ALKALOIDS OF *THALICTRUM*. XXXII. ISOLATION AND IDENTIFICATION OF ALKALOIDS FROM *THALICTRUM REVOLUTUM* DC. FRUIT[1]

JINN WU, JACK L. BEAL, WU-NAN WU[2] and RAYMOND W. DOSKOTCH

Division of Pharmacognosy and Natural Products Chemistry, College of Pharmacy, The Ohio State University, Columbus, Ohio 43210

ABSTRACT.—The fruit of *T. revolutum* DC. yielded nineteen alkaloids which were identified by spectral and chemical methods. Nine alkaloids, argemonine, eschscholtzidine, thalicarpine, *N*-demethylthalphenine, thalmelatine, allocryptopine, *O*-methylthalicberine (**1**), revolutinone (**2**) and neothalibrine (**3**) were isolated from the tertiary nonphenolic fraction, while the tertiary phenolic fraction afforded platycerine, thalirevoline, thalipine and *N*-methylcoclaurine. From the quaternary alkaloid fraction, argemonine methochloride (**8**), eschscholtzidine methochloride (**9**), armepavine methochloride (**10**), berberine chloride (**11**), choline chloride (**12**) and *N*-methyl-6,7-dimethoxyisoquinolinium chloride (**13**) were identified.

The alkaloid constituents of *Thalictrum revolutum* DC. have been studied extensively. Twenty alkaloids were isolated from the roots (1, 2) and eighteen alkaloids from the tops (3, 4, 5). We report in this paper the nineteen alkaloids obtained from the fruit, an achene.

Of the nineteen alkaloids isolated from this source, nine were from the tertiary nonphenolic fraction. These are argemonine, eschscholtzidine, thalicarpine, *N*-demethylthalphenine, thalmelatine, allocryptopine, *O*-methylthalicberine (**1**), revolutinone (**2**) and neothalibrine (**3**). The first six alkaloids are found, also, in the tops (3), and *O*-methylthalicberine occurs in the roots (1), while revolutinone (**2**) and neothalibrine (**3**) are new. Their structures were determined from spectral analyses and partial chemical transformations. The four alkaloids from the tertiary phenolic fraction, namely, platycerine, thalirevoline, thalipine and *N*-methylcoclaurine, are present also in the tops (5). The quaternary alkaloid fraction yielded argemonine methochloride (**8**), eschscholtzidine methochloride (**9**), armepavine methochloride (**10**), berberine chloride (**11**), choline chloride (**12**), and *N*-methyl-6,7-dimethoxyisoquinolinium chloride (**13**).

EXPERIMENTAL

FRACTIONATION AND INITIAL ISOLATION PROCEDURES.—Powdered fruit (528 g) was defatted with light petroleum ether (b.p. 30–60°) in a Soxhlet extractor. The fat-soluble material (80 g) was studied separately; the results of the study will be published later. The defatted seed was next extracted with cold 95% alcohol followed by hot 95% ethanol for a total of 50 liters. The alcohol extracts were concentrated at reduced pressure in a rotary evaporator to give 183 g of a dark brown semi-solid residue, which was divided into ether-soluble tertiary nonphenolic (3.36 g), phenolic (1.54), chloroform-soluble tertiary (0.54) and quaternary fractions (3.0) according to the published procedure (1).

ISOLATION OF ALKALOIDS FROM THE ETHER-SOLUBLE TERTIARY NONPHENOLIC BASE FRACTION.—The crude nonphenolic alkaloids (3.3 g) were chromatographed on a silica gel column (E. Merck No. 7747, 174 g) and eluted with chloroform followed by chloroform with increasing amounts of methanol, absolute methanol and 10% ammoniacal methanol. Effluent volumes of 40 ml were analyzed by tlc. The results of the chromatographic separation are given in table 1.

The compounds isolated from this fraction were very similar to those isolated from the tops (3) except for revolutinone, *O*-methylthalicberine, and neothalibrine; since the isolation and purification were identical to those published (3), we give details only of the isolation and identification of *O*-methylthalicberine (**1**) and the structure elucidation of revolutinone (**2**) and

[1]For paper XXXI see H.-Y. Cheng and R. W. Doskotch, *J. Nat. Prod.*, **43**, 151 (1980).

