

Iboga/Voacanga Chemistry

How to get the ibogaine needed
for use in addiction treatment



Dr. Chris Jenks

Goals for an Ibogaine Production Method

Ensure that there is enough ibogaine for everyone who wants it for treatment

Let ibogaine be affordable for everyone who wants it for treatment

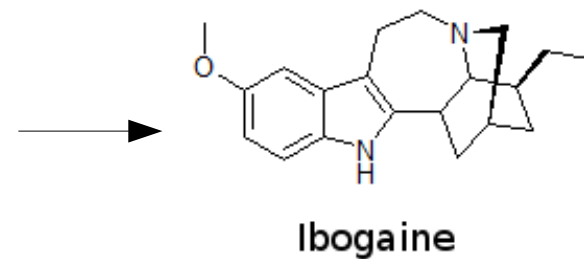
Allow ibogaine to be produced in all places there is likely to be a demand, including developing countries

Ideal Conditions to Reach the Goals

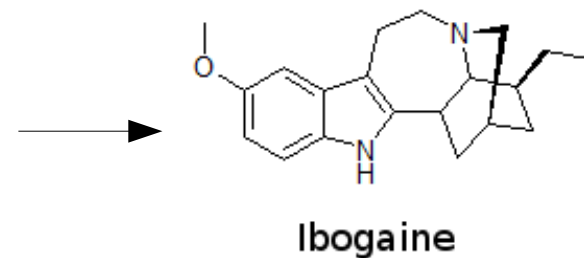
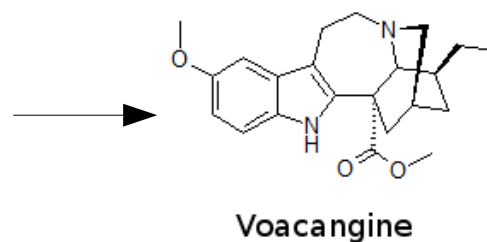
1. The method should be inexpensive
2. The method should be easy and safe enough to reproduce without professional chemical training
3. The method should use materials and equipment available most places in the world
4. The ibogaine should be produced in a stable form
5. Impurities present in the ibogaine should not contribute significant side effects
6. Waste produced by the process should not damage the environment
7. The demands of production should not endanger the species providing the ibogaine

What Kinds of Methods Can Produce Ibogaine?

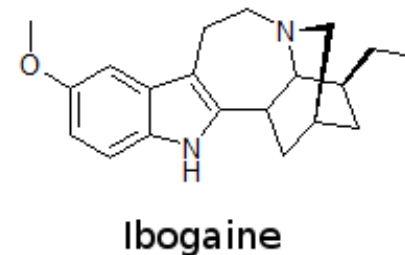
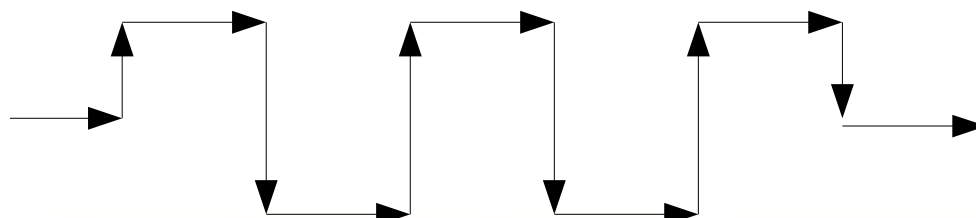
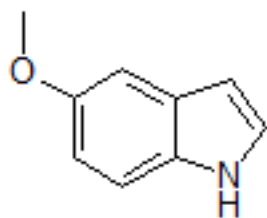
Extraction from a plant



Semisynthesis from a plant substance



Complete synthesis from a petrochemical



Extraction from *Tabernanthe iboga* Root Bark

To begin:

Weigh some root
or bark powder

Batches shown
here are two
kilograms each



Dissolve the Ibogaine in Vinegar

This is fun.

Uses about half a liter of distilled vinegar and 4.5 liters of water. Stir a few times over an hour.



Filter out the Root Pulp

This is hard work.

We used pillow cases, which had to be wrung out. This is the most labor intensive step.



Use a Serial Extraction for Large Operations



Precipitate Ibogaine with Ammonia

The middle bucket has had ammonia added.



Filter the Ibogaine Out and Rinse



This can take a day or two, with frequent checking.

