

Topics in Current Chemistry

112

Managing Editor: F. L. Boschke

Editorial Board: M. J. S. Dewar J. D. Dunitz

K. Hafner E. Heilbronner S. Ito J.-M. Lehn

K. Niedenzu K. N. Raymond C. W. Rees

K. Schäfer F. Vögtle G. Wittig

I. Szele and H. Zollinger

Azo Coupling Reactions –
Structures and Mechanisms

A. Suzuki

Some Aspects of Organic Synthesis
Using Organoborates

E. M. Kosower

Stable Pyridinyl Radicals

J. Káš and P. Rauch

Labeled Proteins,
Their Preparation and Applications



Preparative Organic Chemistry

Springer-Verlag Berlin Heidelberg New York Tokyo

Preparative Organic Chemistry

With Contributions by
J. Káš, E. M. Kosower, P. Rauch,
A. Suzuki, I. Szele, H. Zollinger

With 41 Figures and 21 Tables



Springer-Verlag
Berlin Heidelberg New York Tokyo
1983

This series presents critical reviews of the present position and future trends in modern chemical research. It is addressed to all research and industrial chemists who wish to keep abreast of advances in their subject.

As a rule, contributions are specially commissioned. The editors and publishers will, however, always be pleased to receive suggestions and supplementary information. Papers are accepted for "Topics in Current Chemistry" in English.

ISBN 3-540-12396-2 Springer-Verlag Berlin Heidelberg New York Tokyo
ISBN 0-387-12396-2 Springer-Verlag New York Heidelberg Berlin Tokyo

Library of Congress Cataloging in Publication Data. Main entry under title: Preparative organic chemistry.

(Topics in current chemistry = Fortschritte der chemischen Forschung; 112)

Includes bibliographies and index.

1. Chemistry, Organic—Addresses, essays, lectures.

I. Káś, J. II. Series: Topics in current chemistry; 112.

QD1.F58 vol. 112 [QD255] 540s [547] 83-660

This work is subject to copyright. All rights are reserved, whether the whole or part of the material is concerned, specifically those of translation, reprinting, re-use of illustrations, broadcasting, reproduction by photocopying machine or similar means, and storage in data banks. Under § 54 of the German Copyright Law where copies are made for other than private use, a fee is payable to "Verwertungsgesellschaft Wort", Munich.

© by Springer-Verlag Berlin Heidelberg 1983

Printed in GDR

The use of registered names, trademarks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

2152/3020-543210

112

Topics in Current Chemistry

Fortschritte der Chemischen Forschung

Managing Editor: F. L. Boschke

Managing Editor:

Dr. Friedrich L. Boschke

Springer-Verlag, Postfach 105 280, D-6900 Heidelberg 1

Editorial Board:

- Prof. Dr. *Michael J. S. Dewar* Department of Chemistry, The University of Texas
Austin, TX 78712, USA
- Prof. Dr. *Jack D. Dunitz* Laboratorium für Organische Chemie der
Eidgenössischen Hochschule
Universitätsstraße 6/8, CH-8006 Zürich
- Prof. Dr. *Klaus Hafner* Institut für Organische Chemie der TH
Petersenstraße 15, D-6100 Darmstadt
- Prof. Dr. *Edgar Heilbronner* Physikalisch-Chemisches Institut der Universität
Klingelbergstraße 80, CH-4000 Basel
- Prof. Dr. *Shô Itô* Department of Chemistry, Tohoku University,
Sendai, Japan 980
- Prof. Dr. *Jean-Marie Lehn* Institut de Chimie, Université de Strasbourg, 1, rue
Blaise Pascal, B. P. Z 296/R8, F-67008 Strasbourg-Cedex
- Prof. Dr. *Kurt Niedenzu* University of Kentucky, College of Arts and Sciences
Department of Chemistry, Lexington, KY 40506, USA
- Prof. Dr. *Kenneth N. Raymond* Department of Chemistry, University of California,
Berkeley, California 94720, USA
- Prof. Dr. *Charles W. Rees* Hofmann Professor of Organic Chemistry, Department
of Chemistry, Imperial College of Science and Technology,
South Kensington, London SW7 2AY, England
- Prof. Dr. *Klaus Schäfer* Institut für Physikalische Chemie der Universität
Im Neuenheimer Feld 253, D-6900 Heidelberg 1
- Prof. Dr. *Fritz Vögtle* Institut für Organische Chemie und Biochemie
der Universität, Gerhard-Domagk-Str. 1,
D-5300 Bonn 1
- Prof. Dr. *Georg Wittig* Institut für Organische Chemie der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1

Reactivity and Structure

Concepts in Organic Chemistry

Editors: K. Hafner, J.-M. Lehn, C. W. Rees,
P. v. R. Schleyer, B. M. Trost, R. Zahradnik

