THE PREPARATION AND PROPERTIES OF METALLOCENETHIOLCARBOXYLATE ESTERS

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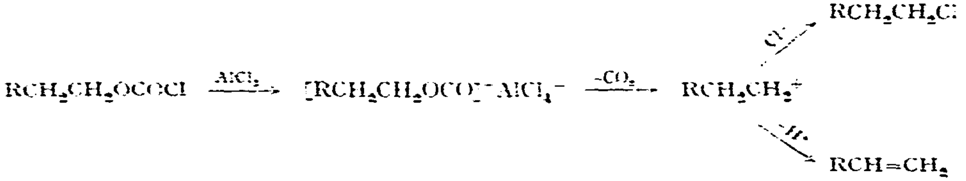
The discovery of the aromatic nature of ferrocene has precipitated numerous investigations into its behavior in electrophilic substitution reactions. These investigations have been extended to the other metallocenes, ruthenocene and osmocene, and the categorically related cyclopentadienylmanganese tricarbonyl[1]. Friedel–Crafts acylation reactions are among those most frequently employed as they lead to products which are useful as synthetic intermediates. The usual reagents such as carboxylic acids, their anhydrides and chlorides have been used as sources of the acylium ion.

In benzene chemistry the introduction of one acyl group deactivates the molecule and precludes further substitution. The metallocenes, however, are more reactive towards this type of electrophilic substitution. By appropriate choice of reagents and reaction conditions one can obtain either the mono- or the disubstituted material as the principal product[1].

The reaction between an aliphatic chloroformate and aluminium chloride has been shown to produce carbon dioxide, and a mixture of the corresponding alkyl halide and olefin[2]:



$$RCH_2CH_2OCOCl \xrightarrow{AlCl_3} [RCH_2CH_2OCO]^+AlCl_4^- \xrightarrow{-CO_2} RCH_2CH_2^+ \begin{cases} \xrightarrow{Cl^-} RCH_2CH_2Cl \\ \xrightarrow{-H^+} RCH{=}CH_2 \end{cases}$$

When the reaction is carried out in the presence of an aromatic hydrocarbon, alkylation occurs via the carbonium ion formed. If phenyl chloroformate is used, loss of carbon dioxide does not occur and no arylation attributable to the phenonium ion is observed. The product is the phenyl ester which results from attack of the phenoxycarbonylium ion.

One might anticipate, on the basis of the above reaction pathways of alkyl and aryl chloroformates, a similar sequence of reactions to occur with chlorothiolformates. It has recently been shown, however, that benzenoid aromatic hydrocarbons, rather than undergoing alkylation, are converted to the corresponding thiolesters when treated with substituted chlorothiolformates in the presence of aluminium chloride[3].

We now wish to report that this reaction is applicable for aromatic systems of an organometallic nature. Thus, ferrocene, ruthenocene and cyclopentadienylmanganese tricarbonyl have been shown capable of reacting with substituted chlorothiolformates to provide the appropriately substituted thiolester derivatives. In addition, ferrocene can be converted to the corresponding 1,1'-bis derivative under appropriate reaction conditions. A variety of substituted chlorothiolformates has been used. The compounds prepared by this method are presented in the table.

The structural assignments of the reaction products are based on infrared and nuclear magnetic resonance spectra in conjunction with microanalytical data (see table). The infrared spectra, determined in carbon tetrachloride solution, exhibited carbonyl absorbtions varying from 6.02 to 6.07 μ with an accompanying absorbtion in the region of 8.02–8.10 μ. In addition, a weak peak in the region of 14.32–14.35 μ, absent in methyl ferrocenoate, was observed in each of the thiolesters. The shift of $\nu_{C=O}$ to the region of 6.0–6.1 μ is in accord with other data for thiolesters[4]. The lack of absorption attributable to C–O–C vibration in the 8.7–9.0 μ region is further evidence of a thiolester. For comparison methyl ferrocenoate exhibits absorption at 5.86, 7.86 and 8.83 μ.

