

GEORGIA INSTITUTE OF TECHNOLOGY  
OFFICE OF CONTRACT ADMINISTRATION  
SPONSORED PROJECT INITIATION

*Red*

Date: March 6, 1979

Project Title: The Chemistry of New Functional Groups In Enzymes

Project No: G-33-N01 *Green Card*

Project Director: Dr. Edward M. Burgess

Sponsor: DHEW/PHS/NIH - National Institute of General Medical Sciences;  
Bethesda, Maryland 20014

Agreement Period: From March 1, 1979 Until February 29, 1980 (09 year)

Type Agreement: Grant No. 2 R01 GM12672-09A1

Amount: \$85,807 New PHS Funds (G-33-N01)  
8,037 GIT Contribution (G-33-339)  
\$93,844 Total

Reports Required: Annual Progress Reports with Continuation Applications;  
Terminal Progress Report upon Grant Expiration

Sponsor Contact Person (s):

Technical Matters

Contractual Matters  
(thru OCA)

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Program Administrator  
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National Institute of General Medical  
Sciences  
Bethesda, Maryland 20014  
Phone: (301) 496-7166

NOTE: Continuation of G-33-678 (07 & 08 Budget Periods).

Defense Priority Rating: None

Assigned to: Chemistry (School/Laboratory)

COPIES TO:

- Project Director
- Division Chief (EES)
- School/Laboratory Director
- Dean/Director-EES
- Accounting Office
- Procurement Office
- Security Coordinator (OCA)
- Reports Coordinator (OCA)

- Library, Technical Reports Section
- EES Information Office
- EES Reports & Procedures
- Project File (OCA)
- Project Code (GTRI)
- Other \_\_\_\_\_

GEORGIA INSTITUTE OF TECHNOLOGY  
OFFICE OF CONTRACT ADMINISTRATION  
SPONSORED PROJECT TERMINATION

Date: March 6, 1980

Project Title: The Chemistry of New Functional Groups in Enzymes

Project No: G-33-N01

Project Director: Dr. Edward M. Burgess

Sponsor: DHEW/PHS/NIH - National Institute of General Medical Science;  
Bethesda, Maryland 20014

Effective Termination Date: February 29, 1980 (end of 09 year)

Clearance of Accounting Charges: ---

Grant/Contract Closeout Actions Remaining:

- Final Invoice and Closing Documents
- Final Fiscal Report
- Final Report of Inventions
- Govt. Property Inventory & Related Certificate
- Classified Material Certificate
- Other Annual Report of Expenditures due by 5/31/80

NOTE: FOLLOW-ON PROJECT (10 YEAR) IS G-33-N02

TERMINATED

Assigned to: Chemistry (School/~~Laboratory~~)

COPIES TO:

Project Director	Library, Technical Reports Section
Division Chief (EES)	EES Information Office
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Dean/Director-EES	Project Code (GTRI)
Accounting Office	Other _____
Procurement Office	
Security Coordinator (OCA)	
Reports Coordinator (OCA)	
Research Property Coordinator (OCA)	

SECTION IV

APPLICANT: REPEAT GRANT NUMBER SHOWN ON PAGE 1 →		GRANT NUMBER	
SECTION IV—SUMMARY PROGRESS REPORT		GM 12672-10	
		PERIOD COVERED BY THIS REPORT	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Last, First, Initial)		FROM	THROUGH
Burgess, Edward M.		03/01/79	12/01/79
NAME OF ORGANIZATION			
Georgia Inst. of Technology			
TITLE (Repeat title shown in Item 1 on first page)			
The Chemistry of New Functional Groups in Enzymes			

- List publications: (a) published and not previously reported; (b) in press. Provide five reprints if not previously submitted.
- List all additions and deletions in professional personnel and any changes in effort.
- Progress Report. (See Instructions)

- None
- Professional Personnel

Deletions:

Pulcrano, Maria C. Res. Assistant graduated (Ph.D.) 08/01/79.  
 Yoshimura, Toshiaki Postdoctoral Assoc. terminated 02/31/79.

