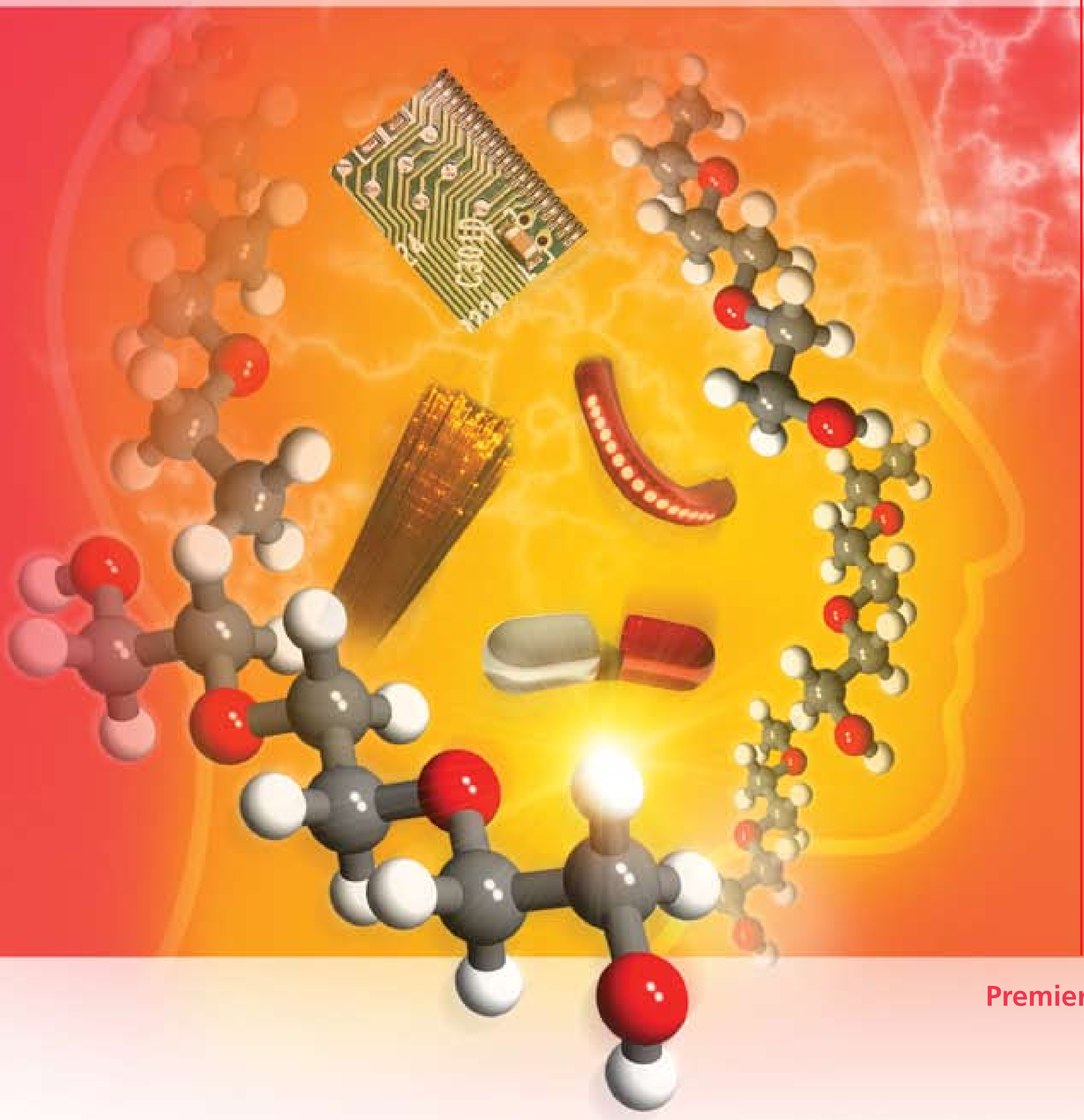
Material Matters
Chemistry Driving Performance

Vol. 1 No. 1

Polymerization for Advanced Applications



Initiator/Stabilizer FAQs

Polymer Analysis by NMR

Fluorinated Hyperbranched Polymers

Etch-Resistant Block Copolymers

Bioactive Hydrogels

Anionic Polymerization

Premiere Issue

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Introduction

Welcome to the premiere issue of Material Matters, a technical guide from Sigma-Aldrich dedicated to addressing research needs in materials science and technology. The theme for this issue is polymerization. Innovative polymers are helping advance almost every field of materials science, from alternate energy to organic electronics. Included in this guide are reviews from researchers in relevant technical fields that discuss a subset of some of the tools available to scientists and engineers.

Our mission at Sigma-Aldrich is to inspire and advance your research. I hope that by highlighting the innovations and products featured in this technical guide, we will help generate the next ideas to significantly impact research in polymerization.

Sincerely,

Luke Grocholl

Luke Grocholl, Ph.D.
Materials Science Team
Sigma-Aldrich Corporation

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- Cross-linkers, chain transfer agents, plasticizers, and stablizers for polymer modification

About Our Cover

Central to advances in science and engineering are the dedicated researchers whose ideas drive tomorrow's technologies. This premiere issue of *Material Matters* features advanced and unique Sigma-Aldrich materials for polymerization such as monomers, cross-linkers, and functional polymers. The cover depicts how our products combine with your ideas to yield the next generation of nanolithography, fiber optics, flexible LEDs and bioactive polymers for drug delivery. *Material Matters—Chemistry Driving Performance.*

Material Matters
Chemistry Driving Performance
Vol. 1 No. 1

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Initiator/Stabilizer FAQs

Dr. S. S. Newaz
Polyorganix Inc.
Houston, TX

Q. How does one choose an appropriate initiator?
In a free-radical addition polymerization, the choice of polymerization initiator depends mainly on two factors: a) its solubility and b) its decomposition temperature. If the polymerization is performed in an organic solvent, then the initiator should be soluble in that solvent, and the decomposition temperature of the initiator must be at or below the boiling point of the solvent. Commonly, AIBN (2,2′-Azobis(2-methylpropionitrile)) (**441090**, dec.102–104°C) and BPO (2-(4-Biphenyl)-5-phenyloxazole) (**216984**, mp 115–119°C) suit these requirements. If the desired polymerization occurs at or below 20 °C, then special, low-temperature free-radical initiators need to be used. Various azo-type initiators can be chosen to satisfy the decomposition temperature requirement.

For emulsion polymerization or polymerization in an aqueous system, a water-soluble initiator like $K_2S_2O_8$ (**379824**) or an organic, water-soluble initiator (4,4′-Azobis(4-cyanovaleric acid)) (**118168**, dec.118–125 °C) would be suitable.

