



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.

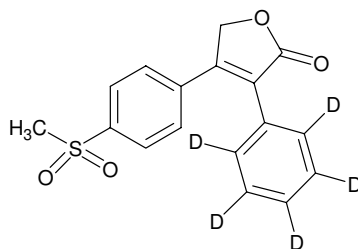
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated in this data sheet.

Barry Dent

Barry R. Dent, PhD, Director
18 January 2007

Name: Rofecoxib-d₅
CAS Number: none (162011-90-7 unlabelled)

Structure:



Molecular Weight: C₁₇H₉D₅O₄S = 319.39
Lot Number: BDG 6626.1
Appearance: White, crystalline solid
Corrected Purity: 99.5 % (HPLC) – 1.1 % (dichloromethane) = 98.4 %
Isotopic Purity: Under 0.5 % d₀
Expiry Date: 18 January 2012

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 absent, compared with the spectrum of unlabelled material, indicating clean deuteration. Integration of the methylene signal at 5.4 ppm indicates that approximately 33 % of rofecoxib-d₆ is present.

Residual solvents: a small amount of dichloromethane (1.1 % w/w) is observed.

Impurities: no significant impurities are evident in the spectrum.

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 clean deuteration.

High-resolution mass spectrum (EI+): found m/z 319.0925. C₁₇H₉D₅O₄S [M]⁺ requires m/z 319.0927.

The deviation of 0.5 ppm is within normally accepted limits for the establishment of identity by HRMS.

There is an M+1 peak at greater than the intensity expected for the contribution from ¹³C, and this is attributed to the presence of d₆ material as discussed for the NMR spectra. No signal for d₀ material was seen (detection limit about 0.5 %).

HPLC: A somewhat broadened, symmetrical peak is observed (99.5 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.

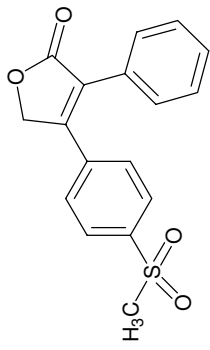
Elemental Analysis: Found: C 63.64, H 2.92, D 3.24 %
C₁₇H₉D₅O₄S requires: C 63.93, H 2.84, D 3.12 %

The elemental analyses fall within generally accepted limits for establishing the molecular formula given.

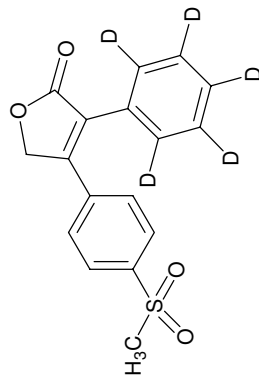
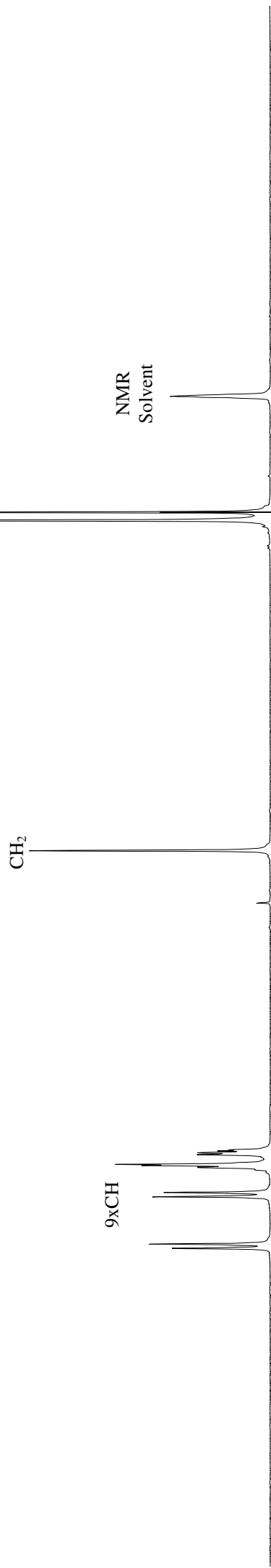
The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).



