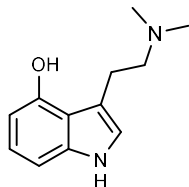
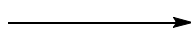
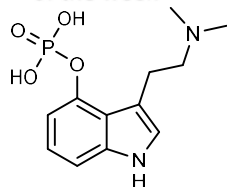


Psilocybin (Indocybin)



- 1957: Isolated from *Psilocybe Mexicana*
 - Hofmann ingested 2.4 g of the dried mushrooms to convince himself that the mushrooms were indeed active
- 1960-1966: marketed by Sandoz as Indocybin (2 mg tablets), proposed to be useful as a drug adjuvant to psychotherapy
- 1971: classified as a Schedule I drug
- Agonist of cortical serotonin 5-HT_{2A} (psilocin)
 - Half life (in healthy adults) ~3 h
- Psychedelic-induced alteration in brain connectivity is characterized by a synchronization of sensory functional networks and disintegration of associative networks
 - Disrupts normal organization and strong, topologically long-range functional connections emerge
- Has potential for treatment of OCD, addiction, major depressive disorder (MDD), depression in terminally ill cancer patients
 - Was given "breakthrough therapy" status by FDA for treatment-resistant depression and MDD

Table 2. Reported Effects of Psilocybin Ingestion

commonly reported effects of psilocybin ingestion	
physiologic effects	mild sedation with compulsive yawning; stimulation; physical euphoria; feelings of weightlessness; tactile enhancement; rhinorrhea; mydriasis; hypersalivation; increased systolic pressure; slight elevation in body temperature
visual effects	enhancement: color saturation; pattern recognition; visual acuity (at lower doses) distortions: flowing/breathing/melting of objects and colors; tracers; perspective distortion hallucinations: bright and colorful shapes and figures seen with eyes closed and with eyes open at higher doses
cognitive effects	increased empathy; simultaneous emotions; enhanced objective and situational analysis; music appreciation; ego loss; catharsis; rejuvenation; addiction suppression; time distortion
auditory effects	sound enhancement and distortion
multisensory effects	synesthesia
transpersonal effects	increased spirituality and a sense of interconnection between humanity and a higher power

