POTENTIAL ANTIDEPRESSANTS. SYNTHESIS OF 6,11-DIHYDRODIBENZO[*b*,*e*]THIEPIN-11-YL (DIMETHYLAMINOMETHYL)PHENYL ETHERS, SULFIDES, AMINES AND SOME RELATED COMPOUNDS

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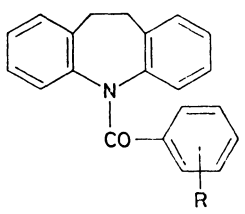
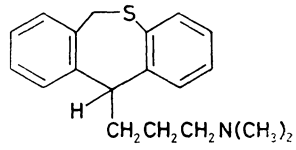
Dedicated to Professor Otto Exner on the occasion of his 65th birthday.

Reactions of 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin and its 2-bromo derivative with the isomeric (dimethylaminomethyl)phenols, (dimethylaminomethyl)thiophenols, and (dimethylaminomethyl)anilines in toluene afforded the title compounds *IIIb,c*, *Va*, *VIIIa,b,c*, and *Xa,b,c*. Reactions of 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin and its 2-chloro and 2-methyl derivatives with N,N-dimethyl-2-(4-aminophenoxy)ethylamine and N,N-dimethyl-3-(4-aminophenoxy)-propylamine by heating in dimethylformamide in the presence of sodium carbonate gave the diamino ethers *XI*—*XIV*. The compounds showed only indications of the antidepressant agents profile and some antimicrobial effects in vitro.

The announcement of psychotropic activity of compounds *Ia,b,c* and analogues[1] induced us to synthesize somewhat similarly constructed analogues of our experimental antidepressant agent "hydrothiadene" (*II*) (refs[2-6]) with the inserted benzene nucleus between the terminal dimethylaminomethyl group and the tricycle and connected with position 11 of this tricycle by an atom of oxygen, sulfur, and nitrogen. In this way the title compounds were designed and the present communication deals mainly with their synthesis.



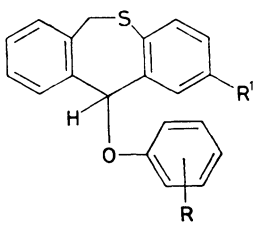
I



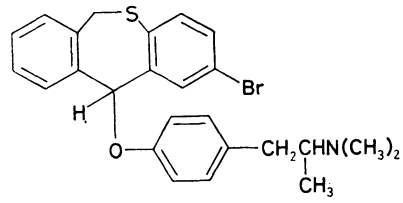
II

In formulae *I*, *III*–*V*, *VIII* and *X*: *a*, R = 2-$CH_2N(CH_3)_2$
b, R = 3-$CH_2N(CH_3)_2$ *c*, R = 4-$CH_2N(CH_3)_2$

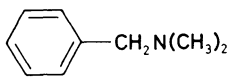
In the ether series, the tricyclic starting compounds were 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3], 2,11-dichloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[7], and 2-bromo--11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[8]. The other reaction components – 2-, 3-, and 4-(dimethylaminomethyl)phenol – were obtained by demethylation of the corresponding (dimethylaminomethyl)anisoles by heating with hydrobromic acid according to Stedman[9]. Reactions of the components mentioned proceeded in boiling toluene and it proved indispensable to process the crude reaction mixtures by chromatography. In this way the bases *IIIb* and *IIIc* were obtained as homogeneous oils giving crystalline salts with weak organic acids, and the base *Va* was obtained as a crystalline substance. The identity of the products was corroborated by spectra, especially by mass and ^{1}H NMR spectra. In some cases attempts were made to isolate the basic ethers by extraction from the crude reaction mixtures with dilute hydrochloric acid for separating the basic and neutral components of the mixtures. These attempts were unsuccessful due to high sensitivity of the ethers formed to strong acids; they are rapidly cleaved. From such attempt to prepare *IVc* only the neutral product was isolated and identified as 2-chloro-6,11-dihydrodibenzo-[*b*,*e*]thiepin-11-ol[7,10]. A similar result gave an attempt to prepare the ether *VI*



III, R' = H
IV, R' = Cl
V, R' = Br



VI



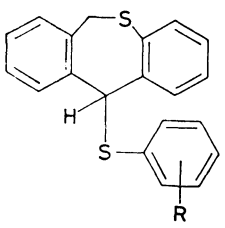
VII

by reaction of 2-bromo-11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[8] with N,N-dimethyl-1-(4-hydroxyphenyl)-2-propylamine[11–13] and by the following extraction of the product with dilute hydrochloric acid. Treatment of the acid layer with aqueous ammonia, extraction with benzene and chromatography on alumina gave first the starting N,N-dimethyl-1-(4-hydroxyphenyl)-2-propylamine which was characterized

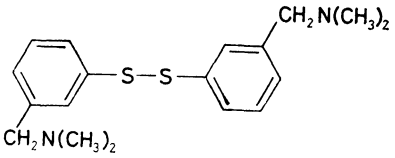
as the hydrochloride. The second compound eluted was identified as 2-bromo-6,11--dihydrodibenzo[*b*,*e*]thiepin-11-ol[8]. In both cases the cleavage was evidently of the usual type of acid cleavage of the benzyl ethers. From a similar attempt to prepare *IVa* only the basic product of the cleavage was isolated in the form of hydrogen oxalate. It was identified, surprisingly, as N-benzyldimethylamine (*VII*) (refs[14,15]). We have no explanation for the formation of this cleavage product.

