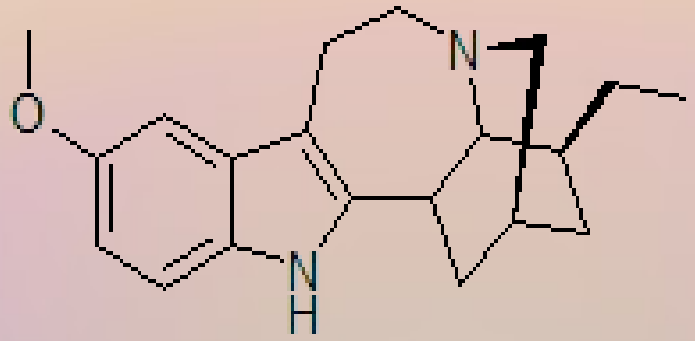
Research on Production of Ibogaine from *Voacanga* and *Iboga*



Ibogaine

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Iboga extraction, review

Powder the bark
Extract it with dilute acid (vinegar)
Filter out the bark
Make the extract basic (ammonia)
Filter, dry and powder the TA (Total Alkaloid)

Extract the TA with acetone
Filter out the spent TA
Titrate the extract with hydrochloric acid
Filter and dry the PTA HCl (Purified Total Alkaloid)

Iboga vs. *Voacanga*

1 kg *Iboga* root bark
(~3% ibogaine)
↓ Extraction
100 g Total Alkaloid (TA)
(~40% ibogaine)
↓ Precipitation
40 g Purified TA HCl
(~80% ibogaine)

1 kg *Voacanga* bark
(~0.35% voacangine)
↓ Extraction
115 g Total Alkaloid (VTA)
(~3% voacangine)
↓ Purification
↓ (chromatography?)
3 g Voacangine
↓ Hydrolysis Reaction
Crude ibogaine
↓ Purification
2 g Ibogaine HCl

Advantages/Disadvantages of *Voacanga*

Advantages

- Sustainable, takes pressure off *iboga*
- Decreasing cost
- May make ibogaine affordable in poor countries

Disadvantages

- Less familiar than *iboga* derived ibogaine
- More complicated production requires central facility

Ideas to Reduce Cost of Voacangine Extraction

- Instead of separating the *Voacanga* bark, use the whole wood, including the trunk, to save labor.
- Instead of extracting the plant material with organic solvent, use dilute acid (as for *iboga*).
- Instead of separating the voacangine from the other alkaloids by chromatography, use an extraction process where solvent is recycled.
- Do all this as close to the farm as possible.

Voacanga Alkaloid Extraction

Extracting *Voacanga* alkaloid is very much like extracting *iboga* alkaloid.

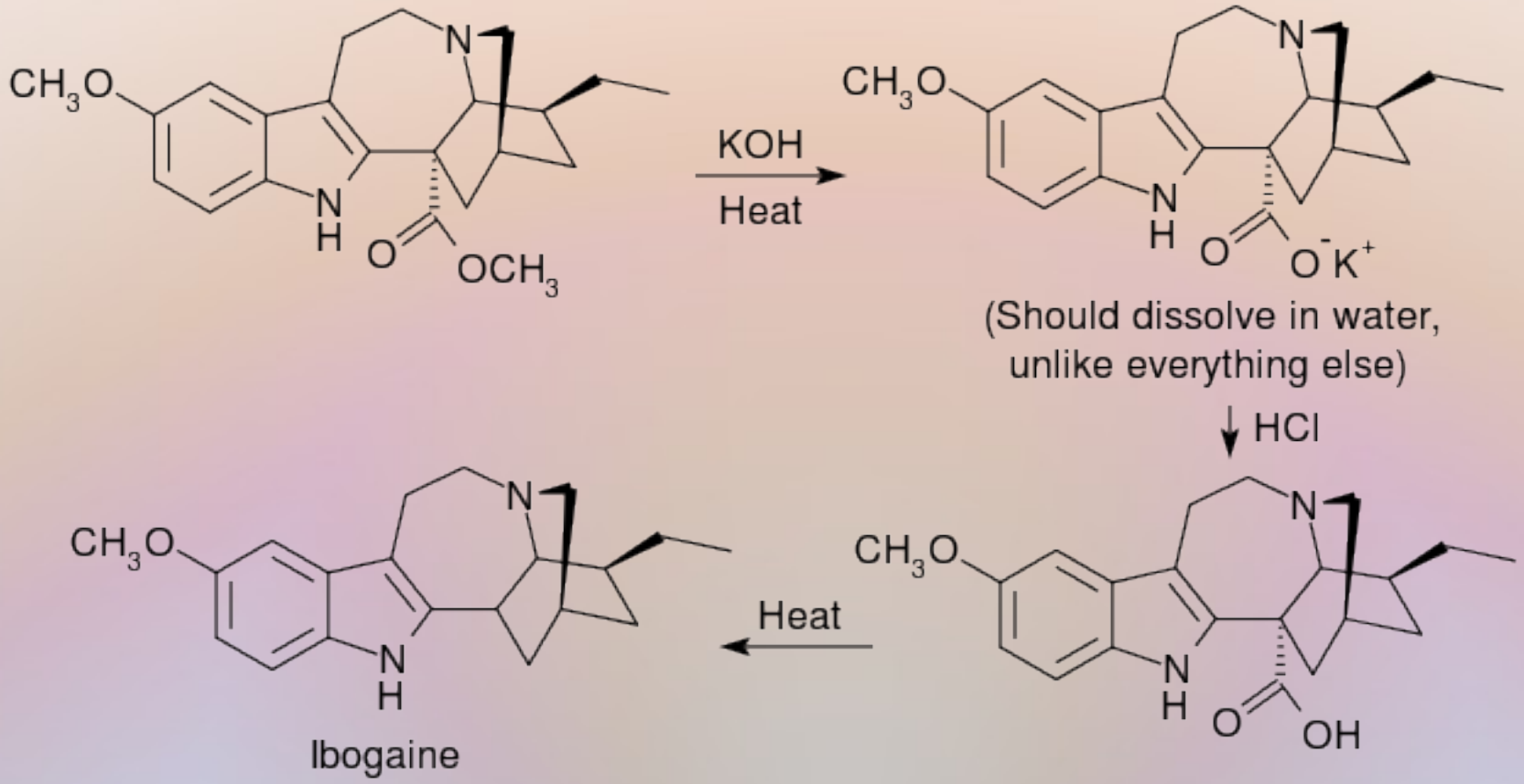
VTA (*Voacanga* Total Alkaloid)

And it produces a similar, solid total alkaloid which contains most of the voacangine.

