POTENTIAL ANTIHISTAMINE AGENTS: 4-(6,11-DIHYDRODIBENZO[*b*,*e*]THIEPIN-11-YLIDENE)-1--METHYLTETRAHYDROTHIOPYRANIUM IODIDE AND SIMILAR SULFONIUM SALTS DERIVED FROM RELATED TRICYCLIC SYSTEMS

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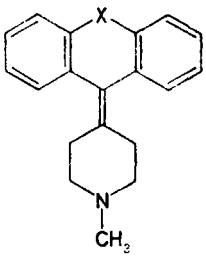
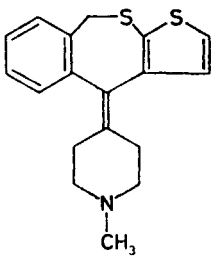
Thioxanthone, 10,11-dihydrodibenzo[*a*,*d*]cyclohepten-5-one, dibenzo[*b*,*e*]thiepin-11(6*H*)-one, its 2-methyl derivative, and thieno[2,3-*c*]-2-benzothiepin-4(9*H*)-one were reacted with 4-tetrahydrothiopyranylmagnesium bromide and the obtained tertiary alcohols *IVabc*, *VIc*, and *XIX* were dehydrated to the olefinic sulfides *IXabc*, *Xc*, and *XXI*. Addition of methyl iodide afforded the title compounds *XIabc*, *XIIc*, and *XXII*. The Grignard reactions were accompanied by the 1,6-addition giving the ketones *XVI*—*XVIII* as by-products. The reductive properties of tetrahydrothiopyranylmagnesium bromide were most striking in the case of reaction with 2-chlorothioxanthone; the isolation of thioxanthene and thioxanthone showed that nuclear dehalogenation took also place. Reactions of 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin and benzhydryl chloride with tetrahydrothiopyran-4-ol gave the sulfides *XXV* and *XXVIII*; whereas the latter reacted with methyl iodide under the formation of sulfonium salt *XXIX*, the former was cleaved and gave 4-hydroxyl-1-methyltetrahydrothiopyranium iodide (*XXVI*). The sulfonium salts are free of the central effects but their antihistamine activity is rather low.

1-Methyl-4-piperidylidene derivatives of thioxanthene (pimethixene, *Ia*) (ref.[1]), 10,11-dihydrodibenzo[*a*,*d*]cycloheptene *Ib* (ref.[2]), 6,11-dihydrodibenzo[*b*,*e*]thiepin *Ic* (refs[3,4]), and 4,9-dihydrothieno[2,3-*c*]-2-benzothiepin (pipethiadene, *II*) (refs[5,6]), having the piperidine residue attached to the central atom of the tricyclic skeletons, have important H_1 antihistamine activity which, however, is accompanied by the unwanted central depressant effects. This fact is due to their ability to penetrate through the blood-brain barrier. It is well known that the onium salts lack this ability and in our previous studies[7] we found high antihistamine activity with the sulfonium analogues of compounds of the diphenhydramine type. This led to the project of preparing and testing the sulfonium salts analogous to compounds *Ia*—*Ic* and *II*; the corresponding work is being reported in the present communication. In compounds prepared, the atom of sulfur is in the saturated six-membered ring for which we prefer this time – because of the nomenclature of the corresponding sulfonium

salts – the name tetrahydrothiopyran (*III*) (*cf.* our previous communications[8,9] dealing with this system).



I



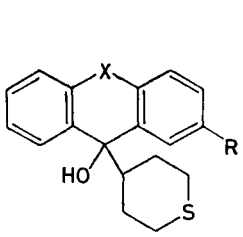
II

III

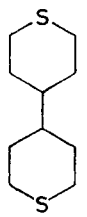
In formulae *I*, *IV–VI*, *IX–XV*: *a*, X = —S—, *b*, X = —CH_2CH_2—, *c*, X = —CH_2S—

Syntheses of the title compounds were carried out from the corresponding tricyclic ketones by reactions with 4-tetrahydrothiopyranylmagnesium bromide, by the following dehydration of the formed tertiary alcohols, and by the final addition of methyl iodide. Mixtures were formed in the first step and partly also in the second step which required separations by chromatography. The course of reactions and the pattern of products were different in individual cases which makes necessary to describe every case separately.

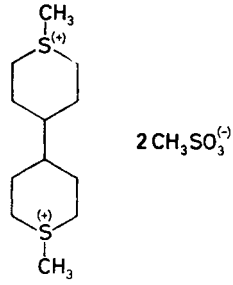
The starting 4-bromotetrahydrothiopyran was obtained from tetrahydrothiopyran-4-ol[8] by treatment with phosphorus tribromide at 80°C according to the literature[10] and the crude product (only this was described) was distilled and characterized. Its transformation to the Grignard reagent in a mixture of ether and tetrahydrofuran proceeded with the usual magnesium activation and initiation with a small amount of 1,2-dibromoethane. Thioxanthone[11,12] was the first ketone to be used. Its reaction with 4-tetrahydrothiopyranylmagnesium bromide gave a mixture from which crystallization afforded a part of the tertiary alcohol *IVa*. Chromatography of the mother liquors on silica gel gave as the first fraction 4,4'-bis(tetrahydrothiopyranyl) (*VII*), *i.e.* the usual by-product resulting from the reaction of the Grignard reagent with the unreacted 4-bromotetrahydrothiopyran. It reacted rather slowly with methyl methanesulfonate[13] in a mixture of benzene and acetone and gave the bis-onium salt *VIII*. Further to be eluted was the recovered thioxanthone which was followed by further quantity of *IVa*. An attempt to dehydrate *IVa* by treatment with thionyl chloride in dichloromethane in the presence of pyridine at room temperature was unsuccessful (no reaction). On the other hand, treatment with acetyl chloride in boiling chloroform effected the dehydration and gave the olefinic sulfide *IXa*. It was characterized by spectra and transformed by reaction with methyl iodide to the sulfonium iodide *XIa*.



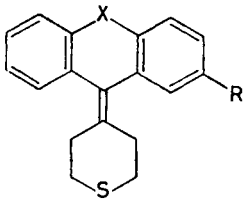
IV, R = H
V, R = Cl
VI, R = CH_3



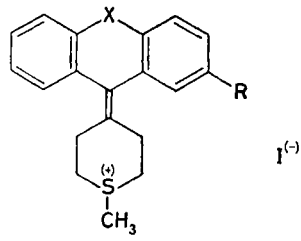
VII



VIII



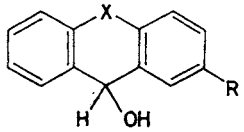
IX, R = H
X, R = CH_3



XI, R = H
XII, R = CH_3

Reaction of 2-chlorothioxanthone[14] with 4-tetrahydrothiopyranylmagnesium bromide gave a mixture which was separated by chromatography on silica gel. Six homogeneous products were obtained and identified. The least polar one was tetrahydrothiopyran (*III*) (ref.[15]), formed by hydrolysis of the Grignard reagent. It was characterized by its methiodide[16] which was prepared by reaction of *III* with methyl iodide. The second to be eluted was thioxanthene[17,18]. This was followed by a small amount of a high-melting (255–257°C) inhomogeneous solid consisting according to the mass spectrum and analysis of the prevailing amount of compound $C_{26}H_{17}ClS_2$ and of a small quantity of compound $C_{26}H_{18}S_2$. Their separation did not succeed which prevented further characterization and identification. Further to be eluted was the compound *VII* in a rather important quantity. This was followed by 11% of the recovered 2-chlorothioxanthone. The next was a solid $C_{13}H_8OS$ melting at 214–217°C, which was identified by means of UV and IR spectra, and by direct comparison with an authentic sample[11] as thioxanthone. The last to be eluted was the desired tertiary alcohol *Va* whose structure was confirmed by spectra. In this experiment, the appearing of the dechlorinated compounds, thioxanthene and thioxanthone, is most surprising and needs at least attempts at explication. We have to assume that there are two different processes behind the formation of these un-

