ELSEVIER

Journal of Organometallic Chemistry 507 (1996) 215–220

Journal of Organometallic Chemistry

Ferrocene compounds XXII [☆]. Synthesis and reactions of some ferrocenylthiaaliphatic acids

S. Lisac, V. Rapić *

Faculty of Food Technology and Biotechnology, University of Zagreb, 41000 Zagreb, Croatia

Received 24 April 1995

Abstract

Condensation of several ferrocenylcarbinols (**1**) with thioglycolic acid, β-mercaptopropionic acid or β-mercaptoisobutyric acid in the presence of trifluoroacetic acid have given the corresponding ferrocenylthiaaliphatic acids (**2–4**) with 65–99% yields. Instead of the expected intramolecularly cyclized products, reactions of the acids **2–4** with trifluoroacetic anhydride give 23–30% of the 1,2-disubstituted 1,2-diferrocenylethanes (**8**), 15–26% of trimeric species (**9**), and about 30% of oligomeric species (**10**). The mechanism of the reactions is discussed.

Keywords: Iron; Ferrocene

1. Introduction

The preparation and some reactions of a few ferrocenylthiaaliphatic acids have been described previously. In general, they can be made by condensation of ferrocenylcarbinols with appropriate mercaptoaliphatic acids in a strongly acidic medium [2]. (±)-*S*-(1-Ferrocenylalkyl)-2-mercaptoaliphatic acids can be resolved into enantiomers by fractional crystallization of their diastereomeric ephedrine salts. Owing to the stereospecific cleavage of the C–S bond in the resolved enantiomers to give the corresponding appropriate carbinols, these acids have been used for the purification and preparation of the optically active 1-ferrocenylalkanols [2] and the corresponding tertiary alcohols [3].

Recently, *S*-(1-ferrocenylalkyl)thioglycolic acids have been converted into amides *N* substituted with penicillanic acid and cephalosporanic acid [4]. Neuse and coworkers [5] have described the electrochemical behaviour of *S*-ferrocyl-3-mercaptoaliphatic acids (ferrocyl = ferrocenylmethyl) and the corresponding fericenium tetrachloroferrates.

Nesmeyanov et al. [6] have described the homoannular cyclization of *S*-ferrocylthioglycolic acid by a conventional Friedel–Crafts reaction with oxalyl chloride in the presence of stannic chloride. To our knowledge this is the only reported example to date of intramolecular cyclization of ferrocylthiaaliphatic acids.

In the light of the above reports and in continuation of our programme on ferrocenylaliphatic acids [1] we decided to prepare some ferrocenylthiaaliphatic acids and to investigate the possibilities of bringing about their intramolecular cyclization by use of trifluoroacetic anhydride (TFAA) or polyphosphoric acid (PPA).

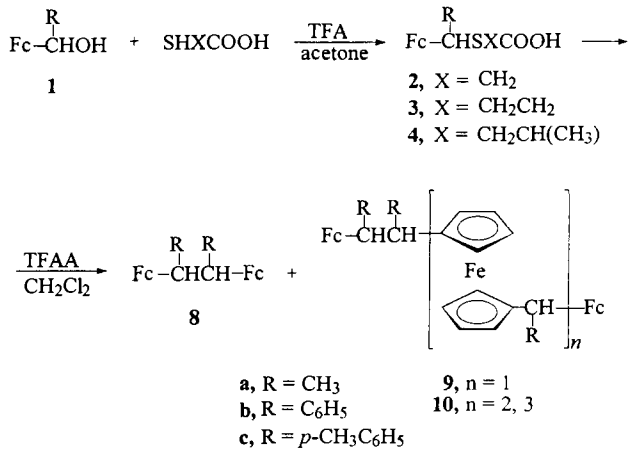
2. Results and discussion

We made ferrocenylthiaaliphatic acids (**2–4**) by the procedure described previously [2], involving treatment of 1-ferrocenylethanol (**1a**), ferrocenyl(phenyl)methanol (**1b**) or ferrocenyl(*p*-tolyl)methanol (**1c**), with thioglycolic acid (X = CH_2), β-mercaptopropionic acid (X =

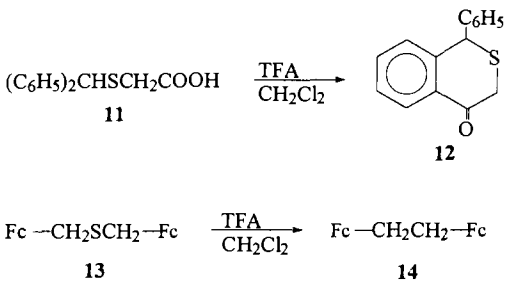
☆ For Part XXI, see [1].