Volume 15

A. J. Kirby

The Anomeric Effect and Related Stereoelectronic Effects at Oxygen

1983. 20 figures, 24 tables. VIII, 149 pages
ISBN 3-540-11684-2

Volume 14

W. P. Weber

Silicon Reagents for Organic Synthesis

1983. XVIII, 430 pages
ISBN 3-540-11675-3

Volume 13

G. W. Gokel, S. H. Korzeniewski

Macrocyclic Polyether Syntheses

1982. 89 tables. XVIII, 410 pages
ISBN 3-540-11317-7

Volume 12

J. Fabian, H. Hartmann

Light Absorption of Organic Colorants

Theoretical Treatment and Empirical Rules
1980. 76 figures, 48 tables. VIII, 245 pages
ISBN 3-540-09914-X

Volume 11

New Syntheses with Carbon Monoxide

Editor: J. Falbe

With contributions by H. Bahrmann, B. Cornils,
C. D. Frohning, A. Mullen
1980. 118 figures, 127 tables. XIV, 465 pages
ISBN 3-540-09674-4

Volume 10

J. Tsuji

Organic Synthesis with Palladium Compounds

1980. 9 tables. XII, 207 pages
ISBN 3-540-09767-8

Volume 9

J. R. Blackborow, D. Young

Metal Vapour Synthesis in Organometallic Chemistry

1979. 36 figures, 32 tables. XIII, 202 pages
ISBN 3-540-09330-3

Volume 8

C. Birr

Aspects of the Merrifield Peptide Synthesis

1978. 62 figures, 6 tables. VIII, 102 pages
ISBN 3-540-08872-5

Volume 7

D. I. Davies, M. J. Parrott

Free Radicals in Organic Synthesis

1978. 1 figure. XII, 169 pages
ISBN 3-540-08723-0

Volume 6

M. L. Bender, M. Komiyama

Cyclodextrin Chemistry

1978. 14 figures, 37 tables. X, 96 pages
ISBN 3-540-08577-7

Volume 5

N. D. Epiotis

Theory of Organic Reactions

1978. 69 figures, 47 tables. XIV, 290 pages
ISBN 3-540-08551-3

Volume 4

W. P. Weber, G. W. Gokel

Phase Transfer Catalysis in Organic Synthesis

1977. out of print. New edition in preparation

Volume 3

H. Kwart, K. King

d-Orbitals in the Chemistry of Silicon, Phosphorus and Sulfur

1977. 4 figures, 10 tables. VIII, 220 pages
ISBN 3-540-07953-X

Volume 2

K. Fukui

Theory of Orientation and Stereoselection

1975. 72 figures, 2 tables. VII, 134 pages
ISBN 3-540-07426-0

Volume 1

J. Tsuji

Organic Synthesis

by Means of Transition Metal Complexes
A Systematic Approach
1975. 4 tables. IX, 199 pages
ISBN 3-540-07227-6



Springer-Verlag Berlin Heidelberg New York Tokyo

Inorganic Chemistry Concepts

Editors: C. K. Jørgensen, M. F. Lippert, S. J. Lippard, J. L. Margrave, K. Niedenzu, H. Nöth, R. W. Parry, H. Yamatera

Volume 8: M. T. Pope

Heteropoly and Isopoly Oxometalates

1983. 71 figures, 40 tables. Approx. 190 pages.
ISBN 3-540-11889-6

Contents: Introduction. – Preparation, Structural Principles, Properties and Applications. – Isopolyanions. – Heteropolyanions. – Heteropolyanions as Ligands. – Redox Chemistry and Heteropoly Blues. – Organic and Organometallic Derivatives. – Polyoxometalate Chemistry. Current Limits and Remaining Challenges. – Appendix: Nomenclature of Polyoxanions. – References. – Subject Index.

Volume 7: H. Rickert

Electrochemistry of Solids

An Introduction
1982. 95 figures, 23 tables. XII, 240 pages. ISBN 3-540-11116-6

Contents: Introduction. – Disorder in Solids. – Examples of Disorder in Solids. – Thermodynamic Quantities of Quasi-Free Electrons and Electron Defects in Semiconductors. – An Example of Electronic Disorder. Electrons and Electron Defects in α -Ag₂S. – Mobility, Diffusion and Partial Conductivity of Ions and Electrons. – Solid Ionic Conductors, Solid Electrolytes and Solid-Solution Electrodes. – Galvanic Cells with Solid Electrolytes for Thermodynamic Investigations. – Technical Applications of Solid Electrolytes – Solid-State Ionics. – Solid-State Reactions. – Galvanic Cells with Solid Electrolytes for Kinetic Investigations. – Non-Isothermal Systems. Soret Effect, Transport Processes, and Thermopowers. – Author Index. – Subject Index.

