DEA TOX
DRUG ENFORCEMENT ADMINISTRATION
TOXICOLOGY TESTING PROGRAM

UCSF Clinical Toxicology and Environmental Biomonitoring Laboratory

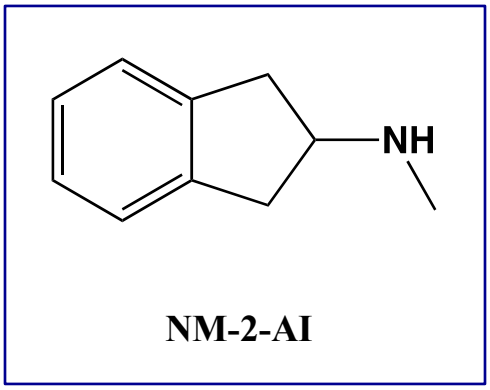
Alert Regarding N-Methyl-2-Aminoindane (NM-2-AI) – May 13, 2021

The US Drug Enforcement Administration (DEA) in collaboration with the University of California San Francisco Clinical Toxicology and Environmental Biomonitoring (CTEB) Laboratory has identified an aminoindane, N-methyl-2-aminoindane (NM-2-AI), in urine samples submitted to our New Psychoactive Substances (NPS) surveillance program[1].

Cohort: In April 2021, cohorts of urine samples from California (25) and Minnesota (25) were submitted to our NPS surveillance program for drug analysis.

Drugs Detected: NM-2-AI was confirmed and quantified in six of the samples submitted. In these same six samples, methamphetamine was also identified. The major substances detected in the cohorts collectively included 11-nor-9-carboxy-THC, methamphetamine, amphetamine, and morphine. The other NPS confirmed include ethylamphetamine, buphedrone, NRG-3, acetylfentanyl, 4CN-AMB-BUTINACA, MEPIRAPIM, and flualprazolam.

NM-2-AI: A member of the aminoindane class of substances, NM-2-AI is sold online as a research chemical. Aminoindanes have been investigated for their biological effects since the 1980s[2]. In the 1990s, aminoindane derivatives of MDMA were found to be a highly selective serotonin releasing agent with putative entactogenic properties[3]. The procedures for synthesizing aminoindanes are well described in the literature. In the past decade, numerous aminoindanes have been detected in drugs promoted as legal substances capable of producing euphoria[4].



NM-2-AI

Analysis: NM-2-AI was detected, confirmed, and quantified in urine samples using liquid chromatography-quadrupole time-of-flight mass spectrometry. Details of the method used along with the chromatogram and mass spectra associated with the compound are presented in the attached supporting documents.

Reference Standard: The reference standard for NM-2-AI is commercially available.

National Forensic Laboratory Information System (NFLIS)[5]: Six exhibits submitted to NFLIS confirmed the presence of NM-2-AI: Alabama (2014); Pennsylvania (2015, 2017); Tennessee (2015); Oklahoma (2 exhibits, 2016).

Additional Cases: As relayed by Dr. Michael Lynch, Medical Director for the Pittsburgh, PA Poison Center, 2 cases in 2020 and 5 cases (2 cases in March, 2 cases in April, 1 case in May) in 2021 have preliminarily identified NM-2-AI and are awaiting final confirmation. In addition, the CTEB laboratory identified NM-2-AI (95.4 ng/mL) in whole blood from an overdose death case in Sioux City, IA in 2015. NM-2-AI was confirmed in addition to the synthetic cannabinoid MAB-CHMINACA (2.7 ng/mL).

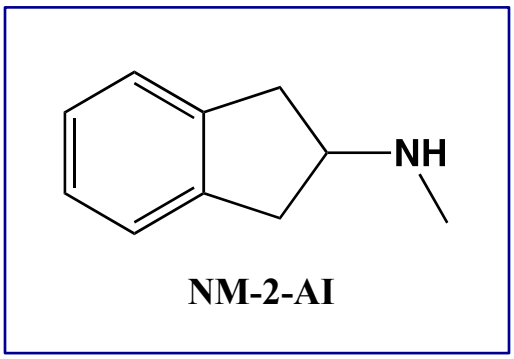
Pharmacological Data: Limited pharmacological data for NM-2-AI is currently available. In animal studies, NM-2-AI was noted to increase the hot plate test reaction time and inhibit exploratory activity without eliciting dopaminergic effects in mice[2].

