tallization loosely, whereas water is tightly bound in the phases existing above 4.6 kb and below 2.2 kb.

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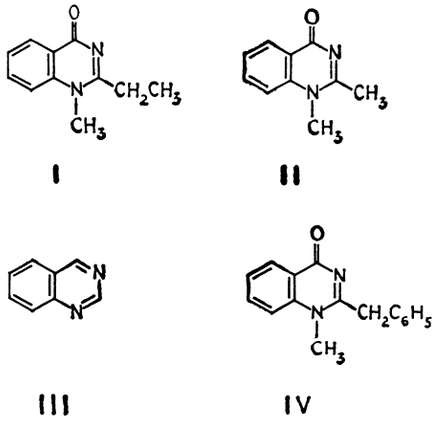
1,2-Dialkyl-4(3H)-Quinazolinones in the Defensive Secretion of a Millipede (Glomeris marginata)

Abstract. *Two crystalline components isolated from the defensive secretion of the glomerid millipede,* Glomeris marginata, *are identified as 1-methyl-2-ethyl-4(3H)-quinazolinone and 1,2-dimethyl-4(3H)-quinazolinone. These heterocyclic compounds bear a close structural resemblance to arborine, the chief alkaloid of the Indian medicinal plant,* Glycomis arborea *Correa.*

Many millipedes, in common with a diversity of insects, phalangids, and other terrestrial arthropods, respond to disturbance by ejecting a noxious fluid from special glands. These defensive secretions have recently been investigated intensively, and in a variety of millipedes the active principles of the discharge have been identified (*1*). Species of the orders Julida, Spirobolida, and Spirostreptida produce *p*-benzoquinones and, in one exceptional case, 2-dodecenal. Members of Polydesmida produce hydrogen cyanide and benzaldehyde. The single species of Chordeumida that has been studied secretes *p*-cresol. Several orders remained to be investigated. One of these, the Glomerida, includes an interesting European species, *Glomeris marginata*, the anomalous secretion of which is the subject of this report (see *2*).



Glomeris is a small millipede, about 1.5 cm long when fully grown. It bears a striking resemblance to the familiar isopod crustaceans called "sow bugs" and shares with some of these animals the characteristic habit of coiling into a tight sphere when disturbed. *Glomeris* discharges its secretion in response to pinching, tapping, or, on occasion, even mere prodding. The liquid oozes as single droplets from eight pores spaced evenly in a row along the dorsal midline of the animal (Fig. 1).

We collected the secretion for chemical analysis by seizing individual millipedes with forceps and aspirating their secretion into capillary tubing. The tubing was pulverized under methylene chloride, and the insoluble residue was separated by centrifugation. The residue was extracted repeatedly with methylene chloride to ensure complete extraction of the soluble components. Careful evaporation of the solvent under nitrogen gave a crystalline residue (40 mg from approximately 1000 animals), melting point 140° to 160°C, resolved into two chief zones by thin-layer chromatography on silica gel (5 percent methanol in methylene chloride). The infrared spectrum of the mixture showed intense maxima at 6.05 and 6.24 μ; these maxima are indicative of conjugated carbonyl and imine groups. In the ultraviolet region, the mixture showed absorptions at 230, 265, 275, 305, and 315 mμ (ethanol), which are suggestive of a bicyclic aromatic nucleus (*3*).

Preparative thin-layer chromatography separated this mixture into its two main constituents, the less polar compound A (23 mg, mp 145° to 147°C) and the more polar compound B (16 mg, mp 198° to 200°C). Sublimation at 120° to 140°C at 0.1 mm gave, for A, mp 146° to 147°C, and for B, mp 200° to 201°C. The infrared and ultraviolet spectra of the separate constituents were very similar to those of the original mixture.

Table 1. High-resolution mass spectra.

Mass			Composition
Nominal (*m/e*)*	Measured	Calculated	
	Compound A		
188	188.094803	188.094958	$C_{11}H_{12}N_2O$
160	160.063766	160.063659	$C_9H_8N_2O$
133	133.052463	133.052761	C_8H_7NO
105	105.033888	105.034037	C_7H_5O(10%)
	105.057786	105.057846	C_7H_7N(90%)
	Compound B		
174	174.079270	174.079308	$C_{10}H_{10}N_2O$
146	146.084385	146.084394	$C_9H_{10}N_2$
145	145.076795	145.076569	$C_9H_9N_2$
133	133.052907	133.052761	C_8H_7NO
105	105.033888	105.034037	C_7H_5O(10%)
	105.057686	105.057846	C_7H_7N(90%)
104	104.049951	104.050022	C_7H_6N

* Mass/charge

Nuclear magnetic resonance spectra of both compounds showed the presence of four aromatic protons, three as a complex multiplet centered at τ 2.5, and one as a doublet (9 cy/sec) of closely spaced doublets at τ 1.8. Methyl groups appeared as singlets at τ 6.25 in both compounds, but B showed an additional methyl singlet at τ 7.35, and A showed a typical ethyl group pattern at τ 7.11 (quartet) and τ 8.61 (triplet).

