

2024 Legacy Lecture

Tom J. Maricich, Ph.D.

Seven Decades of Chemistry



2024 Academic Senate Legacy Lecture and Reception

Speaker: **Dr. Tom J. Maricich**

Chemistry & Biochemistry

Presents:

“**Chemistry Lessons in the Lab
and Life**”

The Legacy Lecture series provides an opportunity for honorees to address the University community, thus publicly sharing their wisdom, values, and visions as educators. Honorees are selected based on the legacy they leave to the campus. The series provides an opportunity for faculty to address the key experiences and values that have shaped their lives as educators and scholars-and to share their visions for the future.



CSULB Earl Burns Miller Japanese Garden
Thursday, March 14, 2024, 2:00-5:00pm

RSVP [Here](#)



CALIFORNIA STATE UNIVERSITY
LONG BEACH

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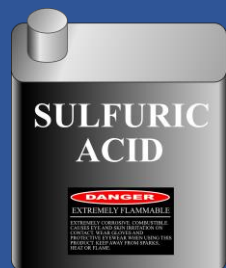
Honorable Mention

Dr. Annie Bianchino



Motivation for a Chemical Career

Ninth Grade Demonstration of the
Reaction of Concentrated Sulfuric Acid with Sugar



+



Carbon

+

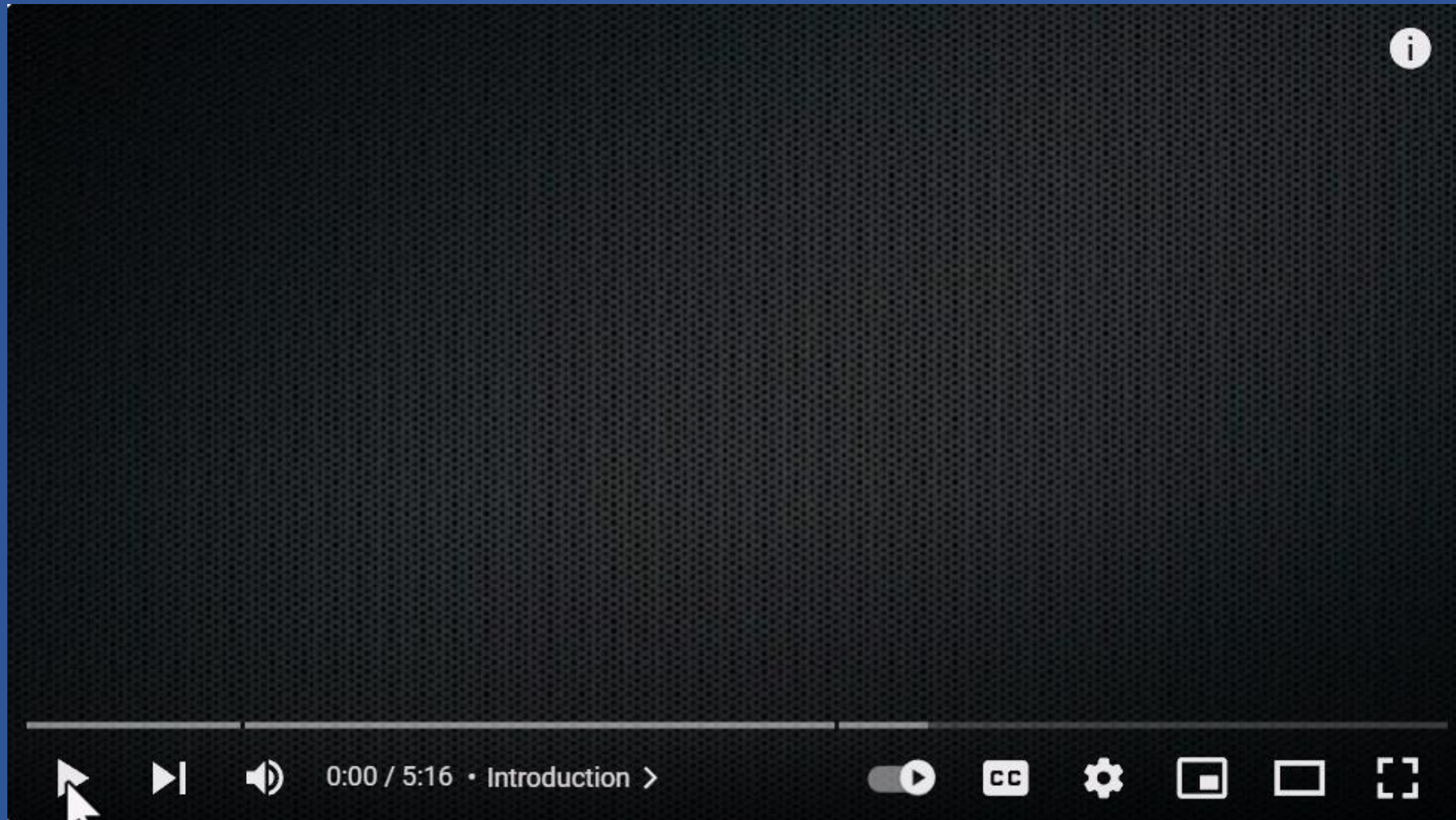


Water

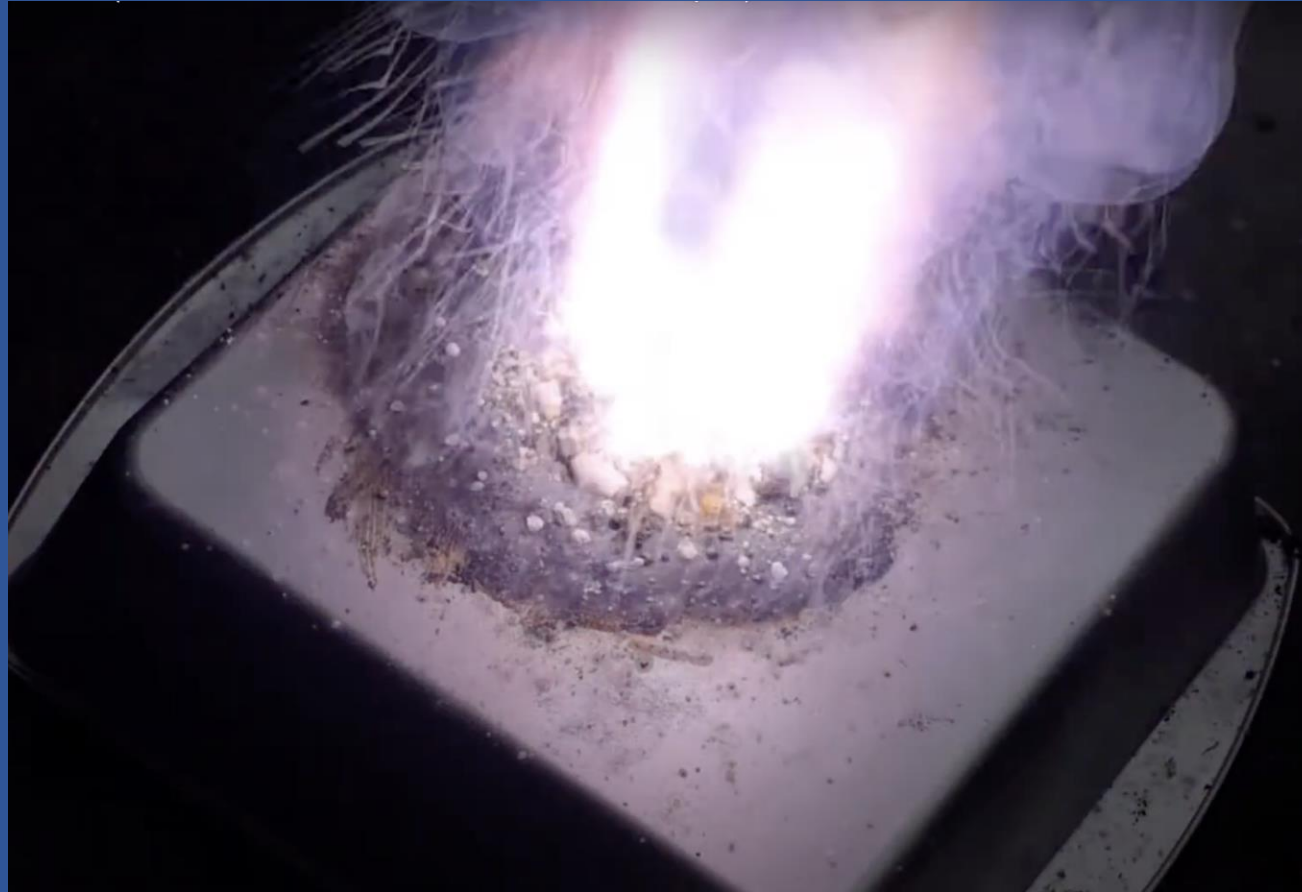
+



This Experiment Made Me Want to Become a Chemist:



Hazards of Chemistry & Importance of Safety In Labs



Reaction of an oxidizer (potassium chlorate) and a fuel (sulfur) – creating sulfur dioxide gas

College and Research Experience



University of Washington

- Extraordinary undergraduate research opportunity
- Traded in summer commercial fishing job for this opportunity



College and Research Experience

Yale University



- Choosing the best advisor with the best/creative and publishable projects gave me many options
- Graduating from Yale opened many doors for me, because of its prestige.



