Cactus Alkaloids XII: β-Phenethylamine Alkaloids of the Genus *Coryphantha*

K. M. KELLEY HORNEMANN, J. M. NEAL, and J. L. McLAUGHLIN*▲

Abstract □ The presence of alkaloids was chromatographically demonstrated in seven species of *Coryphantha*. By using preparative chromatographic techniques, *N*-methyl-3,4-dimethoxy-β-phenethylamine, *N*-methyl-4-methoxy-β-phenethylamine, *N*-methyltyramine, and *N*,*N*-dimethyltyramine (hordenine) were isolated from extracts of *C. cornifera* (DC.) Br. and R. var. *echinus* (Engelm.) L. Benson. In addition, two new cactus alkaloids, *N*-methyl-4-hydroxy-β-methoxy-β-phenethylamine (β-*O*-methylsynephrine) and 4-methoxy-β-hydroxy-β-phenethylamine, were identified spectroscopically in extracts of this species.

Keyphrases □ Alkaloids, cactus—chromatographic identification in seven *Coryphantha* species □ Synephrine—identified in seven *Coryphantha* species □ β-Phenethylamine alkaloids—chromatographic isolation and/or identification from seven *Coryphantha* species □ *Coryphantha*, seven species—chromatographic isolation and identification of β-phenethylamine alkaloids, spectroscopic identification of two new alkaloids and structures proposed, synephrine found in all seven species

The hallucinogenic use of the peyote cactus, *Lophophora williamsii* (Lem.) Coult., in primitive as well as present cults and cultures has prompted phytochemical interest in other members of the Cactaceae (1–4). The genus *Coryphantha* has not been thoroughly examined, although at least one species, *C. palmeri* Br. and R., was reported by Dominguez *et al.* (5) to have folkoric use as a "narcotic" plant and to contain an unidentified alkaloid. These workers also reported that ethanolic extracts of *C. pectinata* (Engelm.) Br. and R. yielded positive alkaloid tests (4). The isolation of macromerine (*N*,*N*-dimethyl-3,4-dimethoxy-β-hydroxy-β-phenethylamine) from *C. macromeris* (Engelm.) Br. and R. (6) and *C. runyonii* Br. and R. (7) demonstrated that the genus, like *Lophophora*, contains simple β-phenethylamine alkaloids. More recently, by combining GLC with mass spectrometry, Agurell (3, 8) detected tyramine, hordenine (*N*,*N*-dimethyltyramine), *N*-methyl-3,4-dimethoxy-β-phenethylamine, and *N*-methyl-4-methoxy-β-phenethylamine in *C. runyonii* [*Lepidocoryphantha runyonii* (Br. and R.) Backbg.]. The present investigation was undertaken to screen additional available species of this genus in a search for new cactus alkaloids that might have psychotropic activity.

EXPERIMENTAL[1]

Plant Material—Seven species of cacti of the genus *Coryphantha* were obtained, and all were identified according to the descriptions of Britton and Rose (9). Included were *C. echinus* (Engelm.) Br. and R.[2], *C. pectinata* (Engelm.) Br. and R.[2], *C. ottonis* (Pfeif.) Lem.[3], *C. elephantidens* Lem.[3], *C. durangensis* (Rünge) Br. and R.[3], *C. cornifera* (DC.) Lem.[4], and *C. poselgeriana* (Dietr.) Br. and R.[5].

Benson (10) recently revised the taxonomy of some members of this genus and included *C. echinus* as a variety of *C. cornifera*. A large quantity of *C. cornifera* (DC.) Br. and R. var. *echinus* (Engelm.) L. Benson (5.0 kg. of dried material) was obtained[2] to permit alkaloid isolation. Confirmation of this identification of the species was obtained by sending freeze-dried specimens to

