

Supplementary Materials

Cardiovascular profile of xanthone-based 1,4 dihydropyridines bearing a lidoflazine pharmacophore fragment

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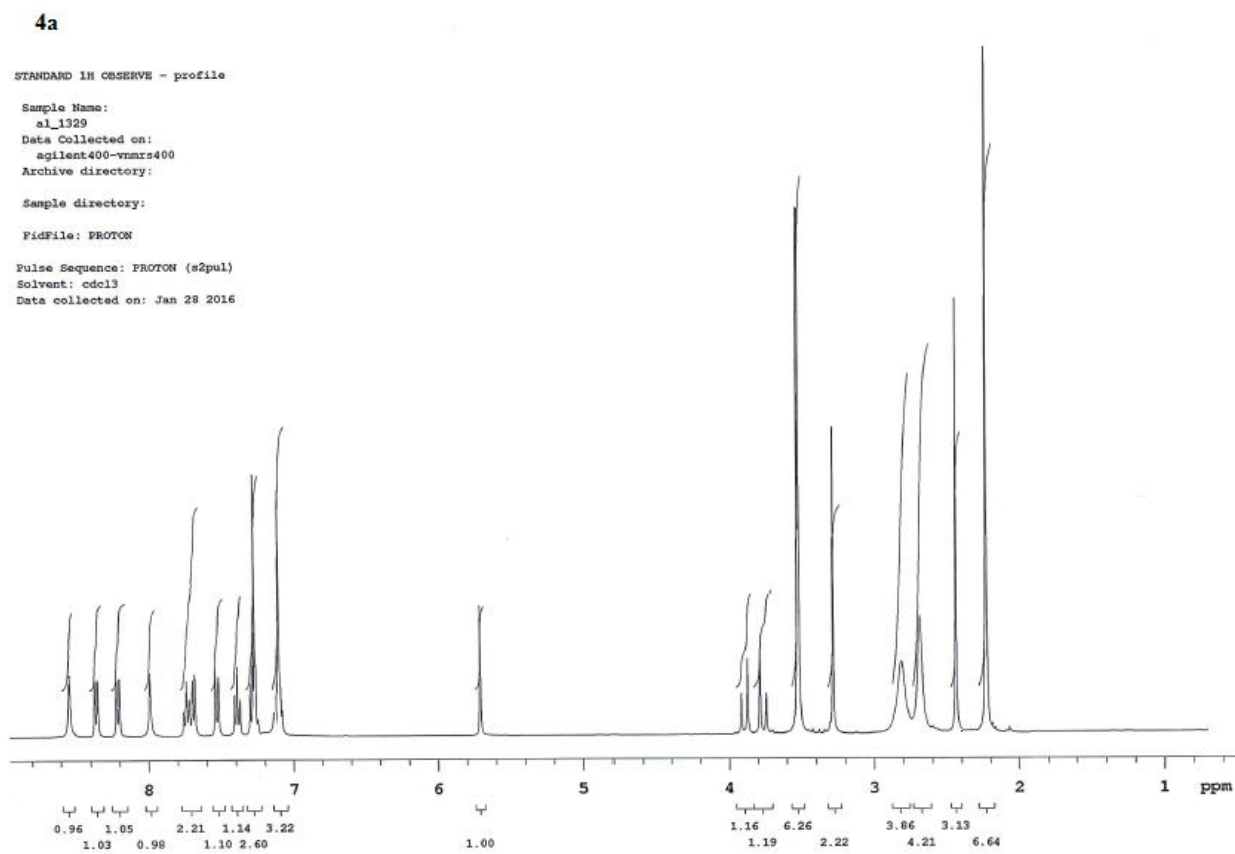
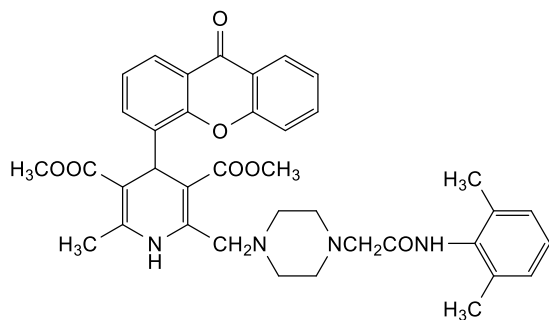
Table S1. Activity of Tested Compounds on K⁺-depolarized Guinea Pig Vascular Smooth Muscle.

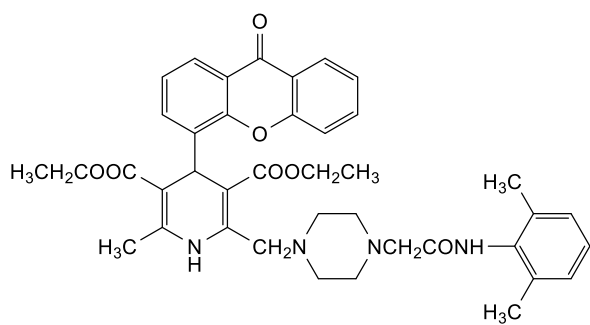
Cpd	Aorta		
	Activity ^d (m ± SEM)	IC ₅₀ ^e (μM)	95% conf lim (x10 ⁻⁶)
Nif.	82 ± 1.3 ^f	0.009	0.003–0.02
Lidofl	42 ± 1.7 ^g		
1^a	59 ± 4.9^g	0.76	0.69–0.85
2^a	7 ± 0.2		
3a^b	51 ± 2.2	2.18	1.88–2.36
4a	16 ± 0.7		
5a	20 ± 0.3		
3b^b	55 ± 1.6	1.04	0.78–1.37
4b	21 ± 1.3		
5b	48 ± 2.1		
3c^c	44 ± 3.4		
4c	6 ± 0.3		
5c	25 ± 2.0		
3d^c	31 ± 2.8		
4d	9 ± 0.9		
5d	36 ± 2.3		
3e^c	33 ± 2.5		
4e	9 ± 0.3		
5e	6 ± 0.2		

^aTaken from ref 1. ^bTaken from ref 2. ^cTaken from ref 3. ^dPercent inhibition of calcium-induced contraction on K⁺-depolarized (80 mM) guinea pig vascular smooth muscle (aortic strips) at 5x10⁻⁵ M. For compounds that reach the maximum intrinsic activity at concentrations different from those indicated in “d” the maximum active concentration is indicated with a specific superscribed letter. ^eCalculated from log concentration-response curves (Probit analysis by Litchfield and Wilcoxon [20])

with $n = 6-7$). When the maximum effect was $<50\%$, the IC_{50} values were not calculated. ^fAt 10^{-6} M. ^gAt 10^{-5} M. Bold: unpublished data. Conf lim: confidential limit.

Figure S1. 1H NMR spectra of new compounds.





4b

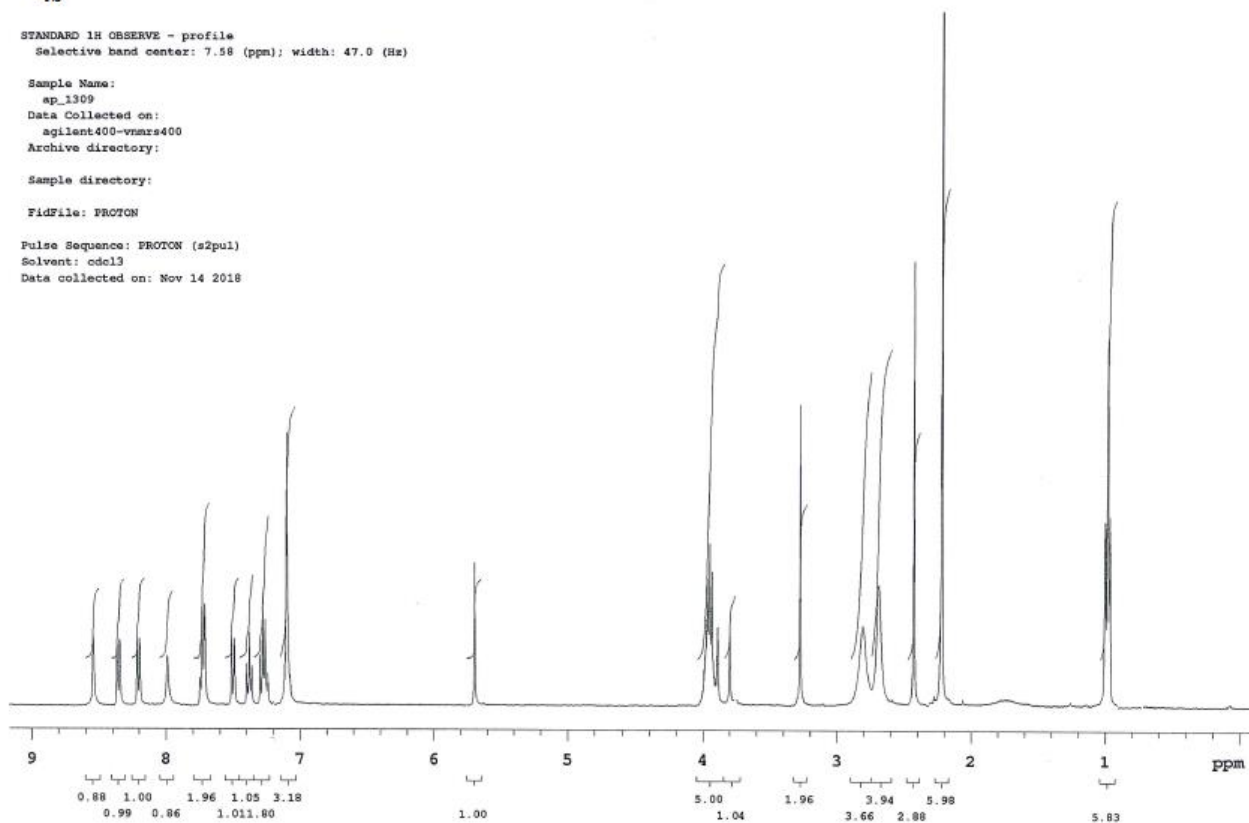
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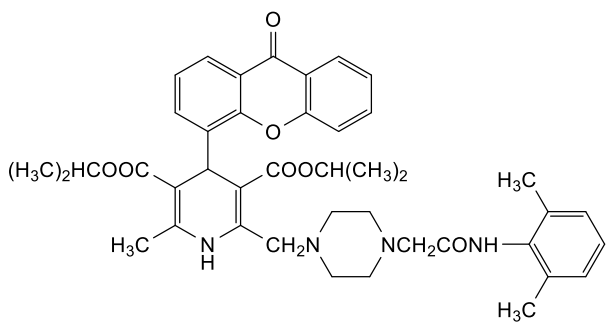
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Pulse Sequence: PROTON (s2pul)
 Solvent: cdcl3
 Data collected on: Nov 14 2018

