DEHYDROHELIAMINE, A TRACE ALKALOID FROM THE SAGUARO, CARNEGIEA GIGANTEA (CACTACEAE)*

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Key Word Index-Carnegiea gigantea; Cactaceae; cactus alkaloids; dehydroheliamine; 3,4-dihydroisoquinolines.

Abstract—Extraction of Carnegiea gigantea yielded a new 3,4-dihydroisoquinoline alkaloid, dehydroheliamine; the structure was confirmed by synthesis.

INTRODUCTION

Prior to our recent studies, seven β -phenethylamines and tetrahydroisoquinolines (carnegine, gigantine, arizonine, salsolidine, dopamine, 3-methoxytyramine and 3,4-dimethoxy- β -phenethylamine) had been identified or isolated from the saguaro cactus, *Carnegiea gigantea* (Engel.) Br. et R. [1]. Subsequent to a chemotaxonomic MS/MS examination of the alkaloids in several species of giant cacti [2], we have previously isolated two new trace alkaloids, dehydrosalsolidine and heliamine (1), from saguaro [3].

Closer examination of the CIMS of the crude extracts of *C. gigantea* revealed a small peak at m/z 192, accompanying the peak at m/z 194 attributed to the [MH]⁺ of heliamine (1) [3]. This new trace alkaloid was, thus, predicted to be dehydroheliamine (2). Synthetic 2 was prepared for reference by cyclization of 3,4-dimethoxyphenethylamine with formic acid [4]. TLC of the nonphenolic portion of extract A from the cactus [5], with UV visualization, detected 2 as a light blue fluorescent spot on the chromatograms.

Column adsorption chromatography of the nonphenolic extract on Si gel yielded an initial abundance of carnegine and salsolidine, but repeated CC of the earlyeluting fractions yielded a trace of 2 (0.0008 % yield) which crystallized as the hydrochloride. The isolated 2 hydrochloride was identical in all respects (TLC, mp, mmp, EIMS, CIMS, and ¹H NMR) to the synthesized 6,7dimethoxy-3,4-dihydroisoquinoline (dehydroheliamine, 2) hydrochloride.

This is, thus, the second simple fluorescent 3,4-dihydroisoquinoline to be reported from nature, dehydrosal-



solidine from this same cactus being the first [3]. These 3,4-dihydroisoquinolines may well be precursors of the more common, tetrahydroisoquinolines [6]. The usefulness of MS/MS [7] for the detection and tentative identification of such trace constituents, necessitating only small quantities of crude extracts, is again emphasized [2, 3].

EXPERIMENTAL

Alkaloid extraction. The pulverized whole plant material was a part of the collection previously described [3]. A total of 1.1 kg was defatted, basified, percolated with $CHCl_3$, and processed to yield fractions A (alkaloids, 33.95 g), B (nonalkaloids, 0.68 g) and C (water-soluble alkaloids, 3.57 g), as previously described [5]. Fraction A was resolved, by the use of 200 g Amberlite IRA-400 (hydroxide form) anion exchange resin, to yield nonphenolic (18.75 g) and phenolic (4.11 g) alkaloid fractions.

Isolation of carnegine and salsolidine. A portion (13.57 g) of the nonphenolic alkaloid fraction was chromatographed on 200 g Si gel, eluting with gradients of CHCl₃, CHCl₃-MeOH (99:1-9:1), CHCl₃-MeOH-NH₄OH (80:20:1-6:4:1) and MeOH-NH₄OH (100:1). A total of 107 fractions of 50 ml each were analysed by TLC (CHCl₃-MeOH, 8:2 on Si gel) and combined according to similar alkaloid patterns. Carnegine hydrochloride (4.58 g, IR, mp, mmp, TLC) was crystallized from fractions 24-69, and salsolidine hydrochloride (3.76 g, IR, mp, mmp, TLC) was crystallized from fractions 70-107.

Isolation of dehydroheliamine (2). Fractions 1–23 (0.071 g) were combined and chromatographed on 10 g Si gel, eluting with a less polar solvent gradient of CHCl₃, CHCl₃–MeOH (995:5–9:1) and CHCl₃–MeOH–NH₄OH (80:20:1). A total of 41 fractions of 20 ml each were collected and analysed by TLC. Fractions 26–33

^{*} Part 55 in the series "Cactus Alkaloids". For Part 54 see Mata, R., Chang, C.-J., and McLaughlin, J. L. (1983) *Phytochemistry* 22, 1263.

