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Synthesis of cyclopeptides from plants, fungi and sea animals*

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Abstract - A very flexible synthesis of non proteinogenic amino acids and an effective ring closure method for formation of macrolactams were elaborated. These methods are prerequisite for economical synthesis of cyclopeptides. The total syntheses of several cyclopeptides which had been isolated from plants, fungi and lower sea animals are described.

INTRODUCTION

The classification of the carbocyclic ring compounds as small, normal, medium and large has been derived from enthalpies, structure and "ease of formation". But this concept cannot be carried over to the characterisation of the overwhelming majority of ring compounds found in nature, all of which contain O, N, or S as endocyclic components. The difference is that in medium heterocyclic rings Pitzer strain does not appear to be chemically significant.

Twelve-membered "medium" rings with one or several heteroatoms as ring components are often closed easily and with high yields. Thus they behave similarly to large ring systems. The 13-membered ring 18 for example is formed with 80 % yield. In many cases high dilution is not required and it may be assumed that the most probable conformation of the linear educt is very favorable for ring closure.

A salient point in forming cyclopeptides concerns the conformations of the amide groups in the ring formed. Cyclotripeptides with at least one amide group in the s-cis conformation have been prepared only with prolines or N-methyl amino acids as ring members (ref. 1). This reflects the difference of enthalpy of s-cis and s-trans amides.

For the most part cyclotetrapeptides containing primary amino acids of the same configuration are accessible only with difficulty. In contrast 12-membered cyclopeptides with at least one amino acid of different configuration or with iminoacids as ring members are formed easily. The compound 19 for example has been prepared in 96 % yield.

The cyclopentapeptides have low strain energy but in synthesis the "dimeric" cyclodecapeptides are also frequently formed as coproducts.

In nature, cyclopeptides and a large number of linear peptides containing non proteinogenic amino acids are not synthesized within ribosomes by protein biosynthesis but rather by multi enzyme complexes which activate the amino acids as thiol esters (ref. 2). They are formed particularly in the metabolism of lower organisms. Since biosynthesis proceeds without RNA and DNA non essential amino acids are often included as well. Salient components of cyclopeptides from plants, bacteria, fungi and lower sea animals are amino acids of "exotic" structure. R-amino acids, dehydroamino acids, aminoalkylthiazole carboxylic acids and aminoalkyloxazoline carboxylic acids (formed from cysteine and threonine peptides) are found.

In looking for biologically active compounds especially cytostatics of new structural types, a lot of cyclopeptides have been isolated from lower organisms in the last twenty years. Often only very small amounts have been obtained.
Prerequisites for an economical preparation of such compounds are: a suitable synthesis of the "exotic" amino acids (f.e. 9, 22, 43) and an efficient method of ring closure under very gentle conditions.

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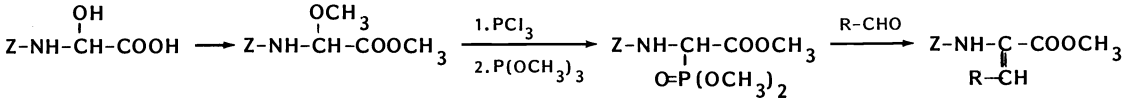
SYNTHESIS OF DEHYDROAMINO ACIDS AND AMINO ACIDS FROM N-ACYL-2-(DIALKYLOXYPHOSPHORYL)-GLYCINE ESTERS

We described (ref. 3,4) an effective three-step synthesis of N-acylphosphoryl glycine esters starting with hydroxyglycine (1) which is readily accessible from technical glyoxylic acid hydrate and benzylcarbaminate (ref. 5). After esterification and acetalisation the semi-aminal was successively treated with PCl_3 and triethyl phosphite to produce alkyl 2-benzyloxycarbonylamino-2-dialkyloxyphosphorylacetate (2) (scheme 1). Acyl-2-(dialkyloxyphosphoryl)-glycine esters with various N-protecting groups are accessible by catalytic hydrogenolysis of the benzyloxycarbonyl protecting group and acylation. The esters are suitable starting materials for preparation of dehydroamino acids which in turn can be easily hydrogenated enantioselectively to amino acids with, in most cases, high optical induction. The route shown in scheme 1 is therefore, a novel synthesis of amino acids (ref. 3,4). Starting from aldehydes, protected amino acid esters having two additional carbon atoms are formed in a Horner type condensation. Because of the very mild reaction conditions, amino acids with acid labile groups can be synthesized. The reaction leads directly to the amino acid with the desired protecting groups for its amino and carboxylic function.

Scheme 1



$R^1HN-CH(O=P(OCH_3)_2)-COOR^2$

2-6

	2	3	4	5	6
R^1	$PhCH_2-O-C(=O)-$	$PhCH_2-O-C(=O)-$	$t\text{-}C_4H_9-O-C(=O)-$	$t\text{-}C_4H_9-O-C(=O)-$	$ClCH_2C(=O)-$
R^2	CH_3	$t\text{-}C_4H_9$	CH_3	$t\text{-}C_4H_9$	CH_3

Since N-methylation and subsequent enantioselective hydrogenation of the N-acyl-N-methyl--dehydroamino acids proceed without difficulty, optically active N-methylamino acids are accessible.