expected products which are probably not interrelated. The first of them is very likely reduction of a part of 2-chlorothioxanthone by the secondary Grignard reagent (*cf.*[19,20]) to 2-chlorothioxanthene-9-ol (*XIVa*) which was not isolated because it is very acid-unstable and only the acidity of the ammonium chloride solution must have effected the abstraction of HO^- and the formation of the corresponding thioxanthylium cation. It is well known[18,21] that cations of this type undergo by hydrolysis disproportionation to the corresponding thioxanthene and thioxanthone. The disappearance of the atom of chlorine from the aromatic nucleus is a more tricky phenomenon. The only hypothesis we have, presumes displacement of the chloride anion by $MgBr^-$ of the Grignard reagent (transmetallation, *cf.*[22]) and the following hydrolysis of the new Grignard reagent formed. The formation of thioxanthene and thioxanthone could then be the result of combination of both mechanisms. The little amount of the isolated thioxanthene, contrasting with the rather important quantity of thioxanthone, indicates that the ketone was formed by both mechanisms, *i.e.* directly from 2-chlorothioxanthone by dechlorination as well as by the reduction-disproportionation mechanism combined by previous or following dechlorination (*e.g. via XIIIa*).

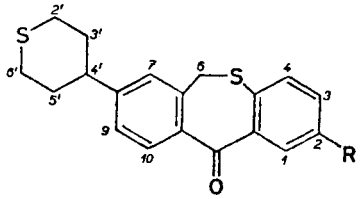


XIII, R = H
XIV, R = Cl
XV, R = CH_3

In the dibenzo[*a*,*d*]cycloheptene series the situation was much easier. The mixture, obtained by reaction of 10,11-dihydrodibenzo[*a*,*d*]cyclohepten-5-one[23] with 4-tetrahydrothiopyranylmagnesium bromide, was separated by chromatography on silica gel. In addition to small amounts of *III*, *VII*, and the starting ketone, there was btained the crude tertiary alcohol *IVb* in the yield of almost 70%. Pure product was prepared by rechromatography of a sample on aluminium oxide. The crude *IVb* was dehydrated with thionyl chloride in dichloromethane in the presence of pyridine under cooling. The mixture obtained was chromatographed and the first product to be eluted was the desired olefin *IXb* which was transformed by treatment with methyl iodide to the sulfonium salt *XIb*.

Dibenzo[*b*,*e*]thiepin-11(6*H*)-one[24] reacted with 4-tetrahydothiopyranylmagnesium bromide similarly and gave in addition to *VII* 61% of the tertiary alcohol *IVc* which was purified by crystallization and characterized by spectra. Secondary alcohol *XIIIc* (ref.[24]) was proven by TLC in the most polar fraction which contained a further

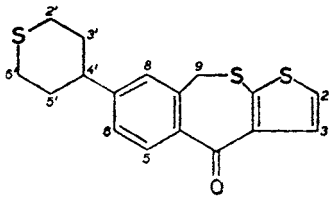
compound which was not possible to separate at this stage. Dehydration of the pure *IVc* with thionyl chloride similarly like in the preceding case gave in good yield the olefinic product *IXc* which was transformed to the sulfonium salt *XIc*. On the other hand, dehydration of crude *IXc*, containing the more polar products of the Grignard reaction, led to a mixture which was rather easily separated by chromatography on silica gel. The very lipophilic *IXc* was eluted with the first fraction and was then followed by a more polar compound $C_{19}H_{18}OS_2$ (mass spectrum) melting at 209–210°C. The UV and IR spectra characterized the compound as a diaryl ketone. A detailed analysis of the ^1H NMR spectrum (200 MHz) led to assignment of structure *XVI* to this product. We already met with a product of this type in reaction of thieno[2,3-*c*]-2-benzothiepin-4(9*H*)-one with 1-methyl-4-piperidylmagnesium chloride[5] where it appeared also as a by-product. The explanation of formation of *XVI* must be the same like in the mentioned former case: The product results from 1,6--addition[25] of the Grignard reagent, the following hydrolysis and elimination of two hydrogen atoms (apparently by oxidation with the air oxygen).



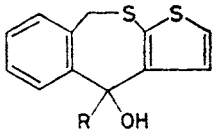
XVI, R = H
XVII, R = CH_3

The reaction sequence starting with 2-methyldibenzo[*b*,*e*]thiepin-11(6*H*)-one[26] took a very similar course like in the preceding case. Reaction with 4-tetrahydrothiopyranylmagnesium bromide gave a mixture which was chromatographed and *III*, *VII*, and the tertiary alcohol *VIc* were successively eluted. The last fractions of *VIc* were contaminated by more polar components, one of which was chromatographically identified as the secondary alcohol *XVc* (ref.[27]). The other was again isolated only after the following step. The alcohol *VIc* was purified by crystallization with difficulties and in this way only the analytical sample was prepared. The crude carbinol *VIc* was dehydrated and the mixture obtained was again easily separated by chromatography. The unsaturated compound *Xc* was obtained in high yield in the first fractions and was followed by a compound $C_{20}H_{20}OS_2$ (mass spectrum and analysis), a diaryl ketone with only six aromatic protons which corresponds to the by-product of the preceding series and must be *XVII*. Compound *Xc* gave by treatment with methyl iodide the sulfonium salt *XIIc*.

Reaction of thieno[2,3-*c*]-2-benzothiepin-4(9*H*)-one[28] with 4-tetrahydrothiopyranylmagnesium bromide gave five identified products. The first two were *III*

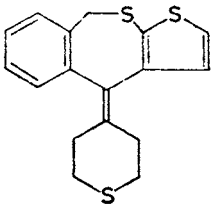


XVIII

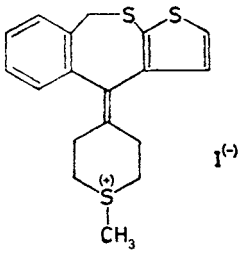


XIX, R =

XX, R = H

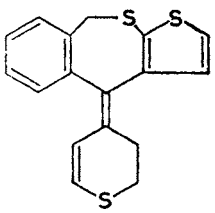


XXI

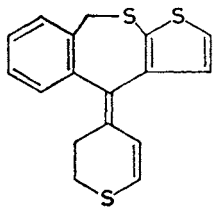


XXII

and *VII*. They were followed by about 10% of the diaryl ketone $C_{17}H_{16}OS_3$ which was identified on the basis of a detailed analysis of its ^1H NMR spectrum (200 MHz) as *XVIII*, *i.e.* a product of the 1,6-addition mechanism[25]. This product was followed by 30% of the tertiary alcohol *XIX*. In the most polar fractions, the secondary alcohol *XX* (ref.[28]) was proven by TLC. Dehydration of *XIX* with thionyl chloride in dichloromethane in the presence of pyridine under cooling gave a crude product which was chromatographed on silica gel; in this way the olefinic sulfide *XXI* was obtained in a high yield and was transformed to the methiodide *XXII*. The first chromatographic fraction crystallized and afforded a minor product $C_{17}H_{14}S_3$ melting at 166–168°C. In comparison with *XXI*, the molecule of the minor product must contain either an additional double bond or a further cycle. ^1H NMR spectrum characterized the product as a 1 : 1 mixture of the geometrical isomers *XXIII* and *XXIV*. The mode of introduction of the additional double bond is unclear.

