POTENTIAL ANTIDIARRHEAL AGENTS: 1-(11-CYANO-6,11-DIHYDRODIBENZO[*b*,*e*]THIEPIN-11-YL-ALKYL)- AND 1-(10-CYANO-10,11-DIHYDRODIBENZO[*b*,*f*]THIEPIN-10-YL-ALKYL)-4-SUBSTITUTED PIPERIDINES

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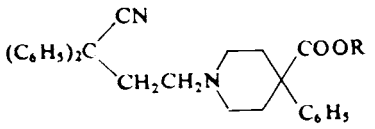
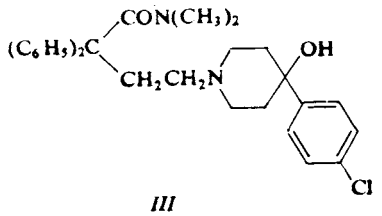
Substitution reactions of 11-(2-bromoethyl)- and 11-(3-bromopropyl)-6,11-dihydrodibenzo[*b*,*e*]-thiepin-11-carbonitrile and further of 10-(2-bromoethyl)- and 10-(3-bromopropyl)-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-carbonitrile with ethyl 4-phenylpiperidine-4-carboxylate, 4-phenylpiperidin-4-ol, 4-(2-tolyl)piperidin-4-ol, 4-(4-fluorophenyl)piperidin-4-ol, 4-(2-oxobenzimidazolin-1-yl)-piperidine and 1-phenyl-1,3,8-triazaspiro[4,5]decan-4-one afforded the tricyclic piperidinoalkyl nitriles *IV*—*XIII* which are cyclic analogues of the antidiarrheal agents diphenoxylate (*I*) and loperamide (*III*). Out of the compounds prepared only *IV* and *XI* showed a significant inhibitory effect towards diarrhea elicited by intravenously administered serotonin in mice.

The development of symptomatic antidiarrheal drugs was started more than 25 years ago[1]; the method of designing such compounds was structural manipulation in the series of 1,4-substituted piperidines aiming at separation of the narcotic and the constipation producing effect of morphine-like substances. The first success in this line was represented by the substituted 2,2-diphenyl-4-piperidinobutyronitrile ("diphenoxylate", *I*) (ref.[1,2]) which is still in practical use. A higher degree of antidiarrhoic activity was shown by its metabolite ("difenoxin", *II*) (ref.[3,4]). A further improvement was achieved by the substituted 2,2-diphenyl-4-piperidinobutyramide ("loperamide", *III*) (ref.[5,6]). Several review articles[7–9] deal with these three therapeutic agents. Their common structural feature is the 2,2-diphenyl-4-piperidinobutyrate fragment with one quaternary carbon in the diphenylmethane part of the molecule and with the second one in position 4 of the piperidine residue. The more recent development[10] differs somewhat from this type but the diphenylmethane fragment with the quaternary carbon and with the freely rotating benzene nuclei remains preserved. Recently, we have synthesized two tricyclic nitriles, *i.e.* 6,11-dihydrodibenzo[*b*,*e*]thiepin-11-carbonitrile[11] and 10,11-dihydrodibenzo[*b*,*f*]thiepin-10-carbonitrile[12], which have now been used to synthesize compounds *IV*—*XIII*. These substances are analogues of the antidiarrheal agents *I* and *III*; their difference consists mainly in the fact that their benzene nuclei are not freely mobile but form a part of the relatively rigid tricyclic systems. The purpose of the present work was to esta-

blish the influence of this rather important structural change on the antidiarrhoic activity.