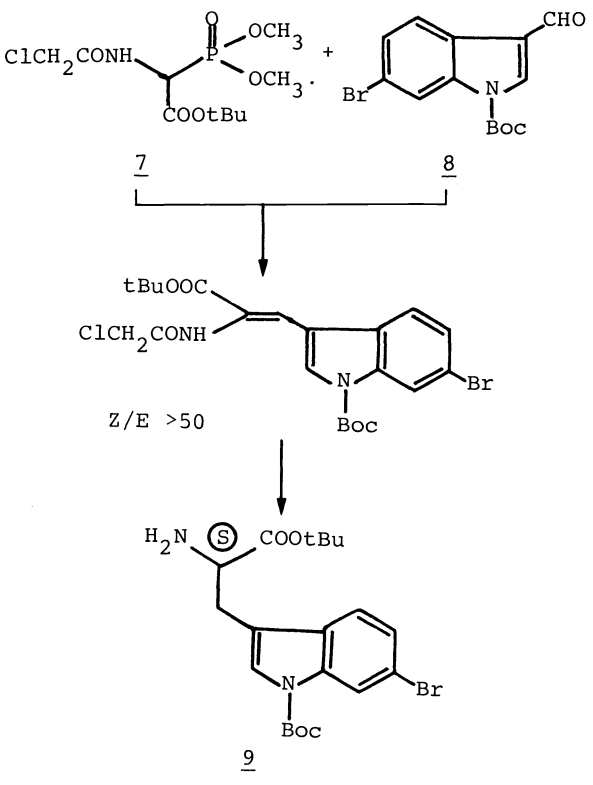
Except for mesoxalic esters the condensation of phosphorylglycine esters with ketones fails. Other aldehydes (with the exception of 2-alkenals), including heterocyclic aldehydes condense with high yield. Sodium hydride is used for the condensation of aromatic aldehydes. The use of lithium diisopropylamide at low temperature was found to be necessary in the reaction of aliphatic aldehydes. The base of choice for all types of aldehydes is potassium t-butoxide suspended in dichloromethane at -70°C. Using this base, the (Z)-isomers are formed predominantly.

By this method and followed by enantioselective hydrogenation particularly with the Monsanto catalyst $[Rh(1.5\text{-}COD)diPAMP]^+BF_4^-$ (ref. 6), the following acid labile amino acid derivatives were prepared. Yield of the condensation reaction and % ee of the amino acid formed by the enantioselective hydrogenation: 9, 80 %, ee >98 %; 22, 90 %, ee >98 %; 43, 90 %, ee >98 %.

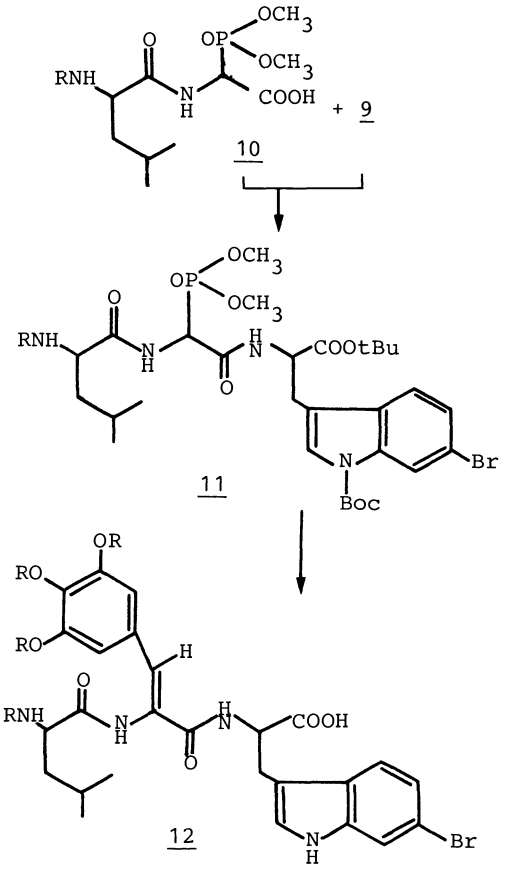
SYNTHESIS OF DEHYDROPEPTIDES FROM (DIALKYLOXYPHOSPHORYL)-GLYCINE PEPTIDES: TOTAL SYNTHESIS OF THE LINEAR PEPTIDE ALKALOID HEXAACETYLCELENAMIDE A

Because of the very mild reaction conditions the condensation of dialkyloxyphosphoryl glycine derivatives can be applied to the synthesis of di- and tri-peptide esters containing a C=C double bond. For that purpose a peptide containing a phosphorylglycinate unit is formed and condensed with an aldehyde. This sequence is illustrated by the synthesis (ref. 7) of Hexaacetylcelenamide A (15), a linear peptide alkaloid, isolated from pacific sponge Cliona celata and elucidated by R.J.Andersen (ref. 8). This dehydrotripeptide with an additional enamide function contains S-6-bromotryptophan the t-butylester of which was synthesized by condensation of the aldehyde 8 and the phosphoryl glycine 7, followed by enantioselective hydrogenation (ee >99 %) and cleaving the chloroacetyl protecting group (scheme 2).

