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Synthetic Methods of Organic Chemistry

Synthetische Methoden
der Organischen Chemie

9

Jahrbuch

An Annual Survey

new Trends
Neue Folge in Synthetic Organic Chemistry

Deutscher Register-Schlüssel

BASEL

S. KARGER

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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. Starting with Volume 5, a table indicating 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 subject index. Another innovation is the indexing of complex compounds 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.

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 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 ihren 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. Beginnend mit Band 5 ist eine Tafel 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 so häufig gebrauchte Hilfsstoffe wie NaOH und HCl, die im alphabetischen Register nicht aufgeführt sind. Neuartig ist ferner die Registrierung der komplizierten Verbindungen. Auf Sammelbegriffe wie Aufbau, Austausch, Heterocyclen sei noch besonders hingewiesen.

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 ermöglichen es, Referate aus früheren Bänden auf den neuesten Stand zu bringen.

Um ferner das Material nicht zu sehr auf Kosten der Uebersicht 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.

Preface to Volume 9

Most of the abstracts in this volume are of papers published between 1952 and 1954. As Volume 8 it contains 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 index covers only Volume 9, as the next volume, which concludes the second series, will contain both a cumulative index and arrangement of all titles of Volumes 6 to 10.

I want to thank Dr. John T. Plati once more for having checked the manuscript and Dr. Bernhard Prijs for his thorough proof-reading. I also greatly appreciate the valuable advice they have given me. Thanks are due again to Dr. J. A. Aeschlimann, Vice President of Hoffmann-La Roche, Inc., for liberally providing me with library and office facilities.

Nutley, New Jersey, U.S.A., May 1955.

W. Th.

Vorwort zu Band 9

Der vorliegende Band 9 der «Synthetischen Methoden» bringt hauptsächlich Referate von Arbeiten aus dem Jahren 1952—1954. Auch dieser Band enthält einen kurzen Ueberblick, «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.

Das Register umfaßt diesmal nur einen Band, da der nächste Band, der die zweite Serie abschließt, sowohl ein Generalregister als auch alle Titel der Bände 6—10 enthalten wird.

Nutley, New Jersey, U.S.A., im Mai 1955.

W. Th.

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 the same as in *Chemisches Zentralblatt* and in Beilstein's *Handbuch der organischen Chemie*: 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 methods of formation. Four types are distinguished: addition ($\Downarrow$), rearrangement ($\curvearrowright$), exchange ($\nleftrightarrow$), and elimination ($\Uparrow$). 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 anorganic reactants, such as nitric acid, are therefore not expressed in the reaction symbols.

Examples:

see Volume II, page viii (Interscience Publishers)

Systematic Survey

see page 473

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 477.

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 die gleiche wie im Chemischen Zentralblatt und in Beilsteins Handbuch der organischen Chemie: H, O, N, Hal (Halogen), S, Rem (Uebrigere 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 ($\downarrow$), Umlagerung ($\curvearrowright$), Austausch ($\updownarrow$) und Abgabe ($\uparrow$).

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 473.

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 Tafel der in diesem Band verwendeten Reihenfolge der Hilfsstoffe befindet sich auf Seite 477.

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

1955

For a number of years, new catalytic high pressure and temperature syntheses have been developed by Reppe et al. (cf. *Synth. Meth.* **3**, 588) who used acetylene and carbon monoxide as their principal starting materials. We do not intend to repeat the contents of several comprehensive publications on the subject¹. More processes of this type, however, will eventually find their way into the current literature, and from there into future volumes of *Synthetic Methods*. In this connection, we mention the addition of HCN to unactivated carbon-carbon double bonds², and the preparation of formamides with carbon monoxide³.