* Corresponding author.

SSDI 0022-328X(95)05745-5



Scheme 1.



Scheme 2.

CH_2CH_2) or β-mercaptoisobutyric acid (X = CH_2-$CH(CH_3)$) in the presence of trifluoroacetic acid (TFA). Most of the acids obtained are well defined crystalline compounds and were identified from their spectral data and by conversion into the methyl esters **5–7**.

Attempts to cyclize the thiaaliphatic acids **2–4** were made by employing the procedure used for intramolecular cyclization of their benzenoid analogues [7], i.e. by refluxing 1 mmol of **2–4** in dichloromethane with 1–2 ml of TFAA for about 1 h. However, instead of the expected cyclic products (analogues of **12**) we isolated 23–30% of 1,2-disubstituted 1,2-diferrocenylethanes (**8**), 15–26% of trimers (**9**) and about 30% of oligomeric products (**10**) (Scheme 1). Longer heating or use of a large excess of the reagent resulted in decomposition, and in such cases we isolated only unidentified products. Use of PPA with the thiaaliphatic acids **2–4** under the same conditions gave either unchanged starting materials or decomposition products.

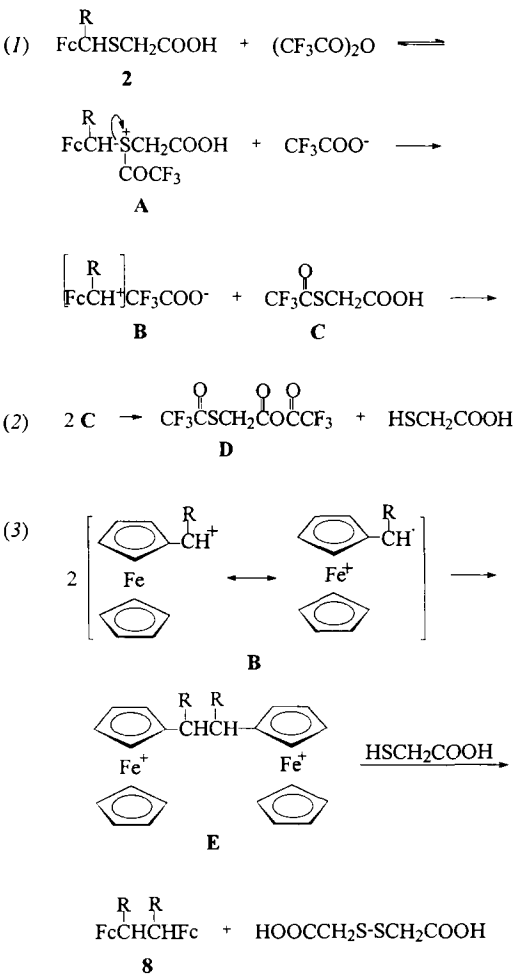
In contrast, we found that *S*-benzhydrylthioglycolic acid (**11**) was readily converted into the corresponding benzothiochromone (**12**) by treatment with TFA in CH_2Cl_2 at room temperature.

To throw light on the mechanism of conversion of **2–4** to **8–10** we performed some additional experiments and found that refluxing of the solutions of the acids in dichloromethane alone or in the presence of TFA left only unchanged starting materials. We also found that diferrocyl sulfide (**13**) is cleaved by means of TFAA to give 1,2-diferrocenylethane (**14**) (Scheme 2).

In considering the possible mechanism we took account of the following points.

(1) In view of the nucleophilic character of thia groups we assumed that the first reaction step involved *S*-acylation, with the formed sulfonium species **A** then being cleaved to give the ferrocyl carbocation **B** and thioester acid **C**. In the light of the conversion **13** → **14** it can be concluded that competitive *O*-acylation of **2–4** plays no part in the reaction. Scheme 3 shows the suggested course of the reaction of acids **2**.

