# Aldrichimica Acta

Volume 17, Number 1, 1984

"Our Chemist-Collector Approaches Sixty"

chemists helping chemists in research & industry
aldrich chemical co.

# Aldrichimica Acta

Volume 17, Number 1, 1984
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## About Our Cover:

This portrait of Adriaen Brouwer by the Flemish artist Joos van Craesbeeck (1605 - 1662) was the first painting acquired by our chemist-collector, Dr. Alfred Bader, and we know it has remained one of his favorites. Consequently, we considered it appropriate for the cover of this issue which features the article "Our Chemist-Collector Approaches Sixty." Furthermore, nothing could better depict the surprise of our chemist-collector upon seeing this *Aldrichimica Acta*.

As our chemist-collector approaches sixty, all his friends and colleagues wish him many more productive years in chemistry and art.

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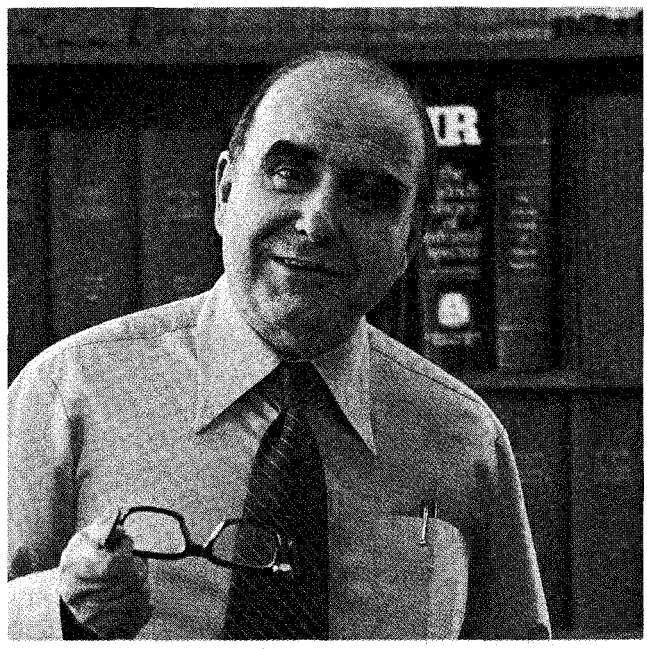
Are you interested in our *Acta* covers? Selections from the Bader Collection, with 30 duotone reproductions, many of previous *Acta* covers, and an introduction by Professor Wolfgang Stechow is available to all chemist art-lovers.

Six beautiful 11 x 14-in., full-color reproductions of paintings on our catalog covers are available, ready for framing, to add beauty to your laboratory.

Many of the early issues of the *Aldrichimica Acta* have become very rare. Please do not throw your issues away. In time, we believe that complete sets will become valuable, and — if you do not want to keep them — there probably are chemists near you who would be interested.

# "OUR CHEMIST-COLLECTOR" APPROACHES SIXTY



*Dr. Alfred Bader*

In 1924, Vienna, so recently the flamboyant capital of the Austrian Hungarian Empire and echoing the strains of the waltzes of Johann Strauss, was hardly recovering from World War I and the effect of the Peace Treaty. The lively, bustling, self-indulgent, high-living Viennese had been forced to change their lifestyle.

This was the world into which our "Chemist-Collector," Chairman of Sigma-Aldrich and Founder of Aldrich, Dr. Alfred Robert Bader, was born. His mother was a Hungarian of noble family. His father, son of the Chief Engineer to Ferdinand de Lesseps, builder of the Suez Canal, had died shortly after his birth, and he was brought up by his dearly loved aunt and uncle. From early childhood on, he was exposed to art in his own home and to the Old Masters at the Kunsthistorisches Museum in Vienna. It should not have been totally surprising, therefore, when at age ten he used money given to him for another purpose to acquire an Old Master drawing at an auction.

By the mid-thirties, Austria was heading towards the Anschluss with Germany. When possible, Jewish youngsters were sent off to presumably friendlier and safer environments. In 1938, saying goodbye to his surrogate parents for the last time, Alfred Bader journeyed to England, a move which may well have saved him from death at the hands of the Nazis.

At fourteen, Alfred found himself at school in Brighton, Southern England, and, despite a strange language and an unfamiliar lifestyle, he was an exceptional student, whose qualities were soon recognized. He received a modest grant (supplemented by the occasional deal in stamps) to study chemistry at the Brighton Technical College. During this period his interest in art continued, and he became immersed in the study of the Bible. This combination of chemistry, art and Bible became his lifelong passion. Even at this early stage, he had begun to shape a future as scientist, businessman and collector.

This relatively settled interval in his life was soon to be disturbed by the German army advancing to the beaches of Northern France, placing England in danger. Fearful of a threatened invasion, Churchill considered that refugees from Europe could be a potential threat to the security of Great Britain. He then made his "Collar The Lot" decision to intern not only potential Nazi-sympathizers but also a great many refugees. Most were interned on the Isle of Man off Britain, but many were shipped overseas. In 1940, Alfred found himself part of a shipload of German Jewish refugees destined for a prisoner-of-war camp on the Richelieu River near Montreal, Canada. However, finding himself interned with able and learned tutors, Alfred put this most difficult period to good use, furthering his learning of the Bible and science.

Being hungry for any kind of news, he, like others in the camp, read through every line of any available newspaper. In doing so, he ran across the obituary of an elderly lady who had been his benefactor in England.

*Editor's Note:* Since our Chemist-Collector would never have permitted us to devote space in the *Aldrichimica Acta* to him, the references to his early days necessarily depended upon recollections of reminiscenses by him to friends and associates and could not be checked for accuracy with the "source." Hence, for any inaccuracies in history, our apologies.

The item listed her son of Montreal among her survivors. Alfred's note of condolence led to a lifelong close association with his second surrogate family, the Wolf family of Montreal. Mr. Wolf helped to arrange for Alfred's parole from the camp in November, 1941, and for his admission to Queen's University in Kingston, Ontario, notwithstanding the absence of standard, formal admission requirements and the fact that the term was well along. His gratitude to Queen's University for this special accommodation is manifested by his service on its Board of Trustees and his contributing to a major collection of Old Masters in its Agnes Etherington Art Centre.

While at Queen's, Alfred overcame the obstacles of English as a second language so well that he entered and won the McColloch speaking contest and the sorely needed prize money associated with it. Thereafter, at the urging of his professors, he became a member of the University's championship debate team. He also served as president of the Hillel House and in other campus leadership positions while earning a B.Sc. degree in Chemical Engineering (1945), a B.A. in History (1946) and a M.S. (1947). During the summer and after graduation, Alfred worked for the Murphy Paint Company of Montreal. Here he generally spent a couple of days visiting customers to discover their needs, then as quickly as possible formulated a suitable paint. Sales soon doubled. Thus Alfred was first shocked to find his job terminated until he realized the company simply wished him to further his education and was prepared to assist with funds.

Alfred attended Harvard which provided him with years of stimulation and excitement. Of course, Alfred began to pursue studies in two distinct disciplines, art history competing with research in chemistry. The contest between the two became concern enough for one chemistry professor to declare anxiously, "Alfred, you haven't made up your mind whether you want to be a chemist or an art historian." Alfred decided perhaps reluctantly for chemistry. As a doctoral research student of the famous Louis Fieser[1], he received great inspiration. Upon receiving his doctorate, Alfred intended to return to his former employer, but in the meantime, the Murphy Paint Company had been sold to Pittsburg Plate Glass, and they placed him in Milwaukee.

There, he was employed as a Research Chemist and later became Organic Group Leader in the paint division. Alfred found it wasteful of research chemists' time and talent to prepare high-purity intermediate compounds necessary to get on with the heart of the research itself. At that time, the only significant U.S. source for such products was a division of Eastman Kodak Company. He suggested to his superior to form a division to augment the list of high-quality intermediates available to research chemists. The proposal was rejected.

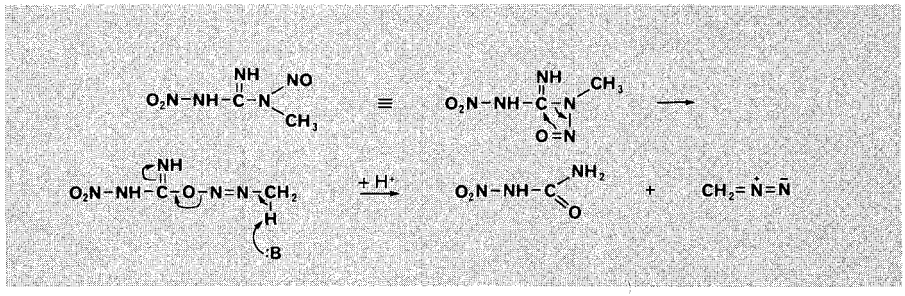
He then requested and received permission to try it on his own during his spare time. In 1951, he rented a $25.00-a-month garage, acquired some basic equipment and made MNNG, 1-methyl-3-nitro-1-nitrosoguanidine which was used as a starting material for diazomethane, and a few other compounds. Not wishing to personalize the company by using his own name he suggested to the attorney preparing the articles of incorporation that they toss a coin between "Daniels" and "Aldrich," the names of his own and the attorney's fiancée. The coin came up "Aldrich."

In 1954, Pittsburgh Glass decided to move its research division to Springdale, Pennsylvania. Although sales from his personal venture were only $15,000 per year, Alfred decided to resign his position and stay in Milwaukee, a city he had come to like. The development of Aldrich now became his full-time occupation.

Alfred began Aldrich with the idea of offering a list of organic chemicals other than those available from Eastman. But, he soon recognized the necessity for developing a complete line of organic chemicals for research. This required the establishment of a network of reliable suppliers to augment Aldrich's then limited production facilities. He also sought close ties with research chemists to enable him to know and even anticipate their needs. Accordingly, he established and developed friendships and working relationships with chemists throughout the world, giving them valuable assistance and promptly responding to their requests and suggestions. Over the years, he has personally helped many able and deserving chemists at universities with research grants underwriting their research, and helping some of them on their way to becoming leading chemists of their time.

While building Aldrich into the world's foremost supplier of high-quality fine organic chemicals, Alfred has been the first to acknowledge his debt to the countless dedicated employees, many of whom are still with the company. But his employees in turn credited him with the vision, drive and readiness to make the pragmatic decisions necessary for such an achievement.

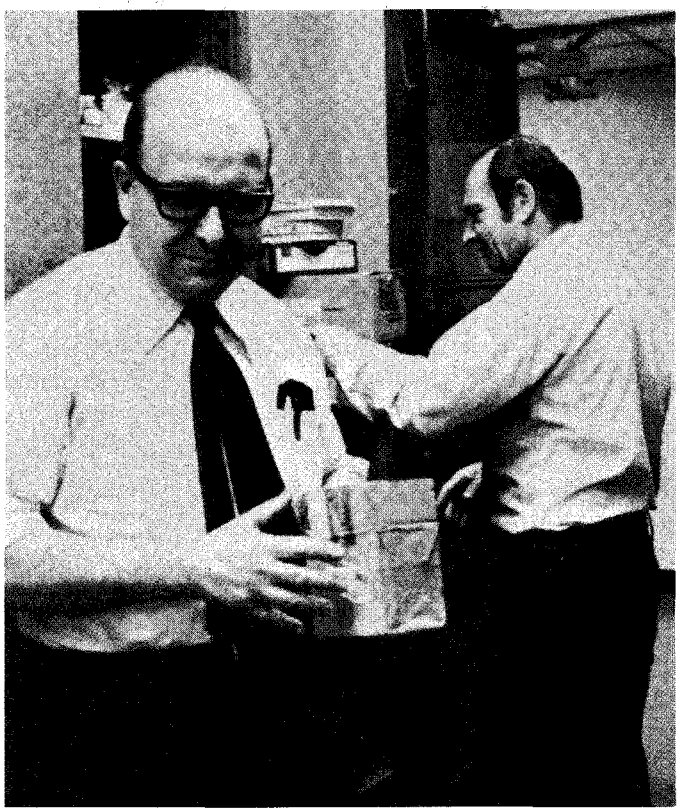
Alfred's enthusiasm and creativity attracted other able chemists who began to cast their lot with Aldrich. Among these was the late John Biel, whose contributions to medicinal chemistry at Lakeside Laboratories, had made him an ideal Director of



*Diazomethane production from MNNG*

Research at Aldrich. This made possible the carrying on of contract work for governmental and pharmaceutical clients with the natural fall-out of both new products and greater insight into the needs of the research chemist.

A catalog evolved which proved to be not only a valuable sales tool but also an indispensable handbook of fine chemicals. This catalog, readily recognized by the Old Master paintings from Alfred's collection reproduced on the front cover with descriptions by "Our Chemist-Collector," soon became Aldrich's hallmark. The 1984-1985 edition will list over 16,000 products.



*Alfred Bader and Professor Gilbert Stork in search of rare chemicals at Columbia University*

In 1967 Alfred launched the *Aldrichimica Acta* to promote Aldrich products and also to disseminate chemical review articles by leading chemists. Today, the *Acta* is perhaps more attentively read than many a scientific journal, and there is no shortage of able prospective authors. With his customary attention to detail, Alfred still zealously guards the quality of the *Acta* which is published quarterly, although for this issue he cannot be held responsible.

Another unique development by Aldrich was the formation of the ABC (Alfred Bader Chemical) Division of Rare Chemicals. This certainly stemmed from Alfred's passion for collecting, in this case, chemicals. But again, he saw the possibilities of acquiring rare and difficult-to-obtain chemicals from universities and laboratories around the world and making them available to others in the research community. Today, over 23,000 such products are offered. The chemicals are featured now in the "Aldrich Microfiche Library of Chemical Indices."

Even in the early days, Alfred revealed that looking for a number of compounds from Aldrich's regular and ABC inventory (over 37,000 chemicals in 1984) containing a particular structural fragment was no easy task. Thus, Aldrich developed a computer-search service capable of locating the required compounds. This unique, free service is now used by scientists worldwide.

Of course, emphasis was placed on supplying quality products. From the infrared spectra taken in the laboratory during routine analyses, there developed "The Aldrich Library of Infrared Spectra" in 1970. Alfred rightly surmised that such a book of quality spectra would be welcomed by the research community. This book, currently in its third edition, and its subsequent companion, "The Aldrich Library of NMR Spectra," have established Aldrich compounds as the standard reference.


*Aldrichimica Acta Preview Issue 1967*

In the leading scientific journals, Aldrich advertisements were soon a regular feature on the back outside cover. The emphasis was generally on promoting new products, often those suggested by Alfred's friends and colleagues at universities.

These varied developments helped establish Aldrich as a major supplier of research chemicals. However, Alfred soon recognized the potential for supplying larger quantities and enlarged Aldrich's production capabilities to become an important source of bulk specialty chemicals. As the business expanded, so did the need for space. After intermediate moves, Aldrich acquired its present St. Paul Avenue headquarters in 1967.

