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SYNTHESIS OF SOME FERROCENE DERIVATIVES

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ABSTRACT

The article provides information on the production of ferrocene and its derivatives, their physical and chemical properties, and their practical importance. Also, the synthesis of the derivative of o-ferroceny lbenzoic acid with dimethylolthiourea - 1-(2-carboxyphenyl)-1'-N-(ferrocenylmethyl)-N'-methyloxycar -boxamide, its structure and chemical composition was given.

KEYWORDS

Ferrocene, cyclopentadienyl ring, aromaticity, ferrocenium ion, nitration, sulfation, organometallic compound, acetic anhydride, copper halides, aminobenzoic acids, biological activity, ferrocenyl nucleus, arylation, alkylation, acylation, elemental analysis.

Introduction

Since the discovery of ferrocene, many of its compounds have been synthesized by scientists and are used in various fields of the national economy. Researchers are interested in its unique properties. This article deals with the synthesis of some practically important compounds of ferrocene.

Ferrocene, a ground-breaking discovery in the realm of organometallic chemistry, has captivated researchers since its serendipitous identification in the 1950s. This molecule, featuring a unique "sandwich" structure composed of an iron atom nestled between two cyclopentadienyl anions, has been a focal point for exploring novel applications and expanding the frontiers of synthetic methodologies. The historical journey of ferrocene research began with the seminal contributions of Wilkinson and Fischer, who laid the groundwork for understanding its fundamental properties. Over the years, this exploration has evolved beyond the confines of ferrocene's intrinsic characteristics to encompass the vast landscape of its derivatives. These derivatives, marked by diverse structural motifs, have emerged as promising candidates for applications ranging from catalysis to medicinal chemistry.

In this context, our current study delves into the synthesis of specific ferrocene derivatives, aiming to contribute to the ongoing narrative of ferrocene chemistry. This article provides a comprehensive overview of the existing literature, examining various synthetic strategies, analysing reactivity patterns, and elucidating structure-property relationships. By amalgamating insights from historical perspectives and recent advancements, we strive to position our work within the broader context of ferrocene research and address pertinent questions in the field.

The subsequent sections will delve into a detailed literature review, where we explore the synthetic methods employed for ferrocene derivatives, analyze reactivity trends, investigate structural diversity, and assess the applications of these derivatives. Following this, the article will present our own synthesis approach, highlighting its novelty and potential contributions to the field.

Literature Review

Ferrocene, a landmark discovery in organometallic chemistry, has spurred extensive research into the synthesis and modification of its derivatives. The journey began with the groundbreaking work of researchers like Wilkinson and Fischer, who elucidated the fundamental properties of ferrocene. Early studies primarily focused on direct substitution reactions, laying the groundwork for subsequent developments. Over time, innovative synthetic strategies emerged, including organometallic transformations and transition metal-catalyzed processes. Notable researchers expanded the scope, exploring diverse functionalizations of the ferrocene core.

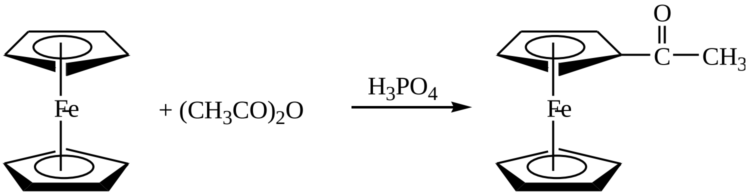
The reactivity of ferrocene derivatives has been a subject of keen interest, with mechanistic studies shedding light on reaction pathways. Challenges, such as regioselectivity and substrate specificity, have been addressed through meticulous synthetic methodologies. Structurally, ferrocene derivatives exhibit a wide range of diversity, influenced by substituents attached to the cyclopentadienyl rings. Electronic and steric effects play a crucial role, dictating the properties and potential applications of these derivatives. Applications of ferrocene derivatives span various fields, including catalysis, materials science, and medicinal chemistry. The unique properties of these compounds make them promising candidates for designing new materials and catalysts with tailored functionalities. Recent literature highlights advances in synthetic methodologies, providing efficient routes to specific ferrocene derivatives. However, gaps in understanding certain reaction mechanisms and the optimization of conditions persist, presenting avenues for future research.

