THE STUDY OF THE ACID CATALYSED MICHAEL ADDITION TO FERROCENE DERIVATIVES OF α,β-UNSATURATED KETONES. KINETICS OF CYCLIZATION OF 1-ACETYL-1′-(*p*-CHLOROCINNAMOYL)FERROCENE

Štefan Toma[a] and Anton Gáplovský[b]

[a] *Department of Organic Chemistry and*
[b] *Chemical Institute, Commenius University, 842 15 Bratislava*

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Cyclization of 1-acetyl-1′-(*p*-chlorocinnamoyl)ferrocene catalysed by H_2SO_4, HCl, CF_3COOH and BF_3. $(C_2H_5)_2O$ has been studied. Kinetic study of the title reaction catalysed by HCl showed that the rate of cyclization increases with the catalyst concentration. Activation parameters of the cyclization are as follows: $\Delta H^{\neq} = 81{\cdot}76$ kJ mol^{-1}, $-\Delta S^{\neq} = 55{\cdot}73$ J mol^{-1} K^{-1}. Attempts at acid catalysed addition of several C-nucleophiles to cinnamoylferrocene and acryloylferrocene have been unsuccessful. The effect of the acidity of reaction medium on the electronic spectra of studied ferrocene derivatives is discussed.

Base catalysed Michael additions are well studied and have been frequently used in organic synthesis[1–5]. Acid catalysed Michael additions are much less frequent and have not a yet been investigated systematically[4]. More detailed study of the acid catalysed addition has been reported for the addition of acetylacetone to 6-hydroxypteridine[6] and 7-hydroxypteridine[7]. Kaplan[8] reported on the kinetics of acid catalysed (CH_3COOH, $HClO_4$) addition of trinitromethane to methyl acrylate. The author found that the reaction is generally acid catalysed and at low perchloric acid concentrations its rate increases with catalyst concentration, *i.e.* the rate determining step is not the addition of C-nucleophile but the protonation of the reaction intermediate. A similar course has been postulated also by Zalutaiev[9] for the addition of 2-nitro-1,3-indanedione to chalcone.

In our previous works[10,11] we have proved that the acid catalysed reaction of 1-acetyl-1′-acylferrocenes with aromatic aldehydes does not stop in the stage of Claisen–Schmidt condensation but it proceeds as the consecutive acid catalysed Michael addition to give [5]-ferrocenophane-1,5-dione derivatives. Intramolecular acid catalysed Michael addition was studied also by Elečko[12] in the case of cyclization of 1-cinnamoyl-1′-phenylacetylferrocenes.

The aim of this work was to examine the possibility of acid catalysed Michael addition to cinnamoylferrocene, acryloylferrocene and cyclization of 1-acetyl-1-(*p*-chlorocinnamoyl)ferrocene as well as to study the kinetics of this acid catalysed cyclization.

Our attempts at the addition of ethyl α-cyanobutyrate, acetylacetone, cyclohexanone, ethyl malonate and 1,3-indanedione to cinnamoylferrocene under different conditions such as CH_3OH/HCl, CH_3COOH/H_2SO_4, CF_3COOH and $(C_2H_5)_2O/$

/$BF_3.(C_2H_5)_2O$ have not been successful. For this reason we made an attempt to realize this addition to the more reactive system, acryloylferrocene. Blank experiments (without C-nucleophile) proved that in most cases there proceeds the addition of solvents (CH_3OH, CH_3COOH) to acryloylferrocene, except for the reaction of ethyl malonate in diethyl ether catalysed by $BF_3.(C_2H_5)_2O$ in which the addition of the reagent has been detected (TLC, ^1H NMR). However, even in this case the pure product could not be isolated and characterized unambiguously.

From the above mentioned facts it follows that the acid catalysed Michael addition has not wide application and can be utilized only with very reactive acceptors or in cases where the addition leads to thermodynamically very stable compounds.

