



## 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.

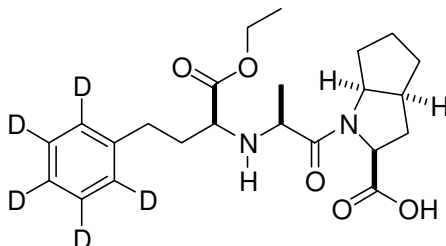
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated in this data sheet.

*Barry Dent*

Barry R. Dent, PhD, Director  
18 January 2007

**Name:** Ramipril-d<sub>5</sub>  
**CAS Number:** none (87333-19-5 unlabelled)

**Structure:**



**Molecular Weight:** C<sub>23</sub>H<sub>27</sub>D<sub>5</sub>N<sub>2</sub>O<sub>5</sub> = 421.54

**Lot Number:** BDG 6635.1

**Appearance:** White, crystalline solid

**Purity by HPLC:** 99.2 %

**Isotopic Purity:** Under 0.5 % d<sub>0</sub>

**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.

1/5

## 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. The complexity of the spectrum indicates two conformers of the product are present in solution.

Isotopic labelling: signals at the sites of deuteration are greatly diminished, compared with the spectrum of unlabelled material, indicating clean deuteration.

Residual solvents: no residual solvents are 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. The majority of signals are duplicated indicating that two conformers of the product are present in solution.

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 (FAB+):** found  $m/z$  422.2717.  $C_{23}H_{28}D_5N_2O_5$   $[M+H]^+$  requires  $m/z$  422.2703. The deviation of 3.3 ppm is within normally accepted limits for the establishment of identity by HRMS. No signal for  $d_0$  material was seen (detection limit about 0.5 %).

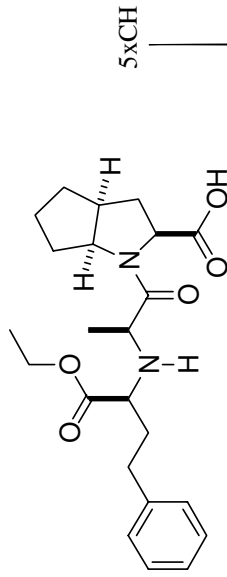
**HPLC:** A sharp, symmetrical peak is observed (99.2 area %). The broad peaks in the baseline are present in the solvent blank. Note: in the absence of reference materials for preparing calibration curves, it is assumed that all peaks have the same detector response. Where possible, the conditions of analysis follow a pharmacopeial or literature method, or have been adapted from same.

**Elemental Analysis:** Found: C 65.80, H 6.59, D 2.44, N 6.64 %  
 $C_{23}H_{27}D_5N_2O_5$  requires: C 65.53, H 6.46, D 2.39, N 6.65 %

