Synthesis, stereochemistry and decomplexation of (η-arene)(η-cyclopentadienyl) iron(II) hexafluorophosphate complexes containing amino acid side chains. A route to N-arylamino acids

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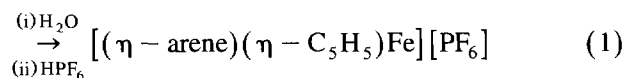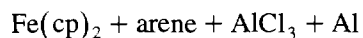
Received 6 February 1997; revised 10 May 1997

Abstract

[(η-Substituted arene)(η-cyclopentadienyl)Fe][PF$_6$] complexes with amino acid side chains on the arene ring have been prepared by reaction of [(η-haloarene)(η-cyclopentadienyl)Fe][PF$_6$] complexes with amino acids and amino acid esters under various conditions. Evidence is presented from ^{1}H- and ^{13}C-NMR spectroscopy for the existence of conformational isomers resulting from restricted rotation about the arene–nitrogen bond. Where a chlorine substituent is also present in the complexed arene, diastereoisomers can be separated by column chromatography. Decomplexation of the complexes is reported in strongly basic media or using 1,8-phenanthroline in light-catalysed reactions offering a new route to N-arylamino acids. © 1997 Elsevier Science S.A.

1. Introduction

We have recently reported a new microwave-mediated synthesis of [(η-arene)(η-cyclopentadienyl)Fe][PF$_6$] complexes. This method reduces reaction times for the ligand exchange process (Eq. (1)) from several hours to a few minutes and involves the simplest of apparatus [1].

$$Fe(cp)_2 + arene + AlCl_3 + Al$$

$$\xrightarrow[\text{(ii)}HPF_6]{\text{(i)}H_2O} [(\eta - arene)(\eta - C_5H_5)Fe][PF_6] \qquad (1)$$

In addition, we have shown that decomplexation occurs when mixtures of these complexes with flaked graphite are subjected to microwave dielectric heating [1]. These iron sandwich complexes are useful as arylating agents since the halogen in [(η-haloarene)(η-C$_5$H$_5$)Fe][PF$_6$]

complexes can be readily displaced by oxygen, nitrogen and sulphur nucleophiles (for a recent review see [2]).
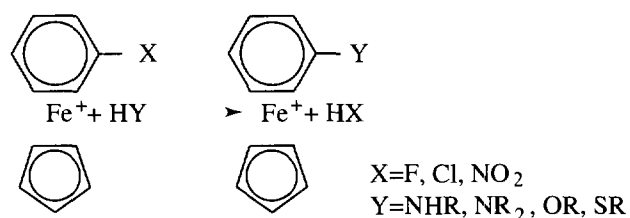
Such S$_N$Ar displacements have been used to synthesise a wide range of iron sandwich complexes. We have recently used this method to make a series of heterocyclic derivatives [3]. Relatively few [(η-arene)(η-C$_5$H$_5$)Fe][X] complexes have been made with chiral or potentially chiral substituents on the arene ring. [(±)-(η-1-Methylethylbenzene) (η-C$_5$H$_5$)Fe][PF$_6$] has been widely used as a catalyst in crosslinking of polymers [4]. Tyrosine substituted complexes linked via the phenolic oxygen have been prepared and used in the synthesis of cyclic antibiotics such as bouvardin and ristocetine [5]. More recently, Abd-El-Aziz and Epp [6] reported the preparation of a potentially chiral sandwich complex, [(η-C$_6$H$_5$CH(CN)SO$_2$Ph) (η-C$_5$H$_5$)Fe][PF$_6$].

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The optically active [(η-α-tetralonoxime)(η-C_5H_5)Fe] cation has been made by deprotonation of the [(η-tetralin)(η-C_5H_5)Fe] cation and subsequent reaction with menthyl nitrite [7]. Hydrolysis of the oxime gave the corresponding chiral ketone.

Although there have been no reports of N-arylation of amino acids using iron sandwich complexes, it has been recently shown that optically pure α-arylamino acids can be made by enantioselective substitution of fluorobenzenetricarbonyl chromium using Schiff Base derivatives of L-alanine methyl ester [8]. Hitherto, most syntheses of N-phenylamino acids have used S_N displacements in haloesters and halonitriles with aniline derivatives [9–12] as the nucleophiles. Another indirect approach involved the reaction of bis-silyl ketene acetals with nitrosobenzene followed by reduction of the product silylated α-hydroxyamino acid silyl esters to give N-phenylamino acids [13].

Earlier work on direct arylation was restricted to the use of aryl halides containing strongly electron withdrawing substituents which promote $S_N Ar$ displacements [14]. More recently, direct N-phenylation of amino acid esters has been reported using triphenylbismuth diacetate as the arylating agent and copper metal or copper(II) salts as catalysts [15]. Moderate to good yields were obtained but the method is rather expensive with a limited range of arylating agents and long reaction times. The method does not work for all amino acids.

The work reported here offers an alternative route to N-arylated amino acids using the readily synthesised [(η-halobenzene)(η-C_5H_5)Fe][PF_6] complexes as arylating agents.

