One-Pot Synthesis of Novel Enantiomerically Pure and Racemic 4-Ferrocenyl-β-lactams and Their Reactivity in Acidic Media

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A series of 4-ferrocenyl- and 4-[(S_{Fc})-2-(*p*-tolylsulfanyl)ferrocenyl]-β-lactams has been synthesized in good yields by a one-pot reaction of achiral and planar-chiral ferrocenylimines with substituted acetic acids. The acid-induced stereoconvergent transformation of *cis*- and *trans*-4-ferrocenyl-β-lactams into (*Z*)-α,β-unsaturated amides by protonation, N–C-4 cleavage and subsequent *exo*-H elimination and the lack of reaction of the *ortho*-*S*-tolylsulfanyl analogs are discussed. (© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2005)

Introduction

Since the introduction of penicillins into clinical practice, β-lactam antibiotics have been recognized as one of the most important classes of compounds possessing antimicrobial activity. For this reason a large number of methods have been developed for the construction of the β-lactam skeleton[1] which also allow control of the functional groups and stereochemistry. Furthermore, it has recently been demonstrated that monocyclic β-lactam derivatives (2-azetidinones) are potent inhibitors of a group of serine proteases, for example, human leucocyte elastase (HLE) implicated in the chronic tissue destruction of several diseases[2] and human cytomegalovirus (HCMV) involved in immunocompromized individuals (AIDS patients).[3] 2-Azetidinones have also been strategically designed to inhibit intestinal cholesterol absorption correlated to atherosclerotic coronary disease.[4]

On the other hand, enantiopure β-lactams have become important as versatile building blocks in the asymmetric synthesis of a variety of proteinogenic and non-proteinogenic amino acids, peptides, peptidomimetics, taxoid antitumor agents, heterocycles and other types of compounds of biological importance.[5] Few works on the influence of the ferrocene residue on the antimicrobial activity of β-lactam antibiotics have been reported,[6] although the aromatic character, stability, low toxicity and ease of substitution of ferrocene makes it ideal for use in drug design.[6b] Furthermore, the sandwich structure of ferrocene, together with the planar chirality present in derivatives possessing at least two different substituents in the same ring,[7] render it completely different from conventional aromatic molecules. A number of ferrocenylpenicillins have been tested[6] in vitro for antibiotic activity against different bacteria, including a penicillase-producing strain; some of these were highly active, while others proved to be potent β-lactamase inhibitors.

2-Azetidinones with a ferrocene moiety directly attached to the four-membered ring are rare. Among them, the biological activity of 4-ferrocenyl-substituted β-lactams, obtained by the cyclocondensation reaction of ferrocenyl Schiff bases, have been extensively investigated.[8]

More recently the synthesis of 3-unsubstituted 4-ferrocenyl-β-lactams by an indium-mediated reaction of imines with ethyl bromoacetate[9] and the preparation of 1-ferrocenyl-, 4-ferrocenyl- and 1,4-diferrocenyl-2-azetidinones by the photochemical reaction of alkoxy(carbene)chromium(0) complexes and mono- and diferrocenyl-substituted imines[10] have been reported. To the best of our knowledge we are the only group to have reported the synthesis of 3-ferrocenyl-substituted β-lactams,[11] achieved through a one-pot reaction of achiral or chiral imines and ferrocenylacetic acid (Staudinger reaction).

In terms of efficiency and stereochemical predictability, the Staudinger reaction[1,12] remains the most widely used route to β-lactams and in more recent times, the asymmetric version of this reaction in the synthesis of optically pure β-lactams has attracted significant interest.[12b]

As a continuation of our studies on ferrocene-containing molecules[13] and our interest on β-lactam derivatives,[11] we herein report the synthesis of 4-ferrocenyl-2-azetidinones, some of which possess planar chirality, through the Staudinger one-pot reaction. We also compare the stability of these derivatives under acidic conditions with that of the previously reported 3-ferrocenyl-substituted 2-azetidinones.

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Results and Discussion

The synthesis of 4-ferrocenyl-substituted β-lactams has been performed starting from achiral (**1a**,**b**)[14] and planar-chiral ferrocenylimines (**1c**)[13g] and substituted acetic acids **2a**–**d**. The reaction was performed in the presence of Et_3N and freshly distilled $PhOP(O)Cl_2$ (Table 1), a commercially available compound used as an acidic activator in the esterification of carboxylic acids[15] and in β-lactam synthesis.[11,16]

With achiral imines **1a**,**b**, the reaction was performed both in CH_2Cl_2 at 30 °C and in C_6H_6 at reflux temperature, since in some cases (Entries 3 and 6) the reaction did not proceed at 30 °C even after 48 h. The 2-azetidinones **3** were obtained in good-to-excellent yields after purification on deactivated neutral alumina. As far as the stereochemistry of the final products is concerned, the reaction performed in CH_2Cl_2 at 30 °C gave either exclusively (Entries 1, 7–10) or mainly (Entry 4) the *cis* isomer. The reaction performed in C_6H_6 at reflux temperature afforded an easily separable mixture of *cis* and *trans* isomers (Entries 2, 3, 5) or only the *trans* isomer (Entry 6). Since many of the routes to β-lactams usually show a strong preference for the formation of the kinetic *cis* derivative,[17] the possible access to both the *cis* and *trans* isomers is noteworthy. The stereochemistry of the products **3** was established on the basis of their ^1H NMR spectra. The coupling constants for the signals corresponding to the C-3 and C-4 protons (5.1–5.5 Hz for the *cis* isomers and 2.0–2.9 for the *trans* isomers) are in agreement with the previously reported values.[11,18]

The planar-chiral derivatives **3e**–**h** (Table 1, Entries 7–10) were obtained in CH_2Cl_2 at 30 °C as *cis* diastereoisomers, as determined by ^1H and ^{13}C NMR analysis of the crude reaction mixture. The absolute configuration of **3h** was established ($3S,4S,S_{Fc}$) by X-ray crystallography (Figure 1).[19]

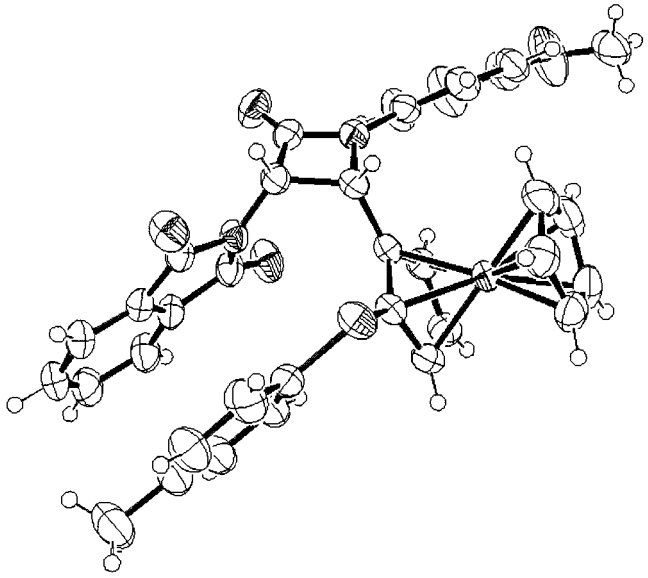
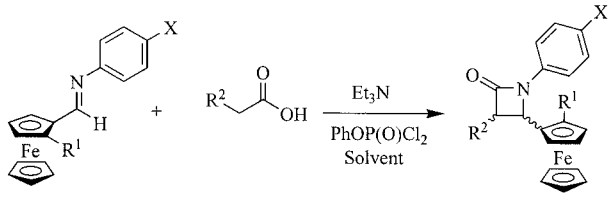


Figure 1. X-ray structure of ($3S,4S,S_{Fc}$)-**3h**.

