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A SIMPLE SYNTHESIS AND PURIFICATION OF 1-FERROCENYLALKYL ALCOHOLS

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Summary

An alternative method for the preparation of 1-ferrocenylalkyl alcohols has been developed. This involves condensation of ferrocene with carbonyl compounds in concentrated sulfuric acid and addition of the resulting solutions of 1-ferrocenylalkylium ions into aqueous sodium bicarbonate. The mixtures are then treated with thioglycolic acid and the *S*-(1-ferrocenylalkyl)thioglycolic acids purified via sodium salts and hydrolysed in the presence of copper powder to give 1-ferrocenylalkyl alcohols in good yields.

Introduction

1-Ferrocenylalkyl alcohols are valuable starting substances for the preparation of ferrocene derivatives, e.g. esters, ethers, alkanes, alkenes and others [1]. Up to now, primary and secondary 1-ferrocenylalkyl alcohols have usually been prepared by reduction of ferrocene compounds bearing a carbonyl group FcCOR with lithium aluminum hydride [1—5]. Tertiary alcohols such as 2-ferrocenylpropanol-2 [4] and 2-ferrocenylbutanol-2 [6] were obtained in 50—75% yields from acetylferrocene by reaction with Grignard reagents.

It has been recently reported that the condensation of ferrocene in solutions of strong acids with carbonyl compounds leads to the formation of stable 1-ferrocenylalkylium ions [7—9], which subsequently react with nucleophilic reagents, e.g. thiols and amines, to form 1-ferrocenylalkyl sulfides [7,8] and 1-ferrocenylalkylamines [9], respectively. The presence of 1-ferrocenyl-2-methylpropylium ion was detected by ^{1}H NMR spectroscopy in a trifluoroacetic acid solution of ferrocene and 2-methylpropanal [8]. Similarly, during condensations of ferrocene with aromatic carbonyl compounds, 1-ferrocenylalkylium ions were obtained as perchlorates in high yields [10].

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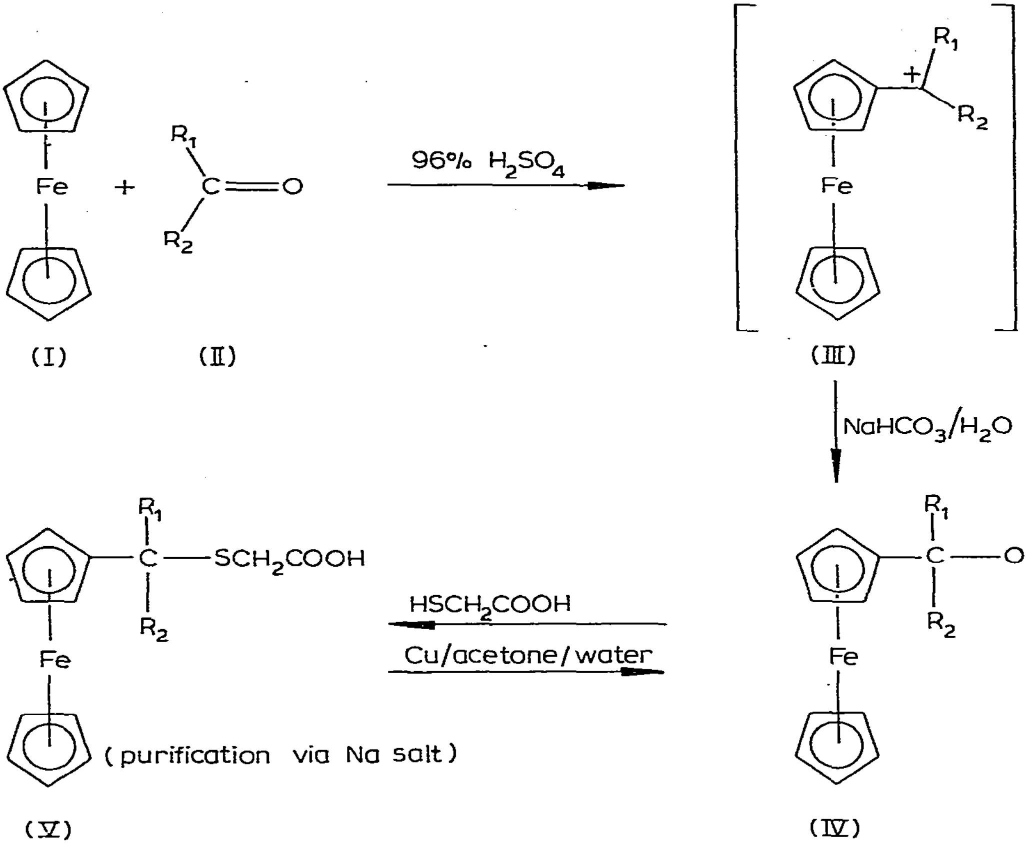
Results and discussion