I, R = C_2H_5
II, R = H

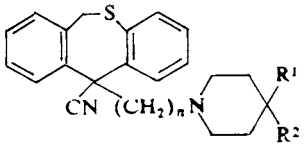


III

Compounds *IV*–*XIII* were obtained by substitution reactions of the recently described 2-bromoethyl and 3-bromopropyl derivatives of the nitriles just mentioned, *i.e.* 11-(2-bromoethyl)-6,11-dihydrodibenzo[*b*,*e*]thiepin-11-carbonitrile (*XIV*) (ref.[13]), 11-(3-bromopropyl)-6,11-dihydrodibenzo[*b*,*e*]thiepin-11-carbonitrile (*XV*) (ref.[13]), 10-(2-bromoethyl)-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-carbonitrile (*XVI*) (ref.[12]) and 10-(3-bromopropyl)-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-carbonitrile (*XVII*) (ref.[12]), with ethyl 4-phenylpiperidine-4-carboxylate[14], 4-phenylpiperidin-4-ol[15], 4-(2-tolyl)piperidin-4-ol[16], 4-(4-fluorophenyl)piperidin-4-ol[15], 4-(2-oxobenzimidazolin-1-yl)piperidine[17] and 1-phenyl-1,3,8-triazaspiro[4,5]decan-4-one[18]. The substitution reactions were carried out in boiling acetone in the presence of potassium carbonate. The racemic basic products were mostly oily (*IV*–*VII*, *XI*) and were then isolated as hydrochlorides. Prior to the preparation of these salts it was necessary in some cases to purify the crude bases by chromatography on silica gel (*IV*, *VII*). In some other cases we found a surprising good solubility of the hydrochlorides in chloroform (*V*, *VII*). Bases *VIII*–*X*, *XII* and *XIII* were crysralline and little soluble in acetone; in these cases they could be obtained by filtration from the reaction mixtures and by removal of the inorganic salts by extraction with water. Most of the products were characterized by the IR and ^{1}H NMR spectra; in cases of crystalline solvates the identity was confirmed also by the mass spectra.

The compounds prepared (*IV*–*XIII*) were pharmacologically tested in the form of bases or hydrochlorides described in the Experimental; they were administered orally and the doses given were calculated for bases. Diphenoxylate (*I*) (ref.[1,2]) was used as a standard. Acute toxicity in mice: compounds *VI*, *VIII*, *IX*, *XI*–*XIII*

were administered in a dose of 500 mg/kg; this dose was practically nontoxic and in the course of 7 days no lethality was noted (a mild central depressant effect was

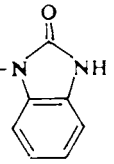


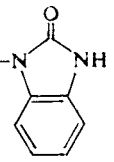
IV, $n = 2$, $R^1 = COOC_2H_5$, $R^2 = C_6H_5$

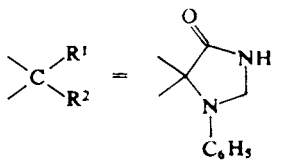
V, $n = 3$, $R^1 = OH$, $R^2 = C_6H_5$

VI, $n = 3$, $R^1 = OH$, $R^2 = 2\text{-}C_6H_4CH_3$

VII, $n = 3$, $R^1 = OH$, $R^2 = 4\text{-}C_6H_4F$

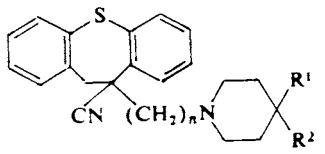
VIII, $n = 2$, $R^1 = H$, $R^2 =$ 

IX, $n = 3$, $R^1 = H$, $R^2 =$ 

X, $n = 3$, 

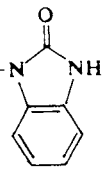
apparent). Compounds *V* and *X* were administered in a dose of 2 500 mg/kg; the former was lethal for 40% animals, the latter did not cause lethality. Diphenoxylate (*I*) was more toxic; LD_{50} = 337 mg/kg. The antidiarrhoic activity was evaluated in mice in which the experimental diarrhoe was elicited by intravenous administration of serotonin in a dose of 10 mg/kg[19]. The new substances were administered in oral doses of 10 mg/kg 60 min prior to the administration of serotonin. Only compounds *IV* and *XI* showed a mild but statistically significant inhibitory effect. Diphenoxylate (*I*) had a significant effect in doses of 5 and 10 mg/kg; morphine was effective starting with a dose of 2 mg/kg. The analgetic activity of the compounds was evaluated in the peritoneal test in mice (chemical stimulation by intraperitoneal injection of acetic acid). The new compounds were administered in an oral dose of 50 mg/kg; for compounds *VI*, *VIII*, *X* and *XII* this dose was approximately equal to the value

