CONCLUSION

The result of the direct bromination of estra-1,3,5(10)-trien-17-one depends substantially on the nature of the substituent at C_3: Estrone and its methyl ether give mainly compounds bromine-substituted in ring A, while the bromination of estrone acetate leads to 16-mono- and 16,16-dibromo-derivatives.

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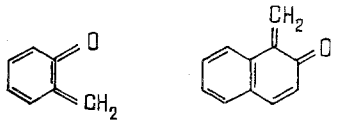
THERMAL DECOMPOSITION OF 2-HYDROXYBENZYLAMINES

V. I. Vinogradova and M. S. Yunusov

UDC 547.233/533

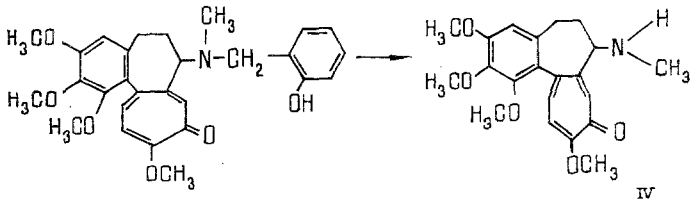
The results are given of the preparation of a number of 2-hydroxybenzylamines and their thermal decomposition. The thermolysis reactions and the formation of the corresponding amines take place smoothly and with good yields.

The convenient method of retrodiene decomposition of 2-hydroxybenzylamines [1, 2] and of 2-hydroxy-1-naphthylmethylamines [3, 4], which is used for the regeneration of O-quinone methide compounds (I, II), has been discussed in the literature.



I II

In the thermolysis of the alkaloids speciosine (III), Kiselev et al. [5] isolated the nitrogen-containing moiety of the molecule — colchamine (IV) — in 52% yield.



III IV

It was of interest to study the possibility of using salicylaldehyde for blocking the amino group and its subsequent debenzylation under pyrolysis conditions. With this aim, we have synthesized a number of substances (Table 1) by condensing amines and salicylaldehyde followed by sodium tetrahydroborate reduction according to the scheme.

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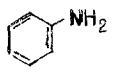
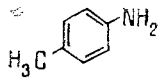
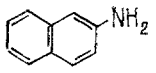
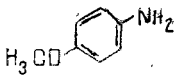
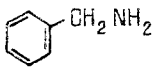
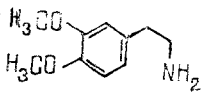
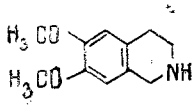
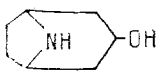
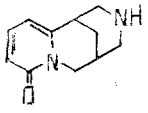
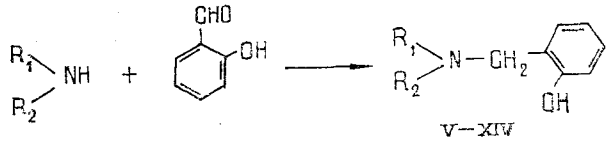
TABLE 1

