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Note

Synthesis, properties and complexation of ($_pS$)-1-isocyano-2-methylferrocene, the first planar-chiral isocyanide ligand

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ABSTRACT

Reaction of enantiomerically pure, planar-chiral ($_pS$)-1-bromo-2-methylferrocene (**1**) with phthalimide in the presence of Cu_2O produces ($_pS$)-1-phthalimido-2-methylferrocene (**2**), quantitative reduction of which with hydrazine hydrate affords ($_pS$)-1-amino-2-methylferrocene (**3**) with >99% ee. Formylation of amine **3** followed by dehydration of the resulting ($_pS$)-1-formamido-2-methylferrocene (**4**) provides ($_pS$)-1-isocyano-2-methylferrocene (**5**), the first example of a planar-chiral isocyanide ligand, in a good yield. Isocyanide **5** reacts with PdI_2 to give the crystallographically characterized chiral complex *trans*-[PdI_2{($_pS$)-1-isocyano-2-methylferrocene}$_2$] (**6**). The redox behavior of **4**, **5**, and **6**, accessed by cyclic voltammetry, is discussed.

1. Introduction

Isocyanides, RN≡C, incorporating chiral substituents R are found in the structures of numerous natural products [1] and constitute important building blocks in contemporary polymer chemistry [2] and materials science [2,3]. To the best of our knowledge, all synthetic and naturally occurring organic isocyanides known to date exhibit *central* chirality. Recent progress in the chemistry of η^5-stabilized organometallic isocyanocyclopentadienides [4], such as isocyanoferrocene (FcNC, Fc = ferrocenyl group), has created an opportunity to pursue a new class of chiral isocyanide compounds featuring *planar*-chiral substituents immediately attached to the isocyano functionality. Substances of this type are particularly intriguing given the vast and ever-growing role of planar-chiral metallocene-based organometallics in synthesis, catalysis, and materials applications [5]. Herein, we describe the synthesis and properties of the first planar-chiral isocyanide ligand, namely ($_pS$)-1-isocyano-2-methylferrocene, as well as those of its crystallographically characterized *bis* adduct with PdI_2. Notably, a few *central*-chiral isocyanide compounds incorporating the ferrocenyl moiety are known [6,7].

2. Results and discussion

Aminoferrocene, $FcNH_2$, has been known for more than fifty years [8]. However, the tedious multi-step procedures and very low overall yields associated with its preparation had prevented further development of aminoferrocene's chemistry until the turn of the century when several improved syntheses of this compound emerged [9–11]. A particularly facile route to $FcNH_2$, published by Bildstein and co-workers in 1999 [9], involves a high yielding sequence ferrocene → lithioferrocene → iodoferrocene → *N*-ferrocenyl phthalimide and constitutes a greatly improved modification of Nesmeyanov's original procedure [12]. We applied the above method to the preparation of optically pure planar-chiral ($_pS$)-1-amino-2-methylferrocene and its ($_pR$)-congener (Scheme 1). Accordingly, refluxing enantiopure ($_pS$)-1-bromo-2-methylferrocene (**1**), the synthesis of which has been developed by Richards *et al.* [13], with phthalimide in the presence of Cu_2O afforded golden crystalline ($_pS$)-1-phthalimido-2-methylferrocene (**2**) in a 55% yield. Reductive cleavage of **2** with hydrazine monohydrate in EtOH quantitatively provided yellow ($_pS$)-1-amino-2-methylferrocene (**3**). Interestingly, compound **3** exhibits somewhat better air and thermal stability compared to $FcNH_2$. The ($_pR$) congener of **3** can be prepared from ($_pR$)-1-bromo-2-methylferrocene following the procedure identical to that described in Scheme 1.