This literature review sets the stage for the current study on the synthesis of specific ferrocene derivatives, aiming to contribute to the ongoing narrative of ferrocene chemistry. The subsequent sections will delve into the methodology, results, and implications of the synthesized derivatives.

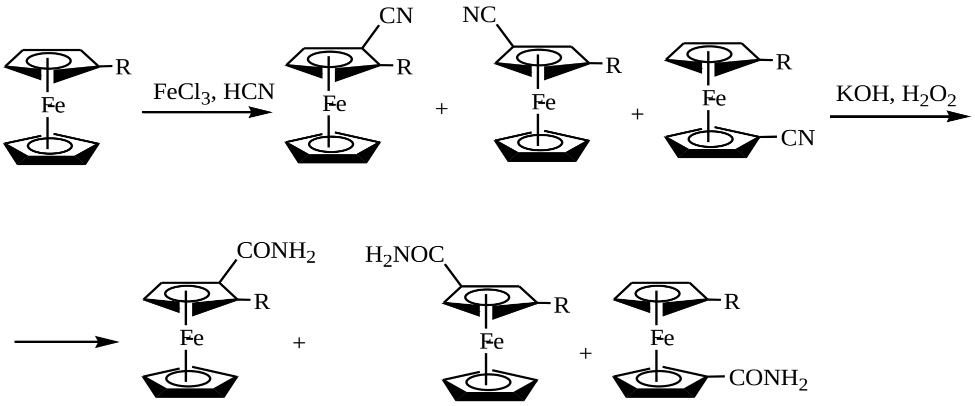
Materials and Methods

The stability of ferrocene in many chemical reactions indicates its aromatic nature. The first type of reaction of ferrocene is reaction with the exchange of hydrogen atoms in the cyclopentadienyl ring. Its aromatic properties are more pronounced than those of other aromatic compounds. The second type of reaction is accompanied by the change of the central metal ion. Reactions such as nitration, sulfonation, and direct halogenation typical of benzene occur in the presence of a ferrocene molecule. Ferrocene is oxidized by $FeCl_3$ in the presence of mineral acids (H_2SO_4 and HNO_3). In this case, a blue ferrocenium ion $(C_5H_5)_2Fe^+$ is formed in the solution. Reactions of the third type proceed with the breaking of the iron-carbon bond [1].

Since ferrocene is an organometallic compound that exhibits the properties of a non-benzoic aromatic compound with a unique structure and is chemically more active than benzene, various derivatives of it have been synthesized and are used in several fields [2]. For example, ferrocene is easily acylated by acetic anhydride. The reaction takes place in the presence of phosphoric acid [3]:

