6. M. Kates, Techniques of Lipidology, North Holland, Amsterdam / American Elsevier, New York (1972).
7. W. M. Ferederiks and S. Brockhoven, J. Chromatogr., 17, 150 (1968).
8. M. E. Mackellian and J. A. G. Larose, Lipids, 9, 455 (1974).
9. É. V. Dyatlovitskaya, T. I. Torkhovskaya, and L. D. Bergel'son, Biokhimiya, 34, No. 1, 177 (1969).

MODIFICATION OF NATURAL COUMARINS REACTION OF KHELLACTONE ESTERS WITH AMINES

Yu. E. Sklyar and N. V. Rodionova

UDC 547.9:582.80

The reaction of diesters of khellactone with primary and secondary amines under mild conditions has given derivatives of 4'-aminodihydroseselin. Under more severe conditions, not only the replacement of a 4'-acyloxy group by an amino group but also the opening of the lactone ring with the formation of the corresponding cinnamamide takes place. The ease of hydrolysis of the 3'-acyloxy group and subsequent esterification of the alcohols formed and also the use of various amines makes it possible to obtain very diverse acyloxy and amino derivatives.

Derivatives of khellactone (I) are widely distributed in plants of the family *Umbelliferae* [1], and a number of these compounds are found in plants of the genus *Seseli* L. [2]. Interest in substances of this type is due to their considerable biological activity and, in particular, their marked spasmolytic action [3] — visnadin, a compound of this class, is used abroad as a spasmolytic agent for the treatment of diseases of the cardiovascular system [4].

The modification of the structure of khellactone esters, for example, by the introduction of an amino group, could considerably modify the activity of these substances and also lead to the formation of compounds, the solubility of salts of which in water would be considerably higher than for the initial lipophilic esters. In order to obtain new biologically

TABLE 1. Synthesis of 4'-Aminocoumarins

Compound	4'-Aminocoumarin		mp, °C	Yield, %	Initial khellactone diester	Method
	R_2	NR_2^3				
IIIa	$COCH_2CH(CH_3)_2$		84	68 9	Ia	A
IIIb	"		142	24,5	Ia	B
IIIc	"	$-\overset{+}{N}H_2-(CH_2)_3CH_3Cl^-$	249 (decomp.)	49,6	Ia	B
IIId	"	$-\overset{+}{N}H_2CH_2CH_2(CH_3)_2Cl$	237 (decomp.)	62,0	Ia	B
IIIe	$COCH_3$		157	53,0	Ib	B
IIIf	"		180	25,0	Ib	B
IIIg	"	$-N(C_2H_5)_2$	111	39,5	Ib	B

All-Union Scientific-Research Institute of Medicinal Plants, Moscow. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 488-499, July-August, 1980. Original article submitted April 8, 1980.

 0009-3130/80/1604-0348$07.50

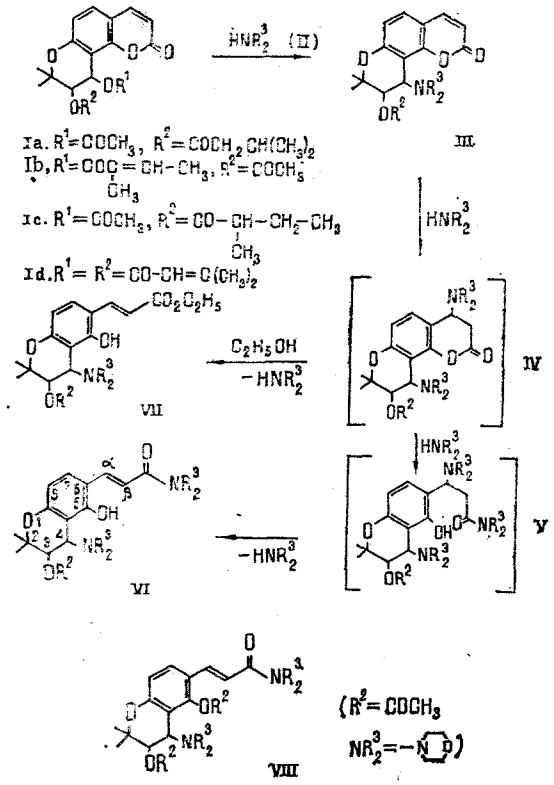
TABLE 2. Characteristics of the PMR Spectra of the 4'-Aminocoumarins

