

NINETEENTH NATIONAL ORGANIC
CHEMISTRY SYMPOSIUM
of the
AMERICAN CHEMICAL SOCIETY

AUSPICES OF THE DIVISION OF ORGANIC CHEMISTRY
AND THE ARIZONA STATE UNIVERSITY



June 13-17, 1965
Tempe, Arizona

NINETEENTH NATIONAL ORGANIC
CHEMISTRY SYMPOSIUM
of the
AMERICAN CHEMICAL SOCIETY



Registration: Gammage Auditorium and Palo Verde Hall

Sunday June 13 - Thursday June 17

Meetings: Gammage Auditorium

Speakers at the Nineteenth National Organic Chemistry Symposium

547
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1965



G. Büchi



J. F. Bunnett



E. J. Corey



W. G. Dauben



W. Herz



H. Muxfeldt



J. D. Roberts



M. Stiles



G. Stork



H. H. Wasserman



K. B. Wiberg

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Program

Monday, June 13

Registration: Gammage Auditorium and Palo Verde Halls

Meetings: Gammage Auditorium

10:00 A.M. Welcome WILLIAM J. BURKE, Vice-President, Arizona State University. Response, T. L. CAIRNS, Chairman, Division of Organic Chemistry, ACS

10:30 A.M. E. J. COREY, "New Methods for the Construction of Complex Molecules."

11:30 A.M. Discussion of Paper 1

2:00 P.M. HARRY H. WASSERMAN, "The Oxidation of Heterocyclic Systems by Molecular Oxygen."

3:00 P.M. Discussion of Paper 2

3:30 P.M. WILLIAM G. DAUBEN, "Some Aspects of the Photochemistry of Conjugated Dienes."

4:30 P.M. Discussion of Paper 3

Tuesday, June 15

9:00 A.M. GILBERT STORK, "Progress in Synthetic Organic Chemistry."

10:00 A.M. Discussion of Paper 4

10:30 A.M. HANS MUXFELDT, "Total Synthesis of Tetracycline Antibiotics."

11:30 A.M. Discussion of Paper 5

8:00 P.M. ARTHUR C. COPE, Roger Adams Award Address, "Resolution and Properties of *trans* Cyclic Olefins; Transition Metal Complexes with Organic Compounds."

Wednesday, June 16

- 9:00 A.M. JOSEPH F. BUNNETT, "Reactions of o-Halophenyl Anions."
10:00 A.M. Discussion of Paper 6
10:30 A.M. MARTIN STILES, "Reactions of Benzyne and Benzyne-Adducts."
11:30 A.M. Discussion of Paper 7
2:00 P.M. GEORGE BÜCHI, "A Topic in Natural Products Chemistry."
3:00 P.M. Discussion of Paper 8
3:30 P.M. WERNER HERZ, "Stereochemistry of the Pseudoguaianolides."
4:30 P.M. Discussion of Paper 9

Thursday, June 17

- 9:00 A.M. JOHN D. ROBERTS, "Studies of Conformational Equilibration."
10:00 A.M. Discussion of Paper 10
10:30 A.M. KENNETH B. WIBERG, "Substituted Bicyclobutonium and Related Ions."
11:30 A.M. Discussion of Paper 11

THE ROGER ADAMS AWARD IN ORGANIC CHEMISTRY

The Roger Adams Award in Organic Chemistry has been established with joint sponsorship by the American Chemical Society, Organic Reactions, Inc. and Organic Syntheses, Inc. The award is made biennially to an individual, without regard to nationality, for outstanding contributions to research in organic chemistry. The award consists of a medal and an honorarium of five thousand dollars. The presentation of the award is made at the biennial National Organic Chemistry Symposium of the Division of Organic Chemistry of the American Chemical Society; and the recipient delivers a lecture as part of the program of the Symposium.

The award recognizes the distinguished career of Roger Adams. He has played a vital role in each of the three organizations sponsoring the award, having been both Chairman of the Board of Directors and President of the American Chemical Society and a co-founder of both *Organic Syntheses* and *Organic Reactions*.

The recipient of the award this year is Arthur C. Cope of the Massachusetts Institute of Technology. His award address is entitled "Resolution and Properties of *trans* Cyclic Olefins; Transition Metal Complexes with Organic Compounds."



Tempe Committees



The Arizona State University is acting as host.

