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Buspar dosing guide

Medication used to treat anxiety disorders Not to be confused with Bupropion or Buprenorphine. Pharmaceutical compound BuspironeClinical dataPronunciation/ˈbjuːspɪroʊn/ (BEW-spi-rohn) Trade namesBuspar, othersOther namesMJ 9022-1[1]AHFS/Drugs.comMonographMedlinePlusa688005License data US DailyMed: Buspirone Pregnancycategory AU: B1[2] Routes ofadministrationBy mouthATC codeN05BE01 (WHO) Legal statusLegal status AU: S4 (Prescription only)[3][4] BR: Class C1 (Other controlled substances)[5] CA: ℞-only UK: POM (Prescription only) US: ℞-only Pharmacokinetic dataBioavailability3.9%[6]Protein binding86–95%[7]MetabolismLiver (via CYP3A4)[11][12]Metabolites5-OH-Buspirone; 6-OH-Buspirone; 8-OH-Buspirone; 1-PPTooltip 1-(2-pyrimidinyl)piperazine[8][9][10]Elimination half-life2.5 hours[11]ExcretionUrine: 29–63%[7]Feces: 18–38%[7]Identifiers IUPAC name 8-{4-[4-(Pyrimidin-2-yl)piperazin-1-yl]butyl}-8-azaspiro[4.5]decane-7,9-dione CAS Number36505-84-7 Yas HCl: 33386-08-2PubChem CID2477IUPHAR/BPS36DrugBankDB00490 YChemSpider2383 YUNIITK65WKS8HLKEGGD07593 YChEBICHEBI:3223 YChEMBLChEMBL49 YCompTox Dashboard (EPA)DTXSID2022707 ECHA InfoCard100.048.232 Chemical and physical dataFormula$C_{21}H_{31}N_5O_2$Molar mass385.512 g·mol^{-1}3D model (JSmol)Interactive image SMILES O=C1CC2(CCCC2)CC(=O)N1CCCCN1CCN(c2ncccn2)CC1 InChI InChI=1S/C21H31N5O2/c27-18-16-21(6-1-2-7-21)17-19(28)26(18)11-4-3-10-24-12-14-25(15-13-24)20-22-8-5-9-23-20/h5,8-9H,1-4,6-7,10-17H2 YKey:QWCRAEMEVRGPNT-UHFFFAOYSA-N Y (verify) Buspirone, sold under the brand name Buspar among others, is an anxiolytic, a medication primarily used to treat anxiety disorders, particularly generalized anxiety disorder (GAD).[13][14] It is a serotonin 5-HT1A receptor partial agonist, increasing action at serotonin receptors in the brain.[6] It is taken orally and takes two to six weeks to be fully effective.[13][14] Common side effects of buspirone include nausea, headaches, dizziness, and difficulty concentrating.[13][15] Serious side effects may include movement disorders, serotonin syndrome, and seizures.[15] Its use in pregnancy appears to be safe but has not been well studied, and use during breastfeeding has not been well studied either.[15][16] Buspirone was developed in 1968 and approved for medical use in the United States in 1986.[13][14] It is available as a generic medication.[15] In 2022, it was the 54th most commonly prescribed medication in the United States, with more than 12 million prescriptions.[17][18] Buspirone is used for the short-term and long-term treatment of anxiety disorders or symptoms of anxiety.[19][20][21][22][23] It is generally preferred over benzodiazepines because it does not activate the receptors that make drugs like alprazolam addictive.[14] Buspirone has no immediate anxiolytic effects, and hence has a delayed onset of action; its full clinical effectiveness may require 2–4 weeks to manifest itself.[24] The drug is similarly effective in the treatment of generalized anxiety disorder (GAD) to benzodiazepines including diazepam, alprazolam, lorazepam, and clorazepate.[6] Buspirone is not known to be effective in the treatment of other anxiety disorders besides GAD.[25] There is some evidence that buspirone on its own may be useful in the treatment of hypoactive sexual desire disorder (HSDD) in women.[26] Buspirone may also be effective in treating antidepressant-induced sexual dysfunction.[14][27][28] Buspirone is not effective as a treatment for benzodiazepine withdrawal, barbiturate withdrawal, or alcohol withdrawal.[29] SSRI and SNRI antidepressants such as paroxetine and venlafaxine, respectively, may cause jaw pain/jaw spasm reversible syndrome, although it is not common, and buspirone appears to be successful in treating antidepressant-induced bruxism.[30][31] Buspirone has these contraindications:[32][33] Hypersensitivity to buspirone Metabolic acidosis, as in diabetes Should not be used with MAO inhibitors Severely compromised liver and/or kidney function Main article: List of side effects of buspirone Known side effects associated with buspirone include dizziness, headaches, nausea, tinnitus, and paresthesia.[6] Buspirone is relatively well tolerated and is not associated with sedation, cognitive and psychomotor impairment, muscle relaxation, physical dependence, or anticonvulsant effects.[6] In addition, buspirone does not produce euphoria[24] and is not a drug of abuse.[20] Buspirone appears to be relatively benign in cases of single-drug overdose, although no definitive data on this subject appear to be available.[34] In one clinical trial, buspirone was administered to healthy male volunteers at a dosage of 375 mg/day, and produced side effects including nausea, vomiting, dizziness, drowsiness, miosis, and gastric distress.[19][20][22] In early clinical trials, buspirone was given at dosages even as high as 2,400 mg/day, with akathisia, tremor, and muscle rigidity observed.[35] Deliberate overdoses with 250 mg and up to 300 mg buspirone have resulted in drowsiness in about 50% of individuals.[35] One death has been reported in a co-ingestion of 450 mg buspirone with alprazolam, diltiazem, alcohol, and cocaine.[35] Buspirone has been shown in vitro to be metabolized by the enzyme CYP3A4.[12] This finding is consistent with the in vivo interactions observed between buspirone and these inhibitors or inducers of cytochrome P450 3A4 (CYP3A4), among others:[32] Itraconazole: Increased plasma level of buspirone Rifampicin: Decreased plasma levels of buspirone Nefazodone: Increased plasma levels of buspirone Haloperidol: Increased plasma levels of buspirone Carbamazepine: Decreased plasma levels of buspirone Grapefruit: Significantly increases the plasma levels of buspirone.[36] See grapefruit–drug interactions. Fluvoxamine: Moderately increased plasma levels of buspirone.[37] Elevated blood pressure has been reported when buspirone has been administered to patients taking monoamine oxidase inhibitors (MAOIs).[32] Buspirone has been found to markedly reduce the hallucinogenic effects of the serotonergic psychedelic psilocybin in humans.[38][39][40] This parallels findings in which serotonin 5-HT1A receptor agonists like 8-OH-DPAT attenuate the head-twitch response, a behavioral proxy of psychedelic effects, induced by serotonergic psychedelics in rodents.[41] Paradoxically however, buspirone enhances the head-twitch response, a behavioral proxy of psychedelic effects, induced by 5-hydroxytryptophan (5-HTP) plus pargyline in rodents.