of PD_{50}. For diphenoxylate (*I*) PD_{50} was 6·8 mg/kg, for morphine 0·24 mg/kg. For compounds *IV*, *V*, *VII*, *XI* and *XIII* PD_{50} was higher than 50 mg/kg. In the rotarod test in mice the tested compounds were administered in doses of 50 mg/kg; they brought about ataxia in 10–20% animals and the discoordinating effect was of short duration. With diphenoxylate (*I*), ED_{50} = 33 mg/kg (maximum effect in 45 min after the administration). Antidiarrhoic effect has thus been proven only with the diphenoxylate analogues *IV* and *XI*; this effect was weaker than that of diphenoxylate (*I*) which. however, is more toxic than compounds *IV* and *XI*.

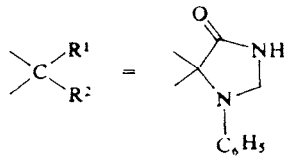


XI, $n = 2$, $R^1 = COOC_2H_5$, $R^2 = C_6H_5$

XII, $n = 3$, $R^1 = H$, R^2 =



XIII, $n = 3$,



EXPERIMENTAL

The melting points of analytical samples were determined in the Mettler FP-5 melting point recorder. The samples were dried *in vacuo* of about 60 Pa over P_2O_5 at room temperature or at 77°C. IR spectra (in Nujol unless stated otherwise) were recorded with a Unicam SP 200G spectrophotometer, ^1H NMR spectra (mostly in C^2HCl_3) with a Tesla BS 487C (80 MHz) spectrometer, and the mass spectra with the spectrometers MCH-1320 and Varian MAT 44S. The homogeneity of the compounds and composition of the mixtures were checked by thin-layer chromatography on silica gel (Silufol).

1-[2-(11-Cyano-6,11-dihydrodibenzo[*b*,*e*]thiepin-11-yl)ethyl]-4-ethoxycarbonyl-4-phenylpiperidine (*IV*)

A mixture of 4·5 g *XIV* (ref.[13]), 2·8 g ethyl 4-phenylpiperidine-4-carboxylate[14], 1·6 g K_2CO_3 and 100 ml acetone was stirred and refluxed for 6 h, filtered while hot and the filtrate was eva-

porated *in vacuo*. The residue was dissolved in chloroform and chromatographed on a column of 180 g silica gel. Elution with chloroform recovered first 1·47 g of the starting *XIV*. Continued elution with chloroform gave then 4·26 g crude *IV* which was transformed with a solution of HCl in ether to the hydrochloride. Its crystallization from a mixture of acetone and ether gave 3·37 g (72% per conversion) pure hydrochloride melting at 192—196°C. IR spectrum (KBr): 700, 760 (5 and 4 adjacent Ar—H), 1 215, **1 718** (RCOOR'), 2 230 (R—CN), 2 510 cm^{-1} (NH^+). ^1H NMR spectrum: δ 7·20 (s, 5 H, C_6H_5), 7·00—7·80 (m, 8 H, remaining ArH), 4·18 (q, 2 H, OCH_2), 1·18 (t, 3 H, CH_3 of ethyl), remaining 7 CH_2 in an undifferentiated multiplet. For $C_{31}H_{33}ClN_2O_2S$ (533·1) calculated: 69·84% C, 6·24% H, 6·65% Cl, 5·25% N, 6·01% S; found: 69·66% C, 6·31% H, 6·70% Cl, 4·98% N, 6·08% S.