Amino-coumarin	δ, ppm (J, Hz)								
	H_3	H_4	H_5	H_6	$H_{3'}$	$H_{4'}$	$(CH_3)_2C$	NR^2_3	Acyl
IIIa	6,10, d (9)	7,50, d (9)	7,19, d (9)	6,65, d (9)	5,10, d (4)	3,79 d (4)	1,28, s 1,48, s 3 H each	1,45, u.m. 6H, (CH_2—C), 2,67, u.m. 4H (CH_2—N)	0,92, d (8), 6H /C—(CH_3)$_2$/, 2,10, u.m. 2H (CH_2—CO)
IIIb	6,13, d (9)	7,52, d (9)	7,22, d (9)	6,68, d (9)	5,14, d (4)	3,83, d (4)	1,30, s 1,51 s 3 H each	2,69, u.m. 4H, (CH_2—N), 3,59, t (5), 4H (CH_2—O)	0,92, d (8), 6H /C—(CH_3)$_2$/, 2,11, u.m. 2H (CH_2—CO)
IIIc*	6,25, d (9)	7,62, d (9)	7,42, d (9)	6,82, d (9)	5,55, d (4)	4,47, d (4)	1,31, s 1,55, s 3 H each	1,96—2,17, u.m 4H (CH_2—C), 0,94, t (3), 3H (CH_3—C), 3,2 —3,55, u.m. 2H (CH_2—N)	0,96, d (8), 6H /C—(CH_3)$_2$, 2,31—2,40, u.m. 2H (CH_2—CO)
IIId*	6,29, d (9)	7,69, d (9)	7,48, d (9)	6,87, d (9)	5,65, d (7)	4,80, d (7)	1,29, s 1,53, s 3 H each	1,00, t (6), 6H/C—(CH_3)$_2$/ 2,30—2,80, u.m. 3H (CH CH_2), 3,00 -3,40, u.m. 2H (CH_2—N)	0,96, d (8), 6H, /C—(CH_3)$_2$/ 2,00—2,30, u.m. 2H (CH_2—CO)
IIIe	6,13, d (9)	7,53, d (9)	7,28, d (9)	6,66, d (9)	5,10, d (5)	3,81, d (5)	1,30, s 1,49, s 3 H each	1,46, u.m. 6H (CH_2—C), 2,69, u.m. 4H (CH_2—N)	2,02, s 3H (CH_3—CO)
IIIf	6,14, d (9)	7,53, d (9)	7,23, d (9)	6,66, d (9)	5,12, d (4)	3,85, d (4)	1,30, s 1,51, s 3 H each	2,60—2,80, u. m. 4H (CH_2—N), 3,51, t (4), 4H (CH_2—O)	2,02, s 3H (CH_3—CO)
IIIg	6,10, d (9)	7,53, d (9)	7,18, d (8)	6,64, d (8)	5,07, d (6)	3,97, d (6)	1,22, s 1,38, s 3 H each	1,00, tr (7), 6H (CH_3—C), 2,67, sept (6), 4H(N<CH_2—, CH_2—)	2,06. s, 3H (CH_3—CO)
IIIh*	6,24, d (9)	7,62, d (9)	7,23, d (9)	6,74, d (9)	3,86, d (8)	3,58, d (8)	1,21, s 1,53, s 3 H each	1,53, s 6H (CH_3—C), 2,40—2,70, u.m. 2H (CH_2—N), 2,90—3,30, u.m. 2H (CH_2—N)	—
IIIi*	6,16, d (9)	7,55, d (9)	7,34, d (9)	6,77, d (9)	5,37, d (4)	4,03, d (4)	1,35, s 1,53, s 3 H each	1,35, s 6H (CH_2—C), 2,65, u.m. 4H (CH_2—N)	7,87, d (8) and 7,89 d (8) (H_2 and H_6 in benzoyl) 7,50—7,20, m, 3H(H_3, H_4 and H_5)

*$CDCl_3$; the spectra of the other compounds were recorded in CCl_4.

active agents we have investigated the reaction of khellactone esters with amines. A number of derivatives of 3'-(α-methylbutyryloxy)-4'-amino-3',4'-dihydroseselin has been synthesized previously [5] by the reaction ofvisnadin with amines. By the same method we have obtained derivatives of 4'-amino-3',4'-dihydroseselin from dihydrosamidin (Ia) and pteryxin (Ib) (Table 1). The structures of the compounds are unambiguously shown by their PMR spectra (Table 2). The presence in a spectrum of the signals of the H_3, H_4, H_5, H_6, H_3', and $(CH_3)_2C$ protons and of those of an acyl residue at C_3' close to the signals of the initial khellactone diester and the upfield shift of the signal from H_4' show that the amino group is present in position 4'. In the hydrochlorides (IIIc) and (IIId), the H_4' signal is shifted downfield as compared with the corresponding signals of the other substances, which were isolated in the form of bases.