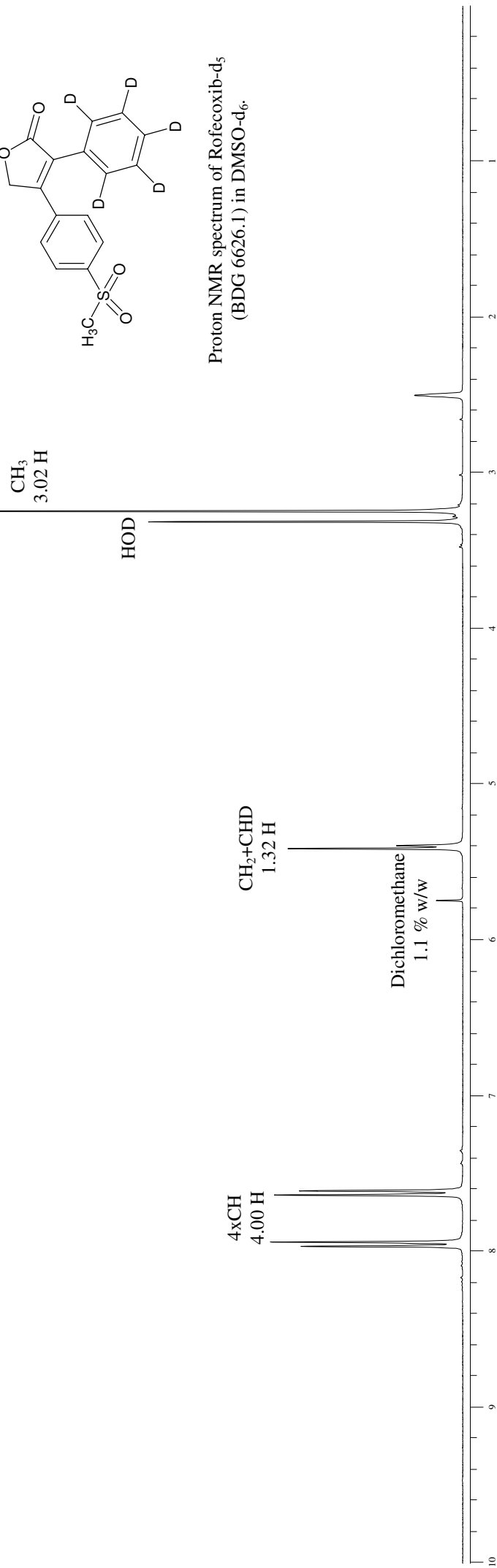
BDG SYNTHESIS



Proton NMR spectrum of Rofecoxib
in DMSO-d₆.

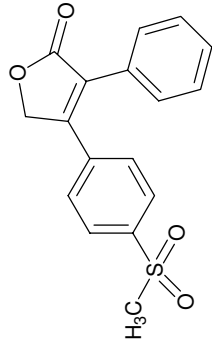


Proton NMR spectrum of Rofecoxib-d₅
(BDG 6626.1) in DMSO-d₆.