[2]Present address: McNeil Laboratories, Fort Washington, PA 19034.

neothalibrine (**3**). The known compounds were identified by direct comparison of spectral and physical properties (tlc, ir, nmr and cd).

TABLE 1. Chromatographic separation of *T. revolutum* ether-soluble tertiary nonphenolic alkaloids from fruit.

Fraction number (40 ml)	Eluent composition	Weight (mg)	Compounds
	$CHCl_3$, 1–2% MeOH–$CHCl_3$	450	nonalkaloids
1–10	4% MeOH–$CHCl_3$	17	"
11–13	"	2	"
14–15	"	30	*N*-demethylthalphenine revolutopine
16–18	"	20	eschscholtzidine
19–24	"	220	argemonine
25–27	"	267	argemonine and thalicarpine
28–37	"	818	thalicarpine
38–39	"	38	mixture
40–45	8% MeOH–$CHCl_3$	110	O-methylthalicberine
46–49	15% "	62	O-methylthalicberine, thalmelatine
50–68	15% "	330	thalmelatine
69–87	20% "	240	allocryptopine
88–99	20% "	250	allocryptopine, neothalibrine
100–112	30% "	170	neothalibrine
residue	40% " and greater	140	minor alkaloids

ISOLATION OF *O*-METHYLTHALICBERINE (**1**).—The yellowish-brown residue (110 mg) from fractions 40–45 were combined and crystallized from methanol as colorless needles, 48 mg, mp 186.5–8.5° [lit. (11) 186–187.5°]. The nmr spectrum showed peaks at; δ ($CDCl_3$) 2.09, 2.57 (2s, 2 NCH_3), 3.64, 3.76, 3.85, 3.88 (4s, 4 OCH_3), and 10 aromatic protons at δ 6.06–7.22 (m, 10 ArH). This compound gave identical ir, cd, and nmr spectra, as well as mp and tlc R_f value with those from a reference sample of *O*-methylthalicberine. The mixture mp with an authentic sample gave no depression.

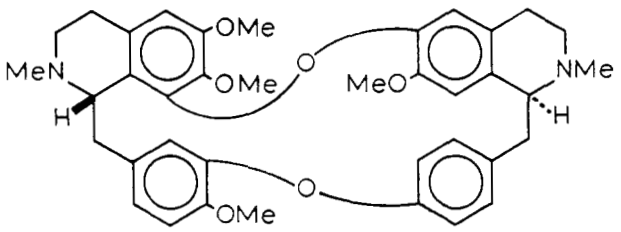
ISOLATION OF REVOLUTINONE (**2**).—The yellowish-brown residue (29 mg) from fractions 14 and 15 was placed on a neutral alumina column (5 g) with benzene and eluted with benzene and chloroform-benzene (1:4). From the benzene effluent a minute quantity (0.5 mg) of *N*-demethylthalphenine was obtained and identified from its nmr (90 MHz), ir, and tlc behavior when compared with a reference sample (3). The chloroform-benzene (1:4) effluent gave 10 mg of revolutinone (**2**) as an amorphous solid: $[\alpha]^{28}$D −10° (c 0.5, MeOH); uv λ max (MeOH) 205 nm (shld, log ϵ 5.13), 250 (4.78), 258 (4.76), 272 (4.69), 280 (shld, 4.66), 301 (shld, 4.31); and ir ($CHCl_3$) ν max 1694 (CH=O), 1644 (NC=O), 2720 cm^{-1} (C*H*O), and no absorption in the hydroxyl region. The nmr spectrum (90 MHz, $CDCl_3$) showed two *N*-methyl peaks at δ 2.27 and 3.09 (lactam), four aromatic *O*-methyls at 3.67, 3.73, 3.85 and 3.86, ten aromatic protons at 6.27 and 6.56 (2s, H-5 and H-5"), 7.63 (s, H-8"), 6.79–7.04 (m, 3H, ABC pattern), 6.92 and 7.77 (AA'BB' q, *J* 8.9), and 9.89 (s, C*H*O); cd spectrum (C 7.7 x 10^{-3}M, MeOH) showed maximum at $[\theta]_{396}$ −2,600, $[\theta]_{260}$ −14,000, $[\theta]_{230}$ +26,000; and ms peaks appeared at *m/e* 652 (0.15%, $C_{35}H_{40}N_2O_5$), 411 (100, 2*a*), 241 (4, 2*b*), 221 (3, 2*a-d*), 205 (2, 2*a-c*), 203 (2, 2*c*), and 190 (3, 2*d*).

