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O-ACETYL-N-(N'-BENZOYL-L-PHENYLALANYL)-L-PHENYLALANINOL. ISOLATION FROM EUPHORBIA FISCHERIANA STEUDEL

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O-Acetyl-N-(N'-benzoyl-L-phenylalanyl)-L-phenylalaninol was isolated from Euphorbia fischeriana Steudel. The structure has been established by nmr spectral analysis and the synthesis of this compound.

Our continuous search for toxic substances in Euphorbiaceae gave several physiologically active compounds[1-3]. From roots of the title plant, Chinese crude drugs "Lang-Tu" shown to contain the toxic principle, we obtained a new phenylalaninol derivative. Now we wish to report the structure and synthesis of this compound.

The roots of this plant were extracted with ethanol for a few days, and the filtrate was concentrated to give an oily material, which was extracted several times with benzene. The combined benzene layers afforded a residue, which was chromatographed on silicic acid. Several fractions eluted by chloroform gave a crystalline compound (crystallization from ether). The physical and spectral data are as follows: $C_{27}H_{28}N_2O_4$ m.p. 185-186° (recrystallized from benzene); Mass m/e 444.2020 (calcd. 444.2049); IR (KBr) 3300 (-NH-), 1730 ($-OCOCH_3$), 1660 (-CONH-), 1630 (-CONH-), 1605, 1530 cm^{-1}; NMR (δ, $CDCl_3$)[4] 2.01 (3H, s, $-OCOC\underline{H}_3$), 2.75 (2H, d, J= 7.0 Hz, H-3), 3.07 (1H, d of d, J= 8.0, 13.5 Hz, H-3'), 3.25 (1H, d of d, J= 6.3, 13.5 Hz, H-3'), 3.90 (2H, d, J= 4.3 Hz, H-1), 4.34 (1H, m, H-2), 4.86 (1H, d of d of d, J= 6.3, 8.0, 9.0 Hz, H-2'), 6.37 (1H, d, J= 8.0 Hz, exchangeable with D_2O on heating, $-^{1'}CON\underline{H}-$), 6.94 (1H, d, J= 9.0 Hz, exchangeable with D_2O on heating, $-N\underline{H}COPh$), 7.0-7.8 (15H, aromatic protons).

From the above data, the working structure (1) for this compound except the absolute configuration was proposed. The structure (1) was confirmed by the synthesis from L-phenylalanine (2). L-Phenylalanine was converted to the methyl ester (3) with methanol-HCl at 45°. Reduction of (3) with lithium aluminum hydride in ether gave L-phenylalaninol (4) [m.p. 85-86.5°][5].

L-Phenylalanine methyl ester (3) on treatment with benzoyl chloride in pyridine at 50° afforded N-benzoyl-L-phenylalanine methyl ester (5) [Mass 283 (m^+)]. Heating the mixture of (4) and (5) at 90° gave a product, which was acetylated with acetic anhydride at 50° to give (1), m.p. 185-186°. Identification of the synthetic and natural products was made by comparison of ir, nmr, and ORD ($[\phi]_{240}^{25} = -8.9 \times 10^3$) spectra, by thin layer chromatography, and the measurement of mixed melting point. Hence the absolute structure (1) was completely defined.

Pharmacognostical studies[6] on the Chinese crude drugs, Lang-Tu, were reported. Our research will be interesting in the chemotaxonomical viewpoint. Actually we have also obtained this compound (1) from Euphorbia kansui Liou.

Acknowledgement.

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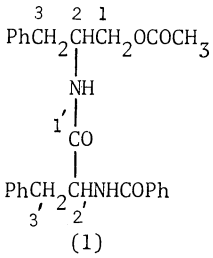
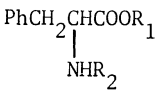


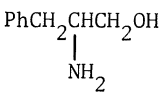
(1)



(2) $R_1 = R_2 = H$

(3) $R_1 = CH_3$, $R_2 = H$

(5) $R_1 = CH_3$, $R_2 = COPh$



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REFERENCES

1) D. Uemura and Y. Hirata, Tetrahedron Letters, 3673 (1971).

2) D. Uemura and Y. Hirata, Tetrahedron Letters, 881 (1973).

3) D. Uemura, Y. Hirata, Y.P. Chen, and H.Y. Hsu, Tetrahedron Letters, in press (1975).

4) The assignment of each proton was secured by nuclear magnetic double resonance experiments.

5) A.R. Battersby and R.S. Kapil, Tetrahedron Letters, 3529 (1965).

6) K. Yoneda, S. Takahashi, and T. Namba, Shoyakugaku Zasshi, 28, 19 (1974).

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