Local Committee in Charge

Executive Myron L. Caspar, Chairman
William J. Burke, Morton E. Munk, Gordon D. Perrine
Housing and Registration Edward E. Burgoyne,
Allan L. Bieber
Transportation Richard J. Guillory, Jay Bishop
Local Arrangements George U. Yuen
Recreation Theodore Brown

Division of Organic Chemistry

The plans and program of the Nineteenth National Organic Chemistry Symposium have been developed by the members of the Executive Committee of the Division of Organic Chemistry who have served during the past two years.

	1963-64	1964-65
Chairman . .	DeLos F. DeTar	T. L. Cairns
Chairman- Elect . . .	T. L. Cairns	Herbert O. House
Secretary . .	Herbert O. House	Norman A. LeBel
National Symposium Officer . .	Howard E. Zimmerman Virgil C. Boekelheide Joseph F. Bunnett C. H. DePuy Jack Hine	Howard E. Zimmerman C. H. DePuy Jack Hine Cheves Walling Harry H. Wasserman

SOME NEW SYNTHETIC METHODS

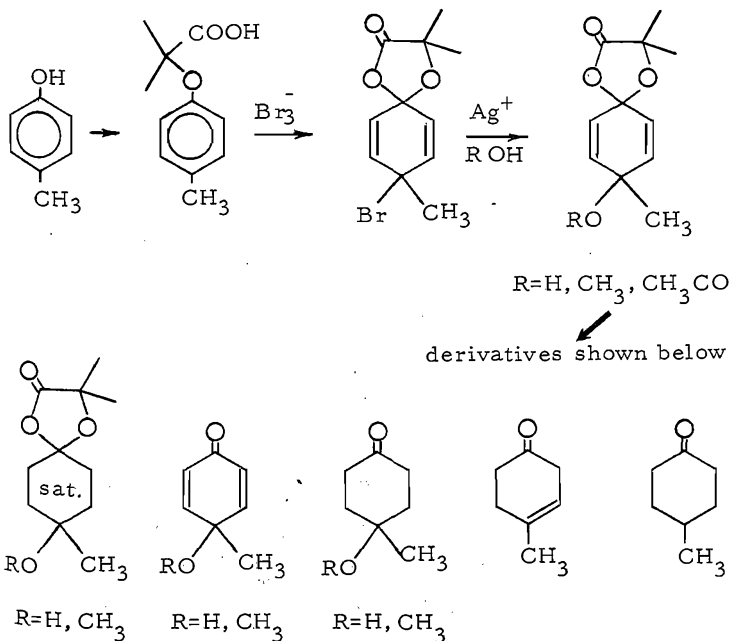
E. J. Corey

Based on studies by

S. Barcza, F. A. Carey, M. Chaykovsky, E. Hamanaka,
A. G. Hortmann, G. Klotmann, M. Semmelhack and R. Winter

The power of organic synthesis can be extended greatly by research which is specifically directed toward the modification of organic structures in certain new ways as can be seen, for example, by the recent development of a wide variety of useful techniques for the selective introduction of functional groups at unactivated sites in complex molecules. This presentation deals with several studies in this vein on new synthetic methodology.

I. A New Method for the Selective Reduction of Aromatic Rings. (Illustrated with p-Cresol):

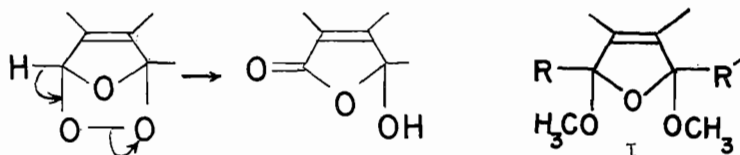


THE OXIDATION OF HETEROCYCLIC SYSTEMS BY MOLECULAR OXYGEN

Harry H. Wasserman

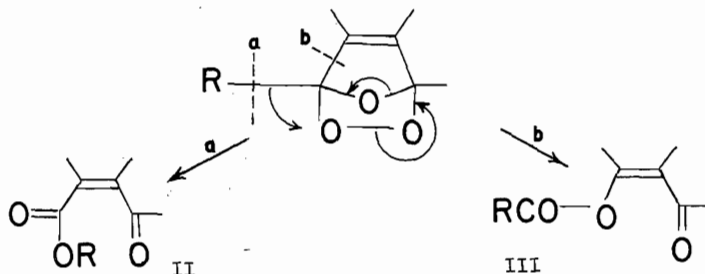
Furans

Photooxidation of furans, studied extensively by Schenck leads to products derivable from intermediate transannular peroxides. With a proton at the α -position, hemiacetal-lactone or (with alcohols as solvents) ψ -ester formation takes place.

