MODERN NOTIONS OF THE MECHANISM OF α-TOCOPHEROL SYNTHESIS. HOMOGENEOUS CATALYSIS BY LEWIS ACIDS

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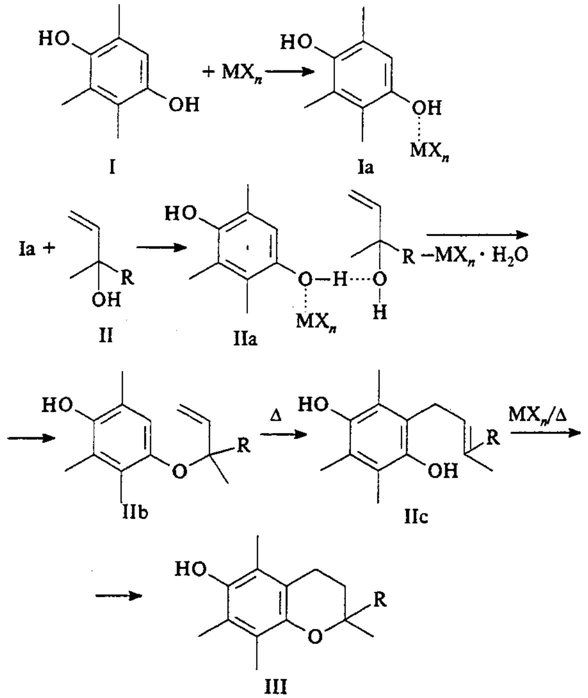
In the study of the synthesis of α-tocopherol from trimethylhydroquinone (I), Wehrli et al. [1] were the first to note the important role of a complex involving trimethylhydroquinone and a Lewis acid. It was suggested that the role of the Lewis acid is to create a complex possessing the properties of the Brönsted acid, which allows the reaction to develop by the carbo-cation mechanism (see the previous article).[2] However, modern experimental data indicate that the formation of α-tocopherol (III) in the presence of Lewis acids proceeds by a mechanism differing from that taking place in the case of catalysis by the Brönsted acids:



$R = C_{16}H_{33}$.

$MX_n = AlCl_3, ZnCl_2, SnCl_4$.

In our opinion, the Lewis acid plays a very important role in the process under consideration, acting not only as a catalyst, but as a reagent and a dehydrating agent as well. On reacting with hydroquinone I, MX_n forms a complex Ia [2, 3] that is especially stable at low temperatures. On adding isophytol (II) the complex yields an allyl ester of trimethylhydroquinone IIb (whereby the Lewis acid binds the water liberated in this reaction, forming a hydrate of the $MX_n \cdot H_2O$ type). Subsequent heating readily leads to a Claisen rearrangement, and the resulting intermediate compound IIc exhibits (on heating in the presence of a catalyst) easy cyclization to form chroman III.

This mechanism is confirmed by our experimental results [2], data on the reaction kinetics [4], spectral characteristics of complexes Ia with Lewis acids [3], liberation of water in the phase appearing at the moment of formation of the intermediate compound IIb (from GC and TLC data), a high yield of compound III, and a very small amount of chromatographically detected impurities [4].

We have established that the initial stage of this process is described by the following kinetic equation for the reaction rate:

$$V = k\,C_{\mathrm{I}} \cdot C_{\mathrm{ZnCl_2}} \cdot C_{\mathrm{II}}^{0.3}$$

where k is the reaction rate constant, and C_{I}, C_{II}, and $C_{\mathrm{ZnCl_2}}$ are the concentrations of compounds I, II, and $ZnCl_2$, respectively (M).

As is seen from this expression, the reaction has first order with respect to trimethylhydroquinone and catalyst ($ZnCl_2$), while the reaction order with respect to isophytol is close to zero. The latter agrees with experiment, since the most complete reaction is observed on gradually adding II to I.

The fact that the concentration of the catalyst enters into the kinetic equation confirms the conclusion that the catalyst (Lewis acid) acts as a reagent in the stage of complex formation. In turn, the complex formation is the limiting factor in the subsequent chain of conversions leading to the formation of a stable chroman nucleus of α-tocopherol. The rate of

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[2] *Khim.-Farm. Zh.*, 31(2), 51 – 52 (1997).

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these subsequent reactions (detachment of water, rearrangements, and cyclization) is determined to a greater extent by the entropy factor.

It is interesting to note that this mechanism is observed in the pure form only for equimolar amounts of the Lewis acid and hydroquinone. At a lower ratio, the reaction proceeds by a mixed mechanism. In the presence of catalytic amounts of the Lewis acid, the reaction involves the carbenium ions (as in the case of the Brönsted acids) and is accompanied by all the undesirable side effects that one usually tries to avoid.

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