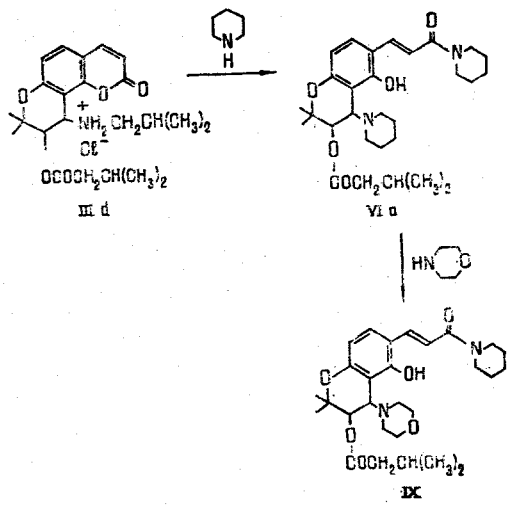
However, even when the reaction was performed under mild conditions, together with derivatives of 4'-amino-3',4'-dihydroseselin, a more polar substance with a blue fluorescence in UV light was formed. When a mixture of compound (Ia) and pyridine was heated without a solvent, the main product was a substance with mp 194-195°C. The NMR spectrum of this reaction product, $C_{29}H_{42}N_2O_5$, showed the signals of groups of protons interacting with one another (J = 9 Hz) geminal to the acloxy and amino groups (5.40 ppm, d, and 4.08 ppm, d, respectively), of ortho aromatic protons (6.16 ppm, d, and 7.19 ppm, d, J = 9 Hz), and of transprotons on a double bond (7.41 ppm, d, and 6.83 ppm, d, J = 16 Hz). The IR spectrum showed a strong amide band at 1640 cm^{-1} and absorption bands of the OH group at 3400 and 3200 cm^{-1}. These facts correspond to the structure (VIa).



Scheme 1. Reaction of khellactone diesters with amines.

Thus, the reaction of compound (I) with an amine leads to an opening of the lactone ring with the formation of a 4-aminochromane derivative. The reaction apparently takes place via the intermediate compounds (IV) and (V), since the lactone ring in 3,4-dihydrocoumarins opens far more readily; the splitting out of pyridine from the unstable intermediate compound (V) leads to the more stable trans derivative (VI). At the same time, the reaction of compound (IVa) with ethanol formed the ester (VII) (R^2, isovaleroyl: NR_2^3, piperidino), which it was possible to isolate in very small amounts from the mother liquor remaining from the crystallization of (VIa).

The structure (VI) contains two fragments which, according to available information, may be responsible for a psychotropic action of substances containing them — trans-cinnamamide and 4-aminochromane [6, 7]. In view of this, we have prepared by a monotypical method from dihydrosamidin (Ia), pteryxin (Ib), visnadin (Ic), and khellactone diseneciоate (Id) and



Scheme 2. Transamination reaction.

various amines a series of 4-aminochromates the constants and main characteristics of which are given in Table 3, and their PMR spectra in Table 4.

The acyl residues in the aminocoumarins (III) and aminochromanes (VI) were the same as in the initial natural khellactone esters (I). For the synthesis of compounds (III) and (VI) containing other acyl residues it was necessary to obtain the corresponding alcohols. The acid or alkaline hydrolysis of (IIIa) gave a good yield of (IIIh) (R^2 = —H). The alkaline hydrolysis of (VIa) and (VIb) likewise gave the alcohols (VIi) (R^2 = H, NR_2^3 = piperidino) and (VIk) (R^2 = H, NR_2^3 = morpholino), respectively, but in the acid hydrolysis of (VIa), as the result of the saponification of the amide, isomerization, and subsequent closure of a lactone ring, the alcohol (IIIh) was obtained. The acylation of (IIIh) with acetic anhydride and with benzoyl chloride gave the acetate (IIIc) and the benzoate (IIIi) (R^2 = —COC_6H_5). The acetylation of (VIi) under mild conditions gave (VId); under more severe conditions the phenolic hydroxyl also took part in the reaction, which led to the formation of the diacetate (VIII) from (VIk).

