Studies of alkaloids isolated from the skins of neotropical poison frogs (Dendrobatidae) have led to the discovery of nearly 500 compounds, representing over 20 alkaloid structural classes. The skin alkaloids of dendrobatids, are acquired from the ants mites, and other leaf-litter arthropods that these frogs eat, generally are believed to deter vertebrate predators, e.g., snakes and birds. The biological activities of alkaloids from dendrobatids and other anurans, however, are known primarily from neuromuscular preparations designed to uncover pharmacological modes of action. We test the hypotheses that: 1) poison dart frog skin alkaloids, acquired in part from ants, are an effective deterrent to ant predation and 2) poison dart frog skin alkaloids deter predatory ants even if the alkaloids are derived from that predatory ant. To do this we developed a very sensitive contact bioassay using *Solenopsis invicta* as the test ant. We challenged the ants in this bioassay with 20 alkaloids (12 structural classes) identified from dendrobatids or other anurans. Results clearly demonstrate that not all frog alkaloids deter fire ants at concentrations that would be found in nature, but others were highly active. We also found that the ant, *Solenopsis geminata*, originates in Central America and is sympatric with a poison dart frog, *Oophaga pumilio*, that sequesters the main piperidine alkaloid produced by *S. geminata*. The contact bioassay showed that this piperidine alkaloid was not effective against *S. invicta*. How this impacts the relationship between the ant and poison dart frog will be discussed.