Fluorocarbonylferrocene. A Versatile Intermediate for Ferrocene Esters and Amides

Trent H. Galow,† Jason Rodrigo,† Katherine Cleary,† Graeme Cooke,‡ and Vincent M. Rotello*,†

Department of Chemistry, University of Massachusetts, Amherst, Massachusetts 01003, and Department of Chemical and Life Sciences, Ellison Building, University of Northumbria, Newcastle Upon Tyne, NE1 8ST, U.K.

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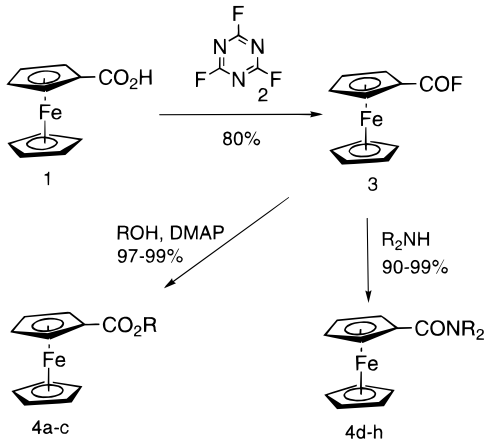
In recent years, considerable interest has been devoted to the creation of ferrocene-based catalysts,[1] sensors,[2] and devices.[3] Examples of such systems in this diverse field include redox-modulated recognition sensors,[4] redox-active self-assembled monolayers (SAM's),[5] redox switches,[6] and redox-switchable membranes.[7] A commonly used intermediate in the synthesis of these systems is chlorocarbonylferrocene. Formation of this acid chloride from the corresponding acid is capricious and can often result in low yields.[8] These difficulties arise from the high nucleophilicity of the ferrocene nucleus. This reactivity results in the formation of dimers and oligomers arising from intermolecular Friedel−Crafts acylations. Purification of the reaction mixtures is then hampered by the reactivity of the acid chloride toward both heat and hydrolysis. To circumvent these difficulties, we have investigated the use of the corresponding acid fluoride as a synthetic intermediate. We report here the synthesis of fluorocarbonylferrocene (**1**) and the application of this intermediate to the synthesis of ferrocenyl esters and amides.

Reaction of ferrocenecarboxylic acid **1** with cyanuric fluoride **2** and pyridine in dichloromethane provides the acid fluoride **3** reproducibly as an orange solid in 80% yield (Scheme 1).[9,10] Generation of the acid fluoride occurs under mild conditions and proceeds with a high level of functional group compatibility.[9] In contrast to the acid chloride, **3** is very stable to recrystallization, sublimation, and chromatography and may be stored at room temperature indefinitely without decomposition.

Scheme 1. Synthesis of Fluorocarbonylferrocene (3) and Its Utility in the Formation of Amides and Esters



Normally associated with the coupling of an acid chloride and an amine is the addition of base to prevent protonation of the attacking nucleophile. When acid fluoride **3** is used, surprisingly *no base* is required. Obviously this presents new advantages for **3** rather than applying the acid chloride strategy. First, no functionality incompatibilities arise when base sensitive groups are present in the substrates of interest. Second, no aqueous workup is necessary. The reaction of **3** proceeds rapidly and efficiently with 1 equiv of primary and secondary amines to provide the corresponding amides **4d**−**h** in excellent yield (Table 1). Poorly nucleophilic aniline reacts sluggishly with **3**, but it was found that 4-(dimethylamino)pyridine (DMAP) effectively catalyses the reaction.[11]

The reactions of **3** with alcohols and weakly nucleophilic phenol were also sluggish, even in the presence of excess alcohol. With the addition of DMAP, however, the esters **4a**−**c** were synthesized in excellent yield (Table 1), using essentially stoichiometric quantities of alcohol.[12]

In summary, we have shown fluorocarbonylferrocene to be a useful and versatile synthetic intermediate for

† University of Massachusetts.

‡ University of Northumbria.

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(10) Ferrocenyl-1,1′-diacid fluoride can be prepared by a slight modification of this method in 88% yield (for diacid fluoride synthesis, refer to the Experimental Section).

