Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Organometallic Chemistry 689 (2004) 1472–1480
Journal of Organometallic Chemistry
www.elsevier.com/locate/jorganchem

Reaction of ferrocenecarboxylic acid with *N*,*N*′-disubstituted carbodiimides: synthesis, spectroscopic and X-ray crystallographic analysis of *N*,*N*′-disubstituted *N*-ferrocenoylureas and identification of a one-pot coupling reagent for the formation of ferrocenecarboxamides in a non-aqueous solvent

Bernd Schetter, Bernd Speiser *

Institut für Organische Chemie, Universität Tübingen, Auf der Morgenstelle 18, D-72076 Tübingen, Germany

Received 3 November 2003; accepted 10 December 2003

Abstract

N,*N*′-dicyclohexyl-*N*-ferrocenoylurea **2**, *N*,*N*′-diisopropyl-*N*-ferrocenoylurea **3**, *N*,*N*′-di-*p*-tolyl-*N*-ferrocenoylurea **4** and *N*,*N*′-di-*tert*-butyl-*N*-ferrocenoylurea **5** were obtained by reaction of ferrocenecarboxylic acid **1** with *N*,*N*′-dicyclohexylcarbodiimide (DCC), *N*,*N*′-diisopropylcarbodiimide (DIC), *N*,*N*′-di-*p*-tolylcarbodiimide **10** and *N*,*N*′-di-*tert*-butylcarbodiimide **11**, respectively. Both *N*-*tert*-butyl-*N*′-ethyl-*N*-ferrocenoylurea **6** and *N*′-*tert*-butyl-*N*-ethyl-*N*-ferrocenoylurea **7** were obtained by reaction of **1** with *N*-*tert*-butyl-*N*′-ethylcarbodiimide **12**. In all cases a small amount of ferrocenecarboxylic anhydride **8** was formed as a by-product. All compounds were characterized by ^{1}H NMR, ^{13}C NMR, IR and MS. Single crystal X-ray structural analyses were made of **2**, **3** and **4**. From the consistent results, the reaction products of **1** with carbodiimides appear different from those proposed by some earlier workers. With *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimidehydrochloride **9** ferrocenoylurea was not isolated, but the main product was rather **8**. The suitability of **8** as acylation reagent was applied by using **9** to obtain *N*-(3-triethoxysilyl)-propylferrocenecarboxamide in a one-pot reaction from **1** and 3-(triethoxysilyl)-propylamine.

Keywords: Ferrocene; Ferrocenecarboxamide; Urea; Condensation; Coupling reaction; Activation

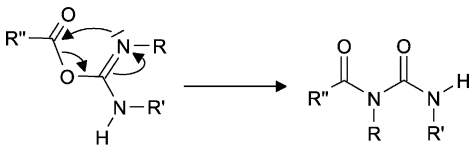
1. Introduction

Carbodiimides are versatile reagents in organic synthesis [1]. *N*,*N*′-dicyclohexylcarbodiimide (DCC) and *N*,*N*′-diisopropylcarbodiimide (DIC) are particularly well-known activators for the formation of amides and esters directly from carboxylic acids and amines or alcohols, respectively, under mild conditions in good yields. The carbodiimide and the carboxylic acid normally form an *O*-acylisourea **A**, a reactive intermediate that can easily be transformed into the amide or ester by reaction with an amine or an alcohol. Sometimes **A** partly converts to an *N*-acylurea **B** (Scheme 1) which is then obtained as an unwelcome by-product [1]. In some special cases, the anhydride is formed in the reaction, which is often also an effective intermediate for the reaction to amides and esters [1].

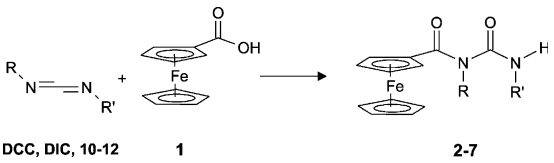
Ferrocenecarboxylic acid **1** reacts in a different way with DCC, and *N*,*N*′-dicyclohexyl-*N*-ferrocenoylurea **2** (structure **B**) is the main product, as already discussed in the literature [2–6], but either no spectroscopic investigation was made [2,3], the ^{1}H NMR and the IR spectra were incorrectly interpreted [4], or the substance was erroneously identified as *N*,*N*′-dicyclohexyl-*O*-ferrocenoylisourea [5]. One report [6] about the formation of **2** from DCC and **1** in the presence of 2-(6-hydroxy-

* Corresponding author. Tel.: +49-7071-2976-205; fax: +49-7071-295-518.
E-mail address: bernd.speiser@uni-tuebingen.de (B. Speiser).

0022-328X/$ - see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.jorganchem.2003.12.045



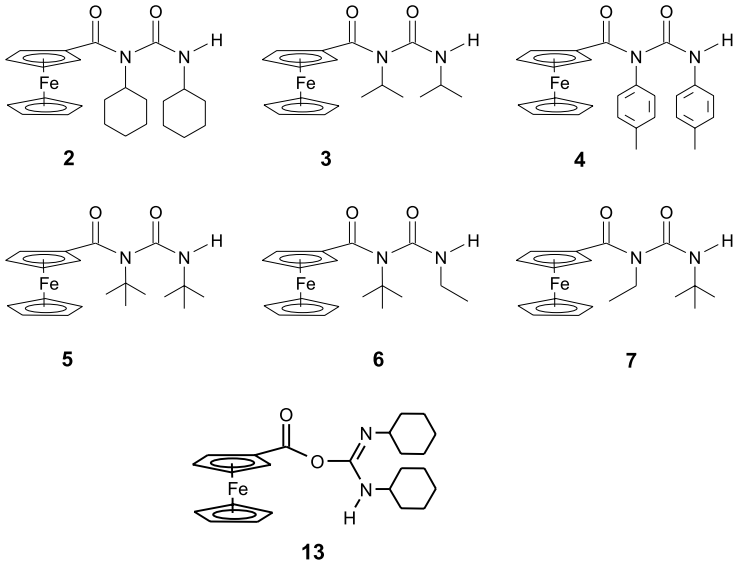
Scheme 1. Conversion of *O*-acylisoureas to *N*-acylureas.