---

[1] This report was prepared by Roy Gerona, Ross Ellison, Deborah French, Sara Love, and Jordan Trecki.
[2] Cannon JG, Perez JA, Pease JP, Long JP, Flynn JR, Rusterholz DB, Dryer SE (July 1980). "Comparison of biological effects of N-alkylated congeners of beta-phenethylamine derived from 2-aminotetralin, 2-aminoindan, and 6-aminobenzocycloheptene". Journal of Medicinal Chemistry. 23 (7): 745–9.
[3] Nichols DE, Brewster WK, Johnson MP, Oberlender R, Riggs RM (February 1990). "Nonneurotoxic tetralin and indan analogues of 3,4-(methylenedioxy)amphetamine (MDA)". Journal of Medicinal Chemistry. 33 (2): 703–10.
[4] Pinterova N, Horsley RR, Palenicek T. Synthetic Aminoindanes: A Summary of Existing Knowledge. Front Psychiatry. 2017 Nov 17;8:236. doi: 10.3389/fpsyt.2017.00236.
[5] NFLIS is a national forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by Federal, State, and local forensic laboratories in the United States.

N-Methyl-2-Aminoindane

I General Information



NM-2-AI

Synonyms: NM-2-AI

IUPAC Name: N-2,3-dihydro-1H-inden-2-yl-N-methylamine

InChi String: InChI=1S/C10H13N/c1-11-10-6-8-4-2-3-5-9(8)7-10/h2-5,10-11H,6-7H2,1H3

InChi Key: SXWZQUCTTOBHJT-UHFFFAOYSA-N

SMILES: CNC1CC2=CC=CC=C2C1

CAS Number: 24445-44-1

CFR: Not Scheduled

II Physical Properties

Solubility: DMF: 25 mg/mL

DMSO: 20 mg/mL

Ethanol: 3 mg/mL

PBS (pH7.2): 10 mg/mL

Melting Point: 230°C

III Chemical Characterization

GC-MS: The GC-MS spectrum for NM-2-AI is available at Cayman Chemical.
https://www.caymanchem.com/gcms/14897-0521204-GCMS.pdf

IV LC-QTOF/MS Analysis

Instrument: Agilent 1260 Infinity, Agilent 6550 QTOF-MS/MS

Sample Preparation: Enzymatic deconjugation with *H pomatia* glucuronidase followed by dilution

Chromatography

***Column*:** Agilent Poroshell 120 EC-C18 (100 mm x 2.1 mm, 2.7 µm)

***Column Temperature*:** 50 °C

***Injection Volume*:** 2.5 µL

***Mobile Phase*:** A: Ammonium formate (5 mM) and Formic Acid (12.6 mM) in H_2O

B: Formic Acid (12.6mM) in acetonitrile

***Flow rate*:** 0.5 mL/min

***Elution Profile*:** Gradient- 95A:5B initially; 70A:30B from 0.5 to 1.5 min; 30A:70B from 1.5 to 4.5 min; 0A:100B from 4.5 to 7.5min; 95A:5B from 10.0 to 14.0 min