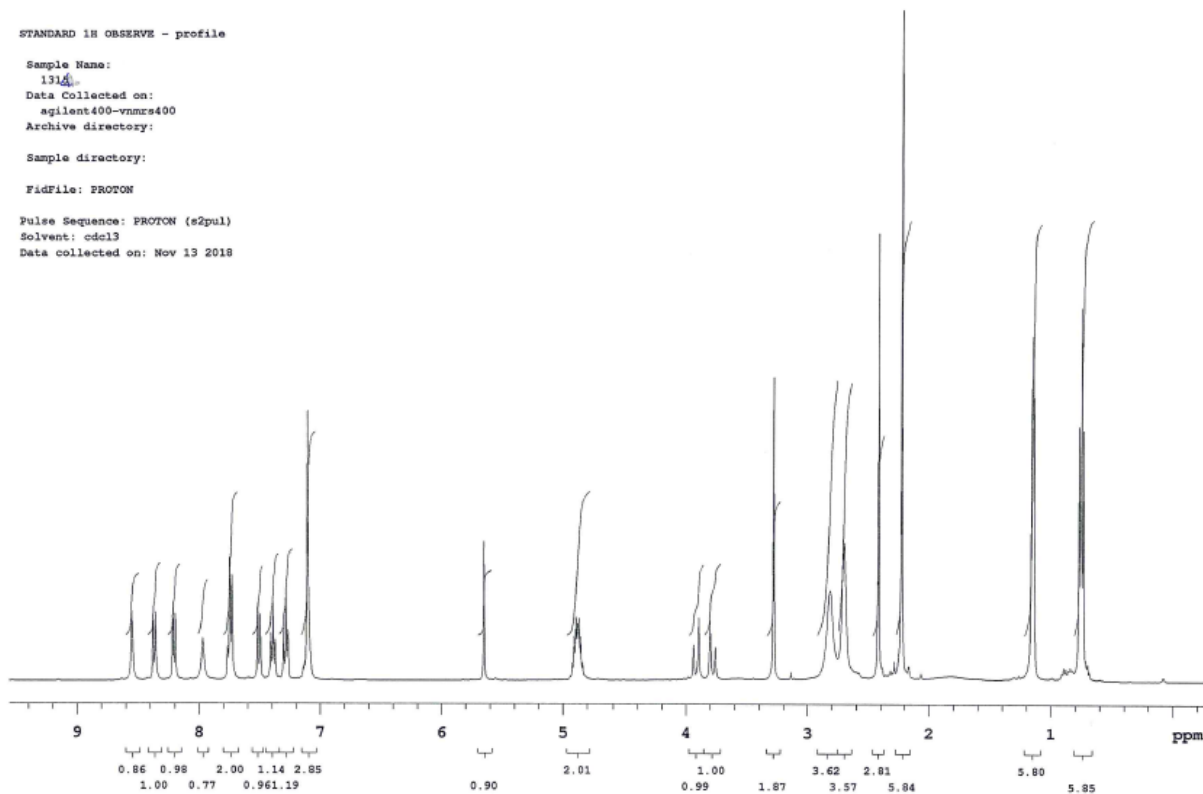


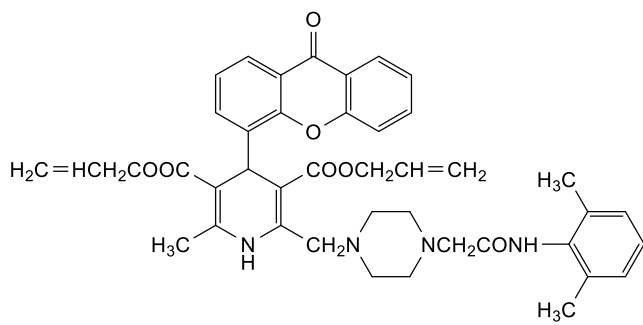


4c

STANDARD 1H OBSERVE - profile

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 Solvent: cdcl3
 Data collected on: Nov 13 2018

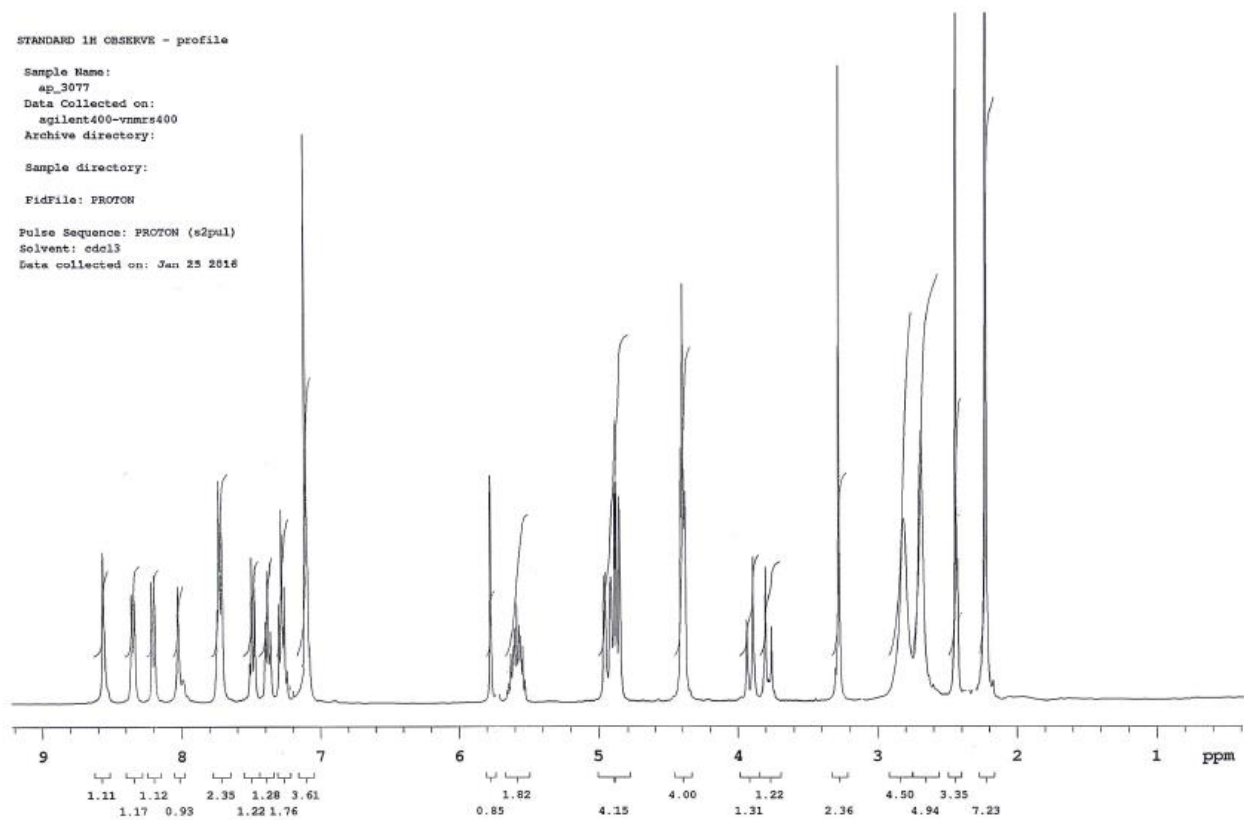


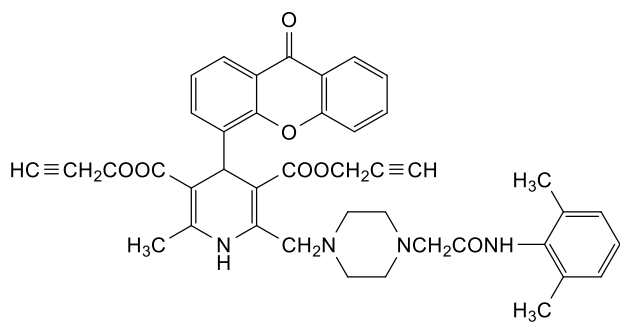


4d

STANDARD 1H OBSERVE - profile

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 Solvent: cdcl3
 Data collected on: Jan 23 2016

