EIGHTEENTH NATIONAL ORGANIC CHEMISTRY SYMPOSIUM of the AMERICAN CHEMICAL SOCIETY

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Registration: Steeb Dormitory, Ohio State University
Sunday, June 16, 2-11 p.m.
Mershon Auditorium, Ohio State Univesrity
Monday, June 17, 8 a.m. to 10 p.m.
Tuesday, June 18, 8 a.m. to 10 p.m.
Wednesday, June 19, 9 a.m. to 6 p.m.
Thursday, June 20, 9 a.m. to noon

Meetings: Mershon Auditorium

Speakers at the Eighteenth National Organic Chemistry Symposium

J. A. Berson

D. J. Cram

S. J. Cristol

C. H. DePuy

J. Hine

J. Meinwald

K.Mislow

E. E. van Tamelen

F. H. Westheimer

B. Witkop

P. Yates

Program

Monday, June 17

10:00 a.m. Welcome. NOVICE G. FAWCETT, President, The Ohio State University. Response. WILLIAM G. DAUBEN, Chairman, Division of Organic Chemistry, ACS.

10:30 a.m. D. J. CRAM, "Carbanions".

11:30 a.m. Discussion of Paper 1

2:00 p.m. S. J. CRISTOL, "Reactions and Rearrangements of Dibenzobicyclooctadienes".

3:00 p.m. Discussion of Paper 2

3:30 p.m. J. A. BERSON, "Some Recent Aspects of Molecular Rearrangements".

4:30 p.m. Discussion of Paper 3

Tuesday, June 18

9:00 a.m. C. H. DEPUY, "Synthesis and Rearrangement of Cyclopropanols".

10:00 a.m. Discussion of Paper 4

10:30 a.m. J. MEINWALD, "Recent Advances in the Chemistry of Strained Bicyclic Systems".

11:30 a.m. Discussion of Paper 5

8:00 p.m. P. D. BARTLETT, Roger Adams Medal Award Address, " 'Biradical' Intermediates".

Wednesday, June 19

9:00 a.m. F. H. WESTHEIMER, "Some Aspects of the Chemistry of Phosphate Esters".

10:00 a.m. Discussion of Paper 6

10:30 a.m. B. WITKOP, "Some Recent Studies on Amino Acids, Peptides and Proteins".

11:30 a.m. Discussion of Paper 7

2:00 p.m. E. E. VAN TAMELEN, "Recent Developments in Synthetic Organic Chemistry".

3:00 p.m. Discussion of Paper 8

3:30 p.m. K. MISLOW, "New Directions in Conformational Analysis".

4:30 p.m. Discussion of Paper 9

8:00 p.m. Concert of classical music by the Columbus Baroque Quartet, at the new auditorium of the Battelle Memorial Institute.

Thursday, June 20

9:00 a.m. J. HINE, "Double Bond- No Bond Resonance".

10:00 a.m. Discussion of Paper 10

10:30 a.m. P. YATES, "Chemistry of *a*-Diazoketones".

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 will be 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 will be made at the biennial National Organic Symposium of the Division of Organic Chemistry of the American Chemical Society, and the recipient will deliver 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 Professor Paul D. Bartlett of Harvard University. His award address is entitled "Biradical Intermediates".

Paul D. Bartlett

Columbus Committees

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The Ohio State University, the Columbus Section of the American Chemical Society, the Battelle Memorial Institute and Chemical Abstracts Service are acting as hosts.

Committee in Charge

Executive.....A. L. Henne, Chairman
W. N. White, R. A. Finnegan
Finance.....F. C. Croxton and S. Wetzel
Registration.....W. T. Lippincott
Transportation.....K. W. Greenlee
Social and Entertainment.....M. S. Newman and M. L. Wolfrom
Chairman, Columbus Section.....F. C. Croxton

Division of Organic Chemistry

The plans and program of the Eighteenth 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.

	1961-1962	1962-1963
Chairman	Stanley J. Cristol	William G. Dauben
Chairman-Elect	William G. Dauben	DeLos F. DeTar
Secretary	Herbert O. House	Herbert O. House
National Symposium Officer	Kenneth B. Wiberg	Kenneth B. Wiberg
	E. J. Corey	Virgil C. Boekelheide
	Carl Djerassi	Joseph F. Bunnett
	Richard B. Turner	E. J. Corey
		Richard B. Turner

An Invitation to Organic Chemists who are not members of the Division of Organic Chemistry

The Executive Committee of the Division of Organic Chemistry extends to you a cordial invitation to become a regular member of the division.

