

ORGANIC REACTION MECHANISMS · 1973

*An annual survey covering the literature
dated December 1972 through November 1973*

Edited by

A. R. BUTLER, University of St. Andrews

M. J. PERKINS, Chelsea College, University of London

An Interscience® Publication

JOHN WILEY & SONS

London · New York · Sydney · Toronto

ORGANIC REACTION MECHANISMS · 1973

*An annual survey covering the literature
dated December 1972 through November 1973*

Edited by

A. R. BUTLER, University of St. Andrews

M. J. PERKINS, Chelsea College, University of London

An Interscience® Publication

JOHN WILEY & SONS

London · New York · Sydney · Toronto

An Interscience® Publication

Copyright © 1975 by John Wiley & Sons Ltd.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, without the prior written permission of the Copyright owner.

Library of Congress Catalog Card Number 66-23143

ISBN 0 471 12690 X

Printed in Great Britain by
William Clowes & Sons Limited
London, Colchester and Beccles

Contributors

R. BAKER	Department of Chemistry, The University, Southampton
T. W. BENTLEY	Department of Chemistry, University College of Swansea
R. B. BOAR	Department of Chemistry, Chelsea College, University of London
A. R. BUTLER	Department of Chemistry, The University, St. Andrews
B. CAPON	Department of Chemistry, Glasgow University
M. R. CRAMPTON	Department of Chemistry, Durham University
T. L. GILCHRIST	Department of Organic Chemistry, University of Liverpool
A. C. KNIPE	Department of Chemistry, The New University of Ulster
D. C. NONHEBEL	Department of Pure and Applied Chemistry, University of Strathclyde
M. I. PAGE	Department of Chemistry, The Polytechnic, Huddersfield
F. L. SCOTT	Pennwalt Chemical Corporation, Pharmaceuticals Division, P.O. Box 1710, Rochester, N.Y. 14603, U.S.A.
B. V. SMITH	Department of Chemistry, Chelsea College, University of London
I. D. R. STEVENS	Chemistry Department, The University, Southampton
R. C. STORR	Department of Organic Chemistry, University of Liverpool
J. C. WALTON	Department of Chemistry, St. Salvator's College, University of St. Andrews

Preface

This year's edition of *Organic Reaction Mechanisms*, the eighth in the series, does not differ greatly from the highly successful pattern developed by the previous editors. The literature dated December 1972 to November 1973 has been covered and the aim has been, as in past years, to make the coverage comprehensive. Over 5000 papers have been reported and many of the important ones discussed in some detail.

One modification which will be immediately apparent to those familiar with the series is the changed order of the Chapters. This change has been made to facilitate separate publication of selected sections of the book at prices more likely to be within the reach of the individual researcher. It should be stressed that not all of this book will be available in sectional form; however, if it is successful, sectional publication may be extended with the 1974 Volume. We have also decided to omit the chapter on Photochemistry. This topic is covered comprehensively in a Specialist Report published annually by the Chemical Society.

A further change, made with great reluctance, but as an economy measure necessitated by spiralling publishing costs, has been the relegation of references to the ends of the chapters. If this innovation or any other aspect of the book's format is found irksome, please do not hesitate to let us know. Indeed, it is our intention to offer *Organic Reaction Mechanisms* as a service, and we shall always be pleased to consider suggestions for its improvement.

We are grateful to the established contributors for their continued support, and welcome those who have joined this year. The British office of John Wiley and Sons have given us every possible help and have made the rapid publication of this volume possible. We sincerely hope that *Organic Reaction Mechanisms 1973* will be of as great a value to organic chemists as its predecessors.

August 1974

A. R. B.
M. J. P.

Contents

1.	Reactions of Aldehydes and Ketones and their Derivatives by B. CAPON	1
2.	Reactions of Acids and their Derivatives by M. I. PAGE	21
3.	Radical Reactions by D. C. NONHEBEL and J. C. WALTON	61
4.	Oxidation and Reduction by T. W. BENTLEY	171
5.	Carbenes and Nitrenes by T. L. GILCHRIST	203
6.	Nucleophilic Aromatic Substitution by M. R. CRAMPTON	225
7.	Electrophilic Aromatic Substitution by A. R. BUTLER	243
8.	Carbonium Ions by R. BAKER	261
9.	Nucleophilic Aliphatic Substitution by I. D. R. STEVENS	295
10.	Carbanions and Electrophilic Aliphatic Substitution by R. B. BOAR	339
11.	Elimination Reactions by A. C. KNIPE	361
12.I.	Addition Reactions I. Polar Addition by B. V. SMITH	381
12.II.	Addition Reactions II. Cycloaddition by R. C. STORR	397
13.	Molecular Rearrangements by F. L. SCOTT	415
Author Index, 1973		507
Subject Index, 1973		551

Reactions of Aldehydes and Ketones and their Derivatives

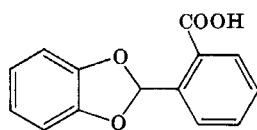
B. CAPON

Chemistry Department, Glasgow University

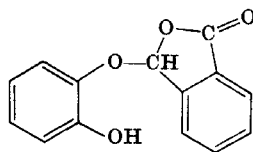
Formation and Reactions of Acetals and Ketals	1
Hydrolysis and Formation of Glycosides	3
Non-enzymic Reactions	3
Enzymic Reactions	3
Hydration of Aldehydes and Ketones and Related Reactions	5
Reactions with Nitrogen Bases	6
Schiff Bases	6
Transamination	7
Enamines	7
Hydrazones, Oximes, Semicarbazones and Related Compounds	7
Hydrolysis of Enol Ethers	8
Enolization and Related Reactions	9
Aldol and Related Reactions	13
Other Reactions	13
References	15

Formation and Reactions of Acetals and Ketals¹

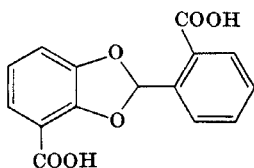
3-(2-Hydroxyphenoxy)phthalide (**2**) is an intermediate in the hydrolysis of *O,O'*-(2-carboxybenzylidene)catechol (**1**) in aqueous buffers of pH 2.9–5. The spontaneous reaction is about 30 times faster than that of *O,O'*-(4-carboxybenzylidene)catechol and may involve nucleophilic catalysis by the carboxylate group. The rate constants for catalysis by acetic and formic acid are similar for the two compounds. The pH-rate profile for the conversion of 2,3-(4-carboxybenzylidenedioxy)benzoic acid (**3**) into the phthalide



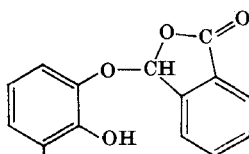
(1)



(2)



(3)

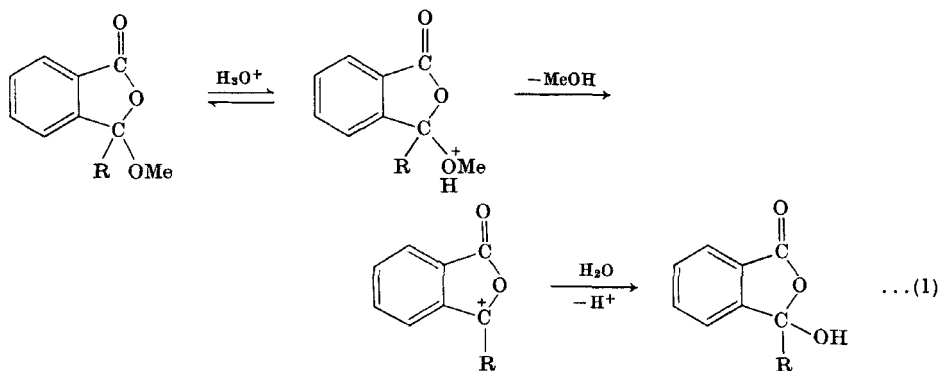


(4)

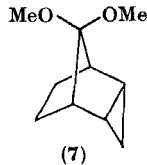
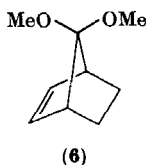
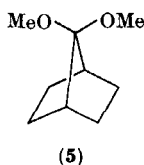
(4) is bell-shaped, but this reaction occurs only about three times faster than the hydrolysis of the acid (3) and hence there can be little nucleophilic assistance.²

Details of Anderson and Fife's work on the hydrolysis of benzaldehyde disalicyl acetal have been published.³

The kinetics of hydrolysis of a series of 3-alkyl-3-methoxyphthalides have been measured and interpreted in terms of the mechanism of equation (1), which was preferred to the A2 mechanism previously proposed.⁴



The relative rates of hydrolysis of compounds (5), (6), and (7) are 1:2.3:120. Therefore, if the faster rates for compounds (6) and (7) are the result of participation by the double bond and the cyclopropane ring, the rate enhancements are much less than found with the analogous *p*-nitrobenzoates and arenesulphonates.⁵ This result is not surprising in view of known reduction of anchimeric assistance brought about by an α -carbonium ion stabilizing group.⁶



The kinetics of alcohol-exchange of acetals and exchange of the α -hydrogen atom have been studied. It was thought that the latter reaction proceeded by way of the vinyl ethers, and the equilibrium constants for the interconversion of the acetals and the vinyl ethers were evaluated from these results together with the rate constants for the addition of alcohols to the vinyl ethers.⁷

Tracer studies have shown that the formation of the formal from benzyl alcohol and paraformaldehyde in aqueous sulphuric acid involves aldehyde-oxygen fission, not benzyl-oxygen fission.⁸

Other related reactions studied include that between acetylferrocene and triethyl orthoformate,⁹ formation of cyclic acetals from enones,¹⁰ formation of 2-furyl-1,3-dioxans catalysed by ion-exchange resins,¹¹ and ketone-exchange of 2,3:4,5-di-isopropylidene- α -L-sorbofuranose with butan-2-one.¹²

There have been numerous investigations of the conformations of cyclic acetals. The classes of compounds studied include 1,3-dioxans,¹³⁻¹⁵ 1,3-dioxolans,¹⁶ spiro-dioxolans,^{17, 18} bicyclic 1,3-dioxans,¹⁹ 1,3-oxathians,^{20a} and 1,3-dioxacycloheptanes.^{20b}

It has been shown that independent estimates of hydrogen-ion activity in moderately concentrated acids are in good agreement. This is of considerable potential use for studies of reaction mechanism.²¹

Hydrolysis and Formation of Glycosides

Non-enzymic Reactions

A reinvestigation of the hydrolysis of ferrocenylmethyl β -D-glucopyranoside has shown that it proceeds with ferrocenylmethyl—oxygen fission, not glucosyl—oxygen fission as previously supposed. Acid-catalysed methanolysis gave glucose and methoxymethyl-ferrocene.²²

