rod, ED_{50} = 11·5 mg/kg *i.v.* In the catalepsy test in rats, it is little active; the intraperitoneal dose of 10 mg/kg produces catalepsy in 30% of the animals. In its whole profile, the compound is very similar to the 2-acetyl derivative of perathiepin[6], described earlier; the result shows that an unsuitable substituent in position 2 is able to destroy completely the pharmacogenic influence of a very favourable substituent in position 8, *viz.* atom of chlorine[1]. The thioxanthene derivative *XXIX* has LD_{50} 35 mg/kg *i.v.*, it is surprisingly highly active as a sedative, its ED_{50} in the test of rotating rod in mice being 0·1 mg/kg *i.v.*; on the other hand, in a dose of 10 mg/kg *i.p.*, it is completely inactive cataleptically in rats. Oral administration of a dose of 150 mg/kg does not produce toxic symptoms in mice, the depressant activity is low (ED_{50} = 27 mg/kg) and a dose of 50 mg/kg is ineffective in the test of catalepsy. The discrepancy between the rather high toxicity and depressant activity after intravenous administration on the one hand, and the low toxicity and activity after oral administration on the other, has probably to be explained by the incomplete resorption from the gastrointestinal tract. Compound *XXX* has the LD_{50} = 66 mg/kg *i.v.*, produces ataxia in mice at the mean effective dose ED_{50} = 13 mg/kg *i.v.* and in a dose of 10 mg/kg *i.p.* brings about catalepsy only in 10% of the animals tested. It is thus sedatively significantly less active than the aminoketone *XXIX*. The homologous amino ketone *XXXI* has LD_{50} = 28 mg/kg *i.v.*, its ED_{50} in the rotating rod test is 1·9 mg/kg *i.v.* and a dose

of 10 mg/kg *i.p.* is completely inactive cataleptically in rats. Parenteral administration is thus connected again with a more significant depressant activity. The important sedative activity of our compounds *XXIX* and *XXXI* is in agreement with the reported[47] strong sedative effect of 9-(dimethylaminomethyl)thioxanthene.

Both of the aminoketones of the thioxanthene series (*XXIX*, *XXXI*) were further evaluated (in the form of the mentioned salts) by Dr A. Šimek, Dr J. Turinová and Dr A. Čapek (bacteriological department of this institute) in the *in vitro* tests for antimicrobial activity toward a standard set of microorganisms (minimum inhibitory concentration in μg/ml given unless they surpass 125 μg/ml): *Streptococcus* β-*haemolyticus*, *XXIX* 25, *XXXI* 25; *Staphylococcus pyogenes aureus*, *XXIX* 25, *XXXI* 25; *Klebsiella pneumoniae*, *XXIX* 50; *Pseudomonas aeruginosa*, *XXIX* 100; *Escherichia coli*, *XXIX* 100; *Salmonella typhi abdominalis*, *XXIX* 100; *Proteus vulgaris*, *XXIX* 100; *Mycobacterium tuberculosis* H37Rv, *XXXI* 3.1; *Trichophyton mentagrophytes*, *XXXI* 125. With regard to the broad spectrum antibacterial activity of compound *XXIX*, some chemotherapeutic trials *in vivo* in mice infected with *Streptococcus* β-*haemolyticus* and *Escherichia coli* were carried out. The substance did not show any protective effect against mortality caused by the mentioned infections.

The semicarbazone of compound *XXVII* (VÚFB-8761) was submitted to a systematic pharmacological screening (Dr J. Němec at the affiliated unit of this institute in Rosice n/L). On oral administration, the mean lethal dose (LD_{50}) of 750 mg/kg was determined. In the *in vivo* tests, the compound was administered orally in doses of 150 mg/kg. Besides some signs of central depression after these high doses, the compound did not produce any other significant effects.

EXPERIMENTAL

The melting points of analytical preparations were determined in Kofler's block and are not corrected; the samples were dried *in vacuo* of about 0·5 Torr over P_2O_5 at room temperature or at 77°C. The UV spectra (mostly in methanol) were recorded on a Unicam SP 8000 spectrophotometer, IR spectra (in KBr unless stated otherwise) on a Unicam SP 200G spectrophotometer, ^{1}H-NMR spectra (in CD_3SOCD_3 unless stated otherwise) for the most part on a Tesla BC 487 (80 MHz) spectrometer and only in some cases on a ZKR 60 (Zeiss, Jena) apparatus. The mass spectra were registered on a MS 902 (AEI) instrument. The homogeneity of the compounds was checked by chromatography on thin layers of silica gel or alumina.

2-(4-Chlorophenylthio)-5-nitrobenzoic Acid (*IVa*)

A mixture of 1 500 ml dimethylformamide, 201·5 g 2-chloro-5-nitrobenzoic acid[7], 160 g 4-chlorothiophenol, 124 g KOH and 8 g molecular copper was stirred and heated for 8 h to 150°C. After standing overnight, the precipitated solid was filtered off, the filtrate evaporated *in vacuo*, the residue diluted with warm water and acidified with hydrochloric acid. The product was filtered and recrystallized from a mixture of benzene and ethanol; 229·5 g (74%), m.p. 235—240°C. Analytical sample melted at 241—242°C (benzene–ethanol). UV spectrum: λ_{max} 217 nm (log ε 4·43), 258·5 nm (3·89), 338 nm (4·19). IR spectrum (Nujol): 823, 890 (2 adjacent and solitary Ar—H), 910, 1 245, 1 692, 2 600 (COOH), 1 344, 1 511 (NO_2), 1 519, 1 579, 1 597 cm^{-1} (Ar). For $C_{13}H_8ClNO_4S$ (309·7) calculated: 50·41% C, 2·60% H, 11·45% Cl, 4·52% N, 10·35% S; found: 50·50% C, 2·70% H, 11·54% Cl, 4·30% N, 10·44% S.

2-(4-Chlorophenylthio)-4-nitrobenzoic Acid (*XVIIa*)

A mixture of 350 ml hexamethylphosphoric triamide, 120·9 g 2-bromo-4-nitrobenzoic acid[15], 88 g 4-chlorothiophenol, 153·5 g K_2CO_3 and 6 g Cu was heated under stirring in a nitrogen atmosphere for 11 h to 170°C. Hexamethylphosphoric triamide was then distilled off *in vacuo*, the residue was dissolved in water, the solution filtered and the filtrate acidified with hydrochloric acid. The product was isolated by extraction with benzene and after processing of the extract, it was recrystallized from aqueous ethanol; 70·7 g (47%), m.p. 218—222°C. Analytical sample melted at 222—225°C (aqueous ethanol). For $C_{13}H_8ClNO_4S$ (309·7) calculated: 50·41% C, 2·60% H, 11·45% Cl, 4·52% N, 10·35% S; found: 50·82% C, 2·75% H, 11·48% Cl, 4·39% N, 10·30% S.

2-(4-Chlorophenylthio)-5-nitrobenzyl Alcohol (*Va*)

A solution of 108·7 g *IVa* in 300 ml tetrahydrofuran was stirred and treated at 20—40°C over 15 min with 14 g $NaBH_4$. Boron trifluoride etherate (50 ml) was then added dropwise at the same temperature in nitrogen atmosphere over 1 h and the mixture was stirred for 6 h. After standing overnight, the mixture was decomposed by a slow addition of 100 ml 10% hydrochloric acid, diluted with water and extracted with benzene. The extract was washed with 5% NaOH, dried with $MgSO_4$ and evaporated; 101·4 g (98%), m.p. 98—99·5°C. Analytical sample melted at 99 to 100°C (benzene–light petroleum). IR spectrum: 825, 909 (2 adjacent and solitary Ar—H), 1 016, 1 025, 1 060, 1 099 (CH_2OH), 1 341, 1 510 (NO_2), 1 577, 1 600 (Ar). 3 210, 3 300 cm^{-1} (OH). For $C_{13}H_{10}ClNO_3S$ (295·8) calculated: 52·79% C, 3·41% H, 11·99% Cl, 4·74% N, 10·84% S; found: 53·03% C, 3·49% H, 11·84% Cl, 4·59% N, 10·57% S.

2-(4-Chlorophenylthio)-4-nitrobenzyl Alcohol (*XVIIIa*)

Similarly as in the preceding case, 52·0 g *XVIIa* were reduced with 6·8 g $NaBH_4$ and 30 ml BF_3 etherate in 200 ml tetrahydrofuran; 37·0 g (75%), m.p. 146—149°C. Analytical sample, m.p. 149—150°C (benzene). UV spectrum: λ_{max} 251 nm (log ε 4·29), infl. 270 nm (4·15), infl. 338 nm (3·13). IR spectrum (Nujol): 794, 821, 840, 883, 890 (2 adjacent and solitary Ar—H), 1 044, 1 069 (CH_2OH). 1 346, 1 520 (NO_2), 1 575, 1 600 (Ar), 3 200 and 3 290 cm^{-1} (OH). ^{1}H-NMR spectrum: δ 8·10 (mcd, J = 8·0; 3·5 Hz, 1 H, 5-H of benzyl alcohol), *c.* 7·70 (m, 2 H, 3,6-H_2 of benzyl alcohol), 7·40 (d, J = 8·0 Hz, 2 H, 3,5-H_2 of chlorophenyl), 7·25 (d, J = 8·0 Hz, 2 H, 2,6-H_2 of chlorophenyl), 5·63 (t, J = 6·0 Hz, disappears after D_2O, 1 H, OH), 4·58 (d, J = 6·0 Hz, after D_2O s, 2 H, $ArCH_2$). For $C_{13}H_{10}ClNO_3S$ (295·8) calculated: 52·79% C, 3·41% H, 11·98% Cl, 4·74% N, 10·86% S; found: 52·79% C, 3·18% H, 11·70% Cl, 4·65% N, 10·91% S.

