NEUROTROPIC AND PSYCHOTROPIC AGENTS. LXIV.*

IODO, ETHOXYCARBONYLAMINO AND METHANESULFONAMIDO DERIVATIVES OF 10-(4-METHYLPIPERAZINO)-10,11-DIHYDRODIBENZO[*b,f*]THIEPIN

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8-Aminodibenzo[*b,f*]thiepin-10(11*H*)-one (*IX*) was converted to 8-iodo- (*X*), 8-ethoxycarbonylamino-(*XI*) and 8-methanesulfonamido- (*XII*) analogues. Ketones *X*—*XII* were reduced to alcohols *XII*—*XV*, these were converted to chlorides *XVI*—*XVIII* which underwent a substitution reaction with 1-methylpiperazine. In addition to the expected 10-(4-methylpiperazino) derivatives *IV*, *VII* and *VIII*, elimination products *XIX*—*XXI* were isolated. 8-Iodo-10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b,f*]thiepin (*IV*) is a very potent neuroleptic, comparable with other 8-halogen analogues (*I*—*III*).

It was found some time ago[1] that 8-halogeno derivatives of 10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b,f*]thiepin (*I*—*III*) possess a pronounced central depressant and neuroleptic activities; the 8-chloro derivative ("octoclothepin")[1-3] was selected[4] for clinical tests and introduced into therapeutical practice for treatment of psychoses of the schizophrenic type[5-9]. So far, the fourth possible 8-halogeno derivative of the parent compound, the 8-iodo derivative *IV*, has not been described. Proceeding from the unsuccessful attempt at preparing the iodinated ketone in the isomeric dibenzo[*b,e*]thiepin series by cyclization of the corresponding acid with polyphosphoric acid[10] the synthetic scheme[1] used for the synthesis of *I*—*III* was considered to be hardly applicable to the preparation of the iodo derivative *IV*. The synthesis of this compound was made possible by employing 8-aminodibenzo[*b,f*]thiepin-10(11*H*)-one[11] (*IX*) as the starting compound since the ketone became relatively readily available by a synthesis recently described[12]. Diazotization of amino ketone *IX* and reaction of the diazonium salt with a solution of potassium iodide and iodine[13,14] led to 8-iododibenzo[*b,f*]thiepin-10(11*H*)-one (*X*). Its reduction with sodium borohydride in a mixture of ethanol and dioxane led to alcohol *XIII* which was converted by hydrogen chloride in chloroform to the chloride *XVI*. Reaction of this compound with excess 1-methylpiperazine in boiling chloroform produced as the

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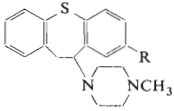
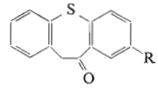
main product the methylpiperazino derivative *IV*, together with a smaller amount of the elimination product, *viz.* 2-iododibenzo[*b*,*f*]thiepin (*XIX*).

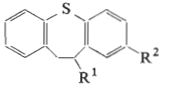


I, R = F
II, R = Cl
III, R = Br
IV, R = I

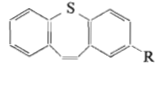
V, R = NH_2
VI, R = $NHCOCH_3$
VII, R = $NHCOOC_2H_5$
VIII, R = $NHSO_2CH_3$



IX, R = NH_2
X, R = I
XI, R = $NHCOOC_2H_5$
XII, R = $NHSO_2CH_3$



XIII; R^1 = OH, R^2 = I
XIV; R^1 = OH, R^2 = $NHCOOC_2H_5$
XV; R^1 = OH, R^2 = $NHSO_2CH_3$
XVI; R^1 = Cl, R^2 = I
XVII; R^1 = Cl, R^2 = $NHCOOC_2H_5$
XVIII; R^1 = Cl, R^2 = $NHSO_2CH_3$