VTA vs. (*iboga*) TA

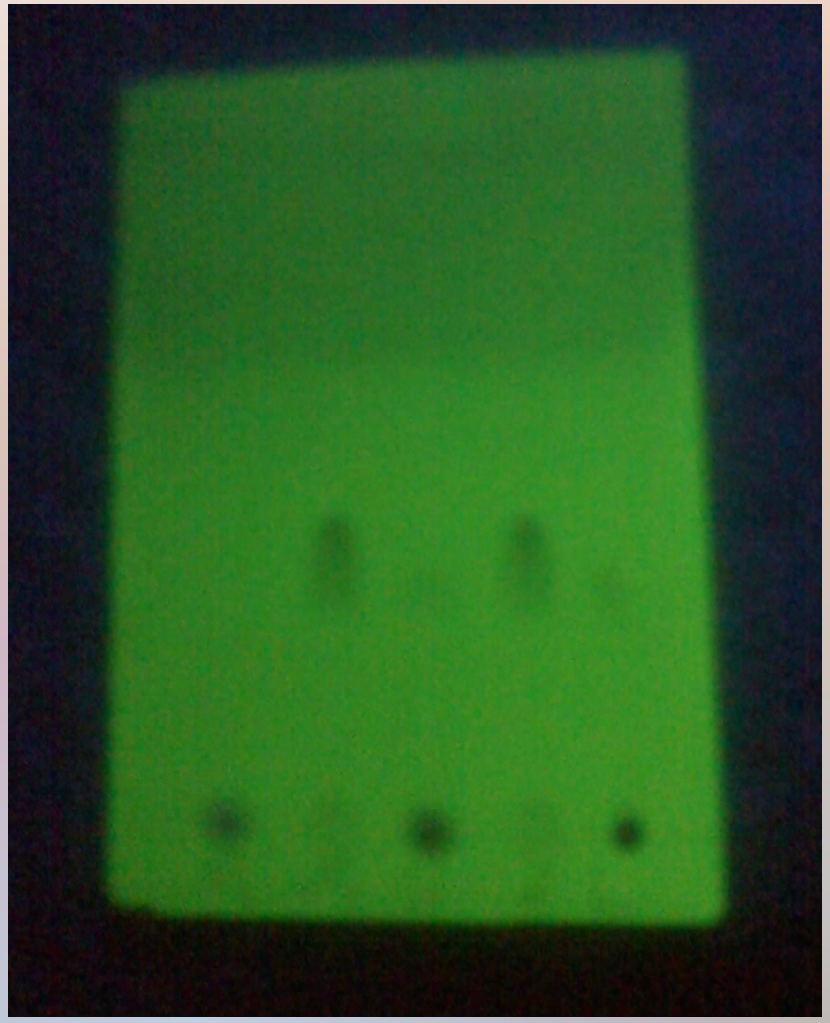
- *Iboga* TA is useful because it normally contains about 50% of the four main *iboga* alkaloiods, ibogaine, ibogaline, ibogamine and tabernanthine.
- *Voacanga* TA (VTA) contains only about 3% voacangine and, unlike TA, seems to be useful only as a stable intermediate on the way to isolating voacangine.
- Since the voacangine is isolated from VTA by extraction of the VTA, there may be no need to isolate VTA as a solid at all.

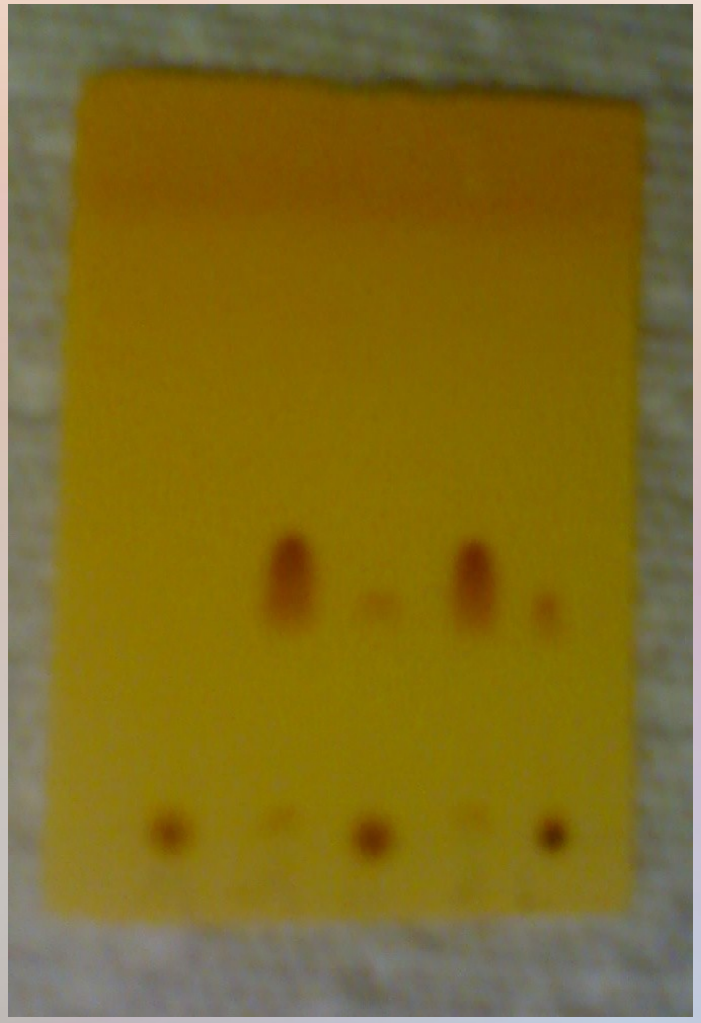
What I Wish Had Worked



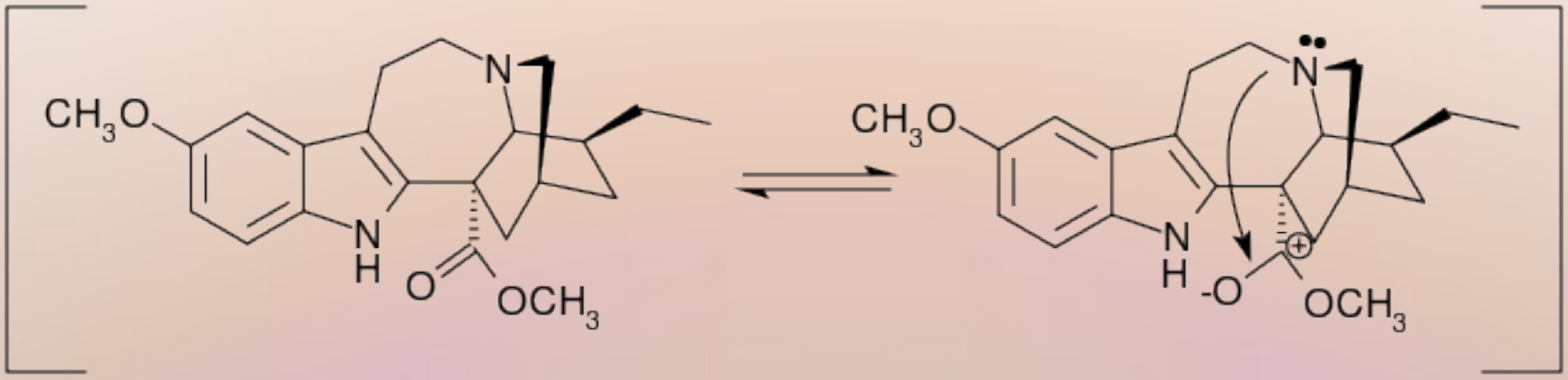
This would have made purification so easy and cheap, if it had worked. But no ibogaine was detected at the end.

The Mystery of the High R_f





Why Voacangine is an Especially Weak Base

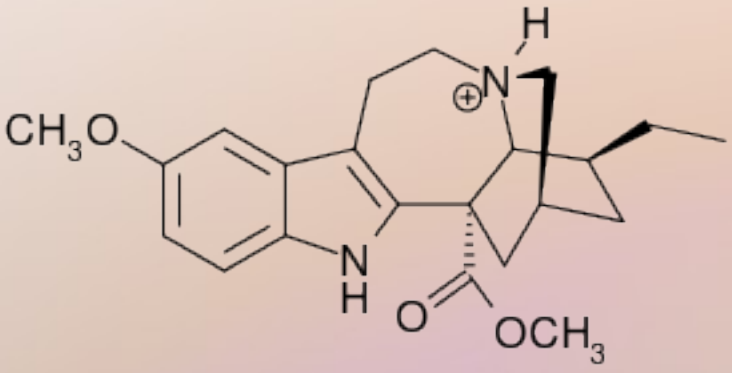


In general, a compound which moves higher on the chromatogram is considered less polar, since it interacts less with the polar silica. But voacangine moves higher than the other *iboga* alkaloids.

Why?

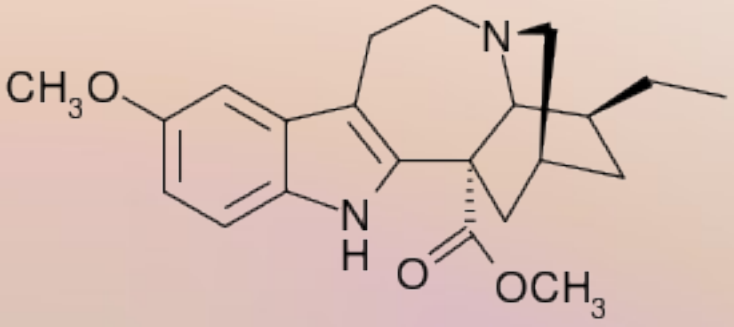
Because it is less basic, due to the ester group.
Silica is not only polar – it is also slightly acidic.

