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SYNTHESES BASED ON β-PHENYLETHYLAMINES
VII. SYNTHESIS AND MASS-SPECTROMETRIC PROPERTIES OF BIS-2-BENZYLTETRAHYDROISOQUINOLINE BASES

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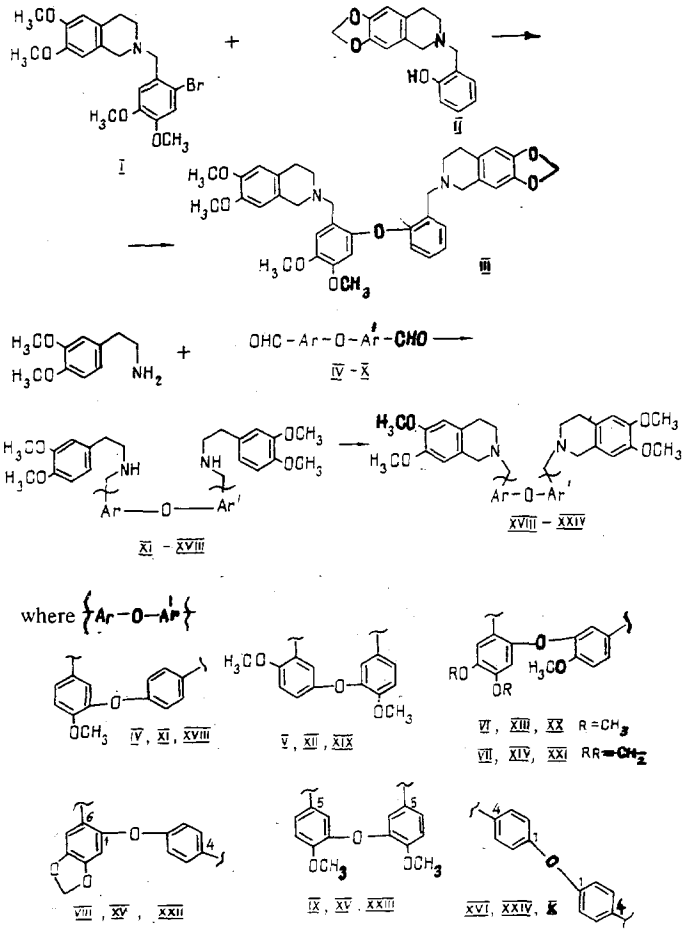
The Pictet–Spengler condensation of bis-β-phenylethylbenzylamines with a central diphenyl ether group has given a new series of substituted bis-2-benzyltetrahydroisoquinolines the fragmentation of which under electron impact is determined by the properties that are characteristic for the monomeric compounds and is associated with the successive elimination of the two tetrahydroisoquinoline nuclei, the features of which depend on the mutual positions of the substituents in the diphenyl ether part of the molecule.

Among the bisbenzyltetrahydroisoquinoline alkaloids and their analogues a number of drugs possessing high biological activity have been found [1, 2]. In view of this, particular interest is presented by the synthesis of compounds of a new bis-2-benzyltetrahydroisoquinoline series consisting of two molecules of a N-benzyltetrahydroquinoline of the type of sendaverine [3] linked by an ether bond. Two approaches to the synthesis of this type of bases are possible that differ by the order of introduction of the oxygen bridge. In the first case, performance of the Ullman condensation of two substituted 2-benzyltetra-



Scheme 1

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TABLE 1. Mass Number (m/z), Letter Designations, Elementary Compositions, and Relative Intensities (%) of the Key Ions in the Spectra of Compounds (XVIII-XXI)