In the sulfide series, 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3] was the tricyclic starting compound. It was reacted with 2-, 3- and 4-(dimethylaminomethyl)thiophenol in toluene at room temperature. These thiophenols have not been described yet. They have been prepared now by reactions of 2-, 3-, and 4-(dimethylaminomethyl)phenylmagnesium bromide with sulfur in tetrahydrofuran. Synthesis of the starting N,N--dimethyl-2-, -3-, and -4-bromobenzylamine was described by Jones and Hauser[16] who stated that in ether only N,N-dimethyl-2-bromobenzylamine afforded the Grignard reagent; the other two isomers did not react with magnesium. It could be established now that all three N,N-dimethyl-bromobenzylamines react smoothly with magnesium in tetrahydrofuran. The importance of this solvent for preparing the "basic" Grignard reagents, e.g. 3-dimethylaminopropylmagnesium chloride and 1-methyl-4-piperidylmagnesium chloride was recognized[17,18] just in the time when the paper of Jones and Hauser[16] appeared. The (dimethylaminomethyl)thiophenols are unstable and it was necessary to process them immediately after their synthesis, i.e. without isolation and characterization. In this way, 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3] and the crude 2-(dimethylaminomethyl)thiophenol afforded 38% of *VIIIa* which was purified by chromatography and was transformed to the crystalline hydrogen oxalate. The identity of the product was confirmed by analysis and by the mass spectrum. Reaction of 3-(dimethylaminomethyl)phenylmagnesium bromide with sulfur gave an inhomogeneous oily product. An attempt at its purification by distillation gave only a small amount of an inhomogeneous distillate. The main product was the distillation residue which was transformed to a crystalline hydrochloride, identified by analysis and spectra as *IX* dihydrochloride. This compound (base) was reduced with lithium aluminium hydride in ether and the crude product (i.e. the corresponding thiophenol) was reacted with 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3] in toluene and gave *VIIIb* in a moderate yield. Chromatography was again necessary for obtaining an almost homogeneous oily product which was transformed to the crystalline hydrogen fumarate. Its mass spectrum and analysis were again the first proof of identity which was confirmed by the ^{1}H NMR spectrum of the released base. Reaction of 4-(dimethylaminomethyl)phenylmagnesium bromide with sulfur gave a mixture of 4-(dimethylaminomethyl)thiophenol and the corresponding disulfide. It was reduced with lithium aluminium hydride in ether and the crude product was again used for reaction with 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3] in toluene. Chromatography of the crude product gave the almost homogeneous oily product in moderate yield; it was transformed to the

crystalline hydrogen oxalate, identified by analysis and the mass spectrum. The ^{1}H NMR spectrum of the released base confirmed the identity.



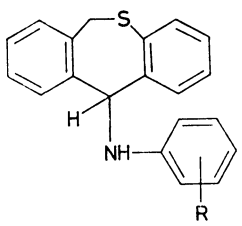
VIII



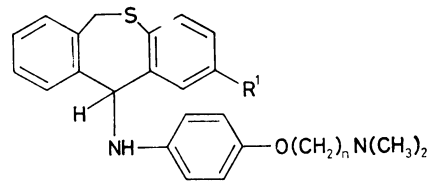
IX

Two series of amines were prepared: *Xa,b,c* and *XI–XIV*. The first three (*Xa,b,c*) were obtained by reactions of 11-chloro-6,11-dihydrodibenzo[*b,e*]thiepin[3] with the isomeric (dimethylaminomethyl)anilines in toluene at room temperature. The preparation of the starting (dimethylaminomethyl)anilines was described by Stedman[9] who reduced the isomeric N,N-dimethyl-nitrobenzylamines[9] by tin and hydrochloric acid. It has now been found that a more suitable method for reducing these nitro compounds consists in reaction with hydrazine hydrate in boiling ethanol in the presence of ferric chloride and active carbon (method[19–21]); the yields are 74–86% and the procedure is described in the Experimental. The amine *Xa* was obtained in a good yield and was crystalline; its identity was confirmed by spectra. It afforded a crystalline oxalate which was used for recording the mass spectrum. The amines *Xb* and *Xc* were oily, they were purified by chromatography on alumina and transformed to crystalline fumarates. The structures were corroborated by spectra.

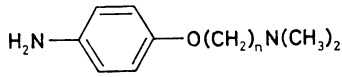
Syntheses of the second group of amines (*XI–XIV*) started on the one hand from 11-chloro-6,11-dihydrodibenzo[*b,e*]thiepin[3] and its 2-chloro[7] and 2-methyl[22] derivatives and from the diamines *XV* and *XVI* on the other. The diamine *XV* (ref.[23]) was prepared by reduction of N,N-dimethyl-2-(4-nitrophenoxy)ethylamine[23–25] with hydrazine and Raney nickel as catalyst (method[26–30]) in a higher yield than stated for the reduction with stannous chloride and hydrochloric acid[23]. The homologous *XVI* was obtained by reaction of potassium 4-nitrophenoxide with 3-dimethylaminopropyl chloride in boiling toluene and by the following reduction of the obtained N,N-dimethyl-3-(4-nitrophenoxy)propylamine with hydrazine and Raney nickel in ethanol (ref.[23] described a different method of preparation). The final products (*XI–XIV*) were prepared from the 11-chloro compounds and *XV* and *XVI* by heating in dimethylformamide (105–125°C) in the presence of sodium carbonate. The oily bases were purified by chromatography, transformed to crystalline salts with dicarboxylic acids (maleic, oxalic) and the released bases were fully characterized by spectra.



X



XI, $R^1 = H$; $n = 2$
XII, $R^1 = Cl$; $n = 2$
XIII, $R^1 = CH_3$; $n = 2$
XIV, $R^1 = H$; $n = 3$



XV, $n = 2$
XVI, $n = 3$

Compounds *IIIb,c*, *VIIIa,b,c*, *Xa,b,c*, and *XI*–*XIV* in the form of salts, described in the Experimental, were tested for ataxic, antireserpine, and antihistamine activity, for affinity to the imipramine and desipramine binding sites in hypothalamus of the rat brain, and finally for potentiating the yohimbine toxicity (oral administration, doses in mg/kg). Ataxic activity was tested in the rotarod test in mice, dose and % of positively responding animals: *IIIb*, *IIIc*, and *VIIIb*, 250, 0; *VIIIa* and *VIIIc*, 100, 0; *Xa*, *Xb*, and *XIV*, 250, 30; *Xc*, 250, 40; *XI*, 50, 0; *XII*, 100, 20; *XIII*, 250, 20. Antireserpine activity in the test of reserpine ptosis in mice: *IIIb,c*, *VIIIa,b,c*, *Xa,b,c*, and *XII*–*XIV*, inactive at 100 mg/kg, *XI*, mild antireserpine activity at 10 and 30 mg/kg. Antireserpine activity in the test of reserpine-induced hypothermia in mice: *XIII* and *XIV*, mild but significant antireserpine effect at 100 mg/kg; *XII*, inactive at 100 mg/kg. Potentiation of yohimbine toxicity in mice, approx. ED_{50} in mg/kg: *IIIc*, 250; *VIIIb*, 250; *Xc*, 250; *XI*, 100; *XIII*, 148; *XIV*, 105; *VIIIa* and *VIIIc*, inactive at 100 mg/kg; *Xa*, at 1 000 mg/kg active in 10% of animals; *Xb*, 250, 40%; *XII*, 100, 40%. Antihistamine activity in the tests of histamine aerosol and histamine detoxication in guinea pigs, *VIIIa*, *VIIIc*, *Xa,b,c*, inactive at 10 mg/kg. Inhibition of binding of 4 nM [^{3}H]imipramine in rat hypothalamus in vitro, *XI*, IC_{50} = = 197 nmol l^{-1}. Inhibition of binding of 4 nM [^{3}H]desipramine in rat hypothalamus in vitro, *XI*, IC_{50} = 1 252 nmol l^{-1}. The affinity of the other compounds to the imipramine and desipramine binding sites in rat hypothalamus was not significant. Only compound *XI* (VÚFB-17 095) is considered a potential antidepressant.