Voacangine Refinement (Step 1)



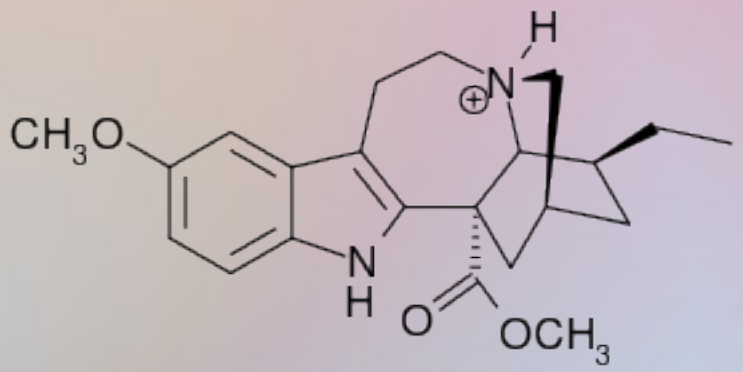
(Dissolved in vinegar extract of VTA, ~3% voacangine)

Extract with toluene



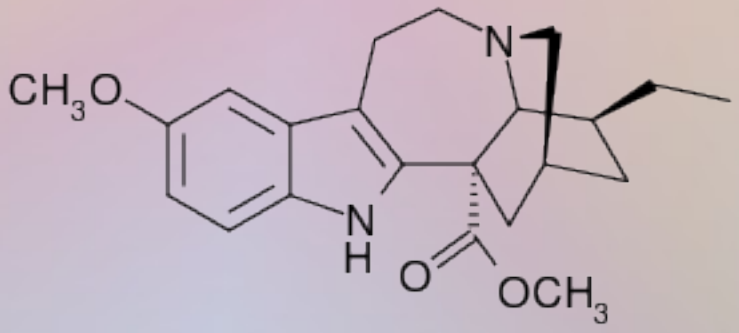
(Dissolved in emulsified toluene)

Extract toluene emulsion with hydrochloric acid



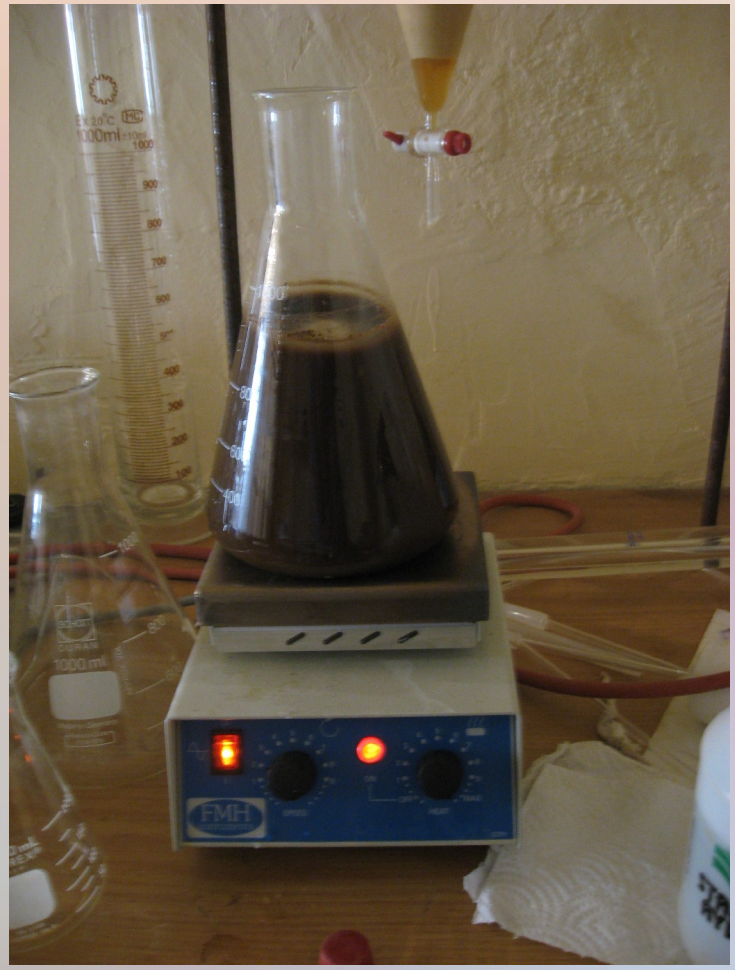
(Dissolved in hydrochloric acid)

Basify with ammonia



(Solid PVTA (Purified Voacanga Total Alkaloid), ~20% voacangine)

Extract VTA with Straight Vinegar



Filter the VTA Extract

Extract the Filtrate with Toluene

By Mixing and Waiting and Draining

(Warning: This and subsequent steps get repeated 3-6 times)

Wash the Toluene Emulsion with Water

The alkaloids in the water washes are precipitated with base and added to the next batch of VTA.

And Extract the Emulsion with 1% HCl

The toluene emulsion gets reused to extract the VTA vinegar extract again.

Add Ammonia and … Oops!

Suspended toluene makes PVTA come out as an oil.
It looks the same after filtering as before,
With little being filtered out.

Extract the HCl with Petroleum Ether

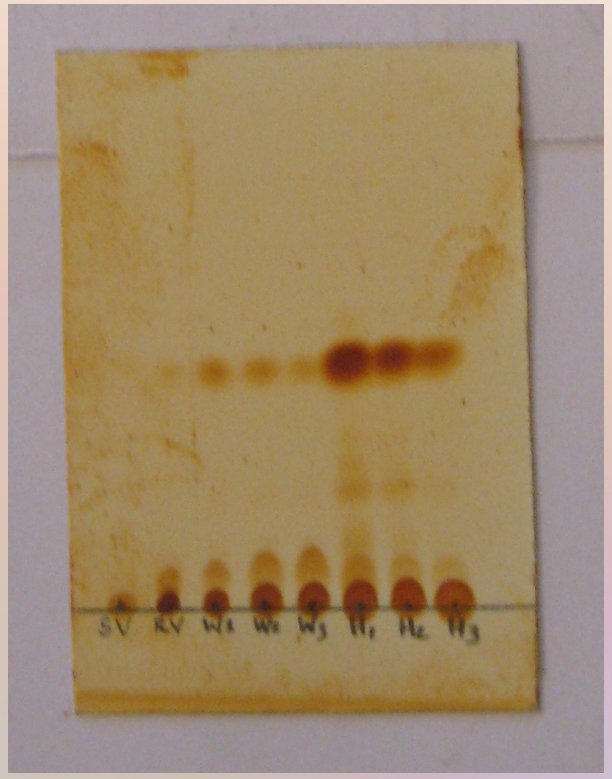
This removes suspended toluene and clarifies the extract.
The petroleum ether can be reused many times and eventually recycled.

Now the Precipitate Filters Nicely

The Filtrate is Nice and Clear

This is How Three Runs Look

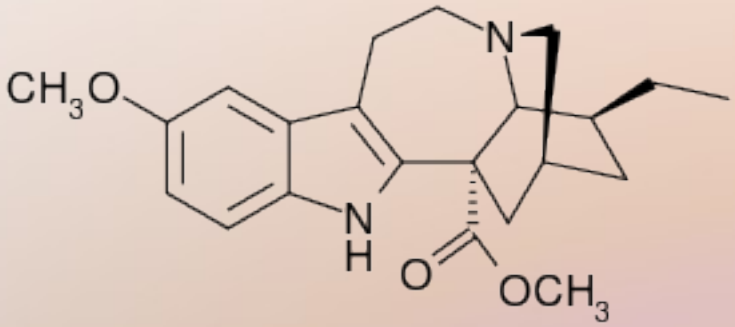
Dried PVTA, ~20% voacangine
Stable intermediate.



