these derivatives with the active site and/or isozyme responsible for the oxidation of tryptamine (22). From these suppositions, it appears that a 3,4-dimethoxyphenethylamine nucleus with a β-hydroxy group cannot properly bind with the active site and/or isozyme associated with both tyramine and tryptamine oxidation.

The monoamine oxidase inhibitory activity of 4-methoxyphenethylamine derivatives has been used to explain the folkloric uses of *D. longimamma* as a psychoactive "peyote" cactus (19). Macromerine and normacromerine are the major alkaloids in *C. macromeris* var. *runyonii* (11), and this cactus was reported to be psychoactive (16, 28). Vogel *et al.* (29) concluded that macromerine and normacromerine were not responsible for the psychoactivity, since they produced no effects on the conditioned avoidance response in rats. Since macromerine and normacromerine are devoid of monoamine oxidase inhibitory activity, there appears to be no correlation between the presence of these compounds and the purported psychoactivity of *C. macromeris* var. *runyonii*.

Harley-Mason (30) predicted that an abnormal methylation of dopamine and/or norepinephrine *in vivo* could produce I or IV. Of these compounds, I received wide attention because of its detection in the urine of schizophrenics (31). Later studies revealed that urinary excretion of I is not unique to schizophrenia (32) and that administration of this compound to humans produces no psychological changes (33, 34). However, the ingestion of cacti containing I and/or its *N*-methyl derivatives together with indirectly acting amines such as synephrine could alter behavior by inhibiting monoamine oxidase and thus potentiating the effects of the indirectly acting amines. This may be the case with the supposedly psychoactive *C. macromeris* var. *runyonii*. Although the major alkaloids do not inhibit monoamine oxidase, this cactus does contain two known monoamine oxidase inhibitors, *N*-methyl-4-methoxyphenethylamine and II, together with several indirectly acting amines (11). This situation may also contribute to the well-documented hallucinogenic activity of the mescaline-containing cacti.

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Alkaloids of *Papaver orientale* L.

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Abstract □ According to the alkaloid profiles, five different chemotypes (A, B, C, D, and E) were classified in *Papaver orientale* L. with haploid chromosome number $n = 14$. Chemotype A had only oripavine; chemotype B contained oripavine and thebaine; chemotype C had isothebaine in addition to oripavine; chemotype D contained oripavine and alpinigenine; and chemotype E had oripavine, thebaine, and alpinigenine. In all chemotypes, oripavine was either the sole alkaloid or the single major alkaloid.

Keyphrases □ *Papaver orientale* L.—chloroform extract of seed capsules, alkaloids isolated and identified, five chemotypes classified □ Alkaloids—isolated and identified, chloroform extract of seed capsules of *Papaver orientale* L., five chemotypes classified

In continuation of a broad study of the Iranian wild Papaveraceae (1–5), alkaloids of *Papaver pseudo-orientale* Fedde. and preliminary results on the alkaloids of *P. orientale* L. were reported (4). In this work, qualitative and

Table I—Classification of *P. orientale* L.

Population	Chemotype	Oripavine[a], %	Thebaine[a], %	Isothebaine[a], %	Alpinigenine[a], %
Khalkhal	A	1.15	None	None	None
	B	0.85	0.15	None	None
	C	0.5	None	0.3	None
Siah Cheshmeh	A	1	None	None	None
	B	0.8	0.1	None	None
	D	0.5	None	None	0.3
Guleh Khaneh	A	1.2	None	None	None
	B	0.88	0.4	None	None
	E	0.8	0.35	None	0.05
Shuran	A	1.25	None	None	None
	E	1.2	0.3	None	0.05

[a] The percentages of the alkaloids were based on the dried seedless capsules.

quantitative results on the alkaloid content of *P. orientale* L.[1] are reported.

BACKGROUND

P. orientale L. is a perennial wild poppy growing in the north and northwest of Iran at 2000–2500 m above sea level. The height of the plant is 30–70 cm (occasionally 1 m), bearing one to four flowering stems and usually four, rarely six, pale-orange petals with no marking above the base. The petals distinguish *P. orientale* L. from *P. bracteatum* Lindl. and *P. pseudo-orientale* Fedde. In addition, *P. orientale* L. lacks bracts while the other two species have bracts.

P. orientale L. is the only species in section oxytona that can be regarded as truly alpine, though it also grows at low altitudes with *P. pseudo-orientale* Fedde. in moist, sheltered areas. It blooms in late June at low elevations, but flowering continues until early September at high altitudes and on open slopes.

Three species of section oxytona were classified according to their haploid chromosome numbers: *P. bracteatum* Lindl., $n = 7$; *P. orientale* L., $n = 14$; and *P. pseudo-orientale* Fedde., $n = 21$ (6).

