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ELECTROPHILIC SUBSTITUTIONS ON SOME FERROCENYL ANALOGUES OF CHALCONES

AN UNUSUAL REACTION CAUSED BY THE HIGH STABILITY OF THE α-FERROCENYLMETHYL CARBENIUM ION

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Summary

Friedel—Crafts acetylation of 5-ferrocenyl-1-phenyl-2,4-pentadien-1-one and 1-ferrocenyl-5-phenyl-1,4-pentadien-3-one has been acomplished. It was found that acetylation takes place on the unsubstituted cyclopentadienyl ring of ferrocene as well as on the double bond of chalcones. In the light of these results the Friedel—Crafts acetylation of 3-ferrocenyl-1-phenyl-2-propen-1-one was reinvestigated and the structures of some derivatives, described earlier, were corrected. The mechanism of the acetylation is discussed briefly.

Friedel—Crafts alkylation and electrophilic bromination of 3-ferrocenyl-1-phenyl-2-propen-1-one have also been attempted.

Introduction

The tendency of the ferrocenyl moiety to stabilize an adjacent electron-deficient centre is clearly shown by the high reactivity of ferrocenylcarbinols [1] or corresponding acetates [2, 3] and ferrocenylmethyltrimethylammonium iodide [4], as well as by the high stability of isolated α-ferrocenylcarbenium ion salts [5, 6].

This paper deals with a new phenomenon, namely electrophilic substitution on the double bond of α,β-unsaturated ketones which occurs due to the pronounced stability of the ferrocenyl carbenium ion.

Results and discussion

The Friedel—Crafts acetylation of 5-ferrocenyl-1-phenyl-2,4-pentadien-1-one (I) and 5-ferrocenyl-1-phenyl-1,4-pentadien-3-one (II) gave rise to two monoacetylated products. In the case of acetylation of I some diacetylated compound was found, the amount of which was dependent to a large extent on the quality of $AlCl_3$ and the molar ratio of ketone/acetyl chloride. The reaction was, in both cases, acompanied by a considerable decomposition of the starting material.

The analysis of PMR spectra of the synthesised compounds showed that the main products (Ib and IIb), the second compounds to be eluted from the columns, have patterns typical of 1,1-disubstituted ferrocene: the signals of both cyclopentadienyl ring protons are split into two triplets of α and β protons (see Table 1). On the other hand, there is a singlet of unsubstituted ring protons in the PMR spectra of the minor monoacetylated products (Ia and IIa). The chemical shifts of α and β protons of the substituted rings of these compounds coalesce into a broad singlet integrated for four protons. This is caused by the shielding of the α protons by the ring current effect of the phenyl group bonded in the *cis* position to the ferrocene; chemical shifts of β protons are less affected.

Similar shielding by the phenyl group was observed by Rausch [7, 8] in the case of 1-ferrocenyl-2,2-diphenylethylene. Raush found that the chemical shift of α (2,5) protons is at higher field than the chemical shifts of the unsubstituted cyclopentadienyl ring protons as well as of the chemical shifts of β (3,4) protons e.g. δ 4.08 (β and C_5H_5; a broad singlet) and δ 3.86 (α, t). This is caused by a different effect and not by the normal shielding due to the polar or anisotropic effects. From the molecular model it seems that the *cis* phenyl ring can rotate above the substituted cyclopentadienyl ring and that α protons are in the shielding area of the ring current of the phenyl group.

The olefinic part of the spectra of compounds Ia and IIa is considerably changed by comparison with the spectra of the starting chalcones I and II, but the aromatic part of the spectra remained unaffected. This can be considered as proof of double bond acetylation.