TABLE I

METALLOCENETHIOLCARBOXYLATE ESTERS

M	*R*	*X*	*M.p.* (°C) or n_D^{25}	*Calcd.*			*Found*		
				C	*H*	*S*	*C*	*H*	*S*
$XC_5H_4MC_5H_4COSR$									
Fe	CH_3	H	45–47	55.40	4.65	12.32	55.71	4.55	12.12
	C_2H_5	H	1.6419	56.95	5.15	11.69	57.48	5.11	11.60
	n-C_3H_7	H	1.6294	58.34	5.60	11.12	58.43	5.42	10.88
	iso-C_3H_7	H	1.6330	—[a]					
	n-C_4H_9	H	1.6195	—[a]					
	n-C_8H_{17}	H	1.5880	63.68	7.32	8.95	64.27	7.17	8.40
	C_6H_5	H	104–105	63.37	4.38	9.96	63.56	4.19	9.85
	CH_3	$COCH_3$	80	55.65	4.67	10.61	55.86	4.64	10.35
	CH_3	$COSCH_3$	77–79	50.30	4.24	19.19	50.26	4.15	19.29
	C_6H_5	$COSC_6H_5$	113–114	—[a]					
	n-C_8H_{17}	COS·n-C_8H_{17}	—	63.39	7.98	12.09	63.25	4.14	11.88
Ru	CH_3	H	81–84	—[a]					
$(OC)_3MnC_5H_4COSR$									
	CH_3		53–58	43.17	2.53	11.57	43.09	2.39	11.52
	C_2H_5		1.6108	45.20	3.11	10.97	45.77	3.10	10.49
	C_6H_5		52–55	52.96	2.67	9.43	53.30	2.78	9.05

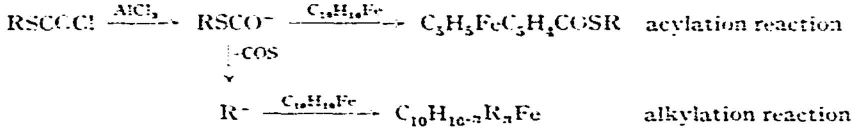
[a] Structure determined by NMR and IR spectra.

The NMR spectra of the thiolesters, determined in deuteriochloroform, consist of two triplets centered in the region of 5.2 τ and 5.6 τ and a singlet at 5.83 τ. The peak areas (2:2:5) and their positions are indicative of an acyl substituted ferrocene[5].

When ferrocene is treated with either an aryl or *n*-alkyl chlorothiolformate the reaction product is the corresponding thiolester. When a 1:1 molar ratio of acylating reagent to ferrocene is used, only very small amounts (*ca.* 1 %) of disubstitution product are observed. Even when four equivalents of acylating reagent are used, complete conversion to the 1,1'-disubstituted material does not occur.

When isopropyl chlorothiolformate is used as the acylating agent, two competitive reactions occur. Analysis of the reaction products by column chromatography on alumina demonstrated the presence of a large amount of alkylferrocenes in addition to a small amount (*ca.* 16%) of the expected thiolester. Infrared and gas-liquid chromatographic (GLC) analysis of the mixture showed it to be comprised of isopropylated ferrocenes. When *tert*-butyl chlorothiolformate was used in this reaction a complex mixture of alkylated ferrocenes was produced composed primarily of mono- and di-*tert*-butylferrocene.