Volume 6: D. L. Kepert

Inorganic Stereochemistry

1982. 206 figures, 45 tables. XII, 227 pages. ISBN 3-540-10716-9

Contents: Introduction. – Polyhedra. – Four-Coordinate Compounds. – Five-Coordinate Compounds Containing only Unidentate Ligands. – Five-Coordinate Compounds Containing Chelate Groups. – Six-Coordinate Compounds Containing only Unidentate Ligands. – Six-Coordinate Compounds [M(Bidentate)₂(Unidentate)₂]. – Six-Coordinate Compounds [M(Bidentate)₃]. – Six-Coordinate Compounds Containing Tridentate Ligands. – Seven-Coordinate Compounds Containing only Unidentate Ligands. – Seven-Coordinate Compounds Containing Chelate Groups. – Eight-Coordinate Compounds Containing only Unidentate Ligands. – Eight-Coordinate Compounds Containing Chelate Groups. – Nine-Coordinate Compounds. – Ten-Coordinate Compounds. – Twelve-Coordinate Compounds. – References. – Subject Index.

Volume 5: T. Tominaga, E. Tachikawa

Modern Hot Atom Chemistry and Its Applications

1981. 57 figures, 34 tables. VIII, 154 pages. ISBN 3-540-10715-0

Contents: Introduction. – Experimental Techniques: Production of Energetic Atoms. Radiochemical Separation Techniques. Special Physical Techniques. – Characteristics of Hot Atom Reactions: Gas Phase Hot Atom Reactions. Liquid Phase Hot Atom Reactions. Solid Phase Hot Atom Reactions. – Applications of Hot Atom Chemistry and Related Topics: Applications in Inorganic, Analytical and Geochemistry. Applications in Physical Chemistry. Applications in Biochemistry and Nuclear Medicine. Hot Atom Chemistry in Energy-Related Research. Current Topics Related to Hot Atom Chemistry and Future Scope. – Subject Index.

Volume 4: Y. Saito

Inorganic Molecular Dissymmetry

1979. 107 figures, 28 tables. IX, 167 pages. ISBN 3-540-09176-9

From the reviews: "... The book is directed towards a general and synthetic understanding of chiral molecules, and their unique property of optical activity, in the field of transition metal chemistry. The level of treatment is suited to graduate or advanced undergraduate teaching. For these roles, and for library reference, the book is strongly recommended." *Nature*

Volume 3: P. Güdlich, R. Link, A. Trautwein

Mössbauer Spectroscopy and Transition Metal Chemistry

1978. 160 figures, 19 tables, 1 folding plate. X, 280 pages
ISBN 3-540-08671-4

From the reviews: "... This volume departs refreshingly from the popular (at least for Mössbauer books) format of a collection of articles by various experts. As a unified treatment and extensive coverage of the literature, it stands up well in comparison to the older book of Greenwood and Gibb (1971)... Workers in the field (who have a knowledge of the MO approach, EFG's etc.) will find the main portion of the book useful. Students will be able to work through the text with profit..." *American Scientist*

Volume 2: R. L. Carlin, A. J. van Duyneveldt

Magnetic Properties of Transition Metal Compounds

1977. 149 figures, 7 tables. XV, 264 pages. ISBN 3-540-08584-X

From the reviews: "... As stated in the Preface by the authors it is a textbook on magnetochemistry presented in the way 'the science of magnetochemistry should be going'. It is no doubt a novel and very useful publication on the subject."

Journal of the Institution of Chemists

Volume 1: R. Reisfeld, C. K. Jørgensen

Lasers and Excited States of Rare Earths

1977. 9 figures, 26 tables. VIII, 226 pages. ISBN 3-540-08324-3

From the reviews: "... The book is clearly written and very useful for laser physicists as well as for chemists or physicists interested in spectroscopy of lanthanide compounds. To understand the conclusions, no deep insight in quantum mechanics or group theory is required. The references include partially the literature of 1976."

European Spectroscopy News



Springer-Verlag Berlin Heidelberg New York Tokyo

Table of Contents

Azo Coupling Reactions — Structures and Mechanisms	
I. Szele, H. Zollinger	1
Some Aspects of Organic Synthesis Using Organoborates	
A. Suzuki	67
Stable Pyridinyl Radicals	
E. M. Kosower	117
Labeled Proteins, Their Preparation and Applications	
J. Káš, P. Rauch	163
Author Index Volumes 101–112	231

Azo Coupling Reactions

Structures and Mechanisms

Ivanka Szele and Heinrich Zollinger

Technisch-Chemisches Laboratorium, Eidgenössische Technische Hochschule (ETH),
CH-8092 Zürich, Switzerland

Table of Contents

1 Introduction	2
2 Structure of Reagents in Azo Coupling Reactions	3
2.1 Diazo Components	3
2.1.1 Aliphatic Diazonium Ions	3
2.1.2 Diazoalkanes, Diazoketones and Diazoesters	6
2.1.3 Diazooxides	8
2.1.4 Heterocyclic Diazo and Diazonium Compounds	11
2.2 Coupling Components	15
2.2.1 Compounds with Activated Methyl, Methylene and Methine Groups	15
2.2.2 Heterocyclic Compounds	17
2.2.3 Isocyclic Aromatic Substrates	21
3 Influence of the Reaction Medium on Azo Coupling Reactions	23
3.1 Azo Coupling Reactions in Organic Solvents	23
3.2 Reactions Catalyzed by Micelles	25
3.3 Phase Transfer Catalysis	27
4 Mechanisms	28
4.1 Acid-base Pre-equilibria	28
4.2 Mixing and Diffusion Effects	33
4.3 The Substitution Proper of C-Coupling Reactions	35
4.4 Mechanisms of N-Coupling: Formation and Rearrangement of Diazoamino Compounds (Triazenes)	49
4.5 Orientation Effects	53
4.6 Comparative Studies of Reactivities	57
5 References	61

1 Introduction

Diazonium ions are Lewis acids in which the β -nitrogen atom is the centre of electrophilic character. The addition of nucleophiles at the β -nitrogen is called an azo (or diazo) coupling reaction and depending on the atom which provides the lone pair of electrons, C-, N-, O-, P- or S-coupling can occur.

