NEUROTROPIC AND PSYCHOTROPIC AGENTS. LXVI.*

6,8-DICHLORO- AND 6,9-DICHLORO-10-(4-METHYLPIPERAZINO)-10,11-DIHYDRODIBENZO[*b,f*]THIEPIN

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The 6,8-dichloro- (*IV*) and 6,9-dichloro derivative (*II*) of 10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b,f*]thiepin (perathiepin) were synthesized. During the synthesis of amine *II*, proceeding from 2,5-dichlorothiophenol, the cyclization of acid *IXb* gave the desired 6,9-dichlorodibenzo[*b,f*]-thiepin-10(11*H*)-one (*XI*), accompanied with a predominant amount of 1,4-dichlorothioxanthene-9-carbaldehyde (*XVI*). Reduction of this mixture with sodium borohydride gave rise to a mixture which, in addition to the desired alcohol *XIIb* and predominating primary alcohol *XVIII*, was found to contain the diol *XXIV*, the ether *XXV* and the thioxanthenes *XXI* and *XXII*. The possibilities of formation of unexpected products, in particular of aldehyde *XVI*, are discussed. Starting from alcohol *XIIb via* chloride *XIIIb*, the synthesis of diamine *II* was concluded, the last step of which resulted mainly in the elimination product *XV*. Pharmacological tests showed the pronounced negative effect of 9-chloro substitution in the perathiepin molecule on the central activity.

After establishing the high degree of central depressant activity of 10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b,f*]thiepin ("perathiepin")[1-4] the problem of most suitable substitution of its molecule was investigated to intensify further this type of activity. The chlorine atom was selected as substituent and, in systematic studies, the 1-, 2-, 3-, 4-, 6-, 7- (ref.[1,5]) and 8-chloro (ref.[1,6]) derivatives were prepared. The synthesis of the 9-chloro derivative *I* was the subject of our further experiments (*e.g.*[7,8]) and it reached a successful materialization only recently[9]. In the meantime, it was attempted to obtain information on the effect of substitution in position 9 on the activity at least indirectly, employing here the preparation and testing of isomeric 6,8-dichloro- and 6,9-dichloro derivatives *II* and *IV*. The two compounds have a common substituent in position 6 and differ in the substitution in position 8 and 9. Substitution in position 8 was chosen because the 8-chloro derivative *III* ("octoclothepin")[1,6,10] was found to be most effective of all the hitherto known monochloro derivatives of the parent compound. In the present communica-

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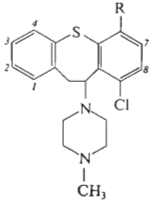
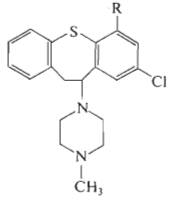
tion, the synthesis of compounds *II* and *IV* and their pharmacological comparison are reported.

The synthesis of the 6,8-dichloro derivative *IV* proceeded in full analogy to the synthesis of the 8-chloro derivative *III* (ref.[6]) with some more recent modifications[10]. 2,4-Dichlorothiophenol[11] was condensed in an aqueous solution of potassium hydroxide and in the presence of copper with 2-iodobenzoic acid[12]. The 2-(2,4--dichlorophenylthio)benzoic acid (*Va*) was reduced with sodium bis(2-methoxyethoxy) dihydroaluminate in benzene to the oily 2-(2,4-dichlorophenylthio)benzyl alcohol (*VIa*) which was used for further work in the crude state. Its reaction with thionyl chloride in the presence of pyridine yielded the chloride *VIIa* which was converted to the nitrile *VIIIa*. Alkaline hydrolysis yielded 2-(2,4-dichlorophenylthio) phenylacetic acid (*IXa*). Cyclization with the aid of polyphosphoric acid at 150°C gave rise to a 80% yield of the sought 6,8-dichlorodibenzo[*b*,*f*]thiepin-10(11*H*)-one (*X*); 18% of the starting acid *IXa* was recovered. It follows that the course of the cyclization reaction was quite homogeneous. Reduction of ketone *X* with sodium borohydride in aqueous ethanol yielded the alcohol *XIIa* which was transformed with hydrogen chloride in benzene to the trichloro derivative *XIIIa*. Its substitution reaction with excess 1-methylpiperazine in boiling chloroform resulted in the oily base *IV* which was characterized as crystalline di(methanesulfonate). The by-product isolated and characterized was 2,4-dichlorodibenzo[*b*,*f*]thiepin (*XIV*), *i.e.* the elimination product.

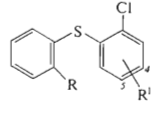
Likewise, the synthesis of the 6,9-dichloro derivative *II* proceeded in the initial stages quite analogously. The starting 2,5-dichlorothiophenol[13,14] was prepared by reduction of 2,5-dichlorobenzenesulfonyl chloride[13,14] with iodine and phosphorus in acetic acid (method[15]). Reaction with 2-iodobenzoic acid yielded 2-(2,5-dichloro-



I, R = H
II, R = Cl



III, R = H
IV, R = Cl



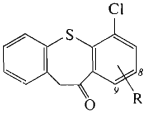
a, R^1 = 4-Cl
b, R^1 = 5-Cl

V, R = COOH
VI, R = CH_2OH
VII, R = CH_2Cl
VIII, R = CH_2CN
IX, R = CH_2COOH

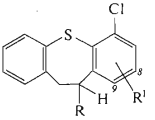
phenylthio)benzoic acid (*Vb*) which was reduced as before to the crystalline alcohol *VIb*. Crystalline compounds are also the chloride *VIIb* and the nitrile *VIIIb* prepared analogously in this series. 2-(2,5-Dichlorophenylthio)phenylacetic acid (*IXb*) was prepared either by an alkaline hydrolysis of nitrile *VIIIb*, or by condensation of 2,5-dichlorothiophenol with 2-iodophenylacetic acid[16].

The course of the attempts to cyclize acid *IXb* was quite different from the preceding case. On heating acid *IXb* with polyphosphoric acid to 120°C no reaction takes place. The desired cyclization was not achieved even in attempts at a reaction of acid *IXb* with polyphosphoric acid in the presence of boiling xylene, with anhydrous hydrogen fluoride at room temperature or with phosphorus pentoxide in boiling xylene. Only on employing polyphosphoric acid at 170°C was the formation of neutral product in an approximately 30% yield observed; even under these conditions most of the starting acid *IXb* was regenerated. The neutral product was characterized by chromatography on a thin layer of silica gel as a mixture in which two components predominate. They were isolated in a small amount from the mixture by crystallization and identified with the aid of analyses and spectra. They are isomers of the expected composition $C_{14}H_8Cl_2OS$, one of which corresponds to the desired 6,9-dichlorodibenzo[*b*,*f*]thiepin-10(11*H*)-one (*XI*), the other is 1,4-dichlorothioxanthene-9-carbaldehyde (*XVI*). When the reaction conditions were strenghtened by using a greater excess of polyphosphoric acid and by heating to 175°C, the yield of the neutral product was increased up to 75%. According to thin-layer chromatography the mixture contains mainly ketone *XI* and aldehyde *XVI* and the aldehyde heavily predominates. The separation of this mixture on a preparative scale was not possible by either crystallization or by chromatography on alumina. A small amount of a high-melting compound $C_{26}H_{14}Cl_4OS_2$ was isolated, according to its IR and mass spectra, apparently the ether *XXII*.