TABLE 3. Synthesis of 4-Aminochromanes

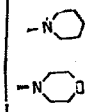
Compound	4-Aminochromane		mp, °C	Yield, %	Initial khellactone diester
	R^2	NR_2^3			
VIa	$COCH_2CH(CH_3)_2$		195	72,2	Ia
VIb	"		202	48,3	Ia
VIc	"		156	54,0	Ia
VId	$COCH_3$		210	50,0	Ib
VIe	$COCH_3$		222	47,5	Ib
VIf	$CO-CH(CH_3)CH_2CH_3$		179	41,4	Ic
VIg	"		189	16,6	Ic
VIh	$CO-CH=C(CH_3)_2$		173	27,3	Id

TABLE 4. Characteristics of the PMR Spectra of the 4-Aminochromanes

Amino chromane	δ, ppm, J, Hz								
	H_3	H_4	H_7	H_8	H_α	H_β	$(CH_3)_2C$	NR^3_2	Acyl
VIa*	5,40, d (9)	4,08, d (9)	6,16, d (9)	7,19, d (9)	7,41, d (16)	6,83, d (16)	1,09, s 1,28, s 3 H each	1,61, u.m. 12H (C—CH_2—), 2,30—3,40, u.m. 4H, (CH_2—N), 3,55, u.m. 4H(CH_2—N)	1,00, d (6), 6H /C—$(CH_3)_2$/, 2,19, u.m. 2H (CH_2—CO)
VIb	5,50, d (9)	4,18, d (9)	6,31, d (9)	7,24, d (9)	7,79 d (16)	6,96, d (16)	1,19, s, 1,31, s, 3 H each	2,40—4,00, u.m. 8H (CH_2—N), 3,67, s 8H (CH_2—O)	1,01, d (6), 6H /C—$(CH_3)_2$/, 2,24, u.m. 2H (CH_2—CO)
VIc	5,54, d (9)	4,47, d (9)	6,28, d (8)	7,25, d (8)	7,79, d (16)	6,85, d (16)	1,21, s, 1,30, s, 3 H each	1,60—2,10, u.m. 8H (CH_2—C), 2,40—3,00, u.m. 4H, (CH_2—N), 3,40—3,65, u.m. 4H, (CH_2—N)	0,99 d (6), 6H /C—$(CH_3)_2$/, 2,21, u.m. 2H (CH_2—CO)
VId	5,47, d (9)	4,19, d (9)	6,31, d (8)	7,28, d (8)	7,89, d (16)	7,03, d (16)	1,18, s, 1,30 s, 3 H each	1,57 u.m. 12H (CH_2—C), 2,30—2,90, u.m. 2H (CH_2—N), 3,00—3,30, u.m. 2H, (CH_2—N), 3,60, u.m. 4H (CH_2—N)	2,13, s, 3H (OC—CH_3)
IVe	5,58, d (9)	4,26, d (9)	6,41, d (9)	7,34, d (9)	7,89, d (16)	7,08, d (16)	1,21, s, 1,33, s, 3 H each	2,40—3,70, u.m. 8H (CH_2—N), 3,70, s, 8H (CH_2—O)	2,17, s, 3H (OC—CH_3)
VIf	5,45, d (9)	4,12, d (9)	6,24, d (8)	7,20, d (8)	7,72, d (16)	6,96, d (16)	1,16, s, 1,27 s, 3 H each	1,57, u.m. 12H (CH_2—C), 2,30—2,90, u.m. 2H, (CH_2—N), 3,00—3,30, u.m. 2H, (CH_2—N), 3,55, u.m), 4H (CH_2—N)	0,92, t (7), 3H (CH_2—CH_3), 1,15, d (7), 3H (CH—CH_3)
VIg	5,00, d (9)	4,10, d (9)	6,32, d (9)	7,17, d (9)	7,81, d (16)	6,97, d (16)	1,16, s, 1,27, s, 3 H each	2,30—3,60, u.m. 8H (CH_2—N), 3,70, s, 8H (CH_2—O)	0,92, t (7), 3H (CH_2—CH_3), 1,15, d (7), 3H (CH—CH_3)
VIh	5,41, d (9)	4,10 d (9)	6,17, d (8)	7,17, d (8)	7,58, d (16)	6,84, d (16)	1,12, s, 1,24, s, 3 H each	1,61, u.m. 12H (CH_2—C), 2,30—2,90, u.m. 2H, (CH_2—N), 3,00—3,30, u.m. 2H (CH_2—N), 3,55, u.m, 4H (CH_2—N)	1,96, s 3H (CH_3—C) 2,23, s, 3H (CH_3—C) 5,67, u.m. 1H (CH)