In this paper reactions of aromatic, heteroaromatic and related diazonium ions with nucleophiles are discussed. In such reactions substitution by the diazonium ion of an electrofugic atom or group bonded to carbon takes place. Occasionally reference is made to N- and P-coupling. In Section 4 the respective substitution at nitrogen (formation of diazoamino compounds) is included for comparative purposes.

The products of these substitution reactions at carbon are azo compounds; azo coupling is the reaction by which about 50 % of all industrial dyes manufactured in the last 100 years have been produced.

The industrial aspects of this reaction will, however, not be discussed in this paper. We will concentrate on structural and mechanistic problems which, to our knowledge, have not been summarized in detail in the last two decades. In the 1950's work on azo coupling reactions with aromatic substrates, e.g. with phenols, naphthols, naphthylamines, as well as with activated methylene compounds such as enols, demonstrated that azo coupling reactions are, in many respects, ideal systems for mechanistic investigations of electrophilic aromatic substitutions: Azo coupling reactions can be run in dilute aqueous buffer solutions, and therefore acid-base phenomena can be studied better than with other electrophilic aromatic substitutions, which often take place in less familiar systems such as concentrated sulfuric acid for nitrations, or apolar solvents for Friedel-Crafts reactions. A clear differentiation between specific and general base catalysis in electrophilic aromatic substitutions was made possible for the first time using an azo coupling reaction. The same is true for a quantitative evaluation of kinetic hydrogen isotope effects.

These results were previously discussed in a monograph published in 1961¹⁾, but were later dealt with only briefly by various authors. In the last twenty years some effects, found many decades ago in coupling and other substitution reactions, could be elucidated with respect to their structural and mechanistic basis, e.g. product ratios due to mixing effects — a phenomenon which was not understandable at all only a few years ago.

This review summarizes such investigations. We hope that it will give suggestions for further work on the understanding and the expansion of the scope of the azo coupling reaction as well as catalyze the transfer of methods used successfully in investigations of the azo coupling to other reactions in organic chemistry.

In order to keep this review to a manageable size we do not discuss in detail related reactions, e.g. additions of diazonium ions to simple anions like OH^- , CN^- , and N_3^- , or the so-called oxidative azo coupling reaction, discovered by Hünig in which electrophilic reagents comparable but not identical with diazonium ions are obtained by oxidation of heteroaromatic hydrazones.

2 Structure of Reagents in Azo Coupling Reactions

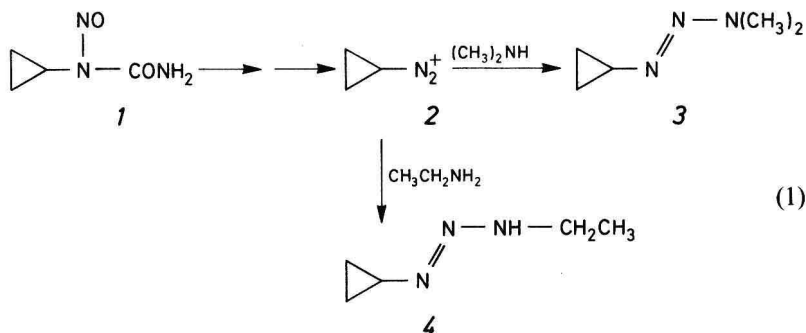
2.1 Diazo Components

By far the most important azo coupling reaction, i.e. the reaction of arenediazonium ions with aromatic coupling components, has been known for many decades and has been extensively reviewed¹⁾. Therefore, in this section we shall concentrate on reactions of aliphatic diazonium ions, diazoalkanes and diazocarbonyl compounds which have not been known previously as well as on coupling reactions which have gained in importance more recently, specifically those of heterocyclic diazonium ions.