CONVERSION OF *O*-METHYLTHALICBERINE (**1**) TO REVOLUTINONE (**2**).—A 15 mg sample of *O*-methylthalicberine was dissolved in 15 ml of acetone and a solution of $KMnO_4$ (6 mg) in acetone (10 ml) was added dropwise during a period of 0.5 hr at room temperature with stirring; then the reaction mixture was stirred for another 8 hrs. The mixture was evaporated, and the residue was chromatographed on a silica gel column (4 gm) using chloroform, 2% methanol-chloroform and 6% methanol-chloroform as solvents. From the 2% methanol-chloroform eluates, a 4.2 mg homogeneous product was obtained which was identical (cd, ir, nmr, ms and R_f on tlc) with revolutinone.

ISOLATION AND IDENTIFICATION OF NEOTHALIBRINE (**3**).—The brownish residue (250 mg) from fractions 88–99 was dissolved in benzene and chromatographed on a neutral alumina column (28 g) with benzene, chloroform-benzene (1:1), chloroform-benzene (4:1), and chloroform. From the chloroform-benzene (4:1) eluates, 66 mg of allocryptopine was obtained. The

chloroform eluate gave 44 mg of neothalibrine as an amorphous solid: $[\alpha]^{27°}D+155°$ (*c* 0.5, MeOH); uv λ max (MeOH) 284 nm (log ε 4.10) and a bathochromic shift in strong base to 285 (4.10), 310 (sh, 3.68); cd spectrum (*c* 8.0×10^{-3}, MeOH) $[\theta]_{288}$ +6,240, $[\theta]_{250}$ −1,250, $[\theta]_{231}$ +29,600; ir ($CHCl_3$) ν max 3540 cm^{-1} (–OH); nmr spectrum (60 MHz, $CDCl_3$) δ 2.43 and 2.51 (2s, 2 NCH_3); 3.59, 3.78 (double intensity), and 3.82 (3s, 4 OMe), 6.09 (H–8″), 6.38 (H–8), 6.46 and 6.56, (2s, 2 ArH), an AA′BB′ quartet at 6.78 and 6.98 (J_{AB} 8.8), an ABC multiplet between 6.6–6.9, and 5.17 ppm (br, OH, lost in D_2O); and ms *m/e* 624 (0.1%, M^+ $C_{38}H_{46}N_2O_6$), 418 (0.3, **3**-*b*), 206 (100, **3***b*), 192 (80, **3***a*).

Additional neothalibrine (96 mg) was obtained from fractions 97–112.



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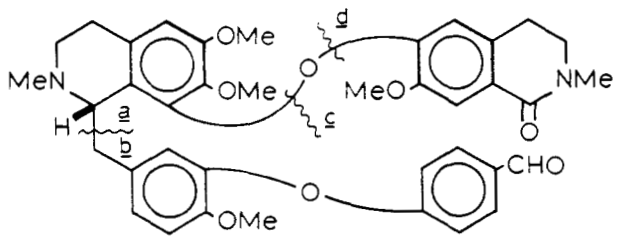

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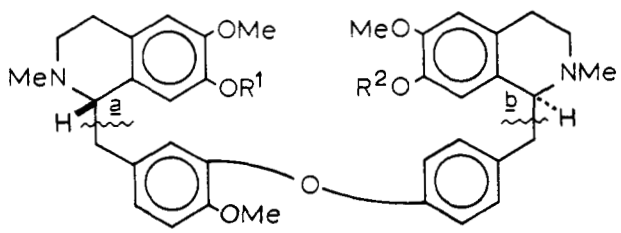