Whereas Reppe chemistry is essentially concerned with one-step syntheses of relatively simple compounds, which, in turn, can be used as building blocks for polymers, Woodward et al. have mastered multi-step syntheses of highly intricate compounds. To the synthesis of quinine, patuline, and the total synthesis of the steroid skeleton, they have recently added a 30-step synthesis of the strychnine molecule⁴, which has long engaged the efforts of many investigators. The total synthesis of lysergic acid in 14 steps has been carried out by a group of the Lilly Research Laboratories⁵. The synthesis of morphine by Gates and Tschudi⁶ should also be mentioned at this point. The total steroid synthesis is attracting the attention of several industrial laboratories⁷. An improved oxidation method for obtaining the 17 α -hydroxy-20-keto group of the cortisone side chain⁸ is a result of these experiments. A number of publications deals with ergosterol as a

¹ W. Reppe, *Chemie und Technik der Acetylen-Druck-Reaktionen*, Verlag Chemie, Weinheim, 1951; A. 560, 1 (1948) and following papers; J. W. Copenhaver and M. H. Bigelow, *Acetylene and Carbon Monoxide Chemistry*, Reinhold, New York, 1949.

² P. Arthur, J., et al., *Am. Soc.* **76**, 5364 (1954).

³ H. Winteler, A. Bieler, and A. Guyer, *Helv.* **37**, 2370 (1954).

⁴ R. B. Woodward et al., *Am. Soc.* **76**, 4749 (1954).

⁵ E. C. Kornfeld et al., *Am. Soc.* **76**, 5256 (1954).

⁶ M. Gates and G. Tschudi, *Am. Soc.* **74**, 1109 (1952).

⁷ e. g. *Helv.* **36**, 1803 (1953); *Am. Soc.* **76**, 1715 (1954); *Am. Soc.* **76**, 5011, 5014 (1954).

⁸ G. I. Poos et al., *Am. Soc.* **76**, 5031 (1954); R. Tull et al., *Am. Soc.* **77**, 196 (1955).

starting material for a partial synthesis of hormones involving side chain degradation⁹.

The arsenal of peptide chemistry has been further enriched by a variety of new methods including the use of phosphorus compounds such as the so-called phosphazo compounds (9, 468), phosphite amides (9, 543), and pyrophosphites as intermediates. Pyrophosphites have been used in the total synthesis of polypeptides such as oxytocin (9, 464), the first natural polypeptide to be synthesized. Recently, activated esters have been introduced as promising acylating agents in peptide chemistry¹⁰. An interesting application of the Smith reaction in this field is the conversion of subst. acetoacetic esters to α -amino esters¹¹. N-Trifluoroacetyl derivatives may prove helpful in peptide chemistry because they are readily cleaved in alkaline media without damage being done to the peptide bond¹². Carbodiimides can be employed in both the synthesis¹³ and the degradation (9, 277) of peptides.

Protecting or blocking operations hitherto essentially confined to functional groups have been extended to the carbon skeleton itself by the use of *tert*-butyl as a blocking group. This group, of all alkyls, is exceptionally easy to remove from aromatic rings¹⁴. Preferential blocking of keto groups may be achieved by interchange with dioxolanes where direct ketalization is unsuccessful¹⁵. A mild two-step procedure for preparing phthalimides to protect sensitive *prim.* amines¹⁶ and O-alkylation of phenolic N-bases without quaternization¹⁷ have been described by Baker et al. In this connection, the temporary modification of a molecule as a means of boosting its reactivity may be mentioned such as the attachment of oxygen to amine-nitrogen to form the more reactive N-oxides¹⁸.

Transfer-hydrogenation¹⁹ with palladium as catalyst and cyclohexene as hydrogen donor is often remarkably selective and may give

⁹ see D. A. Shepherd et al., Am. Soc. 77, 1212 (1955).

¹⁰ R. Schwyzer, M. Feurer, and B. Iselin, Helv. 38, 83 (1955).

¹¹ D. O. Holland and J. H. C. Nayler, Soc. 1953, 280.

¹² F. Weygand and M. Reiher, B. 88, 26 (1955).

¹³ J. C. Sheehan and G. P. Hess, Am. Soc. 77, 1067 (1955).

¹⁴ M. J. Schlatter, Am. Soc. 76, 4952 (1954); M. Kulka, Am. Soc. 76, 5469 (1954).