1-[3-(11-Cyano-6,11-dihydrodibenzo[*b,e*]thiepin-11-yl)propyl]-4-phenylpiperidin-4-ol (*V*)

A mixture of 3·6 g *XV* (ref.[13]), 1·8 g 4-phenylpiperidin-4-ol[15], 1·4 g K_2CO_3 and 30 ml acetone was refluxed for 11 h and filtered while hot. The filtrate was evaporated *in vacuo*, the residue was dissolved in chloroform and the solution was washed with dilute hydrochloric acid. The hydrochloride remained in the organic layer which was then washed with dilute NH_4OH, dried with K_2CO_3 and evaporated. The crude base was dissolved in ether and the solution was treated with a solution of HCl in ether. The crude hydrochloride was filtered and purified by crystallization from ethanol; 2·5 g (51%), m.p. 228—231°C. IR spectrum: 709, 751 (5 and 4 adjacent Ar—H), 1 047 (C—OH in the ring), 2 215 (R—CN), 2 390, 2 420 (NH^+), 3 190, 3 225 cm^{-1} (OH). For $C_{29}H_{31}ClN_2OS$ (491·1) calculated: 70·93% C, 6·36% H, 7·22% Cl, 5·70% N, 6·53% S; found: 70·78% C, 6·50% H, 7·12% Cl, 5·38% N, 6·43% S.

1-[3-(11-Cyano-6,11-dihydrodibenzo[*b,e*]thiepin-11-yl)propyl]-4-(2-tolyl)piperidin-4-ol (*VI*)

A mixture of 6·1 g *XV* (ref.[13]), 2·0 g 4-(2-tolyl)piperidin-4-ol[16], 1·6 g K_2CO_3 and 150 ml acetone was refluxed under stirring for 7 h. The solid was filtered off and the filtrate was evaporated under reduced pressure. The residue was dissolved in ether and the solution was shaken with an excess of dilute hydrochloric acid. The separated oily hydrochloride was combined with the aqueous solution, treatment with NH_4OH released the base which was isolated by extraction with ether. The extract was dried with K_2CO_3, filtered and neutralized with a solution of HCl in ether. The crude hydrochloride was filtered and crystallized from a mixture of 95% ethanol and ether; 1·4 g (16%) hydrochloride monohydrate, m.p. 133—138°C. IR spectrum: 730, 764 (4 adjacent Ar—H), 1 046 (C—OH in the ring), 1 625 (H_2O), 2 215 (R—CN), 2 545, 2 622 (NH^+), 3 005 (Ar), 3 270 cm^{-1} (OH, H_2O). For $C_{30}H_{33}ClN_2OS + H_2O$ (523·1) calculated: 68·88% C, 6·74% H, 6·78% Cl, 5·36% N, 6·13% S; found: 69·14% C, 6·72% H, 6·80% Cl, 5·28% N, 6·18% S.

1-[3-(11-Cyano-6,11-dihydrodibenzo[*b,e*]thiepin-11-yl)propyl]-4-(4-fluorophenyl)piperidin-4-ol (*VII*)

A mixture of 7·7 g *XV* (ref.[13]), 2·8 g 4-(4-fluorophenyl)piperidin-4-ol[15], 1·8 g K_2CO_3 and 100 ml acetone was stirred and refluxed for 10 h. The inorganic salts were filtered off while hot and the filtrate was evaporated *in vacuo*. The residue was treated with NH_4OH and extracted with chloroform. The extract was evaporated and the residue was chromatographed on 200 g silica gel. Chloroform eluted first 0·38 g neutral components and a mixture of chloroform and ethanol eluted 3·25 g (32%) of the oily *VII* which was dissolved in acetone and the solution was treated with a mild excess of HCl in ether. The hydrochloride separated first as an oil which crystallized as a hemihydrate after treatment with a small quantity of water; 2·65 g, m.p. 133—138°C. Mass