Most of the compounds prepared were also tested for antimicrobial activity in vitro (the minimum inhibitory concentrations in mg/l – unless they exceed 128 mg/l

– are given): *Streptococcus* β-*haemolyticus*, *IIIb* 8, *VIIIa* 128, *VIIIb* 4, *Xb* 128, *Xc* 128, *XI* 128, *XII* 128, *XIII* 128, *XIV* 128; *Streptococcus faecalis*, *IIIb* 8, *VIIIb* 4, *Xb* 64, *Xc* 64, *XI* 4, *XII* 8, *XIII* 4, *XIV* 4; *Staphylococcus pyogenes aureus*, *IIIb* 8, *VIIIa* 128, *VIIIb* 4, *Xb* 128, *Xc* 128, *XI* 4, *XII* 2, *XIII* 4; *XIV* 4; *Pseudomonas aeruginosa*, *IIIb* 64, *VIIIb* 64, *XI* 128, *XII* 128, *XIII* 128, *XIV* 128; *Escherichia coli*, *XI* 128, *XII* 128, *XIII* 128, *XIV* 128; *Proteus vulgaris*, *IIIb* 128; *VIIIb* 128, *Xc* 128, *XI* 128, *XII* 128, *XIII* 128, *XIV* 128; *Saccharomyces pasterianus*, *IIIb* 50, *VIIIb* 25, *XII* 50, *XIII* 50, *XIV* 50; *Trichophyton mentagrophytes*, *IIIb* 12·5, *VIIIa* 50, *VIIIb* 6·2, *Xa* 50, *Xb* 25, *Xc* 50, *XI* 25, *XII* 12·5, *XIII* 25, *XIV* 12·5; *Candida albicans*, *IIIb* 50; *Aspergillus niger*, *VIIIb* 50. Compound *VIIIb* (VÚFB-17 136) showed a rather high antimicrobial activity in vitro.

EXPERIMENTAL

The melting points were determined in the Mettler FP-5 melting point recorder or in a Kofler block; the samples were dried in vacuo of about 60 Pa over P_2O_5 at room temperature or at a suitably elevated temperature. UV spectra (in methanol, λ_{max} in nm ($\log \varepsilon$)) were recorded with a Unicam SP 8000 spectrophotometer, IR spectra (mostly in Nujol, ν in cm^{-1}) with a Perkin–Elmer 298 spectrophotometer, ^1H NMR spectra (in $CDCl_3$ unless stated otherwise, δ in ppm, J in Hz) with the CW-NMR spectrometer Tesla BS 487C (80 MHz) or with the FT-NMR spectrometer Tesla BS 567A (100 MHz), and the mass spectra (m/z, fragments and/or %) with MCH 1 320 and/or Varian MAT 44S (GC–MS) spectrometers. The homogeneity of the products and composition of the mixtures were checked by thin-layer chromatography (TLC) on silica gel (Silufol). Column chromatography was carried out on neutral Al_2O_3 (activity II) (unles otherwise stated). The extracts were dried with $MgSO_4$ or K_2CO_3 and evaporated under reduced pressure on a rotary evaporator.

2-(Dimethylaminomethyl)aniline

A solution of 12·0 g N,N-dimethyl-2-nitrobenzylamine[9] in 125 ml ethanol was treated with 25 ml 98% $N_2H_4.H_2O$, 4·1 g charcoal, and a solution of 1·1 g $FeCl_3.6\,H_2O$ in 14 ml ethanol was stirred and heated to 50°C to start an exothermic reaction (under a reflux condenser). After this was over, a solution of further 25·4 g N,N-dimethyl-2-nitrobenzylamine[9] in 40 ml ethanol was slowly added, and the mixture was refluxed for 8 h. The cold mixture was filtered, the filtrate was evaporated, the residue was dissolved in 100 ml chloroform, the solution was dried and evaporated. The residue gave by distillation 26·9 g (86%) of the product, b.p. 113–116°C/2 kPa, m.p. 37–37·7°C. Ref.[9], b.p. 107°C/1·9 kPa, m.p. 36–37°C.

3-(Dimethylaminomethyl)aniline

A similar reduction of 66·2 g N,N-dimethyl-3-nitrobenzylamine[9] with 44 ml 98% $N_2H_4.H_2O$ in 365 ml ethanol in the presence of 7·3 g charcoal and 1·95 g $FeCl_3.6\,H_2O$ gave 46·2 g (84%) of the product boiling at 135–137°C/2 kPa and melting at 45–46°C. Ref.[9], b.p. 129°C/1·73 kPa, m.p. 46°C.

4-(Dimethylaminomethyl)aniline

A similar reduction of 49·6 g N,N-dimethyl-4-nitrobenzylamine[9] with 33 ml 98% $N_2H_4.H_2O$

in 240 ml ethanol in the presence of 5·5 g charcoal and 1·47 g $FeCl_3.6\,H_2O$ gave 30·5 g (74%) of the product, b.p. 130–132°C/2 kPa. Ref.[9], b.p. 133°C/2·13 kPa.

N,N-Dimethyl-2-(4-aminophenoxy)ethylamine (*XV*)

A stirred solution of 24·4 g N,N-dimethyl-2-(4-nitrophenoxy)ethylamine[23–25], 12 ml 99% $N_2H_4.H_2O$ in 100 ml ethanol was heated to 60°C and was slowly treated with 2·9 g moist Raney Ni, added in such small portions that excessive foaming was prevented. The exothermic reaction brought the mixture to boiling under reflux. After this was over, 1·0 g charcoal was added and the mixture was stirred and refluxed for 2 h. After cooling it was filtered and the filtrate was evaporated in vacuo. The residue was dissolved in 80 ml benzene, the solution was washed with water, the washings were extracted with benzene, the benzene layers were combined, dried, and evaporated. The residue was crystallized from a mixture of 8 ml benzene and 25 ml light petroleum; 17·7 g (85%) of *XV*, m.p. 54–56°C. Ref.[23], m.p. 51–52°C.

