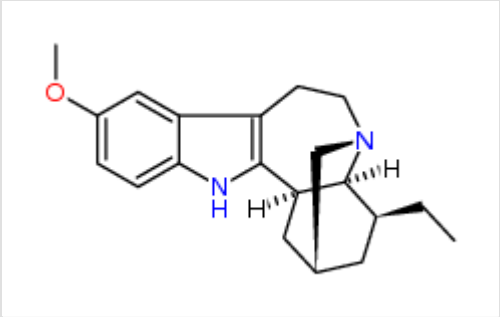
Book II of TiHKAL: The Continuation, by Alexander & Ann Shulgin #25: Ibogaine

#25 Ibogaine: 12-Methoxyibogamine



SYNTHESIS: There have been three total syntheses of ibogaine reported in the chemical literature. The first of these was a thirteen step process published about 30 years ago. The chemistry lab can serve a fine function for both isolation and purification of ibogaine from plant sources, but in the real world, there is no practical way to start from a bottle of nicotinic acid and actually prepare useful amounts. The parent ring system contains two chiral centers, neither of which is amenable to easy manipulation. Because of these two separate and largely inaccessible chiral centers there are, in theory, four distinct isomers of ibogaine which are difficult to resolve. When the term "synthetic" is used in regard to ibogaine in the scientific journals, it usually applies to the resynthesis of the parent alkaloid from the demethylated metabolite. For reference purposes, here are the finger print ~~number~~ numbers from the infrared spectra: For the free base: IR (in cm^{-1}): 741, 799, 830, 1037, 1111, 1148; mp 152–153 °C. For the hydrochloride salt: IR (in cm^{-1}): 638, 810, 832, 925, 1031, 1149; mp 299–300 °C (dec).

DOSAGE: (from hundreds of milligrams up to a gram or more, orally)

DURATION: (quite long)

EXTENSIONS AND COMMENTARY: Here is an example of a most remarkable material that has allowed people to have some rather complex and dramatic experiences. Any effort to present a fair overview of its action, through a selection of individual responses in the "extension and commentary" format would fail, as it would ignore the impact of the set and setting on the subject. Here I will mention a few of these different sets, and a leading author ~~to search out~~ who gives more detail.

There is a well studied history of the use of the iboga plant in the religious rituals in Gabon and its neighboring countries, from the early part of the 19th century. The Buiti religion calls for the use of the root bark of *Tabernanthe iboga* as a sacrament in its religion, and the reports of its psychopharmacological effectiveness reflects these needs (see Samorini).

Another area of reports that can be called upon reflect the exploration of the isolate from this plant, or the isolated active component ibogaine itself, in the study of its use ~~in connection~~ with psychotherapy. Here the reports reflect the physician/patient interaction with an emphasis on early memory and the reliving of past experiences (see Naranjo). In clinical studies such as these, a typical dose would be four hundred milligrams of the chemical, twice this weight of the crude isolate, and perhaps ten times again this weight again if the actual root bark is used.

Yet another source of reports is to be found in some studies that are exploring ibogaine as a treatment for heroin dependency (see De Rienzo and Beal). This end-goal of searching for evidence of addiction confrontation and addiction control

certainly can color any published reports in its own way. Here, its the chemical ibogaine only that is used, and typical dosages are at or above 1000 milligrams.

There is no question but that ibogaine is a rough trip, physically as well as mentally. Here is one report that shows the body aspects of its use.

(with 200 mg, orally) "Subjectively, the most unpleasant symptoms were the anxiety, the extreme apprehension, and the unfamiliar mood associated with visual and bodily hallucinations. The visual hallucinations appeared only in the dark and consisted of blue disks dancing up and down the walls. Dysesthesia of the extremities. a feeling of light-weightedness, and hyperacusis were other symptoms noted. Autonomic signs, such as dryness of the mouth, increased perspiration, slight pupillary dilation, and increase in pulse rate, as well as extrapyramidal syndromes (fine tremors, slight ataxia, enhanced tendon reflexes and clonus) were also present. The peak effect was reached at about 2 hours after swallowing the drug; it subsided gradually, leaving as a residue complete insomnia. No undesirable after-effects, such as exhaustion or depression occurred."

As was pointed out in a pharmacological review (see Popik et al.), as the hallucinogenic dose appears to be several times higher than the stimulant dose, the user must endure intense and unpleasant central stimulation in order to experience the hallucinogenic effects.