Each of the divisions of the American Chemical Society serves a field of specialization and the Organic Division endeavors to serve organic chemists by furthering organic chemistry. To that end, it wishes to have associated with it as many organic chemists as possible.

The requirements for divisional membership are: (1) membership in the American Chemical Society, (2) active interest in organic chemistry, and (3) payment of annual dues of $2.00. These dues are used to pay the expenses involved in the activities of the division which are:

1. Mailing of notices and forms for the presentation of papers at the Spring and Fall Meetings of the A.C.S.
2. Lithoprinting and distributing to members abstracts of the papers to be presented, in advance of the national meetings.
3. Arranging for National Symposia on organic chemistry. These are held every two years and the speakers and program are determined by the members of the Organic Division.
4. Establishing and promoting policies vital to the advancement of organic chemistry.

If you wish to become a regular member of the Organic Division, all that is necessary is to give or send your name, mail address, and $2.00 to:

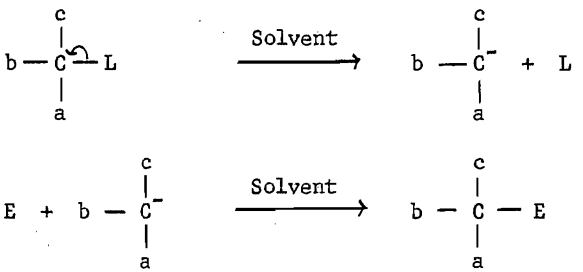
HERBERT O. HOUSE, Secretary
Organic Division, A.C.S.
Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts

Extra copies of the Symposium Abstract Booklet can be obtained at $1.00 each from the Secretary. Abstracts of the 11th, 12th, 14th, 15th, 16th and 17th, but not the 13th, Symposia are also available at the same price.

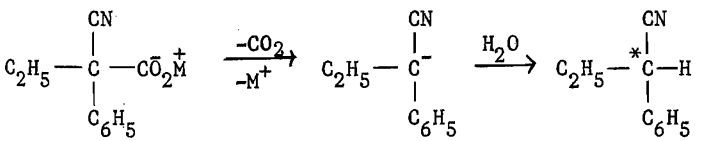
Carbanions

Donald J. Cram

Means of study of carbanions - SE_1 reaction

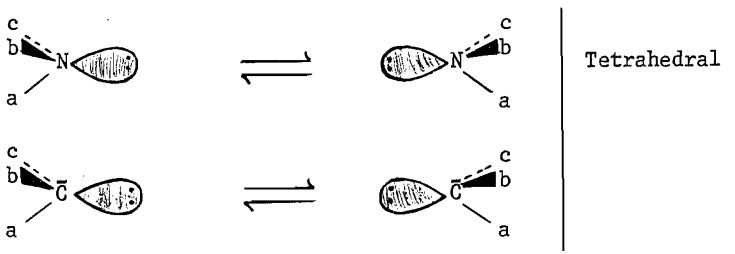


Example:

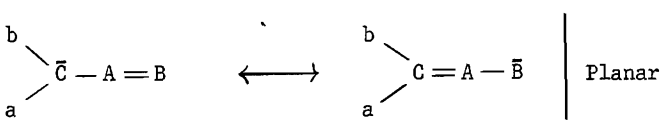


Carbanion structure (preconceptions)

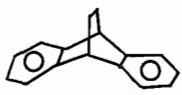
Charge localized - amine, carbanion analogy:



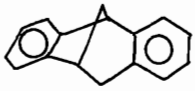
Charge delocalized:



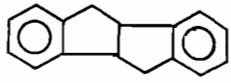
Dibenzobicyclooctadiene Ring Systems Involved in This Work



[2.2.2]

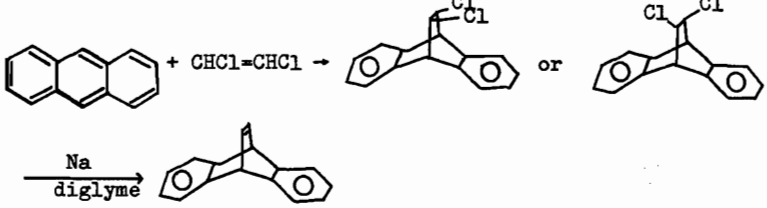


[3.2.1]