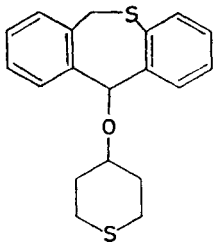


XXIII

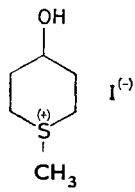


XXIV

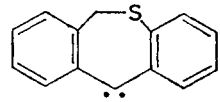
In connection with our previous investigation of sulfonium salts in the ether series of antihistamine agents[7] we wanted to prepare and test one representative of the tricyclic ether series (*cf.*[29]) containing the sulfonium cationic head. To this end we carried out reaction of 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[30] with tetrahydothiopyran-4-ol[8] in boiling xylene in the presence of potassium carbonate. The ether *XXV* was obtained in good yield but its reaction with methyl iodide in a mixture of benzene and nitromethane led to a peculiar cleavage, the product of which was identified as 1-methyl-4-hydroxytetrahydrothiopyranium iodide (*XXVI*). The weakness of the C—O bond in ethers like *XXV* is well known but in the present case there was not any acidic attack. Only the introduction of the positive charge into the molecule must have resulted in increased instability of the C—O bond and in its cleavage having probably the character of an α-elimination. The second product is then probably the carbene *XXVII*, the further fate of which could consist in dimerization to 11,11'-bis(6,11-dihydrodibenzo[*b*,*e*]thiepinylidene) which was not islated. Benzhydryl chloride[31] reacted similarly with tetrahydrothiopyran-4-ol[8] to give the ether *XXVIII* which gave on treatment with methyl iodide in a mixture of benzene and methanol the expected sulfonium salt *XXIX* without difficulties.



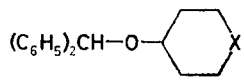
XXV



XXVI



XXVII



XXVIII, X = —S—
XXIX, X = $\overset{(+)}{S}$—CH_3 $I^{(-)}$

Sulfonium salts *XIa*–*XIc*, *XIIc*, *XXII*, and *XXIX* were pharmacologically tested using oral administration. For getting an idea about their acute toxicity, they were administered to mice in doses of 100 and 500 mg/kg. There were either no reaction at all (no influence on the behaviour) or weak sedation lasting for 1–2 h. No lethality was observed until the 7th day after the administration (only with *XIIc* and *XXIX* lethality in 10% animals). LD_{50} in mg/kg: *XIc* c. 2 500, *XIIc* c. 2 500, *XXIX* c. 2 000.

The compounds showed antihistamine activity of medium intensity in the test of histamine aerosol in guinea-pigs, PD_{50} in mg/kg: *XIa* c. 10, *XIb* 1·8, *XIc* 1·1, *XIIc* 4·9, *XXII* 5·30, *XXIX* slightly below 10. Antihistamine activity in the test of histamine detoxication in guinea-pigs was rather low; all compounds were administered in doses of 10 mg/kg: *XXII*, protection with 37·5% animals; *XIa*, *XIb*, and *XXIX*, protection with 12·5–25% animals; *XIc*, *XIIc*, without effect. The compounds were further tested for the ability to protect guinea-pigs from the lethal action of acetylcholine (240 mg/kg *s.c.*); all compounds were administered in doses of 10 mg/kg: *XIa* and *XIb* protected more than 50% animals (significant protection); *XXII* protected 40%; *XIc*, *XIIc*, and *XXIX* were without effect. In doses of 10 mg/kg the compounds had no antiserotonin activity in the test of oedema of the rat paws. In agreement with the expected inability to penetrate through the blood-brain barrier, the tested compounds did not show any central effects: Anticataleptic effect against perphenazine in rats (50 mg/kg), antireserpine action against the ulcerogenic effect in rats (50 mg/kg). Within the general screening program, *XIc* showed some antitussive action at 300 mg/kg in rats (the cough attacks, elicited by the aerosol of citric acid solution, were reduced by 45% in comparison with the control value). The bis-onium salt *VIII* (LD_{50} = 30 mg/kg *i.v.* in mice) in the dose equal to 2 LD_{50} *i.v.* (the animal connected to a respiratory pump) had a significant myorelaxant effect on the gastrocnemius muscle of the rat.

Antimicrobial activity *in vitro* (minimum inhibitory concentrations in μg/ml – unless they exceed 100 μg/ml – are given): *Staphylococcus pyogenes aureus*, *XXII* 12·5; *Proteus vulgaris*, *XXII* 100; *Trichophyton mentagrophytes*, *XIa* 50, *XIIc* 50, *XXII* 50, *XXIX* 50.

EXPERIMENTAL

The melting points were determined in Kofler block and were not corrected; the samples were dried *in vacuo* of about 60 Pa over P_2O_5 at room temperature or at 77°C. The UV spectra (in methanol, λ_{max} in nm (log ε)) were recorded with a Unicam SP 8 000 spectrophotometer, the IR spectra (mostly in Nujol, ν in cm^{-1}) with Perkin–Elmer 298 spectrophotometer, ^1H NMR spectra (in C^2HCl_3 unless stated otherwise, δ, J in Hz) mostly with a CW-NMR spectrometer Tesla BS 487 C (80 MHz) and partly on a FT-NMR spectrometer Varian XL-200 (200 MHz), and finally the mass spectra with MCH 1 320 and Varian MAT 44S spectrometers (m/z and % given), The homogeneity of the compounds and composition of the mixtures were checked by thin-layer chromatography (TLC) on silica gel (Silufol). The extracts were dried with Na_2SO_4 and $MgSO_4$, and evaporated under reduced pressure on a rotating evaporator.

4-Bromotetrahydrothiopyran

Crude product[10], obtained from 32·8 g tetrahydrothiopyran-4-ol[8] and 29·3 g PBr_3, was distilled; 35·1 g (69%), b.p. 72–74°C/1·6 kPa. ^1H NMR spectrum: 1·90–3·10 m, 8 H ($CH_2CH_2SCH_2.CH_2$); 4·25 m, 1 H (CH—Br). For C_5H_9BrS (181·1) calculated: 33·16% C, 5·01% H, 44·12% Br, 17·71% S; found: 33·48% C, 5·20% H, 43·60% Br, 17·74% S.

9-(4-Tetrahydrothiopyranyl)thioxanthen-9-ol (*IVa*)