2.1.1 Aliphatic Diazonium Ions

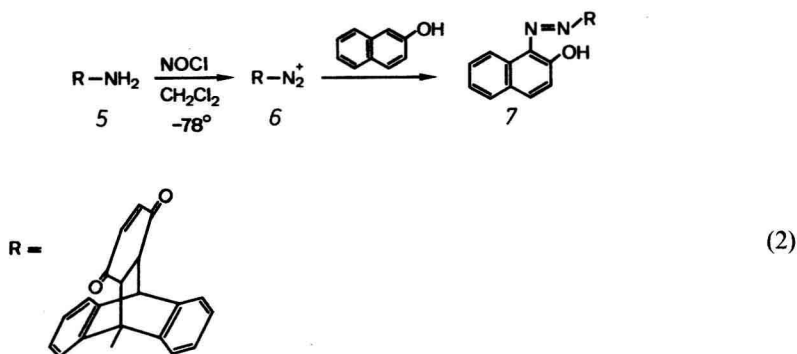
Aliphatic diazonium ions are formed as intermediates in deamination reactions of aliphatic amines. Due to the extremely good leaving group ability of nitrogen, however, they usually cannot be trapped by an azo coupling reaction, but rather undergo rapid dediazonation to give carbocation intermediates²⁾. Recently, however, it has been found that in some alkanediazonium ions azo coupling successfully competes with dediazonation. All the examples known up to now concern cyclopropanediazonium ions³⁻⁵⁾ and bridgehead diazonium ions⁶⁻⁹⁾ in which the loss of nitrogen would lead to a very unstable carbocation.

Kirmse and coworkers have studied the reaction of alkanediazonium ions with amines^{3,4)} and with lithium azide^{3,5)}. Cyclopropanediazonium ions²⁾ give azo coupling products 6 and 7 with dimethylamine and with ethylamine, respectively (1)^{3,4)}. However, no azo coupling of 1 with phenols was observed. In the reaction

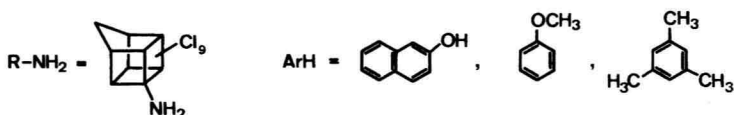
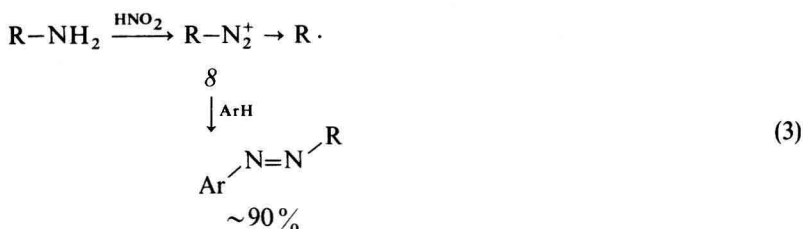


with lithium azide Kirmse and coworkers^{3,5)} determined by ¹⁵N-labelling of the α-nitrogen atom in 1 that only 3% of the product (cyclopropyl azide) was formed by direct substitution of the diazonio group by azide ions, while the major pathway (97%) was an addition of N₃⁻ to the β-nitrogen of the intermediate diazonium ion 2 and dediazonation of the pentazene formed.

Curtin and coworkers have observed the azo coupling of the bridgehead diazonium ion 6 with 2-naphthol at low temperature (2) in 50% yield.



Also Scherer and Lunt⁷⁻⁹⁾ could demonstrate the azo coupling of the extremely electrophilic bridgehead polychlorinated homocubanediazonium ion **8** with several aromatic coupling components (3). The dediazonation of **8** surprisingly yields radical intermediates⁹⁾, thus reflecting the high energy content of the bridgehead perchlorinated homocubyl cation. The hydrogenated analogue of **8**, on the other hand, yields 'normal' ionic intermediates under the same reaction conditions¹⁰⁾.

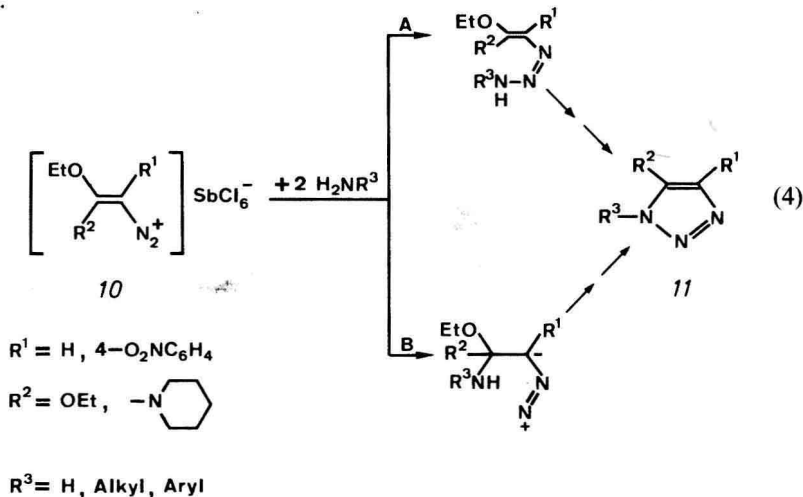


Other alkanediazonium ions, including the bridgehead bicyclo[2.2.1]heptane-1-diazonium ion **9**, do not undergo azo coupling reactions but give only nucleophilic substitution products^{4,5)}. In addition to the examples given above, some alkene-diazonium ions generated from nitrosooxazolidones can also add azide ions^{5,11)}.

