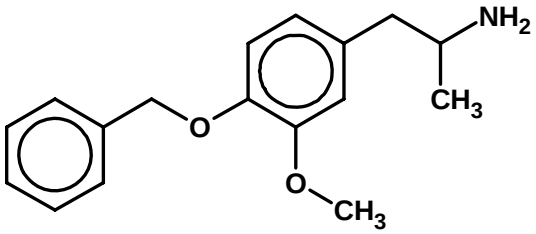
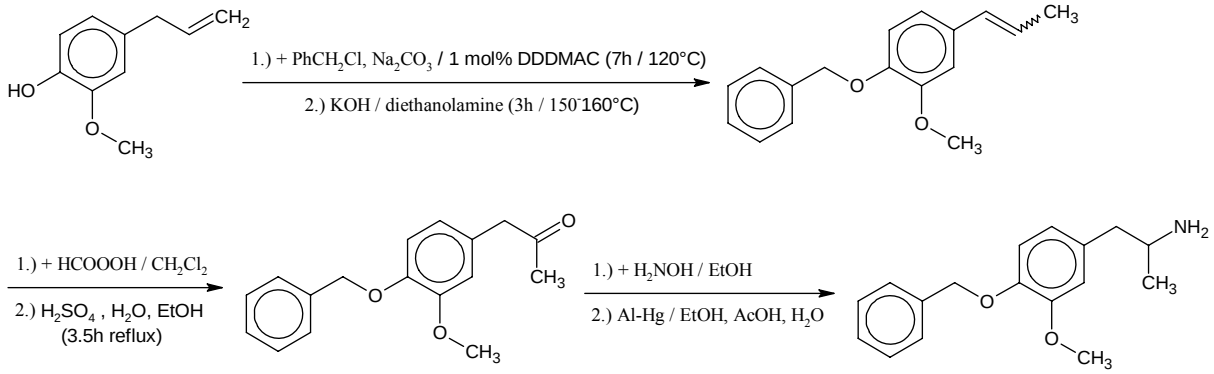
BZOMA

4-benzyloxy-3-methoxyamphetamine hydrochloride

1-[4-(benzyloxy)-3-methoxyphenyl]propan-2-amine hydrochloride



SYNTHESIS:



4-benzyloxy-3-methoxy-propenylbenzene (*O*-benzyl-isoeugenole). In a 250 ml flask there was added 60 g clove oil (0.36 mol; about 95% eugenol), 46 ml benzyl chloride (0.40 mol), 1.3 g didecyldimethylammonium chloride (1 mol%), 12 ml toluene, 45 g anhydrous Na_2CO_3 (0.41 mol). The flask was set in an oil bath and magnetic stirring with a bar long enough to allow for efficient mixing of the slurry. The oil bath was slowly heated to 120°C with the flask left open in order for the toluene vapors and the CO_2 to carry out some water that forms. At this temperature it was left stirring for 7 hours, then when the reaction mixture cooled bellow about 70°C there added 150 ml water for the inorganic salts to dissolve. The liquid organic phase was separated, washed with twice 100 ml 10% NaOH solution, twice 100 ml water (with a couple of drops of HCl in order to break emulsions), 50 ml brine and dried over Na2SO4 which was then washed with a little acetone. The filtrate was stripped under the vacuum of a water jet pump while stirring on an oil bath at 160°C. About 16 ml of unreacted liquid, mostly benzyl chloride, distilled over. There remained 63.5 g of clear, yellow oil (the yields were somewhat higher when up to 4 mol% PTC catalyst was used, but due to emulsion forming is not really worth it). To this oil was added 10 g KOH pellets, 16 ml diethanolamine, and intensively stirred on the oil bath at 150-160°C for 3 hours. When the temperature fell to 80°C there was added 100ml warm water and while still hot the oil was separated. It was then put in a 500 ml beaker where it soon begun to solidify. There was added 400 ml ethanol and heated to boiling in order to dissolve the entire crude product. When it cooled there formed long hair like white fibers that were vacuum filtered and washed with 4 times 30 ml cold ethanol. After drying there remained 48.3 g of white product (47%).