Grignard reagent was prepared from 46·8 g 4-bromotetrahydrothiopyran and 19·1 g Mg in a mixture of 90 ml ether and 35 ml tetrahydrofuran. Mg was activated by washing with chloroform and then with a grain of iodine, and the reaction was started with about 10% of the bromo compound with initiation with several drops of 1,2-dibromoethane. The reaction proceeded without heating and the main part of the bromo compound was added dropwise over 60 min. The mixture was stirred for another 20 min without heating and then refluxed for 60 min for completing the formation of the reagent. It was then diluted with 250 ml tetrahydrofuran, cooled to 8°C, and treated over 20 min at 5—10°C with 27·7 g thioxanthone[11], added in portions. The mixture was maintained for 2 h at 5—10°C, allowed to stand ovrnight at room temperature, and refluxed for 15 min. After cooling it was poured into a mixture of 100 g NH_4Cl, 250 ml water, 400 g ice, and 250 ml benzene. The unreacted Mg was filtered off and the filtrate was extracted with benzene. The extract was washed with 100 ml saturated NaCl solution, dried, and evaporated. The residue was heated with 40 ml boiling benzene and the mixture was allowed for 2 days to crystallize; 24 g inhomogeneous product. It was dissolved in 300 ml boiling benzene, the undissolved solid was removed by filtration (about 1 g), the filtrate was evaporated to 150 ml, and allowed to crystallize overnight; 7·5 g almost pure *IVa*, m.p. 157—161°C. Recrystallization from benzene led to the pure compound melting at 185—187°C which, however, on further crystallization from benzene gave a 3 : 1 benzene solvate, m.p. 166—168°C. Mass spectrum: 314 (M^+, $C_{18}H_{18}OS_2$), 296 (M^+, $C_{18}H_{16}S_2$, product of dehydration evidently formed during the analysis). IR spectrum: 763, 777 (4 adjacent Ar—H); 1 066, 1 070 (C—OH); 1 559, 1 580, 3 000, 3 030, 3 050 (Ar); 3 240, 3 370, 3 440 (OH). ^{1}H NMR spectrum: 1·30—2·60 m, 9 H (4 CH_2 and CH of tetrahydrothiopyranyl); 7·10 m, 8 H (8 ArH). For $C_{18}H_{18}OS_2 + 1/3\ C_6H_6$ (340·4) calculated: 70·57% C, 5·92% H, 18·82% S; found: 70·50% C, 5·92% H, 18·93% S.

All mother liquors were combined, evaporated, and chromatographed on a column of 250 g silica gel. Elution with a 1 : 1 mixture of light petroleum and benzene gave first 6·2 g 4,4′-bis(tetrahydrothiopyranyl) (*VII*), m.p. 118—121°C (benzene–hexane and sublimated at 110°C/40 Pa). Mass spectrum: 202 (M^+, $C_{10}H_{18}S_2$, 100), 169 ($C_{10}H_{17}S$, 53), 155 ($C_9H_{15}S$, 42), 99 (73), 67 (71), 59 (50), 55 (68), 47 (82), 45 (99), 41 (93), 39 (69). IR spectrum (KBr): 1 430, 2 830, 2 850, 2 885, 2 900, 2 923, 2 940 (CH_2, C—H). ^{1}H NMR spectrum: 1·00—2·00 m, 10 H $\left(\begin{matrix}CH_2\\CH_2\end{matrix}\!>\!CH\!-\!CH\!<\!\begin{matrix}CH_2\\CH_2\end{matrix}\right)$; 2·60 m, 8 H ($2\ CH_2SCH_2$). For $C_{10}H_{18}S_2$ (202·4) calculated: 59·35% C, 8·97% H, 31·69% S; found: 59·16% C, 9·11% H, 31·56% S.

A mixture of 5·06 g *VII*, 27·5 g methyl methanesulfonate (was prepared by solvolysis of methanesulfonyl chloride with methanol in ether in the presence of pyridine, b.p. 100—102°C/3·3 kPa; ref.[13], b.p. 202·7—203°C/0·1 MPa), 30 ml benzene, and 25 ml acetone was allowed to stand for 12 days at room temperature; 5·1 g (48%) recrystallized bis(methomethanesulfonate) (*VIII*), m.p. 212—215°C (ethanol–ether). For $C_{14}H_{30}O_6S_4$ (422·7) calculated: 39·78% C, 7·15% H, 30·35% S; found: 39·43% C, 7·25% H, 29·92% S.

Continued elution with the mixture of light petroleum and benzene recovered 7·8 g thioxanthone, m.p. 210—215°C (benzene–hexane). Elution with benzene alone gave then further 14·0 g *IVa*, the total yield thus being 21·5 g (73% *per* conversion).

2-Chloro-9-(4-tetrahydrothiopyranyl)thioxanthen-9-ol (*Va*)

Grignard reagent was prepared similarly like in the preceding case from 17·1 g Mg and 42·0 g 4-bromotetrahydrothiopyran in 80 ml ether and 30 ml tetrahydrofuran. It was diluted with 450 ml

tetrahydrofuran and treated under stirring over 30 min at 10—15°C with 29·0 g 2-chlorothioxanthone[14], added in small portions. The solution was stirred for 2 h at room temperature, allowed to stand overnight in the refrigerator, and decomposed by pouring into the mixture of 90 g NH_4Cl, 220 ml water, and 360 g ice. After the addition of 250 ml benzene, the mixture was filtered, and the aqueous layer of the filtrate was extracted with benzene. The benzene layers were combined, washed (saturated NaCl solution), dried, and evaporated. The residue (39·8 g) was chromatographed on a column of 400 g silica gel. The first to be eluted with a mixture of 10% benzene and 90% light petroleum was tetrahydrothiopyran (*III*) (ref.[15]) (3·1 g). An authentic sample of *III* for comparison was prepared by hydrolysis of a sample of the Grignard reagent. For characterization, a sample (1·6 g) was treated with 22·4 g methyl iodide in 10 ml acetone and the mixture was allowed to stand for 48 h at room temperature; 1·8 g 1-methyltetrahydrothiopyranium iodide, m.p. 175—177°C (ethanol). Ref.[16], m.p. 174—175°C. The same mixture of solvents eluted 3·6 g (10%) thioxanthene, m.p. 130—132°C (benzene–heptane). Mass spectrum: 198 (M^+, $C_{13}H_{10}S$, 65), 197 ($C_{13}H_9S$, 100), 171 ($C_{11}H_7S$, 3), 165 ($C_{13}H_9$, 25), 152 ($C_{12}H_8$, 10). IR spectrum: 760 (4 adjacent Ar—H); 1 567, 1 581, 1 593, 3 010, 3 070 (Ar). ^{1}H NMR spectrum: 3·82 s, 2 H ($ArCH_2Ar$); 7·00—7·50 m, 8 H (8 ArH). Refs[17,18], m.p. 128°C, and 124—128°C, respectively. Mixture of 25% benzene and 75% light petroleum gave first 1·6 g substance melting at 255—257°C (heptane–benzene) which was characterized by the mass spectrum as a mixture of compounds $C_{26}H_{17}ClS_2$ and $C_{26}H_{18}S_2$ and was not identified. Further increase of the proportion of benzene in the eluting mixture (50% benzene, 50% light petroleum) led to washing out of 13·0 g *VII*, m.p. 117—121°C (heptane). Benzene alone recovered first 4·3 g starting 2-chlorothioxanthone, m.p. 154—155°C (heptane–benzene) (ref.[14], m.p. 147—153°C), which was followed by 6·7 g (19%) thioxanthone, m.p. 214—217°C (benzene). UV spectrum: 255·5 (4·67), infl. 285 (3·64), 297·5 (3·49), 377 (3·77). IR spectrum: 735 (4 adjacent Ar—H); 1 592 (Ar); 1 642 (ArCOAr). Ref.[18], m.p. 214—215°C. The last to be eluted with benzene was *Va* (2·2 g, 6%), m.p. 235—237°C (benzene). IR spectrum: 750, 760, 805, 900 (4 and 2 adjacent, and solitary Ar—H), 1 055, 1 065 (C—OH), 1 571, 1 590, 3 050 (Ar), 3 333 (OH). ^{1}H NMR spectrum: 1·20 to 2·60 m, 9 H (4 CH_2 and CH of tetrahydrothiopyranyl); 7·20—7·90 m, 7 H (7 ArH). For $C_{18}H_{17}ClOS_2$ (348·9) calculated: 61·96% C, 4·91% H, 10·16% Cl, 18·38% S; found: 62·26% C, 4·95% H, 9·79% Cl, 18·56% S.

