



Synthesis of Compounds with Isotopic Signatures

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National Stable Isotope Resource at Los Alamos

- **Started in 1975**
- **Efficient separation of isotope as ^{13}C had not lead to available compounds for research**
- **Synthesis of stable isotope-labeled compounds difficult:**
 - Starting materials are expensive
 - There are a limited number of labeled precursors available
- **Synthesis of compounds specifically labeled with ^2H , ^{13}C , ^{15}N , $^{17,18}\text{O}$, and ^{77}Se - could expand to other isotopes.**
- **Started with DOE and NIH Funding**
- **NCRR Resource from 1975-2005**
- **At present funded by users (CDC, DTRA, FBI)**

Isotope Staff

■ Staff Members

- Clifford J. Unkefer, Biochemist/NMR
- Louis (Pete) A. Silks III, Organic Chemist
- David B. Kimball, Organic Chemist
- Siegfried N. Lodwig, Organic Chemist
- Ryszard Michalczyk, Biochemist/NMR
- Jürgen Schmidt, Organic Chemist
- Pat J. Unkefer, Biochemist
- Robert F. Williams, Organic Chemist
- Ruilian Wu, Organic Chemist

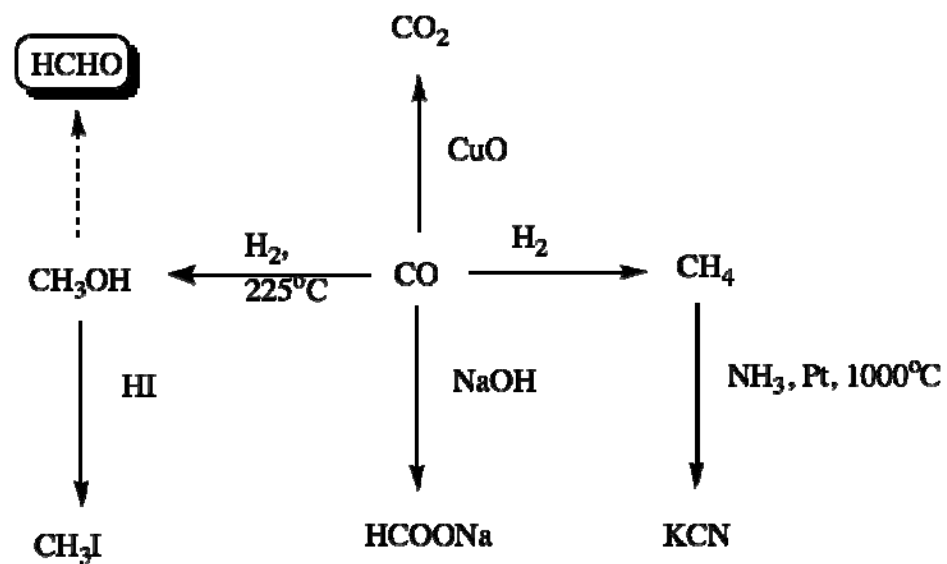
■ Post Doctoral Researchers

- Ricardo Marti-Arbona
- Ramesh Kale

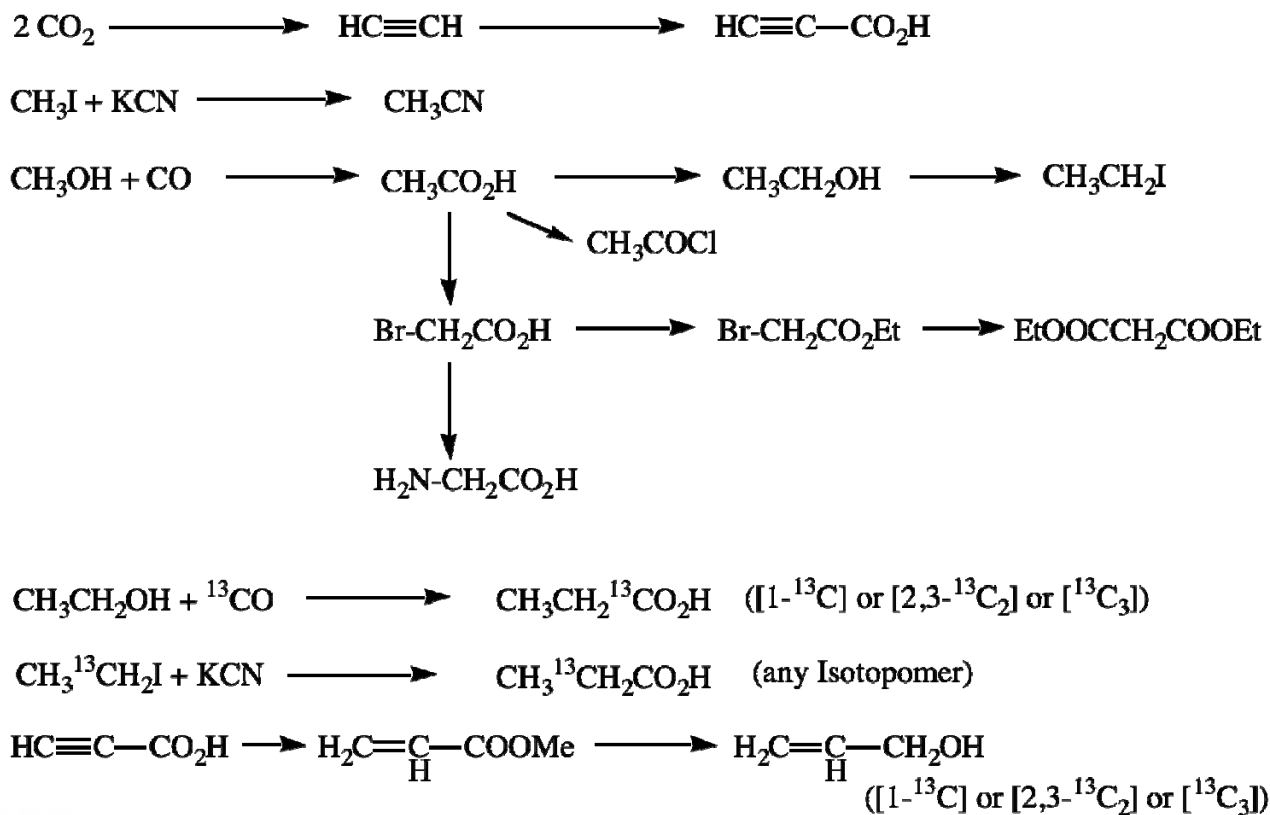
■ Technicians

- Marc A. Alvarez
- Penelope A. Naranjo
- Paulette M. Angel
- Munehiro Teshima

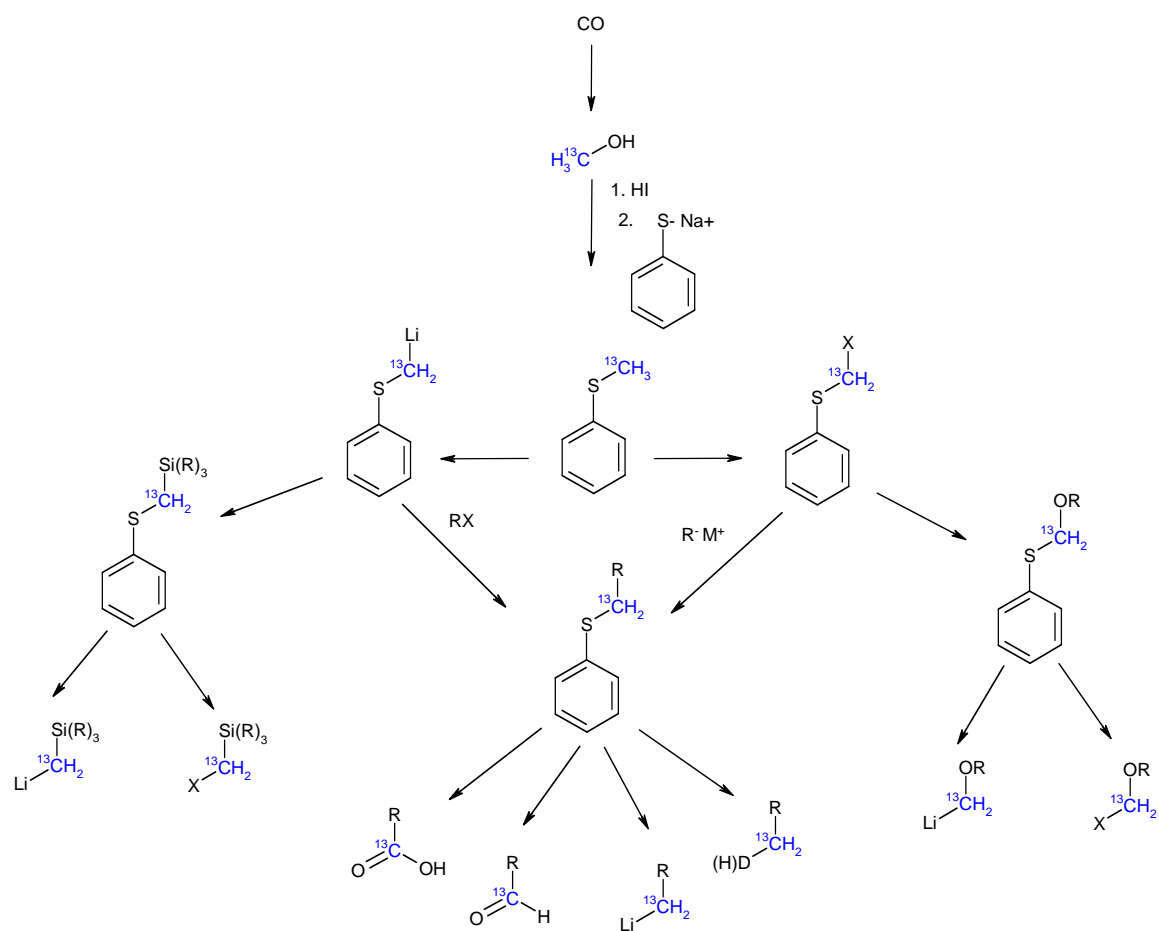
One Carbon Precursors From Carbon Monoxide