spectrum, *m/z* (%): 472 (M^+ corresponding to $C_{29}H_{29}FN_2OS$, 1·8%), 439, 421, 236 (22·4), 208 (100), 190 (30), 84 (16), 56 (21). IR spectrum: 752, 762 (4 adjacent Ar—H), 1 043 (C—OH in the ring), 1 222 (Ar—F), 1 510, 1 600 (Ar), 2 530, 2 620 (NH^+), 3 240 cm^{-1} (OH). For C_{29}. $.H_{30}ClFN_2OS + 0·5\ H_2O$ (518·1) calculated: 67·23% C, 6·03% H, 6·84% Cl, 3·67% F, 5·41% N, 6·19% S; found: 67·31% C, 6·08% H, 6·57% Cl, 3·33% F, 5·24% N, 6·29% S.

1-[2-(11-Cyano-6,11-dihydrodibenzo[*b,e*]thiepin-11-yl)ethyl]-4-(2-oxobenzimidazolin-1-yl)-piperidine (*VIII*)

A mixture of 2·7 g *XIV* (ref.[13]), 1·65 g 4-(2-oxobenzimidazolin-1-yl)piperidine[17], 1·2 g K_2CO_3 and 150 ml acetone was stirred and refluxed for 10 h. After standing overnight the precipitated solid was filtered off, it was suspended in 100 ml water, the insoluble product was filtered, washed with water and dried *in vacuo*; 2·7 g (69%) *VIII* monohydrate, m.p. 202—205°C (98% ethanol–chloroform). Mass spectrum, *m/z* (%): 480 (M^+ corresponding to $C_{29}H_{28}N_4OS$, 5·5%), 440 (3), 357 (2), 345 (7), 265 (15), 245, 246, 247 (10), 82 (100, C_5H_8N). IR spectrum (KBr): 759 (4 adjacent Ar—H), 1 482, 1 590 (Ar), 1 685 (N—CO—NH in the five-membered ring), 2 210 (R—CN), 2 680, 2 715, 2 755 (N—CH_2), 3 010, 3 090, 3 120 cm^{-1} (OH and H_2O). ^1H NMR spectrum ($C^2H_3SOC^2H_3$): δ 10·80 (bs, 1 H, NH), 6·90—7·80 (m, 12 H, ArH), 1·20—3·50 (m, 7 CH_2, CH and H_2O). For $C_{29}H_{28}N_4OS + H_2O$ (498·7) calculated: 69·85% C, 6·06% H, 11·24% N, 6·43% S; found: 69·61% C, 6·07% H, 11·36% N, 6·40% S.

1-[3-(11-Cyano-6,11-dihydrodibenzo[*b,f*]thiepin-11-yl)propyl]-4-(2-oxobenzimidazolin-1-yl)-piperidine (*IX*)

A mixture of 3·6 g *XV* (ref.[13]), 2·2 g 4-(2-oxobenzimidazolin-1-yl)piperidine[17], 1·4 g K_2CO_3 and 50 ml acetone was refluxed for 10 h, diluted with 100 ml boiling acetone and the inorganic salts were removed by filtration while hot. The filtrate was evaporated *in vacuo* and the residue was crystallized from a mixture of acetone and benzene; 2·2 g (44%) base *IX*, m.p. 192—199°C. Analytical sample, m.p. 198—202°C (ethanol–chloroform). IR spectrum: 737, 760 (4 adjacent Ar—H), 1 360 (Ar—N), 1 486, 1 590, 3 090, 3 133 (Ar), 1 680 (N—CO—NH in the five-membered ring), 2 225 (R—CN), 2 740, 2 780 cm^{-1} (N—CH_2). ^1H NMR spectrum: δ 10·70 (bs, 1 H, NH), 6·80—8·00 (m, 12 H, ArH), 4·60 and 4·03 (ABq, J = 14·0 Hz, 1 + 1 H, $ArCH_2S$), 4·30 (bm, 1 H, 4-H of piperidyl), 1·40—3·40 (m, 7 CH_2). For $C_{30}H_{30}N_4OS$ (494·7) calculated: 72·84% C, 6·11% H, 11·33% N, 6·48% S; found: 72·38% C, 6·07% H, 11·09% N, 6·60% S.