Spots are:

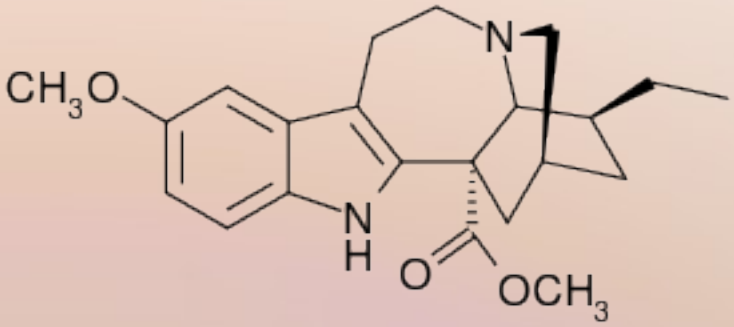
- SV: Spent VTA
- RV: Recovered VTA
- W1 – W3: Water washes 1-3
- H1 – H3: PVTA from HCl extracts 1-3

Voacangine Refinement (Step 2)



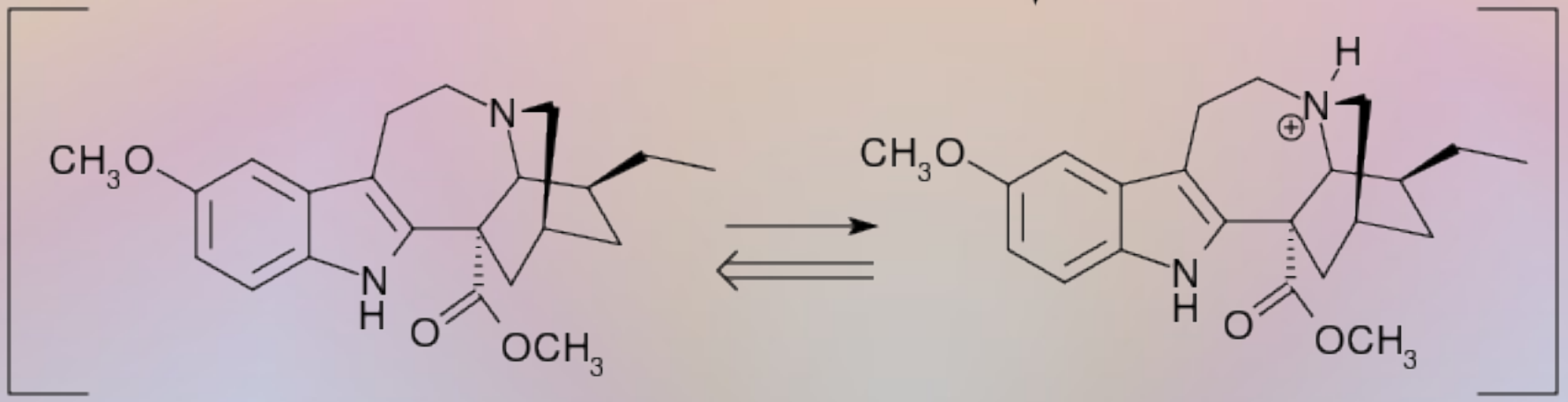
As PVTA, about 20% voacangine

Extract with acetone



More that 20% voacangine, some solid didn't dissolve

Add concentrated HCl



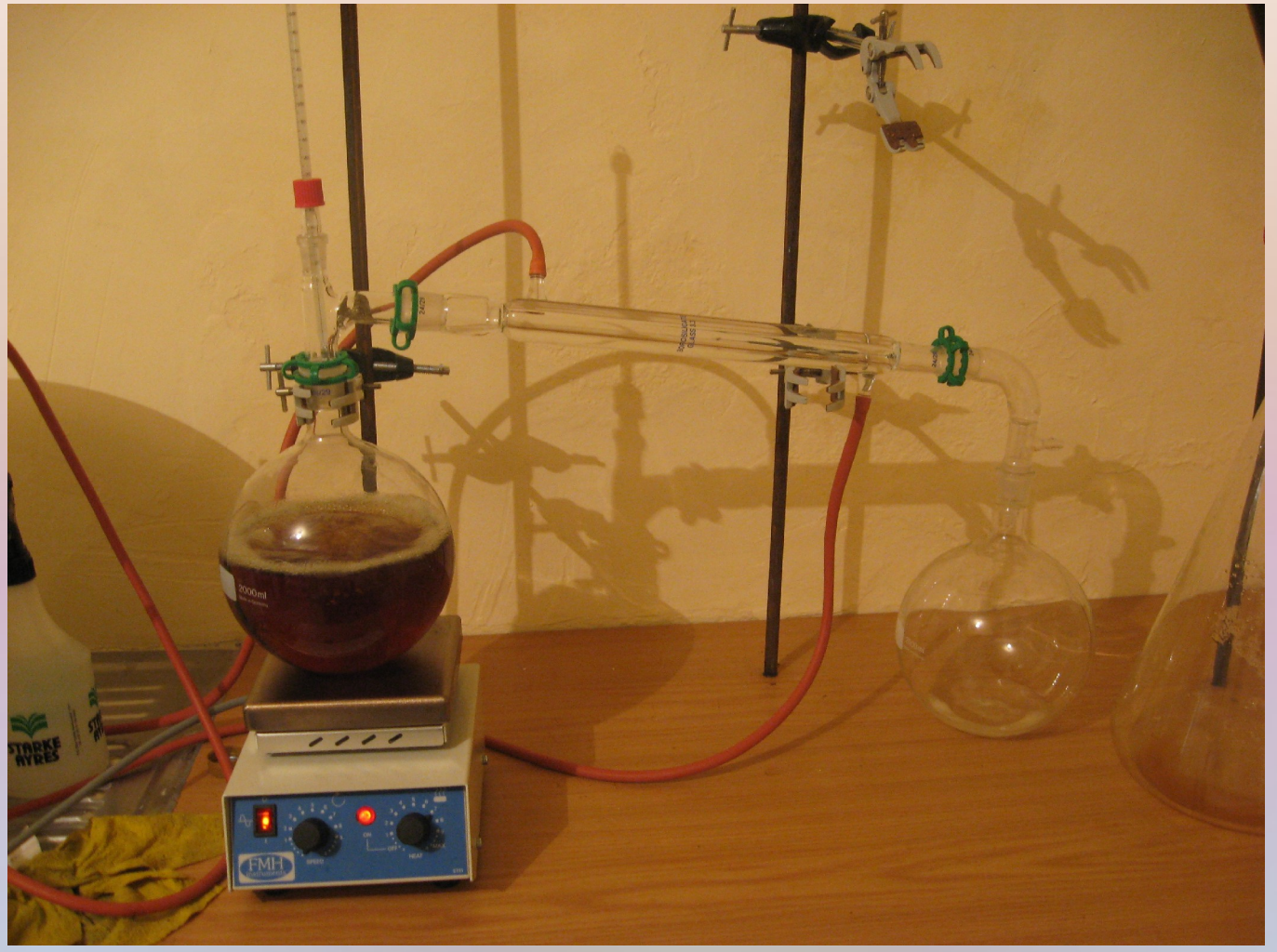
Voacangine, being weakly basic, has more relative stability in unprotonated form in acetone than the rest of the alkaloids.

Extract the Dried PVTA with Acetone

Add HCl and Filter

Unlike with *iboga*, there is less voacangine in this alkaloid salt mixture than was in PVTA. It can be recycled with the next batch of VTA.

