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STUDY OF THE INTERACTION OF GOSSYPOL 15,15′-DIMETHYL ETHER WITH ALKALI

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It has been shown that gossypol 15,15′-dimethyl ether in the dilactol form does not react with aqueous solutions of alkali.

Together with coauthors, we have previously shown that when gossypol is stored in methanol it is converted into gossypol 15,15′-dimethyl ether (GDME) in the dilactol form [1]. This is the first time that such a compound has been obtained, and therefore the study of its chemical properties is of definite interest, and this applies particularly in explanation of the reason for the incomplete elimination of gossypol and its derivatives in the refining of cottonseed oil with sodium hydroxide, since in the production of cottonseed oil the gossypol, reacting with the substances accompanying it, forms the corresponding derivatives.

In view of this, we have investigated the interaction of G-15,15′-DME with aqueous solutions of NaOH having various concentrations. Gossypol is very sensitive to the action of alkali. On the brief action upon it of both weak and concentrated solutions of alkali gossypol salts that have arbitrarily been named "gossypolates," soluble in water and insoluble in oil and organic solvents, are formed. The interaction with alkali takes place quantitatively; the neutralization number (N. No.), characterizing the acidic properties of the substance, is 215 mg KOH, which corresponds to the neutralization of only two of the six hydroxy groups [2]. Some authors consider that these are the phenolic 7,7′-OH groups present in the ortho position to aldehyde groups [3], while others assume the interaction of the alkali, with the 1,1′-OH groups [4].

As in the case of gossypol itself, the reaction of GDME with aqueous solutions of NaOH having various concentrations was studied using short-time action of the alkali upon it. The products that passed into the alkali and those that remained in the ethereal solution were analyzed with the aid of GLC.

When gossypol was present, the sodium "gossypolates" formed passed completely from solution in diethyl ether into the aqueous alkali, and, when the latter was acidified, TLC showed the presence of gossypol. Under the action of weak solutions of NaOH (0.5-2.5%) on GDME, the aqueous solution of alkali contained practically no GDME or gossypol. The GDME remained in solution in the diethyl ether. This shows that the 15,15′-GDME in the dilactol form does not interact with weak solutions of alkali. Raising the concentration of NaOH to 5-10% led to a decrease in the amount of GDME in the solvent, and the main products passing into the alkaline solution were gossypol 15-monomethyl ether (GMME) and gossypol.

When the concentration of alkali was raised further, to 20-40%, no GDME was detected in the diethyl ether, and gossypol with trace amounts of GMME was isolated from the alkaline solution. This can be explained by the assumption that on the action of concentrated alkali the 15,15′-dimethyl ether underwent hydrolysis, leading to the formation of the monomethyl ether and, in the final account, to gossypol, which readily reacts with NaOH and passes into the alkaline solution.

The results of a determination of the neutralization numbers of gossypol, GDME, and GMME that we have carried out — 215.3, 8.77, and 104.2 mg KOH, respectively — serve as conformation of what has been said above. The somewhat high value of the N. No. of GDME as compared with the theoretical value, which is zero, is explained by the fact that in the course of the experiment its partial conversion into the monomethyl ether could take place and this interacts with alkali by the second half of the molecule in the same way as gossypol. The theoretical neutralization number of GMME is 106.4 mg KOH, i.e., close to that which we found.

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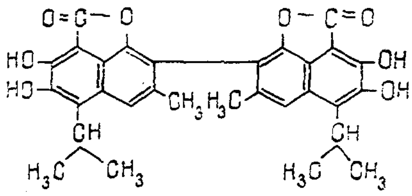
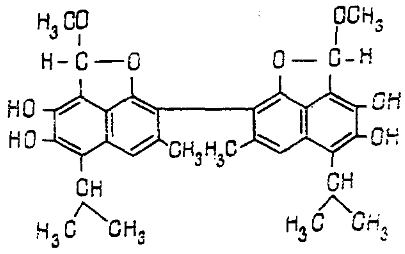
Thus, it has been established that gossypol 15-monomethyl ether interacts with alkali by only one phenolic group while gossypol 15,15′-dimethyl ether in the dilactol form does not react with solutions of alkali at all.

Markman and Vil'kova [4], in studying the influence of the temperature on gossypol dissolved in oil, observed several variants of the mechanism of its oxidation and dwelt upon the fact that a tetrahydrofuran ring is formed, whereupon the aldehyde groups and the acidic 1,1′-hydroxyls that are responsible for the formation of "gossypolates" disappear (see formula).



However, it is known that electron-accepting substituents in the structure of the molecule, such as, in this case, carbonyl groups, must disperse the negative charge and stabilize the anion, and thereby increase the acidity of the hydroxy groups [5]. For this reason, the given substance should interact with NaOH.

From the formula of the GDME that we had obtained and, particularly, from Briegleb–Stuart models and a set of rod-and-ball molecular models of the chemical structures of gossypol and GDME it can be seen that the carbonyl oxygens of the aldehyde groups of gossypol are arranged in space in such a way that, being electron acceptors, they enhance the acidity of precisely the 7,7′-hydroxyls. In view of this, these hydroxyls, possessing an increased acidity in comparison with the other OH groups, react with NaOH.



In the GDME molecule, however, there are no carbonyls, and therefore no reaction with NaOH takes place. Furthermore, it can also be seen from these models that the existence of a hydrogen bond between the oxygens of the aldehyde groups and the hydrogens of the 7,7′-hydroxyls may exert an influence on the increase in the acidity of the 7,7′-hydroxyls. Steric hindrance practically excludes such interaction with the 1,1′-hydroxyls.

In the industrial process of obtaining the oil, an interaction of the aldehyde groups of gossypol with the substances accompanying it takes place, which leads to a decrease in or to the complete loss of acidity of the 7,7′-hydroxyls and, consequently, to the absence of the interaction with NaOH. Remaining in the oil, they adversely affect its color and quality, and other methods must be used for their elimination.

EXPERIMENTAL

GDME was obtained by heating a solution of gossypol in methanol at 50°C for 40 h, and GMME similarly at room temperature for 48 h followed by the TLC isolation of the GMME [6].

The reaction with alkali was conducted in the following way: solutions of gossypol in alcohol were evaporated in a rotary evaporator and the residue was dissolved in diethyl ether in order to prevent possible transformations, after which an aqueous solution of NaOH of the appropriate concentration was added to it to give give pH 8-9. The diethyl ether was separated from the aqueous layer, and after acidification the latter was treated three times with peroxide-free diethyl ether. The combined extracts were washed with water and dried, the ether was distilled off, and the products obtained were analyzed.

TLC was conducted on Silufol in the benzene–ethanol (5:1) system.

The neutralization numbers of gossypol and its derivatives were determined as described in [2, p. 89]. The gossypol, GDME, and GMME were identified by comparison with authentic specimens.

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