2. Results and discussion

2.1. Synthesis of [(η-arene)(η-C_5H_5)Fe][PF_6] complexes with amino acid side chains

The following general route was used for the amino acid ester substituted complexes (PF_6 omitted for clarity).

[R'=H, Me, Et, Pr.]
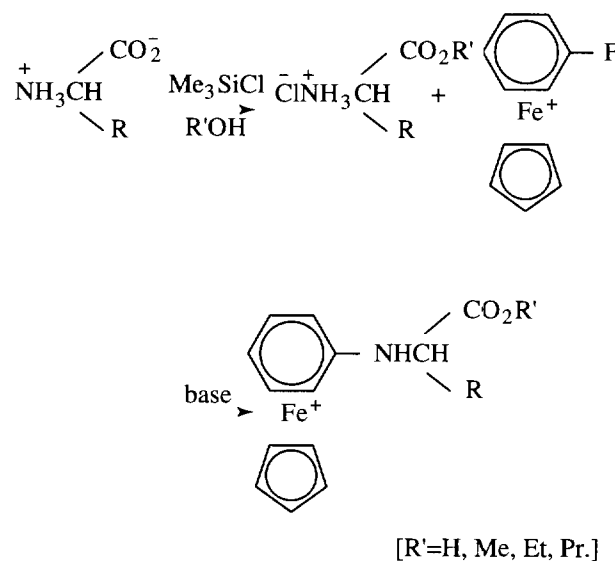
A variety of conditions were employed as indicated in

Table 1
Reaction conditions and yields for the synthesis of amino acid complexes of the type [(η-C_6H_5NHCH(R')CO_2R)(η-C_5H_5)Fe][PF_6]

Amino acid	R	Solvent/base	Temp. (°C)	Reaction time (h)	Yield (%)
Glycine	Me	pyridine	100	1.6	68
L-Alanine	H	MeCN/Et_3N	82	1.0	50
L-Alanine	Me	MeCN/Et_3N	82	0.5	61 [a]
L-Alanine	Me	MeOH/Et_3N	65	1.0	31 [b]
L-Phenylalanine	H	MeCN/Et_3N	82	1.5	40
L-Phenylalanine	Me	MeOH/K_2CO_3	65	1.0	63 [c]
L-Valine	Me	PrOH/Et_3N	97	1.0	62 [c,e,f]
L-Leucine	Me	pyridine	100	1.6	73
L-Isoleucine	H	DMF/Et_3N	120–130	1.0	47 [g]
L-Lysine	H	DMF/Et_3N	120–130	1.0	30
L-Lysine	Me	pyridine	100	4.0	18
D/L-Serine	Me	MeOH/Et_3N	65	2.0	62
L-Proline	Me	pyridine	100	2.5	78
L-Cysteine	Me	MeCN/Et_3N	82	1.5	63 [h]
L-Methionine	H	DMF/Et_3N	120–130	1.0	54 [i]
L-Methionine	Me	MeCN/K_2CO_3	82	1.0	69
L-Threonine	H	DMF/Et_3N	120–130	1.0	40 [j]
L-Glutamic acid	Et	MeOH/Et_3N	65	1.5	38 [k,l]
L-Aspartic acid	Me	MeCN/K_2CO_3	82	1.0	59 [m]
L-trans-Hydroxyproline	H	DMF/Et_3N	120–130	1.0	66
L-Tryptophan	H	DMF/Et_3N	120–130	1.0	43

[a] M^+ 300.5 (300); [b] one-pot reaction; [c] M^+ 345.7 (346); [d] isolated as the BPh_4 salt; [e] propyl group lost during reaction; [f] M^+ 328.2 (328); [g] M +327.9 (328); [h] M^+ 346.3 (346); [i] M^+ 345.7 (346); [j] M^+ 315.8 (316); [k] M^+ 358.5 (358); [l] monoethylester; [m] monomethylester.

Table 2
Yields [a] and mass spectral data for amino acid complexes of the type
$[(\eta\text{-}2\text{-}ClC_6H_4NHCH(R)CO_2H)(\eta\text{-}C_5H_5)Fe][PF_6]$

| Amino acid	Yield (%)	M^+
Glycine [b]	27	–
L-Alanine	52	–
L-Phenylalanine	31	398.3 (398)
L-Valine	51	349.6 (350)
L-Methionine	34	382.0 (382)
L-Glutamic acid I [c,d]	12	394.2 (394)
L-Glutamic acid II [c,d]	18	393.4 (394)

[a] Solvent/base system was DMF/Et_3N with reaction time of 1.0 h at 120–130°C. Methylesters used in all cases but amino acid complexes isolated except where stated.
[b] Na_2CO_3 as base, see Section 3.
[c] Diastereoisomers separated by column chromatography.
[d] Ester group remained intact.

