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SPECTROPHOTOMETRIC DETERMINATION OF COMPLEX OF Zn(II) WITH N-P-BROMOPHENYLTHIOBENZOHYDROXAMIC ACID

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ABSTRACT: A simple , rapid, sensitive and new spectrophotometric method to estimate zinc in pharmaceutical preparations is described. The method depends on the reaction between zinc and the new synthesized reagent [4,5-diphenyl-2-((1E)- (4-(1-(2-phenylhydrazono)ethyl)phenyl)diazenyl)-4H-imidazole] (DPHEDPI) to form a reddish-pink complex at pH 7.5 with a mole ratio (M:L)of (1:2), the complex exhibits a maximum absorbance at 520 nm with molar absorptivity coefficient (Ɛ) of 4.4*102 L.mol-1 cm-1 . Beer's law is obeyed in the range of (0.5–27) ppm for zinc with correlation coefficient of (0.9996) ,and the stability constant was found to be 1*10 12 L.mol-1 . The relative standard deviation for seven replicate measurements, relative error and recovery values of this method were found to be 0.0015 % , -0.778%, and 99.22% respectively. Finally, this proposed method was applied for the determination of zinc in the zinc sulphate capsules drug and the results were compared with atomic absorption method

KEYWORDS: spectrophotometric, zinc, n-p-bromophenylthiobenzohydroxamic, complex, mole ratio, coefficient

I,INTRODUCTION

The method of adsorption of N-p-bromophenylthiobenzohydroxamic acid vanadium(V) complex on microcrystalline naphthalene followed by a solid-liquid separation is described for the trace analysis of vanadium. This complex is stable in naphthalene dimethyl formamide solution. The absorbance has showed a linear relationship to the concentration of vanadium in the range 7-150 µg per 10 mL of dimethyl formamide. The molar absorptivity and sensitivity have been found to be 2.6 7 × 10 4 L mol -1 cm -1 and 0.01346 µg cm -2, respectively for the absorbance of 0.001 with a standard deviation of 0.17 %. 4-Bromophenylacetic acid, also known as p-bromophenylacetic acid, is an organic compound. It is a derivative of phenylacetic acid containing a bromine atom in the para position. 4-Bromophenylacetic acid may be prepared by the addition of a bromine atom to phenylacetic acid through electrophilic aromatic substitution. It was first prepared in the laboratory by treatment of phenylacetic acid with bromine and mercuric oxide; a mixture of the 2- and 4- isomers is made, and the 4- isomer is isolated by fractional crystallization.[1]

It can also be made by condensing 4-bromobenzylbromide with sodium cyanide in ethanol, and the hydrolising the nitrile with sodium hydroxide.[2]

Methyl 2-(4-bromophenyl)acetate is made from 4-bromophenylacetic acid by refluxing it with methanol acidified with sulfuric acid.[3]

An ethyl ester can be made in an analogous way.[4]

A hydrazone derivative, 2-(4-bromophenyl)acetohydrazide, is made by refluxing the methyl ester with hydrazine.[3] Further hydrazone derivatives of 4-bromophenylacetic acid are made by condensing the simple hydrazone with aldehydes, forming a double bond with the second nitrogen.[3] At least 19 of these hydrazones are known.[3]

4-Bromophenylacetic acid is a chemical that can be purchased.[5]

Plant protoplasts conjugate aspartic acid with 4-bromophenylacetic acid to form 4-bromophenylacetyl-L-aspartic acid.[2]

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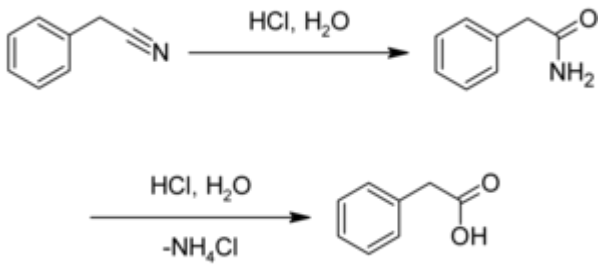
4-Bromophenylacetic acid reacts with sodium tetraphenylborate to form felbinac which can be further converted to xenbucin.[4]

