



BDG SYNTHESIS

Certificate of Analysis

BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

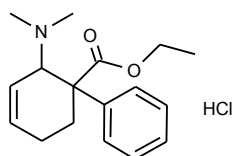
Barry Dent

Barry R. Dent, PhD, Director
22 December 2010

Name: Tilidine HCl

CAS Number: 27107-79-5

Structure:



Molecular Weight: $C_{17}H_{23}NO_2 \cdot HCl = 309.83$

Lot Number: BDG 2374

Appearance: White, crystalline solid

Corrected Purity: 99.0 % (HPLC) - 2.9 % (water) = 96.1 %

Re-test Date: 22 December 2015

Storage and Handling:

Temperature:	refrigerate for prolonged storage; may be handled and shipped at ambient temperature.
Humidity:	may be hygroscopic; store desiccated; recommended to determine water content periodically.
Light:	protect from strong sunlight.
Caution:	only experienced laboratory personnel should handle the material. Do not dry. Drying will remove water of crystallisation and rehydration may be variable.

Identity and Purity

Proton NMR Spectrum

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

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.

High-resolution Mass Spectrum (ESI+)

Found m/z 274.1824. $C_{17}H_{24}NO_2$ $[M+H]^+$ (free base) requires m/z 274.1802. The deviation of 6.9 ppm is somewhat outside normally accepted limits for the establishment of identity by HRMS, and the mass spectral data should be considered in conjunction with other identity criteria.

HPLC

A sharp, symmetrical peak is observed (99.0 %). 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 64.16, H 8.07, N 4.39 %
$C_{17}H_{23}NO_2 \cdot HCl \cdot 0.5H_2O$	Requires:	C 64.04, H 7.90, N 4.39 %
$C_{17}H_{23}NO_2 \cdot HCl$	Requires:	C 65.90, H 7.81, N 4.52 %

The elemental analyses fall somewhat outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the "best-fit" hydrated molecular formula is given.

Karl-Fischer Analysis

	Found:	H_2O 2.9 %
$C_{17}H_{23}NO_2 \cdot HCl \cdot 0.5H_2O$	Requires:	H_2O 2.8 %

Of necessity, only a small sample could be used and only a single or duplicate analysis performed. We are unable to state what the errors in the reported water content are, but recommend that the result be used, as the best available, when determining corrected purity.

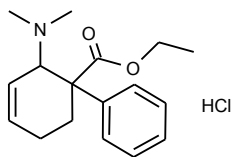
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials 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. This compound is intended for use as an analytical reference material and it is not for human administration. Structures are shown with relative stereochemistry unless otherwise specified.

