Wallach, J, Kavanagh, PV, Mclaughlin, G, Morris, N, Power, JD, Elliott, SP, Mercier, MS, Lodge, D, Morris, H, Dempster, NM and Brandt, SD

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

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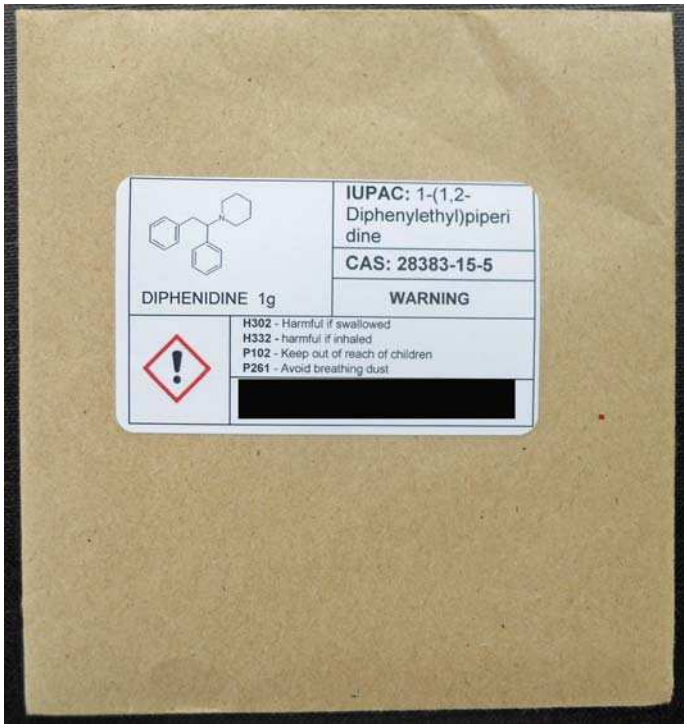
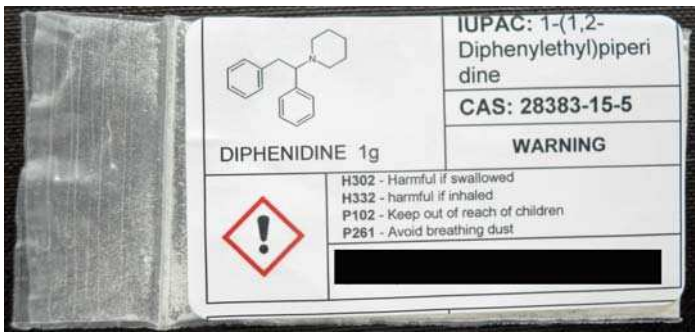
Contents

1) Representative photograph of a diphenidine product obtained online

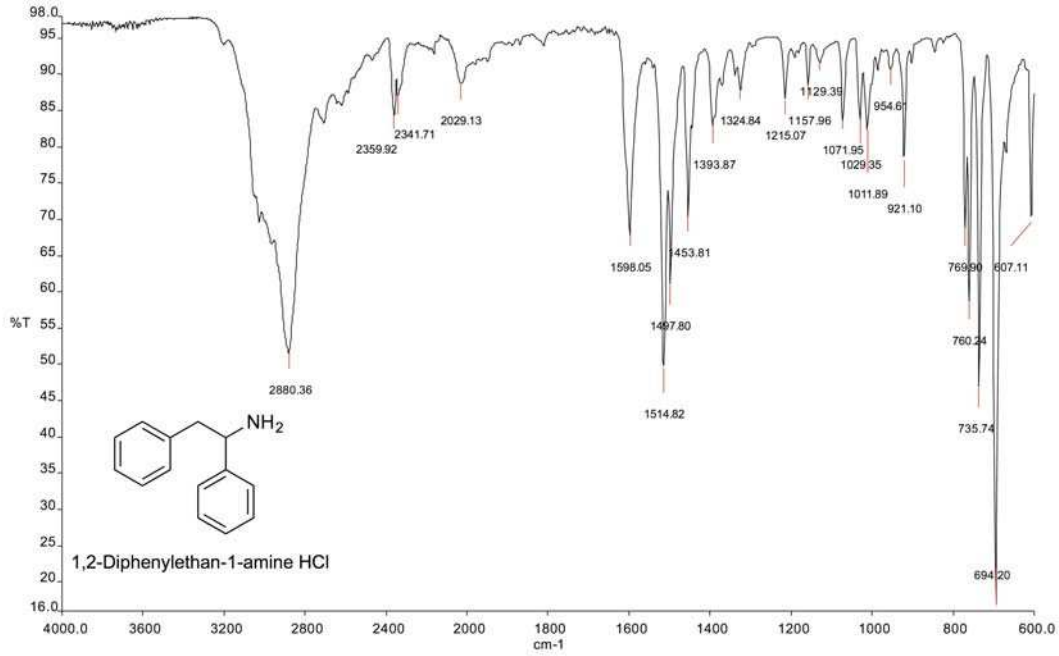


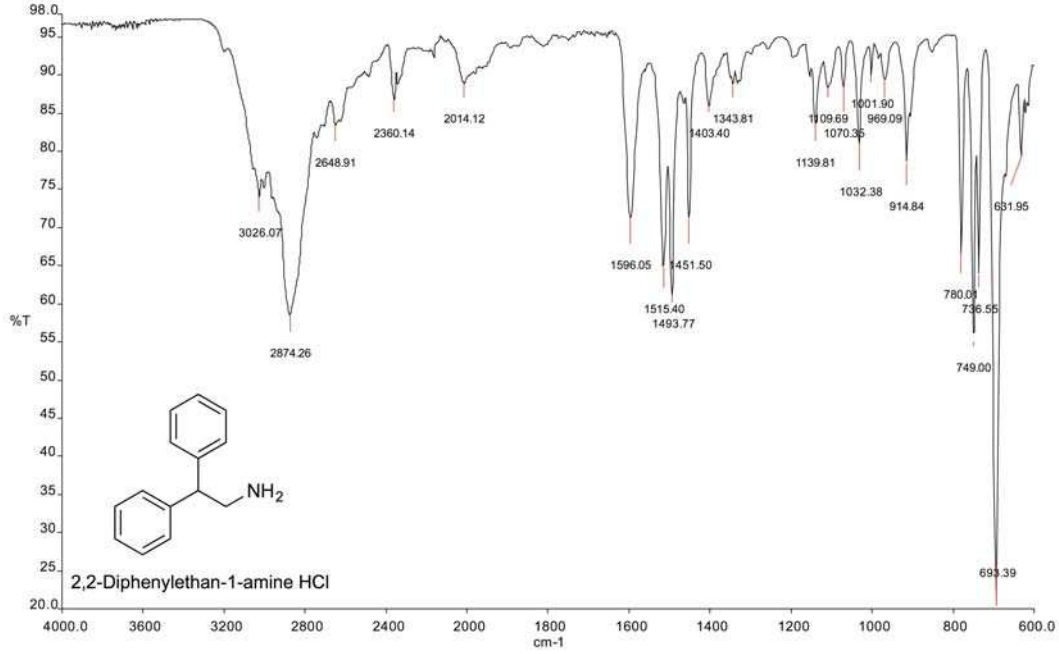
Note: CAS number refers to the hydrochloride salt of diphenidine



