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Preparation and characterization of the 'research chemical' diphenidine, its pyrrolidine analogue, and their 2,2-diphenylethyl isomers

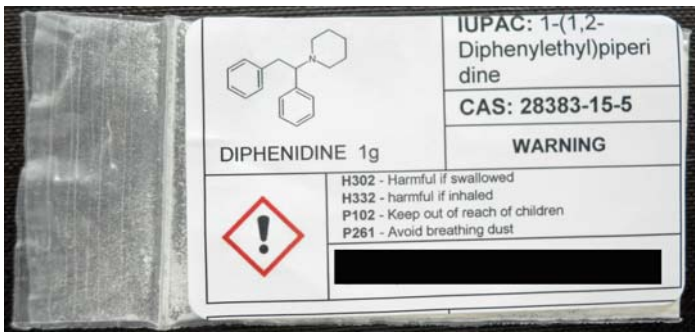
Jason Wallach, Pierce V. Kavanagh, Gavin McLaughlin, Noreen Morris, John D. Power, Simon P. Elliott, Marion S. Mercier, David Lodge, Hamilton Morris, Nicola M. Dempster, Simon D. Brandt

Correspondence to: Simon D. Brandt, School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University, Byrom Street, Liverpool, L3 3AF, UK. E-Mail: s.brandt@ljmu.ac.uk

Contents

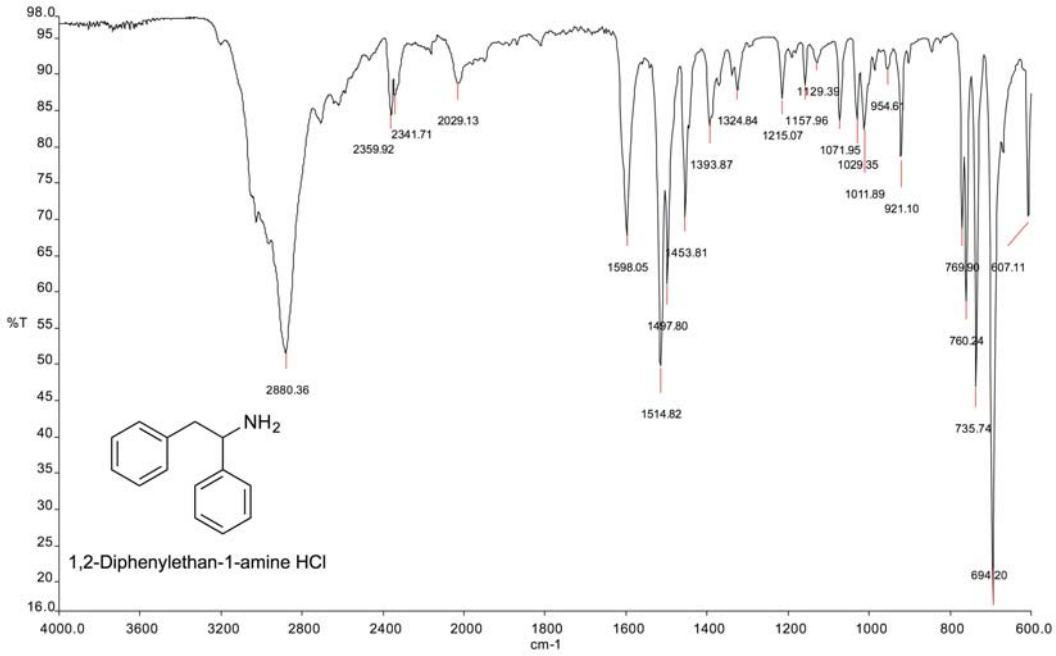
1) Representative photograph of a diphenidine product obtained online

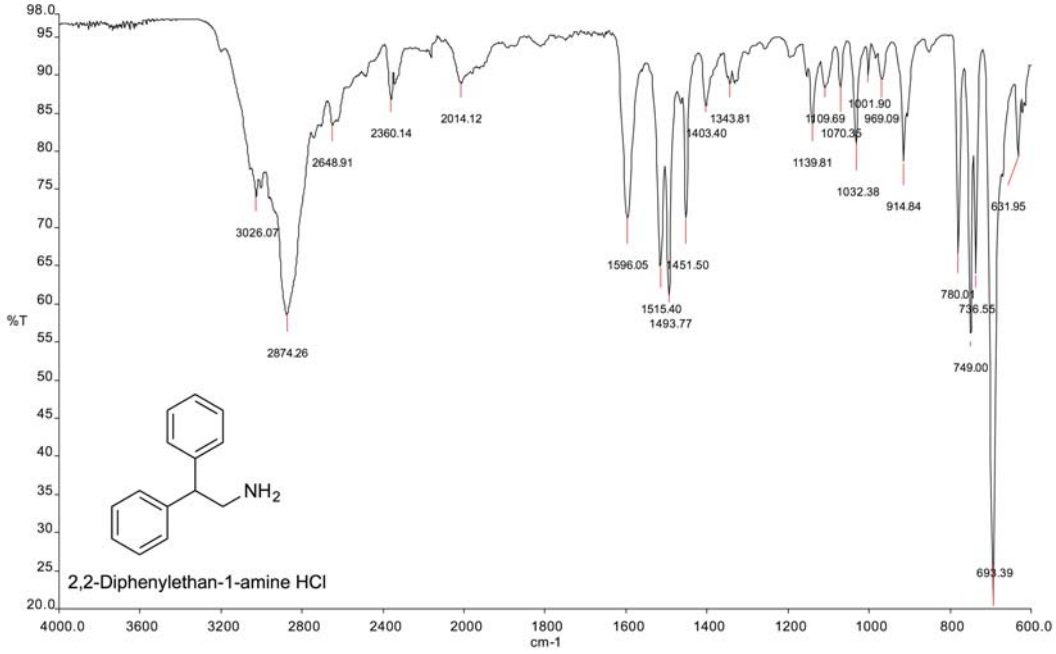
Note: CAS number refers to the hydrochloride salt of diphenidine



Infrared (IR) spectra were obtained on a Perkin Elmer Spectrum BX FTIR model using a Pike MIRacle ATR system. Data were acquired with the Spectrum v5.01 software (scan range 4000_400 cm^{-1}, resolution 4 cm^{-1}, 16 scans).

