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Note

Two convenient new syntheses of ferrocenoyl chloride by triphosgene

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Abstract

Two convenient new syntheses of ferrocenoyl chloride by triphosgene were reported. Firstly, ferrocenoyl chloride was conveniently prepared in 61.5% yield when triphosgene was reacted with ferrocene carboxylic acid in methylene dichloride at room temperature in the presence of triethylamine and DMAP. This new method for the synthesis of ferrocenoyl chloride enjoys a number of advantages in that the reaction is carried out under mild conditions and is cleaner without the formation of $POCl_3$, H_3PO_3 or SO_2 and dark-colored impurities. Secondly, ferrocene underwent reaction with one-third equivalent of triphosgene to give ferrocenoyl chloride in 38.1% yield. The main advantage of the second method for the synthesis of ferrocenoyl chloride is using cheap ferrocene as starting material.

Keywords: Ferrocenoyl chloride; Triphosgene; Ferrocene; Ferrocene carboxylic acid

1. Introduction

Ferrocenoyl chloride is an important synthetic intermediate, and its derivatives exhibit antitumor [1a] and insecticidal activities [1b]. For example, ferrocenoyl acylhydrazines have excellent insecticidal activities against insects of the orders Lepidoptera and Coleoptera. Furthermore, ferrocenyl moiety is recently incorporated into supramolecular arrays and sening devices [2]. Ferrocenoyl chloride has been prepared by the reaction of ferrocene carboxylic acid with a suitable chlorinating agent such as phosphorus pentachloride [3,4], phosphorus trichloride [5], and oxalyl chloride [6]. However, these procedures give dark-colored impurities and provide low yields. Therefore, there exists a need for new and mild synthetic method to the compound. In a search for potentially biological active materials containing the ferrocenyl moiety, the present methods for the synthesis of ferrocenoyl chloride are developed. Herein we report the two new syntheses of ferrocenoyl chloride using triphosgene (bis(trichloromethyl)-carbonate).

2. Results and discussion

The syntheses of thiazolecarbonyl chlorides and *m*-toluyl chloride by triphosgene in the presence or absence of DMF have been reported [7]. When this method was applied to ferrocene carboxylic acid in nitrogen atmosphere, no reaction could be observed. We have found that ferrocenoyl chloride (**3**) was conveniently prepared in 61.5% yield when triphosgene (**2**) was reacted with ferrocene carboxylic acid (**1**) in methylene dichloride at room temperature (r.t.) in the presence of triethylamine and DMAP (Scheme 1). The triphosgene-mediated reaction for the synthesis of ferrocenoyl chloride outlined here enjoys a number of advantages over the existing methods, in that the reaction is carried out under mild conditions and is cleaner without the formation of $POCl_3$, H_3PO_3 or SO_2 and dark-colored impurities.

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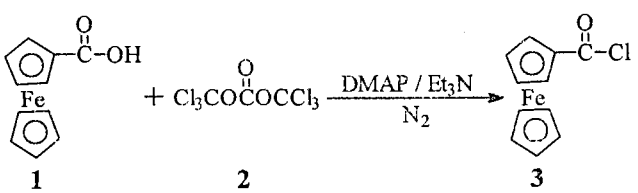
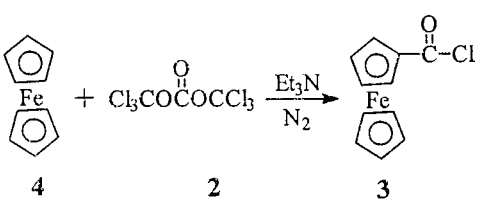
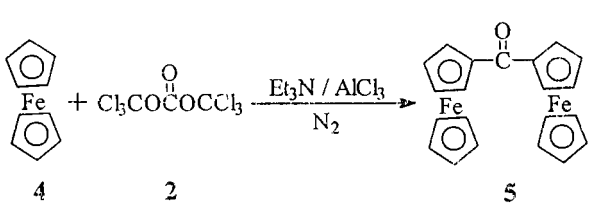
The α carbon in the pyrrole ring can act as a nucleophile with triphosgene and β-amino propionic esters or nitriles to form intermediary pyrrole-2-carboxamides [8]. Encouraged by the work, we developed the idea that the carbon in ferrocene with high partial electron density can also act as a nucleophile with triphosgene to form a C–C bond. As shown in Scheme 2, ferrocene (**4**) underwent reaction with one-third equivalent of triphosgene (**2**) to give ferrocenoyl chloride (**3**) in 38.1% yield. The solvents of choice in our hands have been 1,2-dichloroethane, methylene dichloride, or chloroform, but in principle, other solvents should be equally useful. Other organic bases may substitute for triethylamine in this reaction; however, we decided in favor of triethylamine because of the ease of isolation of its hydrochloride salt from organic solvents; triethylammonium hydrochloride precipitates completely from most organic solvents. When using more than a 1:3 molar ratio of triphosgene to ferrocene only the ferrocenoyl chloride (**3**) was obtained, and difunctional ferrocenyl dicarboxychlorides were not observed. The difficulty of introducing a second chlorocarbonyl group into the ferrocene nucleus is interpreted in terms of deactivation of the nucleus by the first chlorocarbonyl group introduced. This route avoids the use of ferrocene carboxylic acid, which has been prepared by multi-step process [9]. In conclusion, we developed the second efficient new method for the synthesis ferrocenoyl chloride using cheap ferrocene as the starting material. Moreover, the experimental procedure is very simple.



