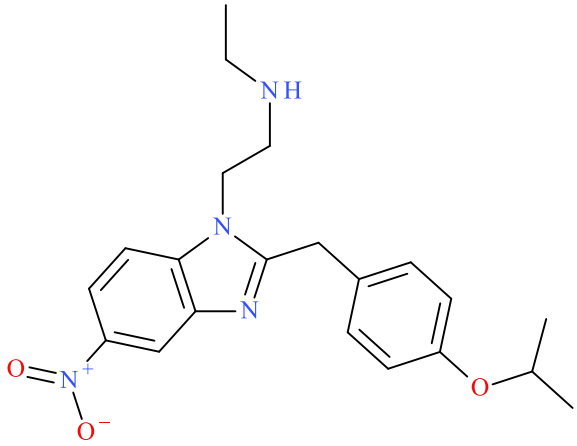
N-Desethyl Isotonitazene

Sample Type: **Drug Material**



Latest Revision: **December 19, 2022**

Date Received: **November 22, 2022**

Date of Report: **December 19, 2022**

1. GENERAL INFORMATION

IUPAC Name:	N-ethyl-2-[2-[(4-isopropoxyphenyl)methyl]-5-nitro-benzimidazol-1-yl]ethanamine
InChI String:	InChI=1S/C21H26N4O3/c1-4-22-11-12-24-20-10-7-17(25(26)27)14-19(20)23-21(24)13-16-5-8-18(9-6-16)28-15(2)3/h5-10,14-15,22H,4,11-13H2,1-3H3
CFR:	Not Scheduled (12/2022)
CAS#	2732926-24-6
Synonyms:	Desethyl Isotonitazene, “Des-Iso”
Source:	Pinellas County Forensic Lab
Appearance:	Round Blue Pill → 

***Important Note**: All identifications were made based on evaluation of analytical data (GC-MS and LC-QTOF-MS) in comparison to analysis of acquired reference material.*

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2. CHEMICAL AND PHYSICAL DATA

2.1 CHEMICAL DATA

Form	Chemical Formula	Molecular Weight	Molecular Ion $[M^+]$	Exact Mass $[M+H]^+$
Base	$C_{21}H_{26}N_4O_3$	382.5	382	383.2078

3. BRIEF DESCRIPTION

N-Desethyl Isotonitazene is classified as a novel opioid of the 2-benzyl benzimidazole sub-class and is structurally dissimilar from fentanyl. Novel opioids have been reported to cause psychoactive effects similar to heroin, fentanyl, and other opioids. Novel opioids have also caused adverse events, including death, as described in the literature. *N*-Desethyl Isotonitazene is a known metabolite of isotonitazene[1]; however, it is now being manufactured and distributed as a parent drug on its own, which has been observed through sales on online gray market sites and demonstrated through the detection of this drug without isotonitazene in drug materials. Etonitazene and its analogue synthetic opioids were first synthesized and reported in the literature in the 1950s.[2] Data suggest that this group of analogues can have potency similar to or greater than fentanyl.[3,4] *In vitro* data shows that *N*-desethyl isotonitazene is similar in potency to etonitazene, and approximately 20 times more potent than fentanyl.[4] Structurally similar drugs include isotonitazene and other nitazene analogues. *N*-Desethyl Isotonitazene is not explicitly scheduled in the United States; however, etonitazene, isotonitazene, and other nitazene analogues are designated as Schedule I substances.

4. ADDITIONAL RESOURCES

1. Krotulski, AJ, Papsun, DM, Kacinko, SL, and Logan, BK. (2020) Isotonitazene Quantitation and Metabolite Discovery in Authentic Forensic Casework. *J. Anal. Toxicol*. **44** (6), 521–530. https://academic.oup.com/jat/article/44/6/521/5753838

2. Hunger, A; Kebrle, J; Rossi, A; Hoffmann, K. (1957) Synthesis of analgesically active benzimidazole derivatives with basic substitutions. *Experientia*, **13**, 400-401. https://link.springer.com/article/10.1007/BF02161116

3. Hoffmann, K; Hunger, A; Rossi, A. (1960). "Patent US2935514A – Benzimidazoles." https://patents.google.com/patent/US2935514A/en