5-(4-Tetrahydrothiopyranyl)-10,11-dihydrodibenzo[*a*,*d*]cyclohepten-5-ol (*IVb*)

Grignard reagent was prepared from 10·9 g Mg and 26·7 g 4-bromotetrahydrothiopyran in 50 ml ether and 30 ml tetrahydrofuran and was diluted with 100 ml tetrahydrofuran. 10,11-Dihydrodibenzo[*a*,*d*]cyclohepten-5-one[23] (17·3 g) was dissolved in 80 ml tetrahydrofuran and the solution was added to the stirred Grignard reagent over 45 min at 3—5°C. The mixture was processed similarly like in the preceding cases. The crude product (29·8 g) was chromatographed on 400 g silica gel. Elution with a mixture of 25% benzene and 75% light petroleum gave 1·0 g *III* (compared by TLC with the standard). A similar 1 : 1 mixture eluted 4·8 g *VII*, m.p. 116—121°C. Starting 10,11-dihydrodibenzo[*a*,*d*]cyclohepten-5-one was proved by TLC in the following fractions but was not isolated (very small amount). Benzene eluted 17·6 g (68%) *IVb*. A sample (2·0 g) was rechromatographed on 120 g neutral Al_2O_3 (activity II), m.p. 169—170°C (benzene–hexane). IR spectrum: 759, 768 (4 adjacent Ar—H); 1 055 (C—OH); 1 479, 3 020, 3 045, 3 055 (Ar); 3 385 (OH). ^{1}H NMR spectrum: 1·60 m, 4 H (H-3, H-3′, H-5, and H-5′ of tetrahydrothiopyranyl); 2·18 s, 1 H (OH); c. 2·50 m, 5 H (H-2, H-2′, H-4, H-6, and H-6′ of tetrahydrothiopyranyl); 2·80—3·70 m, 4 H ($ArCH_2CH_2Ar$); 7·00—7·90 m, 8 H (8 ArH). For $C_{20}H_{22}OS$ (310·5) calculated: 77·38% C, 7·14% H; 10·33% S; found: 77·65% C, 7·22% H, 10·49% S.

11-(4-Tetrahydrothiopyranyl)-6,11-dihydrodibenzo[*b*,*e*]thiepin-11-ol (*IVc*)

Grignard reagent was prepared from 3·65 g Mg and 9·0 g 4-bromotetrahydrothiopyran in a mixture of 25 ml ether and 25 ml tetrahydrofuran; it was reacted with a solution of 5·65 g dibenzo[*b*,*e*]thiepin-11(6*H*)-one[24] in 25 ml tetrahydrofuran and processed similarly like in the preceding cases. Chromatography of the crude product (11·0 g) on 200 g silica gel using benzene as eluent gave first 2·1 g *VII* (m.p. 118–121°C) which was followed by the crude *IVc* (5·0 g, 61%), used for the following step in this state (contained a little more polar impurity which was separated only in the following step). A sample of *IVc* was purified by repeated crystallization from a mixture of benzene and hexane, m.p. 150–155°C. IR spectrum: 746, 754 (4 adjacent Ar—H); 1 120 (C—OH); 1 480, 1 585, 1 600, 3 040 (Ar); 3 440 (OH). ^{1}H NMR spectrum: 1·65 bm, 4 H (H-3, H-3′, H-5, and H-5′ of tetrahydrothiopyranyl); 2·35 s, 1 H (OH); 2·60 bm, 4 H (CH_2SCH_2); 3·50 bm, 1 H (H-4 of tetrahydrothiopyranyl); 3·80 d, 1 H and 4·50 d, 1 H (ABq, $ArCH_2S$, J = 13·0); 6·80–7·80 m, 8 H (8 ArH). For $C_{19}H_{20}OS_2$ (328·5) calculated: 69·47% C, 6·14% H, 19·52% S; found: 69·18% C, 6·10% H, 19·26% S.

In the most polar fractions, the presence of *XIIIc* was detected by TLC using the authentic compound[24] as the standard.

11-(4-Tetrahydrothiopyranyl)-2-methyl-6,11-dihydrodibenzo[*b*,*e*]thiepin-11-ol (*VIc*)

Similarly like in the preceding cases, Grignard reagent was prepared from 15·5 g Mg and 38·0 g 4-bromotetrahydrothiopyran in a mixture of 70 ml ether and 30 ml tetrahydrofuran, it was diluted with 160 ml tetrahydrofuran, and reacted with a solution of 25·5 g 2-methyldibenzo[*b*,*e*]thiepin-11(6*H*)-one[26] in 100 ml tetrahydrofuran. Processing gave 51 g mixture which was chromatographed on 500 g silica gel. Mixtures of benzene and light petroleum eluted 1·5 g *III* (compared by TLC with the standard) and 5·3 g *VII*, m.p. 119–122°C (benzene–hexane). Benzene eluted 13·8 g (38%) crude *VIc* (containing the by-product which was separated in the next step) which was used in this state. A sample was purified by repeated crystallization, m.p. 182–183°C (benzene). IR spectrum: 730, 768, 792, 880 (4 and 2 adjacent, and solitary Ar—H); 1 045 (C—OH); 1 475, 1 600, 3 010, 3 050 (Ar); 3 400 (OH). ^{1}H NMR spectrum: 1·60 m, 5 H (H-3, H-3′, H-5, H-5′ of tetrahydrothiopyranyl, and OH); 2·19 s, 3 H (CH_3); 2·60 bm, 4 H (CH_2SCH_2); 3·55 bm, 1 H (H-4 of tetrahydrothiopyranyl); 3·82 d, 1 H and 4·48 d, 1 H (ABq, $ArCH_2S$, J = 13·0); 6·70–7·80 m, 7 H (7 ArH). For $C_{20}H_{22}OS_2$ (342·5) calculated: 70·13% C, 6·47% H, 18·72% S; found: 70·42% C, 6·43% H, 18·48% S. In the most polar fractions, the presence of *XVc* was detected by TLC using the authentic compound[27] as the standard.

4-(4-Tetrahydrothiopyranyl)-4,9-dihydrothieno[2,3-*c*]-2-benzothiepin-4-ol (*XIX*)

Grignard reagent from 14·1 g Mg and 34·7 g 4-bromotetrahydrothiopyran in 60 ml ether and 25 ml tetrahydrofuran was diluted with 100 ml tetrahydrofuran and reacted with a solution of 22·5 g thieno[2,3-*c*]-2-benzothiepin-4(9*H*)-one[28] in 85 ml tetrahydrofuran, and the reaction mixture was processed similarly like in the preceding cases. The crude product (46·3 g mixture) was chromatographed on 550 g silica gel. Mixtures of benzene and light petroleum eluted 5·8 g *III* (compared by TLC with the standard) and then 3·6 g *VII*, m.p. 119·5–121·5°C (benzene–hexane).

