

Supporting Information

Molecular modelling, synthesis, and biological evaluations of a 3,5-disubstituted isoxazole fatty acid analogue as a PPAR α -selective agonist

Henriette Arnesen¹, Nadia Alazraq¹, Jørn E. Tungen², Helen Södling¹, Jason Matthews¹, Steinar M. Paulsen³, Hilde Nebb¹, Ingebrigt Sylte⁴, Trond V. Hansen² and Thomas Sæther^{1,5}

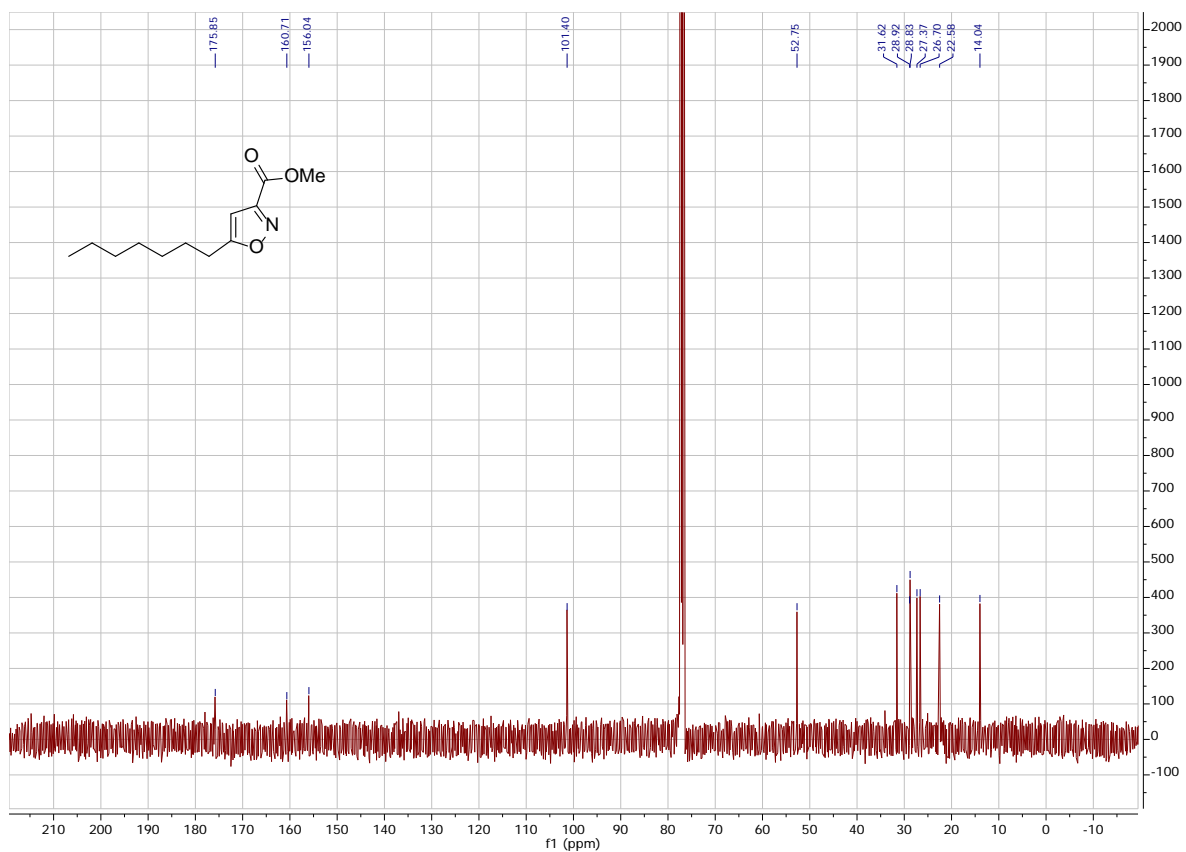
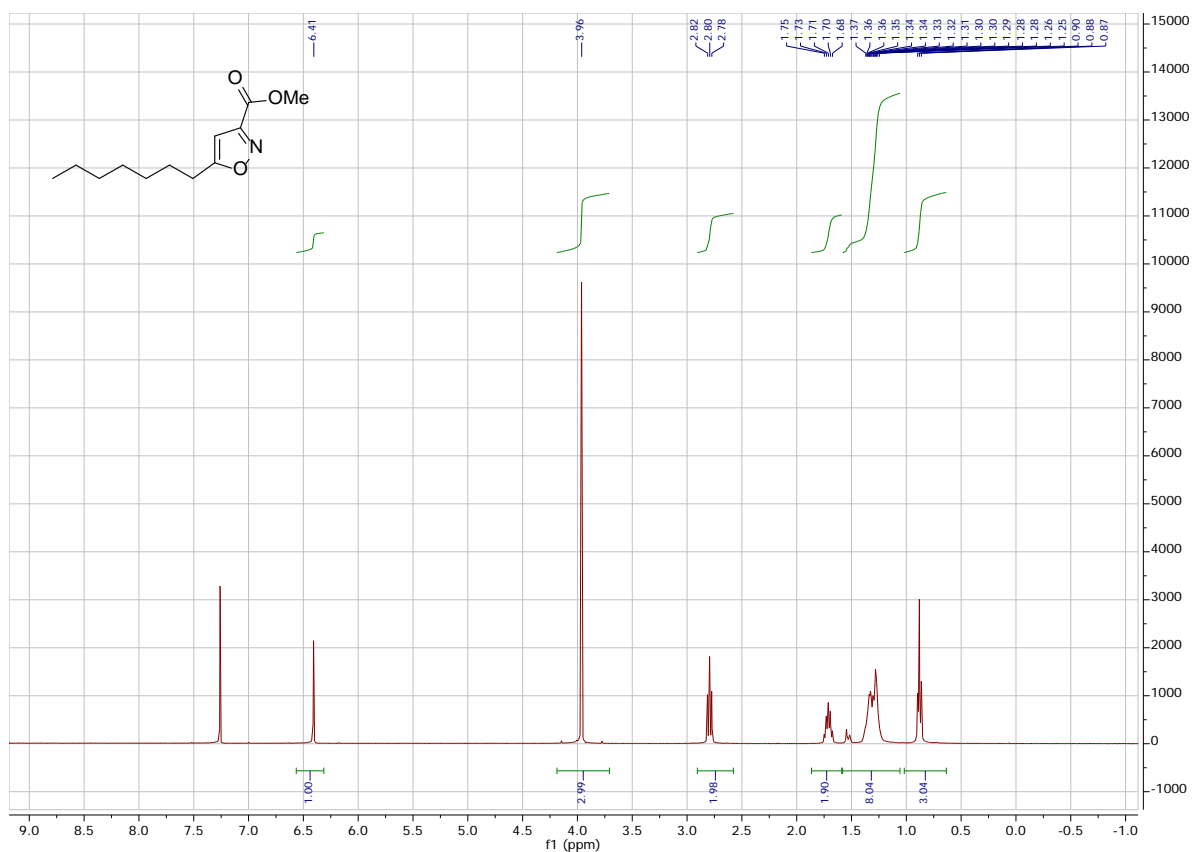
¹Department of Nutrition, Institute of Basic Medical Sciences, University of Oslo, N-0317 Oslo, Norway

