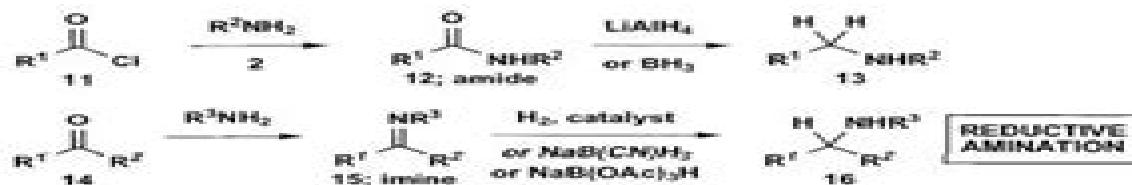
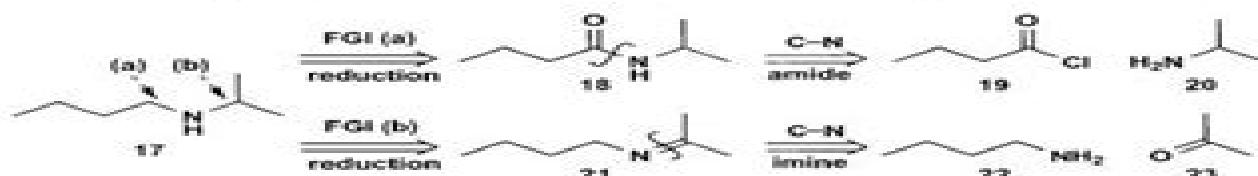


More general solutions come from the replacement of alkylations by reactions with carbonyl compounds. These generally occur once only and in many cases cannot occur twice as the products—amides **12** or imines **15** for example—are much less nucleophilic than the starting amine. The products are reduced to the target amines. The amide route is restricted to amines with a  $\text{CH}_2$  group next to nitrogen **13** but the imine route is very general and is known as reductive amination.<sup>1</sup> It is the most important way to make amines and a recent survey showed that the majority of amines made in the pharmaceutical industry are made this way.



A preliminary PGI is needed before we apply the C–N disconnection. Amine **17** could be made from amide **18** or imine **21** and hence from two different primary amines **20** or **22** and two different carbonyl compounds **19** or **23**. These methods are very versatile.



One published synthesis of this amine **17** is by reductive amination.<sup>2</sup> Note that it is not necessary, nor usually desirable, to isolate the rather unstable imine as reduction with  $\text{NaB}(\text{CN})\text{H}_2$  or  $\text{NaB}(\text{OAc})_3\text{H}$  occurs under the conditions of imine formation.<sup>3</sup> Since the imine is in equilibrium with the starting materials, slightly acidic conditions must be used so that the protonated imine is reduced more rapidly than the aldehyde or ketone. These two reducing agents are stable down to about pH 5.



An example that has been made by the amide route is the cyclic amine **24**. Putting the carbonyl group on the side chain **25** allows us to use readily available piperidine **26** as a starting material. The synthesis<sup>4</sup> uses catalytic reduction to give **24** in 92% yield from the amide **25**.



# Organic Synthesis The Disconnection Approach

**Eliezer Leuschke**

## Organic Synthesis The Disconnection Approach:

**Organic Synthesis** Stuart Warren, Paul Wyatt, 2011-08-24 One approach to organic synthesis is retrosynthetic analysis. With this approach a chemist will start with the structure of their target molecule and progressively cut bonds to create simpler molecules. Reversing this process gives a synthetic route to the target molecule from simpler starting materials. This disconnection approach to synthesis is now a fundamental part of every organic synthesis course. **Organic Synthesis The Disconnection Approach 2nd Edition** introduces this important technique to help students to design their own organic syntheses. There are forty chapters those on the synthesis of given types of molecules alternate with strategy chapters in which the methods just learnt are placed in a wider context. The synthesis chapters cover many ways of making each type of molecule starting with simple aromatic and aliphatic compounds with one functional group and progressing to molecules with many functional groups. The strategy chapters cover questions of selectivity, protection, stereochemistry and develop more advanced thinking via reagents specifically designed for difficult problems. Examples are drawn from pharmaceuticals, agrochemicals, natural products, pheromones, perfumery and flavouring compounds, dyestuffs, monomers and intermediates used in more advanced synthetic work. Reasons for wishing to synthesise each compound are given. This second edition has been fully revised and updated with a modern look. Recent examples and techniques are included and illustrated. Additional material has been added to take the student to the level required by the sequel **Organic Synthesis Strategy and Control**. Several chapters contain extensive new material based on courses that the authors give to chemists in the pharmaceutical industry. **Organic Synthesis The Disconnection Approach 2nd edition** provides a full course in retrosynthetic analysis for chemistry and biochemistry students and a refresher for organic chemists working in industry and academia.