3; R^1 = H, R^2 = Me

4; R^1 = R^2 = Me

5; R^1 = Et, R^2 = Me

14; R^1 = Me, R^2 = H

METHYLATION OF NEOTHALIBRINE (**3**) to *O*-METHYLTHALIBRINE (**4**).—A 10 mg sample of neothalibrine was dissolved in 2 ml of methanol and treated with ethereal diazomethane generated from 0.5 g of *N*-methyl-*N*-nitroso-*p*-toluene-sulfonamide. After 2 days, the solvent was evaporated, and the residue was chromatographed on 10 g neutral alumina with benzene, chloroform-benzene (1:1), and chloroform. The chloroform effluent gave 10 mg of *O*-methylthalibrine (**4**) which was identical (ir, cd, nmr and R_f on tlc) with an authentic sample generated from thalibrine (**14**) (8).

ETHYLATION OF NEOTHALIBRINE (3) TO *O*-ETHYLNEOTHALIBRINE (5).—An 81 mg sample of neothalibrine (3) in 4 ml of methanol was treated with excess ethereal diazoethane generated from *N*-ethyl-*N*'-nitro-*N*-nitrosoguanidine (1.5 g). After 2 days, the reaction mixture was evaporated, and the residue was chromatographed on a 10 g neutral alumina column with benzene, chloroform-benzene (1:1), and chloroform as eluants. The last two solvents eluted 77 mg of *O*-ethylneothalibrine (5): nmr (60 MHz, $CDCl_3$) δ 2.47, 2.52 (2s, 2 NCH_3), 3.58, 3.78 (double intensity), and 3.82 (3s, 4 OMe), 1.33 (t, 3H, $J=7$, OCH_2CH_3), 3.83 (q, 2H, $J=7$, OCH_2CH_3), 6.09 (H-8"), 6.19 (H-8), 6.52 and 6.56 (H-5 and H-5"), AA'BB' quartet 6.78 and 6.99 ($J=8.5$) and ABC multiplet between 6.7–6.9 ppm; ir spectrum showed no hydroxyl absorption; ms *m/e* 652 (0.1%, M^+, $C_{40}H_{48}N_2O_8$), 220 (75, 5*a*), and 206 (100, 5*b*); and cd spectrum (*c* 5.9 x 10^{-3}, MeOH) showed maxima at $[\theta]_{285}$ +18,000, $[\theta]_{259}$ +1,270, $[\theta]_{231}$ +80,500.

NA/LIQ. NH_3 CLEAVAGE OF *O*-ETHYLNEOTHALIBRINE (5).—*O*-Ethylneothalibrine (5, 76 mg) in 5 ml of tetrahydrofuran was added within 1 hr to 25 ml of liq. NH_3 containing 210 mg of Na metal, then reacted 2 hrs more. After the NH_3 was evaporated at room temperature, the residue was treated with excess methanol. The mixture was concentrated to a few ml and dissolved in 200 ml ether. The phenolic products were removed by repeated extraction with 5% NaOH, and the aqueous alkaline solution treated with excess NH_4Cl and extracted with ether to give 41 mg of crude phenolic bases. The ether solution, after extraction with 5% NaOH, was washed with H_2O and dried over anhydrous Na_2SO_4. After evaporation, 43 mg of nonphenolic bases were obtained. The nonphenolic and phenolic base residues were chromatographed on neutral alumina columns (5 g each), with benzene and increasing concentration of chloroform in benzene as eluants. A nonphenolic base (35 mg) was obtained from the 40% chloroform-benzene effluents: nmr (60 MHz, $CDCl_3$) δ 1.31 (t, $J=7$, OCH_2CH_3), 3.78 (q, $J=7$, OCH_2CH_3), 2.51 (s, NCH_3), 3.76 and 3.81 (2s, 2 OCH_3), 6.11 (s, H-8), 6.55 (s, H-5), 6.77, 7.00 (AA'BB', q, $J=8.5$). This compound has structure 7 as shown by direct comparison (ir, cd, nmr and tlc) with a known sample, a product of a similar study on thalrugosidine (9). The phenolic base (28 mg) was obtained from the chloroform effluents: nmr (60 MHz, $CDCl_3$) δ 2.52 (s, NCH_3), 3.53 and 3.81 (2s, 2 OCH_3), 5.99 (s, H-8), 6.55 (s, H-5), 6.63 and 6.88 (AA'BB', q, $J=8.5$), and 6.7 (br, OH, lost in D_2O). The phenolic base was shown to be identical with *S*-(+)-armepavine (6) by direct comparison of physical data (ir, nmr, cd and tlc) with an authentic sample.

