When Bidrin was injected prior to incubation, the nicotinic acid derivative could be injected at any time during the first 4 or 6 days of incubation with great effectiveness, but after about 10 days of incubation the nicotinamide did not alter the teratogenic action of Bidrin. On simultaneous administration of Bidrin and nicotinic acid or nicotinamide at any time between 0 and 12 days, no teratogenic effects were observed.

Bidrin, labeled with both phosphorus-32 and *N*-methyl-C^{14}, was injected at the rate of 1 mg per egg into the yolk on the 4th day of incubation with and without 1 mg of nicotinamide. Only the *cis* crotonamide isomer was used as it was much more potent than the *trans* crotonamide in effecting a teratogenic action. Bidrin was mostly hydrolyzed within a few days, but intermediate nonhydrolytic metabolites were formed. These consisted of Me, Me, H, C(O)NHMe; Me, Me, H, C(O)$NHCH_2OH$; Me, Me H, C(O)NH_2; and possibly also trace amounts of the initial hydroxylation product, Me, Me, H, C(O)$NMeCH_2OH$ (*8*). The concentration of Bidrin, and of these products from successive hydroxylation and *N*-dealkylation, did not vary greatly either in the egg or the embryo as a result of administering nicotinamide. These analyses were made at the 6th, 8th, and 10th days of incubation. Although the metabolism of Bidrin was unaffected, the nicotinamide almost completely reversed the teratogenic effect.

The neurotoxicity of TOCP in adult hens was studied after oral administration of 0.5 ml of TOCP per kilogram of body weight. Analogs of nicotinic acid were injected intraperitoneally, 0.25 to 8 mmole/kg daily, starting 2 days before the administration of TOCP and continuing through 7 days afterward. Some of these analogs prolonged the delay period—that is, the period before the appearance of symptoms—from the 10th day to the 12th or 13th day after the administration of TOCP, and the final severity of the symptoms as determined on the 21st day was much less in such cases. Marked ataxia and general debilitation could be alleviated, sometimes to the point of only mild weakness in the legs. Nicotinamide, 2 to 8 mmole/kg per day, and phenyl nicotinate, 1 to 2 mmole/kg per day, were the most effective. Less effective or inactive were the following compounds (*7*): nicotinic acid and its Me, Et, Pr, *i*-Pr, Bu, Hex, benzyl, and guaiacyl esters; the *N*-substituted nicotinamide analogs with mono- Me, Et, or benzyl and di- Me or Et amide substituents; and 3-pyridyl compounds with Me, CH_2OH, CHO, CN, and C(O)Me radicals.

Nicotinamide and certain analogs are known to protect chick embryos from the teratogenic effects induced by eserine, insulin, sulfanilamide, 6-aminonicotinamide, and 3-acetylpyridine, and to forestall or lessen the effects of pilocarpine and other teratogenic compounds (*5*, *9*). Growth inhibition of certain protozoa by thalidomide was counteracted by nicotinamide and NAD (*10*). The development of glossitis and possibly also polyneuritis upon prolonged therapy with large doses of thalidomide in humans was controlled by the prophylactic use of vitamin-B complex (*11*). Some protection is also offered by nicotinamide and certain analogs against EPN poisoning in mice, guinea pigs, and rats, possibly because they prevent the inhibition of tissue cholinesterase activity (*12*).

The action of nicotinic acid analogs in alleviating the effects of organophosphates might be related to their having an effect on the metabolism of the toxicant, a protective action on the cholinesterase or other active site, or to their providing adequate amounts of a pyridine nucleotide coenzyme to allow a critical enzymatic reaction blocked by the organophosphate to function almost normally through this or an alternate pathway. The experiment in which phosphorus-32 and *N*-methyl-C^{14}-labeled Bidrin was injected into chick embryos failed to support the first hypothesis. The other two hypotheses are under investigation.

J-C. ROGER*
H. CHAMBERS*
J. E. CASIDA*

Department of Entomology, University of Wisconsin, Madison 6

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* Present address: Division of Entomology and Acarology, University of California, Berkeley 4.

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trans-2-Dodecenal and 2-Methyl-1, 4-Quinone Produced by a Millipede

Abstract. *An aldehyde,* trans-2-*dodecenal, heretofore known only from plants, has been identified in the defensive secretion of the spiroboloid millipede* Rhinocricus insulatus. *A second component, 2-methyl-1,4-quinone, was previously known from the secretion of related millipedes.*

The defensive secretions of arthropods are natural products of extraordinary chemical diversity (*1*). Even relatively closely related species may produce secretions of grossly dissimilar composition. Millipedes are a case in point. Some (order Polydesmida) produce a cyanogenic secretion (*2*), others (order Chordeumida) discharge a phenol-containing mixture (*3*), and still others (orders Julida, Spirostreptida, and Spirobolida) secrete *p*-benzoquinones (*4*, *5*). We received recently from Barro Colorado, Panama, a shipment of live *Rhinocricus insulatus* (Chamberlin) (*6*), a species of the Spirobolida, and hence one that could be expected to produce quinones. Although the secretion of this millipede did indeed appear to be quinonoidal (yellow color, ability to tan human skin), it nevertheless seemed worthwhile investigating, since its odor

was distinctly anomalous and suggestive of additional entirely different components (*7*).