VIi†	4,60, d (9)	4,23, d (9)	6,54. d(8)	6,72, d (8)	7,92, d (16)	7,47, d (16)	1,14, s, 1,31, s, 3 H each	1,65, u. m.12H (CH_2—C), 2,80—3,50, u. m. 4H (CH_2—N), 3,69, u. m. 4H (CH_2—N)	—
VIk	5,16, d (9)	4,68, d (9)	6,98, d (9)	7,90, d (9)	8,43, d (16)	7,10, d (16)	1,49, s, 1,79, s, 3 H each	3,20—4,70, u. m. 8H (CH_2—N), 4,27, s, 8H (CH_2—O)	—
VIl	5,79, d (9)	4,39, d (9)	6,38, d (9)	7,54, d (9)	7,84, d (16)	7,00, d (16)	1,33, s, 1,37, s, 3 H each	2,40—3,80, u. m. 8H (CH_2—N), 3,69, s, 8H (CH_2—O)	8,08, d (8) and 8,09, d (8) (H_2 and H_6 in benzoyl), 7,70—7,30, m 3H, (H_3, H_4 and H_6)
VII	5,48, d (9)	4,17, d (9)	6,28, d (9)	7,28, d (9)	7,89, d (16)	6,47, d (16)	1,19, s, 1,30, s, 3 H each	1,40—1,90, u. m. 6H (CH_2—C), 2,40—2,90, u. m. 2H (CH_2—N), 3,00—3,30, u. m. 2H (CH_2—N)	1,01, d (6), 6H /C—$(CH_3)_2$/, 2,24, u.m. 2H (CH_2—C), 1,23 (CO—C—CH_3), (CO—C—CH_3), 4,24, q (7), 2H (CO—CH_2—C)
VIII*	5,20—5,40, u. m.	3,78, d (9)	6,68, d (9)	7,47, d (9)	7,60, d (16)	6,74, d (16)	1,20, s, 1,43, s, 3 H each	2,40—2,70, u. m. 4H (CH_2—N), 3,40—3,55, u. m. 4H (CH_2—N), 3,64, s, 8H (CH_2—O)	2,00, s, 3H (CH_3—COO—Alk), 2,32, s, 3H (CH_3—COO—Ar)
IX	5,53, d (9)	4,21, d (9)	6,34, d (9)	7,79, d (9)	7,79, d (16)	7,01, d (16)	1,21, s, 1,31, s, 3 H each	1,64, u. m. 6H (CH_2—C in piperidine), 2,37—3,06 u. m. 4H (CH_2— in piperidine), 3.49 s, 4H (CH_2—O in morpholine); 3.50-4.00, u. m. 4H (CH_2—N в in morpholine	1,03, d (6), 6H /C—$(CH_3)_2$/, 2,27, u. m. 2H (CH_2—C)

*In $CDCl_4$.

†In $CDCl_3$ + trifluoroacetic acid; the spectra of the other compounds were taken in $CDCl_3$.

In the reaction of the aminocoumarins (III) with amines, in addition to the opening of the ring and the formation of an amide, transamination took place. Thus, the interaction of the aminocoumarin (IIId) with piperidine led to the formation of the compound (VIa), i.e., not only did the opening of the lactone ring take place but also the replacement of an isobutylamino group by a piperidino group. The aminocoumarin benzoate (IIIi), on being heated with morpholine, gave compound (VIIi) (R^2 = —CO—C_6H_5, NR_2^3 = morpholino). The same reaction takes place on the interaction of the aminocoumarins with amines, which provides the possibility of obtaining aminochromanes containing various amino groups. Thus, heating (VIb) with piperidine yielded the aminochromane (IX).