Details of Sinnott and his co-workers' investigation of the hydrolysis of 1-adamantyl glycosides²³ and of Clark and Hay's investigation of the metal-ion catalysis of 8-quinolyl β -D-glucoside²⁴ have been published. It was suggested that the acid-catalysed hydrolysis of 8-quinolyl β -D-glucoside proceeds by an *A2* pathway.²⁴

Other glycosides whose acid-catalysed hydrolysis has been studied include alkyl²⁵ and aryl²⁶ β -D-galactopyranosides, methyl 4-*O*-alkyl- α - and - β -D-galactopyranosides,²⁷ β -D-fructofuranosides,^{28a} the methyl glycoside of *O*-acetylated *N*-acetylneuramic acid,^{28b} sucrose,²⁹ and cellulose.³⁰ The alkaline degradation of sucrose has also been studied.³¹

There has been an investigation of the Fischer glycoside synthesis with glucose and galactose.³²

Brown and Bruice³³ have studied the hydrolysis of 1- β -D-glucopyranosyl benzoate, 2,3-di-*O*-methyl-1- β -D-glucopyranosyl benzoate and a mixture of α - and β -2,3,4,6-tetra-*O*-methyl-D-glucopyranosyl benzoates. These reactions show acid-catalysed and neutral components. The acid-catalysed hydrolysis is 10–100 times faster than that of methyl or phenyl β -D-glucoside and, on the basis of ΔS^\ddagger and the solvent isotope effect, it appears to follow an *A1* mechanism with glycosyl—oxygen fission. The neutral hydrolysis also appears to be a unimolecular process with glycosyl—oxygen fission, as benzoate esters are not normally hydrolysed under these conditions. In alkaline solution the hydrolysis of 1- β -D-glucopyranosyl benzoate shows complex kinetics and must occur with benzoyl migrations. Since complex kinetics are also found with the 2,3-di-*O*-methyl compound, migration to the 6- as well as to the 2-hydroxy-group must occur.³³

Enzymic Reactions³⁴

(a) *Lysozymes*. A detailed kinetic investigation of the hydrolysis of hexa-*N*-acetyl-chitohexaoside (NAG-6) catalysed by lysozyme from hens' egg-white has been reported. From the pH-dependence of k_{cat} and $k_{\text{cat}}/K_{\text{m}}$ it was concluded that the $\text{p}K_{\text{a}}$ of glutamic acid³⁵ is 6.1 in the free enzyme and 6.7 in the non-productive complex of the enzyme and NAG-6, and that the $\text{p}K_{\text{a}}$ of aspartic acid 52 is 3.4–3.7 in the free enzyme and 3.8 in the complex.³⁵

The α -tritium isotope effect on the lysozyme-catalysed hydrolysis of NAG-3 to NAG-2 and NAG is $k_{\text{H}}/k_{\text{T}} = 1.19$, corresponding to an α -deuterium isotope effect $k_{\text{H}}/k_{\text{D}} = 1.14$, from which it was concluded that the rate-limiting step is an $\text{S}_{\text{N}}1$ -type ionization. Unfortunately it is difficult to judge this conclusion since there are few if any models for the possible nucleophilically assisted processes for this system, i.e. reactions at a glycosyl-carbon atom where the nucleophile is an amido or carboxylate group.³⁶

The enthalpy of binding of NAG-4 to lysozyme is 2.8 kcal/mol less negative than that for the binding of NAG-3, but the free energies of binding differ only by 0.3 kcal/mol at 25°. It was suggested that two complexes are formed between lysozyme and NAG-4, one similar to that formed by NAG-3 and the other in which the terminal residue partly fills site D.³⁷

The fluorescence of human lysozyme has been studied. NAG-3 and NAG-4 are bound less strongly to human lysozyme than to lysozyme from hens' egg white.³⁸

The binding of aryl di-*N*-acetylchitobiosides to lysozyme appears to be more complex than hitherto thought. Whereas at 32° only the signal in the PMR spectrum of the acetamido-group proximal to the aglycone of *p*-methoxyphenyl di-*N*-acetyl- β -chitobioside is shifted in the presence of lysozyme, at 65° the signals of both acetamido-groups are shifted so that they coalesce. It was suggested that there was a temperature-dependent transition of the interaction between lysozyme and the aryl di-*N*-acetylchitobioside.³⁹

An X-ray study has confirmed that when 2',3'-epoxypropyl di-*N*-acetylchitobioside reacts with lysozyme it becomes attached to the carboxyl group of aspartic acid 52.⁴⁰ Further work on the reaction of iodine with lysozyme has been reported.⁴¹

A polypeptide with lysozyme activity has been synthesized.⁴²

There have been numerous other investigations of lysozyme from hens' egg white⁴³ and also of the lysozymes from human leukocytes,⁴⁴ baboon milk,⁴⁵ bacteriophage T4,⁴⁶ turkeys' egg white,⁴⁷ and geese's egg white.⁴⁸

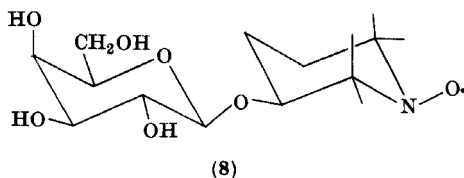
(b) β -Galactosidases. The α -deuterium isotope effect for the hydrolysis of some β -galactosides catalysed by β -galactosidase from *E. coli* has been determined. It was suggested that a conformational change of the enzyme is the rate-limiting step in the reactions of the more reactive galactosides.⁴⁹

Nucleophilic competition by alcohols in the hydrolysis of galactosides catalysed by the β -galactosidase from *E. coli* has been extensively re-investigated. It now seems that the levelling off of the rate at high methanol concentrations arises from factors other than a change in rate-limiting step from degalactosylation to galactosylation.^{50, 51}

The β -D-galactopyranosylpyridinium cation is a poor substrate for β -galactosidase from *E. coli*. As electrophilic catalysis is not possible with this substrate, substrate distortion and electrostatic or nucleophilic catalysis must be responsible for the enzymic catalysis.⁵² The binding of β -D-galactopyranosyltrimethylammonium bromide to β -galactosidase has been studied.^{53a}

Although the acid-catalysed hydrolysis of *tert*-butyl, 1,1-diethylpropyl and diphenylmethyl β -D-galactopyranoside proceed partly with alkyl-oxygen fission, the hydrolyses catalysed by β -galactosidase proceed wholly with galactosyl-oxygen fission.^{53b}

Compound (8) has been used as a spin-labelled substrate for β -galactosidase.⁵⁴



The β -galactosidase from bovine testes has been studied.⁵⁵

(c) *Other glycosidases*. Evidence for the presence of 2-3 carboxyl groups at the active site

of glucoamylase I from *A. niger* has been presented. When the enzyme reacts with glycine methyl ester and a water-soluble carbodiimide, maltose prevents the reaction of between two and three carboxyl groups per molecule of enzyme.⁵⁶

Inhibition of the α -glucosidase from yeast and of the β -glucosidase from almond emulsin by α - and β -D-glucosylimidazole,⁵⁷ and of the glycosidases from almond emulsin by C-glycosides,⁵⁸ has been studied.

Other glycosidases that have been investigated include α -amylases,⁵⁹ β -amylases,⁶⁰ α -mannosidase from bakers' yeast,⁶¹ α -glucosidase from *Mucor javanicus*,^{62a} and rabbit muscle,^{62b} β -L-arabinosidase from *Cajanus indicus*,⁶³ N-acetyl- β -D-glucosaminidase from *A. oryzae*,^{64a} and the β -D-glucuronidases from bovine liver and *E. coli*.^{64b}

Hydration of Aldehydes and Ketones and Related Reactions

Equilibrium constants for the addition of hydroxyl ion to a series of substituted benzaldehydes have been measured and the results used to establish an acidity-function scale.⁶⁵

The kinetics of dehydration of glycolaldehyde hydrate have been measured by determining the rate of scavenging of free aldehyde with semicarbazide and with sulphite. The reaction is general-acid and general-base catalysed.⁶⁶

The kinetics of hydration of isobutyraldehyde have been studied by temperature-jump and NMR spectroscopy,⁶⁷ and the hydration of acetaldehyde has also been studied by NMR spectroscopy.⁶⁸

The effect of pressure on the equilibrium constants for the hydration of aliphatic aldehydes has been determined.⁶⁹

Hydration and polymerization of succinaldehyde, glutaraldehyde, and adipaldehyde,⁷⁰ and the oligomerization reaction of formaldehyde,⁷¹ have been studied. An X-ray structure determination of the dimer of DL-glyceraldehyde has been reported.⁷²

There have been investigations of the chemistry of hemiacetals⁷³ and of ring-chain tautomerism of 8-acyl-1-naphthoic acids.⁷⁴

Diphenyl phosphate, phenylphosphinic acid, and trichloroacetic acid appear to act as tautomeric catalysts for the mutarotation of tetra-O-methylglucose in benzene as they are more effective catalysts than expected from a Brønsted plot for catalysis by phenols.⁷⁵

The mutarotation of glucose in mixtures of water with dimethyl sulphoxide (DMSO) has been studied. The rate of the acid-catalysed reaction varies only slightly with solvent composition, but that for the water-catalysed reaction decreases strongly with increasing DMSO concentration in the range $\chi_{\text{DMSO}} = 0-0.3$ and remains approximately constant at higher concentrations. It was proposed that the acid-catalysed reaction proceeds by a stepwise mechanism without the intervention of a water molecule and that the water-catalysed reaction involves three water molecules.⁷⁶

Glucose shows a complex mutarotation in aqueous dimethylformamide (DMF) at high DMF concentrations. This has been attributed to formation of a furanose form and one has been detected in solutions of glucose in pure DMF by gas chromatography plus mass spectrometry of the trimethylsilyl ethers.⁷⁷

The mutarotation of β -L-arabinopyranose yields furanose forms as well as the α -pyranose form, but the *aldehyde*-form does not appear to cyclize more rapidly to furanose forms than to pyranose as reported for 2-deoxyribose.⁷⁸

The equilibrium composition of fructose 6-phosphate has been shown by ¹³C-NMR to be 19% of α - and 81% of β -furanose with less than 1.5% of the keto-form.⁷⁹

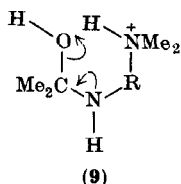
The mutarotatase from bovine kidney cortex has been investigated.⁸⁰

Reactions with Nitrogen Bases

Schiff Bases

On the basis of X-ray crystal-structure determination of compounds that have a carbonyl group close to an amino-group it has been suggested that the preferred angle of attack by nitrogen nucleophiles is not perpendicular to the carbonyl group but at an angle of 107° .⁸¹

