

Pharmaceutical & fine chemicals

Nouryon



Welcome to Nouryon

We are Nouryon, your partner in essential chemistry for a sustainable future

We are a global specialty chemicals leader. Industries worldwide rely on our essential chemistry in the manufacture of everyday products such as paper, plastics, building materials, food, pharmaceuticals, and personal care items. Building on our nearly 400-year history, the dedication of our 10,000 employees, and our shared commitment to business growth, strong financial performance, safety, sustain- ability, and innovation, we have established a world-class business and built strong partnerships with our customers.

We operate in over 80 countries around the world and we supply customers around the world with ingredients for the manufacture of life's essentials. Specialty chemicals are used in, among others, paints, detergents, foods, plastics, cosmetics, construction, pulp and paper, pharmaceuticals, electronics and in agriculture.

Our products can be used in a variety of ways. For example, as basic building blocks of manufactured products, in the

processing of raw materials, as intermediates used to produce finished goods, or they may be used to enhance the functionality and durability of manufactured products. You'll find us in the food you eat, the buildings you live and work in, the vehicles and roads you use to move around, as well as everyday items such as paper products and your children's toys.

We produce everyday essentials for the global polymer and electronic industries. Our product portfolio includes organic peroxides, metal alkyls, metallocenes and single site catalysts and polymer additives, which are essential ingredients for the thermoplastic, composite and rubber industries.

Our products are also used in chemical synthesis of medicines and fine chemicals. In fact, some of the world's best-selling drugs are synthesized using our organometallic specialties or made from our Active Pharmaceutical Ingredients (APIs).



The finest chemical reagents

In pharmaceutical synthesis, our products are especially useful in reduction, addition, alkylation, assymetric oxidation, epoxidation and deprotonation including special reactions like Sharpless & Baeyer Villiger, where our reagents facilitate a wide range of asymmetric steps. Some of our products are presently used in the production of the world's leading drugs.

We invite you to visit our website at www.nouryon.com for complete product listings.

Our expertise and facilities find growing use in the synthesis of APIs and specialty chemicals that are used in the pharmaceutical and fine chemical industries.

We want to be your preferred supplier, producing custom specific products through arrangements protected by confidentiality agreements.

What do you need? From gram-scale to multiple-metric-ton level, we're happy to meet with you and discuss you target molecule.

Nouryon's key commercial API's and specialty chemicals for pharmaceutical synthesis

ORGANOMETALLIC REAGENTS

CAS NO.	ACRONYM	CHEMICAL NAME	FORMULA
1191-15-7	DIBAL-H	Diisobutylaluminum hydride	(i-C ₄ H ₉) ₂ AlH
56252-56-3	DIBAL-BOT	Diisobutylaluminum butylated oxytoluene	$(i-C_4H_9)_2AlO(C_6H_2(CH_3)(t-C_4H_9)_2)$
75-24-1	TMAL	Trimethylaluminum	(CH ₃) ₃ Al
97-93-8	TEAL	Triethylaluminum	(C ₂ H ₅) ₃ Al
96-10-6	DEAC	Diethylaluminum chloride	(C ₂ H ₅) ₂ AlCl
1271-19-8	TDC	Titanocene dichloride or Bis(cyclopentadienyl) titanium (IV) dichloride	$(C_5H_5)_2TiCl_2$
97-94-9	TEB	Triethylborane	(C ₂ H ₅) ₃ B
557-20-0	DEZ	Diethylzinc	$(C_2H_5)_2Zn$
62202-89-2	BEM	n-Butylethylmagnesium	$n-C_4H_9MgC_2H_5$

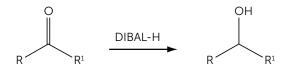
PEROXIDES AND INITIATORS

78-67-1	Perkadox AIBN	2,2'-Azodi(isobutyronitrile)	$(CH_3)_2C(CN)N=NC(CH_3)_2CN$
94-36-0	Perkadox BPO L-W75/78 USP L-DFG API	Dibenzoyl peroxide (API) *USP Grade *EP Grade *Global DMF Grade incl. Japan	(C ₆ H ₅ CO) ₂ O ₂
80-15-9	Trigonox CHP K-84PG K-90PG	Cumyl hydroperoxide or Cumene hydroperoxide	C ₆ H ₅ C(CH ₃) ₂ OOH
937-14-4	МСРВА	m-Chloroperoxybenzoic acid	CIC ₆ H ₄ CO ₃ H
75-91-2	ТВНР	tert-Butyl hydroperoxide	(CH ₃) ₃ COOH