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





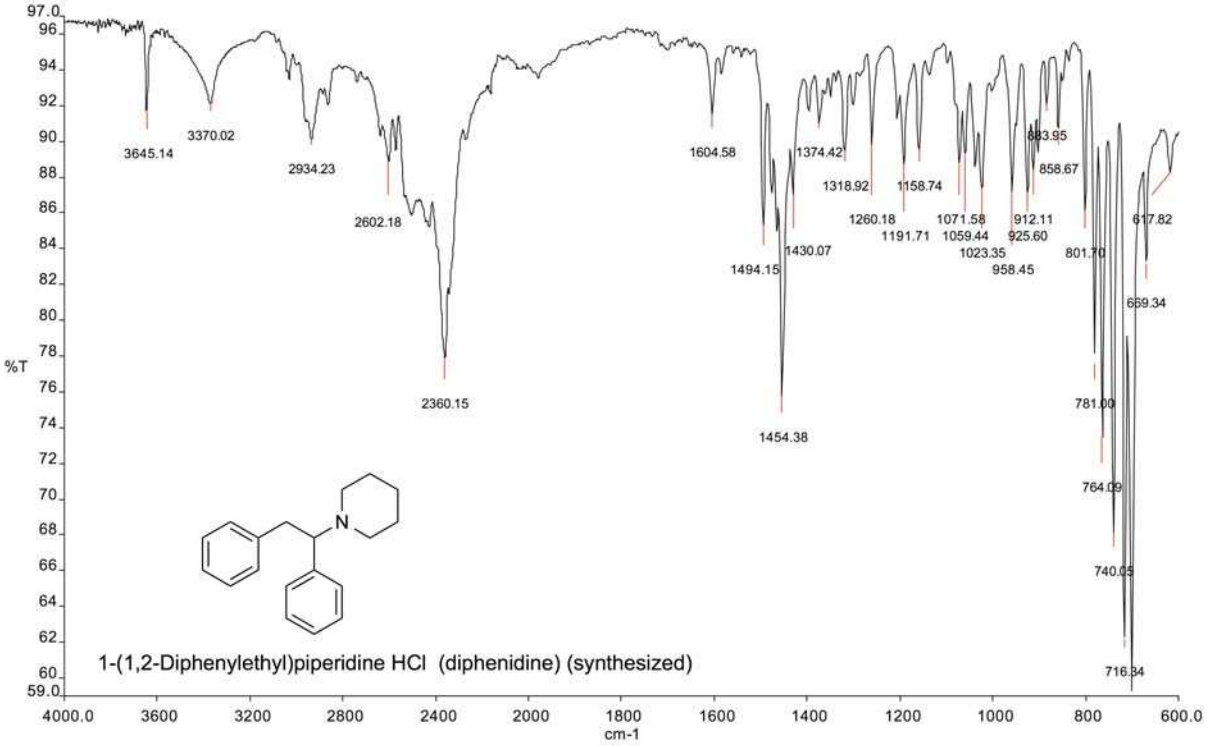
NMR 1,2-diphenylethanamine base (m.p. HCl salt 252.5-254.0 ℃):

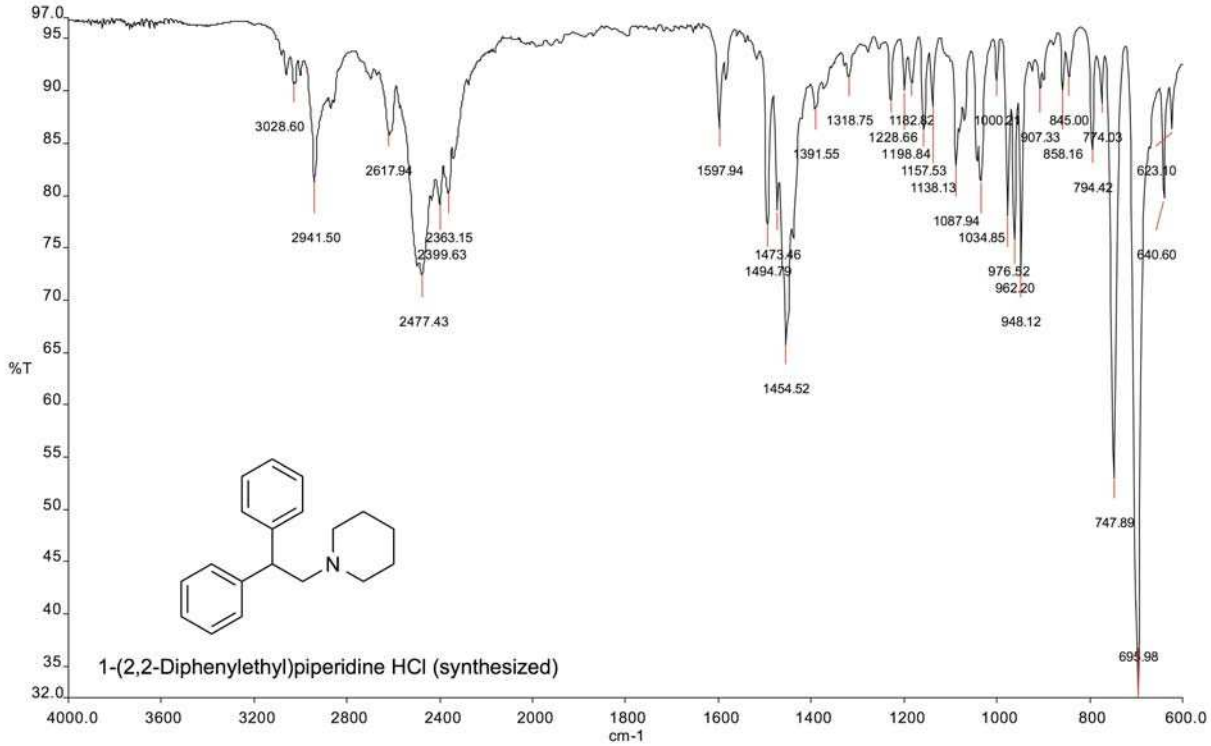
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.11 (10H, m, Ar-H), 4.19 (1H, dd, *J* = 8.8, 4.9 Hz, C_1H), 3.01 (1H, dd, *J* = 13.3, 4.9 Hz, C_2H), 2.83 (1H, dd, *J* = 13.3, 8.8 Hz, C_2H), 1.4 (2H, s, NH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.64 (quat. Ar-C), 139.09 (quat. Ar-C), 129.34 (Ar-CH), 128.39 (Ar-CH),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