Scheme 2. General pathway for the formation of *N*-ferrocenoylureas.

hexyloxy)-3-methoxy-6,7,10,11-tetrahexyloxytriphenylene includes a crystal structure and a ^{1}H NMR spectrum, however without interpretation. No IR investigation was made in [6]. Furthermore, no ^{13}C NMR spectrum of **2** has been published yet, although ^{13}C NMR spectroscopy should allow unequivocal distinction between *O*-acylisourea (**A**) and *N*-acylurea structures (**B**) from the typical strong shift of the carbonyl carbon nuclei.

gated carbodiimides (DCC, DIC, *N*,*N*′-di-*p*-tolylcarbodiimide **10**, *N*,*N*′-di-*tert*-butylcarbodiimide **11**, and *N*-*tert*-butyl-*N*′-ethylcarbodiimide **12**) formed stable *N*,*N*′-disubstituted *N*-ferrocenoylureas (Scheme 2) with small amounts of ferrocenecarboxylic anhydride **8** as the by-product. *N*-(3-dimethylaminopropyl)-*N*′-ethyl-carbodiimidehydrochloride **9** is an exception, which will be discussed separately below. Apart from **4** and **5**, the formation of the *N*,*N*′-disubstituted *N*-ferrocenoylureas



In view of the frequent use of the ferrocene unit as a redox active building block in larger molecular structures (for particularly striking examples see e.g. [7]), or in new medicinal drugs (e.g., [8,9]), where it is often bound by amide linkers, the need arises to activate **1** for the reaction with amines under mild conditions. Obviously, the conventional reagent DCC is not able to promote the desired reaction. It appeared thus of interest to investigate other carbodiimides, which might also be used as an alternative to the active ester pathway [10].

2. Results and discussion

In search of a carbodiimide for the activation of **1**, we tested various derivatives of DCC. Most of the investi-

in dichloromethane proceeds within seconds at room temperature, while **4** needs one day at room temperature and **5** five minutes at 105 °C for complete conversion.

The question if the product of the reaction between DCC and **1** is *N*,*N*′-dicyclohexyl-*O*-ferrocenoylisourea **13** according to [5] or **2** according to [2–4,6] as well as the question if the product between carbodiimides and **1** in general is an *N*,*N*′-disubstituted *O*-ferrocenoylisourea or an *N*,*N*′-disubstituted *N*-ferrocenoylurea was investigated by ^{1}H NMR, as well as ^{13}C NMR spectroscopy, MS and in the case of the reaction between DCC, DIC or **10** and **1** by a single crystal structure analysis of the products.

The similarity of the spectroscopic properties indicates that the products **2**–**7** belong to the same class of compounds. Especially the signals of the two carbonyl carbon nuclei at about 155 and 170 ppm in the ^{13}C

NMR spectrum indicate the formation of *N*,*N*′-disubstituted *N*-ferrocenoylureas. Table 1 summarizes the chemical shifts of these nuclei and compares them with the calculated values of both the corresponding *N*-benzoylureas and the *O*-benzoylisoureas. The benzoyl derivatives were taken as model for the ferrocenoyl compounds since the reliability of shift value calculations for organometallic compounds is rather low. The comparison with values for the model structures is supported by the good correspondence between shift values for ferrocenoyl and benzoyl derivatives. For example, the chemical shifts of the carbonyl carbon nuclei of ferrocenecarboxylic acid and benzoic acid differ less than 1 ppm. In all cases reported in Table 1 the calculated values of the *N*-benzoylureas fit considerably better to the experimental data than those of the *O*-benzoylisoureas.

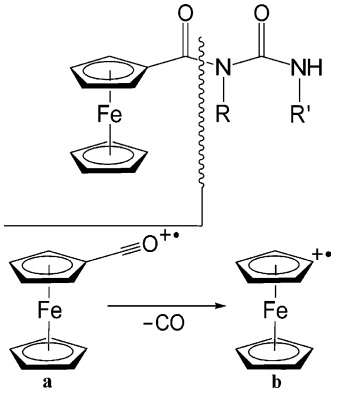
Table 1
^{13}C NMR chemical shifts values for carbonyl carbon atoms C^1 and C^2

		$\delta(C^1)$/ppm	$\delta(C^2)$/ppm
R = R′ = *c*-C_6H_{11}, **2**	A	172.6	154.8
	B	177.2	154.4
	C	163.4	151.4
R = R′ = $CH(CH_3)_2$, **3**	A	172.4	154.6
	B	175.7	153.3
	C	164.5	150.0
R = R′ = *p*-$C_6H_4CH_3$, **4**	A	175.0	152.5
	B	173.6	151.5
	C	164.5	151.5
R = R′ = $C(CH_3)_3$, **5**	A	169.5	153.8
	B	170.7	156.6
	C	165.0	127.3
R = $C(CH_3)_3$,	A	169.3	155.5
R′ = CH_2CH_3, **6**	B	170.7	156.1
	C	164.0	142.1
R = CH_2CH_3,	A	174.8	153.3
R′ = $C(CH_3)_3$, **7**	B	176.4	158.9
	C	165.6	149.8

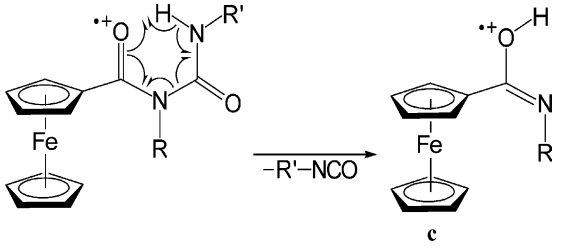
A: experimental values, B: calculated values for *N*-benzoylureas, C_6H_5–(C^1=O)–NR–(C^2=O)–NHR′, C: calculated values for *O*-benzoylureas, C_6H_5–(C^1=O)–O–C^2(NR)(NHR′).

In the ^{1}H NMR spectrum the signal of the N–*H* proton appears at $\delta > 5$ ppm. In dry $CDCl_3$, this acidic hydrogen atom is undergoing an exchange reaction so slowly that the signal is split by coupling with hydrogen atoms that are bound to the neighbouring carbon atom, if these are present (**2**, **3**, **6**). In this way, it was possible to differentiate between the two isomers, **6** and **7**, which were obtained by reaction of **1** with *N*-*tert*-butyl-*N*′-ethylcarbodiimide.

