ACYLATION OF α,β-UNSATURATED KETONES

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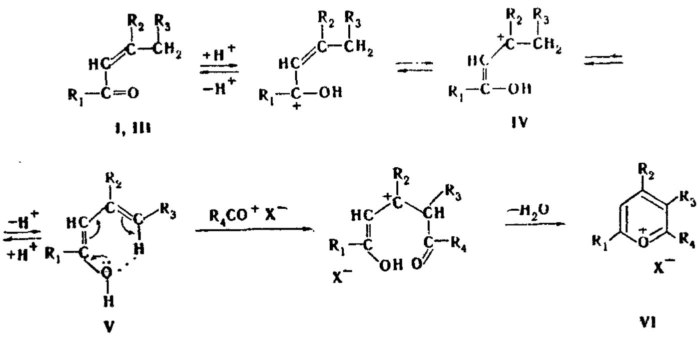
α,β-Unsaturated ketones with a secondary β-carbon atom (ethylideneacetone and n-butylideneacetophenone) undergo acylation to give 2,6-di- and 2,5,6-trisubstituted pyrylium salts. A mechanism is proposed for the reaction.

The first step in the synthesis of pyrylium salts by acylation of α,β-unsaturated ketones (dypnone and mesityl oxide) with anhydrides or acid chlorides in the presence of Lewis acids [1] is conversion of the α,β-unsaturated ketone (I) to the β,γ-unsaturated isomer (II), which undergoes acylation, during which isomerization proceeds through a step involving the formation of a carbonium ion and is the decisive factor that insures the development of the pyrylium salt. Balaban and Nenitzescu assert [2] that only I with a tertiary β-carbon atom can be acylated, since they give a stable carbonium ion that is protonated at the α-carbon atom and is capable of being converted to II. α,β-Unsaturated ketones with a secondary β-carbon atom (ethylideneacetone and crotonaldehyde (III) do not form stable cations and, according to this concept, should not undergo the reaction.

However, there are data [3] that the protonation of ketones proceeds at the oxygen atom of the carbonyl group. In this connection, it seemed more likely to us that the first step in the process is the formation of cation IV, which is converted to enol form V; V is stabilized by the conjugation system and the intramolecular hydrogen bond, and it is precisely V that is then acylated.



VI: a $R_1=R_4=CH_3$; $R_2=R_3=H$; $X=SbCl_6$;
b $R_4=CH_3$
c $R_4=C_2H_5$ } $R_1=C_6H_5$; $R_2=H$; $R_3=C_2H_5$; $X=ClO_4$
d $R_4=C_3H_7$

The development of an intramolecular hydrogen bond in V insures fixing of the active $=CHR_3$ group in the S-cis position, which is favorable for ring closing, and the presence of conjugation leads to the appearance of the +M effect of the hydroxyl group, which creates on the $=CHR_3$ grouping a nucleophilic center that promotes the addition of the acylium cation.

In order to verify this assumption, we carried out experiments involving the acylation of III (ethylideneacetone, ethylideneacetophenone, and n-butylideneacetophenone). As expected, ethylideneacetone (III, $R_1=CH_3$, $R_2=R_3=H$) reacts with acetyl chloride and antimony pentachloride (in a molar ratio of 1:1:2) in

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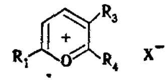
TABLE 1. γ-Unsubstituted Pyrylium Salts

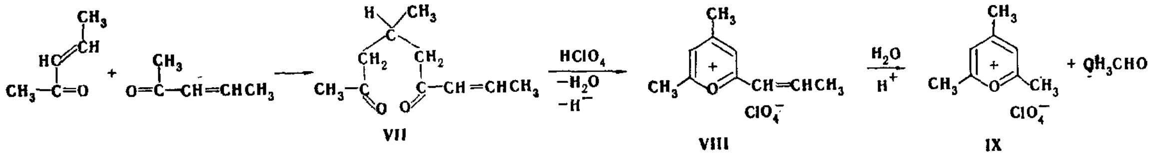


No.	R₁	R₃	R₄	X⊖	mp, °C	Empirical formula	Found, %			Calc., %			Yield, %
							C	H	Cl	C	H	Cl	
VIa	CH_3	H	CH_3	$SbCl_6$	163[5]	—	—	—	—	—	—	—	35
VIb	C_6H_5	C_2H_5	CH_3	ClO_4	160	$C_{14}H_{15}ClO_5$	56,5	5,1	11,7	56,2	5,0	11,8	62
VIc	C_6H_5	C_2H_5	C_2H_5	ClO_4	129	$C_{15}H_{17}ClO_5$	57,7	5,5	11,3	57,6	5,4	11,3	60
VId	C_6H_5	C_2H_5	C_3H_7	ClO_4	140	$C_{16}H_{19}ClO_5$	58,7	5,8	10,9	58,7	5,8	10,8	60

acetic anhydride to give, in ~ 35% yield, 2,6-dimethylpyrylium hexachloroantimonate (VIa) [4, 5], the structure of which was proved by conversion to 2,6-lutidine. This method for the preparation of VIa can be recommended as a preparative method, since it is based on the use of accessible reagents, in contrast to the hard-to-obtain 2,6-heptanedione [5]. The introduction of ethylideneacetophenone (III, $R_1 = C_6H_5$, $R_2 = R_3 = H$) into a similar reaction gives a resinous polymeric product.