5-Amino-2-(4-chlorophenylthio)benzyl Alcohol (*Vb*)

A solution of 146·2 g *Va* in 1·5 l ether was cooled with water and under stirring slowly treated with 452 g $SnCl_2.2\,H_2O$; 400 ml hydrochloric acid were then added dropwise over 90 min maintaining the mixture in gentle boiling. The mixture was refluxed for 4 h, decomposed under cooling by a slow addition of 1·5 l 20% NaOH, the organic layer was separated, washed with 20% NaOH, dried with K_2CO_3 and evaporated; 105 g (80%), m.p. 100—102°C. Analytical sample melts at 102—103°C (benzene–light petroleum). IR spectrum (Nujol): 813, 881 (2 adjacent and solitary Ar—H), 1 009, 1 092 (CH_2OH), 1 307 (Ar—NH_2), 1 472, 1 570, 1 602 (Ar), 1 640 (NH_2), 3 230, 3 355, 3 395 cm^{-1} (OH and NH_2). For $C_{13}H_{12}ClNOS$ (265·8) calculated: 58·74% C. 4·55% H, 13·34% Cl, 5·27% N, 12·07% S; found: 59·11% C, 4·52% H, 13·15% Cl, 5·12% N, 11·95% S.

4-Amino-2-(4-chlorophenylthio)benzyl Alcohol (*XVIIIb*)

A suspension of 34 g *XVIIIa* and 0·8 g 10% Pd catalyst on carbon in 250 ml ethanol was stirred and treated dropwise with 22 ml 100% hydrazine hydrate over 50 min. The mixture was refluxed for 12 h, then treated with 1 g 20% Pd/C and 10 ml hydrazine hydrate, and refluxed for 5 h. The catalyst was filtered off, the filtrate evaporated under reduced pressure, the residue mixed with a small amount of ethanol and filtered; 26·5 g (87%), m.p. 145–148°C. Analytical sample, m.p. 147–150°C (ethanol). IR spectrum: 807, 845, 876 (2 adjacent and solitary Ar—H), 1 088 (CH_2OH), 1 563, 1 595 (Ar), 1 627 (Ar—NH_2), 3 180, 3 270, 3 400 cm^{-1} (OH and NH_2). For $C_{13}H_{12}ClNOS$ (265·8) calculated: 58·74% C, 4·55% H, 13·34% Cl, 5·27% N, 12·07% S; found 58·91% C, 4·68% H, 13·51% Cl, 5·48% N, 11·88% S.

4-Amino-2-(4-chlorophenylthio)benzoic Acid (*XVIIb*)

XVIIa (6·2 g) was dissolved in a mixture of 220 ml water and 10 ml NH_4OH, the solution was treated with a solution of 44·5 g $FeSO_4.7\,H_2O$ in 60 ml water and under stirring, another 25 ml NH_4OH were added dropwise over 10 min. The mixture was stirred for 5 h at 60–80°C, filtered and the filtrate neutralized with acetic acid. The precipitated crude product was filtered and recrystallized from a mixture of aqueous ethanol and dioxane; 2·85 g (39%) of a dioxane solvate were obtained, m.p. 225–232°C with decomposition. Analytical sample, m.p. 230–234°C with decomposition (dioxane). UV spectrum: λ_{max} 226 nm (log ε 4·27), 253 nm (4·30), 289 nm (4·25). IR spectrum (Nujol): 821, 870 (2 adjacent and a solitary Ar—H), 1117 (C—O—C of dioxane), 1 250, 1 279, 1 330 (COOH). 1 546, 1 570 (Ar), 1 592, 1 660 (NH_2...O=C(OH)—), 2 600, 2 660 (NH_3^+), 3 235, 3 350, 3 415 cm^{-1} (NH_2). For $C_{13}H_{10}ClNO_2 + C_4H_8O_2$ (367·9) calculated: 55·51% C, 4·93% H, 9·64% Cl, 3·81% N, 8·71% S; found: 55·50% C, 4·93% H, 9·53% Cl, 3·64% N, 8·48% S.

5-Acetamido-2-(4-chlorophenylthio)benzyl Alcohol (*Vc*)

A mixture of 104·4 g *Vb* and 185 ml isopropenyl acetate was refluxed for 6 h. The acetone formed was distilled off on a column and the residue was refluxed for 14 h with maintaining a temperature of 85°C in the head of the column. The mixture was then diluted with benzene and left overnight in a refrigerator; 108·2 g (83%) of a solvate with 1/3 of benzene molecule crystallized, m.p. 142–143°C. Recrystallization from a mixture of ethanol and benzene does not change the melting point. ^{1}H-NMR spectrum: δ 10·18 (bs, 1 H, NH), 7·84 (mcs, J = 2·5 Hz, 1 H, 6-H of benzyl alcohol), 7·70 (mcd, J = 8·5; 2·5 Hz, 1 H, 4-H of benzyl alcohol), 7·37 (d, J = 8·0 Hz, 1 H, 3-H of benzyl alcohol), 7·34 (d, J = 8·5 Hz, 2 H, 3,5-H_2 of chlorophenyl), 7·02 (d, J = = 8·5 Hz, 2 H, 2,6-H_2 of chlorophenyl), 5·39 (bs, 1 H, OH), 4·56 (bs, 2 H, $ArCH_2$), 2·12 (s, 3 H, $COCH_3$). For $C_{15}H_{14}ClNO_2S + 1/3\ C_6H_6$ (333·9) calculated: 61·16% C, 4·83% H, 10·62% Cl, 4·20% N, 9·60% S; found: 61·15% C, 4·82% H, 10·41% Cl, 3·99% N, 9·45% S.

5-Acetamido-2-(4-chlorophenylthio)benzyl Chloride (*VIc*)

Pyridine (36 ml) was added to a suspension of 108 g *Vc* in 150 ml chloroform and the stirred mixture was treated dropwise at 15°C with 50 g $SOCl_2$ over 30 min. The stirring was continued for 2 h, the mixture left overnight at room temperature, diluted with 850 ml chloroform, decomposed by a slow addition of 100 ml water, the organic layer was separated, washed with 5% NaOH, 5% HCl and water, dried with $MgSO_4$ and after filtration with charcoal, it was evaporated under reduced pressure. The residue was mixed with a small amount of benzene and filtered;

96 g (83%), m.p. 140–142°C. Analytical sample, m.p. 142–143°C (benzene). ^{1}H-NMR spectrum: δ 10·25 (bs, 1 H, NH), 7·93 (mcs, J = 2·0 Hz, 1 H, 6-H of benzyl chloride), 7·64 (mcd, J = 8·5; 2·0 Hz, 1 H, 4-H of benzyl chloride), 7·44 (d, J = 8·5 Hz, 1 H, 3-H of benzyl chloride), 7·36 (d, 8·5 Hz, 2 H, 3,5-H_2 of chlorophenyl), 7·14 (d, J = 8·5 Hz, 2 H, 2,6-H_2 of chlorophenyl), 4·86 (s, 2 H, $ArCH_2Cl$), 2·12 (s, 3 H, $COCH_3$). For $C_{15}H_{13}Cl_2NOS$ (326·2) calculated: 55·22% C, 4·02% H, 21·74% Cl, 4·29% N, 9·83% S; found: 55·23% C, 3·98% H, 21·49% Cl, 4·09% N, 9·80% S.

[5-Acetamido-2-(4-chlorophenylthio)phenyl]acetonitrile (*VIIc*)

A mixture of 350 ml dimethylformamide, 96 g *VIc* and 23 g NaCN was stirred and heated for 8 h to 100°C. The solvent was evaporated under reduced pressure, the residue decomposed with water and the product extracted with chloroform. The extract was washed with water, dried with $MgSO_4$, filtered with charcoal and evaporated. The residue was repeatedly extracted with a boiling mixture 2 : 3 of benzene and light petroleum. The combined extracts were incompletely evaporated and the residue left overnight in a refrigerator; 65 g (70%), m.p. 140–143°C. Analytical sample, m.p. 151–152°C (benzene). IR spectrum: 823, 834, 858 (2 adjacent and solitary Ar–H), 1328, 1553, 1657 (RCONHAr), 1475, 1573, 1605 (Ar), 2255 (R–CN), 3245, 3290 cm^{-1} (NH). For $C_{16}H_{13}ClN_2OS$ (316·8) calculated: 60·66% C, 4·14% H, 11·19% Cl, 8·84% N, 10·12% S; found: 60·93% C, 4·26% H, 11·35% Cl, 8·72% N, 10·10% S.

