W. Theilheimer

Synthetic Methods of Organic Chemistry

19

W. Theilheimer

Synthetic Methods of Organic Chemistry

Yearbook

Synthetische Methoden der Organischen Chemie

Jahrbuch

Vol. 19

Mit deutschem Register-Schlüssel

BASEL (Switzerland) S. KARGER NEW YORK

Preface to Volume 19

Most of the references in this volume concern papers published between 1962 and 1964. The index covers only one volume, as the next volume, which concludes the fourth series, will contain both a cumulative index and arrangement of all titles of Volumes 16 to 20.

I again wish to acknowledge with gratitude the help and advice I have had from Dr. John T. Plati, Dr. Bernhard Prijs, and Mr. Reinhard Zell. I also want to thank Dr. William R. Sullivan, Director of Research Services, for his kind cooperation in matters concerning Hoffmann-La Roche Inc., Nutley, N.J., as headquarters of this enterprise, and Mrs. Carole Majdanski for skilled secreterial help.

Nutley, New Jersey, U.S.A., May 1965.

W. Th.

Vorwort zu Band 19

Die meisten Literaturzitate in diesem Band betreffen Arbeiten aus den Jahren 1962—1964. Das Register umfaßt diesmal nur einen Band, da der nächste Band, der die vierte Serie abschließt, sowohl ein Generalregister als auch alle Titel der Bände 16—20 enthalten wird.

Nutley, New Jersey, USA, im Mai 1965.

W. Th.

From the Prefaces to the Preceding Volumes

New methods for the synthesis of organic compounds, improvements of known methods, and also old proved methods scattered in periodicals, are being recorded continuously in this book series.

An attempt has been made to develop the system of Weygand (Organic Preparations, Interscience Publishers, Inc., New York, 1945), and to group the reactions on a simple, although purely formal, basis. This has led to the invention of reaction symbols that can be classified systematically so that the methods can be

treated without knowledge of the current trivial and author names (e.g., "Oxidation" and "Friedel-Crafts reaction").

Readers accustomed to the common notations will find these in the subject index. In many cases, particularly in searching for complex reactions, use of the classification system may be avoided by consulting the subject index. It is thought that the volumes should be kept close at hand. They should provide a quick survey, and obviate the immediate need for an elaborate library search. Syntheses are therefore recorded in the subject index by starting materials and end products, along with the systematic arrangement for the methods. This makes possible a sub-classification within the reaction symbols by reagents, a further methodical criterion. Complex compounds are indexed with cross references under the related simpler compounds. General terms, such as synthesis, replacement, heterocyclics, may also be brought to the special attention of the reader.

Starting with Volume 5, a table that indicates the sequence of the reagents has been included. It may help the reader to locate reactions in the body of the text, particularly within large chapters. This table also contains such frequently used reagents as NaOH and HCl, which are not included in the alphabetical index.

Volume 8 and subsequent volumes contain a brief review, *Trends in Synthetic Organic Chemistry,* stressing some highlights of general interest and calling attention to developments too recent to be included in the body of the text.

The abstracts are limited to the information needed for an appraisal of the applicability of a desired synthesis. This includes the number and nature of the reaction steps, the yield, and the important literature in question. In order to carry out a particular synthesis it is therefore still necessary to have recourse to the original papers or, at least, to an abstract journal. In order to avoid repetition, selections are made on the basis of most detailed description and best yields, whenever the same method is used in similar cases. Continuations of papers already included will not be abstracted, unless they contain essentially new information. They may, however, be quoted at the place corresponding to the abstracted papers. These supplementary references (see page 483) make it possible to keep abstracts of previous volumes up-to-date.

Furthermore, to avoid a "jungle" of references, the following limitations have been decided on: Papers are not included, if their content does not fit the subject matter of "Synthetic Methods" and if they can be found easily in the indexes of the abstract journals. Less accessible and readable papers, such as the Russian

or Japanese ones, are only abstracted, as a rule, if the method in question is described nowhere else. Since publications dealing with organic chemistry are increasing from year to year, some unintentional omissions may occur as well. Therefore, the editor will be grateful if important methods not yet mentioned are brought to his attention.

Syntheses that are split into their various steps, which are recorded in different places, can be followed with the help of the notations *startg. m. f.* (starting material for the preparation of . . .) and *prepn. s.* (preparation, see).