An NOE experiment, performed by irradiating the C-4 proton of **3h**, showed a positive NOE effect on the C-3 proton, the unsubstituted Cp ring and the C-2 and C-6 protons of the 4-methoxyphenyl protecting group. These observed effects are in agreement with the structure obtained by X-ray analysis. The absolute configurations of the other chiral β-lactams **3e**–**f** were assigned on the basis of the X-ray structure of **3h** and on similar NOE effects on the 4-methoxyphenyl protecting group observed by irradiation of the C-4 protons.

The configuration obtained can be rationalized in terms of the attack of the ketene intermediate on the less congested *Si* face of the imine **1c**, away from the sterically hindered lower cyclopentadienyl ring, with the imine double

Table 1. Synthesis of 4-ferrocenyl-substituted β-lactams **3**.



1a-c **2a-d** **3a-h**

Entry	**1**	X	R^1	**2**	R^2	Solvent	*T* [°C]	**3**	Yield [%][a]	*trans*/*cis* ratio[b]	J_{cis} [Hz]	J_{trans} [Hz]
1	**a**	OCH_3	H	**a**	OPh	CH_2Cl_2	30	**a**	81	only *cis*	5.1	
2	**a**	OCH_3	H	**a**	OPh	C_6H_6	reflux	**a**	60	0.8:1	5.1	2.0
3	**a**	OCH_3	H	**b**	NPht	C_6H_6	reflux[c]	**b**	70	2.3:1	5.4	2.2
4	**b**	Cl	H	**a**	OPh	CH_2Cl_2	30	**c**	5	1:14	5.2	2.1
5	**b**	Cl	H	**a**	OPh	C_6H_6	reflux	**c**	72	5.6:1	5.2	2.1
6	**b**	Cl	H	**b**	NPht	C_6H_6	reflux[c]	**d**	90	only *trans*		2.9
7	**c**	OCH_3	S-*p*-Tol	**a**	OPh	CH_2Cl_2	30	**e**	68	only *cis*	5.1	
8	**c**	OCH_3	S-*p*-Tol	**c**	OAc	CH_2Cl_2	30	**f**	53	only *cis*	5.3	
9	**c**	OCH_3	S-*p*-Tol	**d**	OBn	CH_2Cl_2	30	**g**	78	only *cis*	5.1	
10	**c**	OCH_3	S-*p*-Tol	**b**	NPht	CH_2Cl_2	30	**h**	73	only *cis*	5.5	

[a] Yield of pure isolated products. [b] Determined by ^1H NMR analysis of the crude reaction mixture. [c] No reaction after at 30 °C in CH_2Cl_2 48 h.

bond in an *anti* disposition with respect to the *ortho* substituent on the ferrocene (Figure 2).

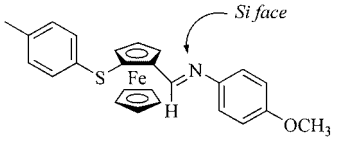


Figure 2. *exo*-Attack of the ketene intermediate on the (S_{Fc})-imine **1c**.

This behavior is in agreement with the highly enantioselective synthesis of β-lactams by the [2+2] cycloaddition reaction of homochiral (η^6-benzaldimine)tricarbonylchromium complexes[20] and ketenes and with the excellent diastereoselective reaction of the imine **1c** with organometallic reagents which occurs on the *Si* face of the imine.[13g]

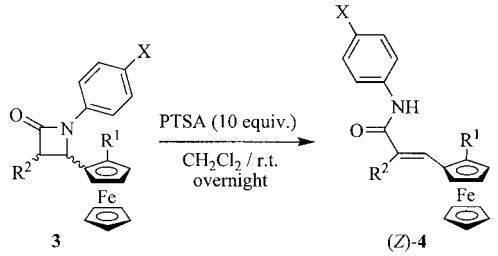
It is well known that β-lactams are very reactive substances; they are susceptible to attack by nucleophilic and electrophilic reagents with resultant cleavage of the β-lactam ring and loss of biological activity in the case of penicillins. Usually, the ring cleavage takes place at the N–C(O) bond.[5b]

In contrast, as we observed during the preparation of β-lactams **3**, the use of the reagent $PhOP(O)Cl_2$ without prior fresh distillation produced, as a by-product, an α,β-unsaturated amide **4** in 5–15% yields, which required cleavage of the N–C-4 bond of the β-lactam. This type of cleavage has been observed in palladium-catalyzed hydrogenolysis reactions and in dissolving-metal reductions of β-lactams when an aryl substituent is attached to the C-4 position.[5b] A similar unsaturated amide was formed[10] by base-promoted Hoffmann-like cleavage during the preparation of 1-(*p*-anisyl)-4-ferrocenyl-3-ferrocenylmethyl-2-azetidinone.

To rationalize this behavior, β-lactams **3** were treated with 10 equiv. of *p*-toluenesulfonic acid (PTSA) in CH_2Cl_2 at room temperature and products **3a–d** were quantitatively transformed overnight into α,β-unsaturated amides **4a–d** (Table 2, Entries 1–7). With regard to the stereochemical outcome of this transformation, starting from either the *cis* or the *trans* derivatives only the (*Z*)-alkene was obtained whose stereochemistry was assigned on the basis of the results of NOE experiments. Note that derivatives **3a–d** afforded the corresponding α,β-unsaturated amides in the presence of both an electron-withdrawing or an electron-donating substituent on the *N*-phenyl group. Moreover, the planar-chiral derivatives **3e–h** (Table 2, Entries 8–11) remained unchanged after treatment with acid.