[5-Amino-2-(4-chlorophenylthio)phenyl]acetic Acid (*VIIIb*)

A warm solution of 41 g *VIIc* in 125 ml ethanol was treated with a solution of 26 g KOH in 52 ml water, the mixture was refluxed for 6 h, diluted with 130 ml water, and ethanol was distilled off at normal pressure. The aqueous residue was acidified with acetic acid and the precipitated product filtered; 37·0 g (97%), m.p. 150–155°C. Analytical sample, m.p. 161–163°C (benzene–light petroleum). IR spectrum (Nujol): 815, 857 (2 adjacent and solitary Ar–H), 917, 1226, 1693, 1710 (COOH), 1477, 1483, 1570, 1596 (Ar), 1620, 3380, 3485 cm^{-1} (NH_2). ^{1}H-NMR spectrum: δ 7·26 (d, J = 8·5 Hz, 2 H, 3,5-H_2 of chlorophenyl), 7·18 (d, J = 8·5 Hz, 1 H, 3-H of phenylacetic acid), 6·94 (d, J = 8·5 Hz, 2 H, 2,6-H_2 of chlorophenyl), 6·64 (mcs, J = 2·5 Hz, 1 H, 6-H of phenylacetic acid), 6·55 (mcd, J = 8·5; 2·5 Hz, 1 H, 4-H of phenylacetic acid), 3·55 (s, 2 H, $ArCH_2CO$). For $C_{14}H_{12}ClNO_2S$ (293·8) calculated: 57·24% C, 4·12% H, 12·07% Cl, 4·77% N, 10·91% S; found: 57·74% C, 4·31% H, 12·09% Cl, 4·75% N, 10·85% S.

(2-Bromo-4-nitrophenyl)acetic Acid (*XXIa*)

2-Bromo-4-nitroaniline[24] (43·4 g) in a mixture of 70 ml hydrochloric acid and 125 ml water was diazotized with a solution of 13·8 g $NaNO_2$ in 20 ml water at 0–5°C. The mixture was stirred for 1 h, the insoluble material was filtered off and the filtrate treated with a solution of 5·4 g CuCl, in 10 ml water. This mixture was added at once into a solution of 34 g 1,1-dichloroethylene[22] in 90 ml acetone. Without cooling, the mixture was stirred and neutralized partly with $NaHCO_3$ and then with MgO. Formation of nitrogen began after dilution with further 100 ml acetone and after attaining the temperature of 20–25°C. The mixture was stirred for 1 h and left overnight at room temperature. Acetone was then distilled off, the residue subjected for a short time to steam distillation and after cooling, the remaining liquid (pH *c.* 4) was extracted with benzene. The extract was dried and evaporated. The residue was dissolved in benzene and the solution filtered through a column of 1 kg Al_2O_3 (act. II). Evaporation of the eluate gave 42·5 g crude intermediate of the type $ArCH_2CCl_3$ with a very unsharp melting point (attempt at its purification by crystallization was unsuccessful), which was subjected to hydrolysis in crude

state. It was dissolved in 200 ml H_2SO_4 at 120—130°C, the solution was stirred for 3 h, cooled, poured on ice and the precipitated product filtered. Separation of neutral and acidic fractions was effected by shaking with chloroform and 5% $NaHCO_3$, the undissolved polymeric products were removed by filtration and the aqueous layer of the filtrate was acidified with hydrochloric acid. The precipitated crude product was filtered and crystallized from water; 5·2 g (10%), m.p. 166—168·5°C. UV spectrum (C_2H_5OH): λ_{max} 268 nm (log ε 3·99). IR spectrum: 830, 860 (2 adjacent and solitary Ar—H), 922, 1246 (COOH), 1353, 1527 ($ArNO_2$), 1600, 1611 (Ar), 1708, 2600—2800, 3139 cm^{-1} (COOH). ^{1}H-NMR spectrum: δ 8·30 (mcs, J = 3·0 Hz, 1 H, 3-H), 8·10 (mcd, J = 8·0; 3·0 Hz, 1 H, 5-H), 7·59 (d, J = 8·0 Hz, 1 H, 6-H), 3·80 (s, 2 H, $ArCH_2CO$). For $C_8H_6BrNO_4$ (260·1) calculated: 5·39% N; found: 5·63% N.

(2-Iodo-4-nitrophenyl)acetic Acid (*XXIIa*)

2-Iodo-4-nitroaniline[25] (105·6 g) was processed similarly as in the preceding case (hydrolysis of the primary product with H_2SO_4 at 80°C) and yielded 18·0 g (15%) product melting at 167 to 168·5°C (water). IR spectrum (Nujol): 821, 850, 872 (2 adjacent and solitary Ar—H), 911, 1236, 1712, 2550, 2640, 2730 (COOH), 1348, 1513 ($ArNO_2$), 1582, 1597, 3095 cm^{-1} (Ar). For $C_8H_6INO_4$ (307·1) calculated: 31·29% C, 1·97% H, 41·33% I, 4·56% N; found: 31·45% C, 2·01% H, 40·82% I, 4·52% N.

(4-Amino-2-bromophenyl)acetic Acid (*XXIb*)

Analogously with the preparation of the acid *XVIIb*, 4·6 g *XXIa* were reduced with ferrous hydroxide, obtained from 40 g $FeSO_4$. 7 H_2O and NH_4OH, and gave 3·39 g (84%) product melting at 182·5—184·5°C (water). IR spectrum: 665 (C—Br), 805, 835, 867 (2 adjacent and solitary Ar—H), 1380 (RCOOH), 1495 (Ar), 1590 (COO^-), 2600 cm^{-1} (NH_3^+). For $C_8H_8BrNO_2$ (230·1) calculated: 34·74% Br, 6·09% N; found: 34·86% Br, 6·28% N.

2-(4-Chlorophenylthio)-4-nitrophenyl Diazomethyl Ketone (*XIXa*)

A mixture of 34·3 g *XVIIa* and 80 ml $SOCl_2$ was refluxed for 2·5 h. Volatile fractions were evaporated, the remnants removed by distillation with toluene, the residue was dissolved in 100 ml dichloromethane and the solution treated dropwise under stirring with a solution of diazomethane in 800 ml ether (prepared by decomposition of 46 g nitrosomethylurea with 130 ml 50% KOH) over 10 min at 5—10°C. The mixture was stirred for 1 h at room temperature, left overnight, the ether was partly evaporated and the product filtered; 31·1 g (84%), m.p. 142—144°C with decomposition. UV spectrum: λ_{max} 247·5 nm (log ε 4·32), infl. 285 nm (4·09), infl. 305 nm (4·01), 362 nm (3·59). IR spectrum: 828, 857, 892 (2 adjacent and solitary Ar—H), 1349, 1360, 1521 ($ArNO_2$), 1573, 1593 (Ar), 1612 (Ar—C=C), 2120 (C=$\overset{(+)}{N}$=$\overset{(-)}{N}$), 3088, 3105 and 3125 cm^{-1} (Ar). ^{1}H-NMR spectrum: δ 7·96 (mcd, 1 H, 5-H of benzoyl), 7·78 (d, 1 H, 6-H of benzoyl), 7·48 (s, 5 H, remaining Ar—H), 6·78 (s, 1 H, $COCHN_2$). For $C_{14}H_8ClN_3O_3S$ (333·8) calculated: 50·38% C, 2·42% H, 10·62% Cl, 12·59% N, 9·61% S; found: 50·20% C, 2·68% H, 10·93% Cl, 12·20% N, 9·66% S.

[2-(4-Chlorophenylthio)-4-nitrophenyl]acetic Acid (*XXa*)

A solution of 30·0 g *XIXa* in 900 ml dioxane was treated at 50°C with 100 ml water and then over 30 min with a suspension of Ag_2O prepared from 15·5 g $AgNO_3$. The mixture was stirred for 30 min at 85°C and after cooling, the precipitated product was filtered. It was decomposed

with hydrochloric acid and the released acid was extracted with benzene. From benzene it was transferred by shaking into an excess of 5% $NaHCO_3$ and released again by acidification with hydrochloric acid. The filtered crude product was crystallized from aqueous ethanol; 13·6 g (47%), m.p. 157–163°C. Analytical sample, m.p. 161–164°C (aqueous ethanol). UV spectrum: λ_{max} 253 nm (log ε 4·28), 272 nm (4·17), 335 nm (3·32). IR spectrum (Nujol): 820, 830, 889 (2 adjacent and solitary Ar—H), 927, 1241, 1707 (COOH), 1350, 1527 (NO_2), 1472, 1481, 1580, 1589 (Ar), 2640, 2735 cm^{-1} (COOH). ^{1}H-NMR spectrum: δ 8·02 (mcd, J = 8·0; 2·0 Hz, 1 H, 5-H of phenylacetic acid), 7·80 (mcs, J = 2·0 Hz, 1 H, 3-H of phenylacetic acid), 7·58 (d, J = 8·0 Hz, 1 H, 6-H of phenylacetic acid), 7·40 (d, J = 8·0 Hz, 2 H, 3·5-H_2 of chlorophenyl), 7·20 (d, J = 8·0 Hz, 2 H, 2,6-H_2 of chlorophenyl), 3·85 (s, 2 H, $ArCH_2CO$). For $C_{14}H_{10}ClNO_4S$ (323·8) calculated: 51·94% C, 3·11% H, 10·95% Cl, 4·33% N, 9·90% S; found: 52·24% C, 3·23% H, 10·78% Cl, 4·72% N, 10·09% S.