[3.3.0]

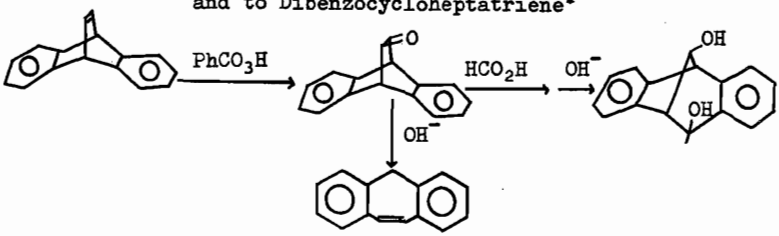
Preparation of [2.2.2] Compounds



S. J. Cristol and N. L. Hause, J. Am. Chem. Soc., 74, 2193 (1952)--modified.

Other [2.2.2] systems available from anthracene via Diels-Alder reactions.

* [2.2.2] Epoxide; Rearrangement of [2.2.2] to [3.2.1] Systems and to Dibenzocycloheptatriene*



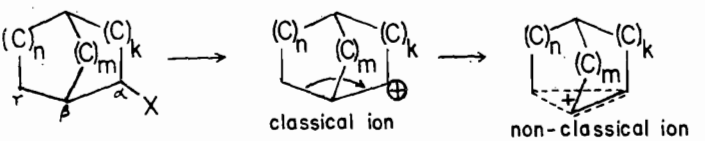
S. J. Cristol and R. K. Bly, J. Am. Chem. Soc., 82, 6155 (1960)

SOME RECENT ASPECTS OF MOLECULAR REARRANGEMENTS

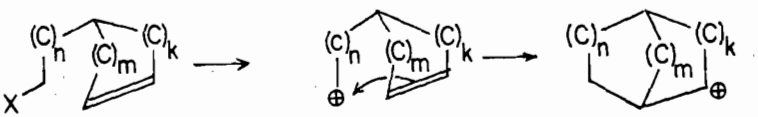
Jerome A. Berson, P. Reynolds-Warnhoff and David Willner

Methods of generating bicyclic carbonium ions:

SIGMA ROUTE



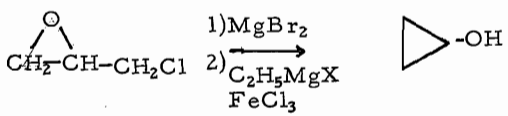
PI ROUTE



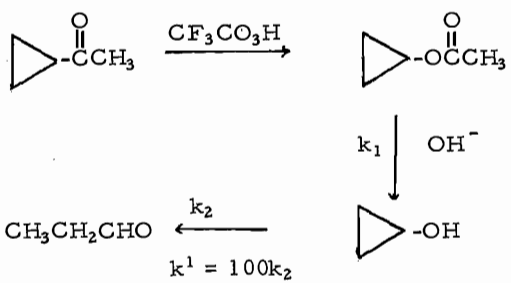
SYNTHESIS AND REARRANGEMENTS OF CYCLOPROPANOLS

C. H. DePuy

Cyclopropanol was first prepared, inadvertently, by Cottle and co-workers (JACS, 1942-3). It could not be prepared pure and it readily isomerized in base.



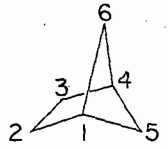
In an attempt to develop a more general synthetic route to substituted cyclopropanols, the hydrolysis of cyclopropyl acetate was investigated kinetically.