Distill Most of the Acetone



And Evaporate the Rest

Until Dry

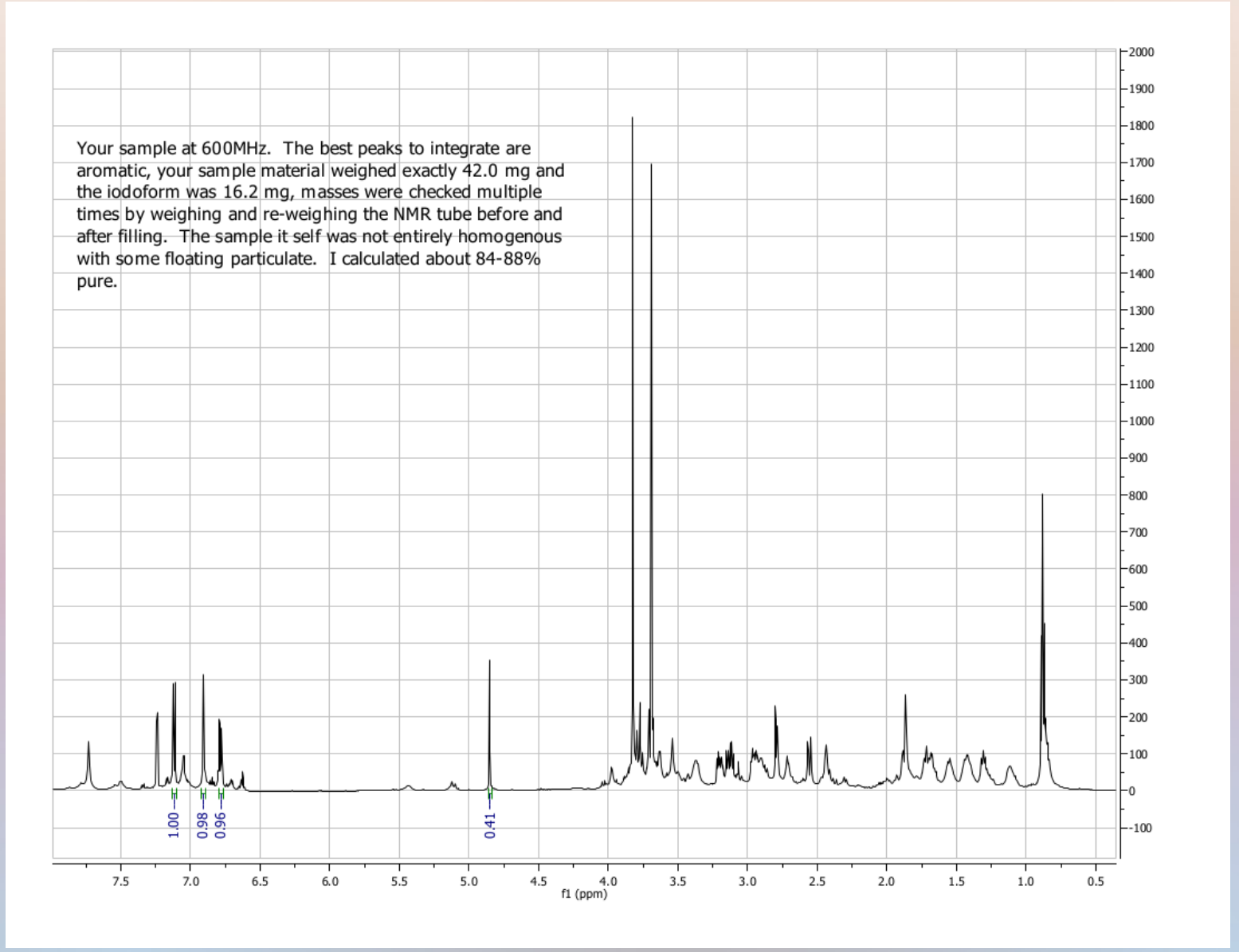
Dissolve this up in Water

And Precipitate with Ammonia

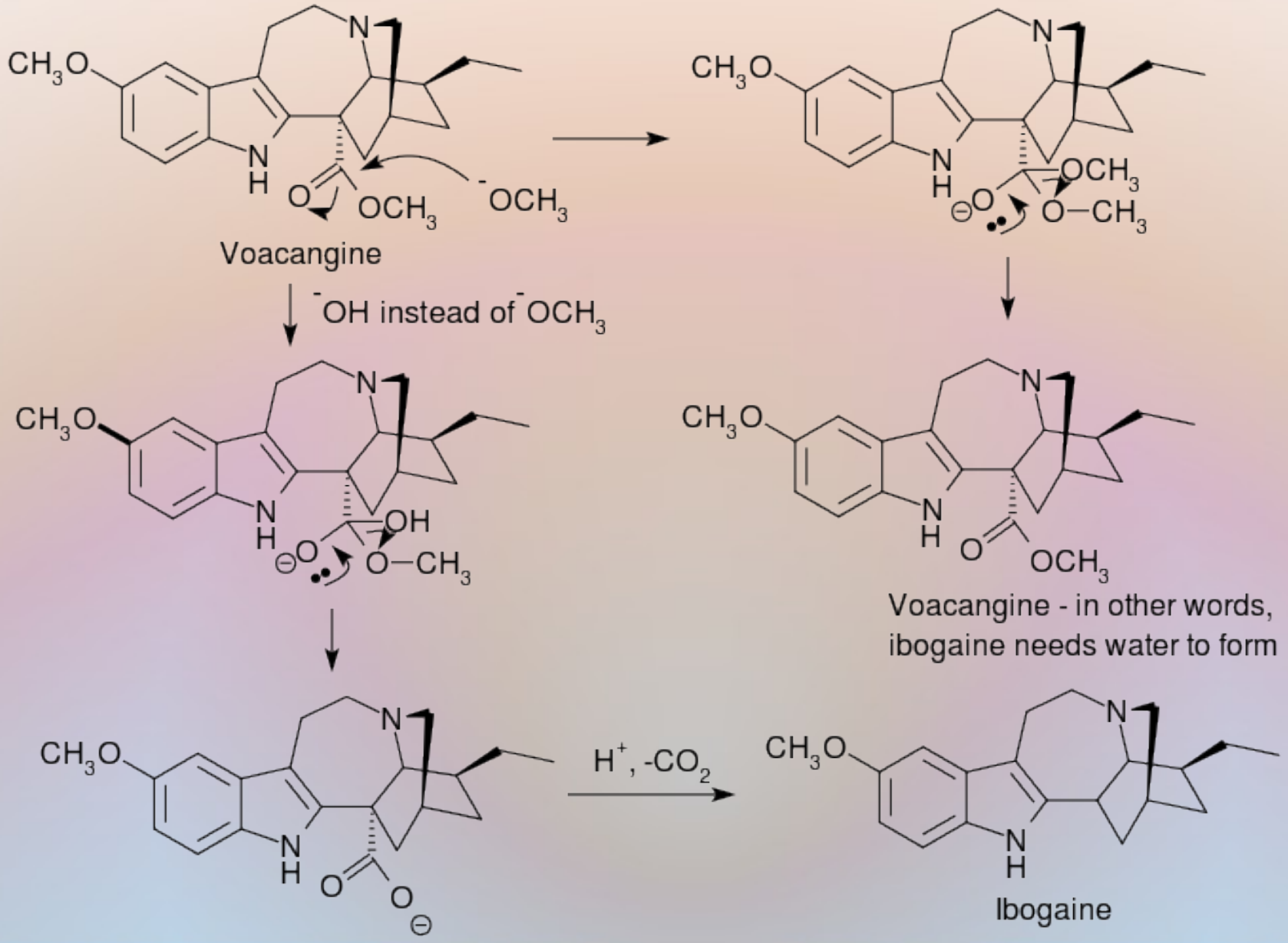
Filer and Dry to get 86% Voacangine (VRA)

Shows the Enrichment of PVTA to VRA

VRA is 86% Voacangine by NMR



Hydrolysis Requires Hydroxide



VRA Hydrolysis

Hydrolysis of voacangine by KOH in 50% refluxing isopropanol for 20 hours gives promising results.

Decarboxylation Results

Voacangine

Ibogaine

Another Promising Decarboxylation Method

From: Renner, U.; Prins, D. A. and Stoll, W. G. "[Alkaloids from *Conopharyngia durissima* Stapf. Isovoacangine, conopharyngine, conodurine, and conoduramine.]", *Helvetica Chimica Acta*, (1959), 42(5), 1572-1581 (German)

1. *Ibogain aus Voacangin.* – a) *Mit Hydrazinhydrat:* 7,36 g Voacangin, 40 ml abs. Äthanol und 40 ml Hydrazinhydrat wurden 48 Std. unter Rückfluss erhitzt. Die beim Abkühlen einsetzende Kristallisation wurde durch vorsichtige Zugabe von Wasser und Eiskühlung vervollständigt. Nach Absaugen 5,13 g Ibogain mit Smp. 144–146°. Nach Umkristallisieren aus Methanol war das Produkt rein; Smp. 149–151°.