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

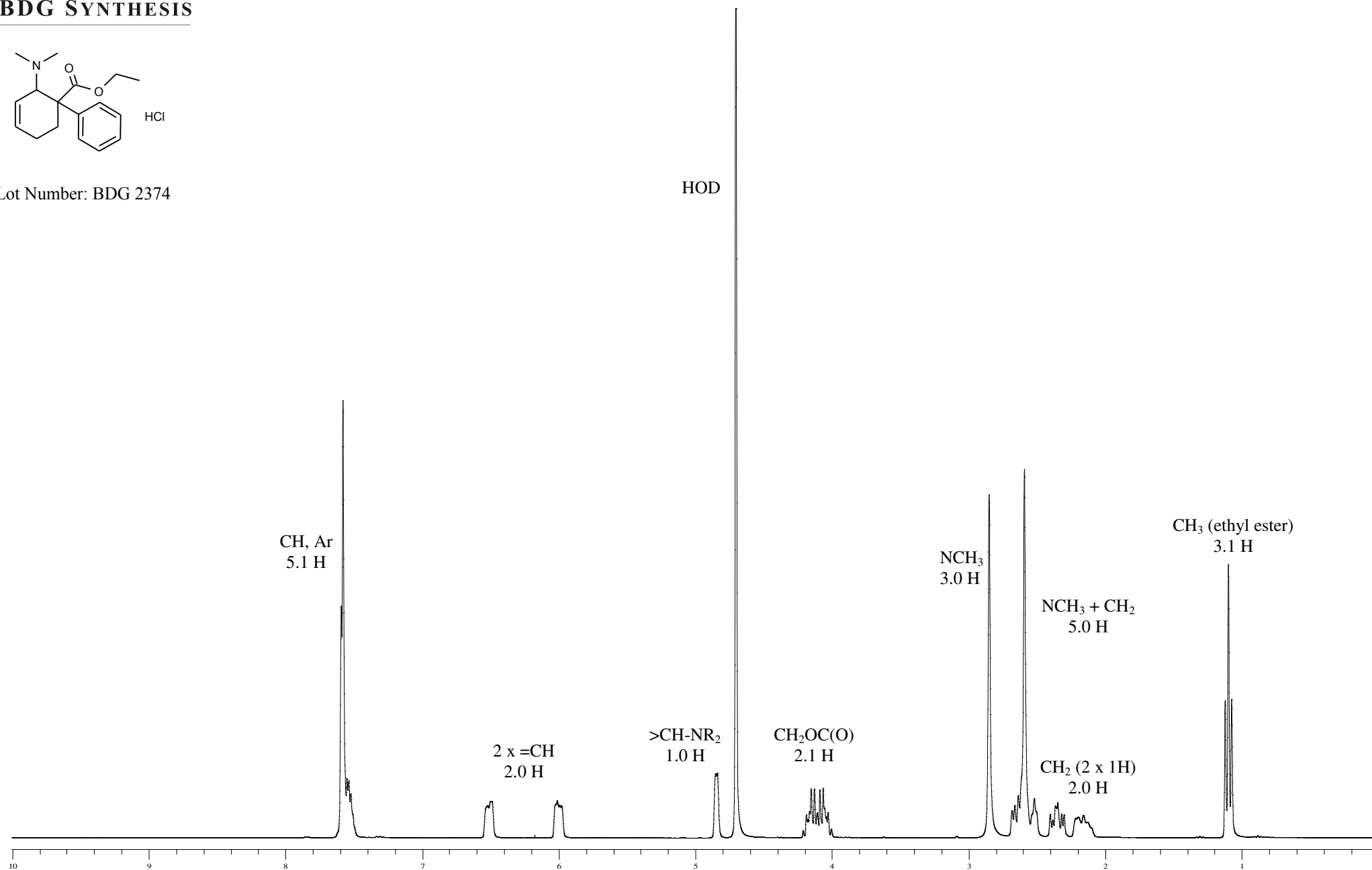


Proton NMR Spectrum of Tilidine HCl in D₂O

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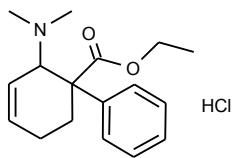
Lot Number: BDG 2374