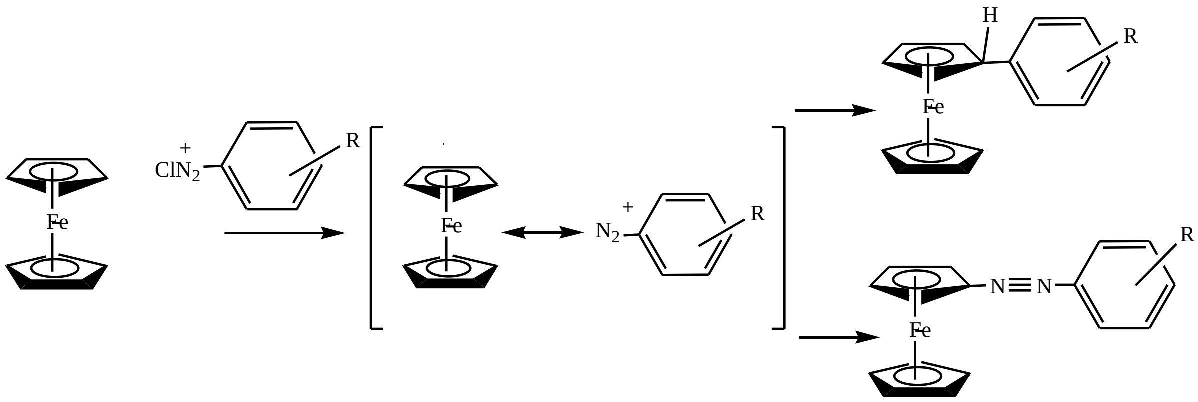


To synthesize β-Ferrocenylethanol, ferrocenylacetic acid is treated with lithium aluminium hydride ($LiAlH_4$) [4]. According to scientists' research, ferrocenylamine is easily oxidized by air oxygen in the presence of copper halides in a benzene solution [5]. Under the catalysis of iron (III) chloride, the substances obtained by the action of HCN on methyl- and ethyl ferrocene are treated with hydrogen peroxide in an alkaline environment, and amides are formed:



When phenyl ferrocene is reacted with cyanide acid under the catalysis of iron (III) chloride, first nitriles are formed, and then a mixture of amides is formed under the influence of H_2O_2 in an alkaline environment [6].

Ferrocene-based *o*-, *m*- and *p*-aminobenzoic acids were synthesized through diazotization reactions. Monoferrocenylbenzoic acids are mainly formed in these reactions. A small amount of hetero-annular diacids was also observed as a byproduct of the reaction. This reaction is mainly carried out in a weakly acidic environment, that is, acetic acid. It can also be carried out in acetone, water-ether and halogen hydrocarbon media [7]. Ferrocene areolation reaction with aminophenols was carried out in different environments [8]:



Alkylation of ferrocene under Friedel-Crafts reaction results in a mixture of mono- and polyalkyl ferrocenes. Haloalkyls, olefins, alcohols and carboxylic acids are used as alkylating agents, $AlCl_3$, BF_3, and H_3PO_4 as catalysts [9]. Mono-, *di-* and poly alkylated ethyl ferrocenes from ferrocene and ethyl bromide; *mono-*, *di-* and polysubstituted butyl ferrocenes from *n*-butyl chloride; synthesized diferrocenylethane and other compounds from dichloroethane. The lower alkyl ferrocenes are red liquids that evaporate without decomposition in a vacuum. Polyalkylferrocenes are dark red oily substances. For example, ethyl ferrocene is released without decomposition even when the reaction mixture is heated to boiling for 5 hours.

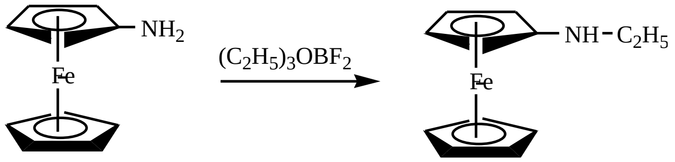
Ferrocene is oxidized to ferrocenium salts along with the alkylation process in the presence of $AlCl_3$ catalyst. This reduces the yield of alkyl ferrocene formation. Because ferrocenium salts are not alkylated. The addition of $LiAlH_4$ to the reaction mixture increases the reaction yield. Alkylation products of ferrocene are of preparative importance due to their difficult decomposition. In addition, ferrocene oxidation is not the only additional reaction, other additional reactions also occur during alkylation [10].

The interaction of ferrocene with 1,2-dichloroethane produces 1,1'-diferrocenylethane as the main product, with a small amount of 1,2-diferrocenylethane. The resulting β-ferrocenyl ethyl cation is isomerized to the more stable α-ferrocenyl ethyl cation. Further heating of ferrocene with aluminium chloride in heptane, benzene, dichloroethane or methylene chloride separates two ferrocenyl compounds and two or one cyclopentane group. It undergoes intramolecular alkylation with aluminium chloride.

Heating aluminium chloride with monoalkyl ferrocene or an equimolar mixture of 1,1'-dialkyl ferrocene and ferrocene produces a mixture of all three compounds [11].

Alkylation of ferrocene with ethyl bromide and tertbutyl chloride in the presence of an equimolar mixture of $AlCl_3$ and $LiAlH_4$ was shown in the works of Sorokin and Domrachev. In this case, the total yield of alkylation products is 80-90%. For example, when ferrocene is ethylated, its 35 alkyl homologues are formed. From monoalkylferrocene to decaalkyl-ferrocene, up to 50% of mono and diethylferrocene can be obtained under the influence of ethyl bromide [13].