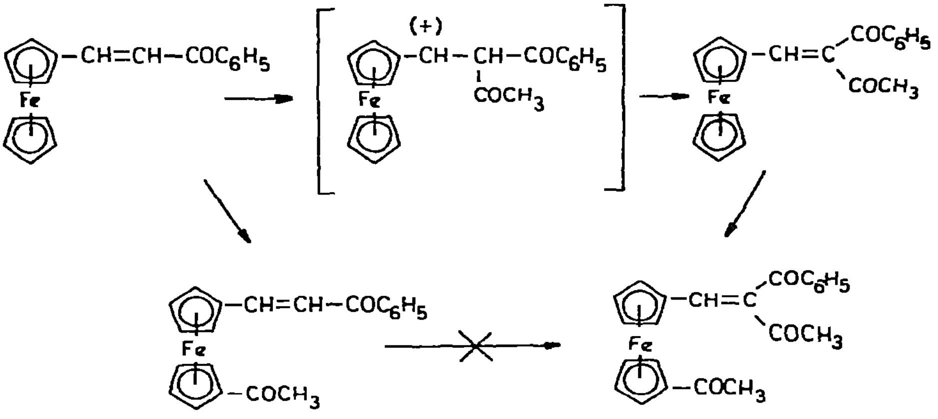
Some years ago we acetylated chalcones [9] of the type FcCH=CH-COAr and diarylethylenes [10] of the type FcCH=CHAr. In the light of the results mentioned above we decided to reinvestigate some of our previous experiments and to reelucidate the structures of the isolated compounds.

During the reinvestigation of the acetylation of 3-ferrocenyl-1-phenyl-2-propen-1-one (III) we have found that two monoacetylated (IIIa and IIIb) and one diacetylated (IIIc) products are formed, as in the acetylation of I.

PMR spectra showed that IIIa is a product of double bond acetylation and IIIc is a product of 1′ and double bond acetylation. Further experiments showed that IIIc is formed through the acetylation of IIIa, e.g. 2-ferrocenylmethylene-1-phenyl-1,3-butanedione, only. The results are summarised in Scheme 1.

We have no direct proof that the acetylation of the double bond passes through the free ferrocenyl carbenium ion: the product observed could

SCHEME 1



alternatively result from an addition—elimination process, but in all cases the pronounced stabilisation effect of ferrocenyl on the adjacent carbenium ion must be responsible for this phenomenon.

The analysis of PMR spectra of acetylated chalcones and diarylethylenes prepared earlier [9,10] (see Table 1) proved that the structure assignments made on the basis of TLC (R_F values) and UV spectra were wrong in all cases when acetylation of position 2 of the substituted cyclopentadienyl ring was anticipated. However, no product of double bond acetylation was found among the acetylation products of chalcones of the type FcCOCH=CHAr when Ar was phenyl, 2-thienyl and 2-furyl. It is evident that neither thiophene nor furane has a stabilising effect on the adjacent carbenium ion similar to that of ferrocene.

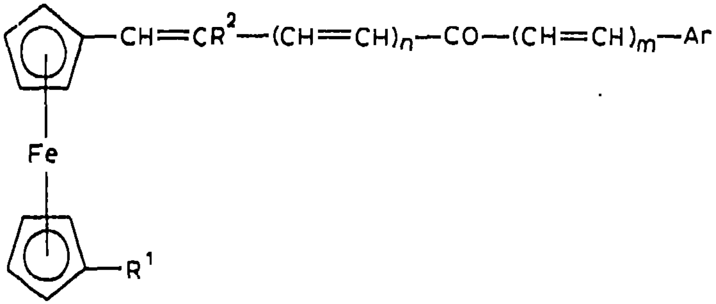
The wrong structure assignement of IIIa (made earlier) led us to another mistake. In a recent paper [11] we described one substance (compound III in the mentioned paper) as 1,15-dioxo[3.3](1,2)ferrocenophane-2,16-diene but in fact it is 1,5-diferrocenyl-1,4-pentadiene-3-one.