(2) As a consequence of the strong acylating ability of thioesters, disproportionation of **C** to give **D** and thioglycolic acid can be expected.



Scheme 3.

Table 1
Physical constants and IR spectral data for FcCHRSXCOOH (**2–4**)

Compound	R	X	Formula (M_r)	Yield (%)	Analysis, found (calculated) (%)			melting point (°C)	IR spectra	
					C	H	S		ν(CH) arom. (aliph.) (cm^{-1})	ν (C=O) (cm^{-1})
2a	CH_3	CH_2	$C_{14}FeO_2S$ (304.19)	99	55.41 (55.28)	5.00 (5.30)	10.92 (10.54)	81–82	3060w (2950 w)	1680 s
2b	C_6H_5	CH_2	$C_{19}H_{18}FeO_2S$ (366.26)	89	61.98 (62.31)	5.16 (4.95)	9.01 (8.75)	97–99	3070 w (2925 w)	1680 s
2c	*p*-$CH_3C_6H_4$	CH_2	$C_{20}H_{20}FeO_2S$ (380.28)	85	63.40 (63.17)	5.17 (5.30)	8.66 (8.43)	101–102	3080 w (2950 w)	1690 s
3a	CH_3	CH_2CH_2	$C_{15}H_{18}FeO_2S$ (318.21)	79 55 [a]	56.30 (56.62)	5.51 (5.70)	10.06 (10.07)	84–85	3090 w (2930 w, 2860 w)	1706 s
3b	C_6H_5	CH_2CH_2	$C_{20}H_{20}FeO_2S$ (380.28)	80 54 [a]	63.39 (63.17)	5.16 (5.30)	8.61 (8.43)	106–107	3080 w (2980 w, 3050 w, 2930 w)	1702 s
4a	CH_3	$CH_2CH(CH_3)$	$C_{16}H_{20}FeO_2S$ (332.24)	65	58.08 (57.84)	6.19 (6.07)	10.01 (9.65)	Resin	3090 w (2970 w, 2930 m)	1705 s
4b	C_6H_5	$CH_2CH(CH_3)$	$C_{21}H_{22}FeO_2S$ (394.31)	77	64.15 (63.97)	5.85 (5.62)	8.33 (8.13)	Resin	3100 w (2980 m, 3030 w, 2920 w)	1705 s

[a] Starting from $CH_3COSCH_2CH(CH_3)COOH$.

(3) The formed carbocations (i.e. cation radicals) **B** can dimerize to dications **E**, which are then reduced to dimers **8** by thioglycolic acid.

(4) Dimers **8** undergo electrophilic attack of ferrocyl carbocations to give oligomers **9** and **10**.

We conclude that the formation of dimers **8** and

Table 2
Physical constants and IR spectral data for $FcCHRSXCOOCH_3$ (**5–7**)

Compound	R	X	Formula (M_r)	Yield (%)	Analysis, found (calculated) (%)			IR spectra	
					C	H	S	ν(CH) arom. (aliph.) (cm^{-1})	ν(C=O) (cm^{-1})
5a	CH_3	CH_2	$C_{15}H_{18}FeO_2S$ (318.21)	73	56.88 (56.22)	5.51 5.70	10.36 (10.07)	3070 w (2940 w, 2905 w)	1725 s
5b	C_6H_5	CH_2	$C_{20}H_{20}FeO_2S$ (380.28)	54	63.35 (63.17)	5.05 (5.30)	8.71 (8.43)	3070 w (2930 m, 2900 m)	1730 s
5c	*p*-$CH_3C_6H_4$	CH_2	$C_{21}H_{22}FeO_2S$ (394.31)	51	64.11 (63.97)	5.93 (5.62)	8.41 (8.13)	3070 w (2940 m, 2900 m)	1730 s
6a	CH_3	CH_2CH_2	$C_{16}H_{20}FeO_2S$ (332.24)	62	58.03 (57.84)	6.23 (6.07)	9.49 (9.65)	3090 w (2970 w, 2930 m)	1735 s
6b	C_6H_5	CH_2CH_2	$C_{21}H_{22}FeO_2S$ (394.31)	70	64.20 (63.97)	5.90 (5.62)	8.41 (8.13)	3080 w 3070 w (2970 m, 2930 m)	1733 s
7a	CH_3	$CH_2CH(CH_3)$	$C_{17}H_{22}FeO_2S$ (346.27)	66	59.15 (58.97)	6.39 (6.40)	9.55 (9.26)	3100 m (2960 w, 2920 m)	1740 s
7b	C_6H_5	$CH_2CH(CH_3)$	$C_{22}H_{24}FeO_2S$ (408.34)	59	64.44 (64.71)	6.12 (5.92)	7.98 (7.85)	3100 w, 3030 w (2960 w, 2920 w)	1735 s

