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SYNTHETIC ANALOGUES OF Peganum ALKALOIDS

VII. BROMINE-SUBSTITUTED QUINAZOLINE ALKALOIDS AND THEIR ANALOGUES

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The quinazoline bases pentamethylenequinazoline and peganol react with bromosuccinimide in glacial acetic acid to form the corresponding 6-bromoquinazoline derivatives. Some by-products of the bromination reaction have been isolated and characterized. 6-Bromopeganol has been subjected to x-ray structural analysis.

We have previously found that the quinazoline alkaloids peganine (I) and deoxypeganine (DOP, II) form the corresponding 6-bromo derivatives (III) and (IV) on interaction with bromosuccinimide (BSI) in glacial acetic acid [1]. We have continued a study of this reaction on homologues of DOP and have also determined the structures of some minor products.

On the reaction of pentamethylenequinazoline (V) with BSI in acetic acid, 6-bromopentamethylenequinazoline (VI) and a base (VII) with mp 95-96°C were isolated as the main products. The structures of these compounds were shown in a way similar to that for the corresponding compounds in [1]. However, the PMR spectrum of (VII) contained, in addition to signals of the protons of the aromatic and azepine rings, a four-proton singlet at 2.70 ppm. The presence of peaks with m/z 292/294 and 99 in the mass spectrum of (VII) led us to the conclusion that the substance under consideration was a molecular complex of 6-bromopentamethylenequinazolone (VIII) with succinimide (SI) in a ratio of 1:1 (PMR spectrum). For a definitive proof, we synthesized this complex by another method. We first obtained 6-bromopentamethylenequinazolone (VIII) [2], the PMR spectrum of which practically coincided with that of compound (VII), with the exception of the signal at 2.70 ppm. In addition, the R_f values and melting points of compounds (VII) and (VIII) proved to be different. A mixed melting point showed a clear depression. Then the 6-bromopentamethylenequinazolone was heated in glacial acetic acid in the presence of an equimolar amount of succinimide. The product isolated was identical with complex (VII) (PMR spectrum). On HPLC analysis it was found that 6-bromopentamethylenequinazolone (VIII), the molecular complex (VII), and succinimide gave individual peaks (Fig. 2). Although the retention times of the latter two substances differed only slightly, the results obtained permitted an unambiguous conclusion in favor of the individuality of compound (VII).

2,3-Polymethylenequinazolones do not form 6-bromo derivatives under the conditions of this reaction, and therefore 6-bromovasicinone (IX), 6-bromodeoxyvasicinone (X), and the complex of 6-bromopentamethylenequinazolone with SI (VII) could be formed only by oxidation from the corresponding 6-bromoquinazolines during the reaction and in the isolation of the products. The ease of oxidation of 6-bromopeganine was confirmed by its conversion into 6-bromoacetylvasicinone (XI) on acetylation. The structures of (IX) and (X) were confirmed by the formation of identical substances on the potassium permanganate oxidation of 6-bromopeganine (III) and 6-bromo-DOP (IV), respectively.

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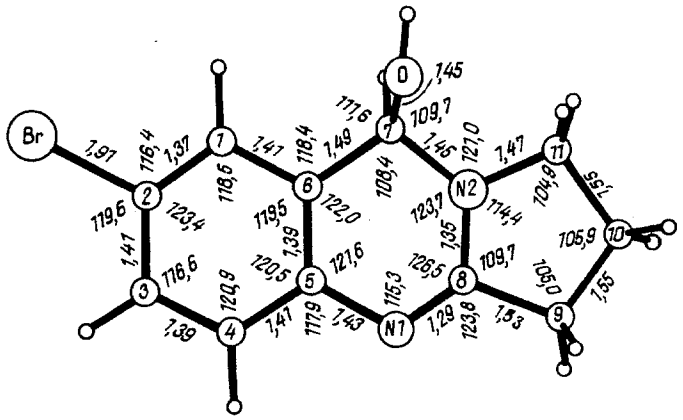


Fig. 1. Structure of the 6-bromopeganol molecule. The errors in the determination of the bond lengths and valence angles are not more than 0.011 Å and 0.7°, respectively.