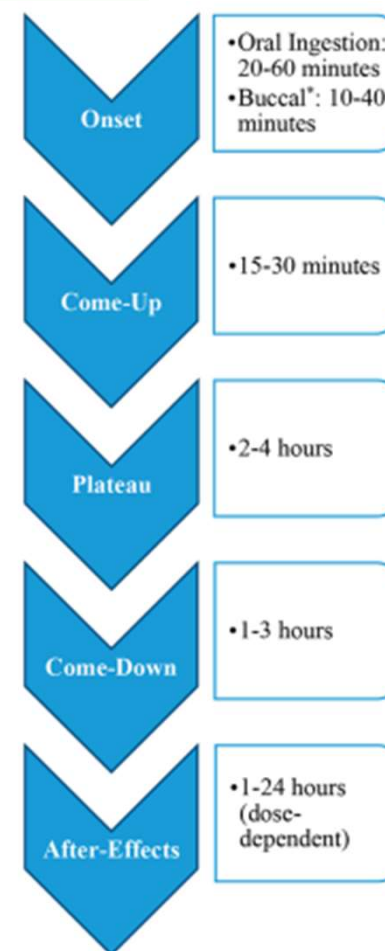
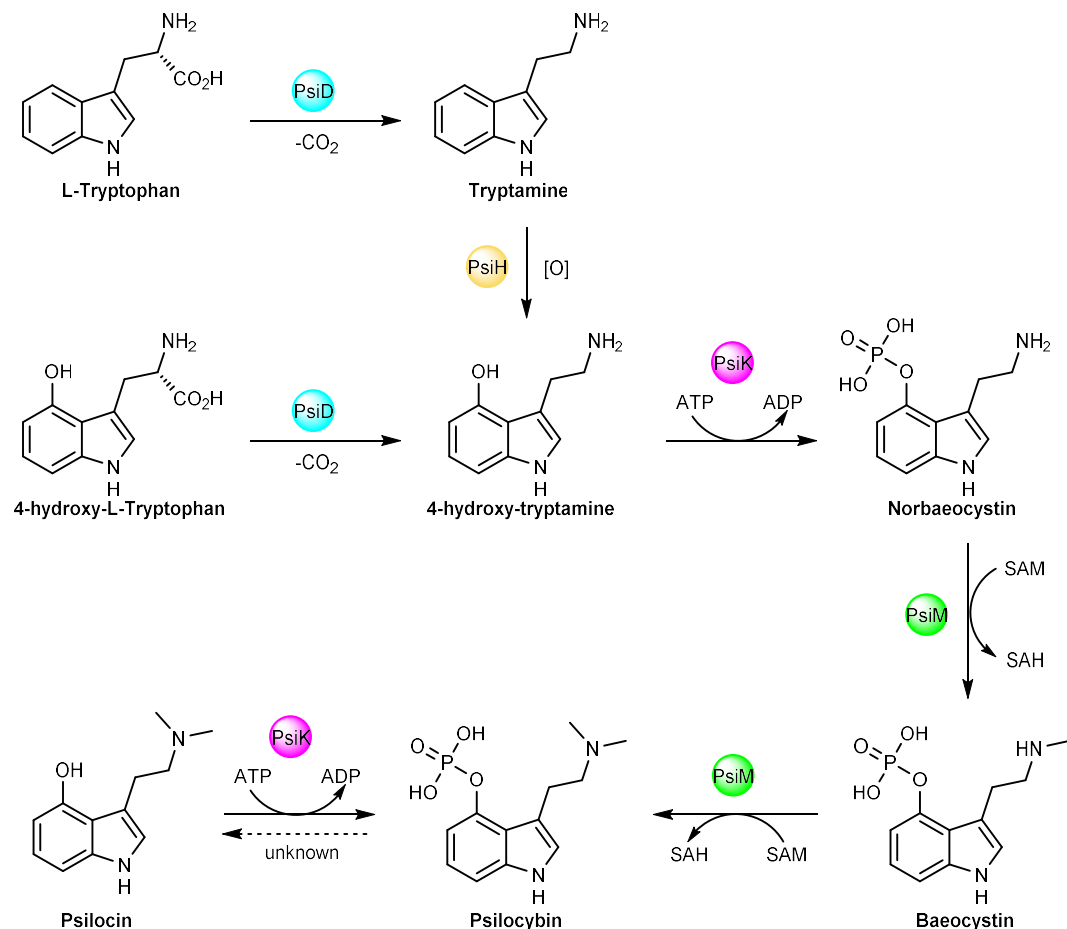