Aus den Vorworten zu den vorhergehenden Bänden

In dieser Buchreihe sollen neue Methoden zur Synthese organischer Verbindungen, Verbesserungen bekannter und auch bewährte ältere Methoden, die sich in den in Fachzeitschriften veröffentlichten Originalarbeiten verstreut vorfinden, laufend registriert werden.

Aufbauend auf der Weygandschen Systematik wurde versucht, alle Reaktionen an Hand weniger einfacher, wenn auch rein formaler Richtlinien zu ordnen. Dies führte zur Ausarbeitung von Reaktions-Formelzeichen, die sich im Gegensatz zu den bisherigen Trivial- bzw. Autorennamen, wie Oxydation, Friedel-Crafts-Synthese, systematisch anordnen lassen. Man kann so die Methoden, ohne ihre Namen zu kennen, mittels des Formelzeichens auffinden.

Benutzer, die an die alten Bezeichnungen gewöhnt sind, finden diese im alphabetischen Register, das in vielen Fällen den Gebrauch der Systematik entbehrlich machen und besonders zum Aufsuchen komplizierter Reaktionen mit Vorteil benutzt werden dürfte. Da die Sammlung für die Handbibliothek am Arbeitsplatz im Laboratorium gedacht ist, soll sie eine rasche Orientierung gestatten, ohne daß fürs erste die Literatur der Instituts- oder Werkbibliothek herangezogen werden muß. Neben der systematischen Registrierung der Methoden werden deshalb im alphabetischen Register auch Synthesen durch ihre Ausgangs- und Endprodukte registriert. Dies ermöglicht es, im Text, innerhalb der Reaktionszeichen, nach einem weiteren methodischen Kriterium, nämlich den Hilfsstoffen, einzuteilen. Neuartig ist ferner die Registrierung der komplizierten Verbindungen. Auf Sammelbegriffe wie Synthese, Austausch, Heterocyclen sei noch besonders hingewiesen.

Von Band 5 an ist eine Tabelle aufgenommen worden, die die Reihenfolge der Hilfsstoffe angibt. Sie dürfte zum Aufsuchen von Reaktionen im Text, besonders in großen Kapiteln, nützlich sein. Sie enthält auch häufig gebrauchte Hilfsstoffe wie NaOH und HCl, die im alphabetischen Register nicht aufgeführt sind.

Band 8 und die folgenden Bände enthalten einen kurzen Überblick, «Trends in Synthetic Organic Chemistry», der einige der wichtigsten Fortschritte allgemeinen Interesses aufzeigt und auf neue Arbeiten hinweist, die nicht mehr in den Hauptteil des Bandes aufgenommen werden konnten.

Die Referate beschränken sich auf das zur Beurteilung der Zweckmäßigkeit einer Synthese Notwendige, wie Zahl und Art der Reaktionsstufen, die Ausbeute, wichtige, die Methode betreffende Literatur usw. Vor Ausführung einer bestimmten Synthese ist es deshalb erforderlich, das chemische Zentralblatt oder ein anderes Referatenblatt und, wenn möglich, auch die Originalarbeit zu Rate zu ziehen. Zur Vermeidung von Wiederholungen wurden bei der Anwendung einer Methode in ähnlichen Fällen diejenigen ausgewählt, die am ausführlichsten beschrieben sind und die besten Ausbeuten geben. Fortsetzungen bereits aufgenommener Arbeiten, die nichts wesentlich Neues bringen, werden nicht mehr referiert, evtl. aber an der Stelle der aufgenommenen Arbeit zitiert. Diese Ergänzungszitate (siehe Seite 483) ermöglichen es, Referate aus früheren Bänden auf den neuesten Stand zu bringen.

Um ferner das Material nicht zu sehr auf Kosten der Übersichtlichkeit anschwellen zu lassen, werden Veröffentlichungen, die nicht ganz in den Rahmen der «Synth. Meth.» passen und die in den Sachregistern der Referatenblätter leicht aufgefunden werden können, nicht aufgenommen. Arbeiten aus schwerer zugänglichen und lesbaren Zeitschriften, wie z. B. den russischen und japanischen, werden im allgemeinen nur dann referiert, wenn die betreffende Methode sonst nirgends beschrieben ist. Da die Zahl der Veröffentlichungen auf dem Gebiete der organischen Chemie von Jahr zu Jahr zunimmt, unterbleibt die Aufnahme von Arbeiten manchmal auch unabsichtlich. Wir wären deshalb dankbar, wenn wir auf wichtige Methoden aufmerksam gemacht würden, die in unserer Sammlung noch nicht enthalten sind.