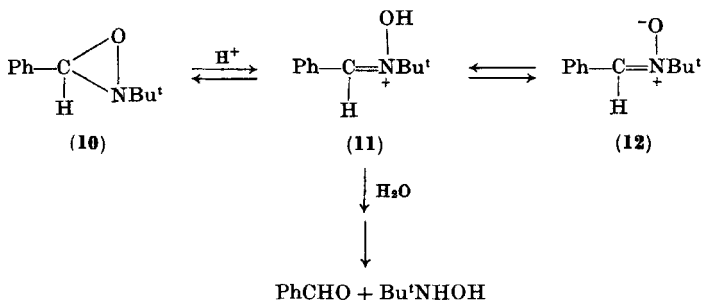
Imine formation from acetone and the monoprotonated forms of 2-(dimethylamino)-ethylamine and *trans*-(2-dimethylaminomethyl)cyclopentylamine is, respectively, 1000- and 60-fold faster than expected on the basis of a Brønsted plot for the reactions with other amines. Smaller rate enhancements are found with the monoprotonated forms of 3-(dimethylamino)propylamine, 4-(dimethylamino)butylamine, and 5-(dimethylamino)pentylamine. It seems likely that intramolecular catalysis of dehydration of the carbinolamine intermediate is occurring, as symbolized by (9).⁸²



The condensation of isobutyraldehyde with diamines to form imidazolines has been studied.⁸³

The rate constants for the uncatalysed reaction of piperazine (pK_a 9.97) and piperazine monocation (pK_a 5.80) with pyridine-4-aldehyde to form the carbinolamine are 2.3×10^5 and $65 \text{ l mol}^{-1} \text{ s}^{-1}$, respectively. The reaction of piperazine shows general-base catalysis which was thought to involve catalysis of the proton-transfer step, i.e. conversion of the zwitterionic carbinolamine into the anionic form.⁸⁴

The hydrolyses of 2-*tert*-butyl-3-phenyloxaziridine (10) and *N*-benzylidene-*tert*-butylamine *N*-oxide (12) are thought to proceed through the same ion (11). The effect of micelles on the rates of these reactions was studied.⁸⁵



The hydrolysis and synthesis of benzylideneaniline in the presence of micelles of sodium dodecyl sulphate^{86a} and the hydrolysis of Schiff bases derived from ferrocenyl aldehyde and ketones^{86b} have been studied.

The kinetics of hydrolysis of salicylideneanilines in acidic solutions with H_0 down to -4 have also been studied.⁸⁷ So have amine exchange reactions of substituted benzylideneanilines.^{88, 89}

The reaction of glycine with benzaldehyde in ethanol in the presence of potassium hydroxide to form phenylserine is thought to involve formation of the Schiff base which forms a carbanion by loss of the α -proton. Reaction of this carbanion with another molecule of benzaldehyde would then lead to the product.⁹⁰

The reaction of substituted benzylideneanilines with diethylmagnesium has been studied. Electron-withdrawing substituents in either benzene ring increase the rate of reaction and electron-releasing substituents decrease it.⁹¹

Dehydration of the β -ketol 9-hydroxy-10-methyl-*cis*-2-decalone by secondary and primary amines proceeds via iminium ions.⁹²

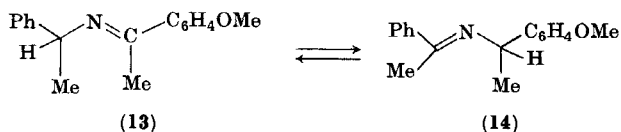
There have been PMR studies⁹³ and MO calculations⁹⁴ on the protonated imine group.

The reaction of the following compounds have been studied: glycine with glyoxal,⁹⁵ imidazole with formaldehyde,⁹⁶ isoxazol-5-ones with Schiff bases,⁹⁷ aldehydes with ammonia,^{98, 99} and Schiff bases with nitrosonium borofluoride.¹⁰⁰

Ring-chain tautomerism of *o*-benzoylbenzamides has been investigated.¹⁰¹

Transamination

The interconversion of *N*-(α -methyl-4-methoxybenzylidene)-1-phenylethylamine (**13**) and *N*-(α -methylbenzylidene)-1-(4-methoxyphenyl)ethylamine (**14**) catalysed by potassium *tert*-butoxide in *tert*-butyl alcohol occurs with about 50% of intramolecular proton-transfer and about 60% of racemization. The starting material also undergoes substantial racemization. It was suggested that reaction proceeds through twisted carbanions.^{102a}



Transamination of the imine derived from 3-hydroxypyridine-4-carboxaldehyde and alanine is 2–3 times faster than racemization in aqueous buffers, the exact value depending on the catalyst and the prototropic state of the imine. This indicates that the intermediate carbanion is protonated with approximately equal facility at the two sites.^{102b}

Other workers on transamination are cited in reference 103.

Enamines

The stereochemistry of the acidic hydrolysis of 2,6-disubstituted cyclohexanone enamines has been studied,¹⁰⁴ as also has the formation of dienamines.¹⁰⁵

Hydrazones, Oximes, Semicarbazones and Related Compounds¹⁰⁶

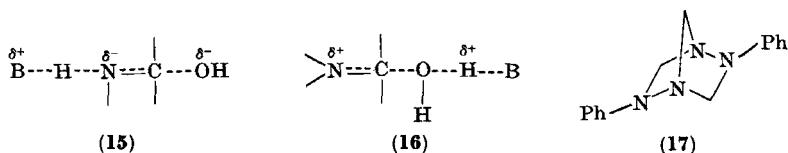
The pH-rate profile for the reaction of methoxyamine with *p*-chlorobenzaldehyde shows two breaks. That at low pH (ca. 1) was interpreted as arising from a change in rate-determining step from attack of the methoxyamine below this pH to proton-transfer to the zwitterionic form of the carbinolamine above it.¹⁰⁷ Details of Sayer and Jencks's investigation of the reaction of 2-methylthiosemicarbazide with *p*-chlorobenzaldehyde have been reported;¹⁰⁸ and there has been a review of "Encounter-Limited Rate-determining Steps in Carbonyl and Acyl Group Reactions".¹⁰⁹

The rate of the base-catalysed dehydration of carbinolamines formed from substituted hydrazines and *p*-chlorobenzaldehyde is enhanced by electron-withdrawing substituents

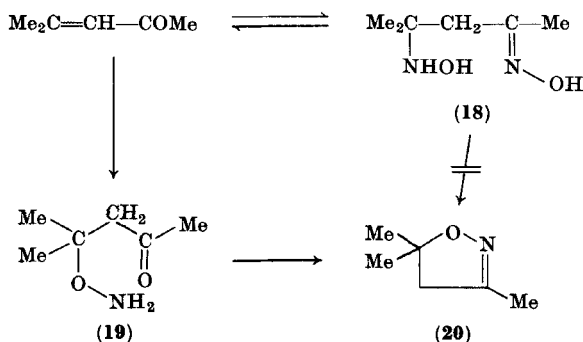
in the hydrazine. A transition state (**15**) involving a large degree of negative charge on nitrogen and little double-bond formation was proposed. The reaction is also general-acid catalysed and the rate of that reaction is also decreased by electron-withdrawing substituents in the hydrazine, a transition state (**16**) being here proposed.¹¹⁰

Details of the investigation by Cordes and his co-workers on the α -deuterium isotope effect for addition of semicarbazide and phenylhydrazine to benzaldehyde have been published.¹¹¹

Other work on hydrazone formation is cited in reference 112. There have been several investigations of the formation of osazones.¹¹³ Molecular-orbital calculations for the products of reaction of glyoxal with phenylhydrazine have been reported.¹¹⁴ Formaldehyde phenylhydrazone reacts with an excess of formaldehyde to yield (**17**).¹¹⁵ The reaction of butane-2,3-dione dihydrazone with formaldehyde in the presence of metal ions has been studied.¹¹⁶



On investigation of the reaction of mesityl oxide with hydroxylamine to form 3,5,5-trimethyl-2-isoxazoline (**20**) it was shown that (**18**) is not an intermediate as it is not converted into (**20**) under the reaction conditions, but an NMR investigation of the reaction solution showed that (**19**) is an intermediate.¹¹⁷



There have been several investigations of the hydrolysis of oximes.¹¹⁸

The reaction of *N*-arylhydroxylamines with nitrosoarenes appears not to be a simple reaction analogous to oxime formation but to be a radical process involving transfer of hydrogen.¹¹⁹

Hydrolysis of Enol Ethers

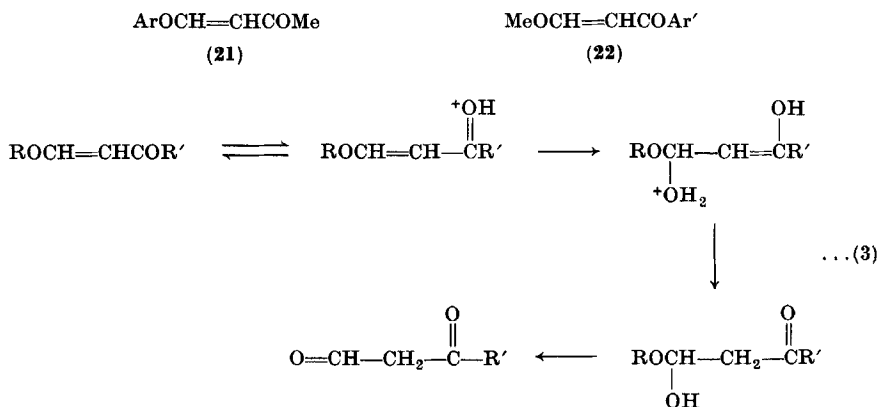
The rate constants for the hydrolysis of ethyl vinyl ether catalysed by positively charged amino-acids gives a Brønsted plot that is almost parallel to that for neutral carboxylic acids but lying about 0.3 logarithm unit below it. On the other hand, the points for negatively charged acids fall above the line for neutral carboxylic acids. An electrostatic interaction in the transition state was proposed as an explanation of these observations.¹²⁰

The hydrolysis of ethoxypropadiene (equation 2) is general-acid catalysed with $\alpha = 0.62$. The rate constant for hydronium-ion catalysis shows a negative deviation from the Brønsted plot. The isotope effect $k(\text{H}_3\text{O}^+)/k(\text{D}_3\text{O}^+) = 3.05$, $\Delta S^\ddagger = -10 \text{ cal mol}^{-1} \text{ K}^{-1}$, and Bunnett's w parameter is 0.36. A mechanism similar to that for the hydrolysis of ordinary enol ethers seems likely.¹²¹



