ACYLATION OF ω-PHENYLALKANOYLFERROCENES BY CINNAMOYL AND PHENYLPROPIOLYL CHLORIDES

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In Friedel–Crafts acylation of ω-phenylalkanoylferrocenes, the site of electrophilic attack depends on the reagent used. The acylation with cinnamoyl chloride yields preferentially the products of substitution of the unsubstituted cyclopentadienyl ring of ferrocene. The acylation with phenylpropiolyl chloride affords the products of acylation of the benzene ring of the starting compound. The different behaviour of both acylating agents is discussed.

In preparing bridged ferrocene derivatives[1] we have found that 1-cinnamoyl-1'--(ω-phenylalkanoyl)ferrocenes can be obtained by acylation of ω-phenylalkanoylferrocenes with cinnamoyl chloride. Analogous acylation with phenylpropiolyl chloride did not result in all cases in formation of the expected 1,1'-disubstituted ferrocene derivatives. The aim of this work has been therefore to study Friedel–Crafts acylation of ω-phenylalkanoylferrocenes by the above acid chlorides and to account for the observed differences. In addition to these aspects, the work was initiated also by the fact that in some studies[2,3] dealing with acylations of aromatic hydrocarbons by cinnamoyl and phenylpropiolyl chlorides such differences have not been reported. The exceptions are some consecutive reactions[4].

EXPERIMENTAL

^{1}H NMR spectra were recorded with Tesla Brno BS 487 spectrophotometer working at 80 MHz or with Bruker 300 instrument, using saturated solutions of the compounds in C^2HCl_3 (99% of ^2H isotope). Tetramethylsilane was used as internal reference. Chemical shifts are given in δ values. Melting points were determined with Kofler hot plate and are not corrected. All reactions were carried out under nitrogen.

Synthesis of ω-Phenylalkanoylferrocenes

A stirred solution of 0·04 mol of the chloride of appropriate ω-phenylalkanoic acid and 0·05 mol of ferrocene in 200 ml of dry dichloromethane was kept at 0—5°C and 0·07 mol of anhydrous $AlCl_3$ was gradually added. The mixture was stirred at 10—15°C for 3 h and then it was poured into 500 ml of ice-cool water. The organic material was extracted with dichloromethane, the dichloromethane solution was washed thoroughly with water and dried (Na_2SO_4). The sodium

sulphate was filtered off and the solvent was evaporated. The residual mixture was chromatographed on a silica gel column, using benzene as an eluent.

Phenylacetylferrocene (I): acylation with phenylacetyl chloride afforded 65% of *I*, m.p. 130 to 134°C (benzene–hexane), in accordance with literature[5]. ^{1}H NMR spectrum: 3·94 (s, 2 H, CH_2); 4·21 (s, 5 H, C_5H_5); 4·56 (t, 2 H, H_β); 4·91 (t, 2 H, H_α); 7·31 (m, 5 H, C_6H_5).

3-*Phenylpropiolylferrocene* (II): acylation with 3-phenylpropiolyl chloride afforded 55% of *II*, m.p. 76—77°C (benzene–petroleum ether). For $C_{19}H_{18}FeO$ (318·2) calculated: 71·71% C, 5·70% H, 17·55% Fe; found: 71·59% C, 5·72% H, 17·59% Fe. ^{1}H NMR spectrum: 3·03 (m, 4 H, CH_2); 4·08 (s, 5 H, C_5H_5); 4·48 (t, 2 H, H_β); 4·78 (t, 2 H, H_α); 7·32 (bs, 5 H, C_6H_5).

4-*Phenylbutanoylferrocene* (III): acylation with 4-phenylbutanoyl chloride afforded 69% of *III*, m.p. 74°C (benzene–petroleum ether). For $C_{20}H_{20}FeO$ (332·2) calculated: 72·30% C, 6·06% H, 16·81% Fe; found: 72·56% C, 6·18% H, 16·21% Fe. ^{1}H NMR spectrum: 2·02 (m, 2 H, CH_2); 2·70 (t, 4 H, CH_2); 4·12 (s, 5 H, C_5H_5); 4·45 (t, 2 H, H_β); 4·72 (t, 2 H, H_α); 7·24 (bs, 5 H, C_6H_5).

