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262. Cyclization of the Enol Esters of *o*-Acyloxyphenyl Alkyl Ketones, IV.

A Kinetic Study of the Steps of the KOSTANECKI-ROBINSON Reaction¹)²)

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(21. VI. 69)

Summary. In a study of the KOSTANECKI-ROBINSON reaction of 2,4-diacetoxy-6-hydroxypropiophenone the rate constants and the order of each step have been approximately determined and compared. Mechanism for the reaction is suggested.

In Part I [1] and II [2] of this series we reported the cyclization of *o*-acyloxyphenyl alkyl ketones into chromones in the presence of bases, in either aqueous or non-aqueous media. In Part III [3] it has been shown that the KOSTANECKI-ROBINSON reaction leading to chromones and isoflavones involves the cyclization of enol esters.

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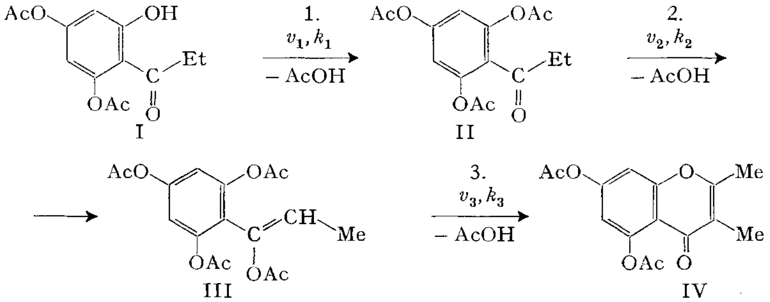
¹) This paper is respectfully dedicated to the memory of ST. VON KOSTANECKI, the famous professor of the University of Bern, for the 60th anniversary of his death.

²) Auf Englisch veröffentlicht gemäss besonderem Beschluss des Redaktionskomitees.

WITTIG *et al.* [4] and later BAKER [5] did considerable research to elucidate the mechanism of this reaction. HEILBRON *et al.* explored the factors affecting the course of the reaction [6]. A kinetical investigation of this reaction has not been reported so far. The present paper deals with a kinetic study of the KOSTANECKI-ROBINSON reaction of 2,4-diacetoxy-6-hydroxy-propiophenone (I). With this model compound the only product is the appropriate chromone IV, *i.e.* no coumarin or 3-acylchromone is produced.

The following reaction steps have been investigated in acetic anhydride in the presence of a base (NaOAc or Et_3N, general symbol B).



Reaction I → II was accomplished in the presence of triethylamine and followed colorimetrically by measuring the rate of disapearance of the orange red colour of the $FeCl_3$ complex of compound I.

Reaction II → III could not be followed satisfactorily in the presence of sodium acetate, since this reaction proceeded to give some IV under these circumstances and the catalyst was slightly soluble at lower temperatures. In the presence of triethylamine and below 120°, however, the reaction practically stopped at the stage of III, and thus v_2 and k_2 could be measured spectrophotometrically.

The last step, *reaction III → IV* was accomplished at higher temperatures in the presence of either sodium acetate or triethylamine, and its rate was followed again spectrophotometrically.

Thus an indirect comparison of the steps of the KOSTANECKI-ROBINSON acylation was possible. Owing to a slight, but definite brownish colour during the reaction, the accuracy of the measurements is estimated to be between 7.5 and 15%.

The results are listed in the Table and in Fig. 1.

Each step was found to be approximately of first order. The rate determining step was the cyclization of the enol ester. The rates were dependent on the base applied, but this had but slight effect upon the overall order of the reaction; the concentration of the base could be considered approximately constant during the reaction. As catalyst sodium acetate is at 180° about 10 times as effective as triethylamine (*cf.* Experiments Nos. 3 and 5) but at lower temperatures (below 100°); the latter becomes slightly superior to sodium acetate.