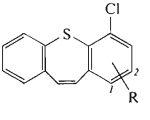
In an attempt to isolate the desired ketone *XI* from the mixture with aldehyde *XVI* we set out to oxidize this mixture, assuming the ready oxidizability of aldehyde *XVI* to acid *XVII*, which should be readily separated from the unaltered neutral ketone *XI*. In the attempt to oxidize with silver oxide (for method see[17]) we obtained a neutral and an acid product but attempts



X, R = 8-Cl
XI, R = 9-Cl



a, R^1 = 8-Cl
b, R^1 = 9-Cl
XII, R = OH
XIII, R = Cl

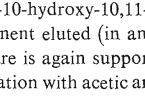


XIV, R = 2-Cl
XV, R = 1-Cl

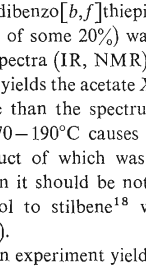
at their crystallization were unsuccessful. When oxidizing with chromic oxide in aqueous acetone in the presence of sulfuric acid, the resulting acid product was 1,4-dichlorothioxanthene-9-carboxylic acid (*XVII*). The neutral fraction yielded as the only crystalline product the ketone $C_{13}H_6Cl_2OS$ which is apparently 1,4-dichlorothioxanthone (*XXIII*). The same ketone was the only crystalline compound isolated on a preparative scale from the oxidation of a mixture of *XI* and *XVI* with potassium permanganate in acetone. The desired ketone *XI* thus could not be isolated from the oxidation product at all.

For this reason, the mixture of *XI* and *XVI* was reduced with sodium borohydride in a mixture of dioxane and aqueous ethanol. The crude product (after washing with dilute hydrochloric acid) dissolved in cyclohexane, crystallized to a small amount of $C_{14}H_{10}Cl_2O_2S$ which, according to the NMR spectrum, is the diol XXIV. The remaining oil was chromatographed on a column of alumina. The least polar component to be eluted was the high-melting compound $C_{28}H_{18}Cl_4OS_2$ which, according to the UV and IR spectrum, is the ether *XXV*. A more polar component isolated in an amount of some 8% (per weight of starting mixture) was $C_{14}H_{10}Cl_2OS$, the IR and NMR spectra of which are compatible with the structure of the desired 6,9-dichloro-10-hydroxy-10,11-dihydrodibenzo[*b*,*f*]thiepin (*XIIb*). Finally, the most polar component eluted (in an amount of some 20%) was the primary alcohol *XVIII*. Its structure is again supported by spectra (IR, NMR) and by further transformations. Acetylation with acetic anhydride yields the acetate *XIX*, the NMR spectrum of which was more readily distinguishable than the spectrum of the alcohol itself. Heating with 85% phosphoric acid to 170–190°C causes a retropinacoline rearrangement of the alcohol *XVIII*, the product of which was 1,4-dichlorodibenzo[*b*,*f*]thiepin (*XV*) (for the sake of comparison it should be noted that the retropinacoline rearrangement of 2,2-diphenylethanol to stilbene[18] was achieved by treatment with phosphorus pentoxide in benzene).

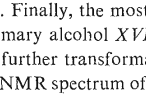
A similarly conducted reduction experiment yielded on crystallization of the crude product some 25% of the main product, *i.e.* the primary alcohol *XVIII*. Crystallization of the mother liquor gave rise to about 3% of ether *XXV*. Chromatography on alumina of the residue produced another substance which is assumed to be bi(1,4-di-



XVI, R = CHO
XVII, R = COOH
XVIII, R = CH_2OH
XIX, R = CH_2OCOCH_3
XX, R = H
XXI, R = CH_3



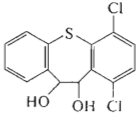
XXII



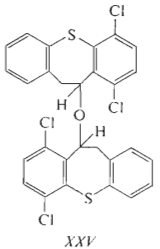
XXIII

chloro-9-thioxanthyl) (*XXVI*). Besides analysis, the structure is supported by the mass spectrum in which the main fragment represented is the ion corresponding to 1,4-dichlorothioxanthene (*XX*) (*m/e* 265) formed apparently by fragmentation of a duplex molecule. A further amount of ether *XXV* was followed by some 25% oil which was redistilled and yielded the satisfactory analysis for $C_{14}H_{10}Cl_2S$. The mass spectrum supported this empirical formula (molecular ion *m/e* = 279·9878); an intense fragment *m/e* 265, corresponding again to 1,4-dichlorothioxanthene (*XX*), suggests a splitting of methyl and identifies the product as 1,4-dichloro-9-methylthioxanthene (*XXI*). Continuation of chromatography then yielded alcohols with gradually increasing polarity: somewhat less than 10% of the desired alcohol *XIIb*, another fraction of primary alcohol *XVIII* and finally a small amount of diol *XXIV*.

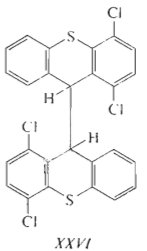
The complicated course of cyclization of acid *IXb* and subsequent reduction of the crude neutral product provokes one to consider the mechanism of formation of the unexpected products. The steric situation in the molecule of ketone *XI* is apparently rather unfavourable so that it is no surprise if in polyphosphoric acid the electrophilic substitution of the primarily formed acylium cation *A* results in a product with a tendency to further transformations; probably even the cation *A* undergoes partly side reactions even before the cyclization. The result is the low final yield of ketone *XI*, formation of a large amount of aldehyde *XVI* and finally the formation of thioxanthene derivatives containing one carbon atom less (*XXII*, *XXVI*). The most critical problem is the formation of aldehyde *XVI*. For unsubstituted thioxanthene-9-carbaldehyde, the literature[19] shows a single method of preparation, consisting in the acid hydrolysis of aziridine *XXVII*; the starting compound is thus the 10,11-bifunctional derivative of 10,11-dihydrodibenzo[*b*,*f*]thiepin and the rearrangement taking place is in apparent analogy with the pinacoline rearrangement[20,21]. This fact supports the view that the source of aldehyde *XVI* in this case might be the diol *XXIV* (which was isolated in a small amount from the mixture after reduction) or the ionic precursor *B* formed in the presence of polyphosphoric acid. The diphenylacetaldehyde (the open analogue of the present *XVI*) is known[22] to be formed through the acid-catalyzed pinacoline rearrangement of hydrobenzoin. In the present case, however, one lacks a plausible explanation of transformation of ketone *XI* or of cation *A* to the diol *XXIV* or to the cation *B* in the presence of polyphosphoric acid and no similar transformation could be found in the literature (see reviews[23–25]). As to the formation of diol *XXIV* it is likely to result from the reduction of the cor-



XXIV



XXV

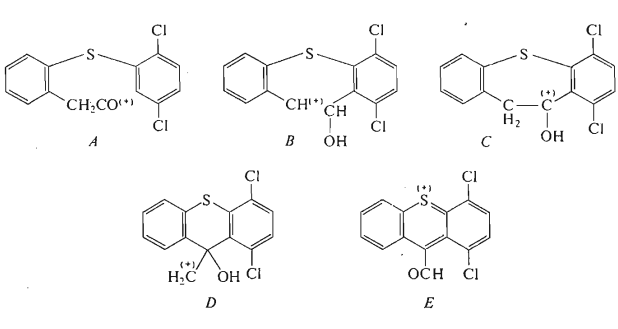


XXVI

responding diketone which might be the oxidation product of a part of ketone *XI* by atmospheric oxygen during the cyclization reaction in polyphosphoric acid at high temperature at which the reaction mixture was not protected from atmospheric oxygen. After all, a case of dehydrogenation in polyphosphoric acid has been described[26].

It is assumed that the formation of aldehyde *XVI* from ketone *XI* may be explained without participation of diol *XXIV*. In the presence of polyphosphoric acid one may assume a protonation of ketone *XI* to the cation *C* (a similar transformation is described in ref.[27]) which, through a migration of the aryl anion, would yield the cation *D* as an immediate precursor of aldehyde *XVI*. One can envisage even other explanations but, in view of the purely speculative nature of these considerations, it would be hardly useful to take up the problem in more detail.