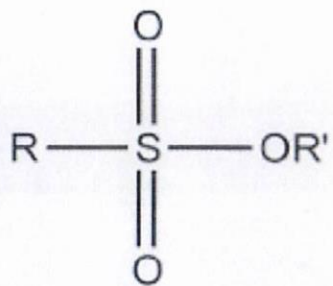
Dr. Walter Lwowski

Research Experience

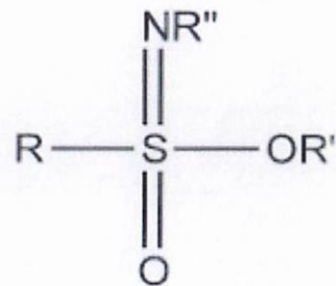
Shell Oil Company



- “Do Something New!”
- I invented several novel classes of sulfur nitrogen compounds, which have dominated the rest of my career.



sulfonate



sulfonimide (iminosulfonate)

Shell Quits Emeryville

Shell Oil Co. announced today it will move its laboratory in Emeryville to Houston as part of a plan to centralize virtually all of its major research activities at the headquarters city.

Discussions will begin shortly to determine which of the present staff of about 1000 will move to Houston, a spokesman said. The phase

out of the East Bay plant is scheduled for mid-1972.

Shell has occupied the 24 acre Emeryville site since 1928. “The buildings and laboratory facilities ultimately will be put up for disposal,” the spokesman said.

In addition to the local facility, three other Shell labs located outside of Houston will be moved there, eventually. They are in Torrance,

Wood River, Ill., and Woodbury, N.J., Shell already has five laboratories in Houston.

The only laboratory not affected by the plan is the company's biological sciences research center at Modesto.

The Emeryville plant has been engaged in research and development in oil and chemical products and processes. The plant's annual payroll is \$17 million.

Teaching and Research Experience

North Dakota State University



**Dr. Tom Albright (Emeritus Prof., U. of Houston)
My First Student:**

“You took me in and showed me what chemical research really entailed. But most of all, you convinced me that I could do better than work as a technician in the paint industry and that I needed to go on and try to get – God-forbid - a PhD!”

