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SIXTEENTH NATIONAL ORGANIC
CHEMISTRY SYMPOSIUM
of the
AMERICAN CHEMICAL SOCIETY.

Division of Organic Chemistry

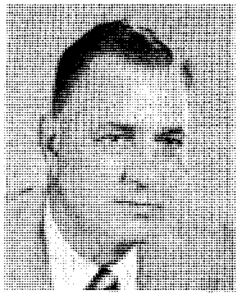
★

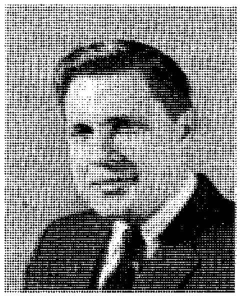
Headquarters and Registration: Men's Residence Hall
(Terry Hall), University of Washington
Sunday, June 14, Noon to Midnight
Monday, June 15, 8:00 a.m. to 8:00 p.m.
Tuesday, June 16, 8:00 a.m. to 8:00 p.m.
Wednesday, June 17, 8:00 a.m. to 3:00 p.m.

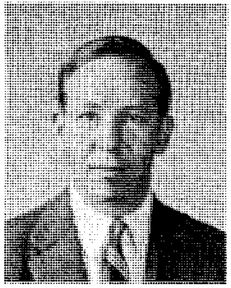
Meetings: Meany Hall

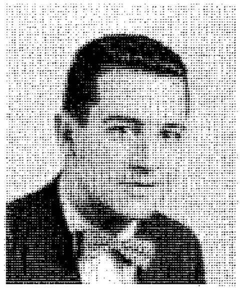
Speakers at the Sixteenth National Organic Chemistry Symposium


P. D. Bartlett


A. T. Blomquist

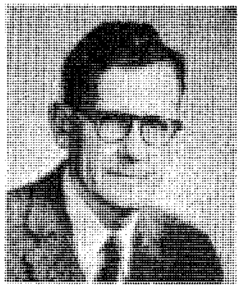

V. Boekelheide


G. Büchi


E. J. Corey

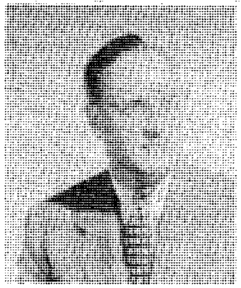

W. von E. Doering

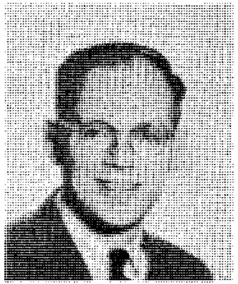

M. S. Newman


J. D. Roberts


G. Stork


A. Streitwieser, Jr.


C. Walling


K. B. Wiberg

Program

Monday, June 15

10:00 a.m.	Welcome. CHARLES ODEGAARD, President, University of Washington Response. KARL FOLKERS, Chairman, Division of Organic Chemistry, A.C.S.
10:30 a.m.	JOHN D. ROBERTS. Rearrangement Reactions of Small-Ring Compounds.
11:30 a.m.	Discussion of Paper 1.
2:00 p.m.	ALFRED T. BLOMQUIST. The Cyclobutadiene Problem.
3:00 p.m.	Discussion of Paper 2.
3:30 p.m.	WILLIAM von E. DOERING. A Few Non-Benzenoid Aromatic Hydrocarbons.
4:30 p.m.	Discussion of Paper 3.
8:00 p.m.	VIRGIL BOEKELHEIDE. Aromatic Character in Polycyclic Molecules.
9:00 p.m.	Discussion of Paper 4.

Tuesday, June 16

9:00 a.m.	MELVIN S. NEWMAN. Reactions of Phenols with Polychlorinated Compounds and Chemistry of the Resulting Products.
10:00 a.m.	Discussion of Paper 5.
10:30 a.m.	GILBERT STORK. Enamines as Synthetic Tools.
11:30 a.m.	Discussion of Paper 6.
2:00 p.m.	GEORGE BÜCHI. The Structure of Ulein.
3:00 p.m.	Discussion of Paper 7.
3:30 p.m.	E. J. COREY. The Mechanism of Oxidation of Ketones by Selenium Dioxide.
4:30 p.m.	Discussion of Paper 8.
8:00 p.m.	Awarding of the Roger Adams Medal to ROGER ADAMS and the Roger Adams Medal and Prize to D. H. R. BARTON.
8:15 p.m.	D. H. R. BARTON. Roger Adams Medal Award Address. Photochemical Rearrangements.
9:30 p.m.	SOCIAL HOUR.

Wednesday, June 17

9:00 a.m.	ANDREW STREITWIESER, JR. Base-Catalyzed Hydrogen-Deuterium Exchange in Hydrocarbons.
10:00 a.m.	Discussion of Paper 9.
10:30 a.m.	CHEVES WALLING. Recent Developments in Free-Radical Chemistry.
11:30 a.m.	Discussion of Paper 10.
2:00 p.m.	PAUL D. BARTLETT. The Oxygen-Oxygen Bond.
3:00 p.m.	Discussion of Paper 11.
3:30 p.m.	KENNETH B. WIBERG. The Mechanisms of Some Chromic Acid Oxidations.
4:30 p.m.	Discussion of Paper 12.

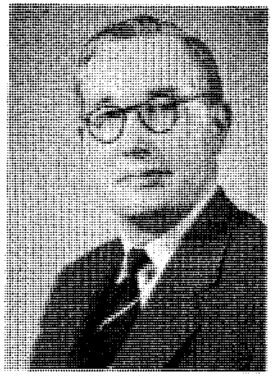
THE ROGER ADAMS AWARD IN ORGANIC CHEMISTRY

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 new 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*. Professor Adams will receive the first impression of the Roger Adams Medal.

The award committee has chosen Professor D. H. R. Barton, of Imperial College, London, as the first recipient of the Roger Adams Award in Organic Chemistry. His award address is entitled "Photochemical Rearrangements."

Roger Adams



D. H. R. Barton

Seattle Committees

* * *

The University of Washington and the Puget Sound Section of the American Chemical Society are acting as hosts

Committees in Charge

General	K. B. Wiberg
Housing	A. G. Anderson and S. G. Powell
Registration	H. J. Dauben, Jr., and W. C. McCarthy
Local Arrangements	W. M. Schubert and A. C. Huitric
Transportation	G. H. Stout
Chairman, Puget Sound Section	R. M. Way

Division of Organic Chemistry

The plans and program of the Sixteenth 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.

	1957-1958	1958-1959
Chairman	Melvin S. Newman	Karl Folkers
Chairman-Elect	Karl Folkers	John C. Sheehan
Secretary	William E. Parham	William E. Parham
National Symposium Officer	Stanley J. Cristol	Stanley J. Cristol
	Alfred T. Blomquist	Alfred T. Blomquist
	Donald J. Cram	Marshall Gates
	David Y. Curtin	William E. Truce

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:

WILLIAM E. PARHAM, Secretary
Organic Division, A.C.S.
Department of Chemistry
University of Minnesota
Minneapolis, Minnesota

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

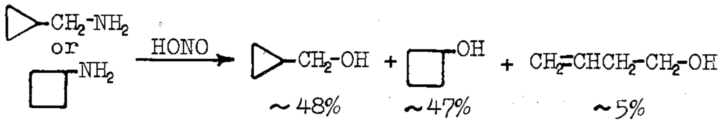
REARRANGEMENT REACTIONS OF SMALL-RING COMPOUNDS

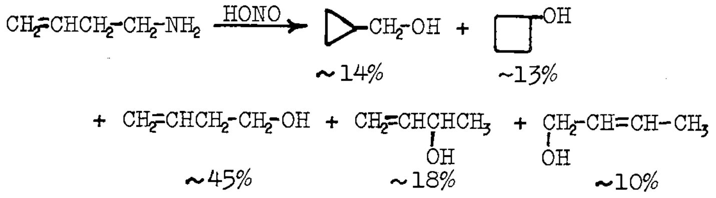
John D. Roberts

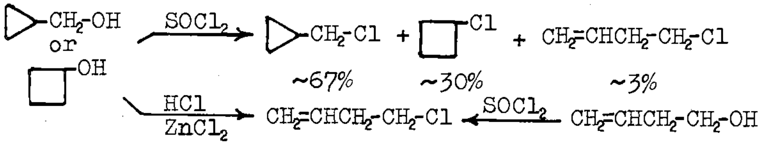
Cyclopropylcarbinyl, cyclobutyl and allylcarbinyl derivatives often undergo interconversion reactions under exceptionally mild conditions in carbonium ion, carbanion and free-radical type reactions. This talk will be primarily concerned with some attempts to correlate and predict the occurence and course of such rearrangements. Only a few simple types of reactions will be discussed. Lack of time will preclude mention or evaluation of most of the contributions of other workers in the field.

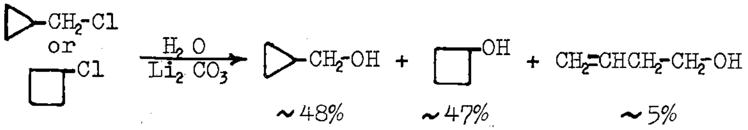
Typical Experimental Observations (MAZUR)

J. Am. Chem. Soc., 73, 2509 (1951)

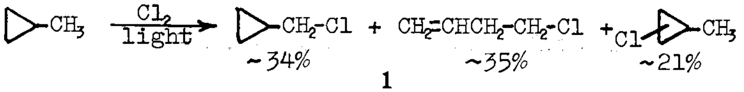


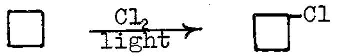


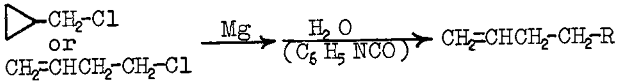


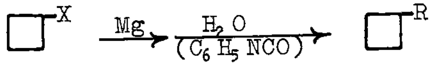


$CH_2{=}CHCH_2{-}CH_2{-}Cl \xrightarrow{H_2O}$ very slow reaction







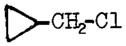
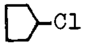
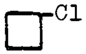
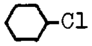
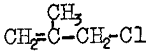


Cason, MAZUR

No skeletal changes have so far been observed in Hofmann, Curtius, Schmidt, Criegee, etc. reactions with cyclopropylcarbinyl and cyclobutyl derivatives.

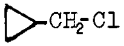
Carbonium ion-type reactions generally give the greatest degree of interconversion of the three radicals. Customarily, relative ease of carbonium ion formation is inferred from solvolysis in ionizing solvents.

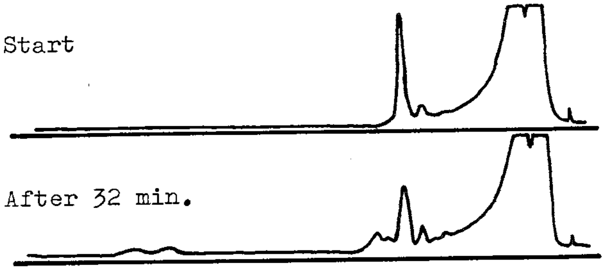
Relative Solvolysis Rates in 50% Ethanol (50°)

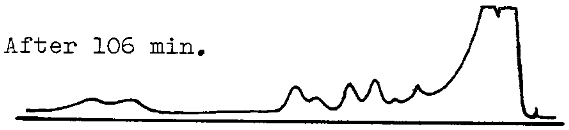
	63		(1)[a]
	3		~0.02[a]
$CH_2{=}CHCH_2{-}CH_2{-}Cl$	≳ 0.005[a]	 $CH_2{=}\overset{CH_3}{C}{-}CH_2{-}Cl$	2

[a] Extrapolated from data at higher temperatures

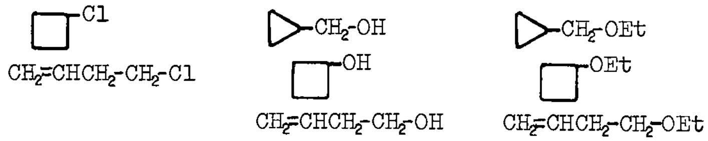
The falloff of the solvolysis rate curve of cyclopropylcarbinyl chloride (99+% pure by VPC) is associated with formation of cyclobutyl and allylcarbinyl chlorides by rearrangement.

Analysis (VPC) of Solvolysis Products of  (94% pure) in 80% EtOH, 97°

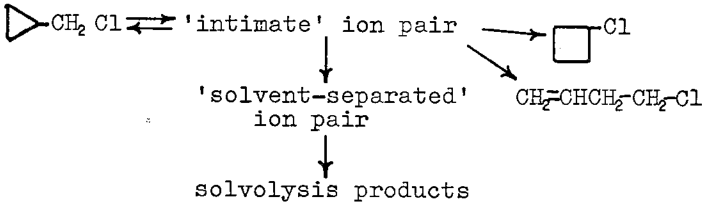


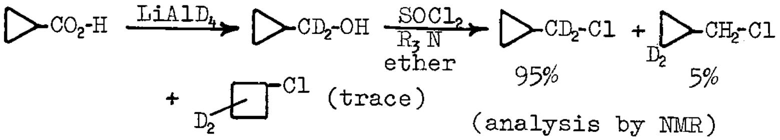


Substances formed:



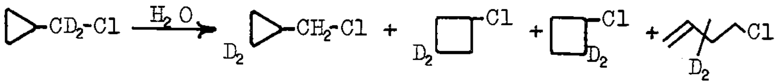
GRAHAM





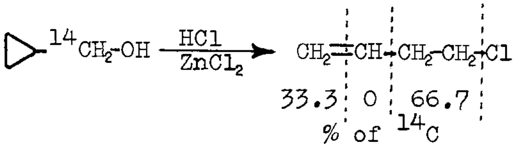
$$CH_2{=}CH{-}\underset{OH}{\overset{*}{C}H}{-}CH_3 \xrightarrow[\text{R}_3\text{N ether}]{\text{SOCl}_2} CH_2{=}CH{-}\underset{Cl}{\overset{*}{C}H}{-}CH_3$$

clean inversion
no rearrangement



No apparent rearrangement in the absence of ionizing agents.

CASERIO



$CH_2{=}CHCH_2{-}CH_2{-}Cl + HCl^* \xrightarrow{ZnCl_2^*} \!\!\!\!\!\!/\!\!/\;\; CH_2{=}CHCH_2{-}CH_2{-}Cl^*$

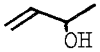
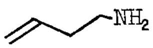
MAZUR

Amine-nitrous acid reactions as non-reversible carbonium ion-type reactions.

$$RNH_2 + HONO\ (N_2O_3) \longrightarrow R\text{-}NH\text{-}N{=}O \longrightarrow R\text{-}N{=}N\text{-}OH$$

$$\xrightarrow{H^+} R\text{-}N{\equiv}N^+ \longrightarrow R^+ + N_2 \longrightarrow ROH \text{ etc.}$$

Product Compositions by VPC (± 1%)

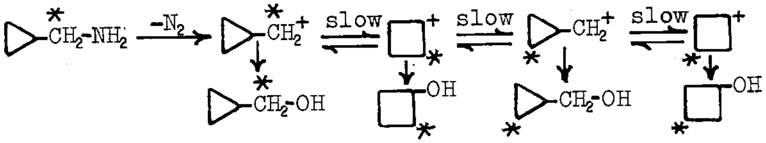
	▷-CH$_2$-OH	□-OH			
▷-CH$_2$-NH$_2$	56	40	4	-	-
□-NH$_2$	51	45	4	-	-
	15.5	13.5	42	22	7.5

RENK

% of ^{14}C

▷-^{14}CH$_2$-NH$_2$	48.3	0	53.2	28.1	71.6	0
CH$_2$=CHCH$_2$-^{14}CH$_2$-NH$_2$	70.3	0	29.7	36.8	63.2	0

MAZUR, LEE, SEMENOW, WHITE, RENK



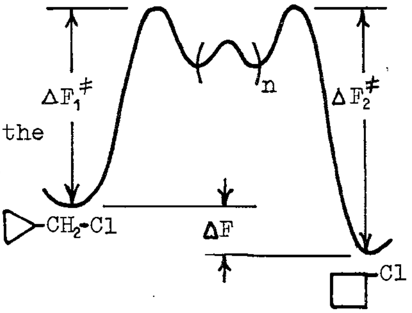
The isotopic tracer results alone do not rule out the above sequence of equilibrating 'classical' ions. However, classical formulations of the intermediates do not account for the abnormal solvolytic reactivities nor the ease of interconversion which the ions possess.

Solvolysis rates ▷-CH$_2$-Cl/□-Cl = 33/1

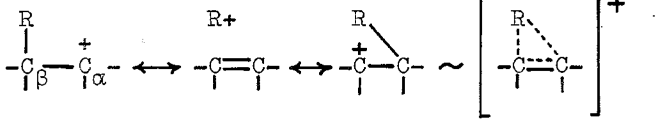
Thermodynamic stabilities ▷-CH$_2$-Cl/□-Cl = 1/36

$$\Delta F_2^{\ne} \approx \Delta F_1^{\ne} + \Delta F$$

n = 0 to ∞ depending on the number of intermediates involved.

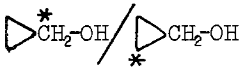
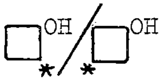
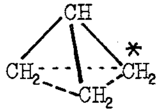
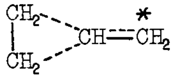
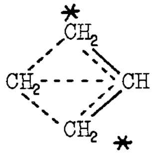
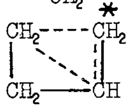


Stabilization of cationic centers by bonding electrons of adjacent R groups.



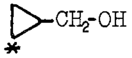
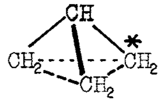
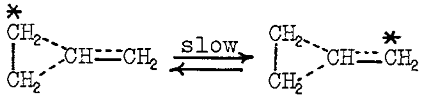
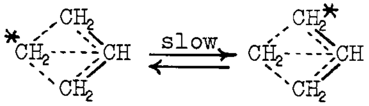
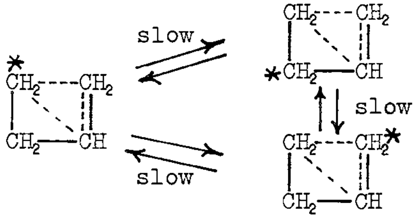
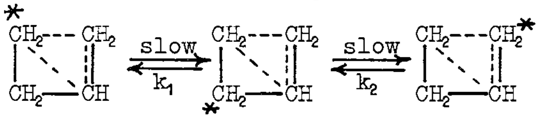
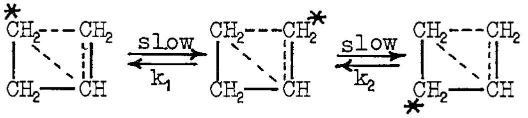
where R can be symmetrically or unsymmetrically located with respect to C_α and C_β.

Possible Stabilized Intermediates and Consequences Thereof.

Symmetry	Structure of first-formed cation	Expected from ▷-$\overset{*}{C}$H$_2$-NH$_2$	
			
3-fold axis		1 : 2	2 : 1
plane		1 : 0	1 : 0
plane		1 : 1	1 : 0
none		1 : 0	1 : 0

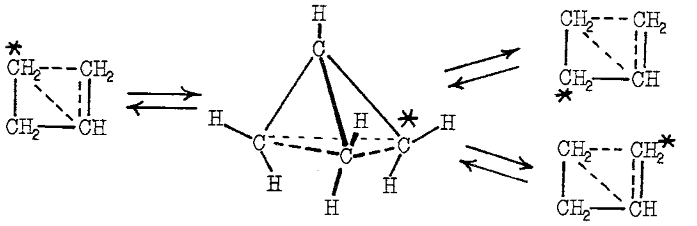
Possible Interconversion Reactions of Cations and Consequences Thereof Starting from $CH_2{=}CHCH_2\text{-}C^*H_2\text{-}NH_2$

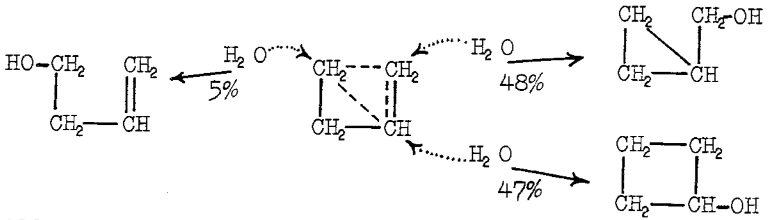
The cyclobutanol formed had 63.2% of the label in the 2-position. This figure was used to compute the % of ring label in the cyclopropylcarbinol produced in the same reaction as a function of the structures and possible interconversion paths of the intermediates.

Sequence of Intermediates	Calcd. % of 
	xx
	73.6
	68.4
	68.4
	73.6[a]-68.4[b]
	63.2[a]-68.4[b]
EXPERIMENT	70.3

[a] If $k_1 >> k_2$. [b] If $k_1 << k_2$.

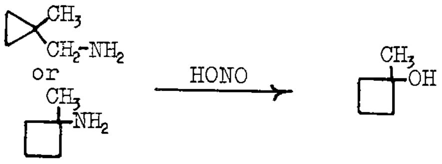
Favored but not established rearrangement path.

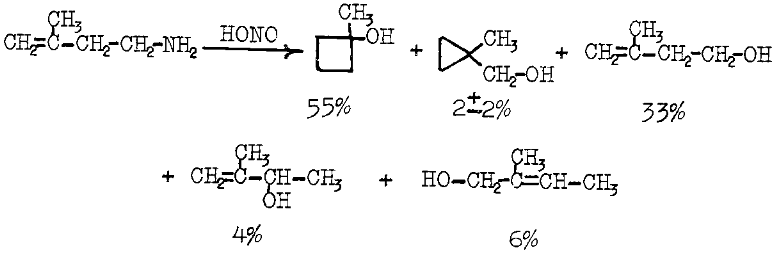


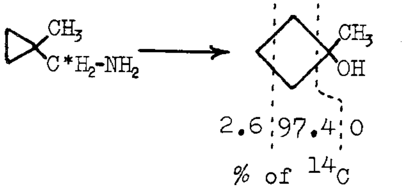


Allylcarbinol formation from cyclopropylcarbinyl- and cyclobutylamines does not arise from the allylcarbinyl cation since no hydrogen migrations are noted of the type found with allycarbinylamine.

Effects of Methyl Substitution

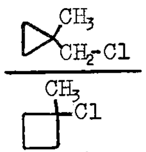




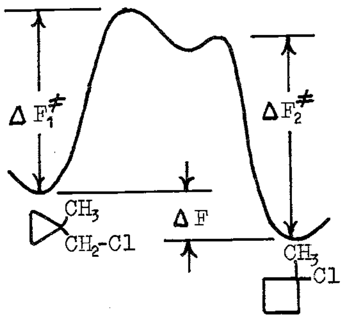


COX

Solvolysis rates



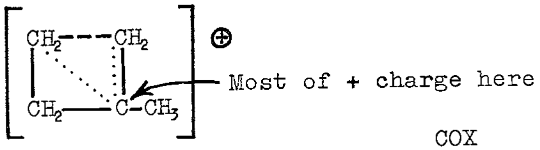
= 9.7 (50°)



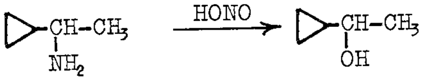
$\Delta F_1^{\neq} + \Delta F > \Delta F_2^{\neq}$

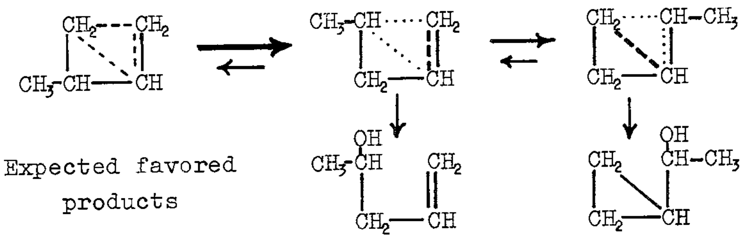
(assuming CH_3 group has no effect on ΔF)

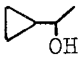
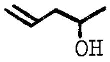
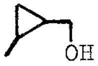
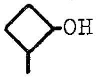
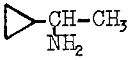
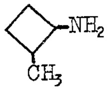
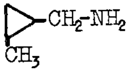
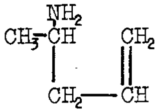
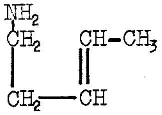
Preferred formulation of the intermediate



COX



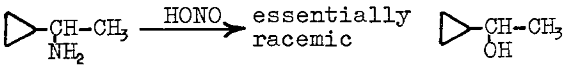


					
	100	0	0	0	0
	100	0	0	0	0
	51	35	13	0	0
	47	39	9	0	5
	17^a	49^a	$3?^a$	0	0
	74^a	0	0	0	0

[a] Plus hydrogen-shift products (allylic alcohols).

SILVER

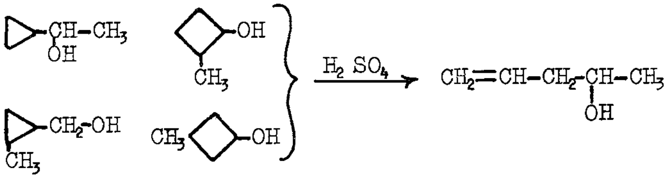
Opt. active

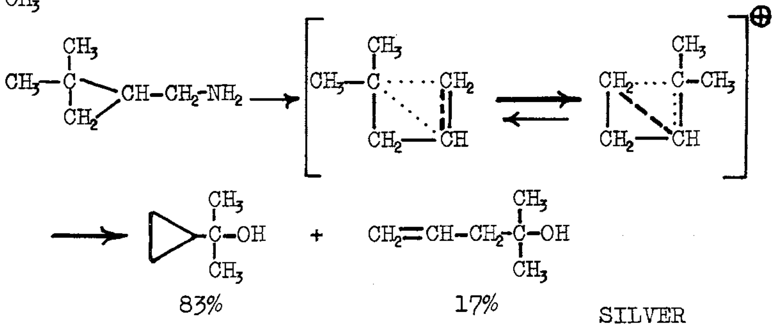


Speaks for equilibration by way of a symmetrical ion.