XVIII	610 ($M^{+\cdot}$, 4), 447 [(a+H)$^+$, (a_1+H)$^{+\cdot}$, $C_{27}H_{31}N_2O_4$, 18], 445 [(a-H)$^+$, 2], 435 ($C_{26}H_{29}NO_5$, 11), 419 [(c+H)$^{+\cdot}$, $C_{25}H_{29}NO_4$, 33], 418 (c^+, 17), 417 [(c-H)$^{+\cdot}$, 8], 406 (4), 405 (4), 404 (4), 285 (4), 284 (5), 272 (4), 254 [(a-d_1)$^+$, $C_{16}H_{15}NO_2$, 36], 243 ($C_{15}H_{15}O_3$, 51), 241 (14), 228 [(c-d_1+H_2)$^{+\cdot}$, 10], 227 [(c-d_1+H)$^+$, $C_{15}H_{15}O_2$, 75], 226 (c-d_1)$^{+\cdot}$, 23], 211 (15), 206 (f^+, 15), 192 (d^+, 100), 189 ($C_{11}H_{11}NO_2$, 42), 164 ($в^{+\cdot}$, 74), 152 (25), 151 (20), 121 (22)
XIX	540 ($M^{+\cdot}$, 7), 491 ($C_{29}H_{35}N_2O_5$, 6), 477 [(a+H)$^+$, 3], 475 [(a-H)$^+$, 1], 449 [(c+H)$^{+\cdot}$, $C_{27}H_{31}NO_5$, 53], 448 (c^+, 14), 447 [(c-H)$^{+\cdot}$, 20], 434 ($C_{26}H_{22}NO_5$, 6], 432 ($C_{26}H_{26}NO_5$, 7), 319 (5), 284 [(a-d_1)$^+$, $C_{17}H_{18}NO_3$, 9], 258 [(c-d_1+H_2)$^{+\cdot}$, $C_{16}H_{18}O_3$, 41], 257 [(c-d_1+H)$^+$, $C_{15}H_{17}O_3$, 53], 256 [(c-d_1)$^{+\cdot}$, $C_{15}H_{16}O_3$, 31], 241 (11), 206 (f^+, $C_{12}H_{16}NO_2$, 19), 204 (5), 192 (d^+, $C_{11}H_{14}NO_2$, 100), 189 (47), 164 ($в^{+\cdot}$, $C_{10}H_{12}O_2$, 63), 121 (23)
XX	670 ($M^{+\cdot}$, 1), 505 [(a-H)$^+$, 1], 479 [(c+H)$^{+\cdot}$, $C_{28}H_{33}NO_5$, 36], 478 (c^+, 10), 477 [(c-H)$^{+\cdot}$, $C_{28}H_{31}NO_6$, 22], 464 (2), 452 (3), 357 (2), 342 (3), 329 (2), 328 (3), 315 (3), 288 [(c-d_1+H_2)$^{+\cdot}$, $C_{17}H_{20}O_4$, 29], 287 [(c-d_1+H)$^+$, $C_{17}H_{19}O_4$, 54], 286 [(c-d_1)$^{+\cdot}$, 55], 285 (15), 271 ($C_{16}H_{15}O_4$, 13), 269 ($C_{17}H_{17}O_3$, 4), 269 ($C_{16}H_{13}O_4$, 3), 255 (28), 239 (7), 224 ($C_{15}H_{12}O_2$, 6), 207 ($C_{12}H_{17}O_2$, 15), 206 (11), 192 (d^+, $C_{11}H_{14}NO_2$, 100), 189 (36), 164 ($в^{+\cdot}$, 42), 137 (13)
XXI	654 ($M^{+\cdot}$, 4), 489 [(a-H)$^+$, 1], 477 (1), 463 [(c+H)$^{+\cdot}$, 57], 462 (c^+, 15), 461 [(c-H)$^{+\cdot}$, 48], 448(3), 446(5), 432(5), 341(3), 326(8), 298 [(a—d_1)$^+$, 2)], 272 (c—d_1+H_2)$^{+\cdot}$, 29], 271 [(c—d_1+H)$^+$, 57], 270 [(c-d_1)$^{+\cdot}$, 69], 269 [(c—d_1—H)$^+$, 19], 255(11), 253(10), 239(32), 206 (f^+, 9), 192(100), 189(29), 176(10), 164($в^{+\cdot}$, 38), 151(10), 121(13)