Applications of our products in pharmaceutical synthesis

DIBAL-H Diisobutylaluminum hydride

Hydride Reduction



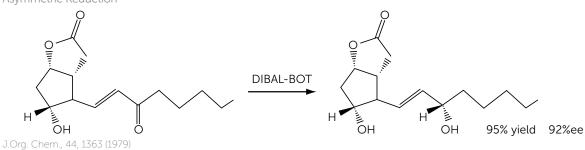
U.S. Patent 5,086,185 (1992)

Hydride reduction, including epoxide to alcohol, enone to allylic alcohol, carboxylic acid to primary alcohol, lactone to cyclic alcohol, amide to aldehyde, amide to amine, and nitrile to aldehyde. For example:

Tetrahedron Lett., 3, 619 (1962)

DIBAL-BOT Diisobutylaluminum butylated oxytoluene

Asymmetric Reduction



DEZ Diethylzinc

Cyclopropanation (Simmons-Smith)

March's Advanced Organic Chemistry, 5th Ed. Wiley, New York (2001),p.1088

Asymmetric Addition

$$\begin{array}{c|c} O & & & HO & Et \\ \hline DEZ & & & & \\ R^1 & & R^2 & & Ti(OiPr)_{4'} \ ligand & & & \\ R^1 & & & R^2 \\ & up \ to \ 99\% \ ee \end{array}$$

U.S. Patent 6,660,884 B2 (2003) J. Am. Chem. Soc., 70, 448 (2005)

TMAL Trimethylaluminum

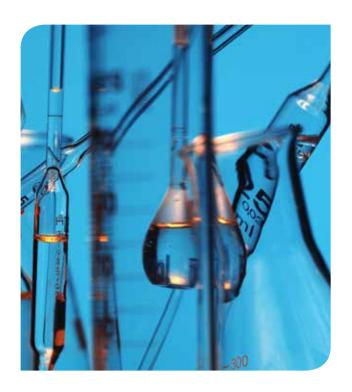
Alkylation

J. Org. Chem., 35, 532 (1970)

J. Chem. Soc. Chem. Comm., 595 (1972)

Weinreb Amidation

J. Org. Chem., 62, 6412 (1997) Org. Syn., 59 49 (1988)





TEB Triethylborane

Asymmetric Reduction

U.S. Patent 4,681,893 (1987) U.S. Patent 5,273,995 (1993)

Asymmetric Reduction (via lithium triethylborohydride)

$$\begin{array}{c|c} \text{LiH} + \text{Et}_3\text{B} & \xrightarrow{\text{THF}} & \text{LiEt}_3\text{BH} \\ & & \\ \hline \\ \text{O} & & \\ \end{array}$$

J. Org. Chem., 45, 1 (1980)

Free Radical Mediated Synthesis

$$O \longrightarrow I + R-CH=CH_2 \longrightarrow H_2O \longrightarrow I$$

Chem. Rev., 101, 3415 (2001)





 $\begin{tabular}{ll} TDC \end{tabular} Titanocene dichloride or Bis(cyclopentadienyl) titanium (IV) dichloride \\ \end{tabular}$

Tebbe Olefination

J. Am. Chem. Soc., 100, 3611 (1978)

BEM

Deprotonation

$$CF_{3} \xrightarrow{Bu_{2}Mg} CF_{3} \xrightarrow{BuLi} CF_{3} \xrightarrow{i) CO_{2} \text{ or } (MeO)_{2}CO} CF_{3} CF_{3}$$

$$CO_{2}R CF_{3} CF_{3} CF_{3} CF_{3} CF_{3}$$

$$Et_{2}O CF_{3} CF_{3} CF_{3} CF_{3}$$

$$CF_{3} CF_{3} CF_{3} CF_{3}$$

$$R=H, 70\%$$

$$R=ME, 74\%$$

Angew. Chem. Int. Ed., 46, 2 (2007).