XIX, R = I
XX, R = $NHCOOC_2H_5$
XXI, R = $NHSO_2CH_3$

In the subsequent part of the present work two novel derivatives of 8-amino--10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b*,*f*]thiepin (*V*) are described. This amine is known[12] to possess a relatively high neuroleptic activity although its 8-substituent is distinguished by its high polarity from the 8-substituents of other highly active compounds of this group[1]. The view was advanced before that blocking of the free amino group by acylation might lead to an increase of activity and hence we prepared the acetamido derivative[12] *VI*. In the context of further pursuit of this view we prepared now the 8-(ethoxycarbonylamino) derivative *VII* and the 8-(methanesulfonamido) derivative *VIII*. Reaction of the amino ketone *IX* with ethyl chloroformate or with methanesulfonyl chloride in pyridine resulted, respectively, in ketones *XI* and *XII*, which were reduced similarly to the preparation of the iodo derivative to alcohols *XIV* and *XV*. Analogously, transformation to chlorides *XVII* and *XVIII* was performed, the chlorides reacting with methylpiperazine to the desired bases *VII* and *VIII*, as well as to a smaller amount of the corresponding elimination products *XX* and *XXI*.

The methanesulfonates of bases *IV*, *VII* and *VIII* were tested pharmacologically for acute toxicity in mice (LD_{50}), influence on motor coordination in the rotating-rod test in mice (the mean effective doses ED_{50}) and in the catalepsy test in rats (the mean effective doses ED_{50}) (for methods see ref.[15]). The results expressed per base are shown in Table I which includes for comparison

also the other 8-halogeno derivatives *I*—*III*, further the amino derivative *V* and the acetamido derivative *VI* (some of the values are taken from the papers cited, some are original).

Table I makes it possible to compare all the four 8-halogeno derivatives of perathiepin. The toxicity decreases gradually from the fluoro, to the chloro, bromo and iodo derivative. The central depressant activity is highest with the chloro derivative and lowest with the iodo derivative. On the contrary, in the catalepsy, the fluoro, chloro and bromo derivatives are practically equivalent, the iodo derivative being most effective. It should be mentioned, however, that the differences are never larger than by a factor of two (an exception is formed here by the strikingly low activity of the bromo derivative *III* in the catalepsy test after oral application) and that for the fluoro derivative *I* we have at our disposal only values after parenteral administration and for the iodo derivative *IV* only those after oral administration. Carbamate *VII* is somewhat more effective as central depressant than the acetamido derivative *VI* but is weaker in the catalepsy test. The sulfonamide *VIII* is less toxic and weaker in both tests. Both new compounds with the blocked amino group are substantially less toxic and less effective than *V* which has a free amino group.

The iodo derivative *IV* was found in *in vitro* tests to be effective antimicrobially over a wide spectrum (determined by Dr A. Šimek and Dr J. Turinová of the bacteriological department of this institute); the minimum inhibitory concentrations in μg/ml are shown: *Streptococcus β-haemolyticus* (12·5), *Staphylococcus pyogenes aureus* (12·5), *Klebsiella pneumoniae* (50), *Myco-*

TABLE I

Pharmacological Properties (in mg/kg) of Compounds *IV*, *VII* and *VIII* in Comparison with Chemically Related Compounds (*I*—*III*, *V*, *VI*)

Compound	Administration	Toxicity LD_{50}	Rotating rod ED_{50}	Catalepsy[a] ED_{50}
I (ref.[1])	*i.v.*	42	0·116	2·7
II (ref.[12])	*i.v.*	46	0·060	2·4
II	*p.o.*	78	2·2	4·3
III (ref.[1])	*i.v.*	78	0·110	2·5
III	*p.o.*	100	2·8	14·0
IV	*p.o.*	185	5·5	2·5
V (ref.[11])	*i.v.*	9·6	0·21	3·4
VI (ref.[12])	*i.v.*	29	2·3	6·0
VII	*i.v.*	35	1·6	>10[b]
VIII	*i.v.*	64	6·0	>10[c]