It would be interesting to find out whether other substitution reactions would proceed analogously. Therefore Friedel—Crafts alkylation with C_2H_5Br/$AlCl_3$ and bromination with $Br_2/AlCl_3$ of III were attempted. No product of alkylation was detected by PMR spectral analysis of all fractions from the chromatography. Bromination of the chalcone III led to the double bond substitution product, the PMR spectrum of which has a similar pattern to that of IIIa (see Experimental).

Bromination of the chalcone $FcCOCH{=}CHC_6H_5$ was carried out for comparison. Elemental analysis and PMR showed that bromine adds only to the double bond. In the PMR spectrum of $FcCOCHBrCHBrC_6H_5$ can be observed a singlet of unsubstituted cyclopentadienyl ring protons [$\delta(C_5H_5)$ 4.40] and multiplets of α and β protons of the substituted ring [$\delta(\alpha) \approx 5.00$ (m, 1H); $\delta(\alpha') \approx 4.90$ (m, 1H); $\delta(\beta) \approx 4.66$ (m, 2H)]. This is the first example of splitting of α (2,5) proton signals caused by the presence of a chiral centre at the side-chain. Nesmeyanov et al. [13] using ^{13}C and ^1H NMR have found a similar non-equivalence of signals of α carbon atoms or α protons in the cases when the chiral centre is bonded directly to the ferrocene (chalcones FcCH=

TABLE 1

PMR SPECTRA OF THE COMPOUNDS UNDER STUDY (δ, ppm)



No.	Ar	n	m	R^1	R^2	α	β	α'	β'	C_5H_5	CH_3	Aromatic, vinylic H
I	Phenyl	1	0	H	H	4.48 t	4.38 t			4.14 s		8.1-6.6
Ia	Phenyl	1	0	H	$COCH_3$	4.36 s				4.09 s	2.30 s	8.0-6.2
Ib	Phenyl	1	0	$COCH_3$	H	4.59 t	4.49 m	4.77 (t)	4.49 (m)		2.30 s	8.1-7.0
II	Phenyl	0	1	H	H	4.67 t	4.46 t			4.16 s		7.9-6.5
IIa	Phenyl	0	1	H	$COCH_3$	4.43 s				4.18 s	2.35 s	7.6-6.7
IIb	Phenyl	0	1	$COCH_3$	H	4.57 t	4.49 m	4.77 (t)	4.49 (m)		2.20 s	7.9-6.5
IIIa^a	Phenyl	0	0		$COCH_3$	4.36 t	4.25 t			4.13 s	2.32 s	8.1-7.4
IIIc	Phenyl	0	0	$COCH_3$	$COCH_3$	4.23 s		4.70 (t)	4.35 (m)		2.30 s	7.9-7.1
IV^a	2-Furyl	0	0		$COCH_3$	4.42 t	4.33 t			4.15 s	2.34 s	7.7-6.5
V^a	2-Thienyl	0	0	$COCH_3$	$COCH_3$	4.39 s		4 81 (t)	4 46 (m)		2.36 s 2.38 s	7.8-7.0
VII^b	Fc-CH=C(Ph)$COCH_3$					3.81 t	4.20 t			4.09 (s)	2.23 (s)	7.6-7.1

[a] These compounds are numbered IIa, IVb, VIc in ref. 9. [b] Compound is numbered IXa in ref. 10.

$CHCOC_6H_5$ or $FcCOCH{=}CHC_6H_5$ are ligands in complexes with $Fe(CO)_4$ and $Fe(CO)_3$ respectively).

Experimental

The PMR spectra were recorded on a Tesla BS 487 instrument with 80 MHz working frequency at 23°C. The spectra were recorded in $CDCl_3$ (99.5% *D*-isomer) solutions with tetramethylsilane as internal standard. The chemical shifts (see Table 1) were read with an accuracy of ± 0.01 ppm. Chromatography was carried out on SiO_2 (Kavalier, Votice) columns, using benzene containing 3-6% of ethyl acetate as the eluent. Melting points were determined on a Kofler apparatus and are uncorrected. All experiments were carried out under purified N_2.