*In other cases the alternative variant of an ion has ben omitted from the Table.

hydroisoquinoline fragments (I and II). In the second case, the preparation of the diphenyl ethers (IV-X), followed by the addition of β-phenylethylamines to them and the Pictet–Spengler cyclization of the resulting compounds (XI-XVII). We have tested both methods of synthesizing bis-2-benzyltetrahydroisoquinolines of this type (scheme 1). The yield of desired product by the first method was 10% (calculated on the (I)), and by the second method 40%, calculated on the corresponding diphenyl ether (VI, VII).

In spite of the fact that the first method permits the synthesis of a molecule the two parts of which differ by the substituents in both the tetrahydroisoquinoline and the benzyl fragments, we performed the syntheses by the second method, which has a clear advantage in the yield of products (XVIII-XXIV). The preparation of the diphenyl ethers (IV-X) and of the amines (XI-XVII) has been described in detail in the preceding communication [4]. The yields of the secondary (XI-XVII) and tertiary (XVIII-XXIV) amines were practically independent of the positions of the substituents in the benzyl parts of the molecules.

The structures of the bis-2-benzyltetrahydroisoquinoline bases synthesized (XVIII-XXIV) were studied by PMR and mass spectrometry (see the Experimental part).

No detailed study of the mass spectra of bis-2-benzyltetrahydroisoquinoline bases with a central diphenyl ether group has previously been made. Nevertheless, the presence of two monotypical structural elements leads to the appearance of unusual fragmentation processes. It is interesting to compare the behavior of these compounds with that of the monomeric N-benzyl-

TABLE 2. Stabilities of the Molecular Ions and Contributions of the Fragments to the Total Ion Currents in the Mass Spectra of Compounds (XVIII-XXI)

Ion	XVIII	XIX	XX	XXI
$M^{+\cdot}$	0.4	1.1	0.3	0.6
$(a+H)^+$	2.1	0.2	—	—
$(a-H)^+$	0.2	0.2	0.1	0.1
$(c+H)^{+\cdot}$	4.0	7.2	5.7	9.1
c^+	2.0	1.8	1.8	2.2
$(c-H)^{+\cdot}$	0.9	2.6	3.6	7.3
$(a-d_1)^+$	4.5	1.2	—	0.2
$(c-d_1+H_2)^{+\cdot}$	0.8	4.0	3.5	3.0
$(c-d_1+H)^+$	8.3	6.8	6.4	6.4
$(c-d_1)^{+\cdot}$	2.5	4.5	9.1	9.1
d^+	10.0	12.7	15.0	15.0
$b^{+\cdot}$	8.1	6.7	6.4	5.5

tetrahydroisoquinolines and the noncyclic bisbenzylphenylethylamines [4]. The former give relatively stable molecular ions, and the main directions of breakdown are: benzyl cleavage with localization of the charge on the benzyl or the tetrahydroisoquinoline fragment, and the retrodiene reaction (RDR) in the heterocyclic nucleus [5, 6]. Pant et al. [5] have also established features of the breakdown of these compounds in the regime of recording negative ions in the EI source. As shown in our previous paper [4], in the spectra of the bis-2-benzyltetrahydroisoquinolines with a central diphenyl group one- and two-stage processes of cleavage of the benzyl bonds compete under the influence of the relative positions of the ether bridge and the phenylalkylamino substituent.

In the present paper we give the results of investigations of the mass spectra of four examples (XVIII-XXI) of the bis-2-benzyltetrahydroisoquinolines synthesized (Table 1). They show a combination of the properties of the two groups of compounds mentioned above. The stability of the molecular ions has an intermediate value (Table 2). With respect to this index the compounds under consideration are greatly inferior to the bis-1-benzyltetrahydroisoquinoline bases [7], which is due to the absence from them of an ether bridge between the tetrahydroisoquinoline nuclei. The instability of the system as a whole leads to a decrease in the contributions of doubly charged ions. Here, simultaneously, the selectivity of fragmentation is lowered, mainly because of the large number of intense peaks in the region of low and medium mass numbers (see Table 1).