[42][43] Buspirone[44] Site Ki (nM) Action Species Ref 5-HT1A 3.98–21421 (median) Agonist Human [44][45] 5-HT1B >100,000 Agonist ? [46] Rat [47] 5-HT1D 22,000–42,700 Agonist ? [46] Human [48][49] 5-HT2A 138–3,240 Antagonist Human 5-HT2B 214 ? Human 5-HT2C 490 Antagonist ? [46] Human 5-HT7 375–381840 Antagonist ? [46] RatHuman [50][51][52] α1 1,000 Antagonist Rat [47] α2 6,000 Antagonist Rat [53] α2A 7.3 (1-PPTooltip 1-(2-Pyrimidinyl)piperazine) Antagonist Human [47] β 8,800 Antagonist Rat [47] D1 33,000 Antagonist Rat [47] D2 484240 Antagonist HumanRat [54][47] D3 98 Antagonist Human [54] D4 29 Antagonist Human [54] mAChTooltip Muscarinic acetylcholine receptor 38,000 ? Rat [47] GABAA(BDZ) >100,000 - Rat [47] Values are Ki (nM). The smaller the value, the more strongly the drug binds to the site. Buspirone acts as a partial agonist of the serotonin 5-HT1A receptor with high affinity.[6][47] It is a partial agonist of both presynaptic 5-HT1A receptors, which are inhibitory autoreceptors, and postsynaptic 5-HT1A receptors.[6] It is thought that the main effects of buspirone are mediated via its interaction with the presynaptic 5-HT1A receptor, thus reducing the firing of serotonin-producing neurons.[6] Buspirone also seems to have lower affinities for the serotonin 5-HT2A, 5-HT2B, 5-HT2C, 5-HT6, 5-HT7 receptors where it probably acts as an antagonist.[46] In addition to binding to serotonin receptors, buspirone is an antagonist of the dopamine D2 receptor with weak affinity.[6][47] It preferentially blocks inhibitory presynaptic D2 autoreceptors, and antagonizes postsynaptic D2 receptors only at higher doses.[6] In accordance, buspirone has been found to increase dopaminergic neurotransmission in the nigrostriatal pathway at low doses, whereas at higher doses, postsynaptic D2 receptors are blocked and antidopaminergic effects such as hypoactivity and reduced stereotypy, though notably not catalepsy, are observed in animals.[6] Buspirone has also been found to bind with much higher affinity to the dopamine D3 and D4 receptors, where it is similarly an antagonist.[54] A major metabolite of buspirone, 1-(2-pyrimidinyl)piperazine (1-PP), occurs at higher circulating levels than buspirone itself and is known to act as a potent α2-adrenergic receptor antagonist.[53][55][56] This metabolite may be responsible for the increased noradrenergic and dopaminergic activity observed with buspirone in animals.[55][57] Buspirone also has very weak and probably clinically unimportant affinity for the α1-adrenergic receptor.[47][58] However, buspirone has been reported to have shown "significant and selective intrinsic efficacy" at the α1-adrenergic receptor expressed in a "tissue- and species-dependent manner".[58] Unlike benzodiazepines, buspirone does not interact with the GABAA receptor complex.[6][59] Buspirone has a low oral bioavailability of 3.9% relative to intravenous injection due to extensive first-pass metabolism.[6] The time to peak plasma levels following ingestion is 0.9 to 1.5 hours.[6] It is reported to have an elimination half-life of 2.8 hours,[6] although a review of 14 studies found that the mean terminal half-life ranged between 2 and 11 hours, and one study even reported a terminal half-life of 33 hours.[8] Buspirone is metabolized primarily by CYP3A4, and prominent drug interactions with inhibitors and inducers of this enzyme have been observed.[11][12] Major metabolites of buspirone include 5-hydroxybuspirone, 6-hydroxybuspirone, 8-hydroxybuspirone, and 1-PP.[60][8][9][10] 6-Hydroxybuspirone has been identified as the predominant hepatic metabolite of buspirone, with plasma levels that are 40-fold greater than those of buspirone after oral administration of buspirone to humans.[9] The metabolite is a high-affinity partial agonist of the 5-HT1A receptor (Ki=25 nM) similarly to buspirone, and has demonstrated occupancy of the 5-HT1A receptor in vivo.[9] As such, it is likely to play an important role in the therapeutic effects of buspirone.[9] 1-PP has also been found to circulate at higher levels than those of buspirone itself and may similarly play a significant role in the clinical effects of buspirone.[55][57] Phase I Metabolism of buspirone in humans[61][62][63][12] Buspirone is a member of the azapirone chemical class, and consists of azaspirodecanedione and pyrimidinylpiperazine components linked together by a butyl chain. Structural analogues of buspirone include other azapirones like gepirone, ipsapirone, perospirone, and tandospirone.[64] A number of analogues are recorded.[65] A number of methods of synthesis have also been reported.[66][67][68] One method begins with alkylation of 1-(2-pyrimidyl)piperazine (1) with 3-chloro-1-cyanopropane (4-chlorobutyronitrile) (2) to give (3). Next, reduction of the nitrile group is performed either by catalytic hydrogenation or with lithium aluminium hydride (LAH) giving (4). The primary amine is then reacted with 3,3-tetramethyleneglutaric anhydride (5) in order to yield buspirone (6).[69][70][71][72][73] Synthesis of buspirone Buspirone was first synthesized by a team at Mead Johnson in 1968[25] but was not patented until 1980.[74][69][75] It was initially developed as an antipsychotic acting on the D2 receptor but was found to be ineffective in the treatment of psychosis; it was then used as an anxiolytic instead.[6] In 1986, Bristol-Myers Squibb gained FDA approval for buspirone in the treatment of GAD.[25][76] The patent expired in 2001, and buspirone is now available as a generic drug. Buspar (buspirone) 10-mg tablets Buspirone is the INNTooltip International Nonproprietary Name, BANTooltip British Approved Name, DCFTooltip Dénomination Commune Française, and DCITTooltip Denominazione Comune Italiana of buspirone, while buspirone hydrochloride is its USANTooltip United States Adopted Name, BANMTooltip British Approved Name, and JANTooltip Japanese Accepted Name.[1][77][78][79] Buspirone was primarily sold under the brand name Buspar.[77][79] Buspar is currently listed as discontinued by the U.S. Food and Drug Administration (FDA).[80] In 2010, in response to a citizen petition, the FDA determined that Buspar was not withdrawn from sale for reasons of safety or effectiveness.[81]