**Organic synthesis : the disconnection approach** Stuart G Warren, 1986     *Organic Synthesis* Stuart Warren, 1982 A workbook providing additional examples, problems and solutions for use with Warren's **Organic Synthesis The Disconnection Approach**. Exercises correspond to chapters in the main text. Problems of special ease or difficulty are labeled for optional use. Workbook includes a formula index of all target molecules contained in the text and workbook.

**Organic Synthesis, Workbook** Stuart G. Warren, Stuart Warren, 1982 A workbook providing additional examples, problems and solutions for use with Warren's **Organic Synthesis The Disconnection Approach**. Exercises correspond to chapters in the main text. Problems of special ease or difficulty are labeled for optional use. Workbook includes a formula index of all target molecules contained in the text and workbook.

**Workbook for Organic Synthesis: The Disconnection Approach** Stuart Warren, Paul Wyatt, 2010-01-11 One approach to organic synthesis is retrosynthetic analysis. With this approach chemists start with the structures of their target molecules and progressively cut bonds to create simpler molecules. Reversing this process gives a synthetic route to the target molecule from simpler starting materials. This disconnection approach to synthesis is now a fundamental part of every organic synthesis course. **Workbook for Organic Synthesis The Disconnection Approach 2nd Edition**

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*Workbook for Organic Synthesis: The Disconnection Approach* 2nd Edition. This workbook provides a full course in retrosynthetic analysis for chemistry and biochemistry students and a refresher course for organic chemists working in industry and academia.

*Organic Synthesis* Stuart Warren, 1982      *Workbook for Organic Synthesis: The Disconnection Approach* Stuart Warren, Paul Wyatt, 2011-08-24

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**Strategic Disconnections in Retrosynthetic Analysis from Pattern Recognition** Claudio Trombini,2025-12-11 Strategic Disconnections in Retrosynthetic Analysis from Pattern Recognition An Applied Approach introduces retrosynthetic analysis through strategic disconnection methods It prioritizes disconnections of general structures characterized by specific functionalization patterns or structural motifs like stereogenic centers or bicyclic frameworks Numerous examples from carefully selected literature illustrate each strategic disconnection organized by functional or structural pattern selected disconnection and polar radical or concerted reaction pathways Developing a deep understanding of these examples enhances 3D visualization skills critical reasoning and expertise in synthetic strategies The book offers insights into advancements in organic synthesis over the last 50 years with cases of varying complexity from curated literature Readers can focus on examples that align with their

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Suggests alternative synthetic strategies     **Fundamentals of Medicinal Chemistry** Gareth Thomas,2004-04-20 Provides a concise introduction to the chemistry of therapeutically active compounds written in a readable and accessible style The title begins by reviewing the structures and nomenclature of the more common classes of naturally occurring compounds found in biological organisms An overview of medicinal chemistry is followed by chapters covering the discovery and design of drugs pharmacokinetics and drug metabolism The book concludes with a chapter on organic synthesis followed by a brief look at drug development from the research stage through to marketing the final product The text assumes little in the way of prior biological knowledge relevant biology is included through biological topics examples and the Appendices

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provides in one text a review of basic techniques and tools of organic chemistry as well as a thorough introduction to the synthesis process The focus of the book is on familiarizing the student with the reactions necessary for synthesis identifying and developing the strategies and methods of doing synthesis as well as developing the mental processes which must be used in planning and executing a synthesis and then doing the synthesis The text includes a unique chapter containing total

synthesis done by students along with instructor commentaries as examples of approaches and potential pitfalls to synthesis

*Organic Synthesis* Tomas Hudlicky, 1993 This fourth volume in the series *Organic Synthesis Theory and Applications* is composed of five chapters that span a wide range of disciplines Alkaloid chemistry total synthesis synthetic methodology carbohydrate technology and spin trapping agents are all covered by experts in these fields The first chapter is one of the finest examples of deductive reasoning in the chemical literature examining the rich history of the chemistry of morphine Within the following chapters synthetic challenges of the marine terpenoids are brought into focus the chemistry and synthetic applications of cyclobutenediones are reviewed and the utility of glycosyl iodides in the preparation of glycosides are summarized Finally a report on a new class of spin trapping agents azulenyl nitrones is covered In all five diverse subdisciplines are brought together and reviewed in this volume

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