Therefore, the kinetic study of the acid catalysed Michael addition has been limited to the cyclization of 1-acetyl-1′-(*p*-chlorocinnamoyl)ferrocene. Preparative experiments proved that the reaction of this compound under various conditions results in formation of 3-(4-chlorophenyl)[5]ferrocenophane-1,5-dione, that is in $CH_3.COOH/H_2SO_4$ (68%), CH_3OH/HCl (95%) and $(C_2H_5)O/BF_3(C_2H_5)_2O$ (85%). The reaction proceeds worst in pure trifluoroacetic acid which gives the expected product (21%) accompanied by the unreacted starting compound and by-products of decomposition of ferrocene derivatives. As the method used did not allow to investigate the kinetics of cyclization catalysed by $BF_3.(C_2H_5)_2O$ and also the work

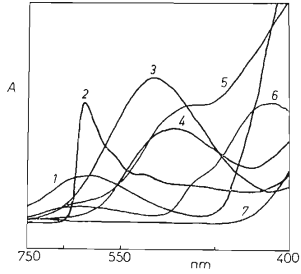


FIG. 1

Electronic spectra of ferrocene derivatives measured in CF_3COOH. *1* *p*-Chlorocinnamoylferrocene, *2* ferrocene, *3* acetylferrocene, *4* 1,1′-diacetylferrocene, *5* 3-(*p*-chlorophenyl).[5]ferrocenophane-1,5-dione, *6* 1-acetyl-1′-(*p*-chlorocinnamoyl)ferrocene, *7* $FeCl_3$

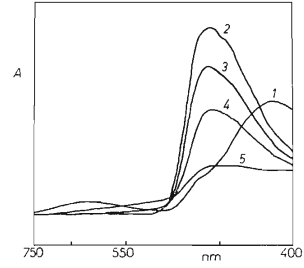


FIG. 2

Time dependence of the spectrum of 1-acetyl-1′-(*p*-chlorocinnamoyl)ferrocene in $CF_3.COOH$; *1* immediately after dissolution, *2* after 120 min, *3* after 225 min, *4* after 300 min *5* after 1 200 min

with CH_3COOH/H_2SO_4 mixture was complicated, we decided to investigate the kinetics of cyclization in trifluoroacetic acid and CH_3OH/HCl mixture.

As shown in Fig. 1, the visible spectrum of 1-acetyl-1 -(*p*-chlorocinnamoyl)ferrocene shows a flat maximum at 600 nm. A similar maximum occurs also in the spectrum of (*p*-chlorocinnamoyl)ferrocene. However, neither 1,1 -diacetylferrocene nor 3-(*p*-chlorophenyl)[5]ferrocenophane-1,5-dione do not absorb in this region (they have λ_{max} 470 nm). Therefore, the maximum at 600 nm can be used to study the reaction. We assume that this maximum belongs only to the $d-d^*$ transition of the protonated starting compound. (The character of this long-wave maximum will be discussed in detail in subsequent work).

The spectrum of ferrocene in CF_3COOH exhibits also the maximum at 600 nm, but the character of this band (very sharp maximum) excludes that we deal here with the $d-d^*$ transition of ferrocene. This can be ascribed to the $d-d^*$ transition of ferricinium cation which absorbs at 617 nm (ref.[13]) in CCl_4 or $CHCl_3$. The time dependence of the spectrum of 1-acetyl-1'-(*p*-chlorocinnamoyl)ferrocene in CF_3. .COOH (Fig. 2) documents that the absorbance of the band at 600 nm decreases with simultaneous increase in the absorbance of the 450 nm band (up to a certain maximum). At 40°C and in CF_3COOH, by following the decrease in the 600 nm band we found $k = 6{\cdot}7 \cdot 10^{-5}\ s^{-1}$ and by following the 450 nm band incerase we obtained $k = 6{\cdot}28 \cdot 10^{-5}\ s^{-1}$. Then also the latter maximum begins to decrease. The above dependence indicates that in this medium the cyclization does proceed (the starting compound absorbance decreases and the product concentration increases), but in further stage the product undergoes decomposition. Especially at higher temperatures the cyclization is complicated from the very beginning by the competition reaction-decomposition of the ferrocene derivative. The decomposition of this derivative is very accelerated by the addition of tetrachloromethane to the solution.

