

BDG SYNTHESIS

Certificate of Analysis

This material is a research-grade material prepared by custom synthesis. The quantity available is limited, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of research-grade materials. Research materials often contain higher levels of residual solvents and/or water, and we urge you to use the corrected purity where needed rather than the raw HPLC purity.

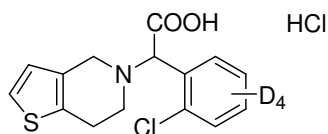
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated in this data sheet.

Barry Dent

Barry R. Dent, PhD, Director
11 May 2009

Name: Clopidogrel acid-d₄ HCl
CAS Number: none (144750-42-5 unlabelled)

Structure:



Molecular Weight: C₁₅H₁₀D₄ClNO₂S•HCl = 348.28
Lot Number: BDG 7838.1
Appearance: Off-white, crystalline solid
Corrected Purity: 99.7 % (HPLC) – 1.8 % (acetone) = 97.9 %
Isotopic Purity: Under 0.5 % d₀
Expiry Date: 11 May 2014

This expiry date is assigned from experience gained with the material in the laboratory and/or on storage. It is not possible to perform formal storage stability studies because of the small amount of material available.

Storage and Handling:

Temperature: ambient laboratory temperature; may be refrigerated.
Humidity: not believed to be hygroscopic; may be handled in normal laboratory atmosphere.
Light: protect from strong sunlight.
Caution: Only experienced laboratory personnel should handle the material.

Identity and Purity:

Source of Material

The material was made by an unambiguous synthetic route, using literature procedures where possible; starting materials were purchased from reputable sources and all intermediates were checked for identity by NMR.

Proton NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.

Isotopic labelling: signals at the sites of deuteration are greatly diminished, compared with the spectrum of unlabelled material, indicating that the material is substantially cleanly deuterated.

Residual solvents: a small amount of acetone (1.8 % w/w) and a trace (under 0.1 %) of ethyl acetate are observed.

Impurities: traces of unidentified impurities are seen in the baseline.

Carbon-13 NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.

Isotopic labelling: signals at the sites of deuteration have collapsed to small multiplets compared with the spectrum of unlabelled material, indicating nearly clean deuteration.

High-resolution mass spectrum (ES+): found m/z 312.0763. $C_{15}H_{11}D_4^{35}ClNO_2S$ $[M+H]^+$ requires m/z 312.0763. The deviation of 0.0 ppm is within normally accepted limits for the establishment of identity by HRMS. Small M-1 and M-2 peaks are observed, but any M-4 peak is at approximately the background level of 0.5%.

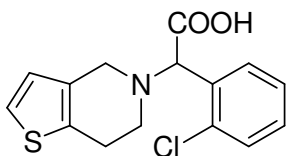
HPLC: A sharp peak is observed (99.7 area %). Note: in the absence of reference materials for preparing calibration curves, it is assumed that all peaks have the same detector response. Where possible, the conditions of analysis follow a pharmacopeial or literature method, or have been adapted from same.

Elemental Analysis:	Found:	C 51.82, H 3.45, D 2.51, N 3.91 %
$C_{15}H_{10}D_4ClNO_2S \cdot HCl$	requires:	C 51.73, H 3.18, D 2.31, N 4.02 %

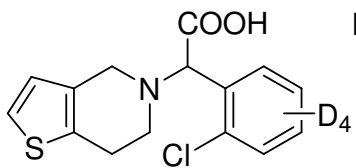
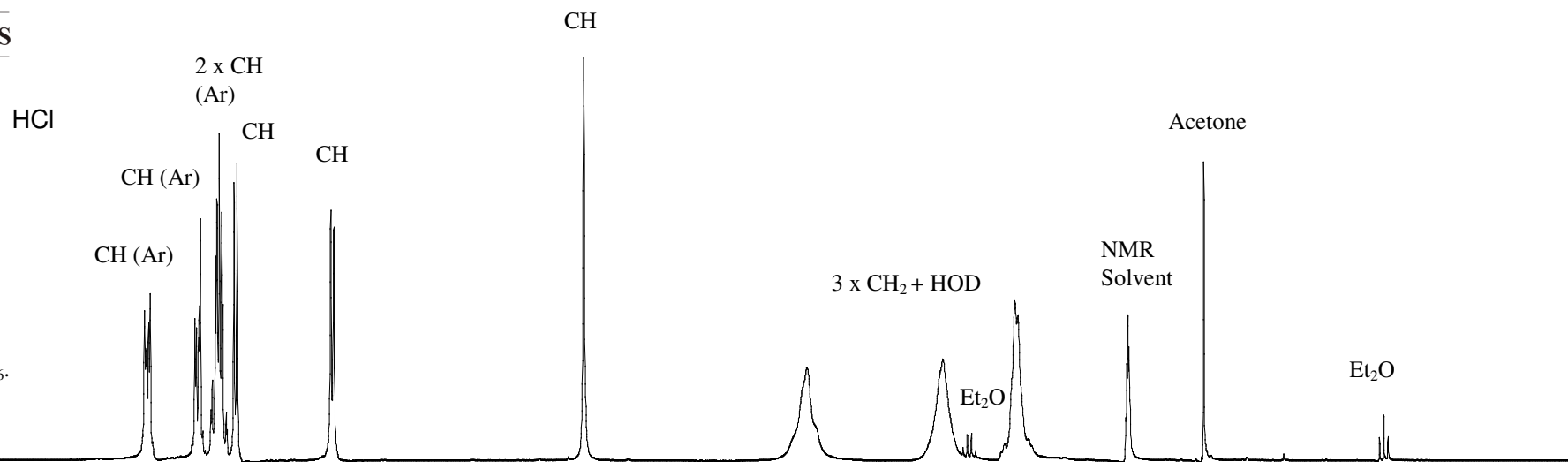
The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).