2) ATR-IR and NMR data of 1,2-diphenylethanamine HCl & 2,2-diphenylethanamine HCl





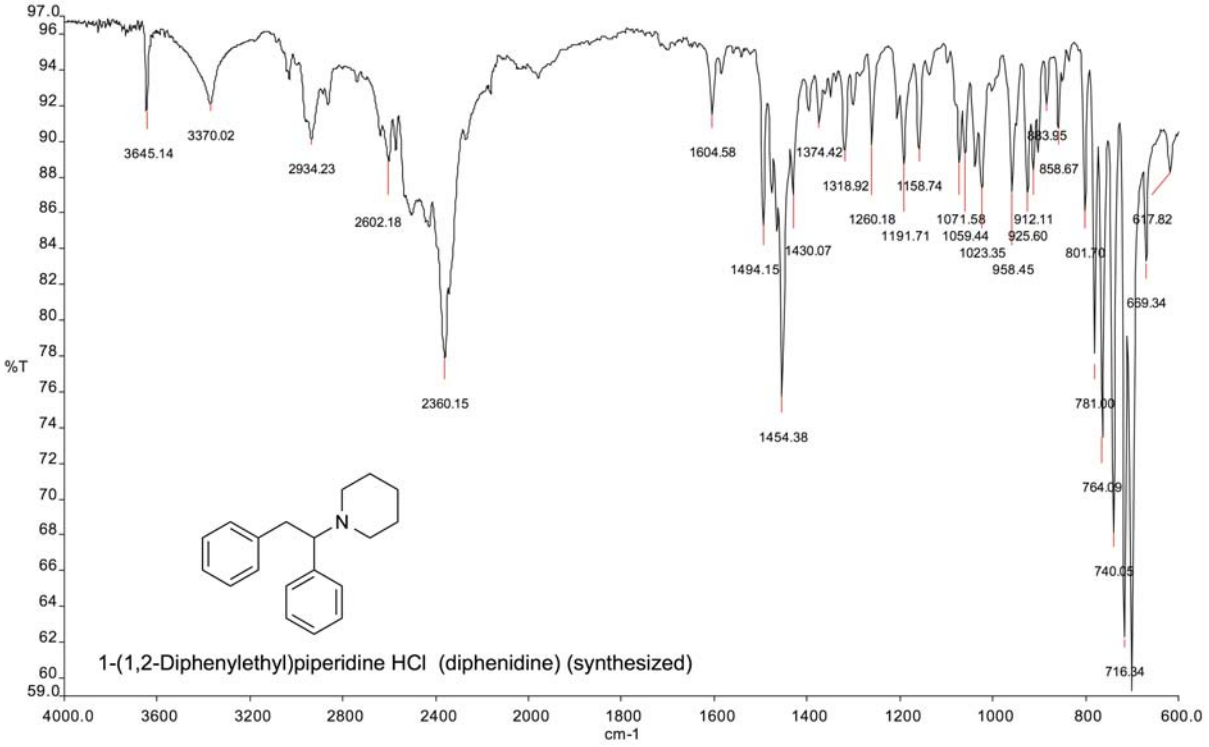
NMR 1,2-diphenylethanamine base (m.p. HCl salt 252.5-254.0 °C):

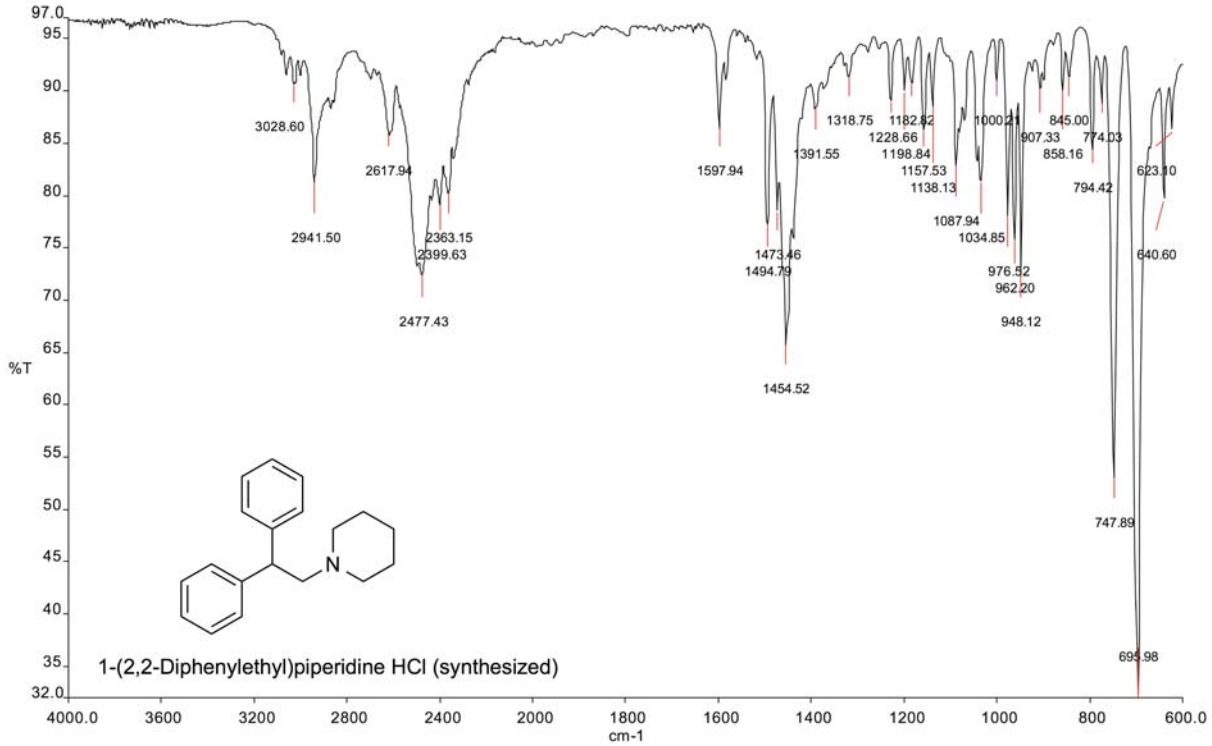
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.11 (10H, m, Ar-H), 4.19 (1H, dd, *J* = 8.8, 4.9 Hz, C_1H), 3.01 (1H, dd, *J* = 13.3, 4.9 Hz, C_2H), 2.83 (1H, dd, *J* = 13.3, 8.8 Hz, C_2H), 1.4 (2H, s, NH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.64 (quat. Ar-C), 139.09 (quat. Ar-C), 129.34 (Ar-CH), 128.39 (Ar-CH), 127.04 (Ar-CH), 126.42 (Ar-CH), 126.35 (Ar-CH), 57.55 (C_1H), 46.59 (CH_2).

NMR 2,2-diphenylethanamine base (m.p. HCl salt > 260 °C):