VOGEL

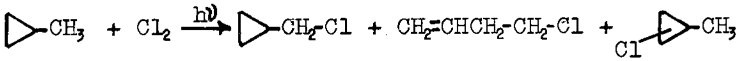
Reversible conditions

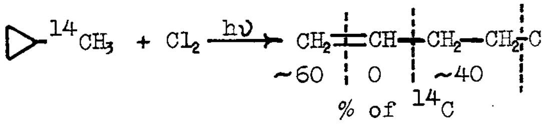




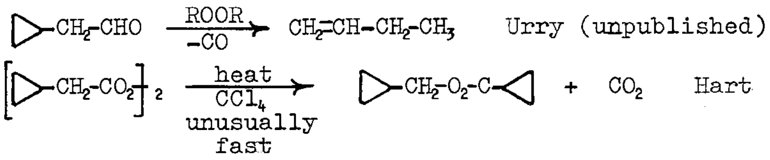
SILVER

Free-radical Reactions





preliminary results, MAZUR

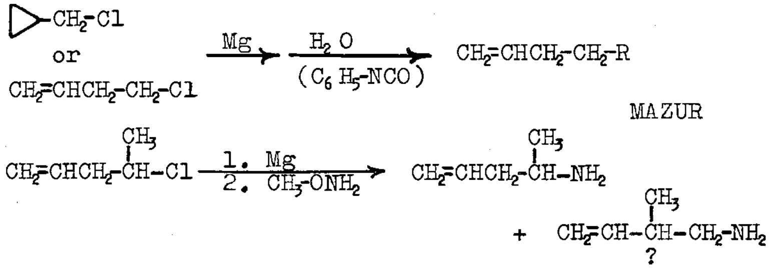


Urry (unpublished)

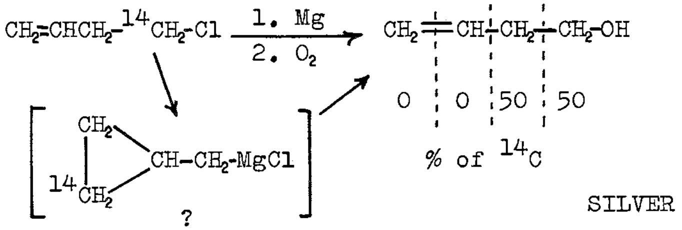
Hart

Carbanion-type Reactions .

Cyclobutyl halides give apparently normal Grignard reagents.

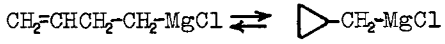


MAZUR



SILVER

However, the NMR spectrum of the Grignard reagent proves it to be allylcarbinylmagnesium chloride. Furthermore, the following equilibrium is not established rapidly (>0.01 sec.).



NORDLANDER, RÜCHARDT

$(C_6H_5-)_2C{=}CH-CH_2-CH_2-Cl \xrightarrow[2.\ CO_2]{1.\ Mg} (C_6H_5-)_2C{=}CH-CH_2-CH_2-CO_2H$

HOWDEN

R. H. Mazur
V. C. Chambers
C. C. Lee
H. E. Rice
E. F. Cox

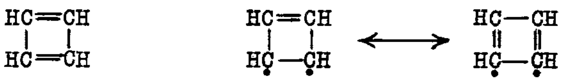
W. N. White
D. A. Semenow
M. S. Silver
E. Renk
W. H. Graham

M. C. Caserio
M. Vogel
J. E. Nordlander
C. Rüchardt
M. E. H. Howden

THE CYCLOBUTADIENE PROBLEM

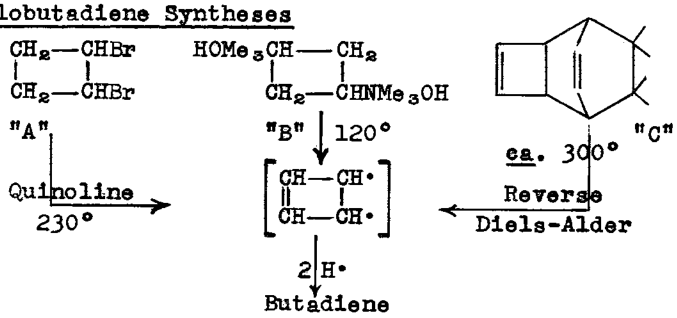
Alfred T. Blomquist

Structure of Cyclobutadiene



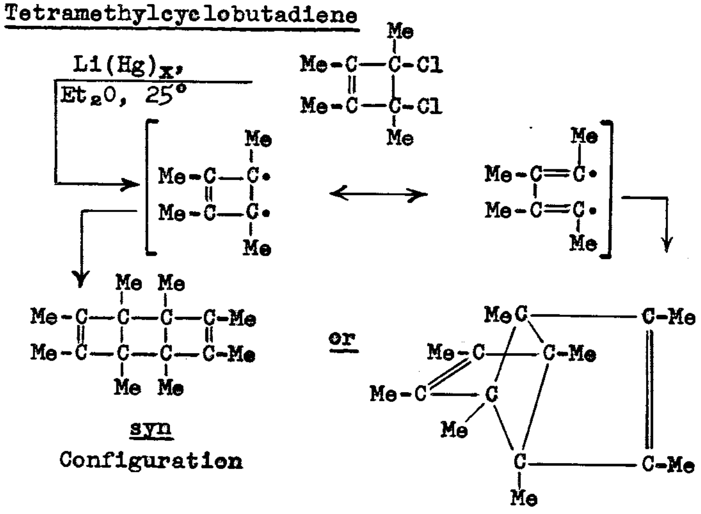
Classical and Biradical Structures

Cyclobutadiene Syntheses



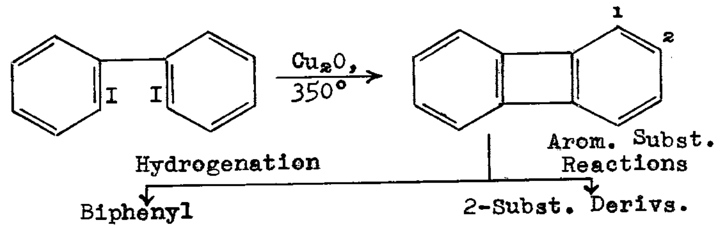
"A"-Willstätter and von Schmaedel, Ber. (1905).
"B", "C"-Nenitzescu and coworkers, Chem. Ber. (1957).

Tetramethylcyclobutadiene



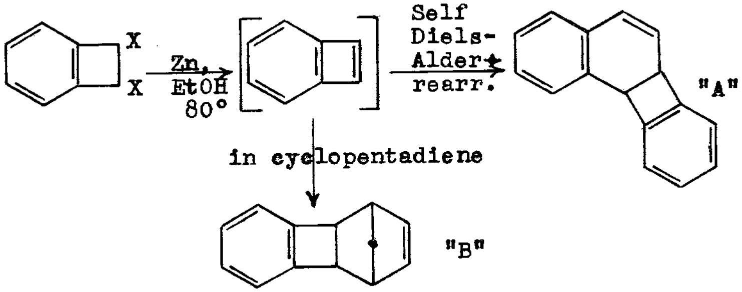
Criegee and Louis, Chem. Ber., 90, 417 (1957).

Diphenylene and Related Hydrocarbons



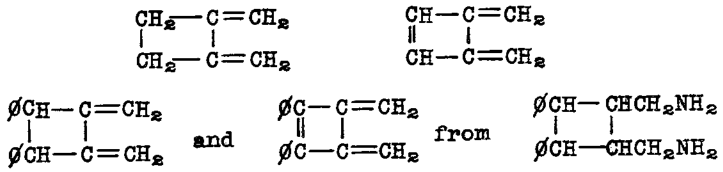
Lothrop, JACS, (1941); Baker, McOmie, "Symposium Paper", Chem. Soc., London (1958); Cava *et al.*, JACS, (1955) *et seq.*

Benzocyclobutadiene

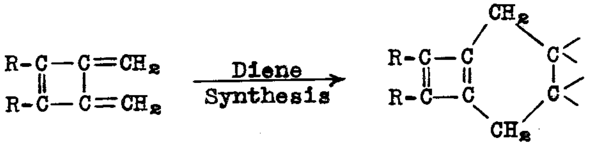


"A"-Cava and coworkers, *vide ante*
"B"-Nenitzescu and coworkers, *Chem. Ber.*, (1957)

Dimethylenecyclobutenes and Related Hydrocarbons

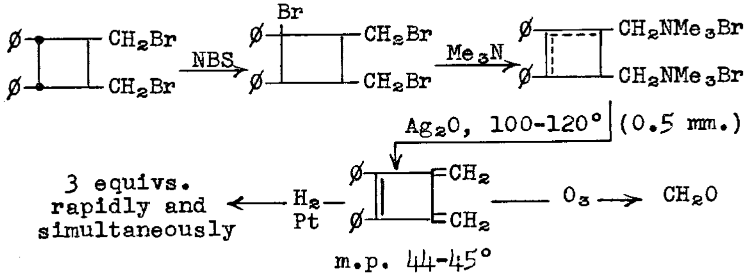


With Joseph A. Verdol and Yvonne C. Meinwald, J. Am. Chem. Soc., (1955-1959)



Diphenyldimethylenecyclobutene

Synthesis



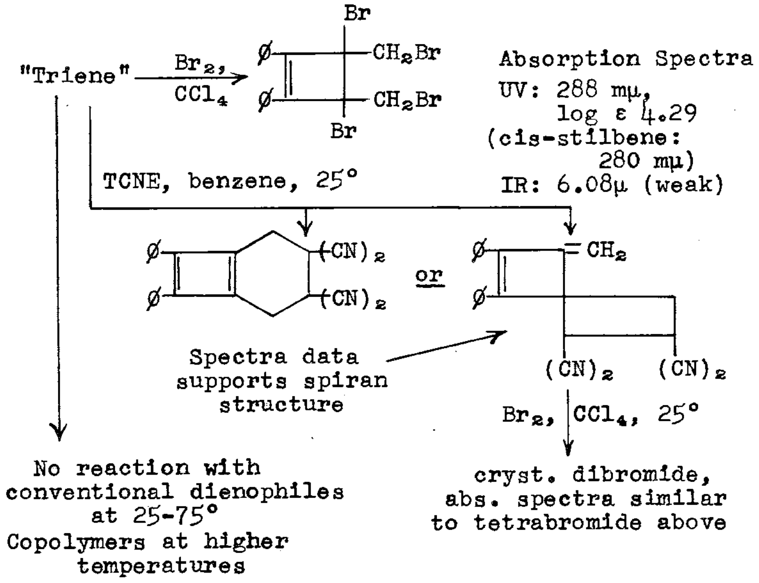
m.p. 44-45°

Colorless, rel. stable at 0° under N_2

Properties

Ultraviolet Absorption
237 mμ, log ε 4.42
262 mμ, log ε 4.50
328 mμ, log ε 4.20

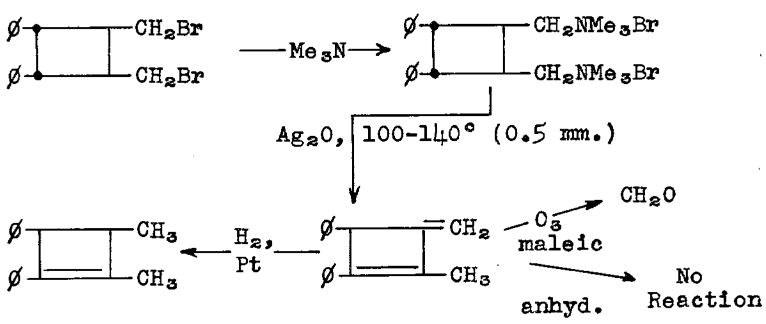
Infrared Absorption
3.29, 5.89 and 11.65μ, =CH_2
3.34, and 6.33μ, C_6H_5-
6.10μ, *cis*-ØCR=CRØ



Absorption Spectra
UV: 288 mμ, log ε 4.29
(cis-stilbene: 280 mμ)
IR: 6.08μ (weak)

3-Methylene-1,4-diphenyl-2-methylcyclobutene (Diene "A")

Synthesis



m.p. 62-64°
Colorless

Properties

Absorption Spectra
IR: 5.97 and 11.60μ
UV: 292 mμ, log ε 4.43
302 mμ, log ε 4.40
316.5 mμ, log ε 4.12 shoulder

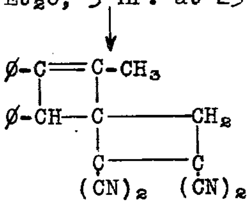
Model Compounds
ØCH=CH-CH=CH₂
λmax 280 mμ

IR: 5.99 and 11.6μ

UV: 291 mμ

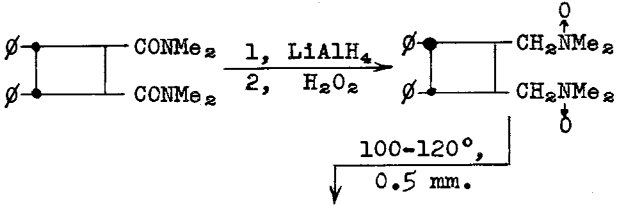
Diene "A" and TCNE
in Et₂O, 3 hr. at 25°

m.p. 139-140°

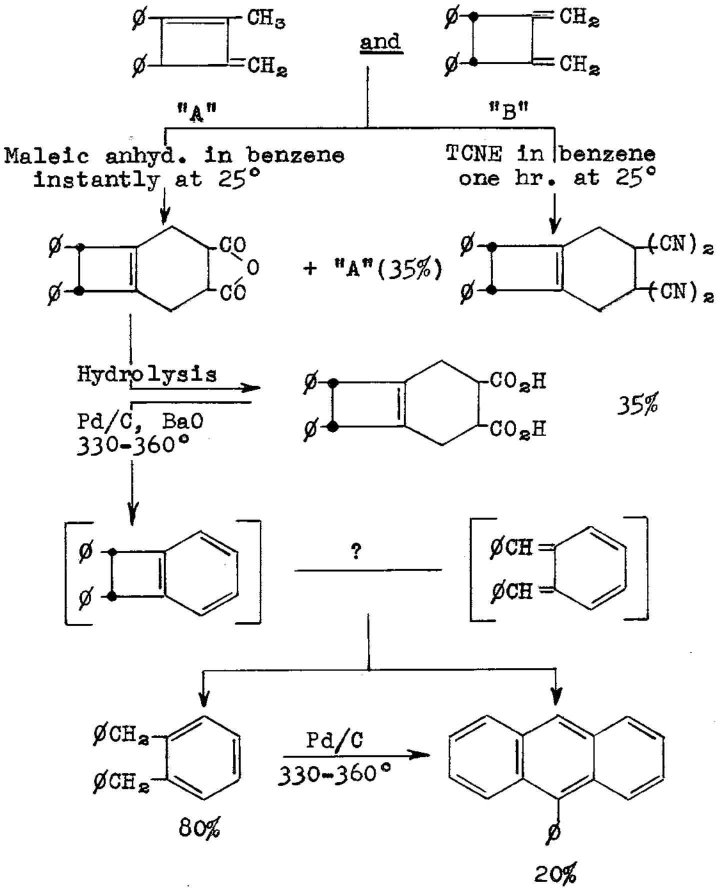


λmax 265 mμ
log ε 4.33

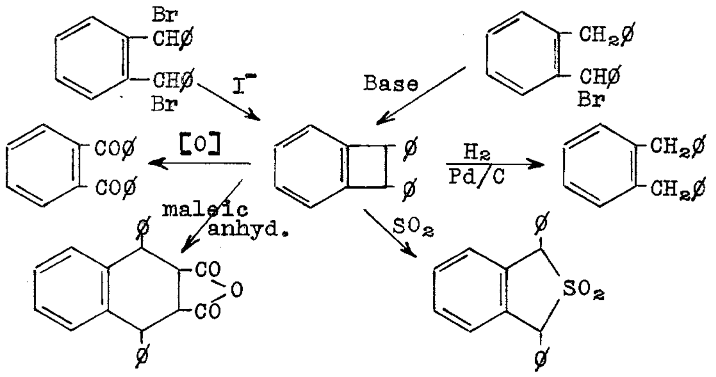
1,2-Dimethylene-3,4-diphenylcyclobutane (Diene "B")



Colorless liquid pyrolyzate: IR similar to diene "A" but also band at 11.30μ



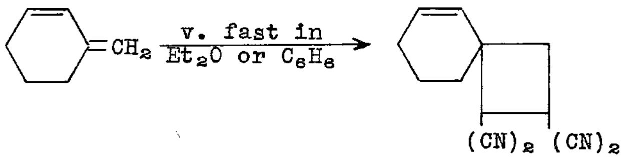
1,2-Diphenylbenzocyclobutene



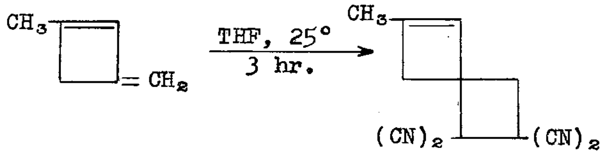
Jensen and Coleman, JACS, (1958)

1,2-Cycloadditions of TCNE

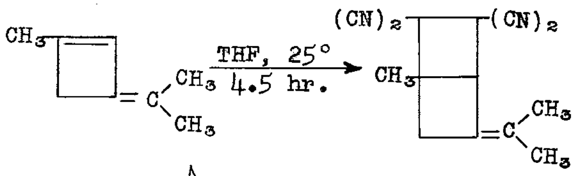
a,



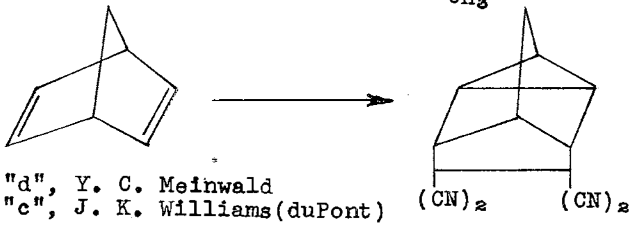
b,



c,

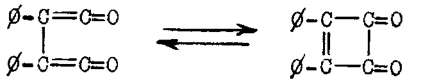


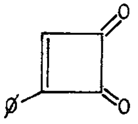
d,



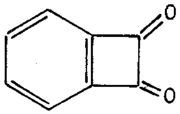
"a" and "d", Y. C. Meinwald
"b" and "c", J. K. Williams(duPont)

Diphenylcyclobutadienoquinone

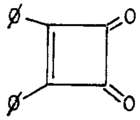




Smutny
and
Roberts



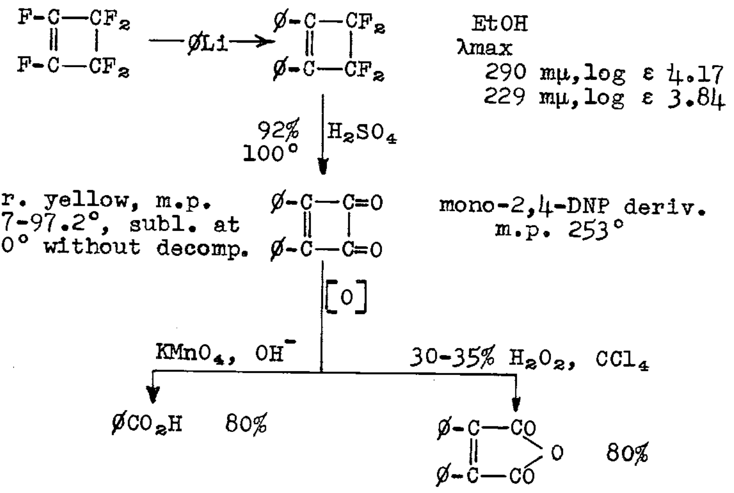
Cava
and
Napier



This Report
(La Lancette)

Smutny and Roberts, JACS., 77, 3420 (1955)
Cava and Napier, ibid., 79, 3606 (1957)
Blomquist and La Lancette, ACS, Boston Meeting, 1959

Synthesis



EtOH
λmax
290 mμ, log ε 4.17
229 mμ, log ε 3.84

br. yellow, m.p. 97-97.2°, subl. at 90° without decomp.

mono-2,4-DNP deriv.
m.p. 253°

Spectral Properties

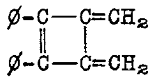
Infrared: 5,60, 5.63μ (doublet); 5.68μ (shoulder)

Ultraviolet:

EtOH λ_{max}
238mμ, log ε 3.86
265mμ, log ε 4.06
320mμ, log ε 4.17
410mμ, log ε 2.21

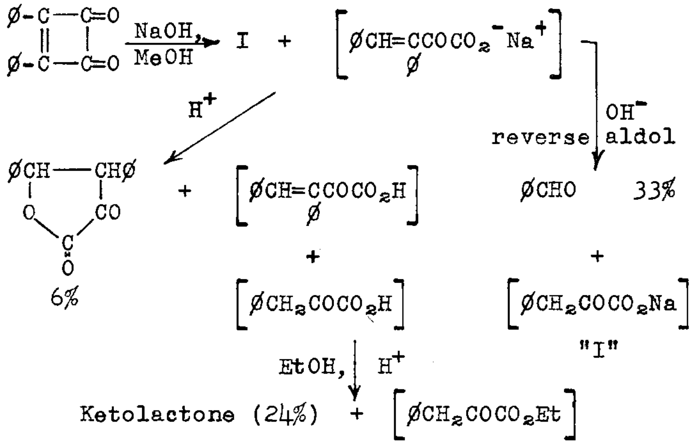
CCl_4 λ_{max}
264mμ, log ε 4.31
320mμ, log ε 4.46
400mμ, log ε 2.48

Model Compound

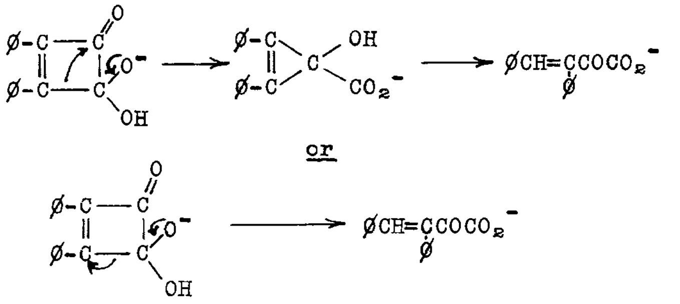


isoöctane λ_{max}
237mμ, log ε 4.42
262mμ, log ε 4.50
328mμ, log ε 4.20

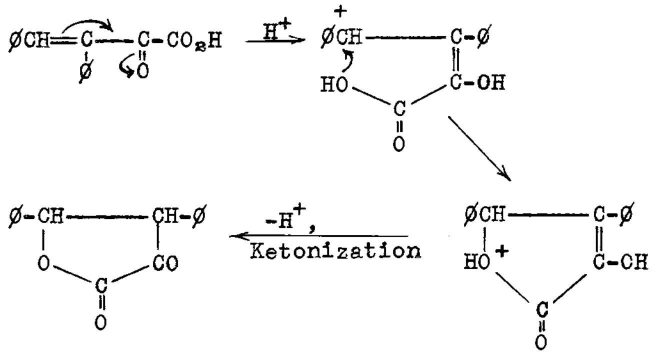
Base Opening



Mechanism (cf. SkattebØl and Roberts, JACS., (1958))

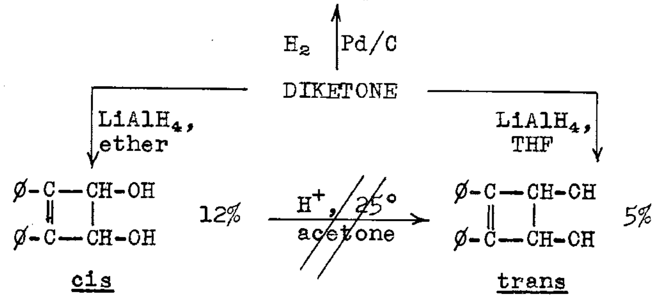


Ketolactone Formation



Reduction of Diketone

Product IR: 2.90, 5.65 and 5.98μ
40% of one equiv. abs.



cis m.p. 135-135.5°

trans m.p. 183-184.5°

Ultraviolet maxima in EtOH

cis	trans
239 mμ (4.27)	238 mμ (4.20)
294 mμ (4.14)	292 mμ (4.10)

log ε's in parentheses

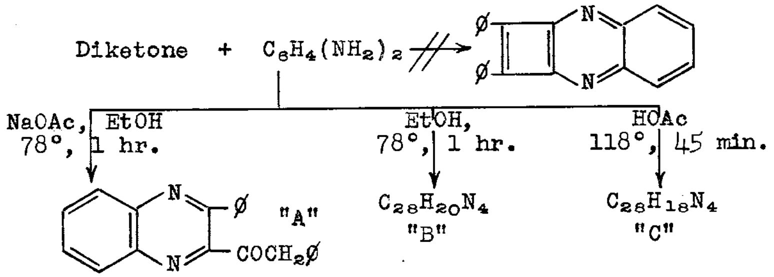
Some other properties of the cis-diol

Infrared Spectrum, $CHCl_3$ soln.