oligomeric products **9** and **10** can be attributed to the extraordinary stability of ferrocyl carbocations [8]. This makes formation of these species the favored process and precludes the expected cyclization analogous to the conversion **11** → **12**.

3. Experimental details

The melting points were determined with a Buchi apparatus. The IR spectra were recorded for KBr pellets or liquid films with a Perkin–Elmer 257 grating IR spectrophotometer. The ^{1}H NMR spectra were recorded on Varian EM 360 or Varian Gemini 300 spectrometer with tetramethylsilane as internal standard. Mass spectra were obtained with a Shimadzu GCNS-QP 1000 spectrometer. Degrees of polymerization of oligomers were determined by gel permeation chromatography (GPC) on a 500 A PL gel column (Varian 8500 pump; tetrahydrofuran as eluent). Products were purified by preparative thin layer chromatography (TLC) on silica gel (Merck, Kieselgel 60 HF_{254}) or by recrystallization.

Ferrocenylcarbinols (**1**) were prepared by reduction of the appropriate acylferrocenes [9].

3.1. S-Ferrocylmercaptoalkanoic acids (2–4)

The appropriate mercaptoaliphatic acid (2.2 mol) was added to a solution of the corresponding carbinol **1** (2 mmol) in 5–10 ml of acetone. The mixture was cooled to 0°C, 0.1 ml of TFA was added with stirring, and the solution was set aside overnight at room temperature. It was then transferred to a separating funnel and was made alkaline by addition of 5% aqueous KOH. The solution was shaken with dichloromethane; the aqueous layer was next separated and acidified with a few drops of 85% H_3PO_4 and then extraction with dichloromethane was carried out. The extract was shaken with water, dried over $MgSO_4$ and evaporated to dryness to leave the crude acids **2–5**, which were recrystallized from hexane–benzene or ethyl acetate (Table 1).

3.2. Methyl S-ferrocylmercaptoalkanoates (5–7)

The methanolic solutions of acids obtained by the above procedure were esterified by treatment with ethereal diazomethane for 12 h in a refrigerator. After evaporation of the solvents the oily residue was purified by preparative TLC on silica gel with benzene–ethanol as eluent (Tables 2 and 3).

3.3. Reactions of S-ferrocylmercaptoalkanoic acids (2–4) with trifluoroacetic anhydride

A solution of 1 mmol of the appropriate acid in 10–20 ml of dichloromethane (dried over P_2O_5) containing 1–2 ml of TFAA was stirred for 0.5–1 h, during which the initial yellow brown solution become darker. The mixture was refluxed for 0.5–1 h, cooled and added to ice–water containing some ascorbic acid. The products were extracted with diethyl ether, and the

Table 3

^{1}H NMR data for $FcCH_cRSCH_aH_bCOOCH_3$ (**5**), $FcCH_cRSC(H_b)(H_a)CCOOCH_3$ (**6**) and $FcCH_cRSC(H_b)(CH_3)CCOOCH_3$ (**7**)

Compound	δ (ppm)								
	Benzene protons	Ferocene protons		Aliphatic protons			OCH_3	CCH_3	
		Unsubstituted ring	Subsituted ring	H_a	H_b	H_c			
5a	—	4.16 (9, m)		3.14 (2, s)		3.90 (1, d)	3.71 (3, s)	1.66 (3, d)	
5b	7.40, 7.30 (5, m)	4.07 (5, m)	4.09, 4.10 (4, m)	2.96 (2, d)		5.02 (1, s)	3.64 (3, s)	—	
5c	7.32, 7.14 (2, d)	4.10 (5, m)	4.13, 4.22 (4, m)	3.05 (1, d)	2.92 (1, d)	5.00 (1, s)	3.69 (3, s)	2.34 (3, s)	
6a	—	4.15 (9, m)		2.49 (2, t)	2.71 (2, t)	3.77 (1, q)	3.67 (3, s)	1.66 (3, d)	
6b	7.39 (5, m)	4.10 (9, m)		2.52 (4, m)		4.84 (1, s)	3.66 (3, s)	—	
7a	—	4.15 (9, m)		2.50 (1, m)	2.76 (2, m)	3.73 (1, m)	3.68 [a] (3, s)	1.64 (3, d)	1.18 (3, d)
7b	7.43 [b] (5, m)	4.09 (9, m)		2.29 (1, m)	2.60 (2, m)	4.82 [b] (1, s)	3.70 [b] (3, s)	1.17 (3, d)	