Scheme 2

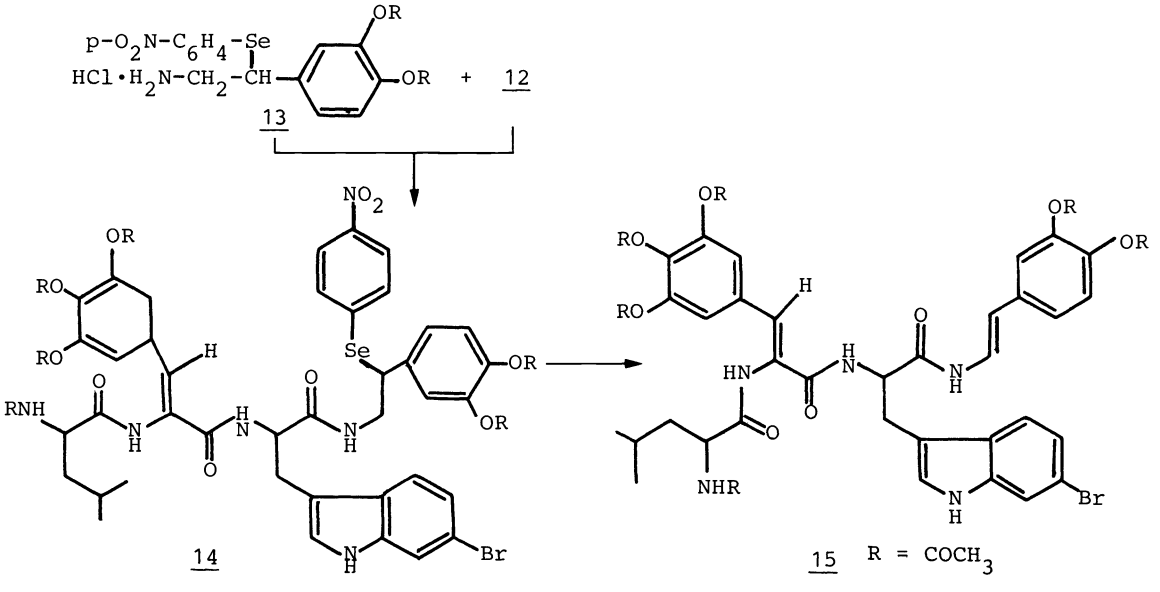


Scheme 3



t-Butyl-S-6-bromotryptophanate (9) was then coupled with the (S)-leucyl derivative 10 to give the phosphono-tripeptide 11, which condensed directly with triacetoxybenzaldehyde to give the E/Z mixture of the two dehydropeptides. These isomers were separated by medium pressure liquid chromatography and further worked up individually. On removing the Boc protecting group, the t-butyl ester was cleaved at the same time, 12 was obtained (scheme 3). Amide formation using the selenium reagent 13 furnished the educt 14 for the oxidative elimination step to the hexaacetylcelenamide 15 (scheme 4). In the cleavage reaction, only the (E)-N-styrylamide was formed.

Scheme 4



SYNTHESIS OF OPTICALLY ACTIVE AMINOALKYLTHIAZOLE CARBOXYLIC ACIDS AND AMINOALKYLOXAZOLINE CARBOXYLIC ACIDS

Lower sea animals produce cyclopeptides with optically active aminoalkylthiazole carboxylic acids and aminoalkyloxazoline carboxylic acids. There are many reasons to believe that they are formed from cysteine or threonine peptides, respectively. In addition aminoalkylthiazole carboxylic acids are known to be components of numerous linear peptides from molds.

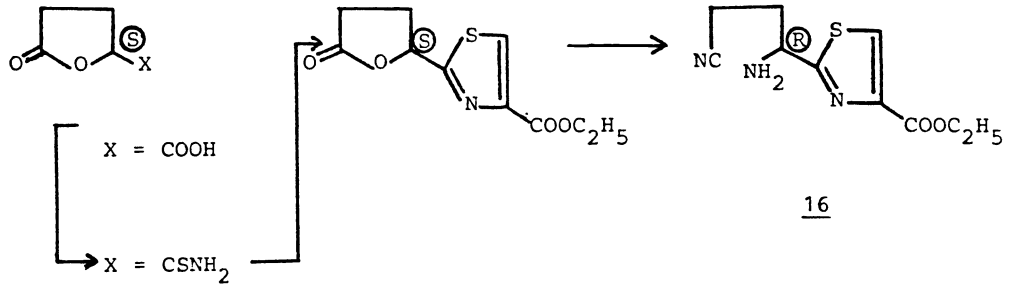
The Hantzsch type synthesis with optically active acylamino acid thioamides and ethyl bromopyruvate results in complete racemisation. - Recently Japanese chemists (ref. 9) formed thiazolidines from cysteine esters and the appropriate α-acylamino aldehydes and obtained optically active aminoalkylthiazole carboxylic acids by subsequent dehydrogenation.

We performed the Hantzsch type synthesis with the easily accessible optically active α-acyloxycarboxylic acid thioamides. The optically active hydroxyalkylthiazole carboxylic acid esters formed with ethyl bromopyruvate could be transformed into the aminoalkylthiazole carboxylic acid derivatives by the Mitsunobu reaction which involves a clean inversion of the configuration.

Since the introduction of the azide functionality proceeds with inversion, whereas the optically active hydroxy acids are formed from α-amino acids with retention of configuration, (R)-aminoalkylthiazol carboxylic acid esters are obtained from natural (S)-amino acids (ref. 10).

Ethyl (R)-2-(1-amino-3-cyanopropyl)-4-thiazole carboxylate (16) is thus accessible from (S)-glutaminic acid. Scheme 5 shows these transformations.

Scheme 5



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The racemisation in the Hantzsch synthesis with optically active α-aminocarboxylic acid thioamides and ethyl bromopyruvate can be avoided by a two step reaction. First, the condensation in acetone leads to the dihydrothiazole which is then dehydrated by cautious reaction with trifluoroacetic acid anhydride and pyridine. By these methods (R)- and (S)-aminoalkylthiazole carboxylic acids are accessible from (S)-amino acids.
Optically active oxazolines were prepared from α-acylamino imidic acid esters and threonine esters, but this synthesis sometimes results in partial racemisation. The NMR analysis of the reaction products is often complicated as the free rotation of the amide bond is hindered.

RING CLOSURE TO FORM CYCLOPEPTIDES

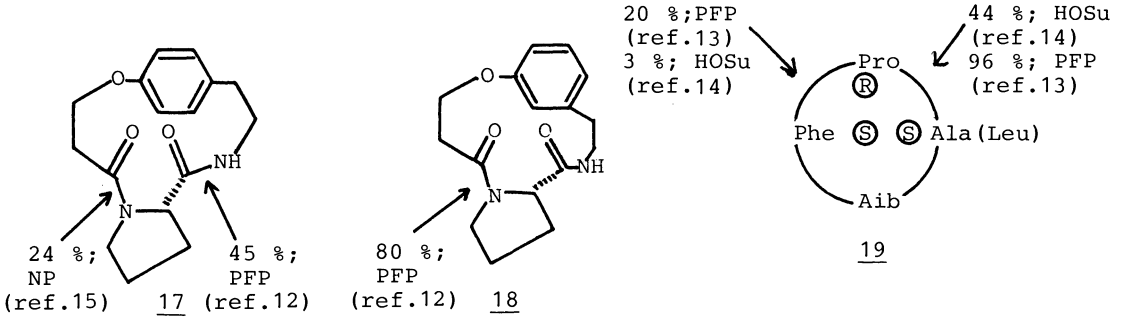
To date ring closure giving rise to cyclopeptides has been performed by nearly all methods which are used to form an amide bond in linear peptides. But for the most part the activation of the carboxylic group as the nitrophenylester, as the hydroxysuccinimid ester or by reaction with diphenylphosphorazidate was preferred. We have developed a new cyclisation method for synthesizing medium and large cyclopeptides which uses pentafluorophenyl esters (ref. 11, 12).