2.75μ (free OH)
2.85μ (internal H-bond)
2.98μ (intermolecular H-bond)

Positive test with Potassium triacetyl osmate

Reaction with o-Phenylenediamine



m.p. 129.5-130°
2,4-DNP deriv.
m.p. 216-217°

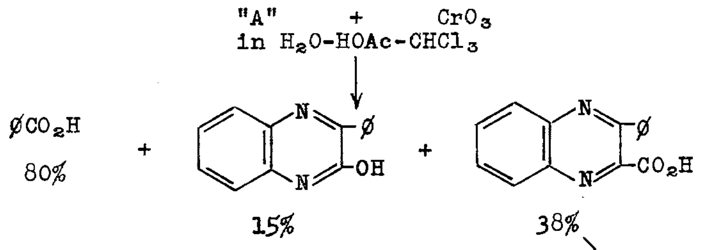
yellow
m.p.'s 209-210°
218-218.5°
(polymorphs)

m.p. 219-219.5°

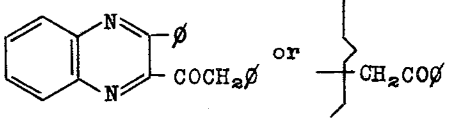
Ultraviolet absorption maxima, EtOH soln.

"A"	"B"	"C"
246 mμ (4.49)	261 mμ (4.62)	246 mμ (4.75)
266 mμ (4.26) (shoulder)	353 mμ (4.24)	342 mμ (4.30)
331 mμ (3.81)	410 mμ (3.74)	

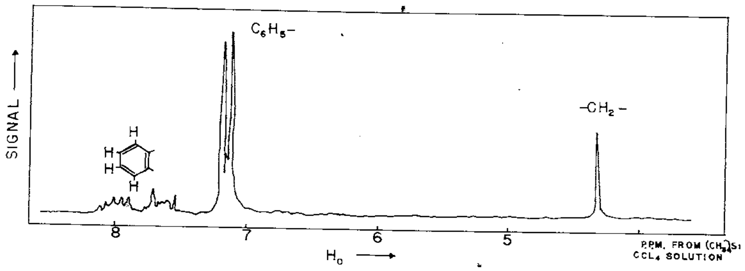
Oxidation of Quinoxaline "A"



∴ "A" must be



NUCLEAR MAGNETIC RESONANCE SPECTRUM
OF QUINOXALINE "A"

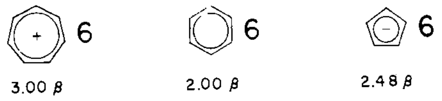


A FEW NON-BENZENOID AROMATIC HYDROCARBONS

William von Eggers Doering

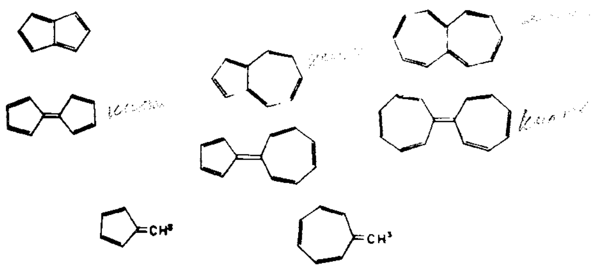
The theory of aromatic character progressed beyond the stage of an empirical generalization - the rule of six - when Erich Hückel formulated the molecular orbital theory in 1931. By means of this quantum mechanical theory, Hückel calculated π-electron delocalization energies for monocyclic arrangements of C-H groups, such as benzene. These "energies" represented differences between delocalized models in which all the available 2p-orbitals - six to use benzene as example - could be hybridized and purely hypothetical models in which the 2p orbitals were localized in pairs - but in which no other changes in bond distances or angles were permitted. This "π-electron delocalization energy" is a purely hypothetical quantity involving the discrepancy - expressed in arbitrary units of energy - between one delocalized but severely simplified model and a non-existent, experimentally inaccessible, localized model. The so-called "observed resonance energy" is the discrepancy between the heat evolved in the reaction of the actual molecule and that expected of an accessible, arbitrarily chosen, and more or less inadequate model.

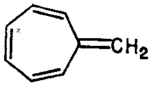
Hückel's prediction that there should be three "aromatic" systems rather than the benzene system alone became a guiding light of great importance. In the last years other



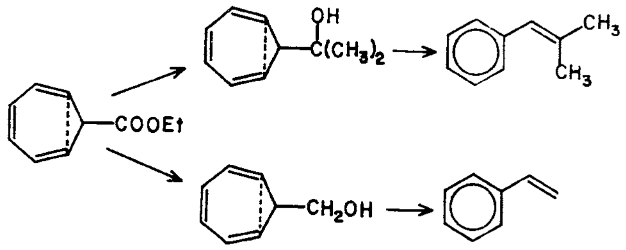
members related to Thiele's cyclopentadienide anion have been sought and found to establish the five-membered, six-electron C_5H_5-H as a second system, and the seven-membered, likewise six-electron C_7H_7+ has been discovered and developed as the third. Despite the impossibility of associating any measureable thermodynamic properties of the 5- and 7-membered parents with the calculated π-electron delocalization energies, the observed physical and chemical properties are sufficiently dramatic to leave one convinced of the qualitative conclusion that the 6-electron cyclic systems are indeed aromatic.

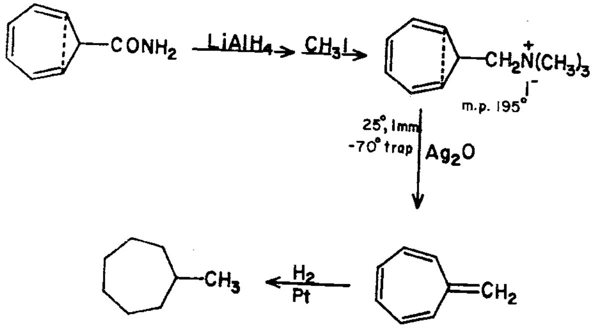
Subsequent to Hückel's pioneering work, molecular orbital theory has been applied enthusiastically in various directions. One of the most stimulating has involved the calculation of π-electron delocalization energies for many new arrangements of double bonds. One group of eight unsaturated hydrocarbons has attracted the attention of theoreticians and synthetic organic chemists alike. This group of eight five- and seven-membered ring compounds contains the known fulvene and azulene and the promise of new non-benzenoid aromatic systems. We wish to discuss the synthesis of three additional members of this group.

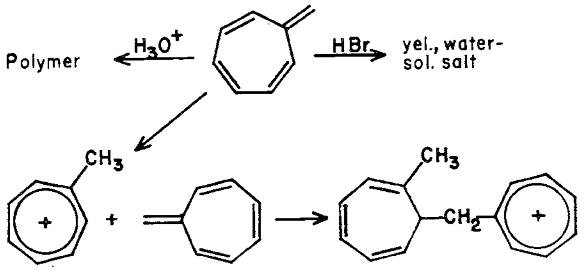


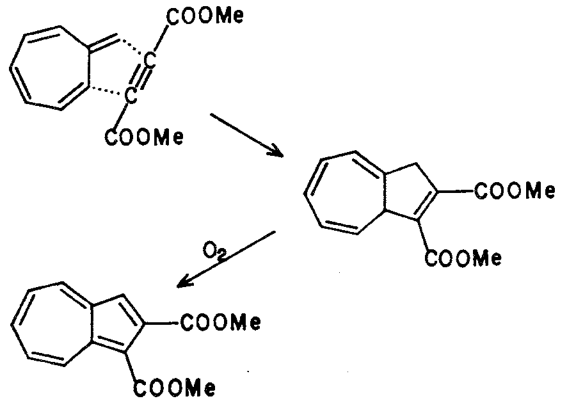


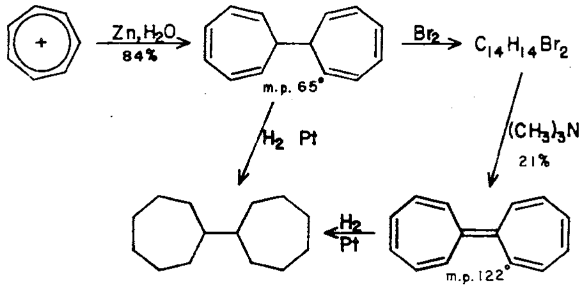
HEPTAFULVENE





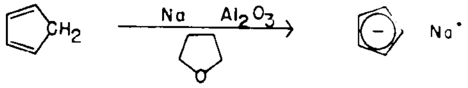




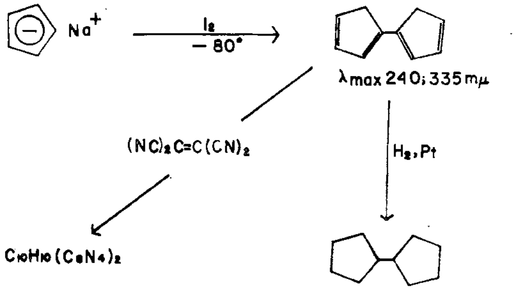


HEPTAFULVALENE

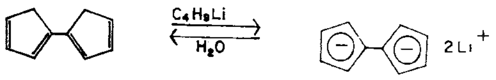
1)



2)



3)



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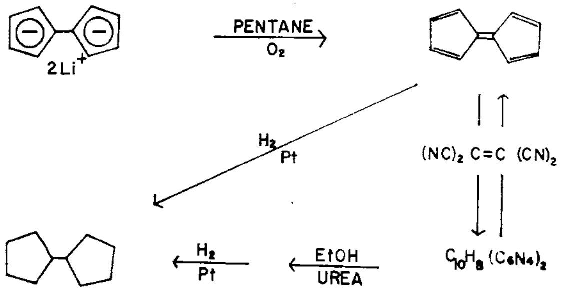
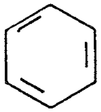


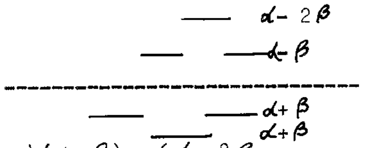
AROMATIC CHARACTER IN POLYCYCLIC MOLECULES

V. BOEKELHEIDE

Molecular orbital theory introduces the concept that the number of available pi electrons is an important consideration. For the special case of simple cycles this requirement can be generalized and $4n + 2$ (Hückel Rule) represents stability.

Energy Levels of Molecular Orbitals



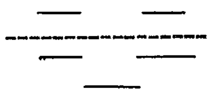


$E_{\text{Total (benzene)}} = 2(\alpha + 2\beta) + 4(\alpha + \beta) = 6\alpha + 8\beta$

$E_{\text{Total (cyclohexatriene)}} = 6\alpha + 6\beta$

Delocalization Energy $= 2\beta$

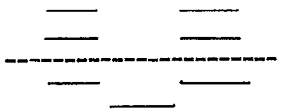
Energy Levels of Molecular Orbitals



Cyclopentadienyl

$\text{D.E.}_{\text{(anion)}} = 2.47\beta$

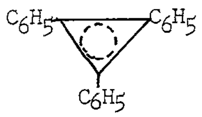
$\text{D.E.}_{\text{(carbonium)}} = 1.24\beta$



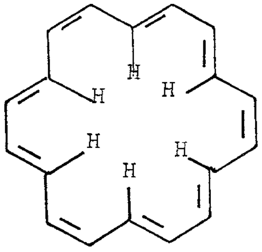
Cycloheptatrienyl

$\text{D.E.}_{\text{(anion)}} = 2.10\beta$

$\text{D.E.}_{\text{(carbonium)}} = 2.99\beta$

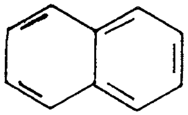


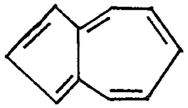
Stable Carbonium Ion
(Breslow and Yuan)



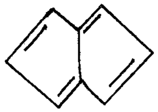
Stable Cyclic Polyene
(Sondheimer and Wolovsky)

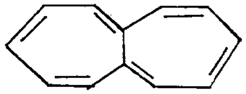
Bridged Cycles





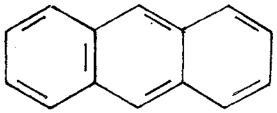
Aromatic



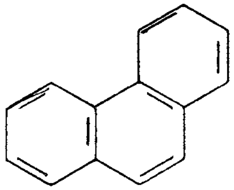


Non-Aromatic

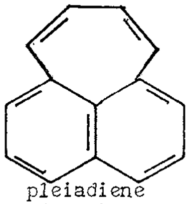
Multi-bridged Cycles



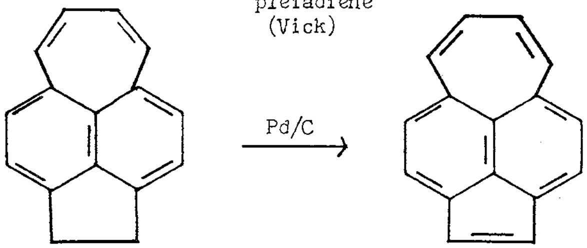
anthracene



phenanthrene



pleiadiene
(Vick)



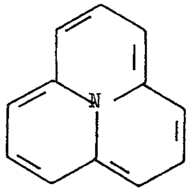
Acepleiadiene

Acepleiadylene
(Vick, Lindsay)

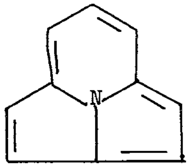
Properties of Acepleiadylene

1. Resonance Energy	(Turner)	77 k cal.
2. Dipole Moment	(Smyth)	0.49 D

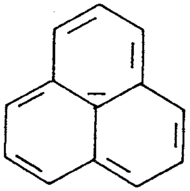
Cyclazines



Cycl(3.3.3)azine



Cycl(3.2.2)azine



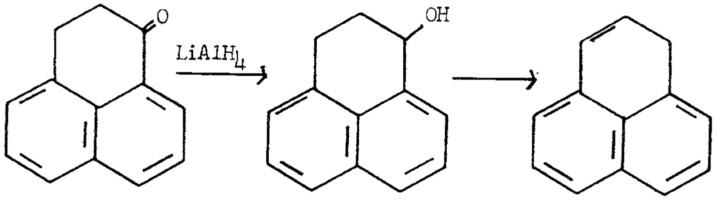
$E_{Total} = 14\alpha + 19.827\beta$
D.E. $= 5.827\beta$

Energy Levels of Molecular Orbitals (Saunders)

$\alpha + k\beta$

+ 2.450	- 2.450
+ 1.732	- 1.732
+ 1.732	- 1.732
+ 1.000	- 1.000
+ 1.000	- 1.000
+ 1.000	- 1.000
0.000	

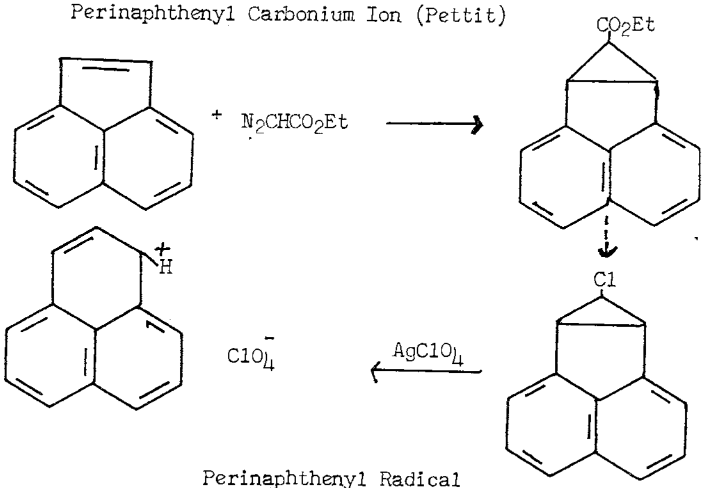
Synthesis of Perinaphthalene (Larrabee)



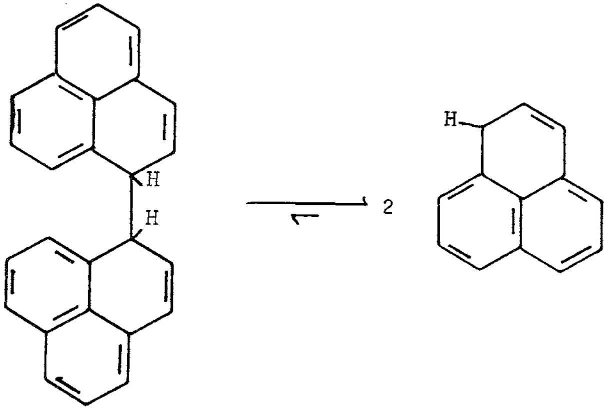
Hydrocarbon Acidities

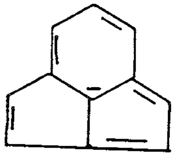
Cyclopentadiene >	indene ≅	perinaphthene >	fluorene
pK$_a$ 17 (predicted)	21	22	25

Perinaphthenyl Carbonium Ion (Pettit)



Perinaphthenyl Radical (Reid)





$E_{Total} = 12\alpha + 15.256\beta$
D.E. $= 5.256\beta$

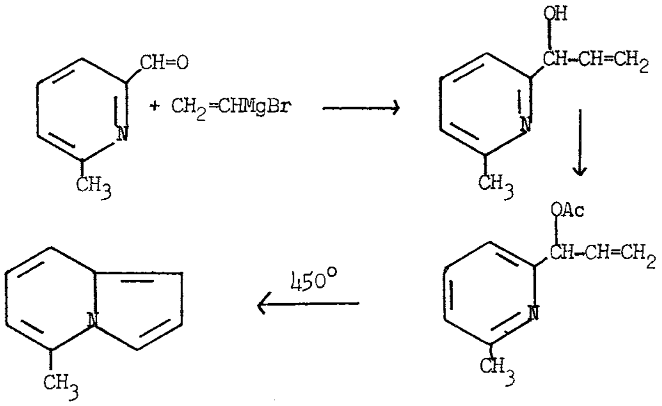
Energy Levels of Molecular Orbitals

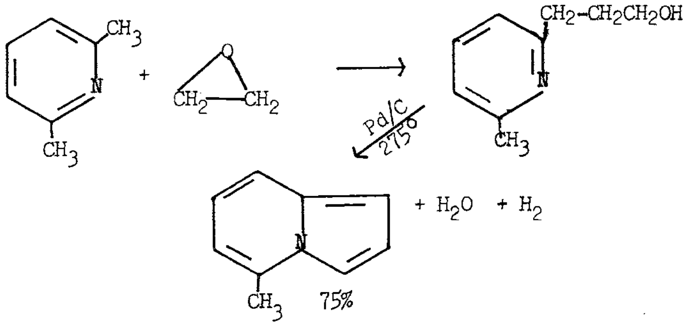
Values of k (Saunders)

+ 2.492	- 2.264
+ 1.627	- 1.941
+ 1.618	- 1.618
+ 0.811	-1.213
+ 0.618	- 0.618
+ 0.462	

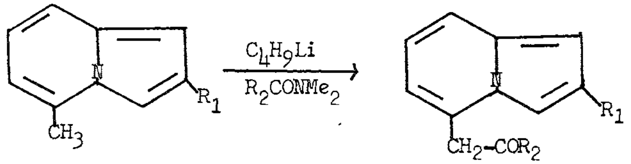
A similar calculation for cycl(3.2.2)azine making allowance for the greater electronegativity of nitrogen than carbon ($\alpha_N = \alpha_C + 0.5\beta$) predicts a delocalization energy of $4.923\,\beta$.

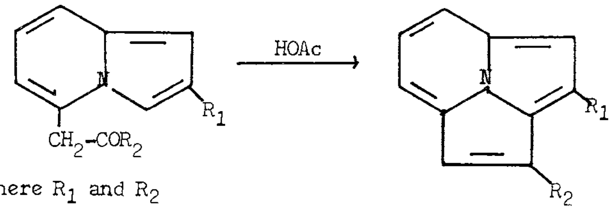
New Syntheses of Pyrrocolines (Windgassen)



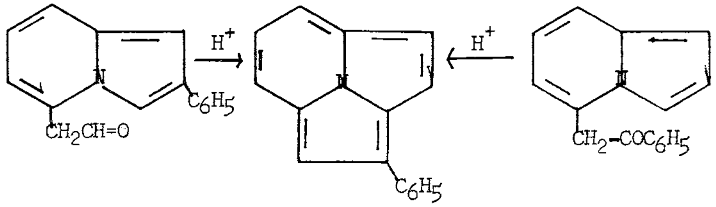


Synthesis of Cycl(3.2.2)azine (Windgassen)



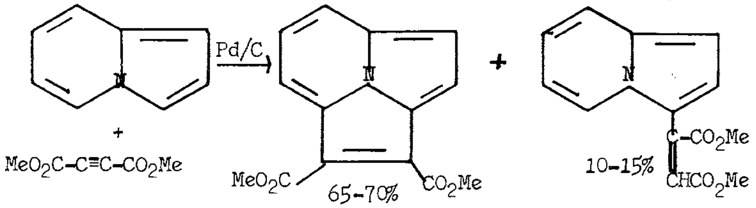


where R_1 and R_2 are -H or $-C_6H_5$.

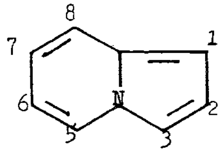


Both cyclizations give the same product.

An Alternate Cycl(3.2.2)azine Synthesis (Galbraith, Small)

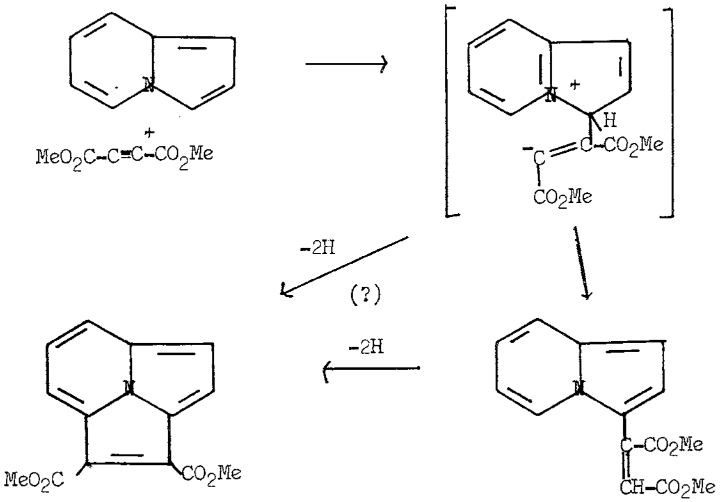


M.O. Calculations for Diels Alder Addition (Barnes)

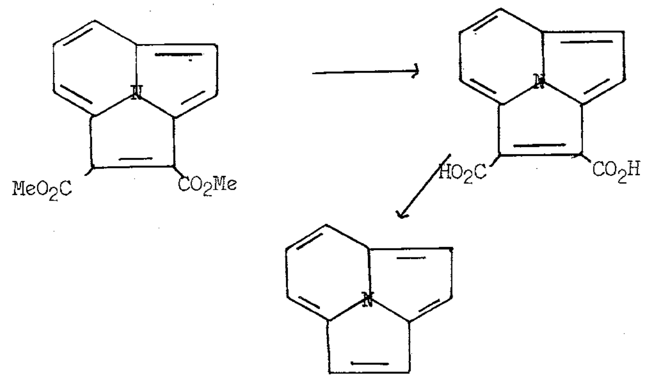


Localization Energies	
Addition at C5-C8	2.385β
Addition at C3-C5	4.255β
Addition at C1-C8	4.329β
Electrophilic Attack at C3	1.854β

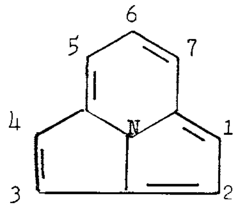
Presumed Mechanism



Proof of Structure



Properties of Cycl(3.2.2)azine



1. Non-basic, as predicted

   D.E. = 5.256 (or 4.923) β

   $D.E._{Periphery} = 2.94\ \beta$

2. Electrophilic Substitution

   Undergoes nitration, bromination and Friedel-Crafts reactions.

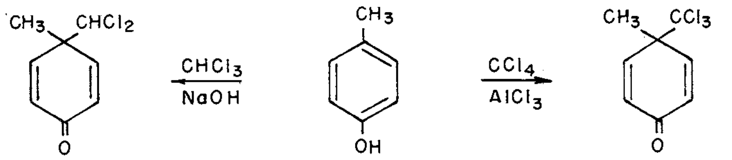
3. Predicted Positions for Substitution

   Electrophilic - 1 and 4
   Nucleophilic - 5 and 7
   Radical - 2 or 5

Reactions of Phenols with Polychlorinated Compounds and Chemistry of the Resulting Products.