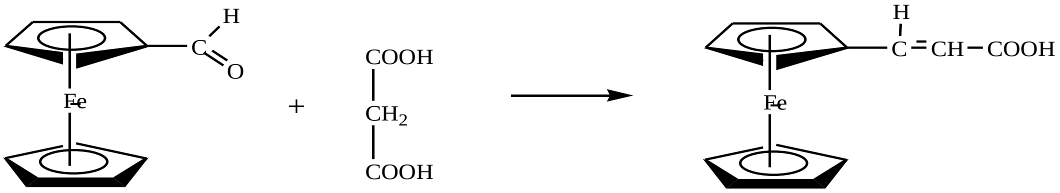
Ferrocenylamine, a derivative of ferrocene, is easily alkylated in the presence of triethyl oxonium borofluoride:



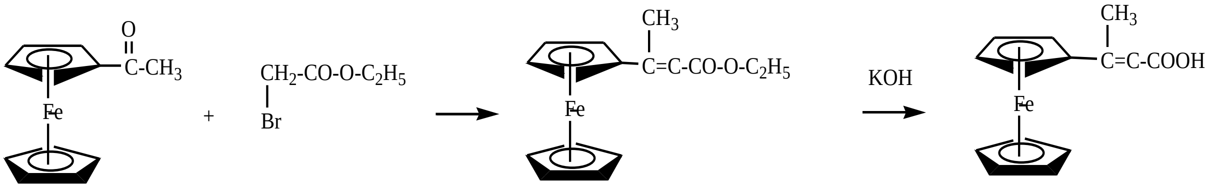
Ferrocenylamine is mixed with borofluoridetriethyloxonium in the cooled solution. The reaction mixture is treated with an alkali solution. The yield of the reaction is 77%. A solution of monoethylferrocenylamine oxalic acid in water decomposes under the influence of light to form iron oxalate [6].

Along with aryl ferrocenes, many aliphatic derivatives of ferrocene have been synthesized [14]. Ferrocenylacetic acid is obtained by hydrolyzing ferrocenacetonitrile in an alkaline environment [15]. Chloroanhydride was obtained from ferrocenylacetic acid under the influence of phosphorus (III) chloride [17].

Several unsaturated carboxylic acids of ferrocene have also been obtained, mainly using the condensation of formyl ferrocene and its derivatives and the Reformatsky reaction. When formyl ferrocene is heated in pyridine with malonic acid, β-ferrocenyl acrylic acid is formed:



The same acid was obtained by reacting formylferrocene with lithium tert-butylacetate [18]. According to the Reformatsky reaction, unsaturated acids were obtained from several carbonyl derivatives of ferrocene. Acetylferrocene was treated with ethyl bromoacetate in the presence of zinc and 3-ferrocenyl crotonic acid was obtained:



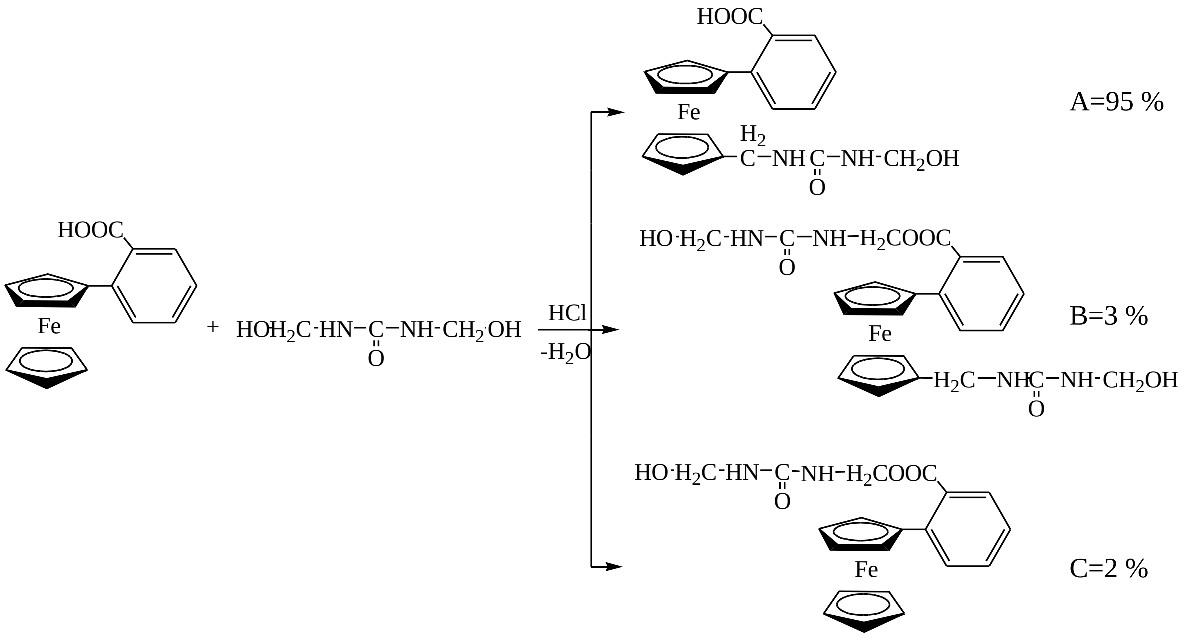
Halogens in halo ferrocenes are exchanged with other halogens in the presence of copper salts under mild conditions. Halogens in halo ferrocenes without copper salts are inert in nucleophilic exchange reactions [22; 1-160-p, 23; 63-73-b].

Synthesis of 1-(2-carboxyphenyl)-1'-N-(ferrocenylmethyl)-N'-methyloxycarboxamide. 6 g (0.05 mol) of dimethylolurea solution and 3.65 ml of concentrated hydrochloric acid were added to 3.06 g of o-ferrocenyl benzoic acid dissolved in 100 ml of diethyl ether. The yield of the obtained product is 2.04 g (50%). $T_{s.}$=161-162°C.

Gross formula: $C_{20}H_{20}O_4N_2Fe$.

Results and Discussion

The synthesis of 1-(2-carboxyphenyl)-1'-N-(ferrocenyl methyl)-N'-methyloxycarboxamide was carried out in an acidic environment according to the following reaction scheme:



The resulting products (A - (1-(2-carboxyphenyl)-1'-N-(ferrocenylmethyl)-N'-methyloxycarboxamide), B, C were isolated. Substance B was hydrolyzed in an alkaline medium, resulting in substance B from substance A - (1 A salt of -(2-carboxyphenyl)-1'-N-(ferrocenylmethyl)-N'-methyloxycarboxamide) was formed in 98% yield.

The wave number of peaks observed experimentally in the IR spectrum of 1-(2-carboxyphenyl)-1'-N-(ferrocenylmethyl)-N'-methyloxycarboxamide and the calculated values of the wave number of the absorption region maximum corresponding to the corresponding vibration of the molecule 1- given in the table.

Table 1. Theoretically calculated and experimentally obtained wavenumber values cm-1) in the IR spectrum of 1-(2-carboxyphenyl)-1'-N-(ferrocenylmethyl)-N'-methyloxycarboxamide.

No	Type of vibration	Absorption region maximum wave number, cm-1	
		Calculated	Received
1	$\delta_{s(C-H)(Cp)}$	596	592
2	$\nu_{as(C-H)(Cp)}$	848	848
3	$\delta_{s(C-H)(C6H4)}$	870	867
4	$\nu_{s(C-C)(Cp)}$	1016	1016
5	$\nu_{(>NH)}$	1419	1414
6	$\nu_{s(C-H)(C6H4)}$	1471	1450
7	$\nu_{s(>C=O)}$	1684	1686
8	$\nu_{as(O-H)}$	3460	3460

Analysis of the results is presented in Table 1. From the groups and bonds in the molecule of 1-(2-carboxyphenyl)-1'-N-(ferrocenylmethyl)-N'-methyloxycarboxamide, it can be seen that the CH bond of the C_p ring, the CH bond of the C_6H_4 ring.