Table 1, leading to moderate to good yields. In some cases (solvent methanol, base triethylamine) the amino acid esterification [16] and S_NAr displacement were combined to give a one-pot synthesis. These reactions are readily monitored since the fluorobenzene complex is only slightly soluble in methanol whereas the product dissolves readily. No evidence was found for the formation of the anisole complex from fluoride displacement by methanol reflecting the much greater nucleophilicity of the nitrogen nucleophile. It was noted that loss of the ester methyl or alkyl group sometimes occurred during reaction. This was particularly true for the 2-chloroarene complexes (Table 2), though the mechanism for this dealkylation is not clear. Only one of the chlorine substituents in the 1,2-dichlorobenzene complex was displaced in these reactions.
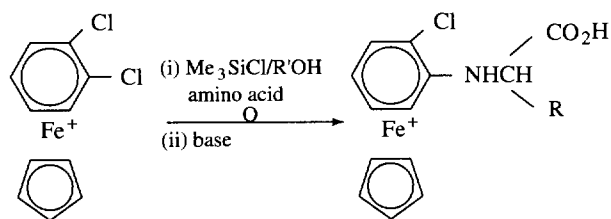

Direct N-arylation of the amino acids themselves was accomplished using DMF/Et_3N as the reaction medium (Table 1). In one case it was possible to separate, by careful chromatography, two diastereomeric forms of the L-glutamic acid derivative of the 2-chlorobenzene sandwich complex (Table 2). The nature of these diastereomers is discussed below.

2.2. Configurational analysis of iron sandwich complexes with chiral amine substituents

Chiral complexes formed by S_NAr displacement of chlorine from the chlorobenzene iron sandwich complex

by the chiral amine, α-methylbenzylamine have been reported from these laboratories [17]. Using the $S(-)$ isomer as the nucleophile, a product complex was formed whose ^{13}C-NMR spectrum showed apparent magnetic non-equivalence of both *ortho* and *meta* carbon atoms in the complexed ring. This was attributed to a long range effect of the chiral centre causing diastereotopic behaviour. A similar phenomenon was noticed for the ^1H spectrum where the *ortho* protons appeared as two distinct doublets at 5.72 and 5.67 ppm. Crucially, two signals appeared for both the CH and CH_3 carbons in the ^{13}C-NMR spectrum which suggests a rather different explanation of these observations. It has now been possible to N-phenylate S-$(-)$-α-methylbenzylamine by the following route:
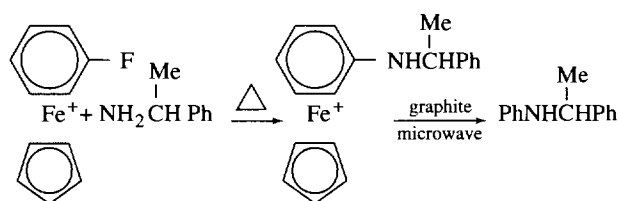
The ^1H-NMR spectrum of PhNHCH(Me)Ph shows only one doublet at 6.55 ppm for the *ortho* protons of the N-substituted phenyl ring. Similarly only one signal was found at 113.86 ppm for the *ortho* carbons in the ^{13}C spectrum. This suggests that an additional factor is causing the magnetic non-equivalence observed when the N-substituted ring is complexed with $Fecp^+$.

The normally rapid inversion of nitrogen is slowed down by the presence of electron withdrawing substituents. The increased barrier to inversion is due to increased p character of the bonds to nitrogen causing more strain in the transition state for inversion (for a discussion of inversion at nitrogen see [18]). The $CpFe^+$ moiety is generally thought to be equivalent in electron withdrawing power to two nitro groups and thus barriers to nitrogen inversion in N-substituted $[(\eta\text{-arene})(\eta\text{-}C_5H_5)Fe][PF_6]$ complexes could be increased ultimately leading to a chiral nitrogen atom and diastereoisomer formation. However, the presence of bulky substituents on nitrogen coupled with delocalisation of the lone pair should result in the nitrogen having more sp^2 character and hence the inversion barrier would be lowered. We are inclined to the view that the observed magnetic non equivalences are due to restricted rotation about the arene–nitrogen bond. Evidence for such restricted rotation in carbanion derivatives of $[(\eta\text{-arene})(\eta\text{-Cp})Fe]^+$ complexes has been reported [19].

Such rotational barriers could result in two conforma-

Table 3
^{1}H-NMR chemical shifts (δ) for selected $[(\eta\text{-}C_6H_5NHCH(R)CO_2CH_3)(\eta\text{-}C_5H_5Fe][PF_6]$ complexes

Amino acid	Solvent	H2,6	H3,5	H4	Cp	OCH$_3$	Other resonances
Glycine	[^{2}H$_6$]-Acetone	5.92d	6.20t	6.05t	5.03s	3.79s	4.24s, 4.23s(CH$_2$)
L-Alanine	D$_2$O ^{a}	5.40d	6.01brs	5.88t	4.88s	3.21s	3.90q(CH), 1.44d(CH$_3$)
		5.59d					
L-Isoleucine	D$_2$O:[^{2}H$_6$]-DMSO (10:1)	6.33d	6.74brs	6.61brs	5.64s	– ^{b}	4.36d(CH), 2.32brs(CH), 2.05m(CH$_2$)
		6.43d					1.77d(CH$_3$), 1.67t(CH$_3$)
trans-4-Hydroxy-proline ^{c}	D$_2$O:[^{2}H$_6$]-DMSO (10:1)	5.89d	6.47m	6.36t	5.37s	– ^{b}	5.07brs(H4'), 4.73t(H2'),4. 19dd(H5A'),
		6.00d					3.96d(H5B'), 2.89m(H3B')

^{a} Reference, sodium 3-(trimethylsilyl-1-propanesulfonate).
^{b} Amino acid complex.
^{c} Numbering of heterocyclic ring denoted with primes starting at carboxylate carbon. H3A' signal masked by solvent. Diastereotopic proton signals labelled A, B as in Ref. [22].