Benzene eluted then 2·5 g 7-(4-tetrahydrothiopyranyl)thieno[2,3-*c*]-2-benzothiepin-4(9*H*)-one (*XVIII*), m.p. 234–236°C (toluene). Mass spectrum: 332 (M^+, $C_{17}H_{16}OS_3$), 299 ($C_{17}H_{15}OS_2$), 229 ($C_{13}H_9S_2$), 128 ($C_{10}H_8$), 115 (C_9H_7). UV spectrum (saturated solution in methanol): 349, 263. IR spectrum: 840, 848, 895 (2 adjacent and solitary Ar—H); 1 600 (Ar); 1 615 (ArCOAr′). ^{1}H NMR spectrum (200 MHz): 1·87 m, 2 H (H-3′(ax) and H-5′(ax), J(3′(ax), 3′(eq)) = 13·6;

J(3'(ax), 2'(ax)) = 11·9; J(3'(ax), 2'(eq)) = 3·6; J(3'(ax), 4') = 12·1); 2·16 m, 2 H (H-3'(eq) and H-5'(eq), J(3'(eq), 3'(ax)) = 13·6; J(3'(eq), 2'(ax)) = 2·7; J(3'(eq), 2'(eq)) = 3·6; J(3'(eq), 4') = = 3·2); 2·58 tt, 1 H (H-4', J(4', 3'(ax)) = J(4', 5'(ax)) = 12·1; J(4', 3'(eq)) = J(4', 5'(eq)) = 3·2); 2·71 dt, 2 H (H-2'(eq) and H-6'(eq), J(2'(eq), 2'(ax)) = 13·8; J(2'(eq), 3'(ax)) = 3·6; J(2'(eq), 3'(eq)) = 3·6); 2·85 ddd, 2 H (H-2'(ax) and H-6'(ax), J(2'(ax), 2'(eq)) = 13·8; J(2'(ax), 3'(ax)) = = 11·9; J(2'(ax), 3'(eq)) = 2·7); 4·15 s, 2 H ($ArCH_2S$); 7·05 d, 1 H (H-8, J(8, 6) = 1·8); 7·06 d, 1 H (H-3, J(3, 2) = 5·6); 7·24 dd, 1 H (H-6, J(6, 5) = 8·1; J(6, 8) = 1·8); 7·71 d, 1 H (H-2, J(2, 3) = 5·6); 7·79 d, 1 H (H-5, J(5, 6) = 8·1). For $C_{17}H_{16}OS_3$ (332·5) calculated: 61·41% C, 4·85% H, 28·93% S; found: 61·90% C, 5·05% H, 28·83% S.

The following product eluted with benzene was *XIX* (9·6 g, 30%), m.p. 201—202°C (toluene). IR spectrum: 760, 765, 845 (4 and 2 adjacent Ar—H); 1 105 (C—OH); 3 335 (OH). ^{1}H NMR spectrum ($C^2H_3SOC^2H_3$): 1·20—2·70 m, 9 H (4 CH_2 and CH of tetrahydrothiopyranyl); 3·90 d, 1 H and 4·85 d, 1 H (ABq, $ArCH_2S$, J = 13·0); 5·75 bs, 1 H (OH); 7·00—7·90 m, 6 H (6 ArH). For $C_{17}H_{18}OS_3$ (334·5) calculated: 61·04% C, 5·42% H, 28·76% S; found: 61·26% C, 5·55% H, 28·53% S. In the most polar fractions, the presence of *XX* was detected by TLC using the authetic compound [28] as the standard.

4-(9-Thioxanthylidene)tetrahydrothiopyran (*IXa*)

A mixture of 13·6 g *IVa*, 85 ml chloroform, and 10·2 g acetyl chloride was stirred and refluxed for 2·5 h, and evaporated *in vacuo*. The residue was diluted with 100 ml water, made alkaline with 50 ml 20% NaOH and the mixture was extracted with dichloromethane. Processing of the extract gave 13·2 g crude product which was dissolved in 100 ml benzene and the solution was filtered through a column of 60 g silica gel. The column was washed with 200 ml benzene and the filtrates were evaporated; 8·6 g (66%) 6 : 1 solvate of *IXa* with benzene, m.p. 170—171°C (benzene). Mass spectrum: 296 (M^+, $C_{18}H_{16}S_2$, 95), 263 ($C_{18}H_{15}S$, 25), 249 ($C_{17}H_{13}S$, 95), 235 ($C_{16}H_{11}S$, 88), 221 ($C_{15}H_9S$, 100). UV spectrum: 231 (4·46), 264 (4·23), 307 (3·54). IR spectrum: 756, 775 (4 adjacent Ar—H); 1 590, 3 090 (Ar); 1 630 (C=C). ^{1}H NMR spectrum: 2·30—3·20 m, 8 H ($CH_2CH_2SCH_2CH_2$); 7·00—7·60 m, 8 H (8 ArH). For $C_{18}H_{16}S_2 + 1/6\,C_6H_6$ (309·5) calculated: 73·74% C, 5·54% H, 20·72% S; found: 73·68% C, 5·49% H, 21·01% S.

4-(10,11-Dihydrodibenzo[*a*,*d*]cyclohepten-5-ylidene)tetrahydrothiopyran (*IXb*)

A solution of 8·5 g *IVb* and 14·6 g pyridine in 130 ml dichloromethane was added dropwise over 80 min to a stirred solution of 7·3 g $SOCl_2$ in 40 ml dichloromethane at —10— —5°C. The mixture was stirred for 1 h at 0°C and decomposed under stirring and cooling by a solution of 30 g tartaric acid in 150 ml water, added over 10 min. It was extracted with dichloromethane, the extract was washed with 2% KOH and water, dried, and evaporated. The residue (9·4 g) was chromatographed on a column of 130 g silica gel. *IXb* (4·2 g, 53%) was obtained in the first fractions by elution with a mixture of 20% benzene and 80% light petroleum, m.p. 129—131°C (hexane). UV spectrum: infl. 240 (4·14). IR spectrum: 750, 775 (4 adjacent Ar—H); 1 483, 3 000, 3 055 (Ar); 1 640 (Ar—C=C). ^{1}H NMR spectrum: 2·40—3·60 m, 12 H ($CH_2CH_2SCH_2CH_2$ and $ArCH_2CH_2Ar$); 7·10 m, 8 H (8 ArH). For $C_{20}H_{20}S$ (292·4) calculated: 82·14% C, 6·89% H, 10·96% S; found: 82·37% C, 6·94% H, 11·02% S.

4-(6,11-Dihydrodibenzo[*b*,*e*]thiepin-11-ylidene)tetrahydrothiopyran (*IXc*)

A solution of 5·3 g crude *IVc* and 8·7 g pyridine in 70 ml dichloromethane was added over 30 min to a stirred solution of 4·3 g $SOCl_2$ in 25 ml dichloromethane at —5—0°C. The mixture was

stirred at this temperature for another 2 h, then decomposed under cooling by a slow addition of 75 ml 3% hydrochloric acid, the aqueous layer was separated, the organic layer was washed with 2% NaOH and water, dried, and evaporated. The residue (6·5 g) was chromatographed on a column of 80 g silica gel. Elution with a mixture of 25% light petroleum and 75% benzene gave 4·2 g (84%) *IXc*, m.p. 194—196°C (cyclohexane). UV spectrum: infl. 226 (4·37), infl. 269·5 (3·91), 300 (3·31). IR spectrum: 750, 764 (4 adjacent Ar—H); 1 480, 3 050 (Ar). ^{1}H NMR spectrum: 2·20—2·80 m, 8 H ($CH_2CH_2SCH_2CH_2$); 3·31 d, 1 H and 4·80 d, 1 H (ABq, $ArCH_2S$, J = 13·1); 6·80—7·30 m, 8 H (8 ArH). For $C_{19}H_{18}S_2$ (310·5) calculated: 73·50% C, 5·84% H, 20·66% S; found: 73·83% C, 5·85% H, 20·28% S.

