

Acylation of metallocenes with ω -oxo- ω -phenylalkanoyl chlorides Chlorides of oxo acids as acylating agents

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Dedicated to Professor RNDr. V. Sutoris, CSc., in honour of his 60th birthday

Ferrocene, ruthenocene, and tricarbonyl(η -cyclopentadienyl)manganese were acylated with chlorides of oxo acids $C_6H_5CO(CH_2)_nCOCl$. Expected unsymmetrically substituted diketones were isolated in reactions with ferrocene (for $n=3-8$), ruthenocene ($n=8$), and tricarbonyl(η -cyclopentadienyl)manganese ($n=4, 6$). Being accompanied with unsaturated lactones the chlorides with $n=2, 3$ gave complicated mixtures of products with ferrocene but did not react with tricarbonyl(η -cyclopentadienyl)manganese.

Ферроцен, рутиноцен и циклопентадиенилмарганецтрикарбонил были ацилированы хлоридами кетокислот $C_6H_5CO(CH_2)_nCOCl$. Были выделены ожидаемые несимметричные diketоны в реакциях с ферроценом ($n=3-8$), рутиноценом ($n=8$) и циклопентадиенилмарганецтрикарбониллом ($n=4, 6$). Хлориды кислот с $n=2, 3$ сопровождаются ненасыщенными лактонами и дают сложную смесь продуктов с ферроценом, но не реагируют с циклопентадиенилмарганецтрикарбониллом.

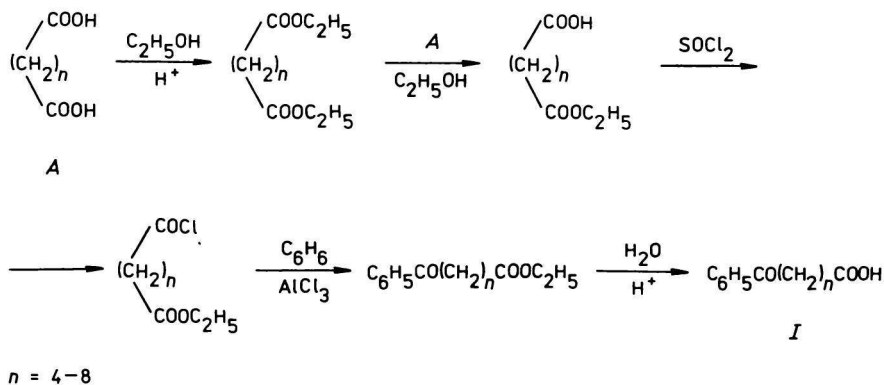
One of our previous papers [1] deals with the competitive intramolecular Michael addition performed on ferrocene derivatives containing one activated methylene group and two activated carbon-carbon double bonds. Another one [2] was devoted to the same reaction on substrates with one activated unsaturated bond and two, nonequally, activated methylene groups.

The aim of the present work involves both the preparation of unsymmetrically substituted diketones $C_6H_5CO(CH_2)_nCOFc$ (e.g. compounds which we needed as starting material in our previous study [2], where Fc = ferrocenyl) and exploring possibility to employ chlorides of oxo acids in acylation reactions with various aromatic systems. So far, almost no attention has been paid to preparation of oxo acid chlorides and their use as acylating agents [3].

The synthesis of ω -oxo- ω -phenylalkanoyl acids (*I*) was accomplished in two steps. Friedel-Crafts acylation of benzene with ester chlorides of dicarboxylic acids ($n=4-8$) (Scheme 1) gave corresponding esters which were subsequently

hydrolyzed to the free acids. In the case of $n = 2, 3$ succinic and glutaric anhydrides were used as acylating agents.

Thionyl chloride and phosphorus trichloride were attempted to convert oxo acids (*I*) to the corresponding chlorides (*II*). The reaction with an excess of thionyl chloride in anhydrous benzene was found to be a convenient route to the chlorides with $n = 4-8$. (Later it was shown, however, that PCl_3 gave better results, at least in the case of $n = 4$.) Crude chlorides which remained after stripping off the solvent and thionyl chloride were used in the next step without further purification. This method failed in the case of 4-oxo-4-phenylbutanoic and 5-oxo-5-phenylpentanoic acids. Evaporation of volatile liquids left an oily material which did not react with ferrocene. When SOCl_2 was replaced by PCl_3 , formation of H_3PO_3 was observed in these reactions, though longer time was required for their completion (in comparison with, for instance, the acid with $n = 4$). In this case the oily product did react with ferrocene.