ISOLATION OF ALKALOIDS FROM QUATERNARY BASE FRACTION.—The alkaline solution which was extracted with ether and chloroform to remove tertiary base was made slightly acidic with citric acid to pH 5–6. Freshly prepared 2% aqueous ammonium Reinecke solution was added to precipitate the quaternary alkaloids. The collected precipitate (yellowish-brown) was washed with water and air dried. The precipitate (~9 g) was dissolved in 50% aqueous acetone and stirred with 90 g IRA-40 (Cl−) ion exchange resin. After filtration, the filtrate was evaporated *in vacuo* to dryness to give 3.0 g of quaternary chlorides.

Chromatography of quaternary bases was performed on a neutral alumina (180 g) with chloroform and increasing amounts of methanol in chloroform. Effluent volumes of 50 ml were collected and analyzed by tlc.

The chromatographic results are summarized in table 2.

TABLE 2. Chromatographic results of quaternary alkaloids.

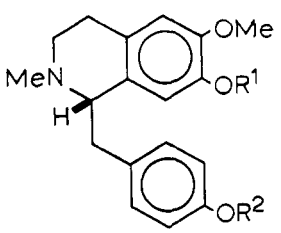
Fraction number (50 ml)	Elution solvent	Weight (mg)	Compound isolated (as chlorides)
1–8	$CHCl_3$, 1–5% MeOH–$CHCl_3$	251	nonalkaloid
9–11	5% and 10%	160	*N*-methylargemonine
12–17	10%	128	*N*-methyl-eschscholtzidine
18–22	"	15	minor alkaloid
23–24	"	37	*N*-methyl-6,7-dimethoxy isoquinolinium
25–41	11%	201	mixture
42–49	15%	73	*N*-methyl armepavine
50–51	"	142	mixture
52–61	"	136	choline
62–67	"	25	berberine

ISOLATION OF *N*-METHYLARGEMONINE CHLORIDE (8).—The residue from fraction 9 (47 mg) crystallized from methanol as colorless needles (4.4 mg): mp 149–152°C, mp 170–172° (crystallized from Abs. EtOH); uv λ max (MeOH) 286 nm (log ϵ 3.86); cd (*c* 5.7 x 10^{-3}M, MeOH) $[\theta]_{277}$ +7,490, $[\theta]_{239}$ −82,400; nmr (60 MHz, $CDCl_3$) at δ 3.68 (s, (+)NMe_2); 3.80 and 3.88 (2s, 2 OCH_3

each), 6.52 and 6.84 (2s, 2 Ar*H* each), and a broad doublet at 5.40 (2H); ms *m/e* 370 (0.4%, M^+, $C_{22}H_{23}NO_4$) 356 (10), 355 (41, M^+-Me), 354 (26), 340 (5), 205 (15) and 204 (100).

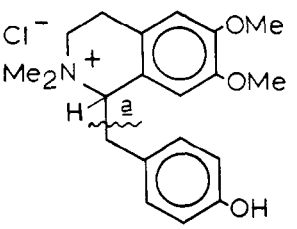
An additional 30 mg of this compound was crystallized from fractions 10 and 11.

SYNTHESIS OF ARGEMONINE METHIODIDE FROM ARGEMONINE.—Argemonine (60 mg) was dissolved in 5 ml MeOH in a 50 ml round-bottom flask to which 1.5 ml of fresh distilled methyl iodide was added dropwise and refluxed on a steam bath for 3.5 hrs. The reaction mixture, after evaporation of solvent, gave from methanol 82 mg of argemonine methiodide as colorless needles; mp 272–3°C (dec.) with same cd and uv spectra as *N*-methylargemonine chloride. The chloride was prepared by stirring 30 mg of the iodide with IRA-410 (chloride form) resin in water-methanol (2:8), filtering off the resin and crystallizing the product, which was identical (tlc, ir, nmr and mp) with the natural product.