EXPERIMENTAL

The elementary analyses of the compounds obtained corresponded to the calculated figures. The PMR spectra of the substances were taken on a Varian HA-100D spectrometer. The dihydrosamidin (Ia) with mp 115-117°C and visnadin (Ic) with mp 85-87°C used for the syntheses were isolated from *Phlojodicarpus sibiricus* (Steph.) (K.-Pol., the pteryxin (Ib) with mp 79-80°C from *Seseli condensatum* (Crantz.) M. Pimen. et Sdobn., and the khellactone diseneciоate (Id) with mp 109-110°C from *Seseli talassicum* (Korov.) M. Pimen. et Sdobn. The authenticity of the substances was shown by their PMR and IR spectra, and their individuality by TLC on Silufol in the petroleum ether—ethyl acetate (1:1) system.

Preparation of 4'-Aminocoumarins. A. A mixture of 0.02 mole of a khellactone diester and 0.06 mole of an amine in 100 ml of dioxane was left at 20°C for 72 h, and then the solution was evaporated, the residue was washed with water and dissolved in 40 ml of ether, and the aminocoumarin was extracted with 7% hydrochloric acid (10 × 20 ml). The hydrochloric acid extract was neutralized with 25% ammonia solution and extracted with ether, the ethereal extract was evaporated, and the residue was crystallized from 90% methanol.

B. A mixture of 0.02 mole of a khellactone diester and 0.06 mole of an amine in 50 ml of benzene was heated at boiling under reflux for 2 h, and then the solution was evaporated and the residue was worked up as described in method A.

3'-Hydroxy-4'-piperidino-3',4'-dihydroseselin (IIIh). A. A solution of 30.2 g of (IIIa) in 300 ml of a 17.5% solution of hydrochloric acid was heated at 95°C for 4 h. Then the solution was cooled to 20°C and was neutralized with 25% ammonia solution, and the resulting precipitate was separated off, washed with water, and dried. This gave 24.0 g (53.5%) of 3'-hydroxy-4'-piperidino-3',4'-dihydroseselin with mp 109-110°C after recrystallization from ether.

B. A mixture of 200 mg of (IIIa) and 250 mg of KOH in 3 ml of ethanol was kept at 20°C for 5 h, and then the solution was neutralized with acetic acid, diluted sixfold with water, and left in the cold, and the resulting precipitate was separated off and washed with water (2 × 5 ml). This gave 120 mg (75.0%) of (IIIh) with mp 106°C, its IR and PMR spectra being identical with those of the product of acid hydrolysis.

3'-Acetoxy-4'-piperidino-3',4'-dihydroseselin (IIIe) from (IIIh). A solution of 1.04 g of (IIIh) in 5 ml of acetic anhydride was left at 20°C for 24 h, after which 10 ml of water was added, the mixture was neutralized with 25% ammonia, and the resulting precipitate was separated off and washed with water. This gave 1.05 g (89.2%) of (IIIe) with mp 158°C after recrystallization from ethanol. The substances were identicalwith compound (IIIe) obtained by method B from pteryxin (IR spectrum, mixed melting point).

3'-Benzoyloxy-4'-piperidino-3',4'-dihydroseselin (IIIi). A solution of 3.00 g of (IIIh) in 20 ml of pyridine was treated with 6 ml of benzoyl chloride and the mixture was left for a day at 20°C, after which 200 ml of water was added. The resulting precipitate was separated off, washed with water, and crystallized from 20 ml of ethanol. This gave 2.76 g (70%) of the benzoate (IIIi) with mp 223-224°C.

Preparation of 4-Aminochromanes. A mixture of 0.03 mole of a khellactone diester and 0.12 mole of an amine was heated at 120-130°C for 2 h, and then 20 ml of ethanol was added to the reaction mixture and the resulting precipitate was separated off, washed with ethanol, and dried.

Preparation of (VIi). A mixture of 5 g of (VIa) and 50 ml of 5% KOH solution in ethanol was heated at boiling for 1 h, whereupon the solution acquired an orange coloration. The cooled reaction mixture was neutralized with acetic acid, which caused the color of the solu-

tion to change to light yellow. The neutralized solution was added in small portions with stirring to 50 ml of cold water, and the precipitate that deposited was separated off and washed with water (3 × 10 ml). This gave 2.53 g of a yellow substance, and another 0.83 g of the substance was obtained from the mother liquors. The total yield was 2.85 g (68.5%), mp 210°C.