5-*Phenylpentanoylferrocene* (IV): acylation with 5-phenylpentanoyl chloride afforded 56% of *IV*, m.p. 68—70°C (benzene–hexane). For $C_{21}H_{22}FeO$ (346·2) calculated: 72·84% C, 6·40% H, 16·12% Fe; found: 72·96% C, 6·72% H, 15·87% Fe. ^{1}H NMR spectrum: 1·73 (m, 4 H, CH_2); 2·67 (m, 4 H, CH_2); 4·17 (s, 5 H, C_5H_5); 4·45 (t, 2 H, H_β); 4·75 (t, 2 H, H_α); 7·21 (bs, 5 H, C_6H_5).

Acylation of ω-Phenylalkanoylferrocenes with Cinnamoyl Chloride

A stirred solution of 6 mmol of the corresponding ω-phenylalkanoylferrocene and 8·5 mmol of cinnamoyl chloride in 90 ml of dry dichloromethane was cooled to 0—5°C and then at this temperature 30 mmol of anhydrous $AlCl_3$ were gradually added. After addition was completed, the mixture was stirred at 10—15°C for 3 h, poured into 500 ml of ice-cool water. The organic material was extracted with dichloromethane, the dichloromethane solution was washed thoroughly with water and dried (Na_2SO_4). After sodium sulphate had been filtered off, the solvent was distilled off and the residue was chromatographed on a silica gel column, using benzene with addition of 3—15% of ethyl acetate as an eluent. In all cases, in addition to the main products the unreacted starting compound (25—50%) and small amounts of other unidentified substances were isolated.

1-*Cinnamoyl*-1'-*phenylacetylferrocene* (Ia): acylation of compound *I* gave 38% of *Ia*, m.p. 147 to 149°C (benzene–hexane), in accordance with literature[6]. For $C_{27}H_{22}FeO_2$ (434·3) calculated: 74·66% C, 5·15% H, 12·85% Fe; found: 73·98% C, 5·10% H, 12·48% Fe. ^{1}H NMR spectrum: 3·94 (s, 2 H, CH_2); 4·50 (m, 4 H, $H_{\beta,\beta'}$); 4·84 (m, 4 H, $H_{\alpha,\alpha'}$); 7·34 (m, 12 H, C_6H_5 + CH=CH).

2,3-*Diphenyl*[5]*ferrocenophane*-1,5-*dione* (5% yield) was further isolated, yellow crystalline compound melting at 220—222°C, in accordance with literature[7]. For $C_{27}H_{22}FeO_2$ (434·3) calculated: 74·66% C, 5·15% H, 12·85% Fe; found: 73·98% C, 5·16% H, 12·28% Fe. ^{1}H NMR spectrum: 2·588 (dd, 1 H, H_A), J_{AB} = 13·7 Hz, J_{AC} = 4·0 Hz; 3·534 (dd, 1 H, H_B), J_{BC} = = 12·8 Hz; 4·192 (ddd, 1 H, H_C), J_{CD} = 5·7 Hz; 4·523 (d, 1 H, H_D); 4·51 (m, 1 H, Fc); 4·58 (m, 1 H, Fc); 4·60 (m, 1 H, Fc); 4·68 (m, 2 H, Fc); 4·88 (m, 1 H, Fc); 5·06 (m, 1 H, Fc); 5·11 (m, 1 H, Fc); 6·9—7·2 (m, 10 H, C_6H_5). (Designation for H_A—H_D see ref.[7]).