Table I—Reference Cactus Alkaloids and Related Compounds

β-Phenethylamines
Mescaline[a]
N-Methylmescaline[a]
Trichocereine hydrochloride[a]
3,4-Dimethoxy-β-phenethylamine hydrochloride[a]
N-Methyl-3,4-dimethoxy-β-phenethylamine hydrochloride[a]
4-Methoxy-β-phenethylamine hydrochloride
N-Methyl-4-methoxy-β-phenethylamine hydrochloride[a]
N-Methyl-β-phenethylamine hydrochloride
Macromerine[a]
Ephedrine SO_4
N-Acetylmescaline[a]
4-Demethylmescaline hydrochloride
4-Demethyltrichocereine hydrochloride
Synephrine tartrate
Phenylephrine hydrochloride
Metanephrine hydrochloride
Normetanephrine hydrochloride
Octopamine hydrochloride
3-Methoxytyramine hydrochloride[a]
N-Methyltyramine hydrobromide[a]
3,4-Dihydroxynorephedrine hydrochloride
Hordenine[a]
DL-Dopa
Tyramine hydrochloride[a]
Tetrahydroisoquinolines
7-Methoxytetrahydroisoquinoline hydrochloride
6,7-Dimethoxytetrahydroisoquinoline hydrochloride
5,6,7-Trimethoxytetrahydroisoquinoline hydrochloride
Anhalonidine hydrochloride[a]
O-Methylanhalonidine hydrochloride[a]
Anhalamine hydrochloride[a]
N-Methylanhalinine hydrochloride
O-Methylpellotine hydrochloride
Hydrohydrastinine hydrochloride
Salsolidine hydrochloride[a]
Lophophorine hydrochloride[a]
Hydrocotarnine hydrochloride
Corypalline hydrochloride
Salsoline hydrochloride[a]
7-Methoxy-8-hydroxytetrahydroisoquinoline hydrochloride
6-Methoxy-7-hydroxytetrahydroisoquinoline hydrochloride
6-Hydroxy-7-methoxytetrahydroisoquinoline
Gigantine hydrochloride[a]
Pellotine hydrochloride[a]
Anhalinine hydrochloride[a]
Anhalidine hydrochloride[a]

[a] Alkaloids known to occur in cacti.

[1] IR spectra were obtained using KBr pellets and a Beckman IR5A. UV spectra were determined in 95% ethanol with a Beckman DB spectrophotometer scanning from 320 to 205 nm. NMR spectra were obtained using microcells in Varian A-60 or Varian T-60 NMR spectrometers. Mass spectral analyses were determined with an AEI MS 9 spectrometer. Melting points were taken with a Fisher-Johns melting-point apparatus and are uncorrected.

[2] From Homer Jones, Southwest Cactus Co., Alpine, Tex.
[3] From Johnson Cactus Gardens, Paramount, Calif.
[4] From Henrietta's Nursery, Fresno, Calif.
[5] From El Paso Cactus Gardens, Anthony, N. M.

Table II—R_f Values and Reactions of Selected Alkaloids with Detecting Reagents

Alkaloids	Fluorescence with Dansyl Chloride	Color Reaction with Tetrazotized Benzidine[a]	Color Reaction with Wagner's Reagent	Solvent A	Solvent B	Solvent C	Solvent D
Nonphenolics							
4-Methoxy-β-phenethylamine	+	RB	−	0.59	0.42	0.51	0.43
N-Methyl-4-methoxy-β-phenethylamine	+	Y	+	0.63	0.34	0.40	0.34
3,4-Dimethoxy-β-phenethylamine	+	RB	+	0.64	0.31	0.44	0.37
N-Methyl-3,4-dimethoxy-β-phenethylamine	+	Y	+	0.63	0.27	0.33	0.27
Macromerine	−	−	+	0.78	0.51	0.60	0.55
NP[b]	+	Y	−	0.39	0.18	0.60	0.37
Phenolics							
Hordenine	+	G	+	0.59	0.54	0.66	0.54
N-Methyltyramine	+	Y	−	0.28	0.24	0.36	0.23
Tyramine	+	RB	+	0.28	0.24	0.45	0.31
Synephrine	+	Y	−	0.15	0.17	0.37	0.24
P[c]	+	Y	−	0.49	0.41	0.60	0.45

[a] RB = red-brown, Y = yellow, and G = gold. [b] NP denotes the unknown nonphenolic alkaloid from *C. cornifera* var. *echinus* (4-methoxy-β-hydroxy-β-phenethylamine). [c] P denotes the unknown phenolic alkaloid from *C. cornifera* var. *echinus* (β-*O*-methylsynephrine).

Dr. Benson. Living specimens of this species and all others investigated are being maintained in the greenhouses of the Drug Plant Laboratory.