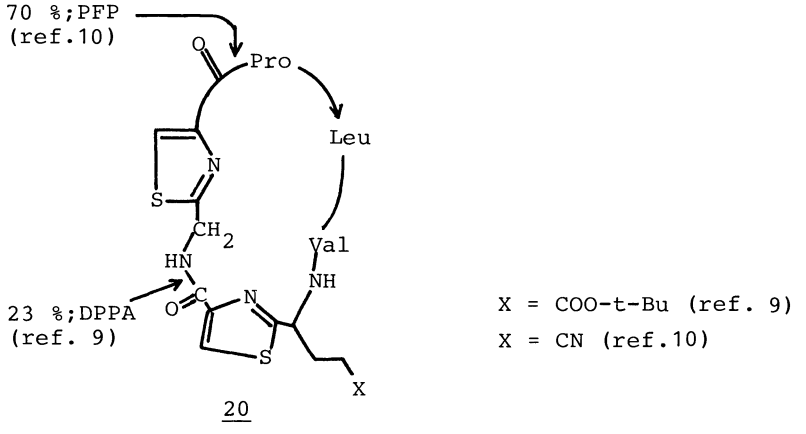
A convenient method of ring closure used a dioxane solution of the carbobenzoxypeptide pentafluorophenyl ester injected slowly to a rapidly stirred suspension of Pd/charcoal in dioxane at 95°C through which hydrogen was bubbled. The solution contained 1 mol 4-pyrrolidinopyridine per mol synthon as catalyst and 2 % alcohol (w.r.t.

solvent). The benzyloxycarbonyl group is first removed by hydrogenolysis, then ring closure occurs. Under conditions of dilution, 45 % of the rigid ring compound 17 was formed. The flexible 13-membered ring 18 was obtained in up to 80 % yield. The yields drop dramatically if alcohol is not added, if its concentration exceeds 5 %, if the reaction temperature is lower than 70°C or if other solvents are used. Compared with similar cyclisations by other methods, the reaction time is rather short; it ranges from 5 h for the ring closure to form 17 to only 0.5 h for 18 but under condition of dilution.

When preparing cyclopeptides with sulfur containing components, catalytic hydrogenation must be avoided. In these cases N-t-butoxycarbonylpeptide-pentafluorophenyl esters are the starting synthons. After acidolytic deblocking of the protecting group with trifluoro acetic acid and evaporation of the excess reagent, the dioxane solution of the peptide-pentafluorophenyl ester trifluoroacetate is added very slowly into dioxane at 95°C. The solution contained at least 1 mol pyrrolidinopyridine and 5-50 % t-butanol (w.r.t. the solvent). In this way, the eight diastereomeric 21-membered ring compounds 20 were obtained in up to 80 % yield. The main advantages of these two ring closure reactions are their high yield and the easy work up of the products since the solvent is low boiling and pentafluorophenol can be removed by destillation with water. The lipophilic cyclopeptides formed were purified by chromatography on silica gel. Scheme 6 represents cyclopeptides formed by several methods.

Scheme 6





Method: PFP = Pentafluorophenyl ester; NP = Nitrophenyl ester;
HOSu = Hydroxysuccinimid ester; DPPA = Diphenylphosphorazidate

TOTAL SYNTHESIS OF PEPTIDE ALKALOIDS

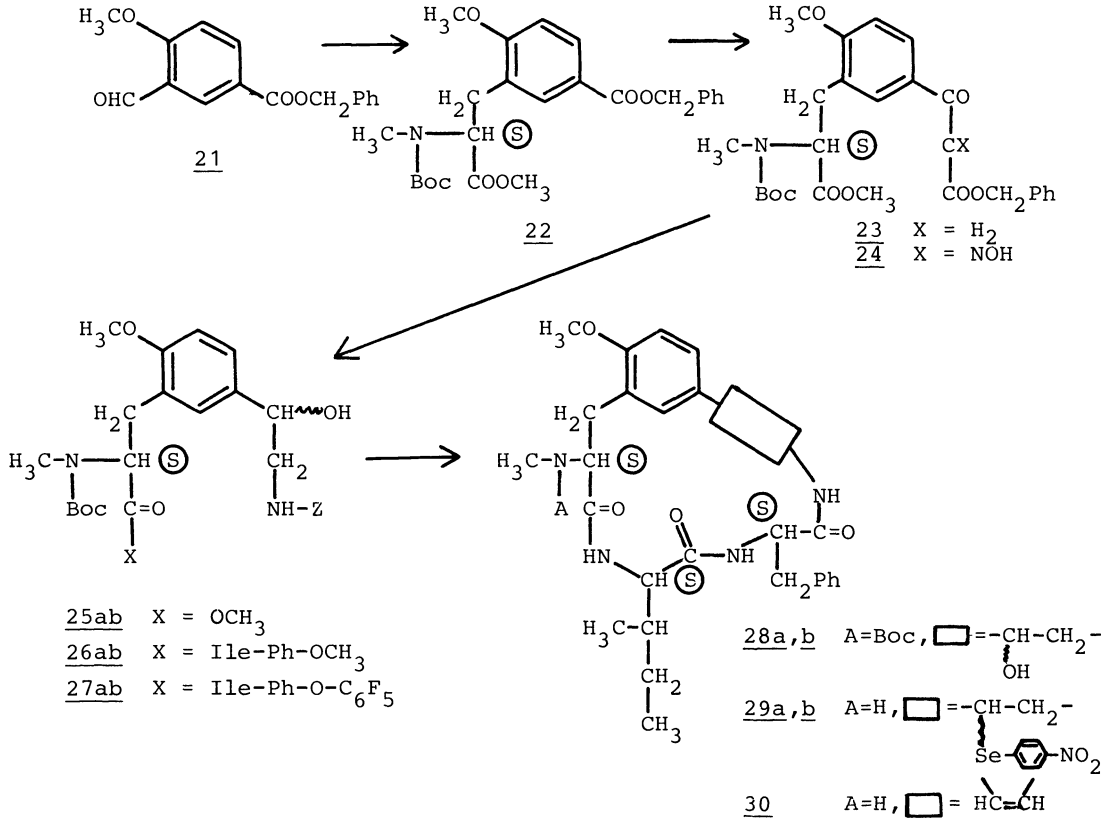
Over the last 20 years ca. 100 peptide alkaloids from Rhamnaceae and Sterculiaceae have been isolated and characterized (ref. 16). They form complexes with alkali earth metal ions and function as ionophores in plants. Most of them show activity against gram-positive bacteria and lower fungi and some inhibit energy transfer processes in chloroplasts.