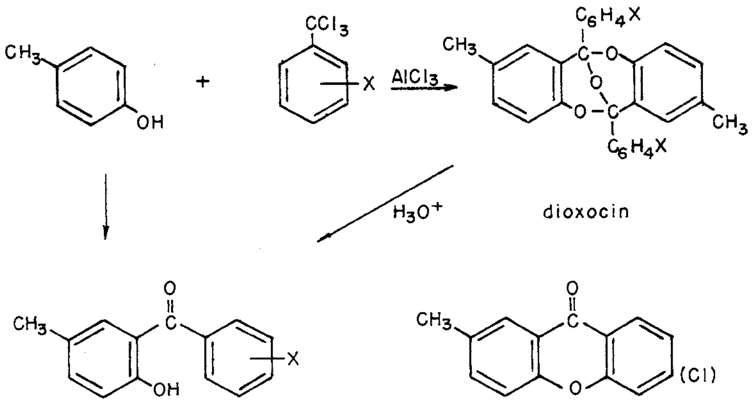
Melvin S. Newman

1. Conversion of p-cresol to chlorinated cyclohexadienones.



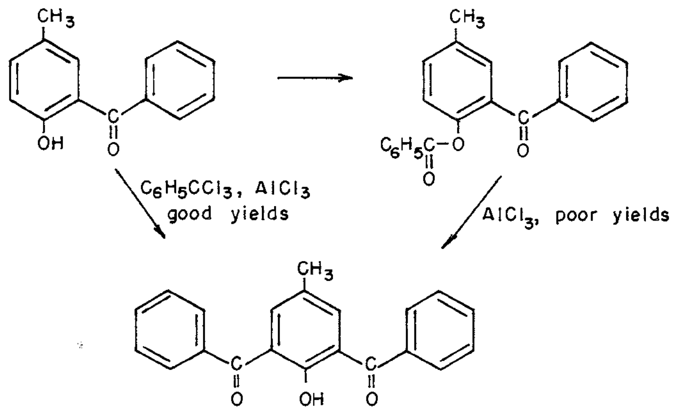
Zincke and Suhl, Ber., 39, 4148 (1906)
Newman and Pinkus, J. Org. Chem., 19, 978 (1954).

2. Reactions of p-Cresol with Benzotrichlorides.



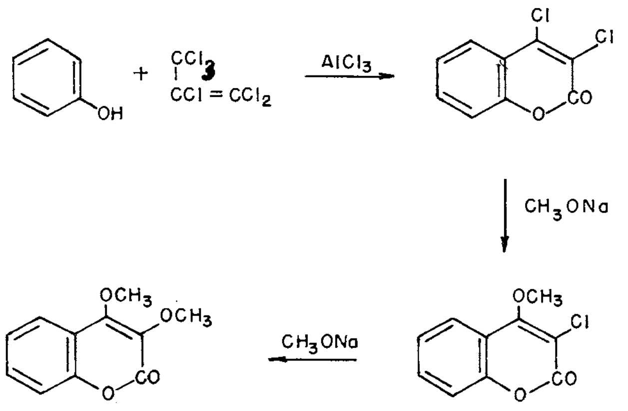
Newman and Pinkus, J. Org. Chem. 19, 985, 996 (1954).

3. Reaction of Hydroxybenzophenones with Benzotrichlorides.



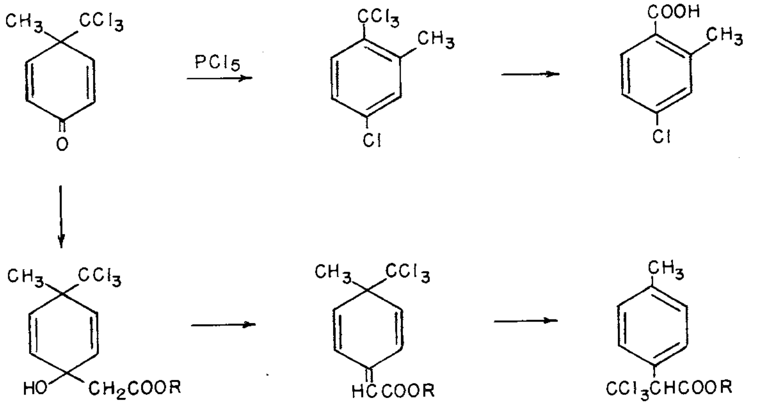
Newman and Pinkus, J. Org. Chem., 19, 993 (1954).

4. Reaction of Phenols with Perchloropropylene.

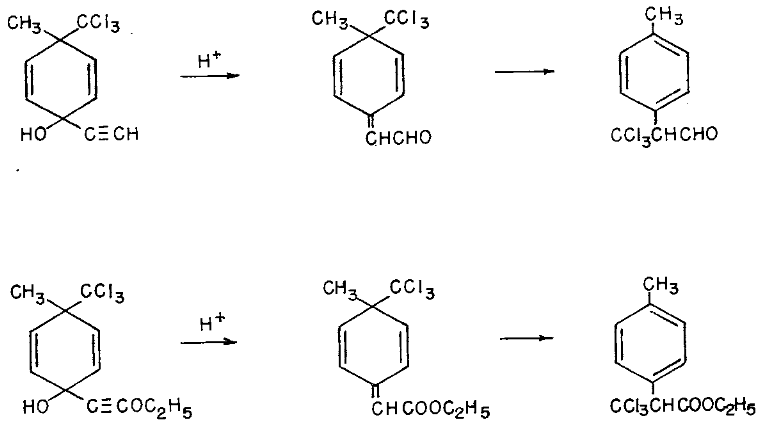


Newman and Schiff, J. Am. Chem. Soc., 81, 0000 (1959).

5. Chemistry of 4-Methyl-4-trichloromethyl-2,5-cyclohexadienone.

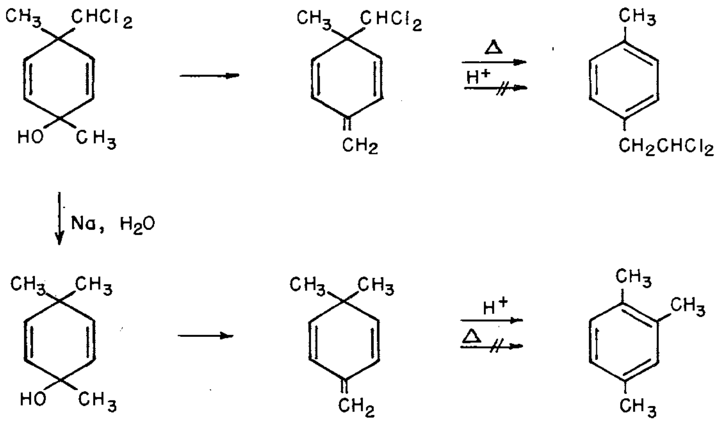


Von Auwers and Julicher, Ber., 55, 2167 (1922).

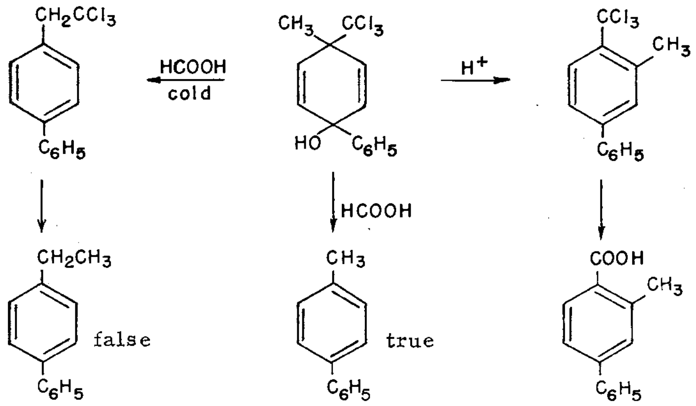


Tse and Newman, J. Org. Chem., 21, 638 (1956).

6. Contrast in Behaviors of Chlorinated and Non-chlorinated Dienones.

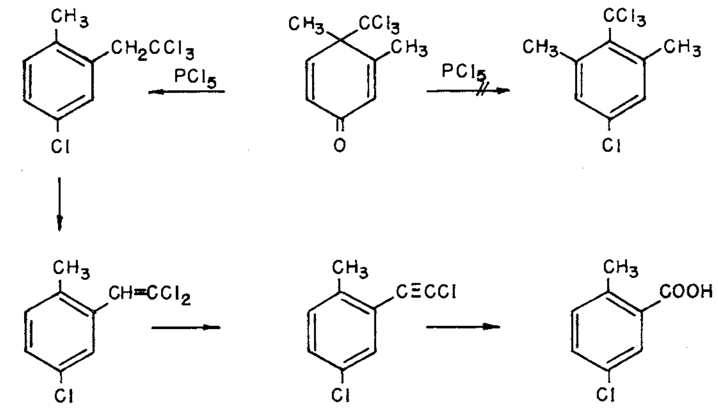


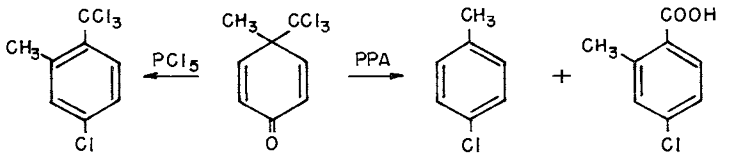
7. Novel Reaction of a Phenyltrichloromethyldienol.

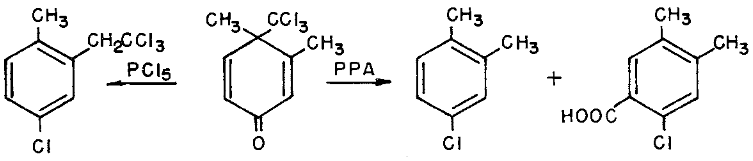


Newman and Wood, unpublished results.

8. New Reactions of Trichloromethylcyclohexadienones.



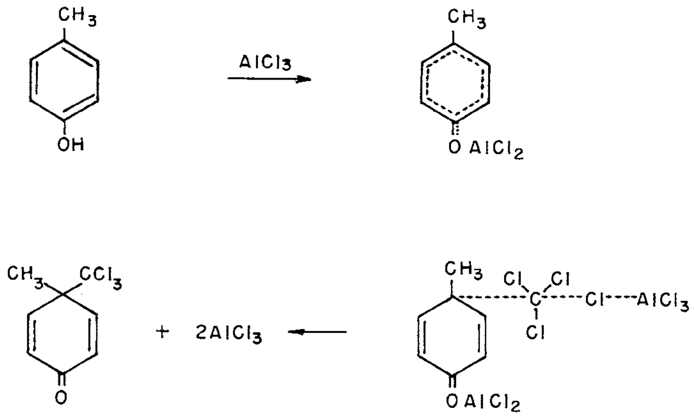




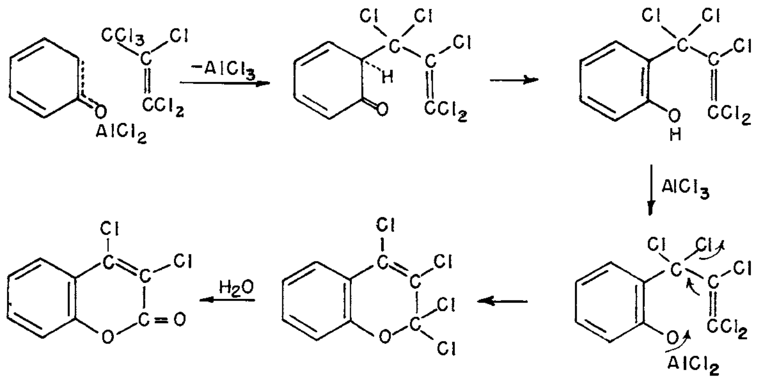
Newman and Wood, unpublished results.

9. Mechanism Portion

I. Zincke and Suhl Reaction

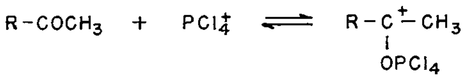


II. Newman and Schiff Reaction

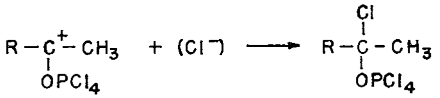


III. Reaction of PCl_5 with Ketones

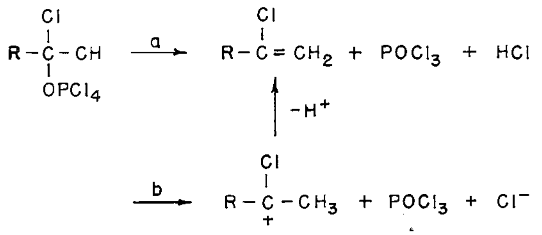
$$2PCl_5 \rightleftharpoons PCl_4^+\,PCl_6^- \qquad (1)$$



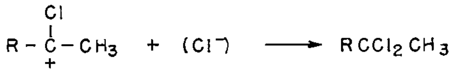
$$R{-}COCH_3 + PCl_4^+ \rightleftharpoons R{-}\underset{OPCl_4}{\overset{+}{C}}{-}CH_3 \qquad (2)$$



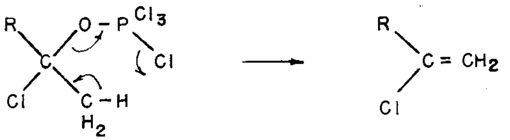
$$R{-}\underset{OPCl_4}{\overset{+}{C}}{-}CH_3 + (Cl^-) \longrightarrow R{-}\underset{OPCl_4}{\overset{Cl}{C}}{-}CH_3 \qquad (3)$$



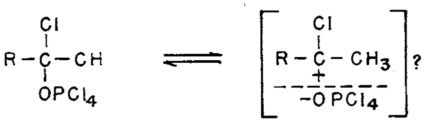
$$\begin{tikzcd} R{-}\underset{OPCl_4}{\overset{Cl}{C}}{-}CH \arrow[r, "a"] \arrow[dr, "b"'] & R{-}\overset{Cl}{C}{=}CH_2 + POCl_3 + HCl \quad (4a) \\ & R{-}\underset{+}{\overset{Cl}{C}}{-}CH_3 + POCl_3 + Cl^- \quad (4b) \arrow[u, "-H^+"'] \end{tikzcd}$$



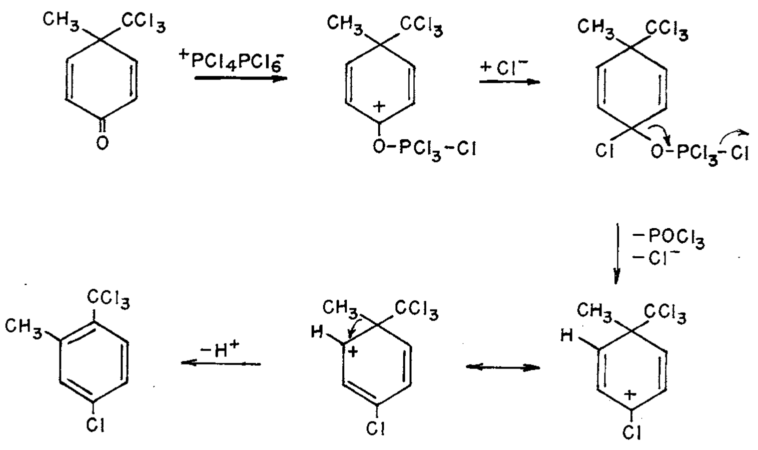
$$R{-}\underset{+}{\overset{Cl}{C}}{-}CH_3 + (Cl^-) \longrightarrow RCCl_2CH_3 \qquad (5)$$

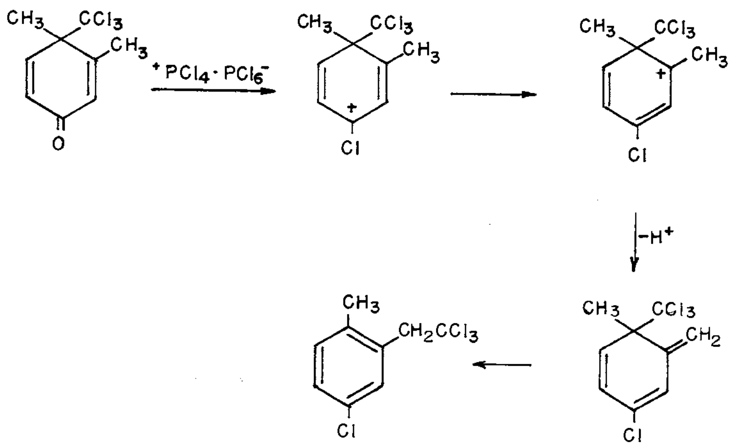


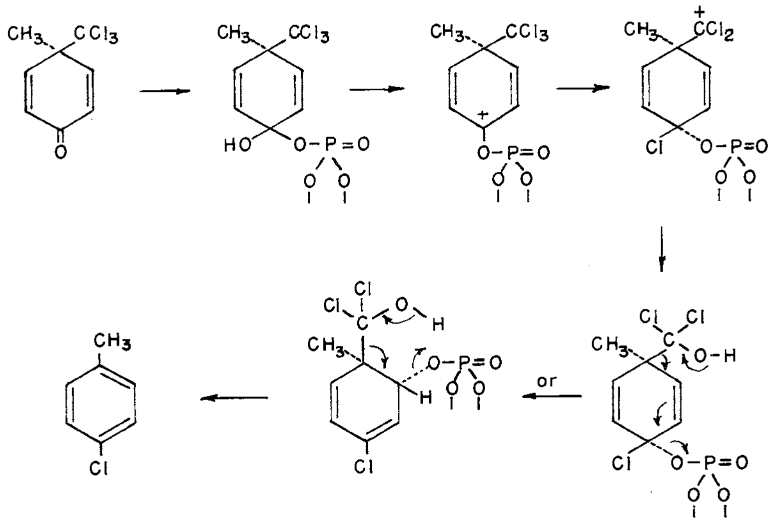
(4a)

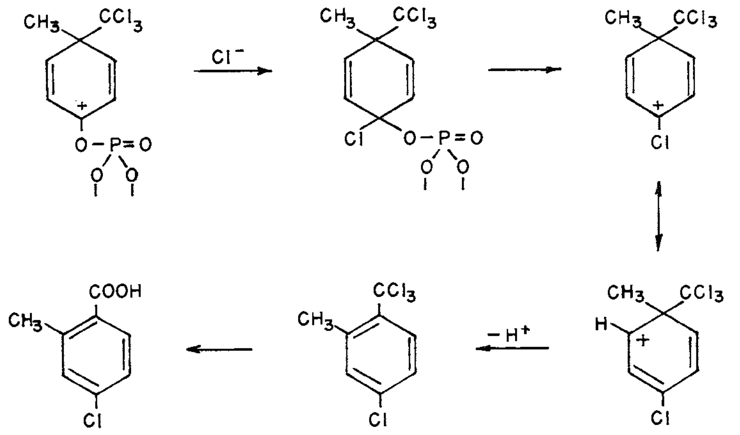


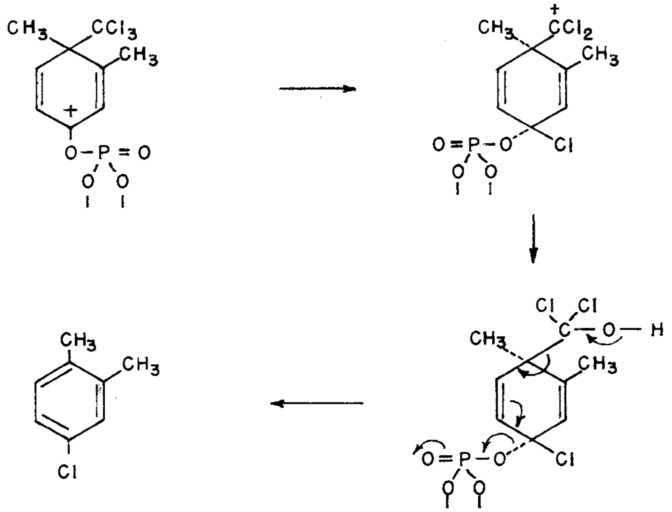
$$R{-}\underset{OPCl_4}{\overset{Cl}{C}}{-}CH \rightleftharpoons \left[\begin{array}{c} R{-}\underset{+}{\overset{Cl}{C}}{-}CH_3 \\ \hdashline {}^{-}OPCl_4 \end{array}\right]?$$

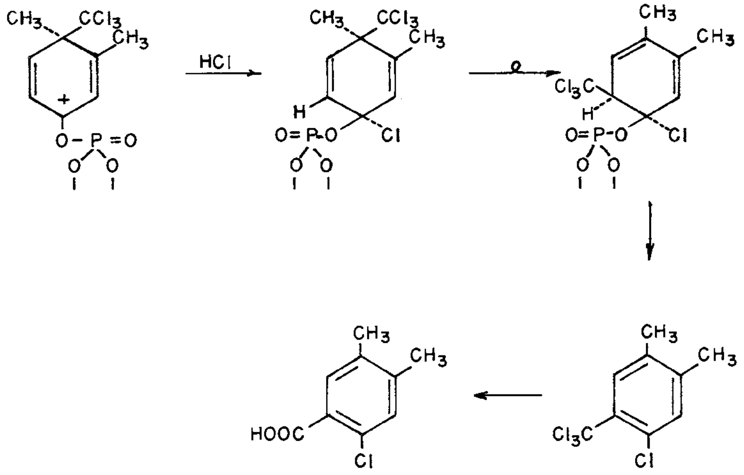





or


Cl⁻
−H⁺




HCl

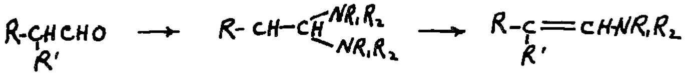
ENAMINES AS SYNTHETIC TOOLS

Gilbert Stork

Enamines of unactivated cyclic ketones and of aldehydes were first prepared by Mannich and Davidsen over twenty years ago (Ber. 69, 2106 (1936)). It was not until 1954, however, that the great potentialities of these substances for the synthesis of a variety of α-substituted carbonyl compounds were discovered (G. Stork, R. Terrell and J. Szmuszkovicz, J. Am. Chem. Soc. 76, 2029 (1954)). Since that time the new synthetic method has found increasing applications as its usefulness and limitations have become more clearly defined.

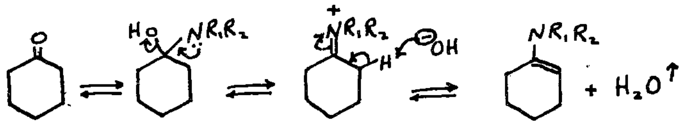
I. Synthesis of Enamines

a) The original Mannich and Davidsen method is still useful for the synthesis of enamines of aldehydes:



$R\text{-}\underset{R'}{C}HCHO \longrightarrow R\text{-}CH\text{-}CH(NR_1R_2)_2 \longrightarrow R\text{-}\underset{R'}{C}{=}CHNR_1R_2$

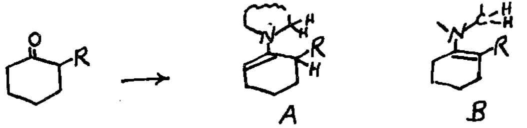
b) In the case of cyclic ketones, however, it is simpler to use the azeotropic method of Herr and Heyl (J. Am. Chem. Soc., 74, 3627 (1952)). This has been used with a variety of ketones up to cyclotridecanone. The general procedure is to heat a mixture of ketone and 50% excess of secondary amine (pyrrolidine, morpholine, hexamethylene imine) with benzene under a water separator. For those ketones which react sluggishly toluene and some p-toluene sulfonic acid are normally used (2-substituted ketones, cycloheptanone and larger ring ketones).



c) Aliphatic methyl ketones give mostly products of aldol condensation but other aliphatic ketones may be used. The reaction, even with toluene and p-toluene sulfonic acid, is very slow requiring about ten days with diethyl or dipropyl ketone to form around 60% yield of the corresponding morpholine enamines. The refluxing period can be cut down to two days in such cases by allowing the condensate from a refluxing solution of an excess of secondary amine and ketone to pass over a bed of Linde No. 4A molecular sieve before returning to the reaction flask.

II. Structure of the Enamines of 2-Substituted Ketones

It is of considerable interest that the enamines of 2-substituted ketones, such as 2-methylcyclohexanone or 2-phenylcyclohexanone are the less substituted isomers



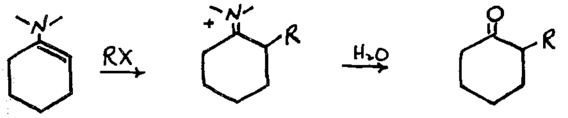
this has been shown in the case of the 2-methyl compound by nuclear magnetic resonance spectroscopy: A($R{=}CH_3$) showed the methyl resonance split into a doublet by the hydrogen on the methyl-bearing carbon while the vinyl hydrogen resonance which would be absent in (B) was split into a triplet by the adjacent methylene. In the case in which R=phenyl, the ultraviolet spectrum shows (private communication from Dr. M. Kuehne) the absence of conjugation with the benzene-ring.

It is assumed that the less substituted enamine is favored in such cases because of steric inhibition of resonance in forms such as B.

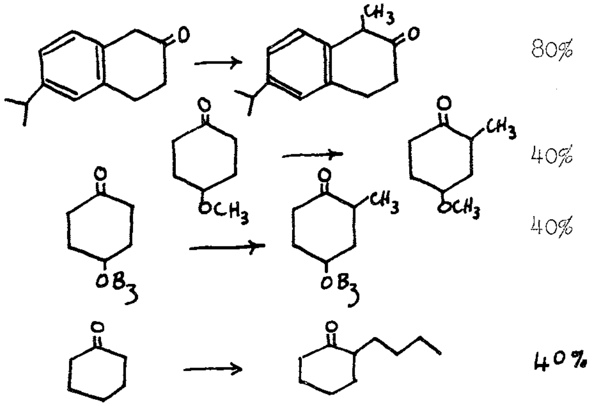
A corollary which will become evident later is that electrophilic reactions of enamines of α-substituted cyclanones takes place on the α′ carbon, rather than on the α-carbon as in base catalyzed reactions of the parent ketones.

