

UC Berkeley

Berkeley Scientific Journal

Title

The Shulgin Legacy: A Profile of 2C-X Psychedelics

Permalink

<https://escholarship.org/uc/item/75q1b2z6>

Journal

Berkeley Scientific Journal, 30(1)

ISSN

1097-0967

Author

Schaupeter, Luke

Publication Date

2026-10-30

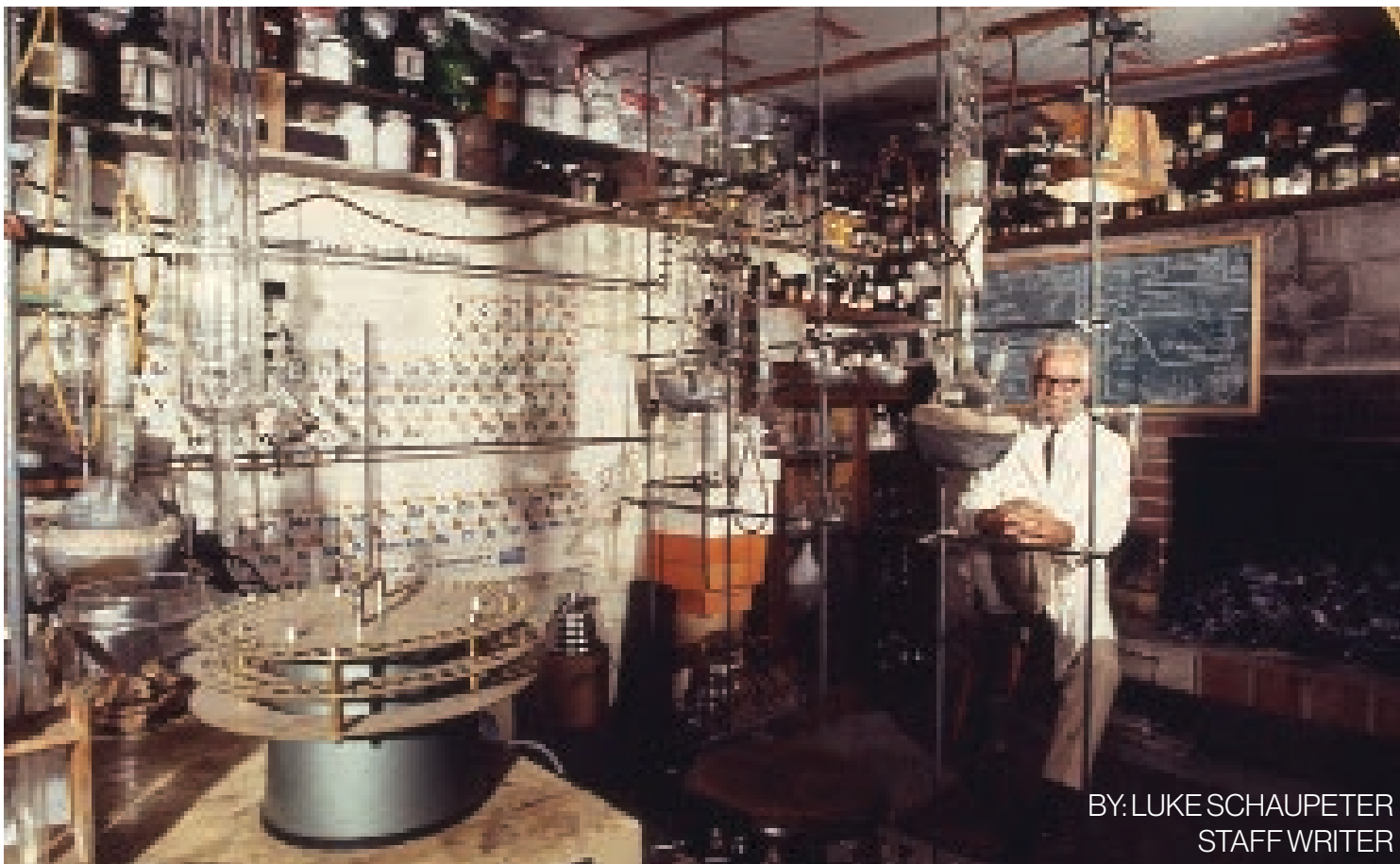
DOI

10.5070/BS3.69971

Copyright Information

This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at <https://creativecommons.org/licenses/by-nc-nd/4.0/>