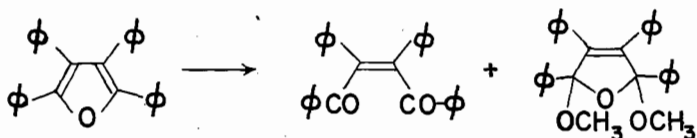


When the 2- and 5- positions of the furan are substituted, other types of products are observed. In reducing solvents such as methanol, reductive cleavage of the O-O bond may occur leading to α,β -unsaturated dicarbonyl derivatives, or the corresponding diketals (I).

In non-reducing solvents, oxidation may yield α,β -unsaturated esters (II) or enol esters (III). Formation of these products may be viewed as rearrangements of the peroxidic system with bond cleavage at a or b as shown.

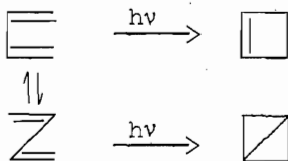
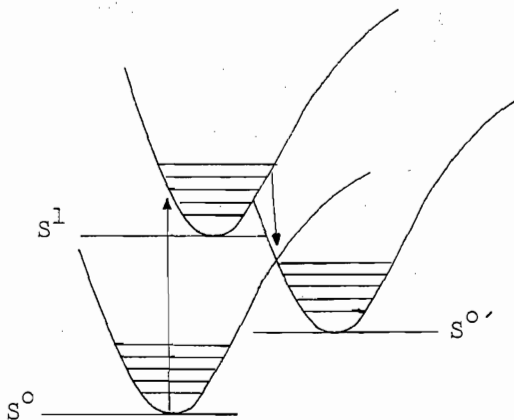
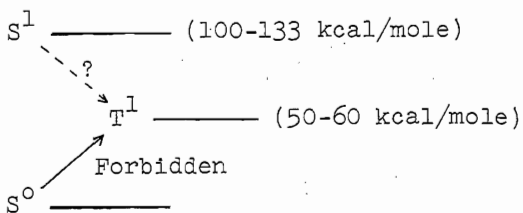


In methanol, in the presence of methylene blue, tetraphenylfuran is photooxidized to cis-dibenzoylstilbene and the corresponding dimethyl ketal (Liberles).