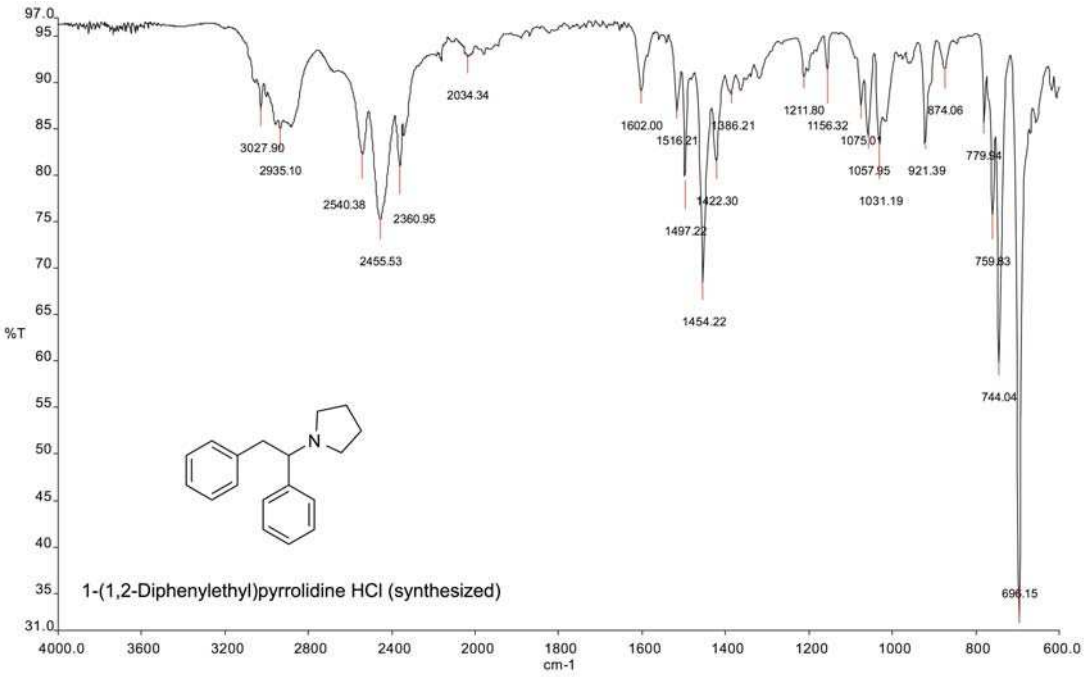
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.14 (10H, m, Ar-H), 3.98 (1H, t, *J* = 7.6 Hz, C_2H), 3.31 (2H, d, *J* = 7.6 Hz, C_1H_2), 1.45 (2H, s, NH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.69 (2 x quat. Ar-C), 128.61 (4 x Ar-CH), 128.08 (4 x Ar-CH), 126.52 (2 x Ar-CH), 55.02 (C_1H_2), 47.01 (C_2H).

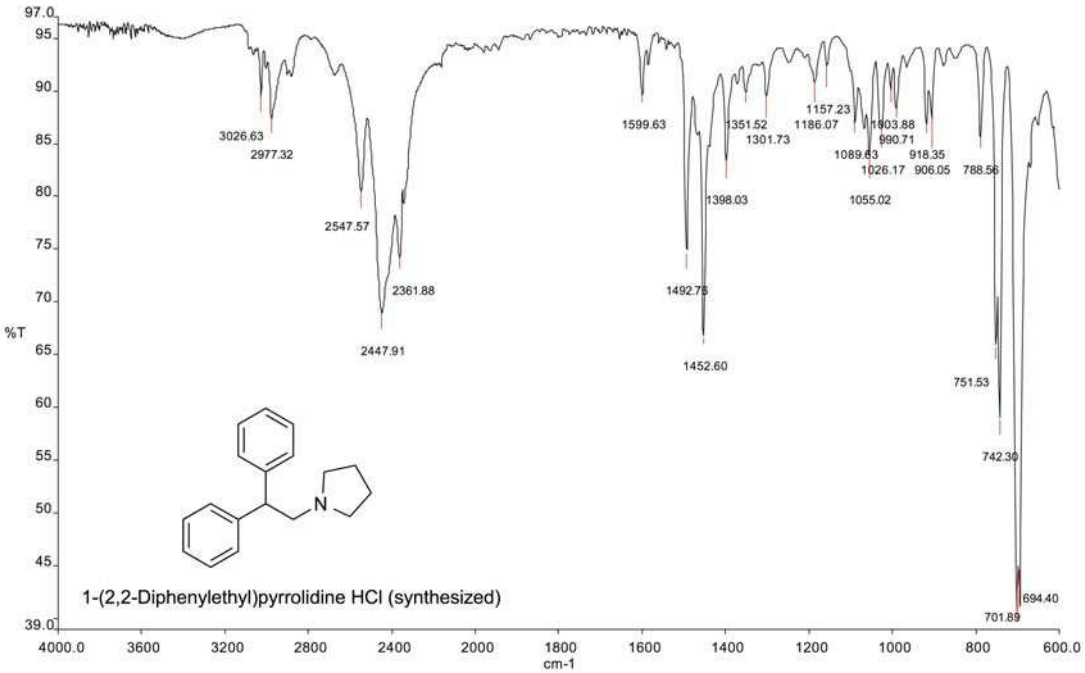
3) ATR-IR of 1-(1,2-diphenylethyl)piperidine (1,2-DEP, diphenidine) (**1**) and 1-(2,2-diphenylethyl)piperidine (2,2-DEP, diphenidine isomer) (**2**)