A compound (XII) with a molecular mass of 370/372/374 was isolated as a minor product of the bromination of pentamethylenequinazoline (V). The absence of a two-proton singlet in the 4.40-4.50 ppm region of the PMR spectrum, the presence of the signals of only two aromatic protons, with meta coupling constants, and the downfield shift of the signal of one of them showed that (XII) had the structure of 6,8-dibromopentamethylenequinazolone. Another minor compound was the tribromo derivative (XIII) with a molecular mass of 448/450/452/454. The proton signals in the aromatic region coincided completely with those for compound (XII), and the third bromine atom was apparently present at C-9. The smallness of the amount of (XIII) did not permit a high-quality PMR spectrum to be obtained. Thus, under the conditions of the given reaction, the most active reaction center is C-6, and C-8 exhibits a far lower activity.

We may mention that we isolated 8-bromodeoxyvasicinone (XIV), together with (X) and (XV), when we performed the reaction of DOP with unpurified BSI in chloroform (see [3]).

The mass spectra of (X) and (XIV) differed by the intensities of certain ions, their UV spectra were very close, their IR spectra had differences in the 1670-1690 and 700-900 cm^{-1} regions, and the most significant differences in their PMR spectra were in the aromatic region, with the signals of the protons of the methylene groups of rings C practically coinciding. In compound (X) the signal of the proton at C-5 was a doublet with a meta coupling constant, and in (XIV) a doublet of doublets with ortho and meta constants.

The main product of this reaction was compound (XV). Its mass spectrum contained the peaks of ions corresponding in mass to 6-bromo-DOP and 6-bromo-DOV and their fragmentation products. However, the PMR spectrum of (XV) differed from that of 6-bromodeoxypeganine by the absence of a two-proton singlet in the 4.30 ppm region, showing the presence of a substituent at C-4. This substituent could not be a carbonyl group, since the UV spectrum of (XV) corresponded to a quinazoline structure. The quniazoline structure was also confirmed by the chemical shifts of the protons in the aromatic region. The presence of the signals from three aromatic protons and of three two-proton multiplets from the methylene groups of ring C was evidence in favor of the assumption that substitution by bromine had taken place in the benzene ring (see top of following page).

On the basis of what has been said above, and taking into account the fact that bromosuccinimide can act as an oxidant and a dehydrating agent [4] we considered two alternatives for (XV): 6-bromopeganol and a symmetrical bimolecular compound consisting of two 6-bromo-DOP molecules linked by an oxygen bridge in the 4–4' position. The choice between the two structures was made on the basis of an x-ray structural analysis unambiguously in favor of the monomolecular structure. The spatial structure of the (XV) molecule is shown in Fig. 1, which also gives the bond lengths and valence angles. When the OH group is left out of account, the molecule is practically planar to within 10.16 Å.

The isolation of the bromopeganol (XV) showed that C-4 is another active center in this reaction. 6-Bromopeganol was isolated as a by-product when the reaction of deoxypeganine with BSI was performed in glacial AcOH. Subsequently, (XV) was obtained by oxidizing 6-bromo-DOP (IV) with potassium permanganate in an acid medium. 6-Bromopeganol was the main

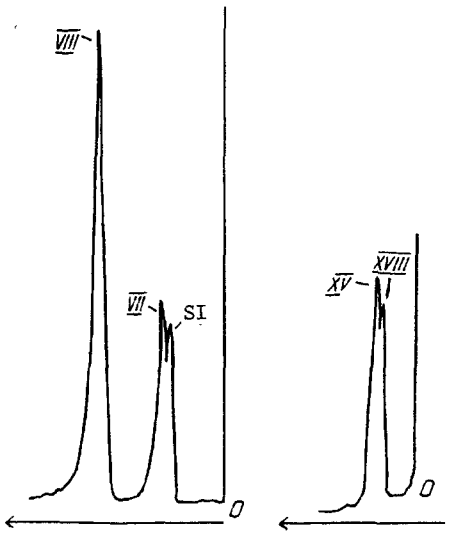
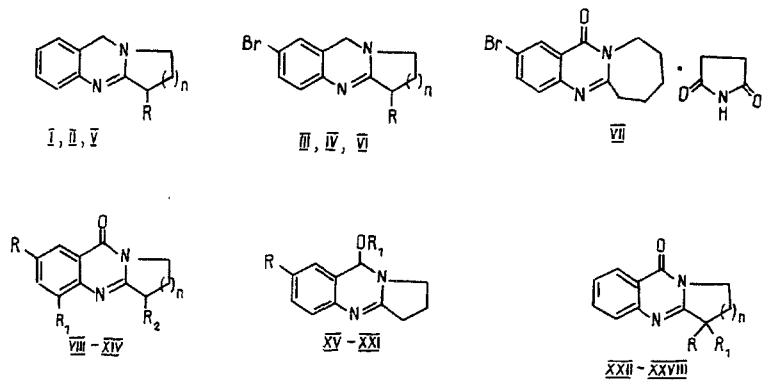


