XtalFluor-E®, A New Deoxygenation Reagent
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The Aldrichimica Acta publishes in-depth review articles on innovative chemistry research written by leading experts from around the world. The reviews cover a variety of topics usually based on a synthetic theme involving organic, organometallic, bioorganic, or inorganic chemistry.

Look for these upcoming authors and topics:

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In 2008, the Aldrichimica Acta was ranked:

• #1 by Impact Factor (16.733, a record!) out of 55 organic chemistry journals
• #1 by Five-Year Impact Factor (12.912)
• #1 by Article Influence™ Score (4.907)
• #1 for the seventh time in the past eight years
Introduction

Haydn Boehm, Ph. D.
Global Marketing Manager: Chemical Synthesis
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Welcome to the third edition of the new Aldrich ChemFiles, our FREE quarterly newsletter written by our experts from Product Management and R&D. Our aim is to keep you informed of the new Aldrich Chemistry products that facilitate the latest research methodologies and trends, and allow you to access key starting materials and reagents more efficiently.

Our cover molecule, XtalFluor-E®, affords us the opportunity to introduce a new line of fluorinating reagents, and also gives us the chance to introduce Troy Ryba as our new Synthetic Reagents Product Manager. Aldrich ChemFiles 10.3 will also introduce our new Buchwald Precatalysts (Catalysis), Leighton Reagents (Asymmetric Synthesis), Trifluoroborates (Organometallic Reagents), and PEG Linkers (Chemical Biology).

We hope that Aldrich ChemFiles will enable you to expand your research toolbox and advance your chemistry more effectively by implementing the latest innovative synthetic strategies.

Kind Regards

Haydn Boehm, Ph.D.

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The reaction scope of these silacycles was extended to a practical method for the enantioselective synthesis of tertiary carbinamines based on the addition of this chiral allylsilane reagent to a structurally diverse array of ketone-derived benzoylhydrazones (Scheme 3). While many methods for the synthesis of quaternary α-amino acids have been published, far fewer reports have dealt with the synthesis of tertiary carbinamines.

86%; 90% ee
76%; 93% ee
80%; 97% ee
70%; 90% ee
80%; 97% ee
78%; 94% ee

Scheme 3: Practical synthesis of tertiary carbinamines by enantioselective allylation of ketone-derived benzoylhydrazones

The free amines are easily accessed in good yields by subjecting the different hydrazones to reduction with SmI2. (409340)

References:

Asymmetric Synthesis
Leighton’s Strained Silacycle Allylation Reagents
The asymmetric alliylation of carbonyl compounds remains one of the most important and fundamental addition reactions for the synthesis of optically active chiral building blocks homoallylic alcohols.
In 2002, Leighton and co-workers developed strained silacycle compounds as versatile reagents for the practical enantioselective allylation of aldehydes.1
A newly developed chiral auxiliary based on the cyclohexane-1,2-diamine scaffold successfully allylated a broad range of aldehydes highly enantioselectively (Scheme 1).2

Scheme 1: Leighton’s silacycle reagent for the enantioselective allylation of aldehydes
The development of practical enantioselective syntheses of chiral amines is of great importance to synthetic organic and medicinal chemists. In 2003, Leighton and co-workers successfully used a pseudoephedrine-derived, five-membered-ring strained silacycle reagent for the enantioselective allylation of acylhydrazones (Scheme 2).3

Scheme 2: Practical, enantioselective allylation of acylhydrazones using strained silacycles

For more information on the applications of the Leighton silacycle reagents, please see Professor Leighton’s recent review in Aldrichimica Acta 2010, Vol. 43, No. 1 or visit aldrich.com/allylation

 sigma-aldrich.com  TO ORDER: Contact your local Sigma-Aldrich office (see back cover), or visit aldrich.com/chemicalsynthesis.
Asymmetric Epoxidation Using Shi Catalyst

Catalytic asymmetric epoxidation of alkenes has been the focus of many research efforts over the past two decades, the best known methods probably being those developed by Sharpless and Jacobsen-Katsuki. Shi has also developed a very efficient method for asymmetric epoxidation, using a ketone-derived organocatalyst based on D-fructose (F0127). This organocatalyst is able to epoxidize trans alkenes and certain cis alkenes with good to excellent yields and selectivities. More recently, Shi has achieved excellent results using hydrogen peroxide as an oxidant instead of OXONE® (228036), which allows a significant reduction in the amount of additional salts introduced and solvent used in the reaction (Scheme 4).

Scheme 4: Enantioselective epoxidation of trans alkenes using Shi organocatalyst

Other groups have used Shi’s methodology in pursuit of a number of unique structural moieties. For example, McDonald and co-workers recently reported a robust and selective synthesis of 2-amino-3,5-diols that employs the Shi epoxidation in a key step (Scheme 5). These 2-amino-3,5-diols are 1-deoxy-5-hydroxyphosphoglycerine analogues, which show promise as anticancer agents.