Looking beyond the confines of the United States, Alfred, during the course of his travels to Europe, found a most useful German supplier - later to become known as EGA Chemie. In England, he persuaded an old friend of his war-time sojourn there, to assist with the development of sales and Ralph N. Emanuel, Ltd. was founded. In 1970, both these European companies became totally owned subsidiaries and ultimately bore the Aldrich name. From such beginnings, Aldrich was to become an international company well known on every continent.

In 1972, Aldrich acquired Diaprep, Inc., an Atlanta, Georgia firm and a small supplier of deuterated com-

pounds. Today, Aldrich is one of the world's major suppliers of such stable isotopes. The same year Alfred established Boranes, Inc., an Aldrich subsidiary, to develop entirely new chemical technology based on borane chemistry discovered by Professor H. C. Brown of Purdue University who was later to be recognized with the Nobel Prize in chemistry. Up to that point, Professor Brown had tried in vain to interest larger companies in the technology. In contrast, Alfred, with characteristic vision and decisiveness, promptly recognized and acted on the opportunity. Today, this activity is carried on at a separate plant in Sheboygan, Wisconsin.

In 1975, Aldrich merged with Sigma Chemical Company to form Sigma-Aldrich Corporation, thus combining the world's leading supplier of research biochemicals with what had become the leading supplier of organic and inorganic research chemicals. Alfred Bader, as well as two of Sigma's founders, Aaron Fischer and Dan Broida, envisioned the opportunity for interplay between the technical, service, and marketing strengths of the two companies in a way which would better serve the research community thus making the combined company greater than the sum of its parts.

Sigma Chemical, having started in a small storefront in 1948, had a similar humble beginning. Its first biochemical product was ATP (adenosine triphosphate), a major source of energy in living organisms. The growth of Sigma had been due mainly to the vision, energy and hard work of its president, Dan Broida. Upon the merger, Dan Broida became Chairman and Alfred Bader President. In 1980, Broida stepped aside, and Bader became the Chairman. Unfortunately, Sigma-Aldrich was not to have the continuing support of Broida for long, for he passed away in 1981. However, as Bader has stated, "Broida was a legend in his own lifetime and probably did more than anyone else to advance biochemistry. Sigma will remain a lasting monument to his vision and untiring work."

At the time of the merger, Sigma also had a subsidiary, B-Line, which manufactured and distributed metal components for strut and cable tray systems used in routing electrical and mechanical services in industrial installations and utilities. Emphasizing the same principles of quality product and service, B-Line has prospered over the years as part of the Sigma-Aldrich organization.

Although some relatively small companies were acquired by Sigma-Aldrich over the years — such as, Makor Chemicals, Ltd. in Jerusalem which had the unique ability to produce bacterial and fungal toxins, and Floyd Green's Dyes and Stains Company — the major growth was internal, based on the development of new products and related product lines supplied at competitive prices backed by unsurpassed service.

Today, Sigma and Aldrich products are purchased by universities, research institutions, hospitals and industry in nearly every country in the world. Over one million catalogs are distributed. Apart from the USA, Sigma-Aldrich now has warehousing and production plants in England, Germany and Israel and sales locations in Canada, Belgium, France and Japan.

Alfred, as Chairman of a company that now employs over 1,800 people, must surely reflect that this is a far cry from his garage of 1951.

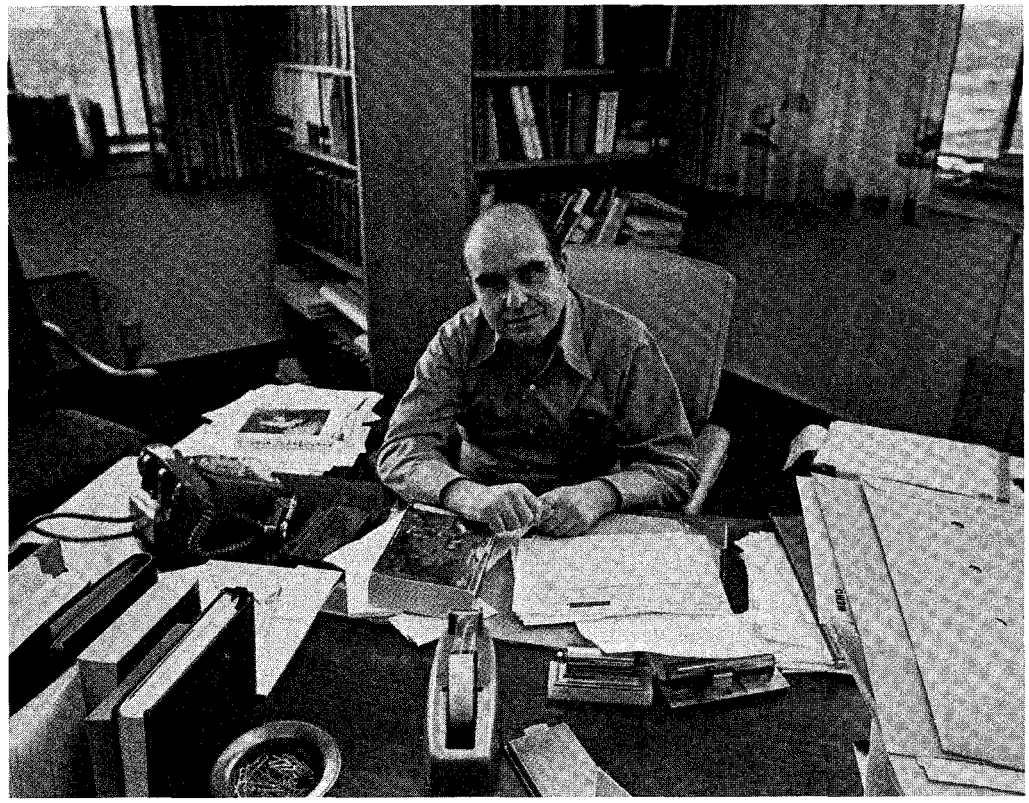
Over the years, Alfred has travelled extensively both in the USA and overseas visiting customers and suppliers. He is known throughout the chemical industry and at many universities. Early on, his main mode of transport was the train, usually at night, while he snatched a few hours sleep to maximize the use of time and minimize expenses. In his customary manner, he soon became an expert on train timetables. As the company grew, Alfred also had the comfort of being driven from place to place by the company's salesmen. Alfred readily adapted to this way of life having the ability to fall asleep quickly, occasionally arousing for a few minutes to comment, "what lovely countryside," without necessarily gazing out of the window. Suitably refreshed between visits to customers and suppliers, Alfred would devote the full day to business. There was hardly any time for eating. A quick sandwich generally sufficed. Even

*Alfred Bader and Dan Broida*

in the evening, little thought was given to culinary delights, for then Alfred either switched his attentions to looking for objects of art or had further business meetings. At the end of such a day, it was not uncommon for Alfred to remark, "put that down to a day's holiday." The Aldrich salesmen, who perhaps had driven hundreds of miles, did not always agree with these well meant comments, but everyone admired his stamina.

During the growth of the company, Alfred continued his intense interest in art — particularly Old Masters — and the Bible. He has assembled an important private collection of 17th-Century Dutch Masters, and found time to teach Bible at a religious school. Being unable to resist fine paintings, Dutch or otherwise, the homes of Alfred's friends and business associates, museums and universities became the beneficiaries of his remarkable eye for those acquisitions which did not fit into his private collection. Apart from Queen's University, institutions benefiting from his Old Master "finds" include The Milwaukee Art Center, the Allen Memorial Art Center, The Minneapolis Institute of Arts, Oberlin College, and the Fogg Art Museum at Harvard.

As a recognized art historian, Alfred was invited to act as guest curator of The Milwaukee Art Center in 1976 and to organize an exhibition "The Bible through Dutch Eyes." He produced a scholarly catalog reflecting his insight and knowledge of painting and the Bible. He is a much sought-after lecturer throughout the USA, Canada and Europe on subjects such as "the Bible as represented by the Dutch Masters" and "the chemistry involved in the restoring of works of art." He was selected as Fellow of the Royal Society of Arts in London in recognition of his achievements as an art collector and historian, and his research in art restorations.

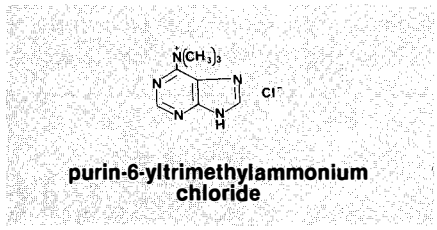


*The chemist-collector at his desk in 1972*

Ten years ago, on the occasion of Alfred's fiftieth birthday, Professor Wolfgang Stechow wrote in the introduction to "Selections from the Bader Collection:" "Lots of art historians could learn a great many things from Alfred Bader; and all art lovers are indebted to his zeal, his perspicacity and his often proven generosity in sharing his treasures with them."

In spite of his enthusiasm for art, chemistry was never neglected. Alfred has authored or co-authored 25 scientific publications covering a wide range of topics in the field of organic chemistry with the emphasis being on practical rather than theoretical chemistry. He also holds 27 patents.

His first scientific publication dealt with the osmium tetroxide oxidation of some long-chain unsaturated fatty acids[2] while the most recent concerned some work on purin-6-yltrimethylammonium chloride.[3] It is interesting to note that Aldrich now offers all the starting materials which Alfred had to prepare for this research.




**purin-6-yltrimethylammonium chloride**

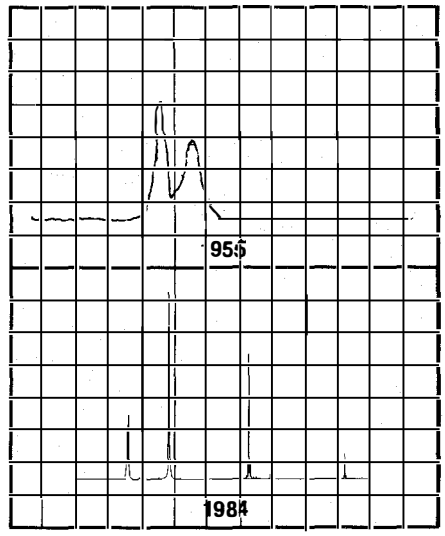
Of course, even Alfred could not completely resist the allure of elucidating structures using new techniques. His 1955 paper on "The Proton Magnetic Resonance Spectrum and Structure of Diketene"[4] confirmed that liquid diketene exists in the 3-buteno-$\beta$-lactone form. The contrast of his spectra with those recently taken on Aldrich's 300MHz (superconducting magnet) NMR equipment dramatically illustrates the strides in technology during the last decades.

While Alfred's practical nature and knowledge of chemistry provided the backbone in building Aldrich, he has also proved to be a most successful businessman. Yet, he is known to his many friends and acquaintances as a person who attaches little importance to the so-called "luxuries of life." Paintings — one of his weaknesses, although he does admit to others — are an exception. He still lives in the

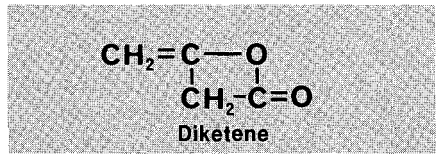
same house, which he himself describes as modest, bought in the early days of Aldrich. He generally drove a car discarded by an Aldrich salesman when it had been driven over 100,000 miles. One of Alfred's own favorite tales concerns the time he drove up to a fund-raising event. The house employee took one look at Alfred and his car and informed him that tradesmen were to use the back entrance.

Kind at heart as many friends can certainly substantiate, Alfred has never suffered fools gladly, and he would be the first to admit that patience is not one of his virtues. Indulging in few hobbies or interests outside of chemistry, the Bible, and art, Alfred's pragmatic, decisive approach and singlemindedness go far toward accounting for his success in the world of both chemistry and art.

Over the years Alfred Bader's contributions to science, industry and art have been recognized in many ways, including an Honorary Doctorate of Science degree from the University of Wisconsin-Milwaukee; the 1983 Engineer-of-the-Year Award given annually to a Milwaukee-area engineer or scientist in recognition of distinguished contributions to the profession and the community; and honorary doctorates from the University of Wisconsin-Madison and Purdue University to be awarded this year.




**Diketene NMR Spectra**




**Diketene**

As Alfred Bader approaches his 60th birthday his coworkers and associates at Sigma-Aldrich wish "Our Chemist-Collector" many more productive and fruitful years of activity as our Chairman and as a renowned art collector and historian.

**References:**

1) Fieser, L.F.; Bader, A.R. *J. Am. Chem. Soc.* **1951**, *73*, 681.
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# The Use of Acronyms in Organic Chemistry

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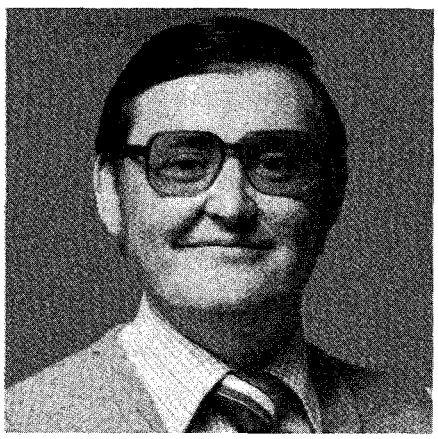

An acronym (Greek, *akros* tip + *onyma* name) is a "word" formed from the first letters or syllables of other words.[1] We constantly encounter acronyms through the news media and even in our daily conversations. Some of the first recalled by one of us (GHD) date back to the Roosevelt (FDR) administration: NRA (**N**ational **R**ecovery **A**ct), CCC (**C**ivilian **C**onservation **C**orps), and WPA (**W**orks **P**rogress **A**dministration). Today most of us are familiar with such acronyms as UN, PLO, and others on the international scene; NAACP, ACLU, LULAC, NOW, and ERA in the national news; and even MTM in the television and entertainment area. Chemists and other scientists understand the meaning of such acronyms as NIH, NSF, PRF and NCI used with reference to important funding agencies which actively support the cost of scientific research. There are hundreds of others and, depending on our income-earning environment or outside interests, we may or may not know the meaning of such acronyms as ACS, CIO, AFL, UAW, or AAA, BMWCCA, USGA, NFL, and NBA. Of course, acronyms relating to chemistry and chemical terms are well known to all chemists, or are they? Each area of chemistry has its own sets of acronyms which are generally understood by those active in that area but may not be familiar to those chemists outside of the particular area. Some acronyms may be well understood by most chemists independent of area: among them are probably NMR, IR, UV, ESR (EPR), CIDNP, FT, FID, HOMO, LUMO, NOE, HPLC, MPLC, LC, PLC, FC, GCMS, SET, VPC, GLC, ICR, ISC, and DNMR.[2] The word LASER which is familiar to the layman is actually an acronym derived from "Light Amplification by the Stimulated Emission of Radiation". Other acronyms recently encountered by the authors are MIRC (Michael-Induced Ring Closure)[3] and $S_NANRORC$ (Nucleophilic Substitution by Addition of Nucleophile, Ring Opening, and Ring Closure).[4]

The use of acronyms in describing reagents, solvents, and selected functional or protecting groups in synthetic chemistry is now widespread in both oral presentations and published work. As early as the nineteenth century chemists have introduced abbreviations for certain common functional groups (Ph, Ac, Me, Et, *etc.*) in the general literature, but it was not until the late 1940's and early 1950's that acronyms started to appear for some common reagents and solvents (DMF, DME, NBS, NBA, *etc.*). Perhaps the most active users of acronyms in the 1950's were those individuals publishing in the biochemical area; however, the use was not general. For example, in one issue of *J. Am. Chem. Soc.* (1958) chosen at random a few acronyms appeared (TETA, TMA, KPP, PMT, $FH_2$ $FH_4$, DNP, TNP, DNPH & TNPH) and all were defined as they appeared either in the text or in a suitable footnote.[5] In recent issues of both *J. Am. Chem. Soc.* and *J. Org. Chem.* (as well as other journals) acronyms abound especially in synthetic papers and in synthetic schemes. In some cases acronyms are defined in the text or in footnotes but in others they are not, especially where the author(s) felt that the acronym was so common that identification was unnecessary.