The Shulgin Legacy: A Profile of 2C-X Psychedelics



BY: LUKE SCHAUPETER
STAFF WRITER

THE FARM

Alexander and Ann Shulgin's farm lies just over the Berkeley Hills in Lafayette, California. The former almond orchard is home to serene views and a clandestine chemistry laboratory. Here, Alexander Shulgin would conduct groundbreaking work in psychedelic research, spanning the 1960s to the late 1990s. Shulgin received his Ph.D. in Biochemistry from UC Berkeley, where he later returned to teach occasional toxicology courses, often delving into relevant tangents like the War on Drugs.^{1,2} Shulgin's work as a pharmacologic researcher and professor cultivated his curiosity of psychedelics that was infectious to those he interacted with.

Shulgin is still renowned for his outstanding work in pharmacologic chemistry. Much of his work revolved around phenethylamines, a chemical family that shares similar structures and

has widely varying applications from stimulants to psychedelics. A compilation of his work, "Phenethylamines I Have Known and Loved" (PiHKAL), details over two hundred phenethylamines from synthesis to subjective effects. This compendium was published in reaction to a series of sting operations performed by the U.S. Drug Enforcement Agency (DEA), which left Shulgin's peers with their life's work destroyed and at the mercy of the judicial system under the Nixon Administration.²

The Controlled Substances Act (CSA) of 1970 created the legal precedent for these raids and led to the establishment of the DEA in 1973.³ The CSA contained five schedules used to categorize substances based on their potential for abuse weighed against their medical application. Schedule I substances are those with no accepted medical use and a high potential for abuse.^{4,5} Immediately following

the CSA, access to these substances was heavily restricted. The act of scheduling substances is often politicized, and many of the psychedelics Shulgin would work with were placed in Schedule I without proper analysis.⁵ While Shulgin and a few colleagues successfully obtained their licensure to continue working, the field of psychedelics research had stalled.^{2,5} An era of discovery had suddenly ended, and the DEA was quickly encroaching on the few prolific pharmacologists still active.

In 1993, just two years after the publication of PiHKAL, the DEA revoked Shulgin's Schedule I clearance and descended on the farm. The sequestration of his lab only reaffirmed Shulgin's determination. In 1997, Alexander and Ann Shulgin would publish a sequel to PiHKAL, detailing a chemical family called tryptamines in the same excruciating detail as PiHKAL.² A vocal critic of these anti-drug

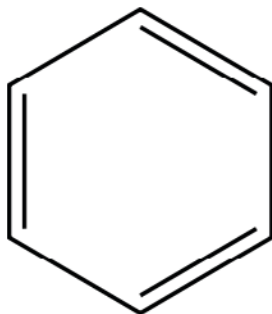


Fig. 1 Phenyl ring. This ring is composed of six carbons, one at each vertex. Alternating double bonds are represented by the three internal lines. By itself, this is a benzene ring, but when bonded or connected to an atom or molecule, this is referred to as a phenyl ring or phenyl functional group.

policies that bolstered the prison-industrial complex, reaffirmed structural racism, and crippled pharmacological research, Shulgin challenged the social perceptions surrounding his work — speculating about the War on Drugs in following toxicology lectures at Berkeley.^{1,3,5} His legacy exists not only in the attitude of active inquiry he cultivated within his students, but also within psychedelic research past and present.

PHENETHYLAMINES

The identity of psychedelics has been long debated. Shulgin describes them as “consciousness-changing chemical compounds,” while others choose the more literal translation “mind-manifesting,” first coined by Humphry Osmond, the creator of the term psychedelic.¹ The term ‘psychedelic’ describes a range of psychoactive compounds. They can differ greatly in form and function. One way to differentiate the thousands of known psychedelics is through structure. A phenethylamine contains two essential components: a phenyl ring (fig. 1) and an ethylamine (fig. 2).¹ Phenyl rings consist of six carbons arranged in a circle with alternating double bonds. An ethylamine describes two carbon atoms attached in line with a nitrogen. This core phenethylamine (fig. 3) structure is endogenous to the human brain, where it acts as a neurotransmitter.¹

Slight modifications of this structure create analogous phenethylamines which affect humans in various ways. For example, the substitution of a methyl group onto the side chain creates amphetamine (fig. 4), a potent central nervous system

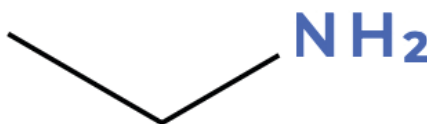


Fig. 2 Ethylamine. The left half is composed of two carbons, one at each vertex, which form an ethyl group. The right has a nitrogen which, when bonded to one carbon, is called a primary amine group.