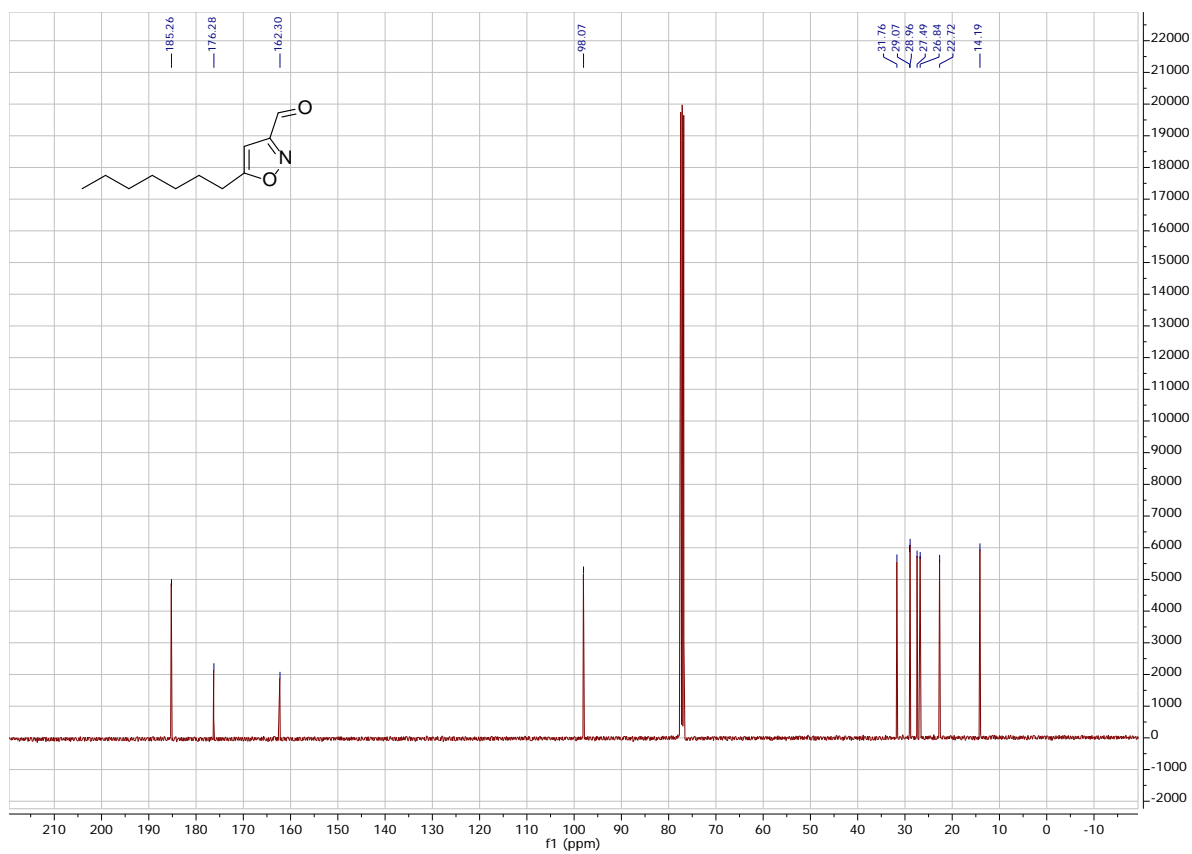
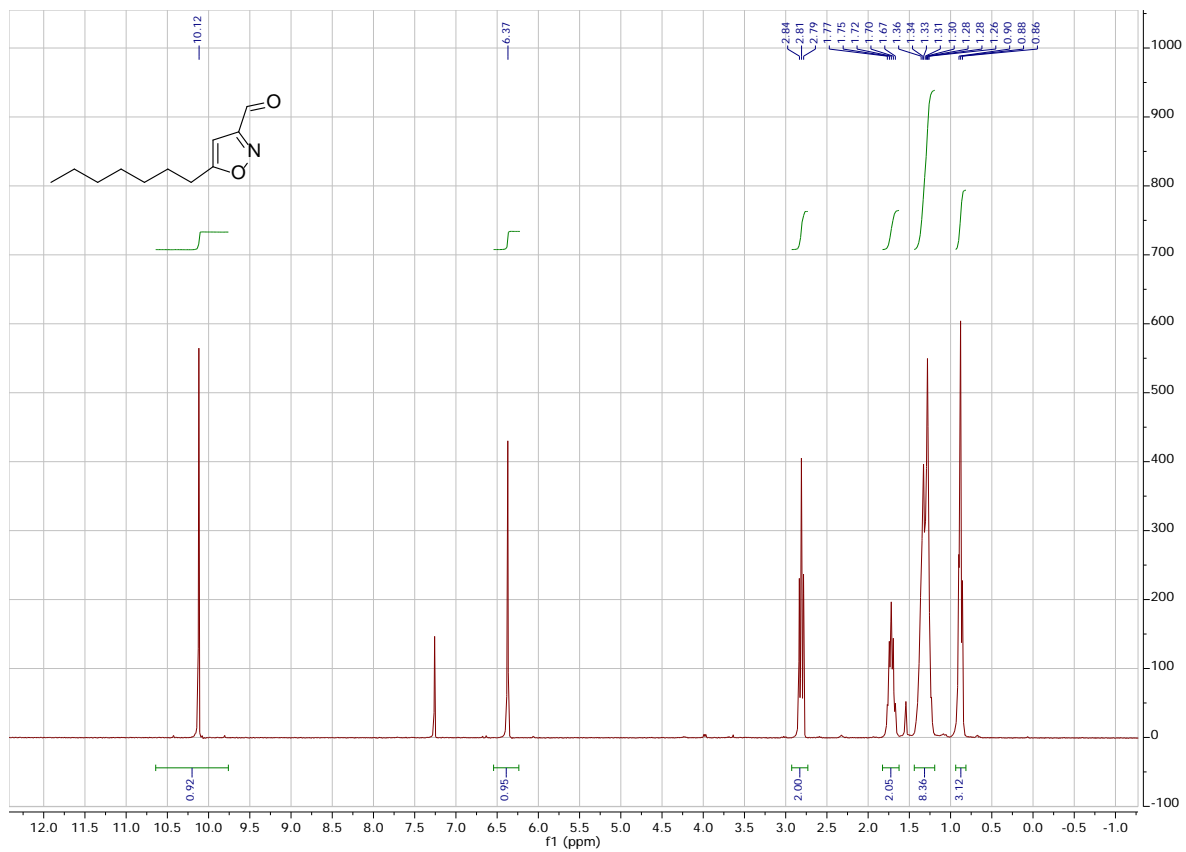
²Department of Pharmaceutical Chemistry, School of Pharmacy, University of Oslo, N-0316 Oslo, Norway