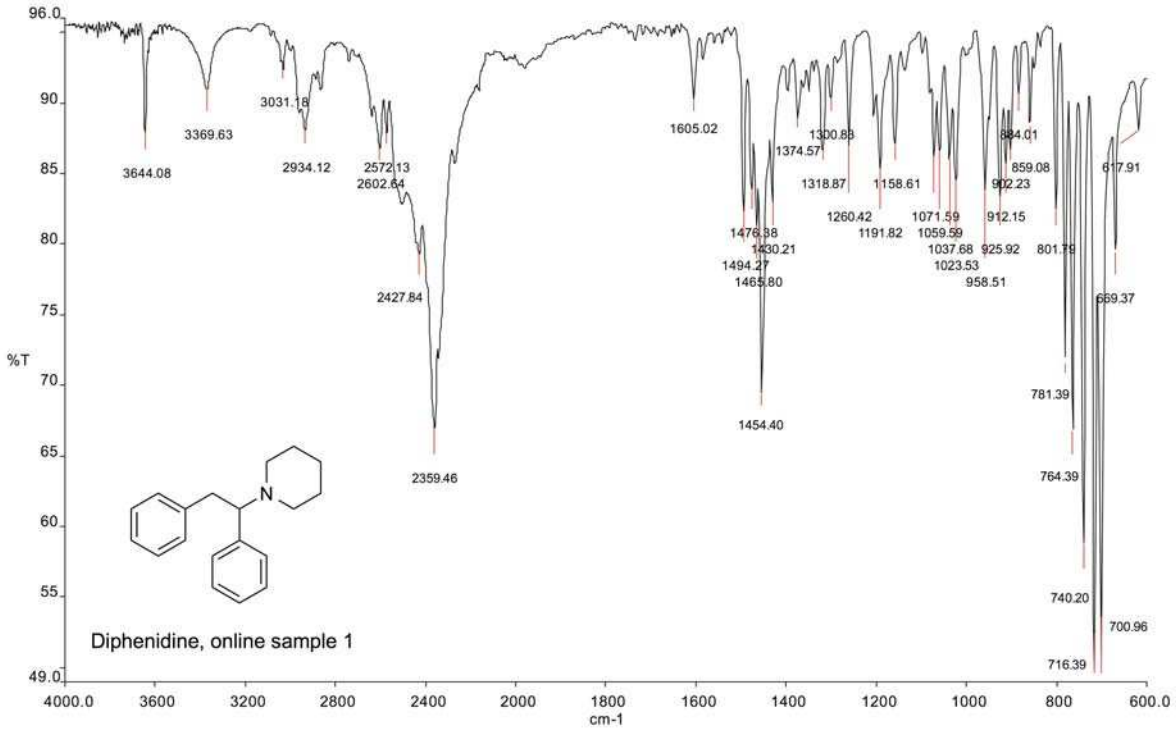


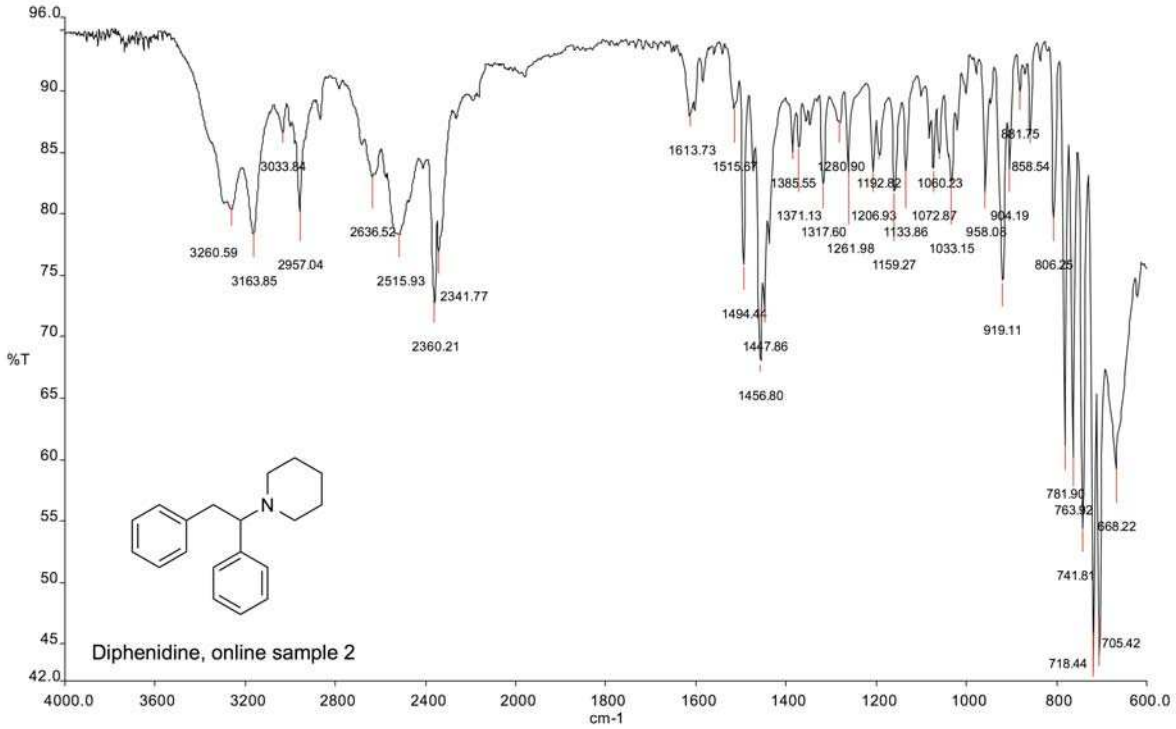
4) ATR-IR of 1-(1,2-diphenylethyl)pyrrolidine (1,2-DEPy) (**3**) and 1-(2,2-diphenylethyl)pyrrolidine (2,2-DEPy) (**4**)