[a] Where intravenous administration is indicated, intraperitoneal application was used for the catalepsy test. [b] A dose of 10 mg/kg brought about catalepsy in only 3 out of ten rats. [c] A dose of 10 mg/kg brought about catalepsy in only 2 out of ten rats.

bacterium tuberculosis H37Rv (50), *Pseudomonas aeruginosa* (50), *Escherichia coli* (50), *Salmonella typhi* (50), *Proteus vulgaris* (50). In an *in vivo* experiment with acute experimental infection with *E. coli* in mice, using 25% LD_{50} as the daily therapeutical dose (*i.e* 46·25 mg/kg), no chemotherapeutic activity was found.

EXPERIMENTAL

The melting points of analytical preparations were determined in Kofler's block; the samples were dried in the usual way. The UV spectra (in methanol) were recorded in a Unicam SP 700 spectrophotometer, the IR spectra (in Nujol unless stated otherwise) in a Unicam SP 200 G spectrophotometer and the NMR spectra (in deuteriochloroform unless stated otherwise) in a ZKR 60 (Zeiss, Jena) spectrometer.

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

Concentrated hydrochloric acid (30 ml) was added to a suspension of 7·24 g amino ketone[11,12] *IX* in 60 ml water; this was followed at 0–5 °C, under constant stirring, by dropwise addition of 2·5 g $NaNO_2$ in 5 ml water. The mixture was stirred under cooling for 1 h and then 10·0 g potassium iodide and 2·2 g iodine in 15 ml water were added. After 5 min of stirring the mixture was overlayered with 30 ml benzene and the whole stirred for another 5 h. After standing overnight, 100 ml benzene were added, the mixture was shaken, the benzene phase was separated, washed with 5% NaOH, 5% $NaHSO_3$ and water, dried with $MgSO_4$ and evaporated. The solid residue (7·9 g, m.p. 100–110°C) is practically homogeneous in thin-layer chromatography. Recrystallization from ethanol yielded 6·60 g (63%) product, melting at 115–117°C. UV spectrum: λ_{max} 231 nm (log ε 4·35), 244 nm (4·31), 268 nm infl. (4·07), 342 nm (3·56). IR spectrum (KBr): 750, 761 (4 vicinal aromatic C—H), 815, 828 (2 vicinal aromatic C—H), 904 (isolated aromatic C—H), 1568 (Ar) and 1665 cm^{-1} (Ar—CO). NMR spectrum: δ 8·53 (d, J = 2·0 Hz, 1 H, aromatic proton in position 9), 7·15–7·85 (m, 6 H, other aromatic protons), 4·30 (s, 2 H, $ArCH_2CO$). For $C_{14}H_9IOS$ (352·2) calculated: 47·74% C, 2·58% H, 36·03% I, 9·11% S; found: 47·75% C, 2·58% H, 35·50% I, 9·28% S.

8-(Ethoxycarbonylamino)dibenzo[*b,f*]thiepin-10(11*H*)-one (*XI*)

Ethyl chloroformate (2·9 ml) was added to a solution of 3·60 g amino ketone[11,12] *IX* in 30 ml pyridine and the mixture was stirred and heated to 90°C. After cooling, it was poured into excess water, the precipitated product was left to stand overnight, filtered, dissolved in chloroform and the solution was washed with 5% hydrochloric acid and water, dried with $MgSO_4$ and evaporated. The residue (4·7 g, quantitative yield) is the desired product, a sample of which was recrystallized for analysis from a mixture of ethanol and benzene; m.p. 198–199°C. UV spectrum: λ_{max} 247 nm (log ε 4·46), 270 nm infl. (4·21), 354 nm (3·63). IR spectrum: 746, 770 and 838 (aromatic C—H), 1230, (C—O), 1540 (CONH), 1662 (Ar—CO), 1732 cm^{-1} (NHCOOR). NMR spectrum (CD_3SOCD_3): δ 10·02 (s, 1 H, NH), 8·30 (d, 1 H, aromatic proton in position 9), 7·00–7·90 (m, 6 H, other aromatic protons), 4·31 (s, 2 H, $ArCH_2CO$), 4·14 (q, 2 H, OCH_2), 1·24 (t, 3 H, CH_3). For $C_{17}H_{15}NO_3S$ (313·4) calculated: 65·16% C, 4·83% H, 4·47% N, 10·23% S; found: 64·77% C, 4·84% H, 4·51% N, 10·28% S.