Scheme 5: Selective route to sphingosine derivatives using Shi’s epoxidation organocatalyst

A recent example of the use of the Shi catalyst is the synthesis of chiral thiosulfonate derivatives. Chiral sulfanyl derivatives have been of interest for the past three decades. This interest stemmed from the use of these molecules as chiral controllers in asymmetric synthesis, as chiral ligands and as Lewis bases. Khiar et al. reported a new method to synthesize enantiomerically pure, functionalized, sterically demanding thiosulfonates. Investigating several catalysts for the oxidation of disulfides, diesters and diethers, Khiar et al. determined that a particular chiral pyranone derived from D-glucose, the Shi catalyst, yielded the best yields and stereoselectivities. Using the Shi catalyst in combination with oxone in acetonitrile and dimethoxymethane, the authors reported up to 89% yield and up to 96% ee for the oxidation of disulfides (Scheme 6).

Scheme 6: Enantioselective disulfide oxidation using Shi catalyst


Expoxidation Catalyst

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Catalysis

Josephine Nakhla, Ph.D.
Market Segment Manager
Organometallics & Catalysis

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Palladium(II) Acetate, Recrystallized

It has been demonstrated that in some applications recrystallized palladium(II) acetate (Pd(OAc)$_2$) performs better than typical grades. White and Overman have both independently demonstrated that in some applications a particular grade of Pd(OAc)$_2$ is necessary. In particular, the preparation of the White catalyst as well as the preparation of the COP catalysts, [COP-Cl]$_2$, by Overman successfully employ and require recrystallized Pd(OAc)$_2$.

Figure 1: Recrystallized palladium(II) acetate (Pd(OAc)$_2$)


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Cationic Palladium Complex, [Pd(dppp)(PhCN)$_2$](BF$_4$)$_2$

Cationic palladium(II) complexes are utilized in a variety of reactions. [Pd(dppp)(PhCN)$_2$](BF$_4$)$_2$ (696617) was shown to catalyze the hetero Diels-Alder reaction of dienes with aldehydes. The reaction yields substituted 5,6-dihydro-2H-pyrans without the use of Lewis acids (Scheme 1). The reaction is believed to proceed through a stepwise mechanism.

Scheme 1: Cationic palladium complex in hetero Diels-Alder reaction


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Air-Stable Precatalysts for Amination

C–N bond forming cross-couplings typically require a palladium source along with the associated ligands. Most Pd(0) sources are not air-stable, while the commonly employed air-stable Pd(0) source, Pd$_2$(dba)$_3$, contains associated ligands which could impede the reaction. Stable Pd(II) precursors require reduction under the reaction conditions. In either case, a ligand must be added to the reaction in order to lead to the active Pd-species. Buchwald and coworkers recently reported the use of highly-active yet air- and moisture-stable precatalysts, which, under the standard reaction conditions, form the active monoligated Pd-species. These precatalysts (704954, 704946, 707589, 708739) are exceptionally efficient even under challenging conditions, such as coupling electron-poor anilines with deactivated aryl chlorides. The catalyst precursors also offer other advantages including low catalyst loadings and short reaction times.

Scheme 2: Buchwald precatalysts in N-arylations of electron-poor amines with electron-rich aryl chlorides


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Buchwald Precatalysts

For more information on our catalysts, visit aldrich.com/catalysis
N-Arylation of Aryl Mesylates and Monoarylation of Primary Amines Using BrettPhos

Buchwald and coworkers recently reported the use of a catalyst system comprised of the highly efficient ligand 2-(Dicyclohexylphosphino)3,6-dimethoxy-2',4',6'-trisopropyl-1,1'-biphenyl (718742; BrettPhos) and a palladium precatalyst (also containing the BrettPhos moiety) for the N-arylation of aryl mesylates with aryl amines (Scheme 4). Aryl mesylates constitute an important class of organic electrophiles due to their reasonable atom economy, cheap cost, and high stability. In addition, BrettPhos was found to be an effective ligand in the unprecedented monoarylation of primary amines with aryl chlorides at exceptionally low loadings (Scheme 5).

Non-Proprietary Catalysts for Cross-Coupling

The cross-coupling reaction of heteroaryl halides is of particular interest to the pharmaceutical industry since many biologically active compounds are accessed through use of the Suzuki-Miyaura reaction. However, the efficient coupling of five-membered heteroaryl halides or six-membered heteroaryl chlorides bearing heteroatom substituents with boronic acids has not been well-developed. Catalysts are thought to form inactive complexes with many of these types of substrates, and thus, they typically require high catalyst loadings in order to achieve good yields. The Guram group at Amgen has recently communicated the development of an air-stable palladium complex, (AtaPhos)₂PdCl₂, for Suzuki-Miyaura cross-coupling reactions. The catalyst was very effective at coupling a wide range of substrates with arylboronic acids, including amino-substituted 2-chloropyridines and five-membered heteroaryl halides. The products are observed in excellent yields and high turnover numbers (up to 10,000 TON) are typically achieved. A series of new PdCl₂{PR₂(Ph-R')}₂ catalysts were developed with various reactivities.