The hydration of the β -oxy- α,β -unsaturated ketones (**21**) and (**22**) is specific-acid catalysed with $k(\text{D}_3\text{O}^+)/k(\text{H}_3\text{O}^+) = \text{ca. } 2.6$. The ρ^+ -values are -0.18 and $+0.26$, respectively. These results are clearly inconsistent with the normal mechanism of vinyl ether hydrolysis and that shown in equation (3) was proposed.¹²²

The alkylation of vinyl ethers has also been studied.¹²³



Enolization and Related Reactions*

A detailed investigation of the halogenation of butan-1-one has shown that the previously reported anomalies can be explained in terms of the heterogeneity of the system, reaction of the halogen with DMF (for reactions in aqueous DMF), formation of iodate, and nucleophilic displacement of the halide by hydroxide ion.¹²⁴

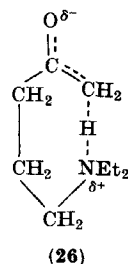
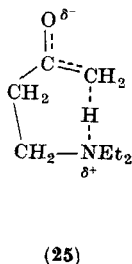
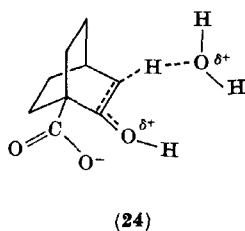
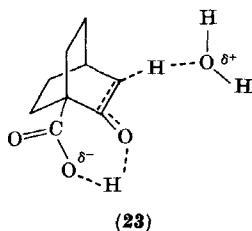
The enolization of 2-oxobicyclo[2.2.2]octane-1-carboxylic acid (RCO_2H) follows a rate law of the form:

$$\text{Rate} = \{k_{\text{H}}[\text{H}^+] + k_0\}[\text{RCO}_2\text{H}]$$

k_{H} is similar to that for the methyl ester. k_0 could arise from the acid-catalysed enolization of the carboxylate form and if this were so the catalytic constant would be 230 times greater than k_{H} for enolization of the methyl ester. This rate enhancement was attributed to hydrogen bonding or electrostatic stabilization as symbolized by (**23**) or (**24**).¹²⁵ More work on the stereochemistry of hydrogen-exchange of bicyclic ketones has also been reported.¹²⁶

The rates of enolization (measured as iodination) of 4-(diethylamino)butan-2-one and 5-(diethylamino)pentan-2-one are much greater than normally found for aliphatic ketones, which was attributed to intramolecular catalysis as symbolized by (**25**) and (**26**).¹²⁷

* See also Chapter 10.



Diamines of type $\text{Me}_2\text{N}(\text{CH}_2)_n\text{NH}_2$, where $n = 2, 3, 4$ or 5 , are not better catalysts than monoamines for the dedeuteriation of $[2\text{-}^2\text{H}]$ isobutyraldehyde, showing the absence of any intramolecularly catalysed reaction of the Schiff base. This was thought to be because the Schiff bases have the *anti*-structure, but even the diamines undecane-1,11-diamine and dodecane-1,12-diamine, which have sufficiently long chains to permit catalysis even with this structure, showed no catalysis. However, evidence for catalysis was found with N^1, N^1 -dimethyloct-2-yne-1,8-diamine.¹²⁸ Catalysis of dedeuteriation of $[2\text{-}^2\text{H}]$ isobutyraldehyde by polyethyleneimines is also thought to involve reversible transformation of the aldehyde group into an iminium ion, followed by intramolecular removal of a deuteron by another amino-group.¹²⁹

Ethylenediamine causes an increase in the rate of deuterium exchange of $[2\text{-}^2\text{H}]$ -isobutyraldehyde (0.06M) up to a concentration of 0.03M and then a decrease at higher concentration. This decrease arises from conversion of the aldehyde into 2-isopropyl-imidazoline. At concentrations of diamine above 1M the rate increases again owing to catalysis by the imidazoline.¹³⁰

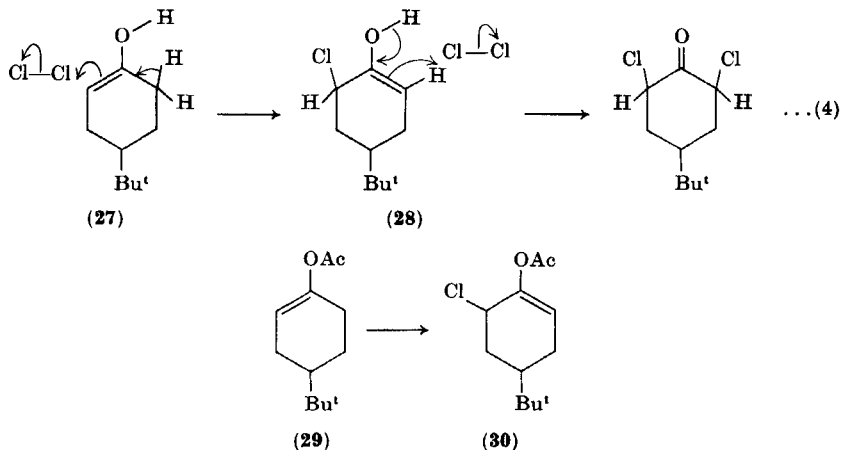
The kinetics of iodination of acetone have a term that is of the second order in amine when this is 2-aminomethylpyridine but not when it is 2-aminoethylpyridine. It was thought that this term arose from a rate-limiting dehydration of a carbinolamine with another molecule of the 2-aminomethylpyridine acting as a bifunctional catalyst. This would yield an imine which should be iodinated rapidly.¹³¹

The Brønsted β -coefficient for the enolization of 3-methylacetylacetone (measured as bromination) is 0.49. The kinetics were also measured in H_2O - D_2O mixtures and the results analysed in terms of the Gross-Butler equation.¹³²

The hydroxide-ion-catalysed enolization of 2,4-dimethylpentan-3-one and 3,5-dimethylheptan-4-one show primary deuterium isotope effects $k_{\text{H}}/k_{\text{D}} = 6.09$ and 3.67 , respectively, at 25° , but no primary tritium isotope effect. Possible explanations of this surprising observation were discussed.¹³³

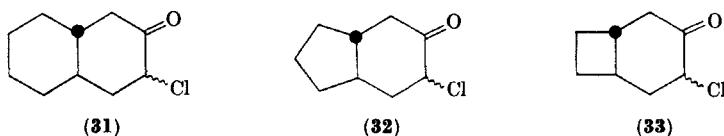
On treatment with chlorine in carbon tetrachloride 4-*tert*-butylcyclohexanone yields 4-*tert*-butyl-*cis-trans*-2,6-dichlorocyclohexanone under conditions where 4-*tert*-butyl-*cis*- and -*trans*-2-chlorocyclohexanone are not further chlorinated. It was suggested that the dichloro-ketone was formed by the mechanism of equation (4). A process analogous

to the conversion of (27) into (28) was demonstrated by treating the enol acetate (29) with chlorine in carbon tetrachloride to yield (30). It seems that, in carbon tetrachloride, C—H bond-cleavage of the enol (27) is competitive with O—H bond-cleavage.¹³⁴ Other work on the halogenation of ketones in carbon tetrachloride solution is reported in reference 135.



The protonation and epimerization of 4-*tert*-butyl-2-halocyclohexanones and of 1-halo-2-decalones in strong acids has been studied. The epimerization was thought to proceed via the enol,¹³⁶ as is that of 1,1-trichloro-2-hydroxy-3-methylhexan-4-one in glacial acetic acid.¹³⁷

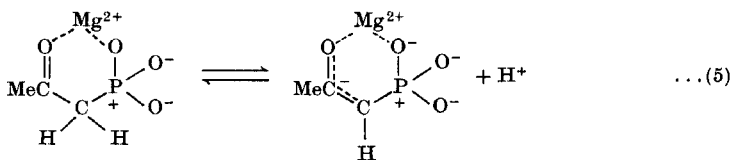
The rates of enolization of the ketones (31), (32) and (33) at the α -carbon atom vary only slightly with the size of the fused ring but the rates of enolization at the α' -carbon decrease strongly as the size of the fused ring is reduced.¹³⁸



The rate constants for the acid-catalysed bromination, chlorination and iodination of acetone under conditions where formation of the enol is not rate-limiting are approximately equal. It seems that the equilibrium constant for enolization is 1.5×10^{-5} , which is considerably smaller than hitherto thought, and that the reactions of the halogens with the enol are diffusion-controlled with rate constant ca. $10^9 \text{ mol}^{-1} \text{ s}^{-1}$.¹³⁹

The kinetic solvent isotope effects for the enolization of ketones in alcohols ROH and ROD have been measured.¹⁴⁰

Magnesium ions catalyse the exchange of hydrogen atoms of the methylene group of acetonyl phosphate in alkaline solutions, the reaction being thought to involve a chelate as shown in equation (5).¹⁴¹



The protolysis and iodination of the copper derivatives of the enolates of α,β -unsaturated carbonyl compounds proceeds with retention of configuration, but the lithium enolates react with racemization. It seems that the latter have the α -carbons *p*-hybridized and that the direction of attack depends on steric factors.¹⁴²

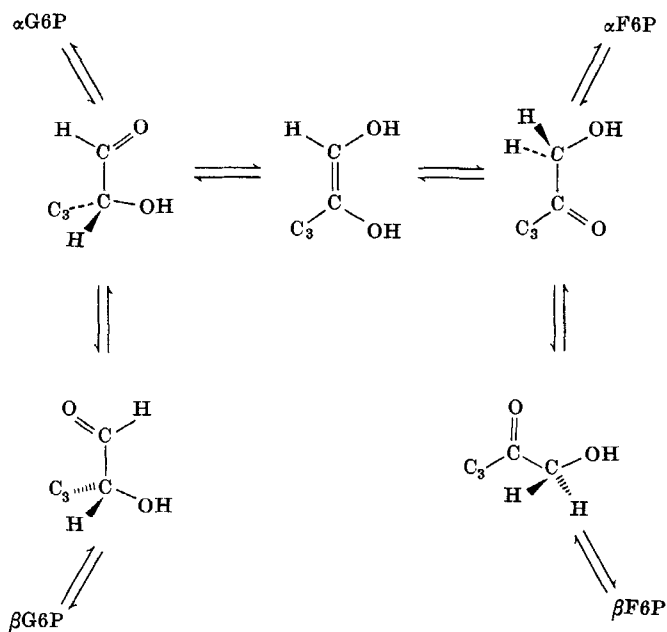
Metal-ion catalysis of the Lobry de Bruyn-Alberda van Eekstein rearrangement has been studied.¹⁴³

More work on the keto-enol tautomerization of 3-hydroxy-2,4-dimethylcyclobutenone has been reported.¹⁴⁴

