Pd-PEPPSI™-IPent: a new and improved catalyst for cross-coupling.
Missing out on the latest research developments in Chemistry?

Aldrichimica ACTA is a complimentary publication, which has been an international forum for the frontiers of chemical research for the past 43 years. Articles, written by chemists from around the world, cover a variety of topics usually based on a synthetic theme involving organic, organometallic, bio-organic, or inorganic chemistry. It has been ranked #1 by Impact Factor in eight of the past nine years in the field of organic chemistry (out of over 50 similar journals), with an Impact Factor of 18.688 (2009).*

Aldrichimica ACTA helps keep you informed of the latest research methodologies and trends, as well as the related Aldrich Chemistry products to support them.

Request your complimentary subscription Aldrich.com/acta

* Thomson Reuters. Journal Citation Reports®, Science Edition.
Dear Fellow Chemists,

Welcome to the second edition of Aldrich ChemFiles for 2011, our complimentary quarterly innovation 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.

As well as introducing all the latest innovations across all of our product lines, in 2011 each edition of Aldrich ChemFiles will be themed to a product line. Aldrich ChemFiles Vol. 11, No. 2 will focus on our Catalysis product line, which is very timely as it affords me the opportunity to welcome Dr. Ronaldo Mariz as our new Catalysis Product Manager. In this “Catalysis” issue Ronaldo highlights our latest palladium and nickel catalysts for Negishi, Suzuki, Heck, Sonogashira and Kumada-Corriu-Tamao cross-coupling reactions. Our cover molecule is PEPPSI™-IPent, developed by Prof. Michael Organ, one of several new molecules to our portfolio of Pd-PEPPSI catalysts, and illustrates how critically important Pd-catalyzed cross couplings are to the chemical community, a fact reflected by the 2010 Nobel Prize for chemistry being awarded to Prof. Richard Heck, Prof. Ei-ichi Negishi and Prof. Akira Suzuki for their pioneering work in this field.

Aldrich ChemFiles Vol. 11, No. 2 will also introduce the latest innovations across all of our product lines including new MIDA boronates (Organometallics), iodinated building blocks and oxetanes (Building Blocks), new novel oxidants (Synthetic Reagents) and the latest isotope labeled organic molecules (Stable Isotopes). I am also pleased to introduce you to Dr. Pietro Butti, our new Green Chemistry Product Manager, who will discuss how Aldrich is using greener methodologies to produce aromatic azides, which have numerous applications for the synthesis of APIs.

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,

Dr. Haydn Boehm
Global Marketing Manager: Chemical Synthesis

Table of Contents

Catalysis ................................................................. 4
Organometallics ..................................................... 10
Building Blocks ....................................................... 12
Synthetic Reagents .................................................. 14
Green Chemistry ..................................................... 16
Stable Isotopes ........................................................ 18
Stockroom Reagents ............................................... 20
Labware Notes ......................................................... 22
Nickamine: Nickel catalyst for Sonogashira and Kumada-Corriu-Tamao (KCT) coupling

- Versatile nickel catalyst
- Excellent functional group tolerance

**Sonogashira coupling**

One of the most widely used methods for introducing the alkynyl moiety in organic substrates is the coupling of an electrophile and a terminal alkyne normally mediated by a palladium catalyst in the presence of copper as co-catalyst. Recently Xile Hu and co-workers reported the use of the nickel catalyst Nickamine (728551) as a versatile alternative to palladium for the Sonogashira coupling (Scheme 1).1

Scheme 1: Nickel catalyzed Sonogashira coupling of non-activated alkyl halides.

Loadings of 5 mol% of the nickel catalyst enabled the coupling of non-activated alkyl iodides with several terminal alkynes. Alkyl bromides and even chlorides in the presence of NaI and n-Bu4NI as additives respectively, were equally effective. It is noteworthy that the catalyst overcomes problems associated with β-H elimination (undesired side reaction) and operates with excellent functional group tolerance for both coupling partners.

**Kumada-Corriu-Tamao (KCT) coupling**

Hu and co-workers have also shown that Nickamine can be successfully employed in the cross-coupling of non-activated alkyl halides and Grignard reagents (Scheme 2).2,3 Despite the reactive nature of the organometallic coupling partner many functional groups were tolerated in the protocols applied. The Kumada-Corriu-Tamao coupling permitted access to a variety of functionalized aryl, heteroaryl and alkyl compounds.

Scheme 2: KCT coupling of non-activated alkyl halides and Grignard reagents.

**Orthogonal Functionalization**

Exploiting the versatility of the catalyst, Hu and co-workers demonstrated that it is possible to make use of both Sonogashira and KCT protocols, as well as the difference in reactivity of the alkyl-X bonds, allowing orthogonal functionalization of substrates with multiple reactive sites (Scheme 3).