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New Polyethylene Glycol Building Blocks for PEGylation

Circulatory half-life is a key success factor for new drugs. In this respect, modification of potential candidates ranging from non-peptidic small molecules to peptides and proteins, antibody fragments, aptamers, and saccharides or oligonucleotides with polyethylene glycol chains (commonly referred to as PEGylation or PEG-ing) offers numerous advantages. PEGylation is considered one of the most successful techniques to enhance the therapeutic and biotechnological potential of peptides and proteins. PEGs are non-toxic, non-immunogenic, non-antigenic, highly soluble in water, and FDA approved. The PEGylated conjugates show a decreased degradation by metabolic enzymes and a reduction or elimination of protein immunogenicity as the PEG coating prevents the approach or recognition by proteolytic enzymes and antibodies. (Scheme 1) Furthermore, PEGylation may favorably alter drug distribution in the organism. While PEGylation may improve the pharmacokinetic properties of a drug, the drug's main activity is predominantly preserved.

Since the first therapeutic PEG-protein conjugate (PEG-adenosine deaminase) had been approved by the FDA in 1990, a large number of new PEGylated drugs was introduced to the market representing a multi-billion dollar business. Table 1 summarizes a selection of FDA approved PEG conjugates including therapeutic peptides, proteins, small molecules, oligonucleotides, and antibodies:

<table>
<thead>
<tr>
<th>Year</th>
<th>Disease</th>
<th>PEG conjugate</th>
<th>Tradename</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>Severe combined immunodeficiency disease (SCID)</td>
<td>PEG-adenosine deaminase</td>
<td>Oncaspar®</td>
</tr>
<tr>
<td>1994</td>
<td>Acute lymphoblastic leukemia</td>
<td>PEG-asparaginase</td>
<td>Adagen®</td>
</tr>
<tr>
<td>2000</td>
<td>Hepatitis C</td>
<td>PEG-interferon α2b</td>
<td>PEG-Intron®</td>
</tr>
<tr>
<td>2002</td>
<td>Hepatitis C</td>
<td>PEG-interferon α2a</td>
<td>Pegasys®</td>
</tr>
<tr>
<td>2002</td>
<td>Treating of neutropenia during chemotherapy</td>
<td>PEG-G-CSF (pegfilgrastim)</td>
<td>Neulasta®</td>
</tr>
<tr>
<td>2002</td>
<td>Acromegaly</td>
<td>PEG-growth hormone receptor antagonist, pegvisomant</td>
<td>Somavert®</td>
</tr>
<tr>
<td>2004</td>
<td>Age-related macular degeneration</td>
<td>Branched PEG-anti-VEGF aptamer, Pegaptanib (oligonucleotide PEG conjugate)</td>
<td>Macugen®</td>
</tr>
<tr>
<td>2005</td>
<td>Ovarian cancer, Kaposi’s sarcoma, AIDS related cancer</td>
<td>Pegylated liposome-encapsulated doxorubicin (small molecule drug)</td>
<td>Doxil®, Caelyx®</td>
</tr>
<tr>
<td>2008</td>
<td>Crohn’s disease</td>
<td>PEGylated fab fragment of humanized anti-tumor necrosis factor (monoclonal antibody), certolizumab pegol</td>
<td>Cimzia®</td>
</tr>
</tbody>
</table>

Table 1: Examples of FDA approved therapeutic PEG conjugates

More recently, researchers have enforced strategies that utilize releasable PEGs in order to control protein release rates. Usually a trigger moiety is introduced between protein and PEG that can be cleaved enzymatically or by aqueous hydrolysis.

Scheme 1: PEGylation may improve the properties of drug candidates
Further important applications of functionalized polyethylene glycols apart from drug discovery are:

- Introduction of solubilizing handles in SPPS
- Soluble polymer supports for Peptide Synthesis
- Soluble polymer supports for Organic Synthesis
- Introduction of hydrophilic amino acids in Peptide Synthesis
- Preparation of PEG-coated surfaces
- Linking of macromolecules to surfaces
- Preparation of PEG-cofactor adducts for bioreactors

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References:

New PEG linkers

(average molecular weight of polymers in brackets)

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Heterocyclic Organotin Reagents for Stille Coupling

Stille reactions remain one of the most viable methods for the formation of C–C bonds in organic chemistry. Their use has been highlighted in various areas, including countless elegant natural product syntheses, material science, and in synthetic methodology. The use of 1-Methyl-5-(tributylstannyl)imidazole (718793) by process chemists at Pfizer in a Stille reaction was reported in 2003. The coupling employed iodothiophenopyridine as the electrophile in the presence of Pd(PPh3)4 as the catalyst. Addition-elimination on the resulting functionalized thiophenopyridine provided bulk material of the desired VEGFR kinase inhibitor. It is worth noting that of several cross-couplings which were examined, the Stille coupling was the only reaction feasible on scales >50 g.