While the same mechanistic pathway involving alkylation is available to all alkyl chlorothiolformates, it appears that the degree to which it is followed parallels the stability of the R cation. Thus the acylation reaction, (alkylthio)carbonylation, occurs exclusively when R is primary alkyl or aryl. When R is the secondary radical isopropyl, evidence of the competitive alkylation reaction is found. When R is the radical *tert*-butyl the alkylation reaction is the sole route followed.



$$\begin{tikzcd}
RSCOCl \arrow[r, "AlCl_3"] & RSCO^+ \arrow[r, "C_{10}H_{10}Fe"] \arrow[d, dashed, "-COS"] & C_5H_5FeC_5H_4COSR \text{ acylation reaction} \\
 & R^+ \arrow[r, "C_{10}H_{10}Fe"] & C_{10}H_{10-n}R_nFe \text{ alkylation reaction}
\end{tikzcd}$$

Methyl thiolferrocenoate is a versatile compound in that it can be converted readily to a variety of derivatives of ferrocenoic acid. Thus, treatment of the thiolester with anhydrous hydrazine results in facile displacement of methyl mercaptan to give ferrocene carboxhydrazide in good yields. Similar reactions have been carried out using an assortment of amines, under varying reaction conditions, providing the corresponding amides. Hydrolysis of either methyl ferrocenethiolcarboxylate or the related 1,1'-derivative provides a route to ferrocenoic acid and ferrocene-1,1'-dicarboxylic acid.

(Alkylthio)carbonylation of ferrocene derivatives by methyl chlorothiolformates in the presence of aluminium chloride proceeds as one would anticipate. Treatment of acetylferrocene by this method has provided 53% of methyl 1'-acetylferrocenethiolcarboxylate. When 1,1'-diethylferrocene was treated with the same reagent a mixture of the 2-, and the 3-substituted isomers was obtained. This mixture was readily separable into its components by column chromatography on alumina.

EXPERIMENTAL

Melting points were determined on a Kofler Hot Bench. Infrared and nuclear magnetic resonance (NMR) spectra were determined on a Beckman IR 5-A spectrophotometer and Varian Associates Model A-60 spectrometer, respectively. Gas-liquid chromatographic analyses were performed on an Aerograph Model A-700P equipped with a 20 ft. × 3/8 in. column packed with 20% S.E.-30 silicone rubber on 60/80 Chromosorb P with helium as the carrier gas.

Methyl ferrocenethiolcarboxylate

A freshly prepared solution containing 11.0 g (0.10 mole) methyl chlorothiolformate* and 13.3 g (0.10 mole) aluminium chloride in 200 ml dry methylene chloride was added dropwise, under nitrogen, to a stirred solution of 18.6 g (0.10 mole) ferrocene in 250 ml dry methylene chloride. The reaction mixture was maintained at reflux for two hours, after completion of the addition, and then allowed to cool. When the cooled solution was poured over ice, the organic phase was separated and allowed to evaporate. The residual red oil was taken up in hexane and chromatographed on activity grade III alumina[6]. Using hexane as eluent, 3.7 g (20%) ferrocene was recovered. When the eluent was changed to 5% ether–hexane 19.2 g (74%) methyl ferrocenethiolcarboxylate was obtained (m.p. 45–47°). When the eluent was changed to 10% ether–hexane 0.28 g (0.84%) of the 1,1′-disubstitution product was removed. It was identical in all respects to that obtained below. The structure of the thiolester was based on infrared and NMR spectra and microanalytical data. (See discussion and table respectively.) Other substituted thiolesters, presented in the table were prepared in a similar fashion.

Dimethyl ferrocene-1,1′-bis(thiolcarboxylate)

The above reaction was carried out using 0.1 moles of acylating reagent and 0.03 mole of ferrocene in carbon disulfide solvent and the normal work-up procedure was carried out. Column chromatography indicated a trace of ferrocene and a small amount (less than 2%) of methyl ferrocenethiolcarboxylate. Elution with 10% ether–hexane removed 5.7 g (51%) of dimethyl ferrocene-1,1′-bis(thiolcarboxylate) (m.p. 77–79°), identified by means of its infrared, NMR spectra and microanalytical data. Other 1,1′-bis-thiolesters prepared in a similar manner are listed in the table.