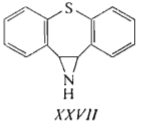
It is further worthwhile to consider the formation of thioxanthene derivatives *XXII* and *XXVI*, the principal skeleton of which has one less carbon atom than the parent acid *IXb*. Two possibilities may be envisaged. The first of these is a decarbonylation of the acylium cation *A* and an electrophilic alkylation by the cation formed which contains one less carbon atom. It is true that the literature[28–33] cases concern all acyls with a branching of the chain in α-position. On the other hand, it follows from the papers that the decarbonylation of the acylium cation is facilitated by the lower reactivity of the aromatic acceptor. This decreased reactivity of the sterically hindered aromate may be assumed in the present case. The primary product would then be the undetected 1,4-dichlorothioxanthene (*XX*) which could be transformed to *XXII* and *XXVI* by oxidation reactions under the influence of atmospheric oxygen in polyphosphoric acid at an elevated temperature (in the first case *via* the corresponding thioxanthylium cation, in the second case directly; for analogy see the nonchlorinated compounds[34–39]). It cannot be excluded that 1,4-dichlorothioxanthone (*XXIII*) isolated only after oxidation of the crude product of cyclization is present as such in the cyclization product. It should be formed as a product of disproportionation taking place during hydrolysis of the corresponding thioxanthylium cation, which is assumed to exist in the presence of polyphosphoric acid. On the other hand, the thioxanthone *XXIII* can be formed through oxidation of thioxanthene derivatives *XVI*, *XVII* and *XX*, or from the diketone corresponding to the diol *XXIV*, through a benzil rearrangement and subsequent degradation of the corresponding hydroxy acid as was observed in the unsubstituted series[4]. The second possibility of formation of thioxanthenes with 13 carbon atoms in the principal skeleton is represented by decarbonylation of aldehyde *XVI*. Since a reaction of this type (decarbonylation of aldehydes catalyzed by strong acids) has been observed practically only with aromatic



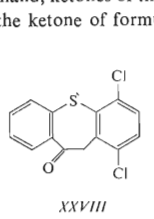
aldehydes[40] one would have to assume in the present case that it proceeds in the form of the aromatic thioxanthylium cation *E*, the formation of which through oxidation of aldehyde *XVI* cannot be excluded.

The formation of 1,4-dichloro-9-methylthioxanthene (*XXI*) is explainable by a hydrogenolysis of aldehyde *XVI* or of alcohol *XVIII*; in this context let us recall the formation of 9-methylthioxanthene in an attempt at reduction of dibenzo[*b*,*f*]thiepin[4]. Finally, the formation of ether *XXV* is accounted for by etherification of alcohol *XIIb* taking place on acidifying the reaction mixture after reduction; we are dealing here with a direct analogy of formation of bis(1,2-diphenylethyl)-ether from 1,2-diphenylethanol under the influence of hydrochloric acid[41].

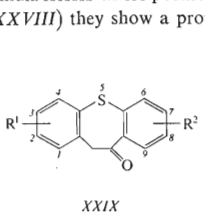
The fact that diphenylacetaldehyde undergoes acid-catalyzed rearrangement to deoxybenzoin[42] makes it useful to discuss in greater detail the structure of the ketone designated here tentatively with formula *XI*. The reaction just mentioned and the formation of aldehyde *XVI* in the course of the work admit the secondary formation of isomeric and sterically more advantageous ketone *XXVIII* which is not known so far; let us attempt to eliminate the structure *XXVIII* on the basis of IR and NMR spectra. It follows from a comparison of formulae *XI* and *XXVIII* that in the first case a chlorine atom is directly adjacent to the keto group. It is known that this may be associated with a shift of the carbonyl absorption to higher values[43]. The present ketone exhibits an absorption band of the aromatic keto group at 1692 cm^{-1}. The only compound that was at our disposal and that had a similar situation in the neighbourhood of the keto group is the 9-chloro ketone (*XXIX*, R^1R^2 = 9-Cl)[9] with an absorption band at exactly the same value, *viz.* 1692 cm^{-1}. For the sake of comparison let us list the positions of the carbonyl absorption of some ketones of the general formula *XXIX* with halogen substitutions in more distant positions, resembling partly the structure of *XXVIII* (the R^1R^2 substitution and the frequency in cm^{-1} is shown): 1-Cl, 1675; 2-Cl, 1670; 2-F, 1665; 3-Cl, 1681; 4-Cl, 1679; 6-Cl, 1675; 7-Cl, 1679; 8-Cl, 1669; 8-F, 1677; 8-Br, 1669; 8-I, 1665; 2,8-Cl_2, 1672; 6,8-Cl_2, 1677.[5,6,10,44,45] The comparison clearly favours the structure of *XI*; the absorption band of the keto group of the present product is shifted by 11 – 27 cm^{-1} in comparison with the compounds shown. As to the NMR spectrum, the aromatic protons of the ketone appear in the form of an indistinguishable multiplet at 7·10 – 7·90 p.p.m; similarly the 9-chloroketone *XXIX* (R^1R^2 = 9-Cl) shows a multiplet at 7·00 to 7·70 p.p.m. (ref.[9]). On the other hand, ketones of the formula *XXIX* where position 9 is not substituted (similarly to the ketone of formula *XXVIII*) they show a proton



XXVII



XXVIII



XXIX

signal in position 9 in the form of a multiplet, separated from the multiplet of other aromatic protons and markedly shifted due to anisotropy of the nearby C=O bond toward higher values of p.p.m.[46]. Thus, *e.g.*, 1-chloro ketone (*XXIX*, R^1R^2 = 1-Cl) exhibits a signal of 9-H in the form of a multiplet at 8·32 p.p.m., while the remaining six aromatic protons possess a multiplet at 6·90–7·80 p.p.m.[45]. Similarly, 2-methoxyketone (*XXIX*, R^1R^2 = 2-OCH_3) shows a signal of 9-H as a multiplet at 8·15 p.p.m., while the signals of the remaining six aromatic protons lie in the region between 6·65 and 7·50 p.p.m. (from these, 1-H and 3-H are doublets at 6·65 and 6·92)[45]. It appears that the NMR spectrum also supports the identity of the present product with *XI*.

Alcohol *XIIb* prepared here was used for completing the synthesis of the piperazine derivative *II*. Treatment with hydrogen chloride in benzene in the presence of calcium chloride yielded the trichloro derivative *XIIIb* which eliminates most of the hydrogen chloride when reacting with excess 1-methylpiperazine in boiling chloroform and yields 1,4-dichlorodibenzo[*b*,*f*]thiepin (*XV*). The substitution product, *viz.* the base *II*, was obtained only as a minor product and was characterized by its NMR spectrum and, for pharmacological tests, converted to the crystalline di(methanesulfonate).

Table I compares the pharmacological properties of *II* and *IV*, listing also octoclothepin (*III*) for the sake of comparison; the compounds were administered intravenously (or intraperitoneally in the catalepsy test) in the form of salts, the values in the table referring to the base. For all the three compounds, the mean effective doses in the rotating-rod test in mice and in the catalepsy test in rats are shown (for methods see ref.[47]). The table shows that while the 6,8-dichloro derivative *IV* is less effective than the 8-chloro derivative *III*, the 6,9-dichloro derivative *II* is ineffective. One can thus draw the tentative conclusion in the sense that substitution in position 9 of the perathiepin molecule has a strongly negative effect from the point of view of central activity. A powerful favourable effect of substitution in position 8 is shown by *IV* mainly in the catalepsy test where the substance almost matches octoclothepin (*III*). On the other hand, its depressant activity is 20 times lower than with octo-

TABLE I
Pharmacological Comparison of *II*–*IV*

Compound	Acute toxicity LD_{50} *i.v.* mg/kg	Rotating rod ED_{50} *i.v.* mg/kg	Catalepsy ED_{50} *i.p.* mg/kg
II		>10	>10
III (ref.[47])	46·3	0·06	2·4
IV	27·0	1·2	2·9

clothepin; we are thus dealing with a neuroleptic with a markedly shifted ratio between depressant and cataleptic activity in favour of the latter.