4-benzyloxy-3-methoxyphenylacetone. In a 250 ml flask there was added 20 g 4-benzyloxy-3-methoxy-propenylbenzene, 80 ml dichloromethane, 3 g Na_2CO_3 and set on magnetic

stirring in an ice bath. In a 100 ml beaker there was prepared the performic acid by adding 12 ml 30% hydrogen peroxide to 50 ml ice cold 85% formic acid and the solution left standing for one hour. The performic acid preparation was then added drop wise to the reaction flask with such speed as to maintain the temperature of the reaction mixture bellow 15°C. After the addition was over the ice bath was removed and the reaction left stirring over night. The organic phase was then washed with twice 50 ml water, put back in a 250 ml flask and the solvent distilled off. To the remaining viscous oil was added 80 ml water, 40 ml ethanol, 40 ml 35% H_2SO_4 and set to reflux with magnetic stirring for 3 hours and half. 100 ml water was added and the water phase decanted from the sticky oil which was then extracted in 60 ml ethyl acetate, washed with 80 ml water, twice 60 ml saturated $NaHCO_3$, 80 ml water, the solvent distilled off and the remains dissolved in 120 ml hot 80% ethanol. The insolubles were removed by filtration and 18 g $NaHSO_3$ was added, heated to boil on a hot plate and left stirring. While cooling a white, voluminous precipitate started to form. After 2 hours when it cooled to the room temperature it was vacuum filtered and washed with 4 times 30 ml 96% ethanol. The precipitate was suspended in 75 ml water in a 250 ml beaker and 50 ml 12% NaOH solution was added, followed by 40 ml dichloromethane. It was left stirring for 15 min and the organic phase separated, washed with 100 ml water, 50 ml brine, dried over Na_2SO_4 and the solvent stripped under vacuum. There was obtained 4.7 g of a thick, brownish oil (22%).

4-benzyloxy-3-methoxyphenylacetone oxime. In a 100 ml flask there was added 1.6 g hydroxylamine hydrochloride, 7.5 ml water, 20 ml ethanol, 4.7 g 4-benzyloxy-3-methoxyphenylacetone and 1.2 g Na_2CO_3. It was set to reflux for one hour. When it cooled, there was added 60 ml water and the precipitated resin was extracted in 40 ml dichlomethane, washed with 40 ml water, and the solvent stripped under vacuum. There remained 5.7 g of a brown resin that crystallized after a couple of days and was used without purification in the next step.

4-benzyloxy-3-methoxyamphetamine hydrochloride. In a 500 ml flask there was added 60 ml 96% ethanol, 5 ml water, 2 ml of 2% $HgCl_2$ solution, 3 g shredded aluminium foil and left stirring for 10 min. Then the flask was immersed in a hot water bath, but taken out as soon as the amalgam begun to dissolve by forming hydrogen. At this point a solution of 5.7 g of the above oxime in 15 ml acetic acid was slowly added drop wise at such speed as to prevent boiling. The reaction mixture was left stirring for 2 hours, then 60 ml of 40% NaOH solution added, extracted with 3 times 20 ml toluene, the combined extracts boiled down to the volume of 40 ml, washed with 3 times 40 ml water and extracted with 3.5 ml of 30% hydrochloric acid in 30 ml water. The water extract was washed with 10 ml toluene, made basic with 5 ml 40% NaOH solution and the precipitated oil extracted in 40 ml toluene, washed with twice 40 ml water and extracted in 2 ml 30% hydrochloric acid in 20 ml water. After washing the extract with 10 ml water it was evaporated to dryness under vacuum at 60 to 80°C. To the remained solid was then added 20 ml isopropanol, stripped off, and this repeated two more times in order to azoetropicaly remove water and hydrochloric acid remains. The crystalline product was triturated in 30 ml acetone, vacuum filtered and washed with 4 times 20 ml acetone. There was obtained 3.9 g (73% from the ketone) of a white crystalline powder: mp 172-173°C (lit.[1] 172-173°C); IR (KBr disc) 2936, 1606, 1518, 1455, 1267, 1235, 1147 cm^{-1}.
Free base mp 56-57°C; ^1H NMR ($CDCl_3$) δ 1.11 (d, J = 6.3 Hz, 3H, CH_3), 1.22 (broad, 2H, NH_2), 2.42-2.64 (dq, 2H, CH2), 3.12 (m, 1H, CH), 3.88 (s, 3H, CH_3O), 5.13 (s, 2H, CH2O), 6.64-6.83 (m, 3H, ArH), 7.25-7.48 (m, 5H, Ph).