At the Spring 1982 National Meeting of the American Chemical Society in Las Vegas, the use of acronyms in oral presentations and on slides illustrating synthetic schemes was common, and the unenlightened chemist or student may have had difficulty interpreting some of the chemistry. In some of the talks, new acronyms were introduced (*e.g.*, NPSP for *N*-phenylselenenylphthalimide).

The use of acronyms in the chemical literature may best be illustrated by a specific example appearing in a relatively recent issue of *J. Org. Chem.*[6] in which the reagents used in a synthetic scheme were presented as follows:

(a) "$Ti(OPr)_4$, (-)-DET, TBHP ($CCl_4$), -20°C, 3h.
(b) Red-Al(THF), 22°C, 3h.
(c) i, 0.8% $H_2SO_4$ (MeOH), 22°C, 15h, 86%;
ii, $(C_3H_3N_2)_2C(=S)$ (THF), reflux, 5h;
iii, $(Me_3O)_3P$, 110°C, 10h;
iv, disiamylborane (THF), NaOH, $H_2O_2$, 50%;
v, NaH, $PhCH_2Br$ (DMF), 50°C, 5h, 87%;
vi, Dowex 50W-X8 resin ($H_2O$), 50°C, 2h, 100%;
vii, $NaBH_4$ (EtOH), 22°C, 2h, 100%.
(d) i, TBDMS-Cl, DMAP ($CH_2Cl_2$), 22°C, 5h;
ii, $H_2$, 5% Pd/C (MeOH), 22°C, 8h;
iii, $Ac_2O$, $C_5H_5N$, 60°C, 5h.
(e) i, $Ac_2O$, $C_5H_5N$, 60°C, 5h;
ii, $H_2$, 5% Pd/C (MeOH), 22°C, 12h;
iii, TBDMS-Cl, DMAP ($CH_2Cl_2$), 22°C, 5h.
(f) $Ti(OPr)_4$, (+)-DET, TBHP ($CH_2Cl_2$), -20°C, 18h.
(g) i, $NaIO_4$ ($H_2O$), 22°C;
ii, $NaBH_4$ (EtOH), 27°C, 10h.
(h) i, TBDMS-Cl, DMAP ($CH_2Cl_2$), 22°C, 5h;
ii, $H_2$, 5% Pd/C (MeOH), 22°C, 8h;
iii, $Ac_2O$, $C_5H_5N$, 60°C, 5h.
(i) i, TBDMS-Cl, DMAP ($CH_2Cl_2$) 22°C, 5h;
ii, $H_2$, 5% Pd/C (MeOH), 22°C, 8h;
iii, $NaIO_4$ ($H_2O$), 22°C;
iv, $NaBH_4$ (EtOH), 22°C, 10h;
v, $Ac_2O$, $C_5H_5N$, 60°C, 5h."

Note that the authors used a combination of chemical formulas, standard abbreviations, abbreviated chemical formulas, commercial names, and acronyms in defining the reagents and conditions for each step in the sequence. The reader must be familiar with all of these terms in order to understand the chemistry presented.

It appears that acronyms are here to stay and well they should since they are very convenient to use; however, a current listing would be helpful to those unfamiliar with some of them. Other forms of notation such as the Wiswesser Line Formula Notation (WLN)[7] could be considered as alternatives to acronyms and for some examples the WLN could be conveniently short. Such examples include: tetrahydrofuran - THF *vs.* T5OTJ; dimethylformamide - DMF *vs.* VHN1&1; dimethyl sulfoxide - DMSO *vs.* OS1&1; *N*-bromosuccinimide - NBS *vs.* T5VNVTJ BE; and *tert*-butyl hydroperoxide - TBHP *vs.* QOX1&1&1. WLN was developed as a succinct and precise description of a molecule with its obvious advantages over what is often a lengthy chemical name. Acronyms, however, are usually only a few characters long and they sacrifice accuracy for convenience. WLN's often can become quite lengthy as illustrated in Table I. Thus, overall, the use of WLN in the chemical literature is unlikely to become a substitute for an acronym but it will continue to retain a place in computer systems for the manipulation of chemical structure information.

**Table I**
**Some Common Acronyms and Their WLN's**

| Material | Acronym | WLN |
|---|---|---|
| Dicyclohexylcarbodiimide | DCC | L6TJ ANUCUN- AL6TJ |
| Diisobutylaluminum hydride | DIBAH | 1Y1&1-AL-H1Y1&1 |
| Ethylenediaminetetraacetic acid | EDTA | QV1N1VQ2N1VQ1VQ |
| Guanosine 5'-monophosphate | GMP | T56 BN DN FMYMVJ GUM D- BT5OTJ CQ DQ E1OPQQO |

One disadvantage of the acronym is that a single acronym has been used to represent more than one chemical compound. For example, TEA has been used as an acronym for *trie*thanol*a*mine, *trie*thyl*a*mine, and *trie*thyl*a*luminum. Other acronyms having more than one meaning include AA, BCP, CMC, DAA, DAP, DDS, DEP, DMAP, DMC, DMP, DNS, DSS, EAA, NIP, OCT, PADA, PCT, PMA, TBP, TCP, TES, TFA, THF, TIBA, TLCK, TNS, and TPP. There are also cases in which a single compound has more than one acronym.

Table II lists mainly acronyms but, in addition, some widely used abbreviations and a few commercial names for organic reagents. This table is not meant to be all inclusive; however, it should be helpful to those not very familiar with the common acronyms. Generally, we have not included those associated with the polymer field (PU, PVA, PVC, DMT, PTA, TDI, *etc.*) or the explosive field (TNT, PETN, TNB, TATB, RDX, HMX, HNS, HNAB, *etc.*) but mainly used those associated with reagents which might appear in organic synthetic papers. Sources for the reagents listed in Table II include selected journals, chemical catalogs and selected reference works bearing a list of abbreviations and acronyms in a Glossary or Appendix.[8]


**References:**

1) Thorndike Barnhart Comprehensive Desk Dictionary, Doubleday, 1952, p 40.
2) In order: Nuclear Magnetic Resonance, Infra Red, Ultra Violet, Mass Spectrometry, Electron Spin Resonance (Electron Paramagnetic Resonance), Chemically Induced Dynamic Nuclear Polarization, Fourier Transform, Free Induction Decay, Highest Occupied Molecular Orbital, Nuclear Overhauser Enhancement, High Pressure Liquid Chromatography, Medium Pressure Liquid Chromatography, Liquid Chromatography, Preparative Liquid Chromatography, Flash Chromatography, Gas Chromatography Mass Spectrometry, Single Electron Transfer, Vapor Phase Chromatography, Gas Liquid Chromatography, Ion Cyclotron Resonance, Intersystem Crossing, and Dynamic Nuclear Magnetic Resonance.
3) Little, R.D.; Verhe, R.; Monte, W.T.; Nugent, S.; Dawson, J.R. *J. Org. Chem.* **1982**, *47*, 362.
4) Van der Plas, H.C. *Acc. Chem. Res.* **1978**, *11*, 462.
5) (a) Jarnagan, R.C.; Wang, J.H. *J. Am. Chem. Soc.* **1958**, *80*, 6477.
(b) Strauss, U.P.; Ander, P. *ibid.* **1958**, *80*, 6494.
(c) Popov, A.I.; Bisi, C.C.; Craft, M. *ibid.* **1958**, *80*, 6513.
(d) Peters, J.M.; Greenberg, D.M. *ibid.* **1958**, *80*, 6679.
6) Ma, P.; Martin, V.S.; Masamune, S.; Sharpless, K.B.; Viti, S.M. *J. Org. Chem.* **1982**, *47*, 1378.
7) Wiswesser, W.J. "A Line-Formula Chemical Notation;" Thomas Y. Crowell Co.: New York, 1954. For a recent description, see Smith, E.G.; Baker, P.A. *The Wiswesser Line-Formula Chemical Notation*, 3rd ed., Chemical Information Management Inc.: Cherry Hill, New Jersey.
8) *J. Am. Chem. Soc.* and *J. Org. Chem.*, 1981 and 1982 issues; Aldrich Catalog/Handbook of Fine Chemicals, Catalog 20, Aldrich Chemical Company, Inc., 1980; Buehler, C.A.; Pearson, D.E. "Survey of Organic Synthesis;" Wiley-Interscience: New York, Vol. I, 1970, Vol. II, 1977; Harrison, I.T.; Harrison, S. "Compendium of Organic Synthetic Methods;" Wiley-Interscience: New York, 1971; Wade, L.G.; O'Donnell, M.J. "Annual Report in Organic Synthesis;" Academic Press: New York, 1979 and 1980; Greene, T.W. "Protective Groups in Organic Synthesis;" John Wiley and Sons, Inc.: New York, 1981; Stowell, J.C. "Carbanions in Organic Synthesis;" John Wiley and Sons, Inc.: New York, 1979; Anand, N.; Bindra, J.S.; Ranganahan, S. "Art In Organic Synthesis;" Holden-Day, Inc.: San Francisco, 1970; Bindra, J.S.; Bindra, R. "Creativity in Organic Synthesis;" Academic Press, Inc.: New York, Vol. I, 1975; Fieser, L.F.; Fieser, M. "Reagents for Organic Synthesis;" John Wiley and Sons, Inc.: New York, Vol. 1-7, 1967-1979; Vol. 8 (Fieser, M.) 1980; Vol. 9 (Fieser, M.; Danheiser, R.L.; Roush, W.R.), 1981.