³MabCent-SFI, UiT – The Arctic University of Norway, N-9037 Tromsø, Norway

⁴Department of Medical Biology, Faculty of Health Sciences, UiT – The Arctic University of Norway, N-9037 Tromsø, Norway

⁵Department of Molecular Medicine, Institute of Basic Medical Sciences, University of Oslo, N-0317 Oslo, Norway





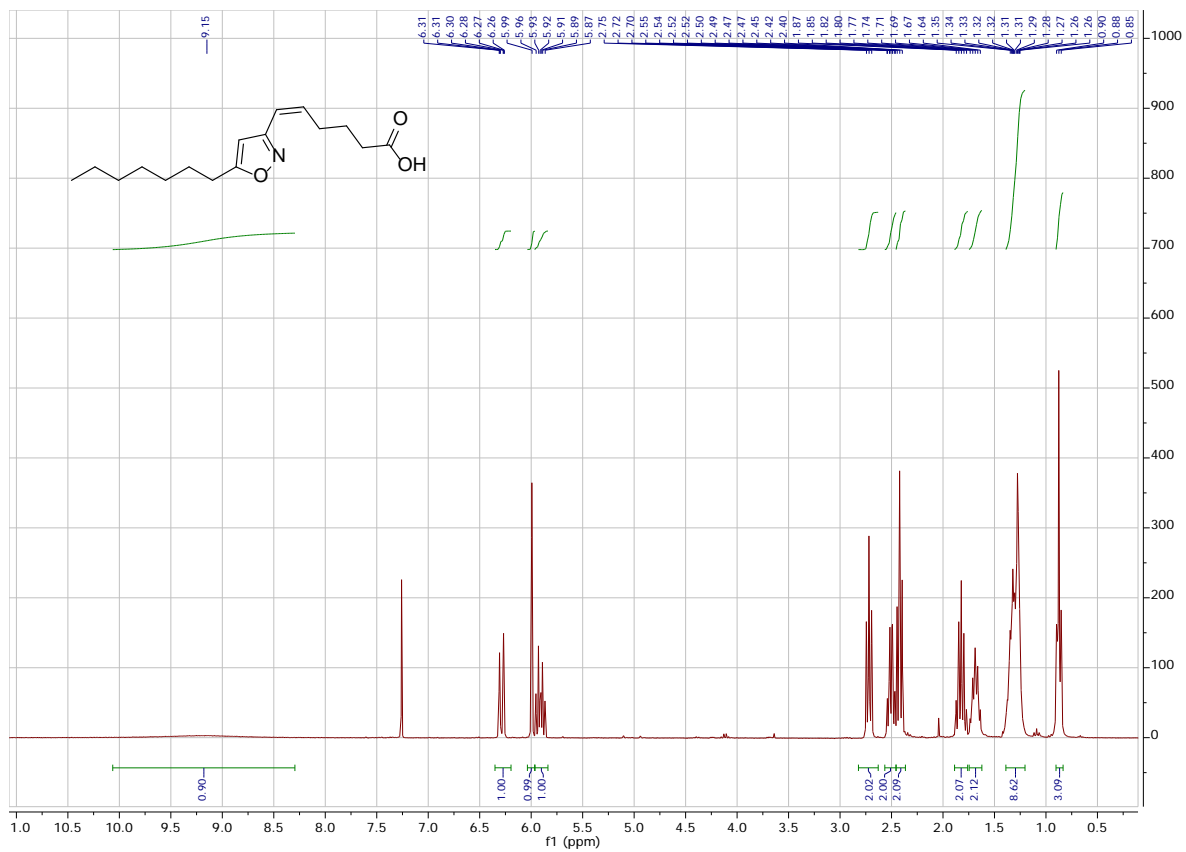


Fig S5. ¹H NMR spectrum of compound 9 in CDCl₃ (300 MHz)