Compound *IV* was evaluated at the bacteriological department of this institute (Dr A. Šimek and Dr J. Turinová) for its antimicrobial activity *in vitro* when it displayed a wide spectrum of inhibition. In the following, the microorganisms tested and the minimum inhibitory concentrations in μg/ml are shown: *Streptococcus* β-*haemolyticus*, 12·5; *Staphylococcus pyogenes aureus*, 12·5; *Mycobacterium tuberculosis* H37Rv, 12·5; *Saccharomyces pasterianus*, 62·3; *Trichophyton mentagrophytes*, 62·3; *Candida albicans*, 125; *Aspergillus niger*, 62·3.

EXPERIMENTAL

The melting points of analytical preparations were estimated in Kofler's block and have not been corrected; the samples were dried at room temperature at 0·5 Torr over P_2O_5. The UV spectra (in methanol) were recorded in a Unicam SP 700 spectrophotometer, the IR spectra (in Nujol, unless stated otherwise) in a Unicam SP 200G spectrophotometer or in an Infrascan (Hilger and Watts) apparatus, the NMR spectra (in deuteriochloroform, unless stated otherwise) in a ZKR 60 (Zeiss, Jena) spectrometer; the mass spectra recorded in a MS 902(AEI) mass spectrometer.

2,5-Dichlorothiophenol

A solution of 120·9 g 2,5-dichlorobenzenesulfonyl chloride (m.p. 35°C)[13,14] in 125 ml acetic acid was added dropwise to a refluxed mixture of 200 ml acetic acid, 45 g red phosphorus and 2.5 g iodine and the mixture was refluxed under stirring for 3 h. After cooling, 50 ml water was added dropwise, the mixture was brought to boiling and refluxed for 1 h; then it was steam-distilled. From the distillate the product was extracted with benzene and from the benzene solution it was transferred by shaking to excess 15% NaOH, liberated by acidification with concentrated hydrochloric acid and isolated by extraction with ether; 55·4 g (63%), b.p. 118—120°C/15 Torr. Ref.[14] reports a b.p. of 112—116°C/50—52 Torr and melting at 27°C.

2-(2,4-Dichlorophenylthio)benzoic Acid (*Va*)

2,4-Dichlorothiophenol[11] (b.p. 108—110°C/10 Torr; 55·1 g) was added to a solution of 50 g KOH in 550 ml water at 50°C and, after 10 min of stirring, this was followed by 2·0 g copper powder and 74 g 2-iodobenzoic acid[12]. The mixture was refluxed under stirring for 7 h (on a 140°C bath), was filtered while hot and the still warm filtrate was made acid with 60 ml concentrated hydrochloric acid. The precipitated product was cooled, filtered and recrystallized from ethanol: 84·5 g (92%), m.p. 232—234°C. For $C_{13}H_8Cl_2O_2S$ (299·2) calculated: 52·19% C, 2·69% H, 23·70% Cl, 10·72% S; found: 52·58% C, 2·72% H, 23·73% Cl, 10·92% S.

2-(2,5-Dichlorophenylthio)benzoic Acid (*Vb*)

As in the preceding case, 120·9 g 2,5-dichlorothiophenol and 173 g 2-iodobenzoic acid[12] reacted to 194 g (90%) product, m.p. 225—227°C (ethanol). For $C_{13}H_8Cl_2O_2S$ (299·2) calculated: 52·19% C, 2·69% H, 23·70% Cl, 10·72% S; found: 52·12% C, 2·67% H, 23·89% Cl, 10·71% S.

2-(2,4-Dichlorophenylthio)benzyl Alcohol (*VIa*)

Sodium bis(2-methoxyethoxy)dihydroaluminate (230 ml of a 50% benzene solution) was added dropwise under stirring over a period of 2 h to a suspension of 84·2 g acid *Va* in 600 ml benzene. The solution heated spontaneously to 50°C and was stirred for 3 h at room temperature; after

standing overnight, it was decomposed under cooling by a slow addition of 400 ml 10% NaOH. It was then stirred for 1 h, the benzene layer was separated, dried with K_2CO_3 and evaporated. The residue (57·3 g, 71%) is oily and, according to thin-layer chromatography in silica gel it is rather homogeneous; on distillation (b.p. 165°C/0·2 Torr) it partly decomposes and hence was used for further work in a crude state.

4-*Nitrobenzoate* was prepared by a reaction of alcohol with 4-nitrobenzoyl chloride in pyridine; it crystallizes as a solvate with 1 molecule methanol, m.p. 98—100°C in a capillary (methanol). IR spectrum (KBr): 765 (4 vicinal aromatic C—H), 811 (2 vicinal aromatic C—H), 862 (isolated aromatic C—H), 1 031 (OH in CH_3OH), 1 099, 1 275 and 1 712 (ArCOOR), 1 349 and 1 522 (NO_2), 1 609 (Ar), 3 480 cm^{-1} (OH). NMR spectrum: δ 8·35 (d, J = 9·0 Hz, 2 H, aromatic protons in the vicinity of the nitro group), 8·10 (d, J = 9·0 Hz, 2 H, aromatic protons in the vicinity of the carbonyl group), 7·40—7·70 (m, 4 H, aromatic protons of the benzyl residue), 7·34 (d, 1 H, aromatic proton between two chlorine atoms), 7·02 (dd, J = 9·0; 2·0 Hz, 1 H, aromatic proton next to a chlorine atom), 6·68 (d, J = 9·0 Hz, 1 H, aromatic proton next to a sulfur atom), 5·55 (s, 2 H, $ArCH_2$), 3·48 (OCH_3 of methanol). For $C_{21}H_{17}Cl_2NO_5S$ (466·4) calculated: 54·09% C, 3·68% H, 15·20% Cl, 3·00% N, 6·88% S; found: 54·08% C, 3·63% H, 14·96% Cl, 3·00% N, 7·10% S.

2-(2,5-Dichlorophenylthio)benzyl Alcohol (*VIb*)

Similarly to the preceding case, 194 g acid *Vb* was reduced to 167 g (90%) crude product melting at 102—107°C. After recrystallization from aqueous methanol, the m.p. was 106—107°C. For $C_{13}H_{10}Cl_2OS$ (285·2) calculated: 54·75% C, 3·53% H, 24·87% Cl, 11·24% S; found: 54·75% C, 3·60% H, 24·76% Cl, 11·43% S.

2-(2,5-Dichlorophenylthio)benzyl Chloride (*VIIb*)

Thionyl chloride (44·5 g) was added dropwise under stirring over a period of 2 h to a mixture of 93 g alcohol *VIb* and 31 g pyridine at 10—20°C, the mixture was stirred for 4 h, after standing overnight it was stirred for 2 h at 40°C and, after cooling, it was decomposed by adding dropwise 120 ml water. The product was extracted with benzene, the extract was washed with 1M-HCl, 5% NaOH and water, dried with $CaCl_2$ and evaporated. A total of 81·7 g (83%) product was obtained, a sample of which crystallized after dissolving in light petroleum: m.p. 50—51°C. For $C_{13}H_9Cl_3S$ (303·6) calculated: 51·42% C, 2·99% H, 35·03% Cl, 10·56% S; found: 52·06% C, 3·10% H, 34·74% Cl, 10·70% S.