1-*Cinnamoyl*-1'-(3-*phenylpropanoyl*)*ferrocene* (IIa): acylation of compound *II* gave 27% of *IIa*, m.p. 146—148°C (benzene–hexane). For $C_{28}H_{24}FeO_2$ (448·3) calculated: 75·01% C, 5·39% H, 12·45% Fe; found: 75·02% C, 5·46% H, 12·07% Fe. ^{1}H NMR spectrum: 3·00 (bs, 4 H, CH_2); 4·40 (t, 2 H, H_β); 4·50 (t, 2 H, $H_{\beta'}$); 4·80 (m, 4 H, $H_{\alpha,\alpha'}$); 6·9—7·9 (m, 12 H, C_6H_5 + CH=CH).

2-Benzyl-3-phenyl[5]ferrocenophane-1,5-dione (IIb) was further isolated, yellow crystalline compound (18% yield) melting at 227—232°C. For $C_{28}H_{24}FeO_2$ (448·3) calculated: 75·00% C, 5·39% H, 12·45% Fe; found: 74·91% C, 5·44% H, 11·87% Fe. ^{1}H NMR spectrum: 2·518 (dd, 1 H, H_A), $J_{AB} = 14·0$ Hz, $J_{AC} = 3·8$ Hz; 2·630 (m, 2 H, CH_2); 3·336 (dd, 1 H, H_B), $J_{BC} = 13·0$ Hz; 3·429 (m, 1 H, H_D); 4·222 (ddd, 1 H, H_C), $J_{CD} = 5·9$ Hz; 4·10 (m, 1 H, Fc); 4·38 (m, 1 H, Fc); 4·42 (m, 1 H, Fc); 4·50 (m, 1 H, Fc); 4·59 (m, 1 H, Fc); 4·78 (m, 1 H, Fc); 4·88 (m, 1 H, Fc); 4·95 (m, 1 H, Fc); 6·9—7·6 (m, 10 H, C_6H_5).

1-Cinnamoyl-1'-(4-phenylbutanoyl)ferrocene (IIIa): acylation of compound *III* afforded 15% of *IIIa*, m.p. 124—126°C (benzene–hexane). For $C_{29}H_{26}FeO_2$ (462·2) calculated: 75·3% C, 5·67% H, 12·09% Fe; found: 75·26% C, 5·51% H, 12·06% Fe. ^{1}H NMR spectrum: 2·01 (m, 2 H, CH_2); 2·67 (t, 4 H, CH_2); 4·52 (t, 4 H, $H_{\beta,\beta'}$); 4·74 (t, 2 H, H_α); 4·85 (t, 2 H, $H_{\alpha'}$); 6·9—7·95 (m, 12 H, C_6H_5 + CH=CH).

1-Cinnamoyl-1'-(5-phenylpentanoyl)ferrocene (IVa): acylation of compound *IV* gave 21% of *IVa*, m.p. 129—131°C (benzene–hexane). For $C_{30}H_{28}FeO_2$ (474·4) calculated: 75·62% C, 5·93% H, 11·72% Fe; found: 76·22% C, 6·25% H, 11·32% Fe. ^{1}H NMR spectrum: 1·68 (m, 4 H, CH_2); 2·62 (m, 4 H, CH_2); 4·07 (m, 2 H, H_β); 4·12 (m, 2 H, $H_{\beta'}$); 4·32 (m, 2 H, H_α); 4·75 (m, 2 H, $H_{\alpha'}$); 6·75—8·13 (m, 12 H, C_6H_5 + CH=CH).

Acylation of ω-Phenylalkanoylferrocenes with Phenylpropiolyl Chloride

Experiments were carried out under analogous conditions to those used in the acylation with cinnamoyl chloride.