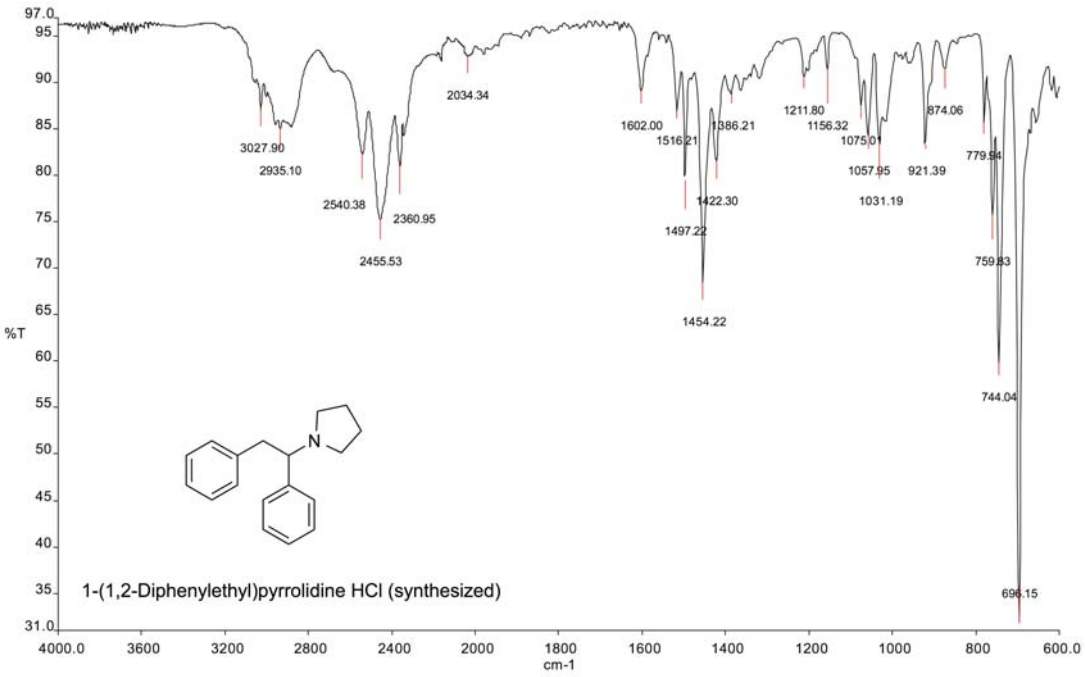
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.14 (10H, m, Ar-H), 3.98 (1H, t, *J* = 7.6 Hz, C_2H), 3.31 (2H, d, *J* = 7.6 Hz, C_1H_2), 1.45 (2H, s, NH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.69 (2 x quat. Ar-C), 128.61 (4 x Ar-CH), 128.08 (4 x Ar-CH), 126.52 (2 x Ar-CH), 55.02 (C_1H_2), 47.01 (C_2H).

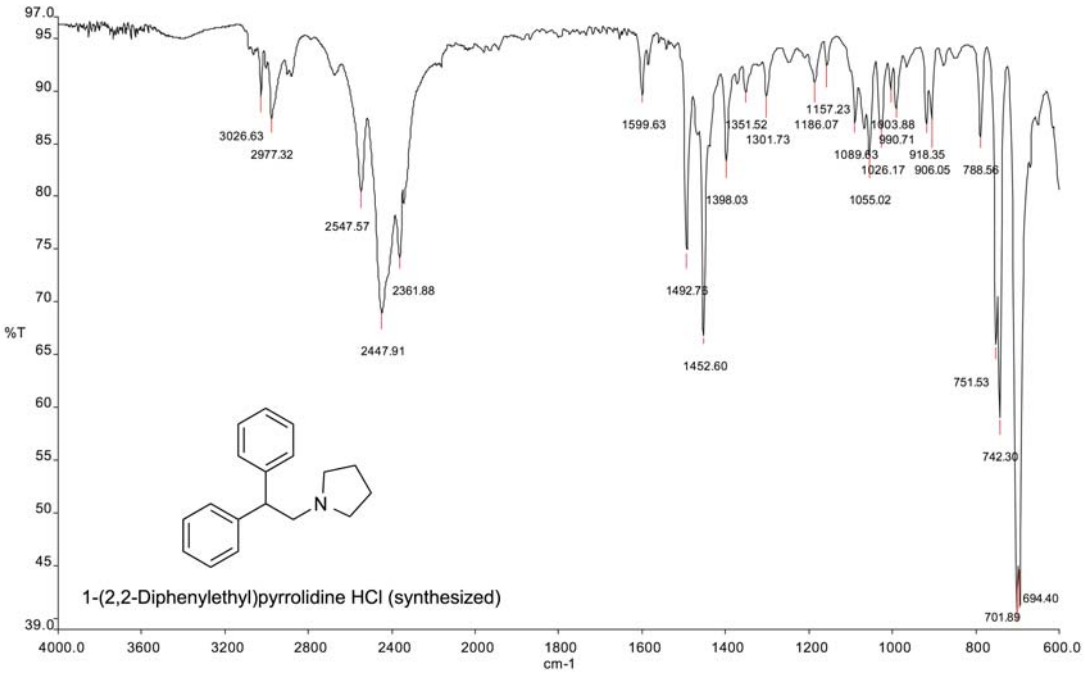
3) ATR-IR of 1-(1,2-diphenylethyl)piperidine (1,2-DEP, diphenidine) (**1**) and 1-(2,2-diphenylethyl)piperidine (2,2-DEP, diphenidine isomer) (**2**)