Table 4
^{13}C-NMR data ^{a} for $[(\eta\text{-}C_6H_5NHCH(R)CO_2Me)(\eta\text{-}C_5H_5)Fe][PF_6]$ complexes

Amino acid	Sol-vent	C1	C2	C3	C4	Cp	C1'	C2'	C3'	C4'	C5'	C6'	OCH$_3$	Other signals
Glycine	^{b}	– ^{d}	69.21	86.64	81.75	76.60	170.83	44.63					52.62	
	^{c}	126.75	65.09	82.77	77.69	72.64	166.96	45.95	–	–	–	–	49.79	–
L-Alanine			63.98	82.38		73.94								
	^{c}	– ^{d}			77.58		165.82	50.48	14.43	–	–	–	50.18	–
			64.11	82.61		74.03								
D/L-Phenyl-alanine	^{b}	125.41	68.56	86.22	81.14	76.09	169.53	57.52	37.89				55.14	130.06, 129.94 C2'',6''
		125.69	68.78	86.38	81.30	76.22	172.26	57.67	37.98	–	–	–		128.96, 128.89 C3'',5''
														127.36, 127.26 C4''
L-Leucine	^{b}	– ^{d}	69.28	86.40	81.63	76.42	173.74	54.32	41.70	25.29	21.72	22.93	52.88	–
			69.48	86.79	81.73	76.46	174.49	54.42	41.75	25.39	21.82	22.97		
D/L-Serine	^{c}	123.38	66.18			73.94								
				84.28	77.58		169.23	56.19	59.83	–	–	–	55.87	
		123.70	66.57			74.03								
L-Proline	^{b}		68.89	86.91	81.78	76.46							53.50	–
		124.64					172.29	61.27	31.17	23.94	49.79	–		
			69.30	87.03	81.91	76.58								
L-Methionine	^{e}		68.97										– ^{f}	15.58 (SCH$_3$)
		126.69		86.85	81.76	76.80	181.10	58.76	32.77	31.22	–	–		
			69.33											
L-Aspartic acid ^{e}		125.63	69.53	86.72	81.83	76.70	174.74	56.60	38.47	– ^{d}	–	–	53.81	–
				86.78										

^{a} The amino acid side chain is numbered using primes, starting at the amino acid carboxylate carbon. The uncomplexed aromatic carbons in D/L-phenylalanine are denoted by double primes.
^{b} Solvent [^{2}H$_6$]-DMSO.
^{c} Solvent [^{2}H$_6$]-acetone.
^{d} Not observed.
^{e} Solvent D$_2$O/[^{2}H$_6$]-DMSO (10:1).
^{f} Complex synthesised using propylester of L-methionine. Propyl group lost during reaction.

tional isomers with the residual lone pair adopting either an *exo* (I) or an *endo* (II) geometry.

(I)   (II)
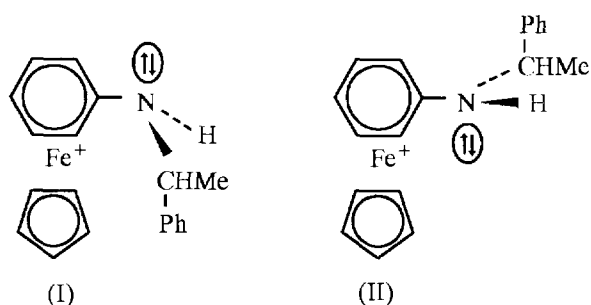
The stabilisation of such structures involving neutral arene substituents by neighbouring metallocene groups has been reviewed by Kerber [20]. One possibility is that conformer I is stabilised via lone pair overlap with ligand-based orbitals whilst in conformer II lone pair overlap with metal-based antibonding orbitals occurs. This situation is reminiscent of the stabilisation of ferrocenyl carbocations in which metal-based orbitals are the donors and the empty p orbital is the acceptor (for a concise review see [21]). However, the lone pair on the nitrogen will be much lower in energy than the antibonding levels on the metal. This would result in weak overlap. An alternative and more likely mode of stabilisation is that of coulombic attraction of the lone pair by the positive metal ion. Of particular note is the magnetic non-equivalence of the methine groups in conformations I and II. This non-equivalence would disappear if the nitrogen hybridisation became pure sp^2. The ^{13}C-NMR spectrum of the S-α-methylbenzylamine complex shows two distinct signals for the methine carbon, and suggests that the nitrogen has a distorted tetrahedral geometry lying between sp^3 and sp^2. Such stereochemical behaviour should be general for such N-substituted complexes.