Q. How does one determine the reactivity of a monomer?
Determination of monomer reactivity is not always obvious or straightforward. Researchers rely on their experience and published data on individual monomers. In general, extent of conjugation in the molecular structure can be viewed as indicative of its tendency to form the initial free radical required for propagating a free-radical polymerization. Usually, a more conjugated system is more likely to undergo free-radical polymerization.

Q. When is it necessary to remove a stabilizer prior to polymerization and how does one do so?
To inhibit polymerization during storage, many monomers are provided with a stabilizer as indicated by the label. Usually, it is not necessary to remove stabilizers. They are typically present in ppm level, and the use of a free radical initiator at the polymerization temperature will overwhelm the effect of the stabilizer. In worst-case scenarios, one may need to add extra amounts of initiator to sustain an acceptable polymerization rate. In most cases, once a polymerization initiates, the rate can be sustained without much difficulty. If, however, it is absolutely necessary to remove the stabilizer, column chromatography is the preferred method (for inhibitor removal columns, see products **306312, 311332, 306320**).

Q. How does one remove residual initiator, stabilizer, and/or unreacted monomer after polymerization?
It is a common practice to dissolve the polymers in a solvent prior to end use, followed by precipitating the polymer using a cosolvent. Usually, the residual initiators and stabilizers will remain in solution and the polymers will separate out as a solid (powder, gum, or fibers). This process may be repeated until desirable polymer characteristics are obtained. This fractional precipitation is also effective in removing lower molecular weight polymers, resulting in narrower molecular weight distribution—of course accompanied with a loss of yield. Typical solvent/cosolvent pairs could be toluene/hexane, toluene/methanol, THF/water, etc., determined by the relative solubilities of the polymer versus the small-molecule component.

For initiator solubilities and decomposition temperatures, visit our Web site at sigma-aldrich.com/poly.

Polymer Analysis by NMR

Sigma-Aldrich Quality Control Team

One of the challenges polymer scientists face is molecular weight (average chain length) determination of their materials. While membrane osmometry, gel permeation chromatography, viscosity analysis and mass spectrometry are typically used for molecular weight determination, the techniques can be time consuming, inaccurate for the molecular weight ranges involved, or require specialized instrumentation. End-group analysis by NMR offers an easy alternative method using an instrument commonly found in many analytical labs. In addition, NMR analysis can also be used to accurately determine monomer ratios for various copolymer.

Scientists at Sigma-Aldrich routinely determine number-average molecular weight (M_n) by ^1H NMR end-group analysis for polymers having M_n values under 3000. Sensitivity of the instrument to detect end-group protons will determine the upper limit that can be measured. In order to use this method, the following criteria must be met:

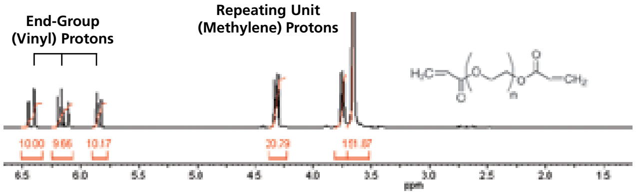
- Identifiable end-group protons distinguishable from repeating monomer-group protons by NMR
- Accurate integration of both end-group and monomer protons
- Knowledge of monomer formula weights

Once the ratio of protons on the end-groups to protons on the polymer chain is determined, using the NMR, simple math can be applied to generate the M_n value.

This example illustrates this method:

437441 Poly(ethylene glycol) diacrylate

$$\text{FW} = \underbrace{H_2CC(H)CO}_{55.06}\text{-}\underbrace{(OCH_2CH_2)_n}_{(44.05)_n}\text{-}\underbrace{OC(O)C(H)CH_2}_{71.06}$$



1) Calculation, integral per proton:

Locate the end-group proton signals (ca. 5.8, 6.2 & 6.4 ppm)

$$\text{integral per proton} = \frac{\text{sum of vinyl proton integrals}}{\text{\# of protons in the two vinyl end groups}}$$

$$= \frac{10.00 + 9.66 + 10.17}{6} = \textbf{4.97 per proton}$$

2) Calculation, number of repeating monomer units, n:

Locate the OCH_2CH_2 proton signals (ca. 3.6, 3.7 & 4.3 ppm)

$$n = \frac{(\text{sum of } CH_2 \text{ proton integrals})/\text{\# of } CH_2 \text{ protons}}{\{\text{integral per proton value}\}}$$

$$= \frac{(20.79 + 151.87)/4}{4.97} = \textbf{8.69 repeating units, n}$$

3) Calculation, M_n:

$$M_n = (\text{FW end groups}) + (\text{FW repeating unit})(n)$$
$$= (55.06 + 71.60) + (44.05)(8.69) = \textbf{509}$$

Therefore, the M_n of this polymer is approx. 509

For questions, product data, or new product suggestions, please contact the Materials Science team at matsci@sial.com.

Fluorinated Hyperbranched Polymers

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Central Michigan University,
Mount Pleasant, MI

Fluorocarbon polymers, like small-molecule fluorocarbons, exhibit increased thermal stability, hydrophobicity, lipophobicity, improved chemical resistance, and decreased intermolecular attractive forces in comparison to their hydrocarbon analogs.[1] These properties derive from the fundamental atomic properties of fluorine: high ionization potential, low polarizability, and high electronegativity. Due to the very high electronegativity, C–F bonds are always strongly polarized. The strength of the C–F bond is due to its highly ionic character, which accounts for the thermal stability of perfluorocarbons. The high ionization potential, combined with the low polarizability, leads to weak intermolecular interactions, which in turn leads to low surface energy and low refractive indices for perfluorocarbons. Therefore, perfluorocarbons have been used to create non-stick and non-wettable surfaces with low surface energies.

Linear fluorinated polymers, such as tetrafluoroethylene (Teflon®) exhibit high crystallinity, which increases the melting point even further. That often leads to inhibitively high processing temperatures. For applications such as mold releases or coatings, high crystallinity is often not needed or even unfavorable.

The superior chemical resistance, hydrophobicity, and low adhesive forces can be coupled with improved processibility (high solubility, low viscosity)[2] by making highly branched fluorocarbon polymers (**Figure 1**).[3] The glass transition temperature of these materials is up to 55 °C (depending on molecular weight), but they are thermally stable to 300 °C, which is sufficient for most applications. The contact angle with water for this hyperbranched fluoropolymer is just below 100° (tetrafluoroethylene: 105°), which can be increased to 120° by substituting one-third of the remaining *p*-fluorines of the structure with longer fluoroalkyl chains.

This material has improved lubricating properties and has been used as an imprinting mold release (**Figure 2**).[4] With a mold coated with the hyperbranched polymer, 250 nm circles and 50–60 nm lines can be imprinted without the pattern being destroyed by removing the imprinter.