Teaching and Research Experience

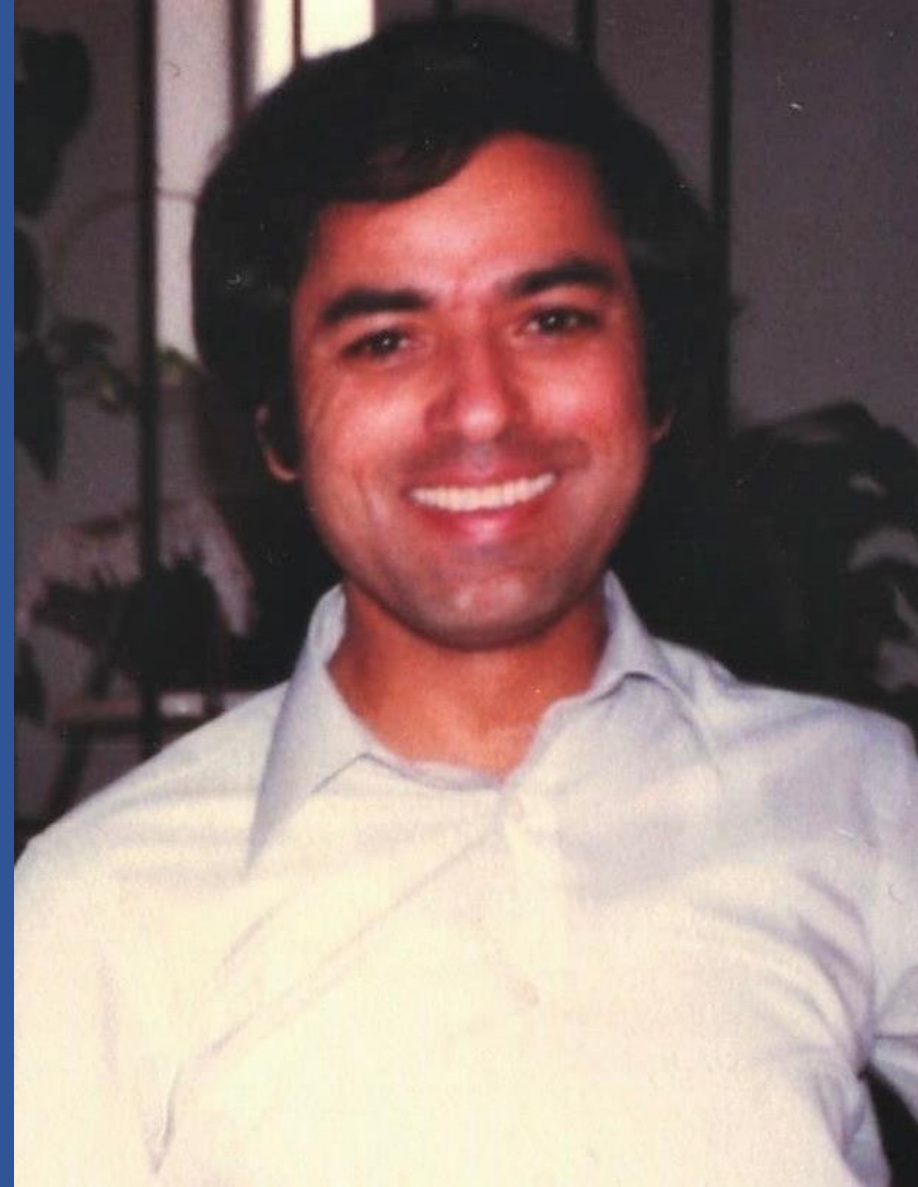
Cal State University, Long Beach

Started in North Dakota + came with me to Long Beach



NUEDEXTA®

(dextromethorphan HBr and $\frac{20}{10}$ mg
quinidine sulfate) capsules



Me



Jeff Cohlberg, last year's legacy lecturer



Teaching and Research Experience

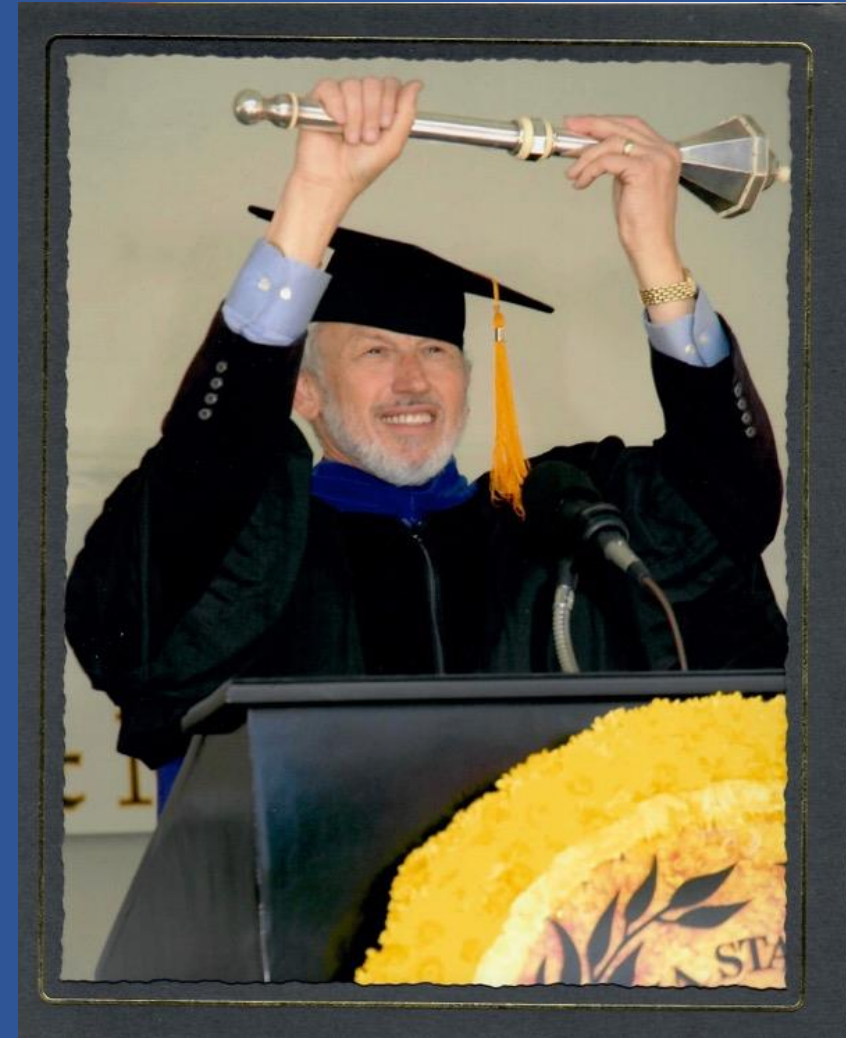
Cal State University, Long Beach

Associate Dean of the
College of Natural Sciences

Professor Emeritus, Department of
Chemistry and Biochemistry

Retired from teaching in 2010

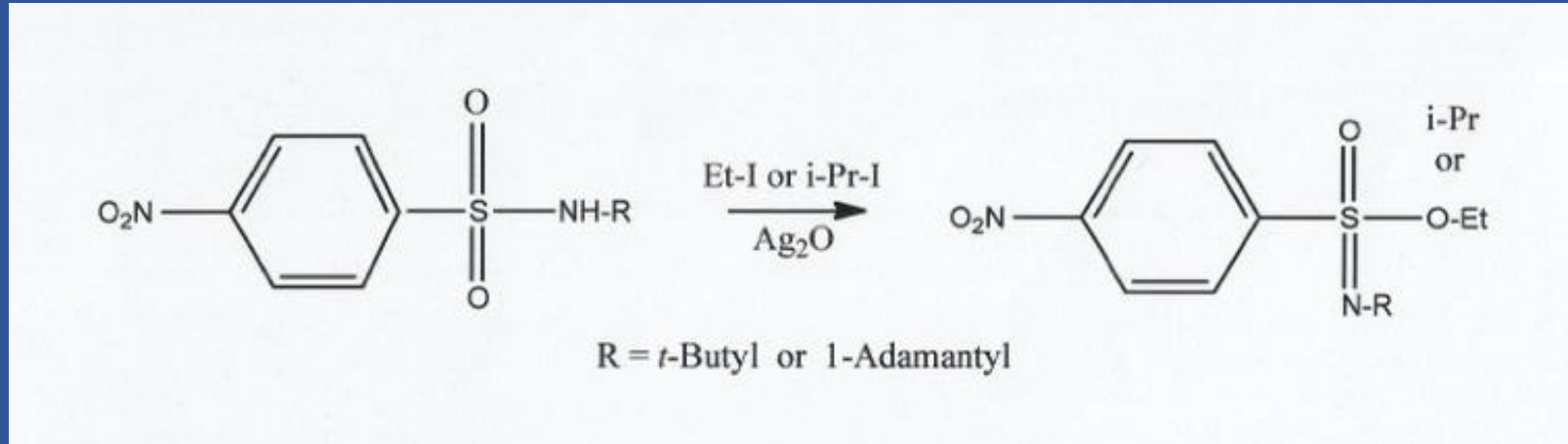
Last publication was with my
students in 2013



Grand Marshal, 2010

