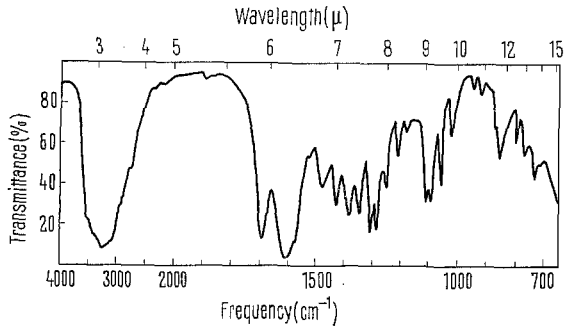

Fig. 1. IR-spectrum of lentinacin Na salt (in KBr).

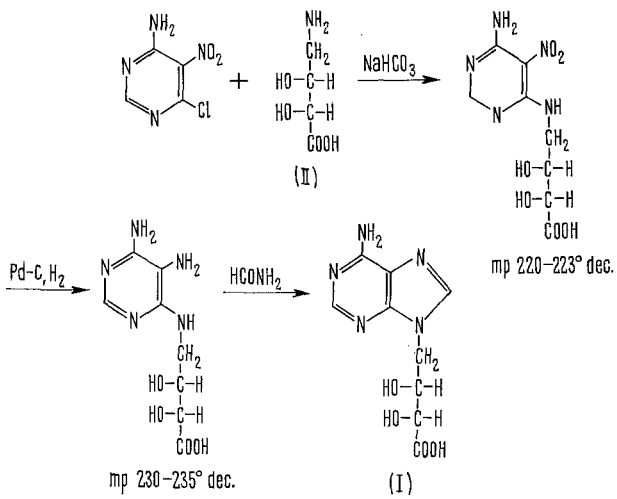

Fig. 2. Synthetic pathway of lentinacin.

Cleavage of lentinacin with 6*N* HCl (110 °C, 72 h) resulted in the liberation of glycine and a new amino acid, 4-amino-2, 3-dihydroxybutyric acid (II). The amino acid (II) was obtained as colourless pillars from water, mp 215–217° (dec.); $[\alpha]_D^{20} = +36.9°$ (C = 0.25 in H_2O, calculated from the ORD curve). Anal. ($C_4H_9O_4N$): C, 35.25; H, 6.68; N, 10.10. The structure of II was confirmed by the synthesis through 4-amino-4-deoxy-2, 3-*O*-isopropylidene-D-erythronic acid[3].

The diol linkage in lentinacin was also elucidated by periodate oxidation.

The degradation studies and spectrometric data indicate I for the structure of lentinacin.

Total synthesis of lentinacin was carried out by the procedure illustrated in Figure 2. The physicochemical properties of synthetic lentinacin coincided with those of natural lentinacin. As presented in the Table, synthetic lentinacin showed completely the same marked hypocholesterolemic effect as natural lentinacin in Sprague-Dawley rats. Its acute and chronic toxicities in experimental animals were extremely low.

Effect of lentinacin on serum total cholesterol levels in rats[a]

Supplement[b]	Serum total cholesterol level[c]		
	Day 0 mg/100 ml	Day 7 mg/100 ml	Decrease[d] %
None	83 ± 3.2	78 ± 3.1	6 ± 2.6
0.005% Lentinacin			
natural	83 ± 4.4	63 ± 4.4	25 ± 1.8
synthetic	83 ± 6.2	62 ± 5.3	25 ± 5.3
0.01% Lentinacin			
natural	83 ± 3.7	60 ± 2.1	28 ± 2.7
synthetic	83 ± 5.2	60 ± 5.0	28 ± 2.3

[a] Male rats of the Sprague-Dawley strain weighing 140–160 g. [b] Lentinacin was supplemented as sodium salt to a commercial stock diet purchased from Japan CLEA Company. [c] Mean values of 5 rats ± S.E. Total cholesterol was determined by the modified method of ZAK[4]. [d] $\left(1 - \frac{\text{Serum total cholesterol on Day 7}}{\text{Serum total cholesterol on Day 0}}\right) \times 100$.

It is very interesting that this newly found and synthesized adenine derivative, which was originally isolated from edible mushroom, shows high hypocholesterolemic activity. We are now investigating the biosynthetic pathway of lentinacin as well as the mechanism of its hypocholesterolemic action.

Zusammenfassung. Aus dem Speisepilz «Shiitake» (*Lentinus edodes*) wurde ein neues Adeninderivat isoliert und Lentinacin genannt. Seine chemische Struktur wurde mit 2(R), 3(R)-Dihydroxy-4-(9-adenyl)-buttersäure durch die vollständige Synthese identifiziert. Lentinacin senkt den Cholesterinspiegel bei Ratten.