[a,b] The compounds **7** consisted of two diastereoisomeric pairs of enantiomers. Besides the given signals, signals corresponding to the other racemate appeared in their spectra. **7a**: 3.70 s ppm. **7b**: 7.34 m; 4.79 s; 3.66 s; 1.17 s ppm.

Table 4
Physical constants and IR spectral data for FcCHRCHRFc (**8**), FcCHRCHRFnCHRFc (**9**) and FcCHRCHR $(FnCHR)_{2,3}Fc$ (**10**) [a]

Compound	R	Yield (%)	Melting point (°C)	IR spectra		
				ν(CH) arom. (cm^{-1})	ν(CH) aliph. (cm^{-1})	ν(C=C) (cm^{-1})
9a	CH_3	15	Resin	3070 m	2960 m, 2913 m	1630 b, 1455 b
8b	C_6H_5	30	187–191	3080 m, 3020 m	2910 b	1600 m, 1450 b
9b	C_6H_5	26	Resin	3085 m, 3030 m	2930 m	1605 m, 1495 m 1455 s
8c	p-$CH_3C_6H_4$	23	93–98	3060 m	2920 m	1600 m, 1510 s, 1450 s
9c	p-$CH_3C_6H_4$	31	Resin	3085 m, 3020 w	2915 b	1600 m, 1510 s, 1455 m
10c	p-$CH_3C_6H_4$	30	Resin	3083 m 3020 w	2915 b	1600 m, 1515 s, 1450 m

[a] Fn = 1,1'-ferrocenylene.

extract was shaken with 5% aqueous $NaHCO_3$, water, dried over $MgSO_4$ and evaporated to dryness. The mixtures of dimeric product (**8**) and oligomeric product (**9**) were separated by TLC with benzene–petroleum ether as eluent (Tables 4 and 5).

3.4. Diferrocyl sulfide (11)

A solution of 500 mg (1.3 mmol) of *N,N,N*-trimethylferrocylammonium iodide and 160 mg (0.66 mmol) of sodium sulfide in 3 ml of water was heated on an oil bath at 100°C, cooled and extracted with diethyl ether. The extract was shaken with water, died over $MgSO_4$ and evaporated to gave 150 mg (48%) of orange crystals melting point (m.p.), 105–108°C (107–108°C [10]).

3.5. 1,2-Diferrocenylethane (12)

A solution of 105 mg (0.25 mmol) of sulfide (**11**) and 0.1 ml of TFAA in 5 ml of dichloromethane was stirred at room temperature for 0.5 h. Work-up and TLC with petroleum ether: benzene (3 : 2) as eluent gave 50 mg (52%) of 1,2-diferrocenylethane (m.p., 194–195°C) (193–195°C [11]).

Table 5
Analyses and ^1H NMR data for oligomers **8–10**

Compound	Formula (M_r calculated)	M_r found	Analysis, found (calculated) (%)		^1H NMR spectra, δ (ppm)				
			C	H	Benzene protons	Ferrocene protons		CH	CH_3
						Substituted ring	Unsubstituted ring		
8b	$C_{34}H_{30}Fe_2$ (550.3)	550	74.49 (74.21)	5.51 (5.50)	7.12 (10, s)	3.88 (8, m)	3.70 (10, s)	3.60 (2,s)	—
9b	$C_{51}H_{44}Fe_3$ (824.5)	—	73.98 (74.29)	5.55 (5.38)	7.59 (15, m)		3.90 (29, m)		—
8c [a]	$C_{36}H_{34}Fe_2$ (578.4)	578	75.11 (74.76)	6.15 (5.92)	6.97 (8, m)	3.85 (8, m)	3.73 (10, s)	3.69 (2, s)	2.32, 2.24 (6, s)
9c [a]	$C_{54}H_{50}Fe_3$ (866.5)	825	74.90 (74.85)	5.65 (5.82)	6.94 (12, m)	3.89 (16, m)	3.68 (13, m)		2.32, 2,27, 2.24 (9, s)
10c [b]	$C_{90}H_{82}Fe_5$ (1442.9)	—	75.13 (74.92)	5.91 (5.73)	7.08 (16, m)		3.89 (38, m)		2.29 (12, m)