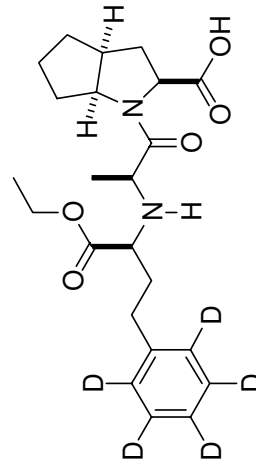
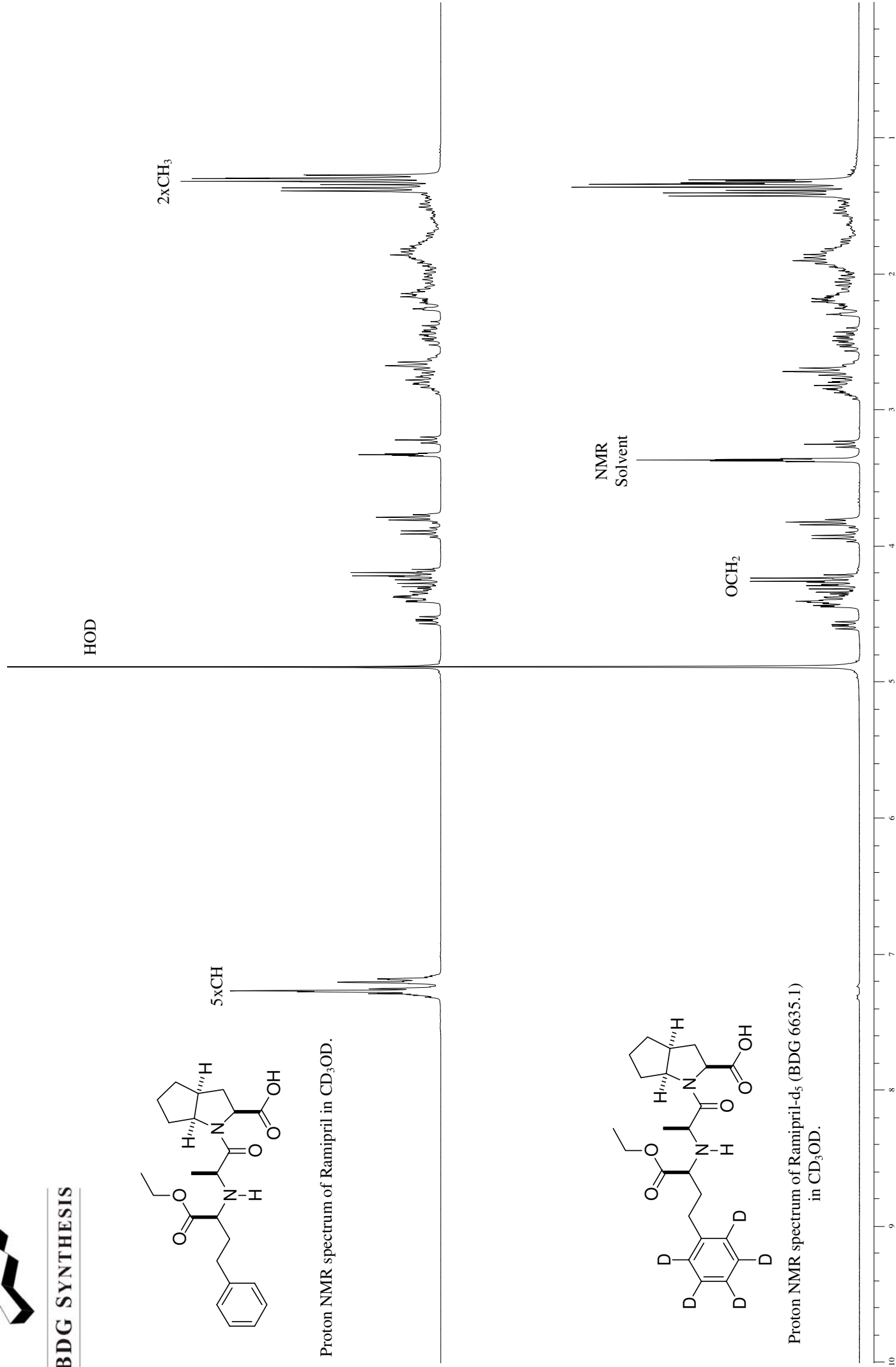
The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).



## BDG SYNTHESIS



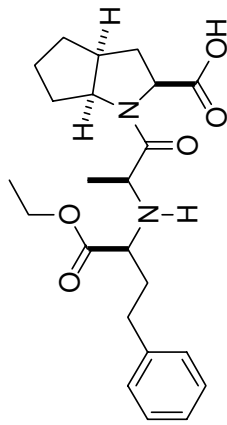
Proton NMR spectrum of Ramipril in CD<sub>3</sub>OD.