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Buspirone, a non-benzodiazepine anxiolytic, have even demonstrated enhancement of sexual function in certain individuals. For this reason, they have been proposed as augmentation agents (antidotes) or substitution agents in patients with emerging sexual dysfunction after treatment with antidepressants. ^ Montejo AL, Prieto N, de Alarcón R, Casado-Espada N, de la Iglesia J, Montejo L (October 2019). "Management Strategies for Antidepressant-Related Sexual Dysfunction: A Clinical Approach". Journal of Clinical Medicine. 8 (10): 1640. doi:10.3390/jcm8101640. PMC 6832699. PMID 31591339. ^ Sontheimer DL, Ables AZ (March 2001). "Is imipramine or buspirone treatment effective in patients wishing to discontinue long-term benzodiazepine use?". The Journal of Family Practice. 50 (3): 203. PMID 11252203. ^ Garrett AR, Hawley JS (April 2018). "SSRI-associated bruxism: A systematic review of published case reports". Neurology. Clinical Practice. 8 (2): 135–141. doi:10.1212/CPJ.0000000000000433. 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Additionally, pretreatment with the 5-HT1A agonist buspirone (20 mg p.o.) markedly attenuates the visual effects of psilocybin in human volunteers.59 Although buspirone failed to completely block the hallucinogenic effects of psilocybin, the limited inhibition is not necessarily surprising because buspirone is a low efficacy 5-HT1A partial agonist.60 The level of 5-HT1A activation produced by buspirone may not be sufficient to completely counteract the stimulation of 5-HT2A receptors by psilocin (the active metabolite of psilocybin). Another consideration is that psilocin acts as a 5-HT1A agonist.30 If 5-HT1A activation by psilocin buffers its hallucinogenic effects similar to DMT58 then competition between psilocin and a weaker partial agonist such as buspirone would limit attenuation of the hallucinogenic response. ^ Pokorny T, Preller KH, Kraehenmann R, Vollenweider FX (April 2016). 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For example, 8-OH-DPAT has been shown to attenuate head twitches induced by 5-HTP or DOI [100], [133], [162], while the partial 5-HT1A agonist buspirone has been shown to increase head twitches induced by 5-HTP plus pargyline [190]. ^ Kitamura Y, Nagatani T, Watanabe T (March 1994). "Buspirone enhances head twitch behavior in mice". Eur J Pharmacol. 253 (3): 297–301. doi:10.1016/0014-2999(94)90206-2. PMID 8200425. ^ a b Roth BL, Driscol J. "PDSP Ki Database". Psychoactive Drug Screening Program (PDSP). University of North Carolina at Chapel Hill and the United States National Institute of Mental Health. Retrieved 14 August 2017. ^ Boess FG, Martin IL (1994). "Molecular biology of 5-HT receptors". Neuropharmacology. 33 (3–4): 275–317. doi:10.1016/0028-3908(94)90059-0. PMID 7984267. S2CID 35553281. ^ a b c d e Sato H, Skelin I, Diksic M (July 2010). 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Pharmaceutical compound 2C-B2C-B structure3D representation of a 2C-B moleculeClinical dataOther names4-Bromo-2,5-dimethoxyphenethylamine; 2,5-Dimethoxy-4-bromophenethylamine; Nexus; Venus; Bromo; Bees; Erox; Synergy; Performax; Toonies[1]Routes ofadministrationBy mouth, insufflation, rectalDrug classSerotonergic psychedelic; Hallucinogen; Serotonin 5-HT2 receptor agonistLegal statusLegal status AU: S9 (Prohibited substance) BR: Class F2 (Prohibited psychotropics) CA: Schedule III DE: Anlage I (Authorized scientific use only) UK: Class A US: Schedule I UN: Psychotropic Schedule II Pharmacokinetic dataMetabolismLiver (MAO and CYP450)[1]MetabolitesBDMPE, BDMPAA, BDMBA, and others[2]Onset of actionOral: 20–90 min[2]Elimination half-life2.48 ± 3.20 h[3]Duration of actionOral: 2–8 hours[2][1]ExcretionUrine[2][1]Identifiers IUPAC name 2-(4-Bromo-2,5-dimethoxyphenyl)ethanamine CAS Number66142-81-2PubChem CID98527DrugBankDB01537ChemSpider88978UNIIV77772N32HKEGGC22775ChEBICHEBI:189669ChEMBLChEMBL292821CompTox Dashboard (EPA)DTXSID10216332 ECHA InfoCard100.164.088 Chemical and physical dataFormula$C_{10}H_{14}BrNO_2$Molar mass260.131 g·mol^{-1}3D model (JSmol)Interactive image SMILES COc1cc(CCN)c(OC)cc1Br InChI InChI=1S/C10H14BrNO2/c1-13-9-6-8(11)10(14-2)5-7(9)3-4-12/h5-6H,3-4,12H2,1-2H3Key:YMHOBZXQZVXHBM-UHFFFAOYSA-N 2C-B, also known as 4-bromo-2,5-dimethoxyphenethylamine or by the slang name Nexus, is a synthetic psychedelic drug of the 2C family, mainly used as a recreational drug.[2][1][4] It was first synthesized by Alexander Shulgin in 1974 for use in psychotherapy. To date, there is limited scientific information regarding the drug's pharmacokinetics and pharmacological effects in humans. The existing studies primarily classify 2C-B as a stimulant and hallucinogen, and less commonly an entactogen and empathogen.[5] 2C-B is also known by a number of slang names and appears on the illicit market in multiple forms:[6][7] as a powder, in capsules or pills. For recreational use, the substance is generally consumed orally or nasally. In Shulgin's book PiHKAL, the oral dosage range is listed as 12–24 mg.[8] 1000mg of 2C-B 2C-B became briefly popular in the United States as substitute for the street drug ecstasy (MDMA) when the latter became illegal in 1985.[9] Many 2C-B users are young adults who attend raves.[6] Although 2C-B is still used in the rave subculture (commonly mistaken for and/or sold as ecstasy), more knowledgable use has become more widespread in the 2000s.[10] In 2011, street prices in the United States ranged between $10 and $30 per tablet when purchased in small quantities.[6] Larger retail purchases cost between $200 and $500 per gram. Wholesale purchases of 2C-B would lower the price ($100 to $300 per gram in 2001, $30 to $100 on the darknet in 2020).[11] There are claims that 2C-B was used as entheogen by the Sangoma, Nyanga, and Amagqirha people in place of their traditional plants; they refer to the chemical as Ubulawu Nomathotholo, which roughly translates to "Medicine of the Singing Ancestors".[12][13][14] The September 1998 issue of Journal of Analytical Toxicology reported that very little data exists about the pharmacological properties, metabolism, and toxicity of 2C-B. The relationship between its use and death is unknown.[11] The common oral recreational dose is around 15–25 mg,[15] at which visual and auditory effects are experienced. Severe adverse reactions are extremely rare, but use of 2C-B was linked to significant brain injury in one case report; the alleged "2C-B" was never actually discovered by testing so the only evidence suggesting 2C-B was the cause was the victim's own words, without taking into consideration that adulteration and impurities are very common in illicit drugs.[16] Oral Insufflated ED_{50} 10 mg 4–6 mg Moderate 15–25 mg 5–9 mg Strong 26–35 mg 10–20 mg Extremely Intense >35 mg >20 mg Duration 4–8 hours 2–4 hours When sold as "Ecstasy", tablets containing 2C-B often contain about 5 mg of the drug, an amount which produces stimulatory effects that mimic the effects of MDMA; in contrast, tablets marketed as 2C-B have larger quantities of the drug (10–20 mg) which cause hallucinogenic effects.[17] Street purity of 2C-B, when tested, has been found to be relatively high.