AcroSeal® Extra Dry Solvents for Moisture Sensitive Applications

10/6/08

Most chemical research disciplines have applications in which moisture-sensitive reagents are employed. Examples of such applications include lithiations, Grignard and Wittig reactions. Solvents used in these applications need to be anhydrous to ensure safe, high yielding and effective reactions. One of the challenges facing researchers, purchasing groups and stockroom managers is the storage of appropriate scale quantities of anhydrous reagents and solvents. After all, the bench chemist's practiced syringe technique and other careful handling efforts alone cannot ensure optimal yields and reduction of undesirable byproducts from reactions if the integrity of the reagents and solvents is easily compromised.

Historically, a research group requiring anhydrous solvents in their protocols had to use solvent stills or distillation equipment (often using sodium metal) in order to secure a routine supply of anhydrous material. However safety concerns as well as a continuous push to reduce time-to-market have led chemists to seek practical alternatives. One option is the routine use of molecular sieves, but this option alone does not meet all needs. Accordingly specialized packaging was introduced several years ago to meet the needs of research groups with moderate requirements for laboratory scale quantities of anhydrous solvents. The first offering of this kind has become familiar at the lab bench, but the introduction of additional packaging choices merits careful examination in order to determine which packaging best serves the needs of the researcher.

Considerations in Selecting a Seal Type

Researchers and stockroom managers cite reliability, integrity, convenience and safety as the most important factors in choosing a brand of packaging for dry solvents. Key packaging features below are organized in terms of these crucial factors.

1. Reliability of the packaging, particularly the seal on a reagent's container. Reliability means that the solvent within the package maintains its anhydrous condition within reasonable period of time.

   With AcroSeal® this is addressed in two ways:

   Septum. AcroSeal® uses a specially designed, multi-layer septum. The AcroSeal® septum consists of a sandwich of three layers of engineering polymer material - an inner silicone layer surrounded by PTFE resin layers. The thickness of AcroSeal® septum is twice as much as that of the septum used in the competitive brand packaging. The thick inner silicone layer allows for better resealing around needle punctures. The outer PTFE layers ensure the chemical compatibility of the septum material with the reagents.

   Secondary Cap Liner. The liner and the septum together create the seal in a closure to resist moisture. To optimize the seal, a cushioned liner in the external cap of the closure is also used.

2. Integrity of the container - one should be able to readily observe that a seal is intact.

   With AcroSeal® this is also addressed in two ways:

   Septum. It should be possible to see that the closure's septum has maintained its shape thereby confirming that it is performing properly. The septum must not deform mechanically or through use over time. The AcroSeal® closure system, for example, features a quadrant-style cap design that holds the septum in place, reducing the risk of bulging or deformation.

   Tamper-evident seal. A seal of this kind on the outer closure of the package assures the researcher that bottle is visibly unopened and the quality has not been compromised.

3. Convenience. Ease of use deserves consideration because items that are easy to use properly encourage good, reproducible technique.

   Again with AcroSeal® this is addressed in three ways:

   Septum. Repeated punctures in the same spot over time increases the risk of deformation and achieving a poor seal with the outer closure in place. With competiting brand packaging, it is very difficult if not all impossible to avoid repeated punctures in the same spot due to very limited septum surface area. AcroSeal® is designed to provide a larger surface area available for syringe punctures, providing more than 15 times the surface area than the septum of the competing brand tested above, leading to better resealing over time.

   Larger sample access. The traditional packaging for the competing brand's dry solvents has a crimp cap design, meaning that the reagent within is only accessible with a syringe unless a special tool is used. Once de-crimped, the cap cannot be replaced. By contrast, the AcroSeal® screw closure allows not only syringe withdrawal of a reagent through the septum but also permits ready access to a larger volume of the solvent with the option to reseal the closure by hand. The AcroSeal® closure design also has a special rim design to prevent an accidental unscrewing of the quadrant-style inner cap that keeps the septum in place.