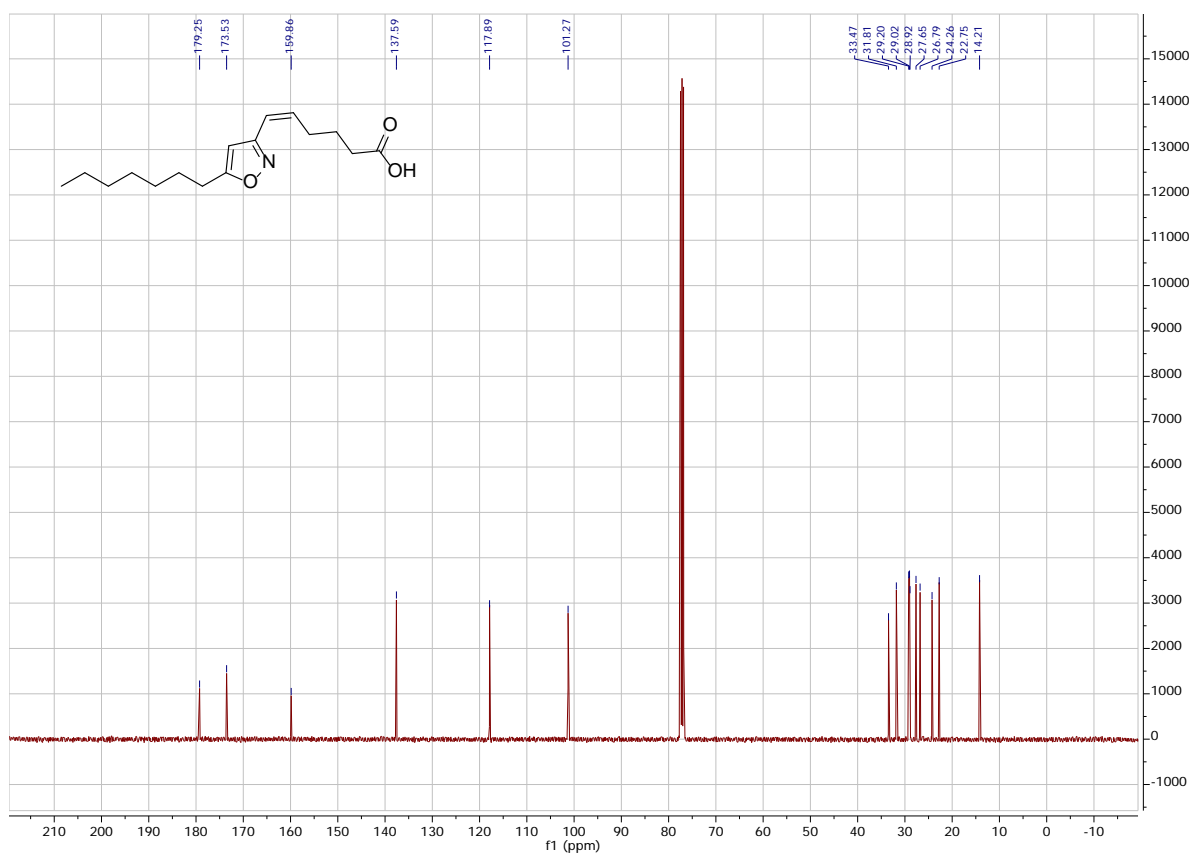


Fig S6. ¹³C NMR spectrum of compound 9 in CDCl₃ (101 MHz)

