

Reaction of ferrocene carboxylic acid with dicyclohexylcarbodiimide[†]

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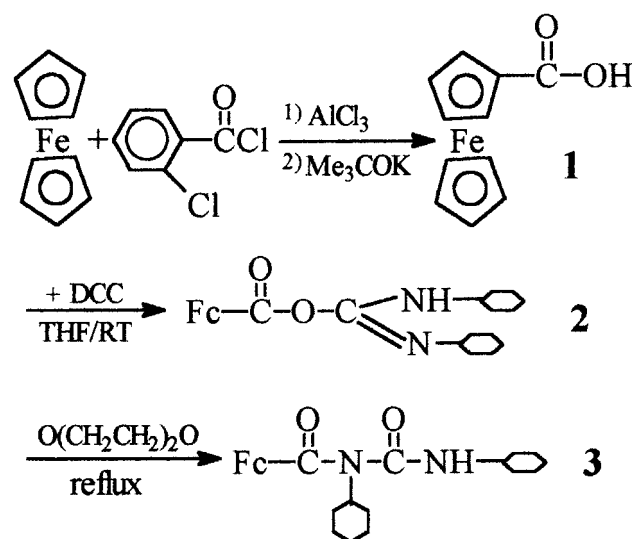
Ferrocene carboxylic acid was reacted with DCC in tetrahydrofuran at room temperature to give N,N'-dicyclohexyl-O-ferrocenoylisourea, which can be converted to N,N'-dicyclohexyl-N-ferrocenoylurea in dioxane at reflux temperature.

Keywords: ferrocene carboxylic acid, dicyclohexylcarbodiimide

In recent years, considerable interest has been devoted to the creation of ferrocene-based bioactive compounds,¹ catalysts, sensors and devices.² A commonly used intermediate in the synthesis of these systems is ferrocenoyl chloride. Formation of this acid chloride from the corresponding acid is capricious and can often result in low yields.³ Hence, it would be useful to synthesise ferrocenyl esters and amides directly from ferrocenecarboxylic acids by using N,N'-dicyclohexylcarbodiimide (DCC) as dehydrating agent. The reactions of other common carboxylic acid with DCC have been studied before including the mechanistic aspects.⁴ However, When ferroceneboxylic acid reacts with DCC, the result is different. Herein we have studied reaction of ferrocene carboxylic acid with DCC.

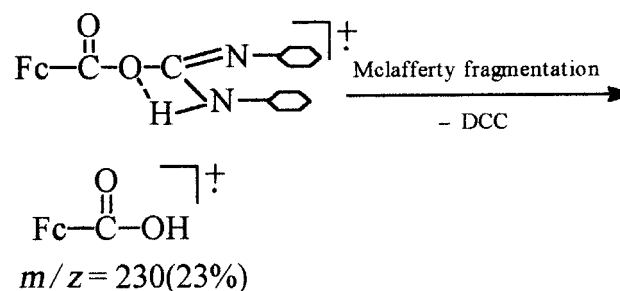
It had been reported that the reaction of ferrocene carboxylic acid with DCC gave N,N'-dicyclohexyl-N-ferrocenoylurea (**3**).^{3a} We have found that this result is incorrect. Furthermore, and its molting point (161°C) is also incorrect, and its molecular formula should be C₂₄H₃₂O₂N₂Fe instead of C₂₄H₃₁O₂N₂Fe.

There has been another report that an attempt to prepare N-2-thiazolylferrocenecarboxamide directly from ferrocenecarboxylic acid and 2-aminothiazole by treatment with DCC in chloroform resulted in the formation of 1-ferrocenylcarbonyl-1,3-dicyclohexylurea (**3**) and a small amount of ferrocenecarboxylic anhydride.⁵ We demonstrated that this result is also incorrect.