[1] Sommers and Weston. *J. Am. Chem. Soc., 73* (**1951**) 5749-5751. DOI: 10.1021/ja01156a077

DOSAGE: 80 – 180 mg (threshold 15 - 30 mg)

DURATION: 12 – 30 h

SUBJECTIVE DESCRIPTIONS OF ACTIVITY:

80 mg (male; 80 kg): I went in the town to meet two friends and we were drinking tea in a bar when at about +1 hour I perceived the first effects, but it took a further hour to properly develop. I was unable to truly follow the conversation and my mood lightened. At +3 hours when it peaked I had the impression that there lacks only a tiny bit more to get to a higher, truly psychedelic level of activity. It is certainly considerably more potent than POMA or IPOMA at the same dose. I later went to visit some other two friends. We were in three, having a beer, and they do not speak my language, I don't speak theirs and we also don't speak a common language so I had to speak a different language with each one. This lead to a very interesting and funny situation especially since they are also younger and we discussed the typical teenager problems like girls and love troubles that I luckily grew over. I was very amused and relaxed and could feel every emotion they talked about. I had the impression I communicated much more easily by having more empathy. I only drunk a small beer and did not felt the effects of alcohol at all, but I also begun to believe that the compound's activity was near to its end. However, when I returned home at about +6 hours and had some dinner I finally realized that the effects are not fading at all, they just stabilized and will probably last for several more hours. There are no visuals and also no negative effects. It does however clench my jaws a little and causes some kind of tension in my head but nothing serious.

140 mg (male; 80 kg): I was at the sea coast on a peninsula. For the first two hours there was essentially nothing. Then it began really, really slowly. I went for a walk by the beach with Lucy and the surroundings become attractive and full of interesting details. The stones had a feeling of softness and liveliness. The intensity grew so slowly that I almost had no conscience of the change. There was some tension at the beginning but no true nausea. At about +6 hours I already thought that it is going to fade away, but when we went to the nearby town I found people still quite alien. I did not felt like I was able of normal communication, as I noticed too many details. At the evening, at about +8h hours we went walking to a lighthouse and I was again convinced that it is already over when some new visuals and moods convinced me the opposite. At one point I looked at the sky and the clouds seamed to bee rolling like two giant cylinders one over the other. The little stones on the road looked like a mosaic with some logic in it. I was also not stimulated at all, just in a good mood. Even at +12 hours when I went to sleep and closed my eyes I saw colorful geometric, kaleidoscope-like patterns in the forms of certain flowers I saw earlier during the day.

200 mg (male; 80 kg): The taste of the aqueous solution was plastic-like, almost unbearable. After an hour and half there were some really slow developments and then ten or twenty minutes later it continued more rapidly becoming quite intense. The transition becomes heavy, confusing me quite a lot. I do not feel any nausea but I'm aware that I'm on the border of feeling it. At +4 hours it stabilized to a not so demanding psychedelic state. I was reading a book on oxidations in organic synthesis. Reading was not easy, also because my focus kept on hooking to the reggae music on the radio. Still, I got a new idea that I would like to try out one day. At +5 hours it seamed to have gotten a bit more intense. However, there are only little visuals. With the eyes open the vision borders flash, but with the closed eyes there are barely any patterns. Mentally I'm in a typically psychedelic cognitive mode, but visual activity is poor in comparison. My thoughts are sharp and tense. There is also that typical

metallic taste in my mouth. It is a relatively fine compound, especially if I consider that it is made from one of the most common essential oils. At +7 hours I feel like I'm still at the same exact level and fear I will not be able to sleep this night, but one hour later I think it will be over soon. Yet, I was unable to fall asleep almost till morning (about +16 hours). Even when I finally made it, I soon woke up due to heavily intense dreams. I slept less than 5 hours and then went at work in the lab. I still felt some effects and was exhausted. I was still exhausted even the day after when I had to wake up very early in order to catch a flight. I spent most of that day on airports which made me extremely tired. It was only the third day that my biorhythm corrected and I was able to get enough rest to normalize.

DISCUSSION: As far as I know this is the first eugenol derived amphetamine that showed real psychedelic activity with visuals bellow 200 mg dose. This is not so surprising given that the 4-benzyloxy group should, according to the known SAR theory, enhance binding trough its high hydrophobicity. However its bulkiness is on the border of agonist activity - just one methylene length further and the compound should be an antagonist.[2] It is also expectably less potent than the related 3C-BZ which has an additional *meta* methoxy group.[3]
Nevertheless, BZOMA is an annoying compound for several reasons. Its duration is way too long. Especially for the today's speed of life, it looks kind of out of place. Also, the quality of the experience pales in comparison to similarly long lasting DOB and its relatives. It simply never develops in such a deep altered state of mind and does not give such rich visuals. Instead it only teases and gives little to compensate the exhaustion of a whole day activity. The required dose is also too large for my taste and leaves me with some fear of potentially cardiovascularly active metabolites (like the debenzylated form might potentially be).
The good properties of BZOMA lie almost exclusively in its chemistry. It is perfect for young enthusiasts interested in the hobby of psychedelic chemistry. At the same time it does not have the risk of being prohibited since it is more or less useless for abuse as a recreational drug. All the required materials can be obtained without big troubles and without going through chemical suppliers. Crude eugenol in the form of clove oil is cheap, benzyl chloride can be prepared from toluene or benzyl alcohol, all is available in various shops. Other reagents are similarly easily obtained. In fact the whole synthesis was developed in such a way to use only easily available reagents. All the synthesis steps are simple, though the ketone formation is terribly low yielding. An alternative route would be to form the 1-(4-bezyloxy-3-methoxyphenyl)-2-nitropropene trough the pseudonitrosite and reduce it by one of the viable methods. The preparation of the psudonitrosite is already described with a 77% yield[4] and its transformation to the nitropropene with a base should not cause troubles.
According to literature, BZOMA has been prepared several times but to my knowledge it never was pharmacologically evaluated before.