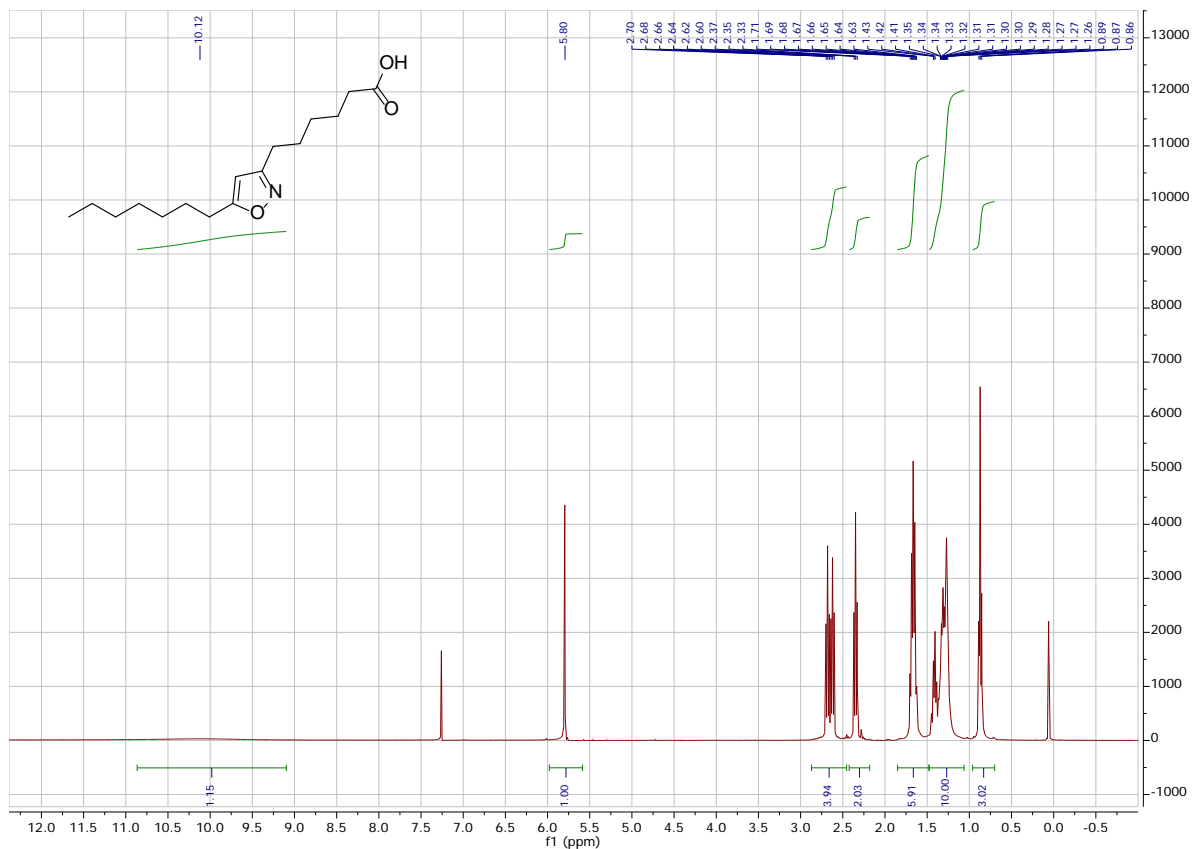


Fig S7. ^1H NMR spectrum of compound **1** in CDCl_3 (400 MHz)

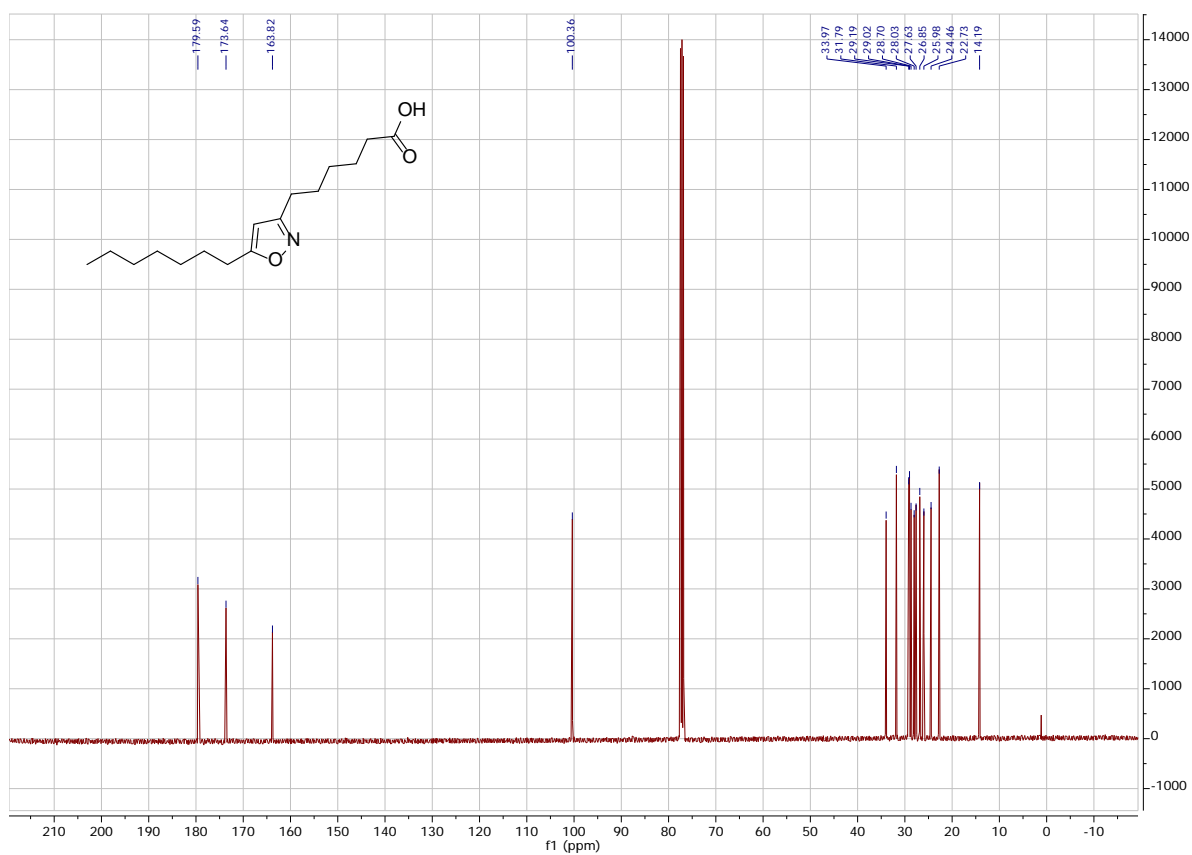


Fig S8. ^{13}C NMR spectrum of compound **1** in CDCl_3 (101 MHz)