Scheme 1

Reaction of ferrocene carboxylic acid with DCC under the reported conditions afforded N,N'-dicyclohexyl-O-ferrocenoylisourea (**2**) (as shown in Scheme 1) rather than N,N'-dicyclohexyl-N-ferrocenoylurea (**3**) as reported.^{3a,5} The carbonyl absorption band at 1699.5 cm⁻¹ (vs) and C=N absorption band at 1596.5 cm⁻¹ (vs) in the infrared spectrum of **2** fell in the range expected.^{4,6} At the same time, it was noted that 1270.2 cm⁻¹ (s) and 1241.8 cm⁻¹ (s) corresponds to the C-O stretching absorption bands in compound **2**. These results are in full agreement with our previous work.⁷ The most interesting feature of the EI fragmentation of the compound **2** is the formation of ferrocene carboxylic acid ion (*m/z* 230) in considerable abundance. The formation of the ion can only be explained by McLafferty rearrangement process as shown in Scheme 2.



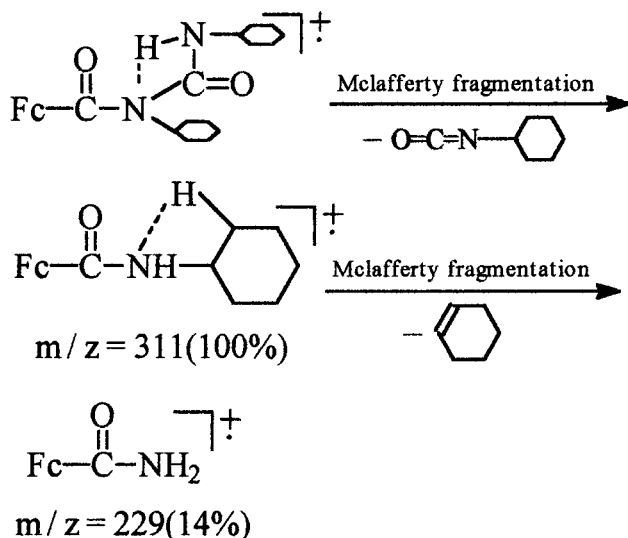
Scheme 2

According to the literature,⁴ acylisoureas are good acylating agents. However, our attempts to prepare N-*t*-butyl-N'-ferrocenoyl-N-benzoylhydrazine as a new class of insect growth regulator⁸ from N,N'-dicyclohexyl-O-ferrocenoylisourea (**2**) and N-*t*-butyl-N-benzoylhydrazine were unsuccessful. It is interesting to note that the compound **2** does not react with primary or secondary amines or hydrazine. In fact, N,N'-dicyclohexyl-O-ferrocenoylisourea is not as reactive as other N,N'-dicyclohexyl-O-acylisoureas, and cannot be transformed into N,N'-dicyclohexyl-N-ferrocenoylurea in THF at reflux temperature. This is probably due to the effects of steric hindrance and the conjugative effect of ferrocene group with carbonyl.

N,N'-dicyclohexyl-O-ferrocenoylisourea (**2**) can be converted to N,N'-dicyclohexyl-N-ferrocenoylurea (**3**) in dioxane at reflux temperature. The carbonyl absorption band at 1621.5 cm⁻¹ (vs) in the infrared spectrum of **3** also fell in the range expected.⁴ Absence of C=N absorption band and C-O stretching absorption bands also confirmed the structure of compound **3**. The electron impact mass spectral behaviour of compound **3** has also been studied. The base peak ion at *m/z* 311 is formed by McLafferty rearrangement of the molecular ion, and further rearrangement yields a characteristic ion at *m/z* 229 [FcCONH₂] as shown in Scheme 3.

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[†] This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.



Scheme 3

In summary, ferrocene carboxylic acid was reacted with DCC in tetrahydrofuran at room temperature to give *N,N'*-dicyclohexyl-*O*-ferrocenoylisourea. This compound is not as reactive as other *N,N'*-dicyclohexyl-*O*-acylisoureas. Compound **2** *N*-ferrocenoylisourea can be converted to **3** *N* in dioxane at reflux temperature. Because of the conjugative effect of ferrocene group with carbonyl, the Fc-C(=O) bond is strong. Hence, in the mass spectra *N,N'*-dicyclohexyl-*O*-ferrocenoylisourea and *N,N'*-dicyclohexyl-*N*-ferrocenoyl-urea can rearrange to form ferrocenecarboxylic acid and amide respectively, whereas it is very difficult to form carboxylic acid and amide by Mclafferty rearrangement for other *N,N'*-dicyclohexyl-*O*-acylisoureas and *N,N'*-dicyclohexyl-*N*-acylisoureas.