Scheme 3: Orthogonal functionalization of substrates.
Frech Pdcat: Piperidinaminophosphine Pincer Palladium catalyst for Suzuki, Heck and Sonogashira coupling

• Palladium catalyst for Suzuki, Heck and Sonogashira coupling at ppm levels

**Suzuki coupling**

The cross-coupling of aryl halides and organoboron nucleophiles is established as one of the most common methods to construct C–C bonds in biaryl frameworks. The Frech group at The University of Zurich has developed a highly active piperidinaminophosphine pincer palladium complex (727733) capable of performing the Suzuki reaction at loadings as low as 0.05 mol% (Scheme 1). The catalyst effectively coupled a wide range of aryl bromides and boronic acids/potassium trifluoroborates with very good functional group tolerance under air atmosphere.

**Heck reaction and Sonogashira coupling**

While Frech’s catalyst demonstrates high activity with just 0.05 mol% for the Suzuki coupling, its performance in both Heck reaction and Sonogashira coupling requires even lower amounts of the metal complex. Excellent yields were obtained at ppm levels (not greater than 50 in most cases) reaching turnover numbers of up to 49000 TON for the Heck reaction (Scheme 2) and 20000 TON for the Sonogashira coupling (Scheme 3).

For a list of homogeneous palladium catalysts available from Aldrich Chemistry, visit Aldrich.com/palladium
Cinchona Based Thiourea Organocatalysts

- Effective organocatalysts for conjugated additions

Catalysis by purely organic small molecules has emerged as a powerful tool in the field of asymmetric synthesis. Among the plethora of chiral organocatalysts developed so far, cinchona alkaloid-based motifs constitute one of the most popular choices. Recent studies have shown cinchona based thiourea (690384, 690600 and 690481), readily accessed from the corresponding amines (713228, 713201 and 713236), as promising organocatalysts. Important features in these types of catalysts are the configuration at C9 as well as the level of saturation at the pendant chain of the bicyclic moiety, found to affect dramatically the performance for a given reaction.\(^1\) For instance, Soós reported enantioselectivities of up to 94% in the 1,4-addition of nitroalkanes to Michael acceptors using thiourea 690384 as the most suitable for this specific transformation. The methodology was used to accomplish the selective synthesis of (R)-rolipram, an antidepressant agent (Scheme 1).\(^2\)

Scheme 1: Thiourea organocatalyzed 1,4-addition of nitromethane to α,β-unsaturated N-acylpyrroles and application in the synthesis of (R)-rolipram.

PEPPSI™-IPent: A New and Improved Catalyst for Negishi Coupling

Pd-Catalyzed cross-coupling reactions are of the utmost importance to chemistry. From the production of pharmaceutical agents to synthetic polymer synthesis, these reactions have proven to be truly versatile for the selective construction of C-C bonds. Within this class of reactions, the coupling of an organozinc nucleophile with a suitable halogenated electrophile, the Negishi reaction, has proven to be particularly useful. Supporting this, the Nobel Prize in chemistry was awarded to Prof. Ei-ichi Negishi, Akira Suzuki, and Richard Heck for their contributions to the field in 2010.

While numerous advances have been made concerning the Negishi reaction, difficulties still remain for the coupling of sterically demanding substrates. To address this issue, efforts have focused on the development of new, more reactive catalysts for cross-coupling. It has been shown that monoligated Pd-N-heterocyclic carbene (Pd-NHC) complexes, with considerable steric bulk around the metal center, are reactive enough to couple even the most sterically demanding substrates, albeit at elevated temperatures. In an attempt to improve this reaction even further, the group of Prof. Michael Organ has developed a new and improved catalyst for cross-coupling at room temperature, Pd-PEPPSI-IPent (Figure 1).

![Figure 1: Pd-PEPPSI-IPent.](image)

Building upon their previous work, Organ and coworkers have developed a powerful catalyst for the cross-coupling of a wide range of organozinc reagents (generated in situ) with various sterically demanding aryl electrophiles at room temperature (Table 1).

<table>
<thead>
<tr>
<th>Ar</th>
<th>Product</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl</td>
<td></td>
<td>90</td>
</tr>
<tr>
<td>Br</td>
<td></td>
<td>80</td>
</tr>
<tr>
<td>TBSO</td>
<td></td>
<td>97</td>
</tr>
<tr>
<td>OBn</td>
<td></td>
<td>87</td>
</tr>
</tbody>
</table>

Table 1: Pd-PEPPSI-IPent catalyzed Negishi cross-coupling.

In addition to simple biaryl systems, Pd-PEPPSI-IPent may also be used to construct an impressive array of heterobiaryl compounds bearing various functional groups and/or congested steric bulk, all in excellent yields under the mildest conditions reported to date (Table 2).

<table>
<thead>
<tr>
<th>Ar</th>
<th>Product</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Br-N</td>
<td></td>
<td>98</td>
</tr>
<tr>
<td>Br-N</td>
<td></td>
<td>61</td>
</tr>
<tr>
<td>Br-N</td>
<td></td>
<td>quant</td>
</tr>
<tr>
<td>Cl-N</td>
<td></td>
<td>79</td>
</tr>
</tbody>
</table>

Table 2: Heterobiaryl synthesis with Pd-PEPPSI-IPent.

