POTENTIAL ANTIDEPRESSANTS: 2-(AMINOALKOXY)BIPHENYLS AND SOME RELATED ω-SUBSTITUTED 2-ALKOXYBIPHENYLS

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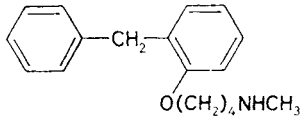
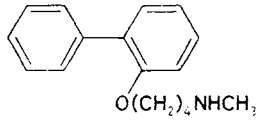
Reactions of 2-hydroxybiphenyl with α,ω-dibromoalkanes gave the 2-(bromoalkoxy)biphenyls *IIIa*—*IIId*. The 2-(dimethylaminoalkoxy)biphenyls *VIa* and *VIb* were transformed via carbamates *VIIa* and *VIIb* to the secodary amines *Va* and *Vb*. Their homologues *Vc* and *Vd* were obtained from the bromo compounds *IIIc* and *IIId* by treatment with methylamine. Bromo compounds *IIIa* and *IIIb* were reacted with 1-methylpiperazine, 2-(1-piperazinyl)ethanol, 3-(1-piperazinyl)-propanol, and 4-amino-1-benzylpiperidine and gave the diamines *VIIIa*, *VIIIb*, *IXa*, *Xa*, *Xb*, and *XIa*. Addition of 2-hydroxybiphenyl to acrylonitrile afforded the nitrile *XIIa*. The homologous nitrile *XIIb* was obtained from the bromo compound *IIIb* and sodium cyanide in dimethyl sulfoxide. Nitriles *XIIa* and *XIIb* were reduced with aluminium hydride to diamines *IVb* and *IVc*. The nitriles were also transformed to hydrochlorides of the corresponding ethyl imidates *XIVa* and *XIVb*. Their hydrolysis resulted in the esters *XVa* and *XVb*. The acid *XIIIa* was obtained by acid hydrolysis of the nitrile *XIIa*; the acid *XIIIb* resulted from the acid hydrolysis of the ester *XVb*. The imidate *XIVb* was transformed to the amidine *XVIb* and to the dihydroimidazole *XVIIb*. Only the amine *Vc* showed properties indicative of potential antidepressant.

In some previous communications[1-3] we have described the synthesis of tricyclic analogues of the atypical antidepressant and cerebral activator „bifemelane" (*I*) (refs[4-6]) in the effort to find further antidepressant compounds. In the present communication we have used the lower homologue of bifemelane, i.e. the biphenyl derivative *II*, as the prototype, and have prepared a series of new 2-(aminoalkoxy)-biphenyls and of some related ω-substituted 2-alkoxybiphenyls for pharmacological testing. A number of various 2-(aminoalkoxy)biphenyls was described in the literature[7]; some of them were characterized as antihistamine agents and adrenergic blocking agents[8-11], coronary vasodilators[12-14], antidepressants and anticonvulsants[15,16], and potential antifungal agents[17]; quaternary salts of some of them were described as ganglionic blocking agents[18].

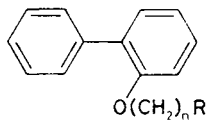


I



II

A survey of the compounds prepared now is given by formulae *III*–*XVII*. Commercial 2-hydroxybiphenyl was the common starting material for the synthesis of the whole series. Its reactions with 1,2-dibromoethane, 1,3-dibromopropane, 1,4-dibromobutane, and 1,5-dibromopentane under various conditions resulted in *IIIa* to *IIId*. Compound *IIIa*, which was mentioned in a patent[19], was obtained by three methods: *a*) by reaction of 2-hydroxybiphenyl with 1,2-dibromoethane and potassium hydroxide in boiling methanol (for analogy, cf. ref.[4]), *b*) by modification of (a) (for analogy, cf. ref.[20]), and *c*) by reaction of 2-hydroxybiphenyl with 1,2-dibromoethane and potassium hydroxide in boiling tert. butyl alcohol in the presence of water[19] (the method of choice). Compounds *IIIb* (ref.[21]) and *IIIc* (refs[15,16,18]) were prepared by described methods. Compound *IIId* was obtained from 2-hydroxybiphenyl, 1,5-dibromopentane, and potassium hydroxide in boiling methanol (literature[18] described a different method).



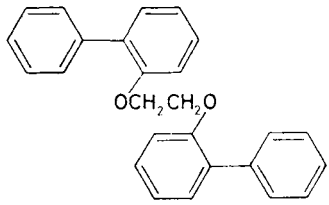
III, R = Br
IV, R = NH_2
V, R = $NHCH_3$
VI, R = $N(CH_3)_2$
VII, R = $N(CH_3)COOC_2H_5$
VIII, R = N(piperazine)–CH_3
IX, R = N(piperazine)–CH_2CH_2OH
X, R = N(piperazine)–$(CH_2)_3OH$
XI, R = NH–(piperidine)–$CH_2C_6H_5$
XII, R = CN
XIII, R = COOH
XIV, R = $C(=NH)OC_2H_5$
XV, R = $COOC_2H_5$
XVI, R = $C(=NH)NH_2$
XVII, R = 2-imidazolyl

In formulae *III*–*XVII*: *a*, n = 2 *b*, n = 3 *c*, n = 4 *d*, n = 5

Compounds *VIa* and *VIb* were prepared by known procedures[7] and were partially demethylated to the coresponding secondary amines *Va* and *Vb*. *VIa* and *VIb* were subjected to treatment with ethyl chloroformate in boiling benzene which resulted in inhomogeneous *VIIa* and *VIIb*. In the first case, crystallization gave the homogeneous *VIIa*, in the second case, chromatography removed the less polar impurity which was then followed by homogeneous *VIIb*; both carbamates were characterized by spectra. Hydrolysis of *VIIa* and *VIIb* with a concentrated boiling solution of potassium hydroxide resulted in *Va* and *Vb* which were transformed to hydrochlorides. The ^1H NMR spectra of the released, homogeneous bases were

measured. Reactions of *IIIa* and *IIIb* with 1-methylpiperazine, 2-(1-piperazinyl)-ethanol, 3-(1-piperazinyl)propanol[22], and 4-amino-1-benzylpiperidine[23] by heating to 130–140°C gave *VIIIa*, *VIIIb*, *IXa*, *Xa*, *Xb*, and *XIa*. The oily bases were transformed to hydrochlorides and the released, homogeneous bases were used for recording the ^{1}H NMR spectra.

