Electronic Supplementary Material (ESI) for Analytical Methods.

Electronic Supplementary Information

External reference ^{1}H qNMR method (PULCON) for characterization of high purity cocaine seizures

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A. Measured T_1 values and literature data.

Table 1. Standard and analytes T_1 values of signals used in determination.

Molecule	Signal (ppm)	T_1 measured (s) / solvent / temperature	T_1 literature (s) / solvent / temperature
Dimethyl sulfone	3.13 ppm	6.3 s / D_2O / 28 °C	6.5 s / D_2O / 25 °C *
Maleic acid	6.43 ppm	6.4 s/ D_2O/ 28 °C	6.3 s / D_2O / 25 °C *
Cocaine (benzoylmethylecgonine)	5.57 ppm	1.1 s/ D_2O / 28 °C	Not found
Cis-cinnamoylcocaine	5.98 ppm	1.5 s/ D_2O / 28 °C	Not found
Trans-cinnamoylcocaine	6.54 ppm	1.3 s/ D_2O / 28 °C	Not found

* Weber, M.; Hellriegel, C.; Rueck, A.; Sauermoser, R.; Wuethrich, J., Using high-performance quantitative NMR (HP-qNMR) for certifying traceable and highly accurate purity values of organic reference materials with uncertainties < 0.1 %. *Accreditation and Quality Assurance* **2013,** *18* (2), 91-98.

B. Purity determination equation development

Equation was based on the original PULCON equation:

$$C_x = kC_{std}\frac{I_x T_x \theta_{90}^{x} n_{std}}{I_{std} T_{std} \theta_{90}^{std} n_x} \quad \textit{Eq. 1}$$

Where x and std refer to sample and reference, respectively, C is the concentration, T the temperature, θ_{90} the value of the 90° pulse, n is the number of scans and k is a correction factor that considers differences in detector gain. This equation is valid when all experiments are obtained within the same probe, provided it is properly matched and tuned for each sample.

To express sample purity (% in mass) it is necessary to expand concentration terms in equation 1:

$$\frac{m_x^{grav} P_x N_{std}}{M_x V_x} = k\frac{m_{std}^{grav} P_{std} N_x}{M_{std} V_{std}} \frac{I_x T_x \theta_{std}^{90} n_{std}}{I_{std} T_{std} \theta_{std}^{90} n_x} \quad \text{Eq. 2}$$

New terms are: the gravimetric mass (m^{grav}), purity (P), the number of protons related to the signal (N), molecular weight of the substance (M) and solution volume (V). Notations *x* and *std* refer to sample and reference, respectively.

Solving equation 2 for analyte purity:

$$P_x = k\frac{I_x N_{std} M_x m_{std}}{I_{std} N_x M_{std} m_x^{grav}} P_{std} \frac{V_x T_x \theta_x^{90} n_{std}}{V_{std} T_{std} \theta_{std}^{90} n_x} \quad \text{Eq. 3}$$

Solution volume can be replaced by a mass/density relation:

$$P_x = k\frac{I_x N_{std} M_x m_{std}}{I_{std} N_x M_{std} m_x^{grav}} P_{std} \frac{m_x^{solv}/d_x^{solv} T_x \theta_x^{90} n_{std}}{m_{std}^{solv}/d_{std}^{solv} T_{std} \theta_{std}^{90} n_x} \quad \text{Eq. 4}$$

Where, m^{solv} and d^{solv} are solvent mass and density, respectively. As the same solution of deuterium oxide was used to prepare the reference and sample solutions, one can assume its ratio as 1:

$$P_x = \frac{I_x N_{std} M_x m_{std}}{I_{std} N_x M_{std} m_x^{grav}} P_{std} k\left(\frac{m_x^{solv} T_x \theta_x^{90} n_{std}}{m_{std}^{solv} T_{std} \theta_{std}^{90} n_x}\right) \quad \text{Eq. 5}$$

Equation 5 can be used to directly calculate analyte purity using PULCON.