Scheme 1.



Scheme 2.



Scheme 3.

In the presence of anhydrous aluminium chloride, the resulting ferrocenoyl chloride was reacted with ferrocene to give diferrocenyl ketone (**5**) in 50.6% yield (Scheme 3).

3. Experimental

3.1. Instruments

All reactions were carried out under a nitrogen atmosphere. Proton NMR spectra were obtained at 200 MHz using a Bruker AC-P 200 spectrometer. Chemical shift values (δ) are given in ppm. IR spectra were recorded on a Shimadu-435 spectrometer. Elemental analyses were determined on an MT-3 elemental analyzer. Melting points were taken on a Thomas–Hoover melting-point apparatus and are uncorrected.

3.2. Synthesis

Triphosgene was prepared from dimethyl carbonate and chlorine gas according to a reported procedure [10], melted at 79°C. Ferrocene carboxylic acid was prepared according to previous reports [9].

3.2.1. Ferrocenoyl chloride (*3*)

Method I. Under a nitrogen atmosphere, to the stirred solution of triphosgene (0.89 g, 3.29 mmol) in methylene dichloride (30 ml), was added dropwise a solution of ferrocene carboxylic acid (0.72 g, 3.13 mmol), distilled triethylamine (3.29 mmol), and DMAP (0.20 g, 1.65 mmol) in methylene dichloride (10 ml) at 0°C. Then the resulting mixture was stirred at 0°C for 1 h, followed by a further 11 h of stirring at r.t. The solution was filtered and the filtrate was evaporated in vacuo to dryness. Trituration with hot hexane precipitated unreacted triphosgene; the mixture was filtered, and the filtrate was concentrated under reduced pressure, and the resulting residue was crystallized from hexane to give a red crystalline solid (0.48 g, 61.5%), m.p. 49–51°C (literature reference [4], m.p. = 49°C); ^{1}H-NMR ($CDCl_3$): δ 4.32 (s, 5H, C_5H_5), 4.63 (s, 2H, C_5H_4), 4.91 (s, 2H, C_5H_4).

Method II. A solution of ferrocene (1.0 g, 5.4 mmol) and distilled triethylamine (0.61 g, 6 mmol) in 1,2-dichloroethane (15 ml) was stirred in an ice bath (nitrogen atmosphere). A solution of triphosgene (0.59 g, 2 mmol) in 1,2-dichloroethane (5 ml) was added dropwise. Then the resulting mixture was stirred in the ice bath for 2 h, and subsequently stirred for a further 12 h at r.t. The solid was filtered and the filtrate was evaporated in vacuo to dryness. The residue was tritu-

rated with hot hexane and filtered. The filtrate was concentrated under reduced pressure, and the resulting residue was crystallized from hexane to give a red crystalline solid (0.51 g, 38.1%), m.p. 49–51°C (literature reference [4], m.p. = 49°C); ^{1}H-NMR ($CDCl_3$): δ 4.32 (s, 5H, C_5H_5), 4.63 (s, 2H, C_5H_4), 4.91 (s, 2H, C_5H_4).

3.2.2. Diferrocenyl ketone (5)

Under a nitrogen atmosphere, to the magnetically stirred and cooled (− 15°C) mixture of ferrocene (1.5 g, 8.06 mmol), anhydrous aluminium chloride (1.07 g, 8.06 mmol) and methylene dichloride (30 ml) were added dropwise a solution of triphosgene (0.4 g, 1.61 mmol) in methylene dichloride (10 ml) and distilled triethylamine (0.49 g, 4.83 mmol) simultaneously from separate addition funnels. Stirring was continued for 2 h at − 15°C and 6 h at r.t. The reaction mixture was then poured into ice-water, and the aqueous phase was extracted with three 10 ml portions of methylene dichloride. The combined methylene dichloride extracts were washed with water, and then dried over magnesium sulfate. The extract was concentrated and chromatographed on a silica gel column. Elution with petroleum ether removed unreacted ferrocene. Elution with ethyl acetate and petroleum ether collected a red band, which gave the desired product. Recrystallization from isopropanol gave an analytical sample as red–violet needles (0.81 g, 50.6%); m.p. 203–204°C (literature reference [4c,11], m.p. = 204°C); IR (KBr) 3113.5, 1607.1, 1462.4, 1382.4, 1291.6, 1102.0, 1059.6, 804.6, 490.3 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 4.23 (s, 5H, C_5H_5), 4.54 (s, 2H, C_5H_4), 5.02 (s, 2H, C_5H_4). Anal. Calc. for $C_{21}H_{18}OFe_2$: C, 63.36; H, 4.56. Found: C, 63.16; H, 4.28%.

Acknowledgements

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