6; R^1 = Me, R^2 = H

7; R^1 = Et, R^2 = Me



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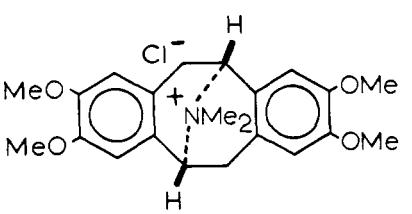

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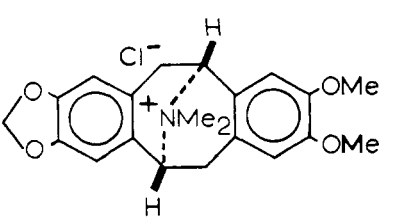

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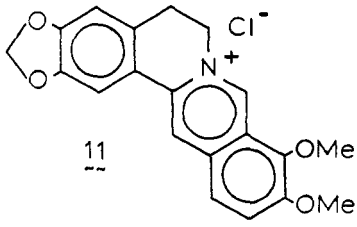
ISOLATION OF *N*-METHYLESCHSCHOLTZIDINE CHLORIDE (**9**).—The residue (128 mg) from fractions 12–17 was collected and rechromatographed on a neutral alumina column (5 g) with chloroform and increasing amounts of methanol in chloroform. The 2% methanol in chloroform eluent gave 25 mg of a colorless amorphous *N*-methyleschscholtzidine chloride: $[\alpha]^{20}D$ −170° (*c* 0.26, MeOH); cd (*c* 3.2 x 10^{-3}M, MeOH) $[\theta]_{282}$ +6,440, $[\theta]_{241}$ −40,600; uv λ max (MeOH) 289 nm (log ε 3.74), 257 (3.46) and 230 (shld, 3.91); and nmr spectrum (60 MHz, $CDCl_3$) indicates peaks at δ 3.68 (broad s, (+)NMe_2), 3.79, 3.86 (2s, 2 OCH_3), 5.89 (brs, OCH_2O), 6.48, 6.55, 6.80, 6.85 (4s, 4 ArH), and a broad doublet centered at 5.57 (2H). Eschscholtzidine methiodide

was prepared by refluxing 10 mg of the tertiary base eschscholtzidine with methyl iodide in methanol for 1 hr.

Evaporation of the reaction mixture gave 9 mg of eschscholtzidine methiodide; nmr (90 MHz, $CDCl_3$) δ 3.59 (broad s, (+)-NMe_2), 3.81, 3.90 (2s, 2 OCH_3), 5.93 (brs, 2H, OCH_2O), 6.52 (s, 2 ArH), 6.79, 6.82 (2s, 2 ArH) and a multiplet centered at 5.37 (2H).

ISOLATION OF *N*-METHYL-6,7-DIMETHOXYISOQUINOLINIUM CHLORIDE (**13**).—Fractions 23 and 24 were combined and evaporated to dryness to give 37 mg of a yellowish-brown residue, which crystallized from ethanol and n-hexane as colorless fine needles (15 mg) of compound **13**: mp 185.5–6.5°C; no optical activity in both [α] D and cd; uv λ max (MeOH) 310 nm (log ϵ 3.95), 253 (4.91); nmr (90 MHz, CD_3OD) δ 4.07, 4.12 (2s, 2 OCH_3), 4.43 (s, (+)N-CH_3), 7.64, 7.71 (2s, H-5, H-8), 9.38 (s, H-1), and an AB quartet for H-2 and H-3 at 8.20 and 8.35 (J 7 Hz); and ms (%) 204 (10, M^-, $C_{12}H_{14}NO_2$), 205 (7, M^- +1), 189 (100%), and 188 (62%).

