Amino Acids (1992) 2: 189–190

Amino
Acids

Asymmetric synthesis of α-aminophosphonic acids

Short Communication

A. Alami[1], F. Ouazzani[1], M.-L. Roumestant[1], Ph. Viallefont[1], and A. el Hallaoui[2]

[1] URA 468, CNRS—Université Montpellier II, Montpellier, France
[2] Faculté des Sciences, FES, Maroc

Summary. The enantiospecific synthesis of several α-aminophosphonic esters starting from enantiomerically pure derivatives of phosphonic analogues of homoserine is reported.

Keywords: Amino acids – Asymmetric synthesis – α-Aminophosphonic acids

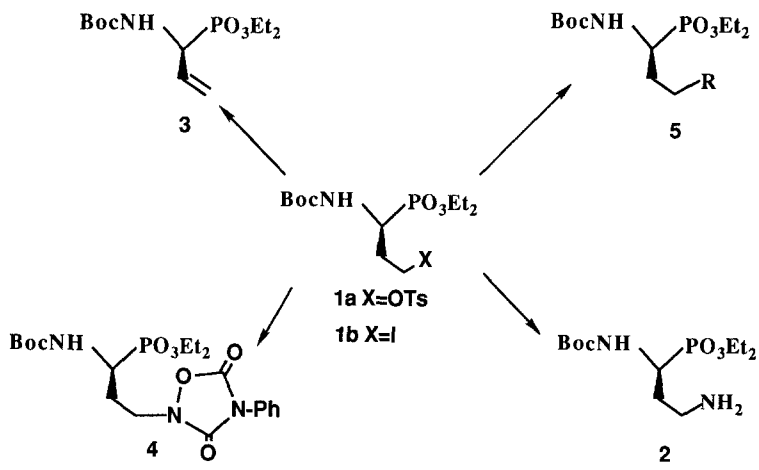
Introduction

The study of phosphorus analogues of the natural α-aminoacids has accelerated in the past ten years, due to the finding of molecules with useful biological activity: potent antibiotics: Atherton (1986), enzyme inhibitors: Giannoussis (1987) Logush (1988) Allen (1989), pharmacological agents: Mastalertz (1983) Hassal (1983). Their activity depends on their configuration. Both the resolution of racemates and their asymmetric syntheses have been reported: Dhawan (1987), Sting (1990) Hannessian (1990).

We have developed an efficient synthesis of several optically pure α-aminophosphonic acids using as chiral auxiliary 2-hydroxy pinan-3 one: Jacquier (1988) and recently have applied this methodology to the obtention of enantiomerically pure phosphonic analogues of homoserine derivatives: Ouazzani (1991). These compounds are precursors of choice for the synthesis of numerous α-aminophosphonic acids and we wish to report here on this work.

Results

The action of several nucleophiles on these derivatives led to the synthesis of phosphonic analogues of biologically active α-aminoacids. Action of sodium azide in dimethylformamide on **1a** (X = OTs) followed by hydrogenation led to the phosphonic analogue of DABA (diaminobutyric acid) **2** in 90% yield.



From the same starting product, phosphonic analogue of vinyl glycine **3** was prepared via the ethylthioderivative which was oxidised by sodium metaperiodate to give the sulfoxide in 90% overall yield. Thermolysis in *o*-dichlorobenzene afforded the phosphonic analogue of vinylglycine in 45% yield.

Reaction on the iodo derivative **1b** of 4-phenyl 1,2,4-oxadiazolidine-3,5-dione led to the phosphonic analogue of homoquisqualic acid **4**, potentially neuroactive compound.

Organocuprates reacted well with the iodo derivative **1b** to afford differently substituted aminophosphonic acids **5**.

References

1. Allen MC, Fuhrer W, Tuck B, Wade R, Wood JM (1989) J Med Chem 32: 1652–1661
2. Atherton FR, Hassal CH, Lambert RW (1986) J Med Chem 29: 29–36
3. Dhawan B, Redmore D (1987) Phosphorus Sulfur 32: 119–144
4. Giannousis PP, Bartlett, PA (1987) J Med Chem 30: 1603–1610
5. Hannessian S, Benani YL, Delorme D (1990) Tetrahedron Lett 31: 6465–6468
6. Hassall CH (1983) In: Hahn FE (ed) Antibiotics, vol 7. Springer, Berlin Heidelberg New York, pp 1–11
7. Jacquier R, Ouazzani F, Roumestant ML, Viallefont Ph (1988) Phosphorus Sulfur 36: 73–76.
8. Logusch EW, Walker DM, Mc Donald JF, Leo CG, Franz JE (1988) J Org Chem 53: 4069–4074
9. Mastalertz P, Kupczyk-Subotkowsica L (1983) Int J Pept Protein Res 21: 485–489
10. Ouazzani F, Roumestant ML, Viallefont Ph, El Hallaoui A (1991) Tetrahedron Asymmetry (in press)
11. Sting M, Steglich W (1990) Synthesis 2: 132–134

Authors' address: M. C. Roumestant, URA 468, CRNS—Université Montpellier II, F-34095 Montpellier Cedex 5, France.