For coatings applications, the hyperbranched fluorinated polymer has to be cross-linked to make it less brittle (fluorocarbon polymers have not only reduced adhesion, but also reduced cohesion). At the same time, the cross-linking molecule can be used to introduce other properties or additional functional groups.[5]

This family of materials thus combines the superior properties of fluorocarbon polymers with an easy synthesis and processibility, allowing for its use in a variety of applications.

References: (1) Chambers, R. D. *Fluorine in Organic Chemistry*; Olah, G.A., Ed.; Interscience Monograph on Organic Chemistry; John Wiley & Sons: New York, 1973. (2) Mourey, Y. H. et al. *Macromolecules* **1992**, *25*, 240. (3) Mueller, A. et al. *Macromolecules* **1998**, *31*, 776. (4) Mueller, A. *Hyperbranched Fluoropolymers: Synthesis, Characterization, Derivatization, and Applications*; Ph.D. Thesis 1998, Wooley, K.L., Adv.; Dept. of Chemistry, Washington University, St. Louis, MO. (5) Gan, D. et al. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*(22), 3531.

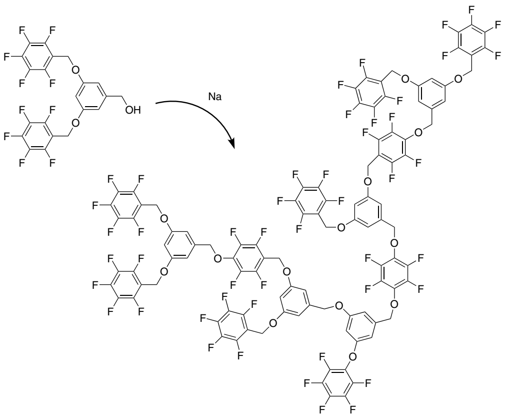


Figure 1. A highly cross-linked fluorinated polymer.

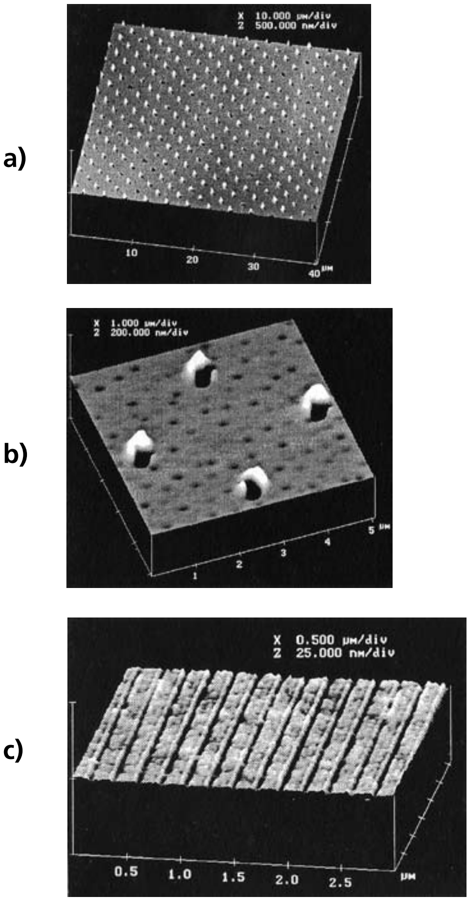
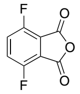


Figure 2. AFM images of a) 250nm punctures in ca. 100 nm thick film of fluoroalkyl-substituted HBFP; b) expelled material adjacent to punctures; c) imprint of 50–60 nm thick lines spaced 210 nm apart. Imprinting: Krchnavek, Dept. of Electrical Engineering, Washington University, St. Louis; AFM: Tomasz Kowalewski, Dept. of Chemistry, Carnegie Mellon University.

Fluorinated Monomers

3,6-Difluorophthalic anhydride, 97%

$C_8H_2F_2O_3$
MW: 184.1
MP: 218–221 °C (lit.)



381128-100MG	100 mg
381128-500MG	500 mg

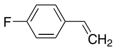
2-Fluorostyrene, 98%

C_8H_7F
MW: 122.14
BP: 29–30 °C (4 mm Hg) (lit.)

290505-1G	1 g
290505-5G	5 g

4-Fluorostyrene, 99%

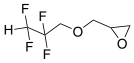
C_8H_7F
MW: 122.14
BP: 67 °C (50 mm Hg) (lit.)



155799-1G	1 g
155799-10G	10 g

Glycidyl 2,2,3,3-tetrafluoropropyl ether, 97%

$C_6H_8F_4O_2$
MW: 188.12
BP: 50 °C (4 mm Hg) (lit.)



474150-5ML	5 mL
474150-25ML	25 mL

Hexafluoroglutaric acid, 97%

$C_5H_2F_6O_4$
MW: 240.06
MP: 88-91 °C (lit.)
BP: 134–138 °C (3 mm Hg) (lit.)

196908-5G	5 g
196908-25G	25 g

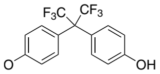
4,4′-(Hexafluoroisopropylidene)dianiline, 98%

$C_{15}H_{12}F_6N_2$
MW: 334.26
MP: 195–198 °C (lit.)

368148-1G	1 g
368148-5G	5 g

4,4′-(Hexafluoroisopropylidene)diphenol, 97%

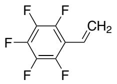
$C_{15}H_{10}F_6O_2$
336.23
MP: 160–163 °C (lit.)



257591-5G	5 g
257591-25G	25 g
257591-100G	100 g

2,3,4,5,6-Pentafluorostyrene, 99%

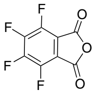
$C_8H_3F_5$
MW: 194.1
BP: 62–63 °C (50 mm Hg) (lit.)



196916-5G	5 g
196916-25G	25 g

Tetrafluorophthalic anhydride, 97%

$C_8F_4O_3$
MW: 220.08
MP: 94–96 °C (lit.)



339016-1G	1 g
339016-5G	5 g

Tetrafluoroterephthalic acid, 97%

$C_8H_2F_4O_4$
MW: 238.09
MP: 275–277 °C (dec.) (lit.)

104418-1G	1 g
104418-5G	5 g

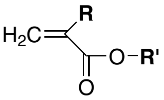
3-(Trifluoromethyl)styrene, 99%

$C_9H_7F_3$
MW: 172.15
BP: 64.5 °C (40 mm Hg) (lit.)

366692-1G	1 g

For halogenated monomers that result in high and low refractive index polymers, see the *Advanced Polymers for Electronic/Optical Devices* technical guide. Request your free copy at matsci@sial.com; reference code GGE.