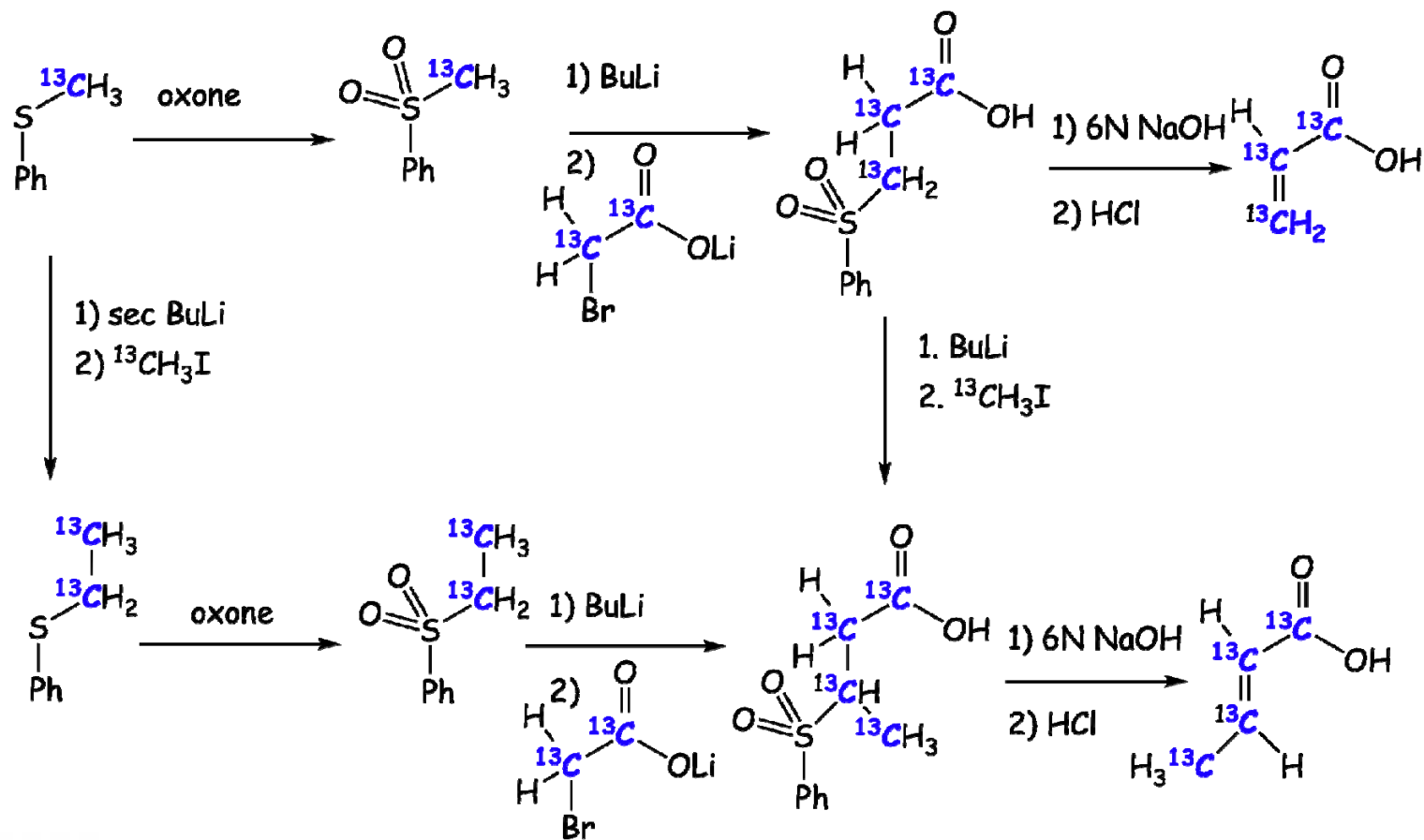
Two and Three Carbon Precursors



Additional Synthons From Thioanisole

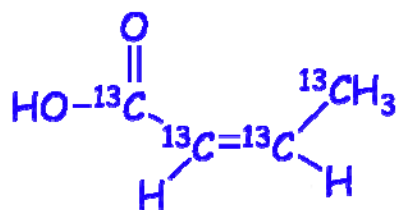


Synthesis of Labeled Acrylic and Crotonic Acids

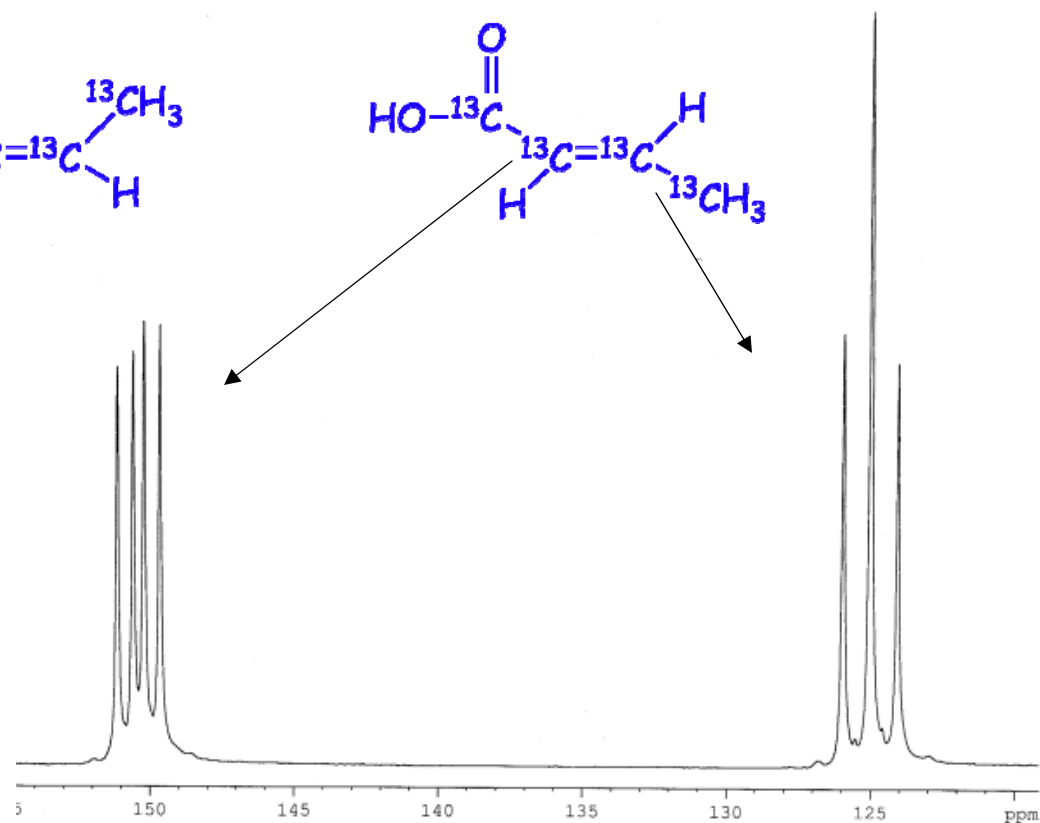
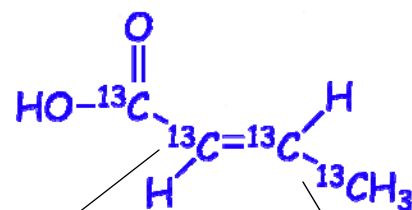