Compounds *II* (refs[15,16]) and *Vd* were obtained by reactions of *IIIc* and *IIId* with methylamine in ethanol at room temperature (analogy of ref.[4]); they were also transformed to hydrochlorides. Addition of 2-hydroxybiphenyl to acrylonitrile, catalyzed by sodium (for method, cf. refs[24,25]), gave *XIIa*. It is a crystalline solid melting at 71–73°C which was characterized by spectra. An attempt to prepare *XIIa* by reaction of *IIIa* with sodium cyanide in dimethyl sulfoxide at 75–80°C (method[26]) resulted in a nitrogen-free compound $C_{26}H_{22}O_2$ (mass spectrum and analysis) melting at 100–102°C which was identified as *XVIII* (IR and ^{1}H NMR spectra). There was the question of origin of *XVIII* in our reaction. *XVIII* is certainly a by-product of formation of *IIIa* from 2-hydroxybiphenyl and 1,2-dibromoethane but under the conditions used, it was not mentioned. The high yield, in which it was now obtained, excludes the possibility that *XVIII* could be an impurity of the used *IIIa*. Our attempt to hydrolyze *XIIa* with potassium hydroxide in aqueous ethanol to the acid *XIIIa* resulted in elimination of acrylonitrile and recovery of 2-hydroxybiphenyl. This result indicated the way how to explain the formation of *XVIII* from *IIIa* and sodium cyanide: *XIIa* was probably primarily formed but after elimination of acrylonitrile the regenerated 2-hydroxybiphenyl reacted with the still unreacted *IIIa* to give *XVIII*, whereas sodium cyanide present participated by forming the sodium salt of 2-hydroxybiphenyl, necessary for the nucleophilic displacement. The nitrile *XIIb* was easily obtained by reaction of *IIIb* (ref.[21]) with sodium cyanide in dimethyl sulfoxide at 55–60°C (method[26]).



XVIII

The nitrile *XIIa* was reduced either with lithium aluminium hydride in ether or better with aluminium hydride (generated from aluminium chloride and lithium aluminium hydride) in ether to the primary amine *IVb*; the oily base gave the hydrochloride and the released, homogeneous base was used for recording the spectra. The homologous amine *IVc* was prepared by similar reduction of *XIIb* with alumi-

nium hydride. This compound was described in patents[15,16] but was evidently prepared differently and the melting point of the hydrochloride given (155–158°C) is by 10° lower than our value (165–168°C). Treatment of the nitriles *XIIa* and *XIIb* with hydrogen chloride in the presence of ethanol gave hydrochlorides of the corresponding ethyl imidates *XIVa* and *XIVb*. Hydrolysis of the imidates gave the esters *XVa* and *XVb*. It was already mentioned that alkaline hydrolysis of *XIIa* resulted in elimination of acrylonitrile but not in the desired acid *XIIIa*. This was obtained by hydrolysis of *XIIa* with 85% phosphoric acid at 150°C. Similar hydrolysis of *XIIb* was not successful and *XIIIb* was finally obtained by hydrolysis of *XVb* with hydrochloric acid at 135–145°C. Ammonolysis of *XIVb* in methanol at room temperature gave the hydrochloride of the amidine *XVIb*. Treatment of *XIVb* with ethylenediamine at 60–75°C gave the 2-imidazoline *XVIIb* which was transformed to the hydrogen succinate.

The compounds prepared were tested pharmacologically (mostly as potential antidepressants, anticonvulsants and antiinflammatory agents), the amines in the form of salts, described in the Experimental (the doses given were calculated per bases); they were administered orally. Acute toxicity in mice, LD_{50} in mg/kg: *IVb*, 411; *IVc*, 306; *Va*, 242; *Vb*, 401; *Vc*, 214; *Vd*, 500; *VIIIa*, 188; *VIIIb*, 308; *IXa*, 200; *Xa*, 296; *Xb*, 371; *XIa*, 599; *XIIIa*, >1 000; *XIIIb*, >1 000; *XVIb*, 351; *XVIIb*, 187.

Ataxic activity in the rotarod test in mice, ED_{50} in mg/kg: *Va*, 17·6, *Vc*, 54; *IXa*, 58·2; *XVIIb*, about 50. Protective effect in the test of maximum electroshock in mice, PD_{50} in mg/kg or dose used and its effect: *IVb*, mild effect at 50 mg/kg (in 20% animals); *IVc*, 10·3; *Va*, 22·7; *Vc*, 34·1; *VIIIa*, about 50; *VIIIb*, mild effect at 50 mg/kg (in 20% animals); *IXa*, mild effect at 50 mg/kg (in 40% animals); *Vd*, *Xa*, *Xb*, *XIa*, *XVIb*, and *XVIIb* were inactive at 50 mg/kg.

Antireserpine effects: (1) inhibition of the reserpine-induced gastric ulcer formation in rats at 50 mg/kg: *Va* and *Vb*, mild effect; *IVb*, *Vc*, *VIIIa*, *VIIIb*, *IXa*, *Xa*, *Xb*, *XIa*, *XVIb*, and *XVIIb* were inactive. (2) Inhibition of the reserpine-induced ptosis in mice: *Vc*, significant effect starting from the dose of 3 mg/kg. (3) Antagonization of the reserpine-induced hypothermia in mice: *Vc*, $D_5^t{}_0 = 9{\cdot}6$ mg/kg. Potentiation of the toxicity of yohimbine in mice: *Vc*, $ED_{50} = 18{\cdot}2$ mg/kg; *IXa*, the dose of 50 mg/kg is active in 30% animals; *XVIIb*, the dose of 50 mg/kg is active in 20% animals.

Antiinflammatory and antinociceptive actions (the compounds were administered in doses of 25 and 100 mg/kg and their activity was evaluated in two types of oedema in rats and the results are expressed as % of inhibition of oedema ($^+$ means statistical significance); the analgetic adtivity was assessed in the test of inhibition of the writhing syndrome in male mice using stimulation with intraperitoneal 0·7% acetic acid (results in % of inhibition of the pain): Carrageenan oedema, *XIIIa*, 25 mg/kg, 21$^+$; *XIIIb*, 100 mg/kg, 3. Adjuvant oedema, *XIIIa*, 100 mg/kg, 16$^+$; *XIIIb*, 100 mg/kg, 19$^+$. Antinociceptive action (100 mg/kg), *XIIIa*, 49$^+$; *XIIIb*, 60$^+$. Ibu-

profen, used as the standard: carrageenan, 25 mg/kg, 32^+; adjuvant oedema, 100 mg/kg, 49^+; antinociceptive action, 100 mg/kg, 39^+.