Fluorinated Acrylates



Monomer	R	R′	Quantity
2,2,3,3,3-Pentafluoropropyl acrylate, 98%	H	$CF_2CF_2CF_3$	470961-5ML 470961-25ML
3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecyl acrylate, 97%	H	$CH_2CH_2(CF_2)_7CF_3$	474487-5ML 474487-25ML
Heneicosafluorododecyl acrylate, 96%	H	$CH_2CH_2(CF_2)_9CF_3$	474355-5G
2,2,2-Trifluoroethyl methacrylate, 99%	CH_3	CH_2CF_3	373761-5G 373761-25G
2-(Trifluoromethyl)acrylic acid, 98%	CF_3	H	369144-1G 369144-5G
Zonyl® TM fluoromonomer	$(CF_2)_nCF_3$, n ~ 7–8	CH_2CH_3	421480-10ML 421480-50ML

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Etch-Resistant Block Copolymers

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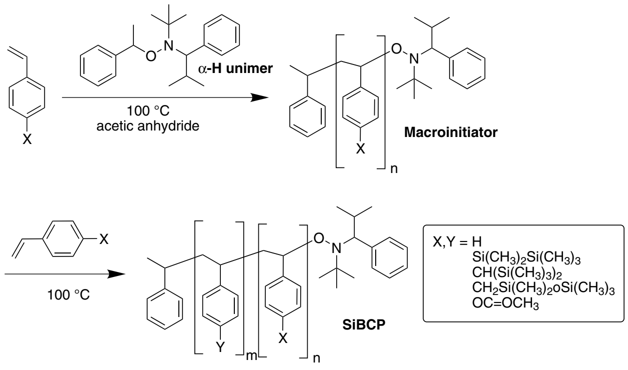
Introduction

Block copolymers offer a means of combining the desirable characteristics of different polymers in a new hybrid material. Polymers consisting of hydrophobic and hydrophilic blocks, for example, can be used to encapsulate organic molecules and deliver them into aqueous media. There has been tremendous interest in the self-assembly of block copolymers in nanoscale dimensions, especially in thin-film configuration.

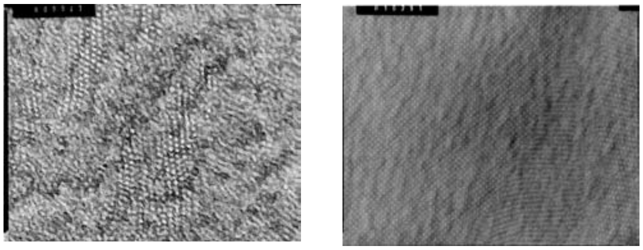
Conventional lithography has its limitations when features of less than 30 nm are desired. Accessibility to a wide range of periodic structures with feature sizes less than 30 nm make block copolymers attractive as templates for nanopatterning.[1–3] Most of the literature approaches use selective ozonolysis or preferential staining of one block with heavy metals to increase etch selectivity between the blocks. Often, an intermediate silicon nitride (SiN) layer and selective etching of one block over another is required for successful pattern transfer. In general, the use of organic block copolymers is limited at high temperatures because of low thermal/mechanical stabilities. Thus, direct patterning of semiconductors that requires high growth temperature (>500 °C) using organic block copolymers as templates is nearly impossible.

It has been well established that incorporation of silicon (at least 10 wt %) in resist polymers provides improved oxygen–RIE (reactive ion etching) etch resistance. When exposed to oxygen plasma, the silicon-containing polymers are oxidized to silicon oxide that is stable in an O_2 environment. The high etch resistance to oxygen plasma compared to organic polymers makes silicon-containing polymers favorable as bilayer resists to pattern high-aspect ratio structures and to create nanoporous ceramic thin films in a variety of morphologies.[4–8] In addition, silicon oxide has high thermal and mechanical stability at a temperature greater than 500 °C, making it a long-time dielectric in microchip fabrication. Thus, the possibility of combining acid labile groups and silicon-containing groups in block copolymers offers a new route to directly pattern nanostructured semiconductors.

As the synthesis of silicon-containing block copolymers is quite challenging using traditional living anionic polymerization, post functionalization of polymers is often used to incorporate silicon. Recent advances in controlled living free-radical polymerization (LFRP),[9–11] including nitroxide-mediated radical polymerization (NMRP), atom transfer radical polymerization (ATRP), and reversible addition fragmentation chain transfer (RAFT), make it possible to design and synthesize a variety of block copolymers with novel functionalities. The LFRP procedures in general are easier to carry out as they are tolerant to a variety of functionalities and do not require stringent purification of the starting materials, unlike living anionic or cationic polymerization. We had recently applied NMRP towards, (i) the synthesis of narrow dispersed silicon-containing homopolymers from three kinds of silicon-containing styrenic monomers, including 4-(pentamethyldisilyl)-styrene (Si_2St), 4-(bis(trimethylsilyl)-methyl)styrene (Si_2-CSt), and 4-(pentamethyldisiloxymethyl) styrene (OSi_2-St) **(Scheme 1)**, each containing two silicon atoms to enhance the etch selectivity, and (ii) the synthesis of block copolymers from silicon-containing styrenic monomers with styrene and acid labile acetoxystyrene by sequential monomer addition using an nitroxide unimer initiator. By optimizing conditions such as solvent polarity, temperature of polymerization, and the monomer addition sequence, well-defined narrow dispersed silicon-containing block copolymers were synthesized from the above monomers. Both TEM (transmission electron microscopy) and SAXS (small angle X-ray scattering) data showed that these polymers formed cylindrical, lamellae, or disordered structures depending on the volume ratio between the blocks and their molecular weights. When the silicon-containing block was the major phase and silicon content was greater than 12 wt %, block copolymer morphology and its domain size were well maintained under exposure to oxygen plasma[12] **(Figure 1)**.



Scheme 1. Synthesis of macroinitiators and SiBCPs by LFRP at 100 °C.



Before **After**

Figure 1. Transmission electron micrograph (TEM) images of PAcOSt-PSi_2St (21/79 v/v) before and after O_2 plasma for 10 minutes, showing intact cylindrical morphology.

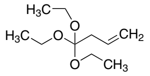
Synthetic access to novel silicon-containing block copolymers via LFRP enables potential applications such as (1) growth of nanostructured semiconductor crystals at high temperatures, (2) formation of nanoporous ceramic films, or (3) creation of hierarchical hybrid nanostructures by combining photolithography and self-assembly of photosensitive silicon-containing block copolymers.

References: (1) Park, M. et al. *Science* **1997**, *276*, 1401. (2) Black, C. T. et al. *Appl. Phys. Lett.* **2001**, *79*, 409. (3) Kim, H. C. et al. *Adv. Mater.* **2001**, *13*, 795. (4) Gabor, A. H. et al. *Chem. Mater.* **1994**, *6*, 927. (5) Zharov, I. et al. *Chem. Mater.* **2002**, *14*, 656. (6) Bowden, M. et al. *J. Photopolym. Sci. Technol.* **2003**, *16*, 629. (7) Avgeropoulos, A. et al. *Chem. Mater.* **1998**, *10*, 2109. (8) Chan, V. Z.-H. et al. *L. Science* **1999**, *286, 1716.* (9) Matyjaszewski, K. *Advances in Controlled/Living Radical Polymerization*; American Chemical Society: Washington, DC, 2003; Vol. 854, p 2. (10) Hawker, C. J. *J. Am. Chem. Soc.* **1994**, *116*, 1185. (11) Benoit, D. et al. *J. Am.Chem. Soc.* **1999**, *121*, 3904. (12) Fukukawa, K. et al. *Macromolecules* **2005**, *38*, 263.