N,N-Dimethyl-3-(4-aminophenoxy)propylamine (*XVI*)

The base was released from 39·5 g 3-dimethylaminopropyl chloride hydrochloride by means of 10·5 g NaOH in 80 ml water and was immediately extracted with 300 ml toluene. The solution was dried with 50 g solid KOH. The dry solution was separated by decantation, treated with 39·2 g potassium 4-nitrophenoxide and the mixture was refluxed for 6 h with vigorous stirring. After cooling the solid was filtered off, the filtrate was evaporated under reduced pressure and the residue was distilled; 23·0 g (47%) of N,N-dimethyl-3-(4-nitrophenoxy)propylamine boiling at 123–125°C/50 Pa which was reduced without further characterization. A stirred solution of 23·0 g of the product and 10·5 ml 99% $N_2H_4.H_2O$ in 100 ml ethanol was slowly treated at 45°C with 2·8 g Raney Ni, added in small portions. The exothermic reaction brought the mixture to boiling under reflux. After the addition of 1·0 g charcoal, the mixture was stirred and refluxed for 2·5 h. Similar processing like in the preparation of *XV* gave 16·9 g (86%) of *XVI* boiling at 103–104°C/30 Pa. ^{1}H NMR spectrum (100 MHz): 1·90 m, 2 H (CH_2 in position 2 of propyl); 2·18 s, 6 H ($N(CH_3)_2$); 2·40 t, 2 H (CH_2N, J = 7·0); 3·40 bs, 2 H (NH_2); 3·90 t, 2 H (OCH_2, J = 7·0); 6·55 d, 2 H (H-3, H-5, J = 9·0); 6·75 d, 2 H (H-2, H-6, J = 9·0). For $C_{11}H_{18}N_2O$ (194·3) calculated: 68·00% C, 9·34% H, 14·42% N; found: 67·75% C, 9·24% H, 14·44% N. Ref.[23], b.p. 128–135°C/30 Pa (different method of preparation).

N,N-Dimethyl-3-(6,11-dihydrodibenzo[*b*,*e*]thiepin-11-yloxy)benzylamine (*IIIb*)

A mixture of 20·0 g 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3], 5·5 g 3-(dimethylaminomethyl)-phenol[9] and 240 ml toluene was refluxed for 12 h. After cooling toluene was removed by decantation and the residue was distributed between 50 ml NH_4OH and 200 ml chloroform. The extract was filtered, the filtrate was evaporated and the residue (9·4 g) was dissolved in 150 ml cyclohexane and chromatographed on 100 g Al_2O_3. Cyclohexane eluted 4·61 g (16%) of almost homogeneous oily *IIIb* which was transformed to hydrogen fumarate, m.p. 138–141°C (ethanol–ether). Mass spectrum: 361 (M^+, $C_{23}H_{23}NOS$, 0·2), 211 (32), 178 (14), 165 (2), 151 (24), 134 (2·5), 108 (18), 107 (26), 98 (18), 88 (7), 77 (14), 58 (100), 45 (17), 44 (67), 40 (2·5). For $C_{27}H_{27}.NO_5S$ (477·6) calculated: 67·90% C, 5·79% H, 2·93% N, 6·71% S; found: 67·70% C, 5·89% H, 3·03% N, 6·87% S.

N,N-Dimethyl-4-(6,11-dihydrodibenzo[*b*,*e*]thiepin-11-yloxy)benzylamine (*IIIc*)

A similar reaction of 7·5 g 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3] with 4·62 g 4-(dimethylaminomethyl)phenol[9] in 200 ml toluene (reflux for 8 h) gave an inhomogeneous product which

was chromatographed on 100 g Al_2O_3. Cyclohexane eluted first 1·45 g of crude 6,11-dihydrodibenzo[*b,e*]thiepin-11-ol (m.p. 107—108°C, ref.[3]). Benzene then eluted 2·40 g (22%) of homogeneous oily product which crystallized from a mixture of cyclohexane and light petroleum and melted at 99—101°C. UV spectrum: 262 (3·93). IR spectrum: 750, 753, 825 (4 and 2 adjacent Ar–H); 1 030, 1 040, 1 240 (Ar–O–R); 1 509, 1 585, 1 610, 3 020, 3 055, 3 060 (Ar); 2 760, 2 810 (N–CH_3). ^{1}H NMR spectrum (80 MHz): 2·15 s, 6 H ($N(CH_3)_2$); 3·28 s, 2 H ($ArCH_2N$); 4·20 d and 4·45 d (ABq), 1 and 1 H ($ArCH_2S$, J = 13·0); 6·50 s, 1 H (Ar_2CH–O); 6·88 d, 2 H (H-3 and H-5 of benzylamine, J = 8·5); 7·00—7·70 m, 10 H (remaining ArH). For $C_{23}H_{23}NOS$ (361·5) calculated: 76·41% C, 6·41% H, 3·88% N, 8·87% S; found: 76·55% C, 6·57% H, 3·65% N, 8·70% S.

Hydrogen fumarate, m.p. 144—146°C (ethanol–ether). Mass spectrum: 361 (M^+, $C_{23}H_{23}NOS$, 0·2), 211 (100), 178 (52), 165 (8), 151 (16), 134 (2·5), 108 (2·5), 107 (22), 98 (19), 88 (6), 77 (7) 74 (75), 58 (24), 45 (65), 44 (40), 40 (67). For $C_{27}H_{27}NO_5S$ (477·6) calculated: 67·90% C, 5·70% H, 2·93% N, 6·71% S; found: 67·80% C, 6·08% H, 2·84% N, 6·71% S.

Hydrogen succinate monohydrate, m.p. (60) — 90°C (ether). Mass spectrum: 361 (M^+, $C_{23}H_{23}$. .NOS, 0·1), 211 (35), 178 (15), 165 (2), 151 (40), 134 (5), 108 (7), 107 (100), 100 (11), 77 (14), 74 (3), 58 (4), 45 (8). For $C_{27}H_{29}NO_5S + H_2O$ (497·6) calculated: 65·17% C, 6·28% H, 2·82% N, 6·44% S; found: 64·99% C, 6·20% H, 2·78% N, 6·41% S.

N,N-Dimethyl-2-(2-bromo-6,11-dihydrodibenzo[*b,e*]thiepin-11-yloxy)benzylamine (*Va*)

A similar reaction of 5·25 g 2-bromo-11-chloro-6,11-dihydrodibenzo[*b,e*]thiepin[8] with 2·44 g 2-(dimethylaminomethyl)phenol[9] in 100 ml toluene (reflux for 14 h) gave 4·48 g (63%) of oily *Va* which crystallized after chromatography on 85 g Al_2O_3, m.p. 125—126°C (benzene–light petroleum). UV spectrum: 270 (4·12). IR spectrum: 750, 805, 852 (4 and 2 adjacent and solitary Ar–H); 1 019, 1 040, 1 245 (Ar–O–R); 1 490, 1 587, 1 600, 3 020, 3 040, 3 065, 3 090 (Ar); 2 760, 2 813 (N–CH_3). ^{1}H NMR spectrum (80 MHz): 2·35 s, 6 H ($N(CH_3)_2$); 3·56 d and 3·78 d (ABq), 1 and 1 H ($ArCH_2N$, J = 14·0); 4·10 d and 4·64 d (ABq), 1 and 1 H ($ArCH_2S$, J = 13·0); 6·50—7·60 m, 11 H (ArH with the exception of H-1); 7·78 d, 1 H (H-1, J = 2·5). For $C_{23}H_{22}Br$. .NOS (440·4) calculated: 62·72% C, 5·04% H, 18·15% Br, 3·18% N, 7·28% S; found: 62·57% C, 5·16% H, 18·30% Br, 3·34% N, 7·52% S.