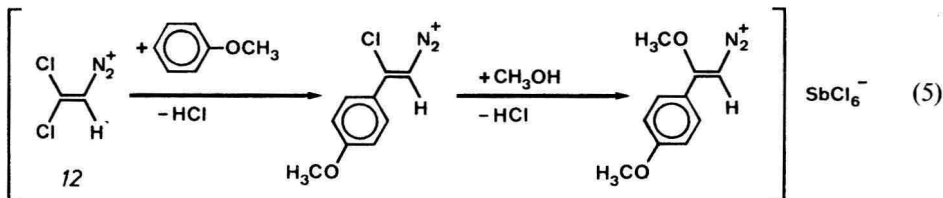


It is interesting to compare the behavior of short-lived diazonium ion intermediates with that of the relatively stable and isolable alkenediazonium ions first prepared

by Reimlinger¹²⁾ and by Bott^{13,14)}. Until now there has been no conclusive evidence that the latter compounds undergo an azo coupling reaction. The reaction of alkenediazonium ions **10** with primary amines, which gives triazoles **11** in reasonable yield^{15,16)}, can be rationalized in terms of an azo coupling reaction (Path A), as well as of a nucleophilic attack on the β -carbon atom of the C—C double bond (Path B) (4).

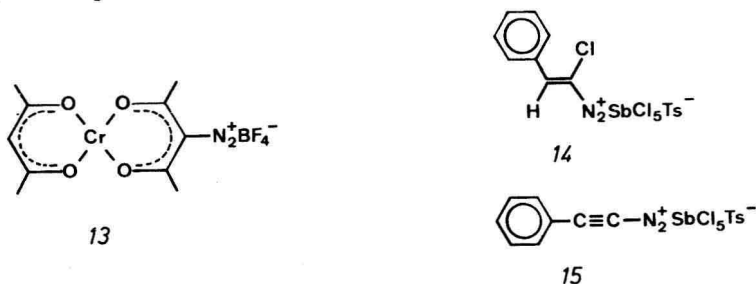


The extremely electrophilic alkenediazonium salt **12** was shown to react with nucleophiles, e.g. with anisole, at the β -carbon atom (5)¹⁴⁾. Compound **12** and other



substituted ethenediazonium ions¹⁷⁾ do not give azo compounds with typical aromatic coupling components.

On the other hand, the diazonium substituted acetyl-acetone complex¹⁸⁾ **13** as well as the mixture of diazonium salts¹⁹⁾ **14** and **15** seem to react with 2- and 1-naphthol, respectively, to give the corresponding azo dyes, which could, however, not be isolated as pure compounds.

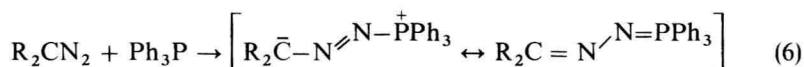


In conclusion it can be said that alkane- and alkenediazonium ions react with nucleophiles by a variety of pathways, one of them, in certain cases, being the azo coupling reaction. Small changes in the substrate structure, as well as in the reaction conditions, can drastically change the reaction pathway, indicating that the energy requirements for the competing reactions are rather similar.

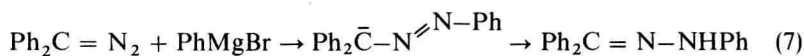
2.1.2 Diazoalkanes, Diazoketones and Diazoesters

Compared to diazonium salts, diazo compounds are generally much less reactive towards nucleophiles than towards electrophiles. As a result of this azo coupling reactions of diazo compounds are the exception rather than the rule. Electron withdrawing substituents on the diazo carbon increase the reactivity towards nucleophiles. Consequently the ability to undergo azo coupling reactions increases from diazomethane to diazocarbonyl- and 2-diazo-1,3-dicarbonyl compounds. Among the earliest reactions known were those with cyanide and sulfite ions ^{1,20}.

Tertiary phosphines, as opposed to amines, can form stable addition complexes with diazoalkanes ^{21,22}, probably due to the ability of phosphorus to stabilize the betaine with its empty d orbitals (6).

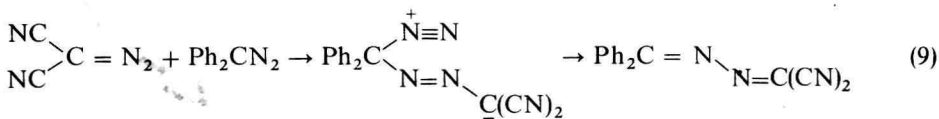
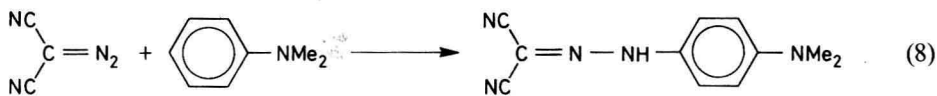


Carbanions derived from organometallic reagents react with aryldiazoalkanes ^{23 to 25}, diazoketones ²⁶ and diazoesters ²⁷ to yield hydrazones after hydrolysis (7).