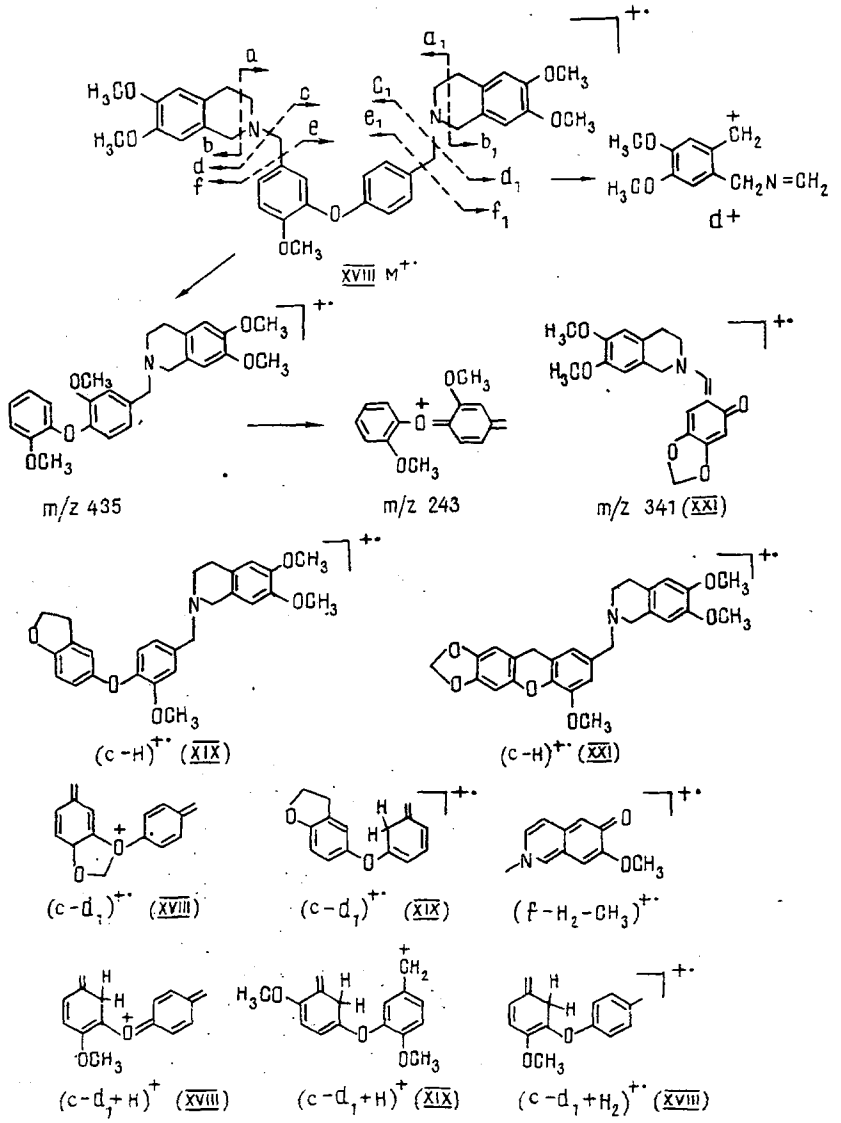
A distinctive feature of the breakdown processes for the bis-2-benzyltetrahydroisoquinoline bases of the given type along the lines a↔b (RDR) and c↔d (scheme 2) consists in the fact that in all cases the probability of an alternative localization of the charge ($a^{+\cdot}$ and $b^{+\cdot}$, c^+ and d^+) is high. However, the contribution of the ions formed in cleavages along the line a↔b was greatly inferior to the contribution of the fragments arising through cleavage along the line c↔d. This difference became greater with an increase in the number of substituents in the diphenyl ether part of the molecule. Thus, the peaks of the $(a + H)^+$ ions had a medium intensity in the spectrum of (XVIII) and a low intensity in the spectrum of (XIX), while in the spectra of (XX) and (XXI) only very weak peaks of the $(a - H)^+$ ions appeared (see Tables 1 and 2).