All of them are meta- or para-ansa compounds with a ten or twelve membered peptide handle. There are three salient groups with a 13-, a 14- or 15-membered ring system. Dihydroderivatives of one of each of the latter two groups have been prepared. The total synthesis of two members, Zizyphin A and Mucronin B with a 13- and a 15-membered ring, have been reported.

Mucronin B was constructed according to Scheme 7 (ref. 17). Starting with aldehyde 21, amino acid 22 was synthesized by condensation with phosphorylglycine ester, N-methylation of the resultant dehydroamino acid ester formed and enantioselective hydrogenation (60 % yield over all; ee >99 %). The benzyl group was removed by catalytic hydrogenation and the carboxylic acid transformed into the β-ketoester 23 by Masamune's method via the acyl-imidazolide and the magnesium salt of monobenzyl malonate.

Subsequent reaction with nitrite afforded the oxime 24. Catalytic hydrogenation of the latter reduced the oximino group, cleaved the benzylester and - after simultaneous decarboxylation - reduced the keto group to form a mixture of two diastereomeric alcohols, which were N-protected with the benzyloxycarbonyl group to form 25a,b. - The non-stereoselective reduction of the carbonyl group is of no account since this new asymmetric center is eliminated in the last step of the synthesis. - After hydrolysis the amino acid was coupled with Ile-Phe-OCH_3 and the tripeptide 26a,b converted into the pentafluorophenyl esters 27a,b. Cyclisation proceeded by catalytic hydrogenation under high dilution conditions with 85 % yield of the two diastereomeric ring compounds 28a,b. For the transformation into the enamide we adopted the selenoxide elimination procedure. The acetates of 28a,b were reacted with trifluoroacetic acid/selenophenol to afford the mixture of two diasteromeric selenides 29a,b. Oxidative elimination to the (Z)-olefine yielded Mucronin B (30).