Other reactions which have been studied include enolization of tetrahydro-2,4-dioxothiophen¹⁴⁵ and isomerization of protonated cyclohepta-3,5-dienones.¹⁴⁶

There have been several investigations of keto-enol equilibria.¹⁴⁷

Phosphoglucose isomerase produces and uses both the α - and β -form of D-fructofuranose 6-phosphate but with a preference for the α -form. The α -anomer of D-glucopyranose 6-phosphate is the preferred substrate, but the β -form also reacts. The mechanism outlined in Scheme 1 was preferred. It seems that the enzyme catalyses the ring-opening processes as well as the interconversion of the ring-opened forms via the enediol.¹⁴⁸ The carboxyl group of a glutamic acid residue has been implicated in the active site of this enzyme by allowing it to react with 1,2-anhydromannitol 6-phosphate, which causes rapid inactivation.¹⁴⁹



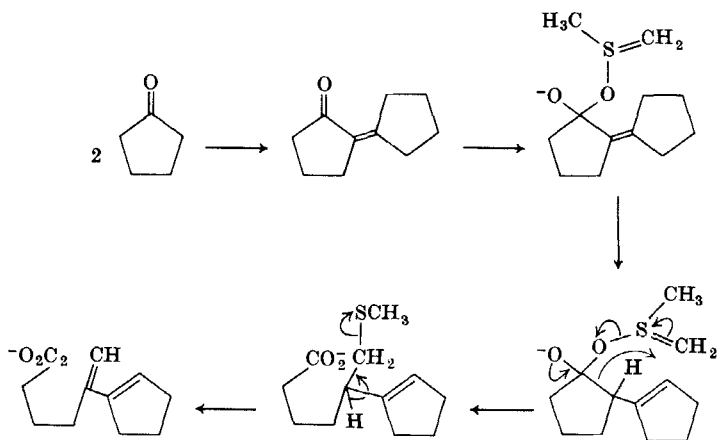
SCHEME 1.

Phosphomannose isomerase uses only the β -anomer of mannose 6-phosphate. This enzyme (or phosphoglucose isomerase) catalyses the anomerization of mannose 6-phosphate.¹⁵⁰

There have also been investigations of enolase¹⁵¹ and triose phosphate isomerase.¹⁵²

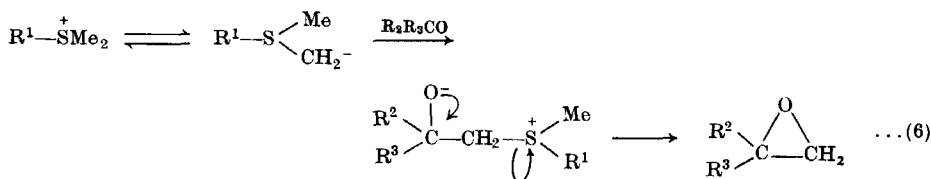
Aldol and Related Reactions

On treatment with methylsulphinyl carbanion, cyclopentanone undergoes an intriguing reaction to form 5-(cyclopent-1-enyl)hex-5-enoic acid. The pathway shown in Scheme 2 was proposed.¹⁵³



SCHEME 2.

Dodecyldimethylsulphonium salts react with carbonyl compounds in a mixture of benzene and aqueous sodium hydroxide to form epoxides, presumably by the pathway shown in equation (6).¹⁵⁴

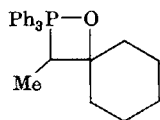


There has also been work on the aldol reaction,¹⁵⁵ the retro-aldol reaction,¹⁵⁶ the Claisen-Schmidt reaction,¹⁵⁷ the Darzens condensation,¹⁵⁸ the Knoevenagel condensation,¹⁵⁹ and the condensation of carbonyl compounds with 3,5-dihydroxy-4-phenylisoxazole.¹⁶⁰ The condensation of acetylenes with aldehydes and ketones has been reviewed¹⁶¹ (in Russian), and the stereochemistry of additions to carbonyl compounds has been discussed.¹⁶²

Pyridoxal phosphate has been shown to form a Schiff base with the amino-group of a lysine residue of rabbit muscle aldolase contained in the sequence Gly—Gly—Val—Val—Gly—Ile—Lys*—Val—Asp—Lys.¹⁶³ Other work on aldolase is reported in reference 164.

Other Reactions

The ³¹P-NMR spectrum of an intermediate in the Wittig reaction of the ylide from ethyltriphenylphosphonium bromide and cyclohexanone has shown that it has the oxaphosphetane structure (34).¹⁶⁵ The kinetics of the Wittig reaction of Ph₃P=CETCO₂Et



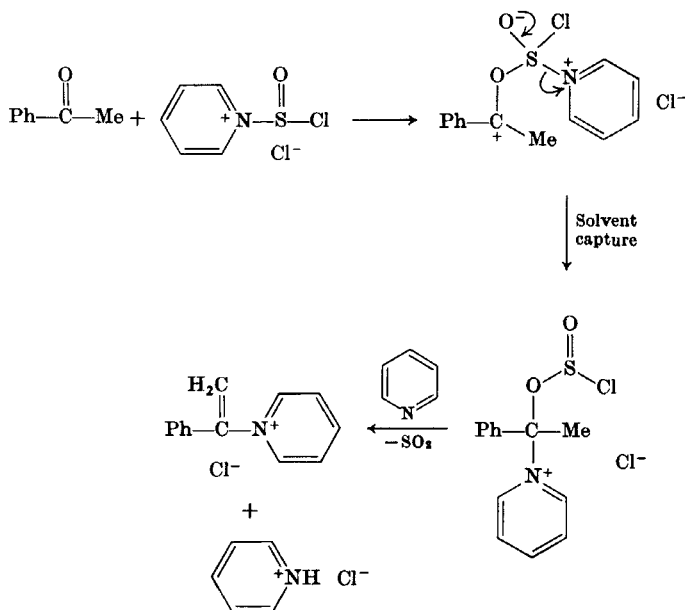
(34)

with substituted benzaldehydes yields a ρ -value of 2.89. The rate of reaction of the compounds $\text{Ph}_3\text{P}=\text{CRCO}_2\text{Et}$ with benzaldehyde decreases as R is changed along the series $\text{Me} > \text{H} > \text{Et} > \text{Bu}^n$.¹⁶⁶ The rate of the Wittig reaction of $\text{Ph}_3\text{P}=\text{CHCOPh}$ with *p*-nitrobenzaldehyde in hydrocarbon solvents decreases with increasing dielectric constant of the solvent.¹⁶⁷ Other work on the Wittig reaction is noted in reference 168.

p-Nitrobenzaldehyde does not undergo the Cannizzaro reaction in aqueous potassium hydroxide but instead yields *p*-nitrosophenol.¹⁶⁹ An investigation of the Cannizzaro reaction is reported in reference 170.

The Schmidt reaction of hydrazoic acid with ketones PhCOR gave a ρ -value of 2.28. The rate-limiting step is addition of hydrazoic acid to the protonated ketone.¹⁷¹

Acetophenone reacts with thionyl chloride in pyridine to form *N*-styrylpyridinium chloride.¹⁷² The mechanism of Scheme 3 was proposed.¹⁷³



SCHEME 3.

Other reactions that have been studied include decarbonylation of tricyclo[2.1.0.0^{2,5}]-penta-3-one catalysed by transition metals,¹⁷⁴ formation of 1,2-dithiolylum tri-iodides from β -diketones, hydrogen sulphide and iodine,¹⁷⁵ and the reaction of disiamyl(3-phenylbut-2-enyl)borane with aldehydes.¹⁷⁶

There have been several investigations of the protonation of carbonyl compounds.¹⁷⁷