## Table II - Acronyms in Organic Chemistry

| Acronym | Description | Aldrich Cat. No. |
|---|---|---|
| A | adenine | 10,496-5 |
| AA | (see ACAC) | |
| AA | anisylacetone | |
| AAA | acetoacetanilide | A873-2 |
| AAAF | 2-(*N*-acetoxyacetylamino)fluorene | |
| AAMX | acetoacet-*m*-xylidide (*m*-aceto-acetoxylidide) | |
| AAO | acetaldehyde oxime | A100-2 |
| AAOA | acetoacet-*o*-anisidide (*o*-acetoacet-anisidide) | A875-9 |
| AAOC | acetoacet-*o*-chloroanilide (*o*-aceto-acetochloranilide) | |
| AAOT | acetoacet-*o*-toluidide (*o*-acetoaceto-toluidide) | |
| ABA | abscisic acid | 86,216-9 |
| ABL | α-acetyl-γ-butyrolactone | A1,340-9 |
| ABTS | 2,2′-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) | 27,172-1 |
| Ac | acetate | |
| Ac | acetyl | |
| 7-ACA | 7-aminocephalosporanic acid | 19,114-0 |
| ACAC (acac) | acetylacetone | P775-4 |
| ACES | *N*-(2-acetamido)-2-aminoethane-sulfonic acid [*N*-(carbamoylmethyl)-taurine] | 85,759-9 |
| ACTH | adrenocorticotropic hormone | |
| ADA | *N*-(2-acetamido)iminodiacetic acid [*N*-(carbamoylmethyl)iminodiacetic acid] | 85,760-2 |
| 7-ADCA | 7-aminodesacetoxycephalosporanic acid | |
| ADDC | ammonium diethyldithiocarbamate | |
| ADMA | alkyldimethylamine | |
| ADP | adenosine 5′-diphosphate | 14,810-5 |
| AEP | aminoethylpiperazine | A5,520-9 |
| AET | *S*-2-aminoethylisothiouronium bromide hydrobromide | A5,460-1 |
| AIBN | 2,2′-azobisisobutyronitrile | |
| AICA | 5(4)-aminoimidazole-4(5)carboxamide | 16,496-8 |
| AIP | aluminum isopropoxide | 22,041-8<br>22,940-7 |
| Ala | alanine | A2,680-2 |
| Am | amyl | |
| AMBA | 3-amino-4-methoxybenzanilide | |
| AMEO | 3-aminopropyltriethoxysilane | 11,339-5 |
| AMMO | 2-aminopropyltrimethoxysilane | |
| AM-ex-OL | 4-chloro-2-phenylquinazoline | 16,243-4 |
| bis-AMP | *N*-bis(hydroxyethyl)-2-amino-2-methyl-1-propanol | |
| AMP | adenosine 5′-monophosphate | A2,500-8 |
| AMPD | 2-amino-2-methyl-1,3-propanediol | A6,517-4 |
| AMPS | 2-acrylamido-2-methylpropanesulfonic acid | |
| AMTCS | amyltrichlorosilane | 26,233-1 |
| AN | acetonitrile | 15,460-1<br>11,008-6 |
| ANM | *N*-(4-anilino-1-naphthyl)maleimide | |
| ANPP | 4-azido-2-nitrophenyl phosphate | |
| ANS-NH4 | 8-anilinonaphthalene-1-sulfonic acid, ammonium salt | 21,690-9 |
| ANT | (see AN) | |
| APAD | 3-acetylpyridine adenine dinucleotide | |
| APAP | *N*-acetyl-*p*-aminophenol | A730-2 |
| APDC | ammonium 1-pyrrolidinecarbodithioate | 14,269-7 |
| APDTC | ammonium pyrrolidinedithiocarbamate | 14,269-7 |
| APG | *p*-azidophenylglyoxal hydrate | |
| *p*-APMSF | (*p*-amidinophenyl)methylsulfonyl fluoride | |
| APS | adenosine 5′-phosphosulfate | |
| APTP | *N*-(4-azidophenylthio)phthalimide | |
| Ar | aryl | |
| Arg | arginine | A9,240-6 |
| ASC | *p*-acetylaminobenzenesulfonyl chloride | 11,274-7 |
| ATA | anthranilamide | A8,980-4 |
| ATC | ethyltrichlorosilane | |
| ATEE | *N*-acetyl-L-tyrosine ethyl ester monohydrate | A2,290-4 |
| ATP | adenosine 5′-triphosphate | A2,620-9 |
| B | nucleoside base (adenine, cytosine, guanine, thymine, or uracil) | |
| BA | benzyladenine | 85,243-0 |
| BAA | Nα-benzoyl-L-arginineamide hydrochloride monohydrate | |
| 1,3-BAC | 1,3-bis(aminomethyl)cyclohexane | 18,046-7 |
| BACO | 1,4-diazabicyclo[2.2.2]octane | D2,780-2 |
| BAEE | Nα-benzoyl-L-arginine ethyl ester | B1,225-3 |
| BAL | 2,3-dimercapto-1-propanol (British anti-Lewisite) | D12,880-5 |
| BAME | Nα-benzoyl-L-arginine methyl ester | |
| BANA | Nα-benzoyl-DL-arginine-2-naphthyl-amide | |
| BANI | Nα-benzoyl-DL-arginine-4-nitroanilide | 85,711-4 |
| BAO | bis(4-aminophenyl)-1,3,4-oxadiazole | |
| BaP (BAP) | benzo[*a*]pyrene | B1,008-0 |
| BAP | benzylaminopurine | 85,243-0 |
| BAPNA | Nα-benzoyl-DL-arginine-*p*-nitroanilide hydrochloride | 85,711-4 |
| 9-BBN | 9-borabicyclo[3.3.1]nonane | 17,871-3<br>19,385-2<br>15,107-6 |
| BBO | 2,5-bis(4-biphenylyl)oxazole | 21,890-1 |
| BBOD | 2,5-bis(4-biphenylyl)-1,3,4-oxadiazole | |
| BBOT | 2,5-bis(5-*tert*-butyl-2-benzoxazolyl)-thiophene | 22,399-9 |
| BBP | benzyl butyl phthalate | |
| BCA | *N*-benzylcyclopropylamine | |
| BCB | bromocresol blue | |
| BCDC | *N*-benzylcinchonidinium chloride | |
| BCG | bromocresol green | 11,435-9<br>11,436-7 |
| BCNC | (+)-*N*-benzylcinchonidinium chloride | |
| BCNU | 1,3-bis(2-chloroethyl)-1-nitrosourea | |
| BCP | bromocresol purple | 11,437-5<br>86,089-1 |
| BCP | butyl carbitol piperonylate | |
| BCPB | bromochlorophenol blue | 21,298-9 |
| BCPC | *sec*-butyl *N*-(3-chlorophenyl)carbamate | |
| BDCS | (see TBSCl) | |
| *t*-BDEA | *tert*-butyldiethanolamine | |
| BDMA | benzyldimethylamine | 18,558-2<br>13,692-1 |
| BDPA | α,γ-bisdiphenylene-β-phenylallyl, free radical | 15,256-0 |
| BES | *N*,*N*-bis(2-hydroxyethyl)-2-amino-ethanesulfonic acid | 16,372-4 |
| BGE | butyl glycidyl ether | |
| BHA | 3-*tert*-butyl-4-hydroxyanisole | |
| BHC | benzene hexachloride | |
| BHMF | 2,5-bis(hydroxymethyl)furan | 19,461-1 |
| BHMT | bis(hexamethylene)triamine | |
| BHT | 2,6-di-*tert*-butyl-4-methylphenol (butylated hydroxytoluene) | 24,002-8<br>D4,740-4 |
| BICINE | *N*,*N*-bis(2-hydroxyethyl)glycine | 16,379-1 |
| BIS-MSB | *p*-bis(*o*-methylstyryl)benzene | 22,244-5<br>25,740-0 |
| BIS-TRIS | 2,2-bis(hydroxymethyl)-2,2′,2″-nitrilo-triethanol [bis(2-hydroxyethyl)amino-tris(hydroxymethyl)methane] | 15,666-3<br>14,609-9 |
| BLO | γ-butyrolactone | B10,360-8 |
| BMS | borane-methyl sulfide complex | 17,982-5<br>19,211-2<br>19,212-0<br>19,303-8<br>19,482-4 |
| Bn | benzyl (also Bz, BZL, or Bnz) | |
| BN | benzonitrile | B895-9<br>15,463-6 |
| BNAH | 1-benzyl-1,4-dihydronicotinamide | |
| BNB | 2,4,6-tri-*tert*-butylnitrosobenzene | 22,378-6 |
| Bnz | (see Bn) | |
| BOC (or Boc) | *tert*-butoxycarbonyl (or carbo-*tert*-butoxy) | |
| *t*-BOC | (see BOC) | |
| BOC-ON | 2-(*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile | 19,337-2 |
| BOC-OSU | *N*-(*tert*-butoxycarbonyloxy)succinimide | |
| BOC-OTCP | *tert*-butyl 2,4,5-trichlorophenyl carbonate | 15,020-7 |
| BON | β-oxynaphthoic acid | H4,600-7 |
| BOP | benzotriazol-1-yloxytris(dimethylamino)-phosphonium hexafluorophosphate | 22,608-4 |
| BPB | bromophenol blue | 11,439-1<br>11,440-5 |
| BPBG | butyl phthalyl butyl glycolate | |

| Acronym | Description | Aldrich Cat. No. |
|---|---|---|
| BPC | *n*-butylpyridinium chloride | |
| BPCC | 2,2′-bipyridinium chlorochromate | 23,674-8 |
| BPO | 2-(4-biphenylyl)-5-phenyloxazole | 21,698-4 |
| BPPM | (2*S*,4*S*)-*N*-*tert*-butoxycarbonyl-4-diphenylphosphino-2-diphenylphosphinomethylpyrrolidine | |
| BPR | bromophenol red | |
| BSA | *N*,*O*-bis(trimethylsilyl)acetamide | 12,891-0 |
| BSC | *N*,*O*-bis(trimethylsilyl) carbamate | |
| BSH | benzenesulfonyl hydrazide | B380-9 |
| BSOCOES | bis[2-(succinimidooxycarbonyloxy)ethyl] sulfone | |
| BST Chloride | 2-(2′-benzothiazolyl)-5-styryl-3-(4′-phthalhydrazidyl)tetrazolium chloride | |
| BSTFA | *N*,*O*-bis(trimethylsilyl)trifluoroacetamide | 15,519-5 |
| BT | blue tetrazolium | B5,480-0 |
| BTA | benzoyltrifluoroacetone | 21,704-2 |
| BTB | bromothymol blue | 11,441-3<br>11,442-1 |
| BTDA | 3,3′,4,4′-benzophenonetetracarboxylic dianhydride | B975-0<br>26,246-3 |
| BTEAC | benzyltriethylammonium chloride | 14,655-2 |
| BTEE | *N*-benzoyl-L-tyrosine ethyl ester | 85,658-4 |
| BTFA | bis(trifluoroacetamide) | |
| BTMSA | bis(trimethylsilyl)acetylene | 18,743-7 |
| Bu | butyl | |
| nBu | *n*-butyl | |
| iBu | isobutyl | |
| sBu | *sec*-butyl | |
| tBu | *tert*-butyl | |
| Bz | benzoyl | |
| BZL | (see Bn) | |
| CAN | ceric ammonium nitrate | 21,547-3<br>22,954-7 |
| CAP | cellulose acetate phthalate | |
| CAP-$Li_2$ | carbamoyl phosphate, dilithium salt | |
| CAPS | 3-cyclohexylamino-1-propanesulfonic acid | 16,376-7 |
| CAT | 2-chloro-4,6-bis(ethylamino)-*s*-triazine | |
| Cathyl | ethoxycarbonyl (or carbethoxy) | |
| *p*-CBA | *p*-carboxybenzaldehyde | 12,491-5 |
| CBC | carbomethoxybenzenesulfonyl chloride | 24,521-6 |
| CBn (or Cb) | benzyloxycarbonyl (or carbobenzoxy) | |
| CBz (or CBZ) | (see CBn) | |
| CBZ-HONB | *N*-benzyloxycarbonyloxy-5-norbornene-2,3-dicarboximide | 20,891-4 |
| CCH | cyclohexylidenecyclohexane | |
| CCNU | 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea | |
| CD | cyclodextrin | 85,609-6<br>85,608-8<br>86,141-3 |
| CDAA | chlorodiallylacetamide | |
| CDC | cycloheptaarylose-dansyl chloride complex | |
| CDEC | 2-chloroallyl *N*,*N*-diethyldithiocarbamate | |
| CDP | cytidine 5′-diphosphate | |
| CDTA | *trans*-1,2-diaminocyclohexane-*N*,*N*,*N*′,*N*′-tetraacetic acid | 12,581-4 |
| CE | cyanoethyl | |
| CEEA | *N*-(2-cyanoethyl)-*N*-ethylamine | |
| CEEMT | *N*-(2-cyanoethyl)-*N*-ethyl-*m*-toluidine | |
| CEMA | *N*-(2-cyanoethyl)-*N*-methylaniline | |
| CEPEA | *N*-(2-hydroxyethyl)-*N*-(2-cyanoethyl)-aniline | |
| CF | 5(6)-carboxyfluorescein | |
| CHAPS | 3-[(3-cholamidopropyl)dimethylammonio]propanesulfonate | 22,694-7 |
| CHES | 2-(cyclohexylamino)ethanesulfonic acid | 22,403-0 |
| CHP | *N*-cyclohexyl-2-pyrrolidone | |
| CHT | cycloheptatriene | C9,920-5 |
| 5-CIA | 5-chloroisatoic anhydride | C4,810-4 |
| CMA | carbomethoxymaleic anhydride | |
| CMC | carboxymethyl cellulose | |
| CMC | 1-cyclohexyl-3-(2-morpholinoethyl)-carbodiimide | 19,756-4<br>C10,640-2 |
| CMDMCS | (chloromethyl)dimethylchlorosilane | 22,618-1 |
| CMP | cytidine 5′-monophosphate | 85,200-7 |
| CNT | cyanotoluene | 11,977-6<br>13,232-2<br>13,233-0 |
| CoA | coenzyme A | |
| COD | cyclooctadiene | C10,920-7 |
| COT | cyclooctatetraene | 13,892-4 |
| Cp (or cp) | cyclopentadiene | |
| Cp* (or cp*) | pentamethylcyclopentadiene | 21,402-7 |
| 6-CP | 6-chloropurine | 16,117-9 |
| 4-CPA | 4-chlorophenoxyacetic acid | 15,316-8 |
| *m*CPBA | *m*-chloroperoxybenzoic acid | C6,270-0 |
| CPR | chlorophenol red | 19,952-4<br>23,548-2 |
| CPTEO | 3-chloropropyltriethoxysilane | |
| CPTMO | 3-chloropropyltrimethoxysilane | 25,457-6 |
| 12-Crown-4 | 1,4,7,10-tetraoxacyclododecane | 19,490-5 |
| 15-Crown-5 | 1,4,7,10,13-pentaoxacyclopentadecane | 18,883-2 |
| 18-Crown-6 | 1,4,7,10,13,16-hexaoxacyclooctadecane | 18,665-1 |
| CSA | camphorsulfonic acid | C210-7 |
| CSI | chlorosulfonyl isocyanate | 14,266-2 |
| CTA | citraconic anhydride | 12,531-8 |
| CTAB (orCTABr) | cetyltrimethylammonium bromide | 85,582-0 |
| CTACl | cetyltrimethylammonium chloride | |
| CTACN | cetyltrimethylammonium cyanide | |
| CTAOH | cetyltrimethylammonium hydroxide | |
| CTP | cytidine 5′-triphosphate | 85,201-5 |
| CYAP | *O*,*O*-dimethyl *O*-(*p*-cyanophenyl) phosphorothioate | |
| cyclic AMP | adenosine 3′,5′-cyclic monophosphoric acid | 85,120-5 |
| CYP | *p*-cyanophenyl ethyl phenylphosphonothioate | |
| CySH | cysteine | 16,814-9 |
| D | 2,2′-dithiodibenzoic acid | D21,940-1 |
| 2,4-D | 2,4-dichlorophenoxyacetic acid | D7,072-4 |
| DAA | diacetone alcohol | H4,154-4 |
| DAA | diacetone acrylamide | 22,234-8 |
| DAB | *p*-dimethylaminoazobenzene | 11,449-9 |
| DAB | diaminobenzidine (usually 3,3′) | D1,238-4<br>26,189-0 |
| DABCO (or TED) | 1,4-diazabicyclo[2.2.2]octane | D2,780-2 |
| DABITC | 4-(*N*,*N*-dimethylamino)azobenzene-4′-isothiocyanate | |
| DABS-Cl | 4-(*N*,*N*-dimethylamino)azobenzene-4′-sulfonyl chloride | 22,626-2 |
| 3,5-DACB | 3,5-diaminochlorobenzene | |
| DACH | *trans*-1,2-diaminocyclohexane | 13,255-1 |
| DACM-3 | *N*-(7-dimethylamino-4-methyl-3-coumarinyl)maleinimide | |
| DAD | (see DEAD) | |
| DAMN | diaminomaleonitrile | 16,388-0 |
| DAMO | *N*-aminoethylaminopropyltrimethoxysilane (diaminotrimethoxysilane) | 23,577-6 |
| DANSYL | 5-dimethylaminonaphthalene-1-sulfonyl | |
| DAP | diammonium phosphate | 21,599-6 |
| DAP | diallyl phthalate | |
| DAPI | 4′,6-diamidino-2-phenylindole dihydrochloride | 21,708-5 |
| DAS | 4,4′-diaminostilbene-2,2′-disulfonic acid | |
| DAST | diethylaminosulfur trifluoride | 23,525-3 |
| DATMP | diethylaluminum 2,2,6,6-tetramethylpiperidide | |
| 2,4-DB | 2,4-dichlorophenoxybutyric acid | 26,188-2 |
| DBA | dibenz[*a*,*h*]anthracene | D3,140-0 |
| DBC•$Br_2$ | dibenzo-18-crown-6/$Br_2$ | |
| DBCP | 1,2-dibromo-3-chloropropane | |
| DBDPO | decabromodiphenyl oxide | 19,442-5 |
| DBIC | dibutylindolocarbazole | |
| DBMIB | dibromomethylisopropylbenzoquinone | |
| DBN | 1,5-diazabicyclo[4.3.0]non-5-ene | 13,658-1 |
| DBP | dibutyl phthalate | 15,243-9<br>24,047-8 |
| DBPC | 2,6-di-*tert*-butyl-*p*-cresol | D4,740-4<br>24,002-8 |
| DBS | dibutyl sebacate | |
| DBU | 1,8-diazabicyclo[5.4.0]undec-7-ene | 13,900-9 |
| 2,4-DCAD | 2,4-dichlorobenzaldehyde | 14,675-7 |
| DCAF | 2′,4′-bis[di(carboxymethyl)aminomethyl]fluorescein | |
| DCB | dicyanobenzene | 14,585-8<br>24,108-3 |
| 2,4-DCBA | 2,4-dichlorobenzoic acid | 13,957-2 |