Further displaying the power of Pd-PEPPSI-IPent for Negishi cross-coupling, the Organ group has also shown that this catalyst can effectively couple sterically demanding substrates at temperatures as low as 0°C (Figure 2). This finding solidifies Pd-PEPPSI-IPent as a truly unique and highly active catalyst for Negishi cross-coupling.
Pd-PEPPSI™ Catalysts for Cross-Coupling

While Pd-catalyzed cross-coupling reactions have proven to be critically important to the chemical community, one dilemma often encountered by chemists is not knowing which Pd-catalyst will be most effective for their desired application. Few catalysts exhibit activity across a wide range of substrates and reaction conditions. While Pd(PPh₃)₄ has developed into one of the most general and commonly used catalysts for cross-coupling, this complex often suffers from poor stability upon storage, as well as the need to handle under inert atmosphere. To address this, the group of Prof. Michael Organ has developed Pd-PEPPSI-IPr as a highly effective and versatile catalyst for cross-coupling (Figure 3).

In addition to Negishi cross-coupling, Pd-PEPPSI-IPr is also useful for Suzuki and Kumada couplings, as well as Buchwald-Hartwig aminations (Figure 5). In addition to Negishi cross-coupling, Pd-PEPPSI-IPr is also useful for Suzuki and Kumada couplings, as well as Buchwald-Hartwig aminations (Figure 5).

Need a MolarMatic™ Measuring Cylinders for your Acid/Base solutions?

Add Aldrich

**Aldrich MolarMatic Measuring Cylinder**

Our MolarMatic graduated measuring cylinder allows you to add concentrated acid to the desired molarity line. Simply pour the measured acid into one liter of water, and your 1 M, 2 M, or 3 M solution is prepared.

- No calculations
- No struggling for the correct cylinder

**Convenient Dual-Scale Graduated Cylinder**

- Class A, 350-mL cylinders
- Graduated in 5.0-mL increments; calibrated “to deliver”
- 1 to 3 molar scale on opposite side
- Eliminates repetitive molar calculations and potential errors
- Set contains one of each cylinder in plastic storage case

<table>
<thead>
<tr>
<th>Acid Type</th>
<th>Cat. No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetic acid</td>
<td>Z683728</td>
</tr>
<tr>
<td>Hydrochloric acid</td>
<td>Z683736</td>
</tr>
<tr>
<td>Nitric acid</td>
<td>Z683744</td>
</tr>
<tr>
<td>Sulfuric acid</td>
<td>Z683752</td>
</tr>
<tr>
<td>Set of four</td>
<td>Z683760</td>
</tr>
</tbody>
</table>

Save time. Add Aldrich.
[Aldrich.com/molarmatic](http://Aldrich.com/molarmatic)
The Utility of MIDA Boronates

Over the past three years Aldrich Chemistry has introduced the MIDA boronates as a powerful new class of boronic acid surrogates that can be used for Suzuki-Miyaura cross-coupling reactions. These useful reagents were developed by the group of Prof. Martin Burke at the University of Illinois, and their work has illustrated the utility of MIDA boronates in the context of both methodological studies and the realm of total synthesis. In doing this, the Burke group has shown that the MIDA boronate platform possesses a number of advantages over their classical boronic acid and boronate ester counterparts (Figure 1).

Figure 1: The advantages of MIDA boronates.

Due to these unique features and advantages, three distinct applications for the MIDA boronates have been disclosed.

Applications of MIDA Boronates

- Iterative cross-coupling
- Advanced building block synthesis
- Slow-release cross-coupling

Importantly, all three of these applications represent unique opportunities for chemists that could not be accomplished with other organoboron species prior to these reagents.

Iterative Cross-Coupling with MIDA Boronates

MIDA boronates have proven to be unreactive under classical non-aqueous cross-coupling conditions. This unique reactivity difference allows for the use of MIDA boronates in iterative cross-coupling sequences. This technique was recently used by the Burke group in their synthesis of all-trans-retinal (Scheme 1). In this synthesis MIDA boronate BB1, containing both electrophilic (vinyl-halide) and nucleophilic (MIDA boronate) moieties was successfully cross-coupled in an iterative fashion. Because of the enhanced stability of the MIDA boronate moiety, BB1 was efficiently coupled with triene boronic acid 1 in 78% yield. Following this, hydrolysis of the MIDA unit with aqueous NaOH revealed the organoboron species that was subsequently coupled in a second Suzuki reaction, yielding all-trans-retinal in a highly efficient manner.

Scheme 1: Iterative cross-coupling of MIDA boronate BB1 in the synthesis of all-trans-retinal.
Advanced Building Block Synthesis Using MIDA Boronates

The Burke group has shown that a diverse range of reactions can be carried out while keeping the MIDA group intact due to its enhanced stability. For example, asymmetric aldol reactions, Horner-Wadsworth-Emmons and Takai olefinations, as well as a range of other reactions can all be carried out in the presence of the MIDA unit in good yields with excellent selectivity (Scheme 2).

Scheme 2: Advanced building block synthesis with MIDA boronates.