The plant material was prepared for alkaloid extraction by drying sliced cacti in a forced air oven at 48°, grinding to a coarse powder, and defatting with petroleum ether in large continuous-extraction (Soxhlet) apparatus.

TLC—Analytical TLC plates were prepared in the usual manner with a 0.25-mm. layer of adsorbent (silica gel G, Merck). Preparative TLC plates were prepared with a 1-mm. layer of adsorbent containing a fluorescent indicator (silica gel PF_{254}, Merck). Two solvents were used routinely for analytical and preparative separations: Solvent A, chloroform–methanol–concentrated ammonium hydroxide (80:20:1); and Solvent B, ethyl acetate–methanol–concentrated ammonium hydroxide (85:10:5). Solvent C, isopropanol–water–concentrated ammonium hydroxide (80:18:2), and Solvent D, benzene–methanol–4% ammonium hydroxide (10:15:2), were only used analytically. The alkaloids were visualized using dansyl chloride, Wagner's, and tetrazotized benzidine spray reagents (11). Reference samples of 24 β-phenethylamine and 21 tetrahydroisoquinoline alkaloids (Table I) were compared with alkaloid extracts of the cacti on the basis of R_f values and color reactions with the spray reagents when 10-mcg. quantities were chromatographed (Table II).

GLC[6]—A prepacked stainless steel column, 1.83 m. × 0.41 cm. (6 ft. × 0.125 in.) o.d., having a solid support of high-performance Chromosorb W acid washed (100–120 mesh, pretreated with 2% KOH) and treated with dimethyldichlorosilane and a liquid phase of 5% silicone gum rubber SE-30[7], was used. Samples were injected in 4-μl. volumes at a concentration of 1 mcg./μl. ethanol and analyzed at both 150 and 170°.

Extraction of Alkaloids—For each species, the defatted plant powder was macerated with a solution of chloroform, methanol, and ammonium hydroxide; it was then extracted with chloroform in the continuous extractors. The chloroform extract was condensed *via* rotary vacuum to a thick syrup. This syrup was dissolved in 1 *N* HCl and extracted with chloroform and with ethyl ether to remove nonalkaloidal materials. The acidic aqueous solution was then neutralized to pH 9.5 with ammonium hydroxide. The alkaloids were extracted from the basic solution with chloroform and with ether. The details of these procedures were described previously (11, 12).

These extracts were condensed, and the combined residue was dissolved in 95% ethanol. The alcoholic solution of the alkaloids was separated into nonphenolic and phenolic fractions using a strongly basic ion-exchange resin[8] (11). The nonphenolic alkaloids were washed through the column with ethanol, and the solution was condensed to a volume of concentration suitable for TLC assay. The phenolic alkaloids were eluted from the resin with 1 *N* HCl. The acidic solution of phenolic compounds was neutralized to pH 9.5 with 7.5 *N* NaOH and freeze dried[9]. The powdered residue was extracted with ethanol in chloroform (1:9). This extract was condensed, and the residue was dissolved in a volume of ethanol for a concentration suitable for TLC assay.

A modification of this procedure was employed in the isolation of alkaloids from *C. cornifera* var. *echinus*. To elute the phenolic alkaloids from the ion-exchange column, a solution of glacial acetic acid in ethanol (1:9) was used. The eluate was condensed *in vacuo*, and the remaining acetic acid solution was diluted with water, filtered to remove a resinous precipitate, and extracted with chloroform. The acidic aqueous solution was then basified with ammonium hydroxide to pH 9.5 and extracted with chloroform (Ext. P-1). The basic aqueous solution retaining alkaloids was freeze dried, the powder was extracted with chloroform and with ethanol, and the extracts were combined (Ext. P-2).

Resolution of Nonphenolic Alkaloids from *C. cornifera* var. *echinus*—The separation of the three major alkaloids (*N*-methyl-3,4-dimethoxy-β-phenethylamine, *N*-methyl-4-methoxy-β-phenethylamine, and an unknown alkaloid) detected in the nonphenolic fraction obtained from 5.0 kg. of this species was performed using preparative TLC. The extract was applied with a syringe to 19 preparative plates and developed in Solvent A. The appropriate zones were visualized under UV light, removed from the plates, and eluted with five successive washings with 5% concentrated ammonium hydroxide in ethanol, using 5 ml. per zone. The lower zone contained an unidentified alkaloid, designated NP, which could not be crystallized as the hydrochloride.