C. Complete assignment of ^{1}H NMR spectrum of cocaine

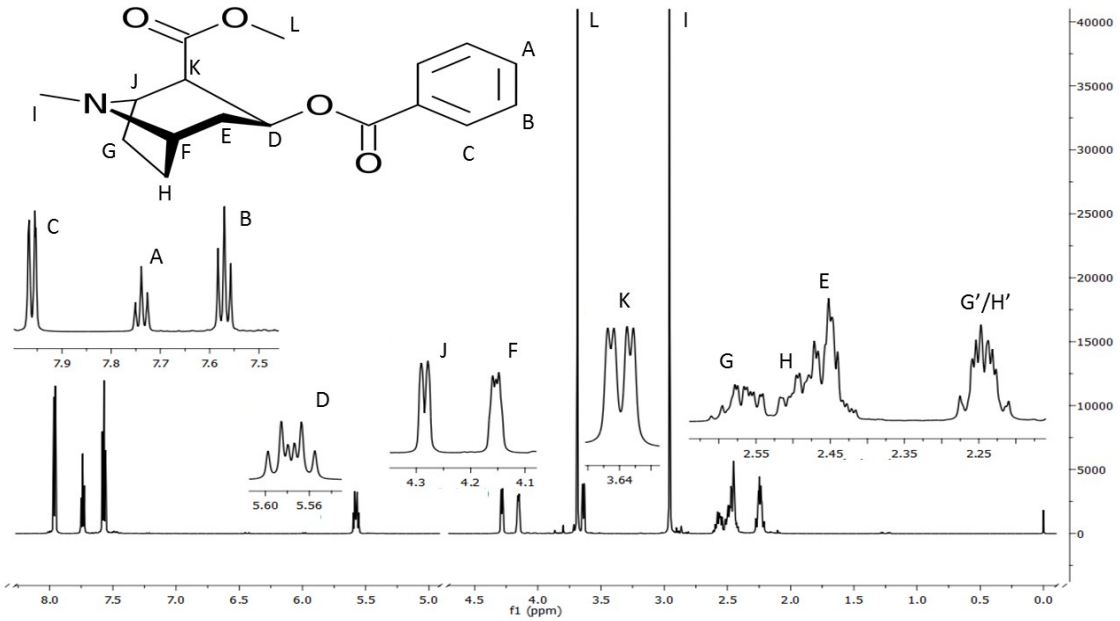

Figure 1. ^{1}H NMR spectrum and signal assignment for cocaine hydrochloride sample in D_2O/TSP at 600 MHz.

Table 2. Chemical shift, multiplicity, coupling constants and approximate integral value for 1H NMR cocaine signals in cocaine hydrochloride sample (D_2O/TSP at 600 MHz).

Site	Chemical Shift (ppm)	Multiplicity	Coupling constants (J)	Int. Valuel
A	7.74	Triplet	7.45 Hz	1
B	7.57	Triplet	7.90 Hz	2
C	7.96	Doublet	8.49Hz	2
D	5.57	Doublet of triplets	11.1 Hz / 7.2 Hz	1
E	2.45	Multiplet	-	-
F	4.15	Multiplet	-	1
G	2.57	Multiplet	-	1
G'/ H'	2.24	Multiplet	-	2
H	2.48	Multiplet	-	-
I	2.96	Singlet	-	3
J	4.28	Doublet	7.4 Hz	1
K	3.64	Doublet of doublets	7.5 Hz / 2.5 Hz	1
L	3.69	Singlet	-	3