2-(2,4-Dichlorophenylthio)phenylacetonitrile (*VIIIa*)

Alcohol *VIa* (49 g) yielded in analogy with the preceding case 51 g oily chloride *VIIa* which was dissolved in 55 ml ethanol, a solution of 12·5 g NaCN in 18 ml water was added and the mixture was refluxed under stirring for 7 h. Ethanol was evaporated, the residue divided between water and benzene, the benzene solution was dried with $CaCl_2$ and distilled: 30·5 g (60%, referred to alcohol *VIa*), b.p. 180—182°C/0·6 Torr. For $C_{14}H_9Cl_2NS$ (294·2) calculated: 10.90% S; found: 11·09%S.

2-(2,5-Dichlorophenylthio)phenylacetonitrile (*VIIIb*)

Starting from 81·7 g chloride *VIIb*, 73·0 g (92%) product was prepared as in the preceding case; m.p. 61—62°C (ethanol). For $C_{14}H_9Cl_2NS$ (294·2) calculated: 57·16% C, 3·08% H, 24·10% Cl, 4·76% N, 10·90% S; found: 57·73% C, 3·08% H, 24·30% Cl, 4·69% N, 10·79% S.

2-(2,4-Dichlorophenylthio)phenylacetic Acid (*IXa*)

A solution of 30 g KOH in 60 ml water was added to a solution of 30·0 g nitrile *VIIIa* in 100 ml ethanol and the mixture was refluxed under stirring for 3·5 h. Ethanol was evaporated, the residue was diluted with 750 ml water, the liquid was washed with benzene and filtered to remove the insoluble portion. Acidification of the filtrate with hydrochloric acid yielded 27·9 g nonhomogeneous product which was crystallized first from aqueous ethanol and then from a mixture of benzene and light petroleum: 14·2 g (44%), m.p. 115—117°C. NMR spectrum: ϑ 10·70 (bs, 1 H, COOH), 7·20—7·60 (m, 5 H, aromatic protons of benzyl and a proton between two chlorine atoms), 7·05 (dd, J = 9·0; 2·0 Hz, 1 H, aromatic proton next to a chlorine atom), 6·65 (d, J = 9·0 Hz, 1 H, aromatic proton next to a sulfur atom), 3·84 (s, 2 H, $ArCH_2$). For $C_{14}H_{10}Cl_2O_2S$ (313·2) calculated: 53·69% C, 3·22% H, 22·64% Cl, 10·24% S; found: 53·96% C, 3·39% H, 22·31% Cl, 10·27% S.

2-(2,5-Dichlorophenylthio)phenylacetic Acid (*IXb*)

A. Similarly to the preceding case, hydrolysis of 72 g nitrile *VIIIb* yielded 64·7 g (84%) homogeneous product; after recrystallization from aqueous ethanol, m.p. 131—133°C. NMR spectrum: ϑ 10·18 (bs, 1 H, COOH), c. 7·50 (m, 4 H, aromatic protons of benzyl), 7·32 (d, J = 9·0 Hz, 1 H, aromatic proton in position 3 of dichlorophenyl), 7·00 (dd, J = 9·0; 2·0 Hz, 1 H, aromatic proton in position 4 of dichlorophenyl), 6·60 (d, J = 2·0 Hz, 1 H, aromatic proton in position 6 of dichlorophenyl), 3·84 (s, 2 H, $ArCH_2$). For $C_{14}H_{10}Cl_2O_2S$ (313·2) calculated: 53·69% C, 3·22% H, 22·64% Cl, 10·24% S; found: 53·89% C, 3·24% H, 22·58% Cl, 10·00% S.

B. To a solution of 52 g KOH in 650 ml water, the following were added in sequence under constant stirring: 55·2 g 2,5-dichlorothiophenol, 78 g 2-iodophenylacetic acid[16] and 3 g copper powder and the mixture was refluxed for 6 h. It was filtered while hot and the warm filtrate was made acid with hydrochloric acid. After cooling, it was filtered to obtain a nonhomogeneous product which was several times recrystallized from aqueous ethanol and benzene; 31·6 g (34%), m.p. 127—130°C. The compound is identical with the product prepared under *A*.

6,8-Dichlorodibenzo[*b*,*f*]thiepin-10(11*H*)-one (*X*)

Acid *IXa* (10·3 g) was added at 125°C to polyphosphoric acid prepared from 60 g P_2O_5 and 40 ml 85% H_3PO_4 and the mixture was heated under stirring for 4 h at 145—150°C. After partial cooling, the mixture was poured into ice and water, the precipitated solid was filtered and dissolved in benzene, the solution was washed with 15% NaOH and water, dried and evaporated. A total of 7·65 g (79%) product was obtained; m.p. 146—149°C. An analytical sample melted at 149 to 150°C (benzene–ethanol). UV spectrum: λ_{max} 248·5 nm (log ε 4·26), 269 nm (3·98), 276 nm (3·93), 340 nm (3·56). IR spectrum (KBr): 749 and 768 (4 vicinal aromatic C—H), 871 (solitary aromatic C—H), 1 566 (Ar), 1 677 cm^{-1} (ArCO). NMR spectrum: ϑ 8·13 (m, 1 H, aromatic proton in position 9), 7·59 (m, 1 H, aromatic proton in position 7), 7·10—7·85 (m, 4 H, aromatic protons in positions 1, 2, 3, 4), 4·30 (s, 2 H, $ArCH_2CO$). For $C_{14}H_8Cl_2OS$ (295·2) calculated: 56·96% C, 2·73% H, 24·02% Cl, 10·86% S; found: 57·00% C, 2·82% H, 23·93% Cl, 11·03% S. Acidification of the washings recovered 1·85 g (18%) acid *IXa*, m.p. 114—116°C.

6,9-Dichlorodibenzo[*b*,*f*]thiepin-10(11*H*)-one (*XI*) and 1,4-Dichlorothioxanthene-9-carbaldehyde (*XVI*)

A. Polyphosphoric acid was prepared by a 4-h heating of a mixture of 120 g P_2O_5 and 80 ml 85% H_3PO_4 to 130°C. After adding 29·8 g acid *IXb* the temperature was raised to 170°C and at

that temperature stirring continued for 3 h. After partial cooling, it was poured into a mixture of 500 g ice and water, left to stand overnight and the product was isolated by decanting the aqueous liquid and dissolved in benzene. The solution was washed with 15% NaOH and water. Acidification of the washings recovered 20·7 g acid *IX*, m.p. 125°C. The benzene solution was evaporated to yield 8·2 g oil which was dissolved in ethanol and the solution was filtered with charcoal. Evaporation of the filtrate yielded 5·75 g oil which, according to thin-layer chromatography on silica gel, consists of two main components with rather similar R_F values. After dissolving in a small amount of benzene and an addition of light petroleum, 0·7 g yellow substance precipitated on standing; m.p. 158—161°C. After repeated crystallization from ethanol the m.p. was 160—162·5°C. According to analyses and spectra the compound is ketone *XI*. UV spectrum: λ_{max} 240 nm infl. ($\log \varepsilon$ 4·08), 272 nm infl. (3·60), 330 nm (3·13). IR spectrum (KBr): 770 (4 vicinal aromatic C—H), 838 (2 vicinal aromatic C—H), 1 553 (Ar), 1 692 cm^{-1} (ArCO). NMR spectrum: δ 7·10—7·90 (m, 6 H, aromatic protons), 4·20 (s, 2 H, $ArCH_2CO$). For $C_{14}H_8Cl_2OS$ (295·2) calculated: 56·96% C, 2·73% H, 24·02% Cl, 10·86% S; found: 56·88% C, 2·92% H, 24·28% Cl, 10·75% S. On standing of the mother liquor, 0·6 g colourless crystals precipitated which, after several crystallizations from a mixture of benzene and light petroleum, melted at 147—149°C. According to analysis and spectra the compound is aldehyde *XVI*. UV spectrum: λ_{max} 224 nm ($\log \varepsilon$ 4·27), 310 nm (3·94). IR spectrum (KBr): 769 (4 vicinal aromatic C—H), 822 (2 vicinal aromatic C—H), 1 726, 2 750 and 2 845 cm^{-1} (CHO). NMR spectrum: δ 9·60 (s, 1 H, CHO), 7·15—7·60 (m, 6 H, aromatic protons), 5·52 (s, 1 H, Ar_2CH). For $C_{14}H_8Cl_2OS$ (295·2) calculated: 56·96% C, 2·73% H, 24·02% Cl, 10·86% S; found: 57·11% C, 2·77% H, 24·24% Cl, 10·65% S.