Synthesen, die in ihre Stufen zerlegt und an verschiedenen Stellen eingeordnet sind, können mit Hilfe der Vermerke *startg. m. f.* (Ausgangsmaterial für die Darstellung von . . .) und *prepn. s.* (Darstellung siehe) zusammengesetzt werden.

Method of Classification

The following directions serve to explain the system of Classification.

1. Reaction Symbols.

The first part of the symbol refers to the chemical bonds formed during the reaction. These bonds appear in the reaction symbols as the symbols for the two elements that have been linked together (e.g., the bond between hydrogen and nitrogen, as HN). The order of the elements is as follows: H, O, N, Hal (Halogen), S, and the remaining elements (Rem). C is always placed last.

The "principle of the latest position" determines the order of the element symbols, and is used whenever possible.

The methods of obtaining a particular chemical bond are subdivided according to types of formation. Four types are distinguished: addition (⇓), rearrangement (↶), exchange (⇅), and elimination (⇑). The last part of the symbol refers to the bonds which are destroyed in the reaction or to a characteristic element of that part of the molecule which is eliminated.

The following simplifying stipulations facilitate the use of the reaction symbols: *(1)* The chemical bond is rigidly classified according to the structure formula without taking the reaction mechanism into consideration. *(2)* Double or triple bonds are treated as being equivalent to two or three single bonds, respectively. *(3)* Generally speaking, only stable organic compounds are taken into consideration. Intermediary compounds, such as Grignard compounds and sodiomalonic esters, and inorganic reactants, such as nitric acid, are therefore not expressed in the reaction symbols.

Examples:

see Volume II, page viii

Systematic Survey

see page 471

2. Reagents.

A further subdivision, not included in the reaction symbols, is made on the basis of the reagents characteristic of the reaction. The order usually follows that of the periodic system. Reagents made up of several components are arranged according to the element significant for the reaction (e.g., $KMnO_4$ under Mn, NaClO under Cl). When a constituent of the reagent goes into the products of the reaction, the remainder of the reagent, which acts as a carrier of this constituent, is the criterion for the classification; for example, phosphorus is the carrier in a chlorination with PCl_5 and sodium in a nitrosation with $NaNO_2$. A table indicating the sequence of the reagents may be found on page 476.

3. The material between the listings of the reagents is arranged with the simple examples first and the more complicated ones following.

4. When changes in more than one chemical bond occur during a reaction, as, for example, in the formation of a new ring, or if the reaction can be carried out in different ways, these reactions are introduced in several places when necessary. The main entry in such cases is placed usually according to the "principle of the latest position"; the other entries are cross-referenced back to it.

Systematik

Für die Reihenfolge der Methoden gelten folgende Richtlinien:

1. Reaktionszeichen.

Die Einteilung erfolgt zuerst nach den Bindungen, die bei einer Reaktion entstehen. Diese erscheinen im Reaktions-Formelzeichen in Gestalt ihrer beiden Elementsymbole, z. B. die Bindung zwischen Wasserstoff und Stickstoff als HN. Die Reihenfolge der Elemente ist wie folgt: H, O, N, Hal (Halogen), S, Rem (Übrige Elemente). C steht an letzter Stelle.

Das «*Prinzip der letzten Stelle*» bestimmt die Reihenfolge der Elementsymbole und ist auch sonst nach Möglichkeit immer angewandt worden.

Die Methoden zur Herstellung einer bestimmten Bindung werden nach ihrer Bildungsweise eingeteilt. Es werden 4 Fälle unterschieden: Aufnahme (⇓), Umlagerung (↶), Austausch (⇵) und Abgabe (⇑).

Der letzte Teil des Reaktionszeichens gibt die Bindung an, die

gelöst wird, oder ein charakteristisches Element desjenigen Molekülteils, der abgespalten wird.

Die Bildung des Reaktionszeichens wird durch folgende vereinfachende Annahmen erleichtert:

1. Die Bindungen für die Registrierung ergeben sich rein formal aus den Strukturformeln, ohne daß auf Reaktionsmechanismen Rücksicht genommen wird.