SOME RECENT ADVANCES IN THE CHEMISTRY OF STRAINED BICYCLIC SYSTEMS

Jerrold Meinwald

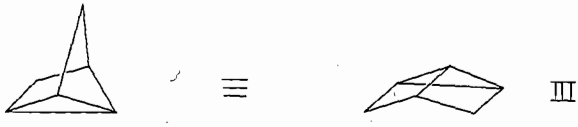
The bicyclo [2.1.1] hexane ring system (I) has been the subject of study in several laboratories in recent years (Büchi, Horner, Srinivasan, Wiberg). Current work at Cornell either



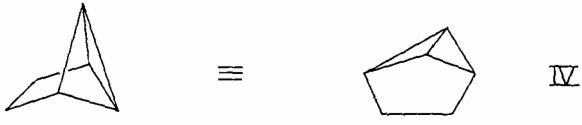
I

II

directly or indirectly related to this nucleus has involved (1) the synthesis and solvolysis of 2-substituted bicyclo-[2.1.1] hexanes, (2) synthetic approaches to bicyclo [2.1.1]-hexanes (II), including studies on nitrosylhalide olefin addition reactions, and (3) studies of the two possible tricyclic skeletons derivable from I, the tricyclo[$2.1.1.0^{2,5}$] hexanes (III) and the tricyclo[$2.1.1.0^{5,6}$] hexanes (IV).



III



IV

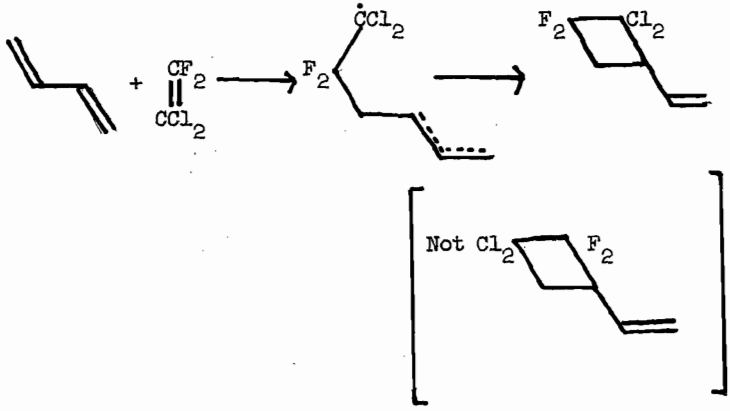
BIRADICAL INTERMEDIATES

Paul D. Bartlett

For the present purpose a biradical is defined as a molecular species having two uncoupled electrons confined to separate atoms or groups of atoms. This definition includes the trimethylene and tetramethylene biradicals, but excludes excited triplet anthracene and similar structures, where the uncoupled electrons are in molecular orbitals of different energies associated with the same group of atoms.

Involvement of biradicals in the 1,2-cycloaddition of fluorinated olefins to dienes (E. C. Coyner and H. S. Hillman, 1949) is supported by the following lines of evidence:

1 - Orientation is "head-to-head", where the "head" of each addend is that location which best accommodates an unpaired electron:



2 - Methyl and chlorine substituents in the diene both direct 1,2-cycloaddition as if they became preferentially 1- or 3-substituents in an allylic radical in the first step.

MECHANISMS OF SOLVOLYSIS OF PHOSPHATE ESTERS

F. H. Westheimer

I. Classification of mechanisms.

The solvolysis of phosphate esters may occur by any of several mechanisms. Although many interesting and important biochemical reactions (e. g., the condensation reactions of mevalonic pyrophosphate to polyisoprenoids) require carbon-oxygen cleavage, such processes are fundamentally similar to reactions of alkyl halides or sulfonates, and will not be further considered here. Reaction at phosphorus may be considered to proceed by either of two general mechanisms: either by way of a transition state (or intermediate) with five groups around phosphorus, or alternatively by way of an intermediate with only three groups around phosphorus. The tricovalent phosphorus compounds postulated for the latter mechanism comprise monomeric metaphosphoric acid, HPO_3, and its derivatives. None of these monomeric metaphosphates has yet been isolated; their assumed role in phosphorus chemistry (Todd, Proc. Nat. Acad. Sci., 45, 1389 (1959); Westheimer, 8th Special Publication of the Chemical Society, 1957, p. 1) resembles that of carbonium ions, or possibly of acylonium ions, in carbon chemistry. Specific examples of various mechanisms are considered below.