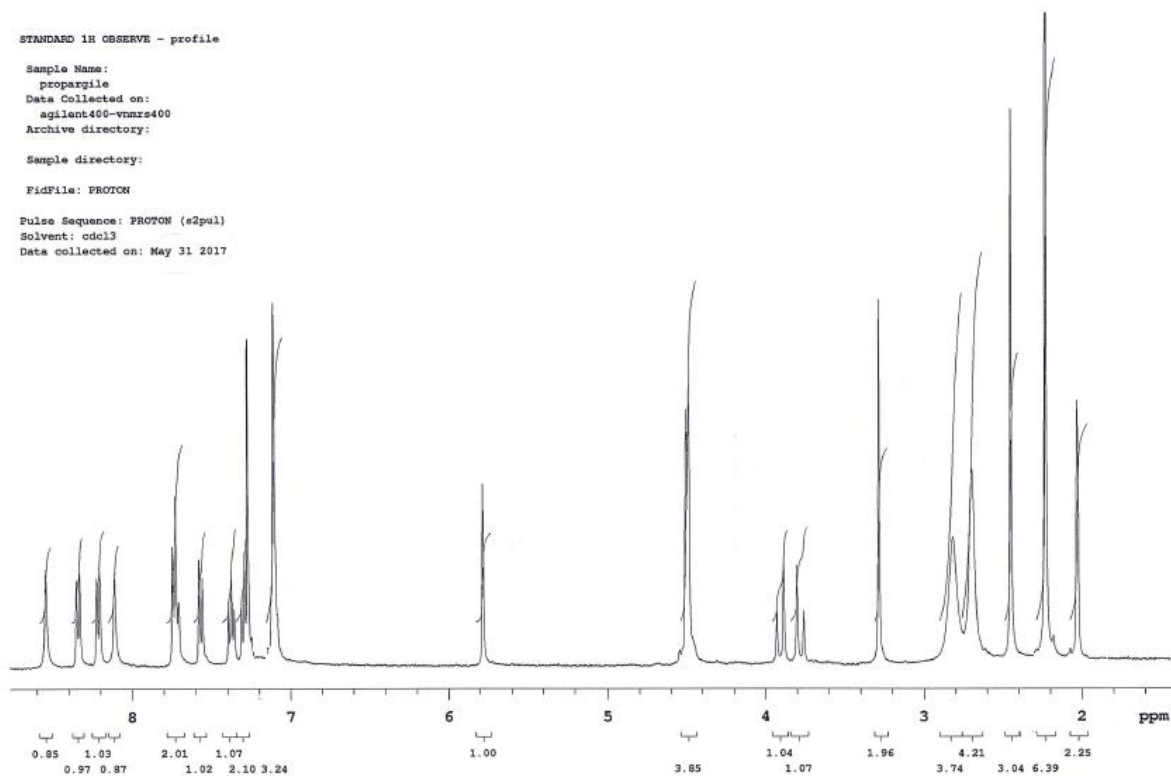


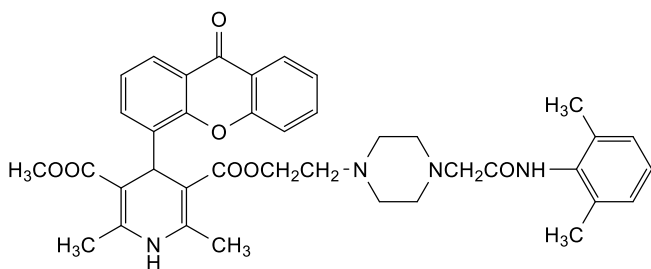


4e

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 Archive directory:
 Sample directory:
 FidFile: PROTON
 Pulse Sequence: PROTON (s2pul)
 Solvent: cdcl3
 Data collected on: May 31 2017

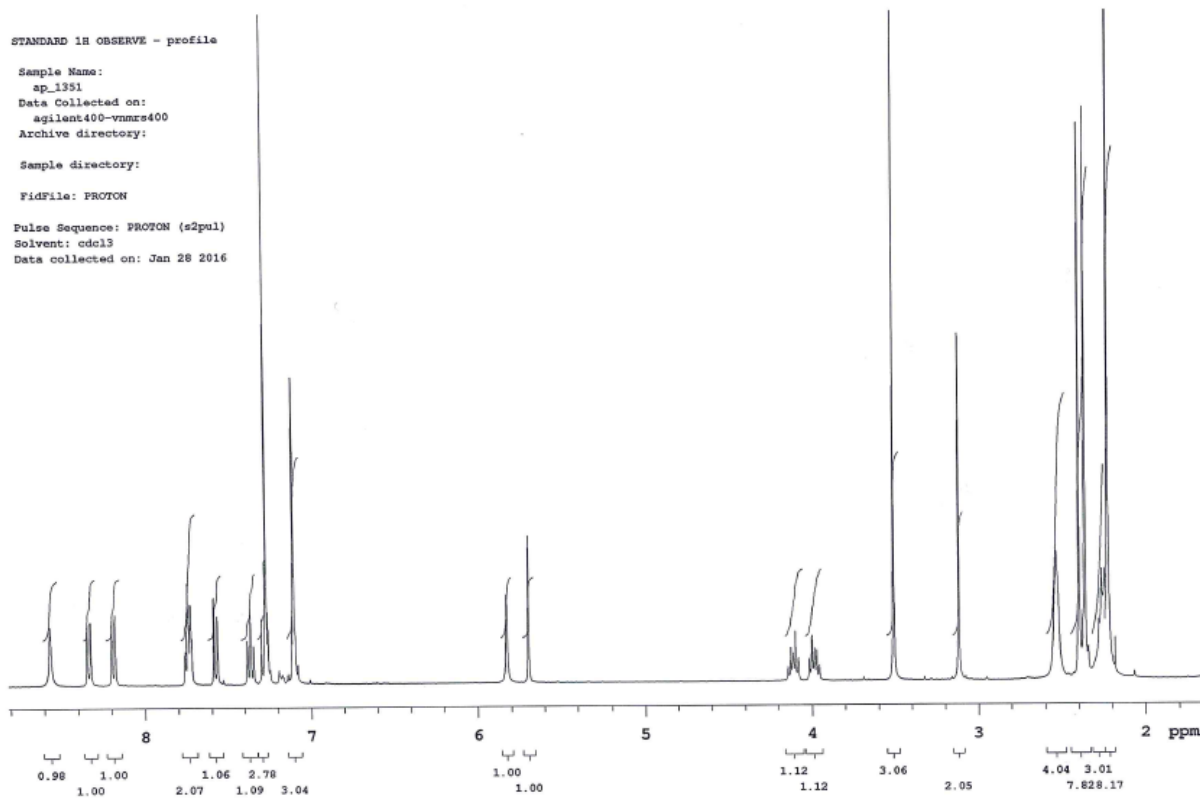


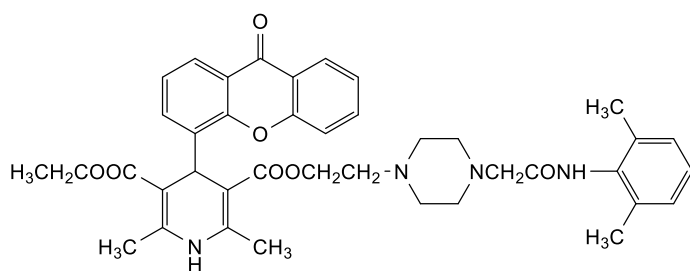


5a

STANDARD 1H OBSERVE - profile

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 Archive directory:
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 Pulse Sequence: PROTON (s2pul)
 Solvent: cdcl3
 Data collected on: Jan 28 2016





5b

PC147 LM

Sample Name:

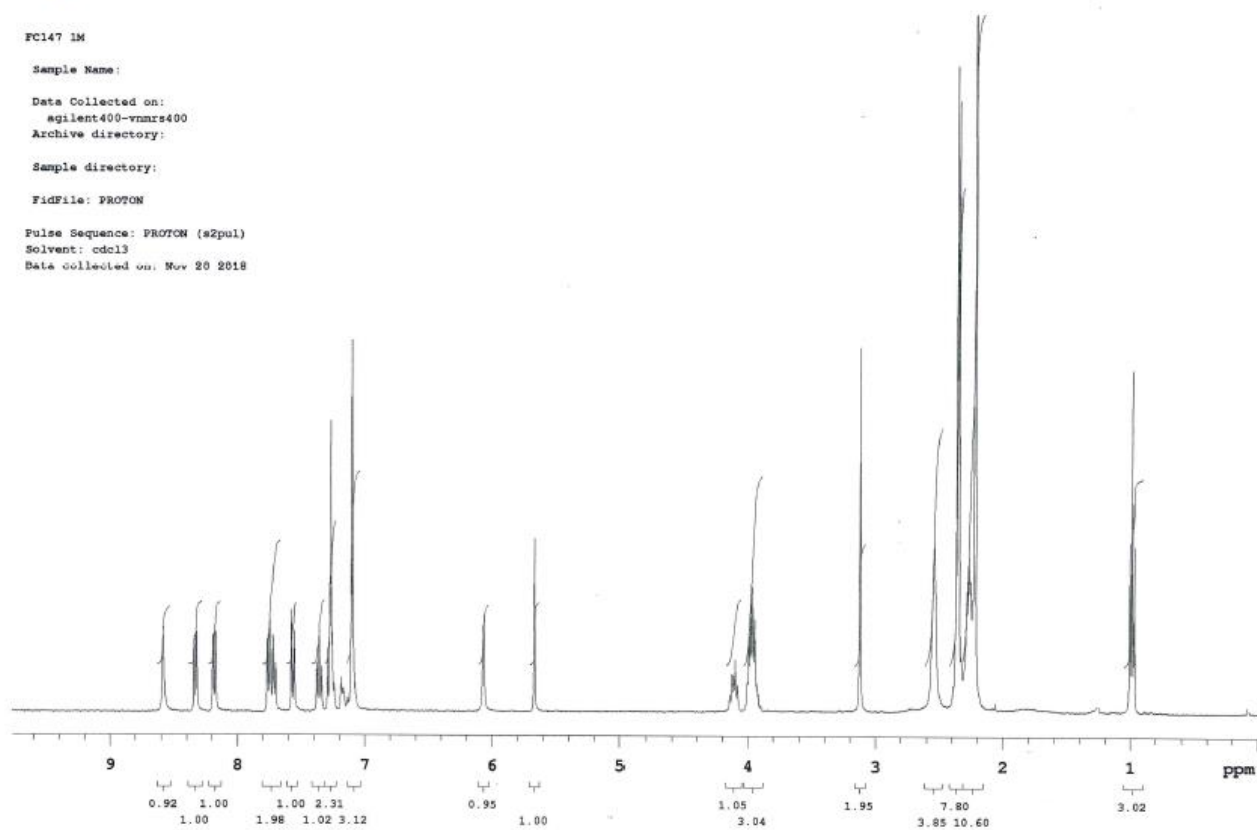
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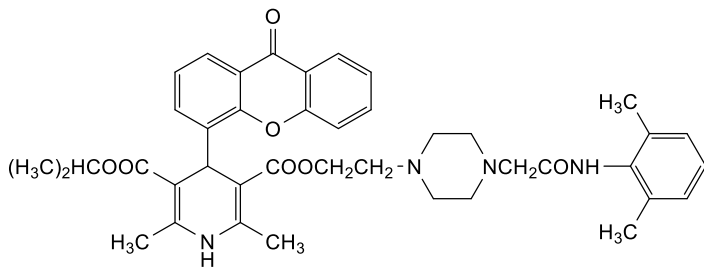
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Sample directory:

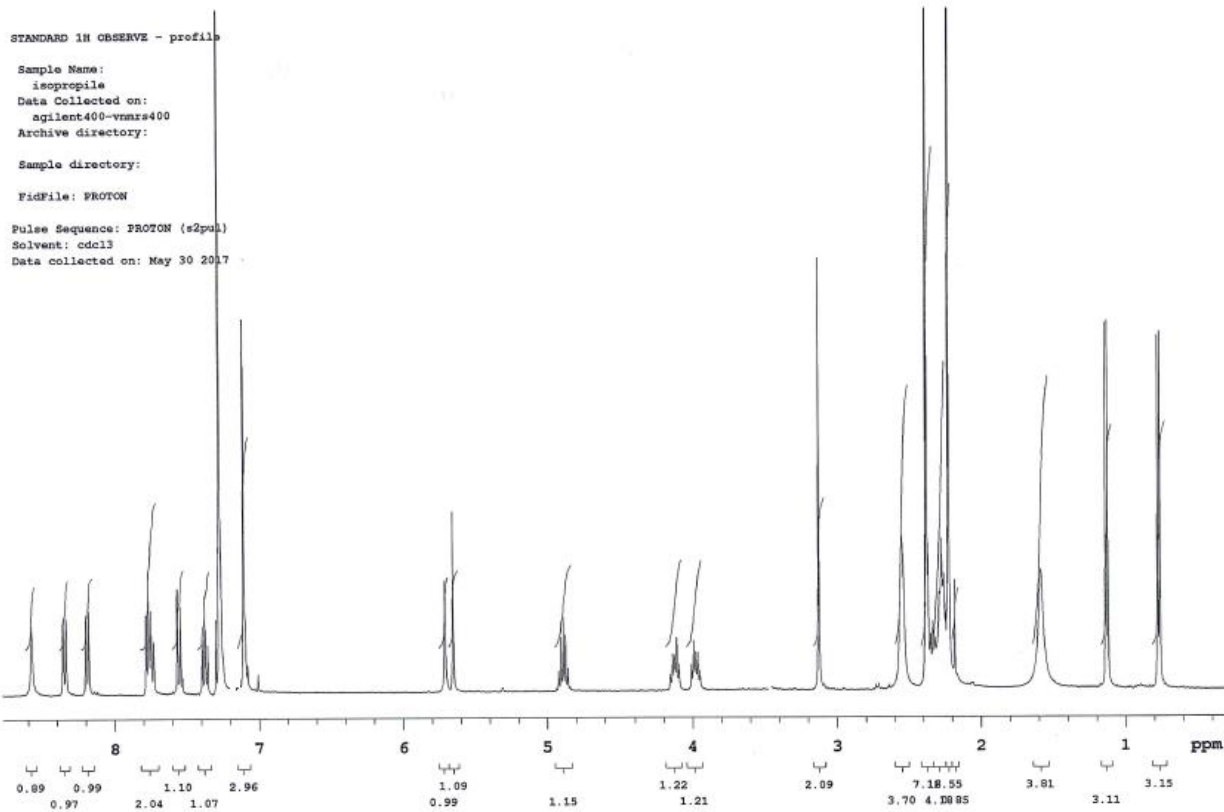
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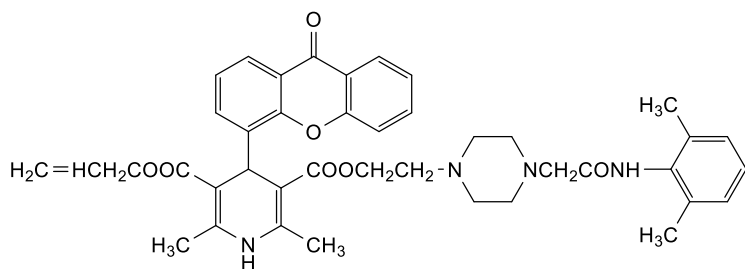
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Solvent: cdcl3
Data collected on: Nov 20 2018