¹⁵ Synth. Meth. 9, 352; F. Sondheimer, M. Velasco, and G. Rosenkranz, Am. Soc. 77, 192 (1955).

¹⁶ B. R. Baker et al., J. Org. Chem. 19, 1786 (1954).

¹⁷ B. R. Baker and F. J. McEvoy, J. Org. Chem. 20, 118, 136 (1955).

¹⁸ Synth. Meth. 6, 389; 8, 260; 9, 243; E. C. Taylor, Jr., and A. J. Croveti. J. Org. Chem. 19, 1633 (1954); R. Adams and S. Miyano, Am. Soc. 76, 3168 (1954).

¹⁹ E. A. Braude, R. P. Linstead et al., Soc. 1954, 3578, 3586, 3595; s. a. Y. Ahmad and D. H. Hey, Soc. 1954, 4516.

higher yields than direct catalytic hydrogenation or other methods of reduction. Phenolic hydroxyl groups may be removed by reducing the corresponding phosphoric esters with sodium or lithium in liquid ammonia²⁰. Reductions with metal hydrides have been performed to advantage in pyridine, which has been used with LiAlH_4 to obtain methylamines from formamides²¹, and with NaBH_4 in the preferential reduction of steroid 3-keto to 3 α -hydroxy groups²². Two new routes from acid derivatives to aldehydes have been found: the reduction of N-methylanilides by LiAlH_4 ²³, which can also lead to the formation of hydroxymethyl compounds, and, recently, the reduction of amidines and imidazolines with sodium and ethanol in liquid ammonia as carried out by Birch²⁴.

Aromatic aldehydes and alkyl aryl ketones can be synthesized by the reaction of diazonium salts with oximes (9, 868). Mannich bases may be converted into the corresponding aldehydes via nitrones (9, 553) or, directly, with hexamethylenetetramine²⁵. N-Bromoacetamide has proved highly selective in the oxidation of certain *sec.* hydroxyl groups, e.g. at the 3 position of steroids²⁶. Another way of achieving this oxidation is by catalytic dehydrogenation with platinum and either oxygen or air²⁷. Bachmann et al. convert *prim.* amines into oxo compounds through N-chloramines and particularly recommend *tert*-butyl hypochlorite for N-chlorination²⁸. Baumgarten and Bower have found a simple preparation of α -aminoketones starting from *sec.* alkylamines and rearranging the corresponding N,N-dichloroamines²⁹. There is also a convenient new procedure for regenerating oxo compounds from their 2,4-dinitrophenylhydrazones³⁰, derivatives used most frequently for purposes of isolation and characterization.

Alkali sensitive and slow reacting α -diazoketones can be converted successfully into acids and esters by irradiation³¹. N-Methyl-N-cyano-

²⁰ G. W. Kenner and N. R. Williams, Soc. 1955, 522.

²¹ B. R. Baker, R. E. Schaub, and J. P. Joseph, J. Org. Chem. 19, 638 (1954).

²² O. Mancera et al., Am. Soc. 75, 1286 (1953); A. J. Lemin and C. Djerassi, Am. Soc. 76, 5672 (1954).

²³ F. Weygand et al., Ang. Ch. 65, 525 (1953); B. 88, 301 (1955).

²⁴ A. J. Birch, J. Cymerman-Craig, and M. Slaytor, Chem. and Ind. 1954, 1559.

²⁵ 9, 290; s. a. M. M. and B. L. Robison, Am. Soc. 77, 457 (1955).

²⁶ R. E. Jones and F. W. Kocher, Am. Soc. 76, 3682 (1954).

²⁷ R. P. A. Sneed and R. B. Turner, Am. Soc. 77, 190 (1955).

²⁸ W. E. Bachmann, M. P. Cava, and A. S. Dreiding, Am. Soc. 76, 5551 (1954).

²⁹ H. E. Baumgarten and F. A. Bower, Am. Soc. 76, 4561 (1954).

³⁰ J. Demaecker and R. H. Martin, Nature 173, 266 (1954); s. a. J. J. Beereboom and C. Djerassi, J. Org. Chem. 19, 1196 (1954).