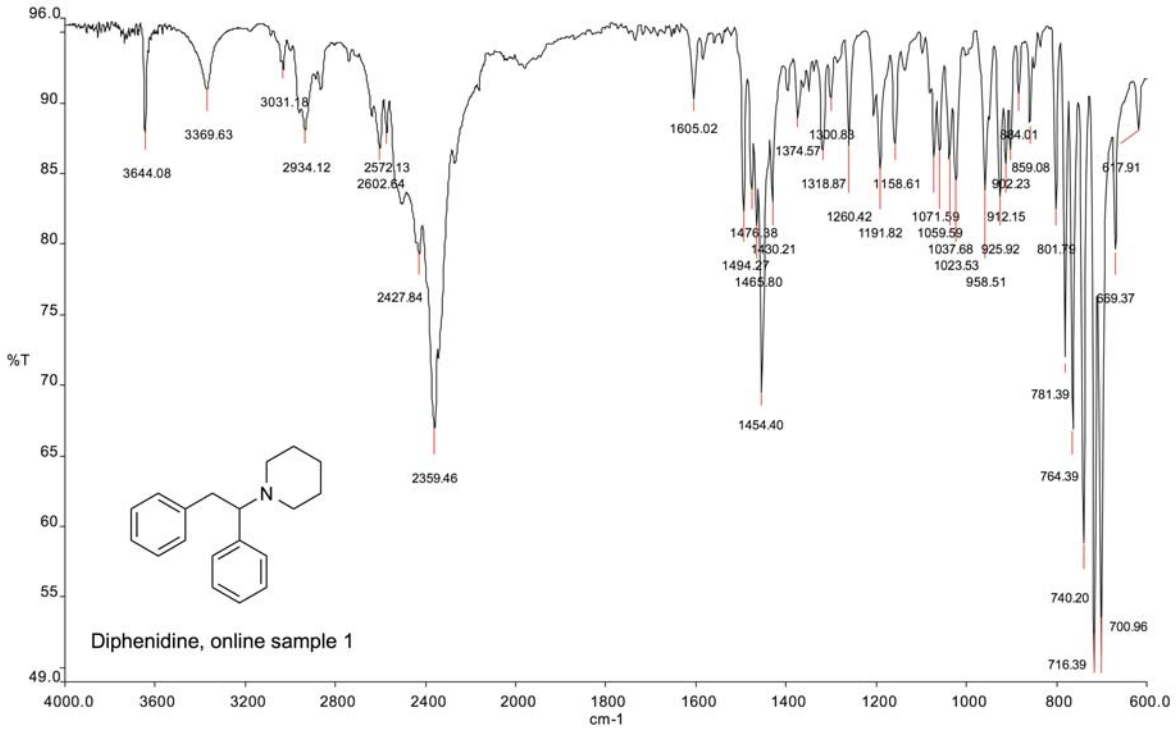


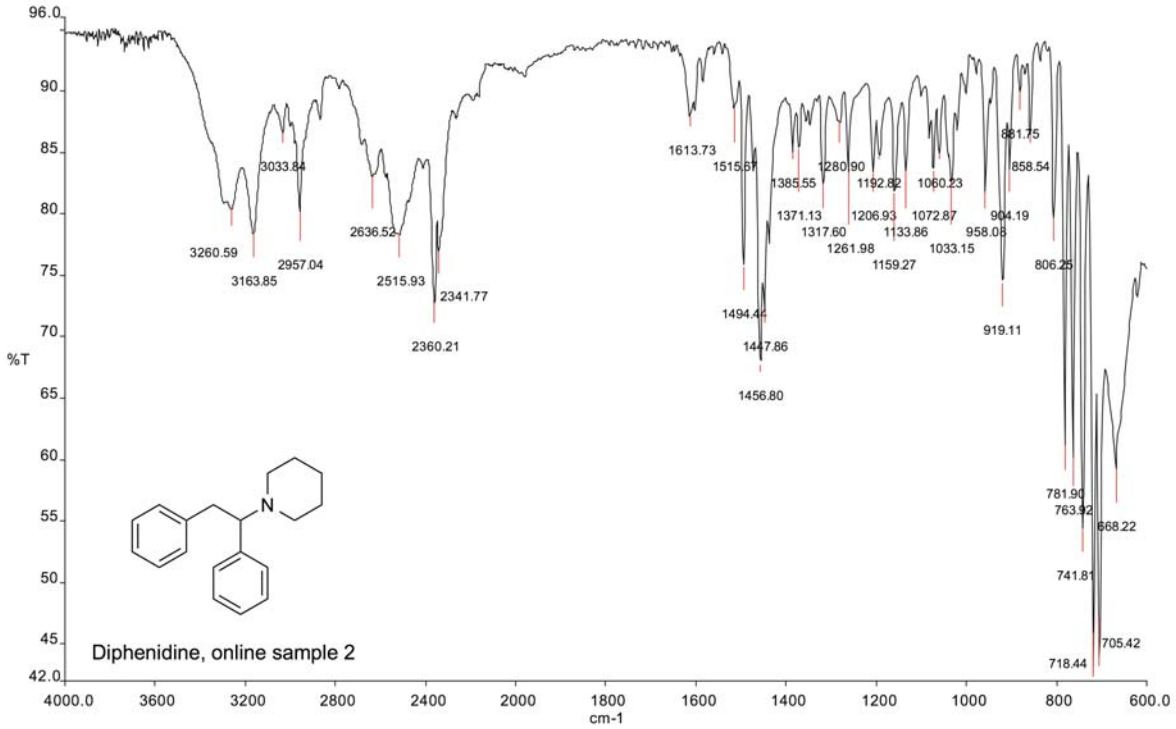
4) ATR-IR of 1-(1,2-diphenylethyl)pyrrolidine (1,2-DEPy) (**3**) and 1-(2,2-diphenylethyl)pyrrolidine (2,2-DEPy) (**4**)