**MIDA Boronates for Building Block Synthesis**

704415  
697494  
721573  
704547  
698008  
698210

**Slow-Release Cross-Coupling of MIDA Boronates**

In addition to iterative cross-coupling and building block synthesis, MIDA boronates have also been shown to undergo the *in situ* slow-release of boronic acids under aqueous basic conditions (Scheme 3). Harnessing the power of this phenomenon, boronic acids that are notoriously unstable can now be effectively utilized when employed as MIDA boronates. The slow-release of sensitive boronic acids can be achieved using mildly basic aqueous K$_3$PO$_4$. This slow-release concept prevents decomposition of the precursor organometallic species and in many cases improves the overall yield of the Suzuki-Miyaura reaction.

Scheme 3: Slow-release of unstable boronic acids from MIDA boronates.

This concept is exemplified by the development of 2-pyridinylboronic acid MIDA ester as a viable 2-pyridinylboron anion equivalent. 2-Pyridinylboronic acids and esters have been developed in the past, but due to their air and moisture sensitivity, cross-coupling with these reagents is often low-yielding and almost always inefficient. Now, via this slow-release methodology, the Suzuki coupling of 2-pyridinylboronic acid MIDA ester with a wide range of aryl- and heteroaryl chlorides is predictable and high-yielding (Scheme 4).

Scheme 4: Suzuki-Miyaura cross-coupling of 2-pyridinylboronic acid MIDA ester.

**Sensitive Organo-Boron Species Ideal for Slow-Release Cross-Coupling**

To view our complete line of MIDA boronates, visit Aldrich.com/mida
Iodinated Building Blocks

• Ease the purification of coupling reactions

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. Iodinated substrates are often preferred to the brominated analog, 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.

New Iodinated Building Blocks

<table>
<thead>
<tr>
<th>Iodinated Substrate</th>
<th>Iodinated Substrate</th>
<th>Iodinated Substrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>779059</td>
<td>730742</td>
<td>722278</td>
</tr>
<tr>
<td>722057</td>
<td>722170</td>
<td>731412</td>
</tr>
<tr>
<td>714364</td>
<td>724092</td>
<td>730564</td>
</tr>
<tr>
<td>724084</td>
<td>720372</td>
<td>729639</td>
</tr>
</tbody>
</table>

Oxetanes

• Oxetanes can improve the pharmokinetic profile and stability of a target molecule when replacing a gem-dimethyl or a carbonyl unit

Oxetanes are the closest homologs to epoxides, but historically have received far less attention than their three-membered-ringed brethren. However, oxetanes are receiving increasing attention as attractive modules for drug discovery, largely due to a recent series of reports from Rogers-Evans, Carreira and coworkers. They have shown how oxetanes can perform as surrogates for carbonyl groups, how certain properties of a target molecule are improved when an oxetane unit replaces a gem-dimethyl unit and also how the use of oxetane-containing scaffolds can be employed as alternatives to unstable 1,3-heteroatom substituted cyclohexanes.

Furthermore, oxetanes are critical moieties in drug-like and various biologically active molecules such as the natural product paclitaxel, or Taxol®, and docetaxel, its synthetic analog (Figure 1). Other oxetane-containing natural products such as Merrilactone A (Figure 2) and the β-amino acid oxetin (Figure 3) have demonstrated therapeutic potential. Brubaker and coworkers have also recently demonstrated the use of oxetan-3-tert-butylsulfinimine, LS00429 as a common synthetic intermediate for the preparation of 3-substituted-3-aminooxetanes (Scheme 1).

Figure 1: Paclitaxel (Taxol®) and Docetaxel

Figure 2: Merrilactone A

Figure 3: β-Amino Acid Oxetin
Scheme 1: Synthesis of Substituted 3-Aminooxetanes

Other New Building Blocks Cont'd

Other New Building Blocks

For a complete list of available oxetanes, visit Aldrich.com/oxetane

Other New Building Blocks Cont'd

For a comprehensive list of Building Blocks, visit Aldrich.com/bb

Ferrate (VI) Chemistry and Application
Summary: A New and Novel Oxidant from Ferratec, LLC*

- One of the strongest known oxidants
- Green oxidant
- Cost-effective, small scale and large

Although discovered in the 1700s, potassium ferrate (VI) K₂FeO₄ (723835) has largely remained an academic curiosity due to the absence of a scalable production process for stable, high purity, chlorine-free, ferrate (VI) salts. However, a commercial process now exists to enable efficient production for specialty and niche applications.

Ferrate is not only more active than conventional commodity disinfectants such as chlorine, permanganate, ozone, monopersulfate, chromic acid and hydrogen peroxide, but it also circumvents the hazardous side products of these chemistries.

