1,3-DIPHENETHYLUREA FROM *STREPTOMYCES* SP. NO. AM-2498

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In the course of screening for new alkaloids from microorganisms, we found 1,3-diphenethylurea[1] as a metabolite in the culture broth of the soil isolate, *Streptomyces* sp. strain No. AM-2498. The sporophore of strain No. AM-2498 was spiral, representative of the section *Spirales* of PRIDHAM *et al.*[2] and the spore was oval with a spiny surface. The aerial mass color was white and melanoid pigment was not produced. The cell wall preparation from strain No. AM-2498 contained LL-diaminopimelic acid.

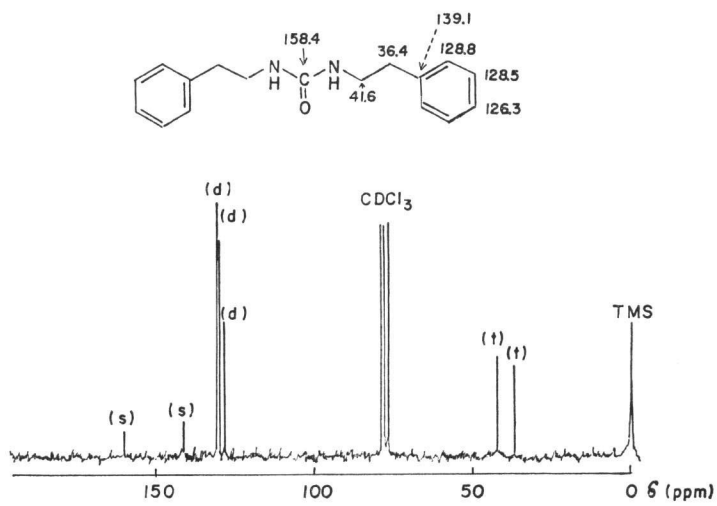
Strain No. AM-2498 was inoculated into 100 ml of medium in a 500-ml SAKAGUCHI flask and incubated at 27°C. A 48-hour culture was transferred into 20 liters of medium in a 30-liter jar fermentor and the fermentation carried out at 27°C for 30 hours. The composition of the seed medium was 2% glucose, 0.5% peptone, 0.5% meat extract, 0.3% dried yeast, 0.5% NaCl and 0.3% $CaCO_3$ (pH 7 before sterilization) and the production medium was 1% glucose, 2% starch, 0.5% yeast extract, 0.5% peptone and 0.4% $CaCO_3$ (pH 7 before sterilization). Adekanol LG-109 (Asahi Electro-Chemical Co., Ltd.) was used as antifoam agent. Metabolite AM-2498 was detected by DRAGENDORFF reaction on silica gel TLC, $CHCl_3$-CH_3OH (10: 1, v/v) (Rf=0.68).

The culture broth was extracted with 4 liters benzene and the solvent layer was dried over anhydrous sodium sulfate and concentrated *in vacuo* to dryness to yield 1.84 g of a brown paste. The paste was treated twice with 100 ml of benzene to give 420 mg of a pale green powder. The powder was recrystallized from methyl alcohol to afford colorless needles (250 mg) of metabolite AM-2498.

Metabolite AM-2498 showed the following physicochemical properties: Melting point 138~141°C, UV λ_{max}^{MeOH} nm (ε) 248 (308), 251 (411), 253 (446), 256 (535), 259 (549), 262 (543), 265 (419), 269 (351). IR ν_{max}^{KBr} cm^{-1}, 3320, 1950, 1875, 1810, 1740, 1610, 1570, 745, 695, PMR (100 MHz, $CDCl_3$) δ 2.70 (4H, sharp triplet, $-CH_2-\times 2$), 3.28 (4H, sharp quartet, $-CH_2-NH-\times 2$), 4.45 (2H, broad singlet, $-NH-\times 2$), 7.12 (10H, sharp doublet, aromatic ring$\times 2$). The molecular formula $C_{17}H_{20}N_2O$ was determined on the basis of elemental analysis (C 76.06, H 7.51, N 10.33%) and its mass spectrum (M^+, *m/e* 268). These spectroscopic properties and proton noise-decoupled ^{13}C-NMR spectrum, are consistent with 1,3-diphenethylurea[1] as the structure of metabolite AM-2498. The ^{13}C-NMR spectrum and signal assignment of metabolite AM-2498 are shown in Fig. 1. The signals in the spectrum were assigned on the basis of their chemical shifts[3], off-resonance decoupling and the comparison with those of dibenzylmethylamine, urea, dimethylurea and their related compounds[4,5].

In a preliminary test the metabolite was found to possess weak antidepressant activity. No acute toxicity of the metabolite was observed in mice after 100 mg/kg intraperitoneal injection.

Fig. 1. Proton noise-decoupled ^{13}C-NMR spectrum of metabolite AM-2498 ($CDCl_3$).
The abbreviations used are as follow: s, singlet; d, doublet; t, triplet.



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