Continued elution with benzene gave 1·0 g 8-(4-tetrahydrothiopyranyl)dibenzo[*b*,*e*]thiepin-11(6*H*)-one (*XVI*), m.p. 209—210°C (benzene). Mass spectrum: 326 (M^+, $C_{19}H_{18}OS_2$), 311 ($C_{18}H_{15}OS_2$), 297 ($C_{18}H_{17}S_2$). UV spectrum: infl. 266 (4·00), infl. 279 (3·95), 351 (3·56). IR spectrum: 740, 766 (4 adjacent Ar—H); 1 584, 1 603 (Ar); 1 625 (ArCOAr'). ^{1}H NMR spectrum (200 MHz): 1·86 m, 2 H (H-3'(ax) and H-5'(ax), J(3'(ax), 3'(eq)) = 13·5; J(3'(ax), 2'(ax)) = 11·9; J(3'(ax), 2'(eq)) = 3·6; J(3'(ax), 4') = 12·1); 2·15 m, 2 H (H-3'(eq) and H-5'(eq), J(3'(eq), 3'(ax)) = = 13·5; J(3'(eq), 2'(ax)) = 2·6; J(3'(eq), 2'(eq)) = 4·0; J(3'(eq), 4') = 3·2); 2·57 tt, 1 H (H-4', J(4', 3'(ax)) = J(4', 5'(ax)) = 12·1; J(4', 3'(eq)) = J(4', 5'(eq)) = 3·2); 2·70 m, 2 H (H-2'(eq) and H-6'(eq), J(2'(eq), 2'(ax)) = 13·8; J(2'(eq), 3'(ax)) = 3·6; J(2'(eq), 3'(eq)) = 4·0; 2·85 ddd, 2 H (H-2'(ax) and H-6'(ax), J(2'(ax), 2'(eq)) = 13·8; J(2'(ax), 3'(ax)) = 11·9; J(2'(ax), 3'(eq)) = 2·6); 4·03 s, 2 H ($ArCH_2S$); 7·03 d, 1 H (H-7, J(7, 9) = 1·7); 7·18 dd, 1 H (H-9, J(9,7) = 1·7; J(9, 10) = = 8·0); 7·22—7·41 m, 3 H (H-2, H-3, and H-4); 7·59 d, 1 H (H-10, J(10, 9) = 8·0); 8·18 m, 1 H (H-1). For $C_{19}H_{18}OS_2$ (326·4) calculated: 19·63% S; found: 19·44% S.

4-(2-Methyl-6,11-dihydrodibenzo[*b*,*e*]thiepin-11-ylidene)tetrahydrothiopyran (*Xc*)

Crude *VIc* (11·1 g) was dehydrated similarly like in the preceding case by treatment with 8·7 g $SOCl_2$ in 200 ml dichloromethane and in the presence of 17·3 g pyridine. Similar processing gave 12·2 g crude product which was chromatographed on a column of 110 g silica gel. Benzene eluted first 8·4 g (80%) *Xc*, m.p. 128—131°C (benzene–hexane). UV spectrum: 227 (4·39), infl. 270 (3·99), 305 (3·33). IR spectrum: 758, 808, 815, 884 (4 and 2 adjacent, and solitary Ar—H); 1 480, 3 015, 3 040, 3 055 (Ar). ^{1}H NMR spectrum: 2·19 s, 3 H (CH_3); 2·30—2·80 m, 8 H ($CH_2CH_2SCH_2CH_2$); 3·33 d, 1 H and 4·80 d, 1 H (ABq, $ArCH_2S$, J = 13·0); 6·70—7·40 m, 7 H (7 ArH). For $C_{20}H_{20}S_2$ (324·5) calculated: 74·03% C, 6·21% H, 19·76% S; found: 74·39% C, 6·36% H, 19·54% S.

Continued elution with benzene afforded 1·5 g 8-(4-tetrahydrothiopyranyl)-2-methyldibenzo-[*b*, *e*]thiepin-11(6*H*)-one (*XVII*), m.p. 180—181·5°C (benzene). In mixture with *VIc* there was an important depression of the melting point (150—163°C). Mass spectrum: 340 (M^+, $C_{20}H_{20}$· .OS_2), 325 ($C_{19}H_{17}OS_2$), 307 ($C_{20}H_{19}OS$), 239 ($C_{15}H_{11}OS$), 74 (C_3H_6S). UV spectrum (saturated solution in methanol): 244, infl. 275, 360. IR spectrum: 749, 761, 819, 898 (4 and 2 adjacent and solitary Ar—H); 1 598, 1 605 (Ar); 1 642 (ArCOAr'). ^{1}H NMR spectrum: 1·70 to 3·10 m, 9 H (4 CH_2 and CH of tetrahydrothiopyranyl); 2·35 s, 3 H (CH_3); 4·00 s, 2 H ($ArCH_2S$); 7·00—7·50 m, 4 H (H-3, H-4, H-7, and H-9); 7·65 d, 1 H (H-10, J = 8·5); 8·10 bs, 1 H (H-1). For $C_{20}H_{20}OS_2$ (340·5) calculated: 70·57% C, 5·92% H, 18·82% S; found: 70·84% C, 5·99% H, 18·43% S.

4-(4,9-Dihydrothieno[2,3-*c*]-2-benzothiepin-4-ylidene)tetrahydrothiopyran (*XXI*)

Dehydration of 3·7 g *XIX* with 2·9 g $SOCl_2$ in 100 ml dichloromethane and in the presence of 5·9 g pyridine was carried out similarly like in the preceding cases. Processing gave 4·2 g crude

product which was chromatographed on a column of 50 g silica gel. Elution with a mixture of 25% benzene and 75% light petroleum gave first 0·25 g seemingly homogeneous fraction which was identified as a 1 : 1 mixture of (*E*)- and (*Z*)-4-(4,9-dihydrothieno[2,3-*c*]-2-benzothiepin-4--ylidene)-3,4-dihydro-2*H*-thiopyran (*XXIII* and *XXIV*), m.p. 166–168°C (benzene–hexane). Mass spectrum: 314 (M^+, $C_{17}H_{14}S_3$), 281 ($C_{17}H_{13}S_2$), 267 ($C_{16}H_{11}S_2$), 253 ($C_{15}H_9S_2$), 235 ($C_{16}H_{11}S$), 221 ($C_{15}H_9S$), 184 ($C_{12}H_8S$), 97 (C_5H_5S). IR spectrum: 743, 749, 766, 774, 839 (4 and 2 adjacent Ar—H); 1 478, 1 553, 1 559, 3 040 (Ar). ^{1}H NMR spectrum: c. 2·90 m, 4 H (SCH_2CH_2); 3·45 d, 1 H and 4·75 d + 4·76 d, 1 H (ABq, $ArCH_2S$, J = 13·0); 6·60 d and 6·76 d (ABq, J = 10·0), and 6·76 d and 7·17 d (ABq, J = 10·0), $\sum$ 2 H (SCH=CH); c. 7·20 m, 4 H (H-7, H-8, H-9, and H-10); 7·26 d and 7·37 d (ABq, J = 5·0), and 7·38 d and 7·52 d (ABq, J = 5·0), $\sum$ 2 H (H-2 and H-3). For $C_{17}H_{14}S_3$ (314·5) calculated: 64·92% C, 4·49% H, 30·50% S; found: 64·54% C, 4·53% H, 30·51% S.

The chromatography was continued by elution with benzene alone and afforded 2·9 g (83%) *XXI*, m.p. 175–177°C (benzene). UV spectrum: 227 (4·34), 241 (4·21), 283 (3·84). IR spectrum: 744, 765, 834 (4 and 2 adjacent Ar—H); 3 060, 3 090 (Ar). ^{1}H NMR spectrum: 2·00–3·00 m, 8 H ($CH_2CH_2SCH_2CH_2$); 3·45 d, 1 H and 4·75 d, 1 H (ABq, $ArCH_2S$, J = 13·0); 6·58 d, 1 H (H-3); 6·90 d, 1 H (H-2, J = 5·0); c. 7·20 m, 4 H (H-7, H-8, H-9, and H-10). For $C_{17}H_{16}S_3$ (316·5) calculated: 64·51% C, 5·10% H, 30·39% S; found: 64·72% C, 5·18% H, 30·15% S.

