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PREPARATIVE SYNTHESIS OF FRAGRANCE SUBSTANCES BASED ON VANILLIN AND VERATRALDEHYDE

Methods of reception of fragrance substances are defined on the basis of vanillin and veratraldehyde by aldol-crotonic condensation with aliphatic and aromatic ketones (acetone, methylethylketone, heptanone-2, β-ionone, acetophenone, *p*-methylacetophenone, *p*-acetyl-anisole). Distinctive feature of the given technique is the use of methanol as solvent and the replacement of potassium hydroxide on sodium hydroxide. For allocation of products of condensation from methanolic solution it is expedient to use 5%-s' solutions of hydrochloric acid instead of acetic acid that allows to receive purer product and raises its yield up to 80–90%. With the help of Infrared Spectroscopy the presence of the functional groups in the received substances was proved.

Introduction. Fragrance substances are organic compounds used in the production of perfumes, cosmetics, soap, detergents, household chemicals and food products.

Depending on the origin of raw materials and methods of producing fragrance substances are conventionally divided into natural and synthetic.

Natural substances are organic compounds derived from natural compounds (essential oils, resins and extracts) without changing the molecular structure of these compounds.

Synthetic fragrance substances include compounds derived from natural or chemical sources by chemical transformations.

One of the ways to promote the products of the Belarusian perfume, food, confectionery and alcoholic beverage companies in the domestic and foreign markets, more competitive and attractive to customers is the development and application of new cheap fragrances, flavors and fragrances based on the available fragrance substances.

Needs in vanillin (4-hydroxy-3-methoxy-benzaldehyde) – one of the few fragrances, are constantly increasing. This is due to a strong growth of food consumption, in which vanillin or its derivatives are used as flavoring agents.

Vanillin has one of the lowest threshold concentration, ie, the minimum concentration at which a person can identify the substance in the air, that is $1.24 \cdot 10^{-10}$g/l. For comparison, the corresponding value for the thiols used in odoration of natural gas is $2 \cdot 10^{-9}$ g/l, which is much higher.

Vanillin is widely used in the food and fragrance industry [1–3]. It is found in significant quantities in the fruit scented Vanillin (Vanilla planifolia Andr. and Vanilla pompona) of the orchid family (Orchidaceae).The content in their dried fruit reaches 3%.

Nowadays most part of vanillin is produced synthetically from guaiacol and lignin – the by-product of the pulp and paper industry. [4] Annual global industrial production of vanillin is 15 thousand tons.

The development of advanced technologies in the food industry requires new perfume with the scent of vanilla, with a higher thermal stability than vanillin, stability in a wide range of pH and in the presence of enzymes. These requirements encourage chemists to synthesize and food workers and perfumers to explore new derivatives of vanillin. It often turns out that many derivatives have more complete (compared to starting compounds) vanilla flavor with a wide range of different colors. This, in turn, stimulates further research in the synthesis of new derivatives of vanillin series and the development of effective methods of their preparation.

The main direction for the synthesis of aromatic compounds based on the reaction of vanillin are functional groups.There are two such groups of vanillin. Therefore vanillin may be modified both on hydroxyl and aldehyde group. In order to obtain new fragrances based on vanillin the method of synthesis of esters of vanillin and vanillal was developed.

The flavor testing of synthesised compounds showed that obtained fragrances have vanilla smell with different shades of flavors including honey, woody, powdery, chocolate, cream and even clove [5, 6].

Another direction in the modification of vanillin is the synthesis on its basis of veratraldehyde which is methylated on hydroxyl group vanillin.

Veratraldehyde (3,4-dimethoxybenzaldehyde) is widely used in perfume and cosmetics industry as an independent fragrance substance and as starting material for the synthesis of fragrance substances with a vanilla flavor with different shades. On its basis esters and oximes with promising flavors and suitable for the use as flavoring agents for cosmetics and detergents are synthesized [7, 8].

1,3-Dioxalanes obtained by condensation of vanillin with 1.2-propylene glycol were used at fragrances [9].

Vanillin can be used as a synthon for the production of biologically active substances [10, 11]. So, using the carbonyl group of esters of vanillin azomethines (Schiff bases) which possess a wide range of biological activity were synthesized and on their basis effective antidepressants, anticonvulsants, antimicrobal, sleeping pills and other drugs were developed.

