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Note

Ferrocene derivatives (II). Synthesis and reactions of 4-ferrocenyl-2-thiazolamine

Huairang Ma *, Yihua Hou, Yinjuan Bai, Jun Lu, Bingqin Yang

Department of Chemistry, Northwest University, Xi'an, 710069, China

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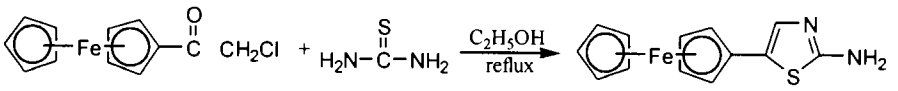
Abstract

4-Ferrocenyl-2-thiazolamine (**1**) was prepared by the reaction of chloroacetylferrocene with thiourea. The thiazolimines **2**–**5** were synthesized by the condensations of the amine with aromatic aldehydes. The reaction of imine **2** with thioglycollic acid produced thiazolidone **6**. All products were characterized by elemental analysis, IR and ^{1}H-NMR spectra.

Keywords: Synthesis; 4-Ferrocenyl-2-thiazolamine; Thiazolimines; Thiazolidone

1. Introduction

The thiazole ring is very important in nature. It occurs, for example, in thiamine, a coenzyme required for the oxidative decarboxylation of α-keto acids. A tetrahydrothiazole also appears in the skeleton of penicillin which is one of the first and still most important of the broad-spectrum antibiotics. Thiazolamines are key intermediates for synthesizing many pharmaceuticals [1]. Some thiazolidones are valuable medicines [2,3]. It is obvious that compounds with the thiazole ring have potential biological activity. We also know that some Schiff bases are effective antitumor drugs and antibacterials [4,5]. The search for biologically active ferrocene derivatives has attracted considerable attention [6,7]. Recently, Zakaria and Chohan reported, respectively, antimicrobial and antibacterial ferrocene derivatives [8,9]. We synthesized and characterized a series of ferrocene derivatives with strong biological activity [10,11]. In order to continue our research project, we prepared another type of ferrocene derivative which contained both the thiazole ring and Schiff base structures. For this purpose, 4-ferrocenyl-2-thiazolamine (**1**) has been prepared. The amine easily condenses with aromatic aldehydes to give the following imines **2**–**5**. The imine **2** cyclizes with thioglycollic acid to produce the thiazolidone **6**.



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* Corresponding author. Fax: +86-29-830-3511.
E-mail address: lujunyue@hotmail.com (H. Ma).

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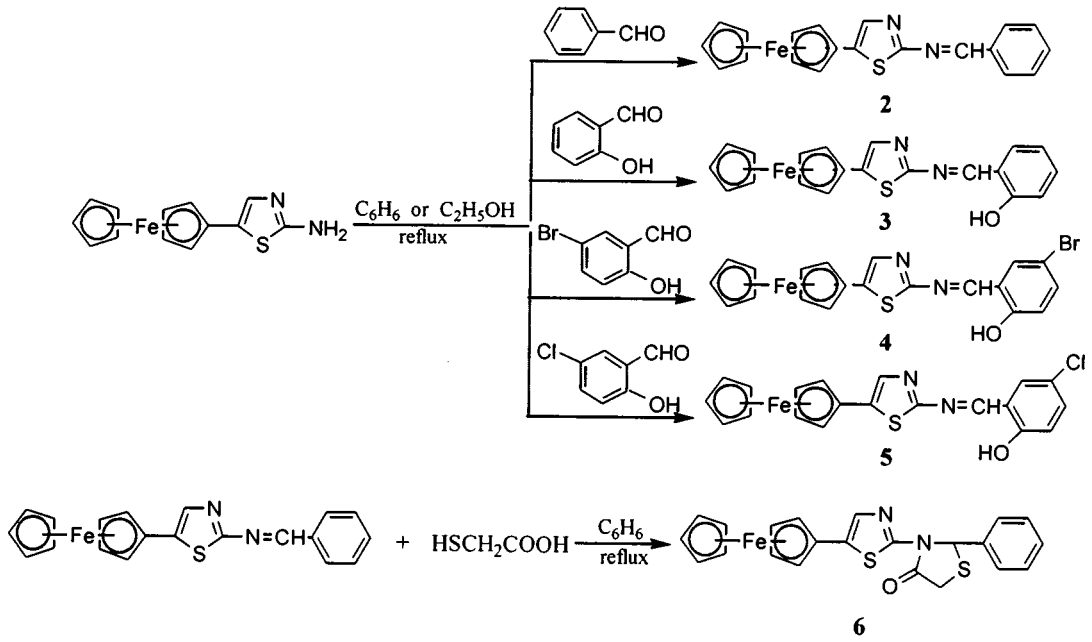