Ferrate Thermodynamic Oxidizing Power

Ferrate has one of the highest standard reduction potentials known, 0.7–2.2 volts. As with many oxidants, there is a pH dependence to the observed standard half-cell potential (E°) values of ferrate (VI) due to a fundamental change in the overall chemical reactions involved. Reduction potential of oxo ions are lowest at high pHs, and greatest at low pHs. For ferrate (VI), this pH dependence is understood using the following reactions:

**Basic Solution**

FeO₄²⁻ + 3e⁻ + 3H₂O = 5OH⁻ + FeOOH  E° = 0.77 V

**Acid Solution (pH 1.7–7.0)**

FeO₄²⁻ + 3e⁻ + 5H⁺ = 2H₂O + FeOOH  E° ~ 1 V

**Acid Solution (pH <1.7)**

FeO₄²⁻ + 3e⁻ + 8H⁺ = 4H₂O + Fe³⁺  E° = 2.2

At neutral pH values the intermediate protonated species HFeO₄⁻ exists and the reduction potential is about one volt (see below). FeOOH precipitate due to the exceptionally broad pH window for this highly insoluble solid (> pH 1.7 to > 10% NaOH) is a valuable trait for water purification. Therefore, neutral and lower pH values can be used to increase the kinetic and thermodynamic aggressiveness of ferrate (VI) for oxidation and disinfection, while maintaining excellent coagulant properties of the FeOOH product.

In line with the well-established reactivity of oxo ions in general, the protonation of the ferrate (VI) ion strongly enhances its reactivity.

FeO₄²⁻ + H⁺ = HFeO₄⁻  pKₘᵢₙ = 7.8

HFeO₄⁻ + H⁺ = H₂FeO₄⁻  pKₘᵢₙ = 3.2

Potassium Ferrate (723835) is also an extremely “green” chemical. When dissolved, K₃FeO₄ completely converts to innocuous minerals: potassium bicarbonate, iron flocs & rust (Fe₂O₃), and oxygen. Furthermore, the FeOOH flocs collected from the water purification or chemical production process are not toxic. The large body of experience of FeOOH/Fe₂O₃- encapsulated contaminants (such as toxic metal ions, phosphate, arsenate, biological cell mass, etc.) indicates that such contaminants are not leachable by the EPA’s TCLP test.

* We would like to acknowledge Ferratec, LLC for providing this article.
Some Applications for Potassium Ferrate

- **Water Treatment** — provides acid neutralization capacity, coagulation and flocculation, precipitation of P and As, disinfection, clarification, taste and odor removal, replenishment of DO, reduction in TOC, BOD, COD, and trace toxic metal ion removal. Its disinfection range includes algae, protozoans, viruses, and bacteria.
- **Soil remediation (heavy metals, organics)**
- **Disinfection of medical equipment**
- **Sanitization of food**
- **Sorbent for odor control** (phenolics, mercaptans, hydrogen sulfide, sulfur dioxide, aldehydes, rancid acids, etc.)
- **Surface finishing of metals** for corrosion protection, especially iron, aluminum, aluminum alloys, stainless steels, and zinc
- **Chemical synthesis oxidation reagents**
- **Chemical and biological warfare agent decontamination**
- **Diesel and military fuel desulfurization.** Achieves > 99% removal of total S and even removes the recalcitrant hindered alkylbenzothiophenes.

**Cathodic material for batteries.** Ferrate(VI) is a 3 or even 4 electron/mole donor. Depending on other battery components, it may be possible to use ferrate(VI) to produce a primary or secondary battery that can be disposed of as a nonhazardous waste. The very high and tunable half cell potential of ferrate(VI) reduction appears to offer the opportunity of new “super iron” battery technology.

### Broad Spectrum and Potent Antimicrobial Activity

**Laboratory test results illustrating the disinfection of B. anthracis**

While the mechanisms for biocidal action by ferrate have not yet been extensively studied, test data show ferrate (VI) ion is a promising broad spectrum biocide: at 25 ppm ferrate(VI) ion, Cryptosporidium spores are disintegrated into fragments with at least a log 4 reduction in viable spores; 1 ppm is effective against pathogenic microorganisms such as *E. Coli*, total fecal Coli forms and others.

#### Comparison of Ferrate(VI) with other Disinfection Systems

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl₂/NaOCl/ Ca(OCl)₂</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td>—</td>
<td>YES (incl. THMs and HAAs)</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>DIFFICULT</td>
<td>YES</td>
<td>Yes (incl. NDMA)</td>
<td>YES</td>
<td>HIGH</td>
</tr>
<tr>
<td>NH₂Cl</td>
<td>YES</td>
<td>WEAK</td>
<td>NO</td>
<td>—</td>
<td>YES (incl. NDMA)</td>
<td>—</td>
<td>YES</td>
<td>YES (NHCl₂, NCl₃)</td>
<td>—</td>
<td>NO</td>
<td>NO</td>
<td>LOWEST</td>
<td>—</td>
</tr>
<tr>
<td>ClO₂</td>
<td>YES</td>
<td>—</td>
<td>SOMETIMES</td>
<td>YES</td>
<td>YES (incl. ClO₃ &amp; ClO₄⁻)</td>
<td>—</td>
<td>NO</td>
<td>NO</td>
<td>DIFFICULT</td>
<td>YES</td>
<td>—</td>
<td>LOW</td>
<td>—</td>
</tr>
<tr>
<td>ClO₃</td>
<td>YES</td>
<td>YES</td>
<td>—</td>
<td>YES</td>
<td>YES (incl. Bromate and bromoform THM in feed waters with Br⁻)</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>—</td>
<td>NO</td>
<td>NO</td>
<td>VERY HIGH</td>
<td>—</td>
</tr>
<tr>
<td>UV (254nm)</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>NO</td>
<td>NA</td>
<td>—</td>
<td>NA</td>
<td>NA</td>
<td>—</td>
<td>YES</td>
</tr>
<tr>
<td>Ferrate(VI)</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td>None known (no THMs and HAAs. Tests with Br⁻ still needed)</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>YES</td>
<td>VERY HIGH</td>
</tr>
</tbody>
</table>