III. Alkylation of Ketones with Alkyl Halides

The reaction has so far been studied only with cyclic ketones (mostly 6-membered). Primary halides give fair to good yields with pyrrolidine enamines. The general procedure is to reflux the halide and enamine in benzene or dioxan for a few hours. Addition of water hydrolyzes the imonium salt to the alkylated ketone:



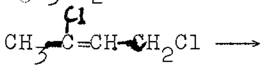
Simple halides carrying no functional groups can of course often be introduced as well or better through the intermediacy of the β-ketoesters derived from the cyclic ketones. However, even with such halides the method is useful when the preparation of the β-keto ester is impossible or unsatisfactory. For instance, with β-tetralones, 4-alkoxy or 4-acyloxy cyclohexanones. In such cases the enamine method is useful:



allyl and benzyl halides (with cyclohexanone)

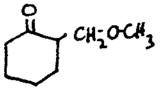
$CH_2{=}CHCH_2Br \longrightarrow$ 60%

$C_6H_5CH_2Cl \longrightarrow$ 60%


$CH_3-\overset{Cl}{C}=CH-CH_2Cl \longrightarrow$ 40% (private com. from Dr. A. W. Lutz)

α-halo ethers

$CH_3OCH_2Cl \longrightarrow$

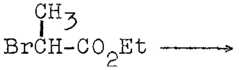


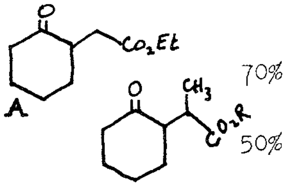
35%

especially interesting since this halide normally gives O-alkylation with β-keto esters.

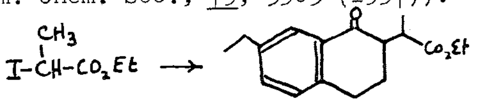
α-halo esters

$BrCH_2CO_2Et \longrightarrow$


$\overset{CH_3}{BrCH}-CO_2Et \longrightarrow$



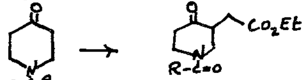
This illustrates the simplicity of the reaction compared with many other methods. Conventional syntheses of A (Dornow, C.Ber., 88, 1340 (1955)) require some five steps from cyclohexanone and produce about 38% overall yield. The enamine synthesis of A has recently been used to synthesize thioctic acid (Segre et al, J. Am. Chem. Soc., 79, 3503 (1957)).



D.M.Locke and S.W.Pelletier, JACS., 80,2588 (1958).

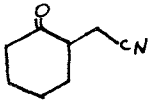
The last reaction shows the utilization of an aromatic ketone. The product was transformed to a dehydrogenation product of atisine.

Heterocyclic ketones may also be used:



(R.L. Augustine, J.O.C., 23, 1853 (1958)).

α-halonitriles

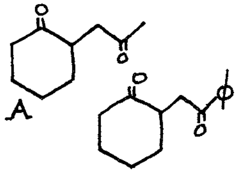


(private com. from Dr. V. Boekelheide)

α-haloketones

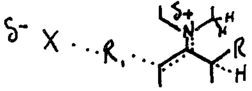
$BrCH_2COCH_3 \longrightarrow$ 40%

$\phi COCH_2Br \longrightarrow$ 55%



(H.E. Baumgarten et al, J. Am. Chem. Soc., 80, 6609 (1958)). Conventional synthesis of A gives 3% yield (Helv. Chim. Acta, 12, 16 (1929)).

One interesting feature of the enamine alkylation procedure is that it gives mostly monoalkylation as a result of the considerably slower rate of alkylation of the monoalkylated compounds. This is of some theorectical interest and is believed to be the result of the higher energy of the transition state(I)when R is alkyl than when R is H. This slows down C-alkylation

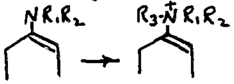


(I)

while N-alkylation is slowed by the increased bulk in the Nitrogen environment (cf. Williamson, Tetrahedron, 3, 314, (1958)).

IV. C vs. N Alkylation

It is of course obvious that the yields with halides are affected adversely by what sometimes becomes the principal reaction: N-alkylation. The latter has been shown to be irreversible and leads to water soluble quaternary salts:



The problem is related to the classical O vs. C alkylation of enolate ions, but is much more simply studied here since the question of the effect of the cation does not come into consideration.

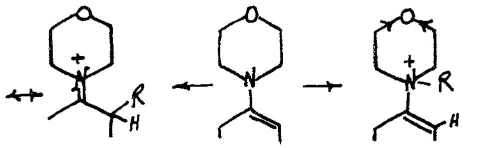
One of the interesting theoretical and practical questions is that of the effect of the structure of the amine on the C/N ratio. It is clear that less hindrance is produced on the α-carbon by cyclic amines than open chain ones. (See e.g. Benkeser, J. Am. Chem. Soc., 80, 6573 (1958)).

It is in the realm of the cyclic amines that the most interesting results have been obtained. Attempts to hinder the Nitrogen but not the carbon, e.g. with 3,3-dimethylpyrrolidine produced only a slight improvement in C/N ratio while 3,3,4,4-tetramethylpyrrolidine does not form enamines at an appreciable rate.

A more fruitful approach which seems very promising at this time follows from the expectation that the rate of N-alkylation should be related to the rate of cyanohydrin formation of the cyclic ketone of the same ring size as that of the amine. This would suggest that pyrrolidine would be a better amine than piperidine for C-alkylation. This is in fact the case. After 18 hours refluxing in toluene with methyl iodide the pyrrolidine enamine of cyclohexanone gives (based on unrecovered cyclohexanone) 29% of 2-methylcyclohexanone. With piperidine the yield is only 11%.

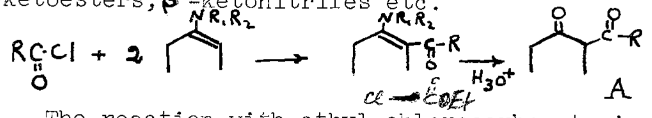
As expected, however, hexamethylene imine (from caprolactam) gave 47% yield of 2-methylcyclohexanone under the same conditions. With the next higher amine we see the effect of increased crowding of the α-carbon and the yield falls to 30%. This demonstrates the possibility of favorably affecting the C/N reatio and the obvious extensions of this finding are being pursued.

The ratio should also be affected favorably by electrostatic means: N-alkylation of a morpholine enamine would be more adversely affected by the inductive effect of the oxygen atom than C-alkylation since the charge is further spread out in the latter case: Actually under our standard conditions the morpholine enamine gave 27% yield of 2-methylcyclohexanone, comparable to that obtained with pyrrolidine. Further extensions of this concept may be envisaged.



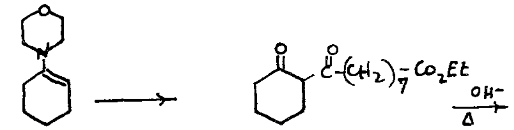
V. Acylation of Carbonyl Compounds

This reaction seems very general and applicable to cyclic or acyclic ketones and leads to β-diketones, β-ketoesters, β-ketonitriles etc.



a) The reaction with ethyl chlorocarbonate in benzene requires two equivalents of enamine (preferably morpholine enamine) since one mole is used up to form the HCl-salt. This also applies to other acid chlorides. Yields of 40-70% are obtained with the enamines of dipropyl ketone, diethyl ketone, cyclohexanones, cyclopentanone, cycloheptanone. The reaction has recently been extended (M. Kuehne, in press) to the synthesis of β-ketonitriles, using cyanogen chloride. Very good yields were obtained using, in this case, pyrrolidine enamines of a variety of ketones.

b) Acid anhydrides or acid chlorides give β-dicarbonyl compounds (A above, R=alkyl or substituted alkyl). The preferred enamine here again is the morpholine enamine and yields of 50-80% of β-diketones are obtained from the enamines of cyclopentanone and cyclohexanone with, for instance, acetyl, capryl, caproyl and benzoyl chloride, as well as with half ester acid chlorides such as that of azelaic acid, or with unsaturated acid chlorides such as that of oleic acid. Some of these compounds are of considerable interest since Hauser has shown that they can be cleaved to keto acids and keto dibasic acids (cf. C. R. Hauser and B. O.Linn JACS., 79, 731 (1957)); (R. M. Manyik, F. C. Frostick, Jr., J. J. Sanderson and C. R. Hauser, JACS, 75, 5030 (1953)). We have, for instance, prepared the C_{15} dibasic acid by this method in about 40% overall yield.



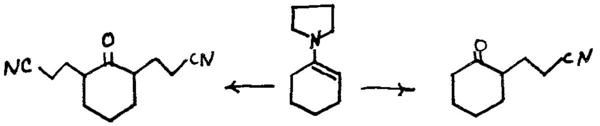
$HO_2C(CH_2)_5CO(CH_2)_7CO_2H \xrightarrow{W.K.} HO_2C(CH_2)_{13}CO_2H$

The reaction leads to chain extension by six carbon atoms (or five, using cyclopentanone). Further examples have been provided by Hünig (S. Hünig and E. Lücke, C. Ber., 92, 652 (1959)).

VI. Addition of Electrophilic Olefins to Carbonyl Compounds

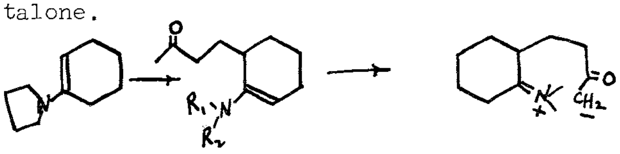
a) α,β-unsaturated esters and nitriles.

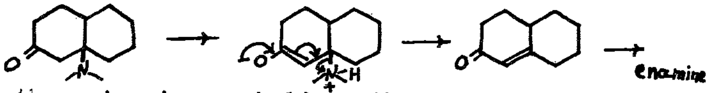
These reactions proceed in very high yields (few hours refluxing) in benzene or dioxane using pyrrolidine enamines and are applicable to practically all enamines cyclic or acyclic. The interesting observation has been made that α,β-unsaturated esters or nitriles give about 80% yield of monoalkylation with the pyrrolidine enamine of cyclohexanone in benzene or the morpholine enamine in alcohol. The pyrrolidine enamine in alcohol gives 80% yields of α,α'-dialkylated products. These would be very difficult to prepare in any other way. These results illustrate the effect of changing the solvent to one favoring charge separation in the transition state, and the effect of increasing amine reactivity.



b) α,β-unsaturated ketones.

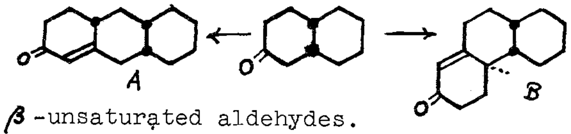
Here again, flexibility is afforded by varying the amine used to form the enamine. For instance, the pyrrolidine enamine of cyclohexanone gives, after standing at room temperature for four hours in dioxane with one equivalent of methyl vinyl ketone, the enamine of $\Delta^{1,9}$-octalone.





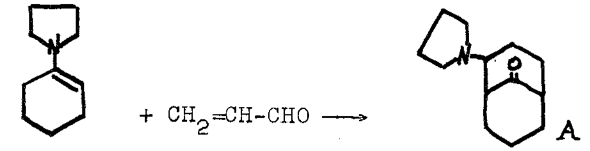
When the amine is morpholine, the reaction stops at the adduct stage (A). Decomposition with water and cyclization produces again the octalone but it is of considerable potential interest that the reaction can be stopped, and operations presumably carried on the side chain after addition. Other applications of the reaction have been reported (G. Stork and H. K. Landesman, JACS, 78, 5128 (1956)).

It is of considerable interest that conversion of cis β-decalone to its pyrrolidine enamine and reaction with methyl vinyl ketone gives roughly equivalent amounts of A and B. This supports the view that there may be no difference in energy between the two possible enols of cis β-decalone (J. Pappas, unpublished).



c) α,β-unsaturated aldehydes.

We have already reported that acrolein reacts with the pyrrolidine enamine of cyclohexanone (or cyclopentanone) to form the interesting bicyclic system A (G. Stork and H. K. Landesman, JACS, 78, 5129 (1956)).

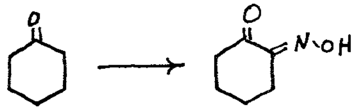


Further studies on the reaction have shown that the reaction is quite general also for substituted cyclic ketones and substituted unsaturated aldehydes. The mechanism could either involve intra or intermolecular transfer of the amine. The evidence which we have obtained demonstrates the intermolecular mechanism (K. Untch, unpublished results).

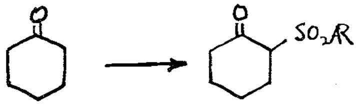
VII. Introduction of Groups other than Carbon.

It is, of course, possible to use enamines to introduce a variety of non carbon groups: cf. reactions below:

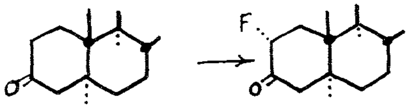
a



b



c



c: R. B. Gabbard and E. V. Jensen, JOC, 23, 1406 (1958).

These are especially interesting reactions since conversion of a 2-substituted ketone to its enamine would not usually give the same result as direct reaction of the ketone with the electrophilic reagent or its equivalent.

The work on the acylation of enamines and C vs. N alkylation with various amines etc. is that of Mr. A. Brizzolara (unpublished and, in the case of acylation, rejected communication (JACS) of Oct. 25, 1958).

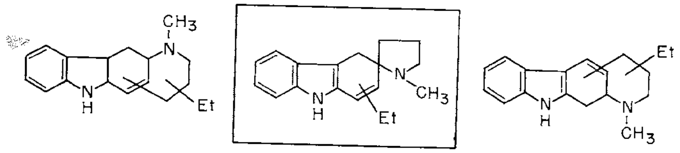
THE STRUCTURE OF ULEIN

G. Büchi and E. W. Warnhoff

Isolation:

From Aspidosperma ulei mgf. in 0.6% yield

Structures proposed:



J. Schmutz, F. Hunziker and R. Hirt
Helv. Chim. Acta, 40, 1189 (1957).

THE FUNCTIONAL GROUPS OF ULEIN

$C_{18}H_{22}N_2$

$[\alpha]_D^{25}$ + 18.5° ($CHCl_3$)

pK MCS 8.23

gives hydrochloride and methiodide

contains one CH_3-N-

Kuhn-Roth oxidation gives 0.72 C-Me

ratio of acetic acid/propionic acid = 1:1

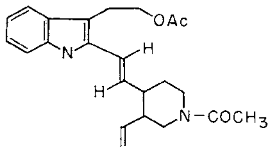
THE CHROMOPHORE OF ULEIN

Ulein λ_{max}^{EtOH} 307 mμ (19500); 316 (19100)

ε at 220 18900

Ulein-hydrochloride identical U.V.spectrum.

I. R. shows N-H at 3540 cm.$^{-1}$ ($CHCl_3$)



λ_{max}^{EtOH} 307 mμ ~ 25000

315 mμ ~ 25000

R. Goutarel, M. M. Janot, V. Prelog and W. I. Taylor
Helv. Chim. Acta, 33, 150 (1950).

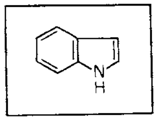
THE CHROMOPHORE OF ULEIN

Ulein $\xrightarrow{H_2,\ Pd/C}$ dihydroulein (only one isomer)

pK* MCS 8.87

Conclusion:

typical for



λ_{max}^{EtOH} 220 mμ ε 43000

281 mμ ε 9000

288 mμ ε 8000

dihydroulein hydrochloride
has identical U.V. spectrum.

THE LOCATION OF THE DOUBLE BOND IN ULEIN

Must be conjugated with indole ring.

Ulein contains a $CH_2 = C\langle$ system.

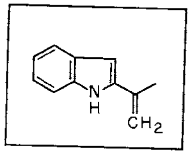
(a) I.R. bands at 877 cm.$^{-1}$, 1635 cm.$^{-1}$, 3030 cm.$^{-1}$

(b) Kuhn-Roth on dihydroulein 0.85 C-Me gives also CH_3CH_2COOH.

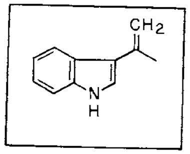
(c) N.M.R. spectrum (60 megacycles)
peaks at 1068 and 1086 c.p.s.
equal intensity; each peak = 1 H

both disappear on reduction. Spectrum shows 4 aromatic H.

Conclusion:



or



FIRST HOFMANN DEGRADATION OF ULEIN

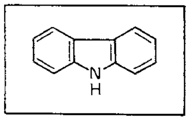
$$\text{Ulein} \xrightarrow{CH_3I} \text{methiodide} \xrightarrow[\substack{(CH_2OH)_2 \\ 150^\circ \\ \text{or} \\ Na_2CO_3/H_2O \\ 100^\circ \\ \text{Fast !}}]{KOH} \text{uleinmethine}$$

<u>Uleinmethine</u>.

Optically inactive (R.D.curve flat); Kuhn-Roth 1.66 of 2 C-Me <u>not</u> resolvable with di-<u>p</u>-toluoyl-D-tartrate.

$\lambda_{max.}^{EtOH}$ 218 mμ ε 32600; 240, 48000; 249, 32000; 261, 21200; 298, 21100; 327, 3700; 340, 28700.

Conclusion:



ring present.

SECOND HOFMANN DEGRADATION

$$\text{Uleinmethine} \xrightarrow{CH_3I} \text{methiodide} \xrightarrow[\substack{(CH_2OH)_2 \\ 150^\circ \\ \text{slow !}}]{KOH} \substack{C_{17}H_{17}N \\ + \\ (CH_3)_3N \\ \text{(picrate)}}$$

$C_{17}H_{17}N$

optically inactive; 1.54 of 2 CMe

$\lambda_{max.}^{EtOH}$
215 mμ ε 24500
248 mμ ε 45200
300 mμ ε 20400

different from uleinmethine !

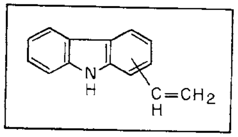
I.R. bands 927; 994; 1625 cm.$^{-1}$

$C_{17}H_{17}N \xrightarrow{H_2/Pd/C}$ dihydro cpd. identical with U.V. uleinmethine $\xleftarrow{Se}$ ulein

ulein $\cancel{\downarrow}$ Pd/C in mesitylene

I.R. vinyl bands disappeared.
2.55 of 3 CMe

Conclusion:



FURTHER DEGRADATION OF SECOND HOFMANN PRODUCT

$C_{17}H_{17}N \xrightarrow[\text{pyridine}]{OsO_4} C_{17}H_{19}NO_2$

U.V. virtually
identical with
uleinmethine

$\downarrow HIO_4$

yellow cpd. + CH_2O
(dimedone)

N-acetyl-aldehyde $\xleftarrow[\text{øSO}_3\text{H}]{CH_3OH}$ triacetate $\xleftarrow{Ac_2O}$ yellow cpd.

$\downarrow KMnO_4$

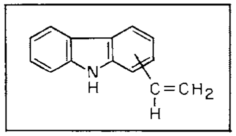
N-acetyl
acid

$C_{16}H_{15}NO$

I.R. 1675 cm.$^{-1}$ (C=O)
1624 cm.$^{-1}$ (C=C conj.)
2800 cm.$^{-1}$ $\left(\mathrm{C}\overset{\mathrm{H}}{\underset{\mathrm{O}}{<}}\right)$

Deuterium exchange 0.2 D
Kuhn-Roth 1.60 of 2-CMe
acetic÷propionic = 2:1

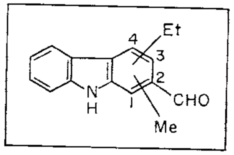
confirms
rigorously



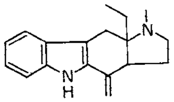
U.V. COMPARISON WITH THE FOUR CARBAZOLE-ALDEHYDES.

Model compounds synthesised by P. H. Carter, S. G. P. Plant and Muriel Tomlinson, Journal Chemical Society, 2210 (1957).

Conclusion:



POSSIBLE STRUCTURES FOR ULEIN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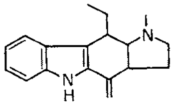
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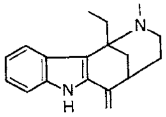
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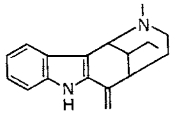
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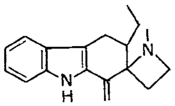
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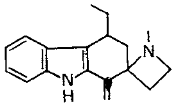
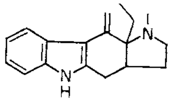

6

(1) not in agreement with: (a) and (b).
(2) not in agreement with: (a), (b), (c) and (d).
(3) not in agreement with: (a).
(4) OK
(5) not in agreement with: (a) and (b).
(6) not in agreement with: (a) and (b).

(a) NMR, (b) mild Hofmann, (c) mercuric acetate oxidation and (d) failure to dehydrogenate without C-N fission.

POSSIBLE STRUCTURES FOR ULEIN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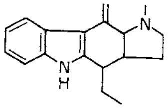
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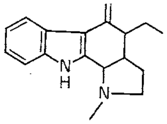
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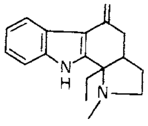
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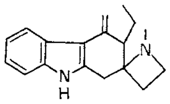
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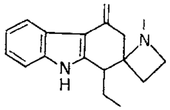
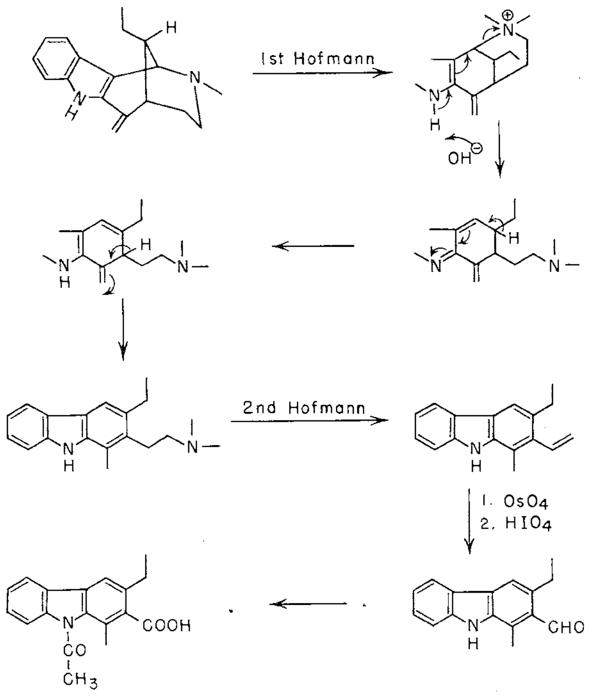

12

(7) not in agreement with: (a) and (b).
(8) not in agreement with: (a), (b), (c) and (d).
(9) not in agreement with: (c) and (d).
(10) not in agreement with: (a).
(11) not in agreement with: (a) and (b).
(12) not in agreement with: (a) and (b).

(a) NMR, (b) mild Hofmann, (c) Hg(OAc)$_2$ and (d) Pd.

STRUCTURE OF ULEIN



THE MECHANISM OF OXIDATION OF KETONES BY SELENIUM DIOXIDE

E. J. Corey

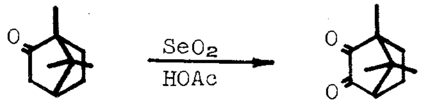
Collaborator: John P. Schaefer

Previous Work

(A) Scope: The oxidation of ketones by selenium dioxide, now a standard synthetic and degradative operation (N. Rabjohn, Org. Reactions, Vol. V) can lead to a variety of products depending on the structure of the ketone and the reaction conditions.

Some illustrations:

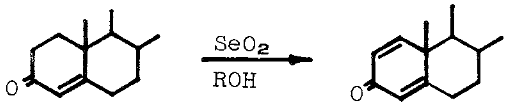
1.



90%

Allard (1934)

2.

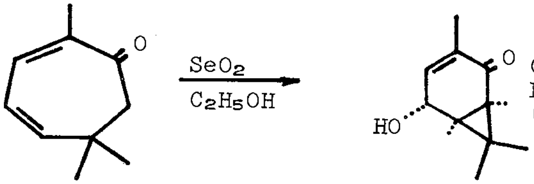


Δ^4-3-ketosteroids $\Delta^{1,4}$-3-ketosteroids

3. $C_6H_5COCH_2Br \xrightarrow[C_2H_5OH]{SeO_2} C_6H_5COCOOC_2H_5$

(J. P. Schaefer)

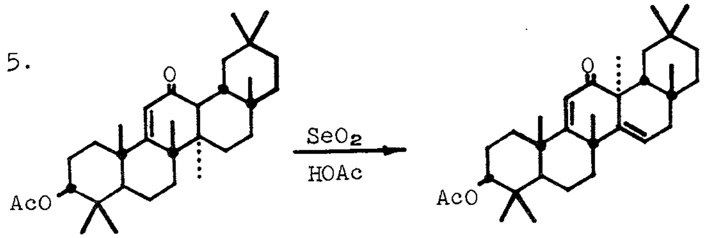
4.



Corey and Burke (1954)

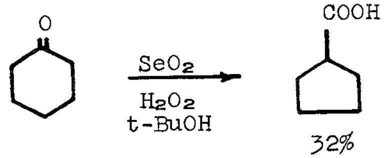
38%

5.



Jeger etal. (1947)

6.



Payne and Smith (1957)

(B) Mechanism: Despite several studies the mechanism of action of selenium dioxide on ketones has remained obscure.

Mel'nikov and Rokitskays reported (1937-1945) the following findings with a series of ketones:

(a) rate = k[ketone][SeO_2]

(on the basis of rough rate measurements)

(b) ketones which enolize readily also undergo oxidation rapidly

(c) $RCH_2O\overset{O}{S}eOCH_2R \xrightarrow[200^\circ]{\Delta} 2RCHO$

proposed mechanism:

$$\text{ketone} \rightarrow \text{enol} \xrightarrow{SeO_2} \text{complex} \rightarrow \text{products}$$

Duke (1948) obtained the following kinetic expression for the oxidation of acetone

$$rate=k[acetone][SeO_2][H^+]$$

proposed mechanism:

rate-determining formation of the complex [acetone. $HSeO_2$ $^+$]

Banerji, Barton and Cookson (1957) on the basis of velocity measurements for the reaction $-CO-\underset{|}{C}H-\underset{|}{C}H-CO \rightarrow -CO-\underset{|}{C}=\underset{|}{C}-CO-$

proposed that two mechanisms are possible: (a) rate-determining enol formation followed by fast reaction with selenium dioxide; (b) a molecular mechanism involving concerted removal of both hydrogens by selenium dioxide.