The ionic conductance has been measured.[6] Phenylacetic acid (PAA; conjugate base phenylacetate), also known by various synonyms, is an organic compound containing a phenyl functional group and a carboxylic acid functional group. It is a white solid with a strong honey-like odor. Endogenously, it is a catabolite of phenylalanine. As a commercial chemical, because it can be used in the illicit production of phenylacetone (used in the manufacture of substituted amphetamines), it is subject to controls in countries including the United States and China.[2] Phenylacetic acid has been found to be an active auxin (a type of plant hormone),[3] found predominantly in fruits. However, its effect is much weaker than the effect of the basic auxin molecule indole-3-acetic acid. In addition the molecule is naturally produced by the metapleural gland of most ant species and used as an antimicrobial. It is also the oxidation product of phenethylamine in humans following metabolism by monoamine oxidase and subsequent metabolism of the intermediate product, phenylacetaldehyde, by the aldehyde dehydrogenase enzyme; these enzymes are also found in many other organisms.

This compound may be prepared by the hydrolysis of benzyl cyanide:[4][5]



Phenylacetic acid is used in some perfumes, as it possesses a honey-like odor even in low concentrations. It is also used in penicillin G production and diclofenac production. It is also employed to treat type II hyperammonemia to help reduce the amounts of ammonia in a patient's bloodstream by forming phenylacetyl-CoA, which then reacts with nitrogen-rich glutamine to form phenylacetylglutamine. This compound is then excreted from the patient's body. It's also used in the illicit production of phenylacetone, which is used in the manufacture of methamphetamine.

The sodium salt of phenylacetic acid, sodium phenylacetate, is used as a pharmaceutical drug for the treatment of urea cycle disorders, including as the combination drug sodium phenylacetate/sodium benzoate (Ammonul).[6]

Phenylacetic acid is used in the preparation of several pharmaceutical drugs, including camylofin, bendazol, triafungin, phenacemide, lorcainide, phenindione, and cyclopentolate.

II.DISCUSSION

Methyl phenylacetate is an organic compound that is the methyl ester of phenylacetic acid, with the structural formula $C_6H_5CH_2COOCH_3$. It is a colorless liquid that is only slightly soluble in water, but soluble in most organic solvents.

Methyl phenylacetate has a strong odor similar to honey. This compound also occurs in brandy, capsicum, coffee, honey, pepper, and some wine. It is used in the flavor industry and in perfumes to impart honey scents.

Methyl phenyldiazoacetate, precursor to cyclopropanation agents, is prepared by treating methyl phenylacetate with p-acetamidobenzenesulfonyl azide in the presence of base.[1]

Cathinone (also known as benzoylethanamine, or β-keto-amphetamine) is a monoamine alkaloid found in the shrub Catha edulis (khat) and is chemically similar to ephedrine, cathine, methcathinone and other amphetamines. It is probably the main contributor to the stimulant effect of Catha edulis, also known as khat. Cathinone differs from many other amphetamines in that it has a ketone functional group. Other phenethylamines that share this structure include the stimulants methcathinone, MDPV, mephedrone and the antidepressant bupropion.

Khat has been cultivated in the Horn of Africa and Arabian Peninsula region of the world for thousands of years. It is most commonly chewed for the euphoric effect it produces. The active ingredient was first proposed in 1930, when cathine was identified as a predominant alkaloid in the plant.[2] Cathine was thought to be the main active ingredient in khat until the 1960s, when it was found that the amount of cathine in the khat leaves is insufficient to produce the effects observed. In 1975, the United Nations Narcotic Laboratory analyzed khat leaves from Yemen, Kenya and Madagascar and found the presence of a different alkaloid, cathinone.[2] Cathinone is a similar

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molecule to cathine, but is much more abundant in younger plants. This finding caused scientists to speculate about whether cathinone was the true active ingredient in khat.[2]

A study was conducted in 1994 to test the effects of cathinone. Six volunteers who had never chewed khat were given an active khat sample and a cathinone-free placebo sample.[3] The researchers analyzed the participants' moods, activity levels and blood pressure before and after consuming the khat or placebo. This analysis showed that cathinone produced amphetamine-like symptoms, leading the researchers to confirm that cathinone, not cathine, is the active ingredient in khat leaves.[3]