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(13.5 mg) were rechromatographed on Si gel (8 g) using a gradient of CHCl₃, CHCl₃-MeOH (98:2-9:1) and MeOH. Twenty fractions of 25 ml each were collected, and **2** hydrochloride (6 mg, 0.008 % yield, mp 194–196°) was crystallized (EtOH-Et₂O) from fractions 9–11.

Synthesis of dehydroheliamine (2) [4]. The free base (10.17 g) of 3,4-dimethoxyphenethylamine (Aldrich) was refluxed for 16 hr with 10 ml 99 $\frac{9}{6}$ HCOOH. The reaction mixture was poured into 200 ml cold H₂O and extracted with C₆H₆ (5 × 100 ml). The C₆H₆ extract was dried and reduced to an oil (7.77 g). The oil was cooled over ice, 5 ml POCl₃ was added, and the mixture was refluxed for 45 min. After cooling, 50 ml petrol was added and then decanted, and 50 ml 10 $\frac{9}{6}$ HCl added. The resultant soln was basified to pHs 7, 8 and 9 with NH₄OH and extracted at each increment with C₆H₆ (100 ml). The C₆H₆ layers were dried and reduced to a brown oil (5.17 g, 48 $\frac{9}{6}$ yield).

This oil then yielded crystalline dehydroheliamine hydrochloride (EtOH-Et₂O) (2) (4.32 g). Mp 195–196°; ¹H NMR (D₂O, 80 MHz): δ 9.13 (1H, br s, H-1), 7.81 (1H, s, H-8), 7.51 (1H, s, H-5), 4.47–4.2 (6H, 2s, OMe-2 overlapped with 2H, m, H-3), 2.56 (2H, br t, H-4); free base: ¹H NMR (CDCl₃, 80 MHz): δ 9.05 (1H, br s, H-1), 7.43 (1H, s, H-8), 6.78 (1H, s, H-5), 4.00–3.82 (6H, 2s, OMe-2 overlapped with 2H, m, H-3), 3.00 (2H, br t, H-4); CIMS m/z 192 [MH]⁺; EIMS m/z (%): 191 (100), 190 (15), 176 (70), 164 (5), 146 (10), 136 (30), 117 (12), 104 (15), 91 (10), 77 (20). The synthetic and isolated **2** hydrochlorides were essentially identical: mmp 195°; cochromatography in five TLC systems [5]. ¹H NMR, CIMS and EIMS.

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ANTIFUNGAL STRESS METABOLITES FROM SOLANUM AVICULARE

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Key Word Index—Solanum aviculare; Solanaceae; solasodine; Solanum alkaloids; stress metabolites; vacuum infiltration.

Abstract—The steroidal alkaloids $\beta\beta$ -solasodan-3-one and solasodenone were isolated as antifungal stress metabolites from leaves of *Solanum aviculare* stressed by vacuum infiltration with water. The constitutive leaf alkaloids, solasodine and solamargine, also showed antifungal activity.

INTRODUCTION

Solanum aviculare L. has been used commercially as a source of 'solasonine', a mixture of steroidal glycoal-kaloids from which solasodine (1), a useful starting material in steroidal drug synthesis, is obtained on hydrolysis [1]. The chemistry of the Solanum alkaloids has recently been reviewed [2]. Fungitoxicity for the steroidal alkaloids and glycoalkaloids of the Solanaceae has been reported for solasodine and solamargine from S. aviculare [3], solanine from the potato (S. tuberosum) [3] and tomatine from the tomato (Lycopersicon esculentum)

[3, 4]. Fungitoxic compounds may also accumulate in plants following fungal infection (phytoalexins) or stress induced by abiotic agents including detergents, metal salts, chloroform vapour, freeze-thaw treatment [5], UV radiation [6] or vacuum infiltration [7, 8]. In tomato and potato the antifungal sesquiterpene rishitin is synthesized under fungal challenge [9]. Here we report the isolation of the *Solanum* alkaloids 5β -solasodan-3-one and solaso-denone as antifungal stress metabolites from the leaves of *S. aviculare* subjected to vacuum infiltration with water.