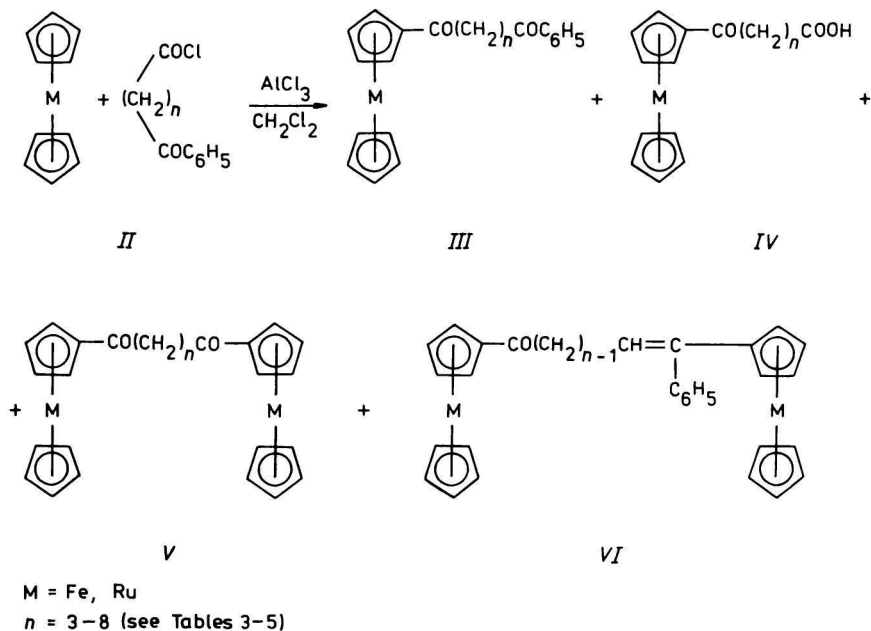
Scheme 1

Reactions of chlorides *II* ($n = 4-8$) with ferrocene and the chloride *II* ($n = 8$) with ruthenocene under AlCl_3 catalysis gave rise to expected unsymmetrically substituted diketones *III* in 7-45 % yields (no attempts to find optimum reaction conditions were made) (Scheme 2).

In some cases, also small amounts of by-products *IV*, *V*, and *VI* were isolated. Contamination of the starting oxo acids *I* with traces of corresponding dicarboxylic acids can account for the formation of oxo acids *IV* and symmetrical diketones *V*. Such an impurity cannot be detected in ^1H NMR spectra of *I*. Its presence was, at last, proved by means of isotachopheresis. (Separation of diesters of dicarboxylic acids from monoesters by rectification cannot exclude the presence of traces of $\text{RO}_2\text{C}(\text{CH}_2)_n\text{CO}_2\text{R}$ in $\text{RO}_2\text{C}(\text{CH}_2)_n\text{CO}_2\text{H}$.) Unsaturated ketones *VI* seem to have

been formed *via* alkylation of ferrocene with ketones *III* followed by elimination of water. Such alkylations of ferrocene with ketones in the presence of AlCl_3 have been described earlier [4].

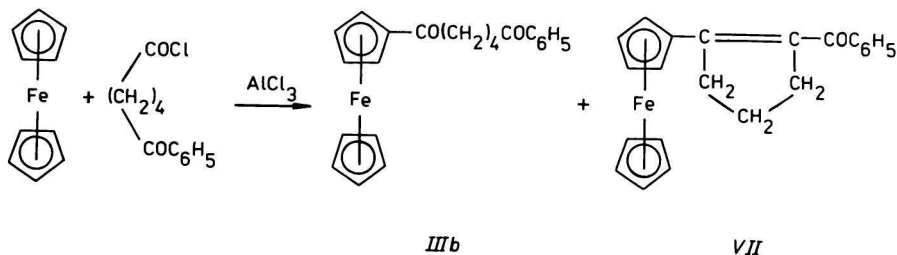
Compounds *IV*—*VI* have been fully characterized and their physical constants together with ^1H NMR data are given in Experimental. In addition, ^1H NMR spectra of *V* were a helpful tool in assignment of signals in ^1H NMR spectra of desired ketones *III*.