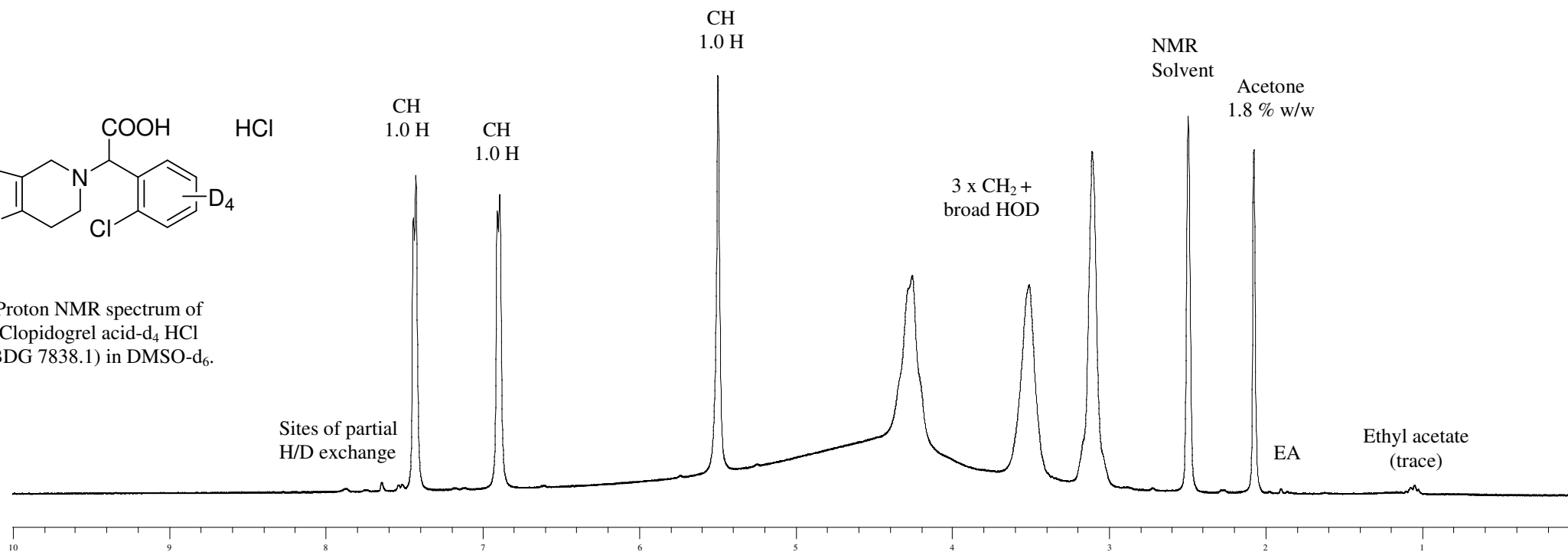
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Proton NMR spectrum of Clopidogrel acid HCl (BDG 6150.1) in DMSO-d₆.

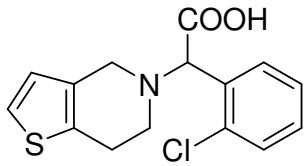


Proton NMR spectrum of Clopidogrel acid-d₄ HCl (BDG 7838.1) in DMSO-d₆.





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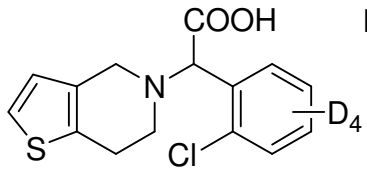
HCl

Carbon-13 NMR spectrum of Clopidogrel acid HCl (BDG 6150.1) in DMSO-d₆.