Additions:

Earnhardt, Laurence Res. Assistant 09/01/79  
 McGraw, Earl C. Res. Assistant 09/01/79  
 Vanderver, Donald Postdoctoral Assoc. 10/01/79

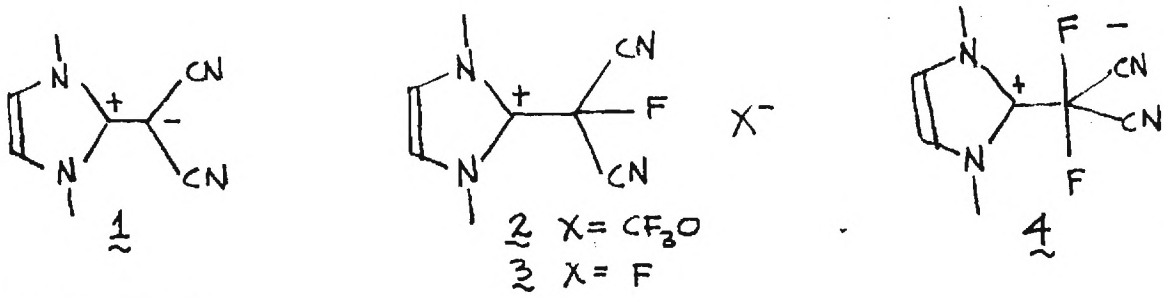
No change in effort.

- Progress Report

The numbering of topics in this report follows from our proposal.

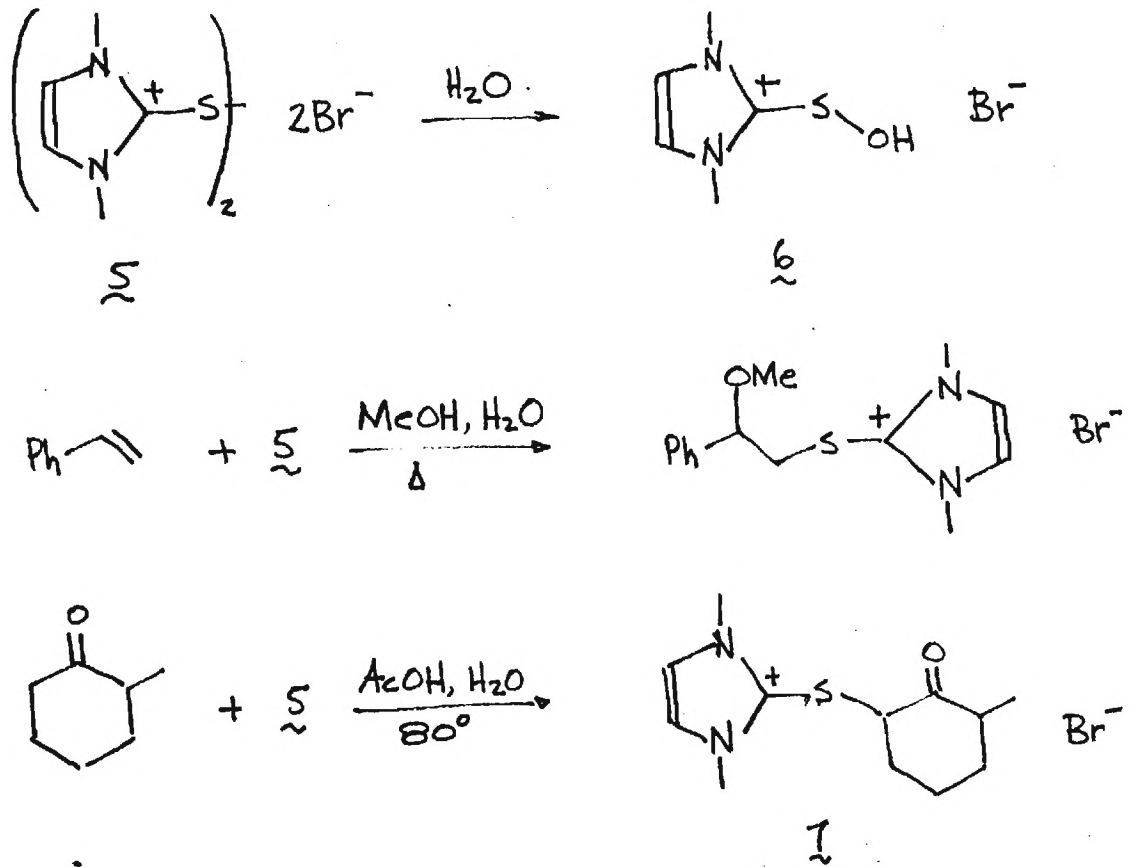
- Hypervalent First and Second Row Molecules.