Synthesis of Labeled Acrylic and Crotonic Acids

cis-crotonic Acid

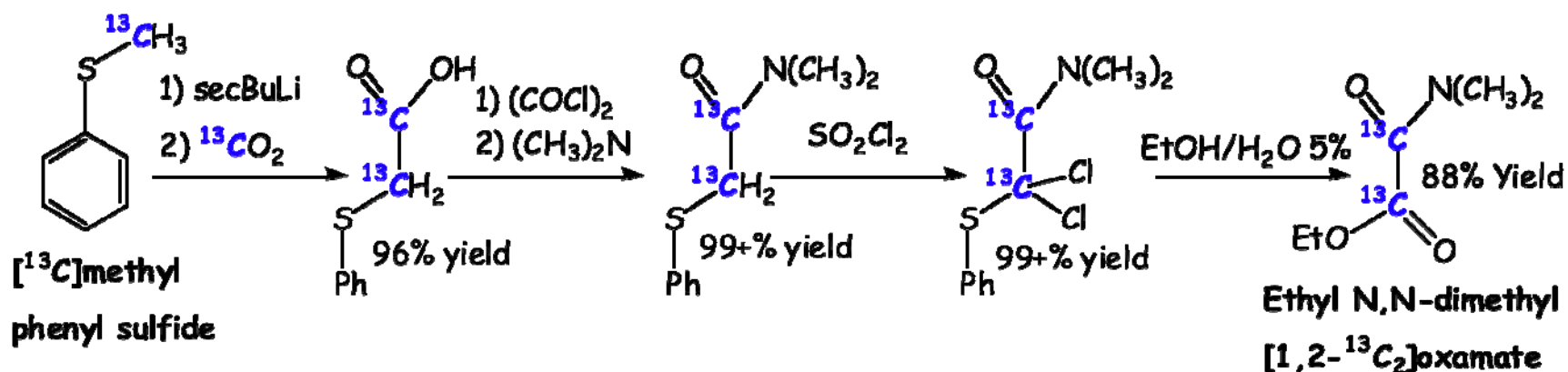


trans-crotonic Acid

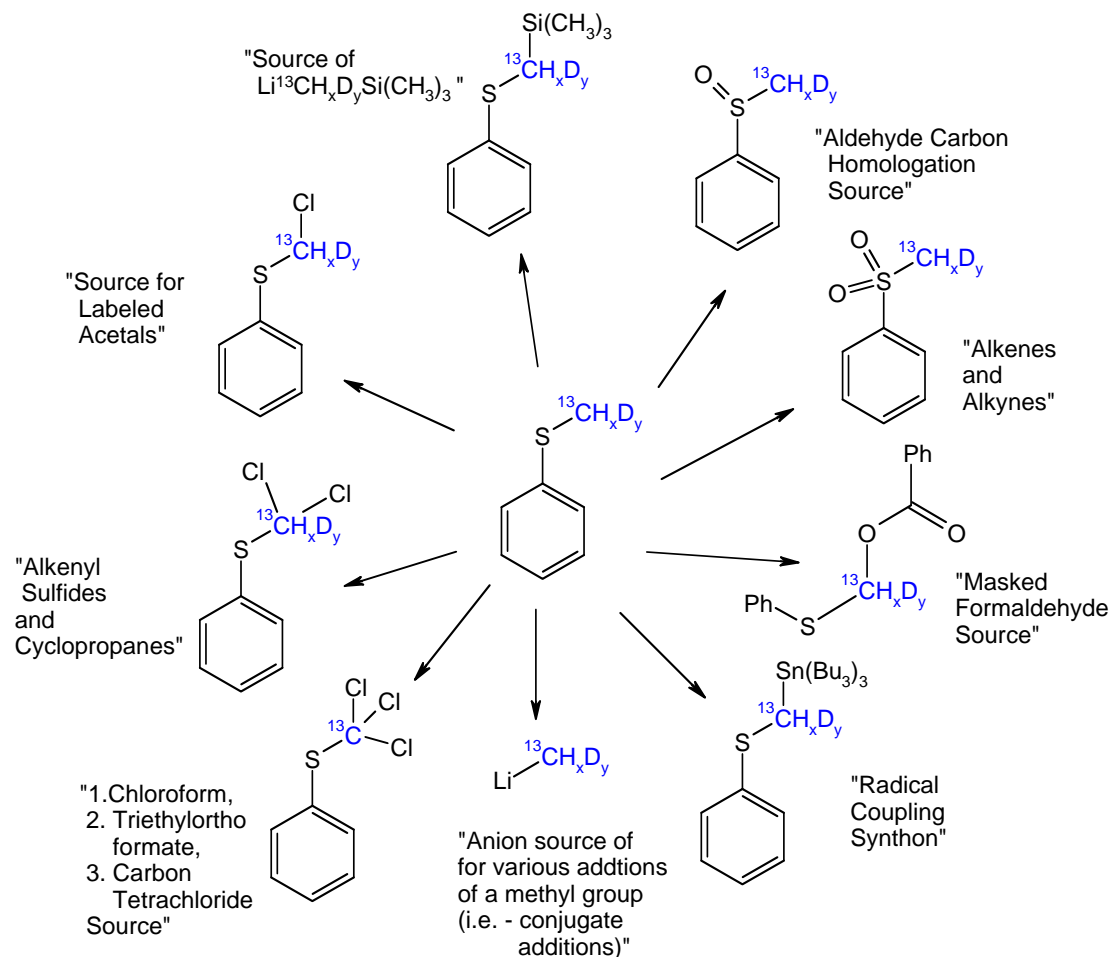


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Synthesis of ^{13}C -labeled Oxamate