[18] Researchers in Spain found that 2C-B samples in the country doubled between 2006 and 2009, switched from primarily powder form to tablets, and exhibited "low falsification rates".[19] An analysis of street samples in the Netherlands found impurities "in small percentages"; only one of the impurities, the N-acetyl derivative of 2C-B, could be identified, and comprised 1.3% of the sample. The authors suggested that this compound was a by-product of 2C-B synthesis.[17] When orally consumed, 2C-B has a much longer delay before the onset of effects than when it is insufflated. Oral ingestion generally takes roughly 45–75 minutes for the effects to be felt, plateau lasts 2–4 hours, and coming down lasts 1–2 hours. Rectal administration onset varies from 5 to 20 minutes. Insufflated onset takes 1–10 minutes for effects to be felt. The duration can last from 4 to 12 hours depending on route of administration, dose, and other factors.[20] With insufflation, the effects are more abrupt and intense but have a significantly shorter duration, while oral usage results in a milder, longer experience. When insufflated, the onset happens very rapidly, usually reaching the peak at about 20–40 minutes and plateauing for 2–3 hours. 2C-B is also considered one of the most painful drugs to insufflate, with users reporting intense nasal burning.[21] The sudden intensity of the experience combined with the pain can often start the experience with a negative imprint and nausea is also increased with insufflation, compounding the issue. 2C-B pill with heart logo Little academic research has been conducted on the effects of 2C-B in humans. The information available is largely anecdotal and limited. Effects are often described as being more easily managed than other psychedelics;[21][22] it is often compared to a mixture of a serotonergic psychedelic and MDMA.[19] At 5–10 mg, experiments with young chickens have shown it to produce effects similar to a low dosage of amphetamines.[23] The anecdotal effects of 2C-B that have been reported by users on online discussion forums include:[20][24][25] At low doses, the experience may shift in intensity from engaging to mild/undetectable. Experienced users report the ability to take control of the effects and switch from engaged to sober at will. The hallucinations have a tendency to decrease and then increase in intensity, giving the users a sense of "waves" or even glowing. These are popularly described as "clichéd '70s visuals" or objects taking on "water color"-like textures. While the effects of the drug often render users unable to concentrate deeply on anything in particular, some can become engrossed in an activity such as watching a movie or playing a video game, thus distracting themselves from the visual and auditory effects of the drug. Excessive giggling or smiling is common, as is a tendency for deeper "belly laughs". Some users say that the effects are more intense when listening to music and report that they can see sounds and noises. Some users experience a decrease in visual acuity, although others report sharper vision. Through increased awareness of one's body, attention may be brought to perceived "imperfections" or internal body processes.The following effects are highly dose-dependent. Open eye visuals (OEVs), such as cartoon-like distortions and red or green halos around objects. Closed eye visuals (CEVs) are more common than OEVs. Affects and alters ability to communicate, engage in deep thought, or maintain attention span. Some users report experiencing frightening or fearful effects during the experience. Users describe feeling frigid or cold on reaching a plateau, while others feel wrapped in comfortable blankets/ultimate pleasure. Coordination may be affected; some users lose balance or have perceptual distinction problems. Onset time of 2C-B is highly dose dependent, but usually from 45 to 75 minutes. Taken on a full stomach, the onset time is increased to two hours or more. Before it was scheduled, 2C-B was sold in small doses as an aphrodisiac (see: § History). Some users report aphrodisiac effects at lower doses.[26][24] Clinical studies in humans suggest that 2C-B is a psychedelic with some possible entactogen-like effects.[5][3][27] Specific effects have included slight hallucinogenic states, perceptual changes, ego dissolution, time dilation, euphoria, feelings of well-being, reduced anger, increased reactivity to negative emotional stimuli, decreased ability to recognize expressions of happiness, augmented emotionality in speech, and mild sympathomimetic effects such as pressor effects, among others.[5][3][27] Some users report mild "jitters" (body tremors), shuddering breath, and/or mild muscle spasms after insufflating 2C-B. Whether or not these effects are enjoyable depends on the user; Mild to intense diarrhea, gas, nausea, and general gastrointestinal discomfort; Severe headaches after coming down from large doses have been reported. However, many users report a lack of "comedown" or "crash", instead noting a gradual return to sobriety; At doses over 30–40 mg the user may experience frightening hallucinations, as well as tachycardia, hypertension, and hyperthermia;[28] 2C-B HCl is very painful to insufflate. Anecdotal evidence suggests that 2C-B HBr, the hydrobromide salt with greater water solubility, is less irritating to the mucous membranes lining the nose but slightly less potent when compared dose-for-dose with the HCl salt;[29] Rectal administration of a water-based solution of 2C-B is known to be less painful than insufflation and much more potent than oral administration. The lethal dosage is unknown. It was reported in PiHKAL, by Alexander Shulgin, that a psychologist had accidentally taken a 100 mg dose orally without apparent harm.[8] See also: Psychedelic drug § Interactions, and Trip killer § Serotonergic psychedelic antidotes 2C-B is metabolized by the monoamine oxidase (MAO) enzymes MAO-A and MAO-B.[30][31] Monoamine oxidase inhibitors (MAOIs) such as phenelzine, tranylcypromine, moclobemide, and selegiline may potentiate the effects of 2C-B.[30][31][32] This may result in overdose and serious toxicity.