Scheme 2

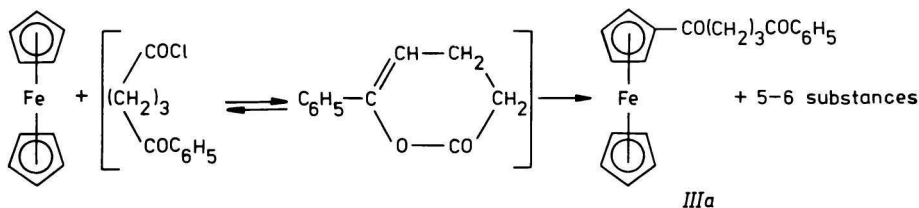
Acylation of ferrocene with 6-oxo-6-phenylhexanoyl chloride (prepared by SOCl_2 method and, hence, contained some HCl) gave diketone *IIIb* in poor yields (7%). *Suschitzky et al.* have reported 12% yield [5]. In this case compound *VII* was the major product (70%) (Scheme 3). *Suschitzky* reported 15 or 55% yield of the same product [6]. Apparently compound *IIIb* underwent Claisen—Schmidt reaction catalyzed by traces of HCl . Such a reaction performed on 1,6-diferrocenyl-1,6-dioxohexane using dried gaseous HCl gave 95% yield of 1-ferrocenyl-2-ferrocenylcyclopentene [7].

When 6-oxo-6-phenylhexanoyl chloride was prepared by PCl_3 method the yield of *IIIb* raised to 40% and *VII* was formed in negligible amounts.



Scheme 3

Both 5-oxo-5-phenylpentanoyl chloride and the corresponding unsaturated lactone are formed upon treatment of the parent acid with PCl_3 (^1H NMR spectra). Acylation of ferrocene with such a mixture led to the formation of great number of products, desired 1-ferrocenyl-5-phenyl-1,5-pentanedione *IIIa* being among them (Scheme 4).

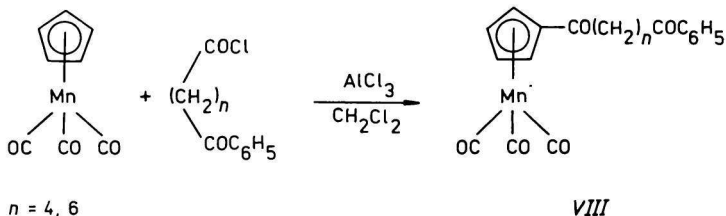


Scheme 4

However, in the case of 4-oxo-4-phenylbutanoic acid, the unsaturated lactone was the major product in the resulting mixture which failed to give 1-ferrocenyl-4-phenyl-1,4-butanedione. Although interesting, this part of our work is a slight deviation from our original project and its results will be published separately.

The last two reactions did not work at all on tricarbonyl(η -cyclopentadienyl)-manganese. Starting material was recovered in 95–98 % and, although, 8–10 additional compounds were detected on TLC plates, they were not isolated due to their rapid decomposition. On the other hand, the chlorides *II* with $n=4$ and 6 reacted smoothly giving 70 % resp. 48 % yields of expected unsymmetrically substituted diketones of the type *VIII*. (Scheme 5).

As reactivity of tricarbonyl(η -cyclopentadienyl)manganese towards electrophiles is regarded to lay between those of benzene and anisole [8, 9], we assume that above chlorides *II* can be utilized in Friedel–Crafts acylations of various kinds of aromatic systems.



Scheme 5

The structures of new compounds have been proved by ^1H NMR spectra and elemental analyses. Signals of methylene groups adjacent to nonequivalent carbonyls in *III* are separated enough (2.7 ppm and 3.0 ppm) to be easily distinguished from each other. These signals were unambiguously assigned to FcCOCH_2- and $\text{C}_6\text{H}_5\text{COCH}_2-$, respectively on the grounds of ^1H NMR spectra of symmetrically substituted diketones *V* (FcCOCH_2- $\delta = 2.68$ – 2.72 ppm). Because protons in $\text{C}_6\text{H}_5\text{COCH}_2-$ moiety are positioned at lower field than those in FcCOCH_2- , one can conclude that they are also more acidic.