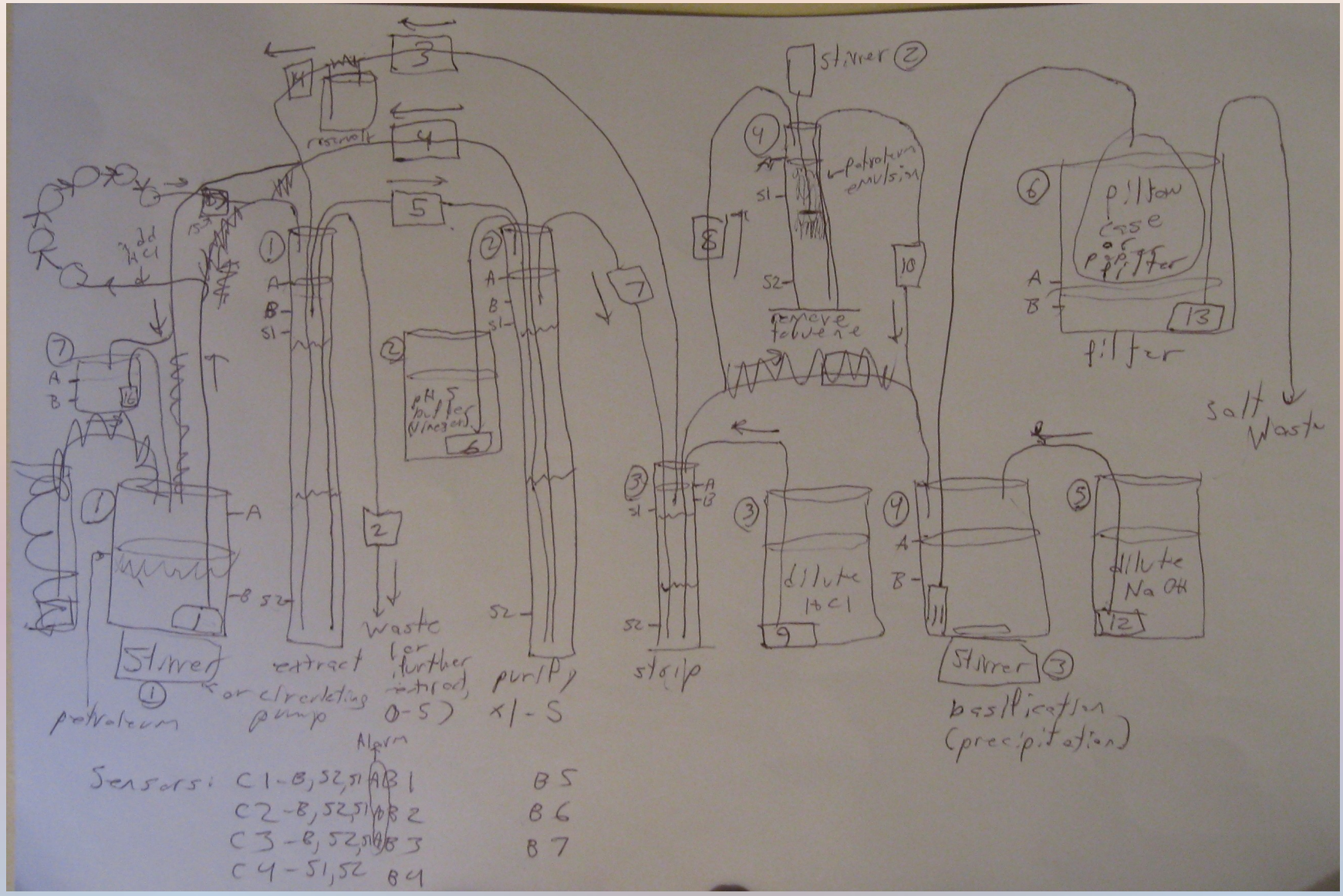
Translation:

Ibogaine from Voacangine - with hydrazine hydrate:

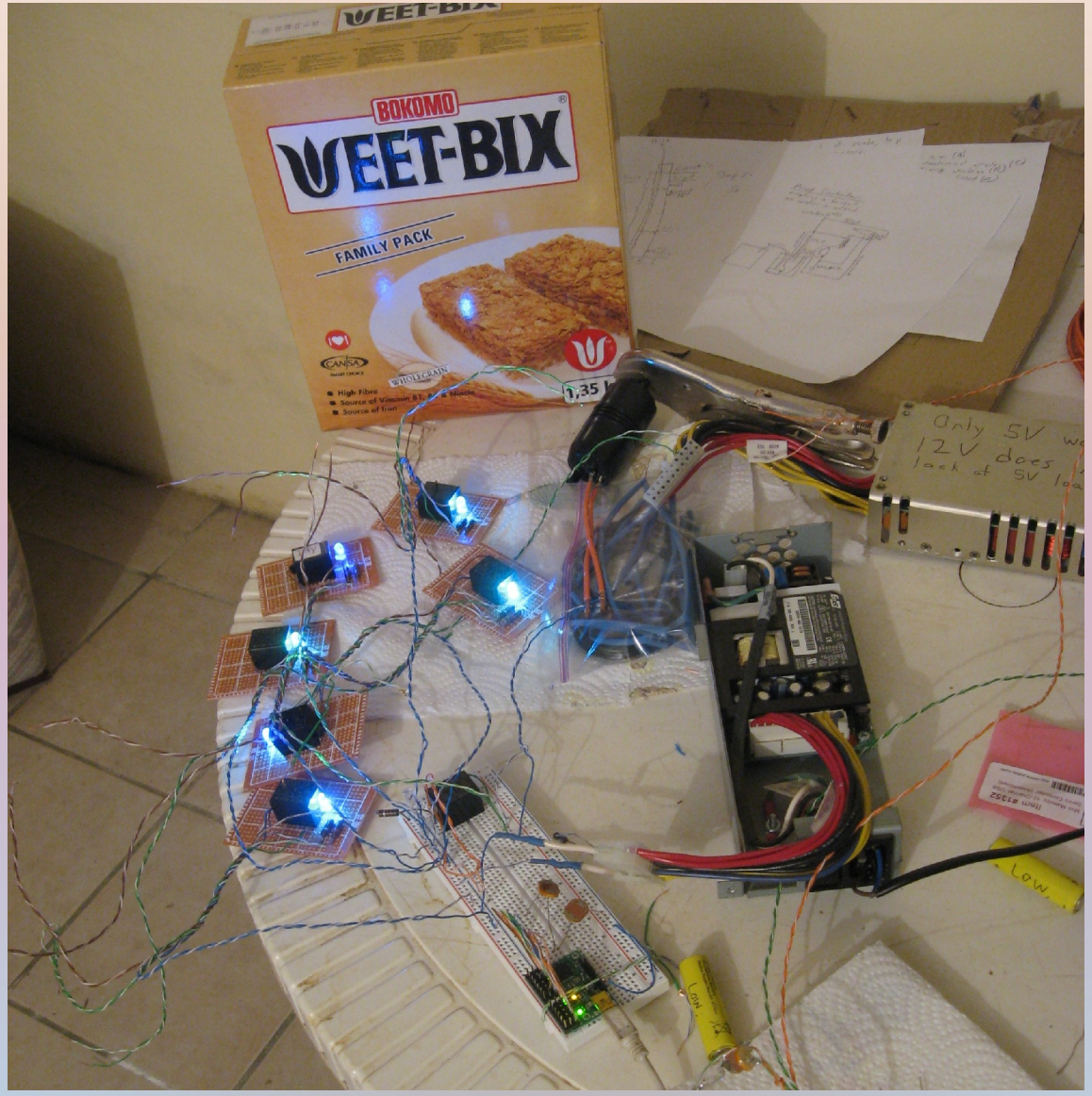
7.36 grams of Voacangine, 40 mL of absolute ethanol and 40 mL of hydrazine hydrate were heated under reflux for 48 hours. The onset of crystallization on cooling was completed by careful addition of water and ice-cooling. After aspirating, 5.13 g ibogaine was collected, mp 144-146. After recrystallization from methanol, the product was pure, mp 149-151.