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Table 1. Preparation of Esters 4a−c and Amides 4e−h from Fluorocarbonylferrocene (3)

Product	Amine / Alcohol	Time	%Yield	mp / lit. mp (°C)
4a	MeOH	12 h	99	70-71 / 70-71[f]
4b	EtOH	12 h	97[a]	60-62 / 60-61[f]
4c	PhOH	12 h	99[b]	124-125 / 124-125[f]
4d	NH_3	15min	99[c]	168-169 / 168-170[g]
4e	$MeNH_2$	15min	99[c]	186-188 / 185-187[g]
4f	Me_2NH	15min	98[d]	119-121 / 118-120[g]
4g	$PhNH_2$	12 h	94[e]	207-209 / 205-207[g]
4h		45min	90	129-130 / 128-130[g]

[a] 1.5 equiv of ethanol (absolute) and 1.5 equiv of DMAP. [b] 1.5 equiv of phenol and 1.5 equiv of DMAP, refluxed in CH_2Cl_2. [c] Added as aqueous solution, with aqueous layer removed prior to purification. [d] Added as a gas. [e] 1.5 equiv of arylamine and 1.5 equiv of DMAP added, refluxed in CH_2Cl_2. [f] See ref 13. [g] See ref 14.

the formation of amides and esters. We are now employing this material to the formation of new ferrocene-functionalized polymers and materials.

Experimental Section

General Methods. Chemicals were purchased from Aldrich, Pharmco, Sigma, and J.T. Baker Chemical Companies and used as received. Thin-layer chromatography (TLC) and column chromatography were carried out on glass precoated TLC plates with silica gel 60 and silica gel 60 (230−400 mesh), respectively. All ^{1}H NMR spectra were recorded using either $CDCl_3$ or DMSO-d_6 as solvent. IR spectra were recorded in $CDCl_3$ solvent. Identity of products **4a**−**h** were further verified by comparing experimental mp's with literature mp's. The melting points presented are uncorrected.

Synthesis of Fluorocarbonylferrocene (3). A suspension of ferrocenecarboxylic acid (**1**) (1.15 g, 5 mmol) and pyridine (0.81 mL, 10 mmol) in dry CH_2Cl_2 (25 mL) was cooled to 0 °C under an an argon atmosphere. To this was added cyanuric fluoride (1.80 mL, 10 mmol), and the contents were stirred for 90 min. A deep red/orange color was observed. Crushed ice/water (25 g) was then added, the suspension filtered, and the organic layer separated and washed with cold water (2 × 25 mL). Concentration in vacuo followed by chromatography (SiO_2, 6:1 Hex/EtOAc) provided 0.93 g (80%) of fluorocarbonylferrocene (**1**) as a dark orange crystalline solid (mp 70−71 °C). The solid can also be sublimed at 68−69 °C (0.1 mmHg) to provide very pure product. Anal. Calcd for $C_{11}H_9FFeO$: C, 56.94; H, 3.91. Found: C, 56.99; H, 3.88.

Synthesis of Ferrocenyl-1,1′-diacid Fluoride. 1,1′-Ferrocenedicarboxylic acid (1.01 g, 3.7 mmol) was added to a 250 mL round-bottom flask under argon, followed successively by additions of dry CH_2Cl_2 (30 mL) and pyridine (1 mL, 12.4 mmol). The suspension was cooled to 0 °C. Cyanuric fluoride was added (2.60 mL, 20 mmol), and the contents were vigorously stirred for 1 h to provide an orange solution. Crushed ice/water (30 mL) was added, the contents were filtered, and the organic layer was separated and washed with cold water (2 × 30 mL). The organic layer was then dried ($CaCl_2$), filtered, and concentrated in vacuo. The solid was then dissolved in acetone and precipitated with cold water. Filtration followed by drying in vacuo provided 0.89 g of the bis-acid fluoride (88%) as a pale orange solid (mp 166.5−167 °C). Anal. Calcd for $C_{12}H_8F_2FeO_2$: C, 51.80; H, 2.90. Found: C, 52.03; H, 3.03.

General Procedure for the Preparation of Amides and Esters Using Fluorocarbonylferrocene. To a solution of fluorocarbonylferrocene (0.2 mmol) in 2 mL dry THF or CH_2Cl_2 (CH_2Cl_2 was used when DMAP (0.2 mmol) was required) was added the appropriate amine or alcohol (0.2 mmol). The mixture was stirred at room temperature (unless otherwise stated) until completion of the reaction (15 min−12 h) and purified by flash chromatography or recrystallization.

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Supporting Information Available: ^{1}H NMR and IR spectra for compounds **3** and **4a**−**h**. This material is available free of charge via the Internet at http://pubs.acs.org.

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