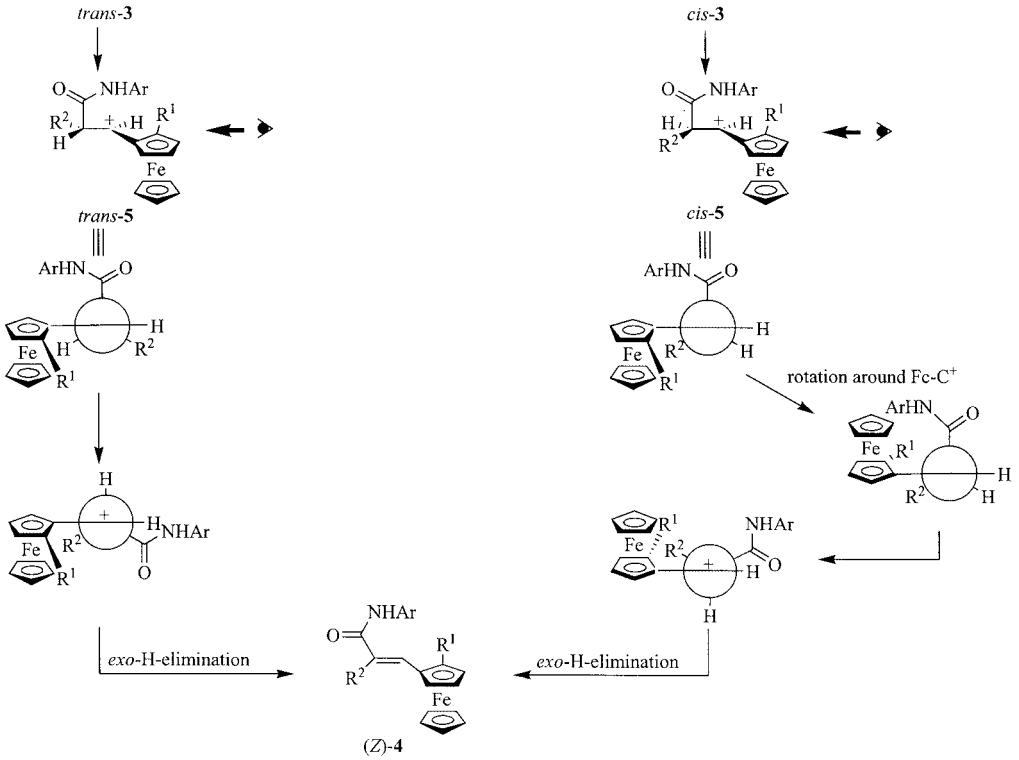
We have previously reported that enantiomerically pure central- and planar-chiral 5-ferrocenyloxazoline, in which the central chirality lies on the C-5 atom adjacent to the oxygen atom, are configurationally unstable and in the presence of traces of acid were partially epimerized at the C-5 atom of the oxazoline ring through a ring-opening/ring-closing mechanism.[13h] A similar acid-promoted ring-opening reaction occurs in β-lactams **3a–d** with the chiral C-4 atom bonded to both the nitrogen atom and the ferrocene moiety. This behavior can be attributed to the outstanding ability of ferrocene to stabilize an adjacent positive charge. In this case, the ring closure to the other diastereoisomer would not occur owing to the amount of strain in the four-membered ring and therefore the fate of the diastereomeric carbocations,[21] *trans*-**5** (R^1 = H) or *cis*-**5** (R^1 = H), is an elimination reaction (Scheme 1). It has been reported[7,22] that the β-hydrogen elimination reaction in ferrocenyl carbocations occurs through the *exo* mode; therefore the *trans*-β-lactams **3a–d** afford the (*Z*)-alkenes **4a–d**. In order to explain the formation of the same alkenes starting from

Table 2. Acid-induced stereoconvergent transformation of 4-ferrocenyl-β-lactams **3** into α,β-unsaturated amides **4**.



Entry	β-Lactam **3**	*cis*/*trans* configuration	Amide **4**	X	R^1	R^2	Yield [%][a]
1	**a**	*cis*	**a**	OCH_3	H	OPh	quantitative
2	**a**	*trans*	**a**	OCH_3	H	OPh	quantitative
3	**b**	*cis*	**b**	OCH_3	H	NPht	quantitative
4	**b**	*trans*	**b**	OCH_3	H	NPht	quantitative
5	**c**	*cis*	**c**	Cl	H	OPh	quantitative
6	**c**	*trans*	**c**	Cl	H	OPh	quantitative
7	**d**	*trans*	**d**	Cl	H	NPht	90[b]
8	**e**	*cis*	**e**	OCH_3	S-*p*-Tol	OPh	no reaction
9	**f**	*cis*	**f**	OCH_3	S-*p*-Tol	OAc	no reaction
10	**g**	*cis*	**g**	OCH_3	S-*p*-Tol	OBn	no reaction
11	**h**	*cis*	**h**	OCH_3	S-*p*-Tol	NPht	no reaction

[a] Yield of pure isolated products. [b] 10% of unreacted starting product.

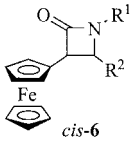


Scheme 1. Plausible explanation for the stereconvergent synthesis of α,β-unsaturated amides **4**.

the *cis*-β-lactams, rotation must occur around the ferrocene–C^+ bond to give the more stable carbocation[22] which by *exo* elimination gives the same (*Z*)-alkenes **4** (Scheme 1).

The stability of the planar-chiral derivatives *cis*-**3e**–**h** under acidic conditions can be attributed to the presence of the S-*p*-tolyl group in the *ortho* position of the ferrocene moiety, which could make the conformations of the *cis*-carbocations **5**, which lead to the (*Z*)-alkenes **4**, less favorable for steric reasons. Nevertheless, we cannot rule out alternative possibilities such as an inductive effect of the S-*p*-tolyl group or its possible hindrance which prevents a proton approaching the amide nitrogen atom.

To compare the stability of 4- and 3-ferrocenyl-β-lactams in acid, we treated compounds of the latter series, selected from our previous work[11] (**6**, Scheme 2), with *p*-toluenesulfonic acid (PTSA) under the same experimental conditions as used for the 4-ferrocenyl series in the present study. Compounds **6a**–**c**, containing only one Fc (ferrocenyl) group at C-3, remained unchanged, in contrast to compound **6d**, which carries two Fc moieties, one each at the C-3 and C-4 positions.

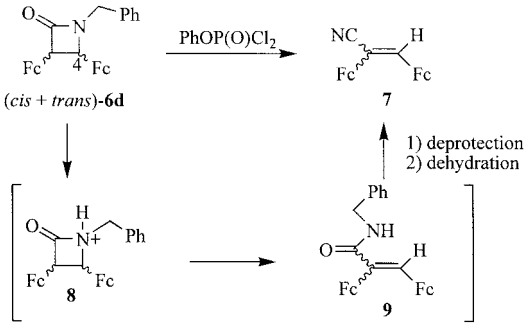


cis-**6**

6a: R^1 = Ph, R^2 = Ph
6b: R^1 = PMP, R^2 = *p*-NO_2-C_6H_4
6c: R^1 = CH_2Ph, R^2 = *p*-NO_2-C_6H_4
6d: R^1 = CH_2Ph, R^2 = Fc

Scheme 2.