Experimental

^1H NMR spectra were measured on a Tesla BS 487 spectrometer with working frequency of 80 MHz as CDCl_3 solutions with tetramethylsilane as internal standard at 23°C . The chemical shifts were read with ± 0.01 ppm accuracy. Column chromatography was performed on a silica (Kavalier, Votice), mixtures of benzene–ethyl acetate being eluant. Melting points were taken on a Kofler hot-stage. All acylation reactions were conducted in anhydrous dichloromethane as solvent and in nitrogen atmosphere.

Diethyl esters, monoesters, and ester chlorides of dicarboxylic acids were prepared according to published procedures [10–12]. Similarly, known procedures were followed in preparation of oxo acids *I* with $n = 4$ – 8 [13] and $n = 2, 3$ [14].

ω-Oxo-*ω*-phenylalkanoyl chlorides *II*

Procedure A: With SOCl_2

A mixture of 0.02 mol of *ω*-oxo-*ω*-phenylalkanoic acid *I* ($n = 4$ – 8), anhydrous benzene (150 cm^3), and freshly distilled thionyl chloride (20 cm^3) was heated to reflux over a period of 3–4 h. After cooling to room temperature the excess of SOCl_2 and benzene were removed under reduced pressure. The residue was heated with an additional dry benzene (100 cm^3) and the evaporation was repeated (to remove the last traces of SOCl_2). The crude product was used in subsequent step without further purification.

Table 1
Characteristic data for compounds of the type III and VIII

Compound	n	Metal	Formula	M _r	w _i (calc.)/% w _i (found)/%			M.p./°C ^a	Yield/%
					C	H	Fe		
IIIa	3	Fe	C ₂₁ H ₂₀ FeO ₂	360.24	70.02	5.59	15.50	94—95	19.5
					70.25	5.66	15.61		
IIIb	4	Fe	C ₂₂ H ₂₂ FeO ₂	374.26	70.60	6.19	14.92	84—86	40.2
					71.21	6.16	15.34		
IIIc	5	Fe	C ₂₃ H ₂₄ FeO ₂	388.29	71.14	6.23	14.38	68—71	20.5
					70.72	6.30	13.94		
III _d	6	Fe	C ₂₄ H ₂₆ FeO ₂	402.32	71.65	6.51	13.88	72—75	39.2
					71.20	6.93	13.76		
III _e	7	Fe	C ₂₅ H ₂₈ FeO ₂	416.34	72.12	6.77	13.41	65—68	46.1
					72.21	6.80	13.39		
III _f	8	Fe	C ₂₆ H ₃₀ FeO ₂	430.37	72.56	7.02	12.97	75—77	45.7
					72.94	7.32	12.86		
III _g	8	Ru	C ₂₆ H ₃₀ RuO ₂	476.23	65.57	6.34	—	94—96	22.3
					65.66	6.44	—		
VIIIa	4	Mn	C ₂₀ H ₁₇ MnO ₅	392.28	61.24	4.37	—	76—84	70.2
					62.06	4.40	—		
VIII _b	6	Mn	C ₂₂ H ₂₁ MnO ₅	420.34	62.86	5.04	—	58—59	51.5
					63.01	5.10	—		

a) Crystallization from the mixture benzene—petroleum ether.

