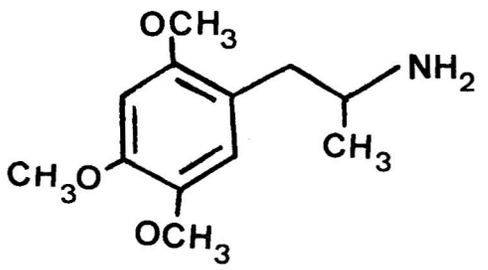

2. TMA-2

Description and Properties: TMA-2, 2,4,5-trimethoxyamphetamine, β-aminodihydroasarone, 1-(2,4,5-trimethoxyphenyl)-2-aminopropane is a colorless, viscous oil with a weak ammoniacal smell. It forms a white hydrochloride salt with a melting point of 188.5-189.5° and an acetamide with m.p. 132-133°. The free base is slightly soluble in water and ether, and easily soluble in methanol and chloroform; the hydrochloride is insoluble in ether and acetone, but dissolves readily in water and alcohol.

History: The first synthesis of TMA-2 was reported in 1933, and its hallucinogenic activity discovered in 1962. The suffix "2" identifies TMA-2 as being the second of the 6 possible isomers of trimethoxyamphetamine to be found with such activity. It has not been reported as occuring in nature, although the corresponding essential oil asarone (2,4,5-trimethoxyphenylpropene) is widely distributed in the plant kingdom. The latter is present in the plant *Acorus calamus* (sweet calamus, sweet flag) which is known as "rat root" in North America and claimed to have intoxicating properties similar to those of LSD. The conversion of asarone to TMA-2 is easily realized chemically, but has not been demonstrated as occuring metabolically.

Human Biochemistry and Pharmacology: Theoretical interest in TMA-2 stems from the recognition of 6-hydroxydopamine as an extremely potent disrupter of the adrenergic nervous system. TMA-2 is structurally related with an identical oxygenation pattern, and has been shown to be partially demethylated *in vivo*. The end product, 2,4,5-trihydroxyamphetamine, has been studied clinically as an antihypertensive, but has not been reported to produce sensory or perceptual changes in humans even at dosages of 200 mg. The metabolism and fate of TMA-2 in humans is unknown.

Human Psychopharmacology: Threshold effects of TMA-2 are evident at dosages of 10 mg, as the hydrochloride salt. The effective oral dose is 16 mg. The first indications of intoxication usually noted are signs of physical disturbance such as nausea, paresthesia and a modest, reflexive mydriasis. The central, sensory changes appear in the second hour and are characterized by some exaggeration of visual input (especially in the appreciation of colors and contrasts of lighting) and of empathy with irrational objects in one's environment. These preludes lead to a plateau, from three to about six hours following administration, which is an impressive altered state of consciousness virtually free of the distortions and portentousness so common with LSD. The experience dissipates gradually, and is usually completed in 8-10 hours. A sharp dose-response curve exists for TMA-2 in that several additional toxic symptoms have been reported at 25-30 mg levels. There can be a pervasive nausea throughout the entire experimental period, accompanied by actual vomiting, apparent fainting and brief but repeated periods of amnesia. Peripheral vision can be lost (this, apparently, of hysteric origin) and the accompanying fear of being irreparably severed from reality has led to situations that have proved difficult to manage. Psycholytic studies with TMA-2 (20 mg) in conjunction with harmaline (250 mg) or ibogaine (250 mg) have resulted in long lasting episodes complicated by severe motor agitation. No information exists concerning the consequences of chronic use.

Legal Status: TMA-2 is implicitly included in the Federal Controlled Substances Act, as it is a "positional isomer" of 3,4,5-trimethoxyamphetamine, itself a Schedule I drug, with registry number 7390.

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