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ATROPISOMERIC CHIRAL 4,4'-BIPYRIDINES

V. MAMANE[1], E. AUBERT[2], P. PELUSO[3], S. COSSU[4]

[1] *Universite de Lorraine, Organic Chemsitry, Vandoeuvre les Nancy, France*
[2] *Universite de Lorraine, Physical Chemsitry, Vandoeuvre les Nancy, France*
[3] *CNR, Istituto di Chimica Biomolecolare, Sassari, Italy*
[4] *Universita Ca' Foscari di Venezia, Scienze Molecolari e Nanosistemi, Venezia, Italy*

4,4'-Bipyridine is one of the most famous ligand used in supramolecular chemistry due to the presence of two donor atoms along a rigid structure. Considering the importance of chiral supramolecular networks in many applications such as asymmetric catalysis, it was surprising to find limited examples of chiral 4,4'-bipyridines in the literature. Based on our recent synthesis of polyhalogenated 4,4'-bipyridines [1], we report herein two methods for the preparation of enantiomerically pure 4,4'-bipyridines. The first method is based on the synthesis of a chiral tetrahalogenated 4,4'-bipyridine (substituted in 3,3',5,5') which after selective cross-couplings yields several atropisomeric derivatives. The enantiomers are separated by chiral HPLC and their absolute configurations are determined by X-ray diffraction (XRD) and electronic circular dichroism (ECD). Alternatively, the chiral tetrahalogenated 4,4'-bipyridine can be first enantioseparated and then involved in cross-coupling reactions without racemization [2, 3]. The second method concerns the direct functionalization in 3-position of an achiral tetrahalogenated 4,4'-bipyridine (substituted in 2,2',5,5') to generate atropisomeric chiral 4,4'-bipyridines; this second method allows for asymmetric synthesis. Chiral HPLC allows easy enantioseparation due to a butressing effect of substituent in 2-position [3] and the absolute configurations of the separated atropisomers are determined by XRD and ECD. In order to show the potential interest of these new chiral ligands for Metal Organic Frameworks (MOFs) synthesis and applications, some metal complexes including tetrahalogenated 4,4'-bipyridines and derivatives will be presented.

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HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY ENANTIOSEPARATION OF ATROPISOMERIC 4,4'-BIPYRIDINES ON IMMOBILIZED POLYSACCHARIDE-BASED CHIRALPAK IA AND CHIRALPAK IC: IMPACT OF SUBSTITUENTS AND ELECTRONIC PROPERTIES

P. PELUSO[1], V. MAMANE[2], E. AUBERT[3], S. COSSU[4]

[1] *CNR - Consiglio Nazionale delle Ricerche, Istituto di Chimica Biomolecolare, Sassari, Italy*
[2] *Universite de Lorraine, Organic Chemistry, Vandoeuvre les Nancy, France*
[3] *Universite de Lorraine, Physical Chemistry, Vandoeuvre les Nancy, France*
[4] *Universita Ca Foscari di Venezia, Scienze Molecolari e Nanosistemi, Venezia, Italy*

More than other techniques [1], high-performance liquid chromatography (HPLC) on chiral stationary phases (CSPs) is the most used for the enantioseparation of chiral compounds. Recently, this technique has been successfully applied to the preparation of pure enantiomers of new atropisomeric 4,4'-bipyridines [2-3]. Due to the novelty of the field, asymmetric procedures devoted to the preparation of optically pure 4,4'-bipyridines are not available yet in the literature. The 4,4'-bipyridyl system is one of the most used connectors between transition metal atoms for building metal organic frameworks (MOFs) due to its structural and topological characteristics. Chiral MOFs are of great interest in asymmetric catalysis and the access to enantiopure 4,4'-bipyridines is therefore highly required. Based on the chromatographic methods recently developed by us for the enantioseparation of atropisomeric 4,4'-bipyridines by using coated polysaccharide-based CSPs [4], we report herein new and efficient methods for the direct enantioseparation of 3,3',5,5'-tetrahalogenated, 2,2',3,3',5-pentahalogenated, 3,3'--dibromo-5,5'-disubstituted and 2,2',3,3'-tetrahalo-5-substituted 4,4'-bipyridines on two immobilized polysaccharide-based CSPs, Chiralpak IA and Chiralpak IC. The impact of structural modifications inside the bipyridyl skeleton on the separation behavior was investigated through a parallel evaluation of experimental data, such as retention (k) and separation factors (α), resolution (R_s) and density functional theory (DFT) computed molecular properties of the analytes. The semipreparative recoveries of optically pure atropisomers of the examined 4,4'-bipyridines provide valuable starting materials for the future preparation of homochiral MOFs.

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