Table 2

¹H NMR chemical shifts (δ /ppm) for compounds of the type *III* and *VIII*

Compound	<i>n</i>	Metal	—CH ₂ —	—CH ₂ COC ₅ H ₄	—CH ₂ COC ₆ H ₅	C ₅ H ₅	H _β	H _α	C ₆ H ₅
<i>IIIa</i>	3	Fe	2.14 q, 2H	2.83 t, 2H	3.09 t, 2H	4.16 s, 5H	4.46 t, 2H	4.78 t, 2H	7.3—8.1 m, 5H
<i>IIIb</i>	4	Fe	1.80 m, 4H	2.75 t, 2H	3.01 t, 2H	4.18 s, 5H	4.47 t, 2H	4.77 t, 2H	7.3—8.1 m, 5H
<i>IIIc</i>	5	Fe	1.2—2.0 m, 6H	2.72 t, 2H	2.99 t, 2H	4.20 s, 5H	4.48 t, 2H	4.77 t, 2H	7.3—8.1 m, 5H
<i>III d</i>	6	Fe	1.2—2.0 m, 8H	2.70 t, 2H	2.96 t, 2H	4.18 s, 5H	4.46 t, 2H	4.75 t, 2H	7.3—8.1 m, 5H
<i>III e</i>	7	Fe	1.2—2.0 m, 10H	2.69 t, 2H	2.96 t, 2H	4.20 s, 5H	4.47 t, 2H	4.77 t, 2H	7.3—8.1 m, 5H
<i>III f</i>	8	Fe	1.2—2.0 m, 12H	2.69 t, 2H	2.95 t, 2H	4.18 s, 5H	4.47 t, 2H	4.76 t, 2H	7.3—8.1 m, 5H
<i>III g</i>	8	Ru	1.1—1.9 m, 12H	2.57 t, 2H	2.95 t, 2H	4.58 s, 5H	4.75 t, 2H	5.08 t, 2H	7.3—8.1 m, 5H
<i>VIII a</i>	4	Mn	1.77 m, 4H	2.70 t, 2H	2.98 t, 2H	—	4.82 t, 2H	5.43 t, 2H	7.1—8.1 m, 5H
<i>VIII b</i>	6	Mn	1.1—1.9 m, 6H	2.58 t, 2H	2.95 t, 2H	—	4.83 t, 2H	5.42 t, 2H	7.1—8.1 m, 5H

¹H NMR (δ /ppm) for *VII*: 1.9—2.2 (m, 2H, —CH₂—), 2.5—3.1 (m, 4H, —C=), 4.07 (s, 9H, Fc), 7.2—7.9 (m, 5H, C₆H₅).

Table 3

Characteristic data for compounds of the type IV—VII

Compound	<i>n</i>	Metal	Formula	<i>M_r</i>	<i>w_i</i> (calc.)/% <i>w_i</i> (found)/%			M.p./°C ^a
					C	H	Fe	
IVa	5	Fe	C ₁₇ H ₂₀ FeO ₃	328.19	62.26	6.14	17.01	98—101
					62.55	6.17	16.35	
IVb	7	Fe	C ₁₉ H ₂₄ FeO ₃	356.25	64.05	6.79	15.67	95—98
					64.17	7.01	16.73	
Va	5	Fe	C ₂₇ H ₂₈ Fe ₂ O ₂	496.22	65.35	5.68	22.50	107—112
					65.49	5.52	21.70	
Vb	6	Fe	C ₂₈ H ₃₀ Fe ₂ O ₂	510.25	65.21	5.92	21.89	112—116
					65.92	6.02	21.12	
Vc	7	Fe	C ₂₉ H ₃₂ Fe ₂ O ₂	524.27	66.43	6.15	21.30	92—95
					66.59	6.30	20.85	
Vd	8	Fe	C ₃₀ H ₃₄ Fe ₂ O ₂	538.30	66.93	6.36	20.75	120—124
					66.58	6.50	20.65	
Ve	8	Ru	C ₃₀ H ₃₄ Ru ₂ O ₂	630.00	57.19	5.43	—	124—128
					57.60	5.59	—	
VIa	5	Fe	C ₃₄ H ₃₄ Fe ₂ O	570.34	71.60	6.00	19.58	104—108
					72.12	6.06	19.35	
VIb	7	Fe	C ₃₆ H ₃₈ Fe ₂ O	598.30	72.25	6.40	18.66	80—83
					72.55	6.61	18.69	
VII	—	Fe	C ₂₂ H ₂₀ FeO	356.25	74.17	5.65	15.67	136—140
					74.23	5.86	15.86	

a) Crystallization from the mixture benzene—petroleum ether.