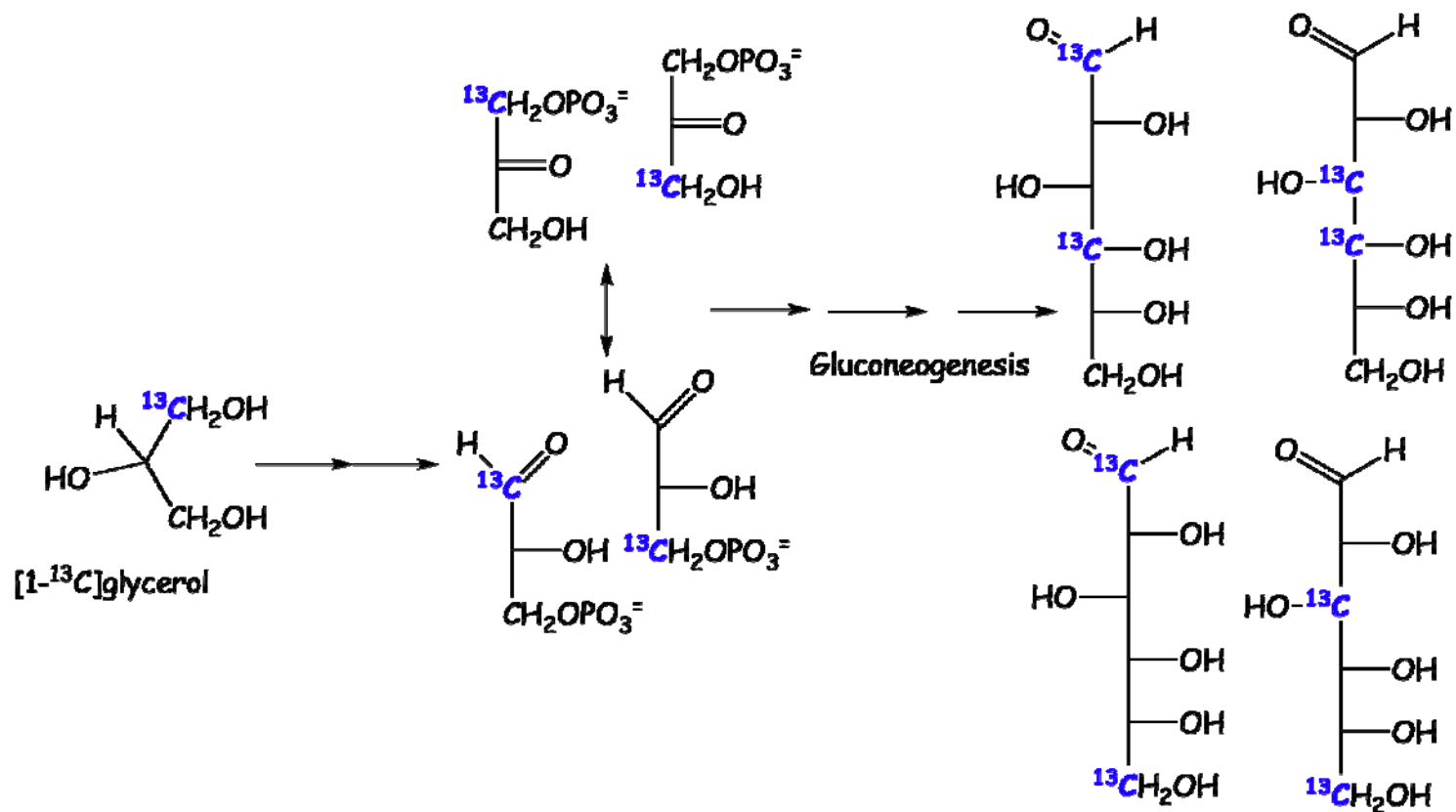


Additional Synthons From Thioanisole

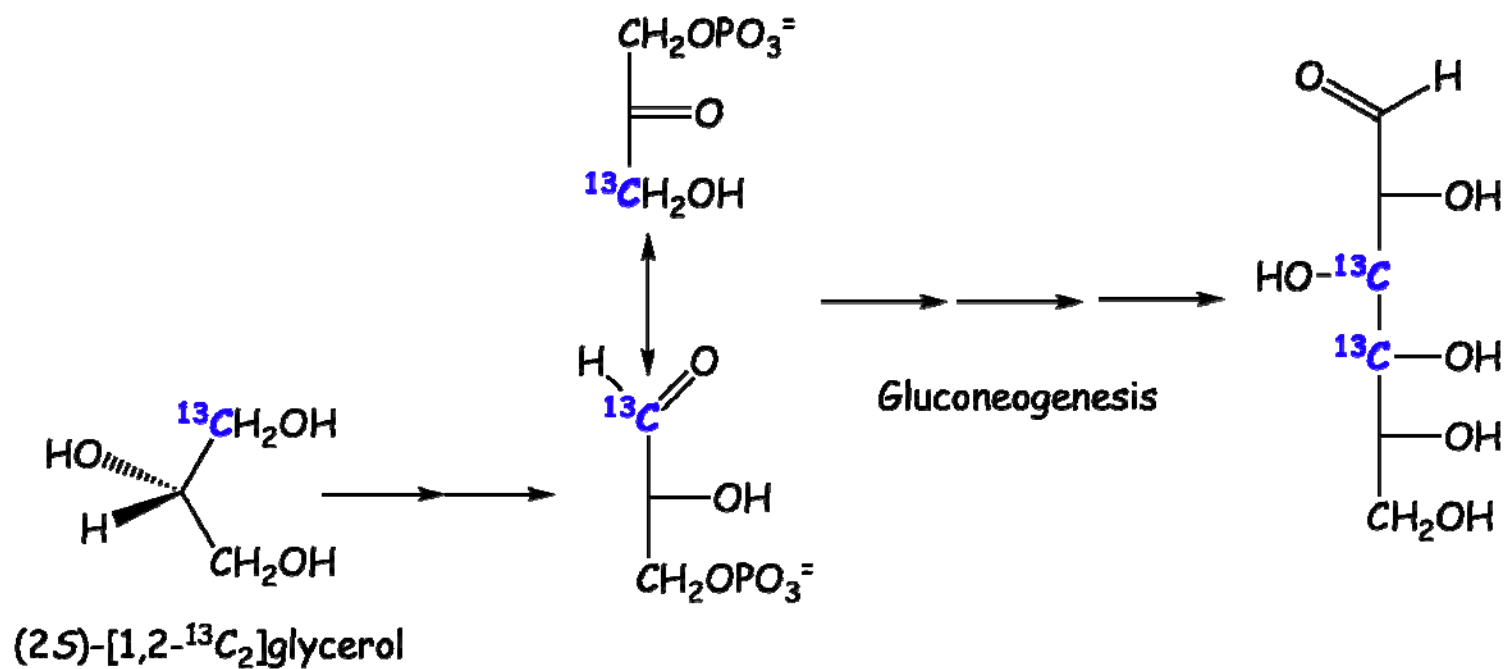