References

- ¹ B. M. Dunn and T. C. Bruice, *Adv. Enzymology*, **37**, 1 (1973).
- ² B. Capon and M. I. Page, *J.C.S. Perkin II*, **1972**, 2057.
- ³ E. Anderson and T. H. Fife, *J. Am. Chem. Soc.*, **95**, 6437 (1973); cf. *Org. Reaction Mech.*, **1971**, 394-395.
- ⁴ D. P. Weeks and J. P. Crane, *J. Org. Chem.*, **38**, 3375 (1973); see *Org. Reaction Mech.*, **1968**, 349.
- ⁵ G. Lamaty, A. Malaval, J.-P. Roque and P. Geneste, *Bull. Soc. Chim. France*, **1972**, 4563, 4567.
- ⁶ See *Org. Reaction Mech.*, **1968**, 30; **1969**, 33; **1970**, 39.
- ⁷ A. Kankaanperä, P. Salomaa, P. Juhala, R. Aaltonen and M. Mattsen, *J. Am. Chem. Soc.*, **95**, 3618 (1973).
- ⁸ N. K. Moshchinskaya and N. I. Parnyuk, *Zh. Org. Khim.*, **9**, 998 (1973); *Chem. Abs.*, **79**, 41624 (1973).
- ⁹ Y. Sasaki and C. U. Pittman, *J. Org. Chem.*, **38**, 3723 (1973).
- ¹⁰ J. W. de Leeuw, E. R. de Waard, T. Beetz and H. O. Huisman, *Rec. Trav. chim.*, **92**, 1047 (1973).
- ¹¹ Z. I. Zelikman and V. G. Kul'nevich, *Geterogen. Kataliz Reakts. Poluch. Prevrashch. Geterotsikl. Sedin.*, **1971**, 93; *Chem. Abs.*, **78**, 15216 (1973).
- ¹² R. S. Glass, S. Kwoh and E. P. Oliveto, *Carbohydrate Res.*, **26**, 181 (1973).
- ¹³ M. Anteunis, D. Tavernier and G. Swaelens, *Rec. Trav. chim.*, **92**, 531 (1973).
- ¹⁴ D. Tavernier and M. Anteunis, *Bull. Soc. Chim. Belges*, **82**, 405 (1973); M. Anteunis and M. Corynon, *ibid.*, p. 413.
- ¹⁵ P. Ayra, *Suomen Kem.*, **B**, **46**, 151 (1973).
- ¹⁶ M. Anteunis, R. Van Cauwenberghe and C. Becu, *Bull. Soc. Chim. Belges*, **82**, 591 (1973).
- ¹⁷ R. A. Y. Jones, A. R. Katritzky, D. L. Nicol and R. Scattergood, *J.C.S. Perkin II*, **1973**, 337.
- ¹⁸ D. Tavernier, M. Anteunis and N. Hosten, *Tetrahedron Letters*, **1973**, 75.
- ¹⁹ A. K. Bhatti and M. Anteunis, *Tetrahedron Letters*, **1973**, 71.
- ^{20a} P. Pasanen, *Suomen Kem.*, **B**, **45**, 363 (1972).
- ^{20b} M. H. Gianni, J. Saavedra and J. Savoy, *J. Org. Chem.*, **38**, 3971 (1973).
- ²¹ K. Yates and R. A. McClelland, *J. Am. Chem. Soc.*, **95**, 3055 (1973).
- ²² P. M. Collins, W. G. Overend and B. A. Rayner, *J.C.S. Perkin II*, **1973**, 310.
- ²³ D. Cocker, L. E. Jukes, and M. L. Sinnott, *J.C.S. Perkin II*, **1973**, 190; see *Org. Reaction Mech.*, **1972**, 394.
- ²⁴ C. R. Clark and R. W. Hay, *J.C.S. Perkin II*, **1973**, 1943; see *Org. Reaction Mech.*, **1970**, 423.
- ²⁵ C. K. De Bruyne and G. van der Groen, *Carbohydrate Res.*, **25**, 59 (1972).
- ²⁶ C. K. De Bruyne, J. Wouters-Leysen and M. Yde, *Carbohydrate Res.*, **29**, 387 (1973).
- ²⁷ J. N. BeMiller and E. R. Doyle, *Carbohydrate Res.*, **25**, 429 (1972).
- ^{28a} J. Szejtli, *Stärke*, **42**, 321 (1972).
- ^{28b} A. Neuburger and W. A. Ratcliffe, *Biochem. J.*, **133**, 623 (1973).
- ²⁹ A. D. Pethybridge, *J.C.S. Perkin II*, **1973**, 102.
- ³⁰ A. Mohn-Wehner, H. K. Rouette and H. Zollinger, *Helv. Chim. Acta*, **56**, 323 (1973).
- ³¹ G. W. O'Donnell and G. N. Richards, *Austral. J. Chem.*, **26**, 2041 (1973).
- ³² R. H. Pater, R. A. Coelho and D. F. Mowery, *J. Org. Chem.*, **38**, 3272 (1973).
- ³³ A. Brown and T. C. Bruice, *J. Am. Chem. Soc.*, **95**, 1593 (1973).
- ³⁴ J. F. Kirsch, "Mechanism of Enzyme Action", *Ann. Rev. Biochem.*, **42**, 205 (1973).
- ³⁵ S. K. Banerjee, I. Kregar, V. Turk and J. A. Rupley, *J. Biol. Chem.*, **248**, 4786 (1973).
- ³⁶ L. E. H. Smith, L. H. Mohr and M. A. Raftery, *J. Am. Chem. Soc.*, **95**, 7497 (1973).
- ³⁷ S. K. Banerjee and J. A. Rupley, *Arch. Biochem. Biophys.*, **155**, 19 (1973); see also *idem.*, *J. Biol. Chem.*, **248**, 2117 (1973); C. Bjurulf and I. Wadso, *Eur. J. Biochem.*, **31**, 95 (1972); S. Kuramitsu, K. Ikeda and K. Hamaguchi, *J. Biochem. (Tokyo)*, **74**, 143 (1973).
- ³⁸ R. S. Mulvey, R. J. Gaultieri and S. Beychok, *Biochemistry*, **12**, 2683 (1973); V. I. Teichberg, T. Plesse, S. Sorell and N. Sharon, *Biochem. Biophys. Acta*, **278**, 250 (1973); S. Kuramitsu, K. Ikeda, K. Hamaguchi, S. Miwa and T. Nishina, *J. Biochem. (Tokyo)*, **72**, 1109 (1972).
- ³⁹ C. S. Tsai, *Biochem. Biophys. Res. Comm.*, **55**, 205 (1973); see also R. Otson, C. Reyes-Zamora, J. Y. Tong and C. S. Tsai, *Can. J. Biochem.*, **51**, 1 (1973).
- ⁴⁰ T. Moulty, Y. Eshdat and N. Sharon, *J. Mol. Biol.*, **75**, 1 (1973); see *Org. Reaction Mech.*, **1970**, 426.
- ⁴¹ T. Imoto, F. J. Hartdegen and J. A. Rupley, *J. Mol. Biol.*, **80**, 637 (1973); F. J. Hartdegen and J. A. Rupley, *ibid.*, p. 649; T. Imoto and J. A. Rupley, *ibid.*, p. 657; see also *Org. Reaction Mech.*, **1970**, 427-428.
- ⁴² J. J. Sharp, A. B. Robinson and M. D. Kamen, *J. Am. Chem. Soc.*, **95**, 6097 (1973).

- ⁴³ N. Hiramatsu, N. Okabe and K. Tomita, *J. Biochem. (Tokyo)*, **73**, 971 (1973); T. Monodane, S. Hora and Y. Matsushima, *ibid.*, **72**, 1175 (1972); Y. Nakae, K. Ikeda, T. Azuma and K. Hamaguchi, *ibid.*, **72**; 1155 (1972); H. Tada and I. Kakitani, *Bull. Chem. Soc. Japan*, **46**, 1226 (1973); N. A. Kravchenko and L. A. Chistyakova, *Biokhimiya*, **37**, 1126 (1972); S. Lapanje and J. A. Rupley, *Biochemistry*, **12**, 2370 (1973); C.-L. Lee and M. Z. Atassi, *ibid.*, p. 2690; N.-I. Yu and B. H. Jo, *ibid.*, **156**, 469; K. J. Kramer and J. A. Rupley, *ibid.*, **156**, 414 (1973); **158**, 566 (1973); K. Y. Chang and C. W. Carr, *Biochem. Biophys. Acta*, **285**, 377 (1972); A. A. Aboderin, E. Boedefeld and P. L. Luisi, *ibid.*, **328**, 20 (1973); V. K. Srivastava and C. C. Bigelow, *ibid.*, **285**, 373 (1972); H. Hayashi, K.-I. Amano, Y. Araki and E. Ito, *Biochem. Biophys. Res. Comm.*, **50**; 641 (1973); M. Kugimiya and C. C. Bigelow, *Can. J. Biochem.*, **51**, 581 (1973).
- ⁴⁴ J. P. Penn and P. Jolles, *Clin. Chim. Acta*, **42**, 77 (1972); *Chem. Abs.*, **78**, 54675 (1973).
- ⁴⁵ J. Hermann, J. Jolles, D. H. Buss and P. Jolles, *J. Mol. Biol.*, **79**, 587 (1973).
- ⁴⁶ B. W. Matthews, F. W. Dahlquist and A. Y. Maynard, *J. Mol. Biol.*, **78**, 575 (1973).
- ⁴⁷ W. L. Riggle, J. A. Long and C. L. Borders, *Can. J. Biochem.*, **51**, 1433 (1973).
- ⁴⁸ N. Arnheim, M. Inouye, L. Law and A. Laudin, *J. Biol. Chem.*, **248**, 233 (1973).
- ⁴⁹ M. L. Sinnott and I. J. L. Souchard, *Biochem. J.*, **133**, 89 (1973).
- ⁵⁰ M. L. Sinnott and O. Viratelle, *Biochem. J.*, **133**, 81 (1973); O. M. Viratelle and J. M. Yon, *Eur. J. Biochem.*, **33**, 110 (1973); G. van der Groen, J. Wouters-Leysen, M. Yde and C. K. De Bruyne, *ibid.*, **38**, 122 (1973).
- ⁵¹ Cf. *Org. Reaction Mech.*, **1970**, 424-425.
- ⁵² M. L. Sinnott, *Chem. Comm.*, **1973**, 535.
- ^{53a} G. S. Case, M. L. Sinnott and J.-P. Tenu, *Biochem. J.*, **133**, 99 (1973).
- ^{53b} M. Maybury and M. Sinnott, *J.C.S. Perkin II*, **1973**, 300.
- ⁵⁴ W. G. Struve and H. M. McConnell, *Biochem. Biophys. Res. Comm.*, **49**, 1631 (1972).
- ⁵⁵ J. J. Distler and G. W. Jourdan, *J. Biol. Chem.*, **248**, 6772 (1973).
- ⁵⁶ C. J. Gray and M. E. Jolley, *FEBS Letters*, **29**, 197 (1973).
- ⁵⁷ E. J. Bourne, P. Finch and A. G. Nagpurkar, *Carbohydrate Res.*, **29**, 492 (1973).
- ⁵⁸ Y. A. Zhdanov and R. M. Kessler, *Dokl. Akad. Nauk SSSR*, **207**, 607 (1972); *Chem. Abs.*, **78**, 68657 (1973).
- ⁵⁹ D. W. Darnall and E. R. Birnbaum, *Biochemistry*, **12**, 3489 (1973); C. E. Weill and J. Guerrero, *Carbohydrate Res.*, **27**, 451 (1973); K. Omechi, T. Ikenaka and Y. Matsushima, *J. Biochem. (Tokyo)*, **73**, 491 (1973); D. J. Stiefel and P. J. Keller, *Biochem. Biophys. Acta*, **302**, 345 (1973); J. Robyt and R. J. Aikerman, *Arch. Biochem. Biophys.*, **155**, 445 (1973).
- ⁶⁰ E. Laszlo, J. Hollo and B. Banky, *Carbohydrate Res.*, **25**, 355 (1972); J. J. Marshall, *Eur. J. Biochem.*, **33**, 494 (1973).
- ⁶¹ T. Kaya, M. Shiband and T. Kutsumi, *J. Biochem. (Tokyo)*, **73**, 181 (1972).
- ^{62a} Y. Yamasaki, T. Miyake and Y. Suzuki, *Agr. Biol. Chem.*, **37**, 251 (1973).
- ^{62b} J. Carter and E. E. Smith, *Arch. Biochem. Biophys.*, **155**, 82 (1973).
- ⁶³ P. M. Dey, *Biochem. Biophys. Acta*, **302**, 393 (1973).
- ^{64a} T. Mega, T. Ikenaka, H. Arita and K. Fukukawa, *J. Biochem. (Tokyo)*, **73**, 55 (1973); T. Mega, T. Ikenaka and Y. Matsushima, *ibid.*, **72**, 1391 (1972); K. Yamamoto, *ibid.*, **73**, 631, 749 (1973).
- ^{64b} J. Tomasic and D. Keylevic, *Biochem. J.*, **133**, 789 (1973).
- ⁶⁵ W. J. Bover and P. Zuman, *J. Am. Chem. Soc.*, **95**, 2531 (1973); *J.C.S. Perkin II*, **1973**, 786; P. Greenzaid, *J. Org. Chem.*, **38**, 3164 (1973).
- ⁶⁶ P. E. Sørensen, *Acta Chem. Scand.*, **26**, 3357 (1972).
- ⁶⁷ L. R. Green and J. Hine, *J. Org. Chem.*, **38**, 2801 (1973).
- ⁶⁸ W. E. Hull, B. D. Sykes and B. M. Babior, *J. Org. Chem.*, **38**, 2931 (1973).
- ⁶⁹ C. A. Lewis and R. Wolfenden, *J. Am. Chem. Soc.*, **95**, 6685 (1973).
- ⁷⁰ P. M. Hardy, A. C. Nicholls and H. N. Rydon, *J.C.S. Perkin II*, **1972**, 2270.
- ⁷¹ T. M. Gorrie, S. K. Raman, H. K. Rouette and H. Zollinger, *Helv. Chim. Acta*, **56**, 175 (1973).
- ⁷² M. Senma, Z. Tara, K. Osaki and T. Taga, *Chem. Comm.*, **1973**, 880.
- ⁷³ G. Siegmund, *Chem. Ber.*, **106**, 2960 (1973); M. Tsuge, T. Miyabayashi and S. Tanaka, *Nippon Kagaku Kaishi*, **1973**, 1016; *Chem. Abs.*, **79**, 31136 (1973).
- ⁷⁴ K. Bowden and A. M. Last, *J.C.S. Perkin II*, **1973**, 1144.
- ⁷⁵ P. R. Rony and R. O. Neff, *J. Am. Chem. Soc.*, **95**, 2896 (1973).
- ⁷⁶ N. M. Ballash and E. B. Robertson, *Can. J. Chem.*, **51**, 556 (1973).
- ⁷⁷ J. A. Hveding, O. Kjølborg and A. Reine, *Acta Chem. Scand.*, **27**, 1427 (1973).
- ⁷⁸ A. H. Conner and L. Anderson, *Carbohydrate Res.*, **25**, 107 (1972); cf. *Org. Reaction Mech.*, **1971**, 403.