³¹ Synth. Meth. 8, 919/20; A. Roedig and H. Lunk, B. 87, 971 (1954).

aniline has been recommended for the introduction of cyano groups (9, 865).

Previously inaccessible hydroperoxides may be obtained from mesylates (9, 166).

There are several new methods of achieving N-alkylation: Acylamines may be reduced with LiAlH_4 ²¹ (9, 113) or LiBH_4 ²². Methylamines, in particular, can be obtained by LiAlH_4 -reduction of urethans²³ or isocyanates (8, 95). Gerrard and Jeacocke²⁴ obtain subst. anilines by the pyrolysis of anilinophosphates. Selective N-alkylation, especially of amido groups, can be performed in acetone in the presence of KOH.

Chloral has been recommended for the formylation of strong organic bases (9, 545).

A new and stable reagent for making diazomethane, p-toluene-sulfonylmethylnitrosamide²⁵, is already commercially available.

Continuing their work with phosphites, Rydon et al. have published an even simpler method of obtaining halides from alcohols²⁶. Polyphosphoric acid, this very versatile reagent, makes possible the direct conversion of acids to α -bromoacids²⁷. Diiodoacetylene has been recommended for the preparation of iodides²⁸.

A new synthesis of thiophenols using 2,4-dinitrobenzenesulfonyl chloride for the introduction of SH-groups into aromatic nuclei has been found²⁹. S-Thiocarbonic acid esters proved to be convenient intermediates for the preparation of ureas, acylureas, and semicarbazides (9, 536). Stabilized liquid SO_3 , e.g. the commercially available Sulfan, is a promising reagent for sulfonations and sulfations³⁰.

In the Friedel-Crafts ketone synthesis, elimination of HCl by a stream of air has been suggested³¹. In specific instances, TiCl_4 may be preferable to AlCl_3 ³². The alkylation and acylation of ketones via enamines may be applied to compounds with base sensitive groups (9, 912). Amino acids are recommended as catalysts in the Knoevenagel

²² M. Bory and C. Mentzer, *Bl.* 1953, 814.

²³ *Synth. Meth.* 8, 95; R. L. Dannley, M. Lukin, and J. Shapiro, *J. Org. Chem.* 20, 92 (1955).

²⁴ W. Gerrard and G. J. Jeacocke, *Chem. & Ind.* 1954, 1538.

²⁵ T. J. de Boer and H. J. Backer, *Org. Synth.* 34, 96, 24 (1954); *R.* 73, 229, 589 (1954).

²⁶ D. G. Coe, S. R. Landauer, and H. N. Rydon, *Soc.* 1954, 2281.

²⁷ E. E. Smisson, *Am. Soc.* 76, 5805 (1954).

²⁸ V. Franzen, *B.* 87, 1148 (1954).

²⁹ N. Kharasch and R. Swidler, *J. Org. Chem.* 19, 1704 (1954).

³⁰ E. E. Gilbert et al., *Ind. Eng. Chem.* 45, 2065 (1953).

³¹ F. Smeets and J. Verhulst, *Bl. Soc. chim. Belg.* 61, 694 (1952).

³² *Synth. Meth.* 7, 800; *Soc.* 1954, 2942.

condensation ⁴³. One advantage is that they facilitate the isolation of the product. Intermolecular ring closure can be achieved without using the high dilution technique ordinarily required when polycondensation is inhibited by steric hindrance (9, 513). The use of trichloroacetic esters opens up a new way of synthesizing 3-subst. 2-oxazolidones and related heterocyclics ⁴⁴.

Braude et al. tested 11 quinones as dehydrogenation agents and found dicyanoquinone rather than chloranil to be the most effective ⁴⁵.