8-(Methanesulfonamido)dibenzo[*b,f*]thiepin-10(11*H*)-one (*XII*)

Methanesulfonyl chloride (1·7 ml) was added dropwise to a solution of 3·60 g amino ketone[11,12] *IX*, the mixture was heated under stirring on a boiling-water bath and processed as before.

A total of 2·53 g (53%) product was obtained m.p. 188—189° (ethanol). UV spectrum: λ_{max} 227 nm (log ε 4·34), 244·5 nm (4·38), 265 nm infl. (4·13), 347 nm (3·62). IR spectrum (KBr): 750 (4 vicinal aromatic C—H), 830 (2 vicinal aromatic C—H), 860 (isolated aromatic C—H), 1155 and 1328 (SO_2N), 1596 (Ar), 1675 (Ar—CO), 3250 cm^{-1} (NH). NMR spectrum (CD_3SOCD_3): δ 10·35 (bs, 1 H, NH) 8·05 (d, 1 H, aromatic proton in position 9), 7·20—7·90 (m, 6 H, other aromatic protons), 4·32 (s, 2 H, $ArCH_2CO$), 3·00 (s, 3 H, SO_2CH_3). For $C_{15}H_{13}NO_3S_2$ (319·4) calculated: 56·40% C, 4·10% H, 4·39% N, 20·08% S; found: 56·55% C, 4·14% H, 4·20% N, 20·22% S.

8-Iodo-10-hydroxy-10,11-dihydrodibenzo[*b,f*]thiepin (*XIII*)

A solution of 0·303 g $NaBH_4$ in 5 ml water (containing 2 drops of 5% NaOH) was added dropwise to a warm solution of 3·80 g ketone *X* in a mixture of 100 ml ethanol and 50 ml dioxane and the mixture was refluxed for 3 h. After standing overnight the solvents were evaporated at reduced pressure and the residue was distributed between water and benzene. The organic phase was washed with 5% hydrochloric acid and water, dried with $MgSO_4$ and evaporated: 3·65 g (94%) m.p. 141—143°C (methanol). UV spectrum: λ_{max} 232 nm infl. (log ε 4·13), 271 nm (4·06). IR spectrum: 750 (4 vicinal aromatic C—H), 805 (2 vicinal aromatic C—H), 885 (isolated aromatic C—H), 1052 (CHOH), 1310 and 3340 cm^{-1} (OH). For $C_{14}H_{11}IOS$ (354·2) calculated: 47·47% C, 3·13% H, 35·83% I, 9·05% S; found: 47·12% C, 3·16% H, 35·62% I, 9·30% S.

8-(Ethoxycarbonylamino)-10-hydroxy-10,11-dihydrodibenzo[*b,f*]thiepin (*XIV*)

Similarly to the above case, 1·30 g ketone *XI* in a mixture of 50 ml ethanol and 20 ml dioxane was reduced with 0·16 g $NaBH_4$. After 5 h of boiling and evaporation, the residue was decomposed with 5% hydrochloric acid and the product was extracted with warm chloroform; 1·23 g (94%), m.p. 176—178°C (benzene–ethanol). IR spectrum: 742 (4 vicinal aromatic C—H), 830 (2 vicinal aromatic C—H), 870 (isolated aromatic C—H), 1010 (ArCHOH in a ring), 1242 (COC), 1545 (CONH), 1610 (Ar), 1700 cm^{-1} (NHCOOR). For $C_{17}H_{17}NO_3S$ (315·4) calculated: 64·74% C, 5·43% H, 4·44% N, 10·17% S; found: 64·99% C, 5·52% H, 4·36% N, 10·08% S.

