CACTUS ALKALOIDS. XLVII. β-PHENETHYLAMINES FROM THE "MISSOURI PINCUSHION", *CORYPHANTHA (NEOBESSYA) MISSOURIENSIS*

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Several species in the large cactus genus *Coryphantha* have yielded β-phenethylamine alkaloids; most of this phytochemical work has been summarized previously (1, 2). Folkloric uses of a few *Coryphanthas* as psychoactive cacti have been documented (3, 4). Following a report that macromerine (*N*,*N*-dimethyl-β-hydroxy-3,4-dimethoxy- β -phenethylamine) is possibly hallucinogenic in squirrel monkeys and cats (5), a purported modern drug use of *Coryphanthas*, as "natural and legal" psychedelics, has evolved (6–10). A subsequent study did not confirm psychoactivity for macromerine, normacromerine, or bisnormacromerine in rats (11), but a more recent study using a battery of tests showed close correlation in psycho-active effects between mescaline and normacromerine (12). The biosynthesis of the major β-hydroxy-β-phenethylamines, in *C. macromeris* (Engelm.) Br. and R. var. *runyonii* (Br. and R.) L. Benson, does not follow the usual mammalian pathways (13, 14).

C. missouriensis (Sweet) Br. and R. is a cold weather cactus named for its type of location on arid hills along the Missouri river of the northern great plains; it is quite widespread, but variable, across western North America (15). Cactologists have also placed this species in the *Mammillaria* and, more commonly, the *Neobessya* genera (16). Its common names include the "Kansas pincushion" and the "Missouri pincushion" (17). In a preliminary thin layer chromatography (tlc) screen, this species was positive for alkaloids, and we wished to examine these compounds further for psychopharmacologic and chemotaxonomic evaluation.

The chloroformic percolate from the basified, freeze-dried, powdered plant material was processed to produce phenolic and nonphenolic portions of alkaloid fractions A and C (18, 19). A tertiary alkaloid hydrochloride crystallized directly from the phenolic portion of fraction A; a further quantity of the same salt was obtained after silica gel column chromatography of the mother liquor. This tertiary phenolic alkaloid was identified (tlc, mp, ir, ms) as hordenine (*N*,*N*-dimethyltyramine).

The more polar eluates from the above column were combined with the phenolic portion of alkaloid fraction C, and the mixture was subjected to preparative tlc. After acid-base partitioning of the tlc eluates, a secondary amine was crystallized as the hydrochloride and identified (tlc, mp, ir, ms) as *N*-methyltyramine. Preparative tlc eluates containing a primary phenolic amine failed to yield a crystalline hydrochloride, but this trace compound was identified (tlc, ms) as tyramine.

The nonphenolic portion of fraction

A contained traces of a secondary amine which, after preparative tlc and acid-base partitioning of the eluates, failed to yield a crystalline hydrochloride. However, this compound was identical (tlc, ms) to *N*-methyl-3,4-dimethoxy-β-phenethylamine.

These four β-phenethylamines (hordenine, *N*-methyltyramine, tyramine, and *N*-methyl-3,4-dimethoxy-β-phenethylamine) have all been isolated and or detected previously in other *Coryphantha* species (1, 2). The absence in *C. missouriensis* and certain other *Coryphanthas* (1, 2) of β-hydroxylated alkaloids, such as synephrine and normacromerine, may be a chemical justification for some taxonomic distinctions within this large genus. Any purported psychoactivity of this species would not likely be explained by the traces of the four β-phenethylamines detected in this study.

EXPERIMENTAL[1]

PLANT MATERIAL.—Whole plants of *C. missouriensis* were collected 16.1 km northeast of Winfield, Cowley County, Kansas (17). Representative specimens were identified by Dr. Edward F. Anderson and deposited in the Herbarium at Whitman College, Walla Walla, Washington. The fresh plants were sliced, frozen, freeze-dried, and pulverized through a 2 mm screen in a Wiley mill.