Preparation of (VIk). A mixture of 2.74 g of (IVb) and 30 ml of 5% KOH solution in ethanol was heated at boiling for 1 h. The cooled reaction mixture was neutralized with acetic acid, and the resulting light yellow solution was poured into 300 ml of cold water. The light yellow precipitate that deposited was separated off and washed with water (2 × 10 ml), giving 1.95 g (85.5%) of a substance with mp 253°C.

Acid Hydrolysis of (VIa). A solution of 1.08 g of (IVa) in 10 ml of 17.5% hydrochloric acid was heated at boiling for 1.5 h, the cooled reaction mixture was neutralized with 25% ammonia, and the resulting flocculent precipitate was separated off. This gave 0.70 g (98.7%) of colorless crystals with mp 102°C identical with (IIIh) according to their PMR spectrum.

Isolation of (VII). The dry residue (46.0 g) after the evaporation of the mother liquor from the preparation of (VIa) was crystallized from 50 ml of ethanol. This gave 3.8 g of combined substances consisting predominantly of (VIa) and a substance having a blue fluorescence in UV light and a considerably higher R_f value (on Silufol in the petroleum ether—ethyl acetate (1:1) system). Of this combined product, 1 g was separated on a column (d = 5 cm) containing 20 g of silica gel L 40/100μ. Elution was carried out with mixtures of petroleum ether and ethyl acetate containing concentrations of the latter rising from 1 to 6%. Fractions with a volume of 100 ml were collected, and the process was monitored with the aid of TLC. Fractions 3-6 yielded 0.04 g of colorless crystals of (VII) with mp 175°C.

Acetylation of (VIi). To 0.42 g of (VIi) was added 0.50 ml of acetic anhydride and 5.00 ml of pyridine, and the mixture was heated on the water bath for 4 h. Then 5.00 ml of water was added to the reaction mixture and it was neutralized with 25% ammonia, and the resinous matter that separated out was crystallized from aqueous ethanol. This gave 0.17 g (35.8%) of colorless crystals with mp 208°C identical according to their IR and PMR spectra with (IVd).

Preparation of (VIII). A solution of 0.858 g of (VIk) in 4.00 ml of pyridine was treated with 2.00 ml of acetic anhydride, and the reaction mixture was heated to boiling in a glycerol bath for 1 h. After cooling to 20°C, the reaction mixture was poured into 200 ml of cold water and was neutralized with 25% ammonia solution. The resin that deposited was titurated in water until it hardened and it was then separated off and was washed with 25% ammonia (2 × 10 ml) and with water (4 × 20 ml), and dried. This gave 0.49 g (47.5%) of a substance with mp 111-113°C.

Reaction of (IIId) with Piperidine. A solution of 0.63 g of (IIId) in 1.2 ml of piperidine was heated at 130°C for 1.5 h. The reaction mixture, after cooling to 20°C, was treated with 15 ml of 75% ethanol, and the precipitate that separated out was separated off. This gave 0.22 g (30.0%) of colorless crystals with mp 195°C. According to its IR and PMR spectra, the substance was identical with (VIa), a mixture with which showed no depression of the melting point.

Reaction of (IIIi) with Morpholine. A solution of 1.26 g of (IIIi) in 2.5 ml of morpholine was heated at 115°C for 1 h. After cooling to 20°C, the reaction mixture was treated with 2.0 ml of ethanol, and the precipitate that deposited was separated off. This gave 1.13 g (72.4%) of a substance with mp 221°C (from ethyl acetate with petroleum ether) — (VIIl) (R^2 = —CO—C_6H_5, NR_2^3 — morpholino).

Preparation of (IX). A solution of 0.66 g of (VIa) in 2.0 ml of morpholine was heated at 120-130°C for 1 h. The reaction mixture, after cooling to 20°C, was treated with 13 ml of 50% ethanol, and the resulting precipitate was separated off. This gave 0.35 g (53.1%) of colorless crystals with mp 183°C.

SUMMARY

The reaction of diesters of khellactone with primary and secondary amines under mild conditions has given derivatives of 4'-aminodihydroseselin. Under more severe conditions not only the replacement of the 4'-acyloxy group by an amino group but also the opening of the lactone ring with the formation of the corresponding cinnamamide took place.