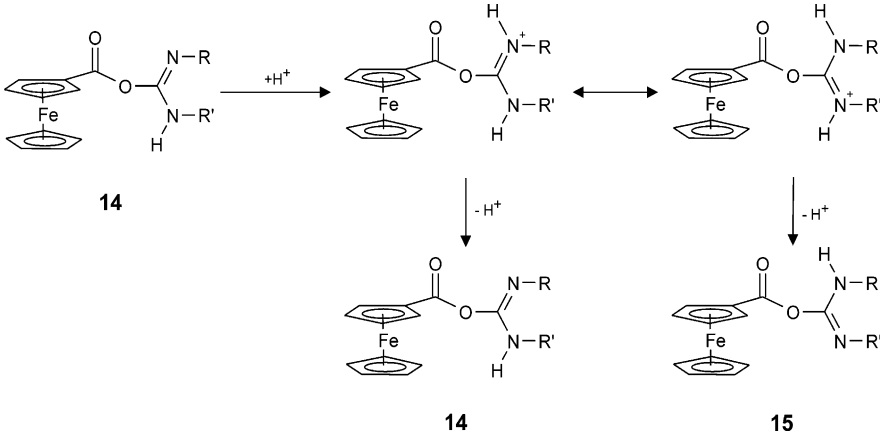
A further chemical argument that confirms the conclusion regarding the structure of the reaction products is as follows: if these isomers were *O*-ferrocenoylisou-



Scheme 4. α-Fragmentation and decarbonylation of *N*-ferrocenoylureas.



Scheme 5. MacLafferty rearrangement of the *N*-ferrocenoylureas.



Scheme 3. Hypothetical acid–base isomerisation between *O*-ferrocenoylisoureas.

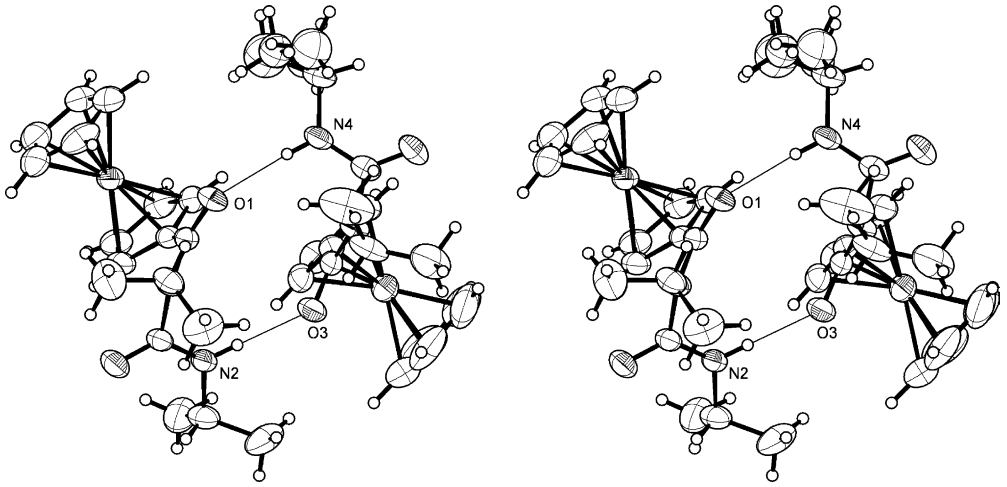


Fig. 1. Crystal structure of **3**, stereoscopic picture.

reas, one should assume that they have amidine like basicities. The take-up and release of a proton by one of the possible isomers, e.g. **14,** should lead to a mixture of **14** and **15** (Scheme 3). We do not observe such an effect in the case of **6** and **7**, which provides evidence that *O*-ferrocenoylisoureas are *not* the products of the reaction between **1** and carbodiimides.

Based on these results, corrections to some earlier work should be considered. In the interpretation of the ^{1}H NMR spectrum of compound **2** [4] the multiplet between 2.20 and 1.00 ppm was erroneously assigned to all 22 instead of 20 protons of the cyclohexyl rings. Furthermore, one of the other two protons of the cyclohexyl rings between 3.5 and 3.6 ppm was erroneously identified as the NH proton, while the second at 4.2 ppm and the NH proton failed to be noticed at all.

The formula weight of **2**–**7** was confirmed by MS. All these compounds show an α-fragmentation (Scheme 4) which leads to fragment **a** ($m/z = 213$). Further decarbonylation yields fragment **b** ($m/z = 185$). Another characteristic is the appearance of a fragment **c** with $m/z = 228 + m(\mathrm{R})$, R being the appropriate carbodiimide substituent (McLafferty rearrangement, Scheme 5). This fragment is not expected for *O*-acylisoureas. The latter should form the ferrocenecarboxylic ion ($m/z = 230$), but this was not detected in our spectra. The observed fragmentation is in full agreement with reported results for other carboxy ferrocenes [11,12]. In the case of **6** and **7** the exchange of the *tert*-butyl-groups against hydrogen and in the case of **5** the exchange of one or both *tert*-butyl-groups is observed and leads to fragments with $m/z = \mathrm{M} - 55$ and $m/z = \mathrm{M} - 110$.

In the IR spectra of **2**–**7** the N–H vibration leads to an absorption at 3300–3150 cm^{-1}, which is quite weak in the case of **4**. Furthermore, in the region between 2800 and 1800 cm^{-1} no significant absorption is detectable. In an earlier IR spectroscopic investigation [4] a band at 2100 cm^{-1} was registered and identified as NH–CO–N–CO stretching band. In this region of wave numbers, however, for **2** no band is detectable and the band discussed in [4] is probably caused by DCC impurities. This starting material gives a strong band at 2117 cm^{-1}.