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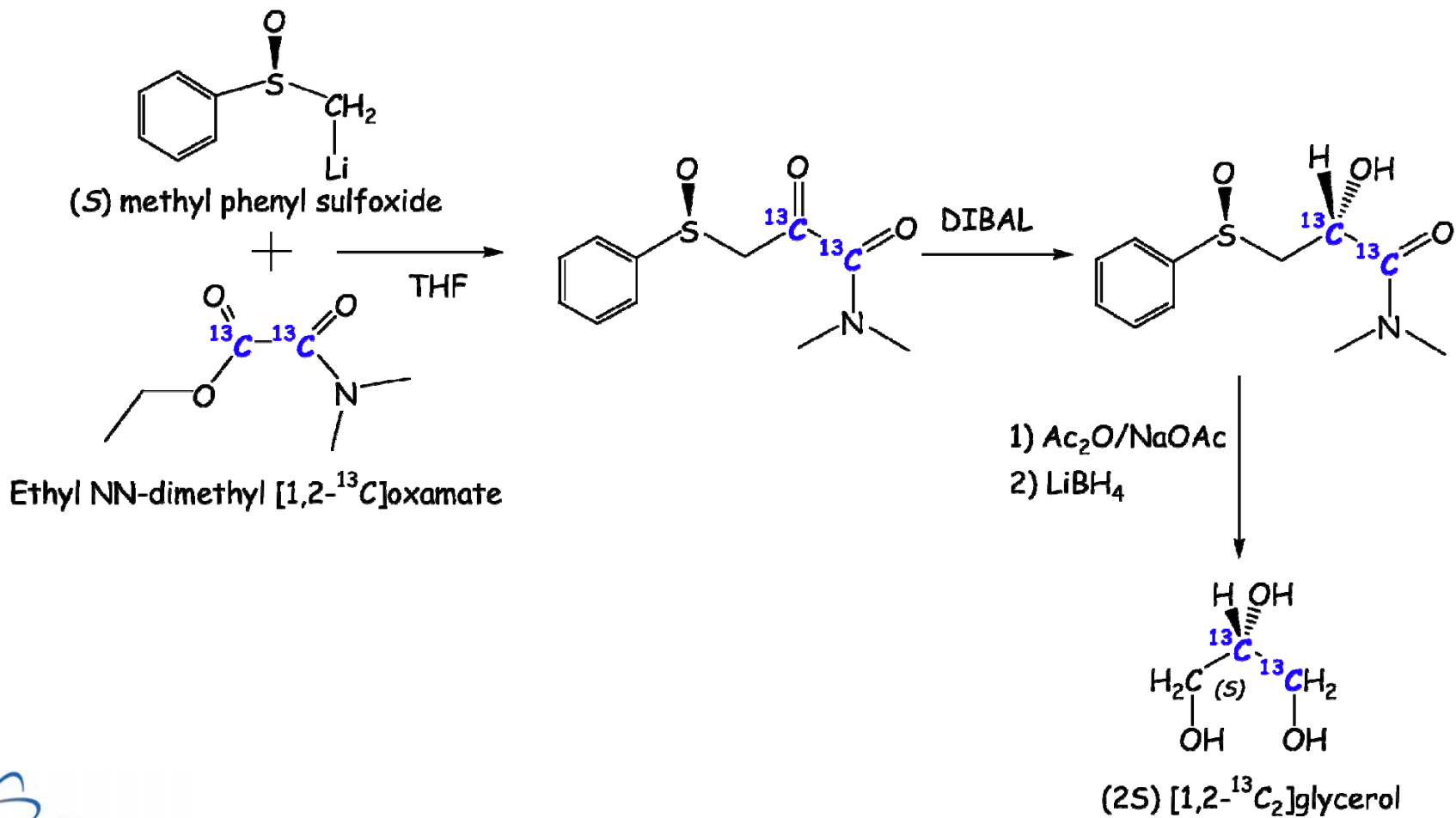
Symmetrical glycerol labeling