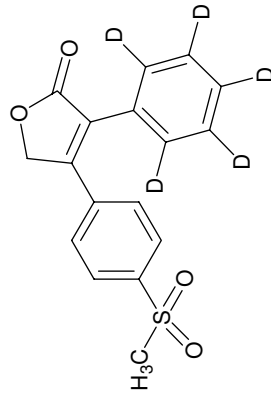
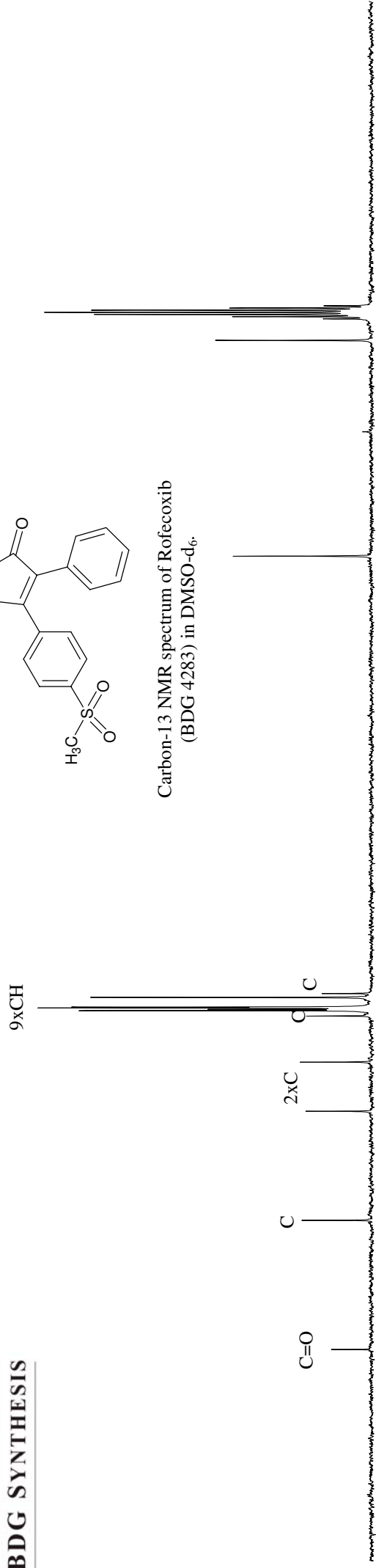




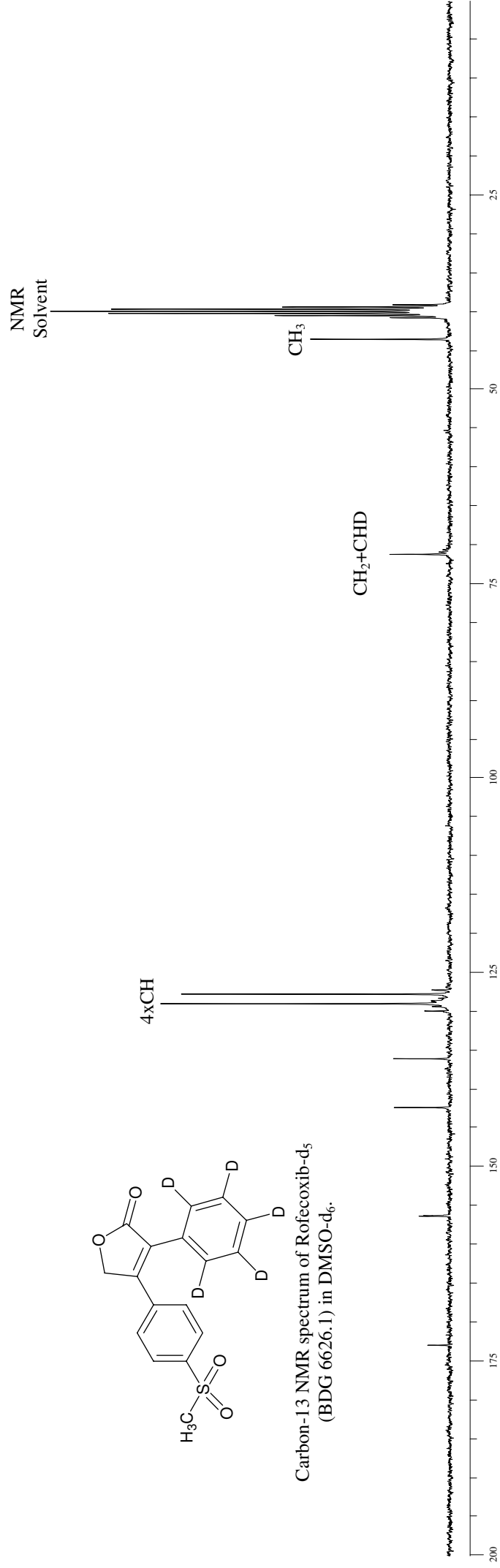
BDG SYNTHESIS



Carbon-13 NMR spectrum of Rofecoxib (BDG 4283) in DMSO-d₆.