By contrast to CF_3COOH, such a modification of the starting compound does not take place in CH_3OH/HCl. In this mixture 1-acetyl-1 -(*p*-chlorocinnamoyl)ferrocene is stable enough but its cyclization procceds at a fast rate. Fig. 3 shows that the reaction rate increases with the concentration of HCl. However, this dependence is not linear. The kinetic study was carried out in CH_3OH/HCl 1 : 1 (v : v) and gave the following rate constants:

t, °C	28·0	36·6	46·5	54·4
$10^4 k$, s^{-1}	1·564	3·086	8·748	21·660

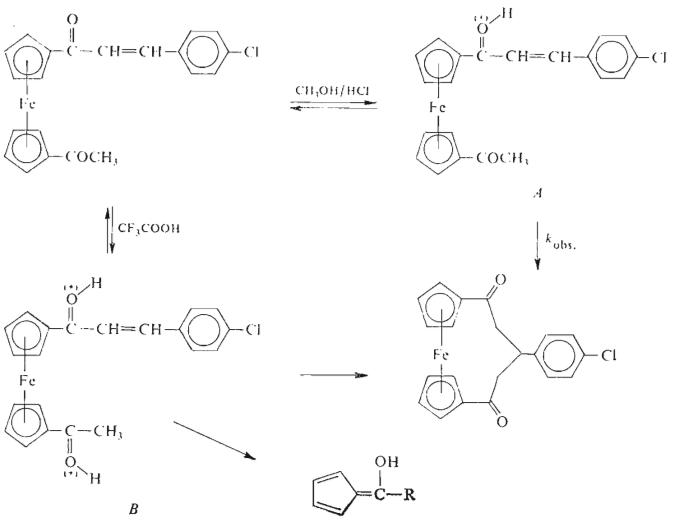
$\Delta H^{\neq} = 81{\cdot}76 \pm 2{\cdot}00$ kJ mol^{-1}, $\Delta S^{\neq} = 55{\cdot}73 \pm 10{\cdot}04$ J mol^{-1} K^{-1}.

Comparison of these data with the values obtained for the cyclization of the same derivative catalysed by sodium methoxide[14,15] allows to conclude that the acid

catalysed cyclization is about twice as fast, but activation parameters (see above) are close to those which were found for the base catalysed reaction, *i.e.* $\Delta H^{\neq} = 82{\cdot}9$ kJ mol^{-1} and $-\Delta S^{\neq} = 60{\cdot}6$ J mol^{-1} K^{-1} (*cf.*[14], repeated experiment) or $\Delta H^{\neq} = 78{\cdot}49$ kJ mol^{-1} and $-\Delta S^{\neq} = 75{\cdot}1$ J mol^{-1} K^{-1} (*cf.*[15]).

Observed dependence of cyclization rate on reaction conditions can be explained by assuming that in CH_3OH/HCl only the oxygen of the more basic carbonyl group (*i.e.* cinnamoyl) is protonated (Scheme 1, intermediate *A*). The increase in the rate of cyclization in dependence on HCl concentration (Fig. 3) can be ascribed to the increasing concentration of intermediate A which undergoes this cyclization. In trifluoroacetic acid both carbonyl groups are protonated to form intermediate *B* which undergoes cyclization at a slower rate. On the other hand, the protonation to the second step accelerates the decomposition of the ferrocene derivative[16].