Elemental Analysis Report

Analysis Info

Sample Name

Method

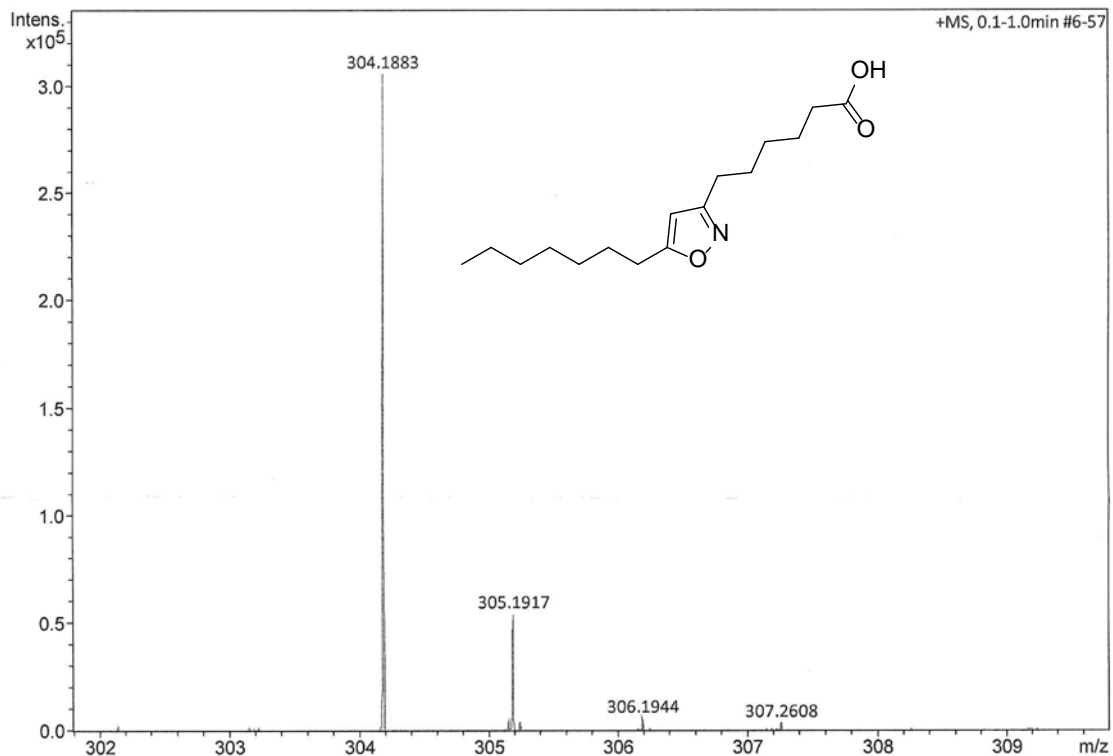
ESI_pos_50_1500_os.m

Acquisition Date 11/22/2018 10:32:17 AM

Analysis Name D:\Data\maxis2018\146706.d

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	3500 V	Set Dry Heater	200 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1500 m/z	Set Charging Voltage	2000 V	Set Divert Valve	Waste
		Set Corona	0 nA	Set APCI Heater	0 °C



Meas. m/z	Ion Formula	m/z	err [ppm]
304.1883	C14H22N7O	304.1880	-0.9
	C16H27NNaO3	304.1883	0.0
	C14H25N4NaO2	304.1870	-4.4
	C12H20N10	304.1867	-5.3
	C16H24N4O2	304.1894	3.5
	C15H28O6	304.1880	-0.9
	C13H26N3O5	304.1867	-5.3
	C18H26NO3	304.1907	7.9

Fig S9. HRMS ESI⁺ spectrum of compound **1** in CH₂Cl₂/MeOH (95:5)