The reaction of  $\overset{1}{\text{C}}$  with  $\text{CF}_3\text{OF}$  in  $\text{MeCl}_2$  solution at  $-78^\circ$  gives the salt  $\overset{2}{\text{C}}$  which upon standing at  $20^\circ$  in  $\text{MeCN}$  solution gives the unstable fluoride  $\overset{3}{\text{C}}$ . Nmr spectroscopy of  $\overset{3}{\text{C}}$  in solvents which are known to stabilize (via H-bonding) fluoride ion reveals a doublet ( $^1\text{H}-^{19}\text{F}$  coupling) for the vinyl protons and thus we may assign a non-hypervalent structure to this species in solution. We are currently determining the solid state structure of  $\overset{3}{\text{C}}$  via x-ray diffraction at  $-60^\circ$  in hopes of uncovering hypervalent structure  $\overset{4}{\text{C}}$ .

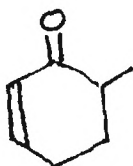
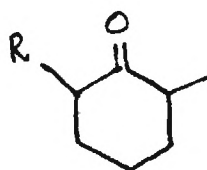


2. Thione Ylides.

A preprint describing some of our completed studies on thione S-imides is included with this report. We have continued our investigation on derivatives of thione ylides including some new reactions of the disulfide  $\text{5}$ . In the presence of one equivalent of water  $\text{5}$  is presumably transformed into the electrophilic species  $\text{6}$  which is capable of reaction with alkenes and enols as illustrated below. The formation of  $\text{1}$  derived from the less stable enol of

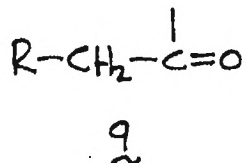
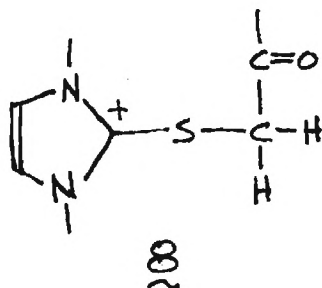


methylcyclohexanone is interesting and we are currently investigating its transformation to such inaccessible model compounds as:

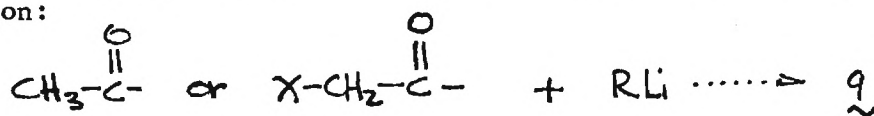


R = alkyl, aryl

which illustrate a potential synthetic use for 5. Furthermore, we found that salts with the general structure 8 react efficiently at  $-78^{\circ}$  with alkyl and aryl lithium compounds to give the  $\alpha$ -substitution product 9 in high yield.