Results of Present Work

System:

$$ArCOCH_2Ar' + SeO_2 \xrightarrow[80-90^\circ]{70\%HOAc^*} ArCOCOAr'$$

yields 95-100%

* $HOAc-H_2O$(7:3 by volume)

Rate Equations: In 70% acetic acid reaction is clearly second order to 70% completion

$$rate=k[PhCOCH_2Ph][SeO_2]$$

The reaction is still first order in desoxybenzoin (I) and in selenium dioxide in the presence of added sulfuric or oxalic acid, but k_{obs} increases linearly with acid concentration giving

$$rate=k[PhCOCH_2Ph][SeO_2]*[H^+]$$

*[SeO_2]= total Se(IV) species, no distinction will be made between H_2SeO_3, SeO_2 etc.

The apparent lack of second-power dependence of rate on selenious acid concentration out to ca. 70% completion in the experiments without added strong acid implies that the medium is a somewhat more important acid catalyst than is the relatively dilute, albeit somewhat stronger acid, selenious acid. (Conductometric measurements in 70% acetic acid at 90° indicate that $K_a(H_2SeO_3)$=10 to 50 x K_a(HOAc)).

The reaction is also subject to catalysis by acetate ion. Rate constant maximized when $[SeO_2] \cong [AcO^-]$.

$$rate=k[PhCOCH_2Ph][SeO_2][AcO^-]$$

The effect is far greater than that obtained with neutral salts.

Sensitivity to Electrical Factors. Effect of para Substituents on Rate:

acid-catalyzed oxidation of $ArCOCH_2Ar'$:

$\rho_{ArCO}=-0.56$ $\rho_{Ar'CH_2}=+0.25$ (excluding p-nitro) acid-catalyzed enolization:

$\rho_{ArCOCH_3} = -0.56$ $\rho_{Ar'CH_2} = +0.5$

acetate-catalyzed oxidation ($k^{max}_{AcO^-}$) at $[AcO^-] = [SeO_2]$:

$\rho_{ArCO} = +0.77$ $\rho_{Ar'CH_2} \cong -0.47$

(excluding p-nitro)

acetate-catalyzed enolization:

$\rho_{ArCOCH_3} = +0.5$ $\rho_{Ar'CH_2} > 1.0$

(Morgan and Watson 1935) (p-nitro exceptionally rapid)

Sensitivity to Steric Factors. Effect of ortho Substituents on Rate:

	$k_2 \times 10^4 \underline{M}^{-1} sec.^{-1}$ (89.2°)	
Ketone	70% HOAc	70% HOAc +[AcO⁻] max
I	2.59	8.03
2,4,6-trimethylphenyl benzyl (II)	4.10	8.25
2,4,6-trimethylbenzyl phenyl (III)	0.43	0.36
2,4,6-triisopropylphenyl benzyl (IV)	-	15.00

for oxidation in 70% HOAc $k_{II}/k_I = 1.58$ for enolization in 70% HOAc k acetomesitylene/k acetophenone =1.47 (Zucker and Hammett 1939)

Kinetic Isotope Effect:

$PhCOCD_2Ph(I\text{-}d_2)$ vs $PhCOCH_2Ph(I)$ at 89.2°

$k_H/k_D = 6.0$ in 70% HOAc

$k_H/k_D = 5.8$ in 1.15$\underline{M}$ oxalic acid/70% HOAc

(in these cases k_D drifts upward only slightly during reaction)

$k_H/k_D = 7.6$ in 70% HOAc + AcO⁻ ($k^{max}_{AcO^-}$)

(k_D shows marked upward drift $k_D^{obs}(t_{1/2}) = 2k_D^{obs}(t=0)$)

Unique Behavior of $PhCOCH_2C_6H_4NO_2(p)$: In 70% HOAc at 89.2° $k^{obs} = 2.15 \times 10^{-4} \underline{M}^{-1} sec.^{-1}$; predicted from Hammett equation: $4 \times 10^{-4} \underline{M}^{-1} sec.^{-1}$ Replacement of water by dioxane or nitrobenzene increases rate, e.g. in $HOAc\text{-}H_2O$-dioxane (7:2:1) at 89.2° $k^{obs} = 3.35 \times 10^{-4} \underline{M}^{-1} sec.^{-1}$

However, in the case of I replacement of water by dioxane produces only a slight decrease in rate; in (7:2:1) solvent at 89.2° $k^{obs} = 2.45 \times 10^{-4} \underline{M}^{-1} sec.^{-1}$

In 70% HOAc + AcO⁻ at equivalent concentrations of AcO⁻ and SeO_2 a large discrepancy between k^{obs} and k(Hammett) is again noted. Enolization is over 10^3 times faster than oxidation. Nitrobenzene increases the rate of oxidation (slight decrease with I).

Salt Effects: In the presence of sodium benzenesulfonate log k/k_0 for I increases linearly with ionic strength, μ, with slope (0.6) consistent with reaction between neutral and charged species (reaction in 70% HOAc).

Miscellaneous:

(a) in 70% HOAc k_2 (benzoin)=1/20 k_2(I)

(b) rate of oxidation of I increases as water concentration is diminished:

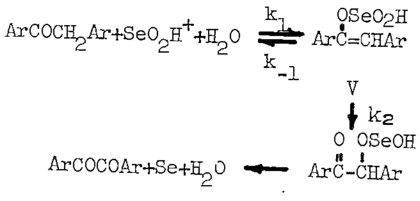
in $HOAc\text{-}H_2O(9{:}1)\,k_2 = 2.92 \times 10^{-4} \underline{M}^{-1} sec.^{-1}$ (89.2°)

in $HOAc\text{-}H_2O(7{:}3)\,k_2 = 2.59 \times 10^{-4} \underline{M}^{-1} sec.^{-1}$ (89.2°)

(c) free-radical initiators and inhibitors produce essentially no change in rate.

Interpretation

(A) Acid-catalyzed Oxidation: In the oxidation of I the intermediacy of the enol can be excluded because of the observed rate equation and isotope effects. Acid-catalyzed addition of a Se(IV) species to the carbonyl carbon is ruled out by the lack of steric retardation with ortho substituents (Hinshelwood and Legard (1935)). The following mechanism for acid-catalyzed oxidation of I is consistent with all our data including the similar characteristics of oxidation and enolization.



$$ArCOCH_2Ar + SeO_2H^+ + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Ar\overset{OSeO_2H}{\overset{|}{C}}{=}CHAr \xrightarrow{k_2} Ar\overset{O}{\overset{\|}{C}}{-}\overset{OSeOH}{\overset{|}{C}}HAr \longrightarrow ArCOCOAr + Se + H_2O$$

V

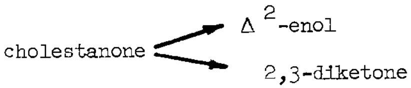
VI

The formation of enol selenite V from I is slow; the rearrangement V → VI is rapid as is further reaction of VI; k_2 is sufficiently greater than k_{-1} so that V does not revert to I appreciably. The change I → V is completely analogous to enolization except that $H_3SeO_3^+$ (or less likely $HSeO_2^+$) is the electrophile. This is probably the mechanism operating with most simple aliphatic and alicyclic ketones.

Some relevent points:

(a) $HSeO_2^+ClO_4^-$ has been obtained as a stable salt (Arlman 1939)

(b) with an unsymmetrical ketone oxidation and enolization occur in the same direction, e.g.



(c) when substantial amounts of unconjugated enol are present, enol selenite will be formed rapidly and directly resulting in facile oxidation. For example enediols of type RCOH=COHR are oxidized very rapidly (Holker 1955).

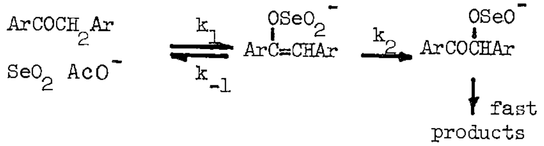
The unique behavior of phenyl p-nitrobenzyl ketone is interpreted as follows: the rearrangement V → VI is retarded by the p-nitro group relative to reversion of V to starting materials; k^{obs} and k(Hammett) for this case indicate $k_2 \cong k_{-1}$. The decrease in k_2 may be associated with destabilization in VI due to p-nitro because of electron demand by selenium(II). Replacement of water in the medium by dioxane diminishes the reversion of V to starting materials causing k^{obs} to approach k(Hammett).

Some relevent points:

(a) conjugated enols such as enolized 1,2-diketones are relatively more stable to oxidation despite the probably ready formation of enol selenite derivatives.

(b) the rate of oxidation of acetone is much greater than that for biacetyl (Mel'nikov (1945)

(B) Acetate-catalyzed Oxidation: All the data are accommodated by the above mechanism with only those changes which are appropriate for a medium of attenuated acidity and enhanced nucleophilicity, specifically:



$$\begin{matrix} ArCOCH_2Ar \\ SeO_2\ \ AcO^- \end{matrix} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Ar\overset{OSeO_2^-}{C}{=}CHAr \xrightarrow{k_2} ArCO\overset{OSeO^-}{C}HAr \xrightarrow{\text{fast}} \text{products}$$

The observed kinetics and isotope effect indicate that as in the case of I, formation of enol selenite is the slow step. Some reversion of enol selenite may occur and this may cause the drift in rate constant for I-d_2 and the observed $\rho_{Ar'CH_2}$ value. For acetate-catalyzed oxidation of phenyl p-nitrobenzyl ketone formation of the Se(II) ester is rate-determining.

Formation of α,β-Unsaturated Ketones: Three possible paths (all via enol selenite) are suggested by our results:

(a) decomposition of enolate-SeO_2H^+ ion pair by transfer of a hydride ion from C_β to SeO_2H^+

(b) concerted 1,4-elimination from enol selenite

(c) 1,2-elimination from the Se(II) ester

Complex Processes: Simple interpretations of reactions such as 4,5 and 6, follow from the above conclusions.

The oxidation of methylated pyridines and quinolines to aldehydes is regarded as analogous to the oxidation of ketones.

Finally, it is possible that the type of mechanism proposed above is operable in other oxidizing systems. For example, α-acetoxylation of ketones by $Pb(OAc)_4$ may involve formation of an enol-lead triacetate directly from the ketone.

Some Rate Data

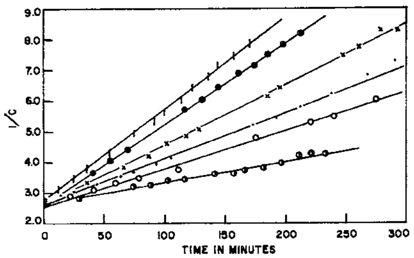


Figure 7. - Rates of Oxidation of Desoxybenzoin at Various Oxalic Acid Concentrations.

Run 10 ●. Run 11 ○. Run 12 •. Run 13 ×. Run 14 ●. Run 15 ǀ.

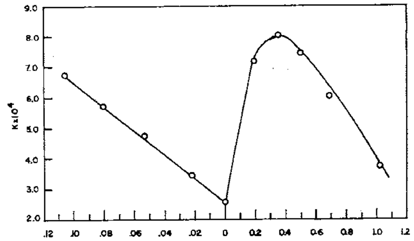


Figure 22. - Rate of Oxidation of Desoxybenzoin as a Function of "Acidity".

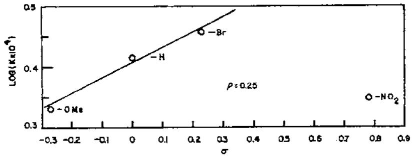


Figure 12. - Hammett Correlation for Rates of Oxidation of $p\text{-}XC_6H_4CH_2COC_6H_5$. t = 89.2°C.

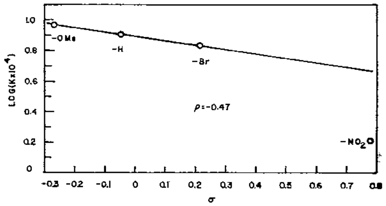


Figure 26. - Hammett Correlation for Rates of Oxidation of $p\text{-}XC_6H_4CH_2COC_6H_5$ in the Presence of Sodium Acetate.

Rate Data (cont.)

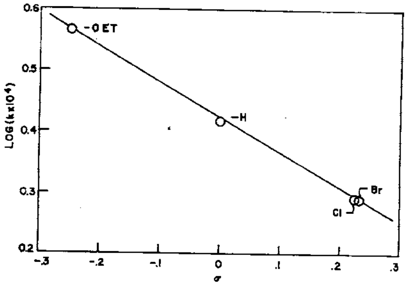


Figure 10a. - Hammett Correlation for Rates of Oxidation of $p\text{-}XC_6H_4COCH_2C_6H_5$. t = 89.2°C.

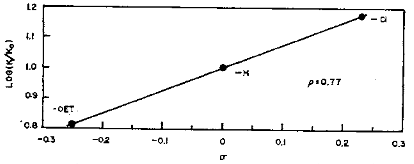


Figure 24. - Hammett Correlation for Rates of Oxidation of $p\text{-}XC_6H_4COCH_2C_6H_5$ in the Presence of Sodium Acetate.

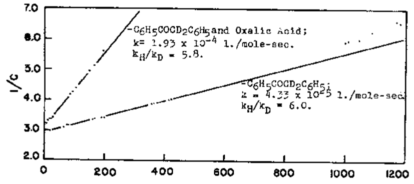


Figure 16. - Isotope Effect Studies. t = 89.2°C.

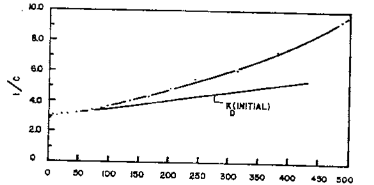


Figure 31. - Isotope Effect in the Presence of Sodium Acetate. t = 89.2°C. k_D (initial) = 1.06×10^{-4} l./mole-sec. k_H/k_D = 7.59.

BASE CATALYZED HYDROGEN-DEUTERIUM EXCHANGE IN HYDROCARBONS

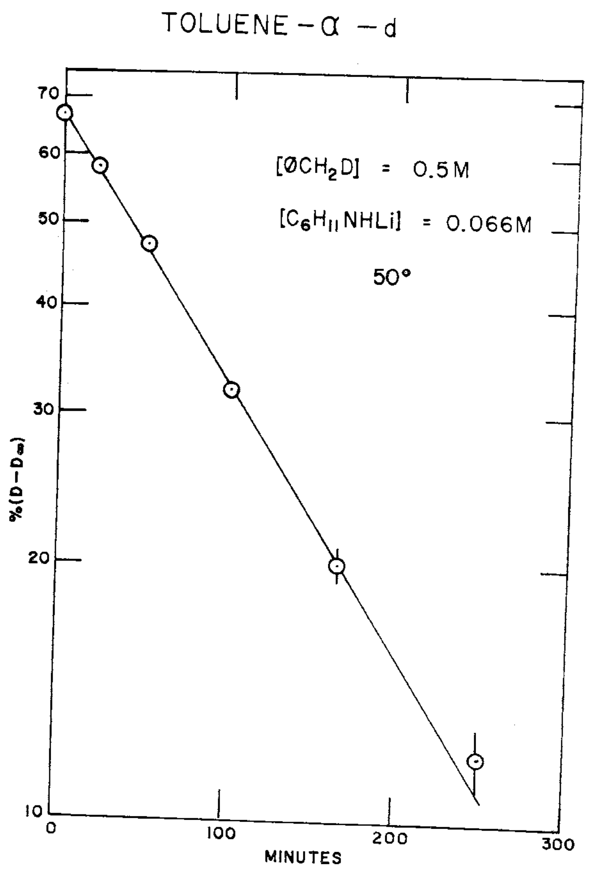
Andrew Streitwieser, Jr.

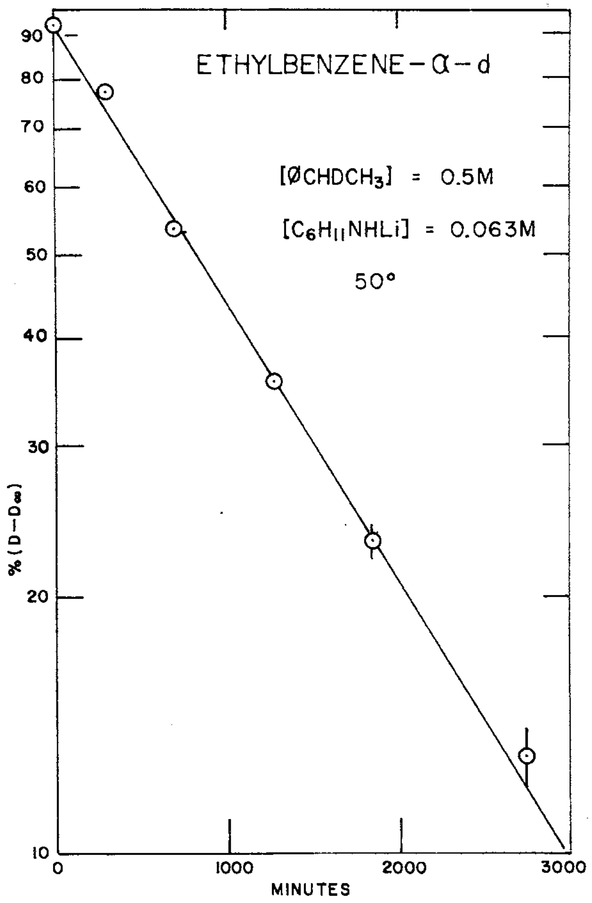
The rate of loss of deuterium from deuterated arylalkanes was studied in cyclohexylamine containing lithium cyclohexylamide:

$$ArCH_2D + C_6H_{11}NH_2 \xrightleftharpoons{C_6H_{11}NHLi} ArCH_3 + C_6H_{11}NHD$$

Vacuum line techniques were used; careful handling was required to exclude moisture and carbon dioxide. With these precautions solutions remained clear and pale pink. Good reproducibility was obtained. A sealed tube technique was used; at intervals hydrocarbon was isolated and analyzed for deuterium in the infrared using the C-D stretching band in conjunction with calibration spectra.

The distribution constant for deuterium is close to unity. Since the solvent is present in large excess the equilibrium position lies far to the right. The reaction follows pseudo-first order kinetics in individual runs. Typical kinetic runs for toluene-α-d and ethylbenzene-α-d follow:





Variation of the hydrocarbon concentration shows the kinetics to be first order in hydrocarbon. In the following table, k_{expl} is the pseudo-first order rate constant obtained directly from the kinetic run; k_{corr} is a pseudo-first order rate constant corrected for the back reaction and for the developing deuterium content of the solvent. Temp. 50°.

[RD] m/l.	$[LiNHC_6H_{11}]$ m/l.	$10^3\ k_{expl}$ min^{-1}	$10^3\ k_{corr}$ min^{-1}
Toluene-α-d			
0.25	0.055	6.0	5.6
0.50	.055	6.7*	5.9
Ethylbenzene-α-d			
0.50	.063	0.74	0.68
0.75	.047	.70	.62

*Taken from curve below

By analogy with related exchange reactions in other systems, a simple general mechanism may be written which should be considered:

$$LiNHC_6H_{11} \overset{K}{\rightleftarrows} Li^+ + C_6H_{11}NH^- \qquad \text{Fast}$$

$$RD + C_6H_{11}NH^- \longrightarrow R^- + C_6H_{11}NHD \qquad \text{Slow}$$

$$R^- + C_6H_{11}NH_2 \longrightarrow RH + C_6H_{11}NH^- \qquad \text{Fast}$$

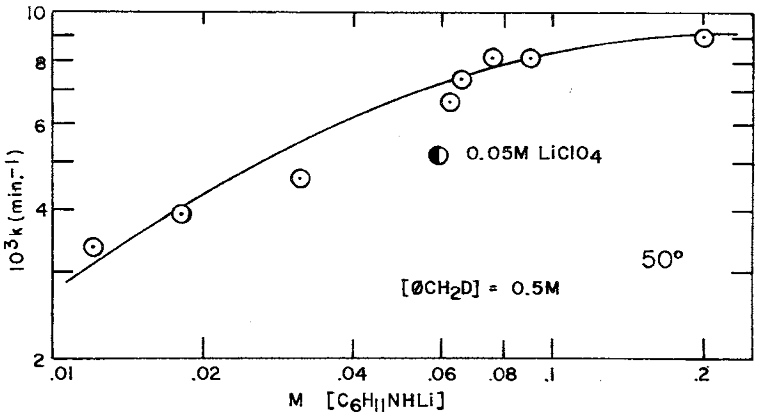
Two limiting cases may be considered:

For $K \gg 1$, kinetics is first order in $[LiNHC_6H_{11}]$.

For $K \ll 1$, kinetics is half-order in $[LiNHC_6H_{11}]$.

In the latter case the addition of an ionic lithium salt should greatly suppress the rate in the absence of compensating salt effects.

The effect on rate of the lithium cyclohexylamide concentration is shown in the following log-log plot:



Neither a line of slope 1 nor of slope 1/2 is obtained; the plot is actually a curve which approximates a line of slope 0.3. The activation parameters give further useful data at this point.

Activation Parameters

Compound	ΔH^* Kcal/mole	ΔS^* e.u.
Toluene-α-d	9.4	-48
Ethylbenzene-α-d	9.8	-51

These data show that the simple mechanism given above is wrong. The varying effect of base suggests a rather low activity coefficient perhaps due to aggregation of the lithium salt at the concentrations used. The large negative entropy of activation indicates a highly ordered transition state although the numbers listed include entropy contributions from prior equilibria and the concentration effect of base in the pseudo-first order rate constants.

The physical chemistry of metal amide-amine solutions will be investigated further; at present the detailed nature of the attacking group is unknown. The mechanism as related to the hydrocarbon substrate, however, was studied further. In order to use this system as a means of assessing relative acidities of various hydrocarbons it is important to evaluate the relative amount of negative charge on the central carbon in the T.S.

β-DEUTERIUM ISOTOPE EFFECT

Deuterium is known to have a significant electron-donating inductive effect relative to hydrogen. Examples:

$$\frac{K_{\phi CH_2COOH}}{K_{\phi CD_2COOH}} = 1.12 \qquad \frac{K_{\phi CH_2NH_3^+}}{K_{\phi CD_2NH_3^+}} = 1.13$$

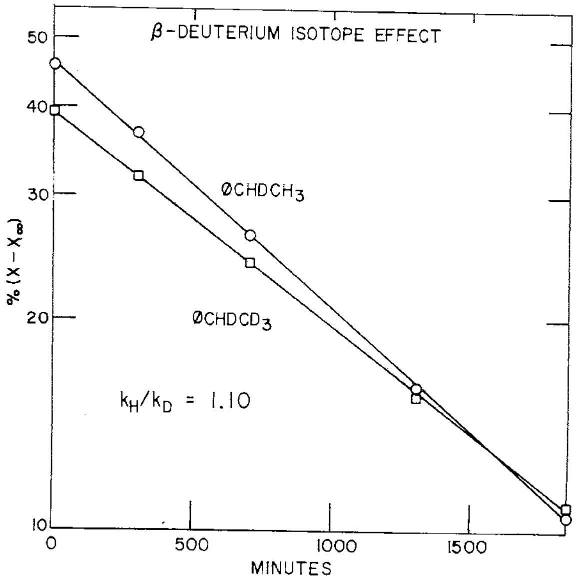
[Halevi and Nussim, Bull. Res. Council Israel, 5A, 263 (1956)]

$$Et_2NR + CH_3OBs \longrightarrow Et_2NRCH_3^+ + OBs^-$$

$$\frac{k_{R = CH_3CD_2}}{k_{R = CH_3CH_2}} = 1.07$$

[Lewis, Tetrahedron, 5, 143 (1959)]

To get some measure of the amount of negative charge developed at the central carbon in our system, a competitive reaction was carried out between ethylbenzene-α-d and ethylbenzene-α,β,-β,β-d_4. The results are shown in the next figure:



The relatively large β-Deuterium isotope effect is taken to indicate that the central carbon has substantial negative charge at the transition state.

α-DEUTERIUM ISOTOPE EFFECT

A competition reaction was run with toluene-α-d and toluene-α,α,α-d_3 in which the following two rates were measured simultaneously:

$$\phi CD_3 \xrightarrow{k_3} \phi CHD_2$$

$$\phi CH_2D \xrightarrow{k_1} \phi CH_3$$

$$3k_1/k_3 = 1.30$$

Both the development of negative charge on the α-carbon and the hybridization change, $sp^3 \longrightarrow sp^2$, are expected to give an isotope effect in this direction. For this and the preceding experiment we are indebted to Dr. D. P. Stevenson, Shell Development Co., for the mass spectral deuterium analyses.

RELATIVE RATES FOR METHYL SUBSTITUENTS

Compound	Relative Rates
$C_6H_5CH_2D$	100
m-$CH_3C_6H_4CH_2D$	69, 66
p-$CH_3C_6H_4CH_2D$	29, 29
$C_6H_5CHDCH_3$	10.6, 10.7, 11.2

Comparison of m-methyl with p-methyl and of α-methyl with p-methyl shows that a substantial amount of negative charge is distributed into the ring. Hence, conjugation between the ring and the central carbon must be important at the transition state.

