chemtos NEWS

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Hope your year has made a great start! Best wishes for an excellent 2018!

We would like to announce our new location in the Austin, Texas area at:

16713 Picadilly Ct, Round Rock, TX 78664

It houses a 500 MHz NMR, 300 MHz NMR, and various other analytical instruments such as HPLC, LC-MS, and GC-MS. We also have a synthesis lab facility here.

In the past, numerous topics have been discussed in these newsletters including concentration dependent stability of solutions of metabolites that degrade by hydrolysis, synthesis challenges of certain types of compounds, etc.

Here we will discuss perspectives on potency determination for analytical reference standards.

Typically, potency (or fraction of active compound in the powder), is determined after analysis by numerous analytical methods and techniques in order to identify all possible impurities that might be present, since all the impurities cannot be detected by just one analytical technique.

These potency determinations normally include orthogonal analysis such as:

(1) UV HPLC purity for assessment of purity of organic components that have UV absorbance (other detectors can also be used instead, GC-MS may also work in cases where compound has sufficient volatility);

(2) A method for residual organic solvent assay such as headspace GC or proton NMR;

(3) KF titration for water/moisture content assay;

(4) Inorganic analysis for salt content assay;

Molecular structure confirmation can include:

(1) UV HPLC retention time under controlled conditions;

(2) LC-MS confirmation of expected m/z;

(3) NMR;

(4) Elemental analysis such as C/H/N;

There is another analytical technique that works very well for simultaneous structure confirmation and potency determination – it is often referred to as "Quantitative Proton NMR". Here, only the organic compound is detected and assayed, irrespective of the types of impurities that might be present.

A measured weight of compound for analysis is mixed with measured weight of another

"As usual, you provide outstanding customer support!" - 01/22/2018

"Your timely updates and follow through on this order is noted and appreciated! " - 01/20/2018

compound (whose potency is known and whose NMR resonance do not overlap with that of the compound for analysis), and dissolved in appropriate deuterated NMR solvent for complete solvation (dilute solution without aggregation). The NMR parameters are optimized to ensure that the observed proton NMR intensities are quantitative, but the largest uncertainty in this method comes from the weighing uncertainty since 1-3 mg is normally weighed for such analysis. Even with a weighing scale that has accuracy of +/1 0.03 mg and readability of 0.01 mg, this represents uncertainty of 1%-3%, which translates to uncertainty of 1%-3% for the calculated potency value. This uncertainty can be minimized by weighing larger quantities.

As you may know, we now have in-stock a number of reference standards available as dilute solutions in flame sealed ampoules with accurate potency values. The potency values of the solutions were confirmed by 500 MHz Quantitative Proton NMR analyses wherein the weighing uncertainties are significantly minimized. We do that by weighing prepared solutions (~500 mg weighed instead of ~1 mg) and use solvent density value in our customized analytical method.

Custom Synthesis of Ref Stds

With years of combined experience in varied chemical synthesis processes and isolation techniques, we have been able to synthesize and isolate compounds and metabolites at high purity, often in short time duration (typically less than 4 weeks). We find innovative ways to insert stable labels in the reference standards that we synthesize, even when others have struggled!

We also have DEA license and quota for manufacture of a number of C-I through C-IV scheduled compounds.

Analytical Services

Our standard GLP Certificate of Analysis includes (i) UV HPLC Purity assessment averaged over multiple absorbance wavelengths; (ii) LC-MS for confirmation of molecular weight; and (iii) Proton NMR analysis for molecular structure confirmation and residual protonated organic solvent determination. We also offer KF titration for moisture content, Residue on Ignition for non-combustible inorganic salt content, Chiral HPLC and Optical Rotation analysis. ATR-FT-IR, GC-MS, and DTA/TGA analysis capabilities are also available in-house.

Catalog of in-stock Ref Stds

We carry a number of Certified Analytical Reference Standards in-stock. Most of these are stable labeled and are accompanied by a comprehensive CoA that includes copies of the analytical data. We are now also offering Analytical reference standard solutions in flame sealed ampoules.

Chemtos on-line catalog

Our web catalog on www.chemtos.com has a list of most of the reference standards that we have in-stock or can re-synthesize. Use of Search bar on top right is quite effective in finding compounds by name or CAS number.

Please do not hesitate to contact me if we can be of any assistance in fulfilling your Certified Analytical Reference Standard needs.

Best regards,

Khalid

Khalid A. Thakur, Ph.D.

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