The high-resolution mass spectra of A and B establish the molecular formula

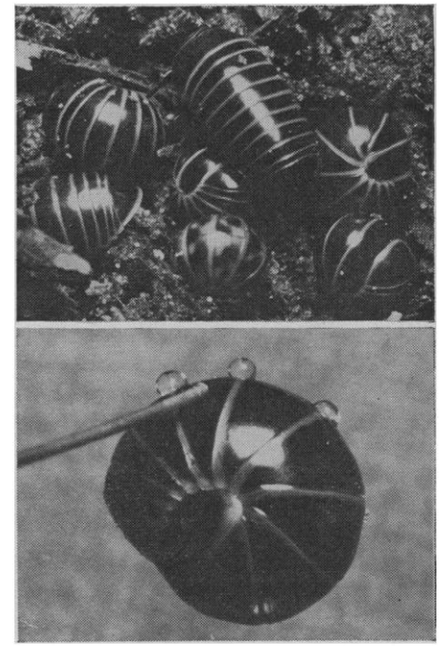


Fig. 1. (Top) *Glomeris marginata* on soil. Several of the millipedes are seen in the typical coiled defensive posture which they assume when disturbed. (Bottom) A coiled *Glomeris* discharging secretion from three of its eight glandular pores in response to prodding with a warm needle.

$C_{11}H_{12}N_2O$ for compound A and $C_{10}H_{10}N_2O$ for compound B (Table 1) (*4*). The facile loss of C_2H_4, HCN, and CO from the former, and of CH_3CN and CO from the latter, considered along with the other spectral data, led us to assign the 1,2-dialkyl-4(3*H*)-quinazolinone structures I and II to A and B, respectively.

A search of the literature showed that both I and II had been synthesized and carefully described in 1961 (*5*). Their published infrared and ultraviolet spectra, as well as their melting points, are in excellent agreement with those of A and B, thus completing the identification.

While our studies on *G. marginata* were in progress, Schildknecht *et al.* (*6*) described the isolation from the same millipede secretion of a crystalline compound which they named "glomerin," for which no structure was deduced. The properties of "glomerin" correspond closely to those of our substance B, and therefore "glomerin" is established to be 1,2-dimethyl-4(3*H*)-quinazolinone (II).

Besides the two heterocyclic compounds, the *Glomeris* secretion must contain other, possibly macromolecular, components. When first discharged, the secretion is translucent and liquid, but within seconds after exposure to air it becomes viscous and sticky, and eventually hardens to an opaque crust. The two identified constituents cannot, by themselves, account for these changes.

Various plant alkaloids are based on the quinazoline ring system (III) (*7*). Both natural and synthetic quinazolines possess significant biological activities, including antimalarial activity (*7*). The most closely related natural product appears to be arborine (IV), the chief alkaloid of the Indian medicinal plant *Glycomis arborea* Correa, in which the propionate and acetate moieties in I and II are replaced by a phenylacetate moiety (*5*). We have recently reported the characterization of a pyrrolizidinone, closely related to the Senecio alkaloids, from the hair-pencil secretion of a danaid butterfly (*8*). The finding of I and II in a millipede secretion now provides the second example of close structural parallelism between an arthropod product and the plant alkaloids.

The defensive behavior of *Glomeris*, the repellent effectiveness of its secretion, and the morphology of the glands have also been studied (*9*).

Note added in proof. Since the submission of this manuscript, a more recent publication of Schildknecht and Wenneis, in which "glomerin" is assigned structure II on the basis of independent evidence, has come to hand (*10*).

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24 August 1966

Light Chains of Mouse Myeloma Proteins: Partial Amino Acid Sequence

Abstract. *Five kappa chains in the urinary proteins of the BALB/c mouse have the same carboxyl terminal amino acid sequence; this sequence resembles that of kappa light chains in human immunoglobulins. The five chains have amino acid sequence variations at the amino-terminal. The genetic basis for the amino-terminal variations is not understood but could be due either to a mechanism for differently translating a single genetic message or to the presence of more than one kappa-type structural cistron in the BALB/c genome.*

The genetic basis of the heterogeneity of the light and heavy chains of related immunoglobulins poses the question of whether the polypeptide chain variants are a consequence of a large number of genes or a consequence of mechanisms for varying the protein product of a single gene by somatic mutation (chemical mutagenesis, crossing over, and others); or, alternatively, whether there is a versatile mechanism for translating a single genetic message (*1*). In an attempt to solve this problem we have investigated the amino acid sequence of related variant polypeptide chains that have originated in genetically similar animals, using the kappa-chain urinary proteins of the inbred BALB/c mouse (*2*) as an experimental model. Partial amino acid sequences of several kappa chains in the urinary proteins of patients with multiple myeloma have been reported (*3*), and we present partial amino acid sequences of several kappa chains in the urinary proteins of mice.

Kappa-chain (*4*) urinary proteins produced by plasma-cell tumors MOPC 70E, MOPC 41, MOPC 157, MOPC 46, and Adj-PC-9 from the highly inbred BALB/c strain of mice were used (*5*). Carboxymethylated preparations of these proteins were electrophoretically homogeneous in polyacrylamide gels, except for the protein MOPC 46, which consistently showed four to five bands.

The NH_2-terminal analyses were performed by the 2,4-dinitrofluorobenzene method (*6*). Phenylisothiocyanate degradation of the proteins was performed by the paper-strip procedure (*6*). Identification of the phenyl-

Table 1. Dinitrophenyl-peptides (S_1, S_2, and S_3) isolated from kappa chains digested with subtilopeptidase A.

Protein	Peptides		
	S_1	S_2	S_3
MOPC-70E	DNP-Asp-(Ile, Val)	DNP-Asp-(Ile, Val, Leu)	DNP-Asp-(Ile, Val, Leu, Thr)
MOPC-41	DNP-Asp-(Ile, Gln)		
MOPC-46	DNP-Asp-(Ile, Val)	DNP-Asp-(Ile, Val, Leu)	
MOPC-157	DNP-Asp-(Ile, Val)		