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Enantiomeric Excess Determination of Amino Acids with Chiral Cyclopalladated Ferrocenylimine

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Abstract: An efficient NMR determination of the enantiomeric excess of the amino acids can be achieved using chloro-bridged dimer R- (+)-{Pd [(η^5-C_5H_5)Fe (η^5-C_5H_3CMe=NAr)] (μ-Cl)}$_2$ (Ar=*p*-$CH_3C_6H_4$) (R-**1**).

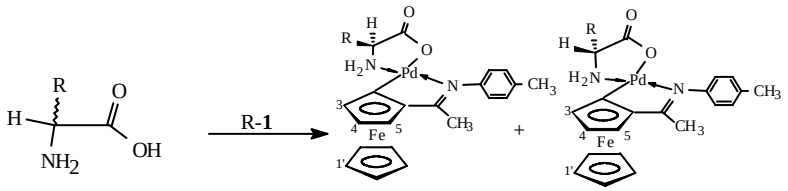
Keywords: Determination; e.e%; amino acids; chiral; cyclopalladated ferrocenylimine.

In recent years amino acids have received much attention because of their important and diverse biological functions and their application for chiral auxiliaries for asymmetric catalyst[1]. Enantiomers of the same amino acid often exhibit different biological activities. Therefore, much effort has done into developing practical methodologies for the enantiomeric excess determination of chiral amino acids[2]. Recent studies have shown that optically active cyclopalladated derivatives have been used for enantiomeric excess determination, optical resolution and determination of the absolute configuration of chiral substrates[3]. In this paper, we report in the first place an efficient method for the determination of e.e% values of three α-amino acids using chiral dimer R- (+)-{Pd [η^5-C_5H_5)Fe (η^5-C_5H_3CMe=NAr)] (μ-Cl)}$_2$ (Ar=*p*-$CH_3C_6H_4$) (R-**1**).

The chiral dimer R- (+)-**1** is readily available. Details concerning the resolution of R-**1** will be reported in another paper. The diastereomeric complexes **3a**-**3c** can be prepared by the method illustrated in **Scheme 1**. A slight excess of racemic α-amino acid was stirred with the chloro-bridged dimer R-**1** and Na_2CO_3 in methanol at room temperature. After evaporation of the solvent *in vacuo*, the crude residue was treated with CH_2Cl_2 and afforded the mixture of diastereomers **3** in 85.4-90.2% yields. Separation of diastereomers **3** was easily achieved by chromatographic or fractional crystallization techniques. In each preparation, the ^{1}H NMR spectra of the crude products were recorded prior to recrystallization to avoid the separation of diastereomers. In all cases, ^{1}H NMR spectra of the substituted ferrocenyl region showed that the chemical shift of the H-3 is indicating an excellent diastereomeric peak separation, since it was adjacent to the metallated carbon of the five membered organometallic ring and protruded into the stereochemical environment of the neighboring N,O chelation. For example, the resonance signals of H-3 in the diastereomers (R,S)-**3a** and (R,R)-**3a** were clearly identified as doublets at δ 4.64 and 4.69 ppm, respectively. So the signal of H-3

was also used as an indication of complete separation of the diastereomers. Selected ^{1}H NMR data and optical rotation values of **3a**-**3c** are given in **Table 1**.

Scheme 1



±**2** R, S-**3** R, R-**3**

R=-CH2 (CH2)2CH3 Norleucine (**a**)

-CH2CH (CH3)2 Leucine (**b**)

-CH2C6H5 Phenylalanine (**c**)

Table 1. ^{1}H NMR data (δ ppm), Optical rotation and EA data of compounds 3

Compound	$[\alpha]_D^{20}$	H-3	H-4	H-5	H-1'	C (%)	H (%)	N (%)
R, S-**3a**	1988.6	4.67d (1.6)	4.38t (2.0)	4.61d (2.0)	4.32s	54.40 (54.32)	5.35 (5.47)	4.98 (5.07)
R, R-**3a**	2186.3	4.71d (1.6)	4.37t (2.0)	4.60d (2.0)	4.30s	54.40 (54.32)	5.32 (5.47)	5.00 (5.07)
R, S-**3b**	2152.2	4.64d (2.0)	4.37t (2.0)	4.60d (2.4)	4.32s	54.13 (54.32)	5.57 (5.47)	4.80 (5.07)
R, R-**3b**	2414.9	4.69d (1.6)	4.38t (2.0)	4.61d (2.0)	4.31s	54.47 (54.32)	5.56 (5.47)	4.88 (5.07)
R, R-**3c**	1726.2	4.62d (2.0)	4.37t (2.0)	4.52d (2.0)	4.29s	57.10 (57.31)	4.60 (4.81)	4.65 (4.77)

The complexes R,S-**3** and R,R-**3** were treated with glacial acetic acid and lithium chloride. The amino acids were recovered without loss of optical activities. Owing to the high molecular weights of the chiral dimer, only small quantities of α-amino acids were required for NMR determinations.

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