Over 20 million people in the Arabian Peninsula and East Africa chew khat leaves daily. It is an important piece of the culture and economy in this region, especially in Ethiopia (where khat is said to have originated), Kenya, Djibouti, Somalia and Yemen. Men usually chew it during parties or other social gatherings while smoking cigarettes and drinking tea. Farmers and other workers also use khat in the afternoon to reduce fatigue and hunger as the day goes on. It functions like the caffeine in a strong cup of coffee as an anti-fatigue drug. Students and drivers have been known to use it to stay alert for longer periods of time.[4]

In order to produce its desired effects, khat leaves should be chewed fresh. The fresh leaves have a higher concentration of cathinone. Waiting too long after cultivation to chew the leaf will allow the cathinone to break down into its less potent form, cathine. Because of the need for quick chewing, it is a habit that has historically been prevalent only where the plant grows. However, in the recent years with improvements in road and air transport, khat chewing has spread to all corners of the world.

The cultivation of khat in Yemen is a highly profitable industry for farmers. Khat plants will grow differently depending on the climate they are grown in and each one will produce different amounts of cathinone.[5] It generally grows best in coastal, hot climates. In Yemen, the khat plant is named after the region in which it is grown. The Nehmi khat plant has the highest known concentration of cathinone, 342.5 mg/100g.[5]

III.RESULTS

Cathinone has been found to stimulate the release of dopamine and inhibit the reuptake of epinephrine, norepinephrine and serotonin in the central nervous system (CNS). These neurotransmitters are all considered monoamines and share the general structure of an aromatic ring and an amine group attached by a two-carbon separator.[5] Because cathinone is a hydrophobic molecule, it can easily cross cell membranes and other barriers, including the blood–brain barrier.[12] This property allows it to interact with the monoamine transporters in the synaptic cleft between neurons. Cathinone induces the release of dopamine from brain striatal preparations that are prelabelled either with dopamine or its precursors.[13]

The metabolites of cathinone, cathine and norephedrine, also possess CNS stimulation, but create much weaker effects.[14] The effects of cathinone on the body can be countered by a preceding administration of a dopamine receptor antagonist.[14] The antagonist prevents synaptic dopamine released by cathinone from exerting its effect by binding to dopamine receptors.

Cathinone can also affect cholinergic concentrations in the gut and airways by blocking prejunctional adrenergic receptors (a2 adrenergic) and activating 5-HT7 receptors, thereby inhibiting smooth muscle contraction.[12] It can also induce dry mouth, blurred vision and increased blood pressure and heart rate.[5] Khat leaves are removed from the plant stalk and are kept in a ball in the cheek and chewed. Chewing releases juices from the leaves, which include the alkaloid cathinone. The absorption of cathinone has two phases: one in the buccal mucosa and one in the stomach and small intestine.[3] The stomach and small intestine are very important in the absorption of ingested alkaloids.[3] At approximately 2.3 hours after chewing khat leaves, the maximum concentration of cathinone in blood plasma is reached. The mean residence time is 5.2 ± 3.4 hours.[3] The elimination half-life of cathinone is 1.5 ± 0.8 hours.[3] A two-compartment model for absorption and elimination best describes this data. However, at most, only 7% of the ingested cathinone is recovered in the urine.[3] This indicates that the cathinone is being broken down in the body. Cathinone has been shown to selectively metabolize into R,S-(-)-norephedrine and cathine. The reduction of the ketone group in cathinone will produce cathine. This reduction is catalyzed by enzymes in the liver. The spontaneous breakdown of cathinone is the reason it must be chewed fresh after cultivation.[3] The first documentation of the khat plant being used in medicine was in a book published by an Arabian physician in the 10th century.[5] It was used as an antidepressant because it led to feelings of happiness and excitement. Chronic khat chewing can also create drug dependence, as shown by animal studies.[5] In such studies, monkeys were trained to push a lever to receive the drug reward. As the monkeys' dependence increased, they pressed the lever at an increasing frequency.[5]

Khat chewing and the effects of cathinone on the body differ from person to person, but there is a general pattern of behavior that emerges after ingesting fresh cathinone:[5]

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1. Feelings of euphoria that last for one to two hours
2. Discussion of serious issues and increased irritability
3. The chewer's imagination is very active
4. Depressive stage
5. Irritability, loss of appetite and insomnia