1-Phenylacetyl-1'-phenylpropiolylferrocene (Ia'): acylation of compound *I* afforded 53% of *Ia'*, m.p. 78—85°C (benzene–hexane). For $C_{27}H_{20}FeO_2$ (432·3) calculated: 75·01% C, 4·66% H, 12·91% Fe; found: 74·82% C, 4·25% H, 12·89% Fe. ^{1}H NMR spectrum: 3·97 (s, 2 H, CH_2); 4·49 (t, 2 H, H_β); 4·57 (t, 2 H, $H_{\beta'}$); 4·88 (t, 2 H, H_α); 4·95 (t, 2 H, $H_{\alpha'}$); 7·1—7·7 (m, 10 H, C_6H_5).

3-(4-Phenylpropiolyl)phenylpropanoylferrocene (IIb'): acylation of compound *II* afforded 17% of *IIb'*, m.p. 114—118°C (benzene–hexane). For $C_{28}H_{22}FeO_2$ (446·3) calculated: 75·3% C, 4·97% H, 12·51% Fe; found: 75·22% C, 4·96% H, 12·71% Fe. ^{1}H NMR spectrum: 3·1 (bs, 4 H, CH_2); 4·1 (s, 5 H, C_5H_5); 4·48 (t, 2 H, H_β); 4·77 (t, 2 H, H_α); 7·05—8·30 (m, 9 H, C_6H_5 + C_6H_4).

1-(3-Phenylpropanoyl)-1'-phenylpropiolylferrocene (IIa') (29% yield) was further isolated, m.p. 112—115°C (benzene–hexane). For $C_{28}H_{22}FeO_2$ (446·3) calculated: 75·3% C, 4·97% H, 12·51% Fe; found: 75·37% C, 5·00% H, 12·75% Fe. ^{1}H NMR spectrum: 2·98 (bs, 4 H, CH_2); 4·43 (t, 2 H, H_β); 4·55 (t, 2 H, $H_{\beta'}$); 4·83 (t, 2 H, H_α); 4·91 (t, 2 H, $H_{\alpha'}$); 7·0—7·7 (m, 10 H, C_6H_5).

1-Phenylpropiolyl-1'-[3-(4-phenylpropiolyl)phenyl]propanoylferrocene (IIc'): the last band yielded 10% of *IIc'*, a red oily substance. For $C_{37}H_{26}FeO_3$ (574·4) calculated: 77·36% C, 4·56% H, 9·72% Fe; found: 76·92% C, 4·45% H, 9·94% Fe. ^{1}H NMR spectrum: 3·05 (bs, 4 H, CH_2); 4·52 (m, 4 H, $H_{\beta,\beta'}$); 4·90 (m, 4 H, $H_{\alpha,\alpha'}$); 7·1—8·25 (m, 14 H, C_6H_5 + C_6H_4).

4-(4-Phenylpropiolylphenyl)butanoylferrocene (IIIb'): acylation of compound *III* afforded 48% of *IIIb'*, m.p. 102—104°C (benzene–petroleum ether). For $C_{29}H_{24}FeO_2$ (460·4) calculated: 75·66% C, 5·26% H, 12·13% Fe; found: 75·86% C, 5·42% H, 12·14% Fe. ^{1}H NMR spectrum: 2·05 (m, 2 H, CH_2); 2·72 (t, 4 H, CH_2); 4·14 (s, 5 H, C_5H_5); 4·46 (t, 2 H, H_β); 4·74 (t, 2 H, H_α); 7·24—8·25 (m, 9 H, C_6H_5 + C_6H_4).

1-Phenylpropiolyl-1'-[4-(4-phenylpropiolyl)phenyl]butanoylferrocene (IIIc') was further isolated, a red oily substance, 7·5% yield. For $C_{38}H_{28}FeO_3$ (588·5) calculated: 77·55% C, 4·79% H, 9·49% Fe; found: 78·02% C, 4·94% H, 9·04% Fe. ^{1}H NMR spectrum: 2·05 (m, 2 H, CH_2); 2·74

(t, 4 H, CH_2); 4·57 (m, 4 H, $H_{\beta,\beta'}$); 4·83 (t, 2 H, H_α); 4·96 (t, 2 H, $H_{\alpha'}$); 7·15—8·25 (m, 14 H, $C_6H_5 + C_6H_4$).

