RULES FOR THE ADDITION OF SECONDARY AMINES TO DIACETYLENIC ALCOHOLS

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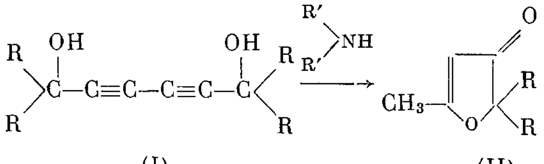
Previously we had shown [1] that unsaturated furanones of type (II) are formed when diacetylenic glycols of general formula (I) are heated with aqueous solutions of secondary amines. To explain the formation of such products we proposed a scheme, according to which the first step of the reaction is the addition of the amine to one of the acetylenic bonds and the subsequent cleavage of acetone from the other end of the molecule.



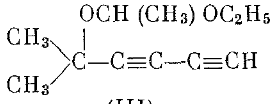
(I) (II)

In connection with this it seemed interesting to study the reaction of tertiary diacetylenic alcohols with secondary amines, since there was reason to believe that in this case the addition of the amine can go in a different manner. In addition, statements exist that diacetylenic alcohols with a free hydroxyl group are capable of giving unsaturated amino ketones when reacted with amines [2]. For this reason, we made a detailed study of the reaction of the acetal derivative of 2-methyl-3,5-hexadiyn-2-ol (III) with a 30% aqueous solution of dimethylamine. It proved that even a short heating of this mixture at 90° yields a mixture of reaction products, from which we were able to isolate two pure compounds – a liquid (IV) and a crystalline compound (V) – the ratio of which depends on the reaction conditions. At a lower temperature the main product is (IV), whereas on longer heating (at 95-100°) the crystalline compound (V) is obtained in good yield. In addition, it was shown that the liquid product (IV) when heated with dimethylamine is easily converted to the crystalline (V) and, consequently, it is the primary reaction product.

Based on its elemental composition, the liquid reaction product (IV) is the product of the addition of one molecule of dimethylamine to the diacetylenic alcohol (III), and based on the data of the infrared spectra it does not contain a terminal acetylene bond. In harmony with this, it can have the structure of either (IV) or (VI). Selecting the first structure was based on the reason that the exhaustive hydrogenation product (VII) obtained from it proved to be different from the authentic 2-methyl-6-dimethylamino-2-hexanol (X), obtained by the hydrogenation of the acetal derivative of 2-methyl-6-dimethylamino-4-hexyn-2-ol (IX), which was synthesized by the Mannich reaction from the acetal derivative of 2-methyl-4-pentyn-2-ol (VIII) [3]. (See scheme on following page.)

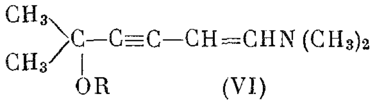
Based on its elemental analysis, the crystalline product (V) has the composition $C_9H_{15}ON$ and its infrared spectrum contains absorption bands corresponding to the presence of a conjugated exocyclic double bond and ether oxygen, and on acid hydrolysis it is easily converted to the previously described furanone (XI). All of this leaves no doubt but that it is the cyclic enamine (V).

As a result, the scheme for the addition of secondary amines to tertiary diacetylenic alcohols may be depicted in the manner shown on the following page.



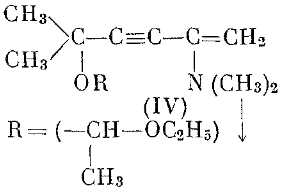
$(CH_3)_2C(OCH(CH_3)OC_2H_5)-C\equiv C-C\equiv CH$

(III)



$(CH_3)_2C(OR)-C\equiv C-CH=CHN(CH_3)_2$

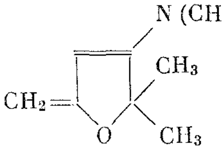
(VI)



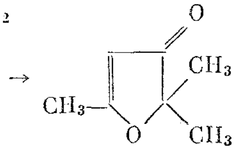
$(CH_3)_2C(OR)-C\equiv C-C(N(CH_3)_2)=CH_2$