The single crystal structure analysis confirms that the products of **1** with DCC, DIC and **10** are **2**, **3**, and **4**, respectively. The structure of **2** is in accordance with [6]. [1] The triclinic unit cell has the space group $P\bar{1}$, and dimers with the symmetry C_i are formed by two hydrogen bonds between the N–H and the carbonyl oxygen of the ferrocenoyl residue. The structure of **3** (Fig. 1) is also characterized by the formation of dimers by hydrogen bonds between N^2 and O^3 as well as between N^4 and O^1, respectively, but these units do not have a centre of inversion. Every forth isopropyl group (one isopropyl group per two molecules) has enough space to occupy split positions. The monoclinic unit cell has the symmetry $P2_1/c$. In contrast, **4** (Fig. 2) is monomeric and forms an *intra*molecular hydrogen bond between O^1 and N^2. The central molecule fragment c-C_5H_4–($C{=}O^1$)–N^1C–($C{=}O^2$)–N^2H–C_6H_4–C is planar, indicating that π-electrons are delocalized over this part of the molecule structure. Furthermore, this shape forces the approach of O^2 to the *ortho*-hydrogen in the tolyl residue, which is bound to N^2. The N^1 tolyl substituent is twisted out of plane by 90° and for this reason the π-electron system of this moiety is isolated from the rest of the molecule. The triclinic unit cell has the space group $P\bar{1}$.

[1] The reference mentions that results of the single crystal structure analysis of **2** were deposited at the Cambridge Crystallographic Data Centre, but the deposition number was not reported. Following the advice of one of the reviewers, the lattice parameters of **2** from our determination are given in the following: $a = 1015.19(9)$ pm, $b = 1068.50(8)$ pm, $c = 1177.53(9)$ pm; $\alpha = 104.369(9)°$, $\beta = 108.628(9)°$, $\gamma = 108.307(9)°$.

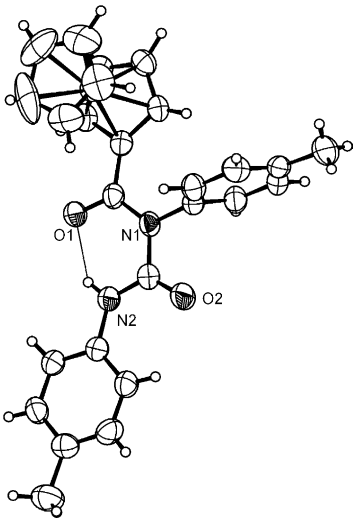


Fig. 2. Crystal structure of **4**.

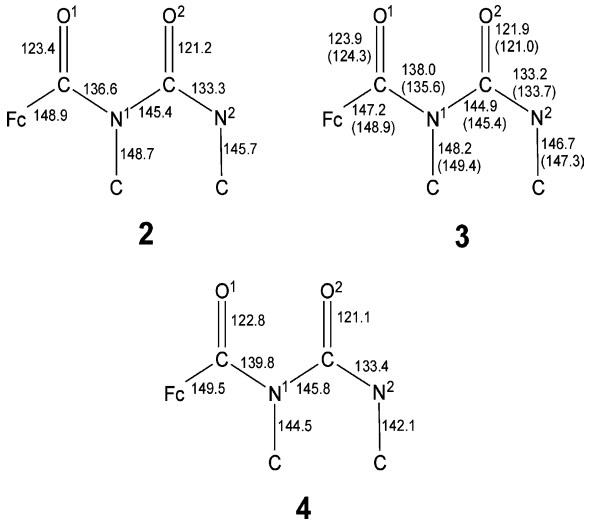
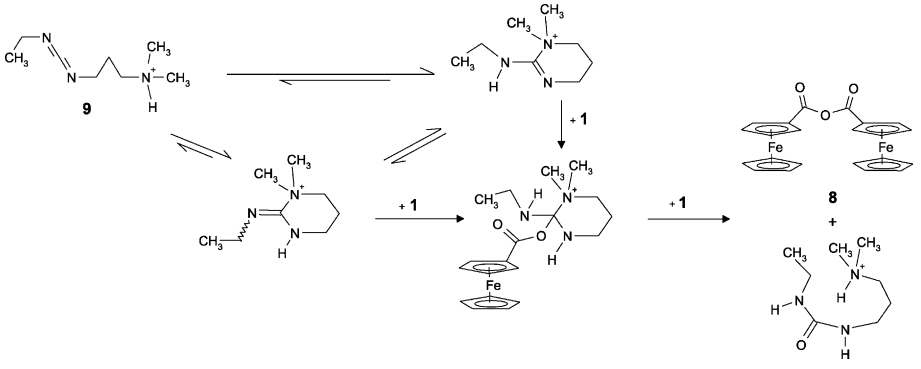


Fig. 3. Selected crystallographic bond lengths for compounds **2**, **3**, and **4**; plain and parenthesized values for **3** refer to the two independent molecules of the compound within the crystal.

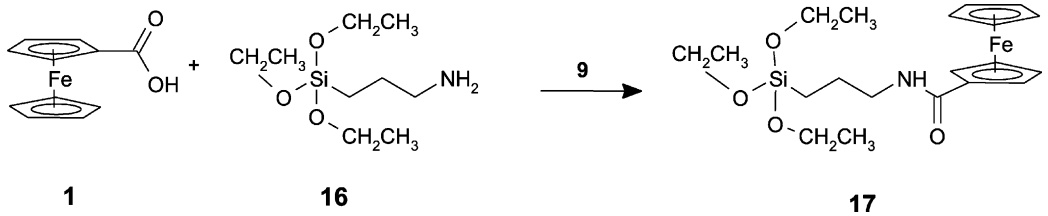
Some selected crystallographic bond lengths of the urea residue are shown in Fig. 3 for species **2**, **3**, and **4**. The urea unit is asymmetric. Especially the N^1–CO^2 bond is remarkably long in contrast to the N^2–CO^2 bond. This could be a reason for the facile McLafferty rearrangement observed in the mass spectra. The N–R bond length depends on the nature of R.

Of course, the stable *N*-ferrocenoylureas are not suitable as coupling reagents for **1**. On the other hand, **9** was found to form anhydride **8** with **1** (Scheme 6). The latter compound is indeed activated with respect to amide formation (see below). We explain this different reaction by the fact that **9** converts in solution to cyclic tautomeric guanidinium ions [13,14]. The reaction product between **1** and these ions is not able to convert to an *N*-acylurea as easily as *O*-acylisoureas do owing to the absence of a double bond and the presence of hydrogen at both nitrogen atoms (Scheme 6).

To demonstrate the activating ability of **9** in a non-aqueous solvent, we used this carbodiimide as a coupling reagent to form an amide from 3-(triethoxysilyl)-propylamin **16** and **1** (Scheme 7) in a one-pot reaction. Indeed, we could prepare the new compound *N*-(3-triethoxysilyl)-propylferrocenecarboxamide **17**, in reason-



Scheme 6. Hypothetical pathway for the formation of **8** from **1** and **9**.