5-(4-*Phenylpropiolyl*)*phenylpentanoylferrocene* (IVb′): acylation of compound *IV* afforded 41% of *IVb′*, m.p. 91—92°C (benzene–petroleum ether). For $C_{30}H_{26}FeO_2$ (474·4) calculated: 75·95% C, 5·32% H, 11·77% Fe; found: 76·13% C, 5·45% H, 11·57% Fe. ^{1}H NMR spectrum: 1·75 (m, 4 H, CH_2); 2·70 (m, 4 H, CH_2); 4·16 (s, 5 H, C_5H_5); 4·46 (t, 2 H, H_β); 4·75 (t, 2 H, H_α); 7·20—8·22 (m, 9 H, $C_6H_5 + C_6H_4$).

1-*Phenylpropiolyl*-1′-[5-(4-*phenylpropiolyl*)*phenyl*]*pentanoylferrocene* (IVc′) was further isolated, a red oily substance, 20% yield. For $C_{39}H_{30}FeO_3$ (602·5) calculated: 77·74% C, 5·01% H, 9·26% Fe; found: 78·23% C, 5·34% H, 8·87% Fe. ^{1}H NMR spectrum: 1·67 (m, 4 H, CH_2); 2·68 (m, 4 H, CH_2); 4·15 (m, 2 H, H_β); 4·57 (m, 2 H, $H_{\beta'}$); 4·82 (m, 2 H, H_α); 4·95 (m, 2 H, $H_{\alpha'}$); 7·0—8·2 (m, 14 H, $C_6H_5 + C_6H_4$).

Acylation of 4-Phenylbutanoylferrocene with t-Butylacetyl Chloride

Reaction was effected under conditions described above. As even after 2 h, the formation of a new substance has not been observed (TLC), t-butylacetyl chloride (twofold excess) and $AlCl_3$ were aded to the reaction mixture and the mixture was refluxed for 3 h.

1-t-*Butylacetyl*-1′-(4-*phenylbutanoyl*)*ferrocene* (65%) was obtained after common work-up and chromatographic separation, m.p. 83—85°C (benzene–petroleum ether). For $C_{26}H_{30}FeO_2$ (430·3) calculated: 72·56% C, 7·02% H, 12·97% Fe; found: 71·94% C, 6·85% H, 12·25% Fe. ^{1}H NMR spectrum: 1·05 (s, 9 H, CH_3); 2·0 (m, 2 H, CH_2); 2·51 (s, 2 H, CH_2); 2·75 (m, 4 H, CH_2); 4·42 (t, 4 H, $H_{\beta,\beta'}$); 4·70 (t, 4 H, $H_{\alpha,\alpha'}$); 7·27 (bs, 5 H, C_6H_5).

### Attempted Acylation of 4-Phenylbutanoylferrocene with Trimethylacetyl Chloride

The reaction was carried out under conditions described in detail for the acylation with t-butyl-acetyl chloride. However, in this case, the reaction did not take place and 92% of the starting compound were isolated from the reaction mixture.

RESULTS AND DISCUSSION

Starting ω-phenylalkanoylferrocenes were prepared by Friedel–Crafts acylation of ferrocene with chlorides of ω-phenylalkanoic acids in 40—70% yields. Optimation of the reaction conditions has not been attempted.

The proper study of the acylation of ω-phenylalkanoylferrocenes with cinnamoyl and phenylpropiolyl chlorides was started with compounds *III* and *IV* (Scheme 1).