An alternative simple method for the preparation of 1-ferrocenylalkyl alcohols has been developed (Scheme 1). During condensations of ferrocene I in concentrated sulfuric acid medium with aldehydes and ketones IIa—IIf, characteristic brown solutions of 1-ferrocenylalkylium ions IIIa—IIIf were formed, but the ions could not be characterized by ^{1}H NMR spectroscopy, probably due to the presence of paramagnetic substances. The solutions of the ions were added to saturated aqueous sodium bicarbonate to yield alcohols IVa—IVf. The crude products were isolated by ether extraction and at first were purified by silica gel column chromatography. However, under these conditions the alcohols IVb—IVf gave small amounts of other products, and during the preparation of ferrocenylmethanol IVa, about 20% of bisferrocenylmethyl ether $(FcCH_2)_2O$ was formed. The removal from the crude alcohols of unreacted carbonyl compounds, particularly IIb, c, d, f, and the products of their intermolecular conden-

SCHEME 1



a, $R_1 = R_2 = H$; b, $R_1 = H$, $R_2 = n\text{-}Pr$; c, $R_1 = H$, $R_2 = i\text{-}Pr$;

d, $R_1 = H$, $R_2 = Ph$; e, $R_1 = R_2 = Me$; f, $R_1 = Me$, $R_2 = Et$.

TABLE 1

EXPERIMENTAL DETAILS

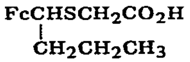
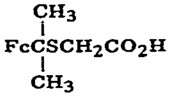
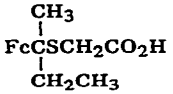
Condensation of ferrocene (1.86 g, 0.01 mol) with carbonyl compound R^1COR^2				Hydrolysis of the obtained acids $FcC(R^1R^2)SCH_2COOH$		
No.	R^1; R^2	Amount of R^1COR^2	Conditions	No.	R^1; R^2	Conditions
IIa	H; H	1.5 g (0.05 mol) [a]	0°C (0.5 h)	Va	H; H	Reflux (2 h)
IIb	H; n-Pr	9.0 cm^3 (0.1 mol)	0°C (0.5 h)	Vb	H; n-Pr	Reflux (2 h)
IIc	H; i-Pr	9.2 cm^3 (0.1 mol)	0°C (0.5 h)	Vc	H; i-Pr	Reflux (2 h)
IId	H; Ph	6.7 cm^3 (0.1 mol)	0°C (0.5 h)	Vd	H; Ph	Reflux (1 h)
IIe	Me; Me	7.3 cm^3 (0.1 mol)	25°C (1 h)	Ve	Me; Me	25°C (2 h)
IIf	Me; Et	9.1 cm^3 (0.1 mol)	25°C (1 h)	Vf	Me; Et	25°C (2 h)

[a] Finely powdered of *para*-form $(CH_2O)_n$.

sation in concentrated sulfuric acid gave problems. Therefore, the alcohols isolated by ether extraction were converted into *S*-(1-ferrocenylalkyl)thioglycolic acids Va—Vf [11—12], which were purified via water soluble sodium salts (Table 2). Unchanged ferrocene and other neutral by-products remained in the organic layer. In this way the by-product bisferrocenylmethyl ether was converted into (ferrocenylmethyl)thioglycolic acid, Va. The acids Va—Vf were hydrolysed in acetone/water (3/1) solution in the presence of copper powder to give the pure alcohols IVa—IVf in high yields (Table 3). When the acids were hydrolysed in the presence of mercuric chloride [11,12], small amounts of by-products were detected in the alcohols by TLC. The hydrolysis of the primary and secondary compounds Va—Vd in the presence of copper powder

TABLE 2

THE CHARACTERISTICS OF THE OBTAINED *S*-(1-FERROCENYLALKYL)THIOGLYCOLIC ACIDS [a]