Experimental

All reactions were carried out under a nitrogen atmosphere. ¹H NMR spectra were obtained at 200 MHz using a Bruker AC-P 200 spectrometer. Infrared spectra were recorded on a Shimadzu-435 spectrometer. Mass spectra were recorded with HP5988A spectrometer using the EI method. Elemental analyses were carried out with a Yanaco CHN Corder MT-3 elemental analyzer. Melting points were taken on a Thomas-Hoover melting-point apparatus and are uncorrected. TLC was carried out on silica gel 60 F₂₅₄ microplates.

N,N'-Dicyclohexyl-*O*-ferrocenoylisourea (**2**): Ferrocene carboxylic acid (0.32 g, 1.40 mmol) and DCC (0.43 g, 2.10 mmol) in anhydrous tetrahydrofuran (15 mL) were stirred for 9 h at room temperature. A few drops of glacial acetic acid were added (to destroy any unreacted carbodiimide) and the mixture was filtered. The filtrate was evaporated in vacuo, the residue was purified by chromatography on a silica gel. Elution with ethyl acetate and petroleum ether (60–90°C) gave the desired product (**2**). Recrystallisation from meth-

ylene dichloride / petroleum ether (60–90°C) gave an analytical sample as a red crystalline solid (0.51 g) in 83.5% yield. m.p. 174–175°C. IR (KBr) ν/cm^{-1} 3218.0(NH), 1699.5(C=O), 1596.5(C=N), 1270.2, 1241.8(C-O). TLC (EtOAc/n-C₆H₁₄, 1:3) R_f 0.51. ¹H NMR(CDCl₃) δ 0.90–2.14 (m, 20H, (CH₂)₅), 3.36–3.70 (m, 2H, NCH), 4.25 (s, 5H, C₅H₅), 4.40 (s, 2H, C₅H₄), 4.76 (s, 2H, C₅H₄), 6.08 (br., 1H, NH). Anal. Calcd for C₂₄H₃₂N₂O₂Fe: C, 66.06; H, 7.39; N, 6.42; Found: C, 66.30; H, 7.28; N, 6.31. MS (EI, 15ev) m/z 436.15 (M, 27.8%), 229.95 (FcCO₂H, 22.7%).

N,N'-Dicyclohexyl-*N*-ferrocenoylurea (**3**). A solution of **2** (0.15 g, 0.34 mmol) in dioxane (20 mL) was refluxed for 36 h. The reaction was monitored by TLC and stopped after complete consumption of **2**. The solvent was removed under vacuum, and the residue was purified by chromatography on a silica gel using a mixture of ethyl acetate and petroleum ether (60–90°C) as the eluent. Finally, a yellow crystalline solid **3** was obtained (0.13 g) in 86.7% yield. m.p. 243–244°C. IR (KBr) ν/cm^{-1} 3274.0(NH), 1621.5(C=O). TLC (EtOAc/n-C₆H₁₄, 1:3) R_f 0.27. ¹H NMR(CDCl₃) δ 1.09–2.09 (m, 20H, (CH₂)₅), 3.74–4.09 (m, 2H, NCH), 4.18 (s, 5H, C₅H₅), 4.32 (s, 2H, C₅H₄), 4.64 (s, 2H, C₅H₄), 5.43 (br., 1H, NH). Anal. Calcd for C₂₄H₃₂N₂O₂Fe: C, 66.06; H, 7.39; N, 6.42; Found: C, 65.68; H, 6.99; N, 6.57. MS (EI, 15eV) m/z 229.00 (FcCONH₂, 14.4%).

We are grateful to the National Natural Science Foundation of China for financial support of this work.

Received 18 December 2000; accepted 13 March 2001

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