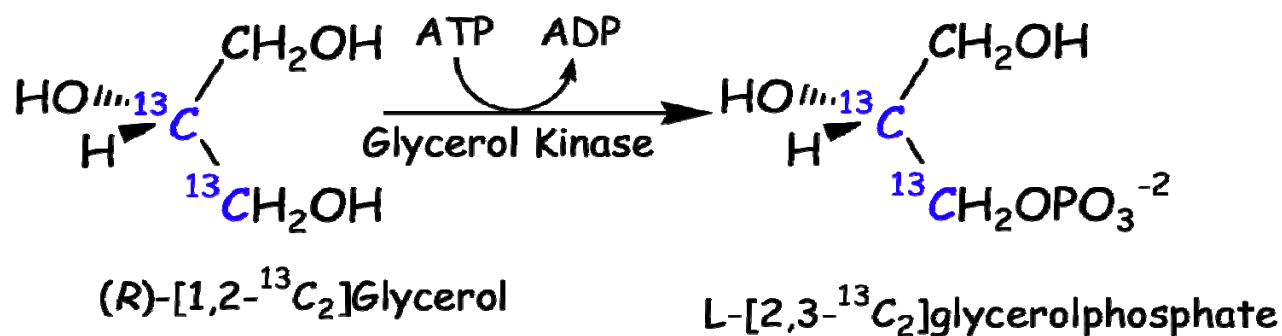
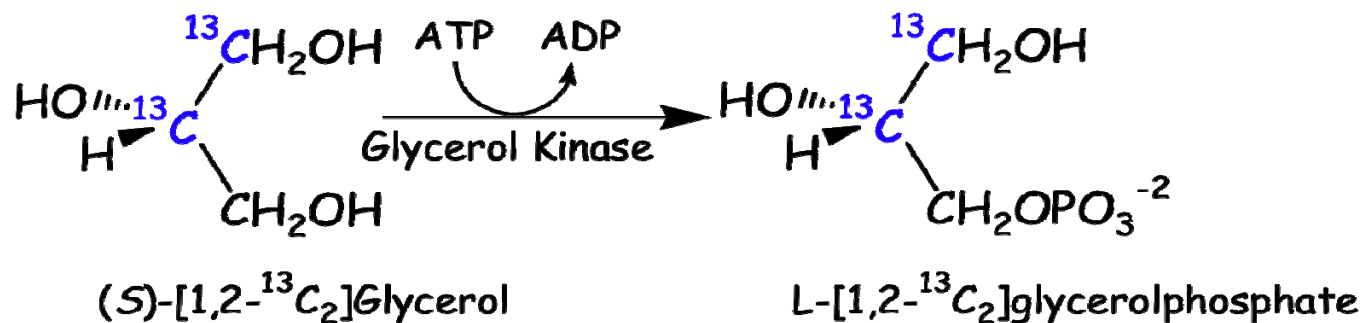
Chiral Labeled Glycerol