No.	Formula	m.p. (°C)	^1H NMR (δ, in $CDCl_3$, 60 MHz)	IR (cm^{-1}) (in CCl_4)	
				C=O band (strong)	OH bands (weak)
Vb	 $\underset{\mathrm{CH_2CH_2CH_3}}{\mathrm{FcCHSCH_2CO_2H}}$	81—82	0.90 (3 H, t, $-CH_3$), 1.30—2.17 (4 H, m, $-CH_2CH_2-$), 3.00 (2 H, s, $-SCH_2$), 3.57 (1 H, m, =CH), 4.07 (9 H, s, ferrocenyl), 10.37 (1 H, s, COOH)	1715	2570, 2680
Ve	 $\mathrm{Fc}\overset{\mathrm{CH_3}}{\underset{\mathrm{CH_3}}{\mathrm{C}}}\mathrm{SCH_2CO_2H}$	112—113	1.60 (6 H, s, $-CH_3$), 2.96 (2 H, s, $-CH_2$), 4.07 (9 H, s, ferrocenyl), 10.13 (1 H, s, COOH)	1715	2565, 2680
Vf	 $\mathrm{Fc}\overset{\mathrm{CH_3}}{\underset{\mathrm{CH_2CH_3}}{\mathrm{C}}}\mathrm{SCH_2CO_2H}$	84—85	0.97 (3 H, t, $-CH_3$), 1.56 (3 H, s, $-CH_3$), 1.80 (2 H, q, $-CH_2$), 2.97 (2 H, s, $-SCH_2$), 4.10 (9 H, s, ferrocenyl), 10.16 (1 H, s, COOH)	1715	2570, 2680

[a] For acids Va, Vc and Vd, m.p., IR and ^1H NMR spectra were identical to those reported previously [11,12].

TABLE 3

PHYSICAL CONSTANTS OF THE 1-FERROCENYLALKYL ALCOHOLS $Fc(CR^1R^2)OH$ [a]

No.	R^1; R^2	m.p. (°C)	lit. m.p. (°C)	Yield (g (%)) [b]
IVa	H; H	80—82	81—82 [2]	(1.60) 74
IVb	H; n-Pr	oil	30—35 [3]	(1.75) 68
IVc	H; i-Pr	oil	56—58 [4]	(1.91) 74
IVd	H; Ph	81—82	81—82 [5]	(2.12) 73
IVe	Me; Me	56—58	56—58 [4]	(1.90) 78
IVf	Me; Et	oil	oil [6]	(1.63) 63

[a] The homogeneity and the identity with authentic samples were confirmed by TLC. [b] Based on ferrocene.

can be performed under reflux, but for the tertiary derivatives Ve and Vf the reaction takes place at room temperature (Table 1). Moreover, it was found by TLC that ferrocene condensed with cyclohexanone and 2-methylcyclohexanone, but not with (—)menthone or (+)camphor.

The method described above can be adapted for the preparation of 1-ferrocenylalkylamines or 1-ferrocenylalkyl ethers [13] by using aminolysis or alcoholysis of the *S*-(1-ferrocenylalkyl)thioglycolic acids.

Experimental

Condensation of ferrocene with carbonyl compounds

Sulfuric acid (7.3 cm³, 96%), cooled to —15°C, was added dropwise with stirring at 0°C to a mixture of finely powdered ferrocene and the appropriate carbonyl compound and the solution was stirred for the time indicated in Table 1. The red-brown oil obtained was added dropwise with stirring to 200 cm³ of water containing 35 g of sodium bicarbonate, and after the addition of a few crystals of sodium dithionite the colour of the solution changed from yellow-green to yellow. The mixture was extracted with ether, and the extract was washed with water and dried (Na_2SO_4), and the ether was evaporated off to give crude 1-ferrocenylalkyl alcohol.

Preparation of S-(1-ferrocenylalkyl)thioglycolic acids

The crude 1-ferrocenylalkyl alcohol obtained by the method described above was dissolved in acetone (10 cm³) and thioglycolic acid (0.7 cm³, 0.01 mol) was added. The mixture was cooled to 0°C, trifluoroacetic acid (0.1 cm³) was added with stirring, and the solution was set aside overnight at room temperature. The dark-red solution was transferred to a separating funnel and 30 cm³ of ether were added. After extraction with 5% NaOH the aqueous layer was carefully washed with ether. The aqueous solution was then acidified by stirring with a few drops of 85% H_3PO_4 until an oily residue separated. This was extracted with ether, and the extract was washed with water, dried (Na_2SO_4) and evaporated to give *S*-(1-ferrocenylalkyl)thioglycolic acid, which was then subjected to hydrolysis. Analytical samples were obtained by recrystallization from hexane/benzene (Table 2).

Hydrolysis of S-(1-ferrocenylalkyl)thioglycolic acids

S-(1-Ferrocenylalkyl)thioglycolic acid was dissolved in 240 cm^3 of the acetone water (3/1) mixture, 12 g of copper powder (POCh Gliwice, Poland, activated at 200°C for 6 h in air) was added, and the mixture was stirred or refluxed as indicated in Table 1. The precipitate was filtered off and washed with acetone. The acetone was evaporated off under reduced pressure and aqueous NaOH (5 cm^3, 5%) was added. Extraction with ether followed by drying (Na_2SO_4) and evaporation of the ethereal layer gave pure 1-ferrocenylalkyl alcohol (Table 3).

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