(CNS) stimulant.¹ Amphetamines are one of the most commonly prescribed treatments for ADHD.⁶ Alternatively, adding three methoxy groups, which contain an oxygen attached to a methyl group, creates the hallucinogen mescaline (fig. 5).¹ Archaeologists posit that for over six thousand years, this psychedelic has been of great cultural significance to groups inhabiting the Americas.⁷

Though their history is not as storied as mescaline, nor medical precedence as well known as amphetamine, Shulgin was fascinated by the 2C-X family of compounds. He featured over twenty in PiHKAL, where he notes effects from aphrodisiac to empathogen which are substances that encourage empathy in the user. 2C phenethylamines (fig. 6) share the core phenethylamine structure, save for one key difference. What separates a 2C molecule from any other phenethylamine are the two methoxy groups that sit opposite each other on the phenyl ring.^{1,8}

2C-X

The 2C family of psychedelics primarily act on serotonin 5-HT₂ receptors in the brain, which are a popular target for many commonly known psychedelics like psilocybin, mescaline, and LSD.^{7,8,9} These receptors play roles in mood, memory, and cognition. They are distributed throughout the brain and can display biased agonism, meaning that the various applications of these receptors may be determined by their location in the brain.⁹ As previously mentioned, small changes in the structures of these molecules, for example, the substitution of one atom, can cause wildly varying effects. The idiosyncrasies of 2C molecules determine whether their action is as an agonist — stimulating the receptor — or an antagonist, blocking receptor

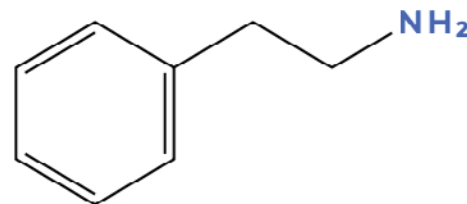


Fig. 3 Phenethylamine. This molecule is formed from the combination of a phenyl ring (left) and an ethylamine (right).

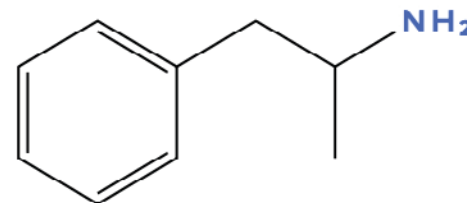


Fig. 4 Amphetamine. This compound is structurally identical to the phenethylamine molecule, save for the substitution of a methyl group on the side chain.

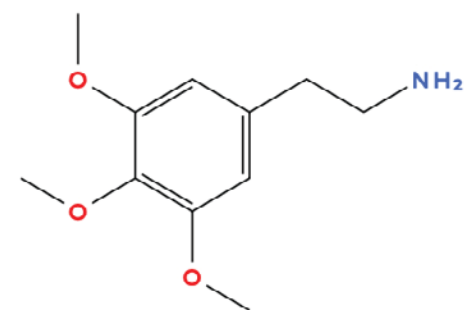


Fig. 5 Mescaline. This molecule shares the same base structure of phenethylamine with the substitution of three methoxy groups on the phenyl ring.

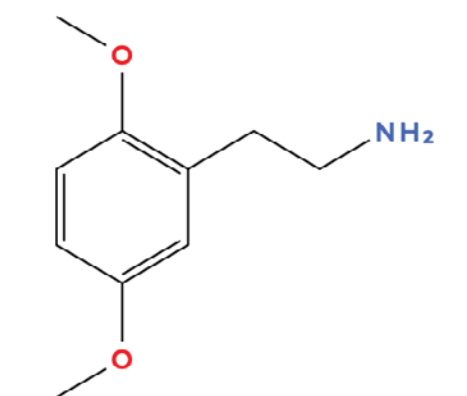


Fig. 6 2C-H (2,5-Dimethoxyphenethylamine). This molecule forms the base structure of all 2C-X compounds. It is analogous to both phenethylamine and mescaline.

activity. They act within the central nervous system and induce intense visual, auditory, and tactile sensations.^{1,8,9}