II. Bimolecular attack at phosphorus.

A. General base catalysis. Those reactions catalyzed by bases (as contrasted to lyate ions) may proceed either by direct nucleophilic attack on phosphorus or by attack of a base in the rate-limiting step on the solvent, to generate an incipient lyate ion. Such general-base catalysis was realized in the solvolysis of tetrabenzylpyrophosphate by propanol, in the presence of 2, 6-lutidine, where the solvent deuterium isotope effect is 3.1 (Dudek and Westheimer, J. Am. Chem. Soc., 81, 2641 (1959)).

$$(RO)_2PO.OPO(OR)_2 + PrOH \longrightarrow (RO)_2PO.OPr + (RO)_2PO_2H$$

Some Recent Studies on Amino Acids, Peptides and Proteins

Bernhard Witkop

Representative Example	Problem	Methodology
Amino Acids: $C_5H_9NO_3$ (131) trans-3-Hydroxy-L-proline cis-3-Hydroxy-L-proline	Isolation from Collagen, Marine Sponge and Telomycin Syntheses, Stereochemistry and Configuration	Selective {Nitrosation, Trinitrophenylation} Preparative Ion-Exchange Chromatography a) Stereospecific Hydroboration of 3,4-Dehydroproline b) Ring-synthesis from Aminomalonic acid and Glycine, Enzymatic Resolution
Peptides: $C_{98}H_{140}N_{20}O_{16}$ (1854) "Valine-Gramicidin A" "Isoleucine-Gramicidin A" "Gramicidin-B" and "C"	Homogeneity, Association, Molecular Weight, Primary and Secondary Structure ortho-Peptide (Cyclol) Arrangement of Aminoethanol Bridge	Thin Layer and Column Chromatography, Polarimetry, Rotatory Dispersion, Ultracentrifuge Nonenzymatic Methods for Preferential and Selective Peptide Cleavage
Proteins: $C_{575}H_{901}N_{171}O_{193}S_{12}$ (13,676.344) Bovine Pancreatic Ribonuclease	Primary Structure: Nonenzymatic cleavage, active or labile fragments, auditing sequences	Cyanogen bromide, N-Bromosuccinimide, Electrolytic cleavage, Sephadex Gel Filtration
	Secondary Structure: How and to what extent does primary structure control secondary and tertiary structure?	Inactivation by reduction, activation by reoxidation of native and modified enzyme
	Tertiary Structure: Chemical probes for tertiary structure	Establishment of vicinal relations to groups between peptide strands by bifunctional reagents Differential reactivity of groups as a function of accessibility Recombination of inactive fragments to active enzymes

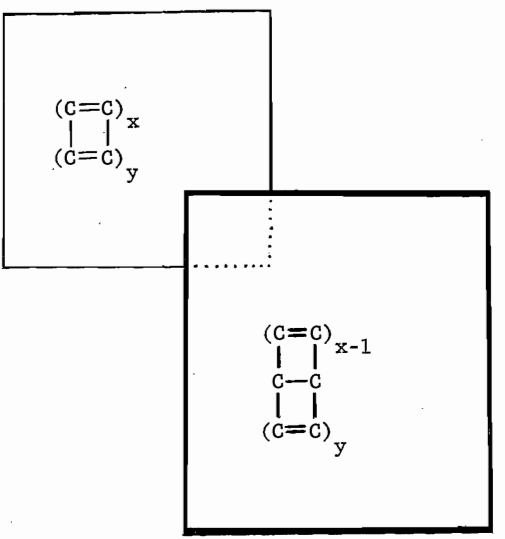
Recent Developments in Synthetic Organic Chemistry:

VALENCE BOND ISOMERS

of

CYCLIC 4n + 2 π-ELECTRON SYSTEMS

E. E. van TAMELEN



....x + y = 2n + 1.....

NEW DIRECTIONS IN CONFORMATIONAL ANALYSIS

Kurt Mislow

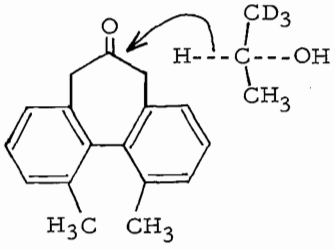
Cyclohexane, norbornane, and closely similar (or derived) structural arrays have proven their versatility in problems of conformational analysis. The system of polycyclic bridged biphenyls possesses features which permit departures from studies in the conventional mode. The present discussion touches on developments in three areas of major interest where this system has played a key role.

On the importance of steric isotope effects

(with A. J. Gordon, R. Graeve, R. E. O'Brien, H. Schaefer, G. H. Wahl, Jr.)