In our previous work, we found that the 3,4-diferrocenyl-β-lactam **6d** was transformed into the alkene **7** in the presence of $PhOP(O)Cl_2$ (Scheme 3).[11] We can now explain this result through the N–C-4 fragmentation reaction of the ammonium salt **8**, which leads to **7** by deprotection and dehydration of the α,β-unsaturated amide **9** in the presence of phosphorus derivatives.[23]



Scheme 3. Ring-opening reaction of 3,4-diferrocenyl-β-lactam **6d**.

From these results we can infer that the presence of the ferrocenyl group in the 4-position of the β-lactam ring is a key feature in the acid-promoted ring-opening reaction.

Conclusions

The one-pot reaction between achiral or planar-chiral ferrocenylimines and substituted acetic acids allows the preparation of 2-azetidinones with a ferrocene substituent at the C-4 atom of the β-lactam ring. A study of the acid-induced ring-opening of the N–C-4 bond showed the stereoconvergent formation of (*Z*)-α,β-unsaturated amides. The notable stability of the planar-chiral derivatives in an

acidic medium could be a useful feature in possible biological applications. A comparison of the stability of 4- and 3-ferrocenyl-β-lactams toward PTSA revealed that the presence of the ferrocenyl group at the C-4 atom of the 2-azetidinone ring (**3a**–**d**, **6d**) is required for the transformation into the corresponding α,β-unsaturated amides (**4a**–**d**, **7**).

Experimental Section

General Methods: Reactions were conducted in oven-dried (120 °C) glassware under a positive pressure of argon. The transfer of anhydrous solvents or mixtures was accomplished with oven-dried syringes/septum techniques. THF was distilled from sodium/benzophenone prior to use and stored under argon. CH_2Cl_2 was passed through basic alumina and distilled from CaH_2 prior to use. Other solvents were purified by standard procedures. Light petroleum ether refers to the fraction with a boiling range of 40–60 °C. Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Thin-layer chromatography (TLC) was performed with plastic plates coated with (0.20 mm) silica gel 60 F_{254} or aluminium oxide 60 F_{254} neutral. Column chromatography was carried out with 70–230 mesh silica gel or 70–230 mesh aluminium oxide 90 active neutral. Preparative thick-layer chromatography was carried out with glass plates using a 1 mm layer of silica gel 60 PF_{254}. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, in $CDCl_3$ as solvent. Chemical shifts are reported on the δ scale and measured in ppm relative to residual $CHCl_3$ (δ = 7.26 ppm) for ^1H NMR and to the central line of $CDCl_3$ (δ = 77.0 ppm) for ^{13}C NMR spectra or to the C_6D_6 solvent residual peak (δ = 7.16 ppm) for ^1H NMR and to the central line of C_6D_6 (δ = 128.0 ppm). *J* values are given in Hz. ^{13}C NMR spectral assignments were based on the results of DEPT experiments. The manufacturer's software was used for DEPT, gradient-enhanced COSY, as well as for the inversed-detected gradient selected heteronuclear correlations gHMBC and gHSQC data analysis. Mass spectra (MS) were obtained using an electrospray ionization source (ESIMS). All the ESIMS spectra were performed by using MeOH as the solvent. $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. The originality of all compounds was checked by a CAS on-line structure search. Ferrocenylimines **1a**,**b**[14] and **1c**[13g] were prepared as described previously. Elemental analyses were performed using Flash EA1112 Automatic Elemental Analyzer CE instruments.

General Procedure for the Synthesis of β-Lactams 3: Freshly distilled $PhOP(O)Cl_2$ (0.6 mmol, 127 mg, 0.09 mL) was added to a solution of ferrocenylimine **1** (0.5 mmol), a substituted acetic acid ($R^2CH_2CO_2H$) (0.55 mmol) and Et_3N (1.5 mmol, 152 mg, 0.21 mL) in dry CH_2Cl_2 (10 mL) or C_6H_6 (10 mL). The mixture was then stirred at 30 °C or reflux temperature (see Table 1) until the starting imine had disappeared (TLC analysis; light petroleum ether/EtOAc, 10:3). The reaction mixture was then poured into water, the organic layer was separated, washed with satd. aqueous $NaHCO_3$, dried, filtered and concentrated under reduced pressure. The crude reaction mixture was carefully analysed by ^1H and ^{13}C NMR spectroscopy with the aim of determining the *cis*/*trans* ratio. Chromatography on deactivated neutral alumina (3%) afforded the desired β-lactam **3**.

4-Ferrocenyl-1-(4-methoxyphenyl)-3-phenoxy-2-azetidinone (3a): According to the general procedure, imine **1a** (160 mg) and phenoxyacetic acid (R^2 = OPh, **2a**) (84 mg), were allowed to react in CH_2Cl_2 at 30 °C for 18 h. ^1H NMR analysis of the crude reaction mixture showed the presence of *cis*-**3a**. Chromatography on deactivated neutral alumina (3%) (light petroleum ether/EtOAc, 10:3) afforded *cis*-**3a** as a yellow solid (81% yield, 0.405 mmol, 184 mg). M.p. 143–145 °C. IR (CCl_4): $\tilde{\nu}$ = 1757, 1508 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.78 (s, 3 H), 4.06 (s, 5 H), 4.18 (m, 2 H), 4.24 (m, 1 H), 4.30 (m, 1 H), 5.29 (d, *J* = 5.1 Hz, 1 H), 5.53 (d, *J* = 5.1 Hz, 1 H), 6.91 (d, *J* = 9.6 Hz, 2 H), 7.03 (t, *J* = 7.4 Hz, 1 H), 7.12 (d, *J* = 8.6 Hz, 2 H), 7.32 (m, 2 H), 7.49 (d, *J* = 9.6 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.7 (CH_3), 59.3, 68.1, 68.6, 69.1, 69.2, 69.25, 80.8 (CH), 81.5 (C), 114.6, 115.9, 120.9, 122.4, 129.8 (CH), 130.3, 157.2, 157.8, 164.0 (C) ppm. MS (ESI): *m*/*z* = 476 [M + Na$^+$]. $C_{26}H_{23}FeNO_3$ (453.31): calcd. C 68.89, H 5.11, N 3.09; found C 68.81, H 5.01, N 3.14. The same reaction was repeated in benzene at reflux for 5 h. ^1H NMR analysis of the crude reaction mixture showed the presence of *trans*- and *cis*-**3a** in a 0.8:1 ratio. Chromatography on deactivated neutral alumina (3%) (light petroleum ether/EtOAc, 10:3) afforded *trans*-**3a** (R_f = 0.60) as a yellow solid (27% yield, 0.135 mmol, 61 mg) and *cis*-**3a** (R_f = 0.47) as a yellow solid (33% yield, 0.165 mmol, 75 mg) in 60% overall yield. *trans*-**3a**: M.p. 184–186 °C. IR (CCl_4): $\tilde{\nu}$ = 1757, 1508 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.74 (s, 3 H), 4.17 (s, 5 H), 4.25 (m, 3 H), 4.42 (m, 1 H), 4.97 (d, *J* = 2.0 Hz, 1 H), 5.45 (d, *J* = 2.0 Hz, 1 H), 6.81 (d, *J* = 8.8 Hz, 2 H), 7.08 (t, *J* = 7.1 Hz, 1 H), 7.30–740 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4 (CH_3), 60.15, 66.5, 68.45, 68.7, 69.8, 70.55 (CH), 81.6 (C), 87.0, 114.2, 116.3, 119.2, 122.6, 129.7 (CH), 130.5, 156.5, 157.5, 163.5 (C) ppm. MS (ESI): *m*/*z* = 476 [M + Na$^+$], 454 [M + H$^+$]. $C_{26}H_{23}FeNO_3$ (453.31): calcd. C 68.89, H 5.11, N 3.09; found C 68.92, H 5.15, N 3.05.