2. Experimental

^{1}H-NMR spectra were recorded on an AM-300 MHz spectrometer with TMS as an internal standard. IR spectra were obtained using KBr pellets on a Bruker Equinox-55 instrument. Elemental analysis was performed using a PE-2000 analyzer.

2.1. Complex *1*

The chloroacetyl ferrocene 0.97 g (3.7 mmol) prepared according to the literature [12] and thiourea 0.40 g (5.3 mmol) were dissolved in 10 ml of warm EtOH. The mixture was refluxed for 1.5 h and then poured into 80 ml of ammonia spirit. The yellow crystals that formed were filtered and dried. After recrystallization from the solvent of a mixture of benzene and petroleum ether, 1.01 g of amine **1** was obtained. ^{1}H-NMR (Me_2CO-d_6, δ ppm): $\delta = 6.45$ (s, 1H), 4.65 (s, 2H), 4.20 (s, 2H), 4.04 (s, 5H), 2.61 (s, 2H). IR ν (cm^{-1}): 3490, 3100, 1640. Anal. Calc. for $C_{13}H_{12}FeN_2S$: C, 54.95; H, 4.26; N, 9.86. Found: C, 55.03; H, 4.49; N, 9.70%. Yield 96%. M.p. 190–192 °C.

2.2. Complexes *2*–*5*

The amine **1** 0.57 g (2 mmol) and corresponding aldehyde (2 mmol) were dissolved in 15 ml of benzene (ethanol for imine **3**). One drop of piperidine was added to the mixture solution. The solution was heated and refluxed in a 50 ml flask equipped with a Dean–Stark trap condenser until no water appeared (ca. 1 h). After the reaction solution was concentrated and allowed to stand overnight at room temperature, the red solid that formed was filtered out. Imine **2** was purified on an aluminum oxide column with a mixture of diethyl ether–petroleum ether (volume ratio: 1:3) as eluent. Imines **3** and **4** were recrystallized from EtOH and imine **5** from a mixture of benzene and petroleum ether.

2.2.1. Complex *2*

^{1}H-NMR ($CDCl_3$, δ ppm): $\delta = 8.98$ (s, 1H), 8.05–6.98 (m, 6H), 4.81 (s, 2H), 4.31 (s, 2H), 4.10 (s, 5H). IR ν (cm^{-1}): 3100, 3050, 1600. Anal. Calc. for $C_{20}H_{16}FeN_2S$: C, 64.53; H, 4.33; N, 7.53%. Found: C, 64.87; H, 4.47; N, 7.51%. Yield 30%. M.p. 105–106 °C.

2.2.2. Complex *3*

^{1}H-NMR ($CDCl_3$, δ ppm): $\delta = 12.31$ (s, 1H), 9.22(s, 1H), 7.54–6.88 (m, 5H), 4.77 (s, 2H), 4.31 (s, 2H), 4.09 (s, 5H). IR ν (cm^{-1}): 3370, 3100, 1605. Anal. Calc. for $C_{20}H_{16}FeN_2OS$: C, 60.59; H, 3.87; N, 6.73%. Found: C, 59.92; H, 4.24; N, 6.95%. Yield 45%. M.p. 164–165 °C.