What differentiated The Shulgin Lab's work from any of the other chemists who had previously synthesized these compounds was their primary assessment of the drugs' subjective effects. With each new molecule, Alexander Shulgin would estimate a safe dosage using structural analogs, which he would ingest while recording diligent notes on their subjective effects. If he thought the compound to be interesting, he would present it to a group of researchers and his wife Ann to consume and document.^{1,2} Their respective knowledge base would build a more robust picture of the subjective effects of nearly all psychoactive 2C compounds. Their reporting was later validated by studies that would show definitively 5HT₂ receptor agonists possess antipsychotic and antidepressant properties, while 5HT₂ agonists are implicated in cognition and hallucination.⁹

2C-B

When asked in his final interview to choose a favorite from the hundreds of novel compounds Shulgin had synthesized and ingested, he answered 2C-B without hesitation.¹⁰ Alexander, Ann, and his testing colleagues authored hundreds of notes on their experiences with 2C-B. Their experiences were, in a somatosensorial sense, rich. Following consumption of 2C-B, Shulgin's team felt every nerve in their body, became completely enveloped in music, and experienced radiating energy emerging from paintings. Shulgin's favorite aspect of 2C-B was its amorous nature. He asserts that, "If there is anything ever found to be an effective aphrodisiac, it will probably be patterned after 2C-B in structure."¹

Shulgin notes that 2C-B has a steep dose-response curve, meaning that its subjective effects scale exponentially as

more is taken.¹ It is one of the shortest-acting of any psychedelic drug, which, in Shulgin's words, keeps the user near "familiar territory".^{1,8} Popular in his testing communities was the combination of MDMA and 2C-B. Reports of 2C-B taken just after the effects of MDMA have become sub-perceptible, suggesting that the undesirable effects of an MDMA crash — depression, apathy, and mental fog — are significantly less noticeable.¹ Synergy between MDMA, an empathogen, and 2C-B, a hallucinogen, raises questions for the clinical application of these substances.

PSYCHEDELIC APPLICATIONS

The attitude surrounding mental health disorders in America largely focuses on the correction of chemical imbalances within the brain. This is the case for common depression, anxiety, and PTSD prescription medications like selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors. Psychedelics challenge this treatment philosophy. Current research suggests that psychedelics in clinical contexts might promote neuroplasticity, or changes within the structure of the brain.^{11,12} Essentially, instead of supplementing a lack or overabundance of some neurotransmitter with psychedelics, the brain learns how to adapt to its environment. Though the possibility of psychedelic therapies has only recently come back into the mainstream, our current state of knowledge is absolutely encouraging. Reappraisal of antiquated Nixon-era policies related to research, scheduling, and sentencing is essential for advancing evidence-based research on the therapeutic potential of psychedelics.⁵

This year marks Alexander Shulgin's 100th birthday. The research he and Ann performed did not exist in a vacuum — their pharmacological discoveries composed one small part of a research vanguard that was unjustly sidelined as a consequence of the War on

Drugs. The 2C compounds represent just one chapter in the book of psychedelics, where an entire class of drugs known to have therapeutic potential were written off. Their recent reappraisal is backed by legions of academics and advocates like Shulgin. What was once a fringe movement, carried out quietly beneath the rolling hills of an almond farm just outside of Berkeley, is now a worldwide campaign that carries incredible promise for improved healthcare outcomes.

ACKNOWLEDGEMENTS

A sincere thank you to Makenzie Wilkinson, Ph.D. candidate in the Helen Wills Neuroscience Institute at U.C. Berkeley. Your thoughtful feedback, review, and guidance were invaluable in creating this article. Additionally, gratitude to BSJ features editors Norah Hom and Sania Moghe; your direction has been incredibly helpful.

REFERENCES

1. Shulgin, A., & Shulgin, A. (1991). PiHKAL: A chemical love story. Transform Press.
2. Bennett, D. (2005, January 30). Dr. Ecstasy. The New York Times. <https://www.nytimes.com/2005/01/30/magazine/dr-ecstasy.html>
3. Mass Incarceration Trends. (2024, May 21). The Sentencing Project. <https://www.sentencingproject.org/reports/mass-incarceration-trends/>
4. Drug Scheduling. (n.d.). Retrieved November 15, 2025, from <https://www.dea.gov/drug-information/drug-scheduling>
5. Henningfield, J. E., Coe, M. A., Griffiths, R. R., Belouin, S. J., Berger, A., Coker, A. R., Comer, S. D., Heal, D. J., Hendricks, P. S., Nichols, C. D., Sapienza, F., Vocci, F. J., & Zia, F. Z. (2022). Psychedelic drug abuse potential assessment research for new drug applications and Controlled Substances Act scheduling. *Neuropharmacology*, 218, 109220. <https://doi.org/10.1016/j.neuropharm.2022.109220>
6. Connolly, J., Glessner, J., Elia, J., & Hakonarson, H. (2015). ADHD & Pharmacotherapy: Past, Present and Future. *Therapeutic Innovation & Regulatory Science*, 49(5), 632–642. <https://doi.org/10.1007/s12220-015-9642-2>

The 2C compounds represent just one chapter in the book of psychedelics, where an entire class of drugs known to have therapeutic potential were written off.