The ease of hydrolysis of the 3'-acyloxy group and of the subsequent esterification of the alcohols formed, and also the use of various amines, provides the possibility of obtaining very diverse acyloxy and amino derivatives.

LITERATURE CITED

1. B. A. Nielsen, Coumarins of Umbelliferous Plants. The Royal Danish School of Pharmacy. Chemical Laboratory B, Copenhagen (1970).
2. M. G. Pimenov, L. I. Dukhovlinova, and Yu. E. Sklyar, Rast. Res., 14, No. 3, 427 (1978).
3. G. P. Sharova, "The spasmolytic properties of pteryxin and dihydrosamidin on cholesterol atherosclerosis in rabbits," Proceedings of a Symposium on Outstanding Advances in the Field of Drugs of Vegetable Origin [in Russian], Poznan (1970), p. 66.
4. H. Erbring, H. Uebel, and G. Vogel, Arzneimittelforsch., 17, No. 3, 283 (1967).
5. M. Pesson (Laboratoire Roger Bellon), French Patent No. 1,261,343, Sept. 8, 1961, 4-Amino-3-α-methylbutyryloxydihydroseselins; Chem. Abstr., 56, No. 9, 10105a (1962).
6. A. Balsamo, P. L. Barili, P. Grotti, B. Macchia, F. Macchia, A. Pecchia, A. Cuttica, and N. Passerini, J. Med. Chem., 18, No. 8, 842 (1975).
7. Schering AG, British Patent No. 758,313, Oct. 3, 1956, 4-Aminochromans; Chem. Abstr., 51, 9708b (1957).

6-CHLOROAPIGENIN FROM *Equisetum arvense* L.

A. I. Syrchina, G. G. Zapesochnaya, N. A. Tyukavkina, and M. G. Voronkov

UDC 547.972

A new compound 6-chloroapigenin, $C_{15}H_9ClO_5$, M^+ 304, mp 305-306°C, λ_{max} 274, 336 (methanol) has been isolated from the ether-soluble fraction of a methanolic extract of the field horsetail. On the basis of the results of UV and PMR spectroscopy and mass spectrometry, the structure of 6-chloro-4',5,7-trihydroxyflavone has been established for this compound.

From the ether-soluble fraction of a methanolic extract of the herbage of *Equisetum arvense* L. (field horsetail) we have isolated a compound (I) with the composition $C_{15}H_9ClO_5$, M^+ 304, mp 305-306°C, λ_{max} 274, 336 nm (methanol). According to its UV spectra in methanol and in the presence of sodium methanolate, aluminum chloride, and sodium acetate, this compound belongs to the flavone group and has free hydroxy groups in positions 4',5, and 7 of the molecule. The mass spectrum of the compound isolated indicated the presence of chlorine in the molecule of (I).

In the region of the molecular ion of compound (I) two peaks are observed with m/e 304 (100%) and 306 (39%), which is characteristic for chlorine-containing compounds with one chlorine atom in the molecule. The peak of any chlorine-containing ion M is always accompanied by the M + 2 peak with approximately one third of the intensity, since the natural ratio of the isotopes ^{35}Cl and ^{37}Cl is 3:1 [1, 2]. A similar ratio of the peaks is preserved for the chlorine-containing fragments A and A + 2: m/e 186 (41%) and 188 (12%).

The presence of chlorine is also confirmed by the qualitative Stepanov reaction and the Beilstein test [3]. For comparison we used flavones (apigenin, genkwanin, and luteolin), and chlorine-containing organic compounds.

In order to establish the position of the chlorine, we compared the peaks of the fragmentary ions of this compound with the peaks of the fragmentary ions of apigenin, genkwanin, and acacetin. Fragmentation peaks with m/e 121 and 118 confirmed that there is a free OH group in ring B in the 4'-position of the molecule. The position of the chlorine in ring A was confirmed by the presence in the mass spectrum of fragmentation ions with m/e 188, 187,

Irkutsk Institute of Organic Chemistry, Siberian Branch of the Academy of Sciences of the USSR, All-Union Scientific-Research Institute of Medicinal Plants, Moscow. I. M. Sechenov First Moscow Medical Institute.

Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 499-501, July-August, 1980. Original article submitted March 20, 1980.

0009-3130/80/1604-0356$07.50