D. Complete assignment of ^{1}H spectrum of trans-cinamoylcocaine

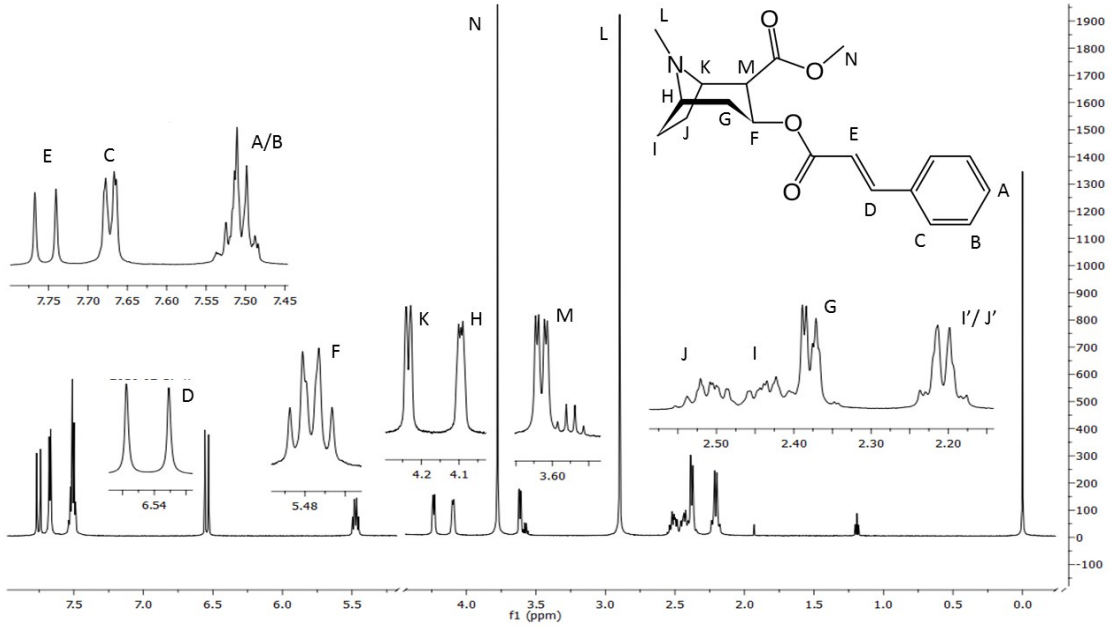

Figure 2. ^{1}H NMR spectrum and signal assignment for trans-cinnamoylcocaine reference material in D_2O/TSP at 600 MHz.

Trans-cinnamoylcocaine present a spectral profile similar to the one of cocaine but with the presence of olefinic hydrogens: signal D (6.50 ppm, doublet, J = 16 Hz) and E (7.76 ppm, doublet, J = 16 Hz).

For cis-cinnamoylcocaine molecule a difference in chemical shift and coupling constant of these signals is observed: signal D (5.98 ppm, doublet, J = 12.4 Hz) and E (7.22 ppm, doublet, J = 12.4 Hz).