In the course of kinetic studies we have found that the spectra of 1-acetyl-1′-(*p*-chlorocinnamoyl)ferrocene change significantly in dependence on the solvent used. In order to explain these changes we have measured electronic spectra of 3-(*p*-chloro-



SCHEME 1

phenyl)[5]ferrocenophane-1,5-dione (Figs 4 and 5), 1-phenyl-3-(*p*-chlorophenyl)--2-propenone (Fig. 6) and *p*-chlorocinnamoylferrocene (Figs 7 and 8) in the 220 to 700 nm region in three solvents (methanol, trifluoroacetic acid and in methanol/HCl 1 : 1 (v : v) mixture. With respect to the decomposition of ferrocene derivatives in trifluoroacetic acid (see above), the values of absorbance are not included in figures.

Spectra of 3-(*p*-chlorophenyl)[5]ferrocenophane-1,5-dione are very similar in all the solvents. The spectrum of 1-phenyl-3-(*p*-chlorophenyl)-2-propenone shows two maxima. One at 240 nm is usually ascribed to the $\pi - \pi^*$ transition of the C=C bond and the second at 310 nm is the so called K band of chalcone type system. On going from methanol to methanol/HCl mixture and to trifluoroacetic acid one observes bathochromic shift of both bands. The K band shifts by 10 or 20 nm. The visible spectrum does not show any maximum.

In addition to analogous bands at 230 nm and 310 nm (K band) the spectrum of *p*-chlorocinnamoylferrocene exhibits a band at 485 nm which can be ascribed[17] to the $d - d^*$ transition. On going from methanol to methanol/HCl mixture one observes a small (10 to 20 nm) bathochromic shift of all three bands. The spectra measured in trifluoroacetic acid show, however, a significant bathochromic shift and that from 315 nm to 415 nm for the K band and from 485 nm to 610 nm for the $d - d^*$ transition. Observed changes in electronic spectra of both chalcones can be explained by the dependence of the structure of protonated chalcone on the structure of starting substance and on the solvent (Scheme 2). The structure of protonated chalcone can be closer to the limit structure *C*, *i.e.* to the complex of proton with the carbonyl group, or to the limit structure *D*, *i.e.* to the hydroxycarbenium ion. The

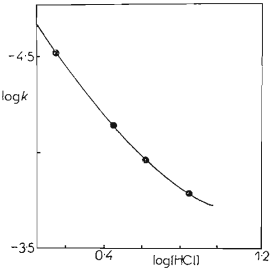


FIG. 3

Dependence of log *k* of cyclization of 1-acetyl-1′(*p*-chlorocinnamoyl)ferrocene on log . [HCl] (*k* in s^{-1}, HCl conc. in mol/dm^3)

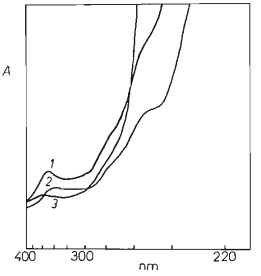


FIG. 4

Electronic spectrum of 3-(*p*-chlorophenyl). .[5]ferrocenophane-1,5-dione in *1* CH_3OH/ /HCl 1 : 1 (v : v), *2* CH_3OH and *3* CF_3COOH

different structure of products of the interaction of 1,5-bis(2-thienyl)-1,4-pentanediene-3-one with trifluoroacetic acid of different concentration has been already proved[18].

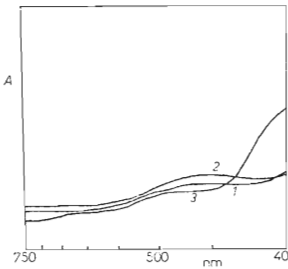


FIG. 5

Electronic spectrum of 3-(*p*-chlorophenyl).[5]ferrocenophane-1,5-dione in *1* CH_3.OH/HCl (1 : 1 (v : v), *2* CH_3OH and *3* CF_3COOH