[32][30] 2C-B activities Target Affinity (Ki, nM) 5-HT1A 240–311 5-HT1B 104 5-HT1D 26 5-HT1E 120 5-HT1F ND 5-HT2A 0.66–32 (Ki)1.20–689 (EC_{50}Tooltip half-maximal effective concentration)4–101% (E_{max}Tooltip maximal efficacy) 5-HT2B 13.5–97 (Ki)12.6–130 (EC_{50})52–97% (E_{max}) 5-HT2C 32–90 (Ki)0.03–493 (EC_{50})50–116% (E_{max}) 5-HT3 >10,000 5-HT4 ND 5-HT5A >10,000 5-HT6 320 5-HT7 210 α1A >10,000 α1B >10,000 α1D ND α2A 309–320 α2B >10,000 α2C 103 β1 >10,000 β2 >10,000 β3 ND D1 12,000 D2 2,200–25,200 D3 7,116–10,000 D4 >10,000 D5 >10,000 H1–H4 >10,000 M1–M2 >10,000 M3 822 M4–M5 >10,000 I1 2,155 σ1 >10,000 σ2 >10,000 TAAR1Tooltip Trace amine-associated receptor 1 90–3,000 (Ki) (rodent)3,300–7,190 (EC_{50}) (human) SERTTooltip Serotonin transporter 9,700–13,300 (Ki)18,000–312,900 (IC_{50}Tooltip half-maximal inhibitory concentration) NETTooltip Norepinephrine transporter 27,400–31,000 (Ki)44,000–67,100 (IC_{50}) DATTooltip Dopamine transporter 6,500–>30,000 (Ki)231,000 (IC_{50}) MAO-ATooltip Monoamine oxidase A 125,000 (IC_{50}) MAO-BTooltip Monoamine oxidase B 58,000 (IC_{50}) Notes: The smaller the value, the more avidly the drug binds to the site. All proteins are human unless otherwise specified. Refs: [33][34][35][36][1][37][38][39][40][41][42][43][44] Unlike most psychedelics, 2C-B has been shown to be a low efficacy human serotonin 5-HT2A and 5-HT2C receptor partial agonist.[45] This suggests that activation of the 5-HT2A-coupled phospholipase D pathway[45] or functional antagonism of 5-HT2A may also play a role. The rank order of 5-HT2A receptor antagonist potency for this family of drugs in Xenopus is 2C-I > 2C-B > 2C-D > 2C-H.[46] Although 2C-B itself was not evaluated, other closely related members of the 2C series, including 2C-C, 2C-D, 2C-E, 2C-I, and 2C-T-2, all showed no activity as monoamine releasing agents of serotonin, norepinephrine, or dopamine (EC_{50}Tooltip half-maximal effective concentration = >100,000 nM or "inactive").[47][48] Likewise, these other 2C derivatives showed little activity as serotonin 5-HT1A receptor agonists (EC_{50} = >3,000 nM).[48] 2C-B has been shown to be metabolized by liver hepatocytes, resulting in deamination and demethylation that produces several products. Oxidative deamination results in the 2-(4-bromo-2,5-dimethoxyphenyl)-ethanol (BDMPE) and 4-bromo-2,5-dimethoxyphenylacetic acid (BDMPAA) metabolites. Additionally, 4-bromo-2,5-dimethoxybenzoic acid (BDMBA) can also be produced by oxidative deamination. Further metabolism of BDMPE and BDMPAA may occur by demethylation. Alternatively, the later metabolites can be generated by demethylation of 2C-B followed by oxidative deamination.[28] There is species differentiation in the metabolism of 2C-B. Mice hepatocytes produce 4-bromo-2,5-dimethoxy-phenol (BDMP), a previously unknown metabolite. Meanwhile, human, monkey and rabbit hepatocytes produce 2-(4-bromo-2-hydroxy-5-methoxyphenyl)-ethanol (B-2-HMPE), but dog, rat and mouse hepatocytes do not.[28] Analogues and derivatives of 2C-B: 25-N: 25B-N1POMe 25B-NAcPip 25-NB: 25B-NB 25B-NB23DM 25B-NB25DM 25B-NB3OMe 25B-NB4OMe 25B-NBF 25B-NBMD 25B-NBOH 25B-NBOMe (NBOMe-2CB) DMBMPP 25-NM: 25B-NMe7BF 25B-NMe7BT 25B-NMe7Bim 25B-NMe7Box 25B-NMe7DHBF 25B-NMe7Ind 25B-NMe7Indz 25B-NMePyr Substituted benzofurans: 2C-B-FLY 2C-B-BUTTERFLY 2C-B-DRAGONFLY 2CBFly-NBOMe (NBOMe-2CB-Fly) DOB-FLY DOB-2-DRAGONFLY-5-BUTTERFLY N-(2C)-fentanyl: N-(2C-B) fentanyl[49] N-(2C-B-FLY) fentanyl[50] Other: BOB BOH-2C-B, β-Hydroxy-2C-B, βOH-2CB[51][52] BMB 2C-B-5-hemifly 2C-B-aminorex (2C-B-AR) 2C-B-AN 2C-B-BZP 2C-B-FLY-NB2EtO5Cl 2C-B-PP 2CB-Ind βk-2C-B (beta-keto 2C-B) N-Ethyl-2C-B TCB-2 (2C-BCB) A variety of N-substituted derivatives of 2C-B have been tested, including N-methyl-2CB, N,N-dimethyl-2CB, N-ethyl-2CB and N-benzyl-2CB. Most simple alkyl derivatives were considerably less potent than 2C-B, with N-ethyl-2CB for instance having a 40 times lower affinity for the 5-HT2A receptor. The N-benzyl derivative however was found to have higher binding affinity than 2C-B itself, with N-(4-bromobenzyl)-2CB binding even more tightly.[53] This initial research did not include functional assays of activity, but later led to the development of potent substituted N-benzyl derivatives such as 25B-NBOMe,[54] and 25B-NBOH. βk-2C-B shows dramatically reduced potency and efficacy as a serotonin 5-HT2A receptor agonist compared to 2C-B.[40] ASR-2001 (2CB-5PrO) is another notable analogue of 2C-B which is under development for treatment of psychiatric disorders.[55][56][57] Exposing compounds to the reagents gives a colour change which is indicative of the compound under test. Marquis Mecke Mandelin Liebermann Froehde Robadope Yellow to green Yellow to olive brownish green Yellow to black Yellow to green Slow pink Ehrlich Hofmann Simon's Scott Folin No reaction No reaction No reaction No reaction (Light) purple 2C-B was synthesized from 2,5-dimethoxybenzaldehyde by American chemist Alexander Shulgin in 1974. It first saw use among the psychiatric community as an aid during therapy, but was abandoned due to gastrointestinal effects and the lack of empathogenic effects.[1] 2C-B was first sold commercially as a purported aphrodisiac[11] under the trade name "Erox", which was manufactured by the German pharmaceutical company Drittewelle.[58] For several years, it was available as tablets in Dutch smart shops under the name "Nexus" and "B-Dub".[citation needed] The UN Commission on Narcotic Drugs added 2C-B to Schedule II of the Convention on Psychotropic Substances in March 2001.[59] 2C-B is a scheduled drug in most jurisdictions.[60] The following is a partial list of territories where the substance has been scheduled. 2C-B is controlled under the List 1, as well as similar substances like 2C-I or 2C-T-2.[61] 2C-B is controlled in Australia and on the list of substances subject to import and export controls (Appendix B). It was placed on Schedule One of the Drugs Misuse and Trafficking Act when it first came to notice in 1994, when in a showcase legal battle chemist R. Simpson was charged with manufacturing the substance in Sydney. Alexander Shulgin came to Australia to testify on behalf of the defense, to no avail. 2C-B is not specifically listed in the Australia Poisons Standard (October 2015), however similar drugs such as 2C-T-2 and 2C-I are making 2C-B fall under the Australian analogue act.[62] In Belgium, 2C-B is a controlled substance making production, distribution, and possession illegal. In Brazil, 2C-B is a controlled substance making production, distribution, and possession illegal. In Canada, 2C-B is classified under Controlled Drugs and Substances Act as Schedule III as "4-bromo-2,5-dimethoxybenzeneethanamine and any salt, isomer or salt of isomer thereof".[63] 2C-B has been rescheduled (Schedule III), in a new amendment, taking effect on October 31, 2016. This is to include the other 2C-x analogues.[64] In August 2007, 2C-B, along with many other psychologically active substances,[65] was added to Ley 20.000, known as the Ley de Drogas [es]. Possession of more than 200 mg of 2C-B is punishable with a two years jail sentence.