Table S1. Human SYBR green RT-qPCR primers

Name	Full Name	Accession Number	5' – 3' Sequence
<i>TBP-F</i>	TATA box binding protein, transcript variant 1	NM_003194.4	TTGTACCGCAGCTGCAAAAT
<i>TBP-R</i>	TATA box binding protein, transcript variant 1	NM_003194.4	TATATTCGGCGTTTCGGGCA
<i>CPT1A-F</i>	Carnitine palmitoyltransferase 1A (liver)	NM_001876.3	CAGGAGACAGAGTTCCTGG
<i>CPT1A-R</i>	Carnitine palmitoyltransferase 1A (liver)	NM_001876.3	TCTAACGTCACGAAGAACGCT
<i>PPARA-F</i>	Peroxisome proliferator-activated receptor alpha	NM_001001928.2	TCGGCGAGGATAGTTCTGGA
<i>PPARA-R</i>	Peroxisome proliferator-activated receptor alpha	NM_001001928.2	TGAAAGCGTGTCCGTGATGA
<i>SCD-F</i>	Stearoyl-CoA desaturase	NM_005063.4	ACACCCAGCTGTCAAAGAGA
<i>SCD-R</i>	Stearoyl-CoA desaturase	NM_005063.4	GCCAGGTTTGTAGTACCTCCTC
<i>SREBF1-F</i>	Sterol regulatory element binding transcription factor 1	NM_001005291.2	CCGCTCCTCCATCAATGACA
<i>SREBF1-R</i>	Sterol regulatory element binding transcription factor 1	NM_001005291.2	GCTGTGTTGCAGAAAGCGAA
<i>PPARG-F</i>	Peroxisome proliferator-activated receptor gamma	NM_015869.4	ACAGATCCAGTGGTTGCAGA
<i>PPARG-R</i>	Peroxisome proliferator-activated receptor gamma	NM_015869.4	TCCACTTTGATTGCACTTTGGT
<i>CEBPA-F</i>	CCAAT/enhancer binding protein (C/EBP), alpha	NM_001287424.1	CCCAGAGGGACCGGAGTTAT
<i>CEBPA-R</i>	CCAAT/enhancer binding protein (C/EBP), alpha	NM_001287424.1	AGACGCGCACATTCACATTG
<i>ACSL1-F</i>	Acyl-CoA synthetase long-chain family member 1	NM_001286708.1	CTTCTGGTACGCCACGAGAC
<i>ACSL1-R</i>	Acyl-CoA synthetase long-chain family member 1	NM_001286708.1	GTCGCTGTCAAGTAGTGCG
<i>CD36-F</i>	CD36 molecule (thrombospondin receptor)	NM_000072.3	CCTGGCTGTGTTTGGAGGTAT
<i>CD36-R</i>	CD36 molecule (thrombospondin receptor)	NM_000072.3	CTTCGAGGACAACCTTGCTTTT
<i>FABP4-F</i>	Fatty acid binding protein 4, adipocyte	NM_001442.2	ATGGGGGTGTCCTGGTACAT
<i>FABP4-R</i>	Fatty acid binding protein 4, adipocyte	NM_001442.2	TCGTGGAAGTGACGCCTTTC
<i>PLIN1-F</i>	Perilipin 1, transcript variant 1	NM_002666	GACAAGGAAGAGTCAGCCCC
<i>PLIN1-R</i>	Perilipin 1, transcript variant 1	NM_002666	GAGAGGGTGTGGTTCAGAGC
<i>ADIPOQ-F</i>	Adiponectin, C1Q and collagen domain containing	NM_001177800	AAGGAGATCCAGGTCTTATTGGT
<i>ADIPOQ-R</i>	Adiponectin, C1Q and collagen domain containing	NM_001177800	GTTCTCCTTTCCTGCCTTGGA
<i>ANGPTL4 -F</i>	Angiopoietin-like 4, transcript variant 1	NM_139314.2	TCCACCGACCTCCCCTTAG
<i>ANGPTL4-R</i>	Angiopoietin-like 4, transcript variant 1	NM_139314.2	GGCCACCTTGTGGAAGAGTT

Table S2. Mouse SYBR green RT-qPCR primers

Name	Full Name	Accession Number	5' – 3' Sequence
<i>Tbp-F</i>	TATA box binding protein	NM_013684.3	GCACAGGAGCCAAGAGTGAA
<i>Tbp-R</i>	TATA box binding protein	NM_013684.3	TAGCTGGGAAGCCCAACTTC
<i>Cpt1a-F</i>	Carnitine palmitoyltransferase 1a, liver	NM_013495.2	GGGCCATCTGTGGGAGTATG
<i>Cpt1a-R</i>	Carnitine palmitoyltransferase 1a, liver	NM_013495.2	ACTGTAGCCTGGTGGGTTTG
<i>Ppara-F</i>	Peroxisome proliferator activated receptor alpha	NM_011144.6	CAACAACCCGCCTTTTGTCA
<i>Ppara-R</i>	Peroxisome proliferator activated receptor alpha	NM_011144.6	TCTTTGTCTTCGACGCCGTT
<i>Scd1-F</i>	Stearoyl-Coenzyme A desaturase 1	NM_009127.4	AAAGCCGAGAAGCTGGTGAT
<i>Scd1-R</i>	Stearoyl-Coenzyme A desaturase 1	NM_009127.4	TACAAAAGTCTCGCCCCAGC
<i>Srebf1-F</i>	Sterol regulatory element binding transcription factor 1	NM_011480.3	GCACACAAAAGCAAATCACTG
<i>Srebf1-R</i>	Sterol regulatory element binding transcription factor 1	NM_011480.3	TCTCCACCACTTCGGGTTTC