Vanillin is of interest as a structural element of the synthesis of fused nitrogen heterocycles in the condensation reaction of aromatic aldehydes with 2-naphthylamine, and CH-acids. Being supplier of methoxyphenol substituent and methane fragment in the structure of azaheterocycles, vanillin plays a major role in the synthesis of biologically active compounds of these classes – analogues of cardioprotectors, enzyme inhibitors, analgesics, drugs with anti-tumor activity and plant alkaloids of acridone series.

However, the resulting heterocycles, due to the complexity of their structure and low solubility in organic solvents, have low reactivity, resulting in their difficult further modification. Introduction of alkylphenoxycarbonyl group with long alkyl radical from C_5 to C_{12} into the heterocyclic molecule changes the hydrophilic-lipophilic characteristics of the compound and increases its biological action.

Vanillin esterification of long-chain aliphatic acid chlorides for the subsequent introduction of esters of vanillin in the reaction with 2-naphthylamine, and CH-acids as synthons of target synthesis of previously unknown alkylcarbonyl derivatives of benzo-[a]-acridine and xanthene [12] was held.

Thus, at present, a lot of work to obtain fragrance substances by modification of vanillin was carried out. But there is no information on the aldol-crotonic condensation of vanillin and its derivatives with aliphatic and aromatic ketones, as a result of new fragrances with promising aromas which may be obtained.

Main part. The objectives of the work were to obtain new synthetic fragrance substances based on vanillin and veratraldehyde by aldol-crotonic condensation with aliphatic and aromatic ketones.

Vanillin (Acros Organics manufacturer, Belgium) of the "puru" mark was used as the starting material with the main substance content of 99%. IR spectroscopic analysis of the synthesized compounds was carried out in the form of solid pellets pressed in potassium bromide.

Veratraldehyde synthesis. Vanillin was dissolved in 10% aqueous sodium hydroxide solution at room temperature. Then the residue relative to the theoretical amount of dimethylsulfate was added in one portion to the solution and the mixture was being stirred with a magnetic stirrer for 7 h at 20°C. After that the mixture was left in the refrigerator at 4–5°C for 12 h. The precipitate of veratraldehyde was filtered with the help of a glass filter and washed with 20 ml of ice water. For further purification veratraldehyde was recrystallized from ethanol. The yield of pure aldehyde was 88% of theoretical one.

Aldol-crotonic condensation of veratraldehyde with aliphatic and aromatic ketones. In a three-necked 100 ml flask equipped with a stirrer, dropping funnel and a thermometer, the solution of 0.1 mol of freshly distilled aldehyde and ketone was placed into 20 ml of methyl alcohol.

Using acetone-ketone with more than one reactive methyl group and having the necessity in the product of monocondensation the molar ratio of ketone and aldechyde was 3 : 1.Sodium hydroxide (0.005 mol) in the form of a 15% solution in methanol was added to this mixture from the funnel with vigorous stirring at 20–25°C in the flask.

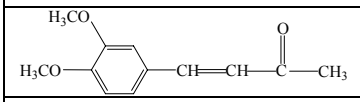
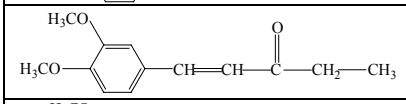
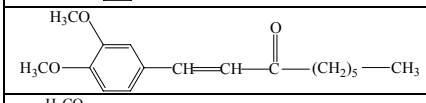
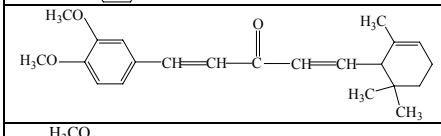
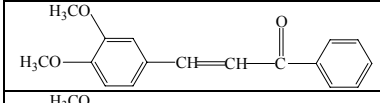
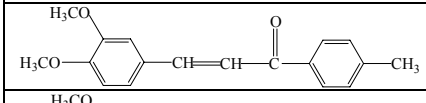
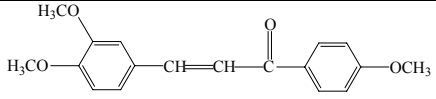
The reaction mixture was being stirred for another 3 h, neutralized with 5% hydrochloric acid solution, and the resulting solid reaction product was filtered on a glass filter and washed with 20 ml of water. After the formation of an oil product the reaction mixture was diluted with water and extracted with ether. The combined ether extracts were washed with water, dried with anhydrous sodium sulfate and ether was distilled on water bath. The product was being crystallized within 2–10 days.

According to this technique, the synthesis of seven products of aldol-crotonic condensation was accomplished.

Due to the optimization of the synthesis conditions sufficiently pure substances were obtained. Their isolation from the reaction mixture was simpler than compared with literary technique. In particular, in most cases it was possible to avoid additional recrystallization. The yield of condensation products was 65–75% (Table 1).