[66] Smaller amount is punishable by a fine. The 200 mg threshold is merely a guideline which the court can reconsider depending on circumstances. In Denmark, 2C-B is listed as a category B drug.[67] In Estonia, 2C-B is classified as Schedule I. In Germany, 2C-B is controlled in the Betäubungsmittelgesetz (BtMG) Anlage I as "Bromdimethoxyphenethylamin" (BDMPEA). 2C-B is schedule I (tabella I).[68] In Japan, 2C-B was scheduled in 1998. It was previously marketed as "Performax". In Luxembourg, 2C-B is a prohibited substance since 2001.[69] In the Netherlands, 2C-B was scheduled on July 9, 1997. In the Netherlands, 2C-B became a list I substance of the Opium Law despite no health incidents occurring. Following the ban, other phenethylamines were sold in place of 2C-B until the Netherlands became the first country in the world to ban 2C-I, 2C-T-2 and 2C-T-7 alongside 2C-B. In Norway, 2C-B was classified as Schedule II on March 22, 2004, listed as 4-bromo-2,5-dimethoxyphenethylamine.[70] 2C-B is schedule I (I-P group) in Poland. Banned as a narcotic drug with a criminal penalty for possession of at least 10 mg.[71] In Spain, 2C-B was added to Category 2 prohibited substances in 2002. 2C-B is currently classified as Schedule I in Sweden. 2C-B was first classified as "health hazard" under the act Lagen om förbud mot vissa hälsofarliga varor (Act on the Prohibition of Certain Goods Dangerous to Health) as of April 1, 1999, under SFS 1999:58[72] that made it illegal to sell or possess. Then it became schedule I as of June 1, 2002, published in LVFS 2002:4[73] but mislabeled "2-CB" in the document. However, this was corrected in a new document, LVFS 2009:22[74] effective December 9, 2009. In Switzerland, 2C-B is listed in Anhang D of the DetMV and is illegal to possess.[75] All drugs in the 2C family are Class A under the Misuse of Drugs Act which means they are illegal to produce, supply or possess. Possession carries a maximum sentence of seven years imprisonment while supply is punishable by life imprisonment and an unlimited fine.[76] In the United States, 2C-B is classified as a Schedule I controlled substance. This became permanent law on June 2, 1995,[77] following a proposal by the Drug Enforcement Administration in December 1994.[78]

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Retrieved 2024-11-12. 2C-B - Isomer Design 2C-B - PsychonautWiki Erowid 2C-B vault 2C-B - PiHKAL - Erowid 2C-B - PiHKAL - Isomer Design 2C-B: Effects, Dosage, & Safety - Tripsitter Retrieved from " 3 Pharmaceutical compound 2C-iBuClinical dataOther names2,5-Dimethoxy-4-isobutylphenethylamine; 4-Isobutyl-2,5-dimethoxyphenethylamine; 2C-iBu; 2C-IB; ELE-02; ELE02; ELEU02Routes ofadministrationOral;[1] Ophthalmic[2][3]Drug classSerotonin 5-HT2A receptor agonist; Serotonergic psychedelic; Hallucinogen; Anti-inflammatory drugPharmacokinetic dataProtein binding74%[4]Duration of action20 hours[1]Identifiers IUPAC name 2-[2,5-dimethoxy-4-(2-methylpropyl)phenyl]ethanamine PubChem CID57486931Chemical and physical dataFormulaC14H23NO2Molar mass237.343 g·mol−13D model (JSmol)Interactive image SMILES CC(C)CC1=C(C=C(C(=C1)OC)CCN)OC InChI InChI=1S/C14H23NO2/c1-10(2)7-12-9-13(16-3)11(5-6-15)8-14(12)17-4/h8-10H,5-7,15H2,1-4H3Key:FLBABUVVTQBINW-UHFFFAOYSA-N 2,5-Dimethoxy-4-isobutylphenethylamine (2C-iBu or 2C-IB), also known by its developmental code name ELE-02, is a serotonin 5-HT2A receptor agonist, serotonergic psychedelic, and anti-inflammatory drug which is under development for the treatment of inflammation.[2][3][4][5][6][7] It is a member of the phenethylamine and 2C families of compounds.[4][5][7] The drug is being developed as a topical eye drop for treatment of inflammatory eye conditions.[2][3] There is also interest in 2C-iBu and related drugs for treatment of systemic inflammation and neuroinflammation.[8][9][10][11][12][5] 2C-iBu was not assessed or discovered by Alexander Shulgin and was not described in PiHKAL (Phenethylamines I Have Known and Loved) (1991).[7][13] However, he did include 2C-iBu (as "2C-IB") as a DOM analogue in a table in The Shulgin Index, Volume One: Psychedelic Phenethylamines and Related Compounds (2011).[1] In addition, he stated in a footnote that a 5 mg oral dose of 2C-iBu produces threshold activity and has a long duration of about 20 hours.[1] The cited source for these observations, however, was only a 2006 personal communication with "M. Mueller." [1] 2C-iBu was subsequently more thoroughly characterized by Charles D. Nichols and colleagues at Louisiana State University School of Medicine as a novel anti-inflammatory drug in the late 2010s.[4][7] Eleusis has licensed 2C-iBu intellectual property from LSU and the drug has reached the preclinical research stage of development, but no recent development has been reported as of October 2023.[2][3] 2C-iBu molecular targets[4] Target Affinity (pKi) 2C-iBu (R)-DOI 5-HT1A 7.1 5.9 5-HT1B 7.3 5.6 5-HT1D 7.2 ND 5-HT2A 8.9 10.4 5-HT2B 7.8 8.6 5-HT2C 9.6 9.2 5-HT6 5.9 ND 5-HT7 6.5 ND 2C-iBu is a highly potent and robustly efficacious serotonin 5-HT2A receptor agonist.[4] Its EC50Tooltip half-maximal effective concentration values are 1.3 nM for calcium mobilization and 57.5 nM for β-arrestin-2 recruitment, whereas its EmaxTooltip maximal efficacy values are 103% for calcium mobilization and 77% for β-arrestin-2 recruitment relative to serotonin.[4] The drug showed higher potency and efficacy as a serotonin 5-HT2A receptor agonist than several other 2C drugs, including 2C-NP, 2C-B, 2C-I, 2C-H, and 2C-iP, whereas its activities were more comparable to or less than those of the DOx drugs DOIB, (R)-DOB, (R)-DOI, and DOiP.[4] 2C-iBu has also been assessed and found to bind to other serotonin receptors, including the serotonin 5-HT2C, 5-HT2B, 5-HT1B, 5-HT1D, 5-HT1A, 5-HT7, and 5-HT6 receptors, in that order of affinity and with varying avidities.[4] 2C-iBu dose-dependently produces the head-twitch response (HTR), a behavioral proxy of psychedelic effects, in rodents.[4] In terms of ED50Tooltip median effective dose, 2C-iBu is about 3-fold less potent than (R)-DOI in producing the HTR.[4] According to Eleusis, it is expected to have "greatly reduced" psychoactivity or hallucinogenic effects compared to related drugs like other members of the 2C family.[6][14] The drug is effective in an allergic asthma model in rodents and showed similar potency as (R)-DOI.[4] Due to its reduced potency in producing the HTR but retained anti-inflammatory potency, 2C-iBu is expected to show greater separation between the desired anti-inflammatory and the undesired psychedelic effects in humans compared to (R)-DOI.[4] In contrast to certain other anti-inflammatory drugs like corticosteroids, serotonin 5-HT2A receptor agonists like 2C-iBu are not immunosuppressants.