Scheme 7. One-pot reaction of **1** with **16** under activation by **9** to form amide **17**.

able yield. Owing to the sensitivity of the silyl moiety to hydrolysis, other pathways, e.g. condensation of an amine with an acyl chloride with liberation of HCl, is not advisable in this case. None of the other carbodiimides, especially DCC and DIC, usually employed in non-aqueous solution, was successful in this case. It is not necessary to prepare the chlorocarbonylferrocene [4] or another activated ferrocene derivative [10] in a separate step. We are currently using **17** as a synthetic building block for the modification of silica nanoparticles [15].

3. Experimental

All reactions and operations were carried out under argon. All solvents were distilled, dried and degassed with Ar.

N,N′-dicylohexyl-N-ferrocenoylurea (**2**), *N,N′-diisopropyl-N-ferrocenoylurea* (**3**), and *N,N′-di-p-tolyl-N-ferrocenoylurea* (**4**) (see Table 2). Acid **1** and the corresponding carbodiimide were suspended in 10 ml dichloromethane in a Schlenk tube with the reactant and solvent by means of an ultrasonic bath and then stirred at room temperature. The clear brown solution was concentrated to 4 ml and separated by column chromatography (CC) with silica gel as the stationary phase and a mixture of acetone and dichloromethane as the eluent. The first coloured fraction was **8** [16] (yields see Table 2), the second was the ferrocenoylurea. The solvent was removed by vacuum and the resulting solid was kept at 0.1 mbar to remove trace amounts of carbodiimide.

2: IR (Atr): $\tilde{\nu}/cm^{-1}$ 3240 (NH), 3150–3000 (CH, ferrocene), 3000–2830 (CH, *c*-C_6H_{11}), 1700 (C═O); ^{1}H NMR ($CDCl_3$): δ 1.00–1.33 (m, 8H, *c*-C_6H_{11}), 1.54–1.65 (m, 4H, *c*-C_6H_{11}), 1.75–1.83 (m, 6H, *c*-C_6H_{11}), 1.97–2.06 (q, $J_{HH} = 9.6$ Hz, 2H, cc-C_6H_{11}), 3.5–3.65 (q, $J_{HH} = 7.6$ Hz, 1H, NH–C*H*), 4.20 (s, 5H, *c*-C_5H_5), 4.20–4.26 (m, 1H, $(C{=}O)_2NCH$), 4.33 (s, 2H, *c*-C–CH–C*H*–C*H*–CH), 4.71 (s, 2H, *c*-C–C*H*–CH–CH–C*H*), 6.20–6.21 (d, $J_{HH} = 7.1$ Hz, 1H, N*H*); ^{13}C NMR ($CDCl_3$): δ 24.6, 25.4, 25.5, 26.2 (*c*-CH–CH_2–CH_2–CH_2–CH_2), 31.0 (*c*-CH(NH)–CH_2–CH_2–CH_2–CH_2), 32.5 (*c*-CH(N)–CH_2–CH_2–CH_2–CH_2), 49.8 (*C*H(NH)), 56.6 (*C*H(N)), 70.2, 70.3, 70.4 (*c*-C_5H_5, *c*-C–*C*H–*C*H–*C*H–*C*H), 77.8 (*c*-*C*–$(CH)_5$), 154.8 (N–(*C*═O)–N), 171.6 (C–(*C*═O)–N); MS (EI, 70 eV): *m*/*z* 436.2, 311.1, 229.0, 213.0, 185.0. Anal. Calc. for $FeC_{24}H_{32}O_2N_2$ (436.37): C, 66.06; H, 7.39; N, 6.42. Found: C, 65.77; H, 7.47; N, 6.17.

3: IR (Atr): $\tilde{\nu}/cm^{-1}$ 3230 (NH), 3150–3000 (CH, ferrocene), 3000–2850 (CH, CH_3CHCH_3), 1700 (C═O); ^{1}H NMR ($CDCl_3$): δ 1.02–1.05 (d, $J_{HH} = 7.5$ Hz, 6H, $NHCH(CH_3)_2$), 1.38–1.41 (d, $J_{HH} = 7.9$ Hz, 6H, $(C{=}O)_2NCH(CH_3)_2$), 3.83–3.87 (m, $J_{HH} = 6.8$ Hz, 1H, NH–C*H*–$(CH_3)_2$), 4.17 (s, 5H, *c*-C_5H_5), 4.32 (s, 2H, *c*-C–CH–C*H*–C*H*–CH), 4.62 (m, 1H, $(C{=}O)_2NCH$–$(CH_3)_2$), 4.67 (s, 2H, *c*-C–C*H*–CH–CH–C*H*), 6.5 (b, 1H, N*H*); ^{13}C NMR ($CDCl_3$): δ 21.1 (NH–CH–$(CH_3)_2$), 22.3 ($(C{=}O)_2NCH$–$(CH_3)_2$), 42.7 (NH–*C*H–$(CH_3)_2$), 48.9 ($(C{=}O)_2NCH$–$(CH_3)_2$), 70.1, 70.2, 70.3 (*c*-C_5H_5, *c*-C–*C*H–*C*H–*C*H–*C*H), 77.8 (*c*-*C*–$(CH)_4$), 154.6 (N–(*C*═O)–N), 172.4 (C–(*C*═O)–N); MS (EI, 70 eV): *m*/*z* 356.1, 271.1, 229.1, 213.0, 185.0. Anal. Calc. for $FeC_{18}H_{24}O_2N_2$ (356.24): C, 60.69; H, 6.79; N, 7.86. Found: C, 60.23; H, 6.75; N, 7.45.