In conclusion: Out of the amines prepared, only *Vc* (VÚFB-17 038) showed thymoleptic (potential antidepressant) pharmacological profile: it was active in two tests for antireserpine activity in mice, potentiated the toxicity of yohimbine in mice, and showed mild anticonvulsant action toward electroshock in mice. The acids *XIIIa* and *XIIIb* showed only slight antiinflammatory activity but are more potent than ibuprofen as analgetics.

The compounds prepared were also tested for antimicrobial activity in vitro (microorganisms and the minimum inhibitory concentrations in mg/l are given unless they exceed 100 mg/l): *Streptococcus β-haemolyticus*, *IVb* 16, *IVc* 16, *Vc* 50, *Vd* 16, *XIa* 12·5, *XVII* 32; *Streptococcus faecalis*, *IVb* 16, *IVc* 16, *Vc* 50, *Vd* 32, *XIa* 50; *Staphylococcus pyogenes areus*, *IVb* 16, *IVc* 16, *Vb* 50, *Vc* 25, *Vd* 16, *VIIIa* 50, *VIIIb* 25, *Xb* 50, *XIa* 25, *XVIIb* 64; *Pseudomonas aeruginosa*, *IVb* 64, *IVc* 64, *Vd* 64; *Proteus vulgaris*, *IVb* 64, *IVc* 32, *Vd* 64; *VIIIb* 50, *XIa* 25, *XVIIb* 64; *Escherichia coli*, *IVb* 16, *IVc* 16, *Vd* 32, *XIa* 25, *XVIIb* 64; *Trichophyton mentagrophytes*, *Vd* 50, *VIIIa* 50, *Xb* 25, *XIa* 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 a suitably elevated temperature. The UV spectra (in methanol, λ_{max} in nm ($\log \varepsilon$)) were recorded with a Unicam SP 8 000 spectrophotometer, IR spectra (in Nujol unless stated otherwise, ν in cm^{-1}) with Perkin–Elmer 298 spectrophotometer, ^1H NMR spectra (mostly in $CDCl_3$, δ, J in Hz) with a Tesla BS 487 C (80 MHz) spectrometer, and the mass spectra (*m/z* and %) with the Varian MAT 44S (GC-MS) spectrometer. The homogeneity of the substances and composition of the mixtures were checked by thin-layer chromatography on silica gel (Silufol). The extracts were dried with $MgSO_4$ (Na_2SO_4) or K_2CO_3 and were evaporated under reduced pressure on a rotating evaporator.

2-(2-Bromoethoxy)biphenyl (*IIIa*)

A) 2-Hydroxybiphenyl (17·0 g) ws added to a solution of 6·5 g KOH in 260 ml methanol, the mixture was treated with 37·2 g 1,2-dibromoethane and refluxed for 9 h. Methanol was evaporated in vacuo, the residue was diluted with 10% NaOH and extracted with benzene. Processing of the extract gave 8·0 g (29%) of crude, oily *IIIa* which crystallized on standing and was recrystallized from ethanol, m.p. 65–67°C. IR spectrum: 700, 734, 754 (5 and 4 adjacent Ar—H); 1 015, 1 227 (Ar—O—R); 1 480, 1 502, 1 582, 1 595, 3 015, 3 025, 3 060, 3 080 (Ar). ^1H NMR spectrum: 3·50 t, 2 H (CH_2Br, J = 6·5); 4·20 t, 2 H (CH_2O, J = 6·5); 6·70–7·60 m, 9 H (ArH). For $C_{14}H_{13}BrO$ (277·2) calculated: 60·67% C, 4·73% H, 28·83% Br; found: 60·67% C, 4·78% H, 29·09% Br.

B) A stirred mixture of 8·5 g 2-hydroxybiphenyl, 37·2 g 1,2-dibromoethane and 35 ml methanol was refluxed and treated over 10 min with a solution of 2·8 g KOH in 35 ml methanol. The mixture was refluxed for 5 h, treated with 10 g 1,2-dibromoethane and 3·0 g KOH in 4 ml water, and the refluxing was continued for 3·5 h. Processing like under *A*) gave 7·3 g (53%) of *IIIa*, m.p. 60–63°C (ethanol).

C) A mixture of 9·2 g 2-hydroxybiphenyl, 3·7 g KOH, 40 g 1,2-dibromoethane, 2 ml water, and 15 ml tert. butyl alcohol was refluxed for 1 h, treated with 20 g 1,2-dibromoethane and 3·0 g KOH in 4 ml water, refluxed for 1·5 h, and allowed to stand overnight. Further 1·5 g KOH in 2 ml water were added, the mixture was refluxed for 1 h and processed; 12·2 g (81%) of *IIIa*, m.p. 59—64°C (ethanol).

2-(5-Bromopentoxy)biphenyl (*IIId*)

A solution of 3·5 g KOH and 8·5 g 2-hydroxybiphenyl in 100 ml methanol was treated with 23 g 1,5-dibromopentane and the mixture was refluxed for 18 h. After cooling, the mixture was filtered, the filtrate was evaporated, the residue was diluted with 2M-NaOH and extracted with a 1 : 1 mixture of benzene and ether. The extract was washed with water and processed; the inhomogeneous residue was chromatographed on 250 g neutral Al_2O_3 (activity II). Elution with benzene gave 7·9 g (50%) of almost homogenenous *IIId* which was distilled, b.p. 188—190°C/1·3 kPa. Ref.[18], b.p. 134—136°C/1·3 Pa (prepared differently). ^{1}H NMR spectrum: 1·60 m, 6 H (3 CH_2 in positions 2, 3, 4 of pentyl); 3·28 t, 2 H (CH_2Br, J = 7·0); 3·78 t, 2 H (CH_2O, J = 7·0); 6·70 to 7·60 m, 9 H (ArH). For $C_{17}H_{19}BrO$ (319·2) calculated: 63·96% C, 6·00% H, 25·03% Br; found: 63·94% C, 6·25% H, 25·14% Br.