[14] 2C-iBu, also known as 2,5-dimethoxy-4-isobutylphenethylamine, is a phenethylamine and 2C derivative.[4][5][7] Related drugs to 2C-iBu include 2C-Bu (the butyl analogue), 2C-tBu (the tert-butyl analogue), 2C-sBu (the sec-butyl analogue), and 2C-CPM (the cyclopropylmethyl analogue).[4] In addition, 2C-iBu is related to DOx drugs such as DOIB (DOiBu).[4][15] According to Charles D. Nichols, 2,5-dimethoxyamphetamine (2,5-DMA) has potent anti-inflammatory activity with weak or no hallucinogenic effects.[7][15] Moreover, DOTFM has potent psychedelic effects with no anti-inflammatory activity.[7][16][17] Hence, it appears that the anti-inflammatory effects and psychedelic effects of serotonin 5-HT2A receptor agonists can be fully dissociated.[7] The chemical synthesis of 2C-iBu has been described.[4][1] 2C-iBu was developed as a novel anti-inflammatory drug by Charles D. Nichols and colleagues at Eleusis in the late 2010s.[7][4] They are developing it for treatment of inflammatory conditions.[2][3] Eleusis was acquired by and merged into Beckley Psytech in October 2022.[2][18][19] The drug has reached the preclinical research stage of development, but no recent development has been reported as of October 2023.[2][3] Eleusis has licensed intellectual property surrounding 2C-iBu and has patent protection for 2C-iBu.[6][4] 2C-iBu is not a controlled substance in the United States as of 2020.[6] Anti-inflammatory § Serotonergic psychedelics ^ a b c d e f Shulgin A, Manning T, Daley PF (2011). "#60. DOM". The Shulgin Index, Volume One: Psychedelic Phenethylamines and Related Compounds. Vol. 1. Berkeley, CA: Transform Press. pp. 118–129. ISBN 978-0-9630096-3-0. OCLC 709667010. 2c-IB: […] (15) Synthesis (from 2,5-dimethoxyisobutylbenzene) (Mueller, 2006); although this compound was reported here, a structure-search in Chemical Abstracts does not produce a CAS registry number (16) Threshold activity in humans at 5 mg orally; long duration (about 20 hours; Mueller, 2006). […] Mueller, M. (2006) Personal communication with A.T. Shulgin. ^ a b c d e f g "ELE 02". AdisInsight. 28 October 2023. Retrieved 16 February 2025. ^ a b c d e f "Delving into the Latest Updates on ELE-02 with Synapse". Synapse. 23 January 2025. Retrieved 16 February 2025. ^ a b c d e f g h i j k l m n o p q r s WO published 2020210823, Nichols CD, Billac G, Nichols DE, "Compounds and methods for treating inflammatory disorders", published 15 October 2020 ^ a b c d Raz S (February 2020). Eleusis Drug Development Overview. LSX World Congress 2020. ^ a b c d Newvine C (8 July 2020). "Eleusis Draws on Research Into Psychedelics To Develop New Medicines for Inflammation". 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ACS Pharmacol Transl Sci. 4 (2): 488–502. doi:10.1021/acsptsci.0c00063. PMC 8033619. PMID 33860179. The nature of the 4-position substituent of phenethylamine psychedelics has been previously linked to 5-HT2 receptor selectivity as well as agonist properties at 5-HT2 receptors.40 Analysis of the 4-position demonstrated that the identity of the moiety at this position was rather flexible. Fully efficacious substitutions at the 4-position included the halogens iodine and bromine (R)-DOI (Figure 3), 2C-B (Figure 7A), methoxy (TMA-2) (Figure 7G), short-chain hydrocarbons (R)-DOM (Figure 7H), (R)-DOET) (Figure 7I), and a branched hydrocarbon (DOiBu) (Figure 7J). […] In a comparison of PenH-AUC values determined for each drug as a proxy measure of anti-inflammatory efficacy (Figure 8A) to either EC50 or EMax for calcium mobilization downstream of 5- HT2A receptor activation (Table 1), […] ^ Flanagan TW, Billac G, Nichols CD (2022). "Differential Regulation of Inflammatory Responses Following 5-HT 2 Receptor Activation in Pulmonary Tissues". The FASEB Journal. 36 (S1). doi:10.1096/fasebj.2022.36.S1.R2617. ISSN 0892-6638. ^ Flanagan TW, Foster TP, Galbato TE, Lum PY, Louie B, Song G, et al. (February 2024). "Serotonin-2 Receptor Agonists Produce Anti-inflammatory Effects through Functionally Selective Mechanisms That Involve the Suppression of Disease-Induced Arginase 1 Expression". ACS Pharmacology & Translational Science. 7 (2): 478–492. doi:10.1021/acsptsci.3c00297. PMC 10863441. PMID 38357283. The effects of (R)-DOTFM were examined in the head-twitch response (HTR) assay. (R)-DOTFM produced a strong HTR with a potent ED 50 of 0.60 μmol/kg. These values are equivalent to (R)-DOI, as previously determined. ^ Gunther M (26 October 2022). "What's the Future of Eleusis Therapeutics After Acquisition by Beckley Psytech?". Lucid News - Psychedelics, Consciousness Technology, and the Future of Wellness. 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Nichols (November 14, 2021) - The Hamilton Morris Podcast (discusses 2C-iBu/ELE-02 from 48:22 to 53:56) Retrieved from " 4 Pharmaceutical compound 2C-BuClinical dataOther names2,5-Dimethoxy-4-butylphenethylamine; 4-Butyl-2,5-dimethoxyphenethylamine; 2C-BUIdentifiers IUPAC name 2-(4-butyl-2,5-dimethoxyphenyl)ethan-1-amine PubChem CID172187929Chemical and physical dataFormulaC14H23NO2Molar mass237.343 g·mol−13D model (JSmol)Interactive image SMILES CCCCC1=CC(=C(C=C1OC)CCN)OC InChI InChI=1S/C14H23NO2/c1-4-5-6-11-9-14(17-3)12(7-8-15)10-13(11)16-2/h9-10H,4-8,15H2,1-3H3Key:WVGDKSDIKCPRKV-UHFFFAOYSA-N 2C-Bu, also known as 2,5-dimethoxy-4-butylphenethylamine, is a chemical compound of the phenethylamine and 2C families.[1] It has been said by Daniel Trachsel to be completely unknown.[1] 2C-Bu is the 2C analogue of the DOx derivative DOBU, which is active but does not appear to have psychedelic-type effects in either animals or humans.[1][2][3] 2C-Bu has several notable skeletal isomers, including 2C-iBu, 2C-tBu, and 2C-sBu.[1][4] 2C-iBu and 2C-tBu are both active and produce hallucinogen-type effects in animals and/or humans.[5][6][7][4] This is in spite of 2C-tBu being predicted to be inactive[4] and DOTB (the DOx analogue of 2C-tBu) being inactive as a hallucinogen in animals and humans.[2][8] 2C-iBu may have reduced hallucinogenic potency than other 2C drugs and is being developed as a potential anti-inflammatory medication.[6][7] 2C-P ^ a b c d Trachsel D, Lehmann D, Enzensperger C (2013). Phenethylamine: von der Struktur zur Funktion [Phenethylamines: From Structure to Function]. Nachtschatten-Science (in German). Solothurn: Nachtschatten-Verlag. pp. 763–764, 766–767, 771, 901. ISBN 978-3-03788-700-4. OCLC 858805226. Retrieved 29 January 2025. ^ a b Shulgin AT, Shulgin A (1991). "#63 DOBU 2,5-DIMETHOXY-4-(n)-BUTYLAMPHETAMINE". PiHKAL: A Chemical Love Story (1st ed.). Berkeley, CA: Transform Press. ISBN 978-0-9630096-0-9. OCLC 25627628. ^ Seggel MR, Yousif MY, Lyon RA, Titeler M, Roth BL, Suba EA, et al. (March 1990). "A structure-affinity study of the binding of 4-substituted analogues of 1-(2,5-dimethoxyphenyl)-2-aminopropane at 5-HT2 serotonin receptors". Journal of Medicinal Chemistry. 