4. Vandeputte, MM; Van Uytfanghe, K; Layle, NK; St. Germaine, DM; Iula, DM; Stove , CP. (2021) Synthesis, Chemical Characterization, and μ-Opioid Receptor Activity Assessment of the Emerging Group of "Nitazene" 2-Benzylbenzimidazole Synthetic Opioids. *ACS Chem. Neurosci*. **12**, 7, 1241–1251. https://pubs.acs.org/doi/10.1021/acschemneuro.1c00064

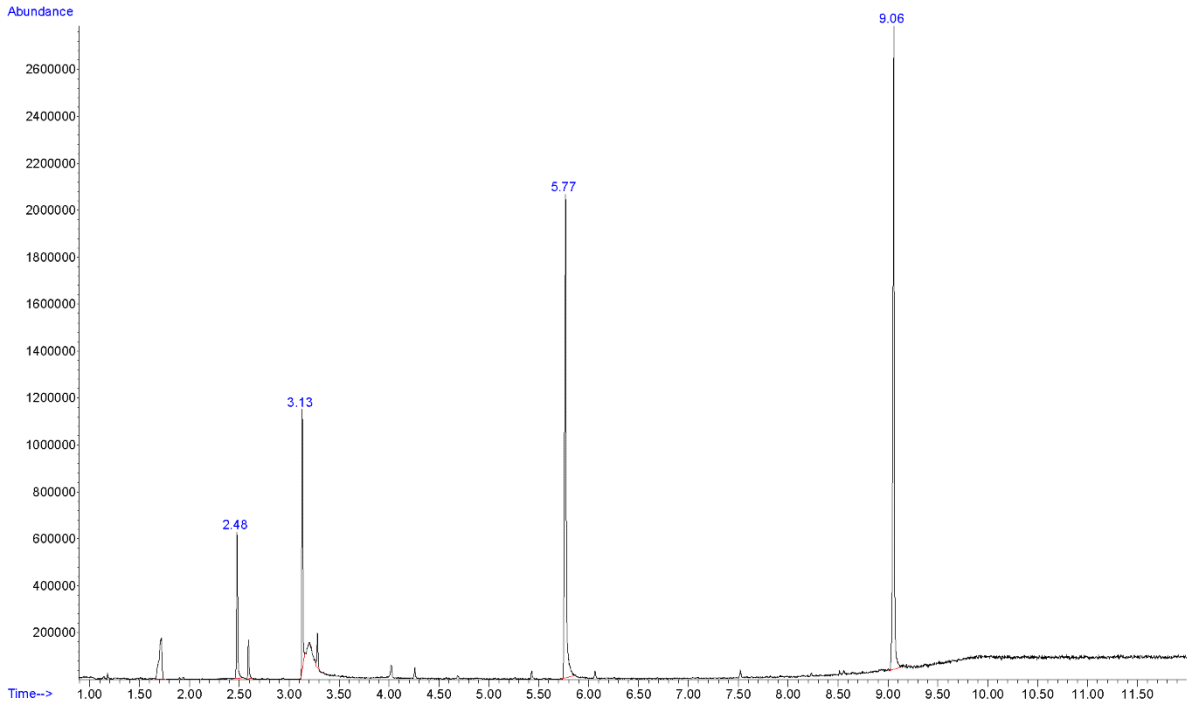
https://www.caymanchem.com/product/30216/n-desethyl-isotonitazene-(hydrochloride)