The eluate of the upper zone, containing *N*-methyl-3,4-dimethoxy-β-phenethylamine and *N*-methyl-4-methoxy-β-phenethylamine, was rechromatographed on eight plates in Solvent B to resolve these two alkaloids. Because there was not a clear separation of the alkaloids, each zone, eluted as already described, was chromatographed again on two plates with the aid of Solvent B. The separated alkaloid fractions were eluted, the eluates were evaporated to dryness, and the residues were subjected to acid–base partitioning. The final residues, dissolved in 3 ml. absolute ethanol and acidified with anhydrous HCl in ethanol (5% w/w), yielded the crystalline HCl salts on addition of ethyl ether.

Resolution of Phenolic Alkaloids of *C. cornifera* var. *echinus*—By using TLC, Ext. P-1 (obtained from the phenolic fraction of 5.0 kg. of plant material) was estimated to contain all of the detectable hordenine but less than half of the other identifiable phenolic alkaloids. Further purification of this extract was achieved by preparative TLC on five plates prepared and developed with Solvent B as al-

[6] GLC analysis was performed on a Hewlett-Packard Chromatograph 5750.
[7] As purchased from Hewlett-Packard.
[8] Amberlite IRA-401.
[9] VirTis Freezemobile.

Table III—Alkaloids Identified with TLC in *Coryphantha* sp.

Alkaloids	*C. cornifera* var. *echinus*	*C. pectinata*	*C. elephantidens*	*C. durangensis*	*C. ottonis*	*C. poselgeriana*	*C. cornifera*
Nonphenolics[a]							
4-Methoxy-β-phenethylamine					x	x	x
N-Methyl-4-methoxy-β-phenethylamine	x	x					
N-Methyl-3,4-dimethoxy-β-phenethylamine	x	x	x	x			x
Macromerine	x	x	x				
NP[b]	x	x	x				x
Phenolics							
Hordenine	x	x	x	x	x	x	x
N-Methyltyramine	x	x	x	x	x	x	x
Synephrine	x	x	x	x	x	x	x
P[c]	x	x					

[a] Identifications of the nonphenolic alkaloids were confirmed by GLC. [b] NP denotes the unknown nonphenolic alkaloid from *C. cornifera* var. *echinus* (4-methoxy-β-hydroxy-β-phenethylamine). [c] P denotes the unknown phenolic alkaloid from *C. cornifera* var. *echinus* (β-*O*-methylsynephrine).

ready described. Eluates of the hordenine fraction and of an unknown alkaloid fraction, designated P, were each evaporated to dryness and partitioned with acid and base; the final extracts were evaporated to dryness under nitrogen. The residue of the hordenine fraction, dissolved in ethanol and acidified with HCl, yielded crystals on addition of ether.

Ext. P-2 was assayed by TLC and found to contain P along with *N*-methyltyramine and synephrine. This extract was resolved on three preparative TLC plates in Solvent A, and the alkaloids were eluted and purified as already described. Attempts to crystallize synephrine as the hydrochloride were unsuccessful. When similar treatment of the combined P fractions failed to produce crystals, the basic aqueous solution from its acid–base partitioning was assayed with TLC and found to have retained most of the alkaloid. The pH of this solution was readjusted to 9.5, and the solution was extracted again with chloroform. The HCl salt was then crystallized as described for the other alkaloids.

The basic aqueous solution, obtained during the partitioning of the hordenine fraction, was readjusted to pH 9.5 and again extracted with chloroform. The extract was evaporated to dryness under nitrogen to yield crystalline hordenine which was recrystallized from benzene.

Isolation of *N*-Methyltyramine from *C. cornifera* var. *echinus*— An earlier shipment of cacti from the same supplier was extracted and resolved into phenolic and nonphenolic fractions according to the method described for the screening, *i.e.*, utilizing 1 *N* HCl to remove the phenolic alkaloids from the ion-exchange resin. The phenolic fraction from 1.5 kg. of dried plant material was subjected to column chromatography. Aluminum oxide (neutral, Merck) was prepared for the column by drying at 105–110° for 24 hr. The adsorbent was packed into a 2 × 60-cm. glass column. The extract was mixed with adsorbent and placed on the column in a 3-mm. band. Development proceeded with 500 ml. chloroform–methanol (4:1), 250 ml. chloroform–methanol (1:1), and 1500 ml. methanol. A fraction collector[10] was used to collect 12-ml. fractions of the column eluate. *N*-Methyltyramine was detected by TLC in all fractions beyond number 60 and was free of other alkaloids beyond number 70. The combined fractions, containing only *N*-methyltyramine, were evaporated to dryness, and the residue was subjected to acid–base partitioning. The HCl salt was crystallized as described for the other alkaloids.