The scheme shows that the acylation with cinnamoyl chloride proceeds, as expected, *via* attack at the unsubstituted cyclopentadienyl ring of ferrocene (and if small amounts of unidentified compounds are disregarded, also quite selectively). In the acylation with phenylpropiolyl chloride, the results are not so unambiguous. The reaction yields a mixture of products of the acylation to the first and the second step, approximately in the ratio of 2 : 1. The most interesting fact is that in the acylation to the first step, the substitution proceeds at the benzene ring and not at ferrocene.
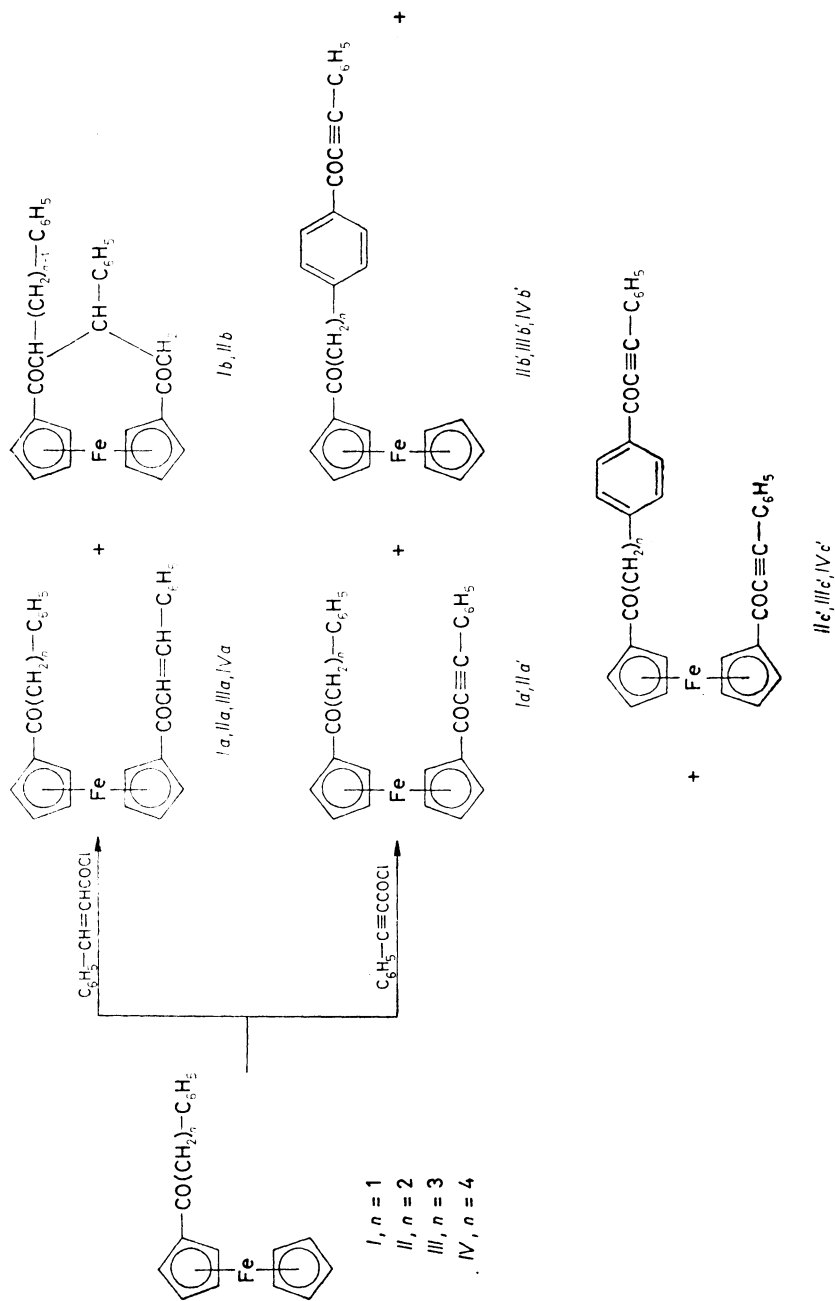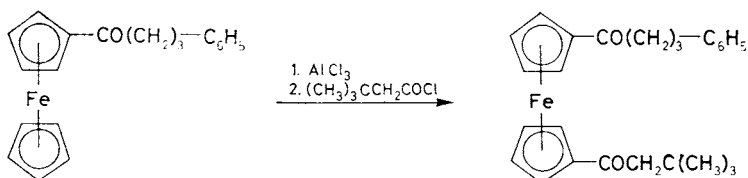
SCHEME 1