B. Similarly to the preceding case, 26·4 g acid *IXb* reacted with polyphosphoric acid (180 g P_2O_5, 100 ml 85% H_3PO_4) at 175°C for 3 h. After pouring on ice, the precipitate was filtered, dissolved in warm benzene, the solution was filtered, washed with 15% NaOH and water, dried with $MgSO_4$ and evaporated. The residue was boiled with 500 ml ethanol, the undissolved fraction was dissolved in 50 ml benzene and the fraction precipitated by adding 300 ml ethanol (1·5 g) was filtered. The combined benzene–ethanol solutions were filtered with charcoal and evaporated to one-half. On cooling, 0·36 g compound precipitated — this was twice crystallized from ethanol to a m.p. of 280—281°C, under decomposition. According to analysis and spectra it has the structure of bis(1,4-dichlorothioxanthen-9-yl) ether (*XXII*). UV spectrum (saturated solution in methanol): λ_{max} 230, 274, 283 infl. and 320 nm infl. IR spectrum (KBr): 752 and 762 (4 vicinal aromatic C—H), 812 (2 vicinal aromatic C—H), 975 (intense band, either in-plane bending of 2 vicinal aromatic C—H or a C—O bond), 1 105 (C—O—C), 1 568 cm^{-1} (Ar). Mass spectrum agrees with the suggested structure; the molecular ion corresponds to the assumed composition and the spectrum contains intense fragments supporting the presence of binding of the two halves of the molecule through an oxygen atom. For $C_{26}H_{14}Cl_4OS_2$ (548·4) calculated: 56·95% C, 2·57% H, 25·86% Cl, 11·70% S; found: 56·89% C, 2·57% H, 25·93% Cl, 12·22% S.

Filtrate after *XXII* was evaporated and the residue (17·9 g) was dissolved in 20 ml benzene. After adding 40 ml light petroleum, 0·69 g aldehyde *XVI* crystallized (m.p. 145—149°C). Evaporation of the mother liquor yielded 17·0 g oil which, according to thin-layer chromatography on silica gel, is a mixture of a predominating amount of aldehyde *XVI* and a smaller amount of ketone *XI*. An attempt at chromatography on alumina did not yield a crystalline compound. The mixture was hence used in its present form for oxidation and reduction experiments.

1,4-Dichlorothioxanthene-9-carboxylic Acid (*XVII*)

A solution of 3·32 g mixture of ketone *XI* and aldehyde *XVI* (prepared according to *B*) in 20 m acetone was combined by a dropwise addition with 3·55 ml solution obtained from 7·0 g CrO_3

6·1 ml H_2SO_4 and 25 ml water at 0°C. The mixture was stirred for 2 h and left at room temperature overnight. After adding 1·0 g $Na_2S_2O_5$, it was stirred for 1 h and extracted with benzene. The benzene solution was washed with 5% NaOH and water. Acidification of the washings with hydrochloric acid yielded 0·65 g acid which, after two recrystallizations from a mixture of benzene and light petroleum, melted at 234—237°C. According to analysis, we are dealing here with a solvate with 1/3 of a benzene molecule. UV spectrum: λ_{max} 232·5 nm (log ε 4·36), 281 nm (3·95). IR spectrum: 750 (4 vicinal aromatic C—H), 818 (2 vicinal aromatic C—H), 930, 1225, 1270, 1710 and 3100 cm^{-1} (COOH). For $C_{16}H_{10}Cl_2O_2S$ (337·2) calculated: 56·98% C, 2·99% H, 21·03% Cl, 9·51% S; found: 56·45% C, 2·93% H, 20·89% Cl, 9·47% S.

1,4-Dichlorothioxanthone (*XXIII*)

A. The benzene solution obtained from the preceding experiment was washed, dried with $MgSO_4$ and evaporated. The residue (2·23 g) was dissolved in ethanol, the insoluble fraction was removed (0·47 g), the solution evaporated again and the residue crystallized from a mixture of benzene and light petroleum; a total of 0·19 g homogeneous substance was obtained which was recrystallized from benzene and melted at 178—180°C. IR spectrum (KBr): 742 (4 vicinal aromatic C—H), 810 and 820 (2 vicinal aromatic C—H), 1295 (CO), 1412 (in-plane bending of aromatic C—H), 1560 (Ar) and 1646 cm^{-1} (ArCOAr). For $C_{13}H_6Cl_2OS$ (281·2) calculated: 55·53% C, 2·15% H, 25·22% Cl; found: 55·89% C, 2·14% H, 24·73% Cl.

B. A solution of 1·26 g $KMnO_4$ in 100 ml acetone was added to a solution of 3·35 g of a mixture of ketone *XI* and aldehyde *XVI* (prepared according to *B*) in 20 ml acetone, the mixture was stirred for 5 h at room temperature, after standing overnight, 0·7 g oxalic acid in 20 ml acetone was added and the solution was stirred for 1 h. Then a solution of 5·0 g $Na_2S_2O_5$ in water was added, the solution was acidified with dilute sulfuric acid and extracted with benzene. The extract was washed with 5% NaOH and water and evaporated to dryness. The residue (3·3 g) was dissolved in a mixture of benzene and light petroleum whereupon 0·36 g product precipitated; it was identical with the compound prepared under *A*. After two crystallizations from benzene it melted at 181—183°C. For $C_{13}H_6Cl_2OS$ (281·2) calculated: 55·83% C, 2·15% H, 25·22% Cl, 11·41% S; found: 55·71% C, 2·39% H, 25·01% Cl, 11·39% S.

6,8-Dichloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-ol (*XIIa*)

A solution of 0·90 g $NaBH_4$ in 10 ml water with 0·2 ml 15% NaOH was added dropwise to a solution of 7·0 g ketone *X* in 200 ml ethanol. The mixture was refluxed for 3 h, left to stand overnight, ethanol was distilled off and the residue was divided between water and chloroform. The organic phase was washed with 5% hydrochloric acid and water and evaporated. The remaining oil crystallized on mixing with cyclohexane; 6·2 g (88%), m.p. 96—97°C (benzene–light petroleum). IR spectrum: 750 (4 vicinal aromatic C—H), 861 (solitary aromatic C—H), 1067, 3230 and 3300 (OH), 1504 and 1556 cm^{-1} (Ar). For $C_{14}H_{10}Cl_2OS$ (297·2) calculated: 56·58% C, 3·39% H, 23·86% Cl, 10·79% S; found: 56·90% C, 3·48% H, 23·35% Cl, 10·97% S.

6,9-Dichloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-ol (*XIIb*) and 1,4-dichloro-9-thioxanthylmethanol (*XVIII*)

A. A solution of 1·15 g $NaBH_4$ in 5 ml water made alkaline with 2 drops of 15% NaOH was added dropwise to a solution of 8·8 g mixture of ketone *XI* and aldehyde *XVI* (prepared according to B) in 50 ml dioxane and 100 ml ethanol. The mixture was refluxed under stirring for 4 h and the organic solvents were evaporated. The residue was divided between water and benzene.