5c

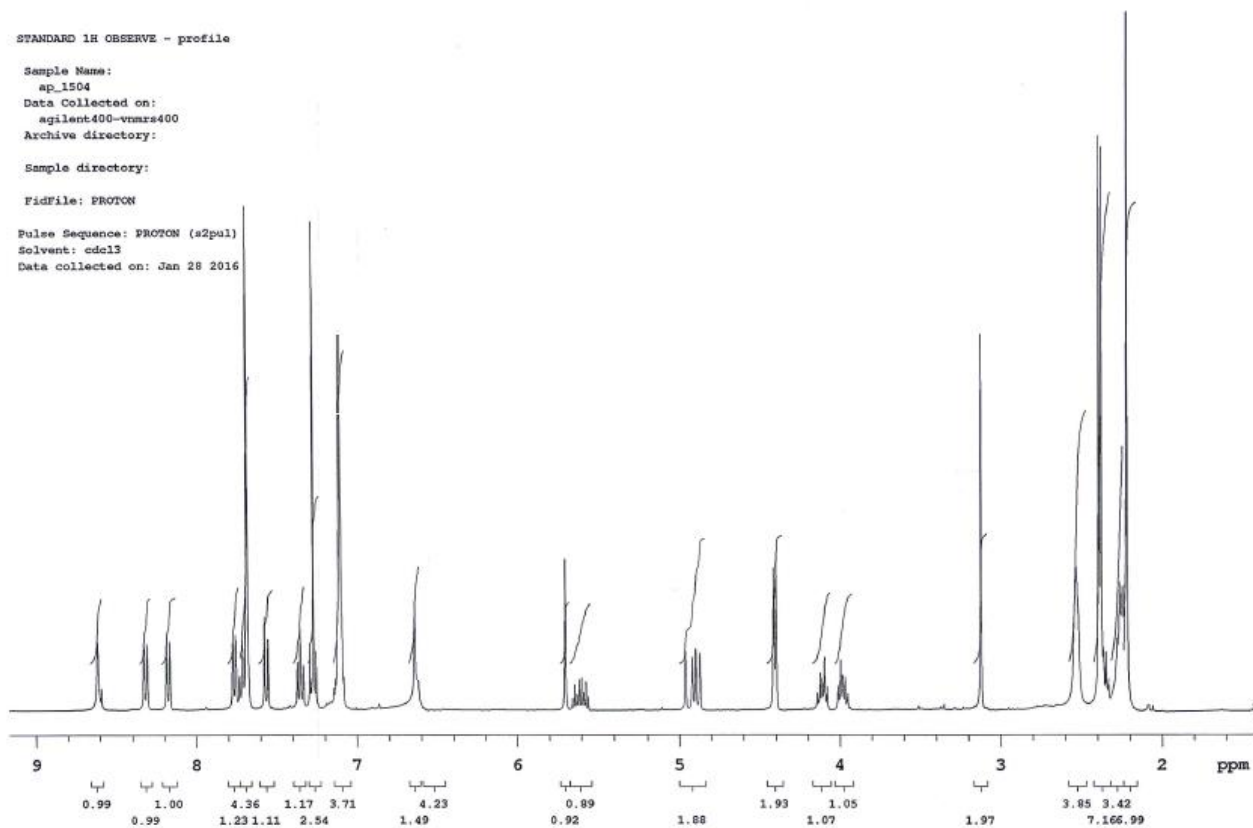




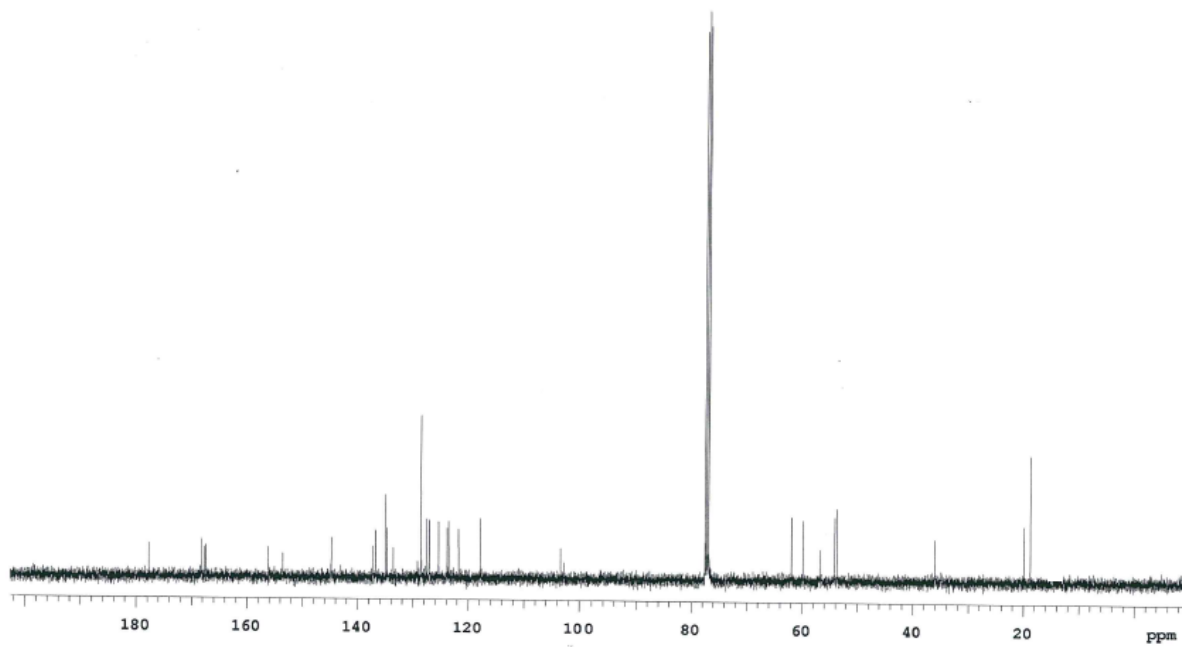
5d

STANDARD 1H OBSERVE - profile

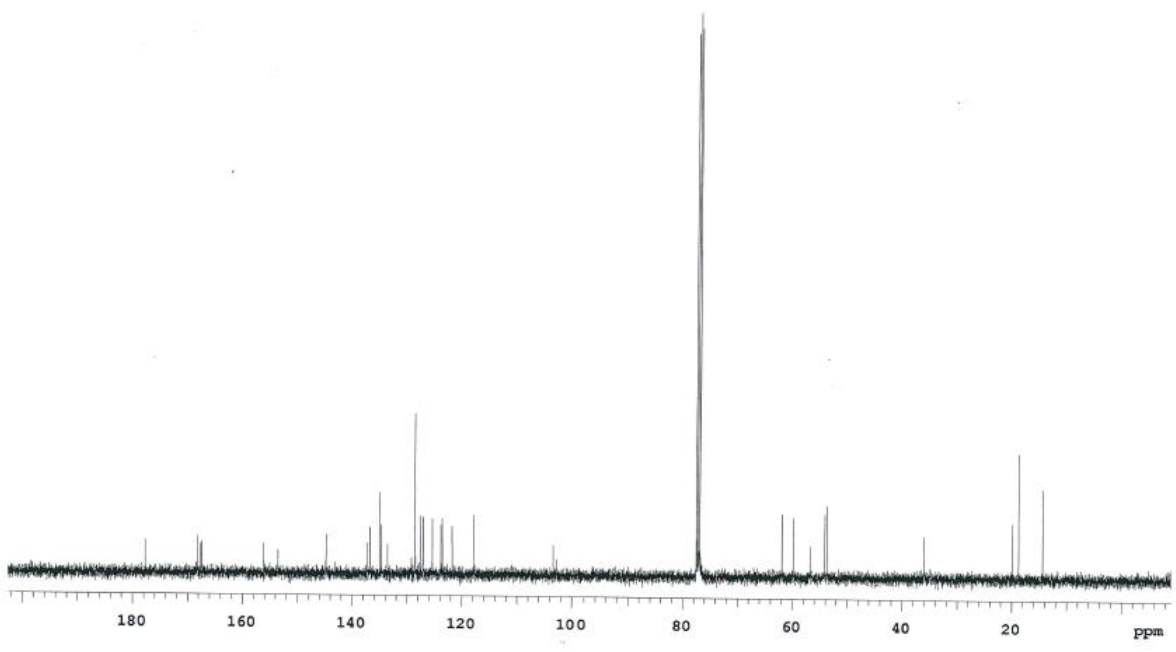
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Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 28 2016



