Calculations of antifriction substances when they are used in combination must be performed in this sequence.

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SYNTHESIS OF 4-METHYL-5-CYANOOXAZOLE AND ITS REACTION WITH 3-METHYL-3-HYDROXYPENT-4-EN-1-YNE

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4-Methyl-5-cyanooxazole (II) is used as the diene component in the synthesis of vitamin B_6 and its analogs [1]. At the present time the best method of obtaining (II) is dehydration of 4-methyloxazole-5-carboxylic acid (I) in the presence of phosphorus pentoxide. We investigated method of synthesizing (II), excluding the use of difficultly available and technologically inconvenient phosphorus pentoxide. In particular, thionyl chloride and titanium tetrachloride were used as the water-removing reagents. In the case of thionyl chloride the reaction was carried out in a dimethylformamide medium, which made it possible to achieve synthesis of (II) in a homogeneous medium. However, in the connection that dimethylformamide and 4-methyl-5-cyanooxazole have similar boiling points, separation of the latter from the reaction mixture and establishing of accurate yield was hindered, as a result of which we developed a spectrophotometric method of determining the yield of (II). Upon using thionyl chloride the yield of compound (II), calculated from its content in the reaction mass, amounted to 45%.

Titanium tetrachloride was used as the other water-removing reagent. The reaction was carried out in the presence of organic base (triethylamine, pyridine), while the least tarring of reaction products was observed in the case of pyridine. The poor solubility of 4-methyloxazole-5-carboxylic acid amide limited the choice of solvent. The best yields of (II) were obtained upon using tetrahydrofuran and dioxane. However, the indicated solvents themselves evidently react with titanium tetrachloride and give chlorine-containing products, hindering separation of pure (II) from the reaction mass. Only after re-

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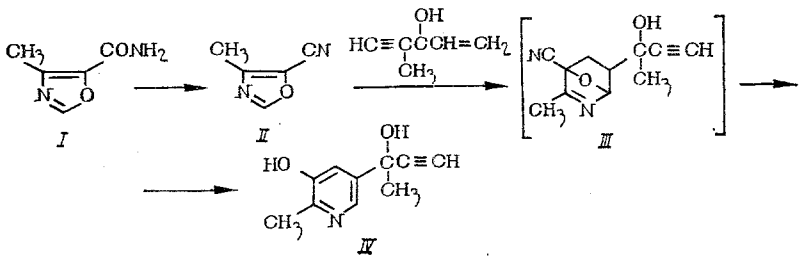
peated distillation can purified samples of (II) be obtained. This disadvantage was removed upon using pyridine as the solvent; however, despite the fact that this method facilitates separation of 4-methyl-5-cyanooxazole from the reaction mixture the yield of compound (II) in this case did not exceed 40%.

4-Methyl-5-cyanooxazole contains an electron-accepting group, which decreases its reactivity as a dienophile in comparison with 4-methyl-5-propoxyoxazole in the heterodiene condensation reaction. We confirmed this on the example of the reaction of (II) with 3-methyl-3-hydroxypent-4-en-1-yne.



The diene condensation reaction was carried out in a nitrogen atmosphere at 120° in the presence of hydroquinone. Evidently adduct (III) is formed at the first stage of synthesis; it is distinguished by high thermal lability and aromatizes rapidly during the synthesis, being transformed to 2-methyl-3-hydroxy-5-(2'-hydroxybut-3'-yn-2'-yl)pyridine (IV). Compound (IV) was obtained in a yield of 11%. We showed that the reaction of this vinylethynylcarbinol with the more active 4-methyl-5-propoxyoxazole leads to formation of (IV) in a yield of 55.5%. Elemental analysis data, UV and IR spectra confirm the structure of compound (IV). A mixed sample with a known sample did not give a melting point depression.

EXPERIMENTAL

UV spectra were measured in methanol on a Specord UV VIS instrument. IR spectra of materials as suspensions in mineral oil were obtained on a UR-10 spectrophotometer. Chromatographic analysis was carried out on a Chrom-4 gas–liquid chromatograph (stationary phase: 15% Carbowax 20M on N-AW-HMDS 0.2-0.25 mm Chromaton), with helium as the carrier gas at a gas rate of 60 ml/min. Thin-layer chromatography was carried out on plates of Silufol in the systems acetone–chloroform, 1:1 (A), acetone–dioxane–ammonia, 9:9:2 (B). Spot detection was achieved in UV light and treatment with Gibbs reagent.

4-Methyloxazole-5-carboxylic Acid Amide (I). Gaseous ammonia was passed through a solution of 17.5 g of 4-methyl-5-carbethoxyoxazole [2] in 90 ml of aqueous ammonia solution with stirring. After 5 h 10.4 g (73%) of (I) was filtered, mp 197-198° [3], R_f 0.30 (system A). UV spectrum [λ_{max}, nm (ε)]:278 (1303).

