

Communication

New Preparation of Ferrocene Carboxylic Acid Benzotriazol-1-yl Ester

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Abstract: Ferrocene and its derivatives are very useful in the fields of chemistry, biomedicine and materials. Herein, a ferrocene derivative was synthesized in one step from benzotriazol-1-yl-oxytripyrrolidino-phosphonium hexafluorophosphate and ferrocenecarboxylic acid. Its accurate structure was determined by ¹H and ¹³C NMR and further confirmed by X-ray diffraction analysis of the corresponding single crystal.

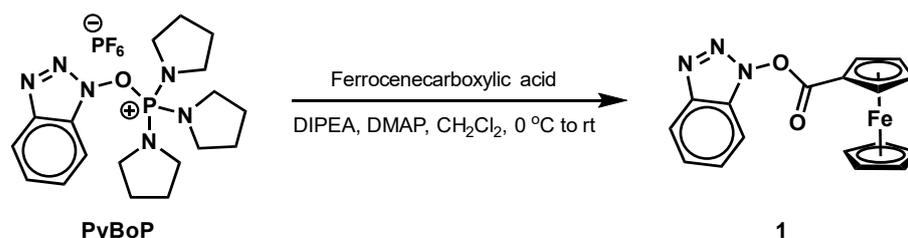
Keywords: ferrocene; synthesis; single crystal

1. Introduction

In the 1950s, iron bis-cyclopentadienyl was first synthesized [1,2], and this unique compound received much attention in the world [3–5]. The initially proposed structure was reassigned as a sandwich-like model by Woodward and co-workers [6], and later confirmed by the X-ray diffraction of its crystal [7–9]. Since the discovery of this unique complex called ferrocene [10,11], new advances in the synthesis of analogs and their properties' studies [12,13] were achieved. No doubt, ferrocene opened up an era of organometallic chemistry and continues to play an important role in many fields, such as asymmetric catalysis [14] and ATP bioconjugates [15] up until now.

2. Results and Discussion

In connection with our continuous research on the synthesis of natural products [16–22] and fluorescent probes [23–27], a ferrocene derivative (**1**, Scheme 1) was obtained serendipitously. When benzotriazol-1-yl-oxytripyrrolidino-phosphonium hexafluorophosphate (PyBoP) was added to a mixture of ferrocenecarboxylic acid [28], *N,N*-diisopropylethyl amine (DIPEA) and 4-dimethylamino pyridine (DMAP) in CH₂Cl₂, compound **1** was formed as an orange solid. This compound had been previously obtained through a different condition [29].



Scheme 1. Preparation of ferrocene derivative **1**.

As shown in Table 1, the reaction could be optimized, and the yield of compound **1** was thus eventually raised to 65%. The extension of the reaction time did not lead to a



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yield increase (entry 1 vs. 2). While a lower yield of **1** was obtained in the diluted solution (entry 3), an excess of PyBoP resulted in more generation of **1** (entry 4). The omission of DMAP even led to a further increase in **1** (entry 5). However, the excess either of DIEPA or DMAP provided inferior results (entries 6 and 7). The replacement of DMAP with 4-pyrrolidinopyridine (PPY) produced a similar result (entries 2, 4 vs. 8). Pleasingly, the addition of 1.5 equivalent of PyBoP can lead to a significant increase in **1** even with the decreased amount of DIEPA and PPY (entry 9).

Table 1. Optimization of reaction.

Entry ^a	PyBoP (equiv.)	DIPEA (equiv.)	DMAP (equiv.)	PPY (equiv.)	1 Yield ^b
1 ^c	1.0	1.8	0.6	/	23%
2	1.0	1.8	0.6	/	25%
3 ^d	1.0	1.8	0.6	/	14%
4	1.5	1.8	0.6	/	30%
5	1.5	1.8	/	/	42%
6	1.0	3.6	0.6	/	9%
7	1.0	1.8	1.5	/	6%
8	1.0	1.8	/	0.6	35%
9	1.5	0.9	/	0.2	52%

^a To a solution of PyBoP and DIPEA in CH₂Cl₂ (4 mL), ferrocenecarboxylic acid (1 mmol) and DMAP or PPY were added at 0 °C, then stirred at 22 °C for 10 h. ^b Isolated yield is shown. ^c Stirred at 14 °C for 28 h. ^d CH₂Cl₂ (10 mL).