Silicone-Containing Monomers

Allyltriethoxysilane, 97%

$C_9H_{20}O_3Si$
MW: 204.34
BP: 78 °C (21 mm Hg) (lit.)



A36301-5G	5 g
A36301-25G	25 g

Diphenylsilanediol, 95%

$C_{12}H_{12}O_2Si$
MW: 216.31

D213705-25G	25 g
D213705-100G	100 g

Octadecyltrichlorosilane, 90+%

$C_{18}H_{37}Cl_3Si$
MW: 387.93
BP: 223 °C (10 mm Hg) (lit.)

104817-25G	25 g
104817-100G	100 g
104817-500G	500 g

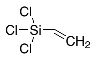
Poly(dimethylsiloxane), vinyl terminated, viscosity 1,000 centistokes

BP: >93 °C (lit.)

433012-100ML	100 mL
433012-500ML	500 mL

Trichlorovinylsilane, 97%

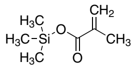
$C_2H_3Cl_3Si$
MW: 161.49
MP: –95 °C (lit.)
BP: 90 °C (lit.)



104876-5G	5 g
104876-100G	100 g
104876-500G	500 g

Trimethylsilyl methacrylate, 98%

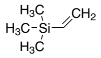
$C_7H_{14}O_2Si$
MW: 158.27
BP: 51–51.5 °C (20 mm Hg) (lit.)



347493-25G	25 g
347493-100G	100 g

Vinyltrimethoxysilane, 98%

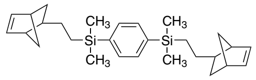
$C_5H_{12}O_3Si$
MW: 148.23
BP: 123 °C (lit.)



235768-5ML	5 mL
235768-100ML	100 mL
235768-500ML	500 mL

1,4-bis(dimethyl(2-(5-norbornen-2-yl)ethyl)silyl)benzene, mixture of endo and exo

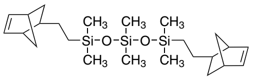
$C_{28}H_{42}Si_2$
MW: 434.8
BP: 314 °C (lit.)



523607-5ML	5 mL

Hexamethyl-1,5-bis(2-(5-norbornen-2-yl)ethyl)trisiloxane, mixture of endo and exo

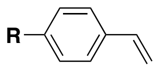
$C_{24}H_{44}O_2Si_3$
MW: 448.86



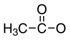
523593-1ML	1 mL
523593-5ML	5 mL

For an up-to-date list of silsesquioxane monomers, visit our nanomaterials Web site at sigma-aldrich.com/nano.

Styrene Monomers



Monomer	R	Quantity
Styrene, reagentplus, 99+%	H	240869-5ML 240869-100ML
4-Bromostyrene, 98%	Br	124141-1G 124141-10G 124141-25G

Monomer	R	Quantity
4-Chlorostyrene, 97%	Cl	C71203-10G C71203-50G
4-Acetoxystyrene, 96%	 $H_3C-\overset{O}{\overset{\|}{C}}-O$	380547-5ML 380547-25ML

For styrenic and other vinyl monomers, use our advanced sub-structure search: sigma-aldrich.com.

For questions, product data, or new product suggestions, please contact the Materials Science team at matsci@sial.com.

Bioactive Hydrogels

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ABTECH Scientific, Inc.
Richmond, VA

The first report of the synthesis of composite materials comprising conducting polymers and hydrogels was in 1994 by Wallace et al.[1] Their objective was to enhance the porosity and ion-transport properties of hydrogels for controlled drug delivery through electrochemically stimulated release of analytes. Since then, the electrochemical and oxidative polymerization of pyrrole, aniline, and thiophene and their derivatives within hydrogel hosts, such as polyacrylamide, poly(acrylic acid), chitosan, and poly(HEMA) have been routinely accomplished for biosensor applications and to achieve voltage-stimulated or controlled release. There have also been several studies conducted on the fabrication of polymer blends of hydrogels, such as poly(methyl methacrylate) (PMMA), poly(vinyl methyl ether) (PVME), poly(4-vinylpyridine),[2] and poly(2-hydroxyethyl methacrylate) (p(HEMA)), primarily for the construction of artificial muscles.[3,4] With hydrogels, high degrees of hydration (ca. 90 %) could be reversibly achieved along with biocompatibility, good refractive index matching with water, and relative ease of molecular engineering. In general, the conducting polymer component of these composites retains their electroactive properties.

Brahim et al.[5] have fabricated bioactive polypyrrole-p(HEMA) composites to function as sensing membranes for clinically important amperometric biosensors. A monomer cocktail containing, among other components, the relevant methacrylate monomers, pyrrole or aniline, and photoinitiator was spin-cast onto microfabricated electrodes and first irradiated by UV to effect polymerization of the hydrogel components. This was immediately followed by potentiostatic electropolymerization of the pyrrole/aniline monomer in a phosphate-buffered potassium chloride solution saturated with further monomer. Amperometric enzyme biosensors for the detection of glucose, cholesterol, and galactose were demonstrated, each possessing extensive linear dynamic response ranges, high sensitivities, and prolonged storage stabilities.[6]

Of particular recent interest is the development of **bioactive** (containing biologically active moieties such as bioactive peptides, growth factors, enzymes and the like) and **biosmart** (responsive to biologically derived external stimuli) electroconductive hydrogels for implant biocompatibility. A novel polymer composite material consisting of a water-dispersed complex of polypyrrole doped with polystyrenesulfonate and embedded in polyacrylamide hydrogel was prepared and evaluated as a matrix for enzyme immobilization.[7] The enzyme glucose oxidase was physically entrapped in the polymer by inclusion in the aqueous phase during emulsion polymerization. The resulting bioactive microparticles (3.5–7.0 µm diameter) were cast onto platinum electrodes and the polymer-modified electrodes used as amperometric glucose biosensors. This configuration displayed rapid response times and efficient screening of interferents.

