natural product was $[\alpha]_D^{15}$ −88° (c 0.1, 0.1 *M* HCOOH). The ratio of amino acids in an acid hydrolyzate: Cys 2.13(2), Ser 2.86(3), Leu 5.10(5), Thr 3.48(4), Val 2.20(2), Gly 3.30(3), Lys 1.98(2), Glu 3.27(3), His 0.95(1), Tyr 0.90(1), Pro 1.96(2), Arg 1.03(1), Asp 2.07(2), Ala 0.94(1). (Average recovery was 89.9%)

The head part of [Asu[1,7]]-E-CT, which corresponds to the sequence (1–10) of the natural hormone, was synthesized as shown in Figure 3. Almost the same procedure used for the synthesis of [Asu[1,6]]-oxytocin[9] was applied to cyclization of the fragment (2–7). The cyclized product was further coupled with Val-Leu-Gly to obtain a protected nonapeptide with a free carboxyl group at the C-terminus. This material was converted to the *N*-hydroxysuccinimide ester, which was then coupled with the fragment I in DMF at 30 °C. The crude product, fully protected [Asu[1,7]]-E-CT, was treated with anhydrous HF as in the case of the synthesis of the natural hormone, and the liberated free peptide was purified by the use of CM-cellulose column chromatography under the same conditions as above, Sephadex G-25 partition chromatography with a solvent system of *n*-BuOH: Pyridine: 1%-AcOH (5:3:11 v/v/v), and gel-filtration with Sephadex LH-20 using 0.1 *M* AcOH as a solvent, successively. Thus, homogeneous [Asu[1,7]]-E-CT was obtained in an over-all yield of more than 30% through the final coupling and purification procedures: Rf 0.71 on cellulose thin layer chromatography using a mixture of *n*-BuOH: AcOH: Pyridine: H_2O (15:3:10:12 v/v/v/v) as the solvent; $[\alpha]_D^{18}$ −95° ± 2° (c 0.54, 1 *M* AcOH). The ratio of amino acids in an acid hydrolyzate: Lys 1.92(2), His 0.89(1), Arg 0.95(1), Asp 1.90(2), Thr 3.88(4), Ser 3.00(3), Glu 3.33(3), Pro 2.16(2), Gly 3.00(3), Ala 0.92(1), Val 2.10(2), Leu 4.95(5), Tyr 0.92(1), Asu 0.99(1), (Average recovery 90.1%).

The synthetic E-CT showed a rat hypocalcemic activity of 4300 MRC U/mg using a similar procedure to that outlined by KUMAR et al.[12]. This potency was reasonably high in comparison with that of the natural hormone as described above. The synthetic [Asu[1,7]]-analog showed a specific activity of 3400 MRC U/mg under the same bioassay system. These findings indicate clearly that the disulfide bond in calcitonin is essential not for the biological activity but for maintainance of the specific conformation by forming an intramolecular bridge, since an open-chain analog of human CT is known to be inactive[13]. During the course of the final purification of the synthetic natural-type E-CT, we were troubled seriously by an unexpected loss of the biological activity; thus, we could not get a reproducible yield of this compound in different runs. In the case of [Asu[1,7]]-analog synthesis, no difficulty was encountered during purification in keeping the biological activity. These fact suggest that the instability of synthetic calcitonin should mainly be attributed to the presence of a disulfide bond, and that, if the Asu-analog were proved not toxic, the use of such an analog must be much more advantageous in developing a hypocalcemic drug because of its ease of manufacturing, enough potency and higher stability during storage.

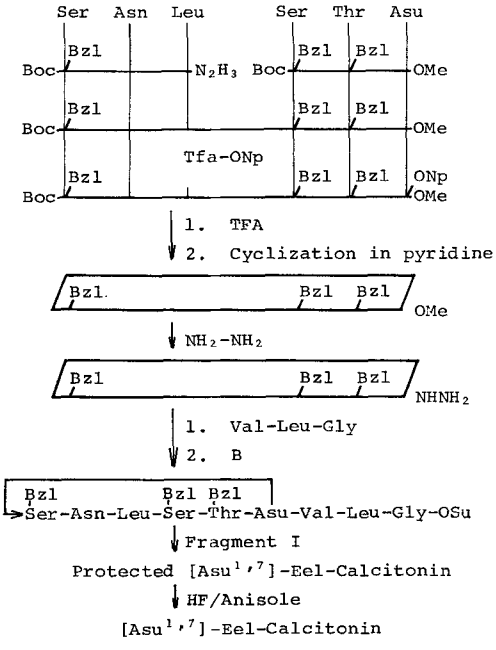

Fig. 3. Synthesis of [Asu[1,7]]-eel-calcitonin[10].

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A Modified Dipeptide from the Alga *Cystoseira corniculata* Hauck

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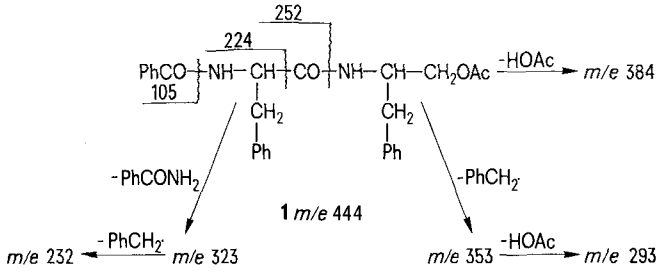
Summary. A modified L-Phe-L-Phe dipeptide has been isolated from the alga *Cystoseira corniculata.*

Although numerous compounds have been isolated from algae in recent years they include, so far as we are aware, only two simple peptides[2,3]. We have now obtained the modified phenylalanine dipeptide 1 by chloroform extraction of *Cystoseira corniculata*[4] collected at Marmaris, Turkey.