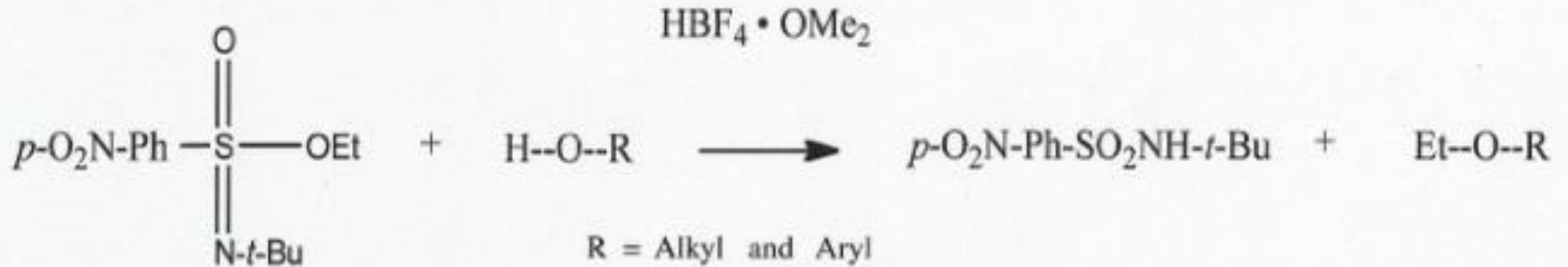


Direct Synthesis of Sulfonimidates:



- One pot syntheses in methylene chloride
- Up to 90% yield with repeat addition of silver (I) oxide [Et]
- Convenient method: reflux for 1 hr [i-Pr] to 3 days [Et]
- Purification: recryst. from pentane [i-Pr] or methanol [Et]

Alkylation of Alcohols and Phenols Catalyzed by $\text{HBF}_4 \cdot \text{OME}_2$



SNAAP[®] Alkylation of Acids, Alcohols and Phenols by Alkyl Sulfonimidates*

Tom J. Maricich

Dept. of Chemistry and Biochemistry
California State University, Long Beach

**Synthesis 2013, 45, (24), 3361-3368*

SNAAP® Alkylations

SNAAP is an acronym for:

Substitution

Nucleophilic

of

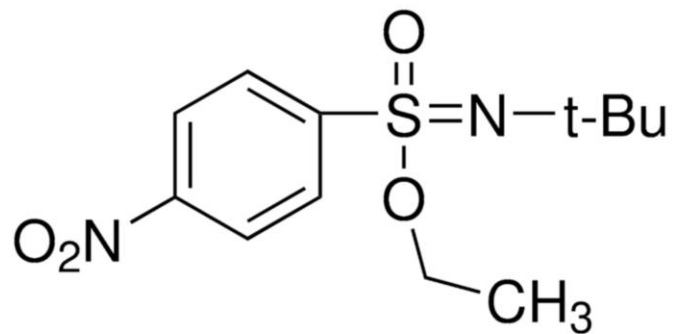
Acids

Alcohols

and

Phenols

A Reagent Named After Me



SNAAP[®] Ethyl Sulfonimidate

★★★★★ (0) [Write a review](#) [Ask a question](#)

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Select a Size

1 G

\$29.80

Synonym(s):

Ethyl *N-tert*-butyl-4-nitrobenzenesulfonimidate **Maricich ethylation reagent**

Empirical Formula (Hill Notation):

C₁₂H₁₈N₂O₄S

Molecular Weight: 286.35

MDL number: [MFCD28053568](#)

PubChem Substance ID: [329817574](#)

United States of America
United States Patent and Trademark Office

SNAAP

Reg. No. 4,973,340

Registered June 7, 2016

Int. Cl.: 1

TRADEMARK

PRINCIPAL REGISTER



Michelle K. Lee

Director of the United States
Patent and Trademark Office

DR. TOM J. MARICICH, PH.D. (UNITED STATES INDIVIDUAL)
1665 CATALINA AVENUE
SEAL BEACH, CA 90740

FOR: CHEMICAL PREPARATIONS, NAMELY, SULFONIMIDATE ALKYLATION AGENTS FOR MODIFYING NATURALLY OCCURRING CHEMICALS AND SYNTHETIC CHEMICALS FOR SCIENTIFIC RESEARCH PURPOSES EXCLUDING FOR MEDICAL DIAGNOSTICS PURPOSES; CHEMICAL PREPARATIONS, NAMELY, SULFONIMIDATE ALKYLATION AGENTS, THAT CONVERT ACIDS INTO ALKYL ESTERS AND THAT CONVERT ALCOHOLS AND PHENOLS INTO ALKYL ETHERS FOR USE IN THE MANUFACTURE OF PHARMACEUTICALS, AND EXCLUDING THE FIELD OF AUTOMOTIVE INDUSTRY AND THE MEDICAL DIAGNOSTICS INDUSTRY, IN CLASS 1 (U.S. CLS. 1, 5, 6, 10, 26 AND 46).

FIRST USE 4-21-2014; IN COMMERCE 4-21-2014.

THE MARK CONSISTS OF STANDARD CHARACTERS WITHOUT CLAIM TO ANY PARTICULAR FONT, STYLE, SIZE, OR COLOR.

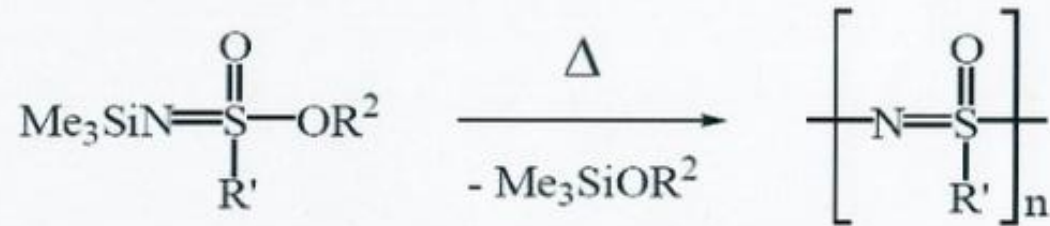
SN 85-360,911, FILED 6-30-2011.

KIM MONINGHOFF, EXAMINING ATTORNEY

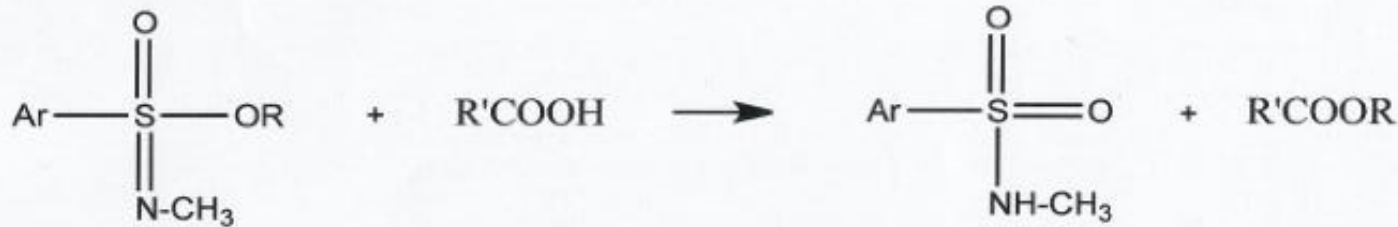


Sulfonimidates Have Been Investigated as

- Potential anti-tumor agents
- Precursors of inorganic polymers

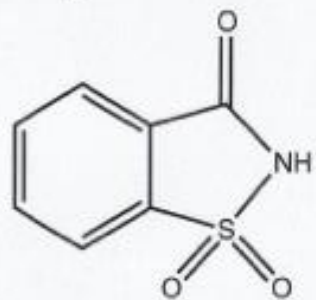


- Alkylating agents



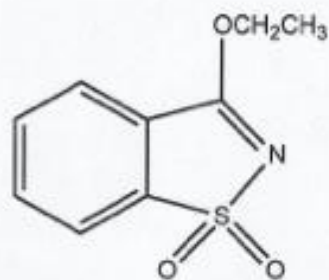
Alkylation of Acids by Sulfonimidates

Acids	pK _a	Rxn. Time [min] at RT	Products	% Yield
CH ₃ SO ₂ OH	-1.9	< 5	CH ₃ SO ₂ OCH ₂ CH ₃	89
CF ₃ COOH	0.0	< 5	CF ₃ COOCH ₂ CH ₃	Quant.
CHCl ₂ COOH	1.35	< 5	CHCl ₂ COOCH ₂ CH ₃	58
4-CH ₃ C ₆ H ₄ S(O)OH	1.99	< 30	4-CH ₃ C ₆ H ₄ S(O)OCH ₂ CH ₃	74
CH ₃ CHClCOOH	2.83	< 60	CH ₃ CHClCOOCH(CH ₃) ₂	45