E. Accuracy for DMS solutions

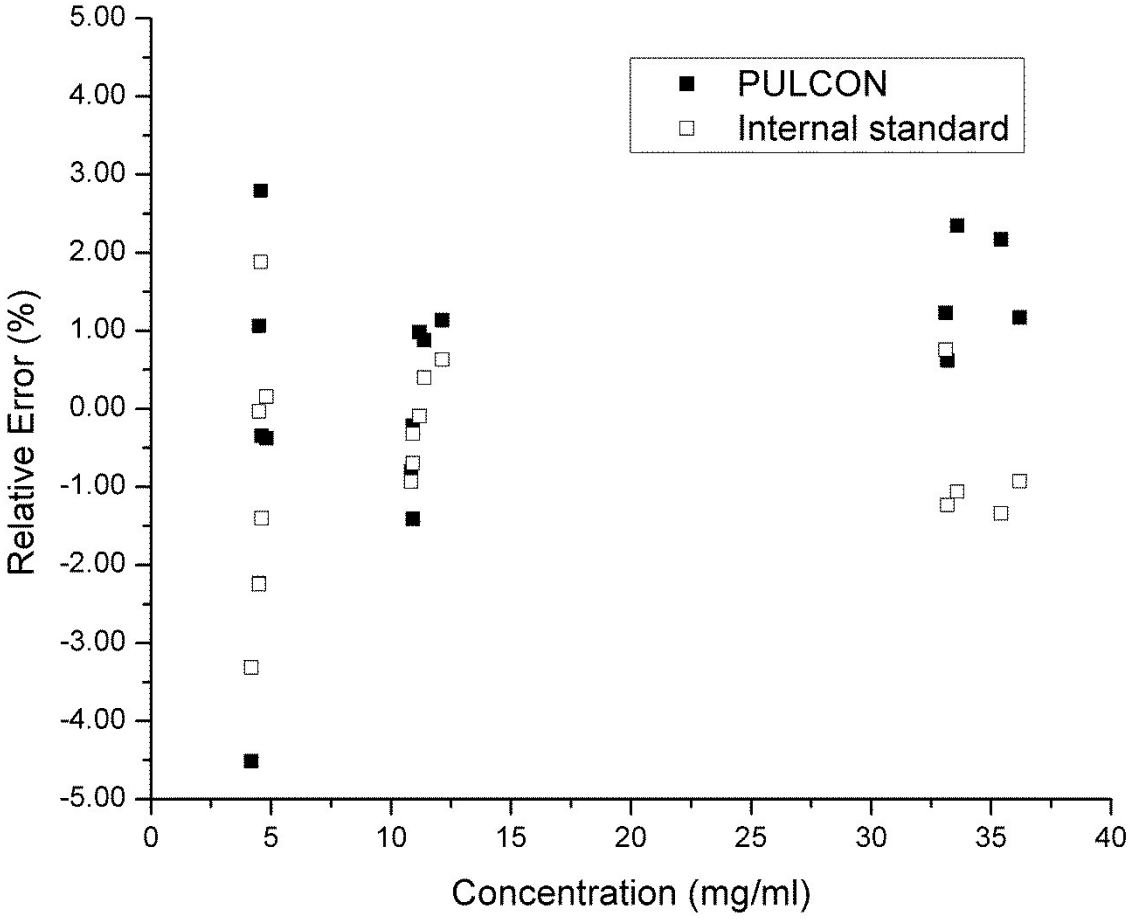

Figure 3

F. Spectra of cocaine sample, reference solution and several adulterants