2-Amino-8-chlorodibenzo[*b,f*]thiepin-10(11*H*)-one (*IX*)

A mixture of 35·0 *VIIIb* and polyphosphoric acid, prepared from 270 g P_2O_5 and 135 ml 85% H_3PO_4, was stirred and heated for 1·5 h to 125°C; after cooling to 70°C it was decomposed with ice and water. After standing overnight, the precipitated product was filtered, suspended in a 5% solution of Na_2CO_3 and after 30 min of stirring filtered again, washed with water and dried in air; 31 g (93%), m.p. 205–210°C. Analytical sample, m.p. 213–215°C (benzene or dioxane). UV spectrum: λ_{max} 229 nm (log ε 4·44), 263 nm (4·27), 355 nm (3·50). IR spectrum: 814, 862, 905 (2 adjacent and solitary Ar—H), 1565, 1572, 1590 (Ar), 1625 (NH_2), 1663 (Ar—CO—R), 3280, 3398 cm^{-1} ($ArNH_2$). ^{1}H-NMR spectrum: δ 7·90 (mcs, J = 2·0 Hz, 1 H, 9-H), 7·55 (m, 2 H, 6,7-H_2), 7·25 (d, J = 8·5 Hz, 1 H, 4-H), 6·65 (mcs, J = 2·0 Hz, 1 H, 1-H), 6·40 (mcd, J = 8·5; 2·5 Hz, 1 H, 3-H), 5·60 (bs, 2 H, NH_2), 4·10 (s, 2 H, $ArCH_2CO$). For $C_{14}H_{10}ClNOS$ (275·8) calculated: 60·97% C, 3·65% H, 12·86% Cl, 5·08% N, 11·63% S; found: 61·04% C, 3·77% H, 12·78% Cl, 5·06% N, 11·42% S.

8-Chloro-3-nitrodibenzo[*b,f*]thiepin-10(11*H*)one (*XXIII*)

Polyphosphoric acid was prepared from 18 g P_2O_5 and 9 ml 85% H_3PO_4; a solution of 4·9 g *XXa* in 60 ml toluene was added and the mixture was stirred and refluxed for 14 h. The toluene solution was separated by decantation, the remnants in the vessel were extracted with boiling toluene and the toluene solutions combined. After washing with 5% NaOH and water, toluene was evaporated; 4·2 g (91%), m.p. 193–194°C. Analytical sample, m.p. 194–195°C (benzene). UV spectrum: λ_{max} 227 nm (log ε 4·34), 264 nm (4·32), 335 nm (3·68). IR spectrum (Nujol): 831, 859, 900, 909 (2 adjacent and solitary Ar—H), 1348, 1533 (NO_2), 1580, 1600 (Ar), 1691 (Ar—CO), 3100 cm^{-1} (Ar). For $C_{14}H_8ClNO_3S$ (305·8) calculated: 55·00% C, 2·63% H, 11·60% Cl, 4·58% N, 10·49% S; found: 54·83% C, 2·74% H, 11·43% Cl, 4·52% N, 10·40% S.

2-Amino-8-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ol (*X*)

A suspension of 24·5 g *IX* in 250 ml dioxane was treated dropwise over 10 min at 20°C with a solution of 3·6 g $NaBH_4$ in 10 ml water containing 3 drops of 20% NaOH. The mixture was stirred for 1 h at 70°C and for 4 h at room temperature. After standing overnight, an insoluble fraction was removed by filtration and the filtrate was evaporated under reduced pressure. The residue was dissolved in benzene, the solution washed with water, dried with $MgSO_4$ and evaporated after filtration with charcoal; 19·0 g (77%), m.p. 122–127°C. Analytical sample, m.p. 130–133°C (benzene). IR spectrum: 814, 860, 873 (2 adjacent and solitary Ar—H), 1058, 1090

(CHOH in a ring), 1557, 1580, 1600 (Ar), 3130 (OH), 3280, 3350 cm^{-1} (NH_2). ^{1}H-NMR spectrum: δ 7·55 (mcs, J = 2·0 Hz, 1 H, 9-H), 7·40 (d, J = 8·5 Hz, 1 H, 6-H), 7·18 (mcd, J = 8·5; 2·0 Hz, 1 H, 7-H), 7·10 (d, J = 8·5 Hz, 1 H, 4-H), 6·52 (mcs, J = 2·0 Hz, 1 H, 1-H), 6·38 (mcd, J = 8·5; 2·0 Hz, 1 H, 3-H), 5·82 (d, J = 5·0 Hz, 1 H, OH), 5·16 (bs, 2 H, NH_2), 5·14 (m, 1 H, Ar—CH—O), *c.* 3·30 (m, 2 H, $ArCH_2$). For $C_{14}H_{12}ClNOS$ (277·8) calculated: 60·53% C, 4·36% H, 12·77% Cl, 5·04% N, 11·54% S; found: 60·78% C, 4·42% H, 12·48% Cl, 5·05% N, 11·37% S.

8-Chloro-3-nitro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ol (*XXIV*)

In analogy to the preceding case but without heating, reduction of 12·6 g *XXIII* with 1·6 g $NaBH_4$ in 180 ml dioxane and 5 ml water was carried out. In this case, it was necessary to chromatograph the crude product on a column of 500 g Al_2O_3 (act. II). After the separation of the least polar fraction by elution with a mixture of benzene and chloroform, the desired product was eluted with chloroform; 8·0 g (63%), m.p. 133·5—134°C (benzene). We are dealing here with the modification *A* of compound *XXIV*. UV spectrum: λ_{max} 266 nm (log ε 4·30), 330 nm (3·09). IR spectrum (Nujol): 779, 825, 841, 891, 906 (2 adjacent and solitary Ar—H), 1056 (CHOH in a ring), 1352, 1524 (NO_2), 1585, 1604 (Ar), 3320, 3390 cm^{-1} (OH). For $C_{14}H_{10}ClNO_3S$ (307·8) calculated: 54·64% C, 3·28% H, 11·52% Cl, 4·55% N, 10·42% S; found: 54·84% C, 3·33% H, 11·60% Cl, 4·69% N, 10·31% S.

In another experiment, crystallization of the product from benzene gave the modification *B* which, when heated, shows at 130—132°C a change of the crystal form and melts at 150—152°C. Its UV spectrum is identical with that of the modification *A*. IR spectrum (Nujol): 779, 804, 824, 846, 872, 897 (2 adjacent and solitary Ar—H), 1060 (CHOH in a ring), 1355, 1518 (NO_2), 1582, 3100 (Ar), 3532 cm^{-1} (OH). IR spectra of both modifications in chloroform solution are completely identical. For $C_{14}H_{10}ClNO_3S$ (307·8) calculated: 54·64% C, 3·28% H, 11·52% Cl, 4·55% N, 10·42% S; found: 55·08% C, 3·38% H, 11·41% Cl, 4·65% N, 10·45% S.

3-Amino-8-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ol (*XXV*)

A warm solution of 6·1 g *XXIV* (modification *A*) in 100 ml ethanol was treated with 6 ml 100% hydrazine hydrate, 1 g charcoal and 0·3 g $FeCl_3$ in 10 ml ethanol and the mixture was refluxed for 6 h. After cooling, it was filtered and the filtrate evaporated *in vacuo*; 5·5 g (100%), m.p. 130—132·5°C. Analytical sample, m.p. 131—132·5°C (aqueous ethanol). IR spectrum: 825, 851, 892 (2 adjacent and solitary Ar—H), 1028, 1064, 1098 (CHOH in a ring), 1500, 1608 (Ar), infl. 1630 (NH_2), 3332 and 3410 cm^{-1} (NH_2 and OH). For $C_{14}H_{12}ClNOS$ (277·8) calculated: 60·53% C, 4·35% H, 12·76% Cl, 5·04% N, 11·54% S; found: 60·79% C, 4·31% H, 12·70% Cl, 5·01% N, 11·49% S.

2-Acetyl-8-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ol (*XI*)

A suspension of 17·5 g *X* in 75 ml hydrochloric acid and 300 ml water was diazotized at 0°C with a solution of 5·0 g $NaNO_2$ in 10 ml water and the mixture was stirred for 1 h at 0°C. After the addition of 1 g urea it was filtered, the filtrate treated with an ice-cold solution of 90 g sodium acetate trihydrate in 90 ml water and the mixture obtained was added at 10°C to a mixture, prepared by mixing solutions of 40 g acetaldehyde semicarbazone[11] in 180 ml water, 40 g sodium acetate trihydrate in 40 ml water, 2·4 g $CuSO_4.5\,H_2O$ in 10 ml water and 0·3 g Na_2SO_3 in 5 ml water. The mixture was stirred for 5 h at room temperature, after standing overnight it was acidified with 50 ml hydrochloric acid, the precipitated solid was filtered and and added to a solu-

tion of 50 g oxalic acid dihydrate in 250 ml water. The mixture was refluxed for 3 h and extracted with a mixture of benzene and chloroform. Evaporation of the extract gave an inhomogeneous product which was chromatographed on a column of 300 g silica gel. 2,8-Dichloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ol (*XII*) (1·54 g) was eluted as the least polar product with a mixture of benzene and chloroform, m.p. 118–119°C. For this product, prepared differently, we reported[12] a m.p. of 120–121°C. IR spectrum: 801, 822, 882 (2 adjacent and solitary Ar—H), 1051, 1091 (CHOH in a ring), 1552, 1575 (Ar), 3245 cm^{-1} (OH). ^{1}H-NMR spectrum ($CDCl_3$): δ 7·50 (mcs, J = 2·0 Hz, 1 H, 9-H), 7·38 and 7·35 (2 d, J = 8·5 Hz, 2 H, 4,6-H_2), 7·00–7·25 (m, 3 H, remaining Ar—H), 5·30 (dd, J = 8·0; 4·0 Hz, 1 H, Ar—CH—O), 3·64 and 3·24 (2 dd, J = 14·0; 4·0 and 14·0; 8·0 Hz, 2 H, $ArCH_2$), 2·28 (bs, disappears after D_2O, 1 H, OH). For $C_{14}H_{10}Cl_2OS$ (297·2) calculated: 56·57% C, 3·39% H; found: 56·51% C, 3·31% H.