Scheme 1: Stille reaction in preparation of VEGFR kinase inhibitor


For a complete list of organotin reagents from Aldrich Chemistry, please visit aldrich.com/organotin
New Method for Stannylation of Cyclopropenes

Due to the wide utility of the cyclopropene ring, methods for the synthesis of highly substituted cyclopropenes are of broad interest to the scientific community. Methods to prepare functionalized cyclopropenes currently include preparation of the cyclopropenyllithium species and subsequent treatment with a trialkyltin chloride, which is then followed by a Stille coupling. However, the obvious limitation to this method is that the cyclopropene ring cannot possess base-sensitive functionalities, which can promote side reactions such as ring opening and formation of stabilized anions. Recently, Lam and coworkers developed a method employing Bu3SnCF2CF3 (711063), which in the presence of stoichiometric KF, allowed for the mild stannylation of otherwise sensitive functionalized cyclopropenes (Scheme 2). These building blocks were further elaborated in a Stille reaction to provide highly functionalized tetrasubstituted cyclopropenes (Scheme 3). A protocol was developed by which the stannylation and Stille coupling were conducted in one-pot, further facilitating access to these useful building blocks.

Method for Introducing Sulfur Linkages

Matzger and co-workers developed a useful method for the introduction of sulfur linkages using Bu3SnSSnBu3 in the preparation of oligothienoacenes. Historically, the preparation of these molecules has been limited and not feasible for longer chain thienoacenes. The low solubility and problematic isolation both contribute to the challenges associated with preparing oligothienoacenes. The synthesis of these molecules in the Matzger lab begins with the introduction of the TIPS group through Li-Br exchange of the precursor dibromide and addition of TIPS-Cl. The bromine at the 2-position was treated with LDA to provide the 3-bromo-substituted isomer. The use of Bu3SnSSnBu3, in a Pd-catalyzed coupling with 2 equivalents of the 3-bromo-substituted precursor provided the thio-linked thienoacene. Incorporating the sulfur linkage typically involves metalation followed by reaction with bis(phenylsulfonyl)sulfide, which often leads to linking at the two- and three-position rather than the 3,3-position. Oxidative ring closure and deprotection yields the final oligothienoacene (Scheme 4). The TIPS groups are strategically placed to avoid competing deprotonation at the 2-position when conducting the oxidative ring closure.

Tributyl(perfluoroethyl)stannane

Bu3SnCF2CF3

711063


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Organotrifluoroborates as Coupling Partners in Suzuki-Miyaura Reactions

Suzuki-Miyaura cross-coupling reactions are some of the most common methods for the formation of C–C bonds in organic chemistry. The use of some boronic acids is complicated by their instability and their propensity for trimerization. The advent of boronic acid surrogates such as trifluoroborates has transformed the field, allowing for shelf-storage and usability of otherwise unstable boronic acids. Trifluoroborates exhibit excellent functional group tolerance and stability towards common reagents, which has also lead to their widespread use. Our platform of trifluoroborate salts is continually growing, with new product introductions occurring regularly. Some of our recent additions are listed below.

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New Trifluoroborates from Aldrich

![Chemical structures](image)


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Building Blocks

Mark Redlich, Ph.D.
Product Manager
mark.redlich@sial.com

Thiazoles and Imidazoles
Thiazoles and imidazoles have been frequently discovered as a vital component of novel and structurally diverse natural products that exhibit a wide variety of biological activities. The exceptional range of antitumor,antiviral, and antibiotic activities, as well as their presence in peptides,or ability to bind to proteins,DNA, and RNA, has directed numerous synthetic studies and new applications of these azole heterocycles.

The thiazole ring has been identified as a central feature of myriad natural products, perhaps the best known being the epothilones (Figure 1). These are antitumor agents that display improved potency against Taxol-resistant tumor cell lines, and variants of epothilone B in particular have been pursued by several major pharmaceutical companies. 

Additionally, thiazoles are frequently cropping up in peptide research. For example, the pseudopeptide dolastatin 10 (Figure 2) is an exceptionally potent antineoplastic agent, and other thiazole-containing marine cyclic peptides have demonstrated significant cytotoxicity. A recent report demonstrates the use of ethyl 2-methylthiazole-4-carboxaldehyde (716308) as a starting material to the pyridine-thiazole structure 1 (Scheme 1), a protected form of the core cluster of thiopeptide antibiotics micrococcin P1-P2, thiocillin I, and YM266183.