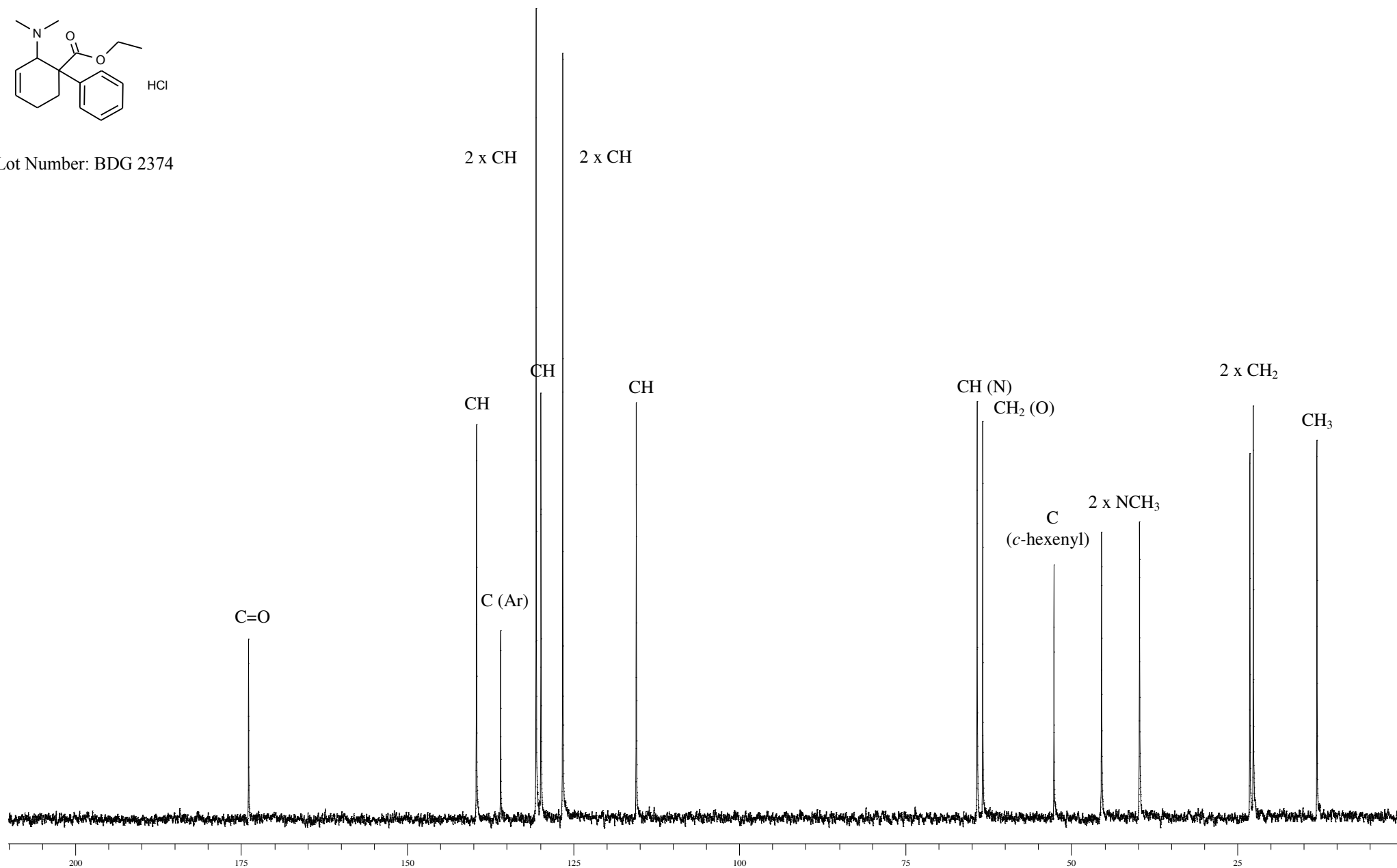


Carbon-13 NMR Spectrum of Tilidine HCl in D₂O

BDG SYNTHESIS



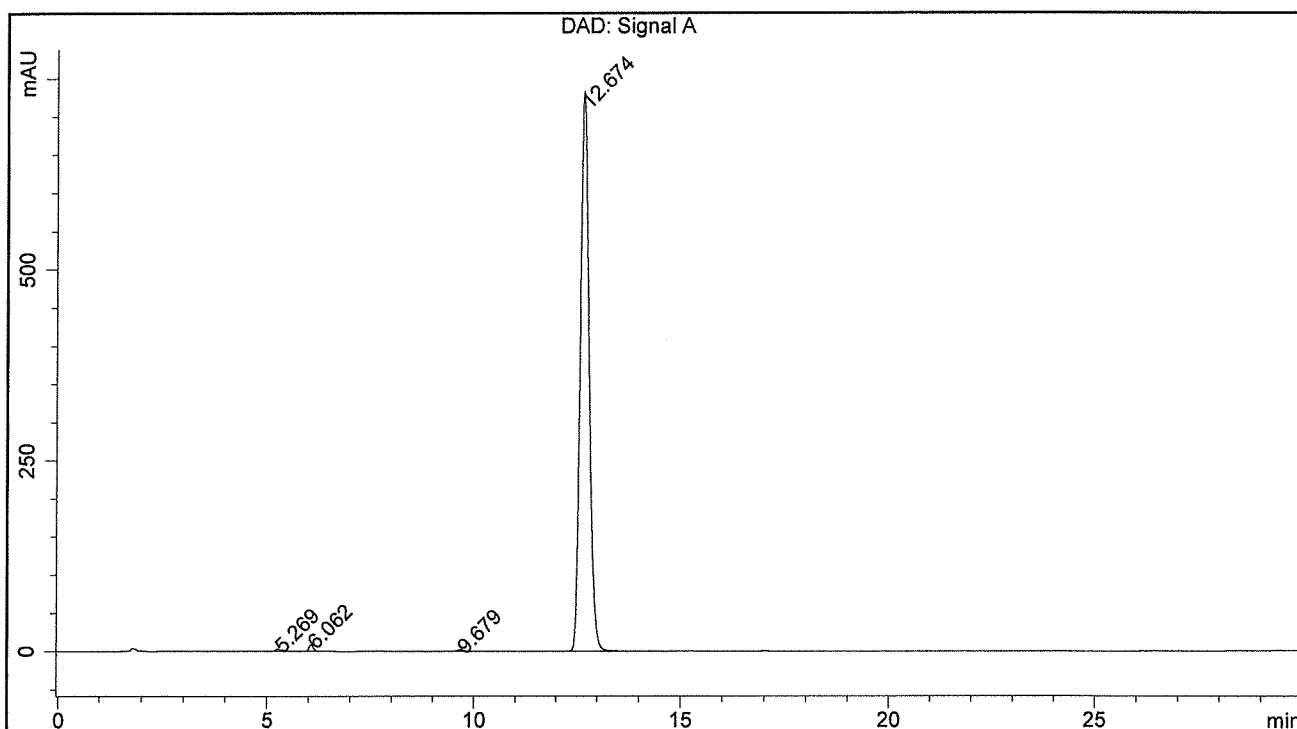
Lot Number: BDG 2374



BDG - Analysis of Tilidine HCl

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase : 30:70 0.98 g/L Ammonium Carbonate : Acetonitrile
 Flow Rate : 1.0 mL/min
 Sample Solvent : Water
 Column Temperature : 20C
 Injection Volume : 10 uL
 Detection : UV at 220 nm

Sample Name	BDG 2374	Instrument	AnalyticalLC01
Acquisition	22/12/2010, 15:45:40	Method (rev.)	LC10255c (6)
Sequence	BDG_22Dec2010b	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	5.27 min	3.0294	23.1074	0.1170 min	0.209 %
2	6.06 min	8.6395	63.6056	0.1139 min	0.576 %
3	9.68 min	1.9142	23.7183	0.1906 min	0.215 %
4	12.67 min	733.9618	10931.2515	0.2298 min	99.000 %