4-Methyl-5-cyanooxazole (II). a. The compound was obtained by dehydration of (I) in the presence of phosphorus pentoxide by the known method [3]. Yield 65%, bp 80° (8 mm), R_f 0.69 (system A), n_D^{20} 1.4691. UV spectrum [λ_{max}, nm (ε)]:263 (9880). Retention time 9 min (120°).

b. To a solution of 0.5 g of (I) in 8 ml of dimethylformamide at 0° was added 0.9 ml of thionyl chloride and the mixture was stirred for 48 h at 20°. The reaction mass was poured into 100 ml of ice water, neutralized with 50% aqueous sodium hydroxide solution to a weakly basic reaction, and extracted with ether (4 × 20 ml). The ether extract was dried with sodium sulfate and the ether was evaporated. The method of UV spectroscopy revealed 0.19 g (45%) of (II) in the residue.

c. To 40 ml of tetrahydrofuran upon mixing and cooling to −5° was consecutively added 9 ml of titanium tetrachloride, a solution of 0.5 g of (I) in 40 ml of tetrahydrofuran, and over 2.5 h, 12,8 ml of pyridine. The reaction mass was left with stirring overnight. The tetrahydrofuran was evaporated and the residue was transferred to 200 ml of ice water and extracted with ether. The ether extract was dried with sodium sulfate and the ether was evaporated. The method of UV spectroscopy revealed 0.29 g (74.2%) of (I). After three distillations 0.1 g (23.5%) of (I) was obtained, bp 93-95° (12 mm) [3], R_f 0.69 (system A). Retention time was 9 min (120°).

d. To 40 ml of pyridine with stirring were added consecutively 8.8 ml of titanium tetrachloride and 0.5 g of (I) in 20 ml of pyridine at −10°. The reaction mass was left overnight with stirring, then poured into 200 ml of ice water, acidified with hydrochloric acid solution, extracted with chloroform (3 × 3 ml), and dried with sodium sulfate. The solvent was evaporated; the residue was distilled in vacuum to give 0.16 g (36.7%) of (I), bp 94-96° (12 mm) [3], n_D^{20} 1.4699, R_f 0.69 (system A). Retention time 9 min (120°).

2-Methyl-3-hydroxy-5-(2'-hydroxybut-3'-ny-2'-yl)pyridine (IV). a. A mixture of 1 g of (I), 1.8 g of 3-methylpent-4-en-1-yn-3-ol and 5 mg of hydroquinone was heated in a nitrogen atmosphere at 120° for 50 h. The method of UV spectroscopy revealed 0.18 g (11%) of (IV). After filtration 0.1 g (5.6%) of (IV) was separated, mp 222-222.5° (from alcohol), R_f 0.58 (system B). Found, %: C 67.56; H 6.30; N 7.98. $C_{10}H_{11}NO_2$. Calculated, %: C 67.78; H 6.26; N 7.90. UV spectrum [λ_{max}, nm (ε)]: 204 (6540), 223 (4970), 284 (6870). IR spectrum (cm^{-1}): ($\nu_{\equiv CH}$, 2120 ($\nu_{C\equiv C}$), 1620, 1520 ($\nu_{C=C}$) .

b. A mixture of 2.0 g of 4-methyl-5-propoxyoxazole, 2.8 g of 3-methylpent-4-en-1-yn-3-ol and 10 mg of hydroquinone was heated for 48 h at 110° in a nitrogen atmosphere. The method of UV spectroscopy revealed 1.39 g (55.5%) of 2-methyl-3-hydroxy-5-(2'-hydroxybut-3'-yn-2'-yl)pyridine (III). Filtration separated 0.71 g (28.3%) of (III), mp 222-222.5° (from alcohol), R_f 0.58 (system B). Found, %: C 67.50; H 6.30; N 7.95. $C_{10}H_{11}NO_2$. Calculated, %: C 67.78; H 6.26; N 7.90. UV spectrum [λ_{max}, nm (ε)]: 204 (6540), 223 (4970), 284 (6870). IR spectrum (cm): ($\nu_{\equiv CH}$), 2120 ($\nu_{C\equiv C}$), 1620, 1520 ($\nu_{C=C}$) .

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PREPARATION OF ARACHIDENE

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The preparation of the drug arachidene, which normalizes lipid metabolism in the organism and is recommended for the medical treatment and prophylaxis of arteriosclerosis [2, 3], was reported earlier [1] by the method of saponification of lipids, tailings of the manufacture of endocrine preparations [4]. We have developed a new, more effective method of obtaining arachidene by alcoholysis of lipids in the presence of acidic catalysts (sulfuric acid, acetyl chloride, hydrogen chloride, p-toluenesulfonic acid, KU-2 ion-exchange resin) [5].

The method consists of subjecting dehydrated lipids to alcoholysis with ethanol in the presence of a catalyst with subsequent removal of ethyl esters of unsaturated fatty acids by low-temperature crystallization and separation of arachidene by vacuum distillation.

When using KU-2 ion-exchange resin as the catalyst, the dehydrated lipids are brought into reaction with ethanol after dissolving them in a sevenfold amount of alcohol and separating the insoluble precipitate. The mixture of acid ethyl esters, after removal of the catalyst, distillation of solvent, and washing with water, is subjected to low-temperature crystallization and fractional distillation in vacuum.

Examples of preparing arachidene by alcoholysis of lipids using acidic catalysts are shown in Table 1.

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