REDUCTION OF *N*-METHYL-6,7-DIMETHOXYISOQUINOLINIUM CHLORIDE (**13**).—A 4 mg sample of compound **13** in 2 ml of methanol was treated with 50 mg of sodium borohydride, portionwise. After 10 min, 20 ml of water was added, and the mixture was extracted with diethyl ether (20 ml x 3). The washed (water) and dried (sodium sulfate) ether extract on evaporation left 3.5 mg of a residue that crystallized from ether: mp 81–3° [lit. (14) mp 83–4°]; and nmr peaks at δ ($CDCl_3$) 2.47 (s, NCH_3), 2.60–2.91 (m, 4H, H-3 and H-4), 3.55 (s, 2H, H-1), 3.84 (s, 6H, 2 OCH_3), 6.51 and 6.60 (2s, 2H, H-5 and H-8).



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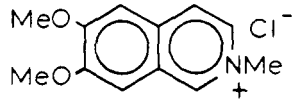

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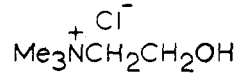

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ISOLATION AND IDENTIFICATION OF *N*-METHYLARMEPAVINE CHLORIDE (**10**).—The brownish residue (73 mg) from fractions 42–49 was crystallized from absolute ethanol as pale yellow prisms (49 mg). Recrystallization from MeOH gave 23 mg of alkaloid **10** as colorless prisms: mp 248–9° (dec.); no optical activity was observed by [α] D and cd; uv λ max (MeOH) 287 nm (log ϵ shld, 3.22), 281 (3.23); ir ν max 3370 cm^{-1} (broad, OH); nmr (90 MHz, MeOH-d_4) δ 3.16 (s, (+)-NMe), 3.45 (s, (+)-NMe), 3.36, 3.80 (2s, 2 OCH_3), 5.69 (s, H-8), 6.82 (s, H-5), and 6.71, 6.85 (AA'BB'q, J 8.9); and ms *m/e* (%) 328 (1.1%, M^-, $C_{20}H_{26}NO_3$), 327 (4, M^+ −1), 206 (100 *a*), 107 (1 *b*), 58 (11, CH_2NMe_2). Armepavine methoiodide (mp 253–255°), obtained by methylation of armepavine with methyl iodide, gave identical uv, nmr and tlc behavior as the isolated compound. Conversion of the isolated chloride salt to the iodide was carried out by adding aqueous potassium iodide to an aqueous solution, then crystallizing from methanol; the mp was the same as for armepavine methoiodide.

ISOLATION AND IDENTIFICATION OF CHOLINE CHLORIDE (**12**).—Fractions 52–61 were combined (136 mg) and crystallized from acetone-methanol (10:1) as colorless hygroscopic plates showing tlc behavior and a nmr spectrum identical to that of authentic choline chloride.

DISCUSSION

Thalictrum revolutum DC. (Ranunculaceae) is a perennial plant, indigenous to the eastern U.S.A. Extensive study of this plant has yielded many alkaloids. From the roots 20 alkaloids were isolated and from the tops 18 alkaloids were isolated (1, 2, 3, 4, 5). Only five alkaloids were common to both roots and tops. In this paper, we wish to report the alkaloids isolated exclusively from the seeds.

There were 9 alkaloids obtained from the tertiary nonphenolic fraction, of which 6 also occur in the tops. These are argemonine, eschscholtzidine, thalicarpine, *N*-demethylthalphenine, thalmelatine, and allocryptopine. The seventh alkaloid, *O*-methylthalicberine (**1**), is absent from the tops but occurs in the roots (1). The two remaining alkaloids are dimeric isoquinolines, revolutinone (**2**) and neothalibrine (**3**), and are new compounds.

Revolutinone (**2**) was obtained as a very minor amorphous base. From spectral evidence, revolutinone (**2**) was formulated as a *seco*-bisbenzylisoquinoline aldehydo lactam type related to baluchistanamine (6). The absorption bands in the ir spectrum at ν max 1644 and 1694 cm^{-1} are due to lactam and aryl aldehyde, respectively. The nmr spectrum indicated two *N*-methyls at δ 2.27 and 3.09, the latter considerably downfield and consistent with an *N*-methyl of an isoquinoline. Four aromatic *O*-methyl signals were at δ 3.67, 3.73, 3.85 and 3.86, and of the ten aromatic protons, three were singlets, four were part of an AA'BB' pattern suggesting a disubstituted phenyl ring, while the other three gave an unresolved multiplet. A very low field one-proton signal at δ 9.89 (not exchangeable with deuterium oxide) was assigned to an aldehydic proton. The mass spectrum showed a molecular ion at *m/e* 652 (0.15%) in agreement with the adopted formula $C_{38}H_{40}N_2O_8$, and the fragmentation pattern, along with the other spectral data, pointed to structure **2** as the most likely possibility.