5. QUALITATIVE DATA

5.1 GAS CHROMATOGRAPHY MASS SPECTROMETRY (GC-MS)

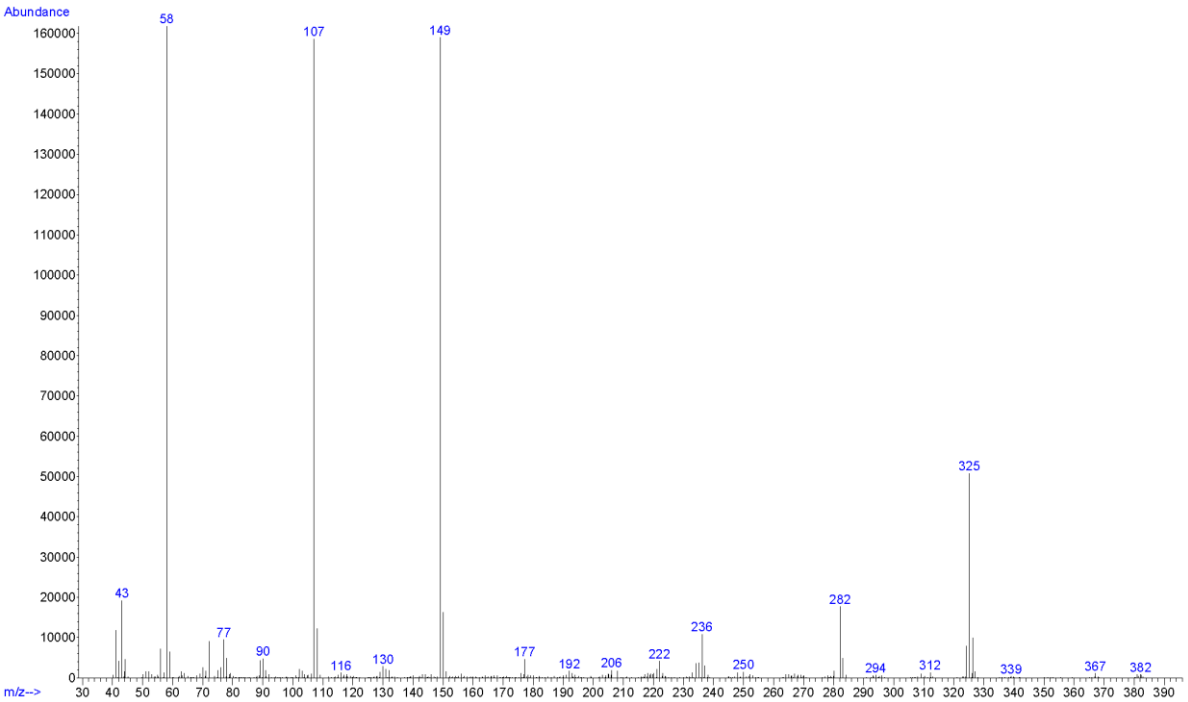
Testing Performed At:	The Center for Forensic Science Research and Education at the Fredric Rieders Family Foundation (Willow Grove, PA)
Sample Preparation:	Dilution in methanol
Instrument:	Agilent 5975 Series GC/MSD System
Column:	Agilent J&W DB-1 (12 m x 200 µm x 0.33 µm)
Carrier Gas:	Helium (Flow: 1.46 mL/min)
Temperatures:	Injection Port: 265 °C, Transfer Line: 300 °C MS Source: 230 °C, MS Quad: 150 °C, Oven Program: 50 °C for 0 min, 30 °C/min to 340 °C for 2.3 min
Injection Parameters:	Injection Type: Splitless, Injection Volume: 1 µL
MS Parameters:	Mass Scan Range: 40-550 m/z Threshold: 250
Retention Time:	9.06 min
Standard Comparison:	Reference material for *N*-desethyl isotonitazene (Batch: 0588587-1) was purchased from Cayman Chemical (Ann Arbor, MI, USA). Analysis of this standard resulted in positive identification of the analyte in the exhibit as *N*-desethyl isotonitazene based on retention time (9.05 min) and mass spectral data. (https://www.caymanchem.com/product/30216/n-desethyl-isotonitazene-(hydrochloride))

Chromatogram: *N*-Desethyl Isotonitazene



Additional peaks in chromatogram: not a controlled substance (2.48 mins) and internal standards (3.13 and 5.77 mins)