2.2

2.5 h



46

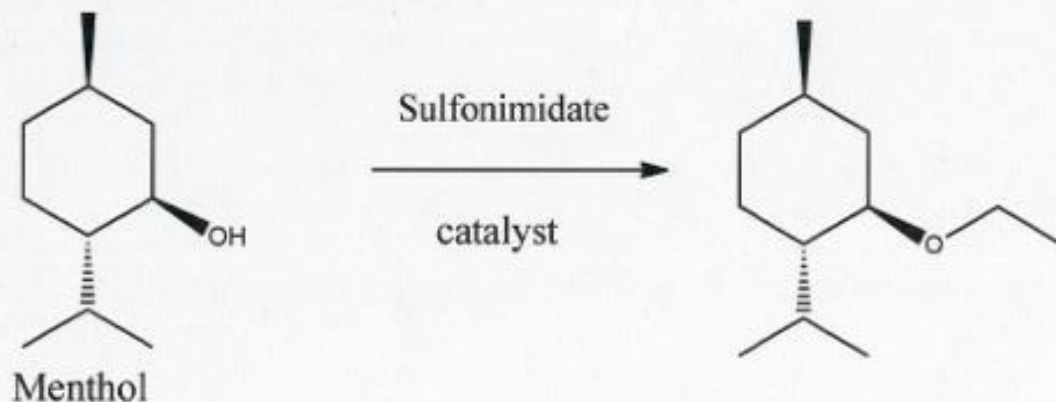
Email from Dr. Robert Rzasas

I received an e-mail from Dr. Robert Rzasas, a graduate of our Department (B.S., 1993).

Dr. Rzasas performed an ethylation reaction on a late-stage pharmaceutical intermediate using our SNAAP reagent and stated:

“To my delight, it worked quite well, giving the desired O-alkylated product. I should note that previous attempts to O-methylate resulted in either complex reaction mixtures or N-methylation.”

Ethylation of Menthol by Sulfonimide



□ Ethylation of Menthol by Sulfonimide

- Ethyl menthyl ether confirmed by 400MHz $^1\text{H-NMR}$, GC/MS
- Percent yield: 72%
- Optical rotation: (c=1, -95.9°), (c=2, -95.4°), (c=4, -95.4°)
- Literature optical rotation: -89.2°
- *N-t*-Butyl-*O*-ethyl-4-nitrobenzenesulfonimide alkylates without rearrangement and with retention of configuration.

SNAAP[®] Isopropylation

Bisp. Nigam* (714-213-8966), Taru Hassala* (310-465-7617), Lori Buehl, Julian Yee, Tom Maricich, Ph.D (562-299-4306) [tom.maricich@csulb.edu]
 Department of Chemistry & Biochemistry, California State University, Long Beach

Introduction

SNAAP[®] is an acronym for:
Substitution **N**ucleophilic of **A**cids **A**lcohols and **P**henols

- > Facile alkylating agents
- > Retention of stereochemistry (R or S)
- > Potential anti tumor agent (bis-sulfonimides)

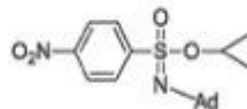


Figure 1 N-1-Adamantyl-O-isopropyl-4-nitrobenzenesulfonimide

Synthesis of Sulfonimide

- > One pot mixture of N-1-adamantyl-4-nitrobenzenesulfonamide, silver oxide, isopropyl iodide and methylene chloride

- > Refluxed for 2 hours

Alkylation of Acids, Alcohols and Phenols

- > 10% excess of sulfonimide and a solvent system of methylene chloride and/or hexane were stirred
- > 10% of catalyst (was added for reactions with alcohols and phenols)
- > Treated with sodium hydride to remove residual substrate and sulfonamide
- > Product obtained through Kugelrohr distillation and/or flash chromatography

Plausible mechanism of alkylation

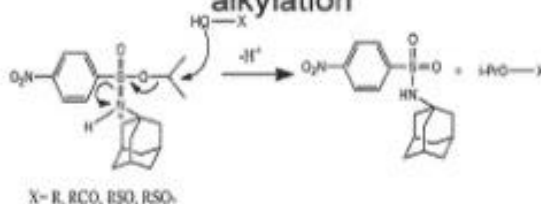


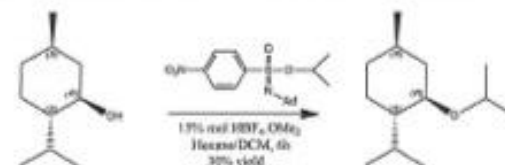
Table 1 Reaction with Phenols

Compound	Run Time	Product	%Yield
	35 min		30
	30 min		35
	40 min		40
	30 min		38

Table 2 Reaction with Acids

Compound	Run Time	Product	%Yield
	< 15 min		52
	-		45
	30 min		83*

*Yields were not optimized



Isopropyl menthyl ether was directly synthesized from L-menthol without racemization

Table 3 Reaction with Alcohols

Compound	Run Time	Product	%Yield
	50 min		40
	10 min		54
	-		35

Conclusions

- > Sulfonimide stable at RT in air
- > Crystalline isopropylating agent
- > Reacts spontaneously with acids: pK_a < 5
- > Isopropylates alcohols and phenols fast with acid catalysis
- > Good to excellent yields [when optimized]
- > No rearrangements or racemization
- > Chemoselective