New Thiazoles

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Scheme 1: Ethyl 2-methylthiazole-4-carboxaldehyde as a starter for pyridine-thiazole structure 1
Thiazoles can also serve as a protected formyl group that can be liberated in the late stages of a complex natural product synthesis. While thiazoles are prevalent in a wide range of bioactive natural products, the imidazole ring occurs largely in the context of the natural amino acid histidine. In addition, the imidazole ring has appeared as a component of unnatural cyclic peptides, and used as an ester isostere in peptidomimetic studies. However, the applications of imidazole are not limited to the realm of peptides and peptidomimetics. They are present in the large family of bromopyrrole-imidazole alkaloids isolated from marine sponges based on the common metabolite oroidin (Figure 3). The imidazole ring is also present in the pilocarpine alkaloids, as well as potential therapeuetic agents for thrombosis, cancer, and inflammatory diseases.
Iodinated Building Blocks

Iodine-containing substrates are valuable building blocks for a diverse array of synthetic methodologies. They have the ability to participate in various cross-coupling reactions for the generation of carbon–carbon, carbon–nitrogen, and carbon–oxygen bonds. Often iodinated substrates are preferred to the brominated analogs, due to cleaner reactions. They are also handy precursors for the formation of organolithium, organozinc, or organomagnesium reagents. Sigma-Aldrich is pleased to offer these useful building blocks for your research.

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With the recent introduction of XtalFluor-E and XtalFluor-M by Couturier and coworkers, however, many of the issues surrounding the safety and handling requirements of traditional fluorination reagents are no longer of concern. XtalFluors, as their name intimates, are crystalline deoxofluorination reagents amenable to short-term handling open to the atmosphere. The substrate and reactivity profiles of the XtalFluors are also comparable to the traditional deoxofluorination reagents (Scheme 1): alcohols are converted to the corresponding alkyl fluorides, aldehydes and ketones to the geminal-difluorides, carboxylic acids to the acyl fluorides, sulfoxides to the fluoromethyl thioethers and hemiacetal sugars to the corresponding glycosyl fluoride donors.

An intrinsic property of the XtalFluors is that they do not generate free HF under anhydrous reaction conditions. While the mechanism is still under investigation, it is thought that the XtalFluors activate the C–O bond without concomitant fluoride release. Only upon subsequent exposure to a promoter such as DBU, Et$_3$N ∙ 3HF, or Et$_3$N ∙ 2HF, does fluoride attack the activated carbon atom. The chemical efficiency of the deoxofluorination is high. As can be noted in Scheme 2, generally, if DAST or Deoxo-Fluor work, so too should the XtalFluors (Scheme 2).

The stability of the XtalFluors has also been investigated by Accelerated Rate Calorimetry (ARC). These studies have shown that the XtalFluors have greater thermal stability than DAST or Deoxo-Fluor (Table 1). This may be of particular practical interest when considering reagents to utilize for scale-up routes.

### Table 1: Accelerated Rate Calorimetry (ARC) data comparisons indicating a higher thermal stability of the XtalFluors.

<table>
<thead>
<tr>
<th></th>
<th>Deoxo-Fluor</th>
<th>DAST</th>
<th>XtalFluor-E</th>
<th>XtalFluor-M</th>
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<tbody>
<tr>
<td>Temperature</td>
<td>60 °C</td>
<td>60 °C</td>
<td>119 °C</td>
<td>141 °C</td>
</tr>
</tbody>
</table>

(higher temperature = more stable)

Scheme 1: Generic substrate scope of XtalFluor-mediated deoxofluorination.
Fluorination Reagents

Specific Examples

<table>
<thead>
<tr>
<th>entry</th>
<th>substrates</th>
<th>XtalFluor-E or -M + promoter*</th>
<th>products</th>
<th>% yield</th>
</tr>
</thead>
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<td></td>
<td></td>
<td>76 %</td>
</tr>
<tr>
<td>2</td>
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<td></td>
<td>72 %</td>
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<tr>
<td>3</td>
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<td></td>
<td>85 %</td>
</tr>
<tr>
<td>4</td>
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<td></td>
<td></td>
<td>68 %</td>
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<tr>
<td>5</td>
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<td></td>
<td>96 %</td>
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<tr>
<td>6</td>
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<td>90 %</td>
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<tr>
<td>7</td>
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<td>72 %</td>
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<tr>
<td>8</td>
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<td>75 %</td>
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<tr>
<td>9</td>
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<td></td>
<td>79 %</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td>89 %</td>
</tr>
<tr>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td>96 %</td>
</tr>
</tbody>
</table>

* promoters: DBU, Et3N·3HF, or Et3N·2HF

Scheme 2: Specific examples of deoxofluorination with XtalFluor-E or XtalFluor-M.