I. CHIBATA, K. OKUMURA,
S. TAKEYAMA and K. KOTERA

Research Laboratories,
Tanabe Seiyaku Co. Ltd.,
Kashima-cho, Higashiyodogawa-ku,
Osaka (Japan), 20 August 1969.

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A New Peptide Coupling Agent – Phosphonitrilic Chloride

Various organic chlorophosphites are employed as coupling agents in peptide chemistry[1]. However, the related inorganic cyclic phosphonitrilic chloride (PNC) has not been evaluated in this aspect, although the chemistry of the compound has been studied for some years[2]. The commercial product contains mostly trimer with some tetramer and a trace of higher oligomers, yet may be fractionated to produce a pure reagent[3].

In a typical experiment, the triethylammonium salt of N-benzyloxycarbonyl-L-phenylalanine (1 mmole) was

stirred with tetrameric PNC (0.25 mmole) in chloroform at room temperature for 30 min, then freshly prepared L-alanine methyl ester (1 mmole) was added, and the mixture was allowed to stand for 24 h. Removal of the solvent, followed by standard washing procedures, gave N-benzyloxycarbonyl-L-phenylalanyl-L-alanine methyl ester: mp 130–131° (65%). Application of the nuclear magnetic resonance spectroscopy method for the determination of racemization revealed no DL dipeptide had formed in the reaction[4].

The reagent was tested on a broader scale by another synthesis of N-*t*-butoxycarbonyl-L-tryptophyl-L-methionyl-L-aspartyl-L-phenylalanine, made previously in a study on the C-terminal sequence of gastrin[5]. The di-, tri-, and tetrapeptide units were formed with the aid of PNC without undue difficulty. The physical properties of the intermediates were in agreement with the literature values. Recently, the trimeric PNC has been shown to produce other tetrapeptides in the glucagon series in moderate amounts[6].

The mechanism here may involve the initial formation of an active ester intermediate, followed by a displacement. Shortly after this investigation was begun, the use of commercial PNC in the formation of various amides and hydrazides, but not peptides, was described in a short note[7,8].

Zusammenfassung. Phosphonitrilchlorid, dessen Verbindung razemisierungsfrei erfolgt, kann als Reagens zur Synthese von Peptiden verwendet werden.

K. C. DAS, YU-YIN LIN, and B. WEINSTEIN

Department of Chemistry, University of Washington, Seattle (Washington 98105, USA), 11 August 1969.

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Synthesis of a Biologically Active Analog of Deamino-8-Arginine-Vasopressin which Does not Contain a Disulphide Bond[1]

The preparation of an analog of deamino-oxytocin, in which the disulphide bond is replaced by an ethylene linkage, was first published in 1967 by RUDINGER and JOŠT[2] who demonstrated that this compound possessed weak but definite oxytocin-like activity. This compound is called deamino-dicarba-oxytocin. Subsequently, we reported the synthesis of the same compound obtained by an independent route[3], and it was found that the rat uterotonic activity of this compound was almost ten-fold higher than that recorded previously[2]. By the same technique we have prepared the corresponding Lys[8]-vasopressin[4]. The preliminary biological activities of this peptide along with those of deamino-dicarba-oxytocin are given in the Table. We now report the synthesis and some preliminary biological activities of deamino-dicarba-Arg[8]-vasopressin.

[1] The tentatively proposed rules by the IUPAC-IBC were followed in the use of abbreviations: J. biol. Chem. *241*, 2491 (1966). Asu, α-aminosuberic acid; –OSu, N-hydroxysuccinimide ester; Aoc–, t-amyloxycarbonyl. The amino acids used were in the L-form.
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Biological activities of deamino-dicarba-Arg[8]-vasopressin and its related compounds

Compounds	Biological activities (IU/mg) Oxytocic (rat)	Depressor (fowl)	Pressor (rat)	Antidiuretic (rat)
Deamino-oxytocin[a]	803 ± 36	975 ± 24	1.44 ± 0.06	19
Deamino-dicarba-oxytocin[b]	96	52	< 0.25	1.78
Deamino-Lys[8]-vasopressin[c]	12 ± 0.5	61 ± 2	126 ± 2	301 ± 11
Deamino-dicarba-Lys[8]-vasopressin[d]	5.1	4.2	10.4	7.8
Deamino-Arg[8]-vasopressin[e]	27 ± 4	150 ± 4	370 ± 20	1300 ± 200
Deamino-dicarba-Arg[8]-vasopressin	11.9[f]	8[g]	23.0[f]	84.5[h]

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