The organic phase was shaken with 5% hydrochloric acid and water and evaporated. The residue was dissolved in ethanol, the solution was filtered with charcoal and the filtrate was again evaporated. The residue (7·7 g) was dissolved in cyclohexane and yielded 0·34 g of a substance melting after recrystallization from benzene at 199—200°C. According to analysis and spectra we are dealing here with 1,4-*dichloro*-10,11-*dihydrodibenzo*[b,f]*thiepin*-10,11-*diol* (XXIV) with an undefined configuration of the hydroxyl groups. NMR spectrum (CD_3SOCD_3): δ 7·15—7·80 (m, 6 H, aromatic protons), 5·91 (d, J = 5·0 Hz, disappears on deuterization, 1 H, OH), 5·26 (bs, disappears on deuterization, 1 H, OH), c. 5·35 (m, after deuterization s at 5·31, 2 H, Ar—CH—CH—Ar). Mass spectrum contains no ions that would be at variance with the suggested structure. The molecular peak at 311·9796 corresponds to the assumed empirical formula: m/e 294 is formed by splitting off water and indicates the presence of at least one OH group which is not bound to the aromatic ring. For $C_{14}H_{10}Cl_2O_2S$ (313·2) calculated: 53·69% C, 3·22% H, 22·64% Cl, 10·24% S; found: 53·74% C, 3·28% H, 22·74% Cl, 10·33% S.

The mother liquor was evaporated and the residue (7·36 g) was chromatographed on a column of 300 g Al_2O_3 (activity II). A mixture of benzene and light petroleum eluted 3·7 g of the least polar fractions from which 0·9 g of not quite homogeneous material crystallized (from ethanol or cyclohexane), the substance melting after two crystallizations from benzene–light petroleum (or from ethanol) constantly at 252—255°C. On the basis of analysis and spectra the compound appears to be *bis*(6,9-*dichloro*-10,11-*dihydrodibenzo*[b,f]*thiepin*-10-*yl*)*ether* (XXV). The compound is very poorly soluble in methanol; its saturated solution does not show any typical absorption in UV light. IR spectrum: 750 and 760 (4 vicinal aromatic C—H), 805 and 815 (2 vicinal aromatic C—H), 1 080 (C—O—C), 1 550 and 1 568 cm^{-1} (Ar). For $C_{28}H_{18}Cl_4OS_2$ (544·3) calculated: 58·35% C, 3·15% H, 24·60% Cl, 11·13% S; found: 58·00% C, 3·07% H, 24·78% Cl, 11·12% S.

Continuation of chromatography resulted in elution of 0·7 g of the polar fractions, from which 0·40 g *alcohol* XIIb crystallized from cyclohexane: m.p. 134—135°C (cyclohexane). UV spectrum: λ_{max} 259 nm (log ε 3·93). IR spectrum: 678 (C—Cl), 750 (4 vicinal aromatic C—H), 815 (2 vicinal aromatic C—H), 1 085 (Ar—CHOH), 1 548, 1 558 and 1 630 (Ar), 3 440 cm^{-1} (OH). NMR spectrum: δ 7·00—7·80 (m, 6 H, aromatic protons), 5·45 (q, after deuterization t, 1 H, Ar—CH—O), 3·60 (d, J = 6·0 Hz, 2 H, $ArCH_2$), 2·90 (d, disappears on deuterization, 1 H, OH). For $C_{14}H_{10}Cl_2OS$ (297·2) calculated: 56·58% C, 3·39% H, 23·86% Cl, 10·79% S; found: 56·26% C, 3·40% H, 23·93% Cl, 10·61% S.

Ether was used for eluting from the column further 1·8 g fractions from which, with the aid of cyclohexane, 0·78 g alcohol *XVIII* crystallized in cyclohexane: m.p. 165—166°C. UV spectrum: λ_{max} 276·5 nm (log ε 4·26). IR spectrum: 750 (4 vicinal aromatic C—H), 800 and 810 (2 vicinal aromatic C—H), 1 050 (CH_2OH), 1 562 and 1 592 (Ar), 3 380 cm^{-1} (OH). NMR spectrum (CD_3SOCD_3): δ 7·20—7·65 (m, 6 H, aromatic protons), 5·00 (t, J = 6·0 Hz, disappears on deuterization, 1 H, OH). 4·80 (t, J = 8·0 Hz, after deuterization no change, 1 H, Ar_2CH), 3·52 (after deuterization d, J = 8·0 Hz, 2 H, CH_2O). For $C_{14}H_{10}Cl_2OS$ (297·2) calculated: 56·58% C, 3·39% H, 23·86% Cl, 10·79% S; found: 56·51% C, 3·44% H, 23·75% Cl, 10·70% S. The last, most polar fraction eluted from the column with ethanol was 0·3 g of a substance, from which crystallization in benzene yielded further 50 mg diol *XXIV*.

B. Reduction of 17·0 g mixture of ketone *XI* and aldehyde *XVI* was carried out similarly to *A* and the reaction mixture was treated similarly. Evaporation of the benzene solution yielded 16 g oil which, after dissolving in 20 ml benzene and 30 ml light petroleum, yielded on crystallization 4·4 g alcohol *XVIII*, m.p. 165—166°C (benzene). On standing, 0·5 g ether *XXV* precipitated; m.p. 252—256°C (benzene). The mother liquor was evaporated and the residue was chromatographed on a column of 1 kg Al_2O_3 (activity II). A mixture of benzene and light petroleum

eluted first 2·5 g of the least polar components of the mixture from which 0·2 g of a compound melting at 279—280°C (under decomposition) crystallized. On the basis of analysis and mass spectrum, it has the structure of *bi*(1,4-*dichloro*-9-*thioxanthyl*) (XXVI). The mass spectrum changes with time and temperature. The most intense peak is at *m/e* 265, corresponding to one-half of the molecule, *i.e.* the 1,4-dichlorothioxanthene ion (*XX*) which apparently represents the main fragmentation product. For $C_{26}H_{14}Cl_4S_2$ (532.4) calculated: 58·66% C, 2·65% H, 26·64% Cl, 12·05% S; found: 59·25% C, 2·72% H, 26·64% Cl, 11·96% S.

The further benzene–light petroleum eluates (3·25 g) crystallized in benzene to 0·4 g ether *XXV*, m.p. 252—255°C. The mother liquors yielded on distillation and four-fold redistillation 0·55 g liquid boiling at 145°C/0·5 Torr which, according to analysis and mass spectrum, is 1,4-*-dichloro*-9-*methylthioxanthene* (XXI). The molecular ion occurring in the mass spectrum corresponds to $C_{14}H_{10}Cl_2S$ (measured as *m/e* 279·9878, theoretically 279·9880). An intense fragment at *m/e* 265 supports the presence of the CH_3 group. For $C_{14}H_{10}Cl_2S$ (281·2) calculated: 59·80% C, 3·58% H; found: 59·99% C, 4·17% H.

The elution continued with chloroform and 5·3 g alcohols *XIIb* and *XVIII* were eluted. On rechromatography on a column of 360 g alumina (activity II), elution with benzene containing 10% chloroform yielded 1·08 g pure alcohol *XIIb*, m.p. 132—136°C. Elution with chloroform alone produced 2·24 g alcohol *XVIII*, melting at 162—166°C. The most polar component to be eluted with a mixture of ether and ethanol was the diol *XXIV* (0·15 g), m.p. 197—199°C (benzene).