The two hundred available *R. insulatus* were "milked" of secretion by the technique used for similar purposes in other species (*5*). In contrast to the secretion of other quinone-producing millipedes, which show a single carbonyl absorption band in the 6.0 μ region, the crude secretion of *R. insulatus*, in methylene chloride, showed two carbonyl absorptions of comparable intensity in its infrared spectrum (5.91 and 6.04 μ). This suggested the presence—in addition to quinone(s)—of a conjugated aldehyde or ketone. Sublimation of the crude secretion (25°C/10 mm-Hg) gave a yellow crystalline sublimate (mp 69°–70°C). This material was identified as 2-methyl-1,4-quinone by comparison of its infrared spectrum with that of an authentic sample (*8*) (6.04, 7.8, 9.2, 11.1, and 12.4 μ), and comparison of gas chromatograms (20 percent Carbowax; 187°C).

The unknown component absorbing at 5.91 μ was isolated by chromatography on activity-III alumina (Merck, 71707) with pentane as eluent. This carbonyl component, which was eluted before the 2-methyl-1,4-quinone, showed characteristic infrared absorption at 3.48, 3.55, 3.70, 5.91, 6.13, 6.9, 8.9, 9.1, and 10.3 μ. The proton magnetic resonance spectrum of this material suggested the partial structure $-CH_2-CH=CH-CHO$ [peaks at 0(doublet)(1),2–4(multiplet)(2), and 7.7(2)τ] with 17 additional protons on saturated carbon. The ultraviolet spectrum, in ethyl alcohol, showed absorption maxima at 223 and 315 mμ, with extinction coefficients of 10,000 and 19, respectively. This spectrum is consistent with a mono-substituted α, β-unsaturated aldehyde.

This aldehyde was identified as *trans*-2-dodecenal by comparison with an independently synthesized authentic sample. Reduction of 2-dodecenoic acid (*9*) with lithium aluminum hydride gave *trans*-2-dodecenol (90 percent) with infrared maxima at 3.1, 3.5, 6.1, 6.9, and 10.3 μ. Oxidation of the alcohol with chromium trioxide-pyridine (*10*) gave *trans*-2-dodecenal (31 percent) (bp 73°–74°C at 0.5 mm-Hg; reported (*11*) 125°–128°C at 10 mm-Hg). The infrared spectra of the synthetic *trans*-2-dodecenal and that of the natural product from the millipede were superposable, and their gas chromatographic retention times were identical (5 percent silicone SE-30; 185°C). A mixture of the natural and synthetic material gave a single symmetrical peak on the same column. Finally, the semicarbazone of the synthetic material melted at 159°–160°C, the reported (*11*) values being 160°C and 165.5°–166°C, and the semicarbazone of the natural product melted at 160°–161°C; the melting point of the mixture was undepressed.

In order to estimate the ratio of aldehyde to quinone in the crude secretion, the infrared spectra of known mixtures of *trans*-2-dodecenal and 2-methyl-1,4-quinone were examined. The known mixture, which showed all the absorptions of the crude secretion except a small peak at 11.3 μ, established the ratio of aldehyde to quinone as 2.5:1. This ratio was confirmed by a comparison of the weights of chromatographic fractions.

Data on the protective action of the secretion will be published elsewhere as part of a comparative study of the repellent effectiveness of a variety of natural products. Suffice it to say, *R. insulatus* is virtually invulnerable to attack by aggressive predators such as ants (*Formica exsectoides* Forel) and grasshopper mice [*Onychomys torridus* (Coues)]. Surprisingly, several of the millipedes were eaten in quick succession by an ornate box turtle [*Terrapene ornata* (Agassiz)], which betrayed no ill effects either during or after the meal.

2-Methyl-1,4-quinone has been obtained not only from other millipedes (*4, 5*) but from other arthropods as well (*1*). *trans*-2-Dodecenal has been found prevoiusly in plants [citrus (*12*), ginger (*13*), and carrot (*14*) families], but although other α,β-unsaturated aldehydes are known from animal secretions (*1, 15*), this appears to be the first reported occurrence of *trans*-2-dodecenal in the animal kingdom.

J. W. WHEELER, J. MEINWALD
J. J. HURST,* T. EISNER
Department of Chemistry and
Department of Entomology,
Cornell University, Ithaca, New York

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Dictyotene Stage of Meiosis in Mosses

Abstract. *The dictyotene stage of first meiotic prophase, characterized by an elongation of the paired chromosomes after diplotene, and known to occur during the growth period of the oocytes of many animals, has a morphologically analogous but relatively short-lived counterpart in the first meiotic prophase of representatives from three moss families.*

A meiotic stage morphologically analogous to the dictyotene stage which occurs during prophase I of oogenesis in many animals has been discovered in three mosses, namely, *Hypnum circinale* Hook., *Brachythecium frigidum* (C. Meull) Besch., and *Claopodium crispifolium* (Hook.) R. & C. The fact that these species represent three families of mosses suggests that the dictyotene stage may be of wider occurrence in this group of plants. This is the first observation of the dictyotene stage in plants and indicates that this meiotic phase is not unique to the animal kingdom. Furthermore, the dictyotene stage, which undoubtedly has some fundamental significance in the meiotic sequence in mosses, may have significance in the evolution and phylogeny of this plant group.

In the three species studied, the stages of first meiotic prophase appear similar except for minor variations. A description of prophase I in *Hypnum circinale* can be taken as representative.

When the archesporial layer of the capsule of *H. circinale* has ceased divid-