4-Ferrocenyl-1-(4-methoxyphenyl)-3-phthalimido-2-azetidinone (3b): According to the general procedure, imine **1a** (160 mg) and *N*-phthaloylglycine (R^2 = NPht, **2b**) (113 mg) were heated to reflux in benzene for 2 h. ^1H NMR analysis of the crude reaction mixture showed the presence of *trans*- and *cis*-**3b** in a 2.3:1 ratio. Chromatography on deactivated neutral alumina (3%) (light petroleum ether/EtOAc, 10:3) afforded *trans*-**3b** (R_f = 0.26) as a yellow solid (49% yield, 0.245 mmol, 124 mg) and *cis*-**3b** (R_f = 0.11) as a yellow solid (21% yield, 0.10 mmol, 53 mg) in a total yield of 70%. *trans*-**3b**: M.p. 208–211 °C. IR (CCl_4): $\tilde{\nu}$ = 1767, 1721, 1508 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.77 (s, 3 H), 4.21 (s, 5 H), 4.30 (m, 2 H), 4.36 (m, 1 H), 4.40 (m, 1 H), 5.27 (d, *J* = 2.2 Hz, 1 H), 5.61 (d, *J* = 2.2 Hz, 1 H), 6.83 (d, *J* = 8.6 Hz, 2 H), 7.34 (d, *J* = 8.6, 2 H), 7.78 (m, 2 H), 7.92 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.7 (CH_3), 58.4, 60.5, 66.4, 68.8, 68.9, 69.9, 70.3 (CH), 82.7 (C), 114.5, 120.2, 124.1 (CH), 130.7, 131.9 (C), 134.9 (CH), 157.0, 162.2, 167.4 (C) ppm. MS (ESI): *m*/*z* = 529 [M + Na$^+$]. $C_{28}H_{22}FeN_2O_4$ (506.09): calcd. C 66.42, H 4.38, N 5.53; found C 66.53, H 4.27, N 5.58. *cis*-**3b**: M.p. 195–200 °C. IR (CCl_4): $\tilde{\nu}$ = 1763, 1721, 1508 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.85 (s, 3 H), 3.92 (m, 2 H), 3.99 (m, 1 H), 4.05 (s, 5 H), 4.14 (m, 1 H), 5.38 (d, *J* = 5.4 Hz, 1 H), 5.49 (d, *J* = 5.4 Hz, 1 H), 6.99 (d, *J* = 8.5 Hz, 2 H), 7.67 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.55 (CH_3), 58.3, 58.9, 65.7, 67.9, 68.6, 68.9, 69.5 (CH), 81.8 (C), 114.3, 121.3, 123.4 (CH), 130.2, 131.4 (C), 134.2 (CH), 157.2, 161.3, 168.0 (C) ppm. MS (ESI): *m*/*z* = 529 [M + Na$^+$]. $C_{28}H_{22}FeN_2O_4$ (506.09): calcd. C 66.42, H 4.38, N 5.53; found C 66.39, H 4.41, N 5.49.

1-(4-Chlorophenyl)-4-ferrocenyl-3-phenoxy-2-azetidinone (3c): According to the general procedure, imine **1b** (162 mg) and phenoxyacetic acid (R^2 = OPh, **2a**) (84 mg) were allowed to react in CH_2Cl_2 at 30 °C for 24 h. ^1H NMR analysis of the crude reaction mixture showed the presence of *trans*- and *cis*-**3c** in a 1:14 ratio. Chromatography on deactivated neutral alumina (3%) afforded

trans- and *cis*-**3c** in a total yield of 5%. The same reaction was repeated in benzene at reflux for 24 h. ^{1}H NMR analysis of the crude reaction mixture showed the presence of *trans*- and *cis*-**3c** in a 5.6:1 ratio. Chromatography on deactivated neutral alumina (3%) (light petroleum ether/EtOAc, 10:1) afforded *trans*-**3c** (R_f = 0.46) as a yellow solid (61% yield, 0.305 mmol, 139 mg) and *cis*-**3c** (R_f = 0.27) as a yellow solid (11% yield, 0.055 mmol, 25 mg) in a total yield of 72%. *trans*-**3c**: M.p. 177–179 °C. IR (CCl_4): $\tilde{\nu}$ = 1763, 1488 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.19 (s, 5 H), 4.27 (m, 2 H), 4.29 (m, 1 H), 4.45 (m, 1 H), 5.00 (d, J = 2.1 Hz, 1 H), 5.51 (d, J = 2.1 Hz, 1 H), 7.06 (t, J = 7.1 Hz, 1 H), 7.23 (m, 2 H), 7.28–7.41 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 59.3, 68.9, 69.5, 69.6, 70.1, 70.4, 80.8 (CH), 81.5 (C), 116.0, 120.1, 122.65, 129.4, 129.9 (CH), 130.2, 135.7, 157.7, 164.3 (C) ppm. MS (ESI): m/z = 480 [M + Na$^+$]. $C_{25}H_{20}ClFeNO_2$ (457.05): calcd. C 65.60, H 4.40, N 3.06; found C 65.49, H 4.43, N 3.12. *cis*-**3c**: M.p. 153–155 °C. IR (CCl_4): $\tilde{\nu}$ = 1765, 1493 cm^{-1}. ^{1}H NMR (400 MHz, C_6D_6): δ = 3.70 (m, 1 H), 3.78 (m, 1 H), 3.83 (m, 1 H), 3.87 (m, 1 H), 3.91 (s, 5 H), 4.54 (d, J = 5.2Hz, 1 H), 5.35 (d, J = 5.2 Hz, 1 H), 6.86 (d, J = 8.4 Hz, 3 H), 7.14 (br. t, J = 7.8 Hz, 2 H), 7.26 (br. d, J = 8.6 Hz, 2 H), 7.47 (br. d, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 60.0, 66.6, 68.5, 68.9, 69.9, 70.6, 81.6 (CH), 87.8 (C), 116.8, 118.8, 123.0, 127.8, 129.2 (CH), 130.0, 136.2, 158.0, 163.8 (C) ppm. MS (ESI): m/z = 480 [M + Na$^+$]. $C_{25}H_{20}ClFeNO_2$ (457.05): calcd. C 65.60, H 4.40, N 3.06; found C 65.68, H 4.35, N 3.11.