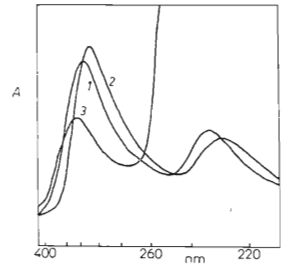


FIG. 6

Electronic spectrum of 1-phenyl-3-(*p*-chlorophenyl)-2-propenone in *1* CH_3OH/HCl 1 : 1 (v : v), *2* CH_3OH and *3* CF_3COOH

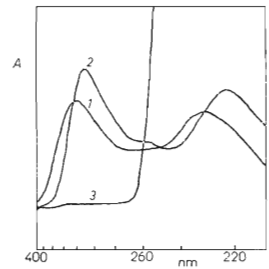


FIG. 7

Electronic spectrum of *p*-chlorocinnamoylferrocene in *1* CH_3OH/HCl 1 : 1 (v : v), *2* CH_3OH and *3* CF_3COOH

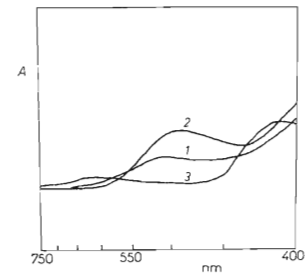
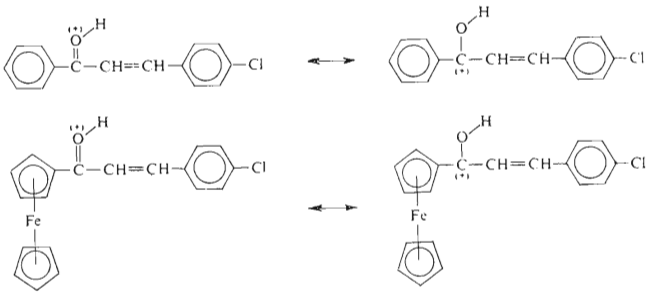


FIG. 8

Electronic spectrum of *p*-chlorocinnamoylferrocene in *1* CH_3OH/HCl 1 : 1 (v : v), *2* CH_3OH and *3* CF_3COOH



C *D*

SCHEME 2

Change of medium containing CH_3OH/HCl does not result in preferential formation of structure *D* in the case of benzene chalcone while in the case of the ferrocene analogue the structure *D* is strongly preferred in trifluoroacetic acid due to the significant stabilization of carbenium ion by ferrocenyl[19,20]. When measuring the spectra of *p*-chlorocinnamoylferrocene in CH_3OH/CF_3COOH mixtures or in CH_2Cl_2 saturated by hydrogen chloride, we have found that in CH_2Cl_2 saturated by hydrogen chloride the band at 610 nm is present while in the CH_3OH/CF_3COOH mixture this band appears in the spectrum at CF_3COOH concentrations exceeding 60%. This is in agreement with the proposed hypothesis, since in CH_3OH/CF_3COOH or CH_3OH/HCl mixture the acid proper which protonates chalcone is $CH_3OH_2^+$, which in turn is weaker acid than anhydrous HCl or CF_3COOH.

EXPERIMENTAL

Synthesis of cinnamoylferrocene, *p*-chlorocinnamoylferrocene and 1-phenyl-3-(*p*-chlorophenyl)--2-propenone was reported earlier[21]. Acryloylferrocene was prepared by reported procedure[22]. 1-Acetyl-1′-(*p*-chlorocinnamoyl)ferrocene and 3-(*p*-chlorophenyl)[5]ferrocenophane-1,5-dione were reported in our previous work[15].

Cyclization of 1-Acetyl-1′-(*p*-chlorocinnamoyl)ferrocene

Procedure A. 1-Acetyl-1′-(*p*-chlorocinnamoyl)ferrocene (0·59 g, 4·5 mmol) was dissolved in 40 ml of methanol and then 40 ml of concentrated hydrochloric acid were added. The reaction mixture was allowed to stand at ambient temperature for 20 h. Then the mixture was transferred into water, the precipitate formed was filtered off, washed with water until neutral reaction and recrystallized from ethanol to yield 0·56 g (95%) of 3-(*p*-chlorophenyl)[5]ferrocenophane--1,5-dione melting at 304°C (with decomposition).