When continuing the chromatography, elution with the same solvent mixture gave 2·06 g of a further fraction melting at 82–83°C (benzene–light petroleum). This fraction is a mixture with 8-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ol (*XIII*) as the main component, for which we earlier reported[1] the m.p. of 84–85°C. The analysis indicates the presence of a nitrogen-containing contaminant (found 2·90% N). The mass spectrum with the molecular ion m/e 262 confirms the presence of compound $C_{14}H_{11}ClOS$, *i.e.* *XIII*. The nitrogen-containing component appears in the mass spectrum as the molecular ion m/e 303, corresponding to the empirical formula $C_{14}H_{10}ClN_3OS$.

Elution with chloroform yielded the desired compound *XI* (5·56 g, 29%), m.p. 120–122°C (ethanol). UV spectrum: λ_{max} 237 nm (log ε 4·17), infl. 256 nm (4·02), 304 nm (4·03). IR spectrum: 807, 816, 872, 899 (2 adjacent and solitary Ar—H), 1029, 1049, 1066 (CHOH in a ring), 1557 and 1580 (Ar), 1672 ($ArCOCH_3$), 3408 cm^{-1} (OH). ^{1}H-NMR spectrum ($CDCl_3$): δ 7·00–7·80 (m, 6 H, Ar—H), 5·44 (dd, J = 8·0; 4·0 Hz, 1 H, Ar—CH—O), 3·65 and 3·34 (2 dd, J = 14·0; 4·0 and 14·0; 8·0 Hz, 2 H, $ArCH_2$), 2·85 (bs, 1 H, OH), 2·53 (s, 3 H, $COCH_3$). For $C_{16}H_{13}ClO_2S$ (304·8) calculated: 63·05% C, 4·30% H; found: 62·97% C, 4·27% H.

3-Acetyl-8-chloro-10,11-dihydrodibenzo[*b,f*]thiepin-10-ol (*XXVI*)

In analogy with the preceding case, 6·3 g *XXV* were processed by diazotization, reaction with acetaldehyde semicarbazone and hydrolysis with oxalic acid (in the diazotization step it was necessary to add 30 ml acetic acid for increase the solubility of *XXV* hydrochloride). An inhomogeneous product (4·8 g) was obtained which was chromatographed on a column of 400 g Al_2O_3 (act. II). A mixture of benzene and chloroform eluted 0·37 g 8-chloro-10,11-dihydrodibenzo-[*b,f*]-thiepin-10-ol (*XIII*), m.p. 79–82°C, melting without depression in a mixture with the authentic product[1]. *XXVI* was obtained by elution with a mixture of chloroform and ethanol; 1·39 g (20%), m.p. 116–118°C (benzene–light petroleum). IR spectrum: 830, 900, 910 (2 adjacent and solitary Ar—H), 1059 (CHOH in a ring), 1470, 1582, 1600 (Ar), 1687 ($ArCOCH_3$), 3060, 3090 (Ar), 3490 cm^{-1} (OH). For $C_{16}H_{13}ClO_2S$ (304·8) calculated: 63·05% C, 4·30% H, 11·63% Cl, 10·52% S; found: 63·10% C, 4·42% H, 11·57% Cl, 10·38% S.

2-Acetyl-8,10-dichloro-10,11-dihydrodibenzo[*b,f*]thiepin (*I*)

A solution of 2·27 g *XI* in 100 ml benzene was treated with 2 g powdery $CaCl_2$ and the suspension was saturated for 2 h with hydrogen chloride at room temperature. After standing overnight, it was filtered and the filtrate was evaporated under reduced pressure. Because it was found by means of TLC that the residue still contains the starting compound, it was dissolved in 50 ml dichloromethane, 3 g $CaCl_2$ were added and the mixture was saturated for 4 h with hydrogen chloride. Evaporation gave 2·33 g (97%) product melting at 116–124°C. Analytical sample,

m.p. 123—125°C (benzene–light petroleum). ^{1}H-NMR spectrum ($CDCl_3$): δ 7·85 (mcs, J = = 2·0 Hz, 1 H, 1-H), 7·76 (mcd, J = 8·5; 2·0 Hz, 1 H, 3-H), 7·56 (d, J = 8·5 Hz, 1 H, 4-H), 7·54 (mcs, J = 2·0 Hz, 1 H, 9-H), 7·35 (d, J = 8·5 Hz,1 H, 6-H), 7·12 (mcd, J = 8·5; 2·0 Hz, 1 H, 7-H), 5·76 (dd, J = 8·0; 4·0 Hz, 1 H, Ar—CH—Cl), 3·98 and 3·65 (2 dd, J = 14·0; 4·0 and 14·0; 8·0 Hz, 2 H, $ArCH_2$), 2·55 (s, 3 H, $COCH_3$). For $C_{16}H_{12}Cl_2OS$ (323·3) calculated: 59·45% C, 3·74% H, 21·94% Cl, 9·92% S; found: 59·34% C, 3·78% H, 21·60% Cl, 9·91% S.

3-Acetyl-8,10-dichloro-10,11-dihydrodibenzo[*b,f*]thiepin (*XIV*)

A mixture of 0·80 g *XXVI* and 5 ml $SOCl_2$ was refluxed for 1·5 h. Volatile fractions were evaporated and the residue (0·80 g, 94%, m.p. 133—140°C) was purified by crystallization; m.p. 138—141°C (benzene–cyclohexane). UV spectrum: λ_{max} 252 nm (log ε 4·33), infl. 295 nm (3·50). IR spectrum: 820, 842, 872, 892 (2 adjacent and solitary Ar—H), 1 582, 1 597 (Ar), 1 693 cm^{-1} (ArCO). ^{1}H-NMR spectrum ($CDCl_3$): δ 8·10 (mcs, J = 2·0 Hz, 1 H, 4-H), 7·85 (mcd, J = 8·0; 2·0 Hz, 1 H, 2-H), 7·51 (mcs, J = 2·5 Hz, 1 H, 9-H), 7·38 (d, J = 8·0 Hz, 2 H, 1,6-H_2), 7·10 (mcd, J = 8·0; 2·5 Hz, 1 H, 7-H), 5·80 (dd, J = 4·0; 8·0 Hz, 1 H, Ar—CH—Cl), 4·05 and 3·68 (2 dd, J = 14·0; 4·0 and 14·0; 8·0 Hz, 2 H, $ArCH_2$), 2·58 (s, 3 H, $COCH_3$). For $C_{16}H_{12}Cl_2OS$ (323·2) calculated: 59·45% C, 3·74% H, 21·94% Cl, 9·92% S; found: 60·16% C, 3·87% H, 21·60% Cl, 10·20% S.

2-Acetyl-8-chloro-10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b,f*]thiepin (*II*)

A mixture of 2·10 g *I*, 10 ml 1-methylpiperazine and 10 ml chloroform was refluxed for 5·5 h. After standing overnight, water was added and the mixture was extracted with benzene. The extract was washed with water and shaken with 10% hydrochloric acid. The precipitated hydrochloride was filtered, combined with the aqueous layer of the filtrate, made alkaline with NH_4OH and the base isolated by extraction with benzene; 1·90 g (76%) oil. Neutralization with maleic acid in ethanol and addition of ether gave the bis(hydrogen maleate) crystallizing from a mixture of 95% ethanol and ether as a hemihydrate of m.p. 73—76°C. For $C_{29}H_{31}ClN_2O_9S + 0{\cdot}5\ H_2O$ (628·1) calculated: 55·46% C, 5·14% H, 5·64% Cl, 4·46% N, 5·10% S; found: 55·87% C, 5·17% H, 5·63% Cl, 4·40% N, 5·30% S.

A sample of the maleate was decomposed with a solution of Na_2CO_3, the precipitated base was filtered, washed with water, dried over P_2O_5 and used for the registration of spectra. UV spectrum: λ_{max} 243 nm (log ε 4·28), infl. 256 nm (4·20), 313 nm (3·93). IR spectrum: 818, 887 (2 adjacent and solitary Ar—H), 1 555, 1 585 (Ar), 1 675 (ArCO), 2765 cm^{-1} (NCH_3). ^{1}H-NMR spectrum ($CDCl_3$): δ 7·86 (mcs, J = 1·5 Hz, 1 H, 1-H), *c.* 7·65 (m, 3 H, 3,4,9-H_3), 7·35 (d, J = = 8·5 Hz, 1 H, 6-H), 7·06 (mcd, J = 8·5; 2·0 Hz, 1 H, 7-H), 3·00—4·00 (m, 3 H, $ArCH_2CHAr$), 2·68 (t, 4 H, $CH_2N^1CH_2$ of piperazine), 2·56 (s, 3 H, $COCH_3$), 2·45 (t, 4 H, $CH_2N^4CH_2$ of piperazine), 2·26 (s, 3 H, NCH_3).