To confirm the above hypothesis, the ^{13}C-NMR spectrum was run at 60° in [^{2}H$_6$]-DMSO. The two doublet signals which had been observed at 53.51, 53.40 ppm (CH) and 24.41, 24.37 ppm (CH$_3$), appeared as two sharp singlets which is the expected result of heating a mixture of rotationally linked conformers. It is worth noting that the C2,6 and C3,5 signals of the complexed arene are still doubled. These carbons are of course diastereomeric due to the chiral centre in the side chain. This phenomenon is independent of rotation about the carbon–nitrogen bond.

Further evidence for restricted rotation comes from the observation that when a strong acid, CF$_3$CO$_2$H, is added to the [^{2}H$_6$]-acetone solution of the complex, both doublets for the CH and CH$_3$ signals collapse to singlets due to protonation of the nitrogen which destroys conjugation with the complexed arene.

2.3. Amino acid complexes

Table 3 lists ^{1}H-NMR data for selected complexes. Two important features emerge from this data. The CH$_2$ signal for the glycine complex appears as two sharp singlets at 4.23 and 4.24 ppm ($J_{gem} \sim 0$). For the chiral amino acid complexes, the H2,6 protons of the complexed aromatic ring appear as two well separated doublets. Both these observations are consistent with the geometries described above.

^{13}C-NMR shift data appear in Tables 4–6. The signals for the complexed arenes were assigned by comparison with data of Sutherland [23] and the signals for the amino acid side chain were identified using published data [24]. The presence of isomers is immediately evident from the doubling of many signals in the ^{13}C spectra of these complexes. Thus for the phenylalanine complex (Table 4), two signals appear for every carbon atom except the ester methyl group. Of particular significance is the doubling of the chiral methine carbon

Table 5
^{13}C-NMR data [a] for [(η-2ClC$_6$H$_4$NHCH(R)CO$_2$Me)(η-C$_5$H$_5$)Fe][PF$_6$] complexes

Amino acid	C1	C2	C3	C4	C5	C6	Cp	C1'	C2'	C3'	C4'	C5'	OCH$_3$	Other signals
L-Phenylalanine	–[b]	89.89	87.06	80.82	85.51		78.50							138.86, 139.96 C1"
						67.26		–		56.12	29.85	–	–	–[c]	129.96, 130.44 C2",6"
		91.38	87.30	81.04	85.68		78.72							130.75 C3",C5", 128.23,
															128.57 C4"
L-Glutamic acid [d]	123.67	90.52	87.63	81.62	85.90	67.67	78.95	177.58	59.12	28.56	31.77	177.58	53.70	–
L-Glutamic acid [d]	124.38	90.69	87.59	81.10	85.81	67.42	78.84	177.15	58.95	27.80	31.75	177.15	53.73	–

[a] Solvent D$_2$O/[^{2}H$_6$]-DMSO (10:1).
[b] Not observed.
[c] Methyl group lost during reaction.
[d] Diastereomers separated by column chromatography.

Table 6
^{13}C-NMR data [a] for $[(\eta\text{-}C_6H_5NHCH(R)CO_2H)(\eta\text{-}C_5H_5)Fe][PF_6]$ complexes

Amino acid	C1	C2	C3	C4	Cp	C1'	C2'	C3'	C4'	C5'	C6'	Other signals
L-Alanine	126.46	68.71 68.93	86.72	81.56	76.66	–	56.00	19.56	–	–	–	–
L-Lysine [b]	127.27	68.47 68.56	86.63	81.22	76.18	180.00	58.20	– [c]	– [c]	25.00	43.53	–
L-Isoleucinene	127.30	68.19 69.31	86.77 86.85	81.58	76.64	180.86	65.03	38.30	26.50	12.07	16.79	–
L-trans-4-Hydroxy-pyroline	125.08	68.84 70.61	86.71	81.55	76.16	– [d]	64.27	31.73	70.29 70.61	58.24	–	–
L-Threonine	126.35	68.47 69.96	86.52 86.68	81.63	76.46	181.01 181.61	65.90	69.15	24.55 24.91	–	–	–
L-Tryptophan [e]	126.52	67.10	85.10 85.21	79.33	74.70	– [d]	– [d]	21.21	–	–	–	[f]126.57 C″, 110.91 C3″, 136.10 C3a″ 111.43 C4″, 120.90 C5″, 118.29 C6″, 123.77 C7″, 127.18 C7a″

[a] Solvent $D_2O/[^2H_6]$-DMSO (10:1).
[b] Solvent $[^2H_6]$-acetone.
[c] Signals masked by solvent.
[d] Not observed.
[e] Solvent $[^2H_6]$-DMSO.
[f] Indole moiety numbered in conventional manner starting at the heteroatom.

(C2′) signal in the amino acid residue. This can again be explained in terms of the conformational analysis previously described. For the 2-chlorobenzene complexes, a further stereochemical complication arises from the chiral nature of the sandwich moiety itself, resulting in two diastereoisomers. Careful chromatography of the L-glutamic acid complex (Table 2, Table 5) resulted in the separation of these diastereoisomers in yields of 12% and 18%.

Attempts to increase stereoselectivity using a chiral base, $(1R,2S)$-(−)-ephedrine, were unsuccessful for the L-alanine complex.