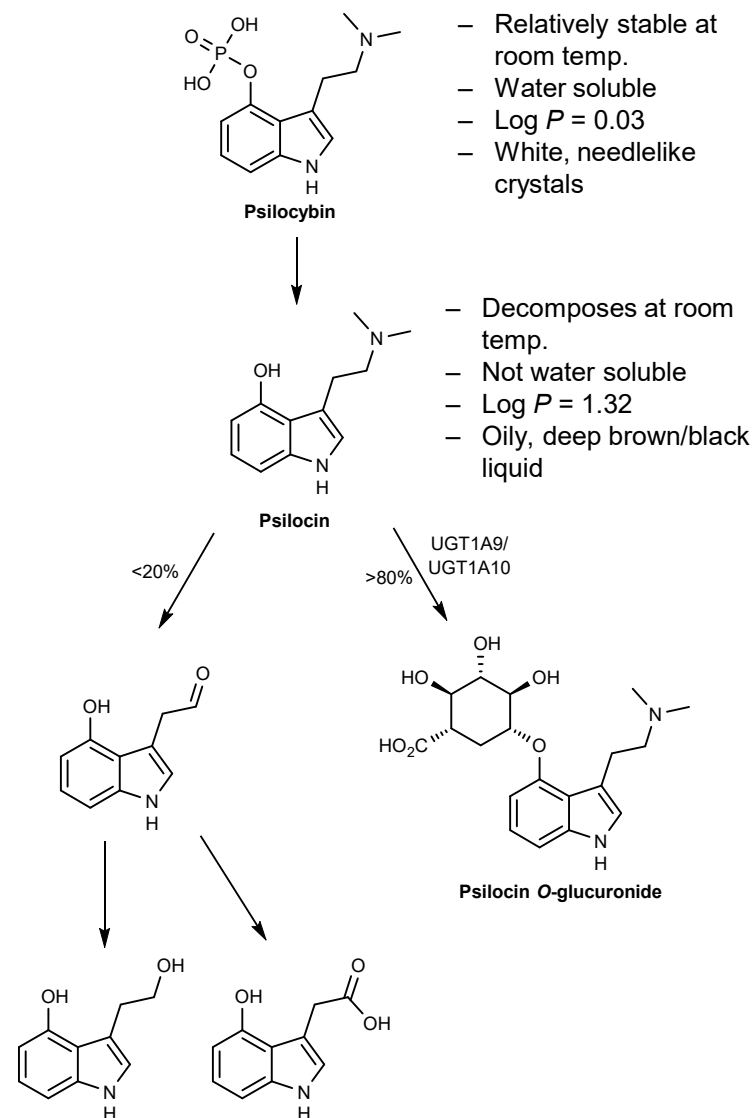
Figure 3. Stages of psilocybin ingestion and effects. *Dried psilocybin-containing mushrooms may be held as a "quid" between the cheek and gum for a potentially faster onset of action.

Biosynthesis:



- Hoffemeister identified a new class of fungal L-tryptophan decarboxylases and provided evidence that N,N,-demethylation is the final step
- Adams made from 4-hydroxyindole in *E. coli* with a fed-batch bioreactor at 1.16 g/L
 - First reported case of *in vivo* psilocybin production with prokaryotic host

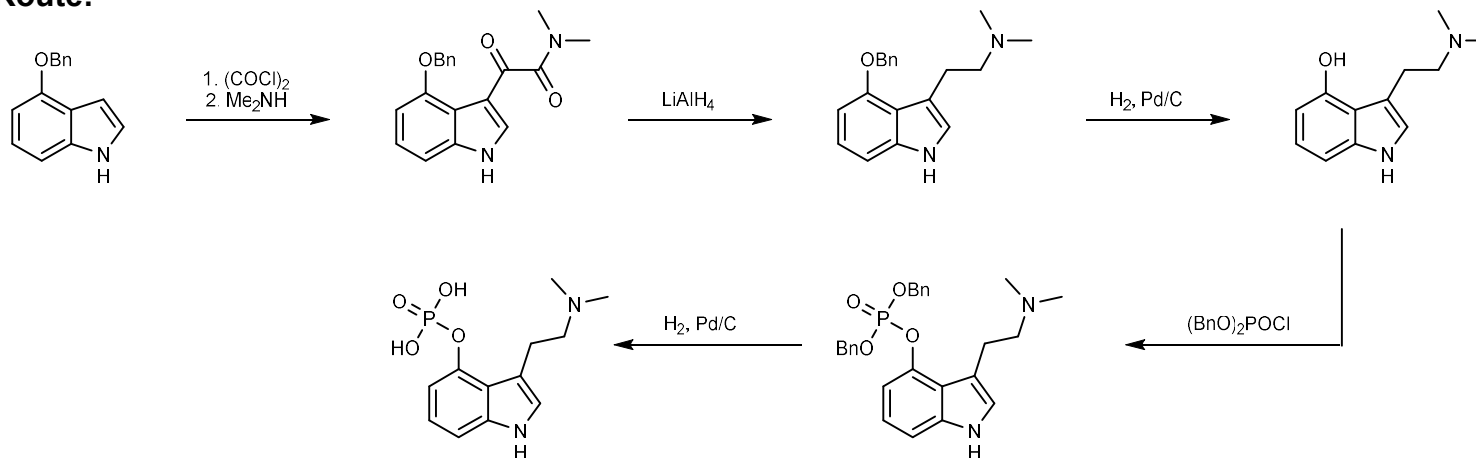
Metabolism:



- Relatively stable at room temp.
- Water soluble
- Log *P* = 0.03
- White, needlelike crystals

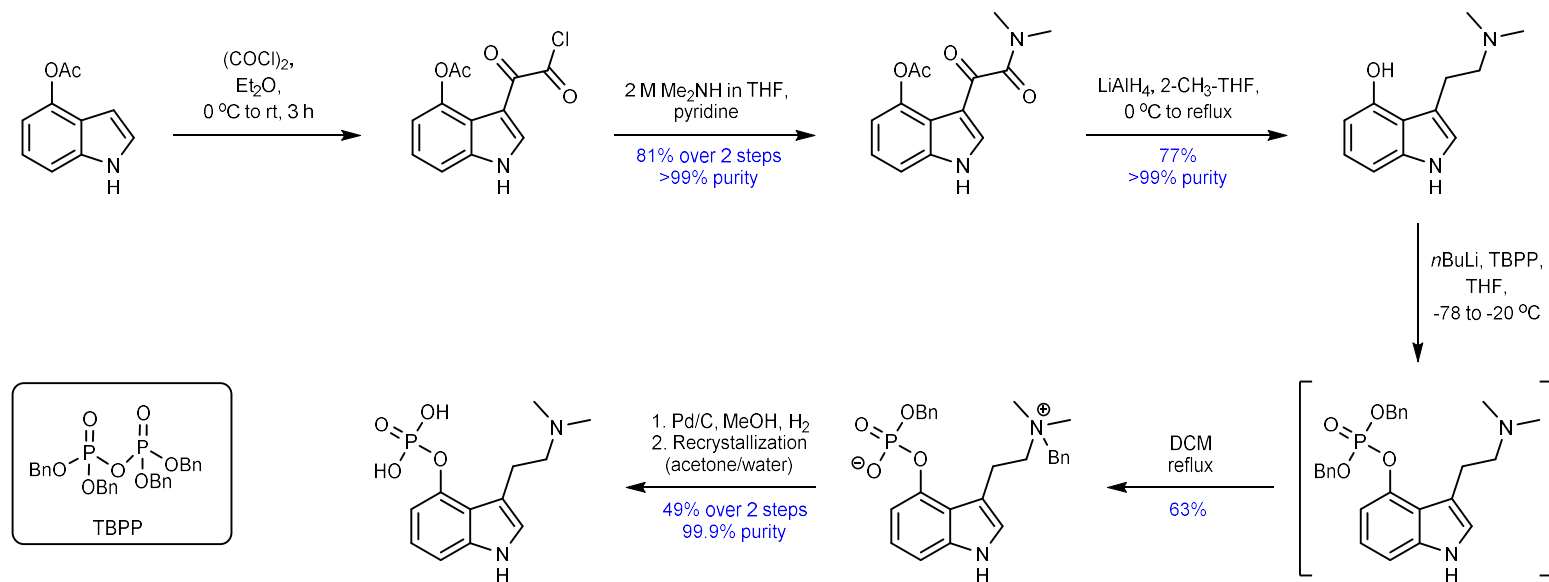
- Decomposes at room temp.
- Not water soluble
- Log *P* = 1.32
- Oily, deep brown/black liquid

Original Route:



Hofmann, A. *Experientia* **1958**, *14*, 397. <https://doi.org/10.1007/BF02160424>

Updated Route:



Kargbo, R. B. *Synthesis* **2020**, *52*, 688. DOI: 10.1055/s-0039-1691565