1,4-Dichloro-9-(acetoxymethyl)thioxanthene (*XIX*)

A mixture of 1·6 g alcohol *XVIII* and 50 ml acetanhydride was refluxed for 2 h, acetanhydride was evaporated in vacuo, the residue was decomposed with 5% $NaHCO_3$ and extracted with benzene. The extract was dried with $MgSO_4$ and evaporated. The residue was distilled to yield 1·2 g of a product boiling at 176—178°C/0·2 Torr, which was redistilled (1·0 g, b.p. unchanged) and crystallized; m.p. 97—98·5°C (light petroleum). IR spectrum: 772 (4 vicinal aromatic C—H), 812 (2 vicinal aromatic C—H), 1230 (C—O), 1740 cm^{-1} (R—COO—R). NMR spectrum: δ 7·15—7·60 (m, 6 H, aromatic protons), 5·09 (t, J = 7·0 Hz, 1 H, Ar_2CH), 4·23 (m, 2 H, CH_2O), 1·93 (s, 3 H, CH_3CO). For $C_{16}H_{12}Cl_2O_2S$ (339·3) calculated: 56·65% C, 3·57% H, 20·90% Cl, 9·45% S; found: 57·01% C, 3·72% H, 21·01% Cl, 9·45% S.

1,4-Dichlorodibenzo[*b,f*]thiepin (*XV*)

A mixture of 2·68 g alcohol *XVIII* and 25 ml 85% H_3PO_4 was heated for 2 h to 170—190°C, after cooling it was poured into water and the product was extracted with a mixture of benzene and chloroform. The extract was dried and evaporated and the residue was extracted with light petroleum. What remained undissolved was 1·1 g alcohol *XVIII* (m.p. 163—165°C). Evaporation of the light petroleum solution produced 1·4 g compound *XV*, m.p. 115—116°C (methanol) which melts without depression in a mixture with the elimination product obtained in the reaction of chloride *XIIIb* with 1-methylpiperazine (see below.) The NMR spectrum exhibits only a multiplet in the region of aromatic protons with which the protons of the CH=CH bond merge. For $C_{14}H_8Cl_2S$ (279·2) calculated: 60·23% C, 2·89% H, 25·40% Cl, 11·48% S; found: 60·38% C, 3·18% H, 25·09% Cl, 11·56% S.

6,8,10-Trichloro-10,11-dihydrodibenzo[*b,f*]thiepin (*XIIIa*)

Powdered $CaCl_2$ (1·0 g) was added to a solution of 5·8 g alcohol *XIIa* in 50 ml benzene and the suspension was saturated under stirring for 4 h with anhydrous hydrogen chloride. After standing

overnight, it was filtered and the filtrate was evaporated. The residue (6·2 g, 100%) crystallizes after dissolving in cyclohexane with an addition of light petroleum; m.p. 90—95°C (light petroleum). For $C_{14}H_9Cl_3S$ (315·7) calculated: 53·27% C, 2·87% H, 33·70% Cl, 10·16% S; found: 53·88% C, 2·96% H, 33·11% Cl, 10·22% S.

6,9,10-Trichloro-10,11-dihydrodibenzo[*b,f*]thiepin (*XIIIb*)

As in the preceding case, 1·05 g alcohol *XIIb* yielded 1·08 g (97%) product, m.p. 165—168°C (cyclohexane). NMR spectrum: δ 7·10—7·80 (m, 6 H, aromatic protons), 5·85 (dd, $J = 6{\cdot}0$; 9·0 Hz, 1 H, Ar—CH—Cl), 3·88 (m, 2 H, $ArCH_2$). For $C_{14}H_9Cl_3S$ (315·7) calculated: 53·27% C, 2·87% H, 33·70% Cl, 10·16% S; found: 53·54% C, 2·91% H, 33·59% Cl, 10·00% S.

6,8-Dichloro-10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b,f*]thiepin (*IV*)

A mixture of 6·2 g chloride *XIIIa*, 15 ml 1-methylpiperazine and 15 ml chloroform was refluxed for 7 h. Chloroform was then evaporated and the residue was divided between water and benzene. The organic phase was washed with water and shaken with 60 ml dilute (1 : 2) hydrochloric acid. The suspension was filtered and the filtered hydrochloride was added to the aqueous phase of the filtrate. Evaporation of the benzene layer of the filtrate yielded 3·2 g neutral product apparently 2,4-*dichlorodibenzo*[b,f]*thiepin* (XIV), m.p. 125—127°C (ethanol). UV spectrum: λ_{max} 267 nm (log ε 4·31), 296 nm (3·73). NMR spectrum: δ 6·80—7·70 (m, aromatic and olefinic protons). For $C_{14}H_8Cl_2S$ (279·2) calculated: 60·23% C, 2·89% H, 25·40% Cl, 11·48% S; found: 60·45% C, 3·05% H, 25·13% Cl, 11·21% S.

Treatment of the aqueous suspension of the hydrochloride with 15% NaOH liberated the base *IV* which was isolated by extraction with benzene; 3·47 g (46%) oil. Conventional procedure was applied to prepare the *di*(*methanesulfonate*), crystallizing from a mixture of ethanol and ether as a monohydrate (4·90 g), m.p. 171—173°C under decomposition. NMR spectrum (CD_3. .$SOCD_3$): δ 7·65 (s, 2 H, aromatic protons in positions 7 and 9), 7·10—7·60 (m, 4 H, remaining aromatic protons), 5·75 (bs, SO_3H and H_2O), 4·50 (m, 1 H, Ar—CH—N), 2·46 (s, 9 H, N—CH_3 and 2 CH_3SO_3). For $C_{21}H_{30}Cl_2N_2O_7S_3$ (589·6) calculated: 42·78% C, 5·13% H, 12·03% Cl, 4·75% N, 16·32% S; found: 43·00% C, 5·04% H, 11·56% Cl, 4·60% N, 15·87% S.

6,9-Dichloro-10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b,f*]thiepin (*II*)

In analogy to the preceding case, 0·94 g chloride *XIIIb* reacted with 10 ml 1-methylpiperazine in 10 ml chloroform. Analogous treatment yielded first of all 0·77 g 1,4-*dichlorodibenzo*[b,f]thiepin (XV), m.p. 111·5—114·5°C (light petroleum), identical with the reported product of Wagner-Meerwein rearrangement of alcohol *XVIII*. UV spectrum: λ_{max} 268·5 nm (log ε 4·24), infl. 295 nm (3·72). IR spectrum: 705 (C—Cl), 740 (4 vicinal aromatic C—H), 815 (2 vicinal aromatic C—H), 888 cm^{-1} (ArCH=CHAr *cis*). NMR spectrum: δ 7·05—7·80 (m, aromatic and olefinic protons). For $C_{14}H_8Cl_2S$ (279·2) calculated: 60·23% C, 2·89% H, 25·40% Cl, 11·48% S; found: 60·48% C, 3·12% H, 25·13% Cl, 11·24% S.

Likewise, in analogy with the preceding case, 0·24 g (21%) crude base *II* was obtained and converted to the di(methanesulfonate), crystallizing from a mixture of ethanol and ether as a monohydrate, m.p. 170—171·5°C. For $C_{21}H_{30}Cl_2N_2O_7S_3$ (589·6) calculated: 42·78% C, 5·13% H, 4·75% N; found: 42·47% C, 5·12% H, 4·74% N. Decomposition of the methanesulfonate with aqueous ammonia liberated the base which was isolated by extraction with benzene; m.p. 142°C (methanol). NMR spectrum: δ 7·15—7·75 (m, 4 H, aromatic protons in positions 1, 2, 3, 4), 7·19 (s, 2 H, aromatic protons in positions 7 and 8), 3·00—4·50 (m, 3 H, $ArCH_2CHAr$), 2·70

(t, 4 H, $CH_2N^1CH_2$), 2·30 (t, 4 H, $CH_2N^4CH_2$), 2·20 (s, 3 H, N—CH_3). For $C_{19}H_{20}Cl_2N_2S$ (379·4) calculated: 60·16% C, 5·31% H, 18·69% Cl, 7·39% N, 8·45% S; found: 60·34% C, 5·58% H, 18·75% Cl, 6·96% N, 8·45% S.

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