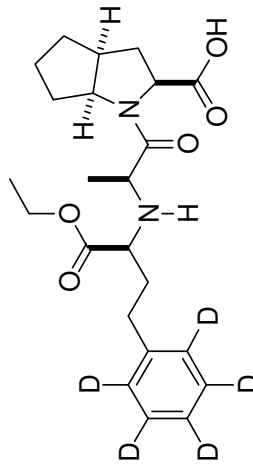
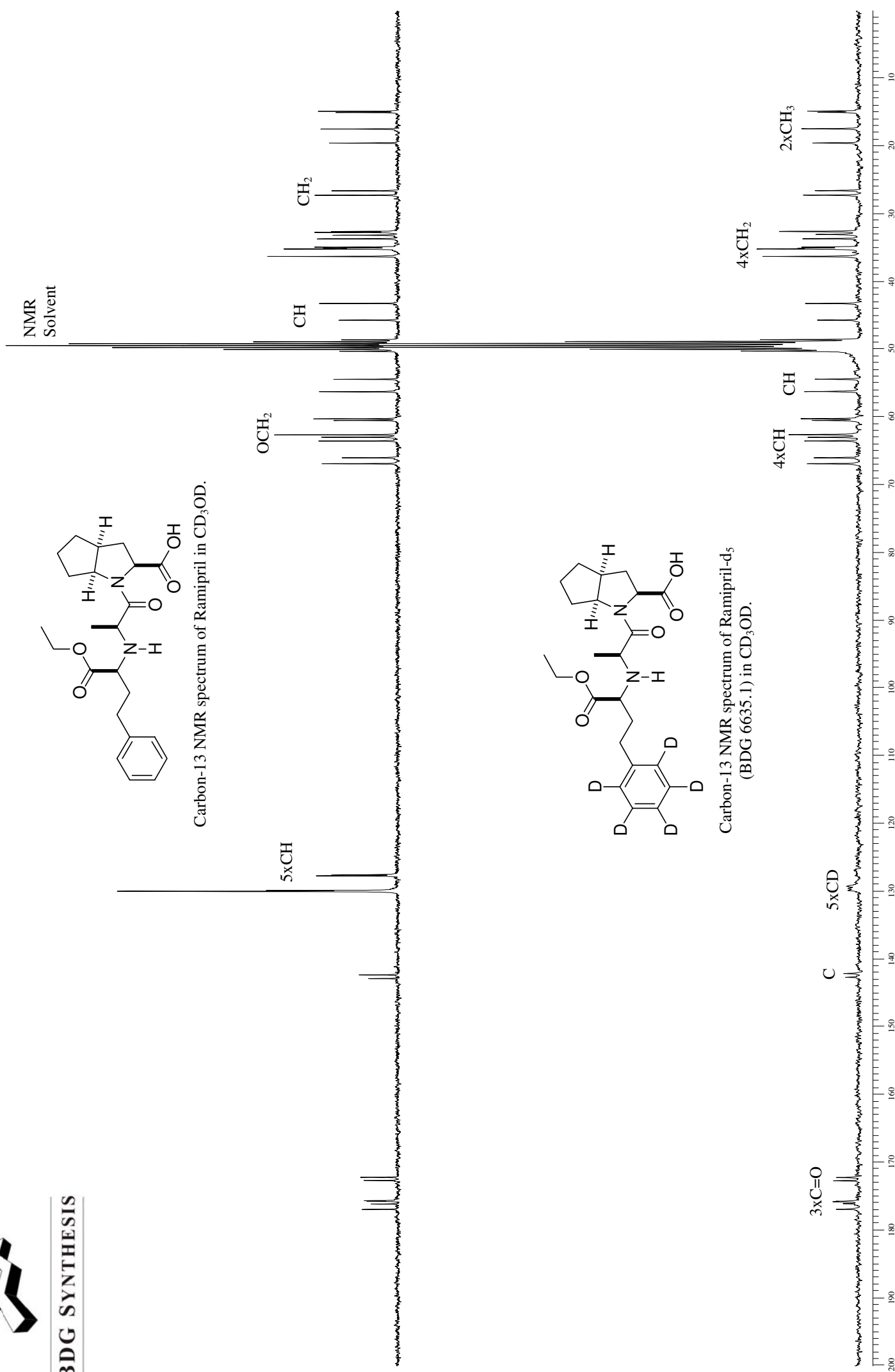
Proton NMR spectrum of Ramipril-d<sub>5</sub> (BDG 6635.1) in CD<sub>3</sub>OD.



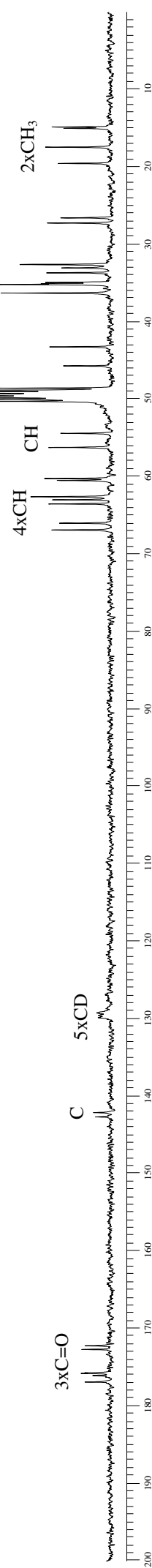
**BDG SYNTHESIS**



Carbon-13 NMR spectrum of Ramipril in CD<sub>3</sub>OD.