For implantable biosensing applications, the synthesis of hydrogel composite polymers consisting of cross-linked p(HEMA) with incorporated polypyrrole and/or polyaniline chains are rendered "bioactive" by the covalent immobilization of oxidoreductase enzymes. Enzymes were first "monomerized" by hetero-bifunctional coupling of the amines of the lysine residues of the enzyme (typically 1:2) with acryloyl (polyethylene glycol)$_{110}$ *N*-hydroxy succinamide ester (Acryl-PEG-NHS). This allowed the covalent immobilization of the tethered oxidoreductase enzyme within the hydrogel milieu. To provide for stabilization of the immobilized enzymes, poly(ethylene glycol)$_{200}$ monomethacrylate (PEGMA) was also included in the monomer cocktail at 0.5 mol %. Together these components allowed photolithographically defined, spin-cast membranes formed on microlithographically defined electrodes to recognize and amperometrically respond to the enzyme's substrate and achieve approximately one year of retained enzyme activity (ca. 80%). For implant biocompatibility, the synthesis of the monomer 2-methacryloyloxyethyl phosphorylcholine (MPC) (**Figure 1**) was accomplished by the coupling of HEMA with 2-chloro-2-oxo-1,3,2-dioxaphospholane (COP).[8] When incorporated into the hydrogels at the level of ca. 5–10 mol %, this monomer conferred nonthrombogenicity, reduced protein adsorption, and supported cell viability. Mimicking the zwitterionic head group of the outer leaflet of cell membranes, phosphotidyl choline, the phosphorylcholine moiety confers the molecular equivalent of "stelt" to the polymer when the biosensor is implanted. When cultured with muscle fibroblasts and endothelial cells, these highly porous hydrogel composites support the migration and mobility of cells within its 3-D network[9]; a property that will render these materials appropriate for the fabrication of nerve electrodes and cellular interfaces as the polymer mimics the biological structures that enable cells to grow.

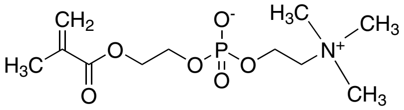


Figure 1. Strucutre of 2-methacryloyloxyethyl phosphorylcholine

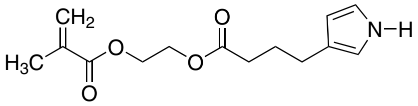


Figure 2. Structure of 2-methacrylooyloxyethyl pyrrolylbutyrate

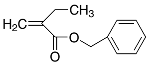
One challenge faced by the use of electroactive polymers as components of hydrogels for mammalian implantation is the potential toxicity. Early work has established polypyrrole as bio-benign. However, to address this issue, bi-functional monomers of pyrrole such as 2-methacrylooyloxyethyl pyrrolylbutyrate (MPB) (**Figure 2**) and aniline that may be UV-polymerized, and hence, covalently coupled into the hydrogel network and also oxidatively polymerized with imbibed free pyrrole or aniline monomer to form the electroactive polymer component were developed. In this way, an interpenetrating network of the electroactive polymer is formed within the preformed hydrogels network that serves as the reactor. Studies are ongoing to evaluate the potential cytotoxicity and biocompatibility of these polymers.

References: (1) Small, C. J. et al. *Polymer Gels and Networks* **1997**, *5*, 251. (2) Asberg, P.; Ingana, O. *Biosens. Bioelectron.* **2003**, *19*, 199. (3) Pich, A. et al. *Polymer* **2002**, *43*, 5723. (4) Douglass, P. M, et al. *Soc. Automotive Eng.* **2000**, 1. (5) Brahim, S. et al. *Biosens. Bioelectron.* **2002**, *17*, 53. (6) Brahim, S. et al. *Electroanalysis.* **2002**, *14*(9), 627. (7) Rubio Retama, J. et al. *Biosens. Bioelectron.* **2004**, *20*, 1111. (8) Brahim, S. et al. *Microchimica Acta* **2003**, *143*, 123. (9) Abraham, S et al. *Biomaterials* **2005**, *26*(23), 4767. (10) Abraham, S.; Guiseppi-Elie, A. *Biomaterials* **2006**, submitted for publication.

Monomers for Bioactive Polymers

Benzyl 2-ethyl acrylate, 99% NEW

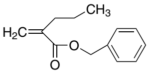
$C_{12}H_{14}O_2$
MW: 190.24



589136-250MG	250 mg

Benzyl 2-propylacrylate, 99% NEW

$C_{13}H_{16}O_2$
MW: 204.26



590126-250MG	250 mg

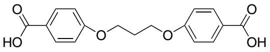
1,6-Bis(*p*-acetoxycarbonylphenoxy) hexane, 97% NEW

$C_{24}H_{26}O_8$
MW: 442.46

657174-1G	1 g

1,3-Bis(4-carboxyphenoxy)propane, 97% NEW

$C_{17}H_{16}O_6$
MW: 316.31
MP: 310 °C(lit.)



655538-5G	5 g

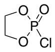
1,6-Bis(*p*-carboxyphenoxy)hexane, 90% NEW

$C_{20}H_{22}O_6$
MW: 358.39

655546-5G	5 g

2-Chloro-1,3,2-dioxaphospholane-2-oxide

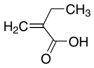
$C_2H_4ClO_3P$
MW: 142.48
MP: 12–14 °C (lit.)
BP: 89–91 at 0.8 mm Hg (lit.)



377953-1G	1 g
377953-5G	5 g

2-Ethylacrylic acid, 98% NEW

$C_5H_8O_2$
MW: 100.12
BP: 176 °C (lit.)



589128-250MG	250 mg

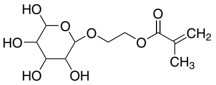
Ethyl 2-propyl acrylate, 99%

$C_8H_{14}O_2$
MW: 142.2
BP: 141 °C (lit.)

590118-250MG	250 mg

Glycosyloxyethyl methacrylate, 5% (w/v) solution in ethanol NEW

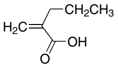
$C_{12}H_{20}O_8$
MW: 292.28



659576-25ML	25 mL

2-Propylacrylic acid, 99% NEW

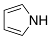
$C_6H_{10}O_2$
114.14
165-188 °C (lit.)



591009-100MG	100 mg
591009-1G	1 g

Pyrrole, 98%

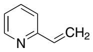
C_4H_5N
MW: 67.09
MP: –23 °C (lit.)
BP: 131 °C (lit.)



131709-25ML	25 mL
131709-100ML	100 mL
131709-500ML	500 mL

2-Vinylpyridine, 97%

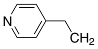
C_7H_7N
MW: 105.14
BP: 79–82 °C (29 mm Hg) (lit.)



132292-5ML	5 mL
132292-100ML	100 mL
132292-500ML	500 mL

4-Vinylpyridine, 95%

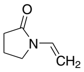
C_7H_7N
MW: 105.14
BP: 62–65 °C (15 mm Hg) (lit.)



V3204-5ML	5 mL
V3204-100ML	100 mL
V3204-500ML	500 mL

1-Vinyl-2-pyrrolidinone, 99+%

C_6H_9NO
MW: 111.14
BP: 92–95 °C (11 mm Hg) (lit.)