DEAC Diethylaluminum chloride

Diels Alder Reaction

See for example J. Am. Chem. Soc., 112, 3018 (1990)

AIBN 2,2'-Azodi(isobutyronitrile)

Radical Initiator

March's ad vanced organic chemistry, 5th ed., wiley, new y ork (2001), p. 911





Trigonox K-84PG/K-90PG CHP Cumyl hydroperoxide or Cumene hydroperoxide

Asymmetric Oxidation

$$R - S - R^{1}$$

$$= \begin{cases}
1. & \text{Ti}(O - iPr)_{4} \\
(S,S) - \text{diethyl tartrate} \\
2. & (iPr)_{2}, NEt \\
CHP & > 95\% \text{ ee}
\end{cases}$$

Tetrahedron asy mmetr y, 11, 3819 (2000)

Perkadox MCPBA m-Chloroperoxybenzoic acid

Baeyer-Villiger Oxidation

J. ORG. CHEM., 63, 1390 (1998)

Oxidation

Epoxidation

March's advanced organic chemistry, 5th ed., wiley, new york (2001) p. 1051

Tetrahedron asy mmetr y, 11, 3819 (2000)

Trigonox A-W70 TBHP tert-Butyl hydroperoxide

Asymmetric Epoxidation (Sharpless)

J. Am. Chem. Soc., 102, 5974 (1980)

Active Pharmaceutical Ingredients (API)

Nouryon markets the widest range of organic peroxides for pharmaceutical applications in the world. Our APIs (Active Pharmaceutical Ingredients) are focused on insuring sustainable supply and regulatory compliance for U.S. Pharmacopeia (USP), Europe Pharmacopoeia (EP) and compliance with cGMPs (current Good Manufacturing Practices) and GDPs (Good Distribution Practices). Our late stage intermediates & fine chemicals are focused on mitigating risk, lowering potential liabilities and insuring security of supply through strict adherence to ISO standards and specific PFC (Pharmaceutical & Fine Chemicals) declarations. We are the world's largest producer of organic peroxides with a global scope using the industry's best safety practices. Our technical, quality

and safety leadership help reduce risk and potential liabilities throughout the entire value chain. We stand ready to partner in drug development as well as commercial opportunities. An example is our dedication to a wide range of Benzoyl Peroxide API's for acne

- Perkadox API US FDA and Japan DMF's
- Perkadox L-DFG >50 EP-DMF's for Europe & Asia (European Pharmacopeia)
- Perkadox L-W78/W75 Powder USP for OTC – DER1, DLC2 & cGMP
- Perkadox L-78W or 75W USP for OTC – DER1, DLC2 & cGMP
- Perkadox PM-W75 M-BPO, new API for new drugs



Logistics and technical support

Nouryon operates manufacturing facilities for organometallic reagents and organic peroxides in the Americas, Europe, and Asia. Our versatile facilities and flexible production schedules enable us to supply your favorite products from a few grams to multiple tons, and anything in between. Our global distribution network allows us to deliver the products to you anywhere in the world.

We at Nouryon always place safety as our top priority in customer service. Our Safety Research laboratory in Deventer, the Netherlands, conducts routine safety tests on our products and develops protocols for your safe handling. Our safety programs combine class- room learning and live demonstrations with on-site consulting, to assist you in receiving and using our products. We also offer design and maintenance services at your sites to support your handling and storage of hazardous materials. All production sites are ISO 9001 and ISO 14001 certified in order to ensure the highest product quality and strictest compliance with



environmental regulations. Additionally, our sites in the Americas have achieved RC 14001 certification. API's from our Mexico site have DMFs (Drug Master Files) in over 30 countries and meet

cGMP (current Good Manufacturing Practices) from over 30 countries including US & Japan and GDP (Good Distribution Practices) worldwide.

Contact us

For product inquiry and ordering information, please contact your regional account manager or sales office.

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Additional information

Product Data Sheets (PDS) and Safety Data Sheets (SDS) for our polymerization initiators are available at www.nouryon.com

On request we also provide specific publications on subjects such as applications of metal alkyls, analytical technique, safe use and storage of metal alkyls, facilities design and maintenance, and unloading procedures.

All information concerning this product and/or suggestions for handling and use contained herein are offered in good faith and are believed to be reliable. Nouryon, however, makes no warranty as to accuracy and/or sufficiency of such information and/or suggestions, as to the product's merchantability or fitness for any particular purpose, or that any suggested use will not infringe any patent. Nouryon does not accept any liability whatsoever arising out of the use of or reliance on this information, or out of the use or the performance of the product. Nothing contained herein shall be construed as granting or extending any license under any patent. Customer must determine for himself, by preliminary tests or otherwise, the suitability of this product for his purposes. The information contained herein supersedes all previously issued information on the subject matter covered. The customer may forward, distribute, and/or photocopy this document only if unaltered and complete, including all of its headers and footers, and should refrain from any unauthorized use. Don't copy this document to a website.

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