Reaction of ferrocene with tert-butyl chlorothiolformate and aluminium chloride

A solution of 15.2 g (0.10 mole) *tert*-butyl chlorothiolformate in 100 ml dry methylene chloride was added dropwise, under nitrogen, to a stirred mixture of 13.3 g (0.10 mole) aluminium chloride and 18.6 g (0.10 mole) ferrocene, in 400 ml dry methylene chloride. The reaction was maintained at 0° during the course of the addition. The solution was then stirred at reflux for two hours then worked up in the usual manner. Column chromatography using hexane eluent removed unchanged ferrocene and alkylated ferrocenes. None of the desired *tert*-butyl ester was observed. Gas–liquid chromatographic analysis of the products demonstrated a multitude of alkylation products derived from the *tert*-butyl cation, consisting mainly of mono- and 1,1′-di-*tert*-butylferrocene.

A reaction carried out in an identical fashion using isopropyl chlorothiolformate gave a mixture of the isopropyl thiolester and isopropylated ferrocenes.

Ferrocenoic acid

A mixture of 6.0 (0.023 mole) methyl ferrocenethiolcarboxylate and 6.0 g (0.11 mole) potassium hydroxide in 100 ml ethanol–water (1:1) was maintained at reflux for two hours. The solution was cooled and the ethanol removed at reduced pressure. The aqueous solution was acidified with phosphoric acid in the cold. After the evolution of methyl mercaptan had subsided the ferrocenoic acid was removed by filtration, re-suspended in water and filtered again. The solid filter cake was then dried *in vacuo* to yield 5.0 g (95%) of ferrocenoic acid, m.p. dec. 200° (Lit.[7] 210°).

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[*] The chlorothiolformates utilized in this study were obtained from the Stauffer Chemical Company, San Francisco, California.

Similar hydrolysis of the dimethyl bis-thiol ester produced a comparable yield of ferrocene-1,1'-dicarboxylic acid. The use of potassium hydroxide instead of sodium hydroxide is preferred due to the greater solubility of the potassium salts of both the mono- and dicarboxylic ferrocene acids in the hydrolysis medium.

Ferrocenecarboxhydrazide and cyclopentadienylmanganese carbohydrazide tricarbonyl

A mixture of 2.6 g (0.01 mole) methyl ferrocenethiolcarboxylate and 0.65 g (0.02 mole) anhydrous hydrazine in 20 ml ethanol was heated on a steam bath for 0.5 h. The mixture was cooled and the solid which precipitated was recrystallized from ethanol to yield 1.40 g (60 %) ferrocenecarbohydrazide of m.p. 160–161° (Lit.[7] 155–156°).

A similar reaction of methyl cyclopentadienylmanganesethiolcarboxylate tricarbonyl with neat hydrazine provided the corresponding hydrazide in 90 % yield (m.p. 163°).

N-Methylferrocenecarboxamide

Methylamine (200 ml) was condensed into a flask containing 7.0 g methyl ferrocenethiolcarboxylate. The mixture was stirred at room temperature overnight allowing the methylamine and methyl mercaptan to evaporate. The residual material was recrystallized from ethanol to give 6.2 g (95 %) N-methylferrocenecarboxamide, m.p. 185–187°. The structure of the amide was proven by its infrared and NMR spectra and microanalytical data.

Similar displacements by ethylamine, piperidine, etc. have been carried out providing the respective amides in varying yields.

SUMMARY

Ferrocene, ruthenocene and cyclopentadienylmanganese tricarbonyl have been shown to undergo either alkylation or conversion to thiolcarboxylate esters when treated with substituted chlorothiolformates in the presence of aluminium chloride. While aryl or primary alkyl chlorothiolformates provide the corresponding thiolesters, *tert*-butyl chlorothiolformate gives only alkylation products derived from the *tert*-butyl cation. Competitive alkylation and acylation reactions occur when isopropyl chlorothiolformate is used. Methyl ferrocenethiolcarboxylate, prepared by this method, has been converted via displacement reactions to ferrocenoic acid, its hydrazide, and several amide derivatives.

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