Fig. 1 compares chiral HPLC traces of ($_pS$)-1-amino-2-methylferrocene and ($_pR$)-1-amino-2-methylferrocene with that of a nearly racemic mixture thereof. The excellent enantiomeric purities (>99% ee) of our samples of **3** and its ($_pR$)-analogue stem from the retention of ($_pS$) or ($_pR$) planar chiralities of their 1-bromo-2-methylferrocene precursors [13a], which in turn originate from the highly diastereoselective (100:1) ortholithiation of the corresponding *central*-chiral isopropyl-substituted ferrocenyloxazolines [14]. Notably, a non-racemic mixture of ($_pR$)- and ($_pS$)-1-amino-2-methylferrocene

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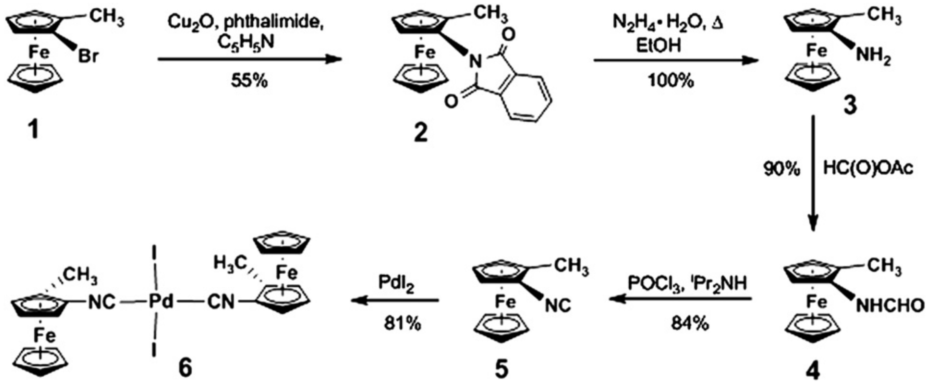

Scheme 1. Synthesis of compounds **2**–**6** from ($_pS$)-1-bromo-2-methylferrocene **1**.

with presumed 56% ee, prepared from the corresponding partially resolved ($_pR$)-methylferrocene-α-carboxylic acid in four steps in an overall 26% yield, has been previously described [15]. This procedure involved alkaline hydrolysis of the *N*-ferrocenylbenzylurethan intermediate product obtained via a Curtius rearrangement of ferrocenylcarbonyl azide in benzyl alcohol [15a].