| Acronym | Description | Aldrich Cat. No. |
|---|---|---|
| 2,4-DCBC | 2,4-dichlorobenzyl chloride | 13,925-4 |
| 2,4′-DCBP | 2,4′-dichlorobenzophenone | |
| 3,4-DCBTE | 3,4-dichlorobenzotrifluoride | 23,580-6 |
| 2,4-DCBTF | 2,4-dichlorobenzotrifluoride | |
| 3,4-DCBTF | 3,4-dichlorobenzotrifluoride | 23,580-6 |
| DCC | dicyclohexylcarbodiimide | D8,000-2 |
| DCCI | (see DCC) | |
| DCDC | 2,4-dichlorodichlorotoluene | |
| DCEE | dichloroethyl ether | |
| DCHA | dicyclohexylamine | D7,950-0 |
| | | 18,584-1 |
| DCHBH | dicyclohexylborane | |
| DCI-HCl | 1-(3′,4′-dichlorophenyl)-2-isopropyl-aminoethanol hydrochloride | D7,175-5 |
| DCOC | 2,4-dichlorobenzoyl chloride | 11,193-7 |
| DCPD | dicyclopentadiene | 11,279-8 |
| 2,4-DCT | 2,4-dichlorotoluene | 14,500-9 |
| 3,4-DCT | 3,4-dichlorotoluene | 16,136-5 |
| 2,4-DCTC | 2,4-dichlorobenzotrichloride | |
| 3,4-DCTC | 3,4-dichlorobenzotrichloride | |
| DCU | *N,N*-dichlorourethane | 14,209-3 |
| DDA | 4,4′-dichlorodiphenylacetic acid | 10,087-0 |
| DDB | 2,3-dimethoxy-1,4-bis(dimethylamino)-butane | 21,296-2 |
| | | 19,548-0 |
| DDD | 2,2′-dihydroxy-6,6′-dinaphthyl disulfide | |
| *o,p′*-DDD | 1-(*o*-chlorophenyl)-1-(*p*-chlorophenyl)-2,2-dichloroethane | C6,380-4 |
| *p,p′*-DDD | 2,2-bis(*p*-chlorophenyl)-1,1-dichloro-ethane | B3,959-3 |
| | | B3,960-7 |
| *o,p′*-DDE | 1-(*o*-chlorophenyl)-1-(*p*-chlorophenyl)-2,2-dichloroethylene | 14,498-3 |
| *p,p′*-DDE | 2,2-bis(*p*-chlorophenyl)-1,1-dichloro-ethylene | 12,389-7 |
| DDH | 1,3-dibromo-5,5-dimethylhydantoin | 15,790-2 |
| DDM | 4,4′-dichlorodiphenylmethane | |
| DDM | diphenyldiazomethane | |
| DDMU | 4,4′-dichlorodiphenyl-2-chloroethylene | |
| DDOH | 4,4′-dichlorodiphenylethanol | 18,888-3 |
| DDP | dichlorodiammineplatinum | 20,407-2 |
| | | 22,691-2 |
| DDQ | 2,3-dichloro-5,6-dicyano-1,4-benzo-quinone | D6,040-0 |
| DDS | *p,p′*-diaminodiphenyl sulfone | A7,480-7 |
| DDS | dihydroxydiphenyl sulfone | 10,303-9 |
| DDSA | dodecenylsuccinic anhydride | D22,190-2 |
| *o,p′*-DDT | 1-(*o*-chlorophenyl)-1-(*p*-chlorophenyl)-2,2,2-trichloroethane | 10,464-7 |
| *p,p′*-DDT | 1,1-bis(*p*-chlorophenyl)-2,2,2-trichloro-ethane | 10,002-1 |
| DDVP | dimethyl 2,2-dichlorovinyl phosphate | |
| DDZ | $\alpha,\alpha$-dimethyl-3,5-dimethoxybenzyloxy-carbonyl | |
| DEA | *N,N*-diethylaniline | D8,990-5 |
| | | 18,586-8 |
| DEAA | *N,N*-diethylacetoacetamide | |
| DEAC | diethylaluminum chloride | 21,280-6 |
| | | 19,273-2 |
| DEAD | diethyl azodicarboxylate | D9,000-8 |
| DEAE-cellulose | diethylaminoethyl cellulose | |
| DEAH | diethylaluminum hydride | |
| DEAI | diethylaluminum iodide | 19,277-5 |
| DEAP | 2,2-diethoxyacetophenone | 22,710-2 |
| DEASA | *N,N*-diethylaniline-3-sulfonic acid | |
| DEC | diethylaminoethyl chloride hydro-chloride | D8,720-1 |
| DEDM | diethyl diazomalonate | |
| DEII | diethylindoloindole | |
| DEP | diethyl phthalate | D9,962-5 |
| DEP | diethyl pyrocarbonate | 15,922-0 |
| DEPC | diethylphosphoryl cyanide | 24,673-5 |
| DEPHA | di-(2-ethylhexyl)phosphoric acid | 23,782-5 |
| DESS | diethyl succinylsuccinate | 12,612-8 |
| DET | diethyl tartrate (+ or −) | 15,684-1 |
| | | 21,396-9 |
| DFP | diisopropyl fluorophosphate | D12,600-4 |
| DHA | dehydroacetic acid | D290-0 |
| DHA | 9,10-dihydroanthracene | 12,617-9 |
| | | 10,755-7 |
| DHBA | 3,4-dihydroxybenzylamine hydro-bromide | 85,878-1 |
| DHBP | dihydroxybenzophenone (usually 4,4′) | D11,050-7 |
| DHEBA | 1,2-dihydroxyethylene-bis-acrylamide | |
| DHET | dihydroergotoxine | |

| Acronym | Description | Aldrich Cat. No. |
|---|---|---|
| DHN | 5,12-dihydronaphthacene | |
| DHP | diheptyl phthalate | |
| DHP | dihydropyran | D10,620-8 |
| DIAD | diisopropyl diazodicarboxylate | 22,554-1 |
| DIB | 1,3-diphenylisobenzofuran | 10,548-1 |
| DIBAC | diisobutylaluminum chloride | 25,680-3 |
| DIBAH | diisobutylaluminum hydride | 19,030-6 |
| | | 21,496-5 |
| | | 25,683-8 |
| | | 21,494-9 |
| | | 21,497-3 |
| | | 25,684-6 |
| | | 25,688-9 |
| | | 25,687-0 |
| | | 21,500-7 |
| | | 21,498-1 |
| | | 19,272-4 |
| | | 25,686-2 |
| | | 21,495-7 |
| | | 25,681-1 |
| | | 25,685-4 |
| DIBAL | (see DIBAH) | |
| DIBAL-H | (see DIBAH) | |
| DIC | (dimethylamino)isopropyl chloride hydrochloride | D14,240-9 |
| DIDP | diisodecyl phthalate | |
| DI-ET | *N,N*-diethyl-*p*-phenylenediamine monohydrochloride | |
| Diglyme | diethylene glycol dimethyl ether | M1,410-2 |
| DiHPhe | 2,5-dihydroxyphenylalanine | |
| Dimsyl Na | sodium methylsulfinylmethide | |
| DIOP | 2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane | 23,765-5 |
| | | 23,766-3 |
| DIPC | dimethylaminoisopropyl chloride hydrochloride | D14,240-9 |
| Diox | dioxane | D20,186-3 |
| | | 15,482-2 |
| DIPHOS | ethylenebis(diphenylphosphine) | 10,649-6 |
| DIPSO | 3-[*N*-bis(hydroxyethyl)amino]-2-hydroxy-propanesulfonic acid | |
| DIPT | diisopropyl tartrate (+ or −) | 22,918-0 |
| | | 22,780-3 |
| DITC | 1,4-phenylene diisocyanate | 26,224-2 |
| DMA | *N,N*-dimethylaniline | D14,575-0 |
| DMA | dimethylacetamide | 15,480-6 |
| | | 18,588-4 |
| | | D13,751-0 |
| 2,6-DMA | 2,6-dimethylanisole | D14,640-4 |
| DMAA | *N,N*-dimethylacetoacetamide | |
| DMAC | (see DMA, dimethylacetamide) | |
| DMAD | dimethyl acetylenedicarboxylate | D13,840-1 |
| DMA-DEA | *N,N*-dimethylacetamide diethyl acetal | |
| DMAEMA | 2-dimethylaminoethyl methacrylate | 23,490-7 |
| DMAP | dimethylaminopropylamine | D14,500-9 |
| | | 24,005-2 |
| DMAP | 4-dimethylaminopyridine | 10,770-0 |
| DMAPMA | dimethylaminopropyl methacrylamide | |
| DMB | 4,4′-dichloro-$\alpha$-methylbenzhydrol | 19,132-9 |
| DMC | 2-(dimethylamino)ethyl chloride | D14,120-8 |
| DMCS | dimethylchlorosilane | 14,420-7 |
| DMDAAC | dimethyldiallylammonium chloride | |
| DME | 1,2-dimethoxyethane (glyme) | 25,952-7 |
| | | 25,638-2 |
| | | E2,740-8 |
| DMECS | dimethylethylchlorosilane | |
| DMEU | *N,N′*-dimethylethyleneurea | 19,345-3 |
| DMF | dimethylformamide | 15,481-4 |
| | | 22,705-6 |
| | | D15,855-0 |
| DMF-DMA | dimethylformamide dimethyl acetal | 14,073-2 |
| DMI | 1,3-dimethyl-2-imidazolidinone | 19,345-3 |
| DMP | dimethyl phthalate | D17,898-5 |
| | | 24,068-0 |
| DMP | dimethyl pyrocarbonate | |
| DMP | 2,2-dimethoxypropane | D13,680-8 |
| 2,6-DMP | 2,6-dimethylphenol | D17,490-4 |
| | | D17,500-5 |
| DMP-30 | 2,4,6-tris(dimethylaminomethyl)phenol | T5,820-3 |
| DMPA | 2,2-dimethoxy-2-phenylacetophenone | 19,611-8 |
| DMPC | dimethylaminopropyl chloride hydro-chloride | D14,520-3 |
| DMPE | 1,2-bis(dimethylphosphino)ethane | 26,193-9 |
| DMPO | 5,5-dimethyl-1-pyrroline-*N*-oxide | 19,458-1 |

| Acronym | Description | Aldrich Cat. No. |
|---|---|---|
| DMPP | 1,1-dimethyl-4-phenylpiperazinium iodide | D17,750-4 |
| DMPS | 2,3-dimercapto-1-propanesulfonic acid (sodium salt) | 19,452-2 |
| DMPU | *N,N'*-dimethylpropyleneurea | 25,156-9 |
| DMS | 4,6-dimethoxybenzene-1,3-disulfonyl chloride | |
| DMSO | dimethyl sulfoxide | 15,493-8<br>M8,180-2 |
| DMSS | dimethyl succinylsuccinate | 18,527-2 |
| DMT | dimethyl terephthalate | 18,512-4 |
| DMTD | dimercaptothiadiazole | D12,900-3<br>13,943-2 |
| DMTSF | dimethyl(methylthio)sulfonium fluoroborate | |
| DNA | deoxyribonucleic acid | |
| DNAP | 4-(2',4'-dinitrophenylazo)-9-phenanthrol | |
| DNBS | 2,4-dinitrobenzenesulfonic acid | 25,993-4 |
| DNBSC | 2,4-dinitrobenzenesulfenyl chloride | 10,545-7 |
| DNF | 2,4-dinitrofluorobenzene | D19,680-0 |
| DNFA | 2,4-dinitro-5-fluoroaniline (Bergmann's reagent) | D19,670-3 |
| DNFB | (see DNF) | |
| DNP | 2,4-dinitrophenylhydrazine | D19,930-3 |
| DNP | dinonyl phthalate | |
| DNPBA | 3,5-dinitroperoxybenzoic acid | |
| 2,6-DNPC | 2,6-dinitro-*p*-cresol | 22,753-6 |
| Dnp-F | (see DNF) | |
| DNPF | (see DNF) | |
| DNS | 5-dimethylamino-1-naphthalene-sulfonic acid | 19,434-4 |
| DNS | 4,4'-dinitrostilbene-2,2'-disulfonic acid, disodium salt | |
| DNS-BBA | *N*-dansyl-3-aminobenzeneboronic acid | |
| DNSA | 5-dimethylaminonaphthalene-1-sulfonamide | 21,889-8 |
| DNTC | 4-dimethylamino-1-naphthyl isothiocyanate | 22,627-0 |
| DOA | dioctyl adipate | |
| DOCA | deoxycorticosterone acetate | |
| DOP | dioctyl phthalate | D20,115-4 |
| DOPA | 3-(3,4-dihydroxyphenyl)-DL-alanine | 10,216-4 |
| DOPET | 3,4-dihydroxyphenethyl alcohol | |
| DOPS | DL-*threo*-3,4-dihydroxyphenylserine | 14,884-9 |
| 2,4-DP | 2,4-dichlorophenoxypropionic acid | 26,187-4 |
| DPB | 1,4-diphenyl-1,3-butadiene | D20,600-8 |
| DPDM | diphenyl diazomalonate | |
| DPH | 1,6-diphenyl-1,3,5-hexatriene | D20,800-0 |
| DPP-Cl | diphenylphosphinyl chloride | 23,023-5 |
| DPPA | diphenylphosphoryl azide | 17,875-6 |
| DPPC | dipalmitoylphosphatidylcholine | |
| DiPT | diisopropyl tartrate (+ or −) | 22,918-0<br>22,780-3 |
| DPS | *trans-p,p'*-diphenylstilbene | D21,375-6 |
| DSAH | disuccinimidyl (*N,N'*-diacetylhomocysteine) | |
| DSP | dithiobis(succinimidyl propionate) | |
| DSS | 3-(trimethylsilyl)-1-propanesulfonic acid (sodium salt hydrate) | 17,883-7 |
| DSS | disuccinimidyl suberate | |
| DSS | 2,2-dimethyl-2-silapentane-5-sulfonate | 17,883-7 |
| DST | disuccinimidyl tartrate | |
| DTE | dithioerythritol | 16,176-4 |
| DTMC | 4,4'-dichloro-α-(trichloromethyl)-benzhydrol | |
| DTNB | 5,5'-dithiobis(2-nitrobenzoic acid) | D21,820-0 |
| DTPA | diethylenetriaminepentaacetic acid | D9,390-2 |
| DTT | dithiothreitol | 15,046-0 |
| DVB | divinylbenzene | |
| DXE | dixylylethane | |
| EAA | ethyl acetoacetate | E964-1<br>24,070-2 |
| EAA | *N*-ethylanthranilic acid | |
| EADC | ethylaluminum dichloride | 19,275-0<br>25,161-5<br>25,691-9<br>25,692-7<br>25,693-5 |
| EAK | ethyl amyl ketone | 13,691-3 |
| EASC | ethylaluminum sesquichloride | 19,276-7<br>25,694-3<br>25,695-1 |
| EBA | *N*-ethyl-*N*-benzylaniline | |
| EBASA | *N*-ethyl-*N*-benzylaniline-4-sulfonic acid | |
| EBSA | *p*-ethylbenzenesulfonic acid | 24,520-8 |
| ECEA | *N*-ethyl-*N*-chloroethylaniline | |
| EAK | ethyl amyl ketone | 13,691-3 |
| EASC | ethylaluminum sesquichloride | 19,276-7<br>25,694-3<br>25,695-1 |
| EBA | *N*-ethyl-*N*-benzylaniline | |
| EBASA | *N*-ethyl-*N*-benzylaniline-4-sulfonic acid | |
| EBSA | *p*-ethylbenzenesulfonic acid | 24,520-8 |
| ECEA | *N*-ethyl-*N*-chloroethylaniline | |
| EDANS | 2-aminoethylamino-1-naphthalene-sulfonic acid (1,5 or 1,8) | 19,387-9<br>19,388-7 |
| EDB | ethylene dibromide | D4,075-2<br>24,065-6 |
| EDC | ethylene dichloride | D6,156-3<br>15,478-4 |
| EDCI | 1-ethyl-3-[3-(dimethylamino)propyl]-carbodiimide hydrochloride | 16,146-2 |
| EDDP | *O*-ethyl *S,S*-diphenyl dithiophosphate | |
| EDTA | ethylenediaminetetraacetic acid | E2,628-2 |
| EDTN | 1-ethoxy-4-(dichloro-*s*-triazinyl)-naphthalene | 16,319-9 |
| EDTP | ethylenediamine tetrapropanol | 12,226-2 |
| EEDQ | *N*-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline | 14,983-7<br>15,207-2 |
| EGS | ethylene glycol bis(succinimidyl succinate) | |
| EGTA | 1,2-di(2-aminoethoxy)ethane-*N,N,N',N'*-tetraacetic acid | 23,453-2 |
| en | ethylenediamine | E2,626-6 |
| EPN | *O*-ethyl *O*-(*p*-nitrophenyl)thiobenzenephosphate | |
| EPPS | 4-(2-hydroxyethyl)-1-piperazinepropanesulfonic acid | 16,374-0 |
| Et | ethyl | |
| ETA | (see EDTA) | |
| ETSA | ethyl trimethylsilylacetate | 20,912-0 |
| EVK | ethyl vinyl ketone | E5,130-9 |
| FA | furfuryl alcohol | F1,990-6<br>18,593-0 |
| FAD | flavin adenine dinucleotide | |
| FAMSO | methyl methylsulfinylmethyl sulfide | 17,795-4 |
| FDMA | perfluoro-*N,N*-dimethylcyclohexylmethylamine | |
| FDNB | (see DNF) | |
| FDNDEA | 5-fluoro-2,4-dinitro-*N,N*-diethylaniline | |
| FDP | D-fructose-1,6-diphosphate | 85,912-5 |
| FHZ | ferritin hydrazide | |
| FITC | fluorescein isothiocyanate | F250-2 |
| Fl | flavin | |
| FMA | fluoroscein mercuric acetate | |
| FMN | flavin mononucleotide | |
| FNPS | bis(4-fluoro-3-nitrophenyl) sulfone | F1,170-0 |
| FS | Fremy's salt (dipotassium nitrosodisulfonate) | 22,093-0 |
| FTN | perfluoro-1,3,7-trimethylbicyclo[3.3.1]-nonane | |
| FUDR | 5-fluorodeoxyuridine | 85,665-7 |
| G | guanine | G1,195-0 |
| GABA | 4-aminobutyric acid | A4,440-1 |
| GAPDH | glyceraldehyde-3-phosphate dehydrogenase | |
| GDP | guanosine 5'-diphosphate | |
| GLDH | glutamate dehydrogenase | |
| gln | glutamine | G320-2 |
| Glu | glutamic acid | 12,843-0 |
| Gly | glycine | G620-1<br>24,126-1 |
| Glyme (glyme) | 1,2-dimethoxyethane (see DME) | |
| GLYMO | 3-glycidyloxypropyltrimethoxysilane | 23,578-4 |
| GMP | guanosine 5'-monophosphate | 85,285-6 |
| GOD | glucose oxidase | |
| G-6-P | glucose-6-phosphate | |
| GSH | glutathione, reduced | G470-5 |
| GSSG | glutathione, oxidized hydrate | 15,056-8 |
| GTP | guanosine 5'-triphosphate | 85,205-8 |
| HABA | 2-(*p*-hydroxyphenylazo)benzoic acid | 14,803-2 |
| HABBA | 2-(4'-hydroxyazobenzene)benzoic acid | |
| Hb | hemoglobin | |