The possibility of the acylation of III with acetyl hexachloroantimonate ($CH_3\overset{+}{C}O\,SbCl_6^-$) in excess antimony pentachloride might have been explained by the effect of the latter, which acts as a strongly polar solvent that stabilizes cation IV. However, III is also acylated by acyl perchlorates. The reaction of n-butylideneacetophenone (III, $R_1 = C_6H_5$, $R_2 = H$, $R_3 = C_2H_5$) with acid anhydrides (acetic, propionic, and butyric) in the presence of equimolecular amounts of 70% $HClO_4$ gave the previously unknown 2-phenyl-5-ethyl-6-alkyl(methyl, ethyl, propyl)pyrylium perchlorates (VIb,c,d) in yields up to 62%. This same compound (III) gives 2-phenyl-5-ethylpyrylium perchlorate [6] on formylation with ethyl orthoformate in the presence of perchloric acid.

Acylation of ethylideneacetone with acetyl perchlorate gave a resinous product, from which 2,4,6-trimethylpyrylium perchlorate was isolated in 11% yield (with respect to the starting ethylideneacetone). It can be assumed that in this case there is side autocondensation of the ethylideneacetone to a 1,5-diketone (VII), which is cyclized to the pyrylium salt (VIII). Then, under the influence of the liberated water in an acidic medium, the double bond in the α-propenyl substituent undergoes acidolysis to give IX.



It is possible that, as in the case of chalcones [7], the C=C bond is initially subjected to acidolysis. However, this assumption requires additional verification.

The data on the properties and structure of the pyrylium salts obtained are presented in Table 1.

From the data presented in Table 1 it can be concluded that the reactivity of V depends on the electronic nature of substituents R_1-R_4. Owing to the conjugation system, electron-donor groups (alkyl) promote electrophilic attack of the acylium cation at the γ-carbon atom. It should be noted that, according to [2], the effect of substituent R_1 should not be manifested in view of the presence of a methylene group between the carbonyl group and the β-C atom. However, when the ethylideneacetophenone is used, weakening of the π bond in the free vinyl group of V apparently creates more favorable conditions for the competitive cationic polymerization because of the −M effect of the phenyl ring (R_1).

It is completely likely that the mechanism under consideration also extends to I with a tertiary β-carbon atom. Thus mesityl oxide can readily form the stable S-cis form of V ($R_1 = CH_3$, $R_2 = CH_3$, and $R_3 = H$) owing to the +I effect of the two methyl groups; however, dypnone, by virtue of steric factors, also exists in the cis form (the methyl group attached to the γ-carbon atom is turned toward the carbonyl group).

EXPERIMENTAL

2,6-Dimethylpyrylium Hexachloroantimonate (VIa). A 15.6-ml (0.1 mole) sample of $SbCl_5$ was slowly added dropwise with stirring and cooling to a cooled (to 0°) mixture of 4.2 g (0.05 mole) of ethylideneacetone, 3.9 g (0.05 mole) of acetyl chloride, and 40 ml of acetic anhydride. The mixture was then held at 0° for 30 min and then at room temperature for 24 h. The precipitated yellow crystals were removed by filtration and washed with dry ether and a small amount of acetone to give 7.7 g (34.8%) of yellowish crystals with mp 163-164° (mp 163° [5]). Dilution of the filtrate with dry ether gave another ~ 8 g of dark crystals that deliquesced in air. They were also identified as VIa, as proved by the production of 2,6-lutidine from them.

2,6-Lutidine. This compound was obtained in almost quantitative yield by treatment of VIa with 25% ammonium hydroxide in the usual manner; mp 142° (mp 140-142° [8]). The picrate was obtained as yellow needles with mp 167° (mp 161, 168° [8]).

2-Phenyl-5-ethyl-6-alkylpyrylium Perchlorates (VIb-d). A 1-ml (0.01 mole) sample of 70% $HClO_4$ was added dropwise to a mixture of 1.8 g (0.01 mole) of n-butylideneacetophenone and 0.06 mole of anhydride at 0°. After 30 min, the mixture was diluted with 100 ml of ether, and the acylation product was removed by filtration and crystallized from hot water containing activated charcoal. IR spectra of the salts: 1618, 1560, 1380, and 1110 cm^{-1}.

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