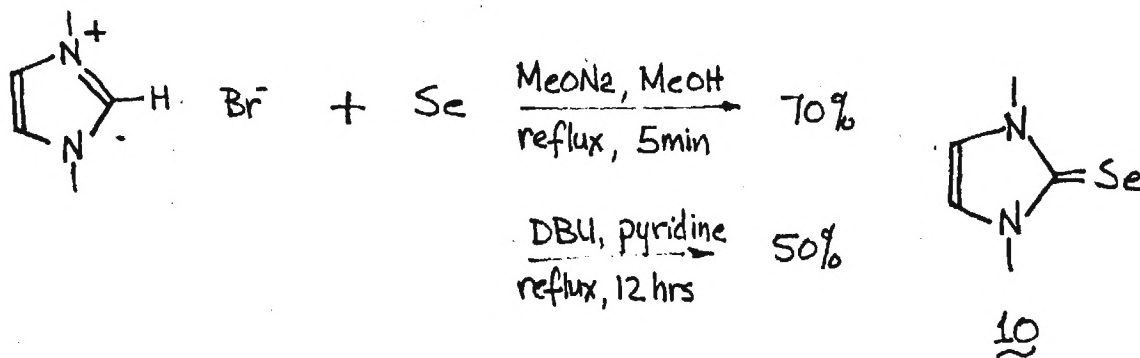


This reaction, which probably proceeds via a single electron transfer, homolysis, and radical pair combination provides an excellent vehicle for the transformation:

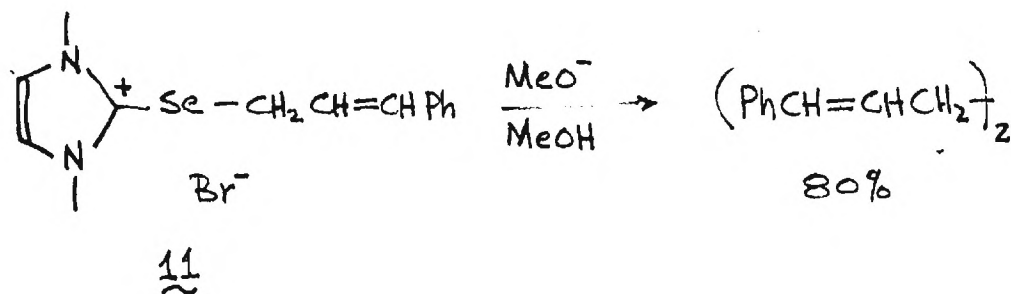


### Selenone Ylides

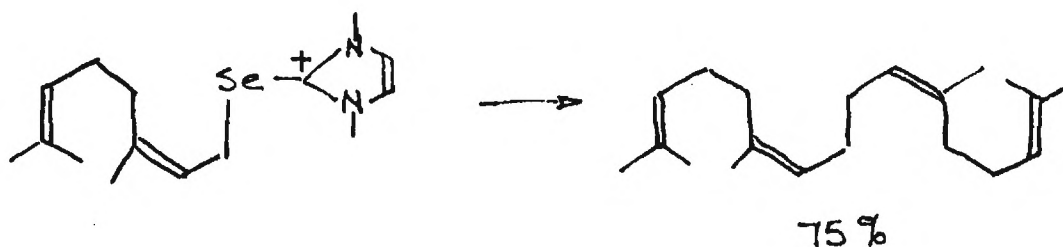
We have initiated studies upon the chemistry of substituent stabilized selenone Se-methylides. The precursor selenone 10 has been prepared by the following reactions:



and readily reacts with alkyl halides to give salts. First, we investigated the base catalyzed deprotonation of such salts derived from allylic halides such as 11. Rapid formation of the reductively coupled allylic system occurred.



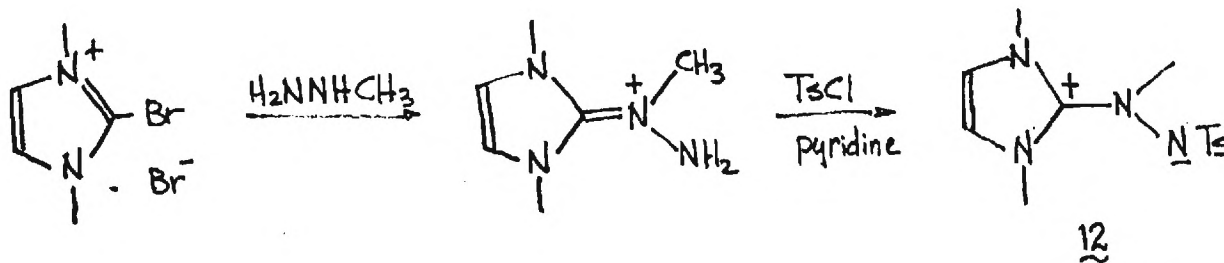
Although the mechanism of this novel reaction remains obscure its synthetic utility is obvious. We have coupled geranyl bromide by this route and are currently studying the farnesyl unit as a precursor to a squalene synthesis.