References:

Fluorination Reagents

For a complete list of fluorination reagents available from Aldrich Chemistry, please visit aldrich.com/fluoro
Stockroom Reagents

Todd Halkoski
Market Segment Manager
todd.halkoski@sial.com

The New Aldrich Sure/Seal™ System

The Ideal Solution for Anhydrous and Air-Sensitive Reagents

As the leader in air-sensitive chemistry, Sigma-Aldrich carries by far the largest breadth of anhydrous solvents and air-sensitive reagents to service the research market. Our traditional Sure/Seal is now undergoing major improvements. During the upcoming months, you will begin experiencing the value of these new design improvements.

New Crimp Cap Design

• Increased puncture area by 4x to accommodate multiple punctures
• Crimp cap helps maintain product quality by providing an air-tight system

New Plug Style

• Maximizes surface area contact with the bottle to prevent moisture and oxygen entry
• More than 50% thicker than competing brands

For additional testing documentation on how the New Aldrich Sure/Seal performs, visit aldrich.com/sureseal

New Elastomer Liner

• Provides outstanding resealing properties
• Secondary resin layer ensures resistance to chemicals
• Outperforms competing seals with respect to moisture uptake

New Aldrich Sure/Seal System

Unpunctured 4 Punctures

Competitor A System

Unpunctured 4 Punctures

Aldrich Sure/Seal Karl Fischer Analysis Results

Utilizes a coulometric titration method to measure the rate of moisture uptake. To determine the effectiveness of the liner’s seals and closure design, a five-week study was conducted.

For additional testing documentation on how the New Aldrich Sure/Seal performs, visit aldrich.com/sureseal

Comprehensive testing confirms the New Aldrich Sure/Seal outperforms other products on the market by maintaining low water absorption even after multiple punctures.
Liner Integrity

When using air-sensitive solvents and reagents, liners should not only seal to maintain product quality, but also consistently hold form after repeated puncture. The New Aldrich Sure/Seal gives you the assurance of safety and a quality product.

Toluene Testing—5 Weeks (20 punctures)

New Aldrich Sure/Seal Chemicals Now Available from United States locations

Below you will find the inventory for these products are using the new Sure/Seal design.

### Solvents

<table>
<thead>
<tr>
<th>Cat. No.</th>
<th>Available sizes with New Design</th>
<th>Product Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>401765</td>
<td>100 mL, 1 L, 6 x 1 L, 2 L</td>
<td>Benzene, Anhydrous, 99.8%</td>
</tr>
<tr>
<td>305197</td>
<td>All Unit Sizes</td>
<td>Benzyl alcohol, anhydrous, 99.8%</td>
</tr>
<tr>
<td>281549</td>
<td>All Unit Sizes</td>
<td>1-Butanol anhydrous, 99.8%</td>
</tr>
<tr>
<td>471712</td>
<td>All Unit Sizes</td>
<td>n-Butanol, anhydrous, 99.5%</td>
</tr>
<tr>
<td>284513</td>
<td>All Unit Sizes</td>
<td>Chlorobenzene, anhydrous, 99%</td>
</tr>
<tr>
<td>372978</td>
<td>All Unit Sizes</td>
<td>Chloroform, anhydrous, ≥99%, contains amylene as stabilizer</td>
</tr>
<tr>
<td>288306</td>
<td>1 L, 2 L, 100 mL</td>
<td>Chloroform, anhydrous, ≥99%, contains 0.5–1.0% ethanol as stabilizer</td>
</tr>
<tr>
<td>294772</td>
<td>100 mL</td>
<td>Decahydronaphthalene, mixture of cis + trans, anhydrous, ≥99%</td>
</tr>
<tr>
<td>457116</td>
<td>All Unit Sizes</td>
<td>Decane, anhydrous, ≥99%</td>
</tr>
<tr>
<td>240664</td>
<td>All Unit Sizes</td>
<td>1,2-Dichlorobenzene, anhydrous, 99%</td>
</tr>
<tr>
<td>284505</td>
<td>All Unit Sizes</td>
<td>1,2-Dichloroethane anhydrous, 99.8%</td>
</tr>
<tr>
<td>270997</td>
<td>100 mL, 1 L, 4 x 2 L</td>
<td>Dichloromethane, anhydrous, ≥99.8%, contains 50–150 ppm amylene as stabilizer</td>
</tr>
<tr>
<td>296082</td>
<td></td>
<td>Diethyl ether, contains 1 ppm BHT as inhibitor, anhydrous, ≥99.7%</td>
</tr>
<tr>
<td>271012</td>
<td>100 mL, 12 x 100 mL, 1 L, 2 L</td>
<td>N,N-Dimethylacetamide anhydrous, 99.8%</td>
</tr>
<tr>
<td>227056</td>
<td>All Unit Sizes</td>
<td>N,N-Dimethylformamide anhydrous, 99.9%</td>
</tr>
<tr>
<td>276855</td>
<td>100 mL, 12 x 100 mL, 1 L, 6 x 1 L</td>
<td>Dimethyl sulfoxide, anhydrous, ≥99.9%</td>
</tr>
<tr>
<td>297897</td>
<td>All Unit Sizes</td>
<td>Dodecane, anhydrous, ≥99%</td>
</tr>
<tr>
<td>459836</td>
<td>All Unit Sizes</td>
<td>Ethanol 200 proof, anhydrous, ≥99.5%</td>
</tr>
<tr>
<td>277649</td>
<td>All Unit Sizes</td>
<td>Ethanol reagent, anhydrous, denatured</td>
</tr>
<tr>
<td>270989</td>
<td>All Unit Sizes</td>
<td>Ethyl acetate, anhydrous, 99.8%</td>
</tr>
<tr>
<td>324558</td>
<td>100 mL, 1 L, 2 L, 6 x 1 L</td>
<td>Ethylene glycol, anhydrous, 99.8%</td>
</tr>
<tr>
<td>246654</td>
<td>All Unit Sizes</td>
<td>Heptane, anhydrous, 99%</td>
</tr>
<tr>
<td>296317</td>
<td>All Unit Sizes</td>
<td>Hexadecane, anhydrous, ≥99%</td>
</tr>
<tr>
<td>296090</td>
<td>All Unit Sizes</td>
<td>Hexane, anhydrous, 95%</td>
</tr>
<tr>
<td>227064</td>
<td>All Unit Sizes</td>
<td>Hexane, mixture of isomers anhydrous, ≥99%</td>
</tr>
<tr>
<td>471402</td>
<td>All Unit Sizes</td>
<td>1-Hexanol, anhydrous, ≥99%</td>
</tr>
<tr>
<td>322415</td>
<td>All Unit Sizes</td>
<td>Methanol, anhydrous, 99.8%</td>
</tr>
<tr>
<td>284467</td>
<td>1 L</td>
<td>2-Methoxyethanol, anhydrous, 99.8%</td>
</tr>
</tbody>
</table>