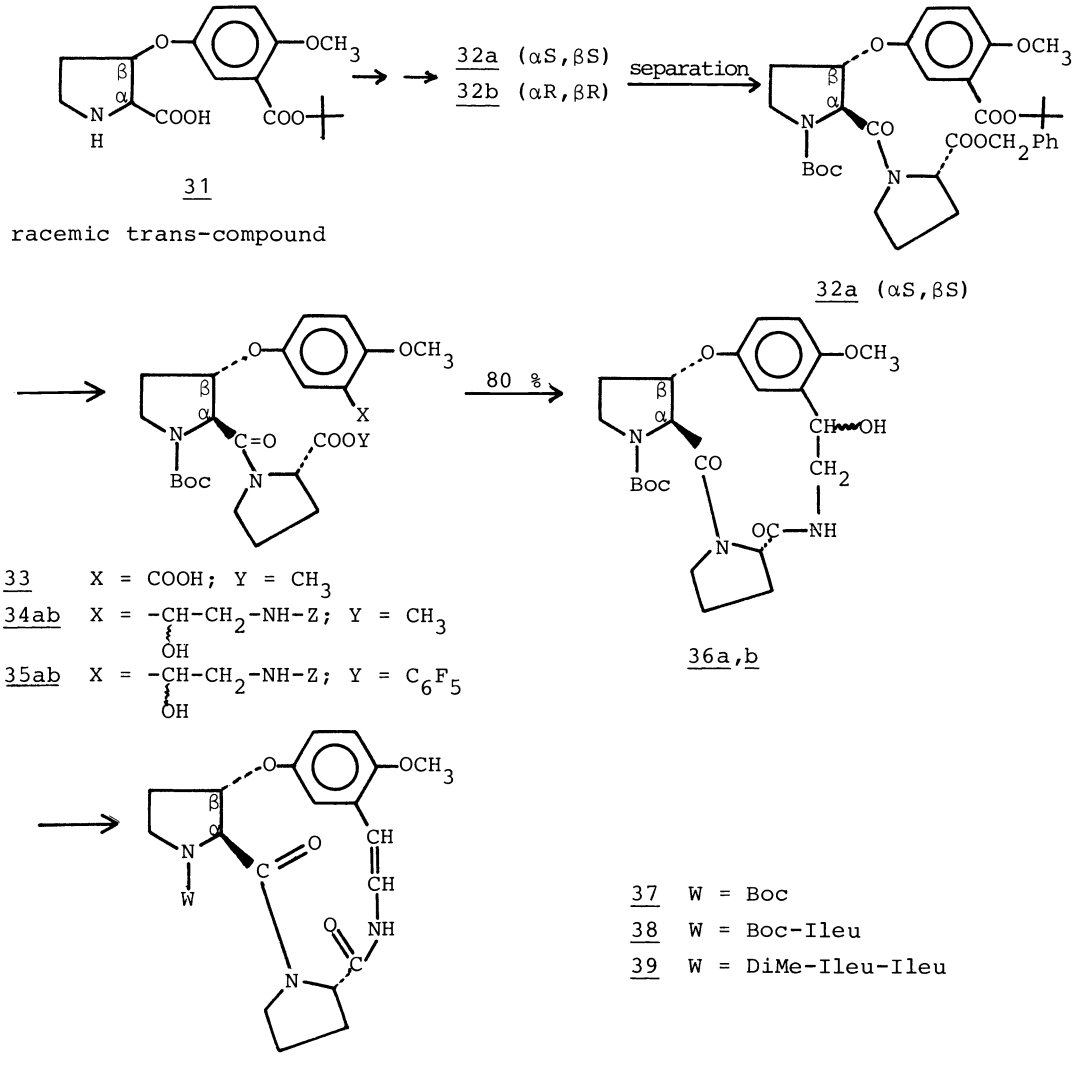
Scheme 7



The total synthesis of Zizyphin is presented in scheme 8 (ref. 18). It starts with the racemic compound 31 prepared by means of the route worked out for the construction of trans-3-phenoxyproline (ref. 19). The further steps are directed toward ring closure on the phenylethylaminenitrogen. This sequence of reactions provides an opportunity for separating the easily accessible diastereomers 32a, 32b resulting from the racemic starting material 31 before ring closure. After hydrogenolysis of the benzyl ester and reaction with diazomethane to give the methyl ester, cleavage of the t-butyl ester and reacylation formed the carboxylic acid 33. Further transformation analogeous to the synthesis of Mucronin B gave the amino ketone unit in high yields. Sodium cyanoborohydride reduced the ketone nonstereoselectively to the diastereomers 34a and 34b. Saponification of the methyl esters and formation of a mixture of the two diastereomeric pentafluorophenyl esters 35a and 35b by DCCD condensation yielded starting material for the ring closure step. Catalytic hydrogenation for 5 h by using dilution techniques afforded, in about 80 % yield, a mixture of the cyclic alcohols 36a and 36b. The non stereoselective introduction of a hydroxy group which is eliminated in the final steps of the synthesis forms two diastereomers and hence leads to a mixture which is difficult to purify. However, this disadvantage is off set by high yields, particularly in the ring closure step.

Transformation of diastereomeric alcohols 36a and 36b into the selenides and oxidative elimination yielded olefin 37 (65 %). After cleavage of the Boc group by trifluoroacetic acid, the amine was first reacted with N(t-butoxycarbonyl)isoleucine hydroxysuccinimide ester, forming 38. After cleavage of the protecting group by trifluoroacetic acid the resulting amine was treated with dimethylisoleucine pentafluorophenyl ester to yield zizyphine 39 (30 % yield from 37) (scheme 8).