The intensities of the peaks of the main products of the RDR — the ions $b^{+\cdot}$ — were far greater, but they decreased in the series of compounds (XVIII—XXI).

The opposite tendency existed in the case of cleavages along the line c↔d. In all the spectra the peaks of the dimethoxydihydroisoquinoline cations $d^{+\cdot}$ with m/z 192 showed 100% intensity, but at the same time the contribution of this ion for the trimethoxy-substituted (XX) was somewhat higher than for (XVIII). The ion $d^{+\cdot}$ was most probably stabilized by an additional cleavage of the C—C bond of the tetrahydroisoquinoline nucleus (scheme 2). Alternative participants in the process of cleavage along line c↔d were stabilized in the form of $(c + H)^+$ ions including a fragment with the methylenecyclohexadiene structure, the probability of the appearance of which rises in the case of *meta*-substitution [4]. In agreement with this rule, the contributions of the $(c + H)^-$ ions had increased in the spectra of (XIX-XXI) as compared with (XVIII) (see Table 2).

In the spectra of compounds (XIX-XXI), as compared with the spectrum of compound (XVIII), the contribution of the $(c - H)^{+\cdot}$ ion had increased. The migration of hydrogen to the more saturated neutral fragment can be explained by the forma-

tion of stable polycyclic ions; with a dihydrofuran structure on the breakdown of compound (XIX) and a xanthene structure in the case of compounds (XX) and (XXI) (see scheme 2).



Scheme 2

For a number of reasons breakdown along the line e↔f was observed in the spectra of compounds (XVIII-XXI). The peaks of the f^+ ions with m/z 206 ($C_{12}H_{16}O_2N$) had intensities of 9-19% (see Table 1). The e^+ ions coincide in mass numbers with the $(c + H - CH_3)^+$ and therefore could not be detected even with he aid of metastable transition spectra.

Of considerable importance in the spectra of the compounds of the series under consideration is the successive elimination of the elements of two tetrahydroisoquinoline nuclei. The greatest contribution among particles of this type was given by the nitrogen-free ions $(c - d_1)^{+\cdot}$, $(c - d_1 + H)^+$, and $(c - d_1 + H)^{+\cdot}$ formed by the cleavage of two benzyl bonds. These ion varieties were present in all the spectra, but their relative amounts depended substantially on the mutual positions of the substituents and the presence of additional functional groups (see Table 2). According to this, the structures of monotypical ions could be different, as, for example, the structures of the $(c - d_1)^{+\cdot}$ ions in the spectra of compounds (XVIII) and (XIX) (see scheme 2). In individual cases (XIX) the $(c - d_1 + H)^+$ ions were formed by the same mechanism as in the bisphenylethylbenzylamines [4], but in the case of compond (XVIII) this ion most probably included elements of a quinoid structure (see scheme 2). A distinguishing property of bis-2-benzyltetrahydroisoquinoline derivatives was the formation of the $(c - d_1 + 2H)^{+\cdot}$ ions (Tables 1 and 2), which obviously contained methylenecyclohexadiene and tolyl fragments. A specific property of compounds (XX) and (XXI) was the formation of the $(c - d_1 - H)^+$ ions. They had as precursors the $(c - H)^+$ ion (Tables 3 and 4) and contained their xanthene structure arising because of the *ortho-* position of the ether bridge and the benzyl substituent [4].