Observed facts can be accounted for by assumption (in accordance with Rosenblum[8]) that in electrophilic substitutions at ferrocene, the initial site of the attack by electrophile is Fe atom, from which the agent migrates to the cyclopentadienyl ring, and also that the structure of the reagent is not the same. It was proved that the structure of the reagent depends on the starting chloride, *i.e.* the equilibrium

$$R\text{—}C\overset{\displaystyle O}{\underset{\displaystyle Cl}{\big<}} \;\rightarrow\; AlCl_3 \;\rightleftarrows\; R\text{—}\overset{+}{C}{=}O \;+\; AlCl_4^-$$
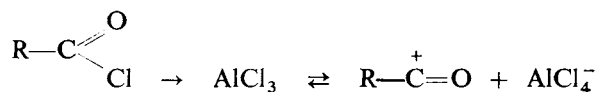
can be shifted either to the left or to the right side[9]. Assuming that in the case of phenylpropiolyl chloride, the equilibrium is shifted to the left, the acylating agent is bulky and can only with difficulty attack Fe atom which is furthermore sterically hindered by the bulky phenylalkyl group attached to ferrocene.

This hypothesis can be tested either by increasing bulkiness of the acylating agent or by decreasing bulkiness of the substituent at ferrocene. The bulkiness of the acylating agent, *e.g.* cinnamoyl chloride, can be increased by using the softer catalyst[9] such as *e.g.* $SnCl_4$ or $TiCl_4$. This approach has not been used, however, in this case as under such conditions the acylation of acylferrocenes did not take place. We have therefore made experiments aimed at acylation of 4-phenylbutanoylferrocene with t-butylacetyl chloride and trimethylacetyl chloride. In the former case under usual conditions $(10-15°C, 2\text{ h})$ the reaction did not proceed. (The quality of the acylating agent, $(CH_3)_3CCH_2COCl/AlCl_3$ was checked by the successful acylation of ferrocene.) On increasing the amount of the acylating agent to double amount and especially the reaction temperature $(35-40°C)$, the acylation took place at the unsubstituted cyclopentadienyl ring of ferrocene. In the case of trimethylacetyl chloride the reaction did not take place even under the just mentioned conditions and the starting chloride underwent decarbonylation[10] (Scheme 2).

SCHEME 2

To complete these experiments, we have also made attempts to acylate phenylacetylferrocene and 3-phenylpropanoylferrocene with cinnamoyl chloride. In the former case we obtained only the product of substitution at the cyclopentadienyl

ring of ferrocene, which underwent partial cyclization to give the already described 2,3-diphenyl[5]ferrocenophane-1,5-dione[7]. In the latter case, the expected 1'--substituted derivative *IIa* was accompanied at higher temperature by its cyclization product (on removing the solvent by distillation).

Our attempts at acylation of phenylacetylferrocene (*I*) and 3-phenylpropanoylferrocene (*II*) with phenylpropiolyl chloride have shown that with decreasing bulkiness of the substituent at ferrocene, the acylation proceeds also on the unsubstituted cyclopentadienyl ring of ferrocene, yielding the products *Ia'* and *IIa'*. In the case of phenylacetylferrocene, the 1'-substituted product *Ia'* is even the only reaction product. It seems likely that this fact is due to the reduced electron density on the benzene ring of phenylacetylferrocene.

Summarizing, the results obtained support the idea that the site of electrophilic attack depends on the bulkiness of the acylating agent as well as on the bulkiness of the substituent attached to ferrocene.

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