2. Doppel- und Dreifachbindungen werden 2 bzw. 3 Einfachbindungen gleichgesetzt.

3. Es werden in der Regel nur stabile organische Verbindungen berücksichtigt. Zwischenprodukte, wie z. B. Grignard-Verbindungen, Na-Malonester und anorganische Reaktionspartner, wie z. B. Salpetersäure, werden deshalb nicht zur Bildung des Reaktionszeichens herangezogen.

Beispiele

siehe Band 2, Seite VI.

Systematische Uebersicht

siehe Seite 471.

2. Hilfsstoffe.

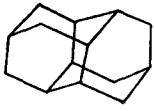
Eine weitere Unterteilung, die im Reaktionszeichen nicht mehr zum Ausdruck kommt, wird nach den für die Reaktion charakteristischen Hilfsstoffen vorgenommen. Ihre Reihenfolge richtet sich im wesentlichen nach dem periodischen System. Hilfsstoffe, die sich aus mehreren Bestandteilen zusammensetzen, werden nach demjenigen eingeteilt, der für die Reaktion verantwortlich ist, z. B. steht $KMnO_4$ bei Mn, NaClO bei Cl. Geht ein Bestandteil des Hilfsstoffs in das Reaktionsprodukt ein, dann ist der Rest als Träger dieses Bestandteils für die Einordnung maßgebend; das ist z. B. bei einer Chlorierung mit PCl_5 Phosphor, bei einer Nitrosierung mit $NaNO_2$ Natrium. Eine Tabelle der Reihenfolge der Hilfsstoffe befindet sich auf Seite 476.

3. Innerhalb dieser Unterteilung sind die einzelnen Referate von einfachen zu komplizierten Beispielen fortschreitend angeordnet.

4. Treten bei einer Reaktion Veränderungen an mehreren Bindungen ein, wie z. B. bei Ringschlüssen, oder kann sie auf verschiedene Art durchgeführt werden, dann wird sie, falls notwendig, an mehreren Stellen eingeordnet. Das Hauptzitat steht in diesen Fällen in der Regel an der letzten Stelle; an den übrigen Stellen befinden sich Hinweise auf dieses.

Trends

in Synthetic Organic Chemistry 1965



The emblem of the 19th International Congress of Pure and Applied Chemistry, London 1963, representing a highly symmetrical molecule with diamond structure, called congressane, has been ingeniously synthezised [1]. At the speed of modern chemical synthesis, a future emblem, no matter how involved in appearance, may well be ready in crystalline form to herald the opening of the new congress.

Starting with the introduction of the Wittig synthesis, phosphorus compounds have gained a prominent place in synthetic organic chemistry. Hydrogen atoms in α-position of phosphonium salts can be easily replaced by deuterium and the resulting phosphonium salts may serve as starting materials for a variety of selectively d-labeled compounds [2]. A remarkably smooth formation of an oxirane ring from dialdehydes has been achieved with trisdimethylaminophosphine [3]. Imino groups can replace oxygen and sulfur under mild conditions by means of phosphoramidate anions [4].

N- and S-Debenzylation with sodium in liq. ammonia is well known. Surprisingly, O-debenzylation by the same reagent has been reported only recently as a convenient and advantageous method, particularly in nucleoside chemistry [5].

Hindered and masked carbonyl groups can be successfully reduced by the Wolff-Kishner-Huang Minlon method if a strong acid is initially added to aid in the formation of the hydrazone [6].

[1] C. Cupas, P. von R. Schleyer, and D. J. Trecker, Am. Soc. *87*, 917 (1965).
[2] M. Schlosser, B. *97*, 3219 (1964).
[3] M. S. Newman and S. Blum, Am. Soc. *86*, 5598 (1964).
[4] Synth. Meth. *17*, 426; J. Org. Chem. *29*, 2816 (1964).
[5] E. J. Reist, V. J. Bartuska, and L. Goodman, J. Org. Chem. *29*, 3725 (1964).
[6] Synth. Meth. *19*, 84.

Hydrogenolysis of hydroxyl groups during reduction with lithium in liq. ammonia can be prevented by pretreatment with lithium hydride [7]. Iodine can be replaced by hydrogen with copper and ascorbic acid as reducing agent without affecting the easily reducible nitro group [8].

The introduction of a functional group at the γ-position of an α-amino acid can be achieved by a scheme which requires a preliminary protonation and subsequent treatment by a free-radical type agent capable of overcoming the inertness of the hydrocarbon chain. The protonation serves to protect the functional groups already present, as well as that part of the hydrocarbon chain to which they are attached [9].