Rival hypotheses have served to account for numerous secondary deuterium isotope effects: the effects may be chiefly hyperconjugative (cf. V. Shiner, Tetrahedron, 5, 243 (1959)) or steric (cf. L. S. Bartell, J. Am. Chem. Soc., 83, 3567 (1961)) in origin. Attempts have been made to separate these factors and to remove some of the ambiguity.

1. Asymmetric hydride transfer (J. Am. Chem. Soc., 84, 1940 (1962)).



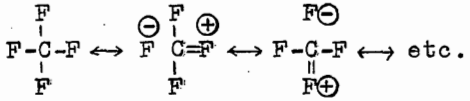
Result: $\frac{k_R}{k_S} = 1.000$

Conclusion: a) negligible difference in "bulk" of $-CH_3$ and $-CD_3$ and/or b) test is not sufficiently sensitive.

DOUBLE BOND-NO BOND RESONANCE

Jack Hine

L. O. Brockway, in 1937, suggested the following type of resonance,



which will be referred to as double bond-no bond (DB-NB) resonance, to explain the shortened carbon-fluorine bond distances observed in several methane derivatives with more than one fluorine atom attached to the same carbon atom. Subsequently, the relatively stable character of a number of compounds with several fluorine atoms attached to the same carbon atom has been explained in terms of such resonance. Only rarely has DB-NB resonance been considered for fluorine-free compounds, however. Some of the data on fluorine compounds that have been explained in terms of DB-NB resonance will be discussed. The relative importance that would be expected of such resonance in various types of fluorine-free compounds will be considered and data that may be interpreted in terms of DB-NB resonance in such compounds (particularly those with more than one oxygen atom attached to the same carbon atom) will be described.

From the carbon-fluorine bond energies in methyl fluoride, methylene fluoride, fluoroform, and carbon tetrafluoride (107, 109.6, 114.6, and 116 kcal/mole, respectively), the latter three compounds may be said to be stabilized by 5.2, 22.8, and 36 kcal/mole, respectively. This corresponds to about 3.2 kcal per DB-NB resonance structure or 6.4 kcal per fluorine-fluorine interaction. According to Pitzer's calculations these fluorine-fluorine interactions are too strong to be explained in terms of electron-correlation energies (London forces). Destabilization would be expected to result from ordinary polar interactions or steric repulsions between geminate fluorine atoms.

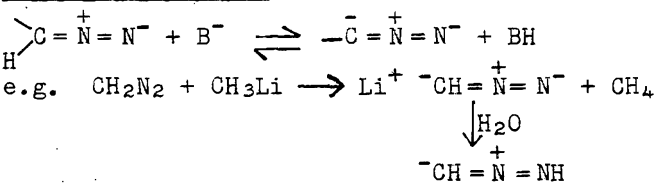
Swarts' synthesis of trifluoroacetic acid by the oxidation of benzotrifluoride (1922) provided one of the earliest illustrations of the stability of trifluoromethyl groups. Henne has provided much additional evidence for the stability of trifluoro-

CHEMISTRY OF α-DIAZO KETONES

Peter Yates

Primary Reactions of Aliphatic Diazo Compounds with Nucleophiles

I Proton Abstraction



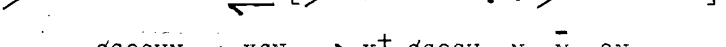
e.g. $CH_2N_2 + CH_3Li \longrightarrow Li^+ {}^-CH=\overset{+}{N}=N^- + CH_4$

$\downarrow H_2O$

${}^-CH=\overset{+}{N}=NH$

[E. Müller and W. Rundel, Chem. Ber., 88, 917 (1955)]

II Addition (i) terminal addition



e.g. $\emptyset COCHN_2 + KCN \longrightarrow K^+ \emptyset COCH=N-\bar{N}-CN$

$\downarrow H_3O^+$

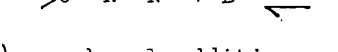
$\emptyset COCH=NNHCN$

[L. Wolff, Ann., 325, 129, (1902)]

$\emptyset_2CN_2 + \emptyset_3P \longrightarrow \emptyset_2C=N-\bar{N}-\overset{+}{P}\emptyset_3$

[H. Staudinger and J. Meyer, Helv. Chim. Acta, 2, 619 (1919)]

(ii) C-addition



(iii) carbonyl addition