Acknowledgements



National Cancer Institute
 CSULB CRSM





SNAAP[®] Conclusions

- N-t*-Butyl-*O*-ethyl-*p*-nitrobenzenesulfonimidate is:
- Stable at RT in air
- Crystalline ethylating agent
- Reacts spontaneously with acids: $pK_a < 5$
- Ethylates alcohols and phenols fast with acid catalysis
- Good to excellent yields [when optimized]
- No rearrangements or racemization
- Chemoselective



Hazards of Bleach

Dr. Tom Maricich
California State University, Long Beach

Scalp Burns Visual

P. Goon, A. Misra/Burns 31 (2005) 530-531



04.12.2011

Fig. 1. A 4 cm × 4 cm defect on the occiput of the scalp at 2 weeks following hair-highlighting treatment.

Missing Explanation

Chemical burns do not explain burns when the scalp is protected by plastic hoods or aluminum foil

Best Explanation

- These are **thermal scalp burns**:
 - Due to exotherms of chemical reactions and/or heat of hydration of strong bases with the water in hydrogen peroxide
 - Do not require chemical contact with scalp

Which Chemical Causes the Exotherm?

Most likely:

Sodium Metasilicate

Effect of Adding Extra Sodium Metasilicate to Activator



Bleaching Results on Wig



Results of Exotherm on Mannequin

- Nice Highlights on Hair
- Scalp would have been **scalded within two seconds** at 152.2 °F
- Mannequin would have **filed a lawsuit** against the salon and manufacturer of the bleach!



The Perfect Storm of Conditions Causes Burns to the Scalp

- Too much sodium metasilicate
- Too little ammonium persulfate
- Too much bleach is used
- Ratio of bleach powder to peroxide is too high
- Too much heating on client's head
- Too much insulation of scalp



What Happened to Create This Problem?

- The Bleach Activator formulas were changed to reduce the smell of Ammonia in salons.
- Sodium Metasilicate replaced Ammonium Persulfate because the **Ammonium Persulfate smelled bad**
- **The irony** is that Ammonium Persulfate cools down when it mixes with water but heats up with Sodium Metasilicate
- **So, taking out the smelly ingredient made the formula unsafe!**

Take-Home Messages

- Hair Bleaches Can Cause Thermal Burns to the Scalp
- Read Fine Print on Labels
- Do Not Heat Bleaches
- Test New Bleaches for Exotherm



Acknowledgements

This research was funded by:

National Cancer Institute

California State University, Long Beach, Women and Philanthropy Org.

CSULB Provost's Undergraduate Summer Stipend Program for Research

McNair Scholars Program

Howard Hughes Medical Institute Program

President's Scholars Program

NIH RISE Program

CSULB Research Released Time Program

Acknowledgements of Former and Current Students

- Matthew Allan (MS, 1998) and Brett Kislin (MS, 1987)
- 2002-2006: Andrea Chen (MS, 2004), Daniel Savino (President's Scholar), Christine Bradford (President's Scholar), Gretchen Witowich (President's Scholar), Alethea Poste (HHMI Scholar), Omonigho Aisagbonhi (HHMI Scholar), Dustin Wride, Sylvia Kim (summer research assistant from Wellesley College), Andrew Roberts (summer research assistant from UC San Diego), Naoki Kodama
- 2007-2010: Fan-Chun (Renata) Meng (MS, 2008), Nai-Chia Kuan (Provost Scholar), Jeremy Wood (Provost Scholar), Francisco Rodriguez (Robert B. Henderson Memorial Scholar, Robert D. Rhodes Award), Marilyn Ton, Holly Phung.
- 2011-2016: Michael Fimbres (MS, 2014), Jessica Burton, Sarah Tabayoyong, Hai Nguyen, Glen Soxman, Haydi Elia, Andrew Sykahua, Joseph Kaladjian, Dianne Choi, Therese Santos, Ali Abou-Zahr, Arturo Mejia, Hiep Nguyen, Roy Santos, Faraz Hussain, Lori Digal, Matthew Huynh, Julian Yano (summer research assistant from Columbia U.) and Marie Donato.

Honorable Mention

Christos Angeletakis Ph.D.



Chris graduated from CSULB with a B.S. and then an M.S. in Chemistry with Dr. Maricich in 1978. Chris then earned a Ph.D. at UCI in 1982 doing research on organic sulfur compounds. He later became a member of our department advisory council.

Maricich

Marie D.

Kate K.

Briana L.

Emily B.

Ian F.

Faraz H.

Jose C.

Brian V.

Dr. R. Tang

Robert C.

Gurshan S.

Continuing My Legacy

Working as an Expert Witness – Chem Consulting



Concentrated
Sulfuric Acid –
Previously used as
drain cleaner

VERY DANGEROUS

Continuing My Legacy

Working as an Expert Witness – Chem Consulting

Concentrated Sulfuric Acid spilled on a 3-year-old boy



The effects of concentrated sulfuric acid on a chicken leg

Continuing My Legacy

Working as an Expert Witness – Chem Consulting

The home improvement store took the concentrated sulfuric acid drain cleaner out of every store shortly after the case ended, due to my testimony.