8-[3-(11-Cyano-6,11-dihydrodibenzo[*b,e*]thiepin-11-yl)propyl]-1-phenyl-1,3,8-triazaspiro[4,5]-decan-4-one (*X*)

A mixture of 3·6 g *XV* (ref.[13]), 2·32 g 1-phenyl-1,3,8-triazaspiro[4,5]decan-4-one[18], 1·4 g K_2CO_3 and 150 ml acetone was stirred and refluxed for 15 h. The solid was filtered off and extracted with water to remove the inorganic salts. The filtrate was evaporated *in vacuo* and the residue crystallized from acetone. The substance obtained was combined with the water-insoluble product and the whole was crystallized from a mixture of chloroform and ethanol; 3·57 g (61%) 2 : 1 : 1 solvate of *X* with chloroform and ethanol, m.p. 210—213°C. Mass spectrum, *m/z* (%): 508 (M^+ corresponding to $C_{31}H_{32}N_4OS$, 3%), 475 (4), 272 (26), 244 (100), 203 (10), 187 (10), 175 (10), 151 (10), 130 (10), 99 (27), 84 (35), 77 (18), 70 (20), 56 (16). For $C_{31}H_{32}N_4OS$ + 0·5 $CHCl_3$ + 0·5 C_2H_6O (581·4) calculated: 67·14% C, 6·15% H, 9·64% N, 5·51% S; found: 67·38% C, 6·30% H, 9·63% N, 5·06% S.

1-[2-(10-Cyano-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-yl)ethyl]-4-ethoxycarbonyl-4-phenylpiperidine (*XI*)

A mixture of 2·4 g *XVI* (ref.[12]), 5·65 g ethyl 4-phenylpiperidine-4-carboxylate[14], 1·0 g K_2CO_3 and 50 ml acetone was stirred and refluxed for 26 h. The solid was filtered off and washed with acetone, the filtrate was evaporated *in vacuo*, the residue was dissolved in 100 ml chloroform and the solution was washed with 50 ml 1 : 1 dilute hydrochloric acid. The hydrochloride of the starting ethyl 4-phenylpiperidine-4-carboxylate was extracted into the aqueous layer whereas the hydrochloride of *XI* remained in chloroform. The solution was further washed with 50 ml 15% Na_2CO_3, dried with K_2CO_3 and evaporated under reduced pressure; 3·2 g (93%) oily *XI*. It was dissolved in ether and neutralized with HCl in ether; 2·62 g hydrochloride which was purified by crystallization from a mixture of acetone and ether, m.p. 169·5—171·5°C. IR spectrum: 698, 730, 760 (5 and 4 adjacent Ar—H), 1 145, 1 160, 1 215, **1 725** (RCOOR'), 2 340 cm^{-1} (a broad band covering NH^+ and R—CN). ^1H NMR spectrum: δ 7·10—7·70 (m, 8 H, ArH of the tricycle), 7·20 (s, 5 H, C_6H_5), 4·30 and 3·40 (ABq, J = 13·0 Hz, 1 + 1 H, $ArCH_2$ in the central ring), 4·18 (q, J = 7·0 Hz, 2 H, OCH_2), 1·16 (t, J = 7·0 Hz, 3 H, CH_3 of ethyl), remaining 6 CH_2 in an unresolved multiplet. For $C_{31}H_{31}ClN_2O_2S$ (531·1) calculated: 70·10% C, 5·88% H, 6·68% Cl, 5·27% N, 6·04% S; found: 69·59% C, 6·22% H, 6·70% Cl, 5·14% N, 6·19% S.