Dehydrations have been carried out with carbodiimides (9, 184), already mentioned as reagents in peptide chemistry. Sulfonic acid anhydrides ⁴⁶ and nucleotides ⁴⁷ have thus been made readily available. Methoxyacetylene has also been used for dehydrations (9, 261). Alkoxyacetylenes ⁴⁸, in general, are among the more interesting compounds that recently appeared in the literature. Here are a few others: *tert*-Nitroparaffins ⁴⁹, 2,4,6-tri-*tert*-butylphenoxyl ⁵⁰, a stable oxygen radical, tritium-labeled compounds ⁵¹, non-classical aromatic compounds, the best known of which are the ferrocenes ⁵², and diketene, which has been the subject of a series of papers ⁵³.

Ethylene oxide is a suitable means of removing hydrogen halides ⁵⁴.

Resins have been used successfully as reagents by Billimoria and Maclagan ⁵⁵. In addition to hydrating the carbon-carbon triple bond with a mercury resin, as was done by Newman (9, 102), they hydrolyze α -ketobromides with a basic ion-exchange resin. Dowex-50 has been used to remove sodium from a liquid ammonia solution (9, 42). Nucleotides have been hydrolyzed with Dowex-50-H⁺ ⁵⁶.

Future developments will show whether electric discharge as a means of gently initiating reactions will find wider application. 9, 198 illustrates its use in the preparation of phenol from benzene.

⁴³ F. S. Prout, J. Org. Chem. 18, 928 (1953).

⁴⁴ G. Y. Leshner and A. R. Surrey, Am. Soc. 77, 636 (1955).

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XVI

The following references, contained in Vol. 8 under Trends, have been entered in this volume ⁵⁷:

4/741; 6/454; 7/452; 8/276; 9/686, 707, 718; 10/169; 11/302; 12/202; 13/735, 737; 14/881; 15/24; 16/44; 17/655; 20/63, 65, 87 a, 112; 21/87; 22/86; 24/363; 27/615; 28/846; 33/749; 34/24; 35/520; 36/968; 37/163; 38/574; 39/897; 40/533.

⁵⁷ The first figure refers to the footnote in Trends, Vol. 8, the second figure to the entry number in this volume.

Formation of H—O Bond

Uptake

Addition to Oxygen

Lithium aluminum hydride

Diols from peroxides

s. 9, 6

HO ↓ OO

LiAlH_4

Addition to Oxygen and Carbon

Zinc/acetic acid

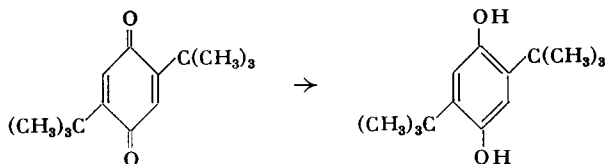
Quinols from quinones

HO ↓ OC

$\text{Zn/CH}_3\text{COOH}$

←

1.



2,5-Di-*t*-butylquinone refluxed with excess Zn-dust and 80% -acetic acid → 2,5-di-*t*-butylhydroquinone. Y: 95%. H. M. Crawford, M. Lumpkin, and M. McDonald, *Am. Soc.* 74, 4087 (1952).

Lithium aluminum hydride

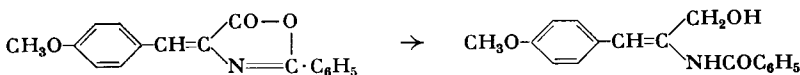
LiAlH_4

2-Acylamino-3-aryl-2-propen-1-ols from azlactones

C

Reductive oxazolone ring opening

2.



2-Phenyl-4-(*p*-methoxybenzylidene)oxazolone allowed to react with LiAlH_4 in tetrahydrofuran at -65 to $-35^\circ \rightarrow$ 2-benzoylamino-3-(*p*-methoxyphenyl)-2-propen-1-ol.—The lower temp. is maintained until the reactants are mixed. Y: 81%. F. e. s. E. Baltazzi and R. Robinson, *Chem. and Ind.* 1953, 541.

Hydrosulfite

$\text{S}_2\text{O}_4^{--}$

Quinols from quinones

←

s. 5, 3; s. a. G. A. Reynolds and J. A. VanAllan, *Org. Synth.* 34, 1 (1954)