Ready to scale up? For competitive quotes on larger quantities or custom synthesis, contact your local Sigma-Aldrich office, or visit safcglobal.com.
Aromatic Azides: Synthesis in a Microstructured Continuous Flow System

- Microreactors improve reaction mixing, heat exchange, and safety
- Solvated azides improve reaction safety

Since the seminal work of Peter Griess in the 19th century, organic azides, thanks to their intriguing nature, attracted the interest of various chemists over the years. Today this kind of compound has found applications in a variety of fields. Organic azides were found to be involved in a number of processes for the synthesis of active compounds (Scheme 1) and many of these compounds are available in the Aldrich Chemistry portfolio.

Scheme 1: Solid phase, microreaction-assisted synthesis of rac-oxomaritidine.

The process (Scheme 2) involves a Sandmeyer reaction on an aromatic amine compound, followed by treatment of the resulting diazonium salt intermediate with an aqueous solution of sodium azide to produce the desired aromatic azide in high yields.

Scheme 2: General method for the synthesis of aromatic azides.

To overcome the lack of aromatic azide products on the chemistry market, Aldrich Chemistry has developed a safe, robust and universal method for the synthesis of aromatic azides using microreaction technologies (Scheme 3).

Continuous flow microreactors have various advantages over larger scale batch processes, especially for the synthesis of highly reactive compounds such as the organic azides.

Scheme 3: Reaction equipment set-up for the synthesis of the aromatic azides.

- High surface-to-volume ratio and the absence of heat and mass transport limitations.
- Opportunity to directly transpose reaction conditions from a small scale to a large scale process.
- Closed system combined with small hold-up volumes offers an intrinsically safe environment for chemicals prone to explosive decomposition.

Using the Microreactor Explorer Kit (19979), all unstable compounds are kept in solution during the entire process, preventing accumulation of labile intermediates or products.

Applying the concept of flow chemistry, the safe preparation of a variety of high purity organic azides has been achieved.

At Aldrich Chemistry, we are committed to the safety of our customers. Therefore, all compounds are offered as a convenient and safe 0.25-0.5M solution in tert-butyl methyl ether.

For a complete list of organic azides available from Aldrich Chemistry, visit Aldrich.com
To discover Microreactor Technology & Flow Chemistry

Microreactor Explorer Kit

Our all-in-one solution allows you to explore innovative new technologies right away at a highly attractive price:

- Improve product profiles, purities and yields of your products
- Perform scale-independent synthesis from mg to kg in a single day
- Control highly exothermic reactions
- Handle unstable or hazardous materials (even explosives) safely
- Minimize the time frame for process development

Improve safety and cost. Add Aldrich.
Aldrich.com/mrt

References:
Stable Isotope Labeled Reagents from ISOTEC®

The labeling of organic molecules with stable isotopes, such as $^{13}$C, D, $^{15}$N, and $^{18}$O, is important to many fields including metabolism, proteomics and ADME. To aid in the synthesis of such molecules, The Next Generation of Labeled Synthons has been developed. This line of products contains labeled reagents which were designed to merge seamlessly into a variety of synthetic routes, providing quick and efficient access to stable isotope labeled compounds.

Ethyl N,N-dimethyloxamates

$\alpha$-Dicarbonyl containing compounds are extremely important in terms of biological relevance as well as synthetic utility. Due to their importance, the synthesis of stable isotope labeled $\alpha$-dicarbonyl compounds is of great value. Synthesizing these types of compounds has been done routinely using labeled diethyl oxalate; however this chemistry provides only symmetrically labeled products. To obtain compounds possessing carbonyls differentiated by a $^{13}$C label, the challenge greatly increases.

To address this deficiency in the methodology of stable isotope labeling, the $^{13}$C labeled ethyl N,N-dimethyloxamates were designed. These reagents are offered in three different labeling patterns and take advantage of the clear reactivity differences between the ester and amide carbonyls which results in regiospecifically $^{13}$C labeled products.

Scheme 1: Pyruvic and Acrylic Acid Syntheses

The utility of these reagents is evident in the efficient, straightforward syntheses of pyruvic and acrylic acids (Scheme 1). One synthetic route and two synthetic steps impressively provide access to these compounds in high yield and isotope enrichment.

New Ethyl N,N-dimethyloxamates

Vinyl Sulfides, Sulfoxides and Sulfones

Organosulfur compounds play an important role in organic chemistry. Due to the multiple strategies available to remove sulfur, combined with its presence in biologically relevant molecules, many applications benefit from the unique reactivity organosulfur compounds possess.