The rates of the different steps may be indirectly and approximately compared as follows:

$v_1 \approx 4.5\, v_2$ at 100° (*cf.* Exp. Nos. 1 and 2) ,
$v_2 \approx 20\; v_3$ at 180° (*cf.* Exp. Nos. 2 and 3) ,
and $v_1 > v_2 > v_3$.

Rate constants of the steps of the KOSTANECKI-ROBINSON *reaction of 2,4-diacetoxy-6-hydroxy-propiophenone*

Exp.	Initial concn. of the base mol · l⁻¹			Rate constants (min.⁻¹) obtained at different temperatures (°C)								
No.	NaOAc	Et_3N		25°	80°	90°	100°	110°	120°	160°	170°	180°
1	–	0.2	k_1	4.0×10^{-2} a)	6.0×10^{-2}	6.3×10^{-2}	6.7×10^{-2}	–	–	–	–	–
2	–	0.2	k_2	0.5×10^{-3} a)	–	–	1.4×10^{-2}	2.1×10^{-2}	2.8×10^{-2}	–	–	1.5×10^{-1}
3	–	0.2	k_3	0.8×10^{-6} a)	–	–	0.17×10^{-3} a)	–	–	0.36×10^{-2}	0.5×10^{-1}	0.76×10^{-2}
4	0.43	–	k_3	$<0.5\times10^{-6}$ a)	–	–	0.2×10^{-3} a)	–	–	0.7×10^{-2}	1.1×10^{-2}	1.75×10^{-2}
5	0.018	–	k_3	$<0.2\times10^{-8}$ a)	–	–	1.25×10^{-5} a)	–	–	0.17×10^{-2}	0.35×10^{-2}	0.65×10^{-2}

The initial concentration of the appropriate ester was always 0.1 mol · l⁻¹.

a) Extrapolated values, obtained from the ARRHENIUS equation.

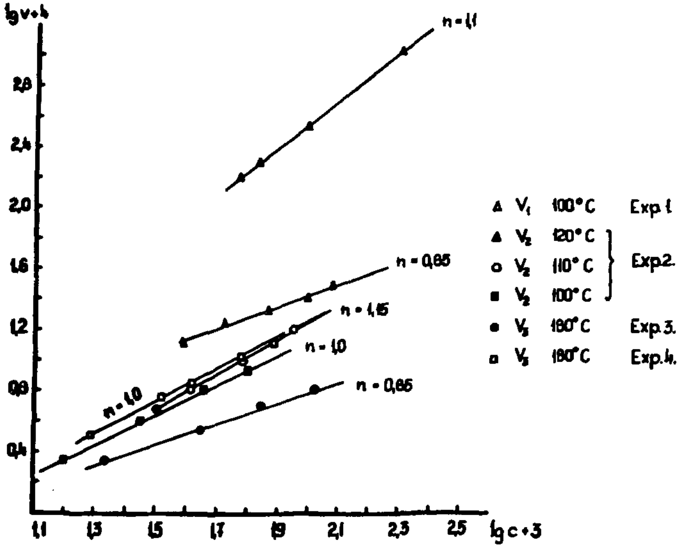
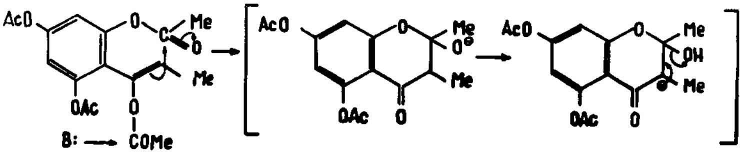


Fig. 1. *Dependence of the rates on the concentration*
(VAN 'T HOFF's differential method applied to single runs)
n = order of the reaction

Extrapolation of the rate constants to 25° is by no means exact, and in case of sodium acetate the rates in reality are smaller than those obtained by extrapolating the rate constants to 25° since the solubility of the catalyst at lower temperature decreases; still it gives a rough idea for the rates of the steps studied. At 25° v_3 becomes very low, this explains and verifies our earlier observation [3] that at room temperature the reaction carried out in the presence of sodium acetate practically stops at the stage of enol acetate with $k_3 < 10^{-9}$. In fact, a recent run kept at 25° for 400 days did not yield any other product than III.