| Acronym | Description | Aldrich Cat. No. |
|---|---|---|
| HBD | hexabutyldistannoxane | B5,338-3 |
| HDCBS | 2-hydroxy-3,5-dichlorobenzenesulfonic acid | 23,882-1 |
| HDODA | 1,6-hexanediol diacrylate | 24,681-6 |
| HDPE | high-density polyethylene | 18,190-0 |
| HEA | *N*-(2-hydroxyethyl)aziridine | 10,690-9 |
| HEDTA | hydroxyethylethylenediaminetriacetic acid | H2,650-2 |
| HEEI | *N*-(2-hydroxyethyl)ethyleneimine | 10,690-9 |
| HEMA | 2-hydroxyethyl methacrylate | 12,863-5 |
| HEPES | 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid | 16,371-6<br>23,388-9 |
| HEPSO | *N*-hydroxyethylpiperazine-*N*′-2-hydroxypropanesulfinic acid | |
| Hex | hexane (or hexyl) | 13,938-6<br>24,887-8<br>20,875-2 |
| HFA | hexafluoroacetone | 13,923-8 |
| HFBA | heptafluorobutyric acid | 16,419-4 |
| HFIP | hexafluoroisopropyl alcohol | 10,522-8 |
| HFP | hexafluoropropene | |
| HFTA | hexafluorothioacetone | |
| HHPA | hexahydrophthalic anhydride | 12,346-3<br>14,829-6 |
| His | histidine | 15,168-8 |
| HMAT | hexa[1-(2-methyl)aziridinyl]-1,3,5-triphosphatriazine | |
| HMB | 2-hydroxy-4-methoxybenzophenone | H3,620-6 |
| HMB | 2-hydroxy-5-methoxybenzaldehyde | 14,686-2 |
| HMDS | 1,1,1,3,3,3-hexamethyldisilazane | H1,000-2 |
| HMDSO | hexamethyldisiloxane | 20,538-9 |
| HMI | hexamethyleneimine | H1,040-1 |
| HMN | 2,2,4,4,6,8,8-heptamethylnonane | 12,851-1 |
| HMPA | hexamethylphosphoramide (hexamethylphosphoric triamide) | H1,160-2 |
| HMPT | hexamethylphosphorous triamide | 14,355-3 |
| HMPTA | (see HMPA) | |
| HMTT | 3-hexadecanoyl-4-methoxycarbonyl-1,3-thiazolidine-2-thione | |
| HOAc | acetic acid | 10,908-8<br>24,285-3 |
| HOBT | hydroxybenztriazole | 15,726-0 |
| HONB | *N*-hydroxy-5-norbornene-2,3-dicarboxylic acid imide | 22,637-8 |
| HOSA | hydroxylamine-*O*-sulfonic acid | 21,313-6<br>22,797-8 |
| HPPH | 5-hydroxyphenyl-5-phenylhydantoin | 16,154-3 |
| HTMP | 2,2,6,6-tetramethylpiperidine | 11,575-4 |
| HVA | homovanillic acid (4-hydroxy-3-methoxyphenylacetic acid) | 14,364-2 |
| Hylv | α-hydroxyisovaleric acid | 21,983-5 |
| I-AEDANS | *N*-iodoacetyl-*N*′-(X-sulfo-1-naphthyl)-ethylenediamine (X = 5, 1,5-I-AEDANS; X = 8, 1,8-I-AEDANS) | |
| 1,5-I-AEDANS | (see I-AEDANS, X = 5) | 85,861-7 |
| 1,8-I-AEDANS | (see I-AEDANS, X = 8) | 85,985-0 |
| IBD | iodobenzene dichloride | |
| IBMX | 3-isobutyl-1-methylxanthine | 85,845-5 |
| IBTMO | isobutyltrimethoxysilane | |
| ICD | isocitric dehydrogenase | |
| ICI | isophthaloyl chloride | I-1,940-3 |
| IDP | inosine 5′-diphosphate | 85,207-4 |
| IDU | 5-iodo-2′-deoxyuridine | I-775-6 |
| IH | immobilized histamine | |
| IIDQ | 2-isobutoxy-1-isobutoxycarbonyl-1,2-dihydroquinoline | 17,824-1 |
| Ile | isoleucine | 15,171-8 |
| IMEO | imidazolinepropyltriethoxysilane | |
| IMP | inosine 5′-monophosphate | 85,206-6 |
| INAH | isonicotinic acid hydrazide | I-1,753-2 |
| INH | (see INAH) | |
| INT | 2-(*p*-iodophenyl)-3-(*p*-nitrophenyl)-5-phenyltetrazolium chloride | I-1,040-6 |
| IPA | isopropyl alcohol | 10,982-7<br>15,497-0<br>19,076-4 |
| IPC | isopropyl *N*-phenylcarbamate | |
| $IpcBH_2$ | isopinocampheylborane | |
| $Ipc_2BH$ | diisopinocampheylborane | |
| IPDI | isophorone diisocyanate (3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate) | |
| IPN | isophthalonitrile | 14,585-8<br>24,108-3 |

| Acronym | Description | Aldrich Cat. No. |
|---|---|---|
| IPOTMS | isopropenyloxytrimethylsilane | |
| IPTG | isopropyl β-D-thiogalactoside | 85,875-7 |
| ITA | itaconic anhydride | 25,992-6 |
| ITP | inosine 5′-triphosphate | 85,208-2 |
| IZAA | 5-chloroindazol-3-acetic acid ethyl ester | |
| KAPA | potassium 3-aminopropylamide | |
| KBA | 3-ketobutyraldehyde dimethyl acetal | A1,220-8 |
| KBT | 4-ketobenztriazine | |
| KDO | 2-keto-3-dioxyoctonate | |
| K-Selectride® | potassium tri-*sec*-butylborohydride | 22,076-0 |
| KS-Selectride® | potassium trisiamylborohydride | 22,077-9 |
| LAH | lithium aluminum hydride | 19,987-7<br>21,277-6<br>21,279-2<br>21,278-4<br>23,605-5 |
| LAP | leucine aminopeptidase | |
| LDA | lithium diisopropylamide | 24,661-1 |
| LDH | lactic dehydrogenase | |
| LDPE | low-density polyethylene | 18,189-7 |
| Leu | leucine | L60-2 |
| $Lgf_2BH$ | dilongifolylborane | |
| LICA | lithium isopropylcyclohexylamide | |
| LPO | lauroyl peroxide | |
| L-Selectride® | lithium tri-*sec*-butylborohydride | 17,849-7 |
| LS-Selectride® | lithium trisiamylborohydride | 22,592-4 |
| LTA | lead tetraacetate | 18,519-1 |
| LTMAC | dodecyltrimethylammonium chloride | |
| Lys | lysine | 16,971-4 |
| M | metal | |
| MA | maleic anhydride | M18-8 |
| MAA | menthoxyacetic acid | M300-0 |
| MAA | methyl acetoacetate | M2,640-2 |
| MAM-acetate | methylazoxymethyl acetate | 85,787-4 |
| MAPO | tris[1-(2-methyl)aziridinyl]phosphine oxide | |
| Phenyl-MAPO | bis[1-(2-methyl)aziridinyl]phenylphosphine oxide | |
| MAPS | tris[1-(2-methyl)aziridinyl]phosphine sulfide | |
| MAPTAC | methacrylamidopropyltrimethylammonium chloride | |
| MASC | methylaluminum sesquichloride | 22,397-2 |
| MBA | *N*,*N*′-methylenebisacrylamide | 14,832-6<br>14,607-2 |
| MBBA | *N*-(*p*-methoxybenzylidene)-*p*-butylaniline | 15,822-4 |
| MBOCA | methylenebis(*o*-chloroaniline) | |
| MBS | *m*-maleimidobenzoyl-*N*-hydroxysuccinimide ester | |
| MBTH | 3-methyl-2-benzothiazolinone hydrazone | |
| MBTH·HCl | 3-methyl-2-benzothiazolinone hydrazone hydrochloride | 12,973-9 |
| MC | magnesium chlorate | |
| 3-MC | 3-methylcholanthrene | 21,394-2 |
| MCA | monochloroacetic acid | C1,962-7<br>24,060-5 |
| MCAA | (see MCA) | |
| 3,3-MCH | 3-methyl-3-cyclohexen-1-one | |
| MCP | *meta*-cresol purple (*m*-cresol purple) | 85,789-0<br>21,176-1 |
| MCP | methylcyclopentane | M3,940-7 |
| MCPBA | *m*-chloroperoxybenzoic acid | C6,270-0 |
| MCPCA | 2-methyl-4-chlorophenoxyaceto-*o*-chloroanilide | |
| MCPDEA | *N*,*N*-di(2-hydroxyethyl)-*m*-chloroaniline | 25,047-3 |
| MCPP | 4-chloro-3-methylphenoxypropionic acid | |
| MDA | 1,8-*p*-menthanediamine | D1,960-5 |
| MDEB | *N*-methyl-*N*-dodecylephedrinium bromide | 23,540-7 |
| MDH | malic dehydrogenase | |
| Me | methyl | |
| MeCCNU | 1-(2-chloroethyl)-3-(4-*trans*-methylcyclohexyl)-1-nitrosourea | |
| MEI | 2-morpholinoethyl isocyanide | |
| MEK | methyl ethyl ketone | 11,026-4<br>23,029-4 |
| MeLeu | *N*-methylleucine | |
| MEM- | methoxyethoxymethyl- | |
| MEMCl | β-methoxyethoxymethyl chloride | 19,354-2 |
| MEMO | 3-methacryloxypropyltrimethoxysilane | 23,579-2 |