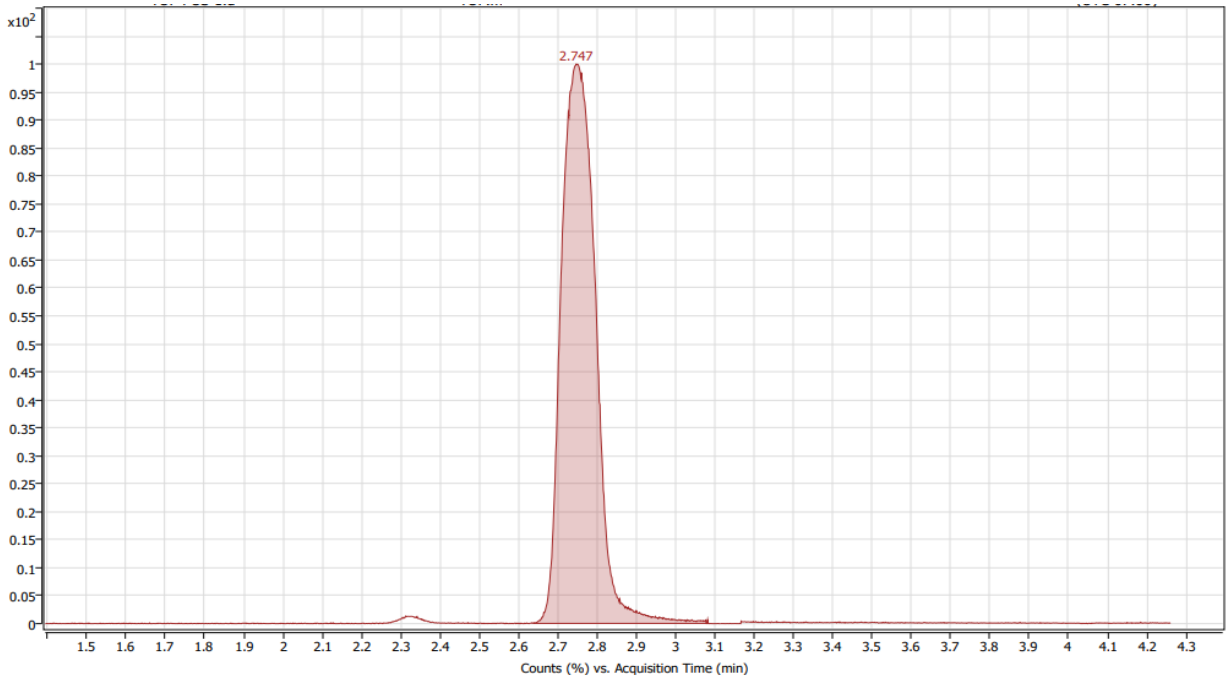
***Run Time*:** 12 min

Mass Spectrometry

***Ion Source*:** Dual Jet Stream Electrospray Ionization
***Polarity*:** Positive
***TOF MS Scan Range*:** 75-1000 Da
***MS/MS Scan Range*:** 50-510 Da
***Gas Temperature*:** 225 °C
***Drying Gas Flow Rate*:** 14L/min
***Sheath Gas Temperature*:** 350 °C
***Sheath Gas Flow Rate*:** 11L/min
***Nebulizer pressure*:** 14psi
***Capillary Voltage*:** 3000 V
***Nozzle Voltage*:** 500 V
***Skimmer Voltage*:** 65 V
***Octopole RF*:** 750 V
***Fragmentor Voltage*:** 380 V
***Internal Reference Masses*:** Purine at m/z 121.0509; HP-921 at m/z 922.0098
***Data Acquisition*:** 2GHz, extended dynamic range
***Fragmentation*:** Auto MS/MS, three maximum precursors (threshold: 500 counts) per cycle with active exclusion after 1 spectrum at a 30s release time