Concerning the finer details of the mechanism, the first step is doubtless a simple esterification shifted to favour the complete formation of II as a result of the presence of the base, the huge excess of the anhydride, and the consecutive reactions. The existence of this step was claimed in the pioneer work of Wittig [4] and also by Baker [5], who completed the picture of the mechanism of the Kostanecki-Robinson reaction. The second step must involve both the enolization and esterification of compound II. On the basis of the bromine consumption, this starting compound is present practically completely in the keto form at the zero time of the reaction. Step 2 is shifted to the right for the same reasons as given for step 1.

For the mechanism of the rate determining third step we suggest the following pattern:



III A B

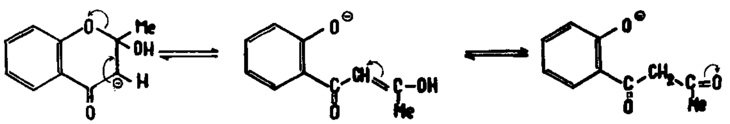
$\downarrow$

IV

The new C–C bond effecting the ring closure of the *trans* isomer of III must be formed earlier than, or simultaneously with, the deacylation of the enolic hydroxyl, otherwise the triacetate II would be obtained, which is known to give chromone only *via* the enolester III [3].

Both, Wittig and Baker suggested the intermediate formation of chromanon-2-ol from the 2-acetoxyphenyl alkyl ketone, which was supposed to lose water to give the end-product. According to Indian authors [7], the dehydration of this intermediate hemiketal begins with the loss of a proton from position 3 to give the anion B whose formation *via* compound A from III is now suggested. The transformation A → B requires participation by a proton source and a base of which there are many possibilities in the reaction mixture of the Kostanecki-Robinson acylation.

If the starting 2-hydroxyacetophenone contains no substituent in the ω position, 3-acylchromones may be formed. In this case the anion corresponding to B can be cleft leading to enol and keto tautomers of a diketone-anion [7] or to their protonated



forms. Any of these compounds available may be the species undergoing O- or C-acylation, to give the parent compound of a 3-acylchromone which may undergo dehydrationas well as further cleavage or Baker-Venkataraman transposition followed by cyclization. This comprehension of the reaction would be in harmony with both, Wittig's and Baker's experimental findings [4] [5][3].

In the case of the Allan-Robinson reaction leading to flavones, the presence of enolbenzoate intermediate could not yet be unambiguously demonstrated, therefore its mechanism may not necessarily be the same as that of the Kostanecki-Robinson reaction, though it must be very similar.

Experimental. – Compounds I, II and III were prepared as described previously [3]. The reaction components were weighed and heated in 10 ml sealed ampoules. At given intervals an ampoule was removed, opened, its content diluted with 96% ethanol, and the concentration determined. In the case of the first step, the concentration of I was measured as its $FeCl_3$-complex by means of a Pulfrich colorimeter, using pH = 7.0 buffer and 4 drops of 20% aqueous $FeCl_3$ solution added to each sample which had been diluted to 2.5 times of the original volume. Reading was taken within 2–3 minutes. In steps 2 and 3 the extinctions were measured on the samples at several wave lengths in a Beckman spectrophotometer, Type D.U. Samples were diluted to 100-fold volume. Spectra obtained in the presence of Et_3N are demonstrated in Fig. 2.