Scaling Up...

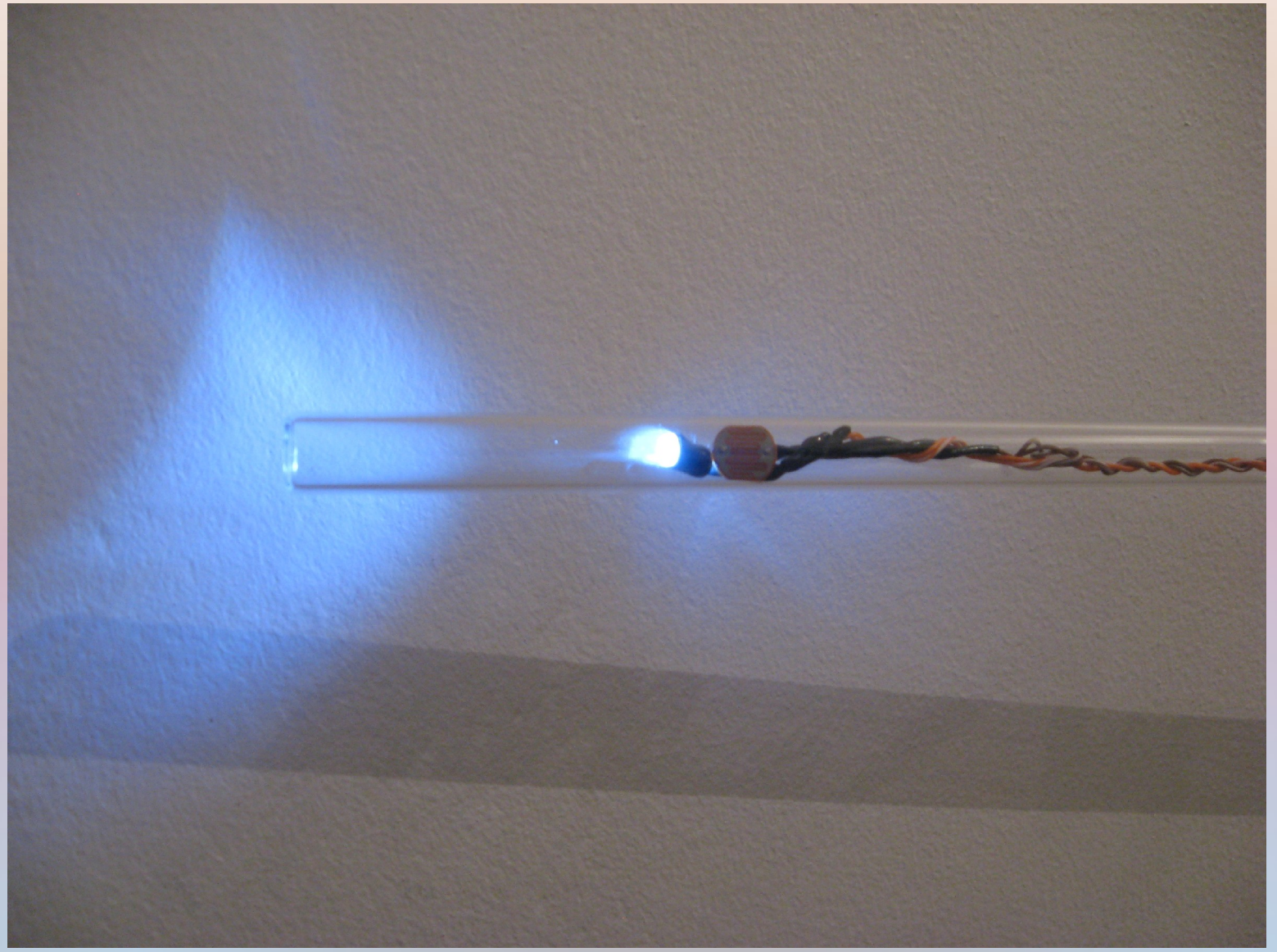
Very Complicated Factory Plan



Very Sophisticated Computerized Controllers



And Space-Age Sensors!



All Ready to Go!

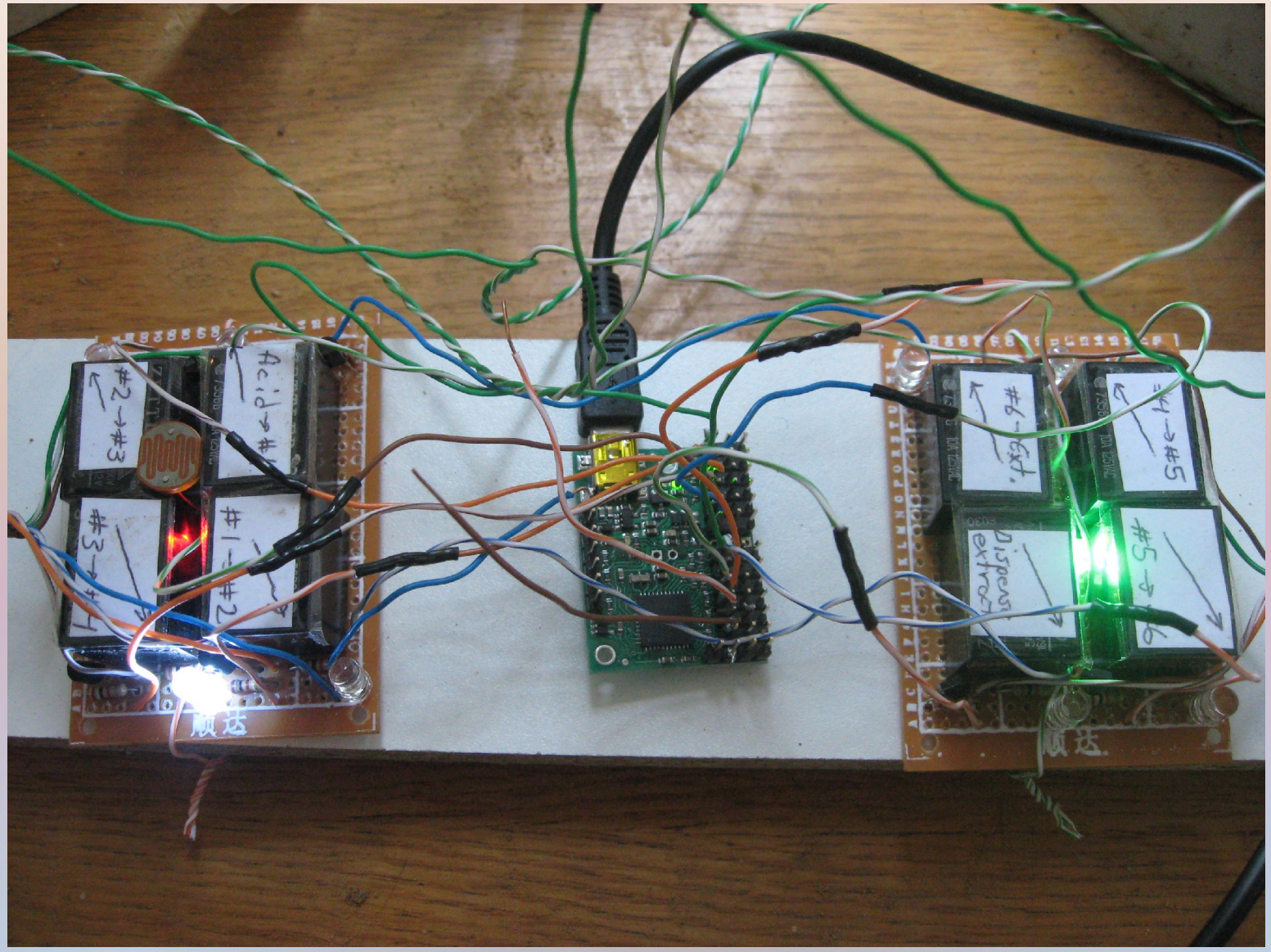
- After months of planning...
- After buying all anticipated equipment and chemicals...
- After remodeling a house into a laboratory...
- After arranging all our lives around this big event...
- All we need is the 50 kilograms of *Voacanga* bark in the other bag...