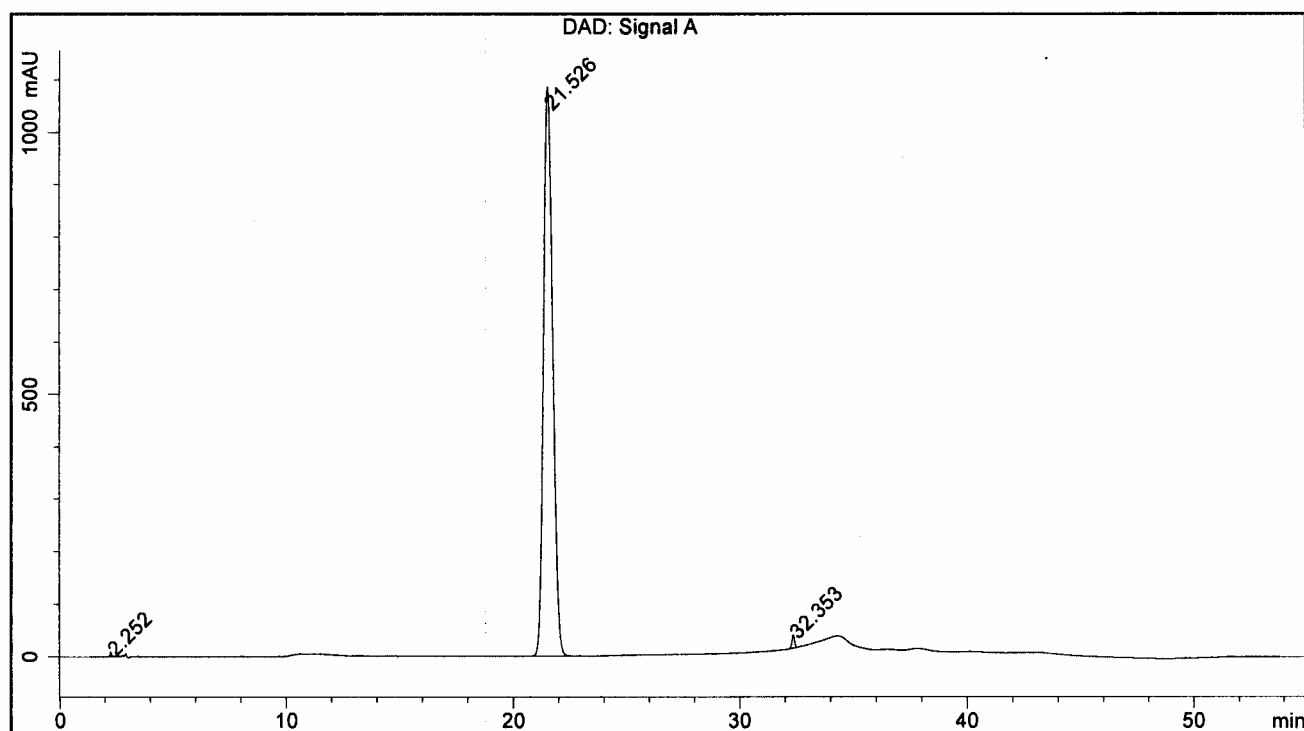
Carbon-13 NMR spectrum of Ramipril-d<sub>5</sub> (BDG 6635.1) in CD<sub>3</sub>OD.



## BDG - Analysis of Ramipril-d5

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm  
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm  
 Mobile Phase A : 80:20 0.2% Sodium Perchlorate + 0.05% Triethylamine pH=3.6 : Acetonitrile  
 Mobile Phase B : 30:70 0.2% Sodium Perchlorate + 0.05% Triethylamine pH=2.6 : Acetonitrile  
 Gradient : T0=90:10, T6=90:10, T7=75:25, T20=65:35, T30=25:75, T40=25:75, T45=90:10, T55=90:10  
 Flow Rate : 1.0 mL/min  
 Sample Solvent : Mobile Phase  
 Column Temperature : 65C  
 Injection Volume : 10 uL  
 Detection : UV at 210 nm

<b>Sample Name</b>	BDG 6635.1	<b>Instrument</b>	AnalyticalLC01
<b>Acquisition</b>	08/01/2007, 18:50:43	<b>Method (rev.)</b>	LC10131a ( 7)
<b>Sequence</b>	BDG_08Jan2007b - Reprocessed	<b>Vial Position</b>	2
<b>Operator</b>	solvation010\cerityadmin	<b>Injection</b>	2 of 2



## Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	2.25 min	8.6685	31.8289	0.0568 min	0.103 %
2	21.53 min	1085.0076	30778.7099	0.4450 min	99.224 %
3	32.35 min	25.2218	208.8692	0.1286 min	0.673 %