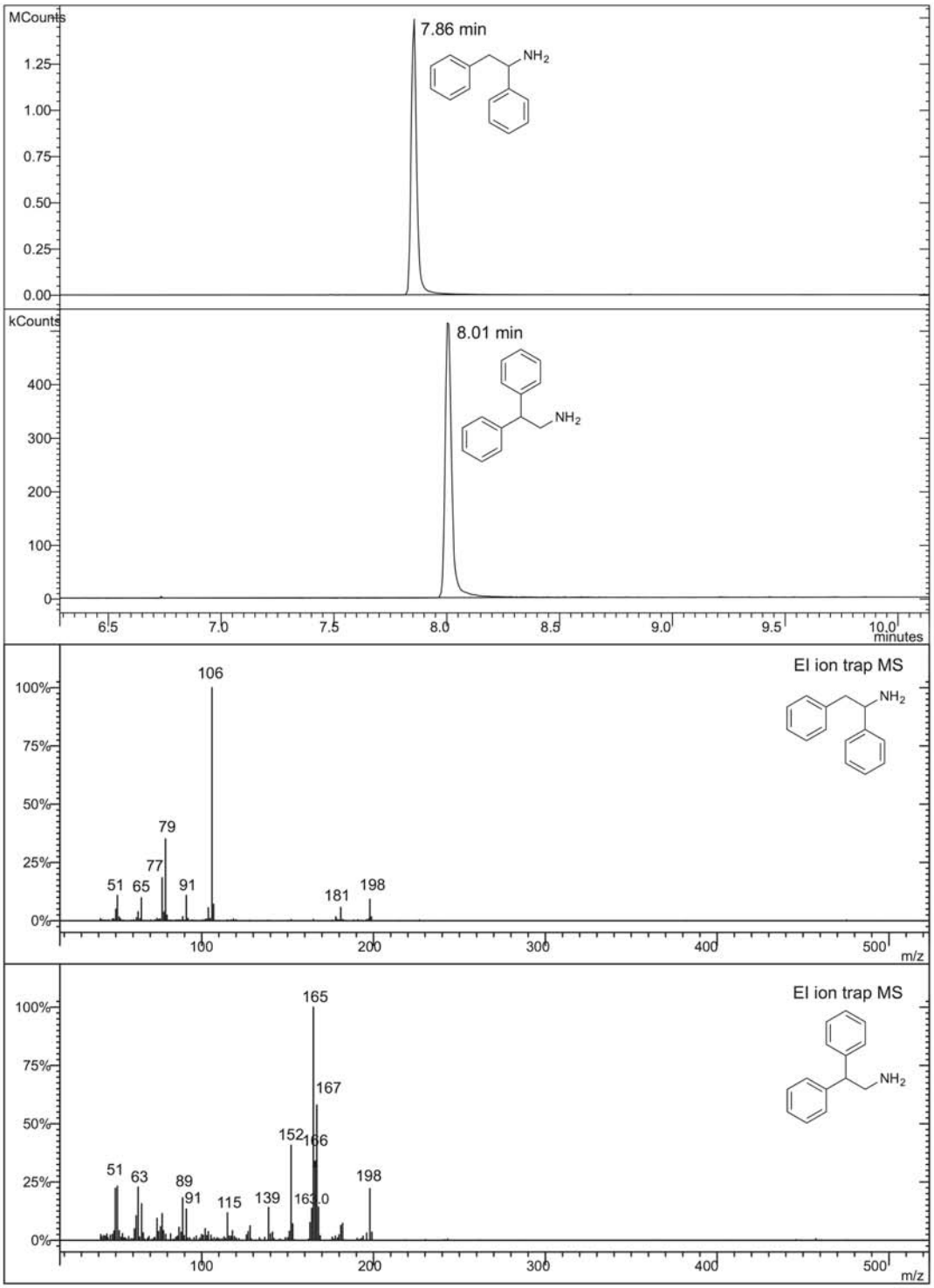


5) ATR-IR of two diphenidine samples obtained online

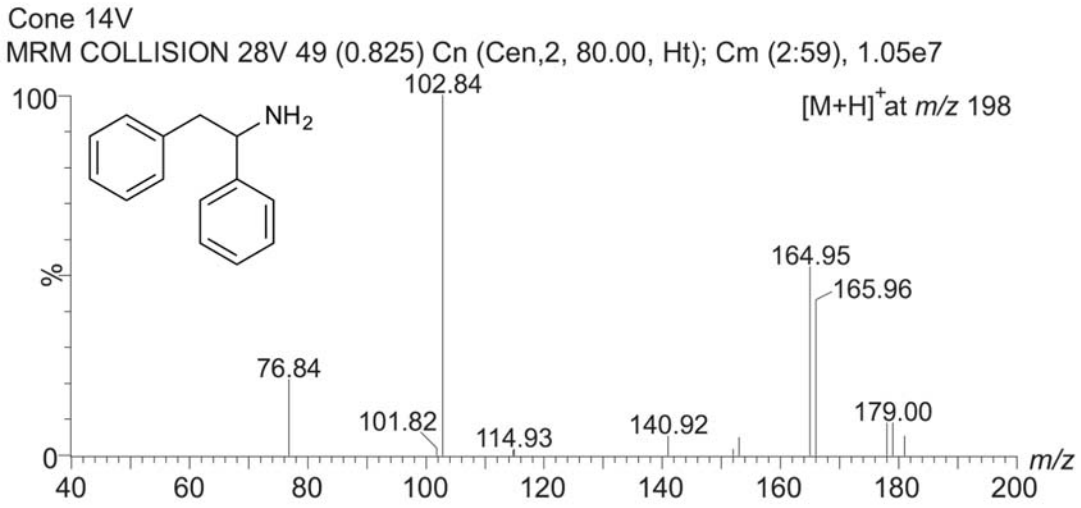


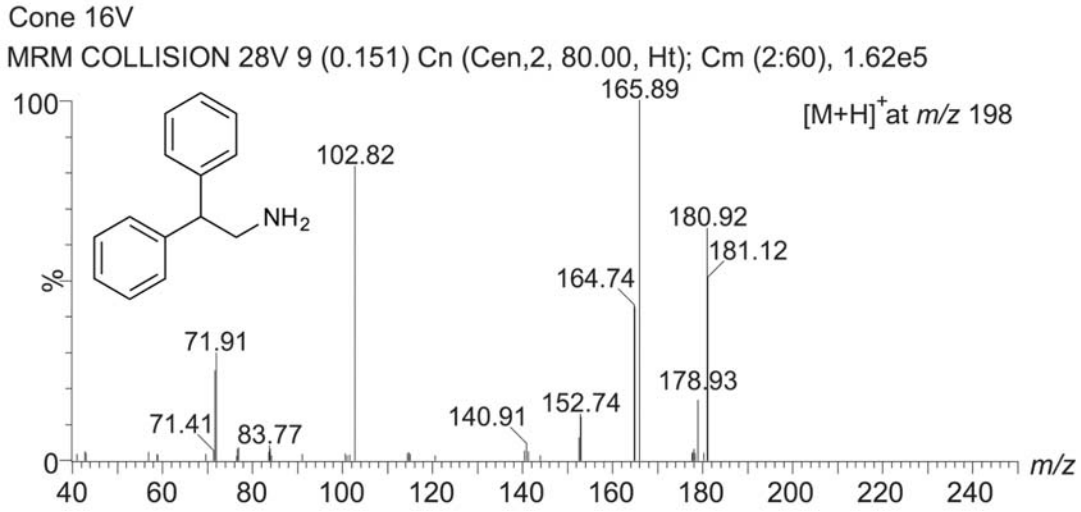


6) GC-MS and EI ion trap MS spectra of 1,2-diphenylethanamine HCl & 2,2-diphenylethanamine HCl

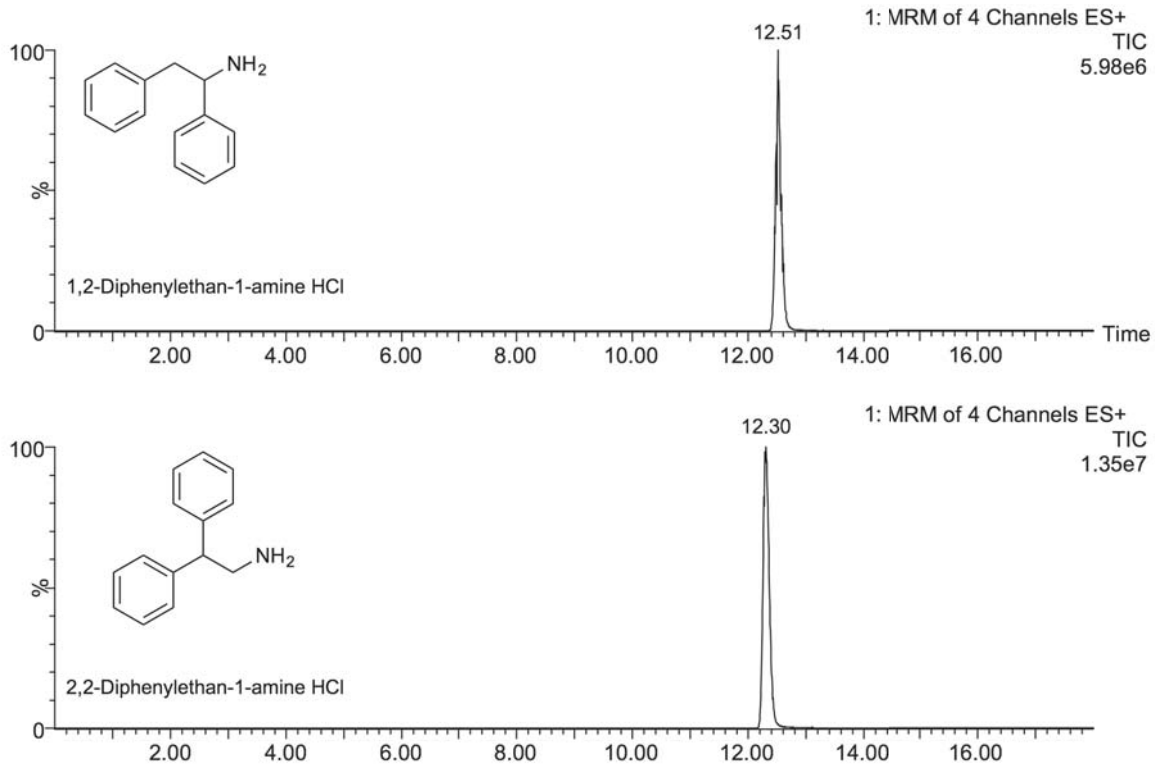


7) ESI-triple quadrupole tandem mass spectra of 1,2-diphenylethanamine HCl & 2,2-diphenylethanamine HCl