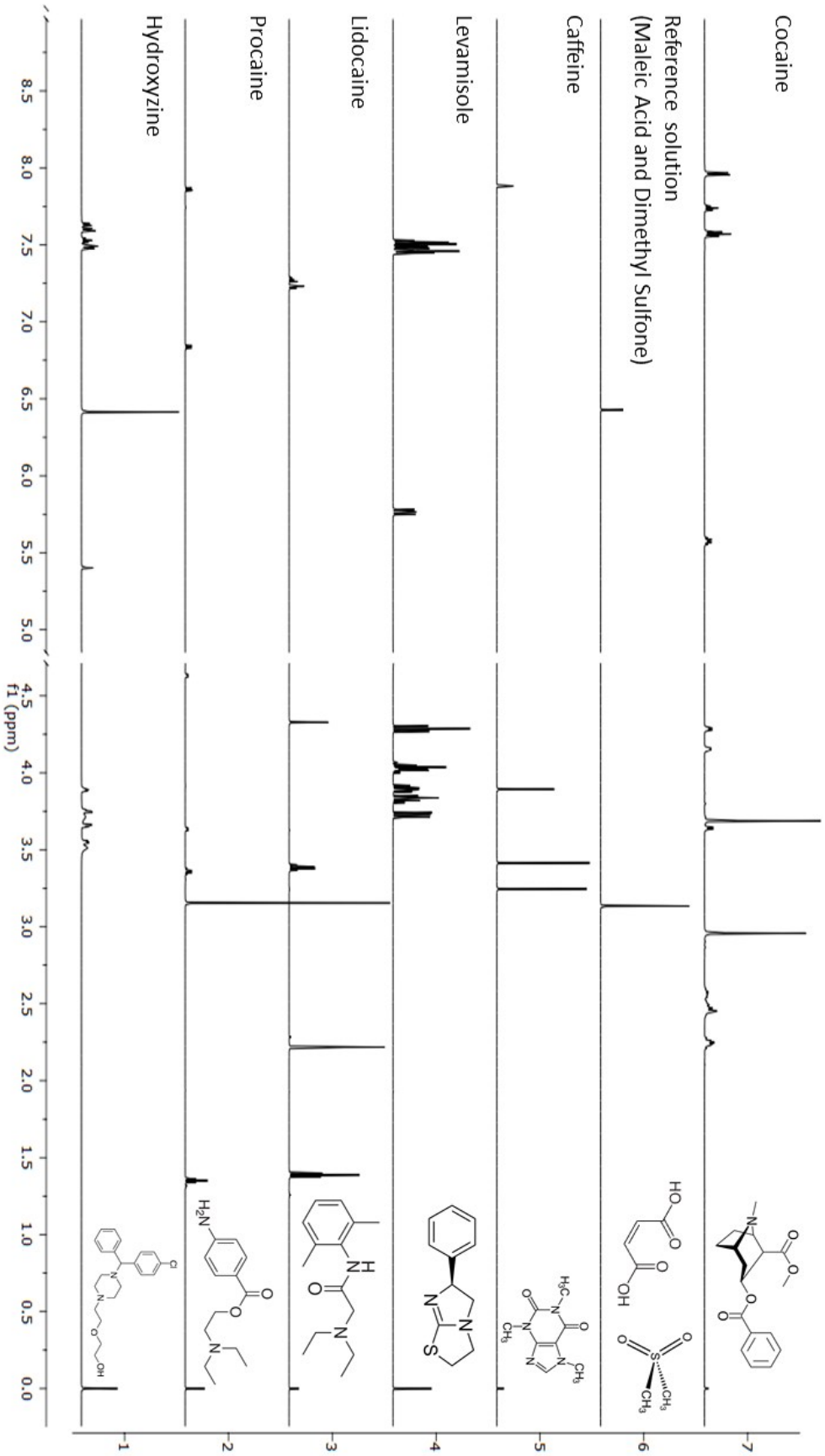

Figure 4

G. GC-FID chromatograms

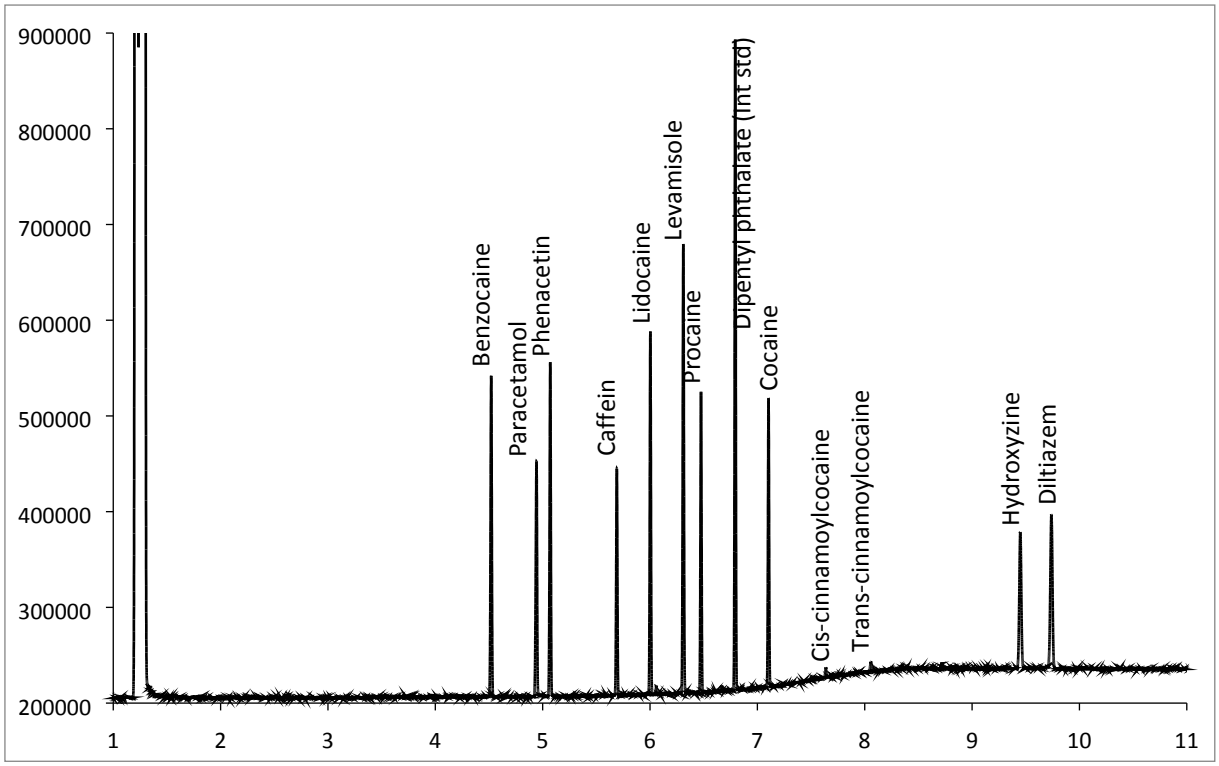

Figure 5 Example of GC-FID chromatogram: Mix of common adulterants, high purity unadulterated cocaine hydrochloride sample and Dipentyl phthalate internal standard.