[a] The separated singlets corresponding to the methyl group protons indicated the presence of the meso and racemic products; the ratio of these signals for **8c** is 3 : 2.
[b] The data for the pentamer ($n = 5$) are given.

3.6. 4,4-Diphenyl-3-thiabutyric acid (13)

In the way described for preparation of the acids **2–5**, benzhydrol was converted into 4,4-diphenyl-3-thiabutyric acid (**13**) with 65% yield m.p., 126–128°C (129–130°C [12]). ^{1}H NMR (acetone-d_6): δ 7.20 (10 H, m, arom.), 5.50 (1H, s, methine), 3.11 (2H, s, methylene) ppm. IR (KBr): ν(O–H) 3000 b, ν(C–H) aliph. 2920 m, ν(C=O) 1690 s, ν(C–O) 1450 m, 1425 m cm^{-1}.

3.7. 1-Phenylisothiochromane-4-one (14)

A solution of 800 mg of **13** in dichloromethane was refluxed with 1 ml of TFAA for 8 h. The usual work-up gave 75% of thiochromone 12 (m.p. (benzene), 117–118°C). Anal. Found: C, 75.20; H, 5.04; S 13.57. $C_{15}H_{12}OS$ Calc.: C, 74.97; H, 5.01; S 13.35%. ^{1}H NMR ($CDCl_3$): δ 7.40 (9H, m, arom.), 5.35 (1H, s, methine), 3.68 (2H, s, methylene) ppm. IR (KBr): ν(C–H) arom. 3060 and 3020 w, ν(C–H) aliph. 2950 w, 2920 m and 2860 m, ν(C=O) 1730 s cm^{-1}.

Acknowledgments

We are indebted to Professor V. Šunjić for helpful discussions. We thank the Ministry for Science, Technology and Information of Croatia, Zagreb, Republic of Croatia, for partial support through a grant.

References

[1] S. Lisac, V. Rapić and S. Kovač, *Croat. Chem. Acta, 67* (1994) 531.
[2] A. Ratajczak and B. Misterkiewicz, *J. Organomet. Chem., 91* (1975) 73; B. Misterkiewicz, *J. Organomet. Chem., 224* (1982) 43.
[3] R. Dabard, B. Misterkiewicz, H. Patin and J. Wasielewski, *J. Organomet. Chem., 328* (1987) 185.
[4] D. Scataru, L. Tataru, I. Mazilu, E. Diaconu, T. Lixandru and Cr. Simionescu, *J. Organomet. Chem., 401* (1991) 81.
[5] E.W. Neuse, F.B.D. Khan and M.G. Meirim, *Appl. Organomet. Chem.*, (1988) 129; N.F. Blom, E.W. Neuse and H.G. Thomas, *Transition Met. Chem., 12* (1987) 301.
[6] A.N. Nesmeyanov, E.G. Perevalova, L.I. Leont'eva and Yu.A. Ustynyuk, *Izv. Akad. Nauk SSSR, Ser. Khim.*, (1965) 1882.
[7] V. Rapić and L. Korontoš, *J. Organomet. Chem., 260* (1984) 219, and references cited therein.
[8] A. Togni and T. Hayashi (eds.), *Ferrocenes*, VCH, Weinheim, 1995, p. 175.
[9] S. Kovač and V. Rapić, *J. Organomet. Chem., 384* (1990) 147, and references cited therein.
[10] A.N. Nesmeyanov, E.G. Perevalova and L.S. Shilovtseva, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, (1962) 1997.
[11] K.L. Rinehart, C.J. Michjeda and P.A. Kittle, *J. Am. Chem. Soc., 81* (1959) 3162.
[12] B. Holmberg, *J. Pract. Chem., 141* (1934) 93.