| Acronym | Description | Aldrich Cat. No. |
|---|---|---|
| 1-MEO-PMS | 1-methoxy-5-methylphenazinium methyl sulfate | |
| MEP | *O,O*-dimethyl *O*-(3-methyl-4-nitrophenyl) phosphorothioate | |
| MES•hydrate | 4-morpholineethanesulfonic acid | 16,373-2 |
| Met | methionine | 15,169-6 |
| Meth | 2-mercaptoethanol | M370-1 |
| MG-Ch | methyl glycol chitosan | |
| MHHPA | methylhexahydrophthalic anhydride | 14,993-4 |
| MIA | *N*-methylisatoic anhydride | 12,988-7 |
| MIBK | methyl isobutyl ketone | M6,710-9<br>24,289-6 |
| MIPK | methyl isopropyl ketone | 23,861-9 |
| MIX | 3-isobutyl-1-methylxanthine | 85,845-5 |
| MMA | methyl methacrylate | M5,590-9 |
| MMAA | mono-*N*-methylacetoacetamide | |
| MMC | methyl magnesium carbonate | 24,840-1<br>24,842-8 |
| MMH | methylmercuric hydroxide | |
| MMS | methyl methanesulfonate | 12,992-5 |
| MMTrCl | monomethoxytrityl chloride | 12,920-8 |
| MMTS | (see FAMSO) | |
| MNA | methylnadic anhydride (methyl-norbornene-2,3-dicarboxylic acid anhydride) | 23,543-1 |
| MNNG | *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine | 12,994-1 |
| MNPT | *m*-nitro-*p*-toluidine | M5,980-7 |
| MO | methyl orange | 11,451-0<br>23,410-9 |
| MOM- | methoxymethyl- | |
| MOPS | 4-morpholinepropanesulfonic acid | 16,377-5 |
| MOPSO | 3-(*N*-morpholino)-2-hydroxypropane-sulfonic acid | |
| 6MP | 6-mercaptopurine | 85,267-8 |
| MPEMA | 2-ethyl-2-(*p*-tolyl)malonamide | 19,496-4 |
| MPP | *O,O*-dimethyl *O*-(4-methylmercapto-3-methylphenyl) thiophosphate | |
| MPPH | 5-(*p*-methylphenyl)-5-phenylhydantoin | 16,145-4 |
| MPS | methyl phenyl sulfide | T2,800-2 |
| Mpt-Cl | methylphosphinothionyl chloride | |
| MR | methyl red | 11,450-2 |
| MRITC | methylrhodamine isothiocyanate | |
| MS (or Ms) | mesyl (or methanesulfonyl-) | |
| MSA | methanesulfonic acid | M860-6<br>M861-4 |
| MsCl | methanesulfonyl chloride | M880-0 |
| MSH | 2,4,6-trimethylbenzenesulfonyl hydrazide | 19,220-1 |
| MSMA | monosodium methanearsonate | |
| MSO | *p*-cresyl methyl ether | 14,809-1 |
| MSOC | *N*-(2-methylsulfonyl)ethyloxycarbonyl | |
| MST | mesitylenesulfonyltetrazolide | |
| MSTFA | *N*-methyl-*N*-trimethylsilyltrifluoro-acetamide | 24,210-1 |
| α-MT | DL-α-methyltyrosine | 12,069-3 |
| MTB | methylthymol blue | B4,200-4 |
| MTBE | *tert*-butyl methyl ether | 17,978-7 |
| MTBSTFA | *N*-(*tert*-butyldimethylsilyl)-*N*-methyl-trifluoroacetamide | 24,205-5 |
| MTC | methyl isothiocyanate | 11,277-1 |
| MTCA | 2-methylthiazolidine-4-carboxylic acid | |
| MTD | *m*-toluenediamine | |
| MTDEA | *N,N*-di(2-hydroxyethyl)-*m*-toluidine (*m*-toluidine-*N,N*-diethanol) | |
| MTES | methyltriethoxysilane | 17,557-9 |
| MTG | methyl β-D-thiogalactoside | |
| MTH | methylthiohydantoin | |
| MTHPA | methyltetrahydrophthalic anhydride | |
| MTM- | methylthiomethyl- | |
| MTMC | 4-(methylthio)-*m*-cresol | |
| MTMS | methyltrimethoxysilane | 24,617-4 |
| MTN | *m*-tolylnitrile | 13,232-2 |
| MTP | 4-(methylthio)phenol | M5,552-6 |
| MTPA | α-methoxy-α-trifluoromethylphenyl-acetic acid | 15,526-8<br>15,561-6 |
| MTT | 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2*H*-tetrazolium bromide | 13,503-8 |
| MTX | (+)-amethopterin | 22,394-8 |
| MUGB | 4-methylumbelliferyl *p*-guanidino-benzoate | |
| MVK | methyl vinyl ketone | M8,750-9 |
| MVP | 2-methyl-5-vinylpyridine | 12,773-6 |
| MXDA | *m*-xylylenediamine | X120-2 |
| 5-NAA | 5-nitroanthranilic acid | |

| Acronym | Description | Aldrich Cat. No. |
|---|---|---|
| NAAD | nicotinic acid adenine dinucleotide | |
| NAC | 1-naphthyl *N*-methylcarbamate | |
| NAD | nicotinamide adenine dinucleotide | |
| NADH | nicotinamide adenine dinucleotide phosphate, reduced | |
| NAI | *N*-acetylimidazole | 15,786-4 |
| NAM | *N*-acetylmethionine | 85,534-0 |
| NANA | *N*-acetylneuraminic acid | 85,565-0 |
| NAP | 4-nitroaminophenol | |
| NB- | *p*-nitrobenzyl- | |
| NBA | *N*-bromoacetamide | 13,513-5 |
| NBDCl | 4-chloro-7-nitrobenzo-2-oxa-1,3-diazole | 16,326-0 |
| NBD-F | 4-nitrobenzol-2-oxa-1,3-diazole-7-fluoro | |
| NBMPR | *S*-(*p*-nitrobenzyl)-6-thioinosine | 86,149-9 |
| NBS | *N*-bromosuccinimide | B8,125-5 |
| NBSac | *N*-bromosaccharin | |
| NBSC | 2-nitrobenzenesulfenyl chloride | 14,089-9 |
| NCA | *N*-chloroacetamide | |
| NCDC | 2-nitro-4-carboxyphenyl *N,N*-diphenyl-carbamate | |
| NCN | cyanonaphthalene | C9,280-4 |
| NCS | *N*-chlorosuccinimide | 10,968-1 |
| NEM | *N*-ethylmaleimide | 12,828-7 |
| NEP | *N*-ethyl-2-pyrrolidinone | 14,635-8 |
| NEPIS | *N*-ethyl-5-phenylisoxazolium-3'-sulfonate | E4,526-0 |
| NesMIC | (+)-(neomenthylsulfonyl)methyl isocyanide | |
| 5-NIA | 5-nitroisatoic anhydride | |
| NIP | 4-hydroxy-5-nitro-3-iodophenylacetic acid | |
| NIP | 2,4-dichlorophenyl 4'-nitrophenyl ether | |
| NM | nitromethane | 10,817-0<br>15,494-6<br>23,073-1 |
| NMA | *N*-methylolacrylamide | 24,580-1 |
| NMO | *N*-methylmorpholine *N*-oxide monohydrate | 22,428-6 |
| NMP | *N*-methylphthalimide | |
| NMP | *N*-methylpyrrolidone | M7,960-3<br>24,279-9 |
| NMSO | 4-methyl-2-nitroanisole | |
| NP- | *p*-nitrophenyl | |
| *p*-NPDPP | *p*-nitrophenyl diphenyl phosphate | |
| α-NPO | 2-(1-naphthyl)-5-phenyloxazole | |
| NPP | 2-nitro-2-propenyl pivalate | |
| NPS- | *o*-nitrophenylsulfenyl- | |
| NPSP | *N*-phenylselenenylphthalimide | 25,461-4 |
| Npys-Cl | 3-nitro-2-pyridinesulfenyl chloride | |
| N-Selectride® | sodium tri-*sec*-butylborohydride | 21,340-3 |
| NTA | nitrilotriacetic acid | N840-7 |
| N-t-B | 2-methyl-2-nitrosopropane | 18,026-2 |
| Nu | nucleophile | |
| OCAD | *o*-chlorobenzaldehyde | 12,497-4 |
| OCBA | *o*-chlorobenzoic acid | 13,557-7 |
| OCBC | *o*-chlorobenzyl chloride | 19,425-5<br>24,118-0 |
| OCBN | *o*-chlorobenzonitrile | C2,479-5 |
| OCCN | *o*-chlorobenzyl cyanide | 18,849-2 |
| OCDC | *o*-chlorodichlorotoluene | |
| OCOC | *o*-chlorobenzoyl chloride | 10,391-8 |
| OCPA | *o*-chlorophenylacetic acid | 19,063-2 |
| OCPT | 2-chloro-4-aminotoluene (*o*-chloro-*p*-aminotoluene) | 10,164-8<br>23,632-2 |
| OCT | *o*-chlorotoluene | 11,191-0 |
| OCT | ornithine carbamyl transferase | |
| OCTC | *o*-chlorobenzotrichloride | C2,540-6 |
| OCTEO | octyltriethoxysilane | |
| ODA | 4,4'-oxydianiline | A7,250-2<br>24,727-8<br>24,839-8 |
| OMH-1 | sodium diethyldihydroaluminate | 18,911-1 |
| OMP | orotidine 5'-monophosphate | |
| OTB | *o*-toluidine boric acid | |
| OTD | *o*-toluenediamine | |
| P | polymer substituent | |
| PABA | *p*-aminobenzoic acid | 10,053-6 |
| PADA | poly(adipic anhydride) | |
| PADA | pyridine-2-azo-*p*-dimethylaniline | |
| Bromo-PADAP | 2-(5-bromo-2-pyridylazo)-5-diethyl-aminophenol | 18,001-7 |
| PAH | polycyclic aromatic hydrocarbon | |
| PAH | *p*-aminohippuric acid | 12,295-5 |
| PAL | phenylalanine ammonia lyase | |
| PAM | pyridine-2-aldoxime methiodide | P6,020-5 |

| Acronym | Description | Aldrich Cat. No. |
|---|---|---|
| 2-PAM | (see PAM) | |
| 2-PAMCl | 2-pyridinealdoxime methochloride | 13,163-6 |
| PAN | 1-(2-pyridylazo)-2-naphthol | 10,103-6 |
| PAP | *O,O*-dimethyl *S*-α-(ethoxycarbonyl)-benzyl phosphorothiolothioate | |
| PAPA | poly(azelaic anhydride) | |
| PAPS | 3′-phosphoadenosine-5′-phosphosulfate | |
| PAR | 4-(2-pyridylazo)resorcinol, sodium salt monohydrate | 17,826-8 |
| PAS | *p*-aminosalicylic acid | A7,960-4 |
| PASAM | *p*-toluenesulfonamide | 10,590-1<br>23,633-0 |
| PBA | *p*-benzoquinone-2,3-dicarboxylic anhydride | |
| PBBO | 2-(4-biphenylyl)-6-phenylbenzoxazole [6-phenyl-2-(4-biphenylyl)benzoxazole] | 23,536-9 |
| PBD | 2-(4-biphenylyl)-5-phenyl-1,3,4-oxadiazole | 25,785-0 |
| Butyl-PBD | 2-(4-biphenylyl)-5-(4-*tert*-butylphenyl)-1,3,4-oxadiazole | 22,400-6 |
| PBI | *p*-benzoquinone-2,3-dicarboxylic imide | |
| PBN | *N*-*tert*-butyl-α-phenylnitrone | 18,027-0 |
| PBP | *p*-(benzyloxy)phenol | |
| PBS | poly(butene-1-sulfone) | |
| PC | propylene carbonate | P5,265-2 |
| PCAD | *p*-chlorobenzaldehyde | 11,221-6 |
| PCB | polychlorobiphenyl | |
| PCBA | *p*-chlorobenzoic acid | 13,558-5 |
| PCBC | *p*-chlorobenzyl chloride | 11,196-1 |
| PCBN | *p*-chlorobenzonitrile | 11,562-2 |
| PCBTF | *p*-chlorobenzotrifluoride | C2,640-2 |
| PCC | pyridinium chlorochromate | 19,014-4 |
| PCCN | *p*-chlorobenzyl cyanide | C2,800-6 |
| PCDC | *p*-chlorodichlorotoluene | |
| P-Cellulose | cellulose phosphate | |
| PCMB | *p*-chloromercuribenzoic acid | C4,960-7 |
| PCMX | *p*-chloro-*m*-xylenol | C3,830-3 |
| PCNB | pentachloronitrobenzene | P220-5 |
| PCOC | *p*-chlorobenzoyl chloride | 11,190-2 |
| PCONA | *p*-chloro-*o*-nitroaniline | 10,166-4 |
| PCOT | 4-chloro-2-aminotoluene (*p*-chloro-*o*-aminotoluene) | C5,120-2 |
| PCP | pentachlorophenol | P260-4<br>14,016-3 |
| PCPA | *p*-chlorophenylacetic acid | 13,926-2 |
| PCT | polychloroterphenyl | |
| PCT | *p*-chlorotoluene | 11,192-9 |
| PCTC | *p*-chlorotrichlorotoluene | C2,580-5 |
| PDA | phorbol 12,13-diacetate | |
| PDBz | phorbol 12,13-dibenzoate | |
| PDC | pyridinium dichromate | 21,469-8 |
| PDEA | *N*-phenyldiethanolamine | P2,240-0 |
| PDQ | sodium (2-methyl-4-chlorophenoxy)-butyrate | |
| PDT | 3-(2-pyridyl)-5,6-diphenyl-1,2,4-triazine | 16,041-5 |
| PEA | *N*-(2-hydroxyethyl)aniline (*N*-phenylethanolamine) | 15,687-6 |
| PEEA | *N*-(2-hydroxyethyl)-*N*-ethylaniline (*N*-phenyl-*N*-ethylethanolamine) | |
| PEEK | poly ether ketone (ICI) | |
| PEG | polyethylene glycol | 20,236-3 to<br>20,246-0 |
| PEI-Cellulose | polyethyleneimine-impregnated cellulose | |
| PEMA | 2-ethyl-2-phenylmalonamide | 19,502-2 |
| PEP | phosphoenolpyruvic acid | 86,007-7<br>85,858-7<br>86,195-2 |
| PET | poly(ethylene terephthalate) | 20,025-5 |
| PETA | pentaerythritol triacrylate | 24,679-4 |
| PG | protective group | |
| PG | prostaglandin | |
| PGE | phenyl glycidyl ether | 24,848-7 |
| Ph | phenyl | |
| Phe | phenylalanine | P1,700-8 |
| PHR | phorbol | |
| Phth | phthaloyl | |
| PIA | phenyliodoso diacetate | 17,872-1 |
| PIPES | 1,4-piperazinebis(ethanesulfonic acid) | 16,375-9 |
| PMA | phorbol 12-myristate 13-acetate | |
| PMA | phenylmercuric acetate | P2,712-7 |
| PMDTA | pentamethyldiethylenetriamine | |
| PMEA | *N*-(2-hydroxyethyl)-*N*-methylaniline (*N*-phenyl-*N*-methylethanolamine) | |
| PMH | phenylmercuric hydroxide | P2,714-3 |
| PMHS | polymethylhydrosiloxane | 17,620-6 |
| PMI | 3-phenyl-5-methylisoxazole | |
| PMI-ACID | 3-phenyl-5-methylisoxazole-4-carboxylic acid | 13,419-8 |
| PMP | *O,O*-dimethyl *S*-(phthalimidomethyl) phosphorodithioate | |
| PMS | phenazine methosulfate | P1,340-1 |
| PNASA | *p*-nitroaniline-*o*-sulfonic acid | |
| PNMT | phenylethanolamine-*N*-methyltransferase | |
| PNOT | *p*-nitro-*o*-toluidine | 14,643-9 |
| PNPDPP | *p*-nitrophenyl diphenyl phosphate | |
| PNPG | α-*p*-nitrophenylglycerine | |
| PNPP | *p*-nitrophenyl phosphate | N2,200-2<br>85,758-0 |
| POBN | α-(4-pyridyl-1-oxide)-*N*-*tert*-butylnitrone | 21,543-0 |
| 4-POBN | (see POBN) | |
| POC | cyclopentyloxycarbonyl | |
| POM | chloromethyl pivalate | 14,118-6 |
| POPOP | 1,4-bis(5-phenyloxazol-2-yl)benzene | B5,080-5 |
| dimethyl-POPOP | 1,4-bis(4-methyl-5-phenyl-2-oxazolyl)-benzene | 22,291-7 |
| POPSO | piperazine-*N*,*N*′-bis(2-hydroxypropanesulfonic acid) | |
| PPA | polyphosphoric acid | 20,821-3 |
| PPDA | phenyl phosphorodiamidate | |
| PPDP | *p*,*p*′-diphenol | 16,873-4 |
| PPE | polyphosphate ester (ethyl *m*-phosphate) | |
| PPNCl | bis(triphenylphosphoranylidene)-ammonium chloride | 22,383-2 |
| PPO | 2,5-diphenyloxazole | D21,040-4 |
| PPTS | pyridinium *p*-toluenesulfonate | 23,223-8 |
| Pr | propyl | |
| PR | phenol red | 11,452-9<br>11,453-7 |
| iPr | isopropyl | |
| Pro | proline | 13,154-7 |
| P2S | 2-pyridinealdoxime methyl methanesulfonate | |
| PS-Cl | 2-pyridinesulfenyl chloride | |
| PSPA | poly(sebacic anhydride) | |
| PTAD | *N*-phenyl-1,2,4-triazoline-3,5-dione | |
| PTAP | phenyltrimethylammonium perbromide | 13,971-8 |
| PTBBA | *p*-*tert*-butylbenzoic acid | 15,035-5<br>23,971-8 |
| PTC | phenyl isothiocyanate | 13,974-2 |
| PTH | phenylthiohydantoin | |
| PTMO | *n*-propyltrimethoxysilane | |
| PTSA | *p*-toluenesulfonic acid | T3,592-0<br>16,199-3<br>25,537-8 |
| PTSI | *p*-toluenesulfonyl isocyanate | 18,927-8 |
| PVA | polyvinyl alcohol | 18,933-2<br>and others |
| PVC | polyvinyl chloride | 18,261-3<br>18,262-1<br>18,956-1<br>18,958-8 |
| PVDF | polyvinylidene fluoride | 18,270-2 |
| PVP | polyvinylpyrrolidone | 23,425-7<br>85,645-2<br>85,647-9<br>85,656-8 |
| PVPDC | poly(4-vinylpyridinium) dichromate | 23,746-9 |
| PVP-I | polyvinylpyrrolidone-iodine complex | 86,056-5 |
| PVSK | potassium polyvinyl sulfate | |
| PyOTs | (see PPTS) | |
| Pyr (or Py) | pyridine | P5,750-6<br>18,452-7 |
| QUIBEC | benzylquinidinium chloride | |
| RDB | sodium dihydrobis(2-methoxyethoxy)-aluminate | 19,619-3 |
| Red-Al® | (see RDB) | |
| RNA | ribonucleic acid | |
| RNase | ribonuclease | |
| SAA | succinic anhydride | 13,441-4<br>23,969-0 |
| SADP | *N*-succinimidyl (4-azidophenyldithio)-propionate | |