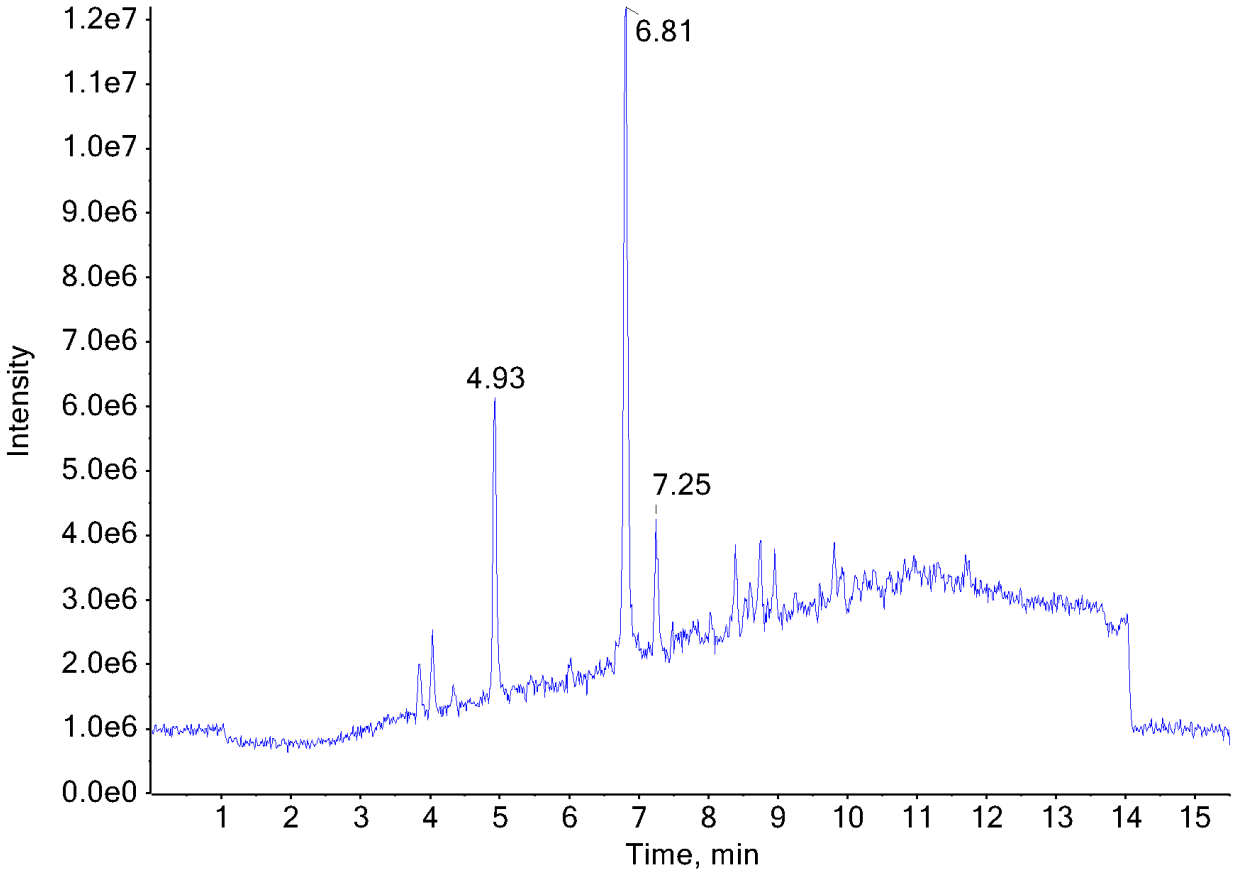
EI (70 eV) Mass Spectrum: *N*-Desethyl Isotonitazene



