Chinese Chemical Letters Vol. 12, No. 6, pp. 497 – 498, 2001

The Synthesis of a Novel Phosphorus Containing Antigen

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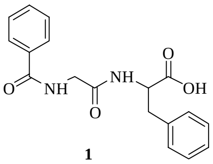
Abstract: Antigen **12**, containing a phosphonyl peptide hapten with free C-terminal carboxylic group, was synthesized by 11 reaction steps. The design of the hapten was based on the transition state of peptide hydrolysis catalyzed by carboxypeptidase A.

Keywords: Phosphonyl peptide, hapten, peptide hydrolysis.

The hydrolysis of peptide is one of the most important chemical processes in life chemistry. It is of great significance to study catalytic antibody, which is capable of catalyzing the hydrolysis on a specific peptide bond. In recent years, we have successfully synthesized some tetrahedral geometry analogues mimicking that of the hippuryl phenylalanine **1** hydrolyzing transition state catalyzed by carboxypeptidase A(CPA)[1,2], which is specific for cleavage of the C-terminal amino acid from an oligopeptide. Catalytic antibodies that mimic the CPA activity of peptidase were generated against antigen **2**.



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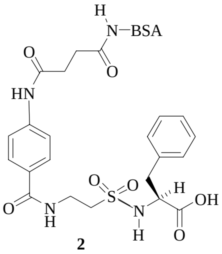

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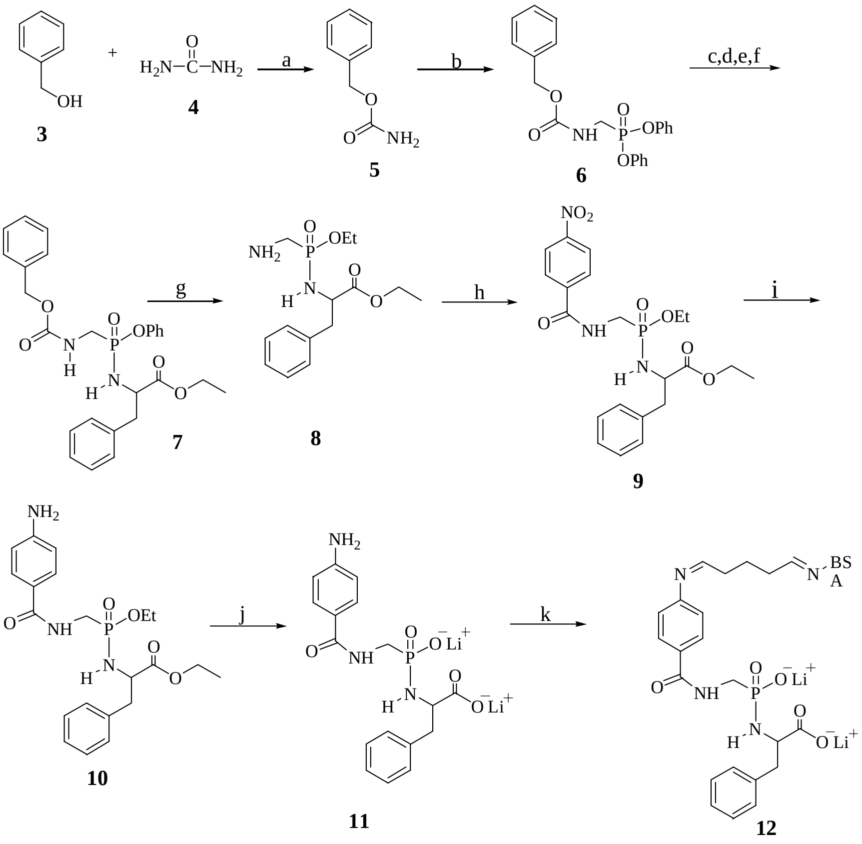
The synthesis of antigen containing phosphonyl peptide with free C-terminal carboxyl group has not been studied. In order to investigate the requirements for the generation of catalytic antibody that catalyzes peptide hydrolysis, we synthesized a novel antigen **12** from the modification of antigen **2** by replacing the sulfonyl group with a phosphonyl group.

The synthetic design is shown in **Scheme 1**. It is noted that the amino group, which next to the methylene group in compound **9,** was not derived from p-nitrobenzamide but from urea or **5**. Hydrogenation of **7**, catalyzed by Pd/C, gave **8**. It was observed that the ester exchange between phenyl ester in **7** and ethyl ester in **8** occurred during the hydrogenation. The exchange of ester group was probably due to the presence of bulky ethanol solvent.

Scheme 1



Reagents and conditions: a. Ni-resin, 150-180℃ 1 h[3]; b. Ac_2O, $(CH_2O)_X$, AcOH, $P(OPh)_3$[4]; c. LiOH, DMF/H_2O[5]; d. 2 N H_2SO_4, $CHCl_3/H_2O$; e. $SOCl_2$ in $CHCl_3$; f. PheOEt, $N(Et)_3$[6]; g. H_2/Pd-C in EtOH; h. p-NO_2PhCOCl; i. H_2/Pd-C in EtOH; j. LiOH, H_2O; k. 0.2% Glutaric dialdehyde/PBS.

References and note

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Received 6 November, 2000