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10. Actually, sodium sulfite was oxidized with O_2^- to sodium sulfate in quantitative yield.
11. 2-Bromo-4-methylthioacetanilide reacted with O_2^- in DMSO at 20°C for 24 h to give the corresponding amide in 5% yield together with the 90% recovery of th starting material, and in 25% yield of amide in the presence of 18-crown-6-ether under the same reaction condition.

An Efficient Route for the Synthesis of Glorin

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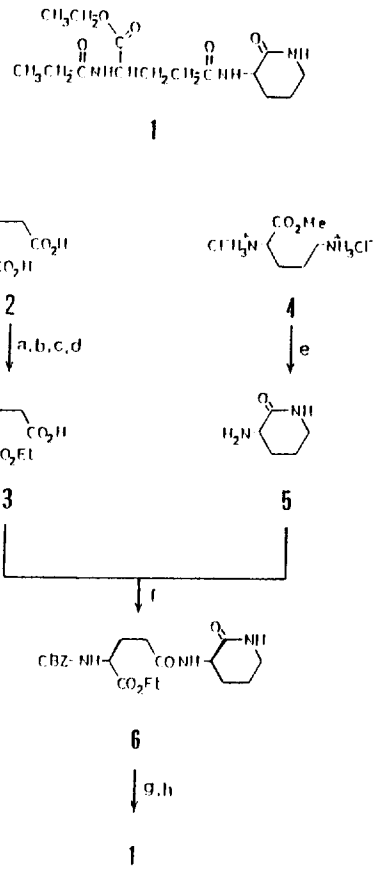
Chemotaxis is referred to the directed movement of cells toward an attractant along a concentration gradient. Many di- or tripeptides with N-formyl-methionine, which are related to inflammation mechanisms of body are well known examples of chemoattractant for neutrophiles and macrophages[1].

Recently, Shimomura *et al.*[2,3] has isolated a chemotactic peptide, N-propionyl-γ-L-glutamyl-L-ornithine-δ-lactam α-ethyl ester (**1**) (glorin) for social amoeba *Polysphondylium violaceum*, and conformed the structure by comparing it with synthetic glorin for its chemotactic activity. To study the relationship between the structures of various derivatives of glorin and their chemotactic activities on amoeba or leukocytes, we had to synthesize them in large quantity. However the reported route for the synthesis of glorin[4] appeared somewhat crude without mentioning of reaction condition. Furthermore, no physical data were available except MS and IR spectra[2].

We now wish to report here a simple and efficient route for the synthesis of glorin and its derivatives. L-Glutamic acid (**2**) was first transformed into N-benzyloxycarbonyl-L-glutamic acid α-ethyl ester (**3**) in the usual manner.[5,6] L-Ornithine-δ-lactam (**5**) was prepared from L-ornithine methyl ester dihydrochloride (**4**)[7] by the known procedures[8]. The two fragments, **3** and **5** were coupled by mixed anhydride method[9] affording N-benzyloxycarbonyl-γ-L-glutamyl-L-ornithine-δ-lactam α-ethyl ester (**6**) in 70% yield. Since **5** was known to be hygroscopic and unstable, 3 eq of **5** was used in the coupling step, and excess of **5** could be removed by washing it with water. The coupled product, **6** was very stable as nice crystalline form[10] and gave satisfactory H-nmr spectral data; NMR ($CDCl_3$): δ 7.35 (5H, 2, phenyl), 6.64 (1H, d, amide), 5.93 (1H, br, amide), 5.74(1H, d, amide), 5.11 (2H, s, $-CH_2-$of benzyl), 4.4-4.0(2H, m, two methines), 4.20 (2H, q, $-OCH_2-$), 3.32 (2H, d of t, $-CH_2$ NH- of lactam), 2.57-1.64 (8H, m, four $-CH_2-$), 1.27 (3H, t, $-CH_3$). Treatment of **6** with H_2/Pd in methanol for 7 h, and evaporation of the solvent gave oily product. It was reacted without further purification with 10 eq of propionic anhydride in CH_2Cl_2 for 10 h at room temperature. Removal of the solvent in high vacuum and crystallization of the resulting solid in EtOH-EtOAc afforded **1** in quantitative yield; MP 139-140°C, TLC, Rf 0.69, silica gel (2-butanone-H_2O-HOAc = 7:1.5:1.5), $[\alpha]_D^{22} = +37.77$ (c = 0.4, $CHCl_3$); NMR($CDCl_3$), δ 6.93 (1H, br, amide), 6.70 (1H, br, amide), 6.15 (1H, br, amide), 4.7-4.0 (2H, br, two methines), 4.20 (2H, q, $-OCH_2-$), 3.37 (2H, m, $-CH_2NH-$ of lactam), 2.6-1.6 (10H, m, five $-CH_2-$), 1.28 (3H, t, $-CH_3$), 1.16(3H, t, $-CH_3$); Anal. calcd. for $C_{15}H_{25}N_3O_5$: C 55.03, H 7.70, N 12.84; found: C 55.26, H 8.13, N 12.52. Unlike the result of Shimomura *et al.*[2], **1** was recovered from the reaction mixture in a highly purified