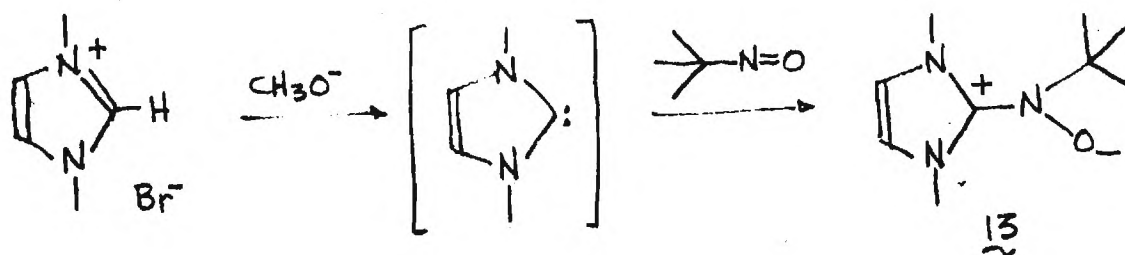
This reaction is not limited to allylic salts, simple alkyl derivatives also undergo base catalyzed reductive coupling. For example, we have converted tetradecyl bromide to the C<sub>28</sub> hydrocarbon in high yield.

### 3. First Row Central Atom Ylides

We have prepared the very stable substituent stabilized azomethine imine, 12, via the following route:



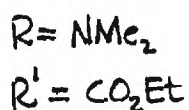
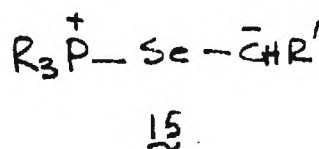
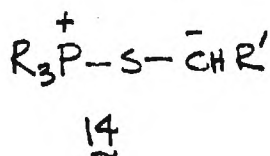
The corresponding nitron  $\underline{13}$  resulted from the reaction:



Both  $\underline{12}$  and  $\underline{13}$  exhibited a  $^1\text{H-nmr}$  singlet for the imidazole N-Me groups at room temperature and therefore are truly 1,3-dipoles. No photochemistry or thermal reactions of these ylides have been investigated to date.

#### 6. Synthetic Application of Hypervalent Intermediates. The Wittig Reaction.

We have made considerable progress in studies of the Wittig Chemistry of the two new classes of 1,3-dipoles, Phosphine S-methylides ( $\underline{14}$ ) and Phosphine Se-methylides ( $\underline{15}$ ).



The requisite precursor salts were obtained via reaction of the phosphine sulfide or selenide with iodoacetic ester in the presence of aqueous sodium fluoroborate. Deprotonation of these salts with sodium methoxide, sodium hydroxide or DBU gave the transient ylides,  $\underline{14}$  or  $\underline{15}$ , which react readily with aldehydes to give the corresponding substituted  $\alpha,\beta$ -unsaturated ester in 70-80% yield. The stereochemistry of this reaction is as follows:

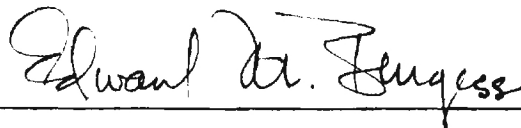
ylide	cis	trans-
$\underline{14}$	50%	50%
$\underline{15}$	60%	40%
$\underline{15} + \text{LiI}$	95%	5%

We are currently investigating the analogous reaction with ketones and plan a synthesis of some vitamin A analogs such as esters of cis-retenoic acid.

The undersigned agrees to accept responsibility for the scientific and technical conduct of the project and for provision of required progress reports if a grant is awarded as the result of this application.

12/19/79

Date



Principal Investigator or  
Program Director