2.4. Decomplexation

Conditions for pyrolytic decomplexation using flaked graphite and microwave dielectric heating [1] proved too severe for the amino acid complexes and resulted in considerable decomposition. Moderate yields of N-arylated amino acids were obtained using either potassium tert-butoxide in DMF [25] or light-mediated decomplexation with 1,8-phenanthroline [25]. Decomplexation of the L-alanine complex using the latter method gave a 32% yield of N-phenylalanine. The ^{13}C-NMR spectrum of the product showed single resonances for all the carbons, unlike the iron sandwich complex pre-

cursor. This is further evidence for the proposed geometries for these complexes.

Overall, this method affords a useful alternative procedure for N-arylation of amino acids and has the advantage that a wide range of substituents on the arene ring can be employed as well as being relatively cheap and involving convenient reaction times.

3. Experimental

The amino acids were obtained from Aldrich Chemical Co. and used without further purification. NMR spectra were run using a JEOL EX270 spectrometer. Chemical shifts δ_H and δ_C were in ppm relative to TMS; coupling constants (J) in Hz; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Microanalyses were performed using in-house facilities (Perkin–Elmer, Series 2 CHN/O Analyser, Model 2400). Mass spectra were obtained from a Kratos MS50 Double Focusing mass spectrometer equipped with a FAB source and using a matrix of 3-nitrobenzyl alcohol. The masses of the cations were reported as M^+ values with accuracies of ±0.5 mass numbers. Calculated values appear in parentheses throughout. Microwave syntheses were performed with a conventional unmodified domes-

tic microwave oven (Sharp Easy Chef, Model R 5A53, 850 W) using the apparatus described in Ref. [1] and using a medium setting.

[(η-fluorobenzene)(η-cyclopentadienyl)Fe)][PF$_6$] and [(η-1,2-dichlorobenzene)(η-cyclopentadienyl)Fe][PF$_6$] were prepared in 25–30% and 40–45% yields, respectively, using the new rapid microwave-mediated ligand exchange reaction pioneered in these laboratories [1]. 10–25 g quantities of these complexes were obtained using irradiation times of 6–10 min [(η-C$_6$H$_5$-S-(−)α-methylbenzylamine)(η-cyclopentadienyl)Fe][PF$_6$] was prepared as previously described [17]. NMR data for this complex is presented below with coupling constants in parentheses and uncomplexed arene signals indicated by primes.

δ_H, [^{2}H$_6$]acetone: 7.62d (7.0) H2',6'; 7.46t (7.0), H3',5'; 7.35t (7.0) H4'; 6.57brs NH; 6.04m H3,5; 5.93t (5.4) H4; 5.72d (6.3); 5.67d (6.3) H2,6; 4.60s Cp; 1.54d (6.6) CH$_3$ (CH signal masked by Cp resonance).

δ_c, [^{2}H$_6$]acetone: 144.40 C1'; 129.94 C3',5'; 128.72 C4'; 127.31 C2'6'; 126.50, 126.43 C1; 86.73, 86.33 C3,5; 81.19 C4; 76.02 Cp; 69.41, 69.34 C2,6; 53.51, 53.41 CH; 24.41, 24.37 CH$_3$.

δ_c, [^{2}H$_6$] DMSO at 60°: 142.89 C1'; 128.27 C3',5'; 126.98 C4'; 125.69 C1',6'; 125.05 C1; 84.97, 84.64C3,5; 79.24C4; 74.17 Cp; 67.29,65.95 C2,6; 51.21 CH; 23.11 CH$_3$.

3.1. Synthesis of amino acid complexes

The amino acid methylester hydrochlorides were made in 80–95% by the elegant and rapid method of Brook and Chan [16]. These were usually prepared in a separate step except where methanol was the solvent, where a one-pot synthesis was devised. This reaction was readily monitored by the disappearance of the sparingly soluble fluorobenzene complex as it is converted to the soluble amino acid complex.

3.2. One-pot synthesis

L-Alanine (0.23 g, 2.5 mmol) was slurried with methanol (15 ml) and Me$_3$SiCl (0.81 g, 7.5 mmol) added. The mixture was stirred until a clear solution was formed. [(η-C$_6$H$_5$F)(η-C$_5$H$_5$)Fe][PF$_6$] (0.72, 2.0 mmol) was added followed by Et$_3$N (1.01 g, 10 mmol) and the whole refluxed for 1 h with stirring. The mixture was filtered and the filtrate evaporated to give an orange-brown solid. This was extracted with acetone (40 ml), the residue comprising triethylammonium salts. Filtration and evaporation gave the crude product (0.60 g, 69%). This was purified by dissolving in a minimum volume of CH$_2$Cl$_2$ and filtering into ether to give a yellow solid, 0.28 g, 31%. Found C, 40.23; H, 4.03; N, 2.69. Calcd. for C$_{15}$H$_{18}$F$_6$FeNO$_2$P: C, 40.48; H, 4.07; N, 3.15.