Table 4

¹H NMR chemical shifts (δ/ppm) for compounds of the type IV and V

Compound	<i>n</i>	Metal	—CH ₂ —	—CH ₂ COOH	—CH ₂ COC ₃ H ₇	C ₃ H ₅	H _β	H _α
<i>IVa</i>	5	Fe	1.2—2.0 m, 6H	2.38 t, 2H	2.70 t, 2H	4.19 s, 5H	4.49 t, 2H	4.77 t, 2H
<i>IVb</i>	7	Fe	1.0—1.9 m, 10H	2.35 t, 2H	2.68 t, 2H	4.18 s, 5H	4.48 t, 2H	4.77 t, 2H
<i>Va</i>	5	Fe	1.3—1.9 m, 6H	—	2.73 t, 4H	4.21 s, 10H	4.48 t, 4H	4.78 t, 4H
<i>Vb</i>	6	Fe	1.2—1.9 m, 8H	—	2.70 t, 4H	4.18 s, 10H	4.46 t, 4H	4.76 t, 4H
<i>Vc</i>	7	Fe	1.2—1.9 m, 10H	—	2.68 t, 4H	4.18 s, 10H	4.46 t, 4H	4.75 t, 4H
<i>Vd</i>	8	Fe	1.0—1.9 m, 12H	—	2.68 t, 4H	4.20 s, 10H	4.48 t, 4H	4.78 t, 4H
<i>Ve</i>	8	Ru	1.1—1.8 m, 12H	—	2.57 t, 4H	4.58 s, 10H	4.76 t, 4H	5.09 t, 4H

Table 5

¹H NMR chemical shifts (δ/ppm) for compounds of the type VI

Compound	n	Metal	—CH ₂ —	—CH ₂ COC ₅ H ₄	C ₅ H ₅	C ₅ H ₅ + C ₅ H ₄
Vla	5	Fe	1.0—2.0 m, 8H	2.62 t, 2H	4.06 s, 5H	4.16 m, 9H
Vlb	7	Fe	1.1—2.0 m, 12H	2.65 t, 2H	4.06 s, 5H	4.16 m, 9H

Compound	n	Metal	H _β	H _α	—CH=	C ₆ H ₅
Vla	5	Fe	4.43 t, 2H	4.73 t, 2H	5.94 t, 1H	7.1—7.5 m, 5H
Vlb	7	Fe	4.45 t, 2H	4.75 t, 2H	5.93 t, 1H	7.1—7.5 m, 5H

Procedure B: With PCl₃

A mixture of 0.03 mol of *ω*-oxo-*ω*-phenylalkanoic acid I, anhydrous benzene (150 cm³), and freshly distilled PCl₃ (25 cm³) was heated at 60—70 °C for 3—10 h (depending on the amount of formed H₃PO₃). The cold benzene solution was decanted from H₃PO₃, the latter was rinsed with dry benzene and the excess of PCl₃ and benzene were removed from the combined solutions under reduced pressure. The residue was dissolved in dry benzene (100 cm³) and volatile liquids were again evaporated (removing of traces of PCl₃). The crude product was immediately used in the next step.

α-Metallocenyl-ω-phenyl-α,ω-alkanediones III

A solution of above prepared chloride (0.03 mol) in dry CH₂Cl₂ (70 cm³) was added to a solution of ferrocene (0.03 mol) in dry CH₂Cl₂ (70 cm³) with stirring at a temperature of 0—5 °C, under nitrogen. Anhydrous AlCl₃ (0.05 mol) was added during 30 min to the stirred mixture. The stirring was continued at temperature 5—15 °C for an additional 1 h and then for 2 h at room temperature. (The course of reaction was monitored on TLC plates.) The reaction mixture was poured into ice-cold water (500 cm³) (sufficient amount of NaHSO₃ was added at this stage to discharge the blue-green colour due to ferricenium salts), and the layers were separated. The aqueous layer was extracted several times with CH₂Cl₂, the combined CH₂Cl₂ solutions were washed with water, dried (Na₂SO₄), and the solvent was removed. The residue was chromatographed on silica using ethyl acetate—benzene mixtures as eluant. There was always isolated unreacted ferrocene (20—40 %) in addition to products III—VII (Tables 1—5).

The same procedure was used with ruthenocene or tricarbonyl(η-cyclopentadienyl)manganese as starting material.

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