Spread Out the Ibogaine to Prepare for Drying



Dry the Ibogaine in a Warm Breeze

This step can take longer than any other unless gentle heat is used.

Much of the moisture seeps into the reusable towel under the paper.



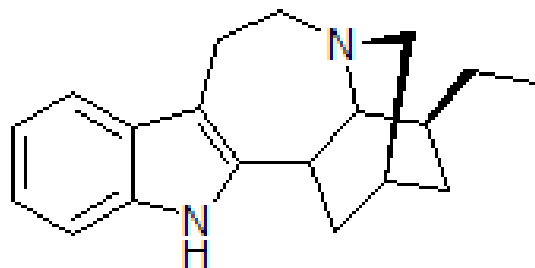
What is this "Ibogaine" We Have Made?

At this stage of purity the mixture is called "total alkaloid" or TA.

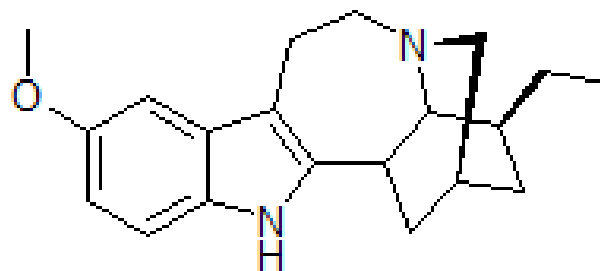
TA is a mixture of all substances in iboga root that dissolve in vinegar but not ammonia, which tend to be nitrogen containing compounds called alkaloids.

TA consists of only about 30% ibogaine.