Procedure B. The reaction mixture containing 0·59 g (1·5 mmol) of 1-acetyl-1′-(*p*-chlorocinnamoyl)ferrocene, 40 ml of acetic acid and 4 ml fo concentrated sulphuric acid was allowed to stand at ambient temperature for 20 h. The the mixture was transferred into water, the organic material was extracted with dichloromethane, the solution was washed with water and dried (Na_2SO_4). After evaporation of the solvent, the residue was crystallized from ethanol, giving 0·40 g (68%) of 3-(*p*-chlorophenyl)[5]ferrocenophane-1,5-dione.

Procedure C. To solution of 0·59 g (1·5 mmol) of 1-acetyl-1′-(*p*-chlorocinnamoyl)ferrocene in 50 ml of dry dioxane, 8 ml of $BF_3.(C_2H_5)_2O$ were added. The reaction mixture was allowed to stand at room temperature for 20 h, then it was transferred into water, the organic material was extracted with dichloromethane. The dichloromethane solution was washed with water and dried over Na_2SO_4. After evaporation of dichloromethane, the residue was crystallized from ethanol, giving 0·50 g (85%) of 3-(*p*-chlorocinnamoyl)[5]ferrocenophane-1,5-dione.

Procedure D. Solution of 0·59 g (1·5 mmol) of 1-acetyl-1′-chlorocinnamoylferrocene in 40 ml of trifluoroacetic acid was allowed to stand at ambient temperature for 20 h. The mixture was transferred into water and the organic material was extracted with dichloromethane. The dichloromethane solution was washed with water and dried (Na_2SO_4). After evaporation of the solvent, the residue was chromatographed on SiO_2, using benzene–ethyl acetate 9 : 1 as the eluent. By this procedure we obtained 0·34 g (58%) of the starting compound and 0·12 g (21%) of 3-(*p*-chlorocinnamoyl)[5]ferrocenophane-1,5-dione.

Measurements

Electronic spectra of all the derivatives were measured with Perkin–Elmer 450 spectrophotometer. As the concentrations of the substance in trifluoroacetic acid (see later) could not be determined with satisfactory accuracy, data on absorbance are not given in figures.

Kinetic measurements were carried out with the use of the same spectrophotometer and kinetic data were treated automatically[14]. The reaction medium was hydrochloric acid (37%) at different ratios with respect to methanol and the pure (98%) trifluoroacetic acid.

The reactions catalysed by hydrochloric acid were followed in 400—280 nm wavelength region, determining the consumption of the starting compound, the initial concentration of which was $5 . 10^{-5}$ mol/dm^3. Solution of the starting compound in methanol (5 ml) and 5 ml of hydrochloric acid were placed in round bottom flasks, the necks of which were connected *via* bent connecting glass tubes equipped with ground glass joint, and were heated to reaction temperature. The experiment was started by mixing these solutions and transferring them several times from one flask to the other and this solution was placed into temperature-controlled cell.

Kinetics of the reactions catalysed by trifluoroacetic acid was determined on the basis of the consumption of the starting compound followed in the region around 600 nm (the initial concentration was $1 . 10^3$ mol/dm^3) and the increase in the product concentration followed in the region of around 450 nm (the initial concentration $5 . 10^{-5}$ mol/dm^3). The sample was disso lved in trifluoroacetic acid by mixing in the flask and the solution was transferred immediately to temperature-controlled cell heated to the reaction temperature.

Note added in proof: The more pronounced red shift was observed in the UV—VIS spectra of cinnamoylruthenocene in CF_3COOH compared with cinnamoylferrocene. The K-band was shifted from 306 nm in CH_3OH to 485 nm in CF_3COOH. This observation is in accord with the our hypothesis, and the more pronounced stabilizing effect of ruthenocenyl on the α-carbenium ion[19].

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