Ethyl N-(2-(2-Biphenylyloxy)ethyl)-N-methylcarbamate (*VIIa*)

A stirred solution of 8·5 g *VIa* (ref.[7]) in 50 ml benzene was treated over 10 min with a solution of 7·8 g ethyl chloroformate in 20 ml benzene, added dropwise. The mixture was stirred for 30 min at 60—70°C and refluxed for 5 h. After cooling the mixture was diluted with benzene, washed with dilute hydrochloric acid (1 : 1) and water, dried, and evaporated; 9·5 g (90%) of oily *VIIa* which crystallized from a mixture of benzene and light petroleum, m.p. 35—38°C. IR spectrum: 701, 729, 752, 770 (5 and 4 adjacent Ar—H); 1 169 (C—O of ester); 1 230 (Ar—O—R); 1 500, 3 060 (Ar); 1 700 (NCOOR); 2 710 (N—CH_3). ^{1}H NMR spectrum: 1·22 t, 3 H (CH_3 of ethyl, J = 7·0); 2·75 bs, 3 H (NCH_3); 3·52 t, 2 H (CH_2N, J = 7·0); 4·08 bt, 2 H (CH_2OAr, J = 7·0); 4·12 q, 2 H ($COOCH_2$, J = 7·0); 6·70—7·60 m, 9 H (ArH). For $C_{18}H_{21}NO_3$ (299·4) calculated: 72·21% C, 7·07% H, 4·68% N; found: 72·06% C, 7·05% H, 4·58% N.

Ethyl N-(3-(2-Biphenylyloxy)propyl)-N-methylcarbamate (*VIIb*)

In analogy to *VIIa*: Refluxing of 17·1 g *VIb* (ref.[7]) with 15·0 g ethyl chloroformate in 40 ml benzene for 6 h gave 19·0 g (90%) of crude, oily *VIIb* which was chromatographed on 480 g neutral Al_2O_3 (activity II). Benzene eluted first the less polar components and then the homogeneous *VIIb* which remained oily. ^{1}H NMR spectrum: 1·20 t, 3 H (CH_3 of ethyl, J = 7·0); 1·90 m, 2 H (CH_2 in position 2 of propyl); 2·75 s, 3 H (NCH_3); 3·28 t, 2 H (CH_2N, J = 7·0); 3·95 t, 2 H (CH_2O, J = 7·0); 4·08 q, 2 H ($COOCH_2$, J = 7·0); 6·80—7·60 m, 9 H (ArH). For $C_{19}H_{23}$·NO_3 (313·4) calculated: 72·81% C, 7·40% H, 4·47% N; found: 72·42% C, 7·69% H, 4·23% N.

N-Methyl-N-(2-(2-Biphenylyloxy)ethyl)amine (*Va*)

A mixture of 23·5 g *VIIa*, 22 g KOH, and 35 ml ethanol was stirred and refluxed for 9·5 h. Ethanol was evaporated in vacuo, the residue was diluted with water and extracted with benzene. From the benzene layer the basic product was extracted with 3M-HCl, the aqueous solution was made alkaline with NH_4OH and the released base was isolated by extraction with benzene; 17·3 g (97%) of oily *Va*. It was dissolved in 20 ml ethanol and the solution was treated with a solution

of HCl in ether; 17·9 g of hydrochloride melting at 153–155°C (ethanol). For $C_{15}H_{18}ClNO$ (263·8) calculated: 68·30% C, 6·88% H, 13·44% Cl, 5·31% N; found: 68·33% C, 6·90% H, 13·34% Cl, 5·34% N.

A sample of this salt was decomposed with NH_4OH and the homogeneous base was isolated by extraction with ether and used for recording the ^1H NMR spectrum: 1·65 bs, 1 H (NH); 2·35 s, 3 H (NCH_3); 2·82 bt, 2 H (CH_2N, $J = 7·0$); 4·03 t, 2 H (CH_2O, $J = 7·0$); 6·80–7·60 m, 9 H (ArH).

N-Methyl-N-(3-(2-Biphenylyloxy)propyl)amine (*Vb*)

In analogy to *Va*: Refluxing of 12·2 g *VIIb*, 11·4 g KOH and 20 ml ethanol for 9 h gave 9·2 g (98%) of crude, oily *Vb*. Hydrochloride, m.p. 141–143°C (ethanol). For $C_{16}H_{20}ClNO$ (277·8) calculated: 69·18% C, 7·26% H, 12·76% Cl, 5·04% N; found: 69·12% C, 7·28% H, 12·68% Cl, 5·21% N. ^1H NMR spectrum of the released base *Vb*: 1·62 bs, 1 H (NH); 1·90 m, 2 H (CH_2 in position 2 of propyl); 2·30 s, 3 H (NCH_3); 2·62 t, 2 H (CH_2N, $J = 7·0$); 4·02 t, 2 H (CH_2O, $J = 7·0$); 6·80–7·70 m, 9 H (ArH).

N-Methyl-N-(4-(2-Biphenylyloxy)butyl)amine (*Vc*)

A solution of 6·0 g *IIIc* (refs[15,18]) in 65 ml ethanol was treated with 32 ml 40% aqueous solution of methylamine and the mixture was stirred for 5 h at room temperature. After standing overnight, 21 ml 40% aqueous methylamine were added and the stirring at room temperature was continued for 8 h. It was evaporated in vacuo, the residue was diluted with 10% NaOH, and extracted with benzene. The extract was washed with water and then shaken with excessive 3M-HCl. The aqueous layer was made alkaline with NH_4OH and the base was extracted with benzene. Processing of the extract gave 3·6 g (72%) of oily *Vc* which was transformed to 3·7 g of hydrochloride, m.p. 141–143°C (ethanol). Ref.[15], m.p. 142–144°C. A sample of this salt was decomposed with NH_4OH, the homogeneous oily base *Vc* was isolated by extraction with ether and used for recording the spectra. IR spectrum: 699, 751 (5 and 4 adjacent Ar—H); 1 053, 1 233, 1 260 (Ar—O—R); 1 500, 1 581, 1 594, 3 020, 3 055 (Ar), 2 790 (N—CH_3); 3 310 (NH). ^1H NMR spectrum: 1·40 bs, 1 H (NH); 1·70 m, 4 H (2 CH_2 in positions 2 and 3 of butyl); 2·32 s, 3 H (NCH_3); 2·51 bt, 2 H (CH_2N, $J = 7·0$); 3·95 t, 2 H (OCH_2, $J = 7·0$); 6·80–7·60 m, 9 H (ArH).

N-Methyl-N-(5-(2-biphenylyloxy)pentyl)amine (*Vd*)

In analogy to *Vc*: A solution of 7·9 g *IIId* in 90 ml ethanol was reacted with 60 ml 40% methylamine in water (stirring for 17 h); 3·7 g (56%) of crude oily *Vd*. Hydrochloride, m.p. 143–145°C (ethanol). IR spectrum: 705, 755 (5 and 4 adjacent Ar—H); 1 043, 1 055, 1 233 (Ar—O—R); 1 482, 1 503, 1 584, 1 586, 3 015 (Ar); 2 440, 2 465, 2 500 (NH_2^+). For $C_{18}H_{24}ClNO$ (305·8) calculated: 70·69% C, 7·91% H, 11·59% Cl, 4·58% N; found: 70·67% C, 8·15% H, 11·85% Cl, 4·36% N.