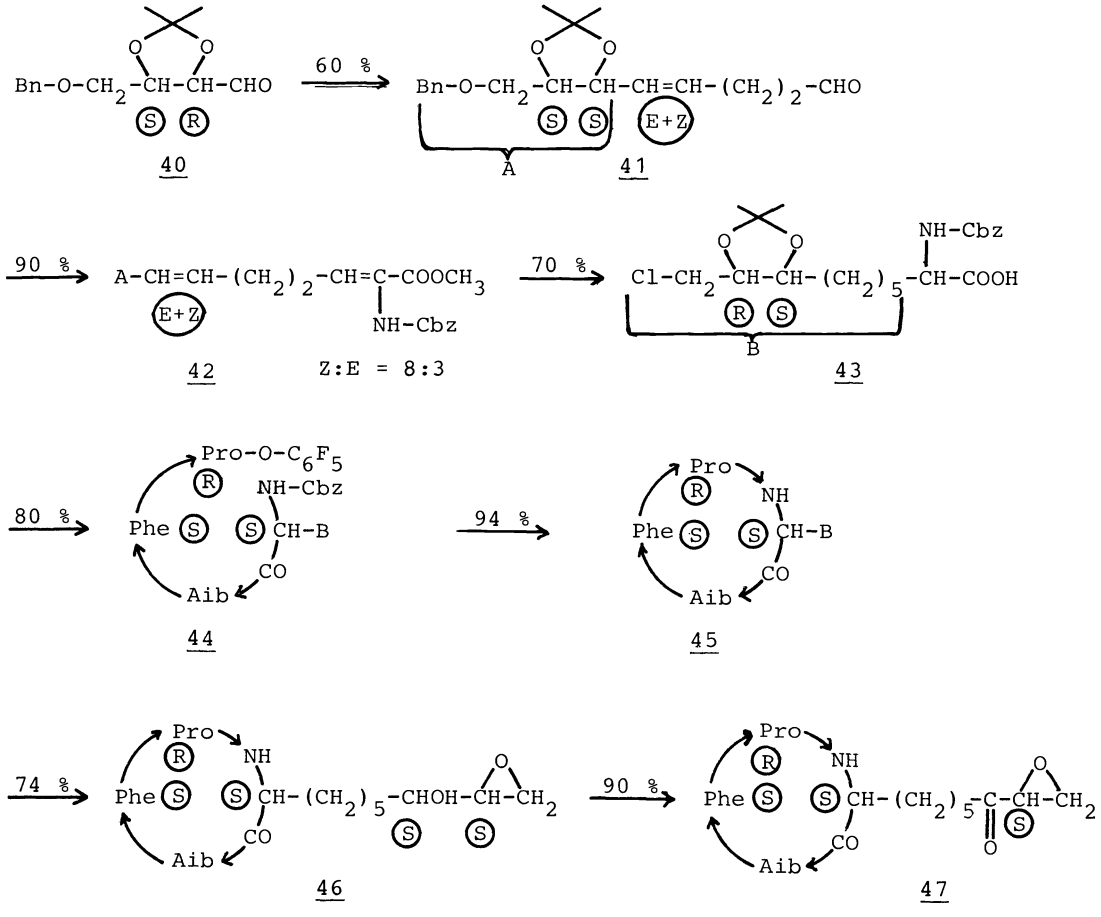
Scheme 8



TOTAL SYNTHESIS OF CHLAMYDOCIN AND DIHYDROCHLAMYDOCIN

Chlamydocin 47, a cyclic tetrapeptide with extremely high cytostatic activity in vitro, was isolated together with dihydrochlamydocin 46 from culture filtrates of Diheterospora chlamydosporia. Its structure and conformation were elucidated in 1976 (ref. 20). In cultures of P-815 mouse mastocytoma cells, it has higher cytostatic activity than actinomycin D, amethopterine, colchicine and vincristine. But in blood the drug is inactivated rapidly in vivo. Four similar biologically active cyclotetrapeptides containing (S)-2-amino-8-oxo-(S)-9,10-epoxidecanoic acid were isolated from molds in the last few years. - Two non stereoselective syntheses of a mixture of chlamydocin and epi-chlamydocin have been reported, one by Rich (ref. 21) and the other by us (ref. 22), which reflects the fact that epoxidation of the corresponding vinyl ketone proceeds without asymmetric induction by the peptide ring. The stereoselective total synthesis of 46 and 47 (scheme 9) was performed by us (ref. 23). The S,S-configuration at C^8 and C^9 of the substituted aminodecanoic acid was achieved with the aid of (R,R)-tartaric acid and the S-configuration at C^2 was formed by enantioselective hydrogenation.

Scheme 9



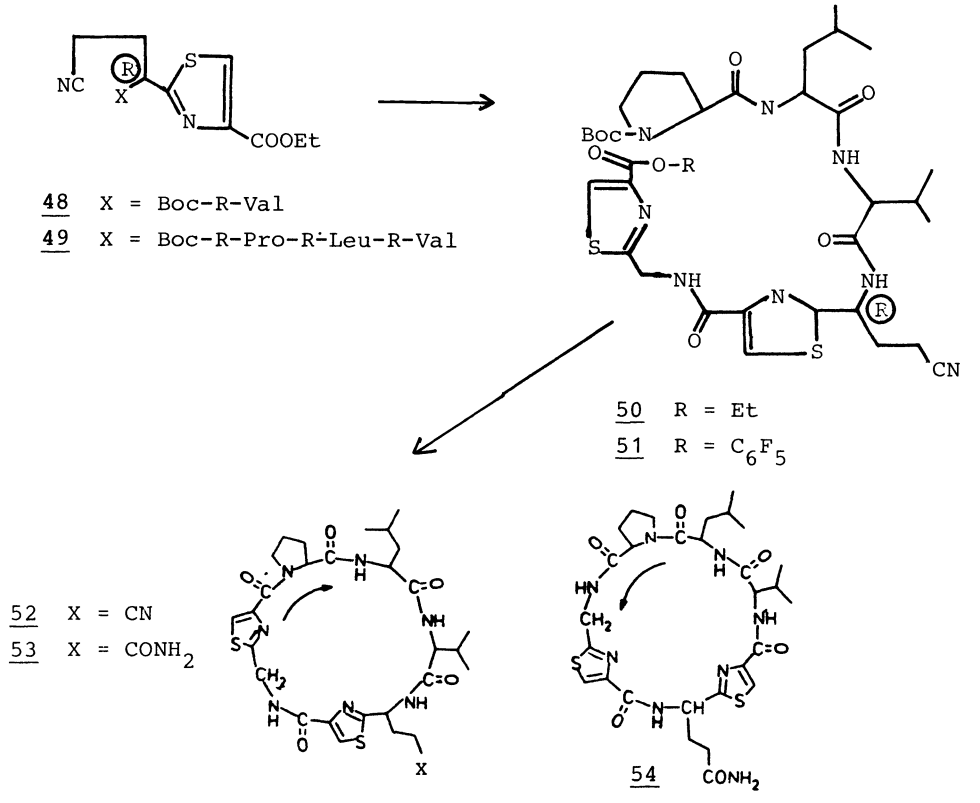
Condensation of the aldehyde 40 - which is readily accessible from (R,R)-tartaric acid - whith triphenyl(4-trimethylsiloxybutylidene)phosphorane and subsequent oxidation led to the C^8-aldehyde 41 (E/Z-mixture), which was condensed with methyl N-benzyloxycarbonyl-2-(dimethoxyphosphoryl)glycinate to give the dehydroamino acid ester 42 (diastereomeric mixture). Enantioselective homogeneous hydrogenation of the E/Z-mixture with the Monsanto catalyst $[Rh(1.5\text{-}COD)diPAMP]^+BF_4^-$ led with high enantioselectivity (ee >98 %) to the (S)-amino acid derivative. Subsequent heterogeneous hydrogenation of the C^6-C^7 double bond, hydrogenolysis of the benzyl ether and the benzyloxycarbonyl protecting group, followed by reincorporation of the protecting group, replacement of OH by Cl and hydrolysis furnished the amino acid 43, from which the tetrapeptide pentafluorophenyl ester 44 was synthesized by conventional methods.

Ring closure "by catalytic hydrogenation under high dilution conditions" afforded the cyclopeptide 45 in high yield. - Absolutely no racemisation at the proline was observed, for this would have led to a cyclotetrapeptide with three (S)-amino acids. In this series, such isomers are formed in only extremely small yields and are easy to recognize on chromatographic separation. - Hydrolysis of the ketal and treatment with base yielded dihydrochlamydocin 46 which was oxidized to the chlamydocin 47 with dicyclohexylcarbodiimide/dimethyl sulfoxide/dichloroacetic acid.