WHAT IS THIS?!
THIS BARK IS ROTTEN!!!

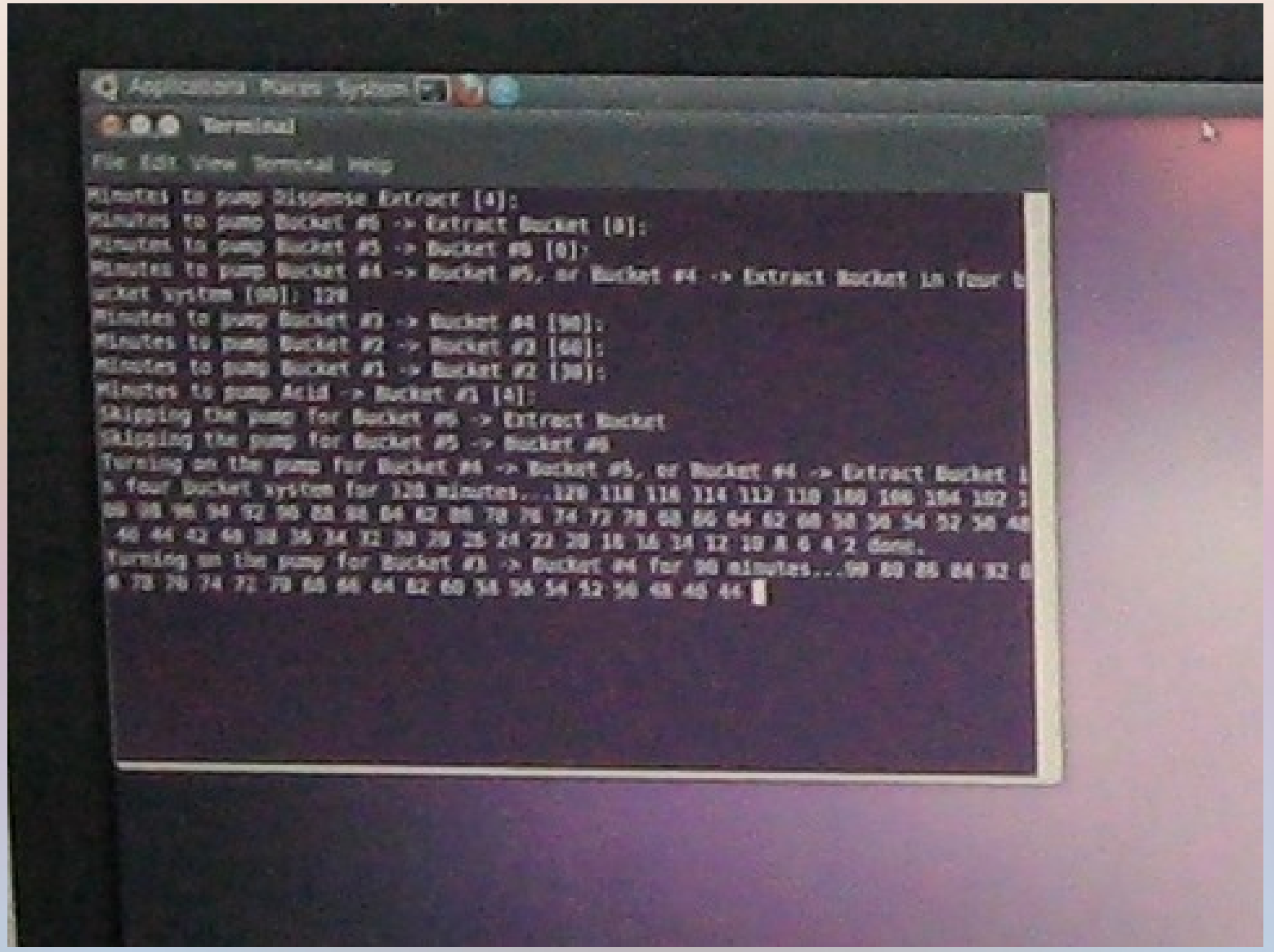
Still Good as Mulch...

So We Repurposed the Equipment to Extract *Iboga* Instead

A Robot Servo Controller Automates the Pumps

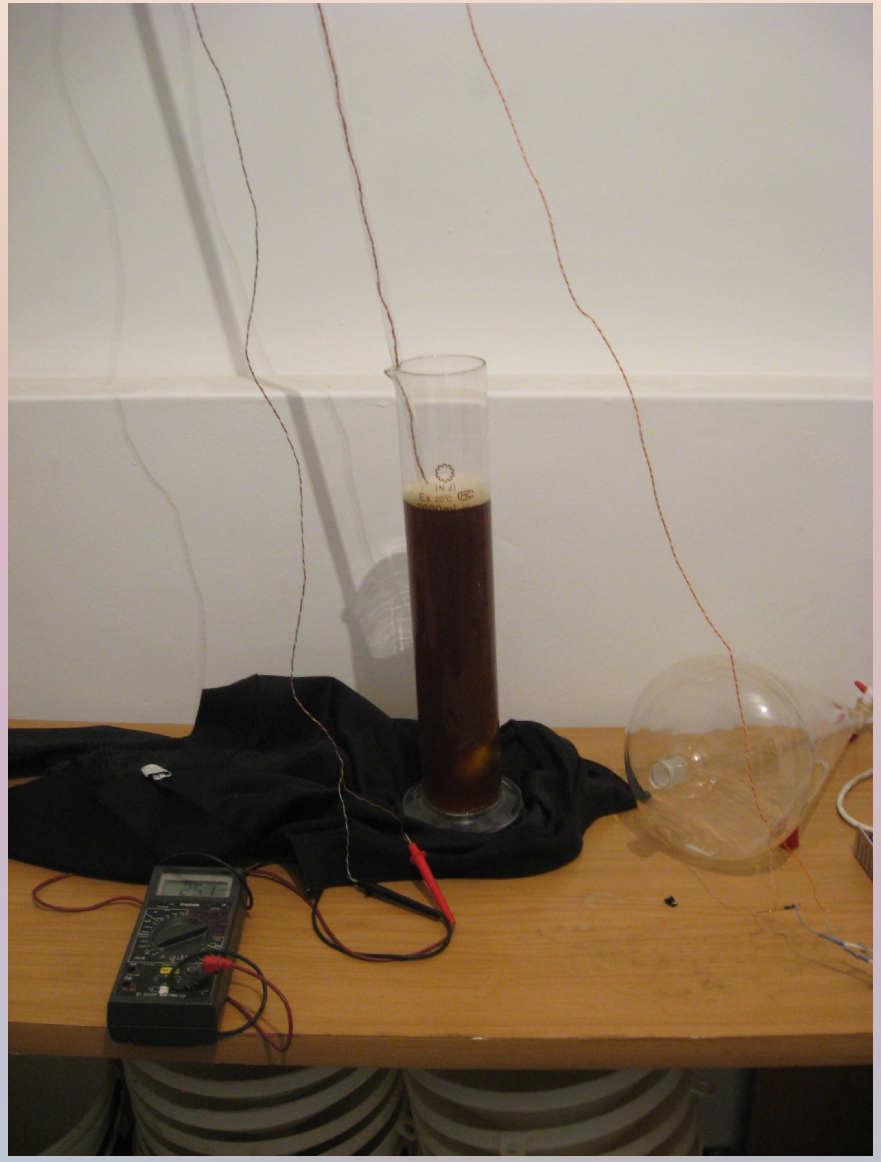


Using Custom Software



Though Grinding Root was Still Tedious

And I Tested What I Could



And Learned Some Strange Lessons

For Our *Voacanga* Factory Someday

Thank You for Your Attention

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