4a



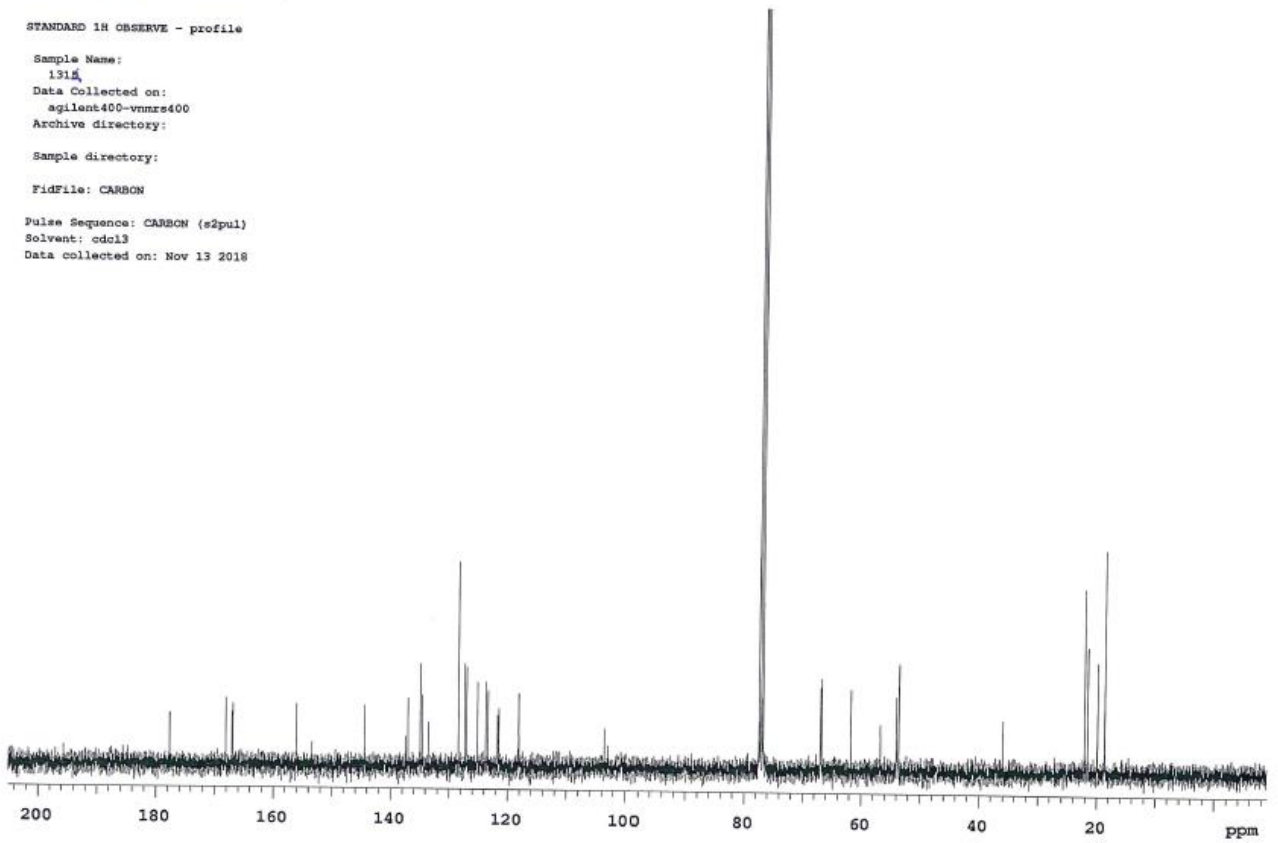
4b



4c

STANDARD IN OBSERVE - profile

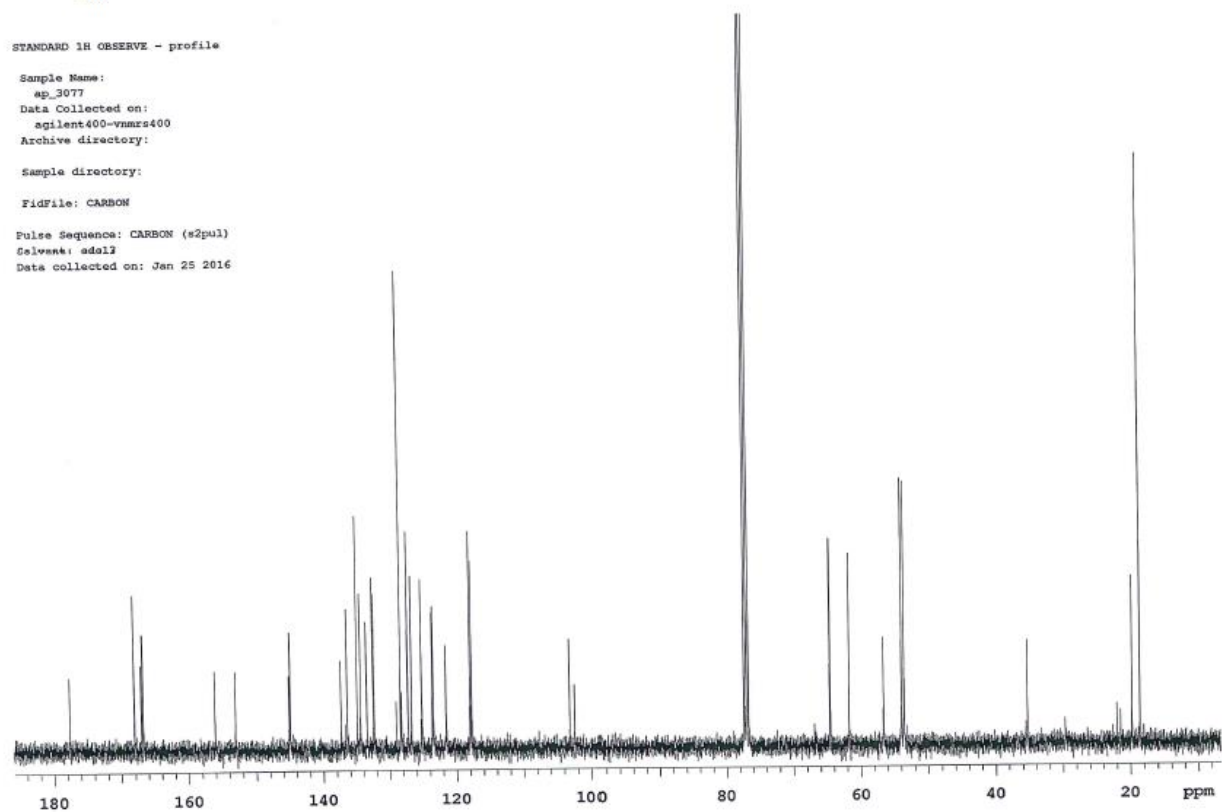
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Archive directory:
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Solvent: cdcl3
Data collected on: Nov 13 2018



4d

STANDARD 1H OBSERVE - profile

Sample Name:
ap_3077
Data Collected on:
agilent400-vnmrs400
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Sample directory:
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Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 25 2016



4e

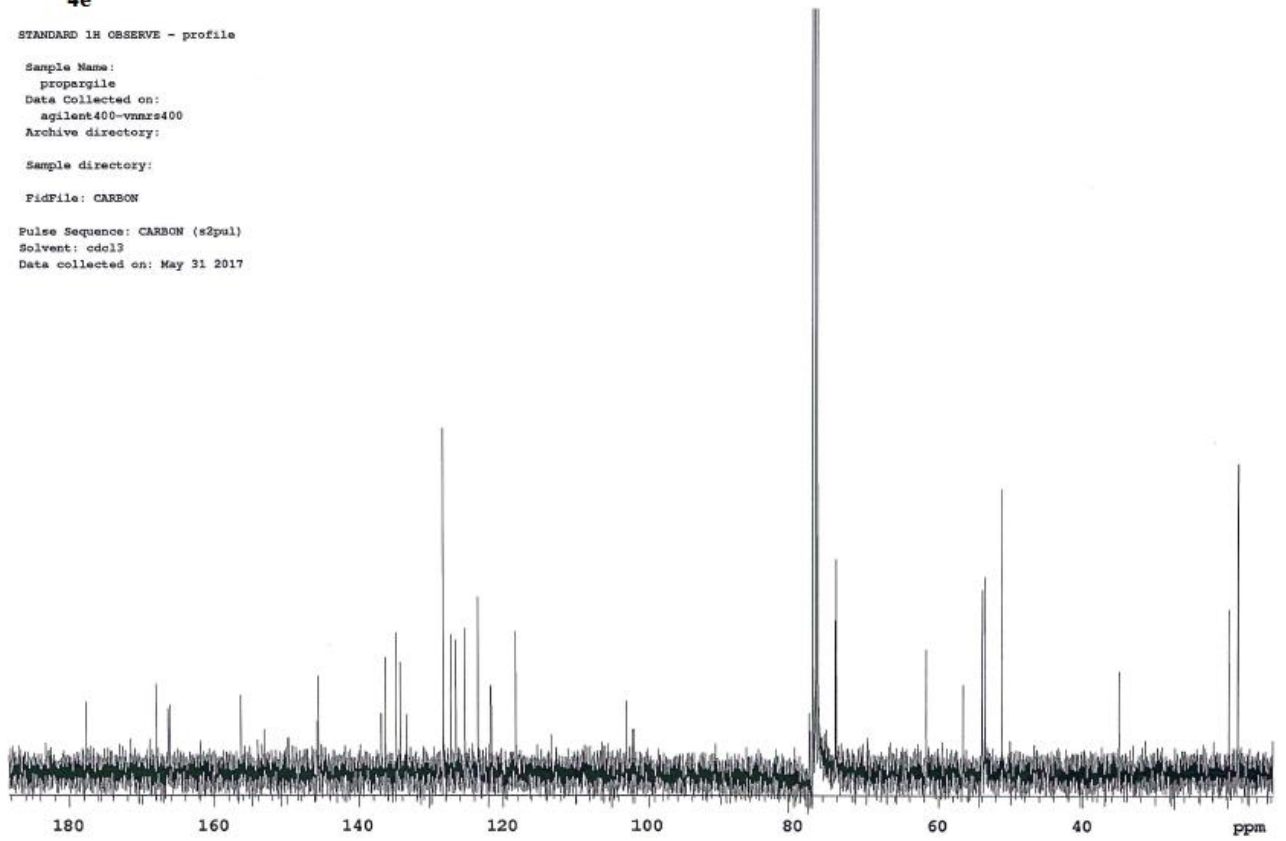
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Archive directory:

Sample directory:

FidFile: CARBON

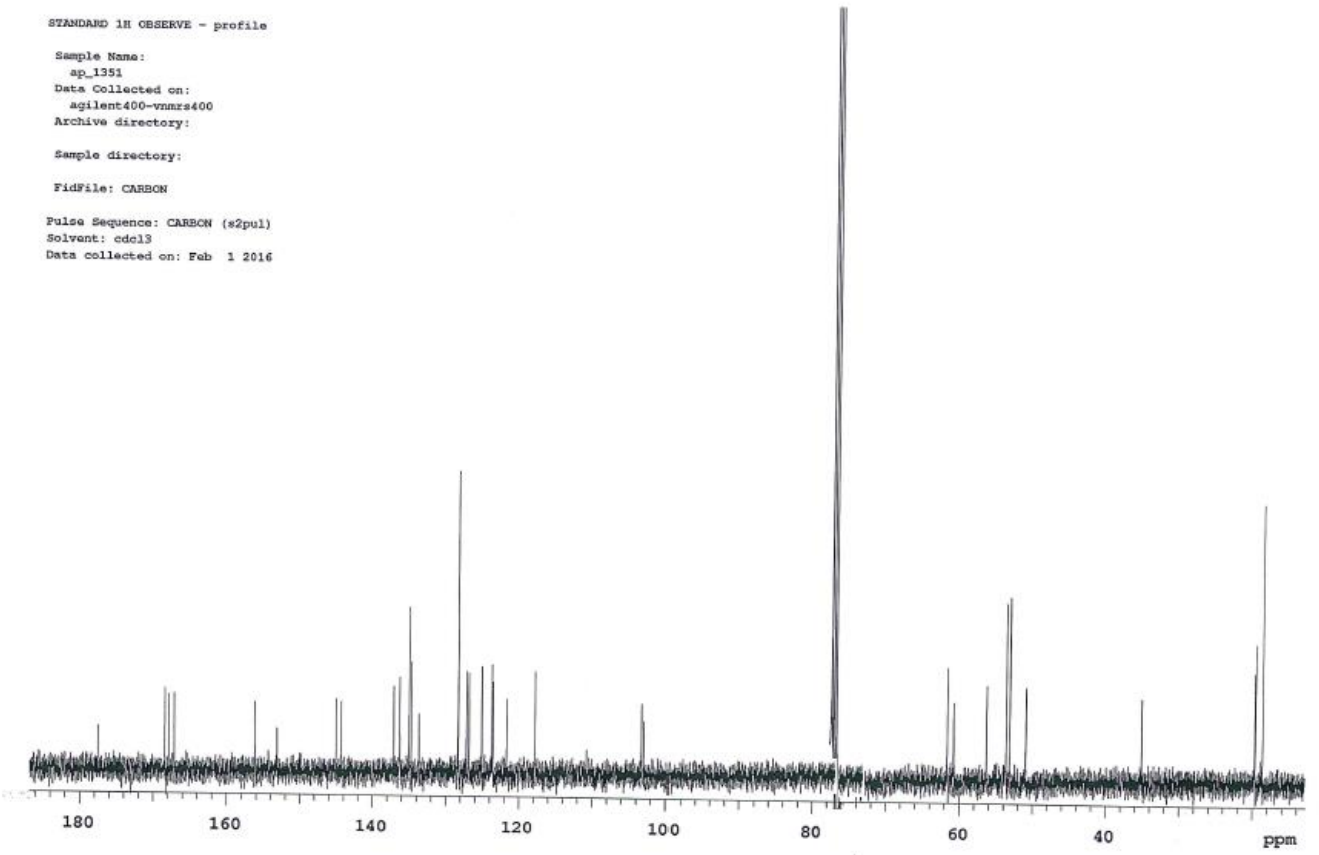
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Solvent: cdcl3
Data collected on: May 31 2017



5a

STANDARD 1H OBSERVE - profile

Sample Name:
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Data Collected on:
agilent400-vnmrs400
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Solvent: cdcl3
Data collected on: Feb 1 2016



5b

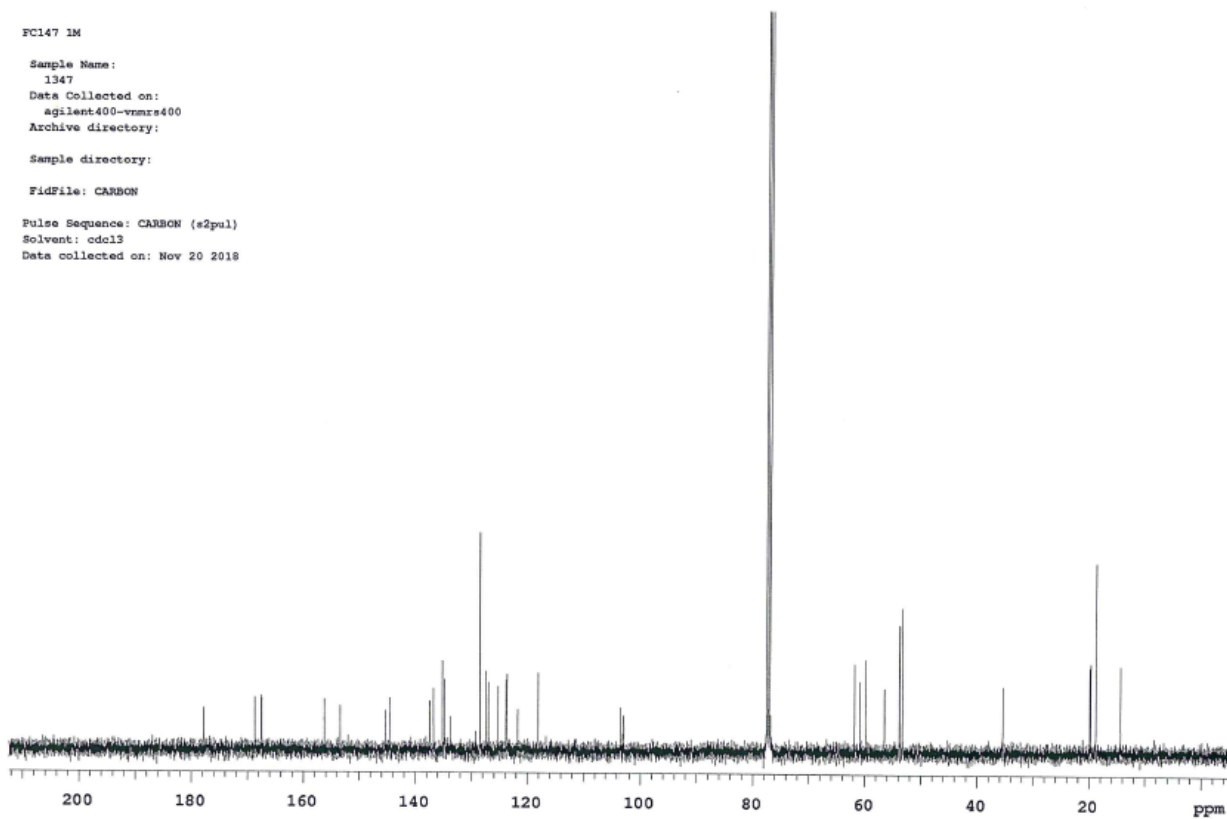
FC147 1M

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5c

FC147 1M

Sample Name:

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Archive directory:

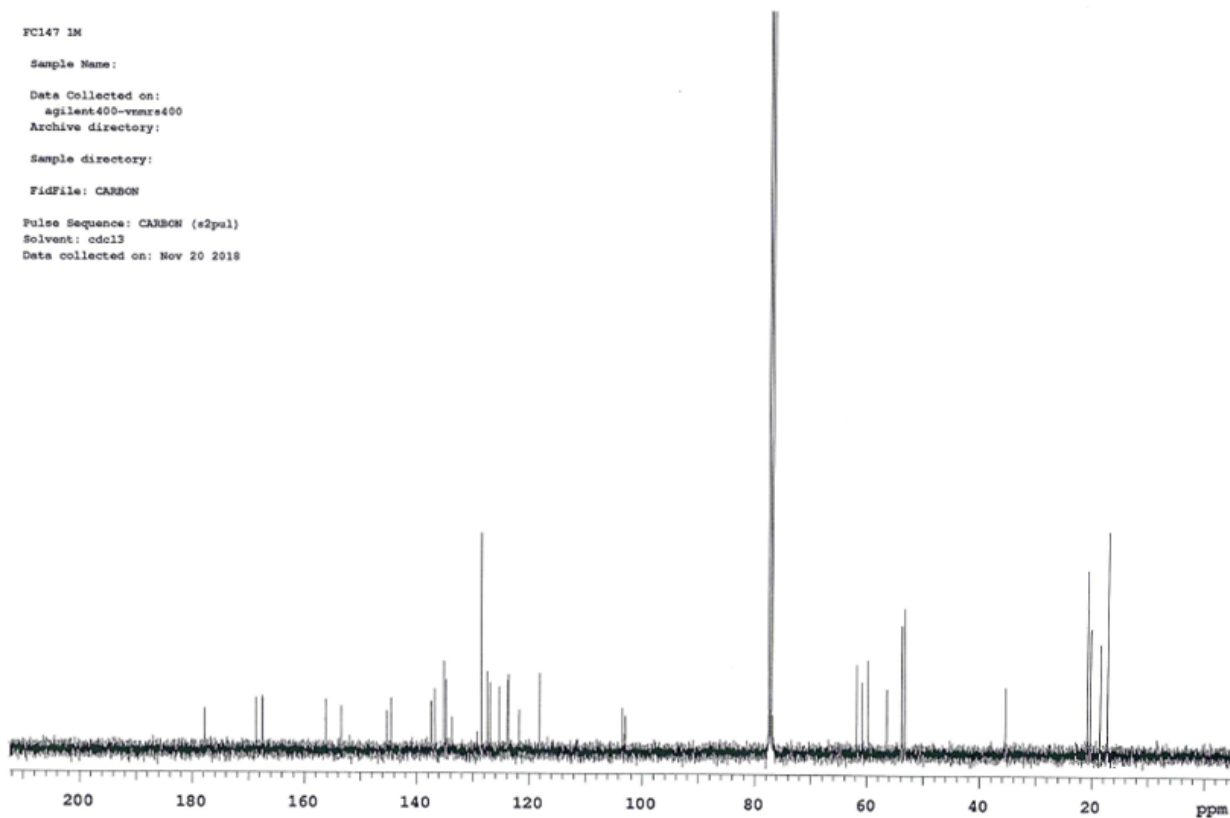
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Pulse Sequence: CARBON (s2pul)