- ⁷⁹ T. A. W. Koerner, L. W. Cary, N. S. Bhacca and E. S. Younathan, *Biochem. Biophys. Res. Comm.*, **51**, 543 (1973).
- ⁸⁰ P. H. Fishman, P. G. Pentchev and J. M. Bailey, *Biochemistry*, **12**, 2490 (1973).
- ⁸¹ H. D. Bürgi, J. D. Dunitz and E. Shefter, *J. Am. Chem. Soc.*, **95**, 5065 (1973).
- ⁸² J. Hine, M. S. Cholod and W. K. Chess, Jr., *J. Am. Chem. Soc.*, **95**, 4270 (1973); see also L. S. Mushketik, N. V. Volkova, E. A. Shilov and A. A. Yasnikov, *Ukr. Khim. Zh.* (Russian Ed.), **38**, 1259 (1972); *Chem. Abs.*, **78**, 96785 (1973); I. E. Kalinichenko and N. A. Emtsova, *Zh. Obshch. Khim.*, **42**, 2223 (1972); *Chem. Abs.*, **78**, 83685 (1973); R. W. Green, P. W. Alexander and R. J. Sleet, *Austral. J. Chem.*, **26**, 1653 (1973).
- ⁸³ J. Hine and K. W. Narducy, *J. Am. Chem. Soc.*, **95**, 3362 (1973); cf. ref. 130.
- ⁸⁴ H. Diebler and R. N. F. Thorneley, *J. Am. Chem. Soc.*, **95**, 896 (1973).
- ⁸⁵ C. J. O'Connor, E. J. Fendler and J. H. Fendler, *J.C.S. Perkin II*, **1973**, 1744, 1900.
- ^{86a} K. Martinek, A. K. Yatsimirski, A. P. Osipov and I. V. Berezin, *Tetrahedron*, **29**, 963 (1973).
- ^{86b} A. Mesli and J. Tirouflet, *Compt. Rend., C*, **275**, 1541 (1972).
- ⁸⁷ J. Hoffmann and V. Štěrbá, *Coll. Czech. Chem. Comm.*, **38**, 2091, 3146 (1973).
- ⁸⁸ P. Nagy, *Szegedi Tanárképző Főiskola Tud. Közlem.*, **1971**, 147; *Chem. Abs.*, **78**, 110162 (1973).
- ⁸⁹ P. Nagy, *Magy. Kem. Folyóirat*, **79**, 145 (1973); *Chem. Abs.*, **78**, 158599 (1973).
- ⁹⁰ Y. Ogata, A. Kawasaki, H. Suzuki and H. Kojoh, *J. Org. Chem.*, **38**, 3031 (1973).
- ⁹¹ J. Thomas, *Bull. Soc. Chim. France*, **1973**, 1296, 1300.
- ⁹² D. J. Hupe, M. C. R. Kendall, G. T. Sinner and T. A. Spencer, *J. Am. Chem. Soc.*, **95**, 2260 (1973); D. J. Hupe, M. C. R. Kendall and T. A. Spencer, *ibid.*, p. 2271.
- ⁹³ G. M. Sharma and O. A. Roels, *J. Org. Chem.*, **38**, 3648 (1973).
- ⁹⁴ P. A. Kollman, W. F. Trager, S. Rothenberg and J. E. Williams, *J. Am. Chem. Soc.*, **95**, 458 (1973).
- ⁹⁵ J. Velisek, J. Davidek, J. Pokorny, K. Grundova and G. Janicek, *Z. Lebensm.-Unters. Forsch.*, **149**, 323 (1972); *Chem. Abs.*, **78**, 70969 (1973).
- ⁹⁶ P. Dunlop, M. A. Marini, H. M. Fales, E. Sokoloski and C. J. Martin, *Bio-Organic Chemistry*, **2**, 235 (1973).
- ⁹⁷ A. M. Knowles and A. Lawson, *J.C.S. Perkin I*, **1973**, 537.
- ⁹⁸ A. T. Nielsen, R. L. Atkins, D. W. Moore, R. Scott, D. Mallory and J. M. LaBerge, *J. Org. Chem.*, **38**, 3288 (1973).
- ⁹⁹ W. E. Hull, B. D. Sykes and B. M. Babior, *J. Org. Chem.*, **38**, 2931 (1973).
- ¹⁰⁰ M. P. Doyle, M. A. Zaleta, J. E. De Boer and W. Wierenga, *J. Org. Chem.*, **38**, 1663 (1973).
- ¹⁰¹ M. V. Bhatt and M. Ravindranathan, *J.C.S. Perkin II*, **1973**, 1160.
- ^{102a} R. D. Guthrie and J. L. Hedrick, *J. Am. Chem. Soc.*, **95**, 2971 (1973).
- ^{102b} J. E. Dixon and T. C. Bruice, *Biochemistry*, **12**, 4762 (1973).
- ¹⁰³ K. Harada and T. Yoshida, *J. Org. Chem.*, **37**, 4366 (1972); A. E. Kitahchi, A. H. Nathans and C. L. Kitchell, *J. Biol. Chem.*, **248**, 841 (1973); H. J. Rhodes, R. B. Kluza and M. I. Blake, *J. Pharm. Sci.*, **62**, 59 (1973).
- ¹⁰⁴ S. Fatutta, A. Risaliti, C. Russo and E. Valentin, *Gazz. Chim. Ital.*, **102**, 1008 (1972).
- ¹⁰⁵ F. Weisbuch, C. Yamagami and G. Dana, *J. Org. Chem.*, **37**, 4334 (1972).
- ¹⁰⁶ J. P. Freeman, "Less Familiar Reactions of Oximes", *Chem. Rev.*, **73**, 283 (1973).
- ¹⁰⁷ S. M. Silver and J. M. Sayer, *J. Am. Chem. Soc.*, **95**, 5073 (1973).
- ¹⁰⁸ J. M. Sayer and W. P. Jencks, *J. Am. Chem. Soc.*, **95**, 5637 (1973); see *Org. Reaction Mech.*, **1972**, 405-406.
- ¹⁰⁹ R. E. Barnett, *Accounts Chem. Research*, **6**, 41 (1973).
- ¹¹⁰ J. M. Sayer, M. Peskin and W. P. Jencks, *J. Am. Chem. Soc.*, **95**, 4277 (1973).
- ¹¹¹ L. do Amaral, M. P. Bastos, H. G. Bull and E. H. Cordes, *J. Am. Chem. Soc.*, **95**, 7369 (1973); see *Org. Reaction Mech.*, **1972**, 405.
- ¹¹² Ya. I. Turyan and O. A. Tohtilcova, *Organic Reactivity (Tartu)*, **9**, 794, 804 (1972).
- ¹¹³ V. A. Afanas'ev and I. F. Strel'tsova, *Zh. Fiz. Khim.*, **46**, 2545 (1972); *Chem. Abs.*, **78**, 58688 (1973); I. Dyong and H. P. Bertram, *Chem. Ber.*, **106**, 1743, 2654 (1973); A. J. Fatiadi, *Chem. Ind. (London)*, **1973**, 38.
- ¹¹⁴ J. Arriau, J. P. Campillo and J. Deschamps, *Bull. Soc. Chim. France*, **1973**, 1398, 1403.
- ¹¹⁵ S. R. Johns, J. A. Lamberton and E. R. Nelson, *Austral. J. Chem.*, **26**, 1297 (1973).
- ¹¹⁶ V. L. Goedken and S.-M. Peng, *Chem. Comm.*, **1973**, 62.
- ¹¹⁷ A. Bely, F. Petrus and J. Verducci, *Bull. Soc. Chim. France*, **1973**, 1395.
- ¹¹⁸ I. Christenson, *Acta Pharm. Suec.*, **9**, 309, 343, (1972); *Chem. Abs.*, **78**, 3450, 3442 (1973); T. Balakrishnan and M. Santappa, *Curr. Sci.*, **42**, 418 (1973); *Chem. Abs.*, **79**, 52522 (1973).