3.3. General synthetic procedure for amino acid or amino acid ester complexes

The amino acid or its ester hydrochloride (2.2 mmol) was slurried or dissolved in the appropriate solvent (15 ml) and the relevant base (6.0 mmol) added. [(η-halobenzene)(η-C$_5$H$_5$)Fe][PF$_6$] (2.0 mmol) was added and the whole refluxed for the times listed in Tables 1 and 2. On cooling, the reaction mixture was filtered into ether to give a golden brown oil. The ether was decanted and the residual oil washed several times with portions of ether (20 ml). The oil was then extracted with acetone (25 ml), filtered, and the filtrate chromatographed on neutral alumina, eluting in the first instance with acetone to remove any unreacted halobenzene complex. Further elution with methanol/water (5:1) and rotary evaporation at 60–70° gave the product as a glassy golden solid. Thus [(η-2-ClC$_6$H$_4$NHCH$_2$CO$_2$CH$_3$)(η-C$_5$H$_5$)Fe][PF$_6$] was prepared in 27% yield. Found C, 36.20; H, 3.29; N, 2.98. Calcd. for C$_{14}$H$_{15}$ClF$_6$FeNO$_2$P: C, 36.12; H. 3.25; N, 3.01.

For the reaction of L-glutamic acid monomethyl ester with the 1,2-dichlorobenzene complex, careful elution with MeOH/H$_2$O (5:1) resulted in the separation of two bands (Table 2) which yielded products whose ^{13}C-NMR spectra were slightly but significantly different (Table 5). As discussed above, two diastereomers are possible in this system but it is not possible to unequivocally identify these diastereomers from the spectroscopic data.

3.4. Decomplexation of amino acid complexes

3.4.1. Decomplexation using potassium tert-butoxide [25]

The glycine complex was made using glycine (0.45 g, 6.0 mmol) [(η-C$_6$H$_5$F)(η-C$_5$H$_5$)Fe][PF$_6$] (2.0 g, 5.5 mmol) and Et$_3$N (1.67 g, 16.5 mmol) in dry DMF (10 ml) at 120–130°C. The reaction was worked up as described above and the acetone extract evaporated then redissolved in dry DMF (5 ml). Potassium tert-butoxide (1.0 g, 8.9 mmol) was added to give a deep red solution. This was heated at 120–125°C for 1.25 h, cooled, and poured into ether (100 ml). The resultant brown precipitate was filtered off and air dried. It was then extracted with methanol (50 ml), filtered and evaporated to give a tan solid which after washing with acetone gave a product (0.44 g, 42%) whose FT–IR spectrum was identical with an authentic sample of PhNHCH$_2$CO$_2$K prepared by neutralisation of N-phenylglycine with KOH.

3.4.2. Decomplexation using 1,8-phenanthroline [25]

The L-alanine complex was made from L-alanine (0.54, 6.0 mmol) [(η-C$_6$H$_5$F)(η-C$_5$H$_5$)Fe][PF$_6$] (2.00 g,

5.5 mmol) and Et_3N (1.67 g, 16.5 mmol) in dry DMF (10 ml) at 120–130°C. The reaction was worked up in the usual manner and the acetone extract evaporated then dissolved in dry pyridine (30 ml). 1,8-Phenanthroline (2.97 g, 16.5 mmol) was added and the whole refluxed for 2 h whilst irradiating with a 500-W halogen lamp. On cooling, the mixture was rotary evaporated to give a red oil which was extracted with acetone (30 ml) and filtered. Isopropanol was added to the filtrate until a red precipitate of $[Fe(phen)_3[PF_6]_2$ was formed. This was filtered off and the filtrate reduced in volume to ~ 20 ml. This was then chromatographed on neutral alumina eluting first with i PrOH. The first band comprised unreacted 1,8-phenanthroline (1.4 g, 47% recovery). Any residual phenanthroline iron complex was washed off the column with methanol. Elution with $MeOH/H_2O/HOAc$ (7:2:1) gave on evaporation 0.9 g of a pink solid which contained some sodium acetate leached from the column. This was removed by treating with conc. HCl (2 ml), diluting with water (2 ml) followed by filtration and evaporation. The residue was extracted with MeOH and a little decolorising charcoal added. Filtration and evaporation gave 0.29 g off white N-phenylalanine (32%–62% conversion based on 1,8-phenanthroline). The structure was confirmed by ^{1}H- and ^{13}C-NMR run in D_2O containing $\sim 10\%$ NaOH.

δ_H, 7.18t ($J = 7.2$ Hz) H3,5; 6.74t (7.0) H4; 6.66d (7.2) H2,6; 3.79 q (6.8) CH; 1.33d (6.8). δ_C, 183.88 $-CO_2^-$, 149.10 C1, 130.88 C3,5, 119.83 C4, 115.60 C2,6, 56.09 CH, 19.97 CH_3.