Vinyl organosulfur compounds are of particular synthetic utility due to the broad range of reactions and conditions with which they are compatible. These reagents are well suited for use as Michael acceptors, in various cyclo-addition reactions and in Heck vinylation (Scheme 2).

Scheme 2: Vinyl Organosulfur Capabilities

$^{13}$C labeled phenyl vinyl sulfide, sulfoxide and sulfone are each offered in three labeling patterns. The natural abundance versions of these reagents and their derivatives have seen success in numerous projects including total syntheses of natural products and preparation of biologically relevant scaffolds like alkaloids and quinolines. With the available literature precedence, as well as convenient labeling patterns, these reagents will fit into any stable isotope labeling project.
New Vinyl Sulfides, Sulfoxides and Sulfones

<table>
<thead>
<tr>
<th>Chemical Structure</th>
<th>Molecular Formula</th>
<th>Aldrich Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Ph-S-13C]</td>
<td>Ph-S-13C</td>
<td>715360</td>
</tr>
<tr>
<td>![Ph-S-13CH2]</td>
<td>Ph-S-13CH2</td>
<td>715379</td>
</tr>
<tr>
<td>![Ph-S-13CO]</td>
<td>Ph-S-13CO</td>
<td>715352</td>
</tr>
<tr>
<td>![Ph-S-13CH2]</td>
<td>Ph-S-13CH2</td>
<td>715883</td>
</tr>
<tr>
<td>![Ph-S-13CH2]</td>
<td>Ph-S-13CH2</td>
<td>715948</td>
</tr>
<tr>
<td>![Ph-S-13CH2]</td>
<td>Ph-S-13CH2</td>
<td>715891</td>
</tr>
<tr>
<td>![Ph-S-13CH2]</td>
<td>Ph-S-13CH2</td>
<td>715875</td>
</tr>
<tr>
<td>![Ph-S-13CH2]</td>
<td>Ph-S-13CH2</td>
<td>715867</td>
</tr>
<tr>
<td>![Ph-S-13CH2]</td>
<td>Ph-S-13CH2</td>
<td>716189</td>
</tr>
</tbody>
</table>

**References:**

For more information on these products, visit [Aldrich.com/sinext](http://Aldrich.com/sinext) or contact:

**Stable Isotope Technical Service**

**Phone:** (937) 859-1808

(800) 448-9760 (US and Canada)

**Fax:** (937) 859-4878

**Email:** isosales@sial.com

---

**ISOTEC® Stable Isotopes**

**Stable Isotopes** have a variety of synthetic reagents ideal for any labeling application.

**Common Laboratory Reagents**

- Acetic acid-13C2 (282022)
- Benzene-13C6 (423637)
- Bromoacetic acid-13C2 (283835)
- Diethyl malonate-2-13C (281859)
- Ethyl bromoacetate-2-13C (293172)
- Hydrazine-15N2 monohydrate (492787)
- Iodomethane-d3 (176036)
- Methyl-d4-magnesium iodide (293091)
- Potassium cyanide-13C15N (490539)

**Derivatizing Reagents**

- Acetic anhydride-13C4 (487821)
- Phenyl-d5 isocyanate (493244)
- 2-Nitrobenzenesulfenyl chloride-13C6 (640492)

**Reducing Reagents**

- Deuterium gas (617474)
- Diborane-d6 (463140)
- LiAlD4 (193100)
- NaBD3CN (190020)
- NaBD4 (205591)

For a complete listing of stable isotope products, visit [Aldrich.com/isotec](http://Aldrich.com/isotec)

©2011 Sigma-Aldrich Co. All rights reserved. ISOTEC and ALDRICH are registered trademarks of Sigma-Aldrich Biotechnology L.P., an affiliate of Sigma-Aldrich Co.
Sigma-Aldrich® is a leading global supplier and manufacturer of high quality, stockroom and essential research products

We specialize in providing the most comprehensive product range and widest selection of purity grades to fulfill your particular application needs.

- **Solvents** — As a leading supplier of high-purity, research grade solvents, we have the solvent to meet your exact needs
- **Acids and Bases** — From ACS grade to TraceSELECT® Ultra for the ultra trace analysis level down to ppb and ppt.
- **Routine Organic and Inorganic Reagents**
- **Adsorbents, Filter Aids and Drying Agents**

You will also find several programs that offer unique solutions to help control your costs. One may be right for you!

**Supply Rewards™ Program**

Get rewarded for choosing Sigma-Aldrich. Earn rewards for your team, your community, or yourself, every time you purchase selected products from Sigma-Aldrich. With over 1,500 eligible common laboratory products to choose from, earning reward points couldn’t be easier.

**New Lab Start-Up Program**

Get your new lab set up in an easy and economical way. Your lab is eligible for the program if:

- You are starting a new lab
- You are moving to a new location
- You have received your first research grant

To learn more, visit Aldrich.com/stockroom

**National Association of Scientific Materials Managers (NAOSMM)**

Sigma-Aldrich is a proud partner of NAOSMM and its members receive savings on a wide range of Sigma-Aldrich Chemistry products.

**By always listening, Sigma-Aldrich delivers.**

**Monthly Savings from Sigma-Aldrich**

Easy-to-find site offers monthly savings on Chemistry, Life Science, Analytical and Labware products.