Its molecular structure was determined by single crystal X-ray diffraction [30]. As shown in Figure 1, two cyclopentadienyl groups were coordinated with an iron atom, which formed a pentagonal prism. The distances of ten Fe–C bonds were from 2.020 to 2.056 Å and the C–C distances of two cyclopentadienyl groups were from 1.384 to 1.428 Å, which were similar to the reported values. The dihedral angle between the C8/C9/C10/C11/C12 and C13/C14/C15/C16/C17 planes was 2.70°, which indicated two cyclopentadienyl groups almost parallel to each other. The dihedral angle between the C1/C2/C3/C4/C5/C6/N1/N2/N3 and C8/C9/C10/C11/C12 planes was 86.48°, which indicated the benzotriazole group and cyclopentadienyl group were almost vertical to each other.

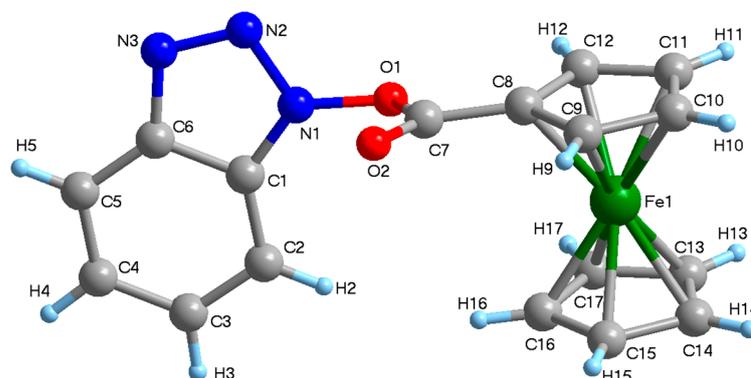


Figure 1. X-ray crystal structure of ferrocene derivative **1**.

3. Materials and Methods

For product purification by flash column chromatography, silica gel (200–300 mesh) and petroleum ether (bp. 60–90 °C) were used. All solvents were purified and dried using standard techniques and distilled prior to use. The following chemicals were purchased and used as received. All of the experiments were conducted under an argon or nitrogen

atmosphere in oven-dried or flame-dried glassware with magnetic stirring, unless otherwise specified. Organic extracts were dried over Na_2SO_4 , unless otherwise noted. ^1H and ^{13}C NMR spectra were taken on a Bruker AM-400 with TMS as an internal standard and CDCl_3 as solvent unless otherwise noted. The X-ray diffraction studies were carried out on a Bruker SMART Apex CCD area detector diffractometer equipped with a graphite-monochromated Cu-K α radiation source (see Supplementary Materials).

To a mixture of ferrocenecarboxylic acid (230 mg, 1.0 mmol), DIPEA (0.15 mL, 0.9 mmol, 0.9 equiv.) and PPY (30 mg, 0.2 mmol, 0.2 equiv.) in anhydrous CH_2Cl_2 (4 mL), PyBoP (520 mg, 1.0 mmol, 1.0 equiv.) was added at 0 °C. The temperature was then raised to room temperature, and the resulting mixture was stirred for 10 h. The reaction mixture was cooled down to 0 °C and quenched with saturated NH_4Cl (5 mL). The aqueous layer was extracted with CH_2Cl_2 (3×5 mL). The combined organic phase was dried over Na_2SO_4 and then concentrated under reduced pressure to produce a crude product, which was purified by flash column chromatography (petroleum ether/EtOAc = 8:1 \rightarrow petroleum ether/EtOAc = 4:1) on silica gel to produce **1** as an orange solid (180 mg, 52% yield). ^1H NMR (400 MHz, CDCl_3): δ = 8.10 (d, J = 8.4 Hz, 1H), 7.56 (t, J = 8.0 Hz, 1H), 7.49–7.42 (m, 2H), 5.10 (t, J = 2.0 Hz, 2H), 4.70 (t, J = 2.0 Hz, 2H), 4.45 (s, 5H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 168.3, 143.6, 128.9, 128.6, 124.7, 120.5, 108.4, 73.5 (2C), 71.0 (2C), 70.9 (5C), 63.8 ppm.

This product was dissolved in EtOAc (0.25 mL), CH_2Cl_2 (0.25 mL) and hexane (0.5 mL). After 4 days, single crystals were obtained by slow evaporation of the solvent at room temperature.

Supplementary Materials: The following are available online: Copies of ^1H , ^{13}C NMR spectra and the cif file of **1**.

Author Contributions: Y.P. conceived and designed the experiments; L.-J.X. and L.-Y.Z. performed the experiments; L.-Y.Z., L.-J.X., Y.-W.W. and Y.P. analyzed the data; Y.-W.W. and Y.P. wrote the paper. All authors have read and agreed to the published version of the manuscript.

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Sample Availability: Samples of the compounds are not available from the authors.

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30. CCDC-2225030 (1) contain the supplementary crystallographic data for this paper. This data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: + 44 1223 336033.

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