1-Methyl-4-(9-thioxanthylidene)tetrahydrothiopyranium Iodide (*XIa*)

A mixture of 4·7 g *IXa*, 33 ml benzene, 56 ml nitromethane, and 22·5 g methyl iodide was allowed to stand for 3 days at room temperature. The precipitated solid was filtered, washed with benzene, and dried *in vacuo*; 5·7 g (82%), m.p. 175–178°C. For $C_{19}H_{19}IS_2$ (438·4) calculated: 52·06% C, 4·37% H, 28·95% I, 14·63% S; found: 52·25% C, 4·34% H, 29·00% I, 14·73% S.

4-(10,11-Dihydrodibenzo[*a*,*d*]cyclohepten-5-ylidene)-1-methyltetrahydrothiopyranium Iodide (*XIb*)

Was prepared similarly from *IXb* in the yield of 90%; m.p. 158–161°C (benzene–nitromethane). For $C_{21}H_{23}IS$ (434·4) calculated: 58·07% C, 5·34% H, 29·21% I, 7·38% S; found: 58·04% C, 5·35% H, 28·94% I, 7·30% S.

4-(6,11-Dihydrodibenzo[*b*,*e*]thiepin-11-ylidene)-1-methyltetrahydrothiopyranium Iodide (*XIc*)

Prepared from *IXc* in the yield of 93%; m.p. 194–196°C with decomposition (benzene–nitromethane). UV spectrum: 265 (3·87), 304 (3·32). IR spectrum: 760 (4 adjacent Ar—H); 1 480, 1 550, 1 580, 3 040 (Ar). For $C_{20}H_{21}IS_2$ (452·4) calculated: 53·10% C, 4·68% H, 28·05% I, 14·17% S; found: 52·67% C, 4·71% H, 27·54% I, 14·15% S.

1-Methyl-4-(2-methyl-6,11-dihydrodibenzo[*b*,*e*]thiepin-11-ylidene)tetrahydrothiopyranium Iodide (*XIIc*)

Prepared from *Xc* in the yield of 97%; monohydrate, m.p. 140–142°C (ethanol–ether). For $C_{21}H_{23}IS_2 + H_2O$ (484·4) calculated: 52·07% C, 5·20% H, 26·20% I, 13·24% S; found: 52·16% C, 5·36% H, 26·13% I, 12·88% S.

4-(4,9-Dihydrothieno[2,3-*c*]-2-benzothiepin-4-ylidene)-1-methyltetrahydrothiopyranium Iodide (*XXII*)

Prepared from *XXI* (2·1 g) and 10 g methyl iodide in a mixture of 20 ml benzene and 15 ml acetone by standing for 4 days at room temperature; 2·8 g (87%), 6 : 1 solvate with benzene, m.p. 173—174·5°C (acetone–benzene). The molecular peak in the mass spectrum corresponds to *XXI*: 316 ($C_{17}H_{16}S_3$, 30); 142, 127, 78 (C_6H_6, 100). For $C_{18}H_{19}IS_3 + 1/6\,C_6H_6$ (471·5) calculated: 48·41% C, 4·28% H, 26·92% I, 20·40% S; found: 48·33% C, 4·39% H, 26·10% I, 20·78% S.

11-(4-Tetrahydrothiopyranyloxy)-6,11-dihydrodibenzo[*b*,*e*]thiepin (*XXV*)

A mixture of 5·3 g 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[30], 2·75 g tetrahydrothiopyran-4-ol[8], 25 ml xylene, and 5·9 g K_2CO_3 was stirred and refluxed for 7·5 h. After cooling the mixture was diluted with 100 ml water and extracted with benzene. The extract was washed with water, dried, and evaporated. The residue (7·0 g) was dissolved in 50 ml benzene and the solution was filtered through a column of 30 g silica gel. The column was washed with 200 ml benzene and the filtrates were evaporated; 5·8 g (88%), m.p. 104—107°C (ethanol–cyclohexane). IR spectrum: 756 (4 adjacent Ar—H); 1 080 (R—O—R'); 1 583, 3 020, 3 055 (Ar). ^{1}H NMR spectrum: 1·80 to 3·20 m, 8 H ($CH_2CH_2SCH_2CH_2$); 3·55 m, 1 H (H-4' of tetrahydrothiopyranyl); 4·25 bs, at 60°C 4·10 bd, 1 H and 4·65 bd, 1 H ($ArCH_2S$, J = 13·0); 5·75 bs, 1 H (H-11); 6·90—7·60 m, 8 H (8 ArH). For $C_{19}H_{20}OS_2$ (328·5) calculated: 69·47% C, 6·14% H, 19·52% S; found: 69·54% C, 5·99% H, 19·50% S.

In an attempt at preparing the corresponding S-methylsulfonium salt, 0·5 g *XXV* were treated with 2·3 g methyl iodide in a mixture of 2 ml benzene and 4 ml nitromethane. After 4 days standing at room temperature the solution was evaporated *in vacuo* and the residue was crystallized from a mixture of methanol and benzene; 0·35 g 4-hydroxy-1-methyltetrahydrothiopyranium iodide (*XXVI*), m.p. 171—172°C. For $C_6H_{13}IOS$ (260·1) calculated: 27·70% C, 5·04% H, 48·78% I, 12·33% S; found: 27·75% C, 5·05% H, 48·75% I, 11·90% S.

4-(Benzhydryloxy)tetrahydrothiopyran (*XXVIII*)

A mixture of 8·1 g benzhydryl chloride[31], 5·2 g tetrahydrothiopyran-4-ol[8], 50 ml xylene, and 5·5 g K_2CO_3 was stirred and refluxed for 5 h. After standing overnight the mixture was diluted with 100 ml water and extracted with benzene. The extract was washed with water, dried, and evaporated *in vacuo*. The residue (15·8 g) was chromatographed on a column of 85 g silica gel. Benzene eluted in the first fractions 7·0 g (62%) *XXVIII*, m.p. 87·5—90°C (hexane). IR spectrum: 710, 755, 766 (5 adjacent Ar—H); 1 069 (R—O—R'); 1 491, 1 589, 1 600, 3 005, 3 030, 3 060, 3 085 (Ar). ^{1}H NMR spectrum: 2·00 m, 4 H (2 CH_2 in positions 3 and 5 of tetrahydrothiopyranyl); 2·20—3·00 m, 4 H (CH_2SCH_2); 3·46 m, 1 H (H-4 of tetrahydrothiopyranyl); 5·50 s, 1 H (Ar_2.CH—O); 7·30 s, 10 H (2 C_6H_5). For $C_{18}H_{20}OS$ (284·4) calculated: 76·01% C, 7·09% H, 11·27% S; found: 76·29% C, 7·16% H, 11·44% S.

4-(Benzhydryloxy)-1-methyltetrahydrothiopyranium Iodide (*XXIX*)

A mixture of 9·3 g *XXVIII*, 20 ml methanol, 30 ml benzene, and 22·8 g methyl iodide was allowed to stand for 4 days at room temperature. There crystallized 12·1 g (87%) *XXIX*, m.p. 151—153°C (methanol–benzene). For $C_{19}H_{23}IOS$ (426·4) calculated: 53·53% C, 5·44% H, 29·76% I, 7·52% S; found: 53·83% C, 5·65% H, 29·44% I, 7·82% S.

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