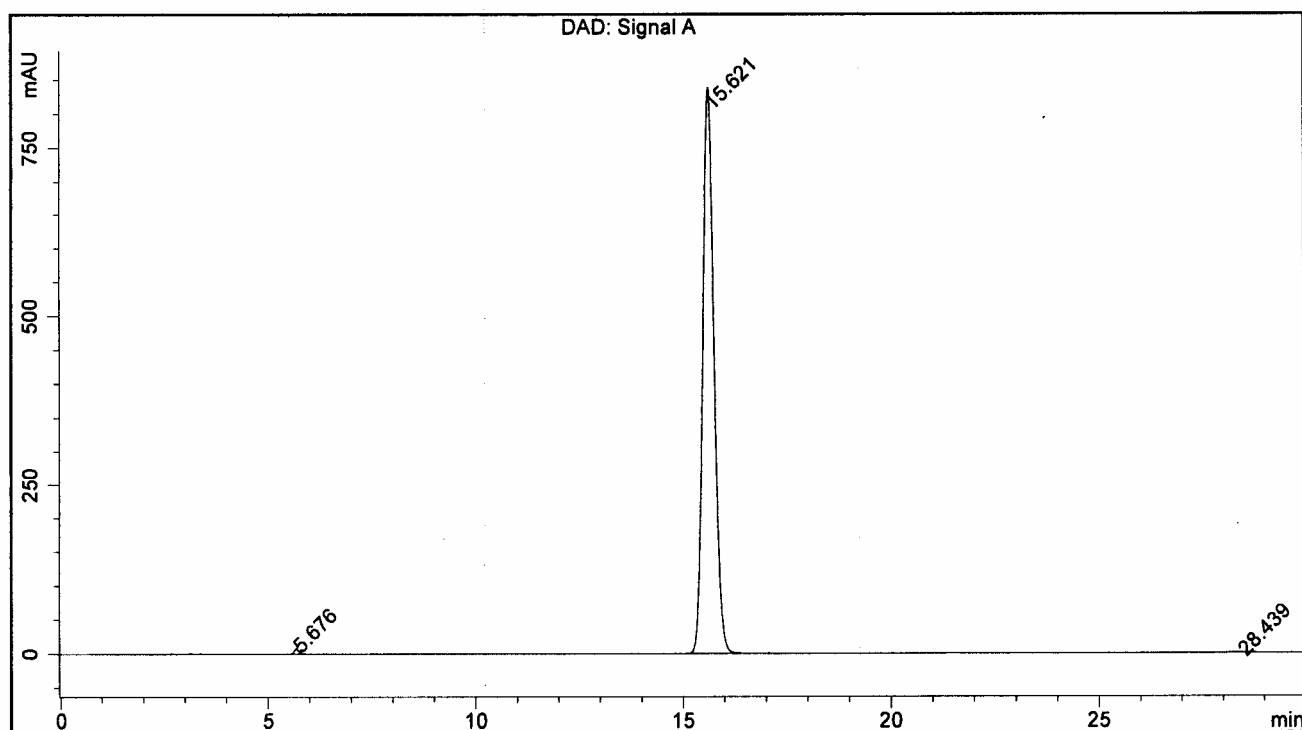
Carbon-13 NMR spectrum of Rofecoxib-d₅ (BDG 6626.1) in DMSO-d₆.



BDG - Analysis of Rofecoxib-d5

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase : 61.6:38.4:0.08:0.024 Water : Acetonitrile : Acetic Acid : Triethylamine
Flow Rate : 1.0 mL/min
Sample Solvent : 1:1 Water : Acetonitrile
Column Temperature : 20C
Injection Volume : 10 uL
Detection : UV at 254 nm

Sample Name	BDG 6626.1	Instrument	AnalyticalLC01
Acquisition	07/01/2007, 19:11:40	Method (rev.)	LC10129a (4)
Sequence	BDG_07Jan2007b - Reprocessed	Vial Position	1
Operator	solvation010\cerityadmin	Injection	2 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	5.68 min	7.3748	54.0159	0.1115 min	0.343 %
2	15.62 min	838.6128	15686.8336	0.2882 min	99.530 %
3	28.44 min	0.5611	20.0760	0.4274 min	0.127 %