Cleavage of *IVc* with Hydrochloric Acid

A similar reaction of 6·1 g 2,11-dichloro-6,11-dihydrodibenzo[*b,e*]thiepin[7] with 3·3 g 4-(dimethylaminomethyl)phenol[9] in 140 ml refluxing toluene (16 h) was carried out. After cooling the mixture was shaken with 150 ml 3M-HCl, the acid layer was separated and made alkaline with 20% NaOH. The lipophilic products were extracted with benzene, the extract was dried, and evaporated; 3·05 g of semi-solid residue which was crystallized from a mixture of 10 ml benzene and light petroleum (1 : 1). There were obtained 0·7 g of homogeneous 2-chloro-6,11-dihydrodibenzo[*b,e*]thiepin-11-ol, m.p. 157—159°C (benzene–light petroleum). The analysis is in agreement with the expected elemental composition $C_{14}H_{11}ClOS$. Ref.[7], m.p. 158—160°C (cf. also ref.[10]). An attempt to isolate the basic product of the cleavage from the mother liquor was not successful.

Cleavage of *VI* with Hydrochloric Acid

A similar reaction of 1·8 g N,N-dimethyl-1-(4-hydroxyphenyl)-2-propylamine[11—13] with 3·3 g 2-bromo-11-chloro-10,11-dihydrodibenzo[*b,e*]thiepin[8] in 100 ml refluxing toluene (10·5 h)

was carried out. After cooling the toluene solution was decanted from the undissolved viscous material, the toluene solution was washed with 10% hydrochloric acid, the acid solution was combined with the toluene-insoluble substance, the mixture was made alkaline with NH_4OH, and extracted with benzene. Processing of the extract gave 3·25 g of semi-solid inhomogeneous substance which was separated by chromatography on 100 g Al_2O_3. Elution with cyclohexane gave 1·23 g of oily base which was transformed to the hydrochloride (0·7 g), m.p. 170—171·5°C. The compound was identified as N,N-dimethyl-1-(4-hydroxyphenyl)-2-propylamine hydrochloride. ^{1}H NMR spectrum (CD_3SOCD_3, 80 MHz): 1·08 d, 3 H ($C-CH_3$); 2·60 m, 1 H (CH–N); 2·74 s, 6 H ($(CH_3)_2N^+$); 3·40 m, 2 H ($ArCH_2$); 6·76 d, 2 H (H-3 and H-5, J = 8·5) 7·10 d, 2 H (H-2, H-6, J = 8·5); 9·46 bs, 1 H (OH). For $C_{11}H_{17}ClNO$ (214·7) calculated: 61·53% C, 7·98% H, 16·51% Cl, 6·52% N; found: 61·35% C, 8·32% H, 16·31% Cl, 6·73% N. A sample of the base melted at (123)—130°C. Refs[11,12], m.p. of the base 133—134°C and 132°C, respectively.

Continued elution with a mixture of cyclohexane and benzene gave 1·28 g of 2-bromo-6,11-dihydrodibenzo[*b*,*e*]thiepin-11-ol, m.p. 164·5—166·5°C (cyclohexane). The analysis was in agreement with the elemental composition $C_{14}H_{11}BrOS$. Ref.[8], m.p. 166·5—167°C.

Cleavage of *IVa* with Hydrochloric Acid

A similar reaction of 4·52 g 2,11-dichloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[7] with 2·44 g 2-(dimethylaminomethyl)phenol[9] in 100 ml refluxing toluene (16 h) was carried out. After cooling the mixture was shaken with 100 ml 3M-HCl, the separated acid aqueous layer was made alkaline with 20% NaOH, and extracted with benzene. Processing gave 3·44 g residue which was chromatographed on 100 g Al_2O_3. Cyclohexane eluted 2·68 g of oil which afforded a very hygroscopic hydrochloride and a crystalline oxalate, m.p. 143—147°C (ethanol–ether). This was identified as N-benzyldimethylamine (*VII*) hydrogen oxalate. ^{1}H NMR spectrum (CD_3SOCD_3, 100 MHz) 2·63 s, 6 H ($(CH_3)_2N^+$); 4·02 s, 2 H ($ArCH_2N$); 6·70 bs (at 100°C), 2 H (2 COOH); 7·24 m, 3 H (H-3, H-4, H-5); 6·90 m, 2 H (H-2 and H-6). For $C_{11}H_{15}NO_4$ (225·2) calculated: 58·65% C, 6·71% H, 6·22% N; found: 58·62% C, 6·83% H, 6·24% N. Refs[14,15] mentioned a hygroscopic hydrochloride.

N,N-Dimethyl-2-(6,11-dihydrodibenzo[*b*,*e*]thiepin-11-ylthio)benzylamine (*VIIIa*)

Grignard reagent was prepared from 21·1 g N,N-dimethyl-2-bromobenzylamine[16] and 2·5 g Mg in 80 ml tetrahydrofuran. After refluxing for 30 min the reagent was stirred and treated over 15 min with 3·0 g S, added in small portions. The mixture was refluxed for 1 h, poured to a mixture of ice and 25 ml hydrochloric acid, it was treated with NH_4OH (to pH 10) and washed with ether. The pH was adjusted to 8 and the product was extracted with chloroform. Processing gave 10·7 g of oil which was considered to be the crude 2-(dimethylaminomethyl)thiophenol and which was used without further purification. It was dissolved in 100 ml toluene, the solution was treated with a solution of 17·0 g 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3] in 100 ml toluene at 50°C, and the mixture was allowed to stand for 2 weeks at room temperature. Toluene was removed by decantation, the residue was treated with NH_4OH and extracted with ether. Processing of the extract gave 18 g of inhomogenéoous oil which was chromatographed on 500 g Al_2O_3. Elution with cyclohexane removed 1·4 g of oil which was not characterized. The following elution with a mixture of cyclohexane and benzene afforded 14·23 g (38% per starting bromo compound) of the almost homogeneous *VIIIa* which was transformed to hydrogen oxalate, m.p. 150—152°C (ethanol). Mass spectrum: 377 (M^+, $C_{23}H_{23}NS_2$, 2), 299 (1), 211 (20), 178 (30), 166 (100), 165 (15), 152 (10), 123 (25), 121 (10). For $C_{25}H_{25}NO_4S_2$ (467·6) calculated: 64·21% C 5·39% H, 3·00% N, 13·71% S; found: 64·17% C, 5·49% H, 3·21% N, 13·75% S.