4. Safety. Because the use of the products involve syringe and needles, it is important that the packaging is designed in such a way that the potential risk of needle puncture can be minimized. The AcroSeal® closure addresses this need by increase the ease of puncturing the septum. With the competitive brand packaging, it requires about 2 lbs. of force to puncture through the septum using a 16 Gauge needle, while for AcroSeal® only 1.2 lbs. of force is required, or a 40% reduction in force. The greater the force required to puncture through the septum, the more likely for needle puncture related accidents to occur.

Demonstrating Reliability in Use and Storage

Comparison of Force Required to Puncture Through Septum[a]		
Puncture Force (Lbs)		
Sample	**Competitive brand**	**AcroSeal®**
1	2.106	1.165
2	2.171	1.195
3	1.979	1.240
Average	2.085	1.200

a. Measurements were carried out by TEN-E Packaging Services, Inc. A. Sixteen Gauge need was used for the measurement.

While AcroSeal® will in principle address the major concerns of chemists, some experienced users of dry solvents may shy away from the convenience of a screw cap as opposed the crimp cap citing concerns over reliability. The next section of this paper addresses the reliability of commercially available seals with a comparison of moisture uptake for AcroSeal® packaging versus the competing crimp-top brands.

The terms "anhydrous" and "dry" lack widely accepted quantitative standards within the research community and the industrial chemicals market. Consequently, competing brands of anhydrous chemicals differ in the initial moisture level prior to using the bottle for the first time. Given the different starting moisture levels of competing products, packaging performance can only be compared properly by examining the increase in water content as moisture penetrates the packaging. For purposes of the comparison described in this paper, graphs presented show the data plotted up to the point at which the average moisture uptake reached a minimum of 100ppm for both of the two competing brands, thereby allowing a comparison of the effectiveness of the packaging.

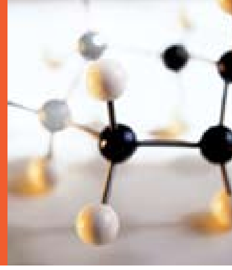
Methods and Instrumentation

AcroSeal® and the competing brand were compared by examining the rate at which moisture was taken up by dry solvents over a period of weeks under conditions of normal use i.e. following septum piercing and subsequent storage. For each brand, the rate of water uptake over time was measured for five dry solvents - DMSO, DMF, methanol, acetonitrile and THF – the hygroscopic solvents most commonly used in synthetic chemistry protocols.

Moisture content levels were determined by the Karl Fischer coulometric method. The procedure for testing used a known amount of solvent (slightly more than 1mL) being drawn into a clean, dry disposable syringe (BD Plastipak™, Disposable Hypodermic syringes with Luer slip tip, 1mL, fitted with a Henke Sass Wolff, HSW FINE-JECT™ needle, Green). Residual air was gently removed from the syringe and the syringe needle was sealed with the protective cap. Then, the syringe was weighed on a 5-decimal place balance prior to the injection of solvent into the coulometer cell. The syringe with the protective cap was then reweighed. Bottle caps for each bottle of solvent were tightened after each test. Solvents were stored at ambient temperature in the open lab between measurements.

Measurements were made using a Metrohm™ Model 831 KF Coulometer with Metrohm Model 703 Pump/Stirrer. Samples were injected into a clean Metrohm coulometric titration cell containing a generator electrode without a diaphragm and a detector electrode.

The initial water content level was then subtracted from the ongoing levels, giving an indication of the increase in water concentration over the time of the experiment. The values presented in the graphs represent the average values of three replicates from each of three bottles of the reagent tested within its brand of packaging.