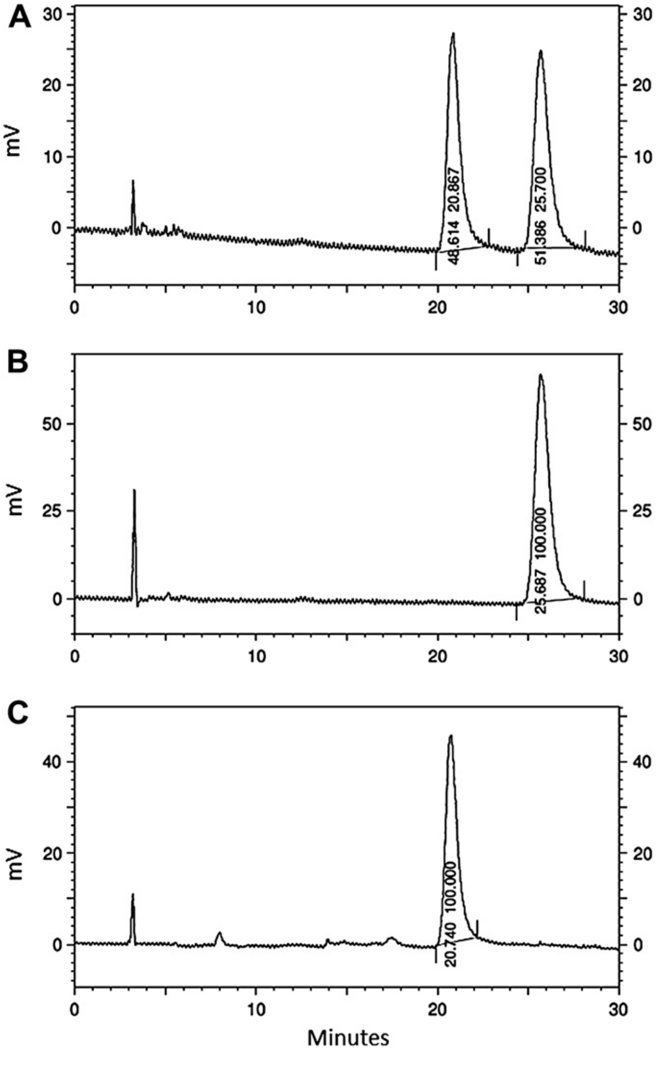

Fig. 1. Chiral HPLC traces (identical conditions) for *rac*-1-amino-2-methylferrocene (A), ($_pS$)-1-amino-2-methylferrocene (B), and ($_pR$)-1-amino-2-methylferrocene (C) synthesized in this work.

Formylation of **3** with excess acetic-formic anhydride under mild conditions gave yellow-orange ($_pS$)-1-formamido-2-methylferrocene (**4**) (Scheme 1). Formamide **4** exists as a mixture of two conformational isomers in dichloromethane solutions because of restricted rotation about the amide C–N bond [16]. The more abundant rotamer of **4** in solution features *trans* relationship of the hydrogen atoms within the H–N–C–H unit (or mutually *cis* orientation of the N–H and C═O bonds) as judged by the relatively large value of $^3J_{HH} = 12$ Hz associated with its formamido moiety. While, generally speaking, this is *not* the thermodynamically preferred orientation of the formamido group [17], such geometry is, in principle, well-suited for supporting intermolecular interactions between the molecules of **4** in solution through hydrogen bonding akin to the dimer formation postulated for solutions of FcNHCHO by Knox *et al.* [18]. Dehydration of **4** with 1.0 equiv of $POCl_3$ provided yellow-orange ($_pS$)-1-isocyano-2-methylferrocene (**5**) (Scheme 1). As in the case of the synthesis of FcNC [19], it is important to avoid using excess dehydrating agent to achieve a high yield of the isocyanide. The spectroscopic signatures of the isocyano group in **5** ($\nu_{CN} = 2127$ cm^{-1} in CH_2Cl_2 and δ (^{13}C) = 164.3 ppm in $CDCl_3$) are very similar to those documented for FcNC ($\nu_{CN} = 2122$ cm^{-1} and δ (^{13}C) = 163.9 ppm) under the same conditions [18,19].

Treatment of PdI_2 with 2 equiv of **5** affords air and thermally stable, red crystalline *trans*-[PdI_2{($_pS$)-1-isocyano-2-methylferrocene}$_2$] (**6**) in a high yield (Scheme 1). The frequency of the ν_{CN} band documented for **6** is 77 cm^{-1} higher compared to that observed for uncoordinated **5** which indicates that the isocyanide ligands in **6** function essentially as σ-donors. Similar changes in the energy of ν_{CN} occur upon coordination of a number of other aryl isocyanides to PdI_2 [20] and are caused by the fact that the lone pair of the terminal isocyanide carbon atom in R–N≡C is antibonding with respect to the N≡C bond [4].

Compound **6** crystallizes in the chiral space group *P*2$_1$. The asymmetric unit contains two crystallographically independent chiral molecules of **6** (A and B) that feature *trans* attachment of the ($_pS$)-1-isocyano-2-methylferrocene ligands to the Pd(II) center (Fig. 2). Selected bond distances and angles for both molecules are provided in Table 1. The metric parameters of their square planar "$PdI_2(CN)_2$" cores are quite similar to those documented for a number of other crystallographically characterized *trans*-PdI_2(CNAryl)$_2$ complexes [20]. All C–N–C angles are essentially linear (175–178°). For **6**, the isocyanide N–C bond lengths vary from 1.144(5) to 1.164(6) Å and are comparable to the corresponding value of 1.157(3) Å found for "free" isocyanoferrocene [21]. The mutual orientation of the two ferrocenyl groups with respect to the C–N–C–Pd–C–N–C axis is best described as *anticlinal* for molecule A and *antiperiplanar* for molecule B because the dihedral