RESULTS AND DISCUSSION

Screening Procedures with TLC and GLC—With selective reagents (11) and various solvent systems (Table II), it was possible to use TLC to identify several alkaloid constituents and to detect other unknown alkaloids of species of the genus *Coryphantha* (Table III). Primary and secondary amines may be detected with dansyl chloride reagent, which forms fluorescent conjugates that are easily visualized when 10 mcg. of alkaloid is present. Plates sprayed with this reagent may be oversprayed with another such as Wagner's reagent, which gives a typical brown stain with the undetected tertiary amines. The colors of complexes formed with tetrazotized benzidine are related to small changes in structural formulas. Primary and secondary amines may be distinguished with this reagent, the former producing a red-brown chromophore and the latter a yellow one. Phenolic β-phenethylamines with aromatic methyl ether substitutes, *e.g.*, 3-methoxytyramine, form brown conjugates with tetrazotized benzidine, whereas 8-hydroxytetrahydroisoquinolines become bright red with this reagent.

GLC has been previously utilized effectively to separate cactus alkaloids (3, 6, 13–15). Information derived from GLC confirmed the TLC identifications of the nonphenolic alkaloids as listed in Table III. The peaks were identified by comparison of retention times with those observed upon injection of reference compounds. Greater resolution was obtained at the lower temperature (150°). The greater sensitivity and/or resolution of GLC over TLC was demonstrated by a larger number of unidentified peaks on the GLC charts compared to spots detected with TLC. The conditions utilized (alkaline) did not permit the analysis of phenolic alkaloids by GLC, because these showed extensive tailing and poor resolution.

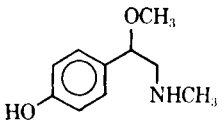
C. pectinata and *C. cornifera* var. *echinus* show identical alkaloidal constituents by both TLC and GLC analyses. Anatomically, these two species are very similar, differing only by the absence of central spines in *C. pectinata*, according to the descriptions of Britton and Rose (9). This suggests that these may be the same species. Indeed, one specimen was received with its major growth having central spines and a smaller growth from the same root system lacking central spines. Surprisingly, the alkaloid composition of *C. cornifera* and *C. cornifera* var. *echinus* was different as evidenced by both GLC and TLC analyses.

Identification of Alkaloid Salts Crystallized from *C. cornifera* var. *echinus*—The identities of salts of known compounds crystallized from *C. cornifera* var. *echinus* were confirmed by comparisons

Table IV—Yields and Melting Points of Products Isolated from *C. cornifera* var. *echinus*

Alkaloid Isolated	Yield, mg.	Percent of Dry Plant Material	Melting Point of Product	Melting Point of Reference
N-Methyl-3,4-dimethoxy-β-phenethylamine hydrochloride	35	0.0007	137–138°	137–138°
N-Methyl-4-methoxy-β-phenethylamine hydrochloride	12	0.0002	183–184°	178–183°
Hordenine hydrochloride	6	0.0001	182–185°	186–187°
Hordenine (free amine)	29	0.0006	114–116°	118°
N-Methyltyramine hydrochloride	3	0.0002	146–147°	146–147°

[10] Gilson Medical Electronics.



β-O-methylsynephrine

of melting points, mixed melting points, and IR spectra of each compound with reference compounds (Table IV). In no case was depression of the melting point of the reference compound on mixing with the product observed. Coincidence of IR spectra of the isolated products with those of the respective references supported the identification of these alkaloids.