A sample of the released, homogeneous base was used for recording the ^1H NMR spectrum: 1·20–2·00 m, 7 H (3 CH_2 in positions 2, 3, 4 of pentyl and NH); 2·35 s, 3 H (NCH_3); 2·48 t, 2 H (CH_2N, $J = 7·0$); 3·88 t, 2 H (CH_2O, $J = 7·0$); 6·70–7·60 m, 9 H (ArH).

1-(2-(2-Biphenylyloxy)ethyl)-4-methylpiperazine (*VIIIa*)

A mixture of 5·6 g *IIIa* and 6·0 g 1-methylpiperazine was stirred and heated to 130°C. The excess of 1-methylpiperazine was evaporated in vacuo, the residue was diluted with water and extracted

with benzene. The benzene layer was shaken with an excess of dilute hydrochloric acid (1 : 1), the aqueous layer was made alkaline with NH_4OH, and the base was extracted with benzene. Processing of the extract gave 5·3 g (88%) of crude oily *VIIIa* which was transformed to the dihydrochloride crystallizing from 98% ethanol as the hemihydrate, m.p. 205–209°C. For $C_{19}H_{26}Cl_2N_2O + 0{\cdot}5\,H_2O$ (378·4) calculated: 60·31% C, 7·19% H, 18·74% Cl, 7·41% N; found: 59·76% C, 6·73% H, 18·82% Cl, 7·27% N.

A sample of the homogeneous oily base was released from the hydrochloride similarly as in the preceding cases and was used for recording the ^{1}H NMR spectrum: 2·20 s, 3 H (NCH_3); 2·40 bs, 8 H (4 CH_2N of piperazine); 2·70 t, 2 H (remaining CH_2N, J = 6·0); 4·03 t, 2 H (CH_2O, J = 6·0); 6·70–7·60 m, 9 H (ArH).

1-(3-(2-Biphenylyloxy)propyl)-4-methylpiperazine (*VIIIb*)

In analogy to *VIIIa* : *IIIb* (5·8 g) and 6·0 g 1-methylpiperazine were reacted for 16 h at 130°C; 5·2 g (84%) of crude, oily *VIIIb*. Dihydrochloride, m.p. 198–202°C (ethanol). For $C_{20}H_{28}Cl_2N_2O$ (383·4) calculated: 62·66% C, 7·36% H, 18·50% Cl, 7·31% N; found: 62·64% C, 7·67% H, 18·50% Cl, 7·20% N.

^{1}H NMR spectrum of the released base: 1·85 m, 2 H (CH_2 in position 2 of propyl); 2·20 s, 3 H (NCH_3); 2·35 bs, 10 H (5 CH_2N); 3·97 t, 2 H (CH_2O, J = 6·0); 6·70–7·60 m, 9 H (ArH).

2-(4-(2-(2-Biphenylyloxy)ethyl)-1-piperazinyl)ethanol (*IXa*)

In analogy to *VIIIa* : *IIIa* (6·9 g) and 10·0 g 2-(1-piperazinyl)ethanol were reacted for 10·5 h at 130°C; 7·7 g (95%) of oily *IXa*, which was transformed to the dihydrochloride, m.p. 188–192°C (methanol–ether). For $C_{20}H_{28}Cl_2N_2O_2$ (399·4) calculated: 60·15% C, 7·07% H, 17·75% Cl, 7·02% N; found: 59·98% C, 7·15% H, 18·00% Cl, 6·96% N.

^{1}H NMR spectrum of the released base: 2·40 s, 8 H (4 CH_2N of piperazine); 2·45 t and 2·65 t, 2 + 2 H (remaining 2 CH_2N, J = 6·0; 6·0); 2·72 bs, 1 H (OH); 3·55 bt, 2 H (CH_2O in the ethanol chain, J = 6·0); 4·03 t, 2 H (CH_2OAr, J = 6·0); 6·70–7·60 m, 9 H (ArH).

3-(4-(2-(2-Biphenylyloxy)ethyl)-1-piperazinyl)propanol (*Xa*)

In analogy to *VIIIa* : *IIIa* (5·5 g) and 8·6 g 3-(1-piperazinyl)propanol[22] were reacted for 12 h at 140°C; 6·3 g (93%) of oily *Xa* which was transformed to the dihydrochloride, m.p. 205–209°C (methanol). For $C_{21}H_{30}Cl_2N_2O_2$ (413·4) calculated: 61·01% C, 7·32% H, 17·15% Cl, 6·78% N; found: 61·29% C, 7·48% H, 17·16% Cl, 6·68% N.

^{1}H NMR spectrum of the released base: 1·65 m, 2 H (CH_2 in position 2 of propyl); 2·40 bs, 8 H (4 CH_2N of piperazine); 2·50 t and 2·63 t, 2 + 2 H (remaining 2 CH_2N, J = 6·0; 6·0); 3·70 t, 2 H (CH_2O in the propanol chain, J = 6·0); 4·00 t, 2 H (CH_2OAr, J = 6·0); 4·30 flat band, 1 H (OH); 6·70–7·60 m, 9 H (ArH).

3-(4-(3-(2-Biphenylyloxy)propyl)-1-piperazinyl)propanol (*Xb*)

In analogy to *VIIIa* : *IIIb* (5·8 g) and 8·6 g 3-(1-piperazinyl)propanol[22] were reacted for 12 h at 140°C; 6·2 g (89%) of oily *Xb* which was transformed to the dihydrochloride, m.p. 210–214°C (ethanol). For $C_{22}H_{32}Cl_2N_2O_2$ (427·4) calculated: 61·82% C, 7·55% H, 16·59% Cl, 6·55% N; found: 62·03% C, 7·75% H, 16·50% Cl, 6·54% N.

Spectra of the released base were measured. UV spectrum: 244 (4·01), 282 (3·57). IR spectrum (film): 699, 751 (5 and 4 adjacent Ar—H); 1 053 (CH_2OH); 1 153, 1 232 (Ar—O—R); 1 481,

1 501, 1 581, 1 594, 3 023, 3 055 (Ar); 3 300 (OH). ^{1}H NMR spectrum: 1·75 m, 4 H (2 CH_2 in positions 2 of the propyl chains); 2·40 m, 12 H (6 CH_2N); 3·75 t, 2 H (CH_2O in the propanol chain, J = 7·0); 3·95 t, 2 H (CH_2OAr, J = 7·0); 4·40 bs, 1 H (OH); 6·80—7·60 m, 9 H (ArH).