PHOTOCHEMISTRY OF CONJUGATED DIENES

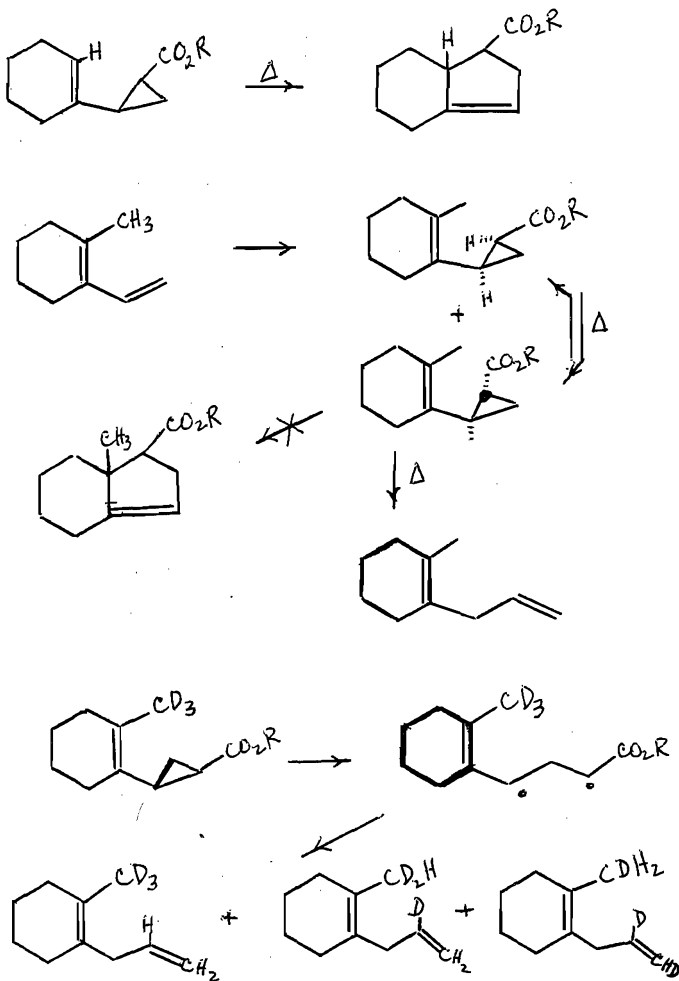
William G. Dauben



PROGRESS IN SYNTHETIC ORGANIC CHEMISTRY

Gilbert Stork

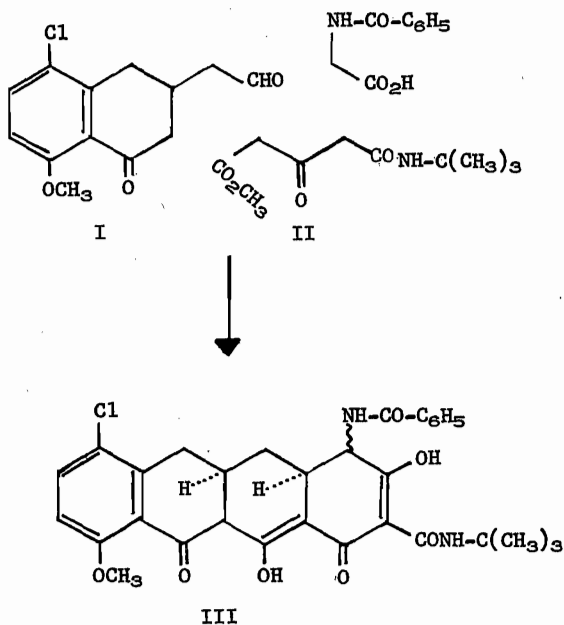
Many problems in the synthesis of polycyclic molecules require methods for the fusion of five-membered rings to a pre-existing system. This lecture will deal with some new syntheses that have recently been developed at Columbia in this area.



Total Syntheses of Tetracycline Antibiotics

Hans Muxfeldt

The following complex reaction will be discussed in detail:



Conditions: Refluxing in tetrahydrofuran and diethylether (1:1). Addition of two equivalents of dicyclohexylcarbodiimid and catalytic amounts of triethylamine was followed by 2 equivalents of sodiumhydride after three hours.

RESOLUTION AND PROPERTIES OF trans CYCLIC OLEFINS;
TRANSITION METAL COMPLEXES WITH ORGANIC COMPOUNDS.

by Arthur C. Cope

The successful resolution of trans-cyclooctene through platinum complexes containing optically active α -methylbenzylamine [J. Am. Chem. Soc., 85, 3276 (1963)] led to many questions involving similar chemistry, some of which have been answered. Levorotatory trans-cyclooctene was shown to have the R configuration by a synthetic method in which (1S:2S)-(+)-1,2-dimethoxycyclooctane (derived from (-)-trans-cyclooctene) was prepared beginning with (2R:3R)-(+)-tartaric acid of known absolute configuration [J. Am. Chem. Soc., 86, 5626 (1964)]. Optically active trans-cyclooctene should racemize thermally at temperatures sufficiently high to permit rotation of the ethylenic unit by 180° through the ring, if the non-bonded interactions between the vinyl type hydrogen atoms and the methylene hydrogen atoms across the ring could be overcome thermally. This has proved to be the case. The rate of racemization of optically active (+ or -)-trans-cyclooctene was studied at 132.7° , 156.4° , and 183.9° . The reaction was found to be first-order in olefin. Half-life values were 122, 15, and 1 hour, respectively, for the three temperatures. The racemization reaction had an activation energy of 35.6 kcal per mole.

Resolution of trans-cyclononene has been accomplished by the scheme employed in the resolution of trans-cyclooctene. It was found that trans-cyclononene racemized spontaneously at room temperature at such a rate that no optical activity could be observed when the olefin was recovered from the pure diastereoisomeric platinum complexes by the procedure which yielded optically active trans-cyclooctene. When the recovery was performed by a fast reaction at room temperature and the rotation of the olefin was measured below 0° , optical activity was observed and rates of racemization could be measured. trans-Cyclododecene that was recovered from pure diastereoisomeric platinum complexes under these conditions was optically inactive.