1-(4-Chlorophenyl)-4-ferrocenyl-3-phthalimido-2-azetidinone (3d): According to the general procedure, imine **1b** (162 mg) and *N*-phthaloylglycine (R^2 = NPht, **2b**) (113 mg) were heated to reflux in benzene for 5 h. ^{1}H NMR analysis of the crude reaction mixture showed the presence of *trans*-**3d**. Chromatography on deactivated neutral alumina (3%) (light petroleum ether/EtOAc, 10:3) afforded *trans*-**3d** as a yellow-brown solid (90% yield, 0.45 mmol, 230 mg). M.p. 183–185 °C (decomp.). IR ($CHCl_3$): $\tilde{\nu}$ = 1773, 1726 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.18 (s, 5 H), 4.28 (m, 1 H), 4.30 (m, 1 H), 4.34 (m, 1 H), 4.36 (m, 1 H), 5.32 (d, J = 2.9 Hz, 1 H), 5.69 (d, J = 2.9 Hz, 1 H), 7.24 (d, J = 8.9 Hz, 2 H), 7.36 (d, J = 8.5 Hz, 2 H), 7.79 (dd, J_1 = 5.5, J_2 = 3.0 Hz, 2 H), 7.92 (dd, J_1 = 5.5, J_2 = 3.0 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.2, 60.5, 66.0, 68.67, 68.73, 69.9, 70.2 (CH), 81.8 (C), 119.1, 123.9, 129.1 (CH), 129.7, 131.5 (C), 134.7 (CH), 135.6, 162.2, 167.0 (C) ppm. MS (ESI): m/z = 533 [M + Na$^+$]. $C_{27}H_{19}ClFeN_2O_3$ (510.04): calcd. C 63.49, H 3.75, N 5.48; found C 63.39, H 3.69, N 5.51.

(3*S*,4*S*)-1-(4-Methoxyphenyl)-3-phenoxy-4-[(*S*$_{Fc}$)-2-(*p*-tolylsulfanyl)-ferrocenyl]-2-azetidinone (3e): Compound **3e** was obtained from imine **1c** (220 mg) and phenoxyacetic acid (R^2 = OPh, **2a**) (84 mg) after 3 h and chromatography in 68% yield (0.34 mmol, 196 mg) as a yellow solid as the *cis* isomer. M.p. 172–174 °C. $[\alpha]_D^{20}$ = –114 (c = 0.515, $CHCl_3$). IR (CCl_4): $\tilde{\nu}$ = 1752, 1513 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.13 (s, 3 H), 3.83 (s, 3 H), 3.87 (s, 5 H), 4.4 (m, 1 H), 4.54 (m, 1 H), 4.55 (m, 1 H), 5.13 (d, J = 5.1 Hz, 1 H), 5.51 (d, J = 5.1 Hz, 1 H), 6.73 (d, J = 8.1 Hz, 2 H), 6.78 (d, J = 7.8 Hz, 2 H), 6.94 (m, 3 H), 7.03 (d, J = 8.8 Hz, 2 H), 7.13 (br. t, J = 7.8 Hz, 2 H), 7.60 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.8, 55.6 (CH_3), 57.4, 68.6, 68.9, 70.4, 75.4, 80.5 (CH), 85.2 (C), 114.5, 115.75, 121.85, 122.7, 126.55, 129.2, 129.5 (CH), 135.1, 135.6, 157.1, 157.7, 164.6 (C) ppm. Proton and carbon assignments were made on the basis of gCOSY and gHSQC experiments. The *cis* configuration was elucidated from the results of NOE experiments. Saturation of the resonance at δ = 5.13 ppm (3-H) produced a significant increase in the intensity of the 4-H signal at δ = 5.51 ppm and the aromatic proton signals at δ = 6.73 ppm (OPh). Saturation of the resonance at δ = 5.51 ppm (4-H) produced a significant increase in the intensity of the 3-H signal at δ = 5.13 ppm and the aromatic proton signals at δ = 7.60 ppm (2-H and 6-H of the 4-methoxyphenyl group). MS (ESI): m/z = 598 [M + Na$^+$]. $C_{33}H_{29}FeNO_3S$ (575.12): calcd. C 68.87, H 5.08, N 2.43; found C 68.91, H 5.04, N 2.39.

(3*S*,4*S*)-3-Acetoxy-1-(4-methoxyphenyl)-4-[(*S*$_{Fc}$)-2-(*p*-tolylsulfanyl)-ferrocenyl]-2-azetidinone (3f): Compound **3f** was obtained from imine **1c** (220 mg) and acetoxyacetic acid (R^2 = OAc, **2c**) (50 mg) after 2 h and chromatography in 53% yield (0.265 mmol, 144 mg) as a yellow solid as the *cis* isomer. M.p. 57 °C. $[\alpha]_D^{20}$ = –38 (c = 0.42, $CHCl_3$). IR (CCl_4): $\tilde{\nu}$ = 1763, 1508 cm^{-1}. ^{1}H NMR (400 MHz, C_6D_6): δ = 1.34 (s, 3 H), 2.0 (s, 3 H), 3.21 (s, 3 H), 3.73 (s, 5 H), 3.91 (dd, J_1 = 2.8 J_2 = 2.4 Hz, 1 H), 4.24 (dd, J_1 = 2.8, J_2 = 1.4 Hz, 1 H), 4.32 (dd, J_1 = 2.4, J_2 = 1.4 Hz, 1 H), 5.15 (d, J = 5.3 Hz, 1 H), 5.63 (d, J = 5.3 Hz, 1 H), 6.75 (d, J = 9 Hz, 2 H), 6.91 (d, J = 9.4 Hz, 2 H), 7.01 (d, J = 9 Hz, 2 H), 7.58 (d, J = 9 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, C_6D_6,): δ = 19.8, 20.7, 54.9 (CH_3), 56.6, 68.1, 68.8, 70.4, 75.5, 75.6 (CH), 77.4, 85.8 (C), 114.5, 122.0, 127.4, 127.8, 128.0, 129.9 (CH), 130.2, 135.6, 136.1, 157.6, 163.0, 167.9 (C) ppm. MS (ESI): m/z = 564 [M + Na$^+$], 541 [M]$^+$. $C_{29}H_{27}FeNO_4S$ (541.10): calcd. C 64.33, H 5.03, N 2.59; found C 64.28, H 5.09, N 2.51.