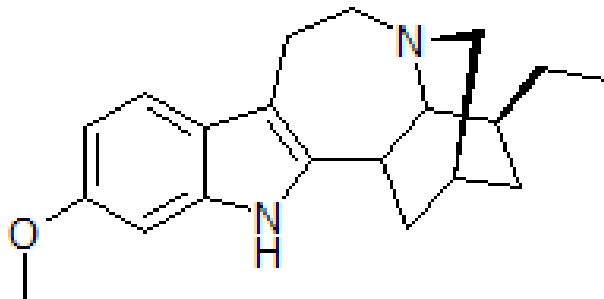
Iboga Alkaloid Structures



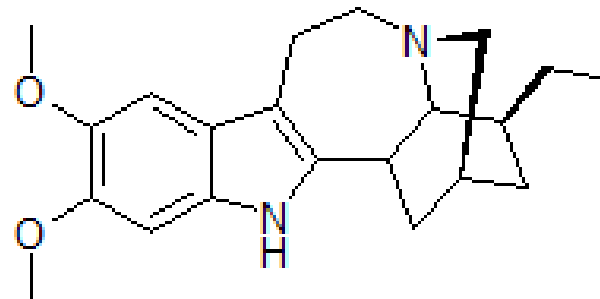
Ibogamine



Ibogaine



Tabernanthine

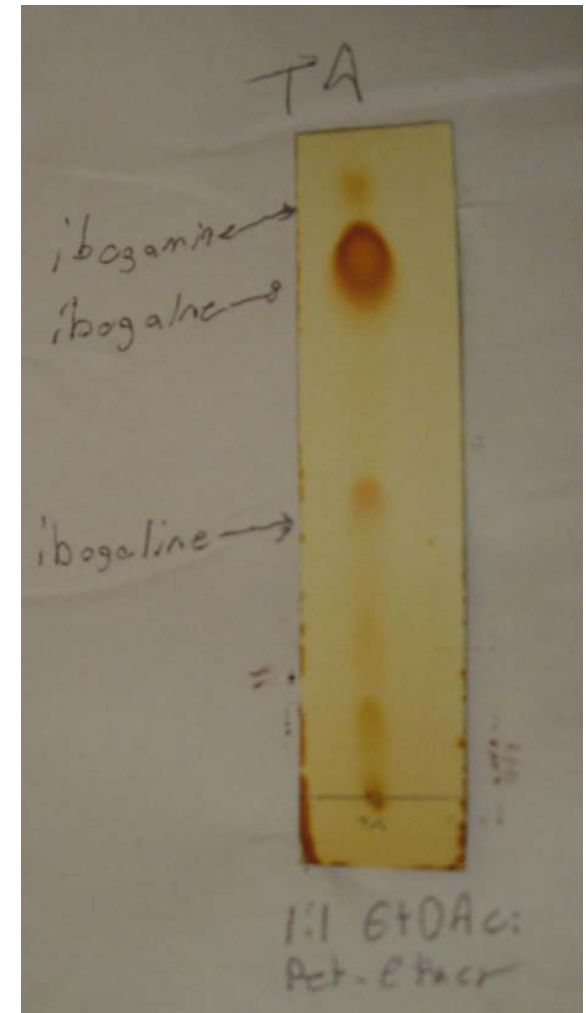


Ibogaline

Present in Tabernanthe iboga root bark

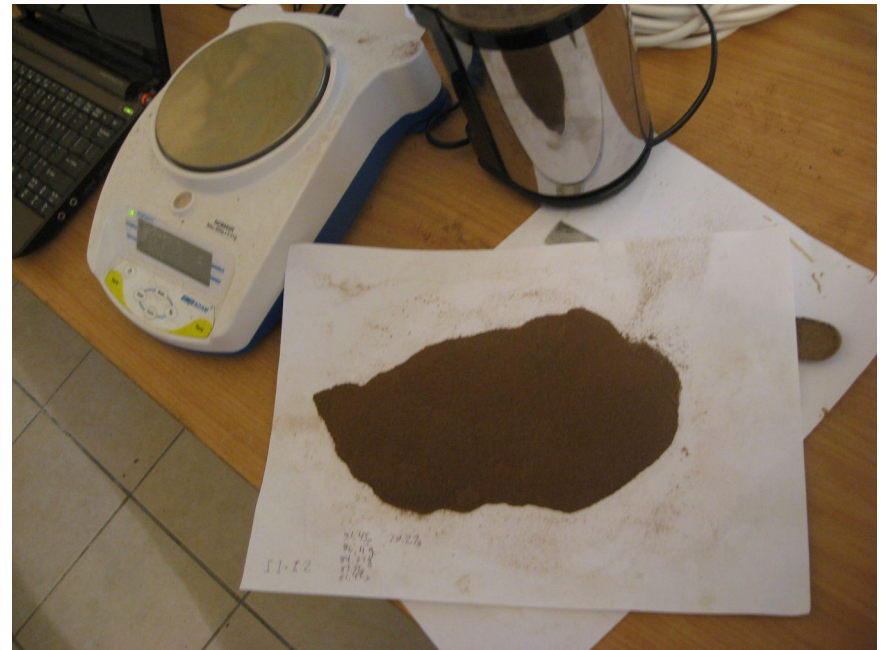
What is Total Alkaloid

This Thin Layer Chromatogram (TLC) shows the components separated into different spots, stained with iodine vapor. The biggest spot is ibogaine, and the next biggest is ibogaline, present only in some batches of iboga. About half of the TA would not dissolve in solvent, so was not applied to the TLC.



Further Purification of TA

After prying the dried TA from the filter paper, the first step is to powder and sift it.



Sure looks better, doesn't it?