Table 1

Properties of the products of aldol-crotonic condensation of veratraldehyde with methylalkyl- and methylaryl ketones

Formula of matter	T_{mt}, °C	Yiel, %
	94	68
	102	70
	111	75
	108	65
	115	68
	122	70
	120	72

Aldol-crotonic condensation of vanillin with aliphatic and aromatic ketones. In a three-necked flask with a capacity of 100 cm^3, equipped with a stirrer, dropping funnel and a thermometer 0.1 mol of aldehyde and ketone was placed into 20 ml of methyl alcohol.

Sodium hydroxide (0.2 mol) in the form of a 15% solution in methanol was added to this mixture from the funnel with vigorous stirring at 30–35°C.

Alkali residue is formed due to the necessity of transfer of vanillin into sodium vanilate as well as to the creation of the required pH medium, which is essential for the aldol-crotonic condensation. The reactive mixture was being stirred for 5 h, resulting in orange-red color.

When finished, the reaction mixture was neutralized with a 5% solution of hydrochloric acid to slightly acid reaction.

In this case two layers were formed – the upper water-alcohol layers, the lower – the condensation product as a heavy oil.

The upper layer was decanted, and the bottom layer was dissolved in diethyl ether, washed with 10% sodium carbonate solution until neutral pH, then with distilled water and saturated sodium chloride solution, after what the ether solution was dried with anhydrous sodium sulfate and the solvent was distilled on water bath. The resulting oil was left in the fridge for a day for crystallization. The yield of condensation products was 76–94% (Table 2).

Distinctive features of the developed method of obtaining fragrance substances based on vanillin by aldol-crotonic condensation are:

– the use of methanol as a solvent;

– the use of sodium hydroxide instead of potassium hydroxide. The use of potassium hydroxide is impractical, since it leads to the formation of the less soluble in methanol potassium vanilate;

– the necessity to use the large residue of sodium hydroxide, because the part of it goes to the formation of salt – sodium vanilate;

– to extract the condensation product from a methanol solution instead of acetic acid is advisable to use a weak solution of a mineral acid, which provides to obtain a purer product in high yield.

The presence of functional groups in the obtained fragrance substances is confirmed by IR spectroscopic analysis. The strips at 2,960, 2,840 cm^{-1} are valence vibrations of –CH methyl group; 1,654 cm^{-1} are valence vibrations of –C=C– in the aliphatic chain; 1,630, 1,336 cm^{-1} are valence vibrations of the carbonyl group; 1,596 cm^{-1} is the group of –C=C– aromatic ring; 1,510 cm^{-1} are – CH deformation vibrations; 1,291 cm^{-1} is –C=C– (trans) group; 1,440 cm^{-1} are deformation vibrations of –CH methylene group; 1,250, 1,030 cm^{-1} are deformation vibrations of C–O–C oxymethyl group.

Table 2

Properties of the products of aldol-crotonic condensation of vanillin with methylalkyl- and methylaryl ketones

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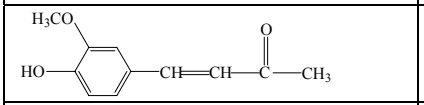
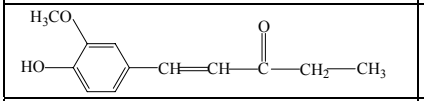
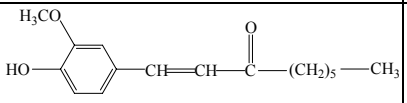
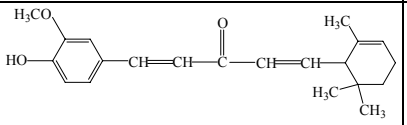
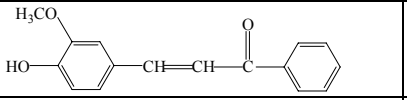
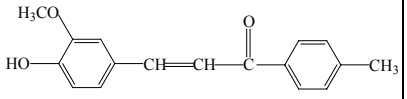
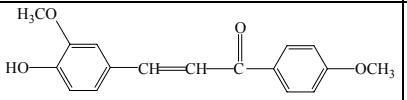
	115	82
	121	93
	128	79
	115	94
	134	88
	145	84
	129	76

Conclusion. Thus, in this paper the synthesis of fragrances based on vanillin and veratr aldehyde by aldol-crotonic condensation is accomplished. Derivatives based on aliphatic and aromatic ketones are prepared. All materials are selected, their melting points are defined and the presence of functional groups is proved by IR spectroscopic analysis.

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