To confirm the proposed structure for revolutinone (**2**) and to establish the stereochemistry, *O*-methylthalicberine (**1**) was oxidized with potassium permangnant in acetone at room temperature (7). The oxidized product gave identical tlc, ir, nmr, and cd behavior as revolutinone, thereby confirming the structure and establishing the stereochemistry as *S*.

Since revolutinone (2) is the second example of this type of alkaloid (baluchistanamine from *Berberis baluchistanica* Ahrendt, the first) and because it coexists with *O*-methylthalicberine in the same fraction, it was of interest to rule out an artifactual origin such as, perchance, by air oxidation on handling. *O*-Methylthalicberine was stirred at room temperature in ethanol for 24 hrs and then refluxed for 2.5 hrs, but no change was observed.

The second new alkaloid, neothalibrine (**3**), isolated as an amorphous base, was also formulated as a bisbenzylisoquinoline with one phenolic group.The phenolic group was supported by the sharp band in ir spectrum at ν max 3540 cm^{-1} and a broad peak at δ 5.1 (D_2O exchangeable) in the nmr spectrum. The 26 nm bathochromic shift in strong base of uv spectrum confirms the existence of a phenolic group. Methylation of neothalibrine (**3**) yielded *O*-methylthalibrine (**4**), with identical physical properties (ir, nmr, cd, and tlc) as *O*-methylthalibrine prepared from thalibrine (10), and also more recently isolated from *T. minus* race B, (8), thereby establishing the carbon skeleton, oxygenation pattern, and stereochemistry for neothalibrine. The mass spectrum gave fragmentation **3***b* at *m/e* 206 (100%) and **3***a* at *m/e* 192 (80%) requiring the phenolic group to be located in one of the tetrahydroisoquinoline units.

O-Ethylation of neothalibrine (**3**) yielded *O*-ethylneothalibrine (**5**), which showed an increase of 28 mass units in the molecular ion of the mass spectrum and a strong peak at *m/e* 220 corresponding to fragment **5***a*, confirmed the presence of one phenolic group and its location on the isoquinoline ring. The exact ring and position remained to be determined, although C–7 on the left-side isoquinoline (as in **3**) was favored, since only one aromatic singlet is present in the upfield position ($\delta \sim 6.0$) in the nmr spectrum. Na/liq. NH_3 degradation of *O*-ethyl-

neothalibrine (**5**) yielded two benzylisoquinoline fragments **6** and **7**. The former was shown to be identical with armepavine, and the latter with one of the cleavage products from thalrugosidine; both were identified by direct comparison of nmr, ir and cd spectra, as well as tlc mobility (9). Therefore, neothalibrine is a thalibrine-type bisbenzylisoquinoline (10) with the phenolic group at C–7.

The four alkaloids from tertiary phenolic fraction, platycerine, thalirevoline, thalipine and *N*-methylcoclaurine, were the same as those contained in the tops. Spectral data and direct comparison of physical properties with known samples characterized these alkaloids.

From the quaternary alkaloid fraction, two pavine-type quaternary alkaloids were obtained, argemonine methochloride (**8**) and eschscholtzidine methochloride (**9**). This is the first report of the isolation of these compounds from a natural source. Argemonine methohydroxide, however, was prepared from argemonine (12). Optically inactive armepavine methochloride (**10**), also reported for the first time as a natural product, was already prepared synthetically as the methiodide (13).

The simple isoquinolinium salt, *N*-methyl-6,7-dimethoxyisoquinolinium chloride (**13**), a new natural product, was characterized from spectral data [uv (14), nmr and ms] and by reduction to the tetrahydro-derivative, whose physical properties were compared to the reported values for *N*-methyl-6,7-dimethoxytetrahydroisoquinoline (15).

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