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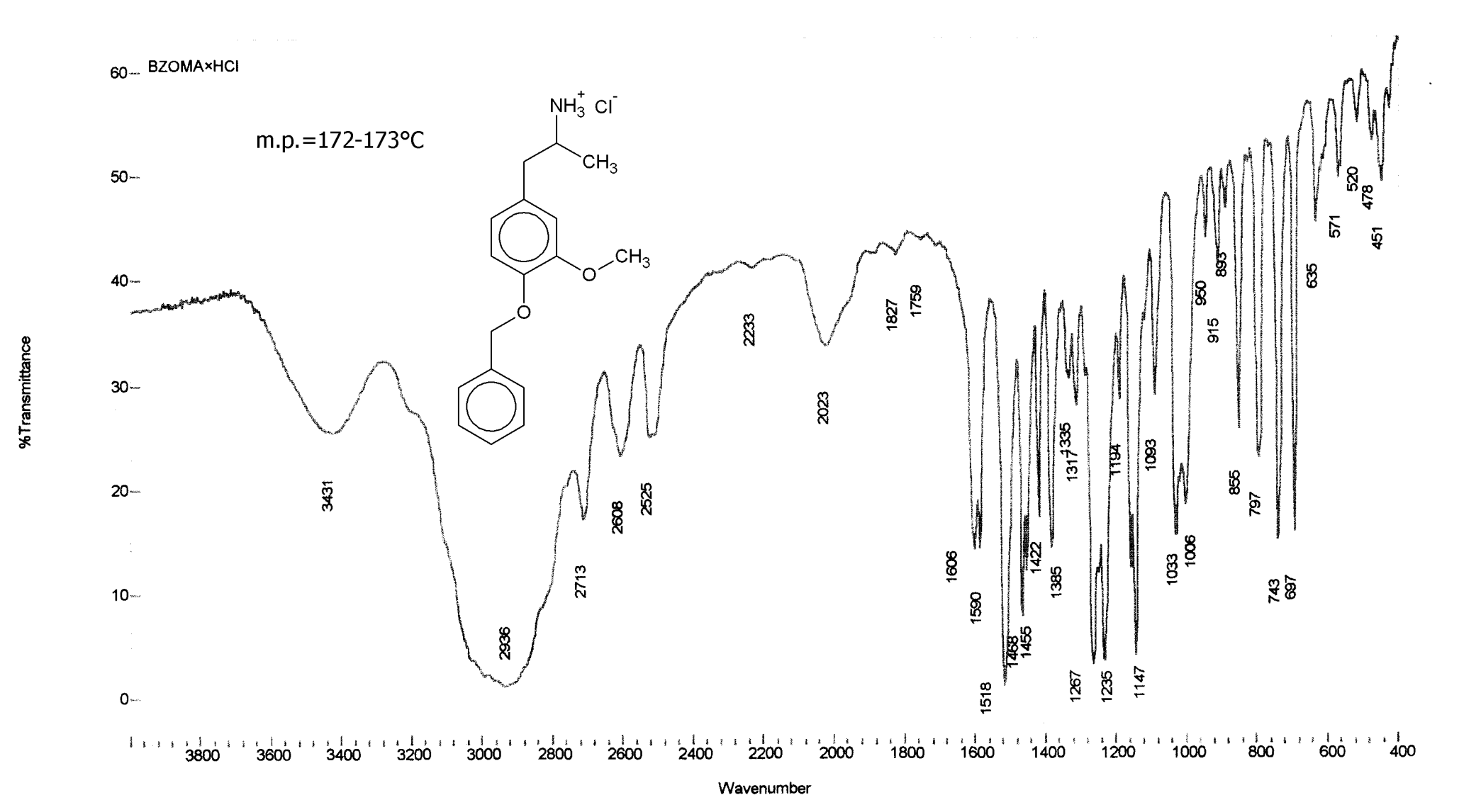
[2] Westkaemper and Glennon. *Current Topics in Medicinal Chemistry*, 2 (**2002**) 575-598. DOI: 10.2174/1568026023393741
[3] PIHKAL #21 3C-BZ: http://www.erowid.org/library/books_online/pihkal/pihkal021.shtml
[4] Fodor. *Chem. Ber., 76* (**1943**) 1216-1219.