N-(1-Benzyl-4-piperidyl)-2-(2-bifenylyloxy)ethylamine (*XIa*)

In analogy to *VIIIa* : *IIIa* (3·3 g) and 5·7 g 4-amino-1-benzylpiperidine[23] were reacted for 12·5 h at 130°C; 4·6 g (theoretical) of the crude, oily *XIa*, which was transformed to the dihydrochloride hemihydrate, m.p. 247—250°C. For $C_{26}H_{32}Cl_2N_2O + 0{\cdot}5\ H_2O$ (468·5) calculated: 66·66% C, 7·10% H, 15·14% Cl, 5·98% N; found: 66·12% C, 7·03% H, 15·45% Cl, 5·74% N.

^{1}H NMR spectrum of the released base: 1·00—2·70 m, 10 H ($CH_2CH_2NCH_2CH_2$ of piperidine and CHNH); 2·80 t, 2 H (CH_2N in oxyethylamino, J = 6·0); 3·40 s, 2 H (NCH_2Ar); 3·98 t, 2 H (OCH_2, J = 6·0); 6·70—7·60 m, 9 H (ArH).

3-(2-Biphenylyloxy)propionitrile (*XIIa*)

Sodium (0·3 g) was added to 51·0 g 2-hydroxybiphenyl, the mixture was heated to 120—135°C and at this temperature, 21·5 g acrylonitrile were added dropwise under stirring. The stirred mixture was heated for 5·5 h to 130—140°C, after cooling the mixture was diluted with 10% NaOH and distributed between water and ether. The organic layer was washed with 10% NaOH, water, and 1·5M-HCl, dried, and evaporated. The residue (38·6 g, 58%) crystallized from ethanol, m.p. 71—73°C. UV spectrum: 243·7 (4·10), 280 (3·62). IR spectrum: 700, 730, 752 (5 and 4 adjacent Ar-H); 1 042, 1 223 (Ar—O—R); 1 500, 1 580, 3 028, 3 065 (Ar); 2 243 (R—CN). ^{1}H NMR spectrum: 2·60 t, 2 H (CH_2CN, J = 7·0); 4·04 t, 2 H (CH_2OAr, J = 7·0); 6·70—7·60 m, 9 H (ArH). For $C_{15}H_{13}NO$ (223·3) calculated: 80·69% C, 5·87% H, 6·27% N; 80·95% C, 5·86% H, 6·14% N.

1,2-Bis(2-biphenylyloxy)ethane (*XVIII*)

Compound *IIIa* (11·1 g) was added over 10 min to a stirred mixture of 2·2 g NaCN and 20 ml dimethyl sulfoxide at 55—60°C. The mixture was stirred for 45 min at 75—80°C and allowed to stand overnight. It was diluted with 100 ml water and extracted with benzene. The extract was washed with 6M-HCl and water, dried, and evaporated. The solid residue (7·2 g) gave by crystallization 5·0 g (69%) of *XVIII* melting at 99—101°C. Analytical sample, m.p. 100—102°C (acetone). Mass spectrum (EI and CI): 367 (M^+, $C_{26}H_{22}O_2$), 197 (96), 181 (54), 179 (80), 169 (68), 152 (100), 141 (37), 115 (40). UV spectrum: 245 (4·35), 283 (3·93). IR spectrum (KBr): 700, 758 (5 and 4 adjacent Ar—H); 1 126, 1 220 (Ar—O—R); 1 480, 1 500, 1 581, 1 600, 3 020, 3 045 (Ar). ^{1}H NMR spectrum: 4·14 s, 4 H (OCH_2CH_2O); 6·70 m, 18 H (ArH). For $C_{26}H_{22}O_2$ (366·4) calculated: 85·21% C, 6·05% H; found: 85·63% C, 6·23% H.

4-(2-Biphenylyloxy)butyronitrile (*XIIb*)

A stirred solution of 2·2 g NaCN in 20 ml dimethyl sulfoxide was treated at 55—60°C with 11·6 g *IIIb*, added over 10 min. The mixture was stirred for 45 min at 75—80°C, after cooling diluted with 100 ml water, and extracted with benzene. The extract was washed with 6M-HCl and water, dried, and evaporated. The residue was distilled in vacuo; 7·8 g (83%), b.p. 210 to 212°C/2·1 kPa. For analysis, a sample of the distillate was chromatographed on silica gel. The homogeneous *XIIb* was eluted with benzene (the less polar components with cyclohexane and cyclohexane–benzene) and was redistilled, b.p. 174°C/1·9 kPa. IR spectrum (film): 700, 754 (5 and 4 adjacent Ar—H); 1 122, 1 230, 1 260 (Ar—O—R); 1 481, 1 502, 1 582, 1 596, 3 020,

3 055 (Ar); 2 245 (R—CN). ^{1}H NMR spectrum: 2·00 m, 2 H (CH_2 in position 3 of butyronitrile); 2·30 t, 2 H (CH_2CN, J = 7·0); 4·00 t, 2 H (CH_2OAr, J = 7·0); 6·80—7·60 m, 9 H (ArH). For $C_{16}H_{15}NO$ (237·3) calculated: 80·98% C, 6·37% H, 5·90% N; found: 81·03% C, 6·30% H, 5·86% N.

3-(2-Biphenylyloxy)propylamine (*IVb*)

A) A solution of 4·5 g *XIIa* in 80 ml ether was added over 20 min to a stirred solution of 3·0 g $LiAlH_4$ in 50 ml ether and the mixture was refluxed for 6 h. After cooling it was decomposed under stirring by slow addition of 3 ml water, 3 ml 10% NaOH, and 9 ml water, the mixture was stirred for 30 min, the solid was filtered off, washed with ether, the filtrate was washed with water and extracted with 3M-HCl. The acid aqueous solution was made alkaline with NH_4OH and extracted with benzene. Processing of the extract gave 1·9 g (41%) of *IVb* which was transformed to the hydrochloride, m.p. 134—137°C (acetone–ether). For $C_{15}H_{18}ClNO$ (263·8) calculated: 68·30% C, 6·88% H, 13·44% Cl, 5·31% N; found: 68·43% C, 6·55% H, 13·28% Cl, 5·35% N.

