Hence, **1** will react with N_2 to some extent in the solid state, and solid **2** releases its N_2 when placed under vacuum for several hours. Complex **2** is best formed by precipitation from solutions of **1** under N_2.[10]

NMR experiments reveal a temperature-dependent equilibrium between **1** and **2** in solution. The ^1H NMR spectrum of **1** prepared in the absence of N_2 contains a single C_5Me_5 resonance in the normal region.[32] After the sample is exposed to N_2, the NMR spectrum contains a small second peak at −0.6 ppm attributed to **2** (ratio of **1**:**2** is approximately 40:1). As the temperatue is decreased, the concentration of **2** increases, but complete conversion of **1** to **2** is not achieved.[33]

The high reactivity of Sm(II)[34–36] and the open coordination environment of $(C_5Me_5)_2Sm$[6,7,34,37] make this molecule one of the most likely f-element systems to form a complex with N_2. Definitive identification of the dinitrogen complex has been difficult due to the delicate balance in the equilibrium in eq 1.[38] The reactivity of the N_2 ligand in the unique planar $M(\mu\text{-}\eta^2\text{:}\eta^2\text{-}N_2)M$ environment in **2** is under study.

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Registry No. 1, 90866-66-3; **2**, 115244-63-8; N_2, 7727-37-9.

Supplementary Material Available: Tables of positional parameters, bond distances and angles, and thermal parameters (3 pages); table of observed and calculated structure factor amplitudes (15 pages). Ordering information is given on any current masthead page.

(32) δ 1–2 ppm. The peak position is concentration dependent.
(33) At −20 °C the ratio of **1** to **2** is approximately 3.5:1.
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(38) This is similar to the $(C_5Me_5)_2Sm + (C_5Me_5)_2Sm(C_5H_5) \rightarrow (C_5Me_5)_2Sm^{II}(\mu\text{-}C_5H_5)Sm^{III}(C_5Me_5)_2$ system.[22]

β-Lactams from Ester Enolates and Silylimines: Enantioselective Synthesis of (+)-PS-5

Gianfranco Cainelli* and Mauro Panunzio

Dipartimento Ciamician, University and C.S.F.M.-C.N.R. Via Selmi, 2 40126 Bologna, Italy

Daria Giacomini, Giorgio Martelli,* and Giuseppe Spunta

ICOCEA-C.N.R. Ozzano. Emilia. Italy

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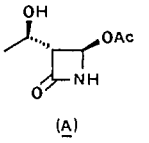
In the course of a general project on the stereocontrolled synthesis of β-lactam antibiotics, we[1] and others[2] recently have demonstrated the versatility of the ester-imine condensation in the production of the azetidin-2-one ring. Through this approach, we have been able to synthesize the optically active 3-(1′-hydroxyethyl)-azetidin-2-one (A),[1a] the key intermediate in the synthesis of thienamycin and related β-lactam antibiotics.[3a] In

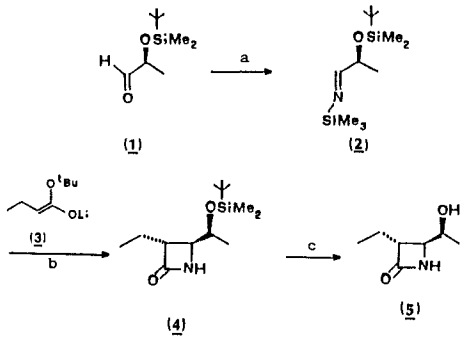


(A)

that synthesis (*S*)-(+)-ethyl 3-hydroxybutanoate was utilized to induce the correct absolute stereochemistry at carbon 3, of the β-lactam ring, in the ester enolate-imine condensation.

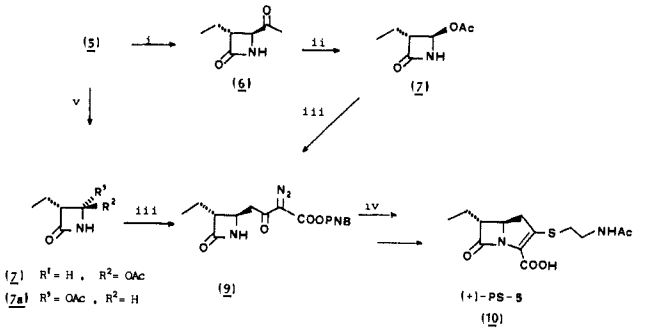
We now report a new enantioselective total synthesis of the carbapenem (+)-PS-5 **10**,[4] in which an optically active silylimine

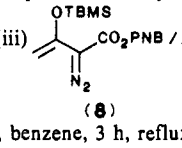
Scheme I[a]



[a] (a) $LiN(SiMe_3)_2$, THF, −40 °C. (b) THF, −78 °C, 15 min, room temperature, 8 h, 61% yield. (c) CH_3CN, HF catalyst, 90 min, 97% yield.

Scheme II[a]



[a] (i) Et_2O, H_2CrO_4, 2 h, room temperature, 76% yield. (ii) MCPBA, EtOAc, 3 h, 50 °C, 72% yield. (iii)  (iv) Reference 4h. (v) $Pb(OAc)_4$, $CaCO_3$, benzene, 3 h, reflux, 61% yield.

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is used for incorporating asymmetry in the ester-imine condensation. This new synthetic strategy relies on our recent report[1e] on the possibility of using enolizable silylimines in the production of the β-lactam ring.