Bis(3-(dimethylaminomethyl)phenyl) Disulfide (*IX*)

Grignard reagent was prepared from 19·0 g N,N-dimethyl-3-bromobenzylamine[16] and 2·3 g Mg in 80 ml tetrahydrofuran. It was refluxed for 30 min and treated over 45 min with 2·7 g S, added under stirring in small portions. It was refluxed for 1 h, poured to ice and 25 ml hydrochloric acid, made alkaline with NH_4OH, and extracted with ether. Processing of the extract by distillation in vacuo gave 2·4 g of unsharply boiling liquid, b.p. 100—130°C/4·7 kPa which was — according to GC — a mixture, probably the impure 3-(dimethylaminomethyl)thiophenol, which was not further processed. The distillation residue was dissolved in ether and transformed by treatment with HCl in ether to a hydrochloride (11·1 g) melting at 205—215°C (ethanol), considered to be *IX* dihydrochloride. Mass spectrum (EI and CI): 311, 300 (M — 32), 268, 267, 266, 265, 258, 253, 243, 238, 236, 235, 221, 211, 197, 166 (M/2), 151, 135, 134, 107, 91, 58 (100). UV spectrum: 240 (4·25), infl. 276 (3·58). IR spectrum: 790, 707, 887 (3 adjacent and solitary Ar–H); 1 573, 1 593, 3 007, 3 038, 3 053 (Ar); 2 410, 2 430, 2 450, 2 575, 2 638 (NH^+). For $C_{18}H_{26}Cl_2N_2S_2$ (405·5) calculated: 53·32% C, 6·46% H, 17·49% Cl, 6·91% N; found: 62·97% C, 6·75% H, 17·56% Cl, 6·67% N.

N,N-Dimethyl-3-(6,11-dihydrodibenzo[*b,e*]thiepin-11-ylthio)benzylamine (*VIIIb*)

The base *IX* (7·3 g) was reduced wit 1·5 g $LiAlH_4$ in 80 ml ether (reflux under stirring for 6 h) under nitrogen, the mixture was allowed to stand for 48 h at room temperature, decomposed under cooling with 10 ml 20% H_2SO_4, the solid was filtered off, treated with 1 ml acetic acid and extracted with chloroform. The organic layers were combined, dried, and evaporated giving 5·6 g of the crude 3-(dimethylaminomethyl)thiophenol which was processed without purification and characterization. It was treated with a solution of 8·6 g 11-chloro-6,11-dihydrodibenzo[*b,e*]-thiepin[3] in 100 ml toluene and the mixture was allowed to stand for 48 h at room temperature. The precipitated solid (the hygroscopic hydrochloride of *VIIIb*) was filtered, washed with benzene, dissolved in water, the base was released with NH_4OH and isolated by extraction with benzene; 8·6 g of oily inhomogeneous substance. It was chromatographed on 100 g Al_2O_3. The first fractions (7·85 g), obtained by elution with benzene, were rechromatographed on 150 g silica gel. The first benzene fractions contained 0·93 g of 6,11-dihydrodibenzo[*b,e*]thiepin-11-ol, m.p. 104·5—105·5°C (cyclohexane); ref.[3], m.p. 107—108°C. Elution with a mixture of chloroform and ethanol gave 4·32 g of the homogeneous oily *VIIIb* which was transformed to the hydrogen fumarate, m.p. 127—129°C (ethanol–ether). Mass spectrum: 377 (M^+, $C_{23}H_{23}NS_2$, 3), 299 (0·1), 211 (100), 178 (50), 166 (3), 165 (10), 152 (5), 123 (5), 121 (2). For $C_{27}H_{27}NO_4S_2$ (493·7) calculated: 65·69% C, 5·51% H, 2·84% N, 12·99% S; found: 65·44% C, 5·75% H, 3·14% N, 12·69% S.

The released base was used for recording the ^1H NMR spectrum (100 MHz): 2·18 s, 6 H ($N(CH_3)_2$); 3·31 s, 2 H ($ArCH_2N$); 5·47 s, 1 H (Ar_2CH–S); 3·75 d and 5·64 d (ABq), 1 and 1 H ($ArCH_2S$, J = 13·0); 6·80—7·30 m, 12 H (ArH).

N,N-Dimethyl-4-(6,11-dihydrodibenzo[*b,e*]thiepin-11-ylthio)benzylamine (*VIIIc*)

Grignard reagent was prepared from 21·3 g N,N-dimethyl-4-bromobenzylamine[16] and 2·6 g Mg in 80 ml tetrahydrofuran, it was refluxed for 30 min and treated under stirring over 15 min with 3·0 g S, added in small portions. The mixture was refluxed for 1 h, poured to a mixture of ice and 25 ml hydrochloric acid, made alkaline with NH_4OH and extracted at pH 8 with chloroform. Processing gave 10·0 g of a mixture of 4-(dimethylaminomethyl)thiophenol and the corresponding disulfide. It was reduced with 2·0 g $LiAlH_4$ in a mixture of 100 ml ether and 50 ml

tetrahydrofuran under nitrogen (stirred and refluxed for 6 h). The mixture was decomposed under cooling with 10 ml 20% H_2SO_4, the solid was filtered off, treated with 1 ml acetic acid and extracted with chloroform. The organic layers were combined and evaporated giving 8·0 g of crude 4-(dimethylaminomethyl)thiophenol which was used without purification and characterization. It was dissolved in 100 ml toluene, the solution was treated with a solution of 9·0 g 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3] in 100 ml toluene and the mixture was allowed to stand for 6 days at room temperature. Toluene was removed by decantation, the residue was treated with NH_4OH and extracted with benzene. Processing of the extract gave 6·65 g of oily mixture which was chromatographed on 140 g silica gel. Benzene and chloroform eluted a small amount of 6,11-dihydrodibenzo[*b*,*e*]thiepin-11-ol[3], m.p. 105—107°C (cyclohexane). Continued elution with a mixture of chloroform and ethanol afforded 3·0 g of homogeneous oil which was shown to be the desired *VIIIc*. It was transformed to the hydrogen oxalate, m.p. 160—163°C (acetone). Mass spectrum: 377 (M^+, $C_{23}H_{23}NS_2$, 2), 299 (0·1), 271 (0·5), 211 (100), 178 (60), 166 (10), 165 (10), 152 (5), 123 (5), 121 (5). For $C_{25}H_{25}NO_4S_2$ (467·6) calculated: 64·21% C, 5·39% H, 3·00% N, 13·71% S; found: 63·96% C, 5·47% H, 3·12% N, 13·62% S.