- org/10.1177/2168479015599811
7. Cassels, B. K., & Sáez-Briones, P. (2018). Dark Classics in Chemical Neuroscience: Mescaline. *ACS Chemical Neuroscience*, 9(10), 2448–2458. <https://doi.org/10.1021/acscchemneuro.8b00215>
 8. Dean, B. V., Stellpflug, S. J., Burnett, A. M., & Engebretsen, K. M. (2013). 2C or Not 2C: Phenethylamine Designer Drug Review. *Journal of Medical Toxicology*, 9(2), 172–178. <https://doi.org/10.1007/s13181-013-0295-x>
 9. Zhang, G., & Stackman, R. W. (2015). The role of serotonin 5-HT_{2A} receptors in memory and cognition. *Frontiers in Pharmacology*, 6, 225. <https://doi.org/10.3389/fphar.2015.00225>
 10. Morris, H., & Smith, A. (2013, May 16). The Last Interview With Alexander Shulgin. *VICE*. <https://www.vice.com/en/article/the-last-interview-with-alexander-shulgin/>
 11. Wallach, J., Cao, A. B., Calkins, M. M., Heim, A. J., Lanham, J. K., Bonniwell, E. M., Hennessey, J. J., Bock, H. A., Anderson, E. I., Sherwood, A. M., Morris, H., de Klein, R., Klein, A. K., Cuccurazzu, B., Gamrat, J., Fannana, T., Zauhar, R., Halberstadt, A. L., & McCorvy, J. D. (2023). Identification of 5-HT_{2A} receptor signaling pathways associated with psychedelic potential. *Nature Communications*, 14(1), 8221. <https://doi.org/10.1038/s41467-023-44016-1>
 12. Nardou, R., Sawyer, E., Song, Y. J., Wilkinson, M., Padovan-Hernandez, Y., De Deus, J. L., Wright, N., Lama, C., Faltin, S., Goff, L. A., Stein-O'Brien, G. L., & Dölen, G. (2023). Psychedelics reopen the social reward learning critical period. *Nature*, 618(7966), 790–798. <https://doi.org/10.1038/s41586-023-06204-3>
- Information (2025). PubChem Compound Summary for CID 241, Benzene. Retrieved November 18, 2025 from <https://pubchem.ncbi.nlm.nih.gov/compound/Benzene>.
3. National Center for Biotechnology Information (2025). PubChem Compound Summary for CID 6341, Ethylamine. Retrieved November 18, 2025 from <https://pubchem.ncbi.nlm.nih.gov/compound/Ethylamine>.
 4. National Center for Biotechnology Information (2025). PubChem Compound Summary for CID 1001, Phenethylamine. Retrieved November 18, 2025 from <https://pubchem.ncbi.nlm.nih.gov/compound/Phenethylamine>.
 5. National Center for Biotechnology Information (2025). PubChem Compound Summary for CID 3007, Amphetamine. Retrieved November 18, 2025 from <https://pubchem.ncbi.nlm.nih.gov/compound/Amphetamine>.
 6. National Center for Biotechnology Information (2025). PubChem Compound Summary for CID 4076, Mescaline. Retrieved November 18, 2025 from <https://pubchem.ncbi.nlm.nih.gov/compound/Mescaline>.
 7. National Center for Biotechnology Information (2025). PubChem Compound Summary for CID 76632, 2,5-Dimethoxyphenethylamine. Retrieved November 18, 2025 from https://pubchem.ncbi.nlm.nih.gov/compound/2_5-Dimethoxyphenethylamine.

IMAGE REFERENCES

1. Shulgin Foundation. (n.d.). [Photograph of Shulgin in his laboratory]. In *The Farm: Photo Gallery*. Retrieved from <https://shulginfoundation.org/the-farm/photo-gallery/>
2. National Center for Biotechnology