(3*S*,4*S*)-3-Benzyloxy-1-(4-methoxyphenyl)-4-[(*S*$_{Fc}$)-2-(*p*-tolylsulfanyl)ferrocenyl]-2-azetidinone (3g): Compound **3g** was obtained from imine **1c** (220 mg) and benzyloxyacetic acid (R^2 = OBn, **2d**) (92 mg) after 3 h and chromatography in 78% yield (0.39 mmol, 230 mg) as a yellow solid as the *cis* isomer. M.p. 62–64 °C. $[\alpha]_D^{20}$ = +59 (c = 0.40, $CHCl_3$). IR (CCl_4): $\tilde{\nu}$ = 1759, 1513 cm^{-1}. ^{1}H NMR (400 MHz, C_6D_6): δ = 1.95 (s, 3 H), 3.21 (s, 3 H), 3.74 (s, 5 H), 3.97 (dd, J_1 = J_2 = 2.5 Hz, 1 H), 4.11 (d, J = 12.0 Hz, 1 H), 4.15 (d, J = 5.1 Hz, 1 H), 4.25 (d, J = 12.0 Hz, 1 H), 4.36 (d, J = 2.5 Hz, 2 H), 5.14 (d, J = 5 Hz, 1 H), 6.72 (d, J = 8.2 Hz, 2 H), 6.77 (d, J = 8.9 Hz, 2 H), 7.0–7.1 (m, 5 H), 7.17 (d, J = 8.2 Hz, 2 H), 7.58 (d, J = 8.9 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ = 20.7, 54.9 (CH_3), 57.0, 68.98, 69.01, 70.7 (CH), 72.0 (CH_2), 75.7, 76.55 (CH), 82.2, 86.4 (C), 114.5, 122.2, 127.3, 127.5, 127.6, 128.3, 129.7 (CH), 130.4, 135.2, 136.7, 137.7, 157.5, 165.3 (C) ppm. Proton and carbon assignments were made on the basis of gCOSY and gHSQC experiments. The *cis* configuration was elucidated from the results of NOE experiments. Saturation of the resonance at δ = 5.14 ppm (4-H) produced a significant increase in the intensity of the 3-H signal at δ = 4.15 ppm and the aromatic proton signals at δ = 7.58 ppm (2-H and 6-H of the 4-methoxyphenyl group). MS (ESI): m/z = 612 [M + Na$^+$], 589 [M]$^+$. $C_{34}H_{31}FeNO_3S$ (589.14): calcd. C 69.27, H 5.30, N 2.38; found C 69.33, H 5.27, N 2.41.

(3*S*,4*S*)-1-(4-Methoxyphenyl)-3-phthalimido-4-[(*S*$_{Fc}$)-2-(*p*-tolylsulfanyl)ferrocenyl]-2-azetidinone (3h): Compound **3h** was obtained from imine **1c** (220 mg) and *N*-phthaloylglycine (R^2 = NPht, **2b**) (113 mg) after 5 h and chromatography in 73% yield (0.365 mmol, 230 mg) as a yellow-orange solid as the *cis* isomer. Crystallization of **3h** from Et_2O furnished suitable crystals for X-ray analysis. M.p. 117–120 °C. $[\alpha]_D^{20}$ = –99 (c = 0.50, $CHCl_3$). IR (CCl_4): $\tilde{\nu}$ = 1768, 1727, 1513 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.0 (s, 3 H), 3.73 (s, 3 H), 3.81 (s, 5 H), 4.17 (m, 1 H), 4.37 (m, 1 H), 4.44 (m, 1 H), 5.45 (d, J = 5.5 Hz, 1 H), 5.62 (d, J = 5.5 Hz, 1 H), 6.37 (d, J = 8.1 Hz, 2 H), 6.54 (d, J = 8.1 Hz, 2 H), 6.93 (d, J = 8.9 Hz, 2 H), 7.25 (br. m, 1 H), 7.49 (br. m, 3 H), 7.52 (d, J = 8.9 Hz, 2 H) ppm. ^{1}H NMR (600 MHz, C_6D_6): δ = 1.88 (s, 3 H), 3.255 (s, 3 H), 3.77 (s, 5 H), 3.85 (t, J_1 = J_2 = 2.6 Hz, 1 H), 4.24 (dd, J_1 = 2.4, J_2 = 1.5 Hz, 1 H), 4.68 (dd, J_1 = 2.7, J_2 = 1.5 Hz, 1 H), 5.38 (d, J = 5.7 Hz, 1 H), 5.58 (d, J = 5.7 Hz, 1 H), 6.43 (d, J = 8.0 Hz, 1 H),

6.7 (dd, J_1 = 5.4, J_2 = 2.9 Hz, 1 H), 6.80 (d, J = 8.9 Hz, 2 H), 6.89 (d, J = 8.0 Hz, 1 H), 7.15 (m, 2 H), 7.61 (d, J = 8.9 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 55.7 (CH_3), 57.8, 59.9 (CH), 66.1 (C), 68.6, 70.7, 71.0, 76.4 (CH), 83.8 (C), 114.6, 123.4, 124.0, 124.9 (CH), 129.2 (C), 129.4 (CH), 131.4, 133.7, 134.1, 135.3, 158.2, 163.1 (C) ppm. Proton and carbon assignments were made on the basis of gCOSY and gHSQC experiments. The *cis* configuration was elucidated from the results of NOE experiments. Saturation of the resonance at δ = 5.38 ppm (4-H) produced a significant increase in the intensity of the 3-H signal at δ = 5.58 ppm and the aromatic proton signals at δ = 7.61 ppm (2-H and 6-H of the 4-methoxyphenyl group). Saturation of the resonance at δ = 5.58 ppm (3-H) produced a significant increase in the intensity of the 4-H signal at δ = 5.38 ppm. MS (ESI): m/z = 651 [M + Na$^+$]. $C_{35}H_{28}FeN_2O_4S$ (628.11): calcd. C 66.88, H 4.49, N 4.46; found C 66.92, H 4.41, N 4.50.

General Procedure for the Synthesis of α,β-Unsaturated Amides 4: *p*-Toluenesulfonic acid (PTSA, 1.0 mmol, 190 mg) was added in one portion to a solution of β-lactam **3** (0.1 mmol) in CH_2Cl_2 (5 mL) at room temperature under nitrogen. The mixture was stirred overnight and then washed with satd. aqueous $NaHCO_3$ (3 × 10 mL) and brine. The organic layer was dried, filtered and concentrated under reduced pressure. The crude reaction mixture was analysed by ^{1}H NMR spectroscopy and then purified by chromatography (if necessary for the characterization) on deactivated neutral alumina (petroleum ether/EtOAc 5:1 or 1:1).