- 119 G. T. Knight and B. Saville, *J.C.S. Perkin II*, **1973**, 1550.
- 120 A. J. Kresge and Y. Chiang, *J. Am. Chem. Soc.*, **95**, 803 (1973).
- 121 I. de Jonge and W. Drenth, *Rec. Trav. chim.*, **92**, 420 (1972).
- 122 L. R. Fedor, N. C. De and S. K. Gurawa, *J. Am. Chem. Soc.*, **95**, 2905 (1973); cf. *Org. Reaction Mech.*, **1969**, 419; **1972**, 407.
- 123 G. Stork and R. L. Danheiser, *J. Org. Chem.*, **38**, 1775 (1973).
- 124 A. C. Knipe and B. G. Cox, *J.C.S. Perkin II*, **1973**, 1391; *J. Org. Chem.*, **38**, 3429 (1973); cf. *Org. Reaction Mech.*, **1972**, 408.
- 125 R. P. Bell and M. I. Page, *J.C.S. Perkin II*, **1973**, 1681.
- 126 G. A. Abad, S. P. Jindal and T. T. Tidwell, *J. Am. Chem. Soc.*, **95**, 6326 (1973); cf. *Org. Reaction Mech.*, **1971**, 410-411.
- 127 R. P. Bell and B. A. Timini, *J.C.S. Perkin II*, **1973**, 1518.
- 128 J. Hine, J. L. Lynn, J. H. Jensen, and F. C. Schmalstieg, *J. Am. Chem. Soc.*, **95**, 1577 (1973); cf. *Org. Reaction Mech.*, **1971**, 409-410.
- 129 J. Hine, E. F. Glod, R. E. Notari, F. E. Rogers and F. C. Schmalstieg, *J. Am. Chem. Soc.*, **95**, 2537 (1973).
- 130 J. Hine, K. W. Narducy, J. Mulders, F. E. Rogers and N. W. Flackham, *J. Org. Chem.*, **38**, 1636 (1973); cf. ref. 83.
- 131 L. P. Koshechikina, I. V. Mel'nichenko and A. A. Yasnikov, *Ukr. Khim. Zh.* (Russian Ed.), **38**, 1248 (1972); *Chem. Abs.*, **78**, 96784 (1973).
- 132 D. B. Dahlberg and F. A. Long, *J. Am. Chem. Soc.*, **95**, 3825 (1973).
- 133 R. A. Lynch, S. P. Vincenti, Y. T. Lin, L. D. Smucker and S. C. S. Rao, *J. Am. Chem. Soc.*, **94**, 8351 (1972).
- 134 K. E. Teo and E. W. Warnhoff, *J. Am. Chem. Soc.*, **95**, 2728 (1973).
- 135 Y. Jasor, M. Gaudry, A. Marquet and M. Bettahar, *Bull. Soc. Chim. France*, **1973**, 2732, 2735.
- 136 P. Moreau, A. Casadevall and E. Casadevall, *Bull. Soc. Chim. France*, **1973**, 1014.
- 137 E. Kiehlmann, F. Masaro and F. J. Slawson, *Can. J. Chem.*, **51**, 3182 (1973).
- 138 P. Metzger, A. Casadevall and E. Casadevall, *Tetrahedron Letters*, **1973**, 2027.
- 139 J. Toullec and J. E. Dubois, *Tetrahedron*, **29**, 2851, 2859 (1973).
- 140 J.-O. Levin, *Chem. Scripta*, **4**, 85 (1973).
- 141 R. Kluger and P. Wasserstein, *J. Am. Chem. Soc.*, **95**, 1071 (1973).
- 142 J. Klein and R. Levene, *J.C.S. Perkin II*, **1973**, 1971.
- 143 B. E. Tilley, D. W. Porter and R. W. Gracy, *Carbohydrate Res.*, **27**, 289 (1973).
- 144 J. S. Chickos and R. E. K. Winter, *J. Am. Chem. Soc.*, **95**, 506 (1973); cf. *Org. Reaction Mech.*, **1972**, 411.
- 145 B. Macierewicz, *Rocz. Chem.*, **47**, 1735 (1973).
- 146 K. E. Hine and R. F. Childs, *J. Am. Chem. Soc.*, **95**, 3289 (1973).
- 147 H. Koshimura, J. Saito and T. Okubo, *Bull. Chem. Soc. Japan*, **46**, 632 (1973); M. C. Fernandez and E. Melendez, *An. Quim.*, **68**, 1035 (1972); A. D. Taneja and K. P. Srivastava, *J. Indian Chem. Soc.*, **49**, 889 (1972); A. D. Taneja, K. P. Srivastava and M. C. Gupta, *J. Chin. Chem. Soc. (Tapei)*, **19**, 115 (1972); *Chem. Abs.*, **77**, 163839 (1972).
- 148 K. J. Schray, S. J. Benkovic, P. A. Benkovic and I. A. Rose, *J. Biol. Chem.*, **248**, 2219 (1973); B. Wurster and B. Hess, *Z. Physiol. Chem.*, **354**, 407 (1973).
- 149 E. L. O'Connell and I. A. Rose, *J. Biol. Chem.*, **248**, 2225 (1973).
- 150 I. A. Rose, E. L. O'Connell and K. J. Schray, *J. Biol. Chem.*, **248**, 2232 (1973).
- 151 T. Y. S. Shen and E. W. Westhead, *Biochemistry*, **12**, 3333 (1973); S.-K. Oh and J. M. Brewer, *Arch. Biochem. Biophys.*, **157**, 491 (1973); T. Nowak, A. S. Mildvan and G. L. Kenyon, *Biochemistry*, **12**, 1690 (1973).
- 152 S. G. Waley, *Biochem. J.*, **135**, 165 (1973); K. J. Schray, E. L. O'Connell and I. A. Rose, *J. Biol. Chem.*, **248**, 2214 (1973).
- 153 W. T. Comer and D. L. Temple, *J. Org. Chem.*, **38**, 2121 (1973).
- 154 Y. Yano, T. Okonogi, M. Sunaga and W. Tagaki, *Chem. Comm.*, **1973**, 527.
- 155 W. L. Dilling, N. B. Tefertiller and J. P. Heesch, *J. Org. Chem.*, **37**, 4159 (1972); L. P. Koshechikina and A. A. Yasnikov, *Ukr. Khim. Zh.* (Russian ed.), **38**, 786 (1972); *Chem. Abs.*, **78**, 3518 (1973); T. Mukaiyama, K. Narasaka and K. Banno, *Chem. Letters (Tokyo)*, **1973**, 1011; A. A. Gallo and H. Z. Sable, *Biochem. Biophys. Acta*, **302**, 443 (1973); J. E. Dubois and P. Fellmann, *Tetrahedron Letters*, **1972**, 5085; J.-E. Vik, *Acta Chem. Scand.*, **26**, 3165 (1972); T. J. Clark, *J. Org. Chem.*, **38**, 1749 (1973).

- ¹⁵⁶ M. Calmon and J.-P. Calmon, *Compt. Rend., C.*, **276**, 197 (1973); M. Calas, B. Calas and L. Giral, *Bull. Soc. Chim. France*, **1973**, 2079.
- ¹⁵⁷ S. A. Fine and P. D. Pulaski, *J. Org. Chem.*, **38**, 1747 (1973).
- ¹⁵⁸ A. Takeda, S. Tsuboi and T. Hongo, *Bull. Chem. Soc. Japan*, **46**, 1844 (1973); E. Elkik and C. Francesch, *Bull. Soc. Chim. France*, **1973**, 1277, 1281.
- ¹⁵⁹ T. I. Crowell and T.-R. Kim, *J. Am. Chem. Soc.*, **95**, 6781 (1973); F. S. Prout, U. D. Beaucaire, G. R. Dyrkarz, W. M. Koppes, R. E. Kuznicki, T. A. Mattewski, J. J. Pienkowski and J. M. Puda, *J. Org. Chem.*, **38**, 1512 (1973).
- ¹⁶⁰ G. Zvilichovsky and U. Fotadar, *J. Org. Chem.*, **38**, 1782 (1973).
- ¹⁶¹ A. V. Shchelkunov, *Vest. Akad. Nauk Kaz. SSR*, **29**, 17 (1973); *Chem. Abs.*, **79**, 104364 (1973).
- ¹⁶² F. Fernandez-Gonzal and R. Perez-Ossorco, *An. Quim.*, **68**, 1411 (1972).
- ¹⁶³ M. Anai, C. Y. Lai and B. L. Horecker, *Arch. Biochem. Biophys.*, **156**, 712 (1973); **158**, 449 (1973).
- ¹⁶⁴ A. L. Crowder, C. A. Swenson and R. Barker, *Biochemistry*, **12**, 2852 (1973); E. Grazi, C. Sivieri-Pecovari, R. Gayliano and G. Trombetta, *ibid.*, p. 2583.
- ¹⁶⁵ E. Vedejs and K. A. J. Snoble, *J. Am. Chem. Soc.*, **95**, 5778 (1973).
- ¹⁶⁶ M. Kuchar, B. Kakac, O. Nemecek, E. Kraus and J. Holubek, *Coll. Czech. Chem. Comm.*, **38**, 447 (1973).
- ¹⁶⁷ G. Aksnes and R. Y. Khalil, *Phosphorus*, **2**, 105 (1972); *Chem. Abs.*, **78**, 70865 (1973).
- ¹⁶⁸ N. A. Nesmeyanov, E. V. Vishtok and O. A. Reutov, *Dokl. Akad. Nauk SSSR*, **210**, 1102 (1973); *Chem. Abs.*, **79**, 91259 (1973); D. W. Allen, B. G. Hutley and T. C. Rich, *J.C.S. Perkin II*, **1973**, 820.
- ¹⁶⁹ I. S. Kislina and M. I. Vinnik, *Organic Reactivity (Tartu)*, **9**, 299 (1972); I. S. Kislina and M. I. Vinnik, *Dokl. Akad., Nauk SSSR*, **206**, 1118 (1972); *Chem. Abs.*, **78**, 71090 (1973).
- ¹⁷⁰ I. V. Andreeva, M. M. Koton, A. I. Turbina and N. V. Kukarkina, *Zh. Org. Khim.*, **9**, 562 (1973); *Chem. Abs.*, **78**, 147018 (1973).
- ¹⁷¹ V. A. Ostrovskii, A. S. Enin and G. I. Koldobskii, *Zh. Org. Khim.*, **9**, 802 (1973); *Chem. Abs.*, **79**, 4770 (1973).
- ¹⁷² R. Varma and B. French, *Carbohydrate Res.*, **71**, (1972).
- ¹⁷³ H. M. Relles, *J. Org. Chem.*, **38**, 1570 (1973).
- ¹⁷⁴ H. Ona, M. Sakai, M. Suda and S. Masarume, *Chem. Comm.*, **1973**, 45.
- ¹⁷⁵ J.-P. Geumas and H. Quiniou, *Bull. Soc. Chim. France*, **1973**, 592.
- ¹⁷⁶ I. Mehrota and D. Devaprabhakara, *J. Organometal. Chem.*, **51**, 93 (1973).
- ¹⁷⁷ P. Talts and U. Haldna, *Organic Reactivity (Tartu)*, **10**, 118 (1973); S. V. Zukerman, C. P. Pivovarevich, L. A. Kutulya, N. S. Pionenko and V. F. Laorushin, *Organic Reactivity (Tartu)*, **9**, 130 (1971); K. L. Cook and A. J. Waring, *J.C.S. Perkin II*, **1973**, 84; D. M. Brouwer and A. A. Kippen, *Rec. Trav. chim.*, **92**, 906 (1973).