Extraction of the dried alga (550 g) gave a thick green oil (2 g) which, after column and repeated thin layer chromatography, afforded the dipeptide (57 mg) as needles, m.p. 185–186° (from chloroform-petrol), $C_{27}H_{28}N_2O_4$ (M^+, 444.2048), $[\alpha]_D$ = −74.0° (c, 0.98; $CHCl_3$); λ_{max} (MeOH) 214, 227sh (log ε 4.18, 4.07); CD, λ_{max} (MeOH) 212 ($\Delta\varepsilon$ −1.27), 227 nm (−4.74); ν_{max} (KBr) 3320 (NH), 1728 (ester CO), 1662 and 1634 cm^{-1} (–NHCO–). The ^1H NMR-spectrum ($CDCl_3$) showed signals for an acetate methyl group (δ 2.00, s), 3 methylene (2.74d, 3.15 m, and 3.88 m), 2 methine (4.34 m and 4.83 q), 2 NH (6.26 d and 6.88 d, exchanged with D_2O), and 15 aromatic protons. Decoupling experiments showed that the methine proton at δ 4.83 was coupled to the methylene group at δ 3.15

and to the NH proton at δ 6.88, while the second methine proton at δ 4.34 was coupled to the other 2 methylene groups and the other NH proton. Confirmatory evidence for all these carbon-containing groups was provided by the ^{13}C NMR-spectrum which also established the presence of 3 carbonyl groups (170.71, 170.41, and 167.17 ppm). These data suggested structure 1 which was supported by the mass spectral fragmentation as indicated.



Structure 1 was confirmed by synthesis from L-phenylalanyl-L-phenylalanine. The methyl ester hydrochloride, m.p. 197–198°, $[\alpha]_D$ = +4.55 (c, 0.91; MeOH), prepared in the usual way[5], was treated with benzoyl chloride in cold pyridine for 30 min. After removal of solvent in vacuo and trituration with ether, the residue crystallized from chloroform-ether to give the *N*-benzoyl methyl ester as needles, m.p. 177–178°, $[\alpha]_D$ = +11.5° (c, 1.08; $CHCl_3$), M^+ 430.1894 ($C_{26}H_{26}N_2O_4$ requires M, 430.1892); δ ($CDCl_3$) inter alia 6.56 and 6.86 (each 1H, d, exchanged with D_2O, 2NH). This ester was reduced with lithium borohydride[6] (2 mols) in dry THF for 30 min in the cold to form the alcohol 1 (OH in place of OAc) which crystallized from chloroform in plates, m.p. 174–175°, $[\alpha]_D$ = –51.1° (c, 1.42; $CHCl_3$), M,+ 402.1945 ($C_{25}H_{26}N_2O_3$ requires M, 402.1943); ν_{max} (KBr) 3400 (OH), 3292 (NH) cm^{-1}. A longer reduction time with $LiBH_4$ led to some degree of racemization. Final acetylation in cold pyridine yielded the acetate 1, m.p. 185–186° (from chloroform-petrol) identical (UV, IR, NMR, MS, CD, $[\alpha]_D$, and mmp) with the natural dipeptide.

Added in proof: Since this Note was submitted the same compound, named asperglaucide, has been reported in *Aspergillus glaucus*.[7]

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Oxygenation of a Dipyrromethene Model for Bilirubin: Formation of a Singlet Oxygen-like Product

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Summary. An oxodipyrromethene model compound for bilirubin is found to undergo oxidation to a blue tetrapyrrole and a water-propentdyopent on a silica gel thin layer chromatography plate. The reaction involves ground state oxygen and requires silica gel, although the propentdyopent is an expected product from reaction with singlet oxygen.

In connection with a widely employed phototherapy for neonatal jaundice due to unconjugated hyperbilirubinemia[2,3], we have been investigating the photooxygenation of bilirubin IXα (BR)[4,5] and various model compounds[6], especially 5′-oxo-3′, 4, 4′-triethyl-3, 5-dimethyl-1′, 5′-dihydro-(2·2′)-dipyrromethene (**1**)[7]. Most of the photochemical investigations of BR reported to date have been in vitro studies in solution[4,8,9], with the exception of some recent work on BR in micelles[10]. Thus environmental effects on the photochemistry have not been studied extensively, and there are only a few reported studies which mimic the environment of (aggregated) BR deposited in the skin[10–12], the presumed major photo-active site. We have studied the reactions of **1**, which serves as a convenient model for one half of BR, in the aggregated state deposited on thin layers of silica gel and alumina.

Materials and methods. Oxodipyrromethene (**1**) was prepared by the base-catalyzed condensation of krypto-

[1] The authors wish to thank the National Science Foundation for generous support of this work. We also thank Mr. Richard Gillespie and Ms. Elizabeth Irwin for running the high resolution mass spectra.

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