The TA is Extracted with Acetone

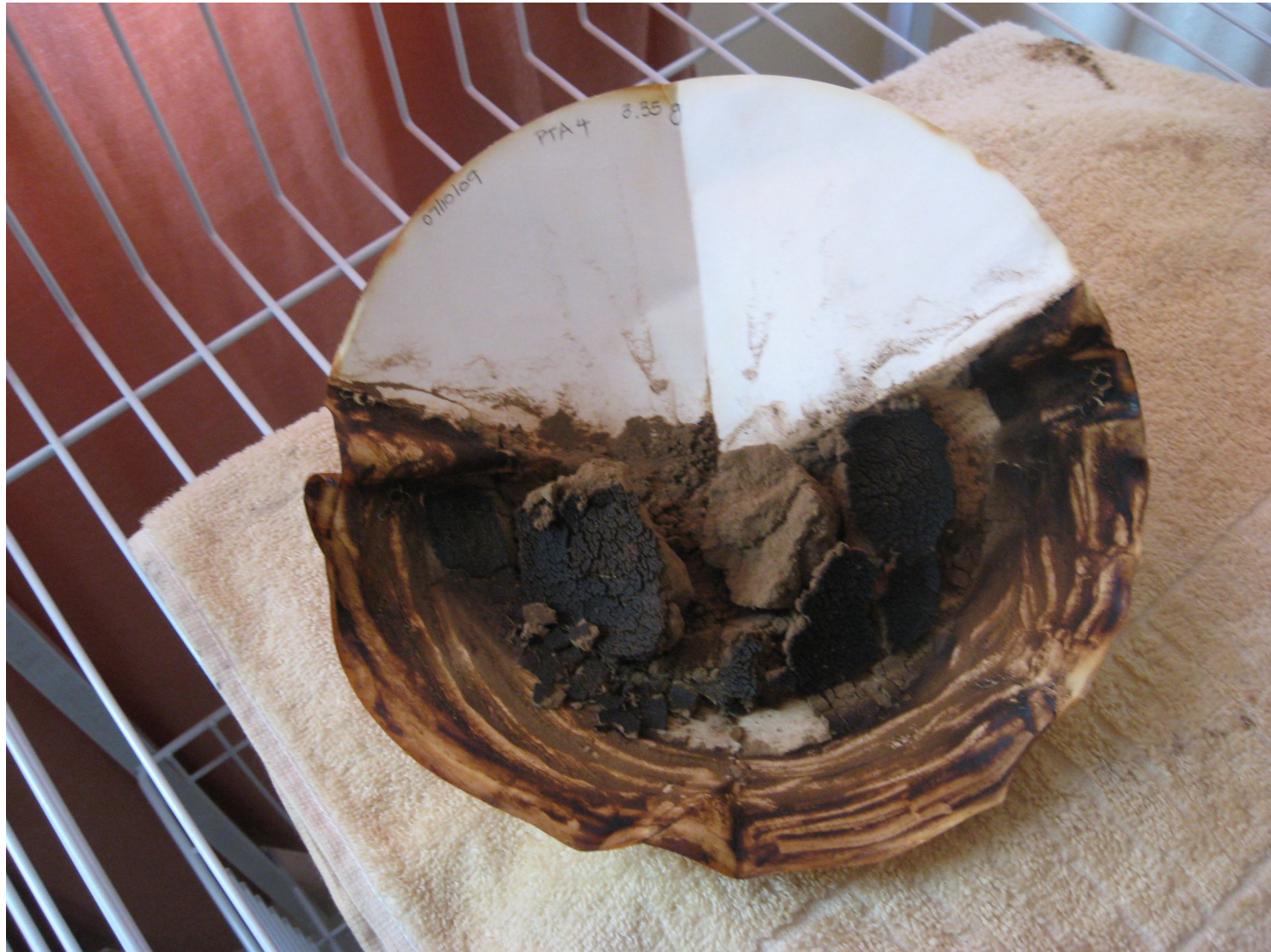


Ibogaine and similar alkaloids dissolve

Leaving Behind Insoluble Alkaloids



Which Look and Taste Like Dirt



The Acetone is Treated with Hydrochloric Acid



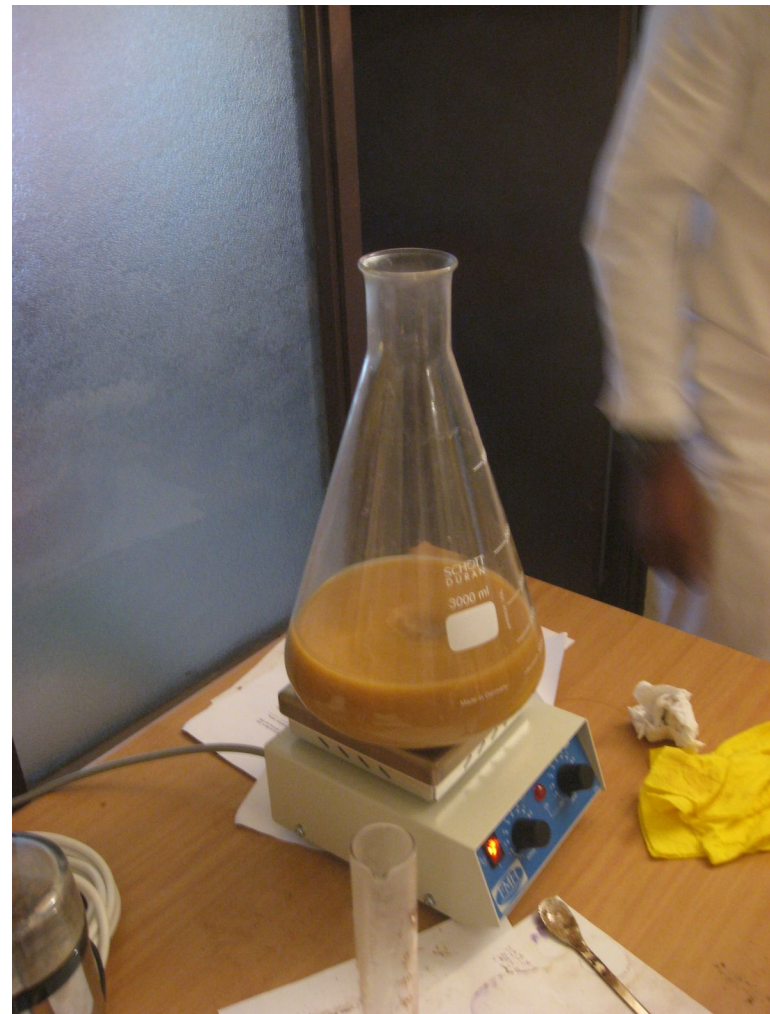
The Hydrochloric Acid is Carefully Measured to Maximize Yield