We began by examining the reaction between the lithium enolate of *tert*-butyl butanoate **3** and the trimethylsilylimine **2**, readily available from (*S*)-lactic aldehyde **1**[5] and lithium hexamethyldisilylamide.[6] Treatment of *tert*-butyl butanoate with lithium diisopropylamide in tetrahydrofuran followed by **2** (−78 → 25 °C overnight) gave a 96/4 mixture of the β-lactam **4** ($[\alpha]^{20}_D$ +23.5° (*c* 1.2, $CHCl_3$)) and **4a**[7] in 61% yield.

The optical purity of **4** as well as its absolute configuration was determined by completing a formal total synthesis of (+)-PS-5 **10** as outlined in Scheme II.

Treatment of **4** with aqueous HF in acetonitrile[8] gave **5** (97%) ($[\alpha]^{20}_D$ +41.8° (*c* 1.14, $CHCl_3$)) which upon oxidation by chromic acid[9] afforded **6** (76%). Baeyer–Villiger oxidation of **6** gave **7** as a single trans isomer in 72% yield ($[\alpha]^{20}_D$ +100° (*c* 1.62, $CHCl_3$)). Reaction of **7** with silyl enol ether **8** and zinc chloride[10] gave trans β-lactam **9** (67.5%) ($[\alpha]^{20}_D$ +63.9° (*c* 1.14, $CHCl_3$, lit.[4h] $[\alpha]^{20}_D$ +64.7° (*c* 1, $CHCl_3$)). Since **9** has previously been prepared in configurationally pure form and has previously been converted to (+)-PS-5 **10**,[4h] this constitutes a formal total enantioselective synthesis of (+)-PS-5 **10**.

In an alternative way **9** was obtained in two steps from **5** through a fragmentation reaction by treating a benzene solution of **5** with lead tetracetate (2 equiv) in the presence of $CaCO_3$ (5 h, reflux)[11] to give **7** and **7a** in 61% as a (30/70) cis–trans mixture and subsequent displacement of the acetoxy group via the above described procedure to give β-lactam **9** in 62% yield as a single trans isomer. By this way the lack of stereoselectivity in the formation of the C-4 stereocenter of the acetoxy derivative appears unimportant since the C-4 center is equilibrated to the more stable 4*R* configuration.

The asymmetric 1,2-lk induction[12] by the electrophilic partner observed in the ester-imine condensation could be explained by assuming a coplanarity between the oxygen and the nitrogen atoms in the imine due to the chelation by lithium cations, present in the reaction medium, and attack of the enolate from the less hindered face of the diastereotopic plane of the imine group.

Work is in progress on mechanistic aspects on the origin of the stereoselectivity of the reaction as well as on the use of other chiral silylimines.

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Registry No. **1**, 87727-28-4; **2**, 116102-34-2; **4**, 116078-97-8; **4a**, 116181-12-5; **5**, 116078-98-9; **6**, 116179-68-1; **7**, 103775-02-6; **7a**, 103775-03-7; **8**, 93788-48-8; **9**, 83997-55-1; **10**, 67007-79-8; *tert*-butyl butanoate, 2308-38-5.

Supplementary Material Available: Preparation and physical data for compounds **4**, **4a**, **5**, **6**, **7**, **7a**, and **9** (4 pages). Ordering information is given on any current masthead page.

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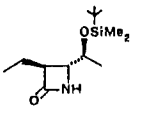
(7) Careful analysis of the 300 MHz ^{1}H NMR spectrum showed the presence of 4% of isomer **4a** which could be separated by flash chromatography and analyzed.



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Basic Polypeptides Accelerate the Hydrolysis of Ribonucleic Acids

Bernard Barbier and André Brack

Centre de Biophysique Moléculaire, CNRS
1A, Avenue de la Recherche Scientifique
45071 - Orléans Cedex 2, France

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Polycationic polypeptides containing arginine or lysine and hydrophobic amino acids are able to accelerate oligoribonucleotide hydrolysis. The greatest effect was observed when the polypeptides are structured in β-sheets.

When mixing an aqueous solution of alternating poly(Leu-Lys) to an aqueous solution of ApAp at pH 8, the solution becomes turbid reflecting the formation of a complex. The mixture was analyzed as a function of time by reversed-phase HPLC, after complete dissociation of the complex. Poly(Leu-Lys) stimulates strongly the rate of hydrolysis as compared to the control run in the absence of polypeptide (Figure 1). From the pseudo-first-order kinetics it can be calculated that the hydrolysis rate is increased by a factor of about 150. HPLC chromatograms show that the hydrolysis produces 2′:3′ cyclic AMP (A > p) together with A2′p and A3′p. This suggests that the polypeptide accelerates the classical alkaline hydrolysis of RNA[1] which is known to proceed in two steps: cleavage of the phosphodiester bond and subsequent formation of a 2′:3′ cyclic phosphate (A > p) followed by the opening of the cycle in a second step. The acceleration of the hydrolysis affects essentially the first step of the mechanism since it has been found that poly(Leu-Lys) increases the rate of A > p hydrolysis only by a factor 5 to produce A2′p and A3′p monomers in a 1.14 ratio in favor of A2′p.

The activity of poly(Leu-Lys) was extended to a mixture of oligo(A)s up to the 25-mer which is well resolved by HPLC on RPC5[2,3] and which can be cheaply obtained on a large scale from commercially available poly A.[4] In a preliminary publication,[5]

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