Continuing My Legacy

Working as an Expert Witness – Chem Consulting

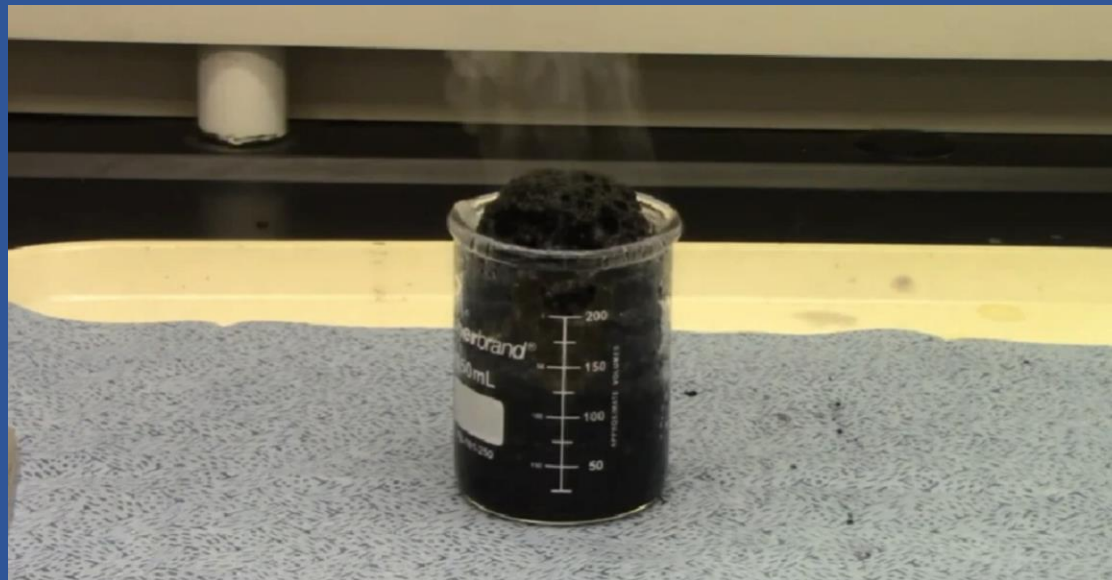
**A Sulfuric Acid Incident at CSULB over 20
years ago**

**Solution: only purchasing concentrated
sulfuric acid in bottles with a plastic
coating going forward**

Continuing My Legacy

Working as an Expert Witness – Chem Consulting

**An uncoated bottle was sold to a junior high school.
This never should have happened!**



The accident occurred when a teacher performed the same experiment that sparked my love for chemistry


Continuing My Legacy

Working as an Expert Witness – Chem Consulting

I recommended connecting the 3-year-old boy (now an adult) to the injured teacher from the experiment at the junior high school, since they had similar experiences.

Lessons in Chemistry and Life

Family + Chemistry Come Together



**Chemistry
is
FUN
With
Dr.
Maricich
4-6-12**

Boron + oxygen +
oxygen + potassium =
BOOK

Uranium + nickel +
cobalt + radon =
UNiCoRn

Do you want to read
about sodium? NA!
Do you want to read
about potassium? K!

Uranium + fluorine +
oxygen = UFO

What do you call iron
blowing in the wind?
Febreeze



Lessons in Chemistry and Life

Family + Chemistry Come Together



Lessons in Chemistry and Life



Work-life balance

Supporting people to do great things

Balance – humanity, family, helping others in addition to academic and professional success

Lessons in Chemistry and Life



Once a fisherman, always a fisherman

Work ethic

Keeping my brain active

My children – now working with CSULB faculty through JAL Therapeutics venture

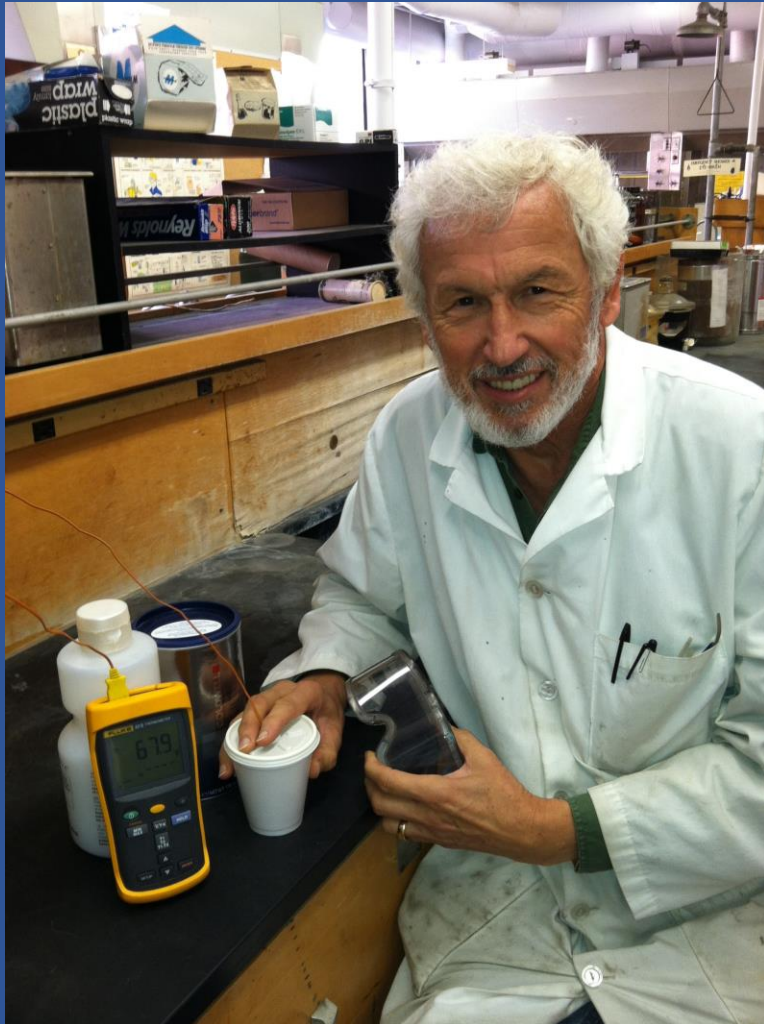
One grandchild – even worked in the CSULB lab one summer!

In Memoriam

Roger A. Acey, Ph.D.



Thank You!



Dr. Maricich and student Dianne Choi, who graduated with honors