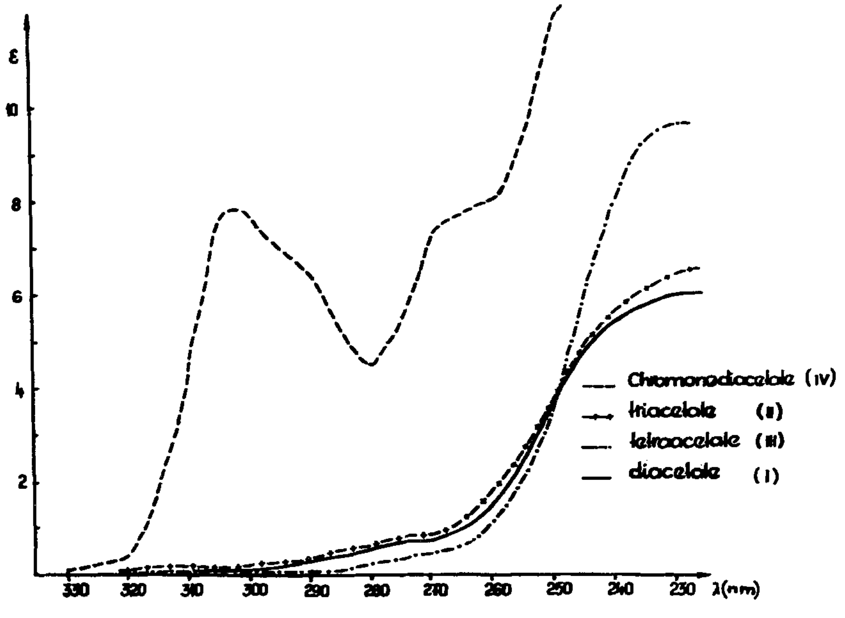


Fig. 2. *Spectra obtained in the presence of Et_3N for compounds I, II, III and IV in 96% ethanol*

The activation energy of step 3 depended on the base applied (and perhaps also on its concentration). Under the conditions of Exp. No. 4 = 21 and in Exp. No. 5 = 25.8 kcal · mol^{-1} · $grade^{-1}$ was found, the mean value being 23.4 ± 3. In the presence of Et_3N in Exp. No. 3 = 16 ± 2 kcal × mol^{-1} · $grade^{-1}$ was determined. Activation energy of step 2 obtained in Exp. No. 2 was found to

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[3] The mechanism of the formation of 3 acylchromones appears to be rather difficult to interpret because there are so many alternative routes for the acylation. The elucidation of the fine details needs extensive further work.

be 10.1 ± 1.5 kcal · mol^{-1} · $grade^{-1}$ and that of step 1 proved to be 1.45 ± 0.3 kcal · mol^{-1} × $grade^{-1}$. Owing to experimental difficulties these values are to be considered just as informative.

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263. Acetylene mit Elektronendonator- und Elektronenakzeptorgruppen 1)

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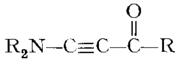
Herrn Prof. Dr. W. FEITKNECHT zum siebzigsten Geburtstag gewidmet

(11. X. 69)

Summary. Acetylenes having both electrondonating and electronaccepting groups (**1**) may be obtained in good yield from the correspondingly substituted olefines *via* bromination and elimination of HBr. The reaction of the acetylene aldehyde **1a** with proton acids yields, after rearrangement of the primary adducts, the β-substituted acrylamides. Addition of nucleophiles leads to the β-disubstituted α,β-unsaturated carbonyl compounds. With hydrazines one obtains pyrazoles and pyrazolones. The acetylenes **1** undergo [2+2]-, [2+3]- and [2+4]-cycloaddition reactions.

Einleitung. – Acetylene mit Elektronendonator- (Push) und Elektronenakzeptorgruppen (Pullgruppen) des Typs **1** enthalten die Bausteine von Alkinaminen **2** [3] und Alkincarbonylverbindungen **3**. Im Vergleich zu Alkinaminen sollte in **1** das die Elektronendonator-Gruppe tragende C-Atom erhöhte elektrophile, im Vergleich zu Alkincarbonylverbindungen das der Elektronenakzeptor-Gruppe benachbarte C-Atom dagegen erhöhte nucleophile Reaktivität aufweisen.

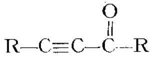


$R_2N-C\equiv C-\overset{O}{\overset{\|}{C}}-R$

1

$R_2N-C\equiv C-R$

2



$R-C\equiv C-\overset{O}{\overset{\|}{C}}-R$

3

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