3.5. Synthesis of N-phenyl-(S)-α-methylbenzylamine

S-($-$)-α-Methylbenzylamine (5.5 g, 45 mmol) and $[(\eta-C_6H_5F)(\eta-C_5H_5)Fe][PF_6]$ (2.0 g, 5.5 mmol) were mixed and heated at 100–110°C for 15 min with stirring. After cooling the mixture was added to ether (100 ml) whereupon $[\eta-(S)-PhNHCH(Me)Ph)(\eta-C_5H_5)Fe][PF_6]$ separated out as an orange-brown oil. This was washed well with ether, extracted with CH_2Cl_2 (30 ml) and filtered. Flaked graphite (4 g) was added to the filtrate and the mixture rotary evaporated. The resultant adsorbate was transferred to a porcelain crucible which was placed in a beaker lined with glass wool. The crucible lid was added and a flanged beaker containing solid CO_2 set in place over the reaction vessel as described in Ref. [1]. The whole was placed in a domestic microwave oven together with a beaker containing water (60 ml) to absorb excess radiation, and irradiated for 2.5 min on a high setting. On cooling the mixture was extracted with acetone (100 ml) and decolorising charcoal added. The mixture was filtered and evaporated to give the product (S)-PhNHCHMePh as a white solid (0.50 g, 46%).

δ_H, $[^2H_6]$-DMSO (alkyl substituted phenyl ring denoted by primes): 8.27brs NH; 7.7–7.2m H2'–6'; 7.00t

($J = 7.8$) H3,5; 6.55d (7.8) H2,6; 6.48t (6.0) H4; 4.39q (7.3) CH; 1.49d (7.3) CH_3.

δ_C, $[^2H_6]$-DMSO: 148.70 C1; 139.27 C1'; 128.78, 128.71 C2',3',5',6'; 128.40 C4'; 126.70 C3,5; 115.64 C4; 113.86 C2,6; 50.01 CH.

3.6. Attempted diastereoselective synthesis

L-Alanine (0.20 g, 2.24 mmol), $[(\eta-C_6H_5F)(\eta-C_5H_5)Fe][PF_6]$ (0.72 g, 2.00 mmol) and $(1R,2S)$-($-$)-ephedrine (0.91 g, 5.50 mmol) were added to MeCN (15 ml) and the whole refluxed for 2.5 h. After the usual work up and chromatographic separation, a product was obtained whose ^{13}C-NMR spectrum showed a 3:2 ratio of proposed conformers, I and II, an identical ratio to that obtained for non-chiral bases.

References

[1] Q. Dabirmanesh, S.I.S. Fernando, R.M.G. Roberts, J. Chem. Soc. Perkin Trans. 1 (1995) 743.
[2] D. Astruc, Topics Curr. Chem. 160 (1991) 47.
[3] S.I.S. Fernando, R.M.G. Roberts, J. Organomet. Chem. 474 (1994) 133.
[4] H.G. Gaube, Polym. Paint Colour J. 177 (1987) 582.
[5] J.R. Hamon, J.Y. Saillard, A. le Beuze, M. McGlinchey, D. Astruc, J. Am. Chem. Soc. 104 (1982) 7549.
[6] A.S. Abd-El-Aziz, K.M. Epp, Polyhedron 14 (1995) 957.
[7] M. Le Rudulier, C. Moinet, J. Organomet. Chem. 352 (1988) 337.
[8] M. Chaari, A. Jehni, J.-P. Lavergne, Ph. Viallefont, J. Organomet. Chem. 401 (1991) C10.
[9] M. Matell, Acta Chem. Scand. 7 (1953) 228.
[10] M. Julia, G. Tschernoff, Bull. Soc. Chim. Fr. (1958) 661.
[11] R.A. Jacobsen, J. Am. Chem. Soc. 67 (1945) 1996; ibid. 68 (1946) 2628.
[12] G. Banti, Gazz. Chim. Ital. 59 (1929) 819.
[13] T. Sasaki, K. Mori, M. Ohno, Synthesis (1985) 280.
[14] F. Sanger, Biochem. J. 39 (1945) 507.
[15] D.H.R. Barton, J.-P. Finet, J. Khamsi, Tetrahedron Lett. 30 (1989) 937.
[16] M.A. Brook, T.H. Chan, Synthesis (1987) 201.
[17] K. Bambridge, R.M.G. Roberts, J. Organomet. Chem. 401 (1991) 125.
[18] J.M. Lehn, Topics Curr. Chem. 15 (1970) 311.
[19] T.D. Turbitt, W.E. Watts, J. Chem. Soc. Perkin Trans. 2 (1974) 177.

[20] R.C. Kerber, J. Organomet. Chem. 254 (1983) 131.

[21] W.E. Watts, in: G. Wilkinson, F.A. Stone, E.W. Abel (Eds.), Comprehensive Organometallic Chemistry, Vol. 8, Pergamon Press, Oxford, 1982, Chap. 59.

[22] M.C. Reddy, B.P. Nagi Reddy, J. Ramakrishna, Spectrochim. Acta 41 (1985) 1229.

[23] B.R. Steele, R.G. Sutherland, C.C. Lee, J. Chem. Soc. Dalton Trans. (1981) 529.

[24] H.-O. Kalinowski, S. Berger, S. Braun, Carbon-13 NMR Spectroscopy, Wiley, Chichester, 1988, ch. 3, p. 227 et seq.

[25] R.A. Brown, S.I.S. Fernando, R.M.G. Roberts, J. Chem. Soc. Perkin Trans. 1 (1994) 197.