Extensive chemical studies in section oxytona revealed that *P. bracteatum* Lindl. contained thebaine (1, 3) or thebaine along with alpinigenine (2, 7, 8). *P. pseudo-orientale* Fedde. contained isothebaine as a major alkaloid and orientalidine, bracteolin, salutaridine, Or_1, Or_2, PO-4, alborine (PO-5), and aryapavine as minor alkaloids (4). Some workers found oripavine in *P. orientale* L. (9, 10), while others reported the same alkaloid in *P. bracteatum* Lindl. (11). These results suggest that the previous alkaloid accounts are unreliable with respect to species determination (6).

To clarify present uncertainties, the alkaloid contents of the capsules of *P. orientale* L., collected from Shuran, Zinjinab, Siah Cheshmeh, Khalkhal, and Guleh Khaneh, were isolated and studied.

EXPERIMENTAL[2]

A small portion (about 100 mg) of individual capsules collected from each region was ground, moistened with ammonia, and extracted exhaustively with chloroform (5 × 5 ml) at room temperature. The solvent was evaporated, and the residue was chromatographed [TLC, silica gel, ethyl acetate–methanol–ammonia (85:10:5)]. The spots were detected first under the UV lamp and then were developed with Dragendorf reagent.

For semiquantitative analysis, the remaining individual capsules, which were chemically similar by TLC and were collected from the same geographical source, were mixed to obtain about 50 g of dried material. These capsules were powdered so that all of the material possessed a mesh size not greater than 0.5 mm. The powder was moistened with ammonia, macerated with 200 ml of chloroform overnight at room temperature, and filtered. This procedure was repeated three more times. The chloroform was evaporated under reduced pressure, and the residue was treated with dilute acetic acid (20%, 20 ml) and filtered. The residue was then washed with water (20 ml).

The combined aqueous solutions were made alkaline with ammonia and extracted with chloroform (4 × 25 ml). The organic layer was dried (sodium sulfate), filtered, and evaporated to give the crude total alkaloids. The crude extract was subjected to preparative TLC [silica gel, ethyl acetate–methanol–ammonia (85:10:5)], and each alkaloid was eluted with chloroform–methanol (80:20). The solvent was evaporated and weighed to determine the percentage of alkaloid. The residue was crystallized from an appropriate solvent and characterized (see *Results and Discussion* and Table I).

RESULTS AND DISCUSSION

The following alkaloids were isolated by TLC and characterized.

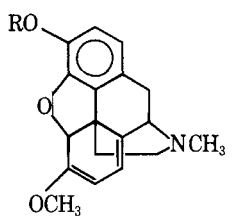
1. Oripavine (I): R_f 0.36, mp 201–203° (ethanol) [lit. (4, 9) mp 201–203°], mixed melting point with an authentic sample 201–203°; NMR (deuterochloroform): δ 6.50 (broad s, 2H, aromatic), 5.90–5.63 (broad s, 1H, OH), 5.50 (d, 1H, H-7 or 8), 5.23 (s, 1H, H-5), 5.0 (d, 1H, H-8 or 7), 3.56 (s, 3H, CH_3O), and 2.43 (s, 3H, NCH_3) ppm; $[\alpha]_D^{20}$ −216.9° (c = 3.44, $CHCl_3$) [lit. (9) $[\alpha]_D^{20}$ −211.8°]; UV_{max} (ethanol): 283 (log ε 3.90) nm; *m/e*: 297 (M^+).

Anal.—Calc. for $C_{18}H_{19}NO_3$: C, 72.73; H, 6.39; N, 4.71. Found: C, 72.85; H, 6.41; N, 4.65.

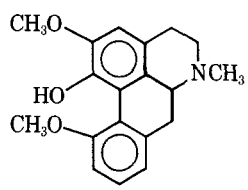
The reaction of oripavine with diazomethane in methanol–ether afforded, in quantitative yield, thebaine (II), mp 193° (ethanol), mixed melting point with an authentic sample 193° (1). The spectral data (IR, UV, NMR, and mass) were identical with an authentic sample.

2. Thebaine (II): R_f 0.36, mp 193° (ethanol) [lit. (1) mp 193°], mixed melting point with an authentic sample 193°. The spectral data (IR, UV, NMR, and mass) were identical with an authentic sample.

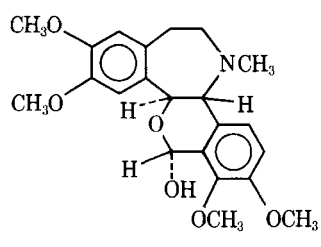
3. Isothebaine: R_f 0.43, mp 203–204° [lit. (4, 12) mp 203–204°], mixed melting point with an authentic sample 203–204°; NMR ($CDCl_3$): δ 7.63 (broad s, 1H, OH), 7.30–6.70 (m, 3H, aromatic), 6.53 (s, 1H, H-3), 3.88 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), and 2.47 (s, 3H, NCH_3) ppm (13); $[\alpha]_D^{20}$ +275° (c = 1.47, $CHCl_3$) [lit. (14) $[\alpha]_D^{21}$ 281 ± 10°]; UV_{max} (methanol): 270



I: R = H
II: R = CH_3



III



IV

[1] The plant was identified by P. Goldblatt, Missouri Botanical Garden, St. Louis, Mo. Herbarium samples were deposited in the Missouri Botanical Garden. (Also see Ref. 6.)