Fig. 2. Chromatogram of a model mixture of 6-bromopentamethylenequinazolone (VIII), the complex compound (VII), succinimide (SI), and 6-bromopeganol (XV) and its ethyl ether (XVIII).



I, III: R=OH, n=1; II, IV: R=H, n=1; V, VI: R=H, n=3; VIII—XIII: R=Br; VIII, XII, XIII: n=3; IX—XI, XIV: n=1, VIII, X: R_1=R_2=H; IX: R_1=H, R_2=OH; XI: R_1=H, R_2=OAc; XII: R_1=Br, R_2=H; XIII: R_1=R_2=Br; XIV: R=R_2=H, R_1=Br; XV: R=Br, R_1=H; XVI: R=R_1=H; XVII—XXI: R=Br; XVII: R_1=CH_3; XVIII: R_1=C_2H_5; XIX: R_1=nC_3H_7; XX: R_1=nC_4H_9; XXI: R_1=t-C_4H_9; XXII, XXIV, XXVIII: n=1; XXIII, XXV: n=2; XXVI, XXVII: n=3; XXII, XXIII, XXVI: R=R_1=H; XXIV, XXV: R=R_1=Br; XXVII, XXVIII: R=H; R_1=Br.

product of the interaction of peganol (XVI) with BSI in acetic acid or chloroform, and also with bromine in chloroform, while DOP (II) did not react with the latter. The reaction of deoxypeganine with bromine in concentrated H_2SO_4 gave both 6-bromo-DOP and 6-bromopeganol.

On being heated with alcohols in an acid medium, 6-bromopeganol readily formed ethers. The hydrochlorides of compounds (XVII)-(XXI) have been obtained. The R_f values of these substances in TLC (SiO_2, Al_2O_3, Silufol; systems: chloroform—benzene—ethanol in various ratios; ethyl acetate—methanol—conc. NH_4OH solution in various ratios) coincided with those of the initial (XV), but it was possible to confirm their formation with the aid of HPLC and mass spectroscopy (see Fig. 2 and the Experimental).

It is known that the reaction of polymethylenequinazolones with BSI in CCl_4 takes place with the formation of 9-monobrominated products. We have shown that when CCl_4 is replaced by acetic acid substitution again takes place at position 9 in ring C, the tri- and tetramethylenequinazolones (XXII) and (XXIII) forming the corresponding 9,9-dibromo derivatives

TABLE 1. Coordinates ($\times 10^4$) of the Nonhydrogen Atoms of the (XV) Molecule

Atom	x	y	z
Br	08671 (2)	2507 (1)	2532 (2)
O	15113 (10)	4064 (4)	7658 (8)
N1	13258 (11)	5817 (5)	4414 (9)
N2	14289 (12)	5540 (5)	7188 (9)
C1	11101 (15)	3761 (6)	4803 (13)
C2	09965 (14)	3587 (7)	3181 (13)
C3	09769 (15)	4137 (7)	1910 (13)
C4	10860 (16)	4884 (7)	2374 (12)
C5	12114 (14)	5063 (6)	4032 (11)
C6	12215 (14)	4516 (6)	5246 (12)
C7	13550 (15)	4674 (6)	7008 (12)
C8	14198 (14)	6007 (6)	5943 (11)
C9	15431 (16)	6809 (7)	6609 (13)
C10	16235 (18)	6767 (7)	8478 (14)
C11	15595 (19)	5909 (7)	8809 (13)

(XXIV) and (XXV), while pentamethylenequinazolone (XXVI) formed only the monobromo derivative (XXVII), as followed from their PMR spectra.