5.2 LIQUID CHROMATOGRAPHY QUADRUPOLE TIME OF FLIGHT MASS SPECTROMETRY (LC-QTOF-MS)

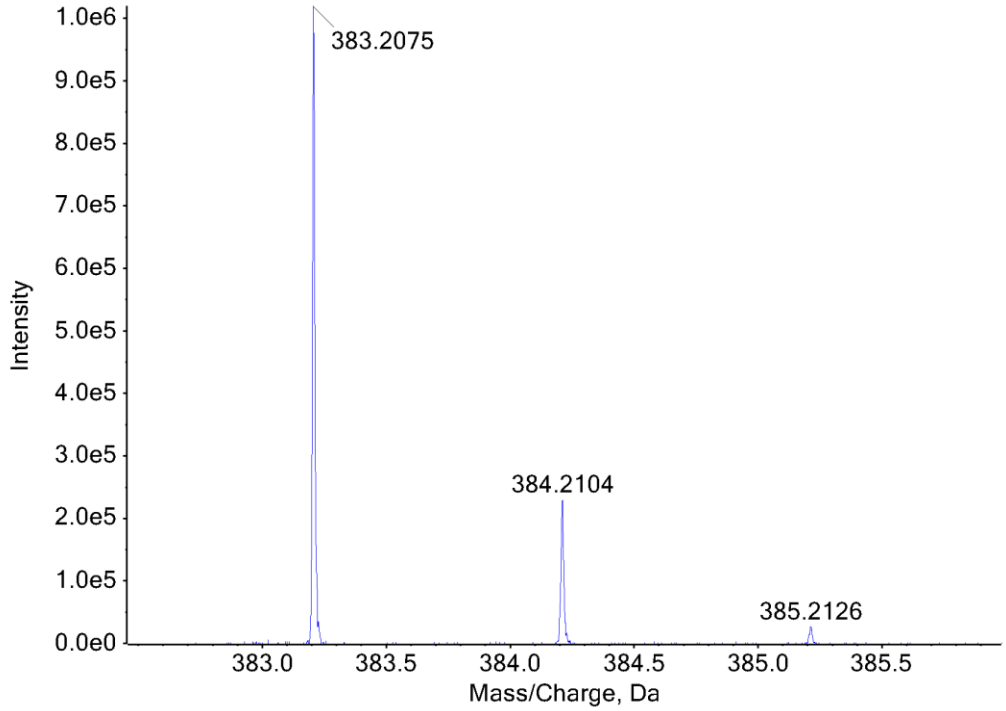
Testing Performed At:	The Center for Forensic Science Research and Education at the Fredric Rieders Family Foundation (Willow Grove, PA)
Sample Preparation:	Dilution in methanol followed by 1:100 dilution of GC-MS sample in mobile phase (CFSRE)
Instrument:	Sciex TripleTOF® 5600+, Shimadzu Nexera XR UHPLC
Column:	Phenomenex® Kinetex C18 (50 mm x 3.0 mm, 2.6 µm)
Mobile Phase:	A: Ammonium formate (10 mM, pH 3.0)
	B: Methanol/acetonitrile (50:50)
	Flow rate: 0.4 mL/min
Gradient:	Initial: 95A:5B; 5A:95B over 13 min; 95A:5B at 15.5 min
Temperatures:	Autosampler: 15 °C
	Column Oven: 30 °C
	Source Heater: 600 °C
Injection Parameters:	Injection Volume: 10 µL
QTOF Parameters:	TOF MS Scan Range: 100-510 Da
	Precursor Isolation: SWATH® acquisition (27 windows)
	Fragmentation: Collison Energy Spread (35±15 eV)
	MS/MS Scan Range: 50-510 Da
Retention Time:	6.81 min
Standard Comparison:	Reference material for *N*-desethyl isotonitazene (Batch: 0588587-1) was purchased from Cayman Chemical (Ann Arbor, MI, USA). Analysis of this standard resulted in positive identification of the analyte in the exhibit as *N*-desethyl isotonitazene based on retention time (6.84 min) and mass spectral data. (https://www.caymanchem.com/product/30216/n-desethyl-isotonitazene-(hydrochloride))

Chromatogram: *N*-Desethyl Isotonitazene

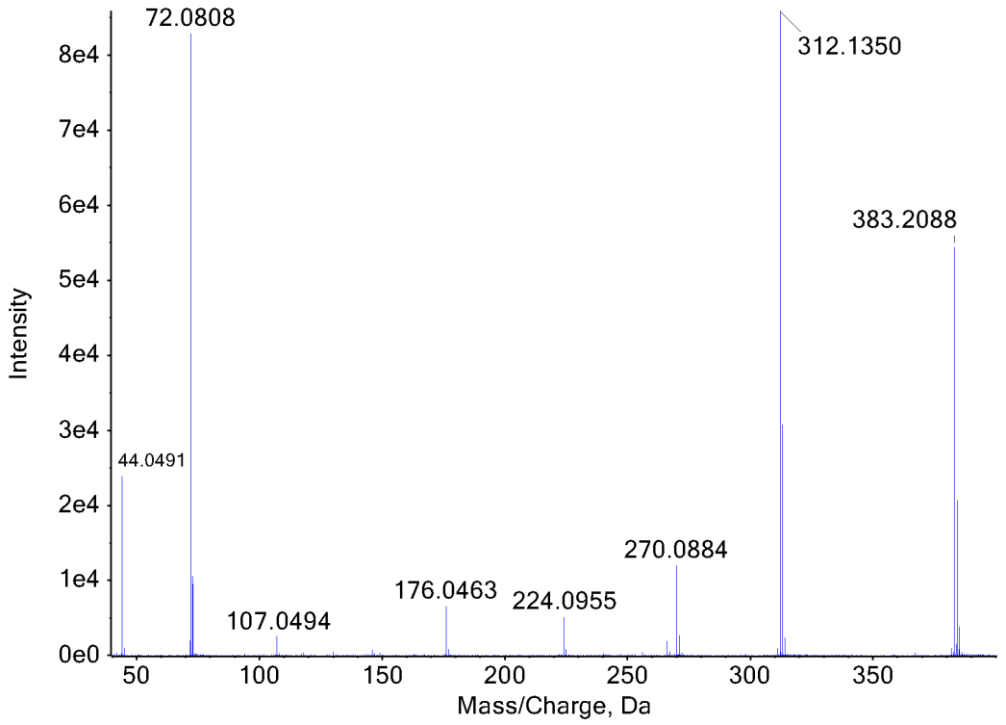


Additional peaks in chromatogram: internal standards (4.93 and 7.25 mins)