4: IR (Atr): $\tilde{\nu}/cm^{-1}$ 3230–3190 (NH), 3150–3000 (CH, ferrocene, tolyl group), 3000–2850 (CH, CH_3), 1712 (C═O); ^{1}H NMR ($CDCl_3$): δ 2.33 (s, 3H, $NHC_6H_4CH_3$), 2.47 (s, 3H, $(C{=}O)_2NC_6H_4CH_3$), 4.22 (s, 5H, *c*-C_5H_5), 3.92, 4.28 (s, each 2H, *c*-C–C*H*–C*H*–C*H*–C*H*), 7.12–7.15 (d, $J_{HH} = 8.1$ Hz, 2H, $(C{=}O)_2N$–(*c*-C–CH–C*H*–$C(CH_3)$–C*H*–CH)), 7.21–7.23 (d, $J_{HH} = 8.1$ Hz, 2H, HN–(*c*-C–CH–C*H*–$C(CH_3)$–C*H*–CH)), 7.31–7.33 (d, $J_{HH} = 7.8$ Hz, 2H, HN–(*c*-C–C*H*–CH–$C(CH_3)$–CH–C*H*)), 7.52–7.54 (d, $J_{HH} = 8.3$ Hz, 2H, $(C{=}O)_2$ N–(*c*-C–C*H*–CH–$C(CH_3)$–CH–C*H*)), 11.82 (b, 1H, N*H*); ^{13}C NMR ($CDCl_3$): δ 20.8, 21.3 (CH_3), 70.2, 71.8, 72.4 (*c*-C_5H_5, *c*-C–*C*H–*C*H–*C*H–*C*H), 74.2 (*c*-*C*–$(CH)_4$), 120.0, 129.4, 129.8, 130.0 (*c*-C–$(CH)_2$–C–$(CH)_2$), 133.3,

Table 2
Reaction conditions and properties of products **2**, **3**, and **4**

Ferrocenoylurea	**2**	**3**	**4**
Amount of carbodiimide	0.625 mmol (129 mg)	0.625 mmol (78 mg)	0.625 mmol (220 mg)
Amount of **1**	0.5 mmol (115 mg)	0.5 mmol (115 mg)	1 mmol (230 mg)
Stirring time/h	15	5	24
Eluent composition CH_2Cl_2/acetone	1/30	1/30	1/60
Carbodiimide removal time and temperature	48 h/50 °C	20 h/30 °C	20 h/30 °C
Yield	122 mg (58%)	94 mg (55%)	280 mg (64%)
Yield of **8**	7.6 mg (5%)	6.3 mg (4%)	13.7 mg (4%)
Product color	Dark orange	Dark orange	Brick red
Mp.	170 °C[a]	121 °C	149 °C[b]

[a] Above slow thermal decomposition.
[b] Above fast thermal decomposition.

135.4, 135.5, 139.1 (*c*-*C*–$(CH)_2$–*C*–$(CH)_2$), 152.5 (N–(*C*=O)–N), 175.0 (C–(*C*=O)–N); MS (EI, 70 eV): *m*/*z* 319.1, 213.1, 185.1, 129.2, 91.2, 77.2, 66.2; MS (FAB): *m*/*z* 452.1, 375.1, 319.1, 213.0, 185.0. Anal. Calc. for $FeC_{26}H_{24}O_2N_2$ (452.38): C, 69.04; H, 5.35; N, 6.19. Found: C, 68.69; H, 5.33; N, 5.91.

N,N′-dicylohexyl-N-ferrocenoylurea **2**, in analogy to Wang and Huang [5]. 0.32 g (140 mmol) of **1** and 0.43 g DCC were dissolved in 15 ml THF and stirred for 9 h. The solvent was removed by vacuum and the solid residue was redissolved with a mixture of petrol ether (60–90 °C) and ethyl acetate 5/1 and separated by CC with a mixture of petrol ether (60–90 °C) and ethyl acetate 7/1. The first fraction obtained was **8**, and the second was **2**, which was purified by recrystallisation from petrol ether (60–90 °C) and ethyl acetate 7/1. Differing from [5], no acetic acid was added to destroy the unreacted carbodiimide.

N,N′-di-tert-butyl-N-ferrocenoylurea (**5**). 1 mmol (230 mg) **1** and 1 mmol (222 mg) *N*,*N′*-di-*tert*-butylcarbodiimide were suspended in 5 ml dichloromethane by application of ultrasound and stirred for 5 min at 105 °C under microwave heating. CC separation with silica gel as the stationary phase and a mixture of ethyl acetate and *n*-hexane 1/6 as the mobile phase yielded a first coloured fraction [**8**, yield: <1 mg (<1%)], and a second one (**5**), closely followed by *N-tert*-butylferrocenecarboxamide [17,18] (22.7 mg, 8%). Because of the insufficient separation, the purification by CC had to be repeated twice. The solvent was removed by vacuum and the orange solid was kept for 5 h at 40 °C at 0.1 mbar to remove any trace amounts of carbodiimide. Yield: 64 mg = 17%; Mp.: 145 °C; IR (Atr): $\tilde{\nu}/cm^{-1}$ 3314 (NH), 3150–3000 (CH, ferrocene), 3000–2850 (CH, CH_3), 1699 (C=O); ^1H NMR ($CDCl_3$): δ 1.12 (s, 9H, $NHC(CH_3)_3$), 1.49 (s, 9H, $(C=O)_2N–C(CH_3)_3$), 4.18 (s, 5H, *c*-C_5H_5), 4.21–4.22 (t, $J_{HH} = 1.6$ Hz, 2H, *c*-C–CH–CH–CH–CH), 4.77–4.78 (t, $J_{HH} = 1.7$ Hz, 2H, *c*-C–CH–CH–CH–CH), 4.99 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 27.9 ($NHC(CH_3)_3$), 28.6 ($(C=O)_2N–C(CH_3)_3$), 51.9 ($NHC(CH_3)_3$), 57.7 ($(C=O)_2N–C(CH_3)_3$), 69.5, 70.0, 70.4 (*c*-C_5H_5, *c*-C–CH–CH–CH–CH), 79.7 (*c*-C–$(CH)_4$), 153.8 (N–(C=O)–N), 169.5 (C–(C=O)–N); MS (EI, 70 eV): *m*/*z* 384.1, 329.1, 285.1, 255.0, 230.1, 213.1, 185.1, 154.1, 136.1. Anal. Calc. for $FeC_{20}H_{28}O_2N_2$ (384.29): C, 62.51; H, 7.34; N, 7.29. Found: C, 62.76; H, 7.56; N, 7.20.