[2] Melting points were taken with a Koffler hot-stage microscope and are uncorrected. UV spectra were recorded on a Varian Techtron 635 instrument. NMR spectra were taken with a Varian A60A instrument. Mass spectra were recorded on a CH5 spectrometer at Aryamehr Technical University. IR spectra were obtained with a Leitz Model III spectrograph. The optical rotation was measured with a Perkin-Elmer polarimeter model 241 instrument. For qualitative detection of alkaloids, the silica gel was DC-Karten SI F from Riedel (West Germany).

(log ϵ 4.16) nm; *m/e*: 311 (M^+).

Anal.—Calc. for $C_{19}H_{21}NO_3$: C, 73.31; H, 6.75; N, 4.50. Found: C, 73.21; H, 6.81; N, 4.58.

4. Alpinigenine: R_f 0.68, mp 185–186° [lit. (2) mp 185–186°], mixed melting point with an authentic sample 185–186°; $[\alpha]_D^{20}$ +230.2° (c = 1.59, $CHCl_3$) [lit. (15) $[\alpha]_D^{20}$ +286°]. The spectral data (IR, UV, NMR, and mass) were identical with an authentic sample (2).

The alkaloid profiles of *P. orientale* L. from different geographical areas suggested classification according to five different chemotypes (Table I). Oripavine was either a sole alkaloid of the poppy (chemotype A) or a single major alkaloid (chemotypes B, C, D, and E).

A literature survey (16) revealed that alpinigenine was not found previously in *P. orientale* L.

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Physiologically Active Substances from Marine Sponges IV: Heterocyclic Compounds

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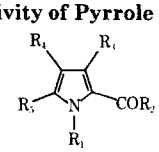
Abstract □ Several guanidine compounds were synthesized by the reaction of acid chlorides of thiophene and furan with guanidines. Some of these compounds showed antibiotic and cytotoxic activities. Series of pyrrole compounds were synthesized and found to have significant antibiotic activity.

Keyphrases □ Pyrroles, various—synthesized, evaluated for antibacterial activity □ Furans, various—synthesized, evaluated for antibacterial and cytotoxic activity □ Thiophenes, various—synthesized, evaluated for antibacterial and cytotoxic activity □ Heterocycles—various pyrroles, furans, and thiophenes synthesized, evaluated for antibacterial and cytotoxic activity □ Antibacterial activity—various pyrroles, furans, and thiophenes evaluated □ Cytotoxic activity—various furans and thiophenes evaluated □ Structure–activity relationships—various pyrroles, furans, and thiophenes evaluated for antibacterial and cytotoxic activity

Several biologically significant pyrrole (1) and indole (2, 3) derivatives have been isolated from marine sources. Most of these compounds show pronounced antibiotic activity. During the present investigation of the sponge *Agelas* sp. (JC-6), a new brominated pyrrole derivative incorporating the guanidine moiety was isolated and showed significant activity against *Escherichia coli* (4). This natural product also showed cytotoxicity against KB carcinoma cells (5). This report describes the synthesis of several pyrrole, furan, and thiophene analogs and their physiological activities.

Table I—Antibiotic Activity of Pyrrole Derivatives



Compound	R_1	R_2	R_3	R_4	R_5	Activity against *E. coli*[a]
XII*a*	H	OCH_3	H	H	H	+++
XII*b*	H	NH_2	H	H	H	++++
XII*c*	CH_3	OCH_3	H	H	H	+++
XII*d*	CH_3	NH_2	H	H	H	++++
XII*e*	H	H	H	Br	H	++++
XII*f*	H	OCH_3	H	Br	H	++++
XII*g*	H	OCH_3	H	Br	Br	++
XII*h*	H	OCH_3	Br	Br	Br	+

[a] After paper disk incubation, zones of bacterial inhibition were measured: +, <15 mm; ++, 15–18 mm; +++, 18–22 mm; and ++++, >22 mm.

EXPERIMENTAL[1]

Chemistry—Since 2-aminopyrimidine (I*a*) and guanidine (II*a*) have a common structural unit, it was considered desirable to synthesize furan, thiophene, and pyrrole derivatives incorporating this structural feature.

[1] All melting points are uncorrected. Microanalyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, N.Y. IR spectra were recorded on a Perkin-Elmer 421 grating IR spectrometer, NMR spectra were recorded on a Varian A-60A spectrometer, and mass spectra were recorded on a Hitachi Perkin-Elmer spectrometer 107.