2.2.3. Complex *4*

^{1}H-NMR ($CDCl_3$, δ ppm): $\delta = 12.30$ (s, 1H), 9.18 (s, 1H), 7.65–6.88 (m, 4H), 4.76 (s, 2H), 4.32 (s, 2H), 4.09 (s, 5H). IR ν (cm^{-1}): 3450, 3100, 1605. Anal. Calc. for $C_{20}H_{15}BrFeN_2OS$: C, 51.42; H, 3.23; N, 5.99%. Found: C, 51.58; H, 3.50; N, 5.74%. Yield 33%. M.p. 159–160 °C.

2.2.4. Complex *5*

^{1}H-NMR ($CDCl_3$, δ ppm): $\delta = 13.11$ (s, 1H), 9.23 (s, 1H), 7.50–7.09 (m, 3H), 4.77 (s, 2H), 4.34 (s, 2H), 4.10 (s, 5H). IR ν (cm^{-1}): 3450, 3100, 1595. Anal. Calc. for $C_{20}H_{14}Cl_2FeN_2OS$: C, 52.54; H, 2.58; N, 6.13%. Found: C, 52.76; H, 2.75; N, 5.92%. Yield 44%. M.p. 169–171 °C.

2.3. Complex 6

The imine **2** (745 mg, 2 mmol), 313 mg (3 mmol) of thioglycollic acid, and 15 ml of benzene were placed in a flask equipped with a Dean–Stark trap condenser. After the mixture solution was refluxed for 4 h, the solvent was removed under reduced pressure. The residue glue was ground together with a saturated aqueous solution of sodium bicarbonate. The formed powder was filtered and washed with water. This crude product **6** was recrystallized from EtOH to obtain orange crystals. ^{1}H-NMR (DMSO-d_6, δ ppm): $\delta = 7.50$ (m, 5H), 7.14 (s, 1H), 6.79 (s, 1H), 4.60 (s, 2H), 4.32 (s, 2H), 4.23 (s, 1H), 4.09 (s, 1H), 3.71(s, 5H). IR ν (cm^{-1}): 3100, 1695, 1560. Anal. Calc. for $C_{22}H_{18}FeN_2OS_2$: C, 59.20; H, 4.06; N, 6.28%. Found: C, 58.83; H, 4.34; N, 6.05%. Yield 60%. M.p. 185–187 °C.

3. Results and discussion

Chloroacetyl ferrocene and ferrocenylthiazolamine cannot be synthesized by any reagents having oxidizing properties, because the ferrocenyl group is easily oxidized. Chloroacetylferrocene was prepared by the reaction of ferrocene with chloroacetyl chloride, with aluminum chloride as catalyst. The yield was only 20%. Several methods for the synthesis of 2-thiazolamine have been reported [13–17]. We first prepared 4-ferrocenyl-2-thiazolamine with Hantzsch's method [18]; the yield was 96%. When the amine condensed with aromatic aldehydes, the yields of imines were lower than those of unsubstituted 2-thiazolamine. The ferrocenyl group has not only an electronic, but also a steric effect. The imine **2** cyclized with thioglycollic acid smoothly to give thiazolidone under the present synthetic conditions. This is consistent with the reported literature [19].

All products were characterized by IR, ^{1}H-NMR and elemental analysis. The spectroscopic data of the prepared complexes are found to be identical with expected structures. In the ^{1}H-NMR spectra of all products, the four protons of the substituted cyclopentadienyl ring form an AA′BB′ system, while the hydrogen atoms of the other Cp moiety appear as a sharp singlet. In the IR spectra of imines **2**–**5**, the strong absorption bands in the 1595–1610 cm^{-1} region correspond to the C=N stretching vibrations, but not absorptions of the C=N in the thiazole ring, because they are very weak.

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