1-[3-(10-Cyano-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-yl)propyl]-4-(2-oxobenzimidazolin-1-yl)-piperidine (*XII*)

A solution of 2·1 g 4-(2-oxobenzimidazolin-1-yl)piperidine[17] in 30 ml chloroform was treated with a solution of 3·5 g *XVII* (ref.[12]) in 100 ml acetone and with 1·4 g K_2CO_3 and the mixture was refluxed for 14 h. The solid was filtered off, washed with acetone and the filtrate was evaporated *in vacuo*. The residue was dissolved in 50 ml benzene and the solution was shaken with dilute hydrochloric acid. The separated oily hydrochloride was isolated by decantation, treated with dilute NH_4OH and the base was isolated by extraction with chloroform. Evaporation of the extract gave the crude base which was chromatographed on 200 g silica gel. Chloroform eluted first a small amount of a less polar impurity and then 4·54 g (94%) oily *XII* which crystallized from cyclohexane and was purified by recrystallization from a mixture of acetone, ethanol and ether. The substance obtained is a 2 : 1 solvate with ethanol, m.p. 118—123°C. IR spectrum: 735, 758 (4 adjacent Ar—H), 1 620 (Ar), 1 690 (N—CO—NH in the ring), 2 220 (R—CN), 2 780, 2 800 (CH_2—N), 3 130, 3 170 cm^{-1} (NH). ^1H NMR spectrum: δ 10·60 (bs, 1 H, NH), 6·90—7·70 (m, 12 H, ArH), 4·28 and 3·40 (ABq, J = 13·0 Hz, 1 + 1 H, $ArCH_2$ in the central ring). For $C_{30}H_{30}N_4OS + 0{\cdot}5\,C_2H_6O$ (517·7) calculated: 71·92% C, 6·43% H, 10·82% N, 6·18% S; found: 72·31% C, 6·57% H, 10·58% N, 6·20% S.

8-[3-(10-Cyano-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-yl)propyl]-1-phenyl-1,3,8-triazaspiro[4,5]-decan-4-one (*XIII*)

A mixture of 2·4 g 1-phenyl-1,3,8-triazaspiro[4,5]decan-4-one[18], 3·5 g *XVII* (ref.[12]), 1·4 g K_2CO_3 and 150 ml acetone was refluxed for 14 h. After cooling the solid was filtered off, washed with acetone and the filtrate was evaporated *in vacuo*. The inhomogeneous residue (5·78 g) was dissolved in chloroform and chromatographed on a column of 180 g silica gel. After removal of a small amount of less polar components by elution with chloroform, the homogeneous oily base was eluted by a mixture of chloroform and ethanol. It crystallized from ethanol as a 1 : 1 solvate; 4·7 g (87%), m.p. 100—107°C. Mass spectrum, m/z: 508 (M^+ corresponding to $C_{31}H_{32}N_4OS$, 5%), 386, 359, 333, 244 (100%). IR spectrum (KBr): 690, 748 (5 and 4 adjacent Ar—H), 1 498, 1 595, 3 050 (Ar), 1 700 (CONH), 2 225 (R—CN), 2 820 cm^{-1} (CH_2—N). ^1H NMR

spectrum: δ 7·85 (bs, 1 H, NH), 6·70—7·70 (m, 13 H, ArH), 4·70 (bs, 2 H, NCH_2N), 4·25 and 3·38 (ABq, J = 13·0 Hz, 1 + 1 H, $ArCH_2$ in the central ring), 3·68 (q, 2 H, CH_2 of ethanol), 1·20 (t, 3 H, CH_3 of ethanol), 1·40—3·00 (m, remaining 7 CH_2). For $C_{31}H_{32}N_4OS + C_2H_6O$ (554·8) calculated: 71·45% C, 6·90% H, 10·10% N, 5·78% S; found: 71·21% C, 6·77% H, 10·40% N, 5·91% S.

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