(IV)

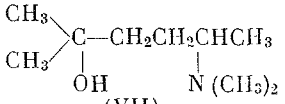
$R=(-CH(CH_3)-OC_2H_5)$



(V)

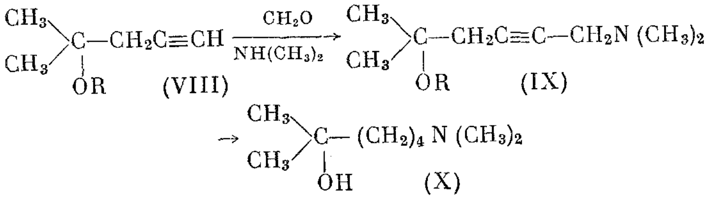


(XI)



$(CH_3)_2C(OH)-CH_2CH_2CH(N(CH_3)_2)CH_3$

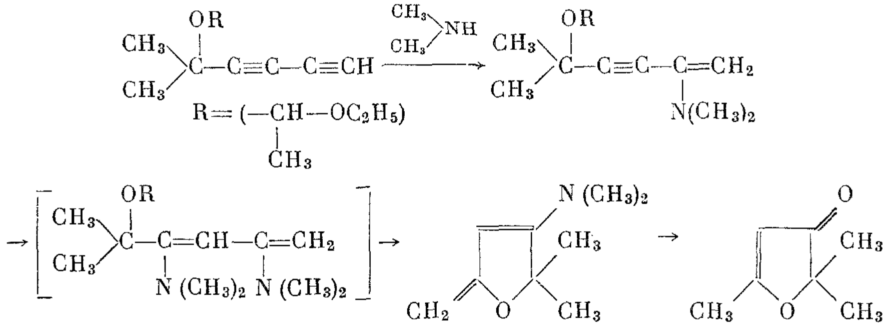
(VII)



$(CH_3)_2C(OR)-CH_2C\equiv CH \xrightarrow[NH(CH_3)_2]{CH_2O} (CH_3)_2C(OR)-CH_2C\equiv C-CH_2N(CH_3)_2 \rightarrow (CH_3)_2C(OH)-(CH_2)_4N(CH_3)_2$

(VIII) (IX) (X)

A characteristic feature of this scheme is the stepwise addition of the amine to the second atom of the terminal acetylene bond. After this, another molecule of the amine adds to the carbon atom adjacent to the hydroxyl group, since it is only in this way that the subsequent formation of the cyclic enamine (V) can be explained.



EXPERIMENTAL

Condensation of Acetal Derivative of 2-Methyl-3,5-hexadiyn-2-ol (III) with Dimethylamine. A mixture of 13 g of (III) and 50 ml of 30% aqueous dimethylamine solution was heated in a metal ampoule for 5 min at 90°. After cooling, the reaction mass was extracted thoroughly with ether, dried over potassium carbonate, and the ether was distilled off. The crystalline portion was filtered and recrystallized from alcohol. We obtained 2.9 g of 2,2-dimethyl-3-dimethylamino-5-methylene-2,5-dihydropyran (V) with m.p. 124-124.5°, λ_{max} 251 mμ (ε 8400); 336 mμ (ε 22,400) (in alcohol); ν 1620, 1547, 3060 cm^{-1} in CCl_4. Found: C 69.92, 70.20; H 9.99, 9.76; N 9.25, 9.26%. $C_9H_{15}ON$. Calculated: C 70.55; H 9.87; N 9.14%.

From the liquid portion after distillation we isolated 4.6 g of the acetal derivative of 2-methyl-5-dimethylamino-5-hexen-3-yn-2-ol (IV) with b.p. 72-74° (0.1 mm); $n^{16}D$ 1.5040; R_f 0.47 (heptane–acetone 1 : 4); λ_{max} 280 mμ (ε 13,100); ν 1636, 2188, 3024 cm^{-1}. Found: C 69.43, 69.44; H 10.49, 10.55; N 6.50, 6.69%. $C_{13}H_{23}O_2N$. Calculated: C 69.29; H 10.29; N 6.22%; picrate, m.p. 128.5-129° (from alcohol).