Initial amine	Substance obtained, bp, yield	Thermolysis product, conditions of decomposition, yield
$(CH_3)_3—CNH_2$	N-(2-Hydroxybenzyl)-tert-butylamine (V), liquid, 95%	Tert-butylamine, mp of the hydrochloride 265-270°; 5 min, 200°C; 86%
	N-(2-Hydroxybenzyl)aniline (VI), 112°C, 83%	Aniline; 5 min, 200°C; acetanilide, mp 107°C, 73%
	N-(2-Hydroxybenzyl)-p-toluidine (VII), 118-120°C, 93%	p-Toluidine, mp 106°C; 5 min, 230°C, 10 mm Hg; 95%
	N-2(Hydroxybenzyl)-β-naphthylamine (VIII), 145-147°C, 92%	β-Naphthylamine, mp 106-109°C; 5 min, 230°C, 10 mm Hg; 95%
	N-(2-Hydroxybenzyl)-p-anisidine (IX), 125-127°C, 90%	p-Anisidine, mp of the hydrochloride 209-210°C; 5 min, 230°C, 10 mm Hg, 99%
	N-(2-Hydroxybenzyl)benzylamine (X), hydrochloride 190-193°C, 91%	Benzylamine, mp of the sulfate 270-273°C; 5 min, 220°C, 10 mm Hg, 95%
	N-(2-Hydroxybenzyl)-3,4-dimethoxyphenylethylamine (XI), mp of the hydrochloride 211-213°C, 80%	Homoveratrylamine, mp of the sulfate 157-158°C, 5 min, 200°C, 10 mm Hg; 80%
	N-(2-Hydroxybenzyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (XII), 200°C, subl., 80%	Decomposition products of 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline; 15 min, 10 mm Hg; 95%
	N-(2-Hydroxybenzyl)nortropine (XIII), 166-170°C, 80%	Nortropine, 150-151°C; 5 min, 230°C, 10 mm Hg; 100%
	N-(2-Hydroxybenzyl)cytisine (XIV), amorphous, 72%	Cytisine, mp 153°C; 5 min, 250°C; 5 mm Hg; 80%

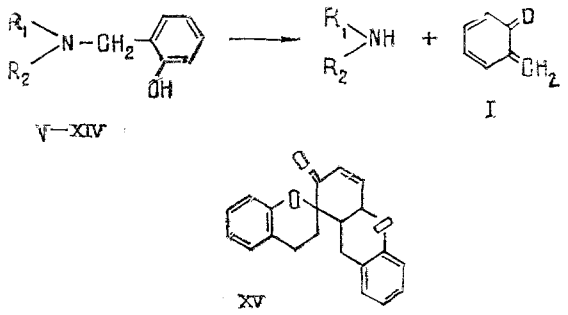
Scheme 1



V—XIV

The structures of the N-substituted bases obtained (V, XI-XIV), see Table 1) that have not been described in the literature were confirmed by mass spectrometry. The other amines (VI-X) were identified by comparison of their physiochemical constants with those given in the literature [6].

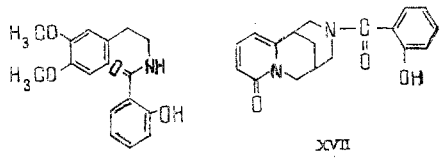
It can be seen from Table 1 that the hydroxybenzylation of both primary (V-XI, 83-95%) and of secondary (XII-XIV, 72-80%) amino groups took place with high yields. The alkylamines obtained (V-XIV) were subjected to thermolysis under various conditions. The performance of the decomposition at a temperature of 200-245°C, as in [5], using tetralin or diethyleneglycol as solvent gave the expected amines as the main product, but their purification was difficult. Good results were obtained when the pyrolysis was performed without a solvent at 200-230°C followed by the distillation of the products in vacuum. The readily volatile amines were distilled off at normal pressure. The retrodiene decomposition took place rapidly and was completed in 5 min by the qualitative dealkylation of the amines. Thermolysis performed in this way permitted the isolation of the initial amines in the pure form since the compound (I) formed in the process gave the trimer (XV) [3, 7] and did not distill off under our conditions.



Scheme 2

In spite of the quantitative decomposition of the alkylamines (V-XIV), the yields of the individual amines were somewhat lower (76-80%) than expected. This is connected with the natural losses, which were appreciable as a percentage, since only small amounts of the substances were subjected to decomposition and subsequent distillation. As was assumed, the decomposition of the 2-hydroxybenzylamines took place very readily and did not depend on the structure of the initial base, but it did depend on the stability of the latter under the thermolysis conditions; thus, for example, 6,7-dimethoxy-1,2,3,4-tetrahydro-isoquinoline proved to be unstable at 210°C.