Amines can be obtained under mild conditions from amides by reduction with borane [10], and also from ethylene derivatives with borane and hydroxylamine-O-sulfonic acid or chloramine [11]. A modified Schmidt reaction gives good yields of N-subst. trifluoroacetamides [12].

High yields of aldehydes and ketones from alcohols under mild conditions can be obtained with lead tetraacetate in pyridine [13]. Also with lead tetraacetate, in the presence of boron fluoride, 21-acetoxylation of certain steroids can be achieved efficiently at room temp. [14]. π-Allylpalladium chloride complexes have found interesting synthetic applications [15].

Non-enolizable ketones can be easily cleaved with potassium tert-butoxide in dimethyl sulfoxide [16], one of the newer powerful basic systems involving the widely applicable and versatile dimethyl sulfoxide, which has also been used for novel oxidative solvolysis reactions, e.g. the preparation of α-hydroxyamides from ketenimines [17].

Carboxylic acids can be converted into p-nitrophenyl esters

[7] E. Grundwell, M. A. Pinnegar, and W. Templeton, J. Med. Chem. *8*, 41 (1964).
[8] S. Safe and R. Y. Moir, Can. J. Chem. *43*, 337 (1965).
[9] Synth. Meth. *19*, 612.
[10] H. C. Brown and P. Heim, Am. Soc. *86*, 3566 (1964); s. a. Z. B. Papanastassiou and R. J. Bruni, J. Org. Chem. *29*, 2870 (1964).
[11] H. C. Brown et al., Am. Soc. *86*, 3565 (1964).
[12] K. G. Rutherford, S. Yuen-Shun Ing, and R. J. Thibert, Can. J. Chem. *43*, 541 (1965).
[13] R. E. Partch, Tetrah. Let. *1964*, 3071.
[14] J. D. Cocker, H. B. Henbest et al., Soc. *1965*, 6.
[15] R. Hüttel and H. Christ, B. *97*, 1439 (1964); W. T. Dent, R. Long et al., Soc. *1964*, 1585, 1588.
[16] P. G. Gassman and F. V. Zalar, Tetrah. Let. *1964*, 3031.
[17] Synth. Meth. *19*, 198.

under mild conditions with p-nitrophenyl trifluoroacetate. This method prevents side reactions such as racemization of α-amino acids [18]. Trifluoroacetic anhydride is used for a simple esterification of hindered acids [19]. Certain esters, e.g. phenacyl esters, employed as protective groups in sensitive molecules, can be cleaved at room temp. by sodium thiophenoxide in dimethylformamide [20].

Alkali amide in liq. ammonia has been used for an efficient N-alkylation of hydrazones [21]. The hydrazide group, well-known for its role in coupling peptide moieties through azides, has also been recommended for the protection of the carboxyl group in peptides, because it can be removed selectively with N-bromosuccinimide or iodine [22]. A comparable removal of protective phenylhydrazide groups has been reported previously [23]. Sulfenyl groups, such as o-nitrophenylsulfenyl, have been used for the protection of N-terminals of peptides. These groups can be removed under very mild conditions with two equivalents of hydrogen chloride [24]. Removal of the nitro part from nitroarginyl groups of peptides by electrolytic reduction has been reported. This method has been successful with sulfur-containing peptides where catalytic hydrogenation has failed [25].

To several known methods for the conversion of aldehydes into nitriles two convenient new ones have been added [26]. Cyanic acid esters, believed to be inaccessible, have been prepared in more than one way and excellent yields [27]. Their reactions have now been investigated extensively [28]. Simple methods for the preparation of diazo compounds by pyrolysis of salts of tosylhydrazones have been found. The tosylhydrazones as well as the diazo