Compounds I and II were prepared [12] by Horner's modification of the Wittig reaction, from β-ferrocenylacrolein and diethylbenzoylmethyl phosphonate, and by condensation of ferrocenecarbaldehyde with benzalacetone, respectively.

Acetylation of 5-ferrocenyl-1-phenyl-2,4-pentadien-1-one (I)

To a stirred solution of 1.7 g (0.005 mol) of I in 50 ml of dichloromethane was added during 30 min a solution of 0.6 g (0.0075 mol) of acetyl chloride and 2.0 g (0.015 mol) of anhydrous $AlCl_3$ in 50 ml of dichloromethane. The mixture was then stirred at room temperature for 4 h. After pouring into cold water the organic material was extracted into dichloromethane; the dichloromethane solution dried over anhydrous Na_2SO_4 and the solvent was evaporated. The residue was dissolved in benzene and chromatographed. Chromatography gave 0.7 g (41%) of the starting material, 0.26 g (13.4%) of 4-ferrocenylmethylene-1-phenyl-2-hexene-1,5-dione (Ia) m.p. 136-139°(petroleum ether) [found: Fe, 14.30; $C_{23}H_{20}FeO_2$ (mol. wt. 384.26) calcd.: Fe, 14.53%]; 0.15 g (7.8%) of 5-(1′-acetylferrocenyl)-1-phenyl-2,4-pentadien-1-one (Ib), m.p. 128-130° (petroleum ether) [found: Fe, 14.25; $C_{23}H_{20}FeO_2$ (mol. wt. 384.26) calcd.: 14.53%]. From the fourth band was isolated 0.1 g (5%) of 4-(1′-acetylferrocenylmethylene)-1-phenyl-2-hexene-1,5-dione (Ic) m.p. 72-77° (petroleum ether) [found: Fe, 12.70; $C_{25}H_{22}FeO_3$ (mol. wt. 426.30) calcd.: Fe, 13.09%].

All the acetylations described below were carried out analogously.

Acetylation of 1-ferrocenyl-5-phenyl-1,4-pentadien-3-one (II) (2.4 g, 0.007 mol) with 0.8 g (0.01 mol) of acetyl chloride and 2.8 g (0.021 mol) of anhydrous $AlCl_3$ yielded: 0.9 g (37.5%) of the starting material, 0.2 g (7%) of 3-ferrocenylmethylene-6-phenyl-5-hexene-2,4-dione (IIa) m.p. 155-160° (benzene—petroleum ether) [found: Fe, 14.51; $C_{23}H_{20}FeO_2$ (mol. wt. 384.26) calcd.: Fe, 14.53%] and 0.7 g (26%) of 5-(1′-acetylferrocenyl)-1-phenyl-1,4-pentadien-3-one (IIb), m.p. 128-132° (benzene—petroleum ether) [found: Fe, 14.79; $C_{23}H_{20}FeO_2$ (mol. wt. 384.26) calcd.: Fe, 14.53%].

Acetylation of 3-ferrocenyl-1-phenyl-2-propen-1-one (III) (3.2 g, 0.01 mol) with 1.2 g (0.015 mol) of acetyl chloride and 4.0 g (0.03 mol) of anhydrous $AlCl_3$ yielded 1.7 g (47%) of the starting material, 0.3 g (9.4%) of 2-ferrocenylmethylene-1-phenyl-1,3-butanedione (IIIa) m.p. 149-150° (ethanol) [9], 0.6 g (18.7%) of 3-(1′-acetylferrocenyl)-1-phenyl-2-propen-1-one, m.p. 129-130°

(ethanol) [9] and 0.07 g (1.7%) of 2-(1'-acethylferrocenylmethylene)-1-phenyl-1,3-butanedione (IIIc) m.p. 115-117° (ethanol) [found: Fe, 14.11; $C_{23}H_{20}FeO_3$ (mol. wt. 400.29) calcd.: Fe, 13.95%]. Note: The amount of IIIc was increased and that of IIIa decreased when the acetylation was carried out with higher $AlCl_3$/chalcone molar ratio.