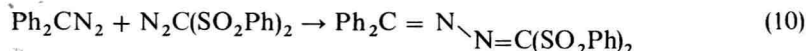


2-Diazo-1,3-dicarbonyl compounds are electrophilic enough to give azo coupling products with reactive aromatic azo coupling components ^{28,29}, as well as with CH acidic compounds ³⁰ such as β -diketones and β -keto-esters.

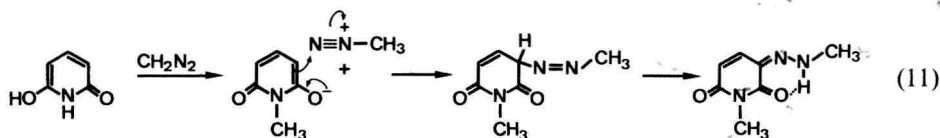
Dicyanodiazomethane ³¹ even gives an azo-coupling product with dimethylaniline (8) and also reacts with diaryldiazomethanes to give the mixed azines (9).



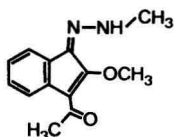
Bisarylsulfonyldiazomethanes can also react with diphenyldiazomethane and the azine is formed without passing through a carbene intermediate (10) ³².



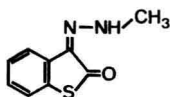
In 1969 the first example was reported of a coupling reaction of diazomethane with



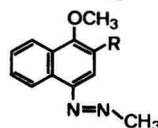
a heterocyclic coupling component ³³⁾ (11). Compounds 16 to 18 can be synthesized in a similar manner ³⁴⁻³⁶⁾.