The homogenenous, oily base *IVb*, released from the hydrochloride, was used for recording the spectra. UV spectrum: 243 (3·94), 280 (3·50). IR spectrum (film): 700, 751 (5 and 4 adjacent Ar—H); 1 121, 1 231, 1 260 (Ar—O—R); 1 481, 1 501, 1 582, 1 594, 3 020, 3 055 (Ar); 3 290, 3 368 (NH_2). ^{1}H NMR spectrum: 1·15 bs, 2 H (NH_2); 1·80 m, 2 H (CH_2 in position 2 of propyl); 2·75 t, 2 H (CH_2N, J = 7·0); 4·00 t, 2 H (CH_2OAr, J = 7·0); 6·80—7·50 m, 9 H (ArH).

B) A solution of 1·8 g $LiAlH_4$ in 50 ml ether was stirred and slowly treated with a solution of 5·1 g $AlCl_3$ in 50 ml ether, the mixture was stirred for 5 min and a solution of 5·0 g *XIIa* in 12 ml ether was added dropwise over 5 min. The mixture was stirred and refluxed for 3 h, after cooling it was decomposed by a slow addition of 20 ml 20% NaOH, diluted with 30 ml benzene, stirred for 10 min, and the solid was filtered off. It was washed with benzene, the filtrate was separated, the aqueous layer was extracted with benzene, and the organic layers were combined. They were extracted with dilute hydrochloric acid (1 : 1), the aqueous solution was made alkaline with NH_4OH and the base was extracted with benzene; 3·8 g (75%) of *IVb* which afforded the hydrochloride, identical with that obtained under *A*).

4-(2-Biphenylyloxy)butylamine (*IVc*)

In analogy to *IVb* under *B*): $LiAlH_4$ (2·1 g) in 40 ml ether was reacted with 6·0 g $AlCl_3$ in 40 ml ether and the reagent obtained was used to reduce 6·2 g *XIIb* in 20 ml ether; 4·3 g (68%) of *IVc*. Hydrochloride, m.p. 165—168°C (ethanol). For $C_{16}H_{20}ClNO$ (277·8) calculated: 69·18% C, 7·26% H, 12·76% Cl, 5·04% N; found: 68·79% C, 7·30% H, 12·68% Cl, 4·95% N. Ref.[15], m.p. 155—158°C (the base was prepared differently).

The released base was used for recording spectra. UV spectrum: 245·5 (3·86), 282 (3·44). IR spectrum (film): 699, 752 (5 and 4 adjacent Ar—H); 1 121, 1 232, 1 260 (Ar—O—R); 1 482, 1 502, 1 581, 1 593, 3 020, 3 058 (Ar); 3 290, 3 368 (NH_2). ^{1}H NMR spectrum: 1·10 bs, 2 H (NH_2); 1·60 m, 4 H (2 CH_2 in positions 2 and 3 of butyl); 2·60 t, 2 H (CH_2N, J = 7·0); 3·92 t, 2 H (CH_2OAr, J = 7·0); 6·80—7·60 m, 9 H (ArH).

Ethyl 3-(2-Biphenylyloxy)propionimidate (*XIVa*)

A solution of 6·7 g *XIIa* in 30 ml ether, 1·5 ml ethanol, and 20 ml chloroform was saturated with dry HCl (2·3 g). The mixture was allowed to stand overnight at 0°C, diluted with ether, the crystalline product was filtered, washed with ether, and dried in vacuo; 8·7 g (96%) of *XIVa* hydrochloride, m.p. 136·5—138°C. IR spectrum: 700, 730, 750 (5 and 4 adjacent Ar—H); 1 040,

1 052, 1 235, 1 260 (Ar—O—R); 1 475, 1 502, 1 563, 1 582, 1 598 (Ar); 1 648 (C=N); infl. 2 660 (NH_2^+); infl. 3 100 (NH). For $C_{17}H_{20}ClNO_2$ (305·8) calculated: 66·77% C, 6·59% H, 11·59% Cl, 4·58% N; found: 66·98% C, 6·56% H, 11·44% Cl, 4·44% N.

Ethyl 4-(2-Biphenylyloxy)butyrimidate (*XIVb*)

In analogy to *XIVa*: *XIIb* (4·7 g) gave similarly 5·9 g (94%) of *XIVb* hydrochloride, m.p. 114 to 117°C (ethanol–ether). IR spectrum: 704, 750 (5 and 4 adjacent Ar—H); 1 056, 1 240 (Ar—O—R); 1 484, 1 502, 1 583, 1 599 (Ar); 1 655 (C=N); 2 660 (NH_2^+); 3 150, 3 230 (NH). For $C_{18}H_{22}Cl.NO_2$ (319·8) calculated: 67·59% C, 6·93% H, 11·09% Cl, 4·38% N; found: 67·24% C, 6·84% H, 11·14% Cl, 4·59% N.

Ethyl 3-(2-Biphenylyloxy)propionate (*XVa*)

Hydrochloride of *XIVa* (3·4 g) was treated with 12 ml water and refluxed for 4 h. After cooling, the product was isolated by extraction with ether and distilled; 2·3 g (77%) of *XVa*, b.p. 170 to 172°C/1·5 kPa. UV spectrum: 245·6 (4·09), 283 (3·66). IR spectrum (film): 700, 732, 755, 770 (5 and 4 adjacent Ar—H); 1 030, 1 180, 1 228, 1 260 (Ar—O—R and C—O of ester); 1 481, 1 500, 1 582, 1 586, 3 020, 3 055 (Ar); 1 732 (RCOOR'). ^{1}H NMR spectrum: 1·20 t, 3 H (CH_3 of ethyl, J = 7·0); 2·65 t, 2 H (CH_2COO, J = 7·0); 4·05 t, 2 H (CH_2OAr, J = 7·0); 4·18 q, 2 H ($COOCH_2$, J = 7·0); 6·80—7·70 m, 9 H (ArH). For $C_{17}H_{18}O_3$ (270·3) calculated: 75·53% C, 6·71% H; found: 75·11% C, 6·72% H.