The released base was used for recording the ^1H NMR spectrum (100 MHz): 2·17 s, 6 H ($N(CH_3)_2$); 3·32 s, 2 H ($ArCH_2N$); 5·42 s, 1 H (Ar_2CH–S); 3·75 d and 5·62 d (ABq), 1 and 1 H ($ArCH_2S$, J = 13·0); 7·18 m, 12 H (ArH).

N-(6,11-Dihydrodibenzo[*b*,*e*]thiepin-11-yl)-2-(dimethylaminomethyl)aniline (*Xa*)

A solution of 9·87 g 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3] and 6·0 g 2-(dimethylaminomethyl)aniline in 260 ml toluene was stirred for 6 h at room temperature and was allowed to stand for 3 weeks. The toluene layer was removed by decantation, the undissolved residue was treated with NH_4OH, and the released base was extracted with chloroform. Processing ofthe extract gave 10·2 g (71%) of crystalline *Xa*, m.p. 158—164·5°C. Analytical sample, m.p.166 to 167°C (benzene–light petroleum). UV spectrum: 248 (4·41), infl. 288 (2·91). IR spectrum: 748 (4 adjacent Ar–H); 1 493, 1 509, 1 587, 3 060 (Ar); 1 609 (ArNH); 2 760, 2 810 ($N–CH_3$); 3 280 (NH). ^1H NMR spectrum (80 MHz): 2·25 s, 6 H ($N(CH_3)_2$); 3·60 s, 2 H ($ArCH_2N$); 4·08 d and 4·73 d (ABq), 1 and 1 H ($ArCH_2S$, J = 13·0); 5·95 bs, 1 H (Ar_2CH); 6·20—7·50 m, 12 H (ArH); 7·70 bs, 1 H (NH). For $C_{23}H_{24}N_2S$ (360·5) calculated: 76·62% C, 6·71% H, 7·77% N, 8·89% S; found: 76·63% C, 6·74% H, 7·59% N, 9·12% S.

Oxalate, m.p. 180—182°C (ethanol). Mass spectrum: 360 (M^+, $C_{23}H_{24}N_2S$, 7), 316 (1), 315 (7), 314 (3), 282 (7), 211 (10), 210 (70), 178 (40), 167 (50), 166 (60), 165 (10), 149 (100). For $C_{25}H_{26}N_2O_4S$ (450·5) calculated: 66·65% C, 5·82% H, 6·22% N, 7·11% S; found: 66·35% C, 5·88% H, 6·65% N, 7·20% S.

N-(6,11-Dihydrodibenzo[*b*,*e*]thiepin-11-yl)-3-(dimethylaminomethyl)aniline (*Xb*)

A similar reaction (cf. *Xa*) of 9·87 g 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3] with 6·0 g 3-(dimethylaminomethyl)aniline in 260 ml toluene at room temperature gave 10·5 g inhomogeneous product which was chromatographed on 100 g Al_2O_3. In the first fractions cyclohexane eluted 6·77 g (47%) of homogeneous oily *Xb* which was transformed to the fumarate, m.p. 100 to 110°C (ether). Mass spectrum: 360 (M^+, $C_{23}H_{24}N_2S$, 3), 314 (1·5), 282 (2) 211 (70), 210 (100), 178 (50). IR spectrum: 700, 752, 790, 890 (4 and 3 adjacent and solitary Ar–H); 980, 1 610 (CH=CH), 955, 1 165, 1 255, 3 080 (COOH); 1 490 (Ar); 1 585 (COO^-); 1 693 (C=C—COOH); 2 480, 2 680 (NH^+), 3 340 (NH). For $C_{27}H_{28}N_2O_4S$ (476·6) calculated: 68·04% C, 5·92% H, 5·88% N, 6·73% S; found: 67·72% C, 6·04% H, 5·51% N, 7·07% S.

N-(6,11-Dihydrodibenzo[*b*,*e*]thiepin-11-yl)-4-(dimethylaminomethyl)aniline (*Xc*)

A similar reaction (cf. *Xa*) of 9·87 g 11-chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3] with 6·0 g 4-(dimethylaminomethyl)aniline in 260 ml toluene at room temperature gave 10·0 g of inhomogeneous product which was chromatographed on 100 g neutral Al_2O_3. Cyclohexane eluted in the first fractions 5·9 g (41%) of homogeneous oily *Xc* which was transformed to the fumarate (microcrystalline hemihydrate), m.p. 117—130°C (ether). Mass spectrum: 360 (M^+, $C_{23}H_{24}N_2S$, 3·3), 316 (1·3), 315 (1), 314 (1·1), 282 (0·7), 281 (0·6), 280 (0·4), 212 (11), 211 (100), 210 (93), 209 (10), 179 (10), 178 (58), 167 (1·9), 166 (2·2), 165 (8), 152 (3·3), 151 (3), 150 (4·4), 149 (3), 106 (16). For $C_{27}H_{28}N_2O_4S + 0{\cdot}5\ H_2O$ (485·6) calculated: 66·78% C, 6·02% H, 5·77% N, 6·60% S; found: 66·41% C, 6·11% H, 5·60% N, 6·78% S.

N-(6,11-Dihydrodibenzo[*b*,*e*]thiepin-11-yl)-4-(2-dimethylaminoethoxy)aniline (*XI*)

A mixture of 2·7 g *XV*, 5 ml dimethylformamide, 4·2 g 11-chloro-6,11-dihydrodibenzo[*b*,*e*]-thiepin[3], and 2·7 g Na_2CO_3 was stirred for 2·5 h at 106—110°C. After cooling the mixture was distributed between 100 ml benzene and 100 ml water, the benzene layer was dried and evaporated. The inhomogeneous residue (7·9 g) was chromatographed on 300 g neutral Al_2O_3. Benzene eluted 4·5 g (77%) of almost homogeneous oily *XI* which was transformed to the maleate crystallizing from ethanol as the hemihydrate, m.p. 154—155°C. For $C_{28}H_{20}N_2O_5S + 0{\cdot}5\ H_2O$ (515·6) calculated: 65·22% C, 6·06% H, 5·43% N, 6·22% S; found: 65·46% C, 6·31% H, 5·38% N, 6·32% S.