Acetylation of 2-ferrocenylmethylene-1-phenyl-1,3-butanedione (IIIa) (0.2 g, 0.55 mmol) with 0.1 g (1.2 mmol) of acetyl chloride and 0.3 g (2.3 mmol) of anhydrous $AlCl_3$ yielded small ammounts of non-identified compounds, 0.1 g (50%) of the starting material and 0.01 g (5%) of IIIc.

Acetylation of 3-(1'-acetylferrocenyl)-1-phenyl-2-propen-1-one (1 g, 3 mmol) with 0.5 g (6 mmol) of acetyl chloride and 1.6 g (12 mmol) of anhydrous $AlCl_3$ yielded small amounts of two unidentified compounds and 0.6 g (60%) of starting material. No product of acetylation has been detected.

Attempted Friedel—Crafts alkylaiton of the chalcone III

To the stirred solution of 1.6 g (5 mmol) of III in 20 ml of CH_2Cl_2 was added (at 0°, over 30 min) a solution of 0.82 g (7.5 mmol) of ethyl bromide and 2 g (15 mmol) of anhydrous $AlCl_3$ in 20 ml CH_2Cl_2. The reaction mixture was stirred at room temperature for 4 h and then worked-up as usual. Chromatography afforded 1.1 g (68%) of the starting material. No product of alkylation was detected.

Bromination of the chalcone III

To the stirred solution of 3.3 g (25 mmol) of anhydrous $AlCl_3$ in 15 ml of $CHCl_3$, cooled to 0° was added a solution of 3.2 g (10 mmol) of III in 15 ml of $CHCl_3$ and then 1.6 g (0.5 ml) (10 mmol) of Br_2 in 10 ml of $CHCl_3$. The reaction mixture was stirred at 0° for 12 h and then poured into cold water. After the usual work-up, chromatography (benzene as eluant) afforded: 0.07 g (1.8 %) of 2-bromo-3-ferrocenyl-1-phenyl-2-propen-1-one, m.p. 142-144° (petroleum ether) [found: Br, 19.70; Fe, 13.95; $C_{19}H_{15}BrFeO$ (mol. wt. 395.09) calcd.: Br, 20.22; Fe, 14.13%]. PMR: $\delta(C_6H_5, =CH)$ 7.8-7.4 (m,6H); $\delta(\alpha)$ 4.95 (t, 2H); $\delta(\beta)$ 4.55 (t, 2H); $\delta(C_5H_5)$ 4.22 (s, 5H). From the second band 1.6 g (50%) of the starting material was recovered.

Bromination of cinnamoylferrocene

The reaction was carried out as described above. 1.6 g (5 mmol) of cinnamolyferrocene were used for the reaction. Chromatography afforded 0.3 g (12.5%) of 2,3-dibromo-3-phenyl-propionylferrocene, m.p. 134-138° (benzene—heptane) [found: Br, 33.19; Fe, 11.70; $C_{19}H_{16}Br_2FeO$ (mol. wt. 474.0) calcd.: Br, 33.72; Fe, 11.73%]. PMR ($FcCOCH_A BrCH_B BrC_6H_5$): $\delta(C_6H_5$ 7.5-7.3 (m, 5H); $\delta(C_5H_5)$ 4.40 (s, 5H); $\delta(\alpha) \approx$ 5.00 (m, 1H); $\delta(\alpha') \approx$ 4.90 (m, 1H); $\delta(\beta) \approx$ 4.66 (m, 2H); and a quartet splitting of AB part of the spectra $\delta(H_A)$ 5.56; $\delta(H_B)$ 5.31; J_{AB} 11.5 Hz. From the second band 0.4 g (25%) of the starting material was isolated.

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