STEREOCHEMISTRY

For the exchange reaction of ethylbenzene-α-d, let

k_D = replacement of D by H
k_H = replacement of H by H
k_H(rac) = replacement of H by H resulting in loss of optical activity

Then, for the observed loss of optical activity, k_{rac}, with optically active ethylbenzene-α-d

$$k_{rac} = k_D + k_H(rac)$$

Let

$$Q = k_H(rac)/k_H$$

Values of Q for different stereochemical possibilities in replacement of H by H are:

Complete retention: Q = 0
Complete racemization: Q = 1
Complete inversion: Q = 2

In a run with optically active ethylbenzene-α-d, k_{rac} and k_D were determined simultaneously:

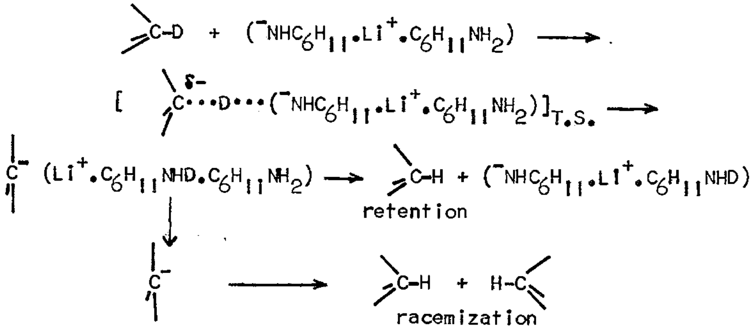
$$k_D = 7.0 \times 10^{-4}\ sec^{-1}$$

$$k_{rac} = 18 \times 10^{-4}\ sec^{-1}$$

$$\text{thus}\quad k_H(rac) = 11 \times 10^{-4}\ sec^{-1}$$

These results demonstrate that the stereochemistry is neither complete inversion nor complete retention. Preliminary experiments with ethylbenzene-α-t give $k_D/k_T \sim 2$, from which $k_H/k_D \sim 5$ [Swain, et al, J. Am. Chem. Soc., 81, 5885 (1958)]; therefore, the stereochemistry of the reaction is partial racemization with some net retention.

PROVISIONAL MECHANISM



COMPARISON OF RELATIVE RATES

In the following table, column two summarizes some of our data on the relative reactivities of different hydrocarbons in our exchange system. The third column lists the comparable relative rates obtained by Shatenshtein and Izrailevich [Zhur. Fiz. Khim., 32, 2716 (1958)] for the exchange reaction of hydrocarbons with potassium deuteroamide in liquid deuteroammonia at 10°. The final column summarizes some of the relative rates obtained by Mr. R. H. Jagow and Dr. R. M. Williams on the solvolysis of arylmethyl tosylates in acetic acid at 40°. A comparison of columns two and four indicates that inductive effects do not suffice to accomodate the stabilization of carbonium ions by methyl groups.

R	RD + $LiNHC_6H_{11}$ 50°	RH + KND_2 10°	ROTs + AcOH 40°
$C_6H_5CH_2$-	1.00	1	1.00
m-$CH_3C_6H_4CH_2$-	.68		2.5
p-$CH_3C_6H_4CH_2$-	.29		57
$C_6H_5CH(CH_3)$-	.11	0.1	$\sim 10^3$ [a]
$C_6H_5C(CH_3)_2$-	.009	.03	$\sim 10^6$ [a]
β-$C_{10}H_7CH_2$-	7		13.8

(a). Estimated

I am indebted to Mr. Dale van Sickle who developed the vacuum line apparatus and experimental procedure and who obtained most of these results. Some of the experiments were run by Miss Liane Reif and Mr. William C. Langworthy. This research was supported by the Air Force Office of Scientific Research. I also wish to thank Professor Richard E. Powell for advice on the solution of some of the kinetic equations.

RECENT DEVELOPMENTS IN FREE RADICAL CHEMISTRY

Cheves Walling

I. Radical reactions of t-butyl hypochlorite

A number of reports in the literature suggest that t-butyl hypochlorite may act as a radical chlorinating agent

toluene	→	benzyl chloride	Clarke, 1931
isobutylene	→	methallyl chloride	Harford, 1939
cyclohexene	→	3-chlorocyclohexene	Kenner, 1945
glycerides	→	allylic chlorides	Teeter, 1949

Reaction of t-Butyl Hypochlorite with Toluene

$$\underset{(0.2\ \text{mole})}{(CH_3)_3COCl} + \underset{(0.6\text{mole})}{\phi CH_3} \xrightarrow[\text{AIBN}\ (1\text{mmole})]{40^\circ C} \phi CH_2Cl\ (94\%) + \phi CHCl_2\ (2\%)$$

$$+ (CH_3)_3COH\ (98\%) + CH_4\ (\text{trace})$$

$$+ (CH_3)_2CO\ (2\%) + CH_3Cl\ (2\%)$$

$$(CH_3)_3COCl \rightarrow (CH_3)_3CO\cdot + Cl\cdot$$

$$(CH_3)_3CO\cdot + H\text{-}R \rightarrow (CH_3)_3COH + R\cdot$$

$$R\cdot + (CH_3)_3COCl \rightarrow R\text{-}Cl + (CH_3)_3CO\cdot$$

$$(CH_3)_3CO\cdot \rightarrow CH_3COCH_3 + CH_3\cdot$$

$$CH_3\cdot + (CH_3)_3COCl \rightarrow CH_3Cl + (CH_3)_3CO\cdot$$

$$CH_3\cdot + H\text{-}R \rightarrow CH_4 + R\cdot$$

Effect of Various Modifiers on the t-Butylhypochlorite - Toluene
Reaction Time, AIBN 40°

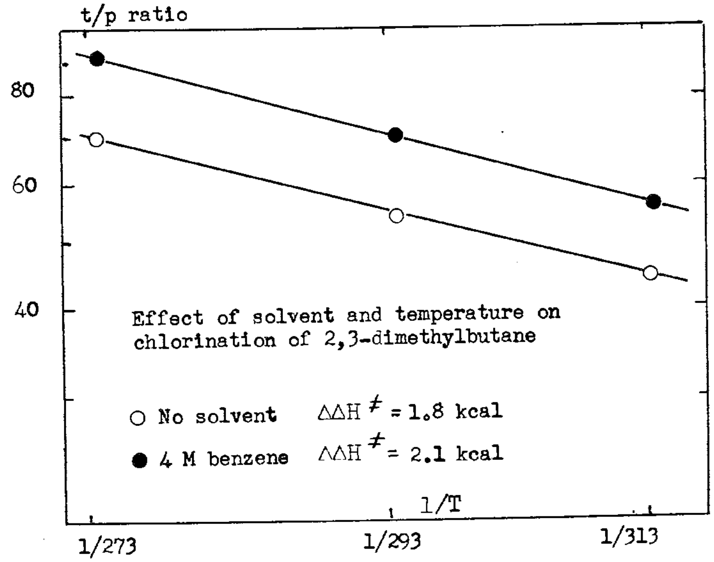
Run	Modifier	Reaction Time
1.	60°	5 minutes
2.	--	250 "
3.	Hydroquinone (0.5 mmole)	1750 "
4.	p-Cresol (0.5 mmole)	No Reaction
5.	Light (No AIBN)	2 minutes

Kinetics: Apparent zero order in hypochlorite
(termination $2RO\cdot \rightarrow ROOR$?)

Relative Reactivity of Hydrocarbons towards t-Butylhypochlorite (40°C)

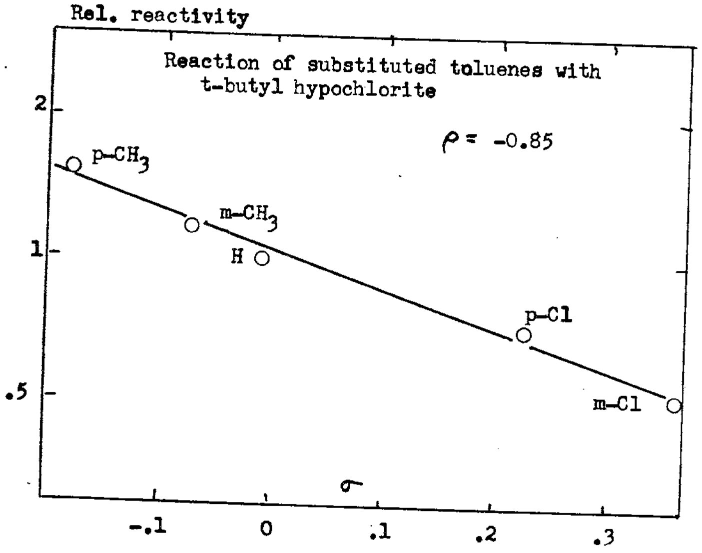
Hydrocarbons	Relative Reactivity Per Molecule	 Per C-H Bond
Triphenylmethane	7.40	22.2
Cyclohexane	6.00	1.50
Mesitylene	4.00	1.33
Diphenylmethane	3.11	4.67
Cumene	2.80	7.65*
p-Xylene	2.80	1.40
m-Xylene	2.05	1.03
Fluorene	2.00	3.00
n-Propylbenzene	2.10	2.04*
Ethylbenzene	1.70	2.13*
Toluene	1.00	1.00
p-Chlorotoluene	0.75	0.75
m-Chlorotoluene	0.55	0.55
t-Butylbenzene	0.40	0.13

* per alpha C-H bond only



Summary of C-H bond reactivities in hydrocarbon - t-butyl hypochlorite reactions
(at 40°)

Alkanes	primary	1	(n-butane)
	secondary	8	(n-butane)
	tertiary	44	(2,3-dimethylbutane)
Benzyl	primary	10.5	(toluene)
	secondary	33	(ethylbenzene)
	tertiary	72	(cumene)
Allylic	secondary	98	(cyclohexene)



Polar effects in t-butyl hypochlorite chlorination
(numbers indicate % substitution at each carbon)

C - C - C - Cl
11 41 48

C - C - C - $OCOCH_3$
26 44 30

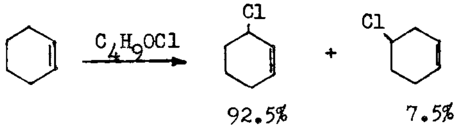
C - C - C - CN
34 44 22

C - C - C - C - Cl
16 44 19 21

C - C - C - C - Cl_2
32 56 12

C - C - C - NO_2
54 33 13

Allylic chlorination, cyclohexene

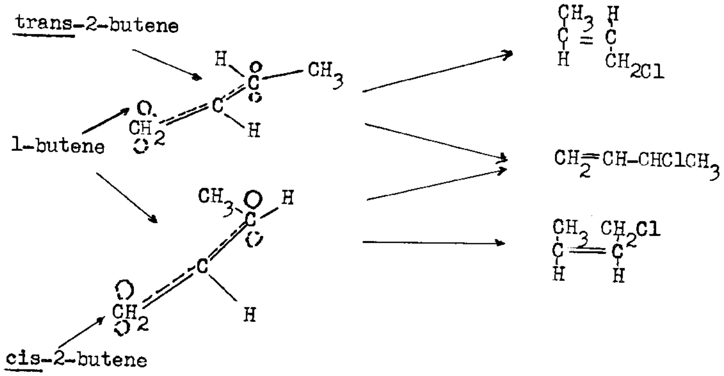


No addition reaction detected.

Butene - t-butyl hypochlorite reactions

	% addn.	rel. react. (allylic)	%1-Cl-2-butene
1-butene	6	1.55	69.6 ± 1
cis-2-butene	28	1.77	63.3 ± 1
trans -2-butene	8	1.67	70.4 ± 1
isobutylene	30	1.0	-

Conformational Stability of Allylic Radicals



II Reaction of Alkoxy Radicals with Trialkyl Phosphites

Cumyl Peroxide: R = $\not{0}C(CH_3)_2-$

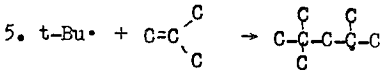
$ROOR + P(OEt)_3 \rightarrow R\text{-}R + OP(OEt)_3$

	25°, U.V.	125°
triethyl phosphate	86%	89%
dicumene	50	72

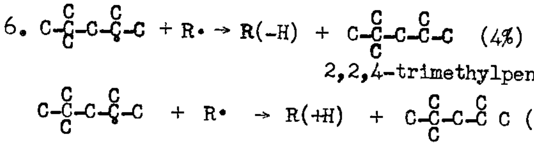
$ROOR \rightarrow 2\ RO\cdot$
$RO\cdot + P(OEt)_3 \rightarrow RO\dot{P}(OEt)_3$
$RO\dot{P}(OEt)_3 \rightarrow R\cdot\ \ OP(OEt)_3$
$2\ R\cdot \rightarrow R\text{-}R$

Di-t-butyl Peroxide - Triethyl Phosphite

1. $\underline{t}\text{-BuOO-}\underline{t}\text{-Bu} \xrightarrow{u.v.} 2\ \underline{t}\text{-BuO}\cdot$
2. $\underline{t}\text{-BuO}\cdot + P\text{-}(OEt)_3 \rightarrow \underline{t}\text{-BuO}\dot{P}\text{-}(OEt)_3$
3. $\underline{t}\text{-BuO}\dot{P}\text{-}(OEt)_3 \rightarrow \underline{t}\text{-Bu}\cdot + OP\text{-}(OEt)_3$
4. (a) $2\ \underline{t}\text{-Bu}\cdot \xrightarrow{disprop.}$ isobutane (30%)
isobutylene (20%)
(b) $2\ \underline{t}\text{-Bu}\cdot \xrightarrow{dimerization}$ hexamethylethane (8%)

5.


$$\text{t-Bu}\cdot + C{=}C\overset{C}{\underset{C}{<}} \rightarrow C\text{-}\overset{C}{\underset{C}{C}}\text{-}C\text{-}\overset{C}{C}\text{-}C$$

6.


$$C\text{-}\overset{C}{\underset{C}{C}}\text{-}C\text{-}\overset{C}{C}\text{-}C + R\cdot \rightarrow R(-H) + C\text{-}\overset{C}{\underset{C}{C}}\text{-}C\text{-}\overset{C}{C}\text{-}C \quad (4\%)$$

2,2,4-trimethylpentane

$$C\text{-}\overset{C}{\underset{C}{C}}\text{-}C\text{-}\overset{C}{C}\text{-}C + R\cdot \rightarrow R(+H) + C\text{-}\overset{C}{\underset{C}{C}}\text{-}C\text{-}\overset{C}{C}\ C \quad (2\%)$$

2,4,4-trimethylpentene-1

$t\text{-}C_4H_9OOH + P(OEt)_3 \xrightarrow{0^\circ} t\text{-}C_4H_9OH + OP(OEt)_3$

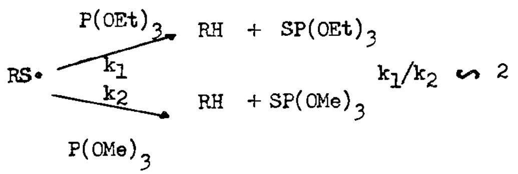
$C_6H_5CO\text{-}O\text{-}O\text{-}COC_6H_5 + P(C_6H_5)_3 \rightarrow C_6H_5CO\text{-}O\text{-}COC_6H_5 + OP(C_6H_5)_3$

$C_4H_9\text{-}O\text{-}O\text{-}C_4H_9 + P(C_6H_5)_3 \overset{?}{\rightarrow} C_4H_9OC_4H_9 + OP(C_6H_5)_3$

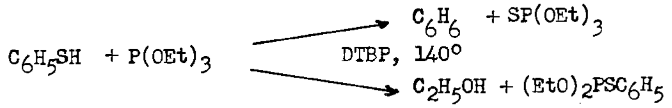
Horner and Jurgeleit (1955)

REACTION OF THIYL RADICALS WITH TRIETHYL PHOSPHITE

1. $RSH + P(OEt)_3 \rightarrow RH + S\text{-}\dot{P}\text{-}(OEt)_3$
2. $RS\cdot + P\text{-}(OEt)_3 \rightarrow R\text{-}S\text{-}\dot{P}\text{-}(OEt)_3$
3. $R\text{-}S\text{-}\dot{P}\text{-}(OEt)_3 \rightarrow R\cdot + S\text{-}P\text{-}(OEt)_3$
4. (a) $R\cdot + RSH \rightarrow RH + RS\cdot$
   (b) $R\cdot + RSSR \rightarrow RSR + RS\cdot$



$k_1/k_2 \backsim 2$



thiophenol inhibits $n\text{-}C_4H_9SH$ reaction, whence

$C_6H_5\dot{S}P(OEt)_3 \longrightarrow C_6H_5\cdot + SP(OEt)_3$ is slow

Limitations of Disulfide Reaction

1. $Me_2\dot{C}CN + RSSR \rightarrow$ too slow

   $RO\cdot + P(OEt)_3 \rightarrow R\cdot + OP(OEt)_3$

2. Benzyl disulfide (low quantum yield)

   $\phi CH_2SSCH_2\phi,\ \phi CH_2SCH_2\phi \xrightarrow{\text{light}} \phi CH_2S\cdot + \phi CH_2\cdot$

   $\phi CH_2S\cdot + P(OEt)_3 \rightarrow SP(OEt)_3 + \phi CH_2\cdot$ (fast)

   $\phi CH_2\cdot + \phi CH_2SSCH_2\phi \rightarrow \phi CH_2S\dot{C}H_2\phi$ (5-10%) $+ \phi CH_2S\cdot$

   $2\phi CH_2 \rightarrow \phi CH_2CH_2\phi$ (26%)

   $\phi CH_2\cdot + RH \rightarrow \phi CH_3$ (20%) $R\cdot$

Thermal Reaction of Disulfides

$C_4H_9S\text{-}SC_4H_9 + P(OEt)_3 \xrightarrow{185^\circ} C_4H_9SC_2H_5$ (50%)

$+ C_4H_9SPO(OEt)_2$ (50%)

via Arbuzov path $C_4H_9\overset{+}{S}P(OEt)_3$ $C_4H_9S^-$

$RSSR + P(OEt)_3 + CO \rightarrow RCOSR + SP(OEt)_3$

via

$RS\cdot + P(OEt)_3 \rightarrow RS\dot{P}(OEt)_3$

$RS\dot{P}(OEt)_3 \rightarrow R\cdot + SP(OEt)_3$

$R\cdot + CO \rightarrow R\dot{C}O$

$R\dot{C}O + RSSR \rightarrow RCOSR + RS\cdot$

Similarly (?)

$R\dot{S}H + P(OEt)_3 + CO \rightarrow RCHO + SP(OEt)_3$

Conversion of Butyl disulfide to Thioester

T	P_{CO}(atm)	Init.	Yield(%)
120-144°	325	DTBP	99
120	7-12	DTBP	47
50	1	UV	18
50	1	UV	36[a]

a) Slow addition of disulfide

Other Examples of Phosphoranyl Radical Reactions

$$\mathrm{CCl_4 + P(OEt)_3 \rightarrow CCl_3PO(OEt)_2 + EtCl}$$

Kamai (1946); Griffin (1958)

$$\mathrm{\cdot CCl_3 + P(OEt)_3 \rightarrow CCl_3\dot{P}(OEt)_3}$$

$$\mathrm{CCl_3\dot{P}(OEt)_3 \rightarrow CCl_3PO(OEt)_2 + Et\cdot}$$

$$\mathrm{Et\cdot + CCl_4 \rightarrow EtCl + \cdot CCl_3}$$

$$\mathrm{CHBr_3 + P(C_6H_5)_3 \rightarrow [CHBr_2P(C_6H_5)_3]^+Br^-}$$

Ramirez and McKelvie (1957)

$$\mathrm{CHBr_2\dot{P}(C_6H_5)_3 + CHBr_3 \rightarrow \cdot CHBr_2 + product}$$

Reactions Involving Oxygen

$$\mathrm{P(OEt)_3 + O_2 \xrightarrow{\underline{DTBP}} OP(OEt)_3}$$

via

$$\mathrm{ROO\cdot + P(OEt)_3 \rightarrow ROOP(OEt)_3 \longrightarrow RO\cdot \quad OP(OEt)_3}$$

$$\mathrm{RH + PCl_3 + O_2 \rightarrow RPOCl_2 + POCl_3 + HCl}$$

Clayton and Jensen (1948)

$$\mathrm{cyclohexene + P_4 + O_2 \rightarrow (C_6H_{10}P_2O_4)_n}$$

Willstatter and Sonnenfield (1914)

THE OXYGEN-OXYGEN BOND

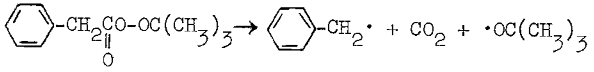
Paul D. Bartlett

The O-O bond, one of the weakest in available organic compounds, shows great versatility in its mechanisms of fission. Ionic cleavage appears in the carboxyl inversion of acyl peroxides (J. E. Leffler, 1950), the Criegee rearrangement of peresters (1948), and the concerted cleavage of primary ozonides (R. Criegee, 1953). Radical (homolytic) fission occurs in a simple form in di-t-butyl peroxide (Raley, Rust and Vaughan, 1948), and as part of a concerted mechanism in the decomposition of peresters $\mathrm{RCO_3C(CH_3)_3}$, where R is benzyl, t-butyl, trichloromethyl, or any group with similar or greater potential stability as a free radical. (P. D. Bartlett, *Experientia*, Suppl. 7, 275 (1957); P. D. Bartlett and R. R. Hiatt, JACS 80, 1398 (1958)). Two striking recent cases of concerted peroxide cleavage are that of peroxy-hemiacetals derived from primary hydroperoxides, in which molecular hydrogen is eliminated (L. J. Durham, C. F. Wurster, Jr., and H. S. Mosher, JACS 80, 332 (1958)), and the anchimerically assisted cleavage in t-butylperoxy-*o*-methylthiobenzoate (J. C. Martin, Boston A. C. S. Meeting, 1959).

Interest is currently centered on such questions as (1) how to determine the mechanism unambiguously in particular cases, (2) Is there a clear boundary between ionic and radical fission? (3) What limits the number of bonds able to undergo simultaneous fission in a concerted mechanism? (4) What is the mode of operation of substituent effects in the various mechanisms? (5) Can the linked changes in enthalpy and entropy of activation in peroxide series be regarded as a model with some generality for other reactions?

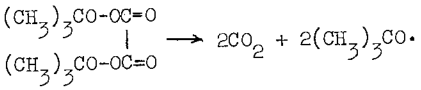
Examples of concerted fission:

(a) at two bonds



$$\Delta H^{\ddagger} = 28.7 \text{ kcal.}$$

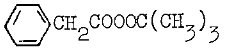
(b) at three bonds



$$\begin{array}{c}(CH_3)_3CO\text{-}OC{=}O\\ \quad\quad\quad\;\;|\\ (CH_3)_3CO\text{-}OC{=}O\end{array} \longrightarrow 2CO_2 + 2(CH_3)_3CO\cdot$$

$$\Delta H^{\ddagger} = 25.5 \text{ kcal.}$$

Radical scavengers contribute to the study of mechanism by providing an independent measurement of rate, by capturing intermediate radicals to form recognizable products, and by distinguishing free radicals on the one hand from caged pairs or nonradical intramolecular reactions on the other.

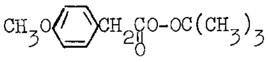
Decomposition of 

in Presence of Iodine in Toluene

Product	Moles per mole perester
CO_2	.956
t-Butyl alcohol	.672
Acetone	.075
Benzyl iodide	1.40
Benzyl t-butyl ether	.165
Iodine consumed	.68
Benzyl group accounted for	.893
t-Butyl group accounted for	.912

The action of scavengers themselves is imperfectly understood. They generally react with zero order kinetics, but do not capture 100% of the potential radicals.

Efficiency of Iodine in Toluene
as Scavenger Toward Different
Radical Sources

Source	T	% of Radicals Captured
$(CH_3)_3C\text{-}O\text{-}O\text{-}C(CH_3)_3$	100.5°	~100
$(CH_3)_2\underset{CN}{C}\text{-}N{=}N\text{-}\underset{CN}{C}(CH_3)_2$	56°	77
	56°	46

Source	T	% of Radicals Captured
$(CH_3)_3CO\text{-}O\underset{O}{C}\underset{O}{C}O\text{-}OC(CH_3)_3$	25°	48

This is not a matter of scavenger concentration.

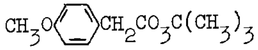
Decomposition of $C_6H_5CH_2CO_3C(CH_3)_3$
in Presence of Iodine in Toluene at 95°, 7 Hours

Compound	Moles per Mole of Perester		
I_2 (initial)	0.78	1.27	1.93
CO_2	.956	.962	.953
$(CH_3)_3COH$	.672	.664	.668
$(CH_3)_2C{=}O$	.075	.046	.043
$C_6H_5CH_2I$	1.40	1.37	1.38
$C_6H_5CH_2OC(CH_3)_3$	.165	.214	.223
Iodine consumed	.68	.72	.73
Benzyl groups accounted for	.893	.920	.934
t-Butyl groups accounted for	.912	.924	.930

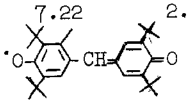
Efficiency of Iodine in Different Solvents
as Radical Scavenger Toward
$C_6H_5CH_2\underset{O}{C}OOC(CH_3)_3$ at 56°

Solvent	[Iodine] x 10^4	Efficiency
Toluene	8.10	48%
Anisole	7.95	50%
Cumene	9.05	25.5%
Chlorobenzene + $(C_6H_5)_3CH$	9.05	25.5%

It has been thought that when some two or more scavengers yield the same percentage efficiency in capturing radicals from a particular reaction, the uncaptured radicals must be reacting by way of caged pairs. However, this conclusion is not firm unless all zero-order reactions of scavengers with higher efficiency can be accounted for.