A sample of the pure salt was decomposed with NH_4OH an the oily base, isolated by extraction with ether, was used for recording the spectra, UV spectrum: infl. 252 (4·15), infl. 302 (3·35). IR spectrum: 747, 759, 819 (4 and 2 adjacent Ar–H); 1 039, 1 229, 1 246 (Ar–O–R); 1 509, 3 020, 3 040 (Ar); 2 770 (N–CH_3); 3 220 (NH). ^{1}H NMR spectrum (80 MHz): 2·25 s, 6 H ($N(CH_3)_2$); 2·62 t, 2 H (CH_2N, J = 7·0); 3·90 t, 2 H (OCH_2, J = 7·0); 4·30 bs, 1 H (NH); 4·28 d and 4·55 d (ABq), 1 and 1 H ($ArCH_2S$, J = 13·0); 5·60 s, 1 H (Ar_2CH–N); 6·50 d, 2 H (H-2 and H-6 of aniline, J = 9·0); 6·72 d, 2 H (H-3 and H-5 of aniline, J = 9·0); 6·90—7·50 m, 8 H (remaining ArH).

N-(2-Chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin-11-yl)-4-(2-dimethylaminoethoxy)aniline (*XII*)

A similar reaction (cf. *XI*) of 6·7 g 2,11-dichloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[7], 3·6 g *XV*, and 4·5 g Na_2CO_3 in 10 ml dimethylformamide (4·5 h at 110—115°C) gave an inhomogeneous product which was separated by chromatography on 400 g Al_2O_3; 5·2 g (61%) of almost homogeneous oily *XII* which was transformed to maleate crystallizing from a mixture of ethanol and 2-propanol (2 : 1) as hemihydrate, m.p. 115—117°C. For $C_{28}H_{29}ClN_2O_5S + 0{\cdot}5\ H_2O$ (550·1) calculated: 61·13% C, 5·49% H, 6·45% Cl, 5·09% N, 5·83% S; found: 61·04% C, 5·33% H, 6·78% Cl, 4·96% N, 5·94% S.

The released base was used for recording the spectra. UV spectrum: 234 (4·27), 263 (4·09), infl. 300 (3·51). IR spectrum: 763, 810, 869 (4 and 2 adjacent and solitary Ar–H); 1 036, 1 044, 1 233 (Ar–O–R); 1 507, 3 015, 3 040 (Ar); 2 770, 2 820 (N–CH_3); 3 390 (NH). ^{1}H NMR spectrum (80 MHz): 2·30 s, 6 H ($N(CH_3)_2$); 2·65 t, 2 H (CH_2N, J = 7·0); 3·95 t, 2 H (OCH_2, J = 7·0); 4·30 bs, 1 H (NH); 4·25 d and 4·50 d (ABq), 1 and 1 H ($ArCH_2S$, J = 13·0); 5·61 s, 1 H (Ar_2CH–N); 6·50 d, 2 H (H-2 and H-6 of aniline, J = 9·0); 6·72 d, 2 H (H-3 and H-5 of aniline, J = 9·0); 6·90—7·50 m, 7 H (remaining ArH).

N-(2-Methyl-6,11-dihydrodibenzo[*b*,*e*]thiepin-11-yl)-
-4-(2-dimethylaminoethoxy)aniline (*XIII*)

A similar reaction (cf. *XI*) of 4·8 g 11-chloro-2-methyl-6,11-dihydrodibenzo[*b*,*e*]thiepin[22], 3·0 g *XV*, and 3·2 g Na_2CO_3 in 5 ml dimethylformamide (4·5 h at 125°C) gave 6·7 g of inhomogeneous product which was chromatographed on 320 g Al_2O_3. Elution with benzene gave 3·1 g (42%) of oily *XIII* which was transformed to the maleate, m.p. 136—139°C (ethanol–ether). For $C_{29}H_{32}N_2O_5S$ (520·6) calculated: 66·90% C, 6·20% H, 5·38% N, 6·16% S; found: 66·70% C, 6·19% H, 5·19% N, 6·30% S.

The released base was used for recording the spectra. UV spectrum: infl. 252 (4·10), infl. 296 (3·35). IR spectrum: 760, 818, 870 (4 and 2 adjacent and solitary Ar–H); 1 039, 1 235 (Ar–O–R) 1 509, 3 020 (Ar); 2 770, 2 818 (N–CH_3); 3 365 (NH). ^{1}H NMR spectrum (80 MHz): 2·18 s, 3 H ($ArCH_3$); 2·25 s, 6 H ($N(CH_3)_2$); 2·62 t, 2 H (CH_2N, J = 7·0); 3·90 t, 2 H (OCH_2, J = 7·0); 4·30 bs, 1 H (NH); 4·20 d and 4·55 d (ABq), 1 and 1 H ($ArCH_2S$, J = 13·0); 5·55 bs, 1 H (Ar_2CH–N); 6·50 d, 2 H (H-2 and H-6 of aniline, J = 9·0); 6·71 d, 2 H (H-3 and H-5 of aniline J = 9·0); 6·80—7·50 m, 7 H (remaining ArH).

N-(6,11-Dihydrodibenzo[*b*,*e*]thiepin-11-yl)-4-(3-dimethylaminopropoxy)aniline (*XIV*)

11-Chloro-6,11-dihydrodibenzo[*b*,*e*]thiepin[3] (6·2 g), 5·05 g *XVI*, and 5·5 g Na_2CO_3 in 8 ml dimethylformamide (4 h at 115—120°C) gave similarly (cf. *XI*) 10 g of inhomogeneous product which was chromatographed on 300 g silica gel. Elution with chloroform, containing 1·5% of methanol, gave 6·0 g (60%) of oily *XIV* which was transformed to the oxalate, m.p. 167—169°C (ethanol). For $C_{27}H_{30}N_2O_5S$ (494·6) calculated: 65·56% C, 6·11% H, 5·67% N, 6·48% S; found: 65·63% C, 5·98% H, 5·52% N, 6·67% S.

The released base remained oily. UV spectrum: infl. 233 (4·10), infl. 304 (3·25). IR spectrum (CS_2): 745, 805, 815 (4 and 2 adjacent Ar–H); 1 016, 1 095, 1 259 (Ar–O–R); 2 760, 2 810 (N–CH_3); 3 015, 3 055 (Ar); 3 385 (NH). ^{1}H NMR spectrum (80 MHz): 1·90 m, 2 H (CH_2 in position 2 of propyl); 1·20 s, 6 H ($N(CH_3)_2$); 1·33 t, 2 H (CH_2N, J = 7·0); 3·88 t, 2 H (OCH_2, J = 7·0); 4·30 bs, 1 H (NH); 4·30 d and 4·58 d (ABq), 1 and 1 H ($ArCH_2S$, J = 13·0); 5·60 bs, 1 H (Ar_2CH–N); 6·50 d, 2 H (H-2 and H-6 of aniline, J = 9·0); 6·71 d, 2 H (H-3 and H-5 of aniline, J = 9·0); 6·90—7·50 m, 8 H (remaining ArH).

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