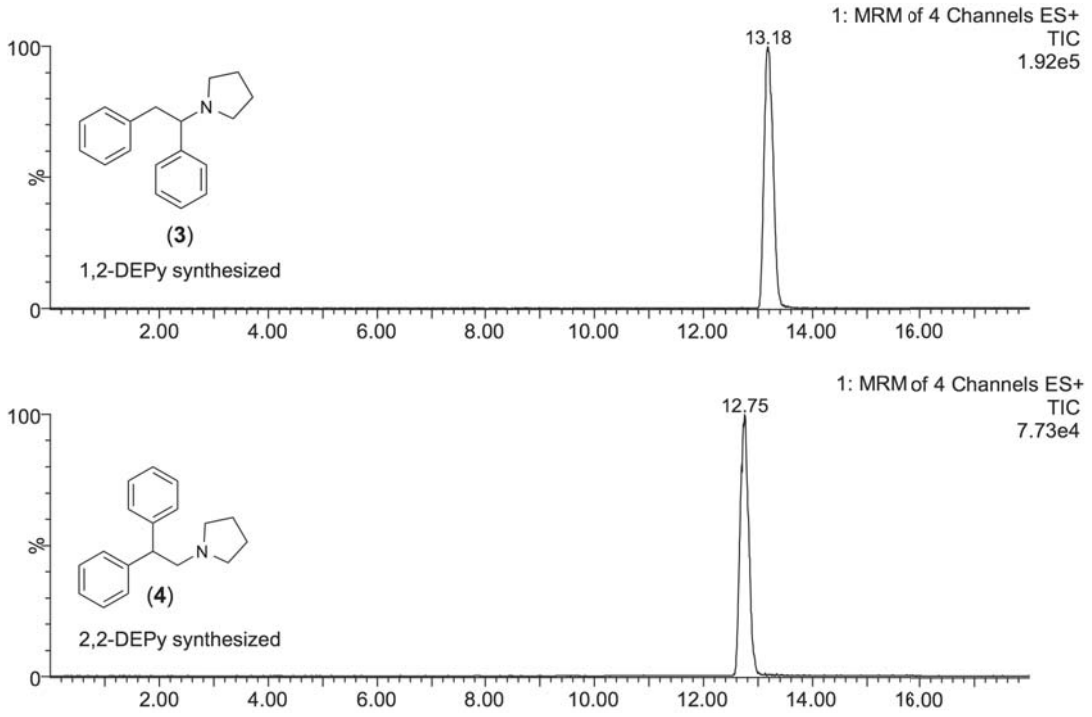
8) LC-ESI-MS/MS chromatograms of 1,2-diphenylethanamine HCl & 2,2-diphenylethanamine HCl



Selected ion transitions:

m/z 198 > 72 (48 eV)
m/z 198 > 103 (35 eV)
m/z 198 > 166 (28 eV)
m/z 198 > 181 (20 eV)

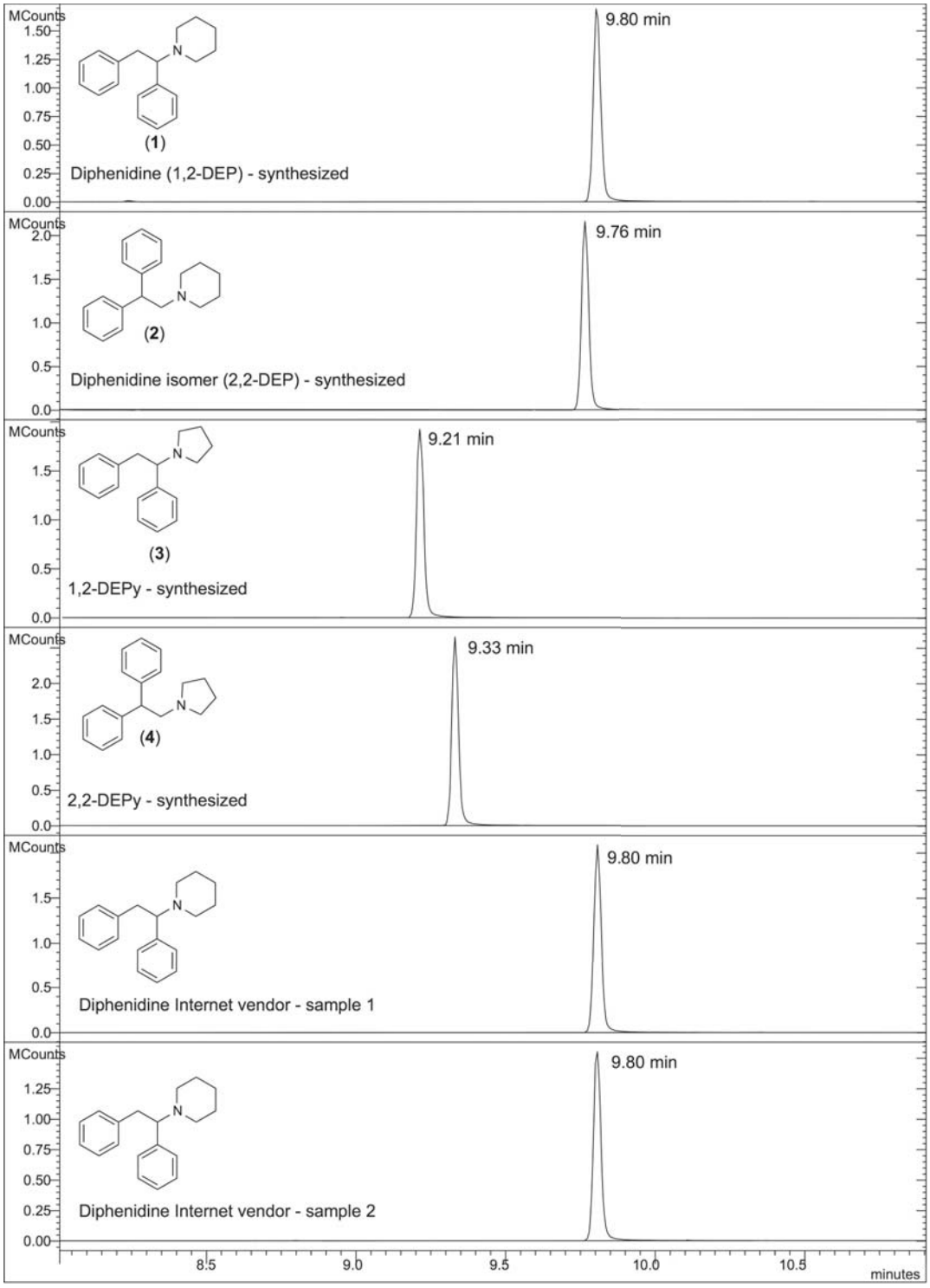
9) LC-ESI-MS/MS chromatograms 1-(1,2-diphenylethyl)pyrrolidine (1,2-DEPy) (**3**) and 1-(2,2-diphenylethyl)pyrrolidine (2,2-DEPy) (**4**)