Ethyl 4-(2-Biphenylyloxy)butyrate (*XVb*)

In analogy to *XVa*: *XVb* hydrochloride (6·4 g) gave by hydrolysis 4·9 g (85%) of *XVb*, b.p. 164 to 166°C/1·3 kPa. IR spectrum: 700, 735, 755, 772 (5 and 4 adjacent Ar—H); 1 055, 1 175, 1 232, 1 260 (Ar—O—R and C—O of ester); 1 485, 1 504, 1 585, 3 020, 3 060 (Ar); 1 730 (RCOOR'). ^{1}H NMR spectrum: 1·21 t, 3 H (CH_3 of ethyl, J = 7·0); 2·05 m, 2 H (CH_2 in position 3 of propionate residue); 2·38 t, 2 H (CH_2COO, J = 7·0); 3·95 t, 2 H (CH_2OAr, J = 7·0); 4·10 q, 2 H ($COOCH_2$, J = 7·0); 6·80—7·70 m, 9 H (ArH). For $C_{18}H_{20}O_3$ (284·3) calculated: 76·03% C, 7·09% H; found: 76·19% C, 7·33% H.

3-(2-Biphenylyloxy)propionic Acid (*XIIIa*)

A mixture of 4·5 g *XIIa* and 18 ml 85% H_3PO_4 was stirred for 2 h at 80°C, for 5 h at 120°C, and for 5 h at 150°C, and was poured into 80 ml ice-cold water. The product was extracted with ether, the extract was shaken with excessive 10% NaOH, the separated aqueous solution was acidified with hydrochloric acid and the released acid was isolated by extraction with ether; 4·4 g(90%) of *XIIIa*, m.p. 93—95°C (benzene–light petroleum). UV spectrum: 244·5 (4·10), 283·4 (3·65). IR spectrum: 705, 759 (5 and 4 adjacent Ar—H); 920, 1 215, 1 710, 2 625, infl. 3 150 (COOH); 1 032, 1 259 (Ar—O—R); 1 486, 1 501, 1 582, 1 598 (Ar). ^{1}H NMR spectrum: 2·72 t, 2 H (CH_2COO, J = 7·0); 4·20 t, 2 H (CH_2OAr, J = 7·0); 6·80—7·60 m, 9 H (ArH); 11·50 bs, 1 H (COOH). For $C_{15}H_{14}O_3$ (242·3) calculated: 74·36% C, 5·82% H; found: 74·19% C, 5·72% H.

4-(2-Biphenylyloxy)butyric Acid (*XIIIb*)

A mixture of 4·7 g *XVb* and 16 ml hydrochloric acid was stirred and heated for 9 h to 135—145°C under reflux. The mixture was then diluted with water and the product was extracted with benzene. From benzene it was transferred into 15% Na_2CO_3, the separated alkaline solution was

acidified with hydrochloric acid, and the released *XIIIb* was isolated by extraction with a mixture of benzene and ether; 3·8 g (90%), m.p. 87—89°C (benzene–light petroleum). UV spectrum: 240·3 (4·09), 282·9 (3·64). IR spectrum: 700, 735, 755 (5 and 4 adjacent Ar–H); 950, 1 052, 1 260, 1 700, 2 570, 2 610, 2 660, infl. 3 060 (COOH); 1 230 (Ar—O—R); 1 480, 1 501, 1 582, 1 592 (Ar). ^{1}H NMR spectrum: 2·00 m, 2 H (CH_2 in position 3 of butyric acid residue); 2·45 t, 2 H (CH_2COO, J = 7·0); 3·98 t, 2 H (CH_2OAr, J = 7·0); 6·80—7·60 m, 9 H (ArH); 11·30 bs, 1 H (COOH). For $C_{16}H_{16}O_3$ (256·3) calculated: 74·98% C, 6·29% H; found: 75·20% C, 6·32% H.

4-(2-Biphenylyloxy)butyramidine (*XVIb*)

A solution of 6·9 g *XIVb* hydrochloride in 17 ml methanol was treated with 5 ml methanol, saturated with NH_3. The mixture was allowed to stand for 6 days at room temperature, the solvent was evaporated in vacuo and the remaining hydrochloride of *XVIb* was crystallized from a mixture of 20 ml acetone and 20 ml 1-butanol; 5·7 g (90%), m.p. 145—147°C. UV spectrum: 245 (4·04), 281 (3·61). IR spectrum: 700, 758 (5 and 4 adjacent ArOH); 1 040, 1 050, 1 122, 1 232, 1 260 (Ar—O—R); 1 482, 1 500, 1 565, 1 581, 1 591 (Ar); 1 690 (C = N^+); 2 715, 2 755, 2 790 (= NH_2^+); 3 218, 3 320, 3 388 (NH, NH_2). ^{1}H NMR spectrum (CD_3SOCD_3): 2·00 bm, 2 H (CH_2 in position 3 of the butyric acid residue); 2·52 bt, 2 H (CH_2 in position 2, J = 7·0); 4·00 bt, 2 H (CH_2OAr, J = 7·0); 6·80—7·60 m, 9 H (ArH). For $C_{16}H_{19}ClN_2O$ (290·8) calculated: 66·08% C, 6·59% H, 12·19% Cl, 9·64% N; found: 66·40% C, 6·63% H, 12·21% Cl, 9·85% N.

2-(3-(2-Biphenylyloxy)propyl)-4,5-dihydroimidazole (*XVIIb*)

A mixture of 14·3 g *XIVb* hydrochloride, 4·5 g ethylenediamine and 15 ml ethanol was kept for 30 h at 65—70°C. The solvent was evaporated in vacuo, the residue was treated with NH_4OH, and the base was extracted with a mixture of benzene and ether. Processing of the extract gave 10·1 g (98%) of *XVIIb*, m.p. 99—101°C (acetone). UV spectrum: 241·4 (4·11), 282·7 (3·63). IR spectrum: 702, 727, 746, 775 (5 and 4 adjacent Ar—H); 1 055, 1 230, 1 259 (Ar—O—R); 1 481, 1 500, 1 581, 1 597 (Ar); 1 609 (C=N); 3 060, 3 130 (NH). ^{1}H NMR spectrum: 2·10 m, 4 H (CH_2CH_2C<); 3·40 s, 4 H (NCH_2CH_2N of imidazoline); 3·98 t, 2 H (CH_2OAr, J = 7·0); 4·20 bs, 1 H (NH); 6·70—7·70 m, 9 H (ArH). For $C_{18}H_{20}N_2O$ (280·4) calculated: 77·11% C, 7·19% H, 9·99% N; found: 77·08% C, 7·29% H, 9·85% N.

Hydrogen maleate, m.p. 81—84°C (acetone–ether). Mass spectrum: 280 (M^+, $C_{18}H_{20}N_2O$, 2), 170 (10), 152 (5), 111 (25), 98 (15), 84 (100). For $C_{22}H_{24}N_2O_5$ (396·4) calculated: 66·65% C, 6·10% H, 7·07% N; found: 66·61% C, 6·31% H, 7·13% N.

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