From the benzene solution, from which the basic product was removed with hydrochloric acid, 0·30 g 2-acetyl-8-chlorodibenzo[*b,f*]thiepin (*III*) were obtained by evaporation and crystallization from ethanol, m.p. 139—140·5°C. UV spectrum: λ_{max} 225 nm (log ε 4·46), 243 nm (4·55), infl. 255 nm (4·44), 279·5 nm (4·31). IR spectrum: 774, 816, 859, 897 (2 adjacent and solitary Ar—H), 1 670 cm^{-1} (ArCOR). ^{1}H-NMR spectrum ($CDCl_3$): δ 7·85 (mcd, J = 2·0; 8·5 Hz, 1 H, 3-H), 7·78 (mcs, J = 2·0 Hz, 1 H, 1-H), 7·52 (d, J = 8·5 Hz, 1 H, 4-H), 7·15—7·50 (m, 3 H, 6,7,9-H_3), 7·10 and 6·90 (2 d, J = 13·0 Hz, 2 H, 10,11-CH=CH), 2·50 (s, 3 H, $COCH_3$). For $C_{16}H_{11}ClOS$ (286·8) calculated: 67·01% C, 3·87% H, 12·36% Cl, 11·18% S; found: 67·55% C, 4·01% H, 12·17% Cl, 11·10% S.

3-Acetyl-8-chloro-10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b,f*]thiepin (*XV*)

Like in the preceding case, 0·70 g *XIV* reacted with 3 ml 1-methylpiperazine in 3 ml boiling chloroform and gave 0·44 g (52%) crude base, which was transformed to the bis(hydrogen maleate), m.p. 101—104°C (ethanol–ether). Its mass spectrum shows the molecular ion of the base with *m/e* 386 corresponding to $C_{21}H_{23}ClN_2OS$. The main fragment has *m/e* 287. IR spectrum: 828, 870 (2 adjacent and solitary Ar—H), 1692 (ArCOR), 2600 cm^{-1} (NH^+). For $C_{29}H_{31}$. $.ClN_2O_9S$ (619·1) calculated: 56·26% C, 5·05% H, 5·73% Cl, 4·52% N, 5·18% S; found: 56·16% C, 5·15% H, 6·13% Cl, 4·99% N, 5·47% S.

The base release from the maleate was used for registration of the ^{1}H-NMR spectrum ($CDCl_3$): δ 8·05 (mcs, 1 H, 4-H), 7·80 (mcd, 1 H, 2-H), 7·60 (mcs, 1 H, 9-H), 6·90—7·50 (m, 3 H, remaining Ar—H), 3·00—4·00 (m, 3 H, $ArCH_2CHAr$), 2·62 (m, 4 H, $CH_2N^1CH_2$ of piperazine), 2·51 (s, 3 H, $COCH_3$), 2·45 (m, 4 H, $CH_2N^4CH_2$ of piperazine), 2·25 (s, 3 H, NCH_3).

7-Acetyl-2-chlorodibenzo[*b,f*]thiepin (*XVI*) was obtained as the neutral product; 0·15 g, m.p. 119—122°C (ethanol). ^{1}H-NMR spectrum ($CDCl_3$): δ 8·02 (mcs, J = 2·0 Hz, 1 H, 6-H), 7·82 (mcd, J = 8·2; 2·0 Hz, 1 H, 8-H), 7·10—7·50 (m, 4 H, remaining Ar—H), 7·00 (s, 2 H, 10,11-CH=CH), 2·60 (s, 3 H, $COCH_3$). For $C_{16}H_{11}ClOS$ (286·8) calculated: 67·01% C, 3·87% H, 12·36% Cl, 11·18% S; found: 67·03% C, 3·88% H, 12·55% Cl, 11·00% S.

2-Acetyl-7-chloro-9-(chloromethyl)thioxanthene (*XXVII*)

A. Acetyl chloride (36·5 g) was added to a mixture of 62·6 g $AlCl_3$ and 300 ml dichloromethane and the solution obtained was treated under stirring dropwise with a solution of 91·7 g 2-chlorodibenzo[*b,f*]thiepin[1] in 175 ml dichloromethane over 1·5 h at room temperature. After dilution with 200 ml dichloromethane, the mixture was refluxed for 5 h. After standing overnight, it was decomposed by pouring into a mixture of 1·25 kg ice and 120 ml hydrochloric acid. The organic layer was separated, the aqueous one extracted with 250 ml dichloromethane, the combined dichloromethane solutions were washed with 5% NaOH and water. After drying with $CaCl_2$, the solution was filtered and the filtrate evaporated. The oily residue crystallized after dissolution in a mixture of 50 ml benzene and 10 ml ethanol; 36·7 g (30%), m.p. 141—142°C. Analytical sample, m.p. 142·5—143·5°C (ethanol). UV spectrum: λ_{max} 241 nm (log ε 4·53), 263 nm (3·91), 312 nm (4·12). IR spectrum: 697 (C—Cl), 814, 826, 880, 903 (2 adjacent and solitaty Ar—H), 1065, 1095, 1105, 1190, 1253 (C—O), 1470, 1594 (Ar), 1682 cm^{-1} (ArCOR). ^{1}H-NMR spectrum ($CDCl_3$): δ 7·90 (mcs, J = 2·0 Hz, 1 H, 1-H), 7·80 (mcd, J = 8·5; 2·0 Hz, 1 H, 3-H), 7·43 (d, J = 8·5 Hz, 1 H, 4-H), *c.* 7·20 (m, 3 H, 5,6,8-H_3), 4·30 (t, J = 7·5 Hz, 1 H, Ar_2CH), 3·62 (d, J = 7·5 Hz, 2 H, CH_2Cl), 2·59 (s, 3 H, $COCH_3$). The mass spectrum shows the molecular ion *m/e* 322 confirming the empirical composition $C_{16}H_{12}Cl_2OS$; the basic fragment has *m/e* 273 corresponding to a cleavage of the CH_2Cl group. For $C_{16}H_{12}Cl_2OS$ (323·2) calculated: 59·45% C, 3·74% H, 21·94% Cl, 9·92% S; found: 59·59% C, 3·78% H, 21·98% Cl, 10·16% S.

Semicarbazone, m.p. 217—220°C (ethanol). ^{1}H-NMR spectrum (ZKR 60): δ 9·60 (s, 1 H, NH), 8·00 (bs, 1 H, 1-H), 7·74 (bd, 1 H, 3-H), 7·20—7·60 (m, 4 H, remaining Ar—H), 6·62 (bs, 2 H, NH_2), 4·56 (t, 1 H, Ar_2CH), 3·71 (bd, 2 H, CH_2Cl), 2·24 (s, 3 H, $COCH_3$). For $C_{17}H_{15}Cl_2N_3OS$ (380·3) calculated: 53·68% C, 3·98% H, 18·65% Cl, 8·43% S; found: 53·70% C, 4·05% H, 18·33% Cl, 8·61% S.

B. A mixture of 20 g $AlCl_3$, 100 ml dichloromethane and 11·5 g acetyl chloride was stirred and without cooling treated dropwise with a solution of 28·1 g 8,10-dichloro-10,11-dihydrodibenzo[*b,f*]thiepin[1] in 100 ml dichloromethane over 1·5 h. After diluting with 100 ml dichloromethane, the mixture was refluxed for 5 h and processed like under *A*. There were obtained 11·1 g

(34%) of a product melting at 137—142°C, which is identical with the product prepared according to A (mixed melting point, TLC).

2-Chloro-9-(chloromethyl)-7-propionylthioxanthene (*XXVIII*)

A mixture of 18·1 g $AlCl_3$, 100 ml dichloromethane and 12·6 g propionyl chloride was stirred and treated dropwise with a solution of 22·0 g 2-chlorodibenzo[*b*,*f*]thiepin[1] in 100 ml dichloromethane over 1 h. After 5 h of refluxing, the mixture was processed similarly as in the preceding cases. The crude product crystallized after addition of light petroleum; 6·3 g (21%), m.p. 141 to 142°C. Crystallization from ethanol did not raise the melting point. For $C_{17}H_{14}Cl_2OS$ (337·3) calculated: 60·54% C, 4·18% H, 21·03% Cl, 9·51% S; found: 60·62% C, 4·33% H, 21·03% Cl, 9·74% S.

2-Acetyl-7-chloro-9-(4-methylpiperazinomethyl)thioxanthene (*XXIX*)

A mixture of 25 g 1-methylpiperazine and 20 g *XXVII* was heated for 4 h to 120—125°C. It was then diluted with benzene and carefully washed with water. The benzene solution was then shaken with 125 ml 3M-HCl. The acid aqueous layer of the hydrochloride was made alkaline with NH_4OH and the base isolated by extraction with benzene; 14·5 g (61%) oil. Neutralization with maleic acid in ethanol gave the bis(hydrogen maleate), m.p. 138—140°C (ethanol). For $C_{29}H_{31}ClN_2O_9S$ (619·1) calculated: 56·26% C, 5·05% H, 5·73% Cl, 4·52% N, 5·18% S; found: 56·37% C, 4·97% H, 6·09% Cl, 4·25% N, 5·30% S.