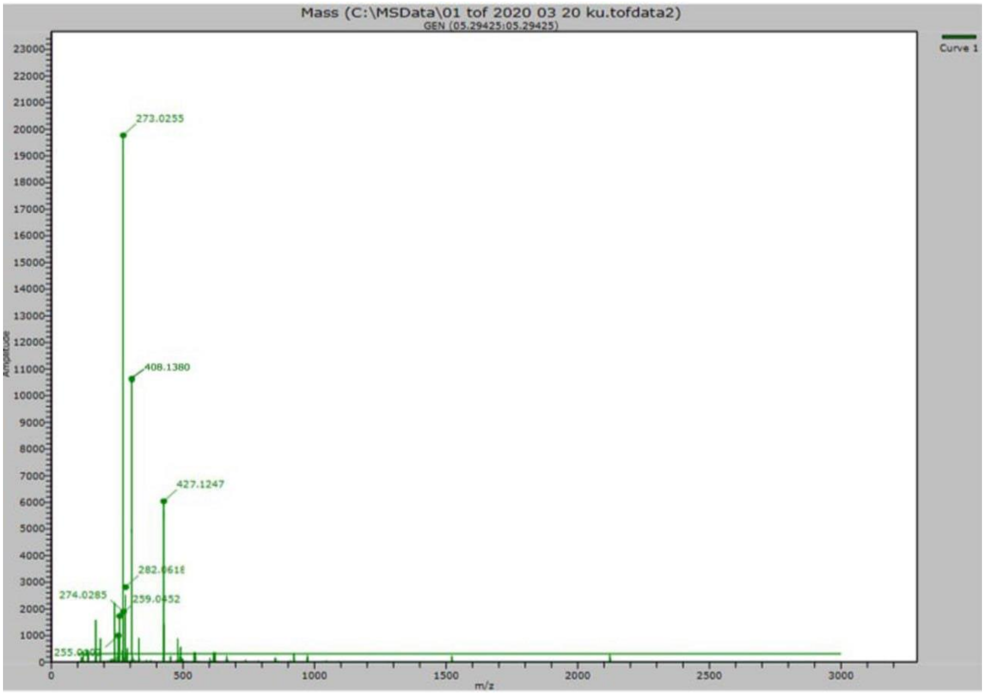


Figure 1. Mass spectrum of 1-(2-carboxyphenyl)-1'-N-ferrocenylamidemethanecarboxamide.

The theoretically obtained values of the deformation vibrations of ' are close to the experimentally obtained values, the coincidence of the valence vibrations of the CH bond and CC bonds of the C_p ring allows us to conclude about the individuality of the obtained substance.

Table 2. 1-(2-carboxyphenyl)-1'-N-(ferrocenyl methyl)-N'-methyloxycarboxamidemass spectrometric indicators

No	Ion	*m/z*	Relative intensity, %
1	[$OOCC_6H_4Fe$]	273	86±1
2	[$HOOCC_6H_4FcCH_2NHC(O)NHCH_2OH$]	408	46±1
3	[$HOOCC_6H_4HFcCH_2NHC(O)NHCH_2OH$]	427	26±1
4	[$HOOCC_6H_4Fe$]	274	8±1

The main peak in the mass spectrum of 1-(2-carboxyphenyl)-1'-N-(ferrocenylmethyl)-N'-methyloxycarboxamide was found to correspond to the molecular ions of the reaction products (Figure 1, Table 2).

It can be seen from Figure 1, Table 2 that the peak with an intensity of 46±1 % refers to the molecular ion of 1-(2-carboxyphenyl)-1'-N-(ferrocenyl methyl)-N'-methyloxycarboxamide ([$HOOCC_6H_4FcCH_2NHC(O)NHCH_2OH$]).

Conclusions

Iron is of particular importance in the vital activity of plants and animals. Iron accelerates the assimilation of nitrogen, phosphorus and potassium in plants. Lack of iron in plants leads to negative consequences, for example, the occurrence of chlorosis, which leads to a violation of the formation of chlorophyll in the leaves and a decrease in the activity of photosynthesis. Effective use of preparations containing iron, such as 1-(2-carboxyphenyl)-1'-N-(ferrocenylmethyl)-N'-methyloxycarboxamide, allows for to prevention of diseases in plants and is widely used in agriculture as stimulators that increase the productivity of crops.

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