And Added Slowly
to Maximize Purity



Until it is All In!



After Sitting In The Refrigerator, an
Attractive Yellow Solid Settles



Filtering and Drying Gives Purified Total Alkaloid (PTA) Hydrochloride



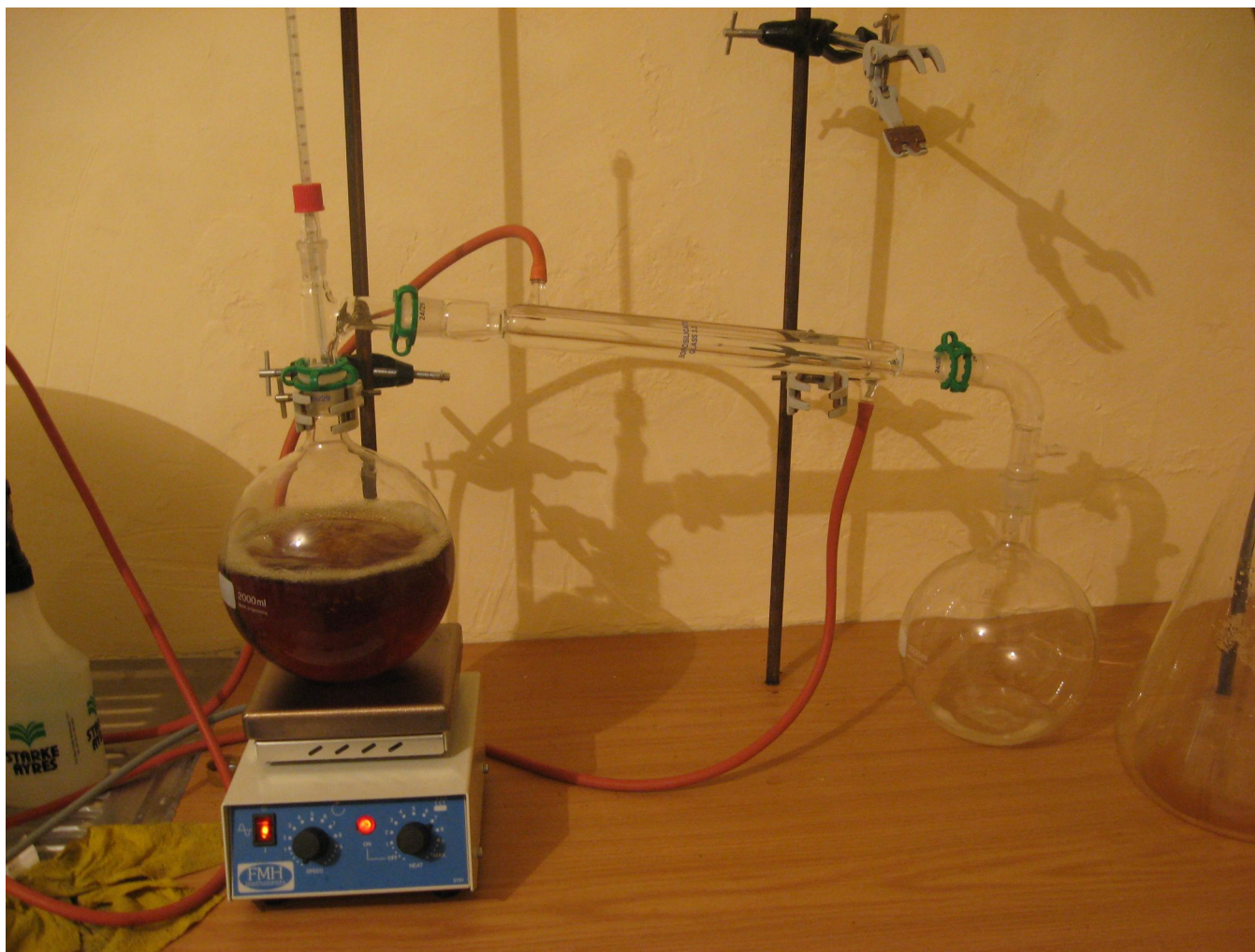
Most treatment providers consider PTA hydrochloride a pure enough (about 80% pure ibogaine) to use in addiction treatment.