Decomposition of a sample of the maleate with NH_4OH and extraction with benzene gave the pure base used for the registration of the ^{1}H-NMR spectrum ($CDCl_3$): δ 7·78 (mcs, 1 H, 1-H), 7·75 (mcd, J = 8·5; 2·0 Hz, 1 H, 3-H), 7·35 (d, J = 8·5 Hz, 1 H, 4-H), 7·20 (m, 3 H, 5,6,8-H_3), 4·12 (t, J = 8·0 Hz, 1 H, Ar_2CH), 2·60 (s, 3 H, $COCH_3$), 2·55 (d, J = 8·0 Hz, 2 H, C^9—CH_2N), 2·35 (bs, 8 H, 4 NCH_2 of piperazine), 2·19 (s, 3 H, NCH_3).

2-Chloro-9-(4-methylpiperazinomethyl)-7-propionylthioxanthene (*XXXI*)

Like in the preceding case, 5·8 g *XXVIII* reacted with 8·0 g 1-methylpiperazine and gave 3·86 g (57%) of an oily base. The crystalline bis(hydrogen maleate) was obtained by neutralization with maleic acid in ethanol; it crystallized from 95% ethanol as a hemihydrate, m.p. 152—153°C. UV spectrum: λ_{max} 235·5 nm (log ε 4·25), 263 nm (3·95), 314 nm (4·11). IR spectrum (Nujol): 869 (Ar—H), 1072, 1089, 1100, 1219 (C—O), 1550 (COO^-), 1620 (CH=CH of maleic acid), 1690 (ArCOR, COOH), 2290, 2390 (NH^+), 3500 cm^{-1} (H_2O). For $C_{30}H_{33}ClN_2O_9S$ + + 0·5 H_2O (642·1) calculated: 56·11% C, 5·34% H, 5·52% Cl, 4·36% N, 5·00% S; found: 56·18% C, 5·33% H, 5·79% Cl, 4·38% N, 5·25% S.

5-Chlorothiosalicylic Acid

A mixture of 51·5 g 5-chloroanthranilic acid[33], 100 g ice and 60 ml hydrochloric acid was diazotized over 10 min with a solution of 21 g $NaNO_2$ in 80 ml water. The mixture was maintained for 30 min by cooling at max. 5°C and added to a solution which was prepared from 78 g Na_2S. .9 H_2O and 10·2 g sulfur in 90 ml water and further 12 g NaOH in 30 ml water. The temperature was first maintained at max. 5°C, then the mixture was stirred for 2 h without cooling, acidified with 60 ml hydrochloric acid and the precipitated 5,5′-dichlorodithiosalicylic acid (m.p. 316 to 320°C) was purified by precipitating from a solution of Na_2CO_3 by acidification. This intermediate was reduced according to the literature[35] with zinc and acetic acid to the desired 5-chlorothiosalicylic acid with a m.p. of 193—195°C (benzene).

2-(4-Acetylphenylthio)-5-chlorobenzoic Acid (*XXXVI*)

A mixture of 10·0 g 5-chlorothiosalicylic acid, 11·2 g 4-bromoacetophenone[36], 7·0 g Na_2CO_3, 0·2 g Cu and 100 ml dimethylformamide was stirred and refluxed for 4 h. Volatile fractions were evaporated *in vacuo*, the residue was mixed with excess of 5% Na_2CO_3 and after shaking with benzene, the mixture was filtered. The aqueous layer of the filtrate was acidified with hydrochloric acid, the crude product isolated by extraction with benzene and crystallized from aqueous ethanol; 8·7 g (57%), m.p. 170–178°C. Analytical sample, m.p. 179–181·5°C (benzene–ethanol). UV spectrum: λ_{max} 242 nm (log ε 4·18), 260 nm (4·13), 314 nm (4·08). IR spectrum (Nujol): 840, 900 (2 adjacent and solitary Ar–H), 935, 1252, (COOH), 1550, 1593, 3065, 3095 (Ar), 1690 (ArCOR, ArCOOH), 2550, 2610, 2655 cm^{-1} (Ar). ^{1}H-NMR spectrum: δ 7·98 (d, J = = 8·0 Hz, 2 H, 3,5-H_2 of acetylphenyl), 7·85 (bs, 1 H, 6-H of benzoic acid), 7·55 (d, J = 8·0 Hz, 2 H, 2,6-H_2 of acetylphenyl), 7·45 (d, J = 8·0 Hz, 1 H, 4-H of benzoic acid), 6·89 (d, J = 8·0 Hz, 1 H, 3-H of benzoic acid), 2·55 (s, 3 H, $COCH_3$). For $C_{15}H_{11}ClO_3S$ (306·8) calculated: 58·73% C, 3·61% H, 11·56% Cl; found: 59·06% C, 3·70% H, 11·48% Cl.

2-Acetyl-7-chlorothioxanthone (*XXXIV*)

A. A mixture of 50 g polyphosphoric acid and 3·0 g *XXXVI* was stirred for 4 h at 55°C and decomposed by pouring into ice and water. The precipitated product was filtered, suspended in 5% Na_2CO_3, filtered again, washed with water and after drying crystallized from a mixture of benzene and ethanol; 0·55 g, needles of m.p. 210 to 212°C. UV spectrum: λ_{max} 265·5 nm (log ε 4·58), 290 nm (4·19), 321·5 nm (4·23), infl. 370 nm (3·72), 382 nm (3·75). IR spectrum: 785, 827, 848 (2 adjacent and solitary Ar–H), 1249 (CO), 1590, 3040, 3090 (Ar), 1636 (Ar_2CO), 1690 cm^{-1} (ArCOR). For $C_{15}H_9ClO_2S$ (288·8) calculated: 62·39% C, 3·14% H, 12·28% Cl, 11·10% S; found: 62·37% C, 3·19% H, 12·10% Cl, 10·89% S.

B. A solution of 3·0 g *XXVII* in 20 ml acetonitrile was treated with a solution of silver *p*-toluenesulfonate (prepared from 1·9 g *p*-toluenesulfonic acid monohydrate and 1·7 g $AgNO_3$) in 10 ml acetonitrile and the mixture was refluxed for 8 h. After addition of the same quantity of Ag tosylate, the refluxing was continued for additional 8 h. Because the reaction mixture still contained mostly the starting material, 20 ml triethylene glycol were added, acetonitrile was evaporated and the mixture stirred for 8 h at 160°C. It was then diluted with water and extracted with benzene. The benzene extract was chromatographed on a column of 200 g silica gel. In the first fractions, 0·71 g of the starting compound *XXVII* (m.p. 138–142°C) were eluted with benzene. After an insignificant high-melting fraction, 0·34 g compound *XXXIV* were eluted with a mixture of benzene and chloroform; needles melting at 211–213°C. In mixture with the product obtained under *A*, it melts without depression. Crystallization from benzene gave a modification melting at 206–208°C (leaflets), which was used for analysis and for the registration of spectra. UV spectrum: λ_{max} 260·5 nm (log ε 4·58), 290 nm (4·19), 321·5 nm (4·23), infl. 370 nm (3·72), 382 nm (3·76). IR spectrum: 789, 828, 850 (2 adjacent and solitary Ar-H), 1249 (CO), 1599, 3060, 3090 (Ar), 1641 (Ar_2CO), 1682 cm^{-1} (ArCOR). Whilst the UV spectrum of this product is completely identical with that of the product obtained by procedure *A*, there are litle difference in the IR spectra caused by the dimorphism. The IR spectrum was therefore recorded in a solution in CS_2 and is then identical for products described under *A* and *B*: 781, 813, 827, 846, 1239, 1630, 1647, 1687 cm^{-1}. The mass spectrum shows the molecular ion *m/e* 288 corresponding to $C_{15}H_9ClO_2S$; main fragments *m/e* 273 and 245. For $C_{15}H_9ClO_2S$ (288·8) calculated: 62·39% C, 3·14% H, 12·28% Cl, 11·10% S; found: 62·44% C, 3·06% H, 11·94% Cl, 10·78% S.

2-Acetyl-7-chloro-9-methylenethioxanthene (*XXXII*)

A. The benzene solution from the preparation of compound *XXIX*, from which the base was removed by extraction with dilute hydrochloric acid, gave by evaporation a neutral product (1·7 g), consisting according to TLC of two components. The separation was carried out by chromatography on a column of 50 g Al_2O_3. Benzene eluted first 1·32 g of the less polar homogeneous compound which crystallized; m.p. 85—95°C. Analytical sample, m.p. 97—99°C (ethanol). We are dealing here with the olefin *XXXII*. For $C_{16}H_{11}ClOS$ (286·8) calculated: 67·01% C, 3·87% H, 12·36% Cl, 11·18% S; found: 66·99% C, 3·95% H, 12·60% Cl, 11·29% S.

Continued elution with benzene yielded 0·18 g of a further homogeneous substance, crystallizing from benzene in needles and melting at 208—210°C. Its analysis, UV and IR spectrum prove its identity as the thioxanthone derivative *XXXIV*.

B. A mixture of 5·0 g *XXVII* and 25 ml 2,4,6-collidine was heated for 1 h to 150—160°C. After cooling, it was diluted with 80 ml water and extracted with benzene. The extract was washed with 3M-HCl and water, dried with $MgSO_4$ and evaporated. The residue yielded by crystallization from 60 ml ethanol 3·35 g (75%) pure olefin *XXXII*, m.p. 97—99°C.