The rate of racemization of trans-cyclononene was followed at -20° to 0° , and was first-order in olefin; the energy of activation for racemization proved to be 20 kcal per mole. The half-life of optically active trans-cyclononene is estimated to be about $\frac{1}{4}$ minutes, 20 seconds, and 6 seconds at 0° , 20° , and 30° , respectively.

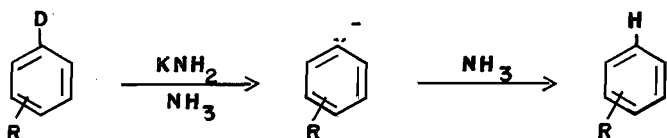
Optically active cis-trans-1,5-cyclooctadiene has been prepared by an asymmetric Hofmann elimination from optically

REACTIONS OF o-HALOPHENYL ANIONS

Joseph F. Bunnett

o-Halophenyl anions are much more easily formed than most other phenyl anions, and they are prone to release halide ion and form an aryne. They are reactive intermediates.

ortho-Halogen substituents strongly accelerate the formation of phenyl anions, and this suggests strong stabilization. Relative rates of exchange are:



R	k(rel.)	R	k(rel.)
H	1	2-OCH ₃	8,000
2-F	4,000,000	2-CF ₃	600,000
3-F	4,000	3-CF ₃	10,000
4-F	200	4-CF ₃	10,000

Hall, Piccolini and Roberts (1955)

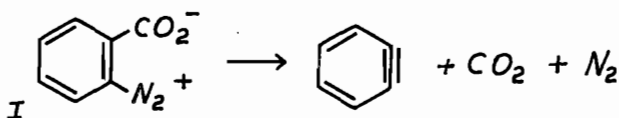
Rates of aryne formation by action of lithium piperidide on substituted bromobenzenes indicate similar substituent effects (Huisgen, Mack, Herbig, Ott and Anneser, 1960).

An anionic center alpha to the benzene ring strongly opposes

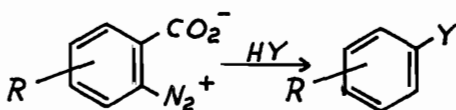
REACTIONS OF BENZYNE AND BENZYNE-ADDUCTS

Martin Stiles

Benzyne was first postulated as a reaction intermediate as a result of careful studies of the mechanism of nucleophilic aromatic substitution. It soon appeared likely that such intermediates would undergo a variety of useful and interesting reactions if other means of generating them could be found. Benzenediazonium -2-carboxylate (I), prepared by the diazotization of anthranilic acid, has proved to be a very useful "benzyne reagent".



Exploratory experiments (Stiles and Miller, J. Am. Chem. Soc., 82, 3802 (1960)) showed that the mild (40-50°) thermolysis of this substance in the presence of furan or anthracene produced the corresponding benzyne adducts. (cf. Wittig and Pohmer, Ber., 89, 1334 (1956).) Both carboxylic acids and alcohols proved quite reactive toward benzyne, and such reactions were used to demonstrate that carbon atoms 1 and 2 become equivalent in the decomposition of I. (Stiles, Miller, and Burckhardt, J. Am. Chem. Soc., 85, 1792 (1963).)



R	Y	para/meta
4-I	C ₆ H ₅ CO ₂ ⁻	1.6 ± 0.2
5-I	"	1.5 ± 0.2
5-F	"	3.5 ± 0.1
5-NO ₂	"	3.8 ± 0.2
5-NO ₂	<u>t</u> -BuO ⁻	3.6

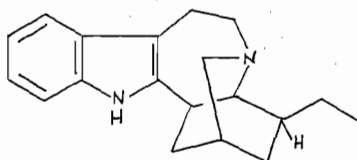
A TOPIC IN NATURAL PRODUCTS CHEMISTRY:

THE TOTAL SYNTHESIS OF IBOGA ALKALOIDS

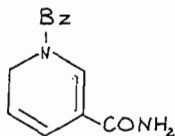
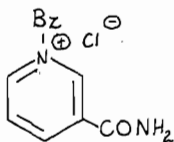
G. Büchi

in collaboration with D. L. Coffen, K. Kocsis, P. E. Sonnet
and F. E. Ziegler.