N-tert-butyl-N′-ethyl-N-ferrocenoylurea (**6**) and *N′-tert-butyl-N-ethyl-N-ferrocenoylurea* (**7**). 1 mmol (230 mg) **1** and 1 mmol (126 mg) *N-tert*-butyl-*N′*-ethylcar-

Table 3
Crystal data for **3** and **4**

Compound	**3**	**4**
Empirical formula	$C_{18}H_{24}N_2O_2Fe$	$C_{26}H_{24}N_2O_2Fe$
Formula weight	356.24	452.32
Temperature (°C)	−60	25
Wavelength (pm)	71.073	71.073
Crystal system	Monoclinic	Triclinic
Space group	*P*21/*c*	$P\bar{1}$
Unit cell dimensions	$a = 1406.77(8)$ pm	$a = 1030.97(11)$ pm
	$b = 1419.02(10)$ pm	$b = 1062.04(11)$ pm
	$c = 1828.18(12)$ pm	$c = 1150.18(11)$ pm
	$\alpha = 90°$	$\alpha = 69.083(11)°$
	$\beta = 99.990(7)°$	$\beta = 79.927(12)°$
	$\gamma = 90°$	$\gamma = 65.890(11)°$
Volume (nm^3)	3.5941(4)	1.07313(19)
Z	8	2
Density (calculated) (g/cm^3)	1.317	1.400
Absorption coefficient (mm^{-1})	0.849	1.457
F (0 0 0)	1504	944
Crystal size (mm^3)	$0.2 \times 0.2 \times 0.4$	$0.2 \times 0.2 \times 0.4$
Theta range	2.47 to 25.79°	3.34 to 24.71°
Index ranges	$-17 \leqslant h \leqslant 16$	$-13 \leqslant h \leqslant 12$
	$0 \leqslant k \leqslant 17$	$-12 \leqslant k \leqslant 12$
	$0 \leqslant l \leqslant 22$	$-13 \leqslant l \leqslant 12$
Reflections collected	6115	7025
Independent reflections	6115	3443
Completeness	to $\theta = 25.79°$: 98.8%	to $\theta = 24.71°$: 93.7%
Refinement method	Full-matrix least-squares on F^2	
Data/restrains/parameters	6115/0/582	3443/0/376
Goodness-of-fit on F^2	0.731	1.073
Final *R* indices [$I \geqslant 2\sigma(I)$]	$R_1 = 0.0379, wR_2 = 0.0815$	$R_1 = 0.0400, wR_2 = 0.0997$
R indices (all data)	$R_1 = 0.0694, wR_2 = 0.0856$	$R_1 = 0.0460, wR_2 = 0.1028$
Largest diffraction peak (eÅ)	0.452	0.707

bodiimide were suspended in 10 ml dichloromethane by application of ultrasound and stirred for 15 h at room temperature. The resulting clear brown solution was concentrated to 4 ml and separated by CC as above. The first coloured fraction was **8** (6.4 mg, 4%), the second was **7** and the third was **6**. Fraction 3 was purified again by CC to remove any traces of **7**. The solvent was removed by vacuum and the red (**7**) and orange (**6**) solids, respectively, were kept for 20 h at 30 °C and 0.1 mbar to remove any trace amounts of carbodiimide. Yields: 104 mg of **6** (29.2%), 123 mg of **7** (34.6%).

6: Mp.: 173 °C; IR (Atr): $\tilde{\nu}/cm^{-1}$ 3270 (NH), 3150–3000 (CH, ferrocene), 3000–2850 (CH), 1645 (C=O); ^{1}H NMR ($CDCl_3$): δ 0.93–0.97 (t, $J_{HH} = 7.4$ Hz, 3H, $NHCH_2CH_3$), 1.52 (s, 9H, $(C=O)_2NC(CH_3)_3$), 3.08–3.15 (quint, $J_{HH} = 7.1$ Hz, 2H, $NHCH_2CH_3$), 4.19 (s, 5H, c-C_5H_5), 4.25–4.26 (t, $J_{HH} = 1.8$ Hz, 2H, c-C–CH–CH–CH–CH), 4.73–4.74 (t, $J_{HH} = 1.8$ Hz, 2H, c-C–CH–CH–CH–CH), 5.30 (t, $J_{HH} = 5.8$ Hz, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 13.9 ($NH–CH_2–CH_3$), 28.6 ($(C=O)_2NC–(CH_3)_3$), 36.2 ($NHCH_2–CH_3$), 48.9 ($N–C–(CH_3)_3$), 69.9, 70.0, 70.1 (c-C_5H_5, c-C–CH–CH–CH–CH), 77.9 (c-C–$(CH)_4$), 155.5 (C–(C=O)–N), 169.2 (C–(C=O)–N); MS (FAB): m/z 356.1, 301.1, 285.1, 255.0, 230.1, 213.0, 185.1, 154.1, 136.1. Anal. Calc. for $FeC_{18}H_{24}O_2N_2$ (356.24): C, 60.69; H, 6.79; N, 7.86. Found: C, 60.33; H, 6.59; N, 7.86.

7: Mp.: 101 °C; IR (Atr): $\tilde{\nu}/cm^{-1}$ 3271 (NH), 3150–3000 (CH, Ferrocene), 3000–2850 (CH), 1699 (C=O); ^{1}H NMR ($CDCl_3$): δ 1.20–1.24 (t, $J_{HH} = 6.9$ Hz, 3H, $(C=O)_2N–CH_2CH_3$), 1.37 (s, 9H, $NHC(CH_3)_3$), 3.94–4.00 (q, $J_{HH} = 7.1$ Hz, 2H, $(C=O)_2N–CH_2CH_3$), 4.23 (s, 5H, c-C_5H_5), 4.38 (s, 2H, c-C–CH–CH–CH–CH), 4.69 (s, 2H, c-C–CH–CH–CH–CH), 9.00 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 15.7 ($(C=O)_2N–CH_2CH_3$), 28.8 ($NHC(CH_3)_3$), 40.4 ($(C=O)_2N–CH_2CH_3$), 50.8 ($NHC(CH_3)_3$), 70.1, 70.3, 70.8 (c-C_5H_5, c-C–CH–CH–CH–CH), 78.3 (c-C–$(CH)_4$), 153.3 (C–(C=O)–N), 174.8 (C–(C=O)–N); MS (FAB): m/z 356.0, 301.0, 257.0, 213.0, 185.1, 136.1, 121.1. Anal. Calc. for $FeC_{18}H_{24}O_2N_2$ (356.24): C, 60.69; H, 6.79; N, 7.86. Found: C, 60.41; H, 6.45; N, 7.54.