SYNTHESIS OF DOLASTATIN 3 ISOMERS

Dolastatin 3, isolated from the Indian Ocean sea hare Dolabella auricularia exhibits strong in vitro antineoplastic activity (P-388 leukemia cells: ED_{50} = $1x10^{-4}$ to $1x10^{-7}$ µg/mL). Pettit et al. (ref. 24), who isolated ca. 1 mg of Dolastatin 3, proposed structure 53 for this compound, but did not rule out the opposite "ring direction". Characteristic building blocks for the cyclopeptide are two 2-(aminoalkyl)-4-thiazolecarboxylic acids. The total synthesis of 8 isomers of the structure 53 is represented in scheme 10 (ref. 10). The optically active R-aminothiazolecarboxylic acid derivative 16 was prepared according to scheme 5 and allowed to react with Boc-R-Val to yield 48, to which Boc-R-Pro-R-Leu is attached. The compound 49 thus obtained is coupled after hydrolysis of the ethyl ester group - to ethyl 2-aminomethyl-4-thiazolecarboxylate to form 50. The pentafluorophenyl ester 51 prepared from this serves as a linear educt for the ring closure. After cleavage of the Boc group cyclisation proceeds upon slow injection of the tris(trifluoroacetate) into a solution of 3 mol pyrrolidinopyridine in alcoholic dioxane at 95°C (80 % yield). Hydrolysis of the nitrile 52 to the amide furnished a product 53 which is not identical to Dolastatin 3. The spectra of the seven other diastereomers containing the R-aminothiazole compound are also not consistent with the data published for Dolastatin 3. In an analogous way, we have also synthesized the eight diastereomers having the reverse order of the amino acids in the ring (54) and containing the R-aminothiazole compound (ref. 10). These compounds were also not identical with Dolastatin 3. The structure proposed for Dolastatin 3 is therefore not correct.

Scheme 10



A few month later Japanese chemists (ref. 9) publicated the synthesis of 16 isomers of Dolastatin as well, but by another route.

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REFERENCES

1) M.Rothe, W.Schindler, R.Pudill, M.Kostrzewa, R.Theyson, R.Steinberger, Pept.,Proc.Eur.Pept.Symp. 11th 1971 (Publ.1973), 388. Edited by H.Nesvadba, North-Holland: Amsterdam, Neth.
2) H.Kleinkauf and H.v.Doeren, Pept.Antibiot.Biosynth.Funct., de Gruyter, Berlin 1982
3) U.Schmidt, A.Lieberknecht, U.Schanbacher, Th.Beuttler and J.Wild,Angew.Chem.Ed. Engl. 21, 770 (1982); Angew.Chem.Suppl. 1982, 1682
4) U.Schmidt, A.Lieberknecht and J.Wild, Synthesis 1984, 53
5) U.Zoller and D.Ben-Ishai, Tetrahedron 31, 863 (1975)
6) B.D.Vineyard, W.S.Knowles, N.J.Sabacky, G.L.Bachman and D.L.Weinkauff, J.Am. Chem.Soc. 99, 5946 (1977)
7) U.Schmidt and J.Wild, Angew.Chem.Int.Ed.Engl. 23, 991 (1984)
8) R.J.Stonard and R.J.Andersen, J.Org.Chem. 45, 3687 (1980)
9) Y.Hamada, K.Kohda and T.Shioiri, Tetrahedron Lett. 25, 5303 (1984)
10) U.Schmidt and R.Utz, Angew.Chem.Int.Ed.Engl. 23, 725 (1984)
11) U.Schmidt, H.Griesser, A.Lieberknecht and J.Talbiersky, Angew.Chem.Int.Ed.Engl. 20, 280 (1981)
12) U.Schmidt, A.Lieberknecht, H.Griesser and J.Talbiersky, J.Org.Chem. 47, 3261 (1982)
13) Th.Beuttler, Dissertation, Universität Stuttgart 1983
14) J.Pastuszak, J.H.Gardner, J.Singh and D.H.Rich, J.Org.Chem. 47, 2982 (1982)
15) J.C.Lagarias, R.A.Houghten and H.Rapoport, J.Am.Chem.Soc. 100, 8202 (1978)
16) R.Tschesche, E.U.Kaußmann "The Cyclopeptide Alkaloids" in "The Alkaloids" (R.F.Manske,Ed.), Vol.XV, Academic Press New York 1975. - U.Schmidt, A.Lieberknecht, E.Haslinger "The Cyclopeptide Alkaloids in "The Alkaloids" (A.Brossi,Ed.), Vol.XXVI, Academic Press New York
17) U.Schmidt and U.Schanbacher, Angew.Chem.Int.Ed.Engl. 22, 152 (1983); Liebigs Ann. Chem., 1984, 1205
18) U.Schmidt, A.Lieberknecht, H.Bökens and H.Griesser, Angew.Chem.Int.Ed.Engl. 20, 1026 (1981); J.Org.Chem. 48, 2680 (1983)
19) J.Häusler and U.Schmidt, Liebigs Ann.Chem. 1979, 1881
20) A.Closse and R.Huguenin, Helv.Chim.Acta 57, 533 (1974)
21) D.H.Rich and J.H.Gardner, Tetrahedron Lett. 24, 5305 (1983)
22) U.Schmidt, Th.Beuttler, A.Lieberknecht and H.Griesser, Tetrahedron Lett. 24, 3573 (1983)
23) U.Schmidt, A.Lieberknecht, H.Griesser and F.Bartkowiak, Angew.Chem.Int.Ed.Engl. 23, 318 (1984)
24) G.R.Pettit, Y.Kamano, P.Brown, D.Gust, M.Inoue and Ch.L.Herald, J.Am.Chem.Soc. 104, 905 (1982)