When this reaction was run at 60° (40 min) we isolated, after distillation, the above-described (IV) in 64% yield.

Operating in the same manner as described above, the heating of a mixture of (III) and dimethylamine at 90-100° for 30 min gave (V) in 48% yield.

Transformations of Acetal Derivative of 2-Methyl-5-dimethylamino-5-hexen-3-yn-2-ol (IV) and 2,2-Dimethyl-3-dimethylamino-5-methylene-2,5-dihydrofuran (V). A mixture of 7.2 g of (IV) and 50 ml of 30% aqueous dimethylamine solution was heated in a metal ampoule for 30 min at 80-90°. After cooling, the reaction mass was extracted with ether, from which we isolated 2.6 g of the above-described enamine (V) with m.p. 124-125° (from alcohol).

A mixture of 3.3 g of the cyclic enamine (V) and 50 ml of dilute (1 : 5) hydrochloric acid was refluxed for 1.5 h. The reaction mass was cooled, extracted with ether, dried over potassium carbonate, and fractionally distilled. We obtained 1.7 g of 2,2,5-trimethyl-2,3-dihydro-3-furanone (XI) with b.p. 47-48° (7 mm); $n^{20}D$ 1.4620; λ_{max} 261 mμ (ε 11,000) (in alcohol); ν 1604, 1703 cm^{-1} (in CCl_4), identical with the previously described compound [1].

A solution of 2.05 g of the acetal derivative of (IV) in 10 ml of methanol was exhaustively hydrogenated at room temperature in the presence of 5% $Pd/CaCO_3$. The alcohol solution of the amine was filtered, the methanol was removed in vacuo, and the residue was distilled. We isolated 1.47 g of 2-methyl-5-dimethylamino-2-hexanol (VII) with m.p. 102-103° (6 mm); $n^{20}D$ 1.4355, from which the methiodide with m.p. 47-48° (from a mixture of acetone and ether) was obtained. Found: C 40.20, 40.11; H 8.13, 8.28; I 41.87, 41.79%. $C_{10}H_{24}ONI$. Calculated: C 39.87; H 8.03; I 42.13%.

Preparation of 2-Methyl-6-dimethylamino-2-hexanol (X). A mixture of 5.3 g of the acetal derivative of 2-methyl-4-pentyn-2-ol (VIII), obtained by the previously described method [4], 1.6 g of dimethylamine, 1.25 g of paraform, and 10 ml of dioxane was heated for 8 h at 110°. After cooling, water was added to the reaction mass and the reaction product was extracted with ether. We isolated 2.4 g of the acetal derivative of 2-methyl-6-dimethylamino-4-hexyn-2-ol (IX) with b.p. 124-125° (12 mm); $n^{22}D$ 1.4475. Found: C 68.69, 68.77; H 10.90, 10.91; N 6.47, 6.48%. $C_{13}H_{25}O_2N$. Calculated: C 68.68; H 11.08; N 6.16%. After exhaustive hydrogenation of the compound in 10 ml of methanol at room temperature in the presence of 5% $Pd/CaCO_3$, and subsequent distillation, we obtained the amine (X) with m.p. 129-131° (22 mm); $n^{20}D$ 1.4317. Methiodide, m.p. 128-129° (from acetone). Found: C 40.12, 39.95; H 8.01, 8.16; I 41.93, 42.01%. $C_{10}H_{24}ONI$. Calculated: C 39.87; H 8.03; I 42.13%.

SUMMARY

The addition of dimethylamine to tertiary diacetylenic alcohols was studied and a scheme was given for the transformations that take place here.

LITERATURE CITED

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