33 (3): 1032–1036. doi:10.1021/jm00165a023. PMID 2308135. ^ a b c Varty GB, Canal CE, Mueller TA, Hartsel JA, Tyagi R, Avery K, et al. (April 2024). "Synthesis and Structure-Activity Relationships of 2,5-Dimethoxy-4-Substituted Phenethylamines and the Discovery of CYB210010: A Potent, Orally Bioavailable and Long-Acting Serotonin 5-HT2 Receptor Agonist". J Med Chem. 67 (8): 6144–6188. doi:10.1021/acs.jmedchem.3c01961. PMID 38593423. The 4-tert-butyl group was considered as a spot for potential hydroxylation by cytochrome P450s to discover analogs with short-lasting effects. However, 2C-t-Bu was a potent agonist at the 5-HT2A receptor (Ki = 9.9 nM, EC50 = 4.2 nM) and elicited a robust HTR (Supporting Information, Table S1), providing in vivo evidence that the tert-butyl group is not rapidly metabolized to an inactive compound in mice, despite predictions. ^ Shulgin A, Manning T, Daley PF (2011). "#60. DOM". The Shulgin Index, Volume One: Psychedelic Phenethylamines and Related Compounds. Vol. 1. Berkeley, CA: Transform Press. pp. 118–129. ISBN 978-0-9630096-3-0. OCLC 709667010. 2c-IB: […] (15) Synthesis (from 2,5-dimethoxyisobutylbenzene) (Mueller, 2006); although this compound was reported here, a structure-search in Chemical Abstracts does not produce a CAS registry number (16) Threshold activity in humans at 5 mg orally; long duration (about 20 hours; Mueller, 2006). […] Mueller, M. (2006) Personal communication with A.T. Shulgin. ^ a b WO published 2020210823, Nichols CD, Billac G, Nichols DE, "Compounds and methods for treating inflammatory disorders", published 15 October 2020 ^ a b Raz S (February 2020). Eleusis Drug Development Overview. LSX World Congress 2020. ^ Oberlender RA (May 1989). "Stereoselective aspects of hallucinogenic drug action and drug discrimination studies of entactogens". Purdue e-Pubs. Purdue University. Retrieved 17 February 2025. Table 7. Hallucinogenic potency of 4-alkyl-2,5-dimethoxyamphetamines.a […] DOTB: […] Hallucinogenic Potencyb: -c. […] c this compound has not been established as hallucinogenic. […] Within this homologous series, optimum activity is straight chain alkyl group, two and three carbons in length 1975). The potency increases by an order of magnitude as associated with a (Shulgin and Dyer, the 4-hydrogen of 2,5-DMA is replaced by a short alkyl chain, then decreases if the chain length exceeds four carbons. In addition, the lack of hallucinogenic activity for the tertiary butyl derivative, DOTB, suggested that branching of the 4-alkyl substituent was not tolerated. […] In a study employing 5-MeO-DMT as the training drug in rats, DOTB and DOAM were distinguishable from this hallucinogen, while 2,5-DMA and DOM were not (Glennon et al., 1981). This was consistent with the studies described above. Surprisingly, however, stimulus generalization was not observed for DOET, DOPR, and DOBU (Glennon et al., 1981a). […] Aldous et al. (1974) noted steric restrictions on the 4-substituent in the rabbit hyperthermia model since the 4-isopropyl derivative was more potent than the 4-tert-butyl analogue, DOTB. Additional studies with DOTB, which contains a more highly hindered benzylic carbon, indicate that hallucinogen-like activity may actually be abolished in man (Shulgin and Dyer, 1975) and drastically attenuated in animals (Glennon et al., 1982). 2C-BU - Isomer Design Retrieved from " 5 Pharmaceutical compound 2C-tBuClinical dataOther names2,5-Dimethoxy-4-tert-butylphenethylamine; 4-tert-Butyl-2,5-dimethoxyphenethylamine; 2C-TBU; 2C-t-BuDrug classSerotonin receptor agonist; Serotonergic psychedelic; HallucinogenIdentifiers IUPAC name 2-(4-tert-butyl-2,5-dimethoxyphenyl)ethanamine PubChem CID117347542ChemSpider76370331Chemical and physical dataFormulaC14H23NO2Molar mass237.343 g·mol−13D model (JSmol)Interactive image SMILES CC(C)(C)C1=C(C=C(C(=C1)OC)CCN)OC InChI InChI=1S/C14H23NO2/c1-14(2,3)11-9-12(16-4)10(6-7-15)8-13(11)17-5/h8-9H,6-7,15H2,1-5H3Key:MHNFTGKRRUDUST-UHFFFAOYSA-N 2C-tBu, or 2C-t-Bu, also known as 4-tert-butyl-2,5-dimethoxyphenethylamine, is a serotonin receptor agonist and putative serotonergic psychedelic of the phenethylamine and 2C families.[1][2] It is a potent serotonin 5-HT2A receptor agonist (Ki = 9.9–35 nM, EC50Tooltip half-maximal effective concentration = 4.2 nM) and also binds to the serotonin 5-HT2C receptor (Ki = 7–24 nM).[1][2] The drug produces a robust head-twitch response, a behavioral proxy of psychedelic effects, in rodents.[2] It also produces hyperlocomotion in rodents.[2] The active dosage in humans is >5 mg per Daniel Trachsel and its duration is unknown.[1] Initial tests with 7 mg and with 10 mg (as 5 mg plus 5 mg 2 hours apart) produced no psychedelic effects in humans, but instead induced a pronounced and long-lasting tiredness.[1] It was hypothesized that 2C-tBu might be a serotonin 5-HT2A receptor antagonist and might thereby be hypnotic,[1] but it was instead shown to be an agonist in subsequent studies.[2] 2C-Bu 2C-iBu DOTB ^ a b c d e Trachsel D, Lehmann D, Enzensperger C (2013). Phenethylamine: von der Struktur zur Funktion [Phenethylamines: From Structure to Function]. Nachtschatten-Science (in German). Solothurn: Nachtschatten-Verlag. pp. 766–767, 771, 901. ISBN 978-3-03788-700-4. OCLC 858805226. Retrieved 29 January 2025. ^ a b c d e Varty GB, Canal CE, Mueller TA, Hartsel JA, Tyagi R, Avery K, et al. (April 2024). "Synthesis and Structure-Activity Relationships of 2,5-Dimethoxy-4-Substituted Phenethylamines and the Discovery of CYB210010: A Potent, Orally Bioavailable and Long-Acting Serotonin 5-HT2 Receptor Agonist". Journal of Medicinal Chemistry. 67 (8): 6144–6188. doi:10.1021/acs.jmedchem.3c01961. PMID 38593423. The 4-tert-butyl group was considered as a spot for potential hydroxylation by cytochrome P450s to discover analogs with short-lasting effects. However, 2C-t-Bu was a potent agonist at the 5-HT2A receptor (Ki = 9.9 nM, EC50 = 4.2 nM) and elicited a robust HTR (Supporting Information, Table S1), providing in vivo evidence that the tert-butyl group is not rapidly metabolized to an inactive compound in mice, despite predictions. 2C-TBU - Isomer Design This psychoactive drug-related article is a stub. You can help Wikipedia by expanding it.vte Retrieved from " 6 The following pages link to 2C-tBu External tools (link count transclusion count sorted list) · See help page for transcluding these entries Showing 50 items. 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