### Kinetic Bases

<table>
<thead>
<tr>
<th>Cat. No.</th>
<th>Available sizes with New Design</th>
<th>Product Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>302120</td>
<td>All Unit Sizes</td>
<td>Butyllithium solution, 2.0 M in cyclohexane</td>
</tr>
<tr>
<td>195596</td>
<td>All Unit Sizes</td>
<td>Butyllithium solution 1.4 M in cyclohexane</td>
</tr>
<tr>
<td>186171</td>
<td>All Unit Sizes</td>
<td>Butyllithium solution 1.6 M in hexane</td>
</tr>
<tr>
<td>230707</td>
<td>All Unit Sizes</td>
<td>Butyllithium solution, 2.5 M in hexane</td>
</tr>
<tr>
<td>186198</td>
<td>All Unit Sizes</td>
<td>tert-Butyllithium solution, 1.7 M in pentane</td>
</tr>
<tr>
<td>561452</td>
<td>25 mL</td>
<td>Ethyllithium solution, 0.5 M in benzene ether</td>
</tr>
<tr>
<td>468568</td>
<td>All Unit Sizes</td>
<td>Hexyllithium solution, 2.3 M in hexane</td>
</tr>
<tr>
<td>529745</td>
<td>100 mL</td>
<td>Isopropyllithium solution, 0.7 M in pentane</td>
</tr>
<tr>
<td>197343</td>
<td>All Unit Sizes</td>
<td>Methylthium solution, 1.6 M in diethyl ether</td>
</tr>
<tr>
<td>277304</td>
<td>100 mL</td>
<td>Potassium bis(trimethylsilyl)amide solution, 0.5 M in toluene</td>
</tr>
<tr>
<td>297054</td>
<td>All Unit Sizes</td>
<td>(Trimethylsilylmethyl)thium solution, 1.0 M in pentane</td>
</tr>
</tbody>
</table>

### Lewis Acids

<table>
<thead>
<tr>
<th>Cat. No.</th>
<th>Available sizes with New Design</th>
<th>Product Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>296112</td>
<td>All Unit Sizes</td>
<td>Diethylzinc solution, 1.0 M in hexanes</td>
</tr>
<tr>
<td>268569</td>
<td>All Unit Sizes</td>
<td>Trimethylaluminum solution, 2.0 M in hexanes</td>
</tr>
<tr>
<td>198048</td>
<td>100 mL, 800 mL</td>
<td>Trimethylaluminum solution, 2.0 M in toluene</td>
</tr>
</tbody>
</table>

### Reducing Agents

<table>
<thead>
<tr>
<th>Cat. No.</th>
<th>Available sizes with New Design</th>
<th>Product Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>214949</td>
<td>All Unit Sizes</td>
<td>Diisobutylaluminum hydride solution, 1.0 M in cyclohexane</td>
</tr>
<tr>
<td>190306</td>
<td>All Unit Sizes</td>
<td>Diisobutylaluminum hydride solution, 1.0 M in hexanes</td>
</tr>
<tr>
<td>215007</td>
<td>All Unit Sizes</td>
<td>Diisobutylaluminum hydride solution, 1.0 M in toluene</td>
</tr>
</tbody>
</table>
Labware Notes

Paula Freemantle
Product Manager
labware@sial.com

Improved NMR Tubes from Sigma-Aldrich

Color coded for easy identification out of the box

Aldrich ColorSpec® NMR tubes are printed with colored bands at the top of each tube and are supplied with colored caps to indicate the quality grade of the NMR tube. In addition, each tube is printed with the MHz rating and a marking spot.