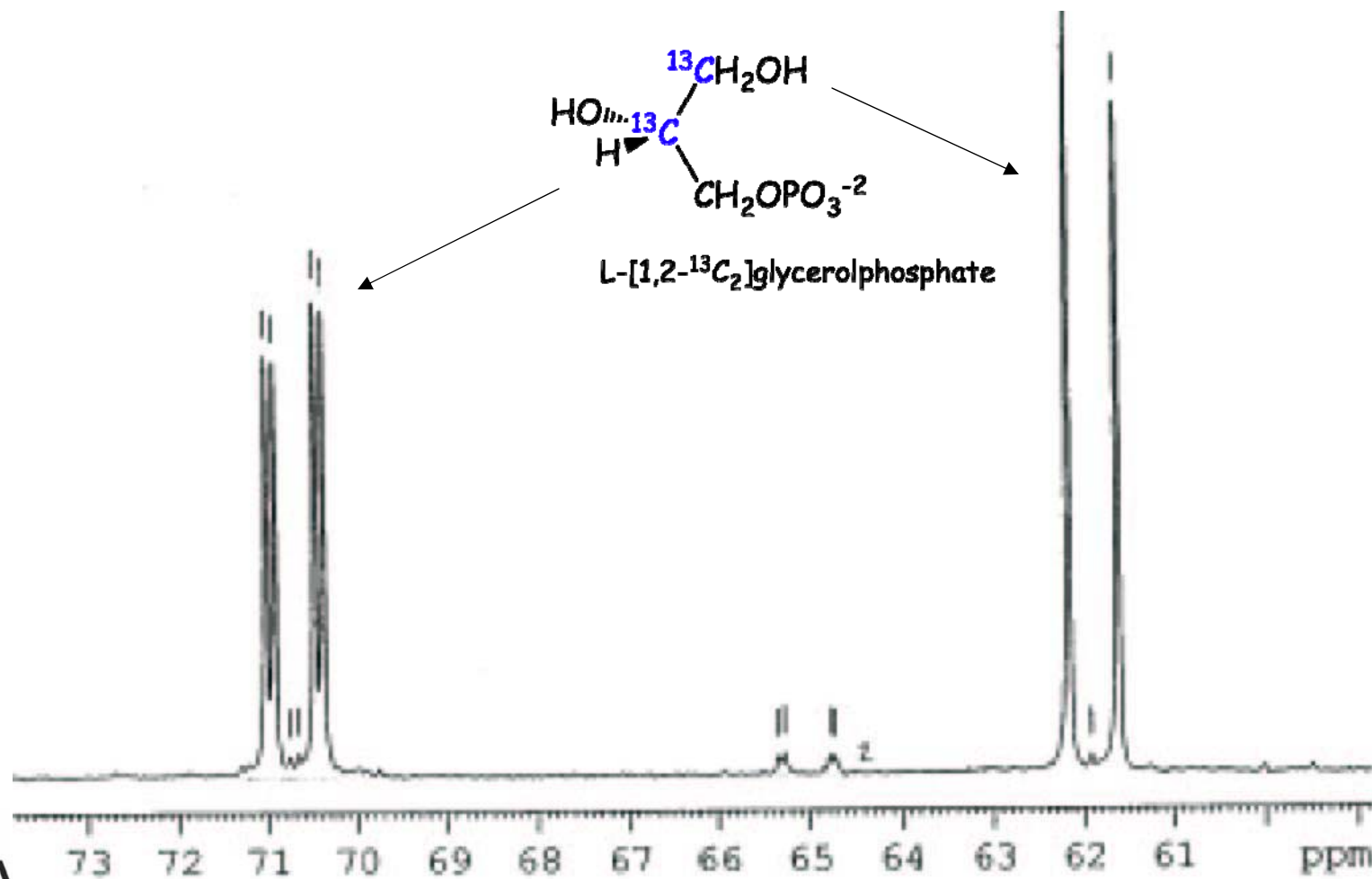
Chiral Synthesis of Glycerol



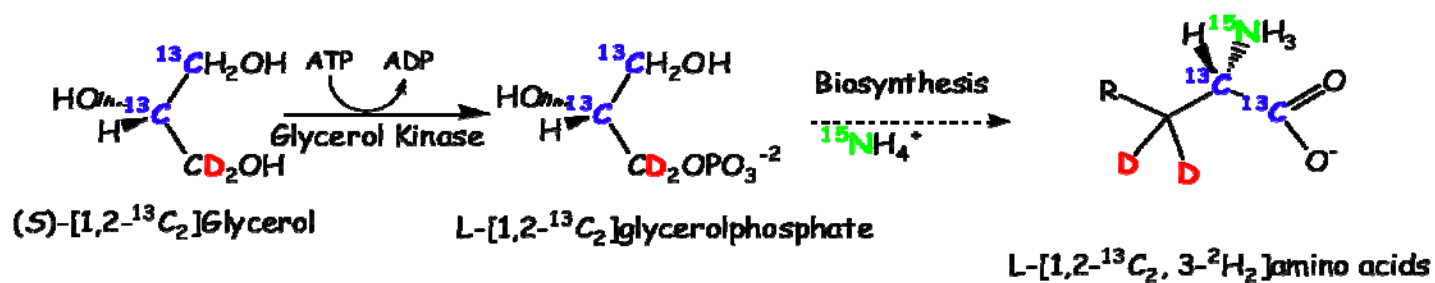
Characterization of Chiral Glycerol



NMR of Chiral Glycerol Phosphate



Amino Acid Labeling



L-[1,2-¹³C₂, 3-²H₂]amino acids

Glycine
 Alanine
 Serine
 Cysteine
 Aspartic acid
 Asparagine
 Threonine
 Methionine
 Lysine
 Tryptophan
 Tyrosine
 Phenylalanine

Glutamate
 Glutamine
 Arginine
 Proline
 Valine
 Leucine
 Isoleucine

Histidine

Synthesis is important

Conclusion:

Plans for production of isotope should include facilities for chemical conversion of isotopes to useful labeled compounds

National Stable Isotope Resource - We Make Labeled Compounds

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Have Gun - Will Travel - Need Funding