BZOMA×HCl
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O
CH_3
O
%Transmittance
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40
30
20
10
0
3431
2936
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2525
2233
2023
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1759
1606
1590
1518
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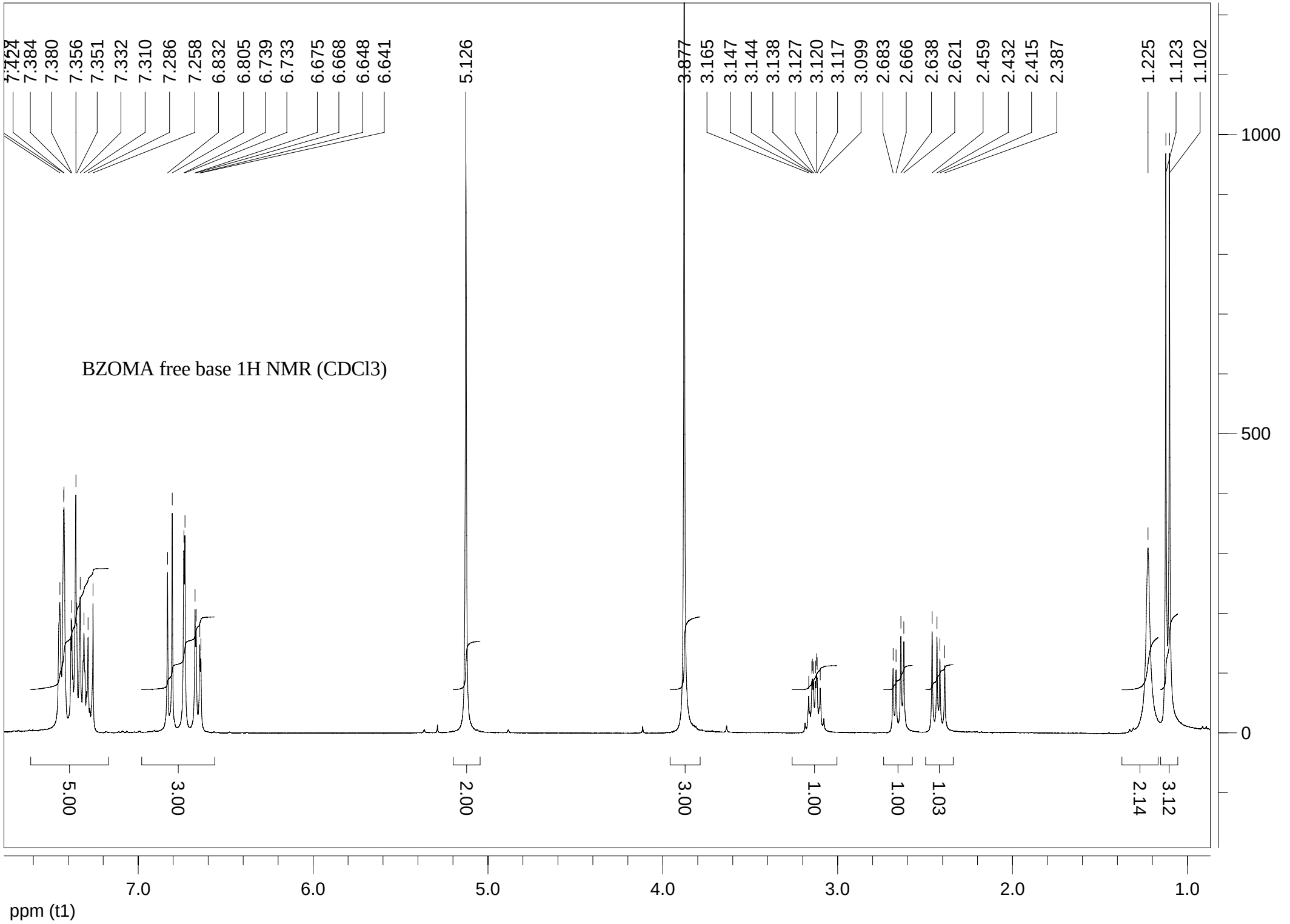
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1.00
1.00
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7.0
6.0
5.0
4.0
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2.0
1.0
ppm (t1)