[18] S. Sakakibara and N. Inukai, Bull. Chem. Soc. Japan *37*, 1231 (1964).
[19] R. C. Parish and L. M. Stock, J. Org. Chem. *30*, 927 (1965).
[20] Synth. Meth. *19*, 6.
[21] W. G. Kenyon and C. R. Hauser, J. Org. Chem. *30*, 292 (1965).
[22] H. T. Cheung and E. R. Blout, J. Org. Chem. *30*, 315 (1965).
[23] Synth. Meth. *18*, 255.
[24] Synth. Meth. *19*, 22; s. a. Am. Soc. *87*, 99 (1965); I. Photaki and V. du Vigneaud, Am. Soc. *87*, 908.
[25] K. B. Walshaw and G. T. Young, Soc. *1965*, 782, 786.
[26] H. G. O. Becker and H. J. Timpe, Z. Chem. *4*, 304 (1964); T. van Es, Soc. *1965*, 1564.
[27] K. A. Jensen, A. Holm, and B. Thorkilsen, Acta Chem. Scand. *18*, 825, 826, 2417 (1964); E. Grigat and R. Pütter, B. *97*, 3012 (1964); D. Martin, Tetrah. Let. *1964*, 2829; B. *97*, 2689 (1964); J. C. Kauer and W. W. Henderson, Am. Soc. *86*, 4732 (1964).
[28] E. Grigat and R. Pütter, B. *97*, 3018 ff. (1964); D. Martin et al., Ang. Ch. *77*, 96 (1965).

compounds may be prepared in situ, the latter subsequently being converted in good yield into carbenes and their transformation products [29].

N-Haloimides in the presence of sulfuric acid have been recommended for aromatic monohalogenation under ionic conditions [30]. High yields of alkyl halides can be obtained from alcohols or ethers with halogen and $LiBH_4$ or $NaBH_4$ [31].

Direct thiation with elementary sulfur has been reported. Imidazole rings can be thiated in good yield by this method [32]. Sulfides can be conveniently obtained from thiolic esters by reduction with $LiAlH_4$ and a large excess of BF_3-etherate [33]. A modified Willgerodt-Kindler reaction with enamines at low temp. has been published [34].

Hydrocarbons such as toluene, containing one mole of tetrahydrofuran per atom of magnesium, have been recommended as a safe and economical medium for the preparation of Grignard reagents [35]. Dicarbanion formation combined with C-arylation by iodonium salts is a good method for the preparation of γ-arylated β-diketones [36]. A new synthesis of α,β-dihydroxyketones from aldehydes through 1,3-dioxaphospholanes has been described [37].

Nucleosides can be prepared directly from imines, such as purines, and acylglycosyl halides in nitromethane containing an HCl-acceptor, e.g. mercuric cyanide [38].

An unusually high degree of stereoselectivity can be achieved in the synthesis of muramic acid by the use of benzyl as the aglycone component [39].

Ketimines may be more easily cyclized than the corresponding ketones, which are usually used for such ring closures. An additional reaction step can thus be avoided when the ketimines are intermediates in the preparation of the ketones [40]. Intramolecular cyclization of phenyldiynes to naphthalene derivatives may occur

[29] G. M. Kaufman et al., Am. Soc. *87*, 935 (1965).
[30] F. L. Lambert, W. D. Ellis, and R. J. Parry, J. Org. Chem. *30*, 304 (1965).
[31] G. F. Freeguard and L. H. Long, Chem. & Ind. *1964*, 1582; *1965*, 223.
[32] A. Giner-Sorolla, E. Thom, and A. Bendich, J. Org. Chem. *29*, 3209 (1964).
[33] Synth. Meth. *19*, 77.
[34] R. Mayer and J. Wehl, Ang. Ch. *76*, 861 (1964).
[35] T. Leigh, Chem. & Ind. *1965*, 426.
[36] K. G. Hampton, T. M. Harris, and C. R. Hauser, J. Org. Chem. *29*, 3511 (1964).
[37] F. Ramirez et al., Am. Soc. *87*, 543 (1965).
[38] N. Yamaoka, K. Aso, and K. Matsuda, J. Org. Chem. *30*, 149 (1965).
[39] T. Osawa and R. W. Jeanloz, J. Org. Chem. *30*, 448 (1965).
[40] F. A. Vingiello, Sih-Gwan Quo, and P. Polss, J. Org. Chem. *30*, 267 (1965).

under remarkably mild conditions [41]. Pyrroles can be easily obtained from 3,4-dichloro-1-cyclobutenes [42]. Polyalkylpyridines can be conveniently prepared from α,β-unsatd. carbonyl compounds and enolethers through 3,4-dihydropyrans [43]. A new synthesis of pyrimidine derivatives from an unusual combination of components has been published [44]. Various heterocyclic salts, such as 3,5-diazapyrylium salts, can be prepared in high yield by reaction of halogenocarbonyl compounds activated by Lewis acids with compounds containing multiple bonds, e.g. nitriles [45].