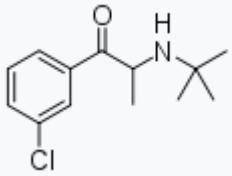
There are other effects not related to the CNS. The chewer can develop constipation and heartburn after a khat session. Long-term effects of cathinone can include gum disease or oral cancer, cardiovascular disease and depression.[5] The withdrawal symptoms of cathinone include hot flashes, lethargy and a great urge to use the drug for at least the first two days.[5]

The synthesis of cathinone in khat begins with L-phenylalanine and the first step is carried out by L-phenylalanine ammonia lyase (PAL), which cleaves off an ammonia group and creates a carbon-carbon double bond, forming cinnamic acid.[15] After this, the molecule can either go through a beta-oxidative pathway or a non-beta-oxidative pathway. The beta-oxidative pathway produces benzoyl-CoA while the non-beta-oxidative pathway produces benzoic acid.[15] Both of these molecules can be converted to 1-phenylpropane-1,2-dione by a condensation reaction catalyzed by a ThDP-dependent enzyme (Thiamine diphosphate-dependent enzyme) with pyruvate and producing CO_2.[15] 1-phenylpropane-1,2-dione goes through a transaminase reaction to replace a ketone with an ammonia group to form (S)-cathinone. (S)-Cathinone can then undergo a reduction reaction to produce the less potent but structurally similar cathine or norephedrine, which are also found in the plant.[15]

Aside from the beta- and non-beta-oxidative pathways, the biosynthesis of cathinone can proceed through a CoA-dependent pathway. The CoA-dependent pathway is actually a mix between the two main pathways as it starts like the beta-oxidative pathway and then when it loses CoA, it finishes the synthesis in the non-beta-oxidative pathway. In this pathway, the trans-cinnamic acid produced from L-phenylalanine is ligated to a Coenzyme A (CoA), just like the beginning of the beta-oxidative pathway.[15] It then undergoes hydration at the double bond. This product then loses the CoA to produce benzaldehyde, an intermediate of the non-beta-oxidative pathway. Benzaldehyde is converted into benzoic acid and proceeds through the rest of the synthesis.[15]

IV.CONCLUSION

Cathinone can be synthetically produced from propiophenone through a Friedel-Crafts acylation of propionic acid and benzene.[12] The resulting propiophenone can be brominated, and the bromine can be substituted with ammonia to produce a racemic mixture of cathinone. A different synthetic strategy must be employed to produce enantiomerically pure (S)-cathinone. This synthetic route starts out with the N-acetylation of the optically active amino acid, S-alanine.[12] Then, phosphorus pentachloride (PCl_5) is used to chlorinate the carboxylic acid forming an acyl chloride. At the same time, a Friedel-Crafts acylation is preformed on benzene with aluminum chloride catalyst. Finally, the acetyl protecting group is removed by heating with hydrochloric acid to form enantiomerically pure S-(-)-cathinone.[12]



Chemical structure of bupropion, a cathinone derivative

Cathinone can be extracted from Catha edulis, or synthesized from α-bromopropiophenone (which is easily made from propiophenone). Because cathinone is both a primary amine and a ketone, it is very likely to dimerize, especially as a free base isolated from plant matter.[16]

The structure of cathinone is very similar to that of other molecules. By reducing the ketone, it becomes cathine if it retains its stereochemistry, or norephedrine if its stereochemistry is inverted. Cathine is a less potent version of cathinone and cathinone's spontaneous reduction is the reason that older khat plants are not as stimulating as younger ones. Cathinone and amphetamine are closely related in that amphetamine is only lacking the ketone C=O group.[17] Cathinone is structurally related to methcathinone, in much the same way as amphetamine is related to methamphetamine. Cathinone differs from amphetamine by possessing a ketone oxygen atom (C=O) on the β (beta) position of the side chain. The corresponding alcohol, cathine, is a less powerful stimulant. The biophysiological conversion from cathinone to cathine is to blame for the depotentiation of khat leaves over time. Fresh leaves have a greater ratio of cathinone to cathine than dried ones, therefore having more psychoactive effects.

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There are many cathinone derivatives that include the addition of an R group to the amino end of the molecule. Some of these derivatives have medical uses as well. Bupropion is one of the most commonly prescribed antidepressants and its structure is Cathinone with a tertiary butyl group attached to the nitrogen and chlorine attached to the benzene ring meta- to the main carbon chain.[17]Other cathinone derivatives are strong psychoactive drugs. One such drug is methylone, a drug structurally similar to MDMA.

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