[a]Z-Cl, H_2O-Et_2O, 0°C, 1.5h and rt, 24h, 91%; [b]Ac_2O, rt, 17h, 80%; [c]EtOH, dicyclohexyl amine, rt, 15h, 70%; [d]Dowex 50 WX4, H_2O-MeOH(1:1), rt, 30 min; [e]NaOMe, MeOH, rt, 3h, 91%; [f]for activation, N-methylmorpholine, $ClCO_2$-isobutyl, -15°C, 5 min; for coupling, -15°C, 30 min and rt, 10h, 70%; [g]H_2, Pd-C, rt, 7h; [h]propionyl anhydride, CH_2Cl_2, rt, 10h.

form, and no chromatographic purification was necessary. Furthermore, this reaction scheme showes a general route for the synthesis of various kinds of N-substituted Glorin.

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4. N-Propionyl-L-glutamic acid-α-ethyl-γ-benzyl ester was prepared from L-glutamic acid. Treatment of the diester with HF give N-propionyl-L-glutamic acid α-ethyl ester, which was coupled with **5** yielding **1**. The final product was purified by coulumn chromatography on Sephadex LH-20 using acetonitrile/water, 9:1 (vol/vol) as the eluent.
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10. The compound, **6** was purified by crystallization in EtOAc. MP 124-126°C; TLC, Rf 0.21, silica gel ($CHCl_3$, 95% EtOH = 15:1); $[\alpha]_D^{18} = +52.6$ (c = 0.5, $CHCl_3$); Anal. calcd. for $C_{20}H_{26}N_3O_6$: C 59.40, H6.48, N10.39; found: C 59.38, H 6.63, N 10.03.

A Biogenetic-Type Synthesis of Rose Furan

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Rose furan(**1**) was isolated from Bulgarian rose oil in 1968 and the structure was assigned and confirmed by synthesis by G. Büchi and coworkers[1]. Since then it has been isolated from other natural sources[2].

Following the first synthesis by Büchi[1], many successful schemes were published. In a number of syntheses[3-8], preformed furan precursors were used and different strategies for intorduction of the prenyl group were investigated. Other synthetic routes involve primarily oxidative furan ring formation of acyclic intermediates[9-11].

In this report, we wish to describe a new biogenetic-type synthesis of rose furan(**1**) from nerol(**2**), one of its probable biogenetic progenitors.

2,3-Epoxynerol(**3**) was prepared by epoxidation of nerol(**2**) with t-butyl hydroperoxide in benzene in the presence of vanadyl acetylacetonate as reported by Sharpless and coworkers[12]. The reaction was complete in 3 hours at room temperature and the product **3** was isolated in almost quantitative yield.

The reaction of 2,3-epoxynerol(**3**) with titanium isopropoxide in dichloromethane at room temperature for 30 hours yielded the enediol **4** in 63% overall yield from nerol(**2**).[13] In the nmr spectrum, a new vinylic proton (H-4) signal appeared at δ 5.36 as a broad triplet and C-5 bisallylic methylene protons gave rise to another broad triplet at δ 2.67.

Partial esterification of **4** with p-toluenesulfonyl chloride in pyridine produced the monotosylate **5** in 89% yield which was cleanly cyclized to yield the epoxide **6** upon treatment with excess sodium hydride in THF for 2 hours. Reaction with methanolic sodium bicarbonate for 36 hours resulted in the formation of several byproducts. In the nmr spectrum of **6**, the characteristic triplet at δ 3.35 was assigned to H-2.