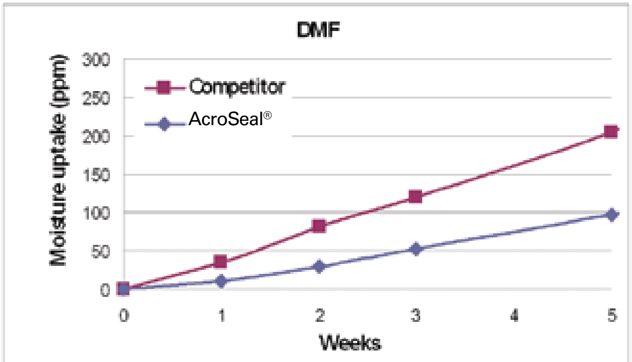


Figure 1. Moisture uptake for DMF.
The increase in water concentration in anhydrous dimethylformamide (DMF) when kept under ambient conditions measured on a weekly basis. At Week 5, the rate of uptake from through the Acroseal® packaging reaches 25ppm/week. The competitor's packaging allows nearly 50ppm/week uptake over the same time frame under identical conditions, nearly twice as fast as the Acroseal® packaging.

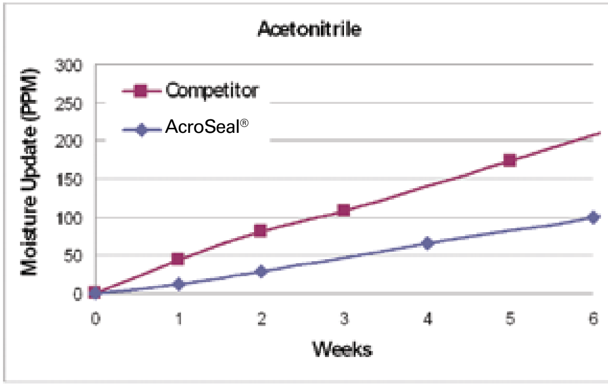


Figure 2. Moisture uptake for acetonitrile.
The increase in water concentration in anhydrous acetonitrile when kept under ambient conditions measured on a weekly basis. At Week 6, the rate of uptake from through the Acroseal® packaging reaches 15ppm/week. The competitor's packaging allows roughly 35ppm/week uptake over the same time frame under identical conditions.

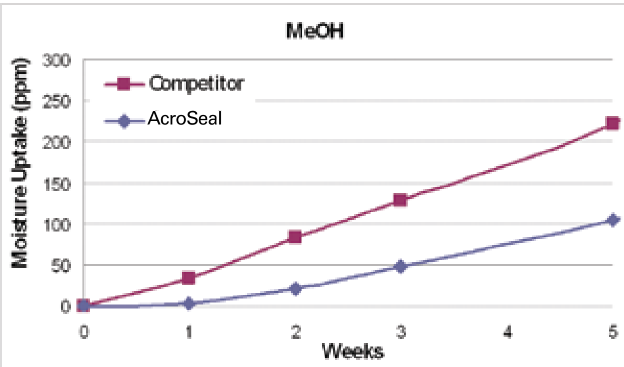


Figure 3. Moisture uptake for MEOH.
The increase in water concentration in anhydrous methanol when kept under ambient conditions measured on a weekly basis. At Week 5, the rate of uptake from through the Acroseal® packaging reaches 28ppm/week. The competitor's packaging allows 46ppm/week uptake over the same time frame under identical conditions.

Figure 4. Moisture uptake for DMSO.
The increase in water concentration in anhydrous DMSO when kept under ambient conditions measured on a weekly basis , At Week 5, the rate of uptake from through the Acroseal® packaging and the competitor packaging is nearly identical, but the overall rate is higher for the competitor seal as the crimp cap has allowed greater rate of ingress of water over the first two weeks.

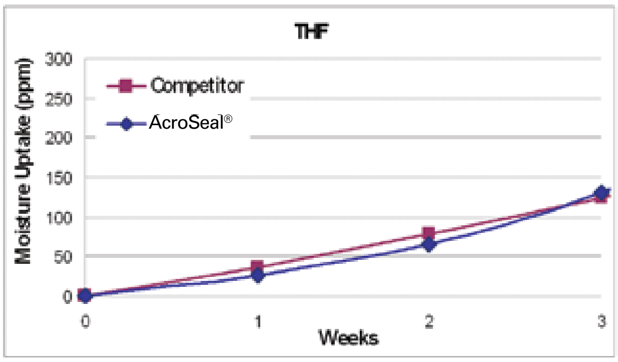
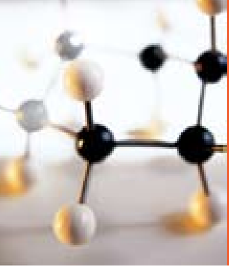