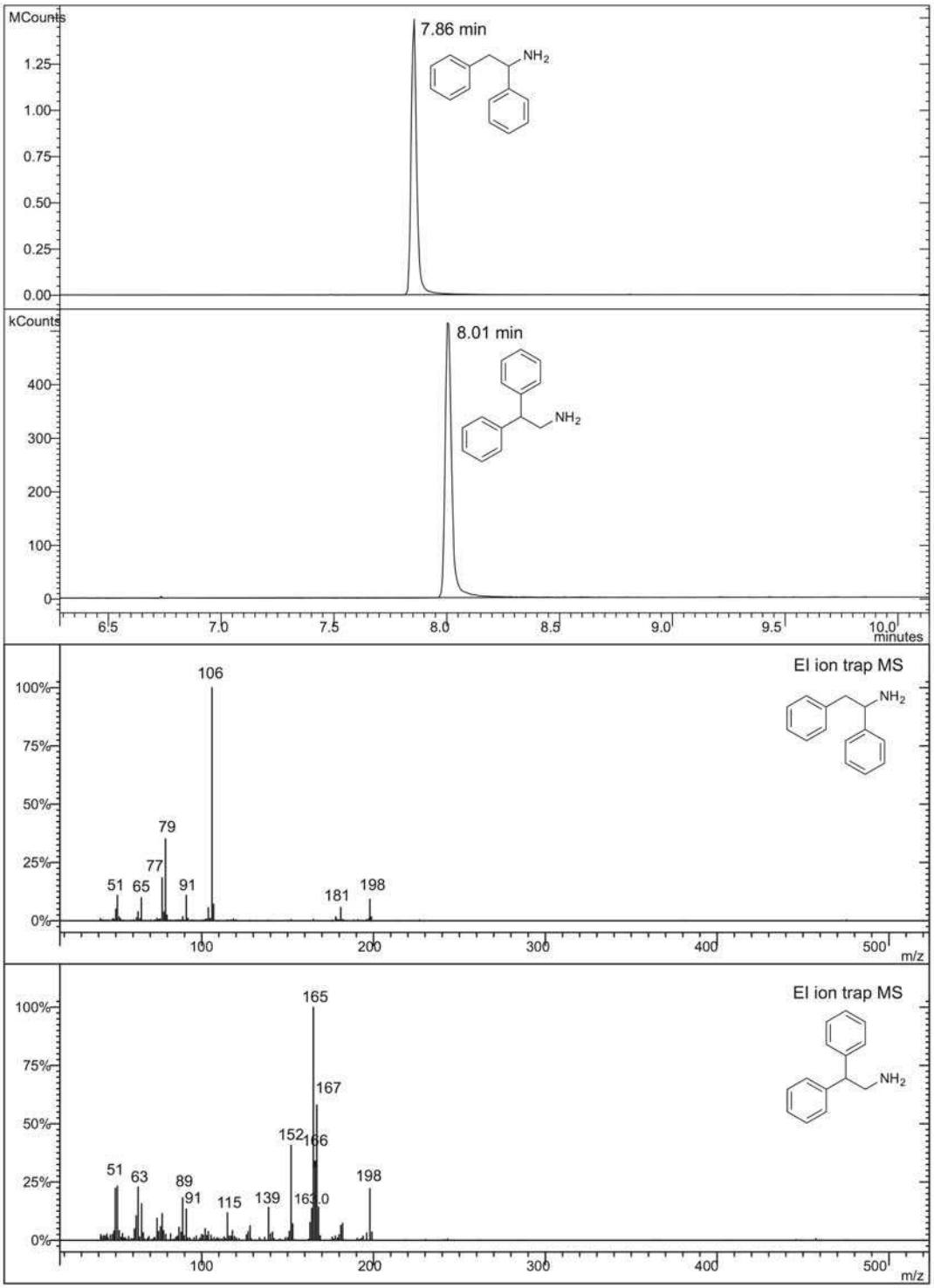


5) ATR-IR of two diphenidine samples obtained online

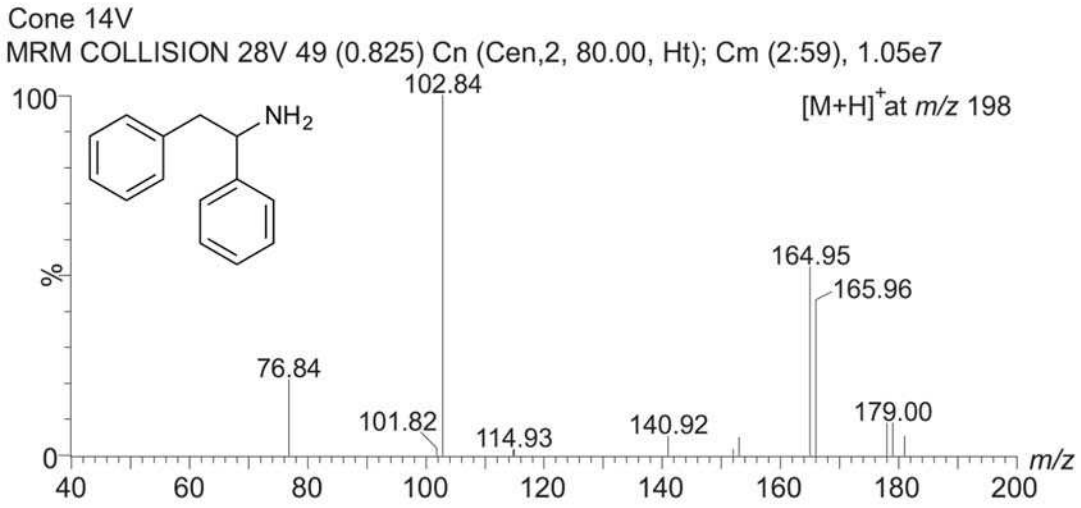


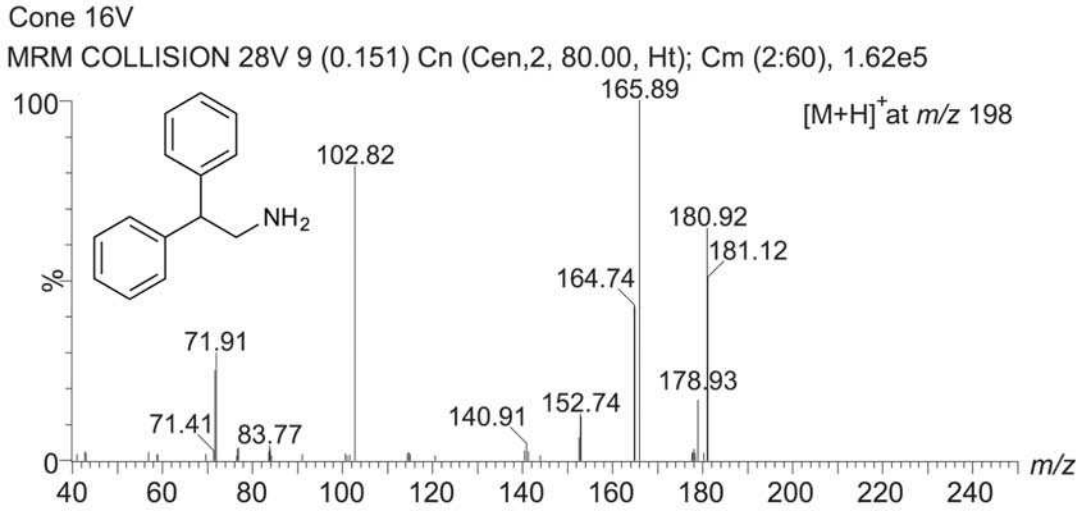


6) GC-MS and EI ion trap MS spectra of 1,2-diphenylethanamine HCl & 2,2-diphenylethanamine HCl