Extracted Ion Chromatogram

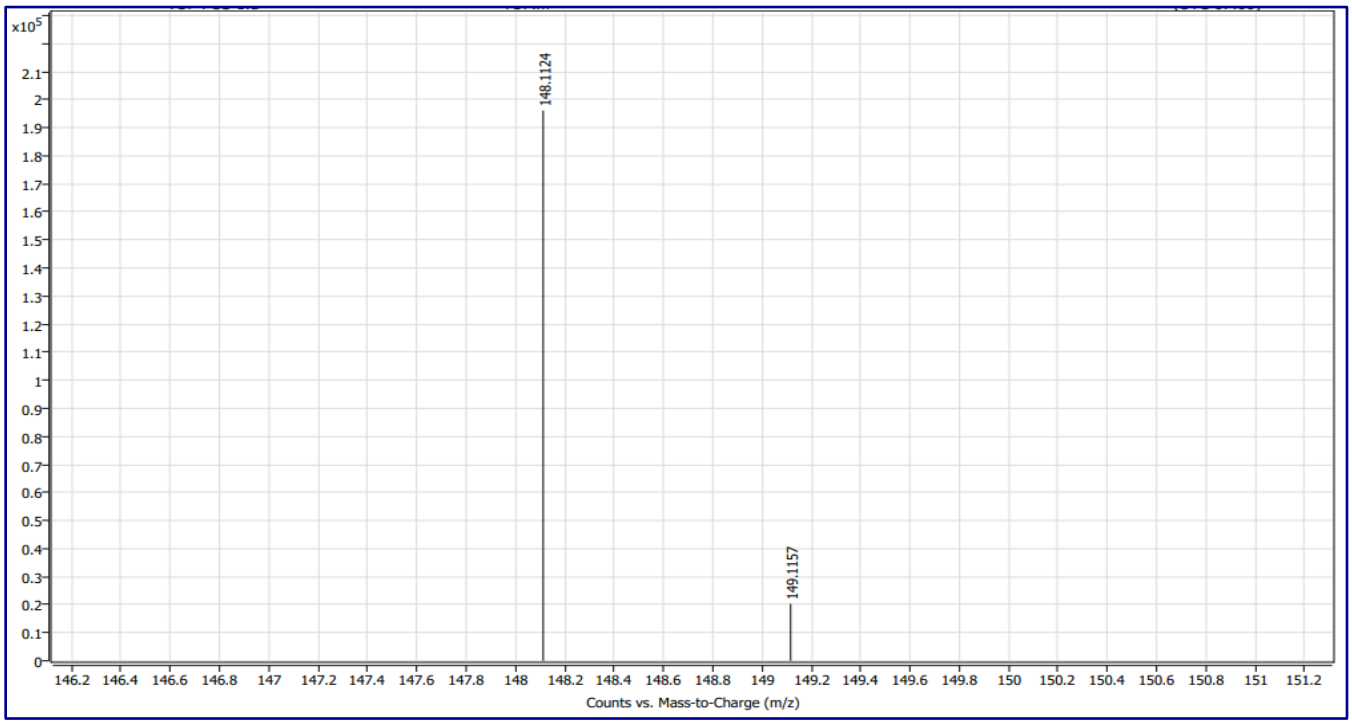
***Retention Time*:** 2.747 min



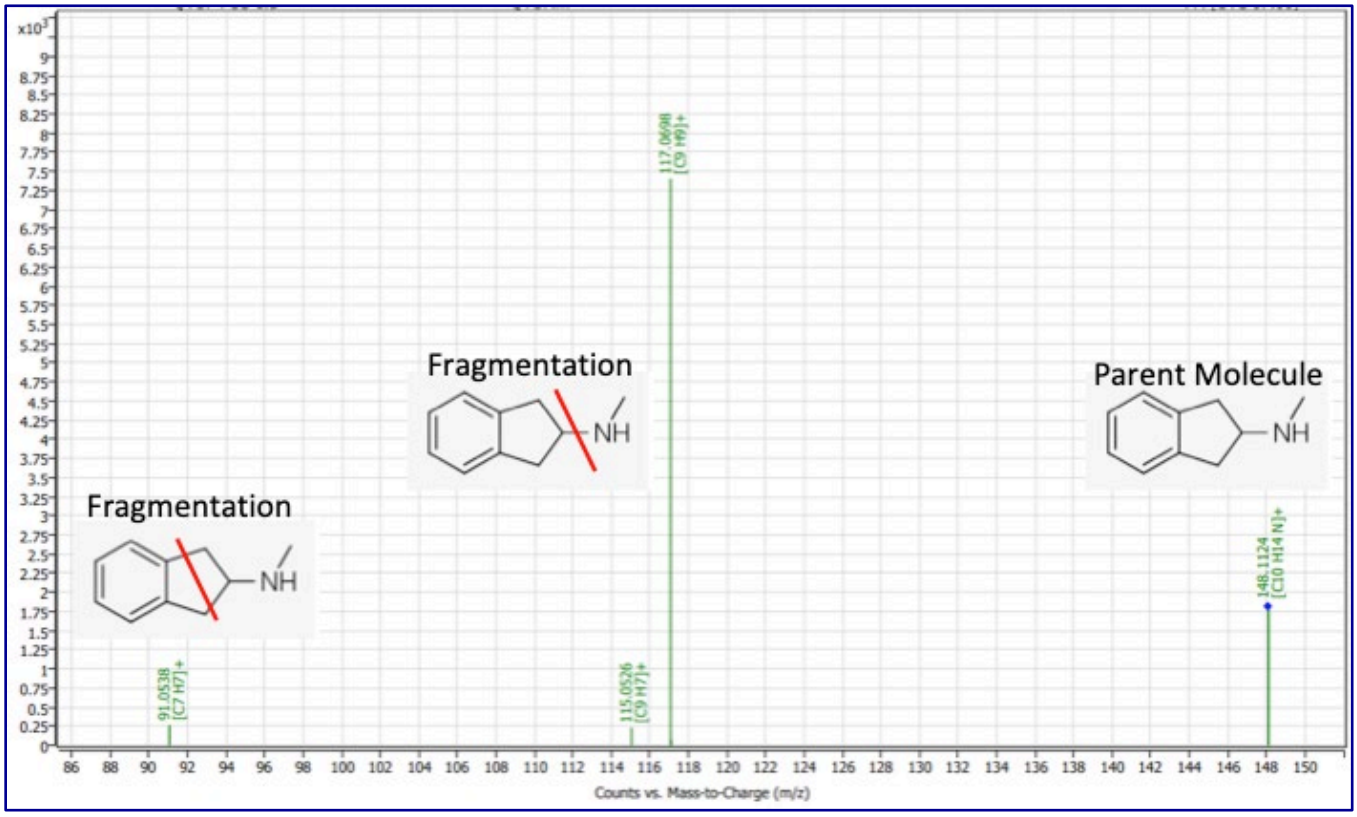
TOF-MS Spectrum

***Exact Mass*:** 147.105

***Accurate Mass*:** $[M+H]^+$= 148.1124 (mass error=-2.15 ppm)



MS/MS Spectrum



DEA TOX
DRUG ENFORCEMENT ADMINISTRATION
TOXICOLOGY TESTING PROGRAM

U. S. Department of Justice
Drug Enforcement Administration
Diversion Control Division
Drug & Chemical Evaluation Section
Toxicology Testing Program
DEATOX@USDOJ.GOV

www.dea.gov

In response to the ongoing synthetic drug epidemic, the Drug Enforcement Administration (DEA) has initiated a contract with the University of California at San Francisco (UCSF) whereby biological samples generated from overdose victims of synthetic drugs can be further analyzed. In many cases, it can be difficult to ascertain the specific substance responsible for the overdose. In the future, we invite you to contact our program if you encounter an overdose of a suspected synthetic drug and desire to have any leftover biological samples (blood preferred) analyzed further for such synthetic substances.

- **Sample Qualifications:**
  - Patients thought to have ingested a synthetic drug, where the traditional drug screen has produced little or no viable options to explain the symptoms exhibited by the patient (alcohol and THC are exempted).
- **How to Contact Us and Send Your Samples:**
  - Once the above qualifications are satisfied:
    - Email DEATOX@USDOJ.GOV with a brief description of the case (including initial toxicology screen and history) and a request for testing.
    - DEA will respond to each inquiry, and if approved, will send the instructions for packing and shipping of sample(s) to UCSF.