Figure 5. Moisture uptake for THF.
The increase in water concentration in anhydrous tetrahydrofuran (THF) when kept under ambient conditions measured on a weekly basis. At Week 3, the rate of uptake from through both products is essentially identical



Results and Discussion

For DMF, methanol and acetonitrile, the competitor's packaging allows water to be absorbed nearly twice as fast as the AcroSeal® packaging. The DMSO testing data also suggest a reduced rate of moisture uptake with the AcroSeal® packaging versus the competitor's packaging. The rate of moisture uptake is comparable only for THF. Overall, the AcroSeal® packaging with its particular closure design appears to allow a slower rate of moisture uptake than the familiar competing brand's closure design.

Conclusion

Many research groups still habitually purchase anhydrous reagents in the familiar sealed packaging first made available several years ago. However, a performance comparison of the older style of packaging with AcroSeal® closure design compels a reconsideration of routine selections of packaging for these reagents. For a complete listing of reagents available with AcroSeal® packaging, see the back panel of this paper or ask your Fisher Scientific Customer Service Representative.

Tamper-evident break ring at the lower end of the protective red cap.
Foolproof guarantee that the customer is the first to open the bottle. The lower ring breaks off with the first opening of the red cap.

Triple sandwich septum with inner silicone layer and double outer PTFE resin coating.
Better chemical compatibility and re-closure of any puncture hole.

Quadrant cap surface.
The quadrant cap promotes the durability of the septum because punctures can be spread over the large septum surface.

Cushioning liner in outer protective cap.
Re-seals perfectly even after the septum has been punctured multiple times.

Rim design at the inner surface of the septum holding quadrant cap will hold and stretch the septum.
Reduces the risk of bulging or deformation of the septum.

Three-plus windings in the septum holding cap for extra security.
Large contact surface prevents infiltration of air and moisture through the screw neck.

Special rim design inside the septum holding cap fits snugly over the glass rim of the bottle neck.
No risk of accidentally unscrewing the septum holding quadrant cap.

Customer Testimonials

"I find occasionally that I need ~100mL from the bottle, so I like the new AcroSeal® top that I can both uncap the septum, and then unscrew the septum itself and pour from the bottle. I then flush with N2 and recap with both caps. I feel that the smaller septum "bottle cap" [used by other suppliers] encourages reusing the same hole until it doesn't seal."

– Hugh Lippincott from the Plastics Engineering Department at University of Massachusetts at Lowell, United States

"I far prefer the AcroSeal® top to the Aldrich™ top because I like the larger the size of the Acros septum and I find that the needle penetrates the Acros septum much easier than the Aldrich. I think that the Aldrich septum tends to harden over time."

– Lead Scientist in the Drug Discovery Group at Schering-Plough NJ facility, United States

"I have used the system once and found that the AcroSeal® system works well."

– Eric Morin, AD Analyst, Ratiopharm, Canada

"I prefer the AcroSeal® system to the Sigma Aldrich™ system as the risk of a needle prick is greatly reduced with the AcroSeal® system."

– Christine Belanger, Chemist, Stability and Reference Standards Les Produits Chimiques DELMAR Inc., Canada

"I can insert a needle 5 times into the AcroSeal® quatrant cap without damaging the septum. So I can use the product several times and save money."

– Organics and Therapeutics Synthesis Researcher at Pharmaceutical University, France

Thermo Fisher Scientific

Acros Organics
Geel West Zone 2
Janssen Pharmaceuticalaan 3a
2240 Geel – Belgium
Tel. +32 14 57 52 11
Fax +32 14 59 26 10

www.acros.com

For more information, please contact your local distributor.