We also carried out the pyrolysis of the amines (XVI and XVII) obtained from the chloride of acetylsalicylic acid and the corresponding amines by the Schotten–Baumann reaction followed by hydrolysis. The amides proved to be stable at 250°C and the decomposition characteristic of the corresponding amines was not observed.



EXPERIMENTAL

Preparation of the Amines (V-XI) via the Imines. A mixture of a primary amine (0.01 mole) and of salicylaldehyde (0.01 mole) was boiled in benzene solution (30 ml) with the azeotropic distillation of water. After the elimination of the water, the benzene was distilled off in vacuum and the imime obtained was reduced with tetrahydroborate in methanol solution (25-30 ml) at 0.10°C. The reaction mixture was concentrated in vacuum and separated between an organic layer (ether or chloroform) and water. The amine was exhaustively extracted from the aqueous layer with the solvent. The solution was evaporated and the residue was crystallized. The amines (V)-(XI) were obtained in this way (see table).

The Preparation of the Amines (XII-XIV) by a Modified Craig Method [8]. N-(2-Hydrobenzyl)cytisine (XIV). A mixture of 1 g of cytisine and 1 ml of salicylaldehyde was boiled in 20 ml of toluene for 4 h. After cooling, the toluene was decanted off and to the reaction product melted in the form of an oil, was added 30 ml of methanol and sodium tetrahydroborate. After a working up process similar to that described above, N-(2-hydroxybenzyl)cytisine was isolated from the reaction mixture by trituration with acetone; it was an amorphous substance with M^+ 296.

N-(2-Hydroxybenzyl)nortropine (XIII). A mixture of 0.5 g of nortropine and 0.5 g of salicylaldehyde was boiled in 2 ml of methanol for 4 h, and then 0.5 g of sodium tetrahydroborate was added to the hot solution over 10 min. After the cessation of the evolution of hydrogen, the solvent was evaporated off. The residue after the appropriate working up gave an amine with mp 166-170°C, M^+ 233.

N-(2-Hydroxybenzyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (XII) was obtained from 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline and salicylicaldehyde by the method described above for the amine (XIII). For (XII) we found M^+ 299.

CONCLUSION

The thermal decomposition of 2-hydroxybenzylamines has been studied. It has been shown that the thermolysis reaction takes place smoothly and the corresponding amines can be obtained in good yield.

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THE NMR STUDY OF ALKALOIDS.

VI. A COMPARISON OF THE STEREOCHEMISTRIES OF PSEUDOCOPSININE AND 14,15-DIHYDROVINDOLININE BY ^{13}C NMR SPECTROSCOPY

M. R. Yagudaev

UDC 547.944.1.92

On the basis of a comparative study of the ^{13}C NMR spectra of the natural alkaloid pseudocopsinine and its synthetic analog 14,15-dihydrovindolinine it has been shown that their stereochemistries are not identical.

The alkaloid pseudocopsinine (I) [mp 136-138°C (benzene), $[\alpha]_D$ −30.4° (c 1.51, methanol); dihydrochloride with mp 266-268°C (methanol, decomp.)] has been isolated from the epigeal part of *Vinca erecta* Regel et Schmalh., family Apocynaceae [1]. A structure was proposed for it on the basis of its chemical and spectral characteristics (UV, IR, PMR, and mass spectra [2, 3]). Then the structure was refined by the method of x-ray structural analysis and the spatial structure and absolute configuration of all the asymmetric centers of (I) were established unambiguously [4-6]. The skeleton of the alkaloid (19R)-pseudocopsinine (I) is identical with the skeleton of (19R)-vindolinine (II) isolated from various species of the family Catharanthus [7].

According to the results of ^{13}C NMR [8] and PMR at a frequency of 300 MHz [9] of (19R)-vindolinine and also its x-ray structural analysis [10], (I) and (II) have identical spatial structures with the cis linkage of rings F and G and with the S configuration of the C_{21} carbon atom except for ring G which contains a C_{14}=C_{15} double bond in (II) and not in (I). Con-

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