Iboga alkaloids are a class of naturally occurring indole bases structurally characterized by the presence of an isoquinuclidine ring and a seven membered ring C. The structures of these alkaloids, were determined by Bartlett, Dickel and Taylor in 1958 and the purpose of this lecture is to describe the total synthesis of the least substituted member of this class namely ibogamine.



Reduction of 3-carboxamido-N-benzylpyridinium chloride with sodium borohydride under special conditions gave a mixture of a 1,6-, a 1,2-dihydropyridine and minor amounts of a tetrahydro-



STUDIES OF CONFORMATIONAL EQUILIBRATION

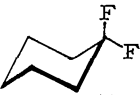
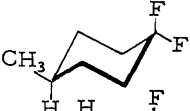
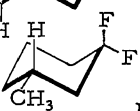
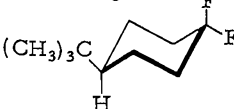
John D. Roberts

California Institute of Technology

Nuclear magnetic resonance spectroscopy is providing a new dimension for the study of dynamic stereochemistry and particularly conformational analysis. A number of papers have already been published describing how n. m. r. may be used to determine conformational populations and rates and activation parameters for interconversion of conformers. In general, the previously reported work has involved the use of proton spectra and as a result has suffered from complications arising from spin-spin splitting (which can usually be alleviated by massive deuteration, F. A. L. Anet) and relatively small chemical shifts which at very low temperatures may be obscured by viscous broadening.

In the present research, we have mostly studied conformational equilibrations of geminal-substituted fluoro compounds because chemical shifts in ^{19}F n. m. r. spectra are ten to fifty times greater than with corresponding proton spectra. Where cross-checks are possible, we find rather close agreement with results obtained with the corresponding nonfluorine-containing compounds, which fact indicates that geminal fluorine substitution does not itself markedly change conformational properties. A great deal of work has been done by Hendrickson, Wiberg, Allinger, and others to calculate the energies of conformations and the energy barriers for conformational equilibration. The results we have obtained are in reasonable qualitative agreement but poor quantitative agreement with theoretical predictions.

Some examples of conformational analysis and conformational equilibration by n. m. r. methods:

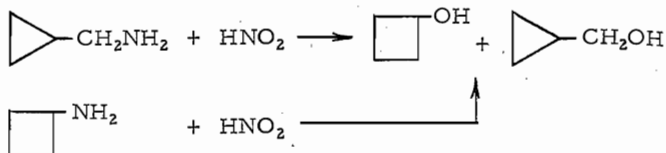
	Room temperature		$\sim -100^\circ$	
	^{19}F Chemical shift, c.p.s.	$J_{\text{F-F}}$, c.p.s.	^{19}F Chemical shift, c.p.s.	$J_{\text{F-F}}$, c.p.s.
	0	0	862	244
	557	241	650	237
	680	241	750	239
	671	240	695	240

BICYCLOBUTONIUM AND RELATED IONS

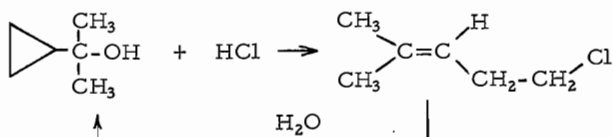
Kenneth B. Wiberg

Examples of Cyclopropylcarbinyl-Cyclobutyl-Allylcarbinyl Interconversions:

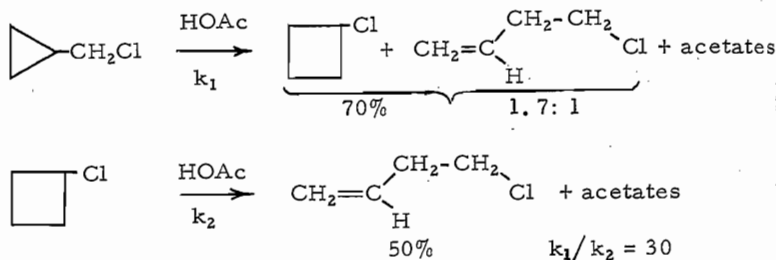
Demjanov (1907):



Bruylants and Dewael (1928):



Roberts and Mazur (1951):



Wallis, Fernholz and Gephart (1937):