The Acetone that went Through the Filter Still Contains Ibogaine

The ibogaine left in the acetone can be recovered in a stable but very impure form which may be purified by technology developed in the future.



Alkaloid Recovery Involves Distillation of the Acetone



The Residue is Precipitated with Ammonia and Filtered



Recovered Alkaloid (RA, ~40% ibogaine) contains about 1/4 of the ibogaine in the original TA, with PTA getting the remaining 3/4.

Does iboga Extraction Have the Ideal Conditions Defined Above?

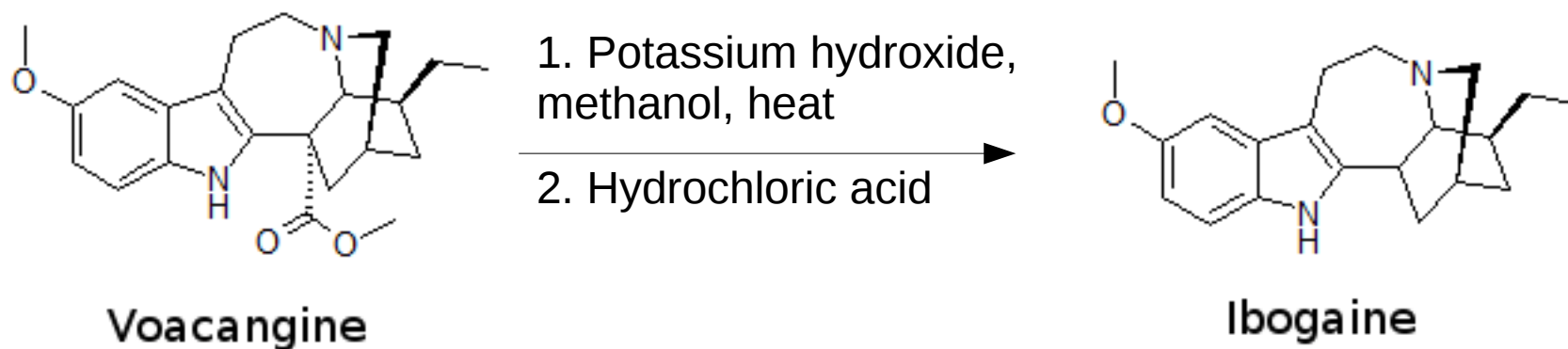
1. Except for the cost of iboga root, this method is very inexpensive.
2. Laypersons have been successfully trained to reproduce the method.
3. The materials needed are some of the most common household chemicals.
4. The TA, PTA hydrochloride and RA all appear completely stable under cool, dark, dry conditions.
5. Both the TA and PTA hydrochloride have been used successfully for addiction treatment and seem to be tolerated about as well as pure ibogaine.
6. The waste from this process makes good garden mulch and fertilizer.
7. **PROBLEM:** Tabernenthe iboga grows in a limited range, is slow growing, not normally farmed, and is normally killed to harvest the root.

What About Semisynthesis from *Voacanga africana*?

From US Patent 2,813,873, Derivatives of the Ibogaine Alkaloids, awarded to Janot and Goutarel in 1957:

"While it would appear logical to produce the new products of the invention [noribogaine] from ibogaine, the applicants have found that it is much more advantageous and desirable to prepare these derivatives by starting with voacangine as a source. It has been found that voacangine is extracted from the bark of the voacanga tree plant. The *Voacanga africana*, stapf, is able to supply up to 5 grs. per kilo, whereas ibogaine is found in the roots of tabernanthe iboga (H.Bn) at a concentration of 3 grs. per kilo. It is both apparent and obvious that gathering the bark is much easier than gathering the roots, and that the former procedure does not bring about the destruction of the plants. It should also be noted that the voacanga is much more prevalent than the iboga."