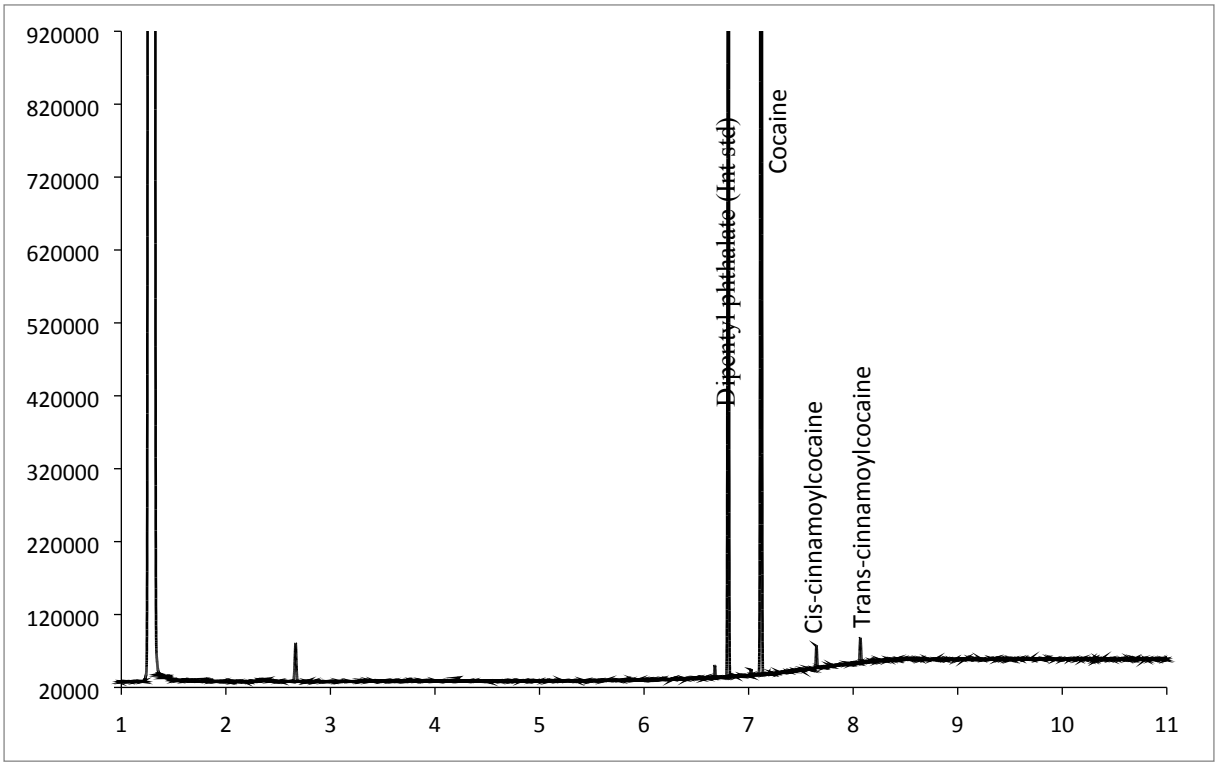

Figure 6 Example of GC-FID chromatogram: high purity unadulterated cocaine hydrochloride sample and Dipentyl phthalate internal standard.

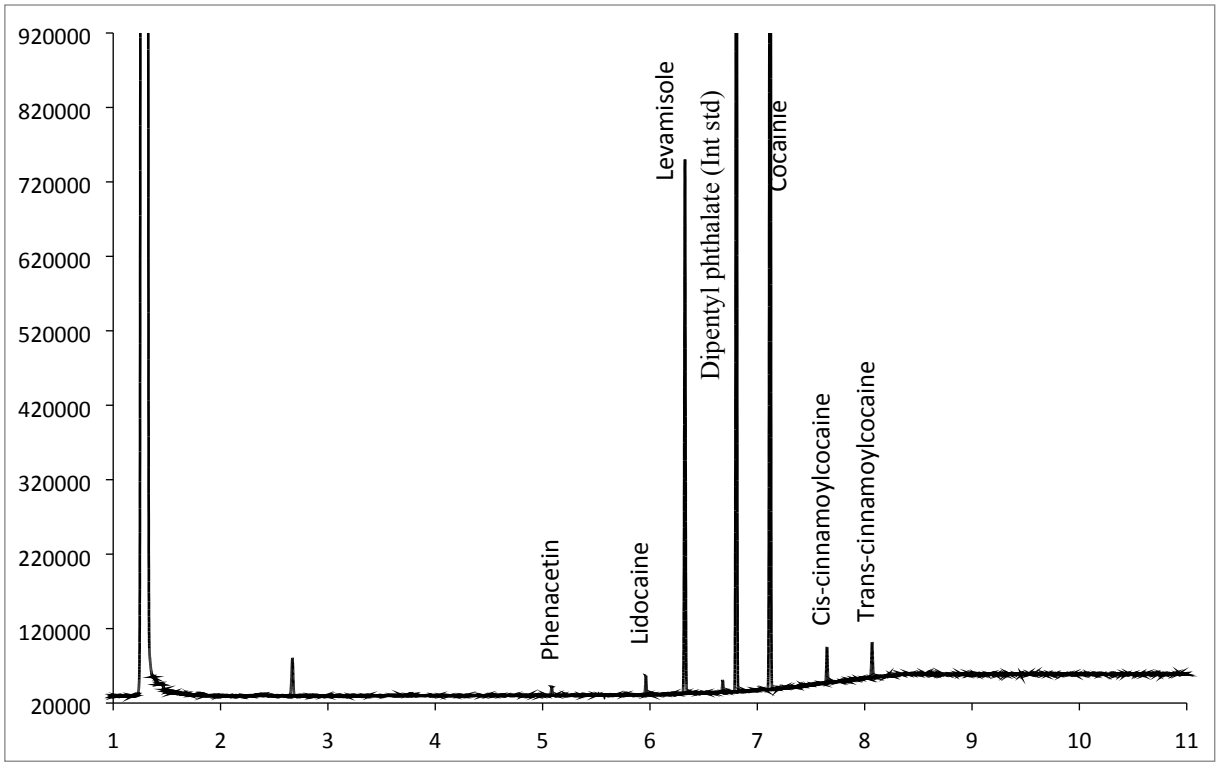

Figure 7 Example of GC-FID chromatogram: adulterated cocaine hydrochloride sample and Dipentyl phthalate internal standard.

End of supplementary material.