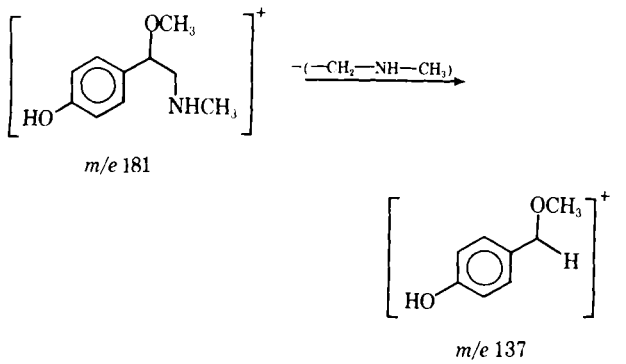
Significance of Isolated Nonphenolic Alkaloids - *N*-Methyl-3,4-dimethoxy-β-phenethylamine previously has been detected in *C. runyonii* Br. and R. (3) and crystallized from *Echinocereus merkeri* Hildm. (16), *Ariocarpus trigonus* (Web.) Schum. (17), *A. fissuratus* (Engelm.) Schum. (18), and *A. retusus* Scheid. (19). *N*-Methyl-4-methoxy-β-phenethylamine has been previously observed in *C. runyonii* (8) and crystallized from only *A. retusus* (19). Thus, these alkaloids have been found previously only in the Cactaceae. No psychopharmacologic studies have been reported with these compounds.

Significance of Isolated Phenolic Products - Hordenine was among the earliest of the cactus alkaloids isolated (20). Since its first detection, this compound has been reported in at least eight plant families (21–24). *N*-Methyltyramine has been more elusive to phytochemical investigations, although it was long presumed to be present in cactus species as the precursor of hordenine. To date, it has been found in at least five plant families (21–23). This alkaloid was first isolated from Cactaceae from *L. williamsii* (11). Both hordenine and *N*-methyltyramine have been demonstrated in several other species of cacti (1, 3, 12, 17, 25–27). The pharmacology of these *N*-methylated tyramines has been studied (28, 29), and weak sympathomimetic responses have been observed. Slight antiseptic activity was reported for hordenine (30).

Detection of Synephrine in *Coryphantha* sp. - Chromatographic evidence suggests the presence of the sympathomimetic synephrine (*N*-methyl-4-hydroxy-β-hydroxy-β-phenethylamine) in all seven species of *Coryphantha* screened. It has not been possible to distinguish chromatographically between synephrine and phenylephrine, the *meta*-isomer. However, it is probable that the *para*-substituted compound should be present rather than the *meta*-substituted analog in view of the biosynthetic derivation of β-phenethylamines from tyrosine. There has been no previous report of synephrine in Cactaceae. However, the compound has been isolated from some citrus fruits (Rutaceae) (31, 32), and its biosynthesis has been investigated there (33). It was recently detected in three other plant families (23). Synephrine, with its β-hydroxyl group, is possibly an intermediate in the biosynthesis of macromerine, also present in *C. cornifera* var. *echinus* as indicated by TLC and GLC.

Structure Elucidation of the Unknown, P - The identity of synephrine in *C. cornifera* var. *echinus* is further supported by the elucidation of the structure of the phenolic unknown, P, isolated from this cactus. UV, NMR, and mass spectral analyses indicate that the compound is β-*O*-methylsynephrine.

The UV spectrum of the alkaloid gave maximal absorption at 276 and 226 nm., corresponding to 4-hydroxy-β-phenethylamine analogs (Table V).



m/e 181

m/e 137

Scheme I

Table V - UV Absorption of Substituted Phenolic β-Phenethylamines

	$\lambda_{max.}$, nm.	
N-Methyltyramine	278	224
Synephrine	276	225
3-Methoxytyramine	282	230
Phenylephrine	276	215
P (unknown phenolic)	276	226

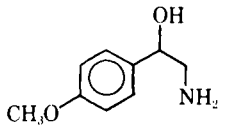
NMR spectra were obtained using 4 mg. of the alkaloid for both the free amine in deuterated chloroform and the HCl salt in deuterated methanol. The spectrum of the free amine showed a pair of doublets (centered at 7.0 δ), integrating for four aromatic protons, and a one proton singlet (7.3 δ); two singlets (2.4 δ and 3.2 δ), each integrating for three protons, indicating an *N*-methyl and an *O*-methyl group, respectively; broad peaks for one proton (1.2 δ) and two methylene protons (2.8 δ); and a quartet for the benzylic proton (4.3 δ). Comparison with the spectrum of the HCl salt in deuterated methanol revealed two exchangeable protons since singlets at 1.2 δ (N–H) and 7.3 δ (Ar–OH) did not appear in this spectrum.