TOF MS Spectra: *N*-Desethyl Isotonitazene



TOF MS/MS Spectra: *N*-Desethyl Isotonitazene



5.3 GAS CHROMATOGRAPHY INFRARED SPECTROSCOPY (GC-IR)

Testing Performed At: Pinellas County Forensic Lab (Largo, FL)

Sample Preparation: Dilution in methylene chloride

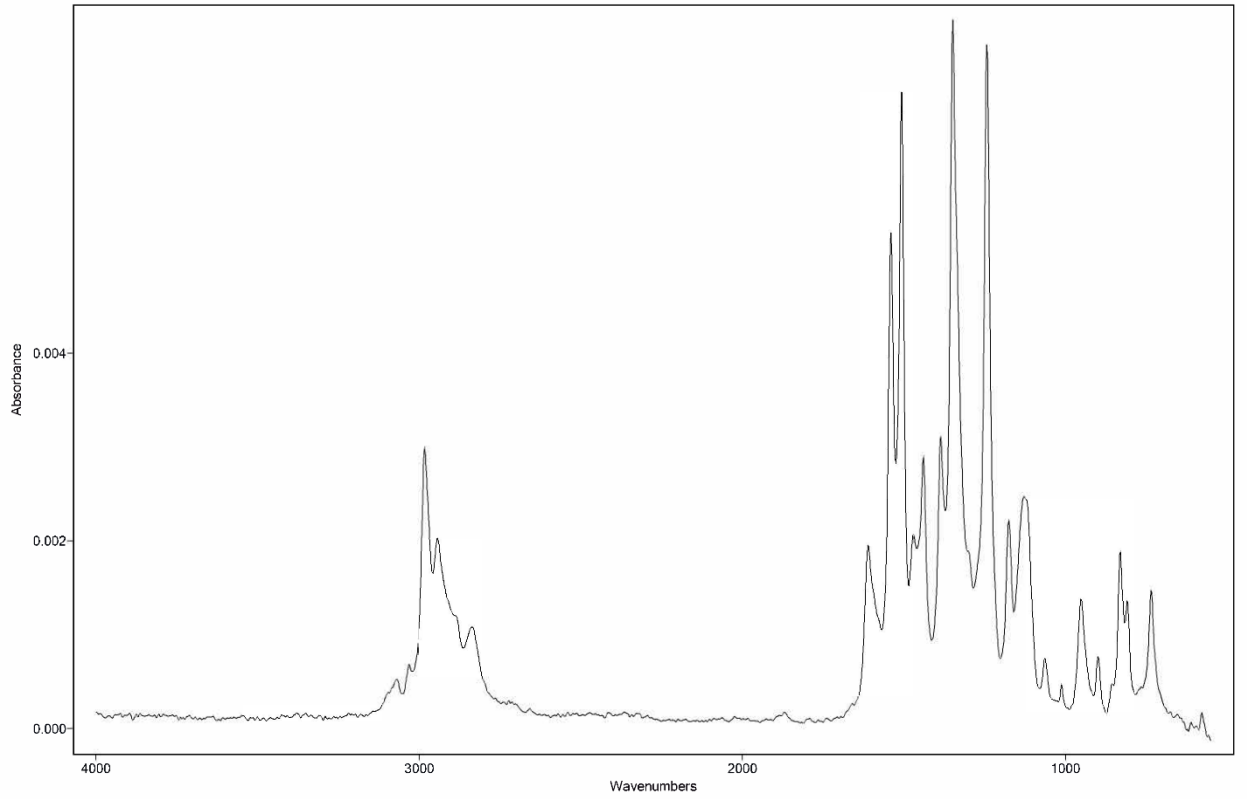
Instrument: Agilent 7890B GC ASAP IRD3

Temperatures: Injector 250 °C, Lightpipe 250 °C, Transfer Lines 275 °C

Oven Program: 80 °C for 1.2 min, 30 °C/min to 320 °C for 4.0 min

Injection Parameters: Injection Type: Splitless, Injection Volume: 1 µL

IR Spectrum: *N*-Desethyl Isotonitazene



6. FUNDING

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