ALKALOID EXTRACTION.—The powdered plant material (626 g) was defatted, basified with methanol-ammonia, and extracted via chloroformic percolation: the chloroform extract when condensed and processed yielded fraction A (alkaloids) (3.2 g), fraction B (nonalkaloidal materials), and fraction C (water soluble alkaloids) (4.5 g) (18). A portion (1.3 g) of fraction A and all of fraction C were separately dissolved in ethanol and resolved into phenolic and nonphenolic portions on columns of 100 g Amberlite IRA-401S (hydroxide form) (19).

[1]Melting points were determined with a Mel-Temp apparatus and are uncorrected. To obtain ir spectra KBr pellets were used in a Beckman IR-33 spectrophotometer. Electron impact and chemical ionization mass spectra (eims and cims) were produced on a Hitachi RMU-6 spectrometer. Reference β-phenethylamines were obtained as previously described (20).

ISOLATION OF HORDENINE.—Analytical tlc (18) of the phenolic portion (1.2 g) of fraction A detected a predominant tertiary amine and small amounts of a secondary and a primary amine (21). A portion of this fraction (0.73 g) was dissolved in absolute ethanol and acidified with 5% HCl gas in absolute ethanol; upon addition of ethyl ether, 422 mg of the tertiary amine hydrochloride crystallized in two batches.

The substances from the mother liquor were dissolved in ca. 30 ml of water, basified with ammonia, and partitioned with two 100 ml portions each of chloroform and ethyl ether. The residue (0.5 g) from the combined chloroform-ether extracts was subjected to chromatography (92 g, silica gel, 0.063–0.22 mm, E. Merck, 3.0 x 60 cm column). Development was made with chloroform (550 ml); chloroform-methanol, 10:1 (1,350 ml); chloroform-methanol, 10:3 (800 ml); chloroform-methanol, 1:1 (300 ml); and methanol (500 ml). The tertiary alkaloid was detected (tlc) in fractions eluted with chloroform-methanol, 1:1, and an additional 167 mg of hydrochloride was crystallized.

The tertiary alkaloid hydrochloride (0.609 g, 0.39% yield) was identical to hordenine hydrochloride: tlc in systems A, C, E, F, and G (18); mp, mmp, lit. mp 181° (2); ir; eims and cims.

ISOLATION OF *N*-METHYLTYRAMINE.—The trace secondary and primary amine alkaloids were detected (tlc) in the methanol eluates of the above column. They were combined with the phenolic portion of fraction C (0.60 g total) and subjected to preparative tlc in solvent G (18) (10 plates, two bands, two developments). The residue from the methanol-chloroform (1:19) eluates of the tlc bands containing the secondary amine was dissolved in 15 ml of 1 N hydrochloric acid and partitioned with two 15 ml-portions each of chloroform and ethyl ether; after basification with ammonium hydroxide, the extractions were repeated. The alkaloid residue from the second combined chloroform-ether extractions yielded a crystalline hydrochloride from acidic ethanol-ethyl ether (8 mg, 0.013% yield). This secondary amine hydrochloride was identified as *N*-methyltyramine: tlc in systems A, C, E, F, and G (18); mp, mmp, lit. mp 149° (18); ir; eims.

IDENTIFICATION OF TYRAMINE.—Eluates of the band containing the primary amine failed to yield a crystalline hydrochloride. However, cims of the residue revealed m/z 138 for the MH^+ indicative of tyramine. Analytical tlc in systems A, C, E, F, and G (18) demonstrated cochromatography with tyramine.

IDENTIFICATION OF *N*-METHYL-3,4-DIMETHOXY-β-PHENETHYLAMINE.—The residue from the nonphenolic portion of fraction A (0.112 g) was dissolved in ethanol and subjected to

preparative tlc in solvent E (18) (4 plates, 1 band, two developments). Methanol-chloroform (1:19) eluates of the major band, containing a secondary amine, failed to yield a crystalline hydrochloride even after acid-base partitioning. However, the residue produced an m/z 196 for the MH^+ in cims, indicative of *N*-methyl-3,4-dimethoxy-β-phenethylamine. Cochromatography with the reference compound in tlc solvents A, C, E, F, and G (18) supported this identification.

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