EXPERIMENTAL

PMR spectra were taken in $CDCl_3$, with the exception of (XVI) – in TFA – and (XXIV) – in $CDCl_3$ + CD_3OD.

Bromination of Pentamethylenequinazoline (V) with Bromosuccinimide. With stirring, a solution of 1.68 g of pentamethylenequinazoline hydrochloride in 10 ml of AcOH was added dropwise to a suspension of 1.9 g of BSI in 15 ml of glacial AcOH. The reaction mixture was heated with stirring in the water bath for 2 h, and the acetic acid was distilled off. The residue was made alkaline with concentrated NH_4OH solution and was extracted with chloroform. The chloroform extract was washed with water, dried with Na_2SO_4, and acidified with an ethanolic solution of HCl. The solvent was evaporated off, and the residue was separated on a column of SiO_2, with the isolation of 0.25 g of (VII), 0.5 g of (VI), and 0.05 g of (XII).

6-Bromopentamethylenequinazoline (VI). mp 124-126°C (lit.: 118-120°C [2]). UV spectrum, $\lambda_{max}^{C_2H_5OH}$, nm: 222, 305 (log ε 3.91; 3.87). Mass spectrum: 278/280 (M^+), 277/279 (100%), 263/265, 238/240. PMR spectrum: 1.73 (6H, m, H-10, H-10', H-11, H-11', H-12, H-12'); 2.48 (2H, m, H-9, H-9'); 3.30 (2H, m, H-13, H-13'); 4.48 (2H, s, H-4, H-4'); 6.78 (1H, d, J = 12 Hz, H-8); 6.90 (1H, d, J_m = 1.5 Hz, H-5); 7.22 (1H, dd, J_o = 12 Hz, J_m = 1.5 Hz, H-7).

Complex of 6-Bromopentamethylenequinazolone with Succinimide (VII). mp 95-96°C [hexane–chloroform (4:1)]; hydrochloride, mp 212-213°C. UV spectrum, $\lambda_{max}^{C_2H_5OH}$, nm: 220, 275, 317, 330 (log ε 4.12; 3.78; 3.29; 3.17). IR spectrum, ν_{max}^{KBr}, cm^{-1}: 1695. Mass spectrum: 292/294, 277/279, 248/250, 238/240, 99. PMR spectrum: 1.80 (6H, m): 2.70 (4H, s); 3.00 (2H, m); 4.33 (2H, m); 7.55 (1H, d, J_o = 9 Hz, H-8); 7.75 (1H, dd, J_o = 9 Hz, J_m = 1.5 Hz, H-7); 8.33 (1H, d, J_m = 1.5 Hz, H-5).

6,8-Dibromopentamethylenequinazolone (XII). mp 163-164°C. Mass spectrum: 374/372/370 (M^+), 358/356/354, 330/328/326, 320/318/316. PMR spectrum: 2.10 (6H, m); 4.03 (2H, m); 5.38 (2H, m); 8.08 (1H, d, J_m = 2.5 Hz, H-7); 8.38 (1H, d, J_m = 2.5 Hz, H-5).

6-Bromopentamethylenequinazolone (VIII). This was synthesized as in [2], mp 100-101°C; hydrochloride, mp 232-234°C (decomp.) (lit.: 103-104°C [2]). Mixed melting point with (VII): 84-85°C.

6-Bromovasicinone (IX). With stirring, a solution of 1 g of $KMnO_4$ in 300 ml of acetone–water (1:1) was added dropwise to a suspension of 2 g of (III) in 50 ml of acetone. The acetone was evaporated off, the solid matter was filtered off, and the filtrate was acidified and was treated with chloroform. The residue [from evaporation of the extract*]

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amounted to 0.5 g, mp 187°C; after recrystallization from ethanol, mp 191-193°C. In a direct comparison it proved to be identical with a sample of 6-bromovasicinone obtained as in [1].

6-Bromoacetylvasicinone (XI). a) A mixture of 0.3 g of (IX), 3 ml of Ac_2O, and 0.5 ml of Py was left at room temperature for 5 days. The reagents were evaporated off, and the residue was recrystallized from petroleum ether–ethyl acetate–acetone. The yield was 0.17 g, mp 146-149°C, M^+ 322/324. UV spectrum, $\lambda_{max}^{C_2H_5OH}$, nm: 223, 277, 313, 324 (log ε 4.53, 4.14, 3.61, 3.53). PMR spectrum: 2.07 (3H, s, AcO-9).

b) The acetylation of 1 g of compound (III) was carried out as described above. The reaction products yielded 0.28 g of (XI), which was identified by a direct comparison with the sample obtained above, and 0.50 g of a compound with M^+ 306/308.