C. A mixture of 3·0 g *XXVII*, 25 ml dimethylformamide and 2·0 g anhydrous potassium acetate was heated for 2 h to 130—140°C. After cooling, it was diluted with water and extracted with benzene. The extract was washed with water, dried and evaporated. The inhomogeneous residue (3·2 g) was chromatographed on a column of 200 g silica gel. A mixture of benzene and chloroform eluted 1·13 g olefin *XXXII*, m.p. 96—100°C (benzene–light petroleum). Continued chromatography with elution with chloroform gave 0·50 g thioxanthone *XXXIV* melting at 206 to 208°C and then, after changing the modification, again at 210—212°C (ethanol–benzene).

D. A solution of 18·3 g 2-chlorodibenzo[*b*,*f*]thiepin[1] and 7·30 g acetyl chloride in 25 ml CS_2 was added dropwise over 1 h at −5°C to a mixture of 12·52 g $AlCl_3$ and 50 ml CS_2. The mixture was stirred for 1 h at −5°C and for 2 h without cooling. After standing overnight, it was poured into a mixture of 250 g ice and 30 ml hydrochloric acid, CS_2 was removed by steam distillation and from the residue, the product was isolated by extraction with chloroform. The crude inhomogeneous product (20·7 g) was chromatographed on a column of 500 g Al_2O_3 (act. II). Benzene eluted 19·0 g substance which was dissolved in 15 ml benzene and the solution treated with 15 ml light petroleum; 2·0 g compound *XXVII* crystallized, m.p. 140—141°C. The rest consisted mostly of the olefin *XXXII*; by the action of semicarbazide, it was possible to prepare a semicarbazone melting at 194—195°C (aqueous ethanol). ^{1}H-NMR spectrum (ZKR 60): δ 9·56 (s, 1 H, NH), 7·20—7·80 (m, 8 H, Ar—H and NH_2), 6·20 (bs, 2 H, C=CH_2), 2·14 (s, 3 H, CH_3). For $C_{17}H_{14}ClN_3OS$ (343·8) calculated: 59·38% C, 4·11% H, 10·31% Cl, 12·22% N, 9·33% S; found: 59·12% C, 4·03% H, 10·89% Cl, 11·52% N, 9·30% S.

2-Acetyl-7-fluoro-9-methylenethioxanthene (*XXXIII*)

A mixture of 18·0 g $AlCl_3$, 30 ml chloroform and 9·5 g acetyl chloride was treated at 0°C with a solution of 15·9 g 10-chloro-8-fluoro-10,11-dihydrodibenzo[*b*,*f*]thiepin[1] in 30 ml chloroform. The mixture was stirred for 5 h at room temperature, after standing overnight it was decomposed with 1 : 3 dilute hydrochloric acid, the organic layer was separated, washed with 5% $NaHCO_3$, dried with $MgSO_4$ and evaporated. The remaining inhomogeneous oil (18 g) yielded by chromatography on a column of 500 g Al_2O_3 (act. II) 8·35 g (51%) homogeneous substance which crystallized from ethanol and in pure state melted at 116—117°C. UV spectrum: λ_{max} 259 nm (log ε 4·23), 322 nm (4·05). IR spectrum: 820, 880 (2 adjacent and solitary Ar—H), 1 262 (CO), 1 556, 1 583, 1 595 (Ar), 1 614 (C=CH_2), 1 690 cm^{-1} (ArCOR). ^{1}H-NMR spectrum

(ZKR 60, $CDCl_3$): δ 8·21 (mcs, J = 2·0 Hz, 1 H, 1-H), 7·85 (mcd, J = 8·5; 2·0 Hz, 1 H, 3-H), 7·40 (d, J = 8·5 Hz, 1 H, 4-H), 6·80–7·50 (m, 3 H, 5,6,8-H_3), 5·63 and 5·58 (2 s, 2 H, C=CH_2), 2·57 (s, 3 H, $COCH_3$). For $C_{16}H_{11}FOS$ (270·3) calculated: 71·09% C, 4·10% H, 7·03% F, 11·86% S; found: 70·82% C, 4·27% H, 7·17% F, 11·93% S.

2-Acetyl-7-(methylthio)thioxanthone (*XXXV*)

A. A solution, obtained by addition of 7·85 g acetyl chloride to a mixture of 13·3 g $AlCl_3$ and 70 ml dichloromethane, was stirred and treated dropwise over 1 h at 20–25°C with a solution of 20·8 g 2-(methylthio)dibenzo[*b*,*f*]thiepin[4] in 330 ml dichloromethane. The mixture was refluxed for 5 h and then processed like in the preceding cases. A crude inhomogeneous product (7·0 g) was obtained which was chromatographed on a column of 170 g Al_2O_3 (act. II). With benzene there were eluted 0·7 g of an almost homogeneous fraction which crystallized after treatment with ether and a small quantity of ethanol; m.p. 200–202°C (benzene). The mass spectrum shows the molecular ion m/e 300 (M^+, 300·0092), correspoding to $C_{16}H_{12}O_2S_2$ (requires 300·0078); main fragments with m/e 257 and 214. For $C_{16}H_{12}O_2S_2$ (300·3). calculated: 64·00% C, 4·03% H, 21·32% S; found: 64·22% C, 4·10% H, 21·20% S.

B. Like in the preceding case, 11·5 g acetyl chloride, 20·0 g $AlCl_3$ and 29·3 g 10-chloro-8-(methylthio)-10,11-dihydrodibenzo[*b*,*f*]thiepin[4] reacted in 300 ml dichloromethane and gave 17·0 g inhomogeneous product which was chromatographed (400 g Al_2O_3, act. II). Elution with a mixture 7 : 3 of light petroleum and benzene gave 5·3 g of a fraction which crystallized and gave a compound identical with that prepared according to *A*; m.p. 198–200°C (benzene).

2-Chloro-7-(1-hydroxyethyl)-9-(4-methylpiperazinomethyl)thioxanthene (*XXX*)

A solution of 13·0 g *XXIX* in 150 ml methanol was stirred and treated dropwise over 20 min at 50°C with a solution of 1·92 g $NaBH_4$ in 10 ml water, containing 0·3 ml 15% NaOH. The mixture was refluxed for 3 h, after cooling it was diluted with 300 ml water and extracted with benzene. The extract was washed with water, dried and evaporated; 12·4 g of an oily base. Neutralization with maleic acid in 200 ml water gave a solution of the maleate which was filtered with 60 g silica, from the filtrate the base was released with NH_4OH and isolated by extraction with benzene. It crystallized after evaporation of the extract and treatment with a small quantity of ether and light petroleum; 9·4 g (72%), m.p. 135–140°C. Analytical sample after repeated crystallization from acetone melted at 164–166°C. IR spectrum (Nujol): 810, 825, 840, 850, 870, 900 (2 adjacent and solitary Ar—H), 1 093 (CHOH), 2 800 (NCH_3), 3 160 cm^{-1} (OH). ^{1}H-NMR spectrum (ZKR 60, $CDCl_3$): δ 7·05–7·55 (m, 6 H, Ar—H), 4·85 (q, J = 6·5 Hz, 1 H, Ar—CH—O), 4·11 (t, J = 8·0 Hz, 1 H, Ar_2CH), 3·30 (bs, 1 H, OH), 2·56 (d, J = 8·0 Hz, 2 H, C^9CH_2N), 2·31 (bs, 8 H, 4 NCH_2 of piperazine), 2·16 (s, 3 H, NCH_3), 1·45 (d, J = 6·5 Hz, 3 H, C—CH_3). For $C_{21}H_{25}ClN_2OS$ (388·9) calculated: 64·85% C, 6·48% H, 9·12% Cl, 7·20% N, 8·24% S; found: 65·00% C, 6·49% H, 9·28% Cl, 7·21% N, 8·47% S.

This homogeneous racemic base gave by neutralization with maleic acid in ethanol and by addition of ether the crystalline bis(hydrogen maleate) melting at 136–137°C (acetone). For $C_{29}H_{33}ClN_2O_6S$ (621·1) calculated: 56·08% C, 5·35% H, 5·71% Cl, 4·51% N, 5·16% S; found: 55·90% C, 5·52% H, 5·60% Cl, 4·16% N, 5·32% S.

10-Acetoxy-10,11-dihydrodibenzo[*b*,*f*]thiepin (*XXXIX*)

A mixture of 5·0 g 10,11-dihydrodibenzo[*b*,*f*]thiepin-10-ol[44], 4·5 ml acetic anhydride and 3·5 ml pyridine was heated for 1 h under reflux in a bath of 140°C. After cooling, it was diluted with

water and the product isolated by extraction with benzene. The extract was washed with dilute hydrochloric acid and 5% $NaHCO_3$, dried with $MgSO_4$ and distilled; 5·3 g (90%), b.p. 157 to 159°C/0·4 Torr. IR spectrum (film): 770 (4 adjacent Ar—H), 1245 (C—O—C), 1445, 1485, 1575, 1600 (Ar), 1735 cm^{-1} (CH_3COOR). For $C_{16}H_{14}O_2S$ (270·4) calculated: 71·08% C, 5·22% H, 11·86% S; found: 70·88% C, 5·39% H, 11·85% S.

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