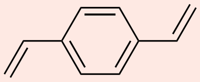


V3409-5G	5 g
V3409-250G	250 g
V3409-1KG	1 kg
V3409-18KG	18 kg

Three grades of HEMA (2-hydroxyethyl methacrylate) are available: 97% (**128635**), 98% (**525464**), 99+% (**477028**).

For a comprehensive list of hydrogel hosts such as polyacrylamide, poly(acrylic acid), chitosan and poly(HEMA), as well as functionalized PEGs (linear, 4-arm and 6-arm), visit sigma-aldrich.com/biocomp.

Cross-linkers



DVB, 85% (535583)

Cross-linking is the formation of chemical links between molecular chains to form a three-dimensional network of connected molecules. The strategy of covalent cross-linking is key to the formation of hydrogels. It is also used in several other technologies of commercial and scientific interest to control and enhance the properties of the resulting polymer system or interface, such as thermosets and coatings.

For a complete list of cross-linkers, visit us at sigma-aldrich.com/biocomp and scroll down to cross-linkers.

Anionic Polymerization

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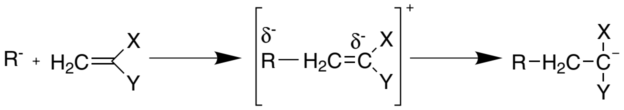
and
Ms. Manuela Ocampo
Maurice Morton
Institute of
Polymer Science
The University of
Akron, Akron, OH

Living anionic polymerization, especially using alkyllithium initiators, has been demonstrated to be a convenient and useful method to make well-defined polymers with low degrees of compositional heterogeneity and with control of the major structural variables that affect polymer properties.[1,2] Living polymerizations are chain-reaction polymerizations that proceed in the absence of the kinetic steps of chain termination and chain transfer. For a living polymerization, one initiator molecule generates one polymer molecule; thus, it is possible to calculate and control the number average molecular weight (M_n) of the final polymer via the stoichiometry of the reaction using the following relationship.

M_n = g of monomer consumed/moles of initiator

Given a comparable or faster rate of initiation relative to propagation, it is possible to obtain narrow molecular weight distribution polymers, i.e., $M_w/M_n \leq 1.1$.[3] Due to the absence of termination and transfer steps, the product after complete monomer consumption is a reactive, polymeric organolithium compound. The living nature of alkyllithium-initiated anionic polymerizations using suitable monomers provides versatile methods for the preparation of well-defined block copolymers by sequential addition of monomers,[4] chain-end functionalized polymers by reaction of the living chain ends with appropriate monomers and/or electrophilic terminating agents[5,6] and branched polymers by linking reactions with multi-functional linking agents.[7]

The monomers that can be polymerized anionically are classified into two categories: (a) unsaturated monomers with one or more double bonds, such as vinyl (e.g., styrenes, vinylpyridines, alkyl methacrylates), dienes (e.g., isoprene, 1,3-butadiene) and carbonyl-type monomers (e.g., formaldehyde); and (b) heterocyclic monomers (e.g., epoxides, thiiranes, lactones, lactams, and siloxanes). In the case of vinyl monomers, the presence of electron-withdrawing substituents (e.g., X, Y) in the double bond is generally required to stabilize the negative charge that develops in the transition state as shown below.



$$R^- + H_2C{=}C(X)(Y) \longrightarrow \left[\overset{\delta^-}{R}{-}H_2C{=}\overset{\delta^-}{C}(X)(Y)\right]^{+} \longrightarrow R{-}H_2C{-}C^-(X)(Y)$$

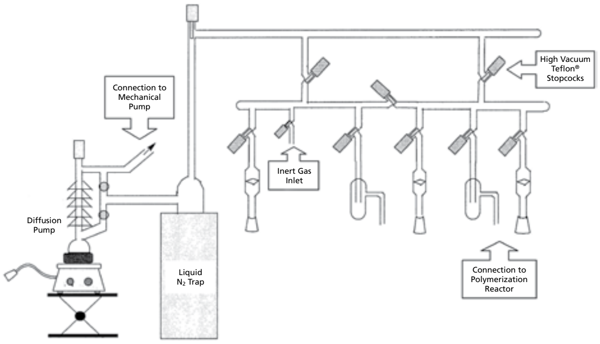


Figure 1. The typical construction of a glass high vacuum line for anionic polymerization.[15–17]

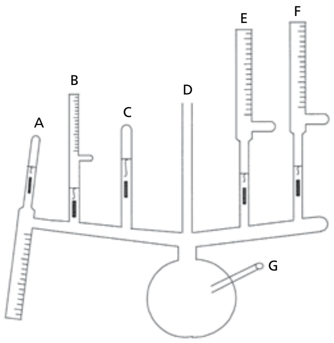


Figure 2. General set-up for a glass polymerization reactor.

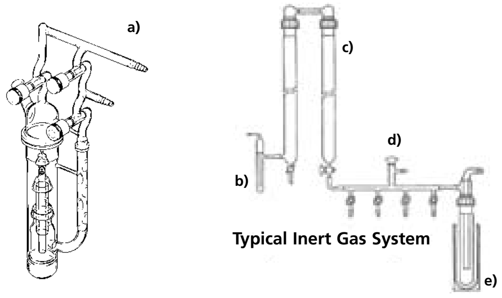


Figure 3. Aldrich products a) Z544787 b) Z173053 c) Z174254 d) Z174432 e) Z220418

Organolithium Initiators

Of all alkali metals, lithium is unique in that it exhibits the highest electronegativity, the smallest covalent and ionic bond radii, along with low-lying, unoccupied p-orbitals available for bonding.[8,9] Organolithium compounds are unique among organoalkali compounds in exhibiting properties characteristic of both covalent and ionic compounds. Thus, they are aggregated in solution, in the solid state and in the gas phase, and they are generally soluble in hydrocarbon solution. In general, the initiation of anionic polymerization of styrene and diene monomers is effected with alkyllithium compounds such as *sec*-butyllithium (**195596**) and *n*-butyllithium (**186171, 230707, 230715, 302104**, and **302120**) in hydrocarbon solution. Under these conditions, the unique ability of organolithium compounds to effect 1,4-enchainment of 1,3-dienes is achieved.[1,10] The concentrations of solutions of active organolithium compounds can be determined using the Gilman double titration method.[11]

Experimental Methods

Due to the reactivity of organolithium compounds and other carbanionic species toward impurities such as oxygen, moisture or carbon dioxide,[12] it is necessary to exclude these contaminants from the reaction environment by the use of an inert gas atmosphere[13,14] or high vacuum techniques.[15–17]

High Vacuum Techniques The use of high vacuum techniques provides the most effective experimental method to exclude impurities from the reaction system.[15–17] In order to attain high vacuum, the combination of a mechanical pump and an oil diffusion pump (**Z220418**) is used in conjunction with a two-stage glass manifold as shown in **Figure 1**.