The reaction of DOP with bromosuccinimide was carried out in a similar way to that of (V). Starting with 3.5 g of (II), after cooling, 0.7 g of the hydrobromide of 6-bromodeoxypeganine (IV) precipitated. The acetic acid mother liquor was evaporated, the residue was converted into a mixture of bases, and from these, by repeated separation on columns of SiO_2 and Al_2O_3, additional amounts of (IV) (1.4%), 6-bromo-DOB (X) (13%), and 6-bromopeganol (XV) (17%) were obtained; when the reaction was conducted at room temperature the ratio between these substances changed (85, 2, and 1.3%, respectively).

6-Bromodeoxyvasicinone (X). mp 161°C (acetone) (lit.: 157-158°C [2]). UV spectrum, $\lambda_{max}^{C_2H_5OH}$, nm: 225, 274, 314, 327 (log ε 3.91; 3.54; 3.03; 2.96). UV spectrum, ν_{max}^{KBr}, cm^{-1}: 1690, 1620. Mass spectrum: 264/266, 238/240, 222/224, 210/208, 197, 196, 185, 184, 170, 168, 156, 155, 129, 118, 115, 102. PMR spectrum: 2.22 (2H, m, H-10; H-10'); 3.05 (2H, m, H-9, H-9'); 4.10 (2H, t, H-11, H-11'); 7.30 (1H, d, J_o = 9 Hz, H-8); 7.65 (1H, dd, J_o = 9 Hz, J_m = 2.2 Hz); 8.20 (1H, d, J_m = 2.2 Hz, H-5).

6-Bromopeganol (XV). mp 190°C (decomp., chloroform). UV spectrum, $\lambda_{max}^{C_2H_5OH}$, nm: 210, 282. Mass spectrum, m/z (%): 264/266 (100), 263/265 (70), 250/252 (37), 249/251 (86). PMR spectrum: 2.40 (2H, m, H-10, H-10'); 3.40 (2H, m, H-9, H-9'); 4.70 (2H, m, H-11, H-11'); 7.50-8.50 (3H, m, Ar–H).

X-Ray Structural Analysis of Compound (XV). Cell parameters and intensities were measured on a Syntex $P2_1$ diffractometer (Cu Kα radiation): a = 8.040(8), b = 15.565(4), c = 9.367(2) Å, β = 119.09(4)°, V = 1024.3 Å^3, d_{calc} = 1.726 g/cm^3. Space group $P2_1/c$.

The structure was determined by the direct method using the SHELXS-86 program [6] and was refined in the full-matrix isotropic-anisotropic approximation by the SHELXS-76 program [7]. In the calculations we used 1322 reflections with $|F| \geq 4\sigma(|F|)$. The H atoms were inserted geometrically (except for the atom in the OH group) and were refined isotropically. The final value of the discrepancy index R = 0.065 (R_w = 0.064). The coordinates of the nonhydrogen atoms are given in Table 1.

The oxidation of 6-bromodeoxypeganine was effected in a similar way to that of 6-bromopeganine. The yield of (VII) from 0.28 g of the starting compound was 0.22 g.