      - The main reason for disapproval of a case would be the identification of substances including methamphetamine, heroin, fentanyl, cocaine, LSD, PCP etc. in a routine toxicology screening at your facility.
      - This program's goal is to connect symptom causation to abuse of newly emerging synthetic drugs (i.e. synthetic cannabinoids, synthetic cathinones, fentanyl-related substances, other hallucinogens etc.).
    - Ensure that you de-identify and label the sample with a numerical value, sex, date of birth or age, and the date and time the sample was collected in accordance with the labeling instructions (sent with shipping instructions).
    - Keep a master list of the patients and the numerical values you allocated to each sample at your institution.
- **Cost of sample analysis:**
  - The DEA will cover the full cost of testing the patient samples.
  - The sender will only be responsible for paying for packing and shipping samples to UCSF.
- **Turn-around Time:**
  - Results are expected within three weeks of receipt of the sample at UCSF except in rare occurrences when a novel substance is identified.

Public Domain Notice

Suggested citation:
U.S. Drug Enforcement Administration, Diversion Control Division. (2021). *DEA-TOX: Advisory on an emerging NPS: N-Methyl-2-Aminoindane (NM-2-AI) – May 13, 2021*. Springfield, VA: U.S. Drug Enforcement Administration.

Obtaining Copies of This Publication

Electronic copies of this publication can be downloaded from the DEA-TOX website at https://www.deadiversion.usdoj.gov/dea_tox/index.html.

This report was produced in conjunction with the CTEB laboratory at UCSF.

Clinical Toxicology
and Environmental Biomonitoring Laboratory

DEA PRB 05-13-21-25