Voacangine into Ibogaine?



Conversion of voacangine into ibogaine requires about the same technology as used to make soap or biodiesel, should give a good (70-85%) yield and little waste.

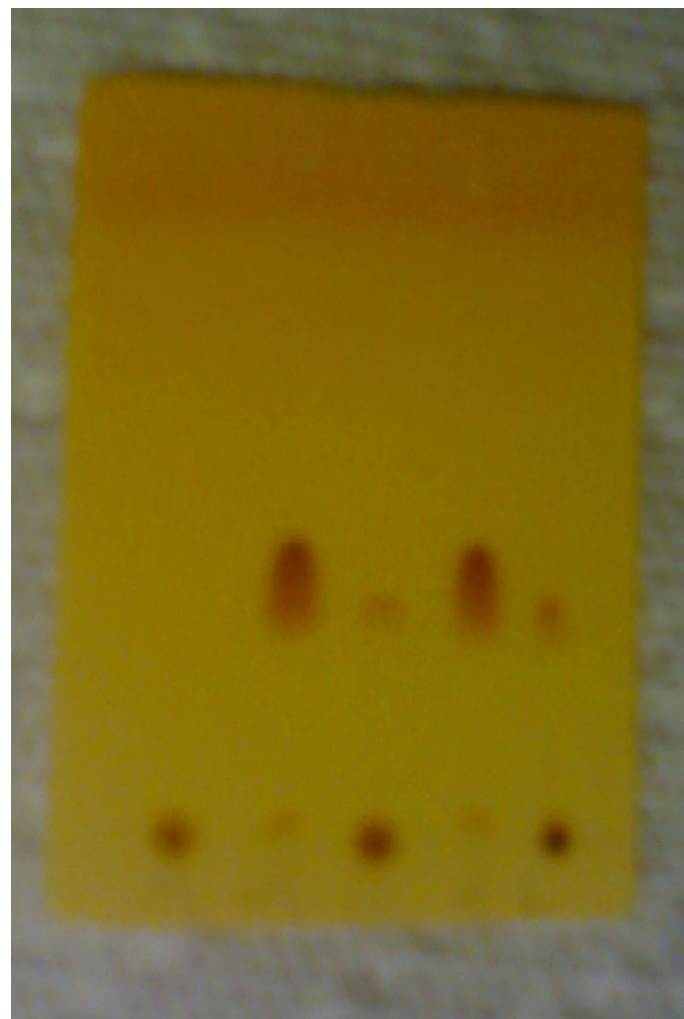
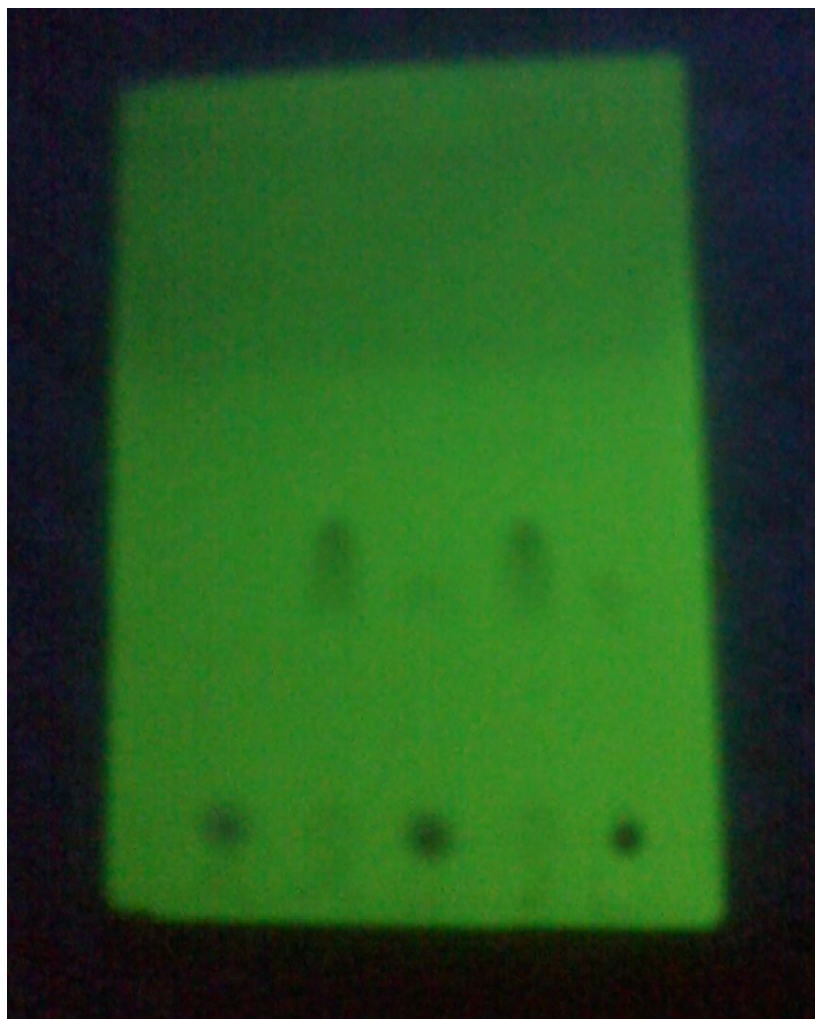
So What's the Problem?