8-(Methanesulfonamido)-10-hydroxy-10,11-dihydrodibenzo[*b,f*]thiepin (*XV*)

Similarly to the preceding case, 2·2 g ketone *XII* in 180 ml ethanol was reduced with 0·261 g $NaBH_4$. After processing, the product was isolated by benzene extraction: 2·2 g (almost theoretical yield), m.p. 171·5—172·5°C (benzene–light petroleum). IR spectrum: 752 (4 vicinal aromatic C—H), 820 (2 vicinal aromatic C—H), 862 (isolated aromatic C—H), 980 and 990 (Ar—CHOH in a ring), 1150 and 1350 (SO_2N), 1595 (Ar), 3270 (NH), 3495 cm^{-1} (OH). For $C_{15}H_{15}NO_3S_2$ (321·4) calculated: 56·05% C, 4·71% H, 4·36% N, 19·95% S; found: 56·33% C, 4·90% H, 4·61% N, 19·48% S.

8-Iodo-10-chloro-10,11-dihydrodibenzo[*b,f*]thiepin (*XVI*)

Powedered $CaCl_2$ (4 g) was added to a solution of 6·95 g alcohol *XIII* in 150 ml chloroform and the suspension was saturated with anhydrous hydrogen chloride for 3 h at room temperature. After standing overnight it was filtered, the filtrate was evaporated at reduced pressure and the residue recrystallized from 20 ml cyclohexane; 6·0 g (82%), m.p. 103—105°C. NMR spectrum: δ 7·81 (m, 1 H, aromatic proton in position 9), 7·00—7·60 (m, 6 H, remaining aromatic protons), 5·66 (q, J = 4·0; 8·0 Hz, 1 H, CH—Cl), 3·94 and 3·59 (2 q, J = 4·0; 14·0 and 8·0; 14·0 Hz, 2 H,

$ArCH_2$). For $C_{14}H_{10}ClIS$ (372·7) calculated: 45·12% C, 2·71% H, 9·52% Cl, 34·05% I, 8·60% S; found: 44·98% C, 2·84% H, 9·82% Cl, 3·80% I, 8·96% S.

8-(Ethoxycarbonylamino)-10-chloro-10,11-dihydrodibenzo[*b,f*]thiepin (*XVII*)

Similarly to the preceding case, 2·24 g *XIV* gave rise to 2·00 g (84%) product, m.p. 141—142·5° (benzene–light petroleum). IR spectrum: 690 (C—Cl), 755 (4 vicinal aromatic C—H), 825 (2 vicinal aromatic C—H), 880 (isolated aromatic C—H), 1 255, 1 520 (CONH), 1 570 (Ar), 1 692 (NHCOOR) 3 290 cm^{-1} (NH). NMR spectrum: δ 7·00—7·80 (m, 7 H, aromatic protons), 6·78 (bs, 1 H, NH), 5·79 (q, J = 5·0; 8·0 Hz, 1 H, CH—Cl), 4·20 (q, J = 7·0 Hz, 2 H, OCH_2), 3·40—4·00 (m, 2 H, $ArCH_2$), 1·20 (t, J = 7·0 Hz, 3 H, C—CH_3). For $C_{17}H_{16}ClNO_2S$ (333·8) calculated: 61·16% C, 4·83% H, 10·62% Cl, 4·20% N, 9·60% S; found: 61·47% C, 4·90% H, 10·49% Cl, 4·08% N, 9·54% S.