Solvent: cdcl3

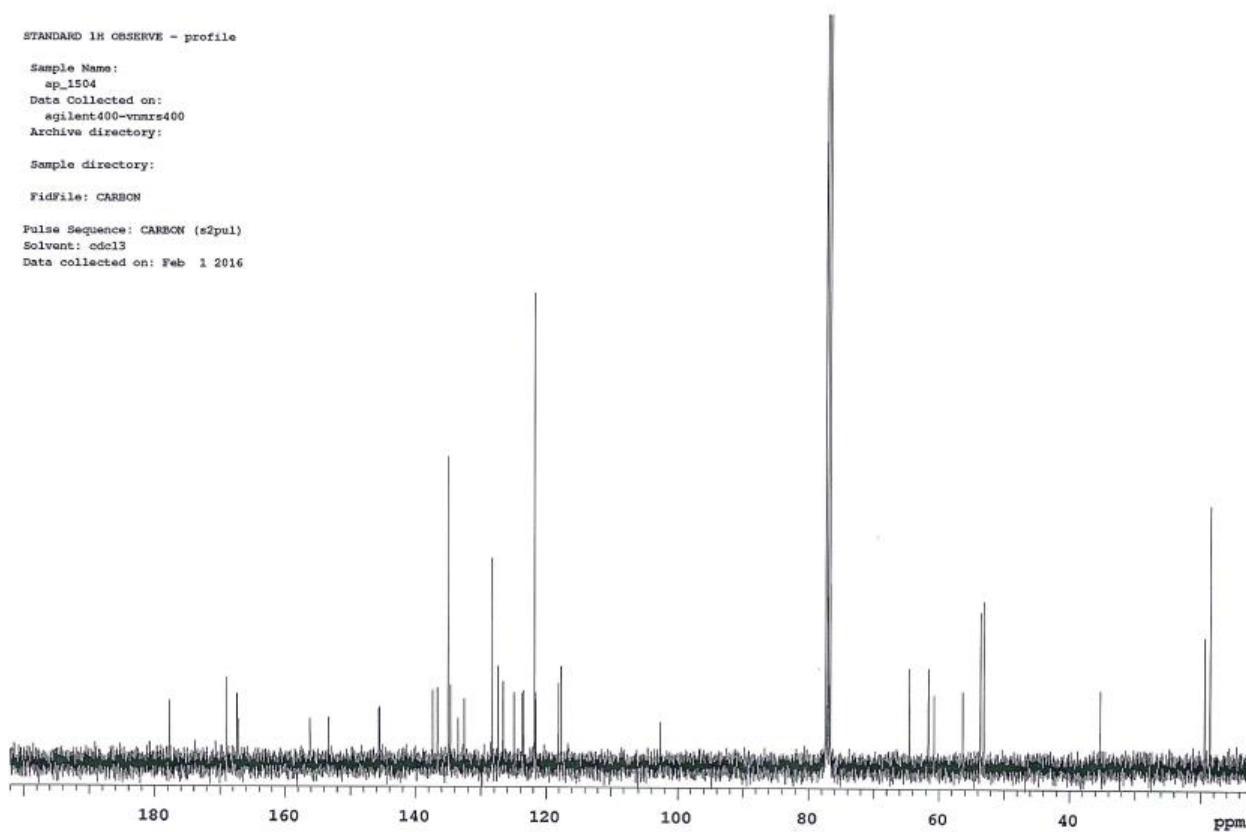
Date collected on: Nov 20 2018



5d

STANDARD 1H OBSERVE - profile

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Pulse Sequence: CARBON (s2pul)
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5e

STANDARD IN OBSERVE - profile

Sample Name:

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Archive directory:

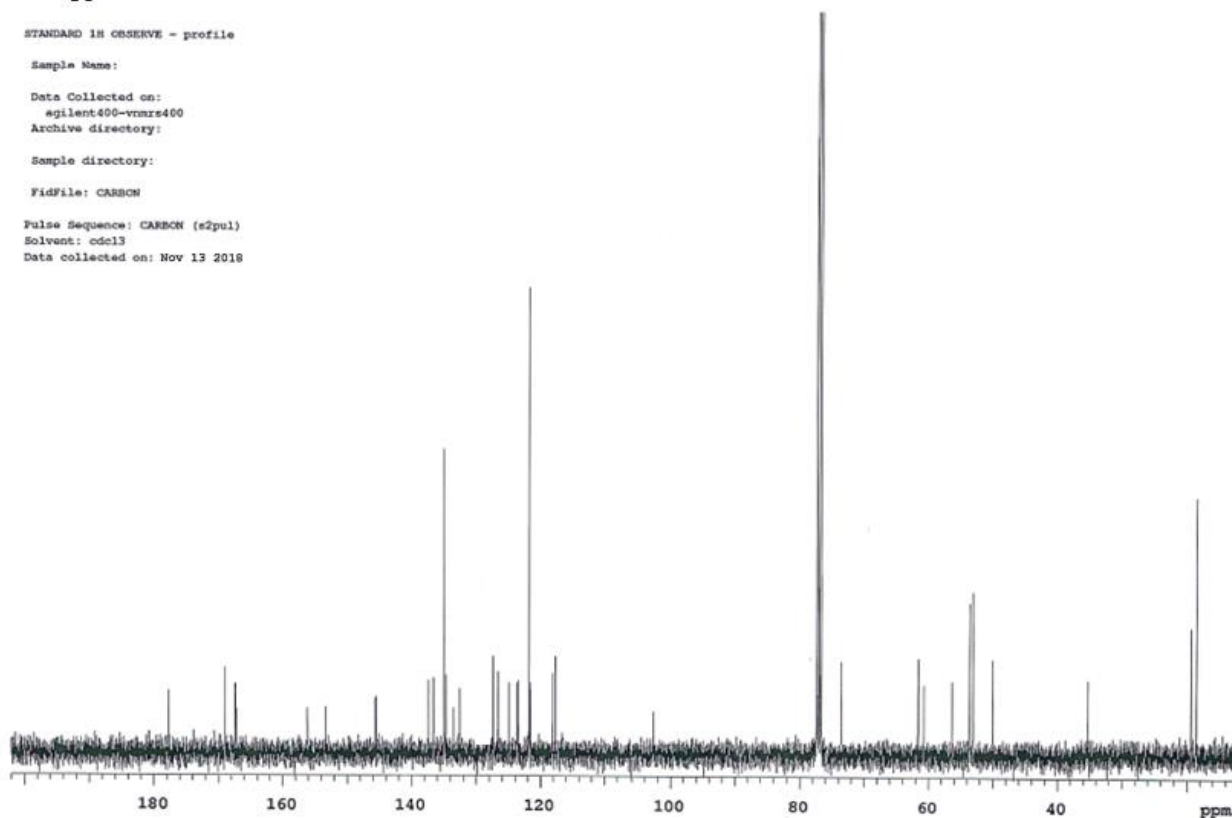
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Solvent: cdcl3

Data collected on: Nov 13 2018



References

1. Chiarini A, Rampa A, Budriesi R, Bisi A, Fabbri G, Valenti P. 1,4-Dihydropyridines bearing a pharmacophoric fragment of lidoflazine. *Bioorg Med Chem.* 1996; 10:1629-1635.
2. Valenti P, Chiarini A, Gasperi F, Budriesi R. Xanthone 1,4-dihydropyridine derivatives with a potent selective bradycardic effect. *Arzneimittelforschung.* 1990; 40:122-125.
3. Chiarini A, Rampa A, Bisi A, Budriesi R, Valenti P. Negative inotropic and chronotropic activity of calcium channel ligands possessing a xanthone 1,4-dihydropyridine backbone. *Arzneimittelforschung.* 1992; 42:797-801.