In order to achieve the desired levels of purity for controlled anionic polymerization, all monomers, reactants, and solvents should be purified, dried, and degassed, preferably on the vacuum line. Solvents are distilled directly into the requisite glass reactors (**Figure 2**) via **D** followed by flame sealing from the vacuum line. Ampules **B, E,** and **F** contain monomers or functionalizing agents. Ampule **C** contains a terminating agent such as degassed methanol. Ampule **A** is equipped with a degassed methanol tube, and it is used to remove a base sample of the living polymer.

Schlenk Line and Glove Box Techniques are often suitable for carrying out many living anionic polymerization procedures. Alkyllithithium-initiated polymerizations are somewhat forgiving in the sense that one can add a calculated excess of initiator to clean the reactor/solvent/monomer system of reactive impurities. See **Figure 3** for representative Schlek Line Glassware. For representative and the Sigma-Aldrich glass center, visit sigma-aldrich.com/glass.

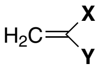
Safety Considerations

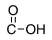
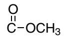
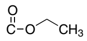
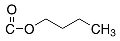
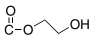
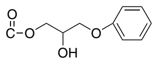
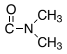
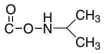
Vacuum traps should be vented while warming because of the possibility of trapped, liquefied gases. Hydrocarbon solutions of alkyllithium compounds are air- and moisture-sensitive; they should be either handled under an inert atmosphere or using syringes and recommended procedures for handling air-sensitive compounds.[13] Carbon dioxide extinguishers should not be used because RLi compounds and many other organometallic compounds react with carbon dioxide exothermically. An all-purpose fire extinguisher, or one designed specifically for combustible metals, should be available when working with these organometallic compounds and alkali metals.[18]

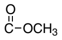
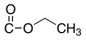
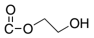
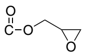
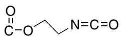
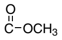
References: (1) Hsieh, H. L.; Quirk, R. P. *Anionic Polymerization: Principles and Practical Applications*; Dekker: New York, 1996. (2) Quirk, R.P. Anionic Polymerization. In *Encyclopedia of Polymer Science and Technology* Kroschwitz, J. I., Ed.; 3rd ed.; Wiley-Interscience: New York, 2003; Vol. 5, p 111. (3) Fetters, L. J. Monodisperse Polymers. In *Encyclopedia of Polymer Science and Engineering* Kroschwitz, J. I., Ed.; 2nd ed.; Wiley-Interscience: New York, 1985; Vol. 2, p 478. (4) Hadjichristidis, N.; Pispas, S.; Flouds, G. A. *Block Copolymers: Synthetic Strategies, Physical Properties, and Applications*; Wiley-Interscience: New York, 2003. (5) Quirk, R. P. Anionic Synthesis of Polymers with Functional Groups. In *Comprehensive Polymer Science, First Supplement*; Aggarwal, S. L., Russo, S., Eds.; Pergamon Press: Oxford, 1992; p 83. (6) Hirao, A.; Hayashi, M. *Acta Polym.* **1999**, *50*, 219. (7) Hadjichristidis, N. et al. *Chem. Rev.* **2001**, *101*, *3747*. (8) Wardell, J. L. Alkali Metals. In *Comprehensive Organometallic Chemistry: The Synthesis, Reactions and Structures of Organometallic Compounds*; Wilkinson, G., Gordon, F., Stone, A. Abel, E. W., Eds.; Pergamon Press: Oxford; 1982; Vol. 1, p 43. (9) Sanderson, R. T. *Chemical Periodicity*; Reinhold: New York; 1960. (10) Bywater, S. In *Comprehensive Polymer Science*; Eastmond, G. C., Ledwith, A., Russo, S., Sigwalt, P., Eds.; Chain Polymerization I; Pergamon Press: Elmsford, New York, 1989, Vol. 3, p. 433. (11) Gilman, H.; Cartledge, F. K. *J. Organomet. Chem.* **1964**, *2*, 447. (12) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon Press: New York; 1974. (13) Shriver, D. F.; Drezdzon, M. A. *The manipulation of Air-Sensitive Compounds*; Wiley: New York, 1986. (Cat. No. Z558486) (14) Ndoni, S.; et al. *Rev. Sci. Instrum.* **1995**, *66*, 1090. (15) Morton, M; Fetters, L. J. *Rubber Chem. Technol.* **1975**, *48*, 359. (16) Hadjichristidis, N. et al. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 3211. (17) Uhrig, D; Mays, J. W. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 6179. (18) Wietelmann, U.; Bauer, R. J. In *Ullmann's Encyclopedia. Industrial Inorganic Chemicals and Products*; Wiley-VCH Verlag: Weinheim, Germany; 1998; Vol. 4, p. 2899.

For the manipulation of air-sensitive compounds, see also Aldrich Technical Bulletins AL-134, AL-136, AL-164, and AL-166.

Monomers for Anionic Polymerization



	X	Y
Vinylidene chloride, 99% 163023-100G 163023-500G	H	Cl
Acrylic acid, 99% 147230-5G 147230-100G 147230-500G	H	 $\overset{O}{\overset{\|}{C}}-OH$
Methyl acrylate, 99% M27301-5ML M27301-250ML	H	 $\overset{O}{\overset{\|}{C}}-OCH_3$
Ethyl acrylate, 99% E9706-5ML E9706-100ML	H	
Butyl acrylate, 99+% 234923-5ML 234923-100ML	H	
2-Hydroxyethyl acrylate, 96% 292818-5ML 292818-250ML	H	
2-Hydroxy-3-phenoxypropyl acrylate 407364-100ML 407364-500ML	H	
***N,N*-Dimethylacrylamide, 99%** 274135-5ML 274135-100ML 274135-500ML	H	
***N*-Isopropylacrylamide, 97%** 415324-10G 415324-50G	H	

	X	Y
Methacrylic acid, 99% 155721-5G 155721-100G 155721-500G	CH_3	 $\overset{O}{\overset{\|}{C}}-OH$
Methyl methacrylate, 99% M55909-25ML M55909-500ML	CH_3	 $\overset{O}{\overset{\|}{C}}-OCH_3$
Ethyl methacrylate, 99% 234893-5ML 234893-100ML 234893-500ML	CH_3	
2-Hydroxyethyl methacrylate, 99+% 128635-5G	CH_3	
Glycidyl methacrylate, 97% 151238-5G 151238-100G 151238-500G	CH_3	
2-Isocyanatoethyl methacrylate, 98% 477060-5ML 477060-50ML	CH_3	
Methyl 2-(bromomethyl)-acrylate, 97% 302546-250MG 302546-1G 302546-5G	CH_2Br	 $\overset{O}{\overset{\|}{C}}-OCH_3$

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