8-(Methanesulfonamido)-10-chloro-10,11-dihydrodibenzo[*b,f*]thiepin (*XVIII*)

Similarly to the preceding cases, 1·85 g *XV* yielded 1·57 g (80%) recrystallized product, m.p. 146·5—147·5°C (benzene). For $C_{15}H_{14}ClNO_2S_2$ (339·9) calculated: 53·01% C, 4·15% H, 10·43% Cl, 4·12% N, 18·87% S; found: 53·23% C, 4·23% H, 10·42% Cl, 4·23% N, 19·15% S.

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

A mixture of 7·0 g chloride *XVI*, 10 ml chloroform and 10 ml 1-methylpiperazine was refluxed for 8 h and chloroform was evaporated. The residue was distributed between benzene and water and the benzene solution was shaken with 100 ml 5% hydrochloric acid. The suspension of the hydrochloride formed was filtered, the filtrated benzene phase was washed with water, dried and evaporated. A total of 1·2 g 2-iododibenzo[*b,f*]thiepin (*XIX*) was obtained, m.p. 117—118°C (ethanol). UV spectrum: λ_{max} 244 nm (log ε 4·45), 235 nm infl. (4·41), 266 nm (4·50), 295 nm infl. (3·82). IR spectrum: 748 and 768 (4 vicinal aromatic C—H), 785 (*cis*-CH=CH in a ring), 810 and 820 (2 vicinal aromatic C—H), 880 and 895 (isolated aromatic C—H), 1 561 cm^{-1} (Ar). NMR spectrum: δ 6·80—7·70 (m, 9 H, aromatic and olefinic protons). For $C_{14}H_9IS$ (336·2) calculated: 50·01% C, 2·70% H, 37·75% I, 9·54% S; found: 50·05% C, 2·72% H, 37·76% I, 9·76% S. The filtered hydrochloride was added to the acid aqueous phase (after separation of the benzene phase), the suspension was made alkaline with 15% solution of NaOH and base *IV* was isolated by extraction with benzene: 6·64 g (81%), m.p. 143—144°C (ethanol). NMR spectrum: δ 7·99 (d, J = 2·0 Hz, 1 H, aromatic proton in position 9), 6·90—7·55 (m, 6 H, remaining aromatic protons), 3·00—3·90 (m, 3 H, $ArCH_2CHAr$), 2·60 and 2·40 (2 m, 8 H, CH_2 groups of piperazine), 2·25 (s, 3 H, N—CH_3). For $C_{19}H_{21}IN_2S$ (436·4) calculated: 52·30% C, 4·85% H, 29·08% I, 6·42% N, 7·35% S; found: 52·38% C, 4·95% H, 29·10% I, 6·57% N, 7·68% S.

Dimethanesulfonate (*hemihydrate*), m.p. 203—204°C (ethanol–ether). For $C_{21}H_{29}IN_2O_6S_3 \frac{1}{2}H_2O$ (637·6) calculated: 39·56% C, 4·74% H, 19·90% I, 4·40% N, 15·09% S; found: 39·49% C, 4·69% H, 19·59% I, 4·68% N, 15·09% S.

8-(Ethoxycarbonylamino)-10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b,f*]thiepin (*VII*)

A mixture of 1·8 g chloride *XVII*, 10 ml chloroform and 10 ml 1-methylpiperazine was refluxed for 12 h, cooled, diluted with benzene and washed with water. The basic product from the organic phase was transferred to 5% hydrochloric acid and, in analogy to the preceding case, 2-(*ethoxycarbonylamino*)*dibenzo*[b,f]*thiepin* (XX) was isolated; 0·32 g, m.p. 166—168°C (benzene–light petroleum). UV spectrum: λ_{max} 225 nm (log ε 4·48), 264 nm (4·57), 296 nm (3·70). IR spectrum:

760 and 770 (4 vicinal aromatic C—H), 790 (*cis*-CH=CH in a ring), 840 (2 vicinal aromatic C—H), 870 (isolated aromatic C—H), 1 530 and 1 575 (CONH), 1 582 (Ar), 1 698 and 1 735 cm^{-1} (NHCOOR). NMR spectrum: δ 7·15—7·70 (m, 7 H, aromatic protons), 7·01 (s, 2 H, CH=CH), 6·80 (bs, 1 H, NH), 4·18 (q, J = 7·0 Hz, 2 H, OCH_2), 1·21 (*t*, J = 7·0 Hz, 3 H, C—CH_3). For $C_{16}H_{15}NO_2S$ (285·4) calculated: 4·91% N, 11·23% S; found: 4·64% N, 10·73% S. Making alkaline of the hydrochloride solution with aqueous ammonia and extraction with benzene yielded the oily base *VII* (1·70 g, 79%) which was converted to *dimethanesulfonate*, crystallizing from ethanol as a solvate with 1 molecule of ethanol; m.p. 206—207°C. IR spectrum: 772, 798 and 860 (aromatic C—H), 1 040 and 1 144 (SO_3H), 1 230 (C—O—C), 1 545 and 1 600 (CONH), 1 725 (NHCOOR), 2 420 (NH^+), 3 165 and 3 230 (NH), 3 420 cm^{-1} (OH). For $C_{26}H_{41}N_3O_9S_3$ (635·8) calculated: 49·11% C, 6·50% H, 6·61% N, 15·13% S; found: 48·90% C, 6·39% H, 6·59% N, 15·62% S.

8-(Methanesulfonamido)-10-(4-methylpiperazino)-10,11-dihydrodibenzo[*b*,*f*]thiepin (*VIII*)

Reaction of 1·72 g chloride *XVIII* and 10 ml 1-methylpiperazine in 10 ml chloroform yielded as in the preceding case 0·36 g 2-(*methanesulfonamido*)*dibenzo*[b,f]*thiepin* (XXI), m.p. 177—178°C (benzene–light petroleum). The compound is a solvate with 1/3 of a benzene molecule. UV spectrum: λ_{max} 224 nm (log ε 4·54), 263 nm (4·50), 296 nm (3·77). IR spectrum: 740 (4 vicinal aromatic C—H), 778 (*cis*-CH=CH in a ring), 838 (2 vicinal aromatic C—H), 850 (isolated aromatic C—H), 1 160 and 1 320 (SO_2N), 1 590 (Ar), 3 220 cm^{-1} (NH). NMR spectrum (CD_3SOCD_3): δ 10·05 (s, 1 H, NH), 7·00—7·65 (m, aromatic and olefinic protons), 3·00 (s, 3 H, SO_2CH_3). For $C_{17}H_{15}$·NO_2S_2 (329·5) calculated: 61·98% C, 4·59% H, 4·25% N, 19·47% S; found: 61·78% C, 4·66% H, 4·05% N, 19·90% S. Processing of an aqueous solution of the hydrochloride yielded 1·60 g (78%) oily base *VIII* which was converted to *dimethanesulfonate*, crystallizing from a mixture of ethanol and ether as a solvate with 1 molecule ethanol and 1 molecule water; m.p. 164—165°C. For $C_{24}H_{41}N_3O_{10}S_4$ (659·9) calculated: 43·68% C, 6·26% H, 6·37% N, 19·44% S; found: 43·66% C, 6·11% H, 6·45% N, 19·51% S. Decomposition of this salt with alkali and extraction with chloroform resulted in a sample of purified base for the NMR spectrum: δ 6·80—7·65 (m, 7 H, aromatic protons), 5·35 (s, 1 H, NH), 3·00—3·95 (m, 3 H, Ar—CH_2CH—Ar), 2·90 (s, 3 H, SO_2CH_3), 2·60 and 2·46 (2 m, 8 H, CH_2 groups of piperazine), 2·24 (s, 3 H, N—CH_3).

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