The main problem developing simple technology to obtain ibogaine from Voacanga seems to be that voacangine is not present in larger amounts than similar alkaloids like vobtusine and voacamine, making it difficult to isolate in pure form. Efforts to convert the voacangine into ibogaine without isolating it first have failed to yield any ibogaine.

Complications and Solutions

The amount of voacangine in different batches of bark has been highly variable, with some batches containing none at all. This could be turned around into an opportunity, since there may be high yielding varieties to identify and select.

Hopeful Analysis



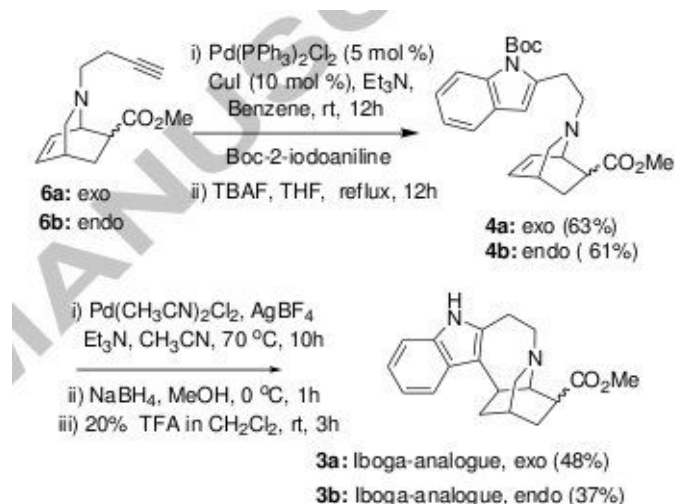
Does Voacanga Extraction Have the Ideal Conditions from Above?

1. This method should be less expensive than iboga extraction because the bark is cheaper.
2. It will probably remain possible to train laypersons to reproduce the method.
3. The final method will probably use common chemicals.
4. Ibogaine produced using this method will probably be stable.
5. Impurities resulting from this method impose more risk than those from iboga extraction because of less human history of Voacanga bark consumption.
6. The waste from this method will be like that from iboga.
7. Voacanga is already farmed at such a high rate that the demand for Voacanga bark could probably be sustainably met already.

Latest Total Synthesis (Leaked)

"A concise route to iboga-analogues via the formation of suitably substituted-2-indoles" by Goutam Kumar Jana and Surajit Sinha, accepted by Tetrahedron Letters *this month*.

Like most complex syntheses, this one requires many steps, some with poor yield, and gives mixtures. Shown here are only two of the key steps.



Scheme 3. Synthesis of iboga-analogues 3

Does Total Synthesis Have the Ideal Conditions from Above?

1. Synthesis of ibogaine requires many chemicals and steps and will probably always be very expensive compared with extraction.
2. A high level of synthetic training would be required to synthesize ibogaine.
3. The chemicals required will be very specialized and be available only from specialized chemical suppliers.
4. Ibogaine produced using this method will probably be stable.
5. Impurities resulting from this method impose much more risk than those from any extraction because nothing is known of their human toxicity.
6. The waste from this method will require extensive processing.
7. Since total synthesis does not depend on any plant source, it should be completely sustainable as long as it can be afforded.

Thank You for Your Attention

