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# New Recyclable Chiral Ligands (Soloshonok-Hamari Ligands) for Dynamic Kinetic Resolution (DKR) and (*S*)/(*R*) Interconversion of Unprotected α-Amino Acids.

## Chiral ligands (*S*)-**1** and (*R*)-**1**.

## CAS Registry Numbers:

161264-49-1, 161264-50-4, 163014-40-6, 163014-43-9

Dynamic kinetic resolution (DKR) of racemates is the most economical and widely used approach for large scale production of tailor-made α-amino acids (α-AAs) [1]. From the methodological standpoint, DKR is entirely dominated by biocatalytic approaches, while chemical methods are relatively underdeveloped. Recently, Soloshonok-Hamari group has developed a new method for DKR of unprotected a-amino acids using new generation of chiral recyclable ligands of type 1 [2]. This new approach can rival convenience, generality and overall economic efficiency of the biocatalytic approaches. Moreover, it was demonstrated that the same reaction principle can be readily applied for α-(S)/(R) interconversion of α-AAs, the methodological versatility unmatched by enzymatic reactions.

Oakwood is proud to present this brand new reagents for an advanced, chemical resolution procedure for preparation of α-AAs in enantiomerically pure form [2]. This approach is the first of its kind as it can be used on *N,C*-unprotected α-AAs and includes only two reaction steps, in situ enantioselective formation of Ni(II) complexes of α-AA Schiff bases followed by their disassembly furnishing the target enantiomerically pure α-Aas (Scheme 1). The whole process can be

conducted under operationally convenient conditions without recourse to inert atmosphere, controlled low temperature or especially purified reagents and solvents. The process features good-to-excellent chemical yields and virtually complete stereoselectivity (up to >99:1).

**Scheme 1.**

| Entry | Ligand 1 | rac-AA 2 | Yield (%) | Ratio (S,R):(S,S) | Time (h) |
|---|---|---|---|---|---|
| 1 | (S)-3 | Trp (a) | 95 | >97:3 | 24 |
| 2 | (S)-3 | Phe (b) | 94 | >97:3 | 24 |
| 3 | (S)-3 | Tyr (c) | 99 | >97:3 | 24 |
| 4 | (S)-3 | Met (d) | 97 | >97:3 | 3 |
| 5 | (S)-3 | Gln (e) | 92 | >96:4 | 3 |
| 6 | (S)-3 | Glu (f) | 92 | >96:4 | 10 |
| 7 | (S)-3 | Lys (g) | 91 | >96:4 | 4 |
| 8 | (S)-3 | Leu (h) | 94 | >96:4 | 24 |
| 9 | (S)-3 | Ala (i) | 97 | >97:3 | 24 |
| 10 | (S)-3 | Val (j) | 93 | >97:3 | 24 |
| 11 | (R)-3 | Tyr (c) | 98 | >97:3 | 24 |
| 12 | (R)-3 | Met (d) | 98 | >97:3 | 5 |
| 13 | (R)-3 | Ala (i) | 96 | >97:3 | 24 |

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The new generation of Soloshonok-Hamari ligands (*S*)- (*R*)-1 are inexpensive and can be quantitatively recycled and reused. Of particular importance is that the axial chirality in the ligands is un-racemizable, therefore the ligands can be recycled with uncompromised opitical purity and reused unlimited number of time for repetative production of α-amino acids. The method can be reliably reproduced on a large-scale.

Furthermore, as shown in Scheme 2, this approach can be easily applyed for (*S*)/(*R*)-interconversion of α-amino acids. This option is of particular imporance for preparation of *(R)* or D stereoisomers starting from very cheap natural (*S*)-α-amino acids.

**Scheme 2.**

The disassembly (Scheme 3) of intermediate Ni(II)-complexes can be also conducted under operationally convenient conditions affording the target α-amino acids isolated in good chemical yield. Moreover, chiral ligand (*S*)-1, can be easily recycled in nearly quantitative yield. Control of enantiomeric purity (99.9% ee) of the recovered reagent (*S*)-1 confirmed that the axial chirality of (*S*)-1 is not stereochemically compromised during the synhesis or disassembly procedures. Thus recovered (*S*)-1 was reused for repetitive DKR of other rac-α-amino acids.

**Scheme 3.**

In overall, application of the ligands (*S*)- and (*R*)-1 are is the first chemical method for preparation of enantiomerically pure α-amino acids that can rival supremacy of the enzymatic methods for economical efficiency and practicality. Thus, if you plan on synthesis of α-amino acids your choice is the Soloshonok-Hamari [2] ligands (*S*)- and (*R*)-1, most recent and advanced development in the area of α-amino acids preparation in enantiomerically pure form.

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**For other new approaches developed by Soloshonok group for preparation of α- and β-amino acids in enantiomerically pure form, see:**


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