(*Z*)-3-Ferrocenyl-*N*-(4-methoxyphenyl)-2-phenoxy-2-propenamide (4a): Starting from *cis*-**3a** (45 mg), according to the general procedure, (*Z*)-**4a** was obtained in quantitative yield (44 mg) as a red solid. M.p. 176–179 °C. IR (CCl_4): $\tilde{\nu}$ = 3424, 1680, 1638, 1508 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.78 (s, 3 H), 4.06 (s, 5 H), 4.31 (m, 2 H), 4.48 (m, 2 H), 6.84 (br. d, J = 8.8 Hz, 2 H), 7.11 (m, 3 H), 7.36 (m, 2 H), 7.41 (br. d, J = 8.8 Hz, 2 H), 7.44 (s, 1 H), 7.81 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.45 (CH_3), 69.3, 70.53, 70.59 (CH), 75.2 (C), 114.1, 114.8, 121.7, 123.0, 126.4, 130.2 (CH), 130.6, 139.2, 156.1, 156.5, 161.1 (C) ppm. Proton and carbon assignments were made on the basis of gCOSY and gHSQC experiments. The (*Z*) configuration was elucidated from the results of NOE experiments. Saturation of the resonance at δ = 7.11 ppm (OPh) produced a significant increase in the intensity of the proton signals at δ = 4.06 (unsubstituted Cp ring) and 4.45 ppm (2-H and 5-H of the substituted Cp ring) and of the aromatic proton signal at δ = 7.41 ppm (OPh). Saturation of the resonance at δ = 4.45 ppm (2-H and 5-H of the substituted Cp ring) produced a significant increase in the intensity of the proton signals at δ = 4.06 (unsubstituted Cp ring) and 4.31 ppm (3-H and 4-H of the substituted Cp ring), the aromatic proton signal at δ = 7.11 (OPh) and the proton signal at δ = 7.44 ppm (CH=). MS (ESI): m/z = 476 [M + Na$^+$]. $C_{26}H_{23}FeNO_3$ (453.10): calcd. C 68.89, H 5.11, N 3.09; found C 68.80, H 5.01, N 3.12. Starting from *trans*-**3a** (45 mg), according to the general procedure, (*Z*)-**4a** was obtained in quantitative yield (43 mg) as a red solid.

(*Z*)-3-Ferrocenyl-*N*-(4-methoxyphenyl)-2-phthalimido-2-propenamide (4b): Starting from *cis*-**3b** (50 mg), according to the general procedure, (*Z*)-**4b** was obtained in quantitative yield (48 mg) as a red solid. M.p. 201–203 °C. IR ($CHCl_3$): $\tilde{\nu}$ = 3434, 1721, 1669, 1617, 1508 cm^{-1}. ^{1}H NMR (400 MHz. $CDCl_3$): δ = 3.785 (s, 3 H), 4.32 (s, 5 H), 4.46 (br. s, 4 H), 6.84 (br. d, J = 8.0 Hz, 2 H), 7.31 (br. s, 1 H), 7.41 (br. d, J = 8.7 Hz, 2 H), 7.87 (br. s, 3 H), 8.01 (br. s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.5 (CH_3), 71.3, 72.8, 72.9 (CH), 77.2 (C), 114.1 (CH), 118.3 (C), 122.6, 124.3 (CH), 130.4 (C), 132.0, 134.8 (CH), 141.0, 156.7, 161.6, 166.7 (C) ppm. MS (ESI): m/z = 507 [M + H$^+$], 506 [M]$^+$. $C_{28}H_{22}FeN_2O_4$ (506.09): calcd. C 66.42, H 4.38, N 5.53; found C 66.38, H 4.34, N 5.58. Starting from *trans*-**3b** (50 mg), according to the general procedure, (*Z*)-**4b** was obtained in quantitative yield (49 mg) as a red solid.

(*Z*)-3-Ferrocenyl-*N*-(4-chlorophenyl)-2-phenoxy-2-propenamide (4c): Starting from *cis*-**3c** (46 mg), according to the general procedure, (*Z*)-**4c** was obtained in quantitative yield (45 mg) as a red solid. M.p. 170–173 °C. IR (CCl_4): $\tilde{\nu}$ = 3414, 1684, 1633, 1518 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.06 (s, 5 H), 4.33 (m, 2 H), 4.48 (m, 2 H), 7.11 (m, 3 H), 7.26 (br. d, J = 8.8 Hz, 2 H), 7.38 (br. t, J = 8.0 Hz, 1 H), 7.46 (s, 1 H), 7.465 (br. d, J = 8.8 Hz, 2 H), 7.89 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 69.6, 70.96, 70.99 (CH), 75.2 (C), 115.0, 121.4, 123.4, 127.5, 129.2 (CH), 129.6 (C), 130.5 (CH), 136.3, 139.0, 156.2, 161.6 (C) ppm. Proton and carbon assignments were made on the basis of gCOSY and gHSQC experiments. The (*Z*) configuration was elucidated from the results of NOE experiments. Saturation of the resonance at δ = 7.11 ppm (OPh) produced a significant increase in the intensity of the proton signals at δ = 4.06 (unsubstituted Cp ring) and 4.48 ppm (2-H and 5-H of the substituted Cp ring) and the aromatic proton signals at δ = 7.38 ppm (OPh). Saturation of the resonance at δ = 4.48 ppm (2-H and 5-H of the substituted Cp ring) produced a significant increase in the intensity of the proton signals at δ = 4.06 (unsubstituted Cp ring) and 4.33 ppm (3-H and 4-H of the substituted Cp ring), the aromatic signal at δ = 7.11 ppm (OPh) and the proton signal at δ = 7.46 ppm (CH=). MS (ESI): m/z = 480 [M + Na$^+$], 457 [M]$^+$. $C_{25}H_{20}ClFeNO_2$ (457.05): calcd. C 65.60, H 4.40, N 3.06; found C 65.68, H 4.43, N 3.00. Starting from *trans*-**3c** (46 mg), according to the general procedure, (*Z*)-**4c** was obtained in quantitative yield (44 mg) as a red solid.

(*Z*)-3-Ferrocenyl-*N*-(4-chlorophenyl)-2-phthalimido-2-propenamide (4d): Starting from *trans*-**3d** (51 mg), according to the general procedure, (*Z*)-**4d** was obtained in 90% yield (46 mg) as a red solid. M.p. >300 °C. IR ($CHCl_3$): $\tilde{\nu}$ = 3430, 1722, 1665, 1508 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.21 (s, 5 H), 4.23 (t, J = 1.9 Hz, 2 H), 4.38 (t, J = 1.9 Hz, 2 H), 7.27 (d, J = 8.9 Hz, 2 H), 7.44 (br. s, 1 H), 7.47 (d, J = 8.9 Hz, 2 H), 7.88 (dd, J_1 = 5.5, J_2 = 3.2 Hz, 2 H), 7.91 (s, 1 H), 8.02 (dd, J_1 = 5.5, J_2 = 3.2 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 70.5, 72.3, 77.6 (CH), 80.12 (C), 122.1, 124.7, 129.3 (CH), 129.9, 130.5, 131.6, 132.3 (C), 135.3 (CH), 136.4 (C), 141.8 (CH), 162.1, 167.1 (C) ppm. MS (ESI): m/z = 533 [M + Na$^+$]. $C_{27}H_{19}ClFeN_2O_3$ (510.04): calcd. C 63.49, H 3.75, N 5.48; found: C 63.41, H 3.69, N 5.41.

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