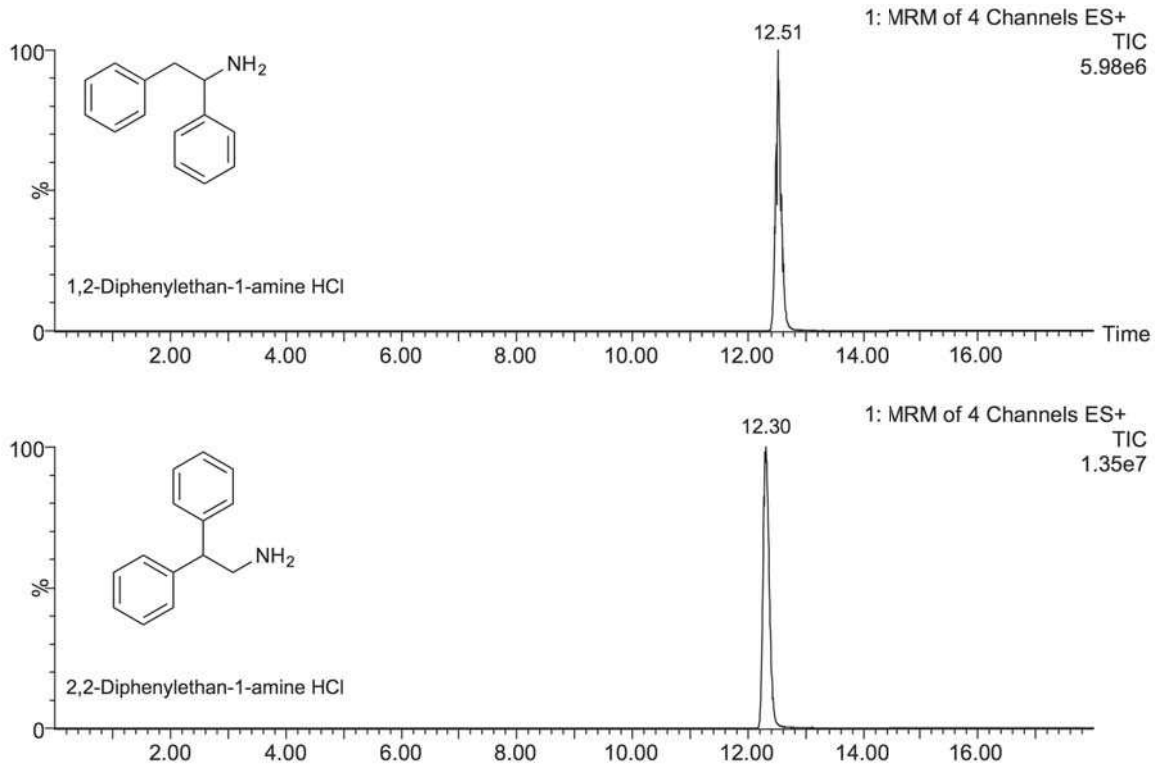


7) ESI-triple quadrupole tandem mass spectra of 1,2-diphenylethanamine HCl & 2,2-diphenylethanamine HCl





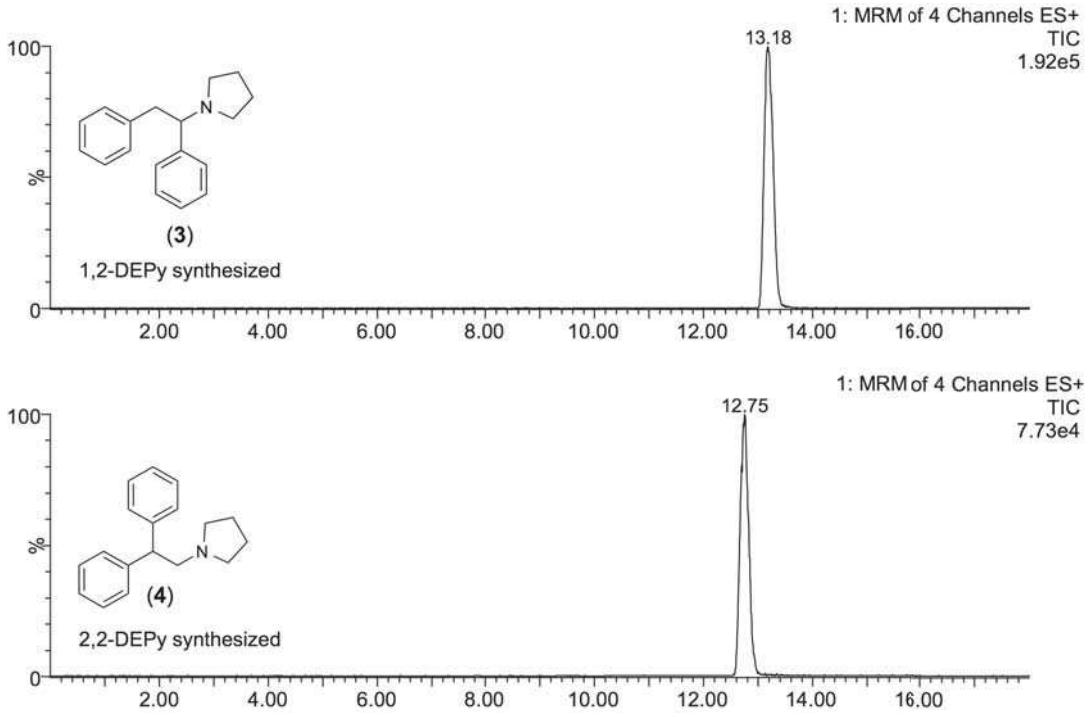
8) LC-ESI-MS/MS chromatograms of 1,2-diphenylethanamine HCl & 2,2-diphenylethanamine HCl



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)