Chemists can easily identify the grade of a ColorSpec® NMR tube at all stages of its use, from opening the box, filling, storage and transport to NMR machine, and even after wash and oven drying.

Avoid poor quality spectra or risk of probe damage from mistaking low grade tubes and using in high frequency instruments.

<table>
<thead>
<tr>
<th>Material</th>
<th>Disposable/Thrift</th>
<th>Precision (Glass)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ASTM Type 1 Class B Borosilicate Glass (commercial name N51A)</td>
<td>ASTM Type 1 Class B Borosilicate Glass (commercial name Pyrex)</td>
</tr>
<tr>
<td>Impact on shimming quality by paramagnetic impurities</td>
<td>Medium (&gt;1,200 ppm Fe₂O₃)</td>
<td>Small (&lt;400 ppm Fe₂O₃)</td>
</tr>
<tr>
<td>Rapid cooling / heating</td>
<td>No</td>
<td>Yes, within 120 °C</td>
</tr>
<tr>
<td>Max. working temperature</td>
<td>Ambient</td>
<td>230 °C</td>
</tr>
<tr>
<td>Sample volume repeatability</td>
<td>1.0%</td>
<td>0.50%</td>
</tr>
<tr>
<td>Cut-off wavelength</td>
<td>320 nm</td>
<td>320 nm</td>
</tr>
<tr>
<td>Recommended application</td>
<td>1D NMR experiments with a small organic molecule (Molecular Weight &lt;1,500) below 600 MHz</td>
<td>Experiments that require critical shimming quality, for example, High/ultra high field, non-spinning, multi-dimensional, multi-nuclei, DNP experiments and studies involving biological samples.</td>
</tr>
</tbody>
</table>

**Note 1:** Impact on shimming quality varies upon magnetic field strength. Disposable/Thrift tubes are recommended for 1D low field experiments.

**Note 2:** Sample volume reproducibility refers to the maximum volume fluctuation when filling different NMR tubes to the same sample height. This number correlates to the reproducibility of time domain signal amplitude between different runs.

For a complete listing of Aldrich ColorSpec NMR tubes, please visit our website at aldrich.com/colourspec
**Aldrich SafetyBarb® NMR tube cleaner**

Z558362 and Z558370

Inner PTFE wash tube with Luer connection prevents NMR tube breakage during the cleaning process. Detaches for thorough cleaning or replacement. SafetyBarb vacuum connection. Washes 3, 5, and 10 mm NMR tubes in both 7 and 8 in. lengths. Order replacement SafetyBarb hose connectors Z547786 (straight) or Z547883 (angled).

**Instructions for use:**
1. Connect the inner PTFE needle to the stainless steel Luer fitting.
2. Assemble the inner and outer glass washer components using silicone grease.
3. Install tube washer into a 24/40 female jointed flask using silicone grease.
4. Attach the SafetyBarb hose connector to the tube washer.
5. Connect vacuum source to the SafetyBarb hose connector.
6. Place one NMR tube, open end down, over the PTFE needle.
7. Fill the tall tube with desired wash solvent.
8. Turn on vacuum to wash NMR tube.
9. Repeat fill process as necessary until NMR tube is clean.

**Aldrich glass combination pH electrodes**

Z113441

BNC, double junction, AgCl electrode with Ultra-thin, long stem for NMR tubes

**Aldrich NMR tube labels**

Z220574

Self-laminating, vinyl labels with white, write-on surface resist oil, water, and solvent. Label wraps around 5 mm tube for positive sample identification. Supplied with 26 labels on a card, 25 cards per pack.

**Aldrich Spectral Viewer FT-NMR**

Spectral Viewer products are electronic reference books on CD-ROM that contains thousands of spectra from the Aldrich spectral libraries. The easy-to-use software is more powerful than a printed book, allowing text and data field searching and the manipulation, printing, and exporting of spectra. There are two FT-NMR libraries available containing over 15,000 compounds in total. The libraries can be used individually and can be combined to create a single powerful, electronic reference. Spectral Viewer is expandable so that when new spectral libraries are released, they can be easily added to the software. Academic and Network versions are available.

- FT-NMR, standard library
  - 11,800 compounds  Z541265
- FT-NMR, 2001 supplemental library
  - 3,500 compounds  Z538086

For additional Spectral Viewer listings, visit our website at [aldrich.com/spectralviewer](http://aldrich.com/spectralviewer)