TABLE 3. Mass Numbers (m/z) and Relative Intensities (%) of the Parental Ions Calculated from the MD Spectra f the Daughter Ions

Compound	Daughter ion	Parental ions
XVIII	419	610(100), 447(8)
	254	447(100), 435(21), 405(13)
	243	435(100), 272(54)
	227	419(100), 406(21), 285(18), 254(30)
	192	447(20), 435(100), 419(73)
XIX	449	640(100)
	284	477(100)
	258	449(100), 284(22)
	192	449(100),
	189	447(20), 432(10), 204(100)
	164	192(100)
XX	479	670(100)
	288	479(100)
	286	477(100), 315(10)
	271	464(45), 286(100)
	269	479(2), 286(100)
	255	286(100)
	192	329(100)

TABLE 4. Mass Numbers (m/z) and Relative Intensities (%) of the Daughter Ions Calculated from the B/E = const. Spectra of the Parental Ions

Compound	Parental ion	Daughter ions
XVIII	610	435(3), 419(100), 241(2), 227(2), 192(3)
	447	419(79), 254(100)
	435	406(90), 404(90), 254(100), 243(25), 192(20)
	419	227(100) 192(60)
	254	227(100), 211(85)
XIX	640	449(100)
	449	434(100), 418(30), 258(23), 257(35), 256(48)
	432	284(22), 256(59), 241(35), 189(100)
	284	256(100), 241(8)

Another pathway of the successive elimination of the tetrahydroisoquinoline substituents was the formation of $(a - d_1)^+$ ions, the magnitudes of the contributions of which decrease in parallel with the fall in the height of the peak of the $(a + H)^+$ ion. The link between these ions was confirmed by the corresponding metastable transitions. In their turn, the $(a - d_1)^+$ ions acted as precursors of the $(c - d_1 + H)^+$ (XVIII) or $(c - d_1)^+$ (XIX) ions (see Tables 3 and 4).

In each of the spectra there was the fairly intense peak of an ion with m/z 189, composition $C_{11}H_{11}O_2N$, coresponding to a dimethoxyquinoline cation. However, the MD and B/E = const. spectra (see Tables 3 and 4) indicated an isomeric structure. Precursors of the ions under consideration in the spectrum of compound (XIX) were fragments with m/z 447, 432, and 204. Taken all together, this means that the origin of the m/z 189 ion was $(f - 2H - CH_3)$ (see scheme 2).

The spectrum of compound (XVIII) contained intense peaks of ions with m/z 435 and 243 having larger numbers of oxygen atoms than could be the case with the standard bond cleavages. On the basis of the spectra of the metastable ions (see Tables 3 and 4) it is possible to assume the following pathway for the formation of these fragments: the m/z 435 ion arose from M^+ on the migation of one of the methoxy groups of the isoquinoline part of the molecule to the diphenyl ether part and phenyl cleavage. Subsequent breakdown took place along the line $c_1 \leftrightarrow d_1$ and gave the m/z 243 ions (see scheme 2).

The compounds in which the ether bridge was present in the *ortho-* position to a benzyl substituent, (XX) and (XXI), were characterized by weakly expressed processes involving breakage of the bridge bond. In addition to the simple cleavage of a C–O bond, leading to ions with m/z 328 and 342 (XX) and 328 and 326 (XXI), a rearrangement with migration of a benzyl hydrogen atom to a carbon atom of the neutral fragment [4, 8] and the formtion of ions with m/z 357 (XX) and 341 (XXI), was observed (see scheme 2).

The authors thank V. V. Takhistov for participating in a discussion of the paper.

EXPERIMENTAL

For the conditions of the mass-spectrometric experiemnt, see [4].

Preparation of the Amine (III). With stirring, 1.12 g (0.008 mole) of potash was added to a solution of 0.6 g (0.002 mole) of N-(2-hydroxybenzyl)-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline in 25 ml of dry pyridine. The mixture was heated in a current of nitrogen at 110-115°C for 3 h, and then 0.8 g (0.0018 mole of N-(6-bromo-3,4-dimethoxybenzyl)-6,7 dimethoxy-1,2,3,4-tetrahydroisoquinoline and 1 g (0.0012) mole of CuO were added. The resulting mixture was heated for 10 h.