N-(3-Triethoxysilyl)-propylferrocenecarboxamide (**17**). 2 mmol (460 mg) **1** and 2.2 mmol (420 mg) *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimidehydrochloride were suspended in 20 ml dichloromethane by application of ultrasound and stirred for 4 h at room temperature. Then the clear brown solution was concentrated to 8 ml and separated by CC with silica gel as the stationary phase and a mixture of dichloromethane and acetone ratio 1/8 as the eluent. After removal of the solvent by vacuum an orange solid was obtained. Yield: 323 mg = 37%; Mp.: 80 °C, above slow thermal decomposition; IR (Atr): $\tilde{\nu}/cm^{-1}$ 3300 (NH), 3130–3050 (CH, ferrocene), 3000–2850 (CH), 1625 (C=O), 1520, 1050; ^{1}H NMR ($CDCl_3$): δ 0.65–0.68 (t, $J_{HH} = 7.8$ Hz, 2H, $Si–CH_2$), 1.18–1.25 (t, $J_{HH} = 7.1$ Hz, 9H, CH_3), 1.67–1.70 (quint, $J_{HH} = 7.6$ Hz, 2H, $CH_2–CH_2–CH_2$), 3.35–3.36 (q, $J_{HH} = 5.5$ Hz, 2H, NCH_2), 3.78–3.83 (q, $J_{HH} = 6.8$ Hz, 6H, $O-CH_2–CH_3$), 4.16 (s, 5H, c-C_5H_5), 4.28 (s, 2H, c-C–CH–CH–CH–CH), 4.65 (s, 2H, c-C–CH–CH–CH–CH), 6.0 (t, $J_{HH} = 5.3$ Hz, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 7.7 ($Si–CH_2$), 18.2 (CH_3), 23.1 ($CH_2–CH_2–CH_2$), 41.7 (NCH_2), 58.3 ($CH_3–CH_2–O$), 68.0, 69.6, 70.1 (c-C_5H_5, c-C–CH–CH–CH–CH), 76.4 (c-C–$(CH)_5$), 169.9 (C=O); MS (EI, 70 eV): m/z 433.1, 388.1, 322.0, 280.0, 229.0, 213.0, 185.0. Anal. Calc. for $FeSiC_{20}H_{31}O_4N$ (433.38): C, 55.43; H, 7.21; N, 3.23. Found: C, 55.19; H, 7.20; N, 2.93.

X-ray crystallography: The crystals of **2**–**4** were obtained by cooling down the solutions of **2**, **3** or **4** from 50 to 10 °C within 2 days. The structures were solved by direct methods using SHELXTL and refined by SHELX-97 [19]. All non-hydrogen atoms were refined anisotropically using full-matrix least squares to give the final R values. Some data are presented in Table 3.

Crystallographic data for the structural analyses reported in this paper have been deposited with the Cambridge Crystallographic Data Centre CCDC and have been allocated the deposition numbers 223438 (**3**) and 223439 (**4**). Copies of this information can be obtained free of charge from: The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: (int code) +44(1223)336-033, E-mail: deposit@ccdc.cam.ac.uk, or www: http://www.ccdc.cam.ac.uk).

Chemical shift calculations: ACD/ChemSketch (Advanced Chemistry Development, Inc.).

Acknowledgements

The authors wish to thank Markus Ströbele, Institut für Anorganische Chemie, Universität Tübingen, for collecting the X-ray data sets for compounds **2**–**4**, and Klaus Eichele for discussion of the analysis results. We also acknowledge Michael Barth, Jörg Bauer and Steffen Weik for the provision of and technical help with the microwave heater and the IR-spectrometer.

References

[1] P. Nuhn, Naturstoffchemie, S. Hirtzel, Stuttgart, 1997, pp. 157–158.
[2] H.H. Lau, H. Hart, J. Org. Chem. 24 (1959) 280–281.
[3] E.M. Acton, R.M. Silverstein, J. Org. Chem. 24 (1959) 1487–1490.
[4] A.F. Neto, J. Miller, V.F. de Andrade, S.Y. Fujimoto, M.M. de Freitas Alfonso, F.C. Archanjo, V.A. Darin, M.L. Andrade e Silva, A.D.L. Borges, G. Del Ponte, Z. Anorg. Allg. Chem. 628 (2002) 209–216.
[5] Q.M. Wang, R.Q. Huang, J. Chem. Res. (S) (2001) 246–247.
[6] G. Cooke, A. Radhi, N. Boden, R.J. Bushby, Z. Lu, S. Brown, S.L. Heath, Tetrahedron 56 (2000) 3385–3390.
[7] D. Astruc, Pure Appl. Chem. 75 (2003) 461–481.

[8] B. Pradines, T. Fusai, W. Daries, V. Laloge, C. Rogier, P. Millet, E. Panconi, M. Kombila, D. Parzy, J. Antimicrob. Chemoth. 48 (2001) 179–184.
[9] R. Kovjazin, T. Eldar, M. Patya, A. Vanichkin, H.M. Lander, A. Novogrodsky, FASEB J. 17 (2003) 467–469.
[10] H.S. Mandal, H.-B. Kraatz, J. Organomet. Chem. 674 (2003) 32–37.
[11] A. Mandelbaum, M. Cais, Tetrahedron Lett. (1964) 3847–3852.
[12] V. Rapić, N. Filipović-Marinić, Org. Mass Spectrom. 20 (1985) 104–109.
[13] T. Tenforde, R.A. Fawwaz, N.K. Freeman, N. Castagnoli Jr., J. Org. Chem. 37 (1972) 3372–3374.
[14] I. Yavari, J.D. Roberts, Org. Chem. 43 (1978) 4689–4693.
[15] K. Albert, G. Fischer, F. Novak, B. Schetter, B. Speiser, unpublished results.
[16] E.J. Kupchik, R.J. Kiesel, J. Org. Chem. 31 (1966) 456–461.
[17] R.L. Cox, T.W. Schneider, M.D. Koppang, Anal. Chim. Acta 262 (1992) 145–159.
[18] M. Oberhoff, L. Duda, J. Karl, R. Mohr, G. Erker, R. Frohlich, M. Grehl, Organometallics 15 (1996) 4005–4011.
[19] G.M. Sheldrick, Structure Determination and Refinement with the Program System SHELX-97, Universität Göttingen, 1997.