8-Bromodeoxyvasicinone (XIV). To 1.22 g of the hydrochloride of (II) were added 150 ml of dry chloroform and, in portions, with stirring, 1.5 g of BSI (unpurified). After it has been stirred for 0.5 h, the reaction mixture was washed with 10% NaOH solution (3 × 10 ml) and with water (3 × 20 ml). After drying and evaporation, a light yellow oil remained which crystallized after trituration with acetone; after several recrystallizations, 0.35 g of 6-bromopeganol was isolated. The mother solution was evaporated, the residue was dissolved in 10% H_2SO_4, and the acid solution was washed with chloroform and was then made alkaline and was treated with chloroform. The two chloroform extracts, individually, were separated on SiO_2 columns; the alkaline extract yielded 6-bromopeganol (XV) (0.07 g), and the acid extract 6-bromo-DOV (X) (0.010 g) and 8-bromodeoxyvasicinone (XIV) (0.17 g), mp 115°C. UV spectrum, $\lambda_{max}^{C_2H_5OH}$, nm: 225, 269, 304, 313, 326. IR spectrum, ν_{max}^{KBr}, cm^{-1}: 1670, 1625. Mass spectrum: 266/264, 240/238, 224/222, 210/208, 202, 200, 197, 196, 186, 185, 184, 168, 167, 160, 157, 149, 130, 129, 119, 118, 117, 103, 102. PMR spectrum: 2.30 (2H, m, H-10, H-10'); 3.12 (2H, t, H-9, H-9'); 4.17 (2H, t, H-11, H-11'); 7.60 (2H, m, H-6, H-7); 8.30 (1H, dd, J_o = 9 Hz, J_m = 1.5 Hz, H-5).

Oxidation of 6-Bromo-DOP (IV). 6-Bromopeganol (XV). With stirring, a solution of 0.77 g of $KMnO_4$ in 40 ml of H_2O was added dropwise to a suspension of 2.46 g of the hydrochloride of (IV) in 15 ml of H_2O and 100 ml of 10% H_2SO_4. After the usual working up, chloroform extracts from acid and alkaline media were obtained: 0.53 and 1.1 g, respectively. The recrystallization of 0.5 g [of the material from the acid extract*] from acetone gave 6-bromo-DOV (X), mp 160°C (lit.: 157-158°C [2]); the material from the alkaline extract was washed with acetone–ethanol (1:1), and 1.03 g of 6-bromopeganol (XV) was isolated, with mp 189°C (decomp.).

Bromination of Peganol (XVI), 6-Bromopeganol (XV). With stirring, a solution of 1 g of (XVI) in 20 ml of chloroform was added dropwise to a suspension of 2 g of BSI and 0.02 g of benzoyl peroxide in 10 ml of chloroform. The mixture was heated with stirring for 1 h. Cooling led to the deposition of 0.98 g of a mixture which, after several recrystallizations from ethanol–acetone, gave 0.32 g of the hydrobromide of (XV). The mother solution was converted into a mixture of bases from which an additional amount of impure (XV) and 0.15 g of deoxyvasicinone (XXII) were isolated.

b) Compound (XVI) (0.55 g) was brominated with the aid of BSI in AcOH, as described above. After the appropriate working up, chloroform extracted from an alkaline solution 0.44 g of material the recrystallization of which from ethanol–chloroform gave 0.26 g of (XV).

c) With stirring, a solution of 0.13 ml of bromine in 10 ml of chloroform was added dropwise to a solution of 1 g of peganol in 10 ml of chloroform. After the mixture had been stirred for 0.5 h, the chloroform solution was decanted off from the precipitate that had formed, which was then washed with acetone, yielding 0.36 g of the hydrobromide of (XV). Compounds (XV) and (XVI) were detected in the mother solution by TLC.

Preparation of the Hydrochlorides of the Ethers (XVII)-(XXI). A mixture of 0.5 g of (XV), 10 ml of the appropriate alcohol, and 10 drops of conc. HCl was heated in the water bath for 2-5 h. The solvent was evaporated off and the residue was washed with ethanol–acetone (1:3) or (1:5). In the mass spectra of compounds (XVII)-(XXI) the peaks of the molecular ions had low intensities (1-15%). In each case the strongest peak was that of an ion with m/z 251/249 $(M - OR)^+$.

HPLC Analysis of Compounds (VII), (VIII), (XV), and (XVII)-(XXI). The high-quality separation of 6-bromopentamethylenequinazolone (VIII), the molecular complex (VII), and succinimide, and also of 6-bromopeganol (XV) and its ethers (XVII)-(XXI), was achieved on a Milikhrom microcolumn chromatograph (USSR) using a 2 × 80 mm column with the support Silasorb-C18 (Czechoslovakia) having a particle size of 6 μm. The mobile phase used for compounds (VII) and (VIII) and succinimide was the methanol–water–perchloric acid (70:30:0.1) system at a rate of flow of eluent of 0.2 ml/min. For (XV) and its ethers (XVII)-(XXI) the mobile phase contained the same components in a ratio of 70:30:0.02, and the rate of flow of eluent was 0.05 ml/min. UV detection was conducted at 254 and 298 nm, respectively (see Fig. 2).