After the end of the reaction, the inorganic substances were filtered off, the solvent was distilled off under vacuum, and the products were extracted with ethyl acetate. The residue after evaporation of the solvent was purified on a column of silica gel (1:15) with elution by benzene and ether. Yield 0.13 g (10%), mp of the hydrochloride 204-210°C (acetone), composition $C_{37}H_{40}O_7N_2$. Mass spectrum, m/z (%), 624 ($M^{+\cdot}$, 3), 192 (100), 176 (83), 164 (35), 151 (28).

General Procedure for the Pictet–Spengler Cyclization of the Amines (XI-XVII). A solution of 0.0034 mole of the hydrochloride of one of the amines (XI-XVII) [4] in 150 ml of methanol was treated with 14 ml of 30% formalin and 3 drops of conc. HCl to give a strongly acid medium, and the mixture was boiled under reflux for 2 h. The methanol was distilled off, and the residue was diluted with water, made alkaline with ammonia, and extracted with ether. The ethereal solution was washed with water and was dried with sodium sulfate. The residue after the solvent had been distilled off yielded the cyclization product, which was purified via the hydrochloride.

The Hydrochlorides of Amines (XVIII-XXIV) were obtined by mixing acetone or acetone-methanol (3:1) solutions of the technical bases (XVIII-XXIV) with conc. HCl to give a weakly acid reaction. The salt that precipitated was separated off and was recrystallized from a suitable solvent.

5″,6′-Bis(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-ylmethyl)-2″-methoxy-3′,4′-methylenedioxydiphenyl ether (XXI) was obtained from 4.1 g (0.0065 mole of the hydrochloride of 5″,6′-bis(3,4-dimethoxyphenethylaminomethyl)-2″-methoxy-3′,4′-methylenedioxydiphenyl ether (XIV). Yield 4.01 g (94%), mp of the hydrochloride 230-232°C (from acetone). Composition $C_{38}H_{42}O_8N_2$. PMR spectrum (δ, ppm): 2.60 (br.s, 8H, CH_2), 3.30-3.60 (8H, $N-CH_2$), 3.70 (s, 15H, OCH_3), 5.80 s (OCH_2O), 6.25-7.15 (11 H, aromatic protons).

5″,6′-Bis(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-ylmethyl)-2″,3′,4′-trimethoxydiphenyl ether (XX) was obtained under analogous conditions from 2.21 g (0.0034 mole) of the hydrochloride of 5″,6′-bis(3,4-dimethoxyphenethylaminomethyl)-2″,3′,4′-trimethoxydiphenyl ether (XIII). Yield 1.37 g (60%), mp of the hydrochloride 205-207°C (from acetone–methanol (3:1)). Composition $C_{39}H_{46}O_8N_2$.

5′,5″-Bis(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-ylmethyl)-2′,2″-dimethoxydiphenyl ether (XXIII) was obtained from 2.81 g (0.0045 mole) of the hydrochloride of 5′,5″-bis(3,4-dimethoxyphenethylaminomethyl)-2′,2″,-dimethoxydiphenyl ether (XVI). Yield 2.33 g (80%), mp of the hydrochloride 168-170°C (from acetone). Composition $C_{38}H_{44}O_7N_2$. PMR spectrum (δ, ppm): 2.60 (8H, $-CH_2$), 3.48 s, 3.51 (s, 8H, $-CH_2$), 3.75 s, 3.77 (s, 18H, OCH_3), 6.30-7.25 (12 H, aromatic protons).

