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SHORT REPORTS

ENTADAMIDE B, A SECOND NEW SULPHUR-CONTAINING AMIDE FROM *ENTADA PHASEOLOIDES**

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Key Word Index—*Entada phaseoloides*; Leguminosae; seed; isolation; synthesis; *N*-(2-hydroxyethyl)-3,3-*bis*(methylthio)propanamide; entadamide B; entadamide A.

Abstract—A second new sulphur-containing amide, entadamide B, has been isolated from the dry seeds of *Entada phaseoloides* Merr. together with entadamide A. Entadamide B was characterized by spectroscopic methods as *N*-(2-hydroxyethyl)-3,3-*bis*(methylthio)propanamide and was synthesized in two steps from propiolic acid.

INTRODUCTION

In the previous paper [1], we reported the isolation and structural elucidation of a new sulphur-containing amide, named entadamide A (**1**), from the dry seed kernels of *Entada phaseoloides* Merr. (Leguminosae). Further studies on the basic components in the same plant led to the isolation of the second sulphur-containing amide, named entadamide B (**2**). In this paper we describe the characterization and synthesis of this new compound (**2**).

RESULTS AND DISCUSSION

From the basic fraction obtained from the 75% EtOH extract of the dry seed kernels of *E. phaseoloides*, collected in Thailand, the new compound (**2**) was isolated by the same procedure as that for entadamide A (**1**) [1]. The purified **2** was a colourless syrup in a 0.004% yield of the dry plant material and behaved like **1** with chromogenic reagents.

Entadamide B (**2**), $C_7H_{15}NO_2S_2$ ($[M]^+$ *m/z* 209.0553, calcd 209.0545), differed in composition by the increment CH_4S from entadamide A (**1**). The IR spectrum ($CHCl_3$) of **2** showed bands at 3250–3550 cm^{-1} (*br*, NH and OH) and 1660 cm^{-1} (amide CO) like the spectrum of **1**. The ^1H NMR and ^{13}C NMR spectra ($CDCl_3$) of **2** also exhibited similar signals to those due to the $-CONHCH_2CH_2OH$ moiety of **1**, as shown in Tables 1 and 2. The other signals of both spectra showed the presence of an isolated $=CH–CH_2–$ moiety and two equivalent *S*-methyl groups in the molecule (**2**). From the

Table 1. ^{13}C NMR spectral data for **2**

Carbon	Chemical shift (δ)
C-1	170.4 (*s*)
C-2	42.9 (*t*)*
C-3	50.4 (*d*)
$NH–CH_2$	42.5 (*t*)*
$CH_2–OH$	61.8 (*t*)
$S–CH_3$	13.4 (*q*)

*Assignments may be interchanged.

Table 2. ^1H NMR spectral data for **2** in $CDCl_3$ (δ ppm)

6.20	(1H, *br*, CONH–, disappears on addition of D_2O)
4.15	(1H, *t*, $J = 7$ Hz, $C\underline{H}–CH_2CO–$)
3.75	(2H, *t*, $J = 5$ Hz, $–OC\underline{H}_2CH_2N–$)
3.45	(2H, *m*, $–OCH_2C\underline{H}_2N–$, becomes a 2H triplet ($J = 5$ Hz) on addition of D_2O)
2.68	(2H, *d*, $J = 7$ Hz, $CH–C\underline{H}_2CO–$)
2.4	(1H, *br*, –OH, disappears on addition of D_2O)
2.16	(6H, *s*, S–Me)

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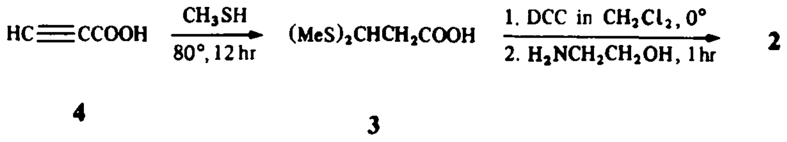
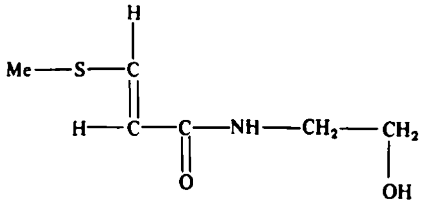
*Parts of this work were presented at the 106th Annual Meeting of the Pharmaceutical Society of Japan at Chiba, 2 April, 1986 (Abstracts p. 180).



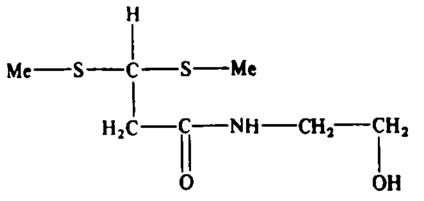
$$\mathrm{HC{\equiv}CCOOH} \xrightarrow[\text{80°, 12 hr}]{\mathrm{CH_3SH}} \mathrm{(MeS)_2CHCH_2COOH} \xrightarrow[\text{2. }\mathrm{H_2NCH_2CH_2OH}\text{, 1 hr}]{\text{1. DCC in }\mathrm{CH_2Cl_2}\text{, 0°}} \mathbf{2}$$

4 **3**

Scheme 1. Synthesis of entadamide B (**2**).



Entadamide A (**1**)



Entadamide B (**2**)

above results, the structure of entadamide B (**2**) was shown to be *N*-(2-hydroxyethyl)-3,3,-*bis*(methylthio)propanamide.

The structure of **2** was also confirmed by direct comparison of the spectral data with those of a synthetic sample, which was prepared by condensation of 3,3-*bis*(methylthio)propionic acid (**3**) with ethanolamine (Scheme 1). The synthetic compound was found to be identical with natural **2** by its spectral data.

EXPERIMENTAL

Plant material. The seeds of *Entada phaseoloides* Merr. were collected in June in the suburbs of Bangkok, Thailand and the air-dried powdered seed kernels (750 g) were used.

Extraction and isolation of entadamide B (**2**) were performed by the procedure of ref. [1]. The purified **2** (28 mg) was obtained in a 0.004 % yield of the dry wt; ^{13}C NMR (100 MHz, $CDCl_3$, TMS): see Table 1; ^{1}H NMR (100 MHz, $CDCl_3$, TMS): see Table 2; EIMS *m*/*z* (rel. int.): 209 $[M]^+$ (6), 194 (14), 162 (8), 88 (18), 75 (100), 70 (30), 45 (25).

Synthesis of entadamide B (**2**). 3,3-*Bis*(methylthio)propionic acid (**3**) was obtained by addition reaction of CH_3SH (0.1 mol) to propiolic acid (**4**, 0.05 mol) according to a modified method of ref. [2] in a 10 % yield. After treated with an equimolar amout of DCC in CH_2Cl_2 at 0°, **3** (0.5 mmol) was allowed to condense with ethanolamine (0.6 mmol) [3] to give **2** in a 23 % yield (Scheme 1).

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