6-Bromopentamethylenequinazolone (XXVII). A mixture of 2.5 g of BSI and 2 g of pentamethylenequinazolone (XXVI) in glacial AcOH was heated at 85°C with stirring for 4 h. After the usual working up, the residue was purified on a column of SiO_2 and was then recrystallized from hexane–chloroform: 2.27 g, mp 120-121°C (lit.: 122-123°C [5]). UV spectrum, $\lambda_{max}^{C_2H_5OH}$, nm: 227, 285, 305, 318, ($\log \varepsilon$ 4.25; 3.86; 3.70; 3.58). IR spectrum, ν_{max}^{KBr}, cm^{-1}: 1685, 880, 600. Mass spectrum: 294/292 (M^+), 213, 185, 160. PMR spectrum: 188 (5H, m, H-11, H-11', H-12, H-12', H-10); 2.88 (1H, m, H-10'); 3.85 (1H, m, H-9); 5.23 (2H, m, H-13, H-13'); 7.38 (3H, m, H-6, H-7, H-8); 8.13 (1H, d, J_o = 8 Hz, H-5).

9,9-Dibromotetramethylenequinazolone (XXV). Compound (XXIII) (1 g) was brominated in a similar way to that described above. After working up, the residue was recrystallized from hexane–chloroform (5:1). This gave 0.72 g of (XXV), mp 109-110°C (lit.: 148-149°C [5]). Mass spectrum: 360/358/356 (M^+), 279/277, 278/276, 199. PMR spectrum: 2.26 (3H, m, H-10, H-11, H-11'); 3.05 (1H, m, H-10'); 4.09 (2H, t, H-12, H-12'); 7.72 (3H, m, H-6, H-7, H-8); 8.21 (1H, d, J_o = 7.5 Hz, H-5).

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9,9-Dibromotrimethylenequinazolone (XXIV). Compound (XXII) (3 g) was brominated under the conditions described above. After the appropriate working up, the residue was recrystallized from ethanol–acetone, to give 3.08 g of a product with mp 175°C (decomp.) (lit.: 189-191°C [5]). Mass spectrum: 346/344/342, 265/263, 185, 184. PMR spectrum: 3.30 (2H, m, H-10, H-10'); 4.15 (2H, m, H-11, H-11'); 7.67 (3H, m, H-6, H-7, H-8); 8.35 (1H, dd, J_o = 7.5 Hz, J_m = 1.5 Hz, H-5). By recrystallization after separation on a column of Al_2O_3 the mother liquors yielded very small amounts of the initial (XXII) and of 9-bromo-DOV (XXVIII).

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ALKALOIDS OF THE EPIGEAL PART OF Aconitum orientale

STRUCTURE OF ORGETINE

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From the total alkaloids of the epigeal part of the plant Aconitum orientale have been isolated the known alkaloid kobusine and a new alkaloid, which has been called orgetine. A structure has been put forward for orgetine on the basis of spectral characteristics (IR, PMR, ^{13}C NMR, and mass spectra) and the production of a triacetate.

Continuing the separation of the total alkaloids of the epigeal part of Aconitum orientale [1], we have isolated kobusine and a new base, which has been called orgetine (I).

Orgetine has the composition $C_{20}H_{27}NO_3$. The IR spectrum of the base contained absorption bands of hydroxy groups at 3300-3500 cm^{-1}. The PMR spectrum revealed the signals of a tertiary C-methyl group and a terminal methylene group, and also one-proton signals at (ppm) 3.00 (doublet, J = 12 Hz), 3.82 (broadened singlet), and 3.97 (doublet, J = 5 Hz).

The acetylation of a mixture of orgetine and kobusine with acetic anhydride in the presence of pyridine led to a triacetyl derivative of orgetine (II) in the IR spectrum of which the absorption bands of hydroxy groups had disappeared, which showed the completeness of acetylation. The absence of the signals of an N-alkyl substituent from the PMR spectra of compounds (I) and (II) and the heterocyclic skeleton of the molecule obtained on replacing the hydroxyls by hydrogen permitted orgetine to be assigned to the alkaloids of the hetisine type and to be considered as an isomer with respect to the positions of the hydroxy groups.

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