United States
Aldrich.com/offers

Europe
Aldrich.com/offerseu

For specific country discounts, visit us at Aldrich.com

The Sigma-Aldrich Pressure-Temperature Nomograph allows you to quickly and easily estimate boiling points at various pressures. Interactive controls simplify calculations to improve the efficiency of your distillation or evaporation process.

**Pressure Conversion Tab:** Use the built-in Pressure Conversion Calculator to convert among five units of pressure using either numeric values or scientific notation.

**Temperature Conversion Tab:** Quickly calculate temperature conversions without leaving the Nomograph.

**Printable:** Need a hard copy to take with you? Simply right-click and select ‘print’.

Aldrich.com/nomograph
Need a Molarity Calculator for your Acid/Base solutions?

Add Aldrich

Aldrich Normality and Molarity Calculator

Features
- Calculates molarity for known acids and bases
- Calculates solutions of a solid reagent
- Dilutes a solution of known molarity
- Gets results at the click of a button
- Runs on your iPhone® and iPad®

Benefits
- Saves time over hand calculations
- Increases accuracy of calculations

Easy-to-Use
1. Select Acid or Base from drop down menu
2. Density, FW, and Wt. % will auto-populate
3. Input desired volume and concentration
4. Click on “Calculate”

Add Aldrich to save time and access the Normality and Molarity Calculator at Aldrich.com/calculator
PureSolv™ Micro Solvent Purification System

Easy Access to Freshly Prepared Anhydrous Solvents

Many organic and organometallic reactions require solvents that are free of water and oxygen. Classically, anhydrous solvents are prepared in the laboratory by refluxing the solvent in the presence of an active metal. This is an intrinsically hazardous operation.

The dangers of this method of solvent purification led Professor Robert Grubbs to investigate alternative methods. In collaboration with Dow, Grubbs published a method to remove water from organic solvents using activated alumina. Reference: Organometallics 1996, 15, 1558.

This approach uses dry nitrogen or argon to push solvent at ambient temperature through a column containing the drying agent. Oxygen is removed by bubbling inert gas through the solvent reservoir prior to pushing it through the drying column.

PureSolv Micro is a bench scale, self-contained system that permits the easy dispensing of small quantities of dry solvent at the turn of a valve. These systems are engineered for safety because they operate at very low pressure, require no electricity, and are bonded and grounded to remove hazards associated with electrostatic discharge.

How PureSolv Micro Works

1. Fill the stainless steel solvent storage reservoir with 4L of HPLC-grade raw solvent.
2. Degas the solvent by connecting the nitrogen line to the reservoir.
3. Pressurize the solvent reservoir to push solvent through the drying column.
4. Dry solvent is stored inside the drying column ready for immediate use.
5. Attach a collection flask to the dispensing joint.
6. Degas the collection flask using vacuum and inert gas cycling.
7. Turn the dispense valve to allow solvent to flow into the collection flask.
8. Refill the flask with inert gas.
9. Your collected solvent is now ready to use.

Flask Joint 24/40
- Z568031 with activated PureSolv media column
- Z568058 with activated molecular sieves
- Z568023 with activated Alumina column

Flask Joint 29/32
- Z683981 with activated PureSolv media column
- Z684007 with activated molecular sieves
- Z683973 with activated Alumina column

For more information about these products or to place an order, visit Aldrich.com/puresolv
Wrap-It-Ties

One-piece nylon fasteners are self-locking fasteners excellent for:

- Securing rubber septa to glass joints
- Attaching tubing to hose barbs
- Closing plastic bags or drum liners

Simply position the tie around the septum, tubing, or bag, and push the narrow end of the fastener through the locking mechanism until finger tight. Complete the operation by clinching the tie with an installing tool (shown in photo). Ties are easily removed with a slide cutter or similar tool.

Wrap-It-Ties
Z256323 Wrap-It Tie set
Z105953 Wrap-It Tie L 4 in.
Z105961 Wrap-It Tie L 5.6 in.
Z256331 Wrap-It Tie L 7 1/2 in.
Z256307 Wrap-It Tie tool heavy-duty version
Z564850 Wrap-It Tie tool economy version

Aldrich® solvent storage/dispensing flask, septum-inlet, with PTFE inlet valve

Designed for use with PureSolv Micro systems. PTFE inlet valve may be closed after filling to isolate dry solvent and to remove flask from PureSolv system and take to different location for use. 100 mL capacity. Use septum Z565695 or Z565679.

Z568538 24/40 Joint
Z684457 29/32 joint

For a complete listing of air-sensitive chemicals and solvents and Labware for handling them, visit the Air-Sensitive Products Guide on line at Aldrich.com/airchem

News and Innovation

Xpell™ indicating pellets for peroxides prevention

- Neutralizes peroxides as they form
- Inert to solvents and non-contaminating
- Distinct blue color indicates the absence of peroxide
- No special disposal requirements
- Not for use with THF

Z683094 80 grams treats up to 8 L of solvent

XploSens PS peroxide detection test strips

Z683108 50 test strips