16

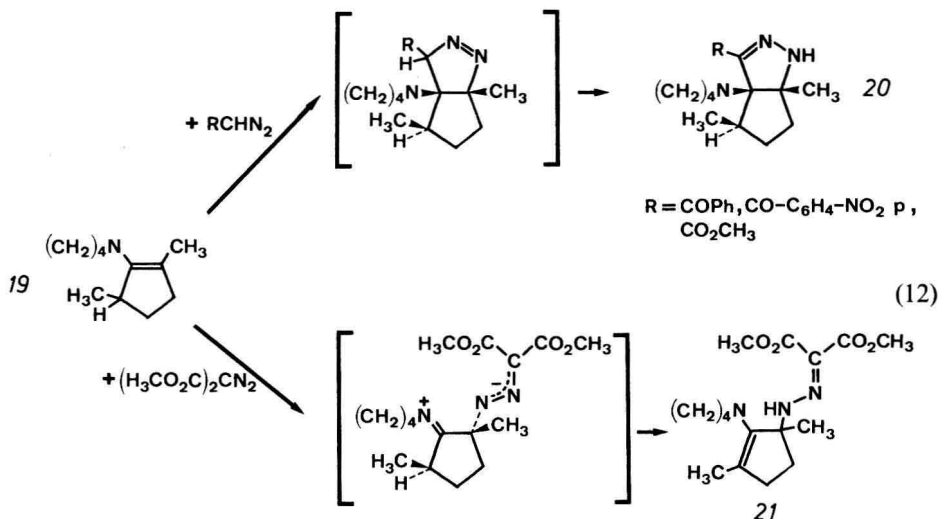


17



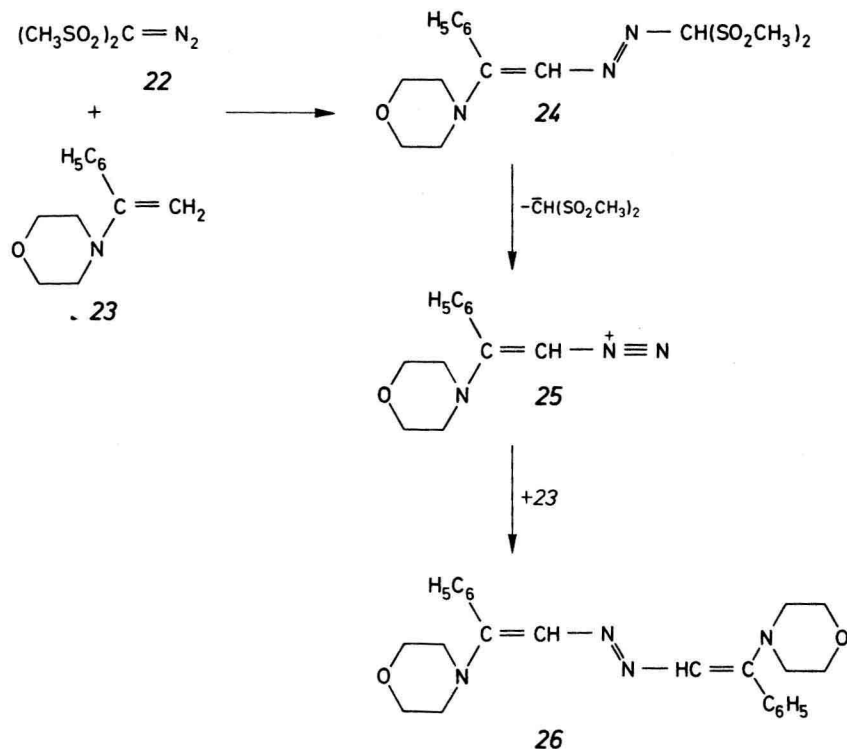
18

An interesting dichotomy of reaction paths was recently observed by Huisgen and coworkers ³⁷⁾ in reactions of diazocarbonyl compounds with enamines: While diazomonocarbonyl compounds react with 2,5-dimethyl-1-pyrrolidinocyclopentene 19 in a cycloaddition reaction to give 2-pyrazolines 20, dimethyl diazomalonate undergoes an azo coupling reaction and the hydrazone 21 is formed (12). This nicely



substantiates the statement that the reactivity of substituted diazo compounds in 1,3-dipolar additions decreases with increasing delocalization of the negative charge on the carbon atom into the substituents. The opposite trend is observed for the reactivity in azo coupling reactions.

Another interesting coupling reaction with enamines was recently observed with bis(methylsulfonyl)diazomethane 22 ⁴⁰⁾.

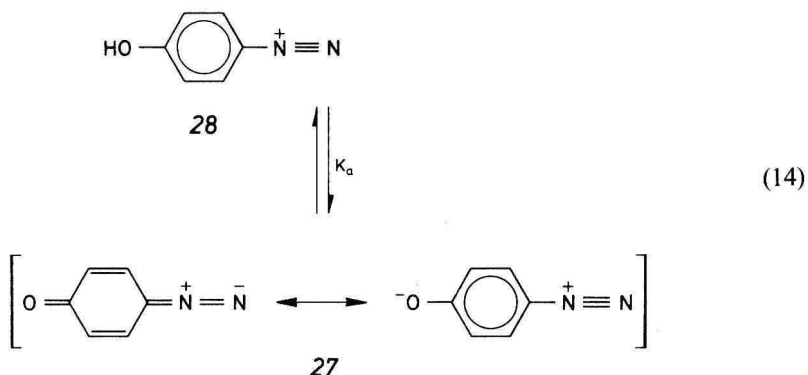


The azo compound 24 is probably formed initially. It decomposes to give the vinyl diazonium ion 25 that in its turn couples with another molecule of 23 to give the final product 26 (13)⁴⁰⁾. Actually the diazodiester 22 acts as a diazo-transfer agent.

2.1.3 Diazooxides¹

p-Diazooxides 27 and their o-isomers simultaneously display the properties of both aliphatic and aromatic diazo components. They can be considered as analogues of conjugated diazoketones. On the other hand, a specific feature of many of their reactions is their conversion to hydroxyarenediazonium ions 28 in the presence of acids (14). The pK_a value of the p-hydroxybenzenediazonium ion 28, for example, is 3.19⁴²⁾, so the reactivity of compounds of this type will depend a lot on the acidity of the reaction medium. 28 is much more electrophilic than 27, and the measured rate therefore depends on the position of equilibrium (14). Recently a comprehensive review on diazooxides has appeared⁴³⁾, also including azo coupling reactions, and therefore only a few selected reactions will be mentioned here.

¹ In this review the name diazooxides will be used for compounds of the type 27, since it seems to be in best agreement with the IUPAC⁴¹⁾ Rules (C10.1 and C84.2). Other names also encountered in the literature are: diazoquinones, quinonediazides and diazophenols.



Diazo oxides react with hydroxyaromatic coupling components in the same manner as diazonium salts, giving dihydroxysubstituted azo compounds. An interesting feature of this reaction is the fact that the reaction rate increases with medium acidity, reaches a maximum (between 50–80% H_2SO_4 in reactions with resorcinol, depending on the diazo oxide under study) and then decreases^{44,45}.

Basically the reactivity in azo coupling reactions of diazonium salts is larger than that of diazo oxides⁴⁶ (1,4-diazo oxides again are more reactive than the 1,2-species), and therefore the concentration of the more reactive form is increasing with the medium acidity. Up to a certain point this compensates for the parallel decrease in the concentration of the more reactive coupling component, the phenolate ion. In principle, however, there are no qualitative differences in the behavior of diazo oxides and arenediazonium salts in azo coupling reactions with hydroxyaromatic compounds. This is also supported by a thorough study of the coupling with 2-naphthol⁴⁶: in a Hammett plot of $\log k$ vs. σ^+ , data for diazonium salts and diazo oxides fall on one straight line ($\rho = 2.55$)⁴², indicating a uniform mechanism of the azo coupling process.

Substituted 1,4-diazo oxides react with secondary aliphatic amines to give the corresponding triazenes (diazo amino compounds) in high yield, while the products with primary amines are surprisingly unstable and decompose by a radical mechanism⁴⁷. Reactions with diazo alkanes yield asymmetrical azines 29 (15) in the case of 1,4-diazo oxides, and cyclic benzoxadiazines 30 with 1,2-diazo oxides (16)⁴⁸.