An interesting smooth ring opening of o-diazides to form 1,4-dicyanobutadiene has been discovered [46]. A selective cleavage of the C_1-N-bond of certain isoquinoline derivatives can be effectively performed with ethyl chloroformate. This little known cleavage was discovered approximately 40 years ago and used recently again with success [47]. Photolysis of solutions of 1,2,3-triazolines results in loss of nitrogen and clean formation of aziridines [48].

Thionyl chloride in dimethylformamide, in addition to its use for the replacement of hydroxyl by chlorine [49], has under careful temp. control proved to be a general and convenient dehydrating agent [50]. In place of peroxybenzoic acid, the more practical m-chloro- [51] and p-nitro- [52] peroxybenzoic acids are used increasingly. A powerful but selective oxidant has been found in the combination of hydrogen peroxide with tungsten trioxide in acidic solution. It was used successfully in the oxidation of a disulfide to a thiolsulfonate where previous methods [53] have failed [54]. Hydroxymethoxycyclohexane can be used with advantage as a precursor of anhydrous gaseous formaldehyde [55].

[41] I. Iwai and J. Ide, Chem. Pharm. Bull. *12*, 1094 (1964).
[42] R. Criegee and M. Krieger, B. *98*, 387 (1965).
[43] Y. I. Chumakov, V. P. Sherstyuk, and S. A. Vereschagina, Tetrah. Let. *1965*, 129.
[44] R. R. Schmidt, B. *98*, 346 (1965).
[45] R. R. Schmidt, Ang. Ch. *76*, 437 (1964); B. *98*, 334 (1965).
[46] J. H. Hall, Am. Soc. *87*, 1147 (1965).
[47] Synth. Meth. *19*, 507.
[48] P. Scheiner, J. Org. Chem. *30*, 7 (1965).
[49] Synth. Meth. *19*, 624.
[50] Synth. Meth. *19*, 563.
[51] N. N. Schwartz and J. H. Blumbergs, J. Org. Chem. *29*, 1976 (1964); L. A. Paquette, Am. Soc. *86*, 4383 (1964); J. Meinwald, J. J. Tufariello, and J. J. Hurst, J. Org. Chem. *29*, 2914 (1964).
[52] Synth. Meth. *19*, 179; M.-M. Janot, X. Lusinchi, and R. Goutarel, Bl. *1964*, 1566.
[53] Synth. Meth. *15*, 486.
[54] L. Field and T. F. Parsons, J. Org. Chem. *30*, 657 (1965).
[55] C. Michel and S. Tchelitcheff, Bl. *1964*, 2230.

The following references in Vol. 18 under Trends have been entered in this volume [56].

1/33; 3/938; 4/962; 5/192; 6/200; 7/240; 8/79; 10/751; 12/307; 13/903; 14/4; 15/9; 16/260; 17/237; 18/949; 19/521; 20/229; 21/494; 22/628; 24/159; 28/905; 30/539; 31/775; 32/769; 35/811, 812; 40/817; 43/761; 45/575; 46/442; 48/482; 49/65; 50/66; 51/62; 52/161; 53/979; 55/861.

[56] The first figure refers to the footnote in Trends, Vol. 18, the second figure to the entry number in this volume.

Contents

Inhalt

Formation of H—O Bond

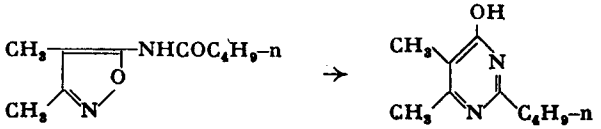
Uptake

Addition to Oxygen and Nitrogen HO⇓ON

Nickel *Ni*

4-Hydroxypyrimidines from 5-acylaminoisoxazoles ←

1.



A soln. of 58.8 g. 3,4-dimethyl-5-valeramidoisoxazole in methanol hydrogenated 24 hrs. with Raney-Ni at 50° and 30 atm. → 40 g. 2-*n*-butyl-4-hydroxy-5,6-dimethylpyrimidine. F. e. s. A. Brossi, Arch. Pharm. *296*, 298 (1963).

Addition to Oxygen and Carbon HO⇓OC

Sodium hydroxide *NaOH*

Cyclonucleoside ring opening C

s. *19*, 168, 206

Zinc/sodium hydroxide *Zn/NaOH*

Quinols from quinones ←

s. *19*, 171

Rearrangement

Oxygen/Carbon Type HO∩OC

Methanol *CH₃OH*

Isomeric dicarboxylic acid monoesters from alkoxyhydroxylactones C

2.