5′,5″-Bis(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-ylmethyl)-2′,4″-dimethoxydiphenyl ether (XIX) was obtained analogously from 0.81 g (0.0013 mole) of the hydrochloride of 5′,5″-bis(3,4-dimethoxyphenethylaminomethyl)-2′,4″,-dimethoxydiphenyl ether. Yield 63 g (75%), mp of the hydrochloride 195-197°C (from acetone–ethanol (3:1)). Composition $C_{38}H_{44}O_7N_2$. PMR spectrum (δ, ppm): 2.60 (t, 8H, CH_2), 3.40-3.50 (8H, $-CH_2$), 3.73 s, 3.75 (s, 18H, OCH_3), 6.30-7.20 (12H, aromatic protons). Mass spectrum (m/z, %): 640 ($M^{+\cdot}$, 0.3), 449 [(c + H)$^{+\cdot}$, 2], 447 (1), 341 ($C_{20}H_{23}NO_4$, 2), 329 (12), 328 (15), 286 (11), 255 [(c-d-H)$^+$, 38], 241 (4), 206 (10), 192 (100), 184 (14), 164 (69), 137 (70).

4″,5′-Bis(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-ylmethyl)-2′-methoxydiphenylether (XVIII) wasobtainedfrom 1.10 g (0.0016 mole) of the hydrochloride of 4″,5′-bis(3,4-dimethoxyphenethylaminomethyl)-2′-methoxydiphenyl ether. Yield

0.75 g (65%), mp of the hydrochloride 160-162°C (from acetone). Composition $C_{37}H_{42}O_5N_2$. PMR spectrum (δ, ppm): 2.62 (t, 8H, CH_2), 3.48-3.52 (8H, $-CH_2$), 3.73 s, 3.75 (s, 15H, OCH_3), 6.40-7.25 (14 H, aromatic protons).

4′,4″-Bis(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-ylmethyl)-diphenyl ether (XXIV) was obtained analogously from 2.11 g (0.0037 mole) of the hydrochloride of 4′,4″-(3,4-dimethoxyphenethylaminomethyl)diphenyl ether (XVII). Yield 2.01 g (90%), mp of the hydrochloride 206-206°C [sic] (from acetone–methanol (4:1)). Composition $C_{34}H_{40}O_5N_2$. PMR spectrum (δ, ppm): 2.70 (t, 8H, CH_2), 3.49 s, 3.52 (s, 8H, $-CH_2$), 3.73 s, 3.75 s (12H, OCH_3), 6.40-7.25 (13H, aromatic protons). Mass spectrum (m/z, %): 580 ($M^{+\cdot}$, 1), 388 (c^+, 6), 376 (2), 348 (2), 346 (2), 313 (6), 312 ($C_{19}H_{22}NO_3$, 6), 302 (5), 282 (2), 208 (7), 192 (d^+, 15), 164 ($b^{+\cdot}$, $C_{10}H_{12}O_2$, 100), 152 (22), 151 (10), 121 (32).

REFERENCES

1. O. N. Tolkachev, Khim. Prir. Soedin., 264 (1981).
2. F. S. Sadritdinov and A. G. Kurmukov, The Pharmacology of Plant Alkaloids and their Use in Medicine [in Russian], Meditsina, Tashkent (1980), pp. 78, 82, 247-245.
3. M. Shamma and J. L. Moniot, Isoquinoline Alkaloids Research 1972-1977, Plenum Press, New York (1978), pp. 97 and 142.
4. N. U. Baratov, E. G. Mil'grom, V. I. Vinogradova, Ya. V. Rashkes, and M. S. Yunusov, Khim. Prir. Soedin., 839 (1993) [in this issue].
5. P. Pant, K. P. Madkusudanan, and D. S. Bkakuni, Indian J. Chem., **25B**, 630 (1986).
6. T. Kametani and K. Ohkubo, Tetrahedron Lett., 4317 (1965).
7. J. Baldas, I. R. C. Bick, T. Ibuka, R. S. Kapil, and G. N. Porter, J. Chem. Soc., Perkin Trans. I, 592 (1972).
8. H. Budzikiewicz, C. Djerassi, and D. H. Williams, Mass Spectrometry of Organic Compounds, Holden-Day, San Francisco (1967), p. 251.