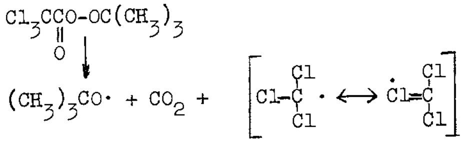
Rate of Decomposition of  in Toluene at 56°

Method	[Perester]$_o$	[Scavenger] x 10^4	k_1 x 10^5, $sec.^{-1}$	% of IR k_1
IR	.0567	(styrene, 3.2%)	4.54	100
IR	.0584	(styrene, 2.0%)	4.60	
Galvinoxyl*	.0556	19.6	4.40	94
"	.0105	20.5	4.16	
Iodine	.0484	9.10	2.02	44
"	.0518	9.10	2.20	
"	.0609	7.22	2.15	
"	.0704	7.22	2.06	
"	.0709	7.22	2.18	

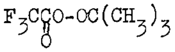
*Galvinoxyl 

(G. M. Coppinger, J. A. C. S. 79, 501 (1957))

Contrast in stabilization between trichloromethyl and trifluoromethyl radicals; example of delocalization using higher orbitals



Half life at 60°, 1.06 x 10^3 min. in ϕCl

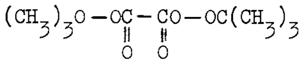


$F_3CCO\text{-}OC(CH_3)_3$

Half life at 60°, 500 x 10^3 min. in ϕCl;
no concerted decomposition.

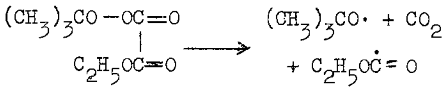
How many bonds participate in decomposition of t-butyl peroxalate?

Products of Decomposition of

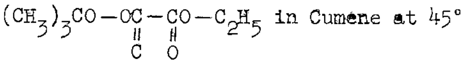


$(CH_3)_3O-OC-CO-OC(CH_3)_3$ at 45°

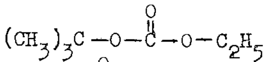
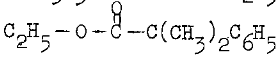
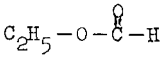
Product	Moles per mole of perester in		
	Benzene	Isopropyl Ether	Cumene
CO_2	1.92	1.95	2.01
t-Butyl alcohol	1.02	2.00	1.77
Acetone	0.76	~ 0	0.03
Methane (+ some CO)	0.14	-	-
Ethane	0.17	-	-
Dicumyl	-	-	0.86



Decomposition Products of



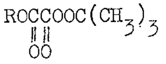
$(CH_3)_3CO-OC-CO-C_2H_5$ in Cumene at 45°

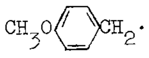
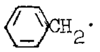
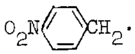
Product	Moles per mole perester
CO_2	1.12
t-Butyl alcohol	0.75
Acetone	none
Ethane (incl. 2-5% ethylene)	0.20
 $(CH_3)_3C-O-C-O-C_2H_5$	0.28
 $C_2H_5-O-C-C(CH_3)_2C_6H_5$	0.23
 $C_2H_5-O-C-H$	0.15
Dicumyl	0.32

Material Balances

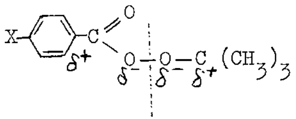
t-Butyl	102%
CO_2	89%
C_2H_5	86%

Decomposition Rates of Peroxalates


$ROCCOOC(CH_3)_3$ with $\overset{\|}{O}$ $\overset{\|}{O}$

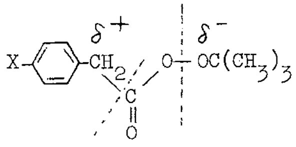
R	Relative rate constant at 45°	ΔH‡	ΔS‡
$(CH_3)_3CO\cdot$	20	25.5	5.1
	5.3	26.2	4.6
$C_2H_5\cdot$	3.5	26.9	6.0
	2.8	26.6	4.5
	1	27.9	6.8

Ionic and radical fission in peresters have opposite signs of ρ in the Hammett Equation (+ for ionic, - for radical). Although t-butyl perbenzoates and phenylperacetates both have negative ρ, the mechanisms are different.



$\overset{\text{ext.}}{\rho_{90}} = -1.04$

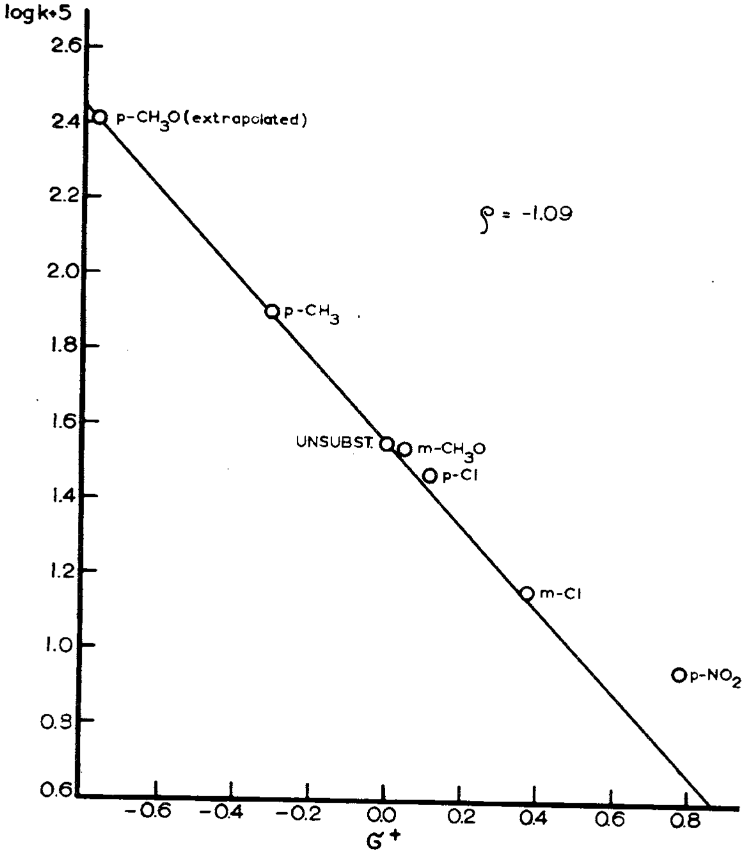
Correlated with σ (Blomquist and Berstein)



ρ_{90} 1.09

Correlated with σ^+

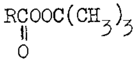
THERMAL DECOMPOSITION OF $X\text{-}C_6H_4CH_2COO\text{-}OC(CH_3)_3$ IN CHLOROBENZENE AT 90.66°C. (observed by I.R.)

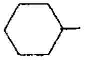
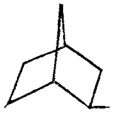
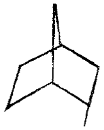


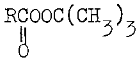
Can ionic transition-state resonance contribute to cleavage into free radicals? Yes; all states are of the same multiplicity because the spins of the partner radicals remain antiparallel.

R = Norbornyl, a borderline case. Norbornyl cations are well stabilized, norbornyl radicals not, through bridging. The results show only borderline driving force.

Peresters Containing Cyclohexyl and Norbornyl Groups


$\underset{\underset{\displaystyle O}{\|}}{RC}OOC(CH_3)_3$

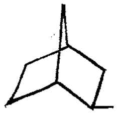
R	Relative Rate at 100°	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$
$(CH_3)_3C-$	2800	30.6	13
	120	31.3	8.6
 (exo)	83	30.9	6.7
 (endo)	20	35.6	16.4
CH_3	1	38.0	17.0

Products from Alicyclic Peresters

$\underset{\underset{\displaystyle O}{\|}}{RC}OOC(CH_3)_3$

Heated in Chlorobenzene at 100° for 22-27.5 Hours

Product	Moles per Mole of Perester R= Cyclohexyl	R= exo-Norbornyl	R= endo-Norbornyl
Gas (CO and CH_4)	.08	.03	.055
CO_2	.75	.76	.58
t-Butyl alcohol	.43	.22	.32
Acetone	.32	.40	.36

Effect of Iodine and Water in Carbon Tetrachloride on Products from t-Butylperoxy-exo-Norbornane-Carboxylate

Product	Moles per mole of perester 3% H_2O	3% H_2O + 1 mole I_2
Gas	none	none
CO_2	.67	.56
CH_3Cl	.30	--
$(CH_3)_2C=CH_2$	--	.13
 COOH	.16	.26

THE MECHANISMS OF SOME CHROMIC ACID OXIDATIONS

Kenneth B. Wiberg

Although much is known about the oxidation of alcohols and of aldehydes, the oxidation of hydrocarbons is relatively poorly understood. Diphenylmethane is a convenient hydrocarbon to study since it gives only one product, benzophenone, and that is formed in high yield. The oxidation was studied in 91% and 95% acetic acid since this medium permits reasonably rapid reactions at moderate acid concentrations (0.1-0.3 M), and permits the reaction to be carried out in homogeneous solution. The presence of some water is desirable since this permits one to specify the nature of the chromium species in the solution.

The rate law for the reaction has been found to be:

$$v = k[\phi CH_2\phi][CrO_3]h_o$$

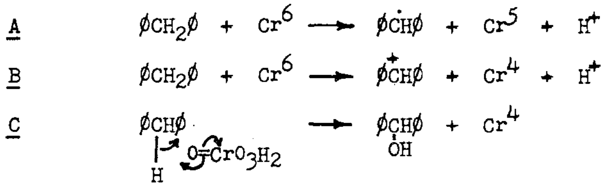
The first order dependence on the organic substrate and on the Hammett acidity function is analogous to most other chromic acid oxidations. However, the first order dependence on chromium trioxide is unusual.

In solutions of chromic acid, there exists an equilibrium between the monomeric form and the dimeric form:

$$2\ HCrO_4^- \rightleftharpoons Cr_2O_7^= + H_2O$$

The equilibrium constant for the reaction may be determined spectrophotometrically using the deviation from Beer's law of chromic acid solutions. The equilibrium constant thereby determined for 91% acetic acid is 25, and that for 95% acetic acid is 65. In the oxidation of alcohols, Westheimer and Novick (J. Chem. Phys. 17, 61 (1949)) have shown that the rate of reaction follows the concentration of the acid chromate ion, and a similar result has been obtained in the oxidation of benzaldehyde (Wiberg and Mill, J. Am. Chem. Soc. 80, 3022 (1958); Westheimer and Graham, ibid., 80, 3030 (1958)). This has been interpreted in terms of the formation and subsequent decomposition of an ester intermediate, and the different result in the oxidation of diphenylmethane lends additional support to this hypothesis.

The rate determining step probably involves the reaction of diphenylmethane with chromic acid or the acid dichromate ion, and this reaction may be either the formation of a complex between the two species, or the abstraction of a hydrogen with one or two electrons. The isotope effect $k_H/k_D = 6.4$ indicates that the latter is the case. There are then three possible mechanisms for this reaction:

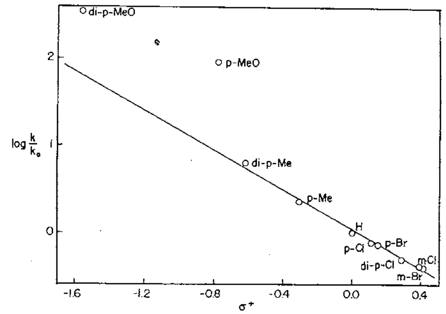


A $\quad \phi CH_2\phi + Cr^6 \longrightarrow \phi\dot{C}H\phi + Cr^5 + H^+$

B $\quad \phi CH_2\phi + Cr^6 \longrightarrow \phi\overset{+}{C}H\phi + Cr^4 + H^+$

C $\quad \phi\underset{H}{C}H\phi \;\; O{=}CrO_3H_2 \longrightarrow \phi\underset{OH}{C}H\phi + Cr^4$

A partial differentiation may probably be made based on the effect of substituents:



With the exception of the p-methoxy substituted compound, which must be considered separately, the rates are correlated well with σ^+, with a slope, ρ^+, of -1.14. This is much smaller than would be expected for mechanism B in which a carbonium ion is formed to a considerable extent in the activated complex (as indicated by the magnitude of the isotope effect). For this mechanism, a ρ value of between 3-5 should be found.

Mechanism A would be expected to give a value of ρ of between -1.0 and -1.5 in analogy with the results obtained in the reaction of toluene with bromine, N-bromosuccinimide (Kooyman, et al., Koninkl. Ned. Akad. Wetenshappen Proc., B56, 75 (1953)) and in the air oxidation of benzaldehyde (Walling and McElhill, J. Am. Chem. Soc. 73, 2927 (1951)). However, mechanism C would also be expected to give a small value of ρ, the direction of which is difficult to predict.

Mechanism C appears the less likely of the two in view of the magnitude of the kinetic isotope effect. A non-linear, activated complex such as would be involved in this case would force the hydrogen to participate in the normal modes of vibration of the activated complex (other than that leading to reaction) and this will in part cancel the zero-point energy difference in the ground state. Since the isotope effect is about as large as any which have been found at the temperature used (30°)

it is unlikely that any such cancellation has occurred. Mechanism A is therefore favored for the first step of the reaction.

Some information concerning the later steps in the reaction may be obtained from a study of the induced oxidation of manganous and cerous ion during the reaction. It can be seen that rate of reaction is reduced to a value less than one-half the original rate, and approaching one-third.

Substituent	$k/k_o(.033\underline{M}\ Ce^3)$	$k/k_o(.0067\underline{M}\ Mn^2)$
H	.47	.58 (.36, 0.04M)
pCl	.44	.56 (.47, 0.06M)
p,p'-diMe	.34	.50

These data rule out a chain process for the reaction since any scheme which can be written for the subsequent steps will lead to a prediction of a rate reduction to one-third of the original value. These data will not however directly indicate what type of reactions must follow the initial step.

It can be shown that in other chromic acid oxidations, Cr^5 invariably reacts by a two electron mechanism. If this is assumed to be the case here also, a possible scheme for the subsequent reactions is:

$$\begin{array}{lcl}
\phi CH_2\phi + Cr^6 & \longrightarrow & \phi\dot{C}H\phi + Cr^5 \\
\phi\dot{C}H\phi + Cr^6 & \longrightarrow & \phi_2CHOH + Cr^5 \\
2\phi CH_2\phi + 2Cr^5 & \longrightarrow & 2\phi_2CHOH + 2Cr^3 \\
\phi_2CHOH + Cr^6 & \longrightarrow & \phi_2C{=}O + Cr^4 \\
Cr^4 + Cr^6 & \longrightarrow & 2Cr^5 \\
2\phi_2CHOH + 2Cr^5 & \longrightarrow & 2\phi_2C{=}O + 2Cr^3
\end{array}$$

The difficulty with a scheme such as this is that it requires that the velocities of the third and the last step be identical (i.e., that exactly one-half of the Cr^5 reacts with the diphenylmethane and the other one-half reacts with the benzhydrol formed in the previous steps). Such a coincidence seems very unlikely, particularly if one remembers that the first reaction involves one species which is in high concentration, whereas the other is between two species which are present in very low concentration.

It is possible to circumvent this difficulty if it is postulated that the benzhydryl radical undergoes a three-electron oxidation directly to benzophenone. Such a scheme is:

$$\begin{array}{lcl}
\phi CH_2\phi + Cr^6 & \longrightarrow & \phi\dot{C}H\phi + Cr^5 \\
\phi\dot{C}H\phi + Cr^6 & \longrightarrow & \phi_2\underset{H}{C}\text{-}OCrO_3H_2 \\
\phi_2\underset{H}{C}\text{-}OCrO_3H_2 & \longrightarrow & \phi C{=}O + Cr^3 \\
\phi CH_2\phi + Cr^5 & \longrightarrow & \phi_2CHOH + Cr^3 \\
\phi_2CHOH + Cr^6 & \longrightarrow & \phi_2C{=}O + Cr^4 \\
\phi CH_2\phi + Cr^4 & \longrightarrow & \phi\dot{C}H\phi + Cr^3 \\
\phi\dot{C}H\phi + Cr^6 & \longrightarrow & \phi_2C{=}O + Cr^3
\end{array}$$

Not only does this scheme eliminate the necessity for a coincidence in velocities of different steps, but it also involves no reactions between species which will be in low concentration.

Possible analogies for the addition of the radical to the Cr^6 species may be found in persulfate oxidations, and other reactions involving the induced decomposition of a species which initiates a reaction. The most novel step is the next to last in which it is proposed that Cr^4 reacts with diphenylmethane to give the benzhydryl radical.

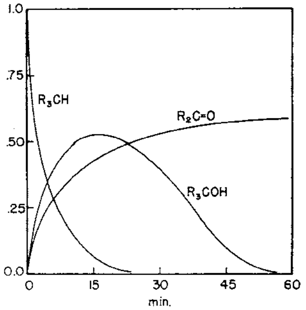
It is difficult to obtain evidence for this type of reaction, but one possible approach is to use an inorganic oxidation-reduction system which produces Cr^4, and to determine the effect of this system on diphenylmethane. One possibility is the ceric-chromic system studied by King and Tong (Abst. 134th Meeting Am. Chem. Soc., Chicago, 1958, p. 85) for which the rate law is

$$v \quad k\frac{[Cr^3][Ce^4]^2}{[Ce^3]}$$

This suggested the mechanistic sequence

$$\begin{array}{lcll}
Ce^4 + Cr^3 & \rightleftharpoons & Ce^3 + Cr^4 & \\
Ce^4 + Cr^4 & \longrightarrow & Ce^3 + Cr^5 & \text{(slow)} \\
Ce^4 + Cr^5 & \longrightarrow & Ce^3 + Cr^6 & \text{(rapid)}
\end{array}$$

The question now remains, are aliphatic hydrocarbons oxidized by a one electron or a two electron process. Sager and Bradley (J. Am. Chem. Soc. 78, 1187 (1956)) have studied the chromic acid oxidation of 3-ethylpentane, analyzing for each of the products as a function of time. Their results were:

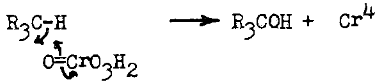


They also observed that there was a kinetic isotope effect when the tertiary hydrogen was replaced by a deuterium. They proposed that the carbinol was the first product formed and that the subsequent reactions depended on a rate controlling dehydration of the alcohol. Roček (Coll. Czech. Chem. Comm. 22, 1509 (1957)) has come to a similar conclusion in studying the oxidation of methylcyclohexane. Since the rate determining step for the initial oxidation is the cleavage of the carbon-hydrogen bond, there are again three possible mechanisms for this step:

A $\quad R_3CH + Cr^6 \longrightarrow R_3C^+ + Cr^4$

B $\quad R_3CH + Cr^6 \longrightarrow R_3C\cdot + Cr^5$

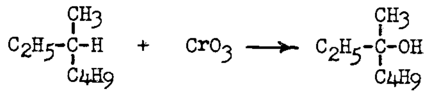
C



$$R_3C{-}H \;\; O{=}CrO_3H_2 \longrightarrow R_3COH + Cr^4$$

One cannot easily use the effect of substituents to differentiate between these three possibilities. However, there exists a more potent and definitive tool, the stereochemistry of the reaction. The formation of a carbonium ion would be similar to a solvolysis reaction and should lead to the same stereochemical result as the latter, inversion accompanying racemization (cf. Streitwieser, Chem. Revs. 56, 571 (1956)). The formation of a radical intermediate should lead to racemic product, whereas the last possibility would lead to retention of configuration.

The hydrocarbon, 3-methylheptane, was prepared from D-(+)-2-methylbutanol, and was oxidized to the carbinol with the following results:



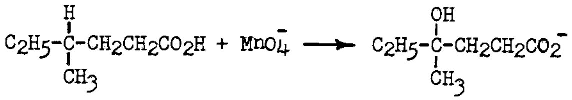
$$C_2H_5{-}C(CH_3)(C_4H_9){-}H + CrO_3 \longrightarrow C_2H_5{-}C(CH_3)(C_4H_9){-}OH$$

$[\alpha]_D = +9.5°$

no Ce^3 $\quad [\alpha]_D = +0.67°$
.013 M Ce^3 $\quad = 0.74°$
.073 M Ce^3 $\quad = 0.85°$

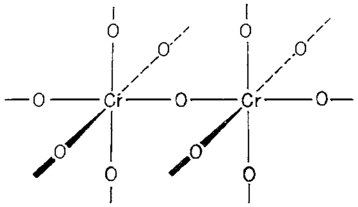
The first value corresponds to the net result of oxidation by Cr^6 and all of the intermediate chromium species. The latter results correspond to progressively less oxidation by the intermediate species. This is indicated by the previous results on the effect of cerous ion on these oxidations, and on the fact that a marked decrease in the amount of alcohol isolated was observed when cerous ion was added. This is the required result since the amount of product was kinetically controlled.

To decide between mechanisms A and C requires that one know the stereochemical relation between the secondary and tertiary alcohols. One method of obtaining this relationship is via the use of the reaction investigated by Kenyon and Symons (J. Chem. Soc. 3580 (1953)):

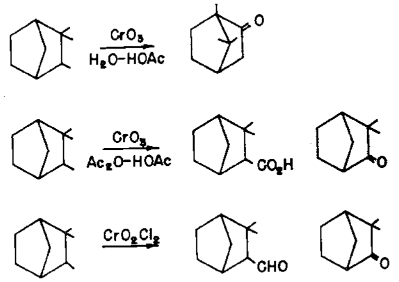


$$C_2H_5{-}C(H)(CH_3){-}CH_2CH_2CO_2H + MnO_4^- \longrightarrow C_2H_5{-}C(OH)(CH_3){-}CH_2CH_2CO_2^-$$

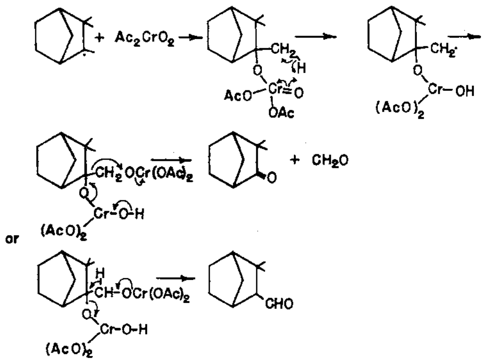
In studying chromic acid oxidations, one must take cognizance of the fact that the form of chromium trioxide present in a solution depends on the solvent used. When water containing solvents are used, it is probably in the form of chromic acid or one of the related ions. However, in acetic anhydride, it is in the form of diacetyl chromate. It is important to note that chromium trioxide is essentially insoluble in glacial acetic acid, and becomes soluble only on the addition of water, acetic anhydride or other compound which will cause depolymerization of chromium trioxide:



The species of Cr^6 present has a marked effect on the products obtained in a chromic acid oxidation, as, for example, in the case of isocamphane:



The oxidation of isocamphane in aqueous acetic acid clearly involves the tertiary carbonium ion as an intermediate. The normal rearrangement of the ion followed by further oxidation would lead to the formation of camphor. The oxidation of isocamphane by diacetyl chromate (Kenyon and Archer, J. Chem. Soc. 4197 (1954)) probably does not involve the carbonium ion, but rather the tertiary free radical. In analogy with the results obtained in the oxidation of diphenylmethane, the radical would be expected to add to the oxidizing agent, and if this occurs, the subsequent reactions may be as follows:



This scheme will account for most of the products of chromic acid oxidations carried out in acetic anhydride.

A closely related reaction is the Etard reaction in which the hydrocarbon is treated with chromyl chloride to give a complex which is then decomposed with water to give mixtures of aldehydes and ketones. The products of the Etard reaction with isocamphane are essentially the same as those obtained using chromyl acetate, and this may be accounted for by a scheme similar to that shown above.

The oxidation of alkylbenzenes is particularly interesting. The Etard oxidation of n-propylbenzene gives 88% benzyl methyl ketone along with 23% propiophenone and 9% benzaldehyde. When propylbenzene-β-d$_2$ is oxidized, the amount of benzyl methyl ketone drops to 14%, and 70% of propiophenone along with 14% of benzaldehyde is obtained. Any mechanism for the reaction will predict this change in product ratio, resulting from a kinetic isotope effect. However, the important fact is that the benzyl methyl ketone contained 60% of one deuterium in the α-position. This can arise only from a rearrangement occurring during the reaction.

The difference in reactivity and products in the oxidation of t-butylbenzene clearly indicates that the initial attack is at the carbon adjacent to the aromatic ring. If a derivative of the corresponding 1,2-diol were formed in the reaction (as was proposed for the diacetyl chromate oxidation above), the formation of both benzyl methyl ketone and benzaldehyde may be accounted for. The former would arise by a pinacol rearrangement, and the latter by the cleavage of the diol. It is known that vic-diols are readily cleaved by chromic acid. The question remains, however, does the rearrangement occur prior to or during the work-up of the complex.

An attempt to answer this question was made by reducing the complex with lithium aluminum hydride in ether. These conditions would appear to be poor ones for promoting rearrangement. The ratio of 1-hydroxy, 2-hydroxy and 1,2-dihydroxy-derivatives was similar to the ratios of 1-keto and 2-keto-derivatives, and benzaldehyde obtained in the usual work-up with water. It is concluded that the rearrangement probably occurred prior to the decomposition of the Etard complex.