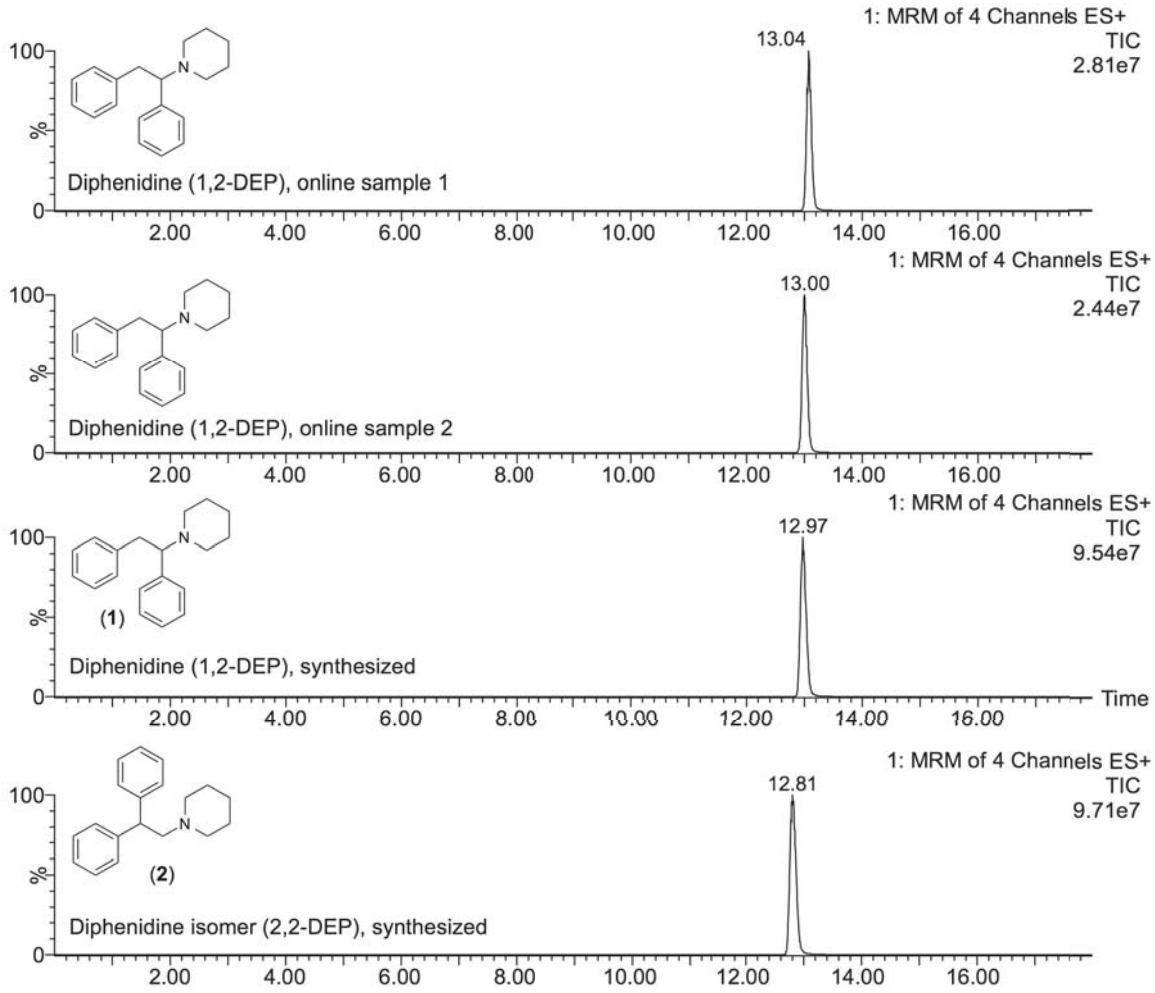
Selected ion transitions:

m/z 252 > 72 (48 eV)
m/z 252 > 103 (35 eV)
m/z 252 > 166 (28 eV)
m/z 252 > 181 (20 eV)

10) GC-EI-MS traces of (**1**) – (**4**) and two diphenidine samples obtained online



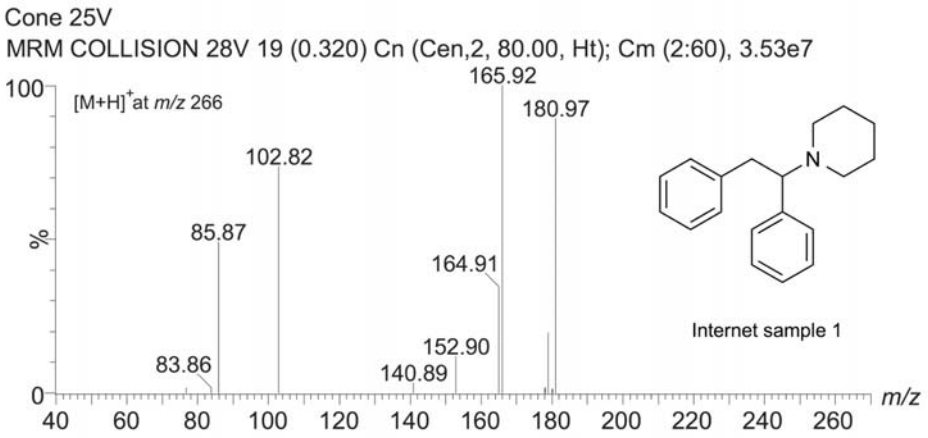
11) LC-ESI-MS/MS traces of synthesized (**1**) and (**2**) and two diphenidine samples obtained online

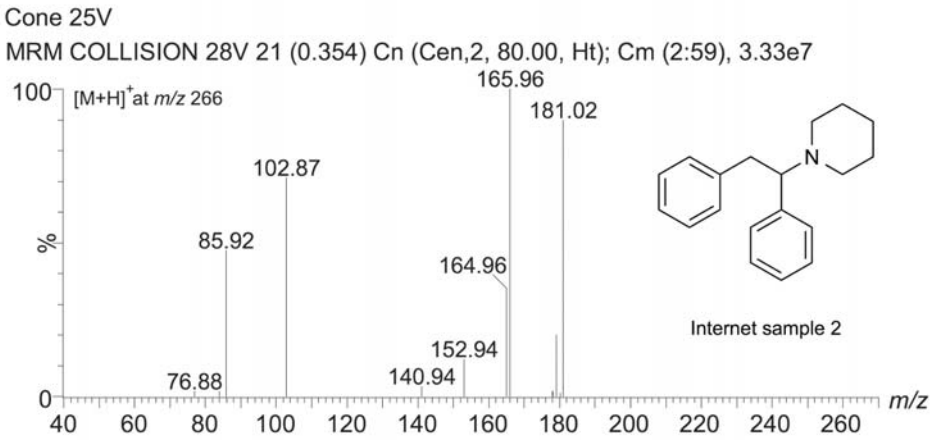


Selected ion transitions:

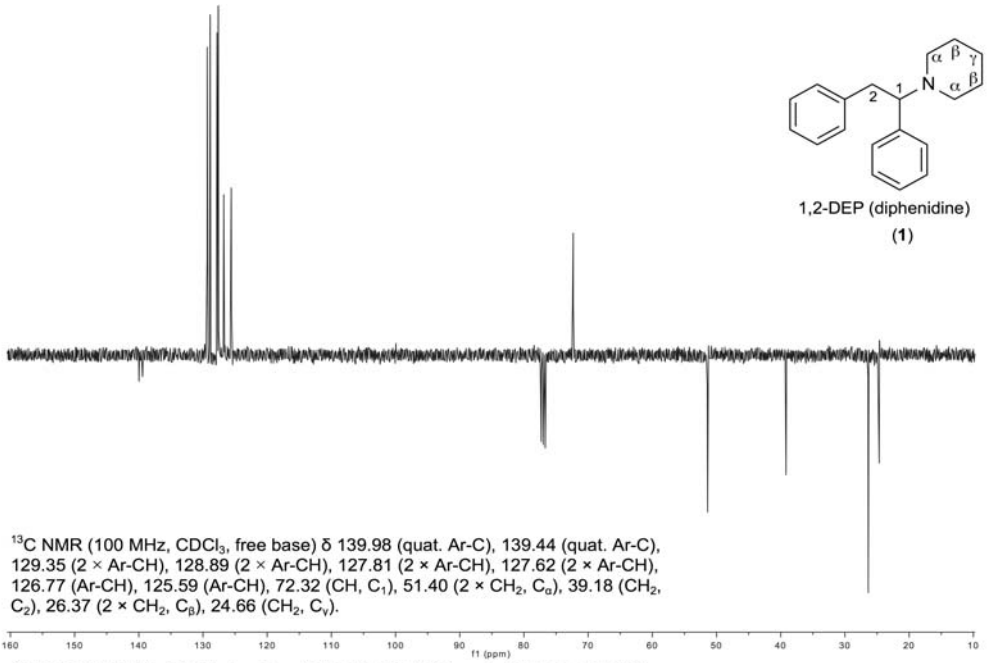
m/z 266 > 72 (48 eV)
m/z 266 > 103 (35 eV)
m/z 266 > 166 (28 eV)
m/z 266 > 181 (20 eV)

12) ESI-triple quadrupole tandem mass spectra of two diphenidine samples obtained online



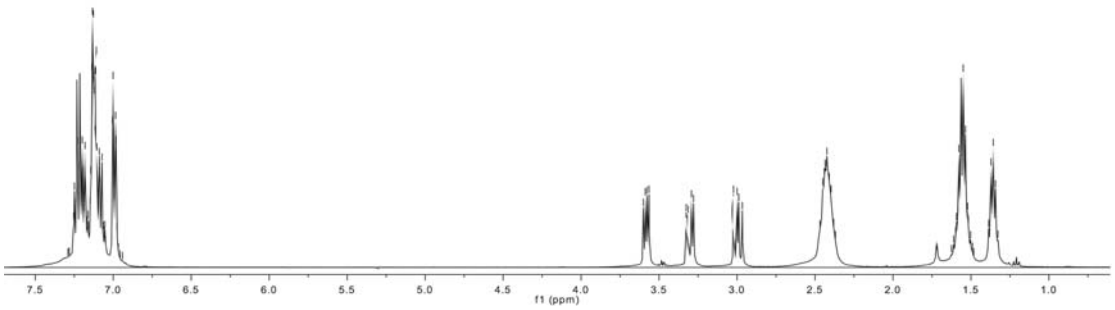


13) ^{1}H and ^{13}C NMR of diphenidine free base



^{13}C NMR (100 MHz, $CDCl_3$, free base) δ 139.98 (quat. Ar-C), 139.44 (quat. Ar-C), 129.35 (2 × Ar-CH), 128.89 (2 × Ar-CH), 127.81 (2 × Ar-CH), 127.62 (2 × Ar-CH), 126.77 (Ar-CH), 125.59 (Ar-CH), 72.32 (CH, C_1), 51.40 (2 × CH_2, C_α), 39.18 (CH_2, C_2), 26.37 (2 × CH_2, C_β), 24.66 (CH_2, C_γ).

^{1}H NMR (400 MHz, $CDCl_3$, free base) δ 7.37–7.03 (8H, m, Ar-H), 7.04–6.95 (2H, m, Ar-H), 3.58 (1H, dd, *J* = 9.4, 5.2 Hz, C_1H), 3.30 (1H, dd, *J* = 13.3, 5.2 Hz, C_2H), 2.99 (1H, dd, *J* = 13.4, 9.4 Hz, C_2H), 2.55–2.29 (4H, m, 2 x $C_\alpha H_2$), 1.64-1.45 (4H, m, 2 x $C_\beta H_2$), 1.36 (2H, quintet, *J* = 5.9 Hz, $C_\gamma H_2$).



14) Assigned ^{13}C and ^{1}H aliphatic and chemical shifts in ppm for compounds (**1**) – (**4**) and (**1**) HCl.

^{13}C Shift	1,2-DEP HCl (**1**)	1,2-DEP (**1**)	2,2-DEP (**2**)	1,2-DEPy (**3**)	2,2-DEPy (**4**)
C_1	72.90	72.32	64.53	73.31	61.74
C_2	36.75	39.18	48.89	42.96	50.87
C_α	53.39 48.81	51.40	54.85	53.0	54.55
C_β	22.71 22.65	26.37	25.99	23.35	23.50
C_γ	22.24	24.66	24.43	-	-

Assigned ^{13}C aliphatic chemical shifts in ppm for compounds (**1**) – (**4**) and (**1**) HCl.

^{1}H Shift	1,2-DEP HCl (**1**)	1,2-DEP (**1**)	2,2-DEP (**2**)	1,2-DEPy (**3**)	2,2-DEPy (**4**)
C_1	4.23 d (11.6, 1H)	3.58, dd (9.4, 5.2, 1H)	2.93, d (7.3, 2H)	3.30, dd (9.9, 4.3, 1H)	3.14, d (7.4, 2H)
C_2	4.04 dd (12.8, 3.1, 1H) 3.46 t (12.2, 1H)	3.30, dd (13.3, 5.2, 1H) 2.99, dd (13.4, 9.4, 1H)	4.21, t (7.3, 1H)	3.36, dd (13.3, 4.3, 1H) 2.96, dd (13.3, 9.9, 1H)	4.22, t (7.1, 1H)
C_α	3.64 d (10.3, 1H) 3.54 d (11.6, 1H) 2.68-2.39 m (2H)	2.55-2.29, m (4H)	2.39, t (5.4, 4H)	2.64, m (2H) 2.45, m (2H)	2.51, t (6.1, 4H)
C_β	2.68-2.39 m (1H) 1.93-1.76 m (3H)	1.64-1.45, m (4H)	1.46, quint (5.5, 4H)	1.77, quint (3.3, 4H)	1.72, quint (3.1, 4H)
C_γ	2.31 q (13.2, 12.2, 1H) 1.27 q (13.4, 12.4, 1H)	1.36, quint (5.9, 2H)	1.37, quint (5.4, 2H)	-	-

Assigned ^{1}H aliphatic chemical shifts in ppm for compounds (**1**) – (**4**) and (**1**) HCl. m = multiplet; d = doublet; t = triplet; q = quartet; quint = quintet.

15) HPLC-DAD traces for synthesized diphenidine isomers (**1**) and (**2**) and comparison with a diphenidine sample obtained from an online test purchase. Note: The overlapping UV maxima for traces (a) and (c) were 257 and 267 nm, respectively.

Analytical details have been described in: Y.N. Soh, S. Elliott. An investigation of the stability of emerging new psychoactive substances. *Drug Test. Anal.* **2013**, in press; doi: 10.1002/dta.1576.