Mass spectral analysis showed a parent ion peak at *m/e* 181.1086 (calc. 181.1103) and a base peak at *m/e* 137.0527 (calc. 137.0603) consistent with the fragmentation shown in Scheme I.

Six milligrams of β-*O*-methylsynephrine or its HCl salt (m.p. 175–181°) was isolated from *C. cornifera* var. *echinus* (yield 0.0001%)[11]. Stewart and Wheaton (34) reported 175–176° as the melting point of this compound isolated from tangerine leaf extracts and prepared synthetically. Synthetic β-*O*-methylsynephrine hydrochloride was prepared from synephrine according to the method of Stewart and Wheaton (34); after recrystallization, it melted at 180–182° and gave NMR spectra identical to that of P. These authors suggest that this product was an artifact of their isolation procedure and synthesized β-*O*-methylsynephrine by eluting synephrine from an acidic Dowex column with 2 *N* NaOH in methanol (34). In this laboratory, the basic Amberlite column used in the isolation procedure did not convert reference synephrine to the β-*O*-methyl derivative, as evidenced by TLC. Unless some previous step in the isolation procedure, *e.g.*, the methanol and concentrated ammonium hydroxide used in the maceration (11), carries out this conversion, it can be concluded that β-*O*-methylsynephrine is, indeed, a natural constituent of *C. cornifera* var. *echinus*.

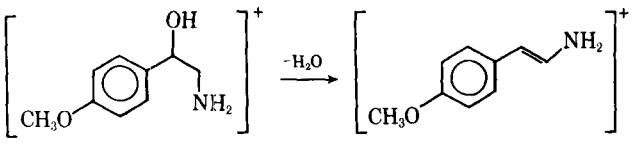
Structure Elucidation of the Unknown, NP - The structure shown here is proposed for the unknown nonphenolic alkaloid, NP, from UV, NMR, and mass spectral analyses. Attempts to crystallize this alkaloid as the HCl salt were futile, due perhaps to the small quantities present and/or to labile properties of the benzylic hydroxyl. However, it was possible to derive sufficiently pure alkaloid from TLC for instrumental analyses.

Comparison of UV spectra ($\lambda_{max.}$ at 224, 276, and 282 nm.) with other analogs of nonphenolic β-phenethylamines (17) indicates *para*-substitution. Further evidence for *para*-substitution is suggested by the NMR spectrum, which was made in deuterochloroform using the free base in eluants from preparative TLC plates. Although the spectrum was obscured by impurities, the symmetric pattern in the aromatic region (6.5–7.6 δ) characteristic of *para*-substitution was evident. Mass spectrometry showed a weak molecular ion peak at *m/e* 167 and a base peak at *m/e* 149 corresponding to a loss of water from the molecule as shown in Scheme II. In view of these limited data, this identification must be regarded as tentative.



4-methoxy-β-hydroxy-β-phenethylamine

[11] This small quantity did not permit determination of optical rotation.



m/e 167 *m/e* 149

Scheme II

4-Methoxy-β-hydroxy-β-phenethylamine has not been reported previously as a natural product. The cinnamide derivative, however, is known as aegeline, an alkaloid of *Aegle marmelos* Correa (Rutaceae) (35). Pharmacologically, the synthetic 4-methoxy-β-hydroxy-β-phenethylamine is found to be a weak vasoconstrictor and, in large doses, a cardiac depressant (36).

SUMMARY

Alkaloid screening of seven species of *Coryphantha* demonstrated the presence of alkaloids throughout the species investigated. From one species, *C. cornifera* var. *echinus*, four known alkaloids isolated were *N*-methyl-3,4-dimethoxy-β-phenethylamine, *N*-methyl-4-methoxy-β-phenethylamine, hordenine, and *N*-methyltyramine. Two alkaloids from *C. cornifera* var. *echinus*, previously unreported in Cactaceae, were isolated and their structures were proposed from spectral analyses to be β-*O*-methylsynephrine and 4-methoxy-β-hydroxy-β-phenethylamine. Chromatographic evidence for the presence of synephrine in all seven species was given.

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