But as fascinating as the pharmacology of ibogaine, it is the chemistry of this alkaloid that is overwhelmingly awesome. The presence of four isomers was mentioned in the chemistry section above, but this fact was not appreciated until the 1960's and even then, a ~~coupe~~ couple of troublesome errors were made that confused the absolute configuration picture quite badly. The story has been accurately told in a (~~almost~~ nearly) hundred page review chapter (see Cordell) which is a "must" for anyone who wants to risk understanding some pretty ~~far-out~~ far-out chemistry. Oh my, there are a lot of closely related alkaloids. As to indolic alkaloids in general, there are well over two thousand of them, with a few dozen ~~being~~ added every year. And most of these are kosher tryptamines in that they carry the tryptamine structural skeleton. And, in turn, a great number of the tryptamine alkaloids are found in the remarkable family Apocynaceae, which is the ultimate treasure-trove of alkaloids, probably the richest single source of pharmacologically active compounds in the entire plant kingdom. It is made up, largely, of tropical shrubs of the ~~dog-bane~~ dogbane group, which almost always ooze out a sticky sap when you break off a twig, which have showy flowers, and which have the reputation of being very poisonous.

And this all leads smoothly to the botany, which is almost as convoluted as the chemistry. Here, let me list the plants that contain ibogaine, or that should contain it. Allow me a brief run-down of binomials. There is a number of species that are, or have been, classified as belonging to the *Tabernanthe* genus and which are reasonable sources of ibogaine, and which are logical alternatives, psychopharmacologically, to the iboga plant itself.

Tabernanthe iboga. This is the major source of ibogaine and is found in Gabon, mentioned above.

Tabernanthe orientalis. This plant is now called *Ervatamia orientalis*, and is found in Western Australia. The leaves contain ibogaine, along with six minor alkaloids that are closely related, structurally.

Tabernanthe pubescens. This is found in Zaire, and contains a number of alkaloids

closely related to ibogaine in structure, as well as ibogaine itself.

Tabernaemontana spp. This genus is from a tribe within the family Apocynaceae that is called the Tabernaemontaneae. As an official sub-family it would be called Tabernaemontanoideae. It is because of the casual use of names such as these that botanical binomialists are rarely invited to social functions. It (this Genus, that is) contains several dozen species, some with ibogaine, many with analgesic or sedative action in experimental animals, and some with a quite a history of native usage either in Africa or Southeast Asia.

And there are many plants in the Apocynaceae family that carry fascinating alkaloids that are closely related in structure to ibogaine and which, potentially, might have a similar psychopharmacology. In most of these, ibogaine is present in very small amounts, if any at all.

Anacampta spp. have usually been published as *Tabernaemontana* spp., as have been species originally published as part of the Genera *Bonafousia*, *Capuronetta* (which has become the species *capuronni* under this Genus), *Conopharyngia*, *Ervatamia*, *Gabunia*, *Hazunta*, *Muntafara*, *Pagiantha*, *Pandaca*, *Peschiera*, *Phrissocarpus*, and *Stenosolen*, . All of these contain alkaloids related to Ibogaine.

Callichilia barteri has appeared as *Hedranthera barteri*, but *C. subsessilis* demands the name *Tabernaemontana subsessilis* in the presentation of its alkaloid content.

Creoceras, *Rejoua*, *Schzozygia*, *Stemmadenia* and *Voacanga*, have, with all their species, remained intact with their original names.

Peschiera echinata. This is one of some ten species within the *Tabernaemontaneae* classification, with some 2% alkaloid content in its leaves. Ibogaine is present.

Voacanga schweinfurthii var. *puberula* (known in the older literature as *Voacanga puberula*) contains some ten related alkaloids, the major one of which is found in the seeds, and is tabersonine present at a rather remarkable 3.5%. Ibogaine is present in the root bark but, at a concentration of 200 mg/kg (0.02%), it is truly a minor constituent.

Naranjo, C. Psychotherapeutic Possibilities of New Fantasy-Enhancing Drugs. *Clin. Toxicol.*, 1969, *2* (2), 209–224. 855 kB. doi:10.3109/15563656908990930

Naranjo, C. Ibogaine: Fantasy and reality. In *The Healing Journey: New approaches to consciousness*; Pantheon Books, New York, 1974; pp 174–228.