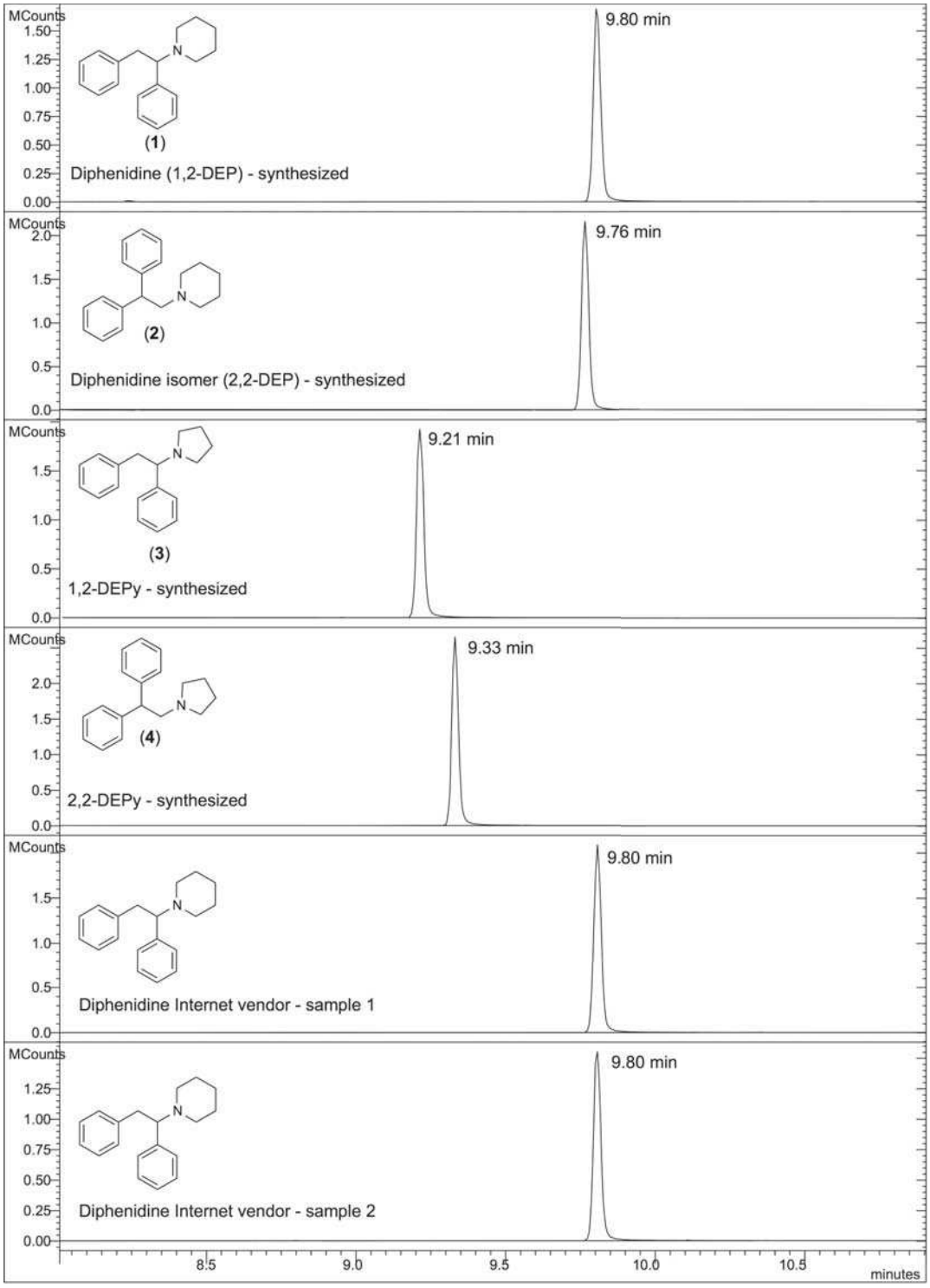
9) LC-ESI-MS/MS chromatograms 1-(1,2-diphenylethyl)pyrrolidine (1,2-DEPy) (**3**) and 1-(2,2-diphenylethyl)pyrrolidine (2,2-DEPy) (**4**)



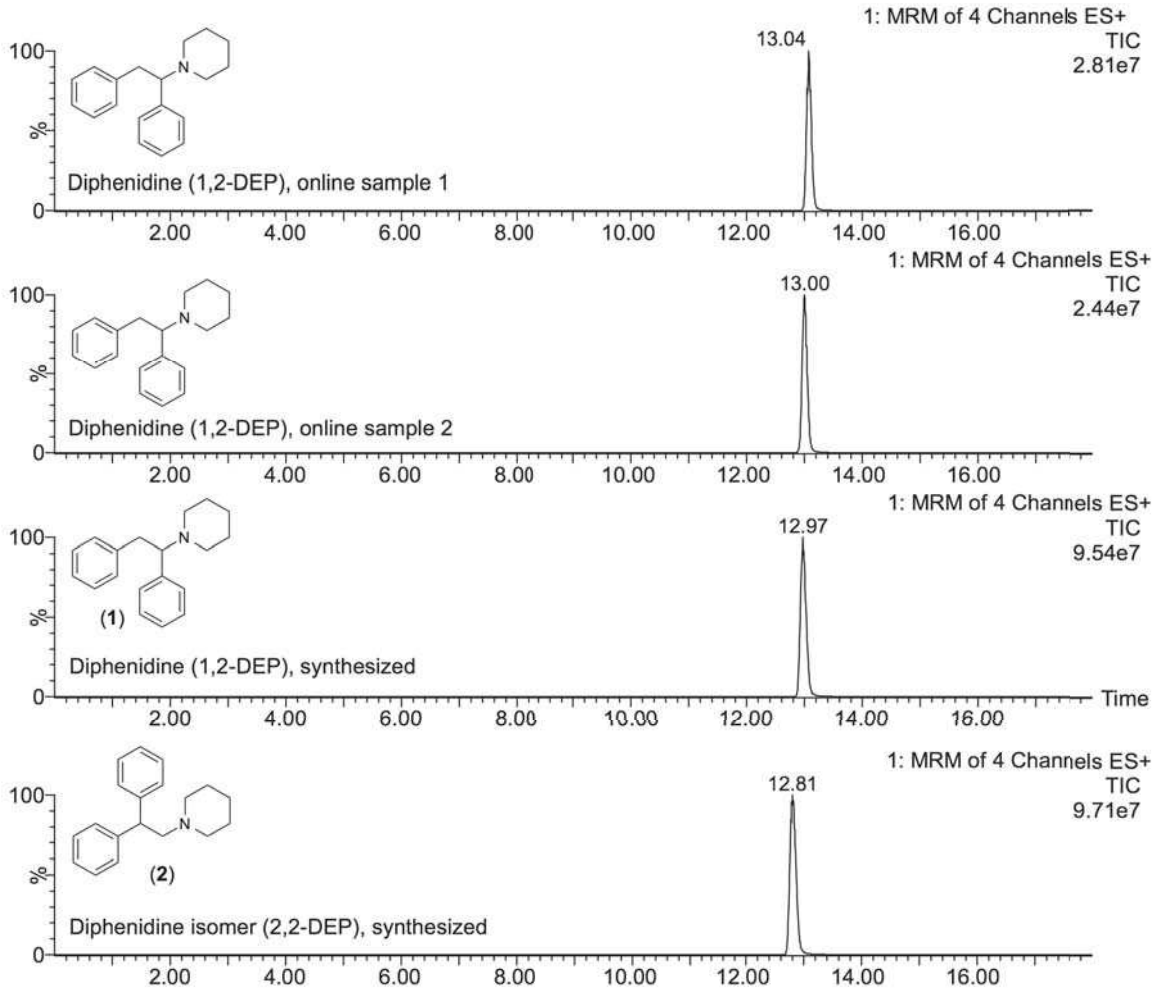
Selected ion transitions:

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



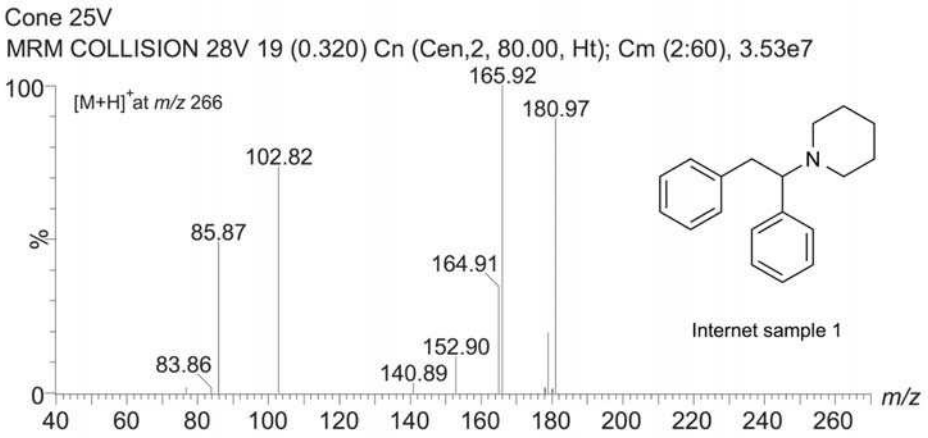
11) LC-ESI-MS/MS traces of synthesized (**1**) and (**2**) and two diphenidine samples obtained online

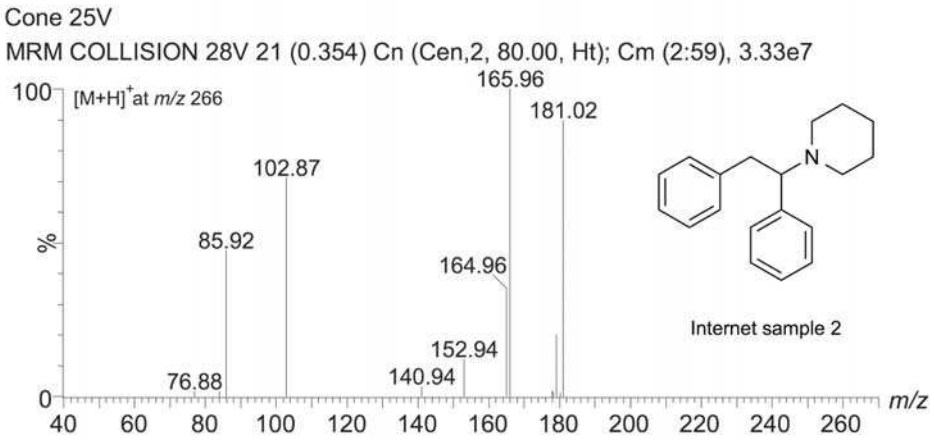


Selected ion transitions:

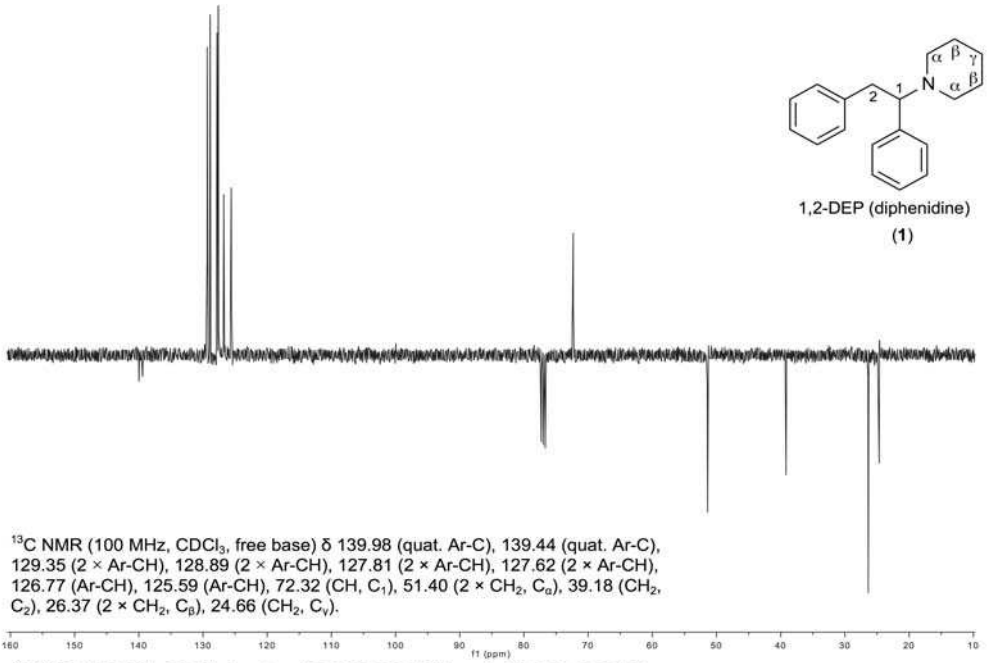
m/z 266 > 72 (48 eV)
m/z 266 > 103 (35 eV)
m/z 266 > 166 (28 eV)
m/z 266 > 181 (20 eV)

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



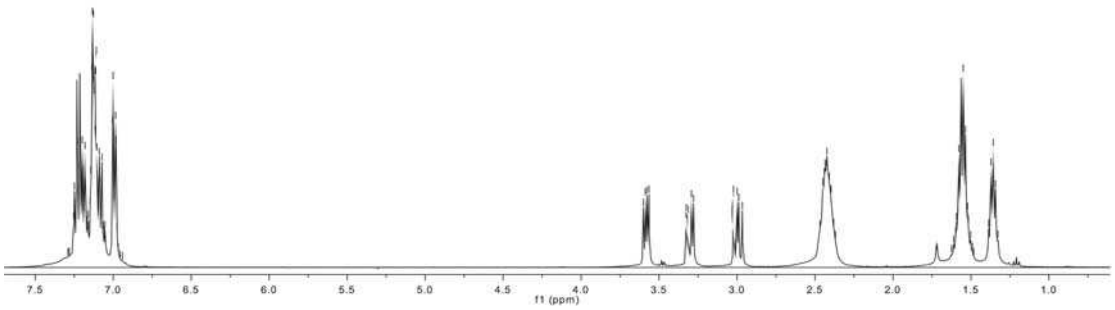


13) ^{1}H and ^{13}C NMR of diphenidine free base



^{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.