4 x C +
4 x CH

2 x CH

NMR
Solvent



HCl

Carbon-13 NMR spectrum of Clopidogrel acid-d₄ HCl (BDG 7838.1) in DMSO-d₆.

CO₂H

4 x C +
4 x CD

2 x CH

NCH

2 x NCH₂

CH₂

Acetone



200

175

150

125

100

75

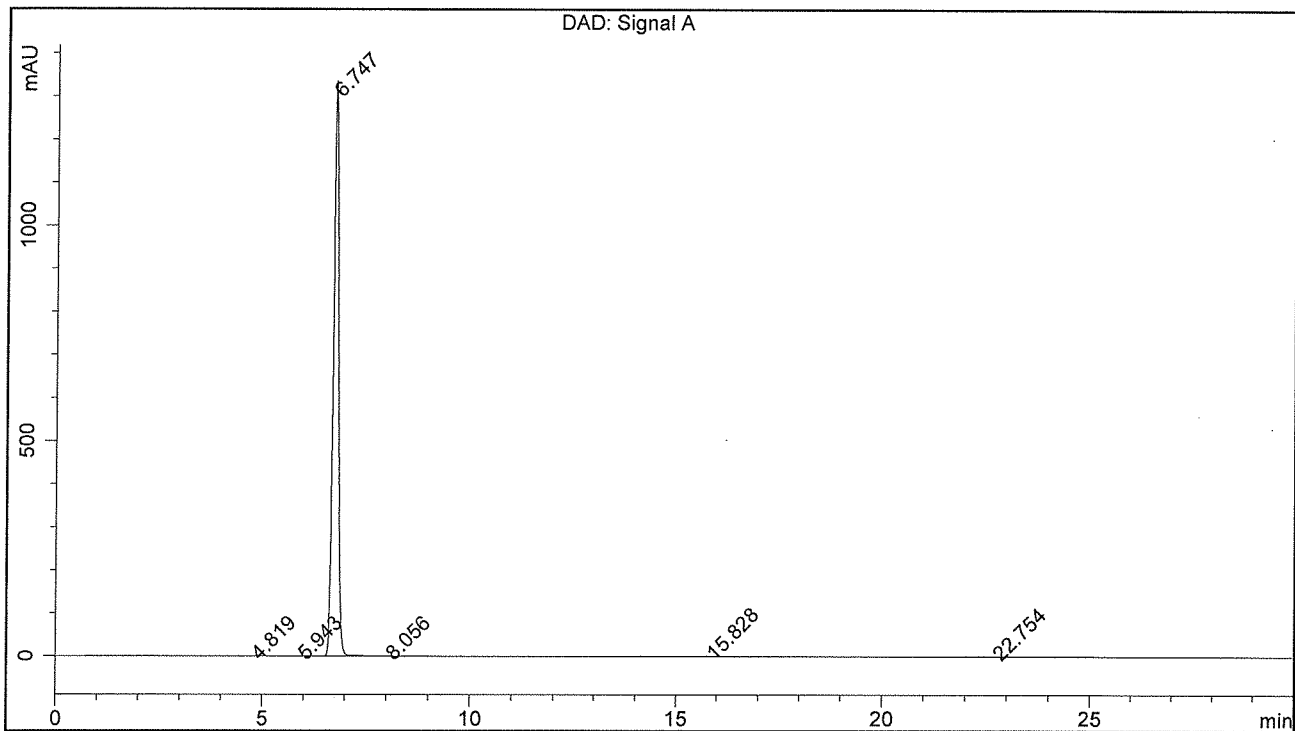
50

25

BDG - Analysis of Clopidogrel acid-d4 HCl

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase : 75:25 0.05M Potassium diHydrogen Phosphate pH=3.0 : Acetonitrile
Flow Rate : 1.0 mL/min
Sample Solvent : Mobile Phase
Column Temperature : 20C
Injection Volume : 10 uL
Detection : UV at 240 nm

Sample Name	BDG 7838.1	Instrument	AnalyticalLC01
Acquisition	11/05/2009, 10:37:02	Method (rev.)	LC10185b (2)
Sequence	BDG_11May2009d	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	4.82 min	0.5193	5.4750	0.1550 min	0.046 %
2	5.94 min	0.2372	2.7048	0.1710 min	0.023 %
3	6.75 min	1336.5447	11845.3278	0.1354 min	99.726 %
4	8.06 min	0.3532	3.6458	0.1584 min	0.031 %
5	15.83 min	0.9388	15.1588	0.2504 min	0.128 %
6	22.75 min	0.2112	5.5184	0.3328 min	0.046 %