| Acronym | Description | Aldrich Cat. No. |
|---|---|---|
| SBH | sodium borohydride | 19,807-2<br>21,346-2<br>21,553-8<br>23,704-3 |
| SDP | 4,4′-sulfonyldiphenol | 10,303-9 |
| SDPP | *N*-succinimidyl diphenyl phosphate | |
| SDS | sodium dodecyl sulfate | 85,192-2<br>86,201-0 |
| SDS | sodium dodecylbenzenesulfonate | |
| Ser | serine | S260-0 |
| SEX | sodium ethyl xanthate | |
| $Sia_2BH$ | disiamylborane | 22,078-7 |
| SLS | sodium lauryl sulfate | 85,192-2<br>86,201-0 |
| SMCC | succinimidyl 4-(*N*-maleimidomethyl-cyclohexane)-1-carboxylate | |
| SMPB | succinimidyl 4-(*p*-maleimidophenyl)-butyrate | |
| Di-SNADNS | 2,7-bis(4-sulfo-1-naphthylazo)-1,8-dihydroxynaphthalene-3,6-disulfonic acid | |
| SPA | super phosphoric acid | |
| SPADNS | 2-(*p*-sulfophenylazo)-1,8-dihydroxy-3,6-naphthalenedisulfonic acid (trisodium salt) | 11,475-8 |
| SPDP | *N*-succinimidyl 3-(2-pyridyldithio)-propionate | |
| SSP | 1,2-distearoylpalmitin | |
| STPP | sodium tripolyphosphate | 23,850-3 |
| Super-Hydride® | lithium triethylborohydride | 17,972-8 |
| T | thymidine | 13,199-7 |
| 2,4,5-T | 2,4,5-trichlorophenoxyacetic acid | 19,712-2 |
| TAC | triallyl cyanurate | 11,423-5 |
| TAMA | *N*-methylanilinium trifluoroacetate | 21,008-0 |
| TAME | *N*α-*p*-tosyl-L-arginine methyl ester hydrochloride | T4,350-8 |
| TAMM | tetrakis(acetoxymercuri)methane | |
| TAPA | α-(2,4,5,7-tetranitro-9-fluorenylidene-aminoxy)propionic acid (+ or −) | |
| TAPS | 3-[tris(hydroxymethyl)methylamino]-1-propanesulfonic acid | 21,993-2 |
| TAPSO | 3-[*N*-(tris(hydroxymethyl)methylamino]-2-hydroxypropanesulfonic acid | |
| TAS- | tris(diethylamino)sulfonium- | |
| TB | thexylborane | 22,079-5 |
| TB | thymol blue | 11,454-5<br>86,136-7 |
| 2,3,6-TBA | 2,3,6-trichlorobenzoic acid | |
| TBAB | tetrabutylammonium bromide | 19,311-9 |
| TBAC | *tert*-butylacetyl chloride | B8,880-2 |
| TBAF | tetrabutylammonium fluoride | 21,614-3<br>24,151-2 |
| TBAF | tetra-*n*-butylammonium fluoroborate | 21,796-4 |
| TBAHS | tetrabutylammonium hydrogen sulfate | 15,583-7 |
| TBAP | tetra-*n*-butylammonium perchlorate | |
| TBAS | tetra-*n*-butylammonium succinimide | |
| TBC | *p*-*tert*-butylcatechol | 12,424-9 |
| TBDA | thexylborane-*N*,*N*-diethylaniline | |
| TBDMS- | (see TBS-) | |
| TBDMSCl | (see TBSCl) | |
| TBDMSI | 1-(*tert*-butyldimethylsilyl)imidazole | 25,023-6 |
| TBE | tetrabromoethane | 13,527-5<br>18,557-4 |
| TBHC | *tert*-butyl hypochlorite | |
| TBHP | *tert*-butyl hydroperoxide | 18,471-3<br>21,312-8 |
| TBO | 3-[(trimethylsilyl)oxy]-3-buten-2-one | |
| TBP | tri-*n*-butyl phosphate | 15,861-5<br>24,049-4 |
| TBP | triphenylbutylphosphonium bromide | B10,280-6 |
| TBS- | *tert*-butyldimethylsilyl- | |
| TBSCl | *tert*-butyldimethylsilyl chloride | 19,050-0 |
| TBTD | tetrabutylthiuram disulfide | |
| TBUP | tri-*n*-butylphosphine | T4,948-4 |
| TC | 2,3,4,5-tetraphenylcyclopentadienone | T2,580-1 |
| TCA | trichloroacetic acid | 11,611-4 |
| TCB | trichlorobenzene (usually 1,3,5) | T5,460-7 |
| Tce | 2,2,2-trichloroethyl- | |
| Tcec | β,β,β-trichloroethoxycarbonyl- | |
| TcecCl | β,β,β-trichloroethoxycarbonyl chloride | 14,207-7 |
| TCl | terephthaloyl chloride | 12,087-1 |
| TCNE | tetracyanoethylene | T880-9 |
| TCNP | 11,11,12,12-tetracyanopyreno-2,7-quinodimethane | |
| TCNQ | 7,7,8,8-tetracyanoquinodimethane | 15,763-5 |
| TCP | tricresyl phosphate | 26,891-7 |
| TCP | trichlorophenol (usually 2,4,5 or 2,4,6) | 15,651-5<br>T5,530-1 |
| TCTFP | 1,1,2,2-tetrachloro-3,3,4,4-tetrafluoro-cyclobutane | |
| TDI | tolylene diisocyanate | 21,683-6 |
| TDP | 4,4′-thiodiphenol | 21,617-8 |
| TEA | triethanolamine | T5,830-0 |
| TEA | triethylaluminum | 19,270-8<br>25,266-2<br>25,716-8<br>25,718-4<br>25,717-6 |
| TEA | triethylamine | 13,206-3<br>23,962-3 |
| TEAB | triethylammonium bicarbonate | |
| TEAE-Cellulose | triethylaminoethyl cellulose | |
| TEAS | tetraethylammonium succinimide | |
| TEBA | benzyltriethylammonium chloride | 14,655-2 |
| TED | (see DABCO) | |
| TEG | triethylene glycol | T5,945-5 |
| TEM | triethylenediamine (1,4-diazabicyclo-[2.2.2]octane) | D2,780-2 |
| TEMPO | 2,2,6,6-tetramethylpiperidinooxy, free radical | 21,400-0 |
| TES- | triethylsilyl- | |
| TES (Aldrich) | 2-[tris(hydroxymethyl)methylamino]-1-ethanesulfonic acid | 22,320-4 |
| TES (Fluka) | *N*,*N*,*N*′,*N*′-tetraethylsulfamide | 25,958-6 |
| TETD | tetraethylthiuram disulfide | T1,160-6 |
| TETM | tetraethylthiuram monosulfide | |
| TETN | triethylamine | 13,206-3<br>23,962-3 |
| TFA | trifluoroacetic acid | T6,220-0 |
| TFA | trifluoroacetyl- | |
| TFAA | trifluoroacetic anhydride | 10,623-2 |
| TFA-ME | methyl trifluoroacetate | 24,983-1 |
| TFE | 2,2,2-trifluoroethanol | T6,300-2 |
| TFMC-Eu | tris[3-(trifluoromethylhydroxy-methylene)-*d*-camphorato]•Eu(III) | 17,649-4 |
| TFMC-Pr | tris[3-(trifluoromethylhydroxy-methylene)-*d*-camphorato]•Pr(III) | 17,770-9 |
| THAM | tris(hydroxymethyl)aminomethane | 15,456-3<br>T8,760-2 |
| THE | tetrahydrocortisone | |
| THF | tetrahydrofuran | 14,722-2<br>17,881-0<br>18,656-2<br>24,288-8 |
| THF | tetrahydrofolic acid | |
| THFA | tetrahydrofurfuryl alcohol | 18,539-6<br>T1,265-3 |
| THFC-Eu | tris[3-(heptafluoropropylhydroxy-methylene)-*d*-camphorato]•Eu(III) | 16,474-7 |
| THIP | 4,5,6,7-tetrahydroisoxazolo[5,4-*c*]-pyrimidin-3(2*H*)-one | |
| THP | tetrahydropyran (or tetrahydropyranyl) | T1,440-0 |
| Thr | threonine | T3,420-7 |
| TIBA | triiodobenzoic acid (usually 2,3,5) | 12,097-9 |
| TIBA | triisobutylaluminum | 19,271-6<br>25,720-6<br>25,721-4 |
| TIPSCl | 1,3-dichloro-1,1,3,3-tetraisopropyl-disiloxane | 23,420-6 |
| TLCK | 1-chloro-3-tosylamido-7-amino-2-heptanone hydrochloride | 85,751-3 |
| TMA | trimethylaluminum | 19,804-8<br>25,722-2<br>25,723-0 |
| TMAC | trimellitic anhydride monoacid chloride | T6,802-0 |
| TMAEMC | 2-trimethylammoniumethylmethacrylic chloride | |
| TMAT | tetramethylammonium tribromide | |
| TMAT | tris-2,4,6-[1-(2-methyl)aziridinyl]-1,3,5-triazine | |
| TMB (Aldrich) | 3,3′,5,5′-tetramethylbenzidine | 86,033-6<br>86,151-0 |
| TMB | *N*,*N*,*N*′,*N*′-tetramethylbenzidine | T1,980-1 |
| TMB-4 | 1,1′-trimethylenebis[4-(hydroxyimino-methyl)pyridinium bromide] | |
| TMBA | 3,4,5-trimethylbenzaldehyde | |
| TMC | 3,3,5-trimethylcyclohexanol | |

| Acronym | Description | Aldrich Cat. No. |
|---|---|---|
| TMCS (Aldrich) | (see TMSCl) | |
| TMEDA | *N,N,N′,N′*-tetramethylethylenediamine | T2,250-0 |
| TMG | methyl β-D-thiogalactoside | |
| TMM | trimethylenemethane | |
| TMO | trimethylamine *N*-oxide | 17,686-9 |
| TMP | 2,2,6,6-tetramethylpiperidine | 11,575-4 |
| TMP | thymidine 5′-monophosphate | |
| TMPTA | trimethylolpropane triacrylate | 24,680-8 |
| TMPTMA | trimethylolpropane trimethacrylate | 24,684-0 |
| TMS- | trimethylsilyl- | |
| TMS | tetramethylsilane | T2,400-7 |
| TMSCl | trimethylsilyl chloride | C7,285-4 |
| TMSCN | trimethylsilyl cyanide | 21,284-9 |
| TMSDEA | *N,N*-diethyl-1,1,1-trimethylsilylamine | 12,725-6 |
| TMTD | tetramethylthiuram disulfide | T2,420-1 |
| TMTM | tetramethylthiuram monosulfide | |
| TNBA | tri-*n*-butylaluminum | |
| TNBT | tetranitro blue tetrazolium | 13,316-7 |
| TNF | 2,4,7-trinitrofluorenone | T8,080-2 |
| TNM | tetranitromethane | T2,500-3 |
| TNPA | tri-*n*-propylaluminum | 25,724-9 |
| TNS | 6-(*p*-toluidino)-2-naphthalenesulfonic acid, potassium salt | 19,426-3 |
| TNT | 2,4,6-trinitrotoluene | |
| Tol | toluene | 15,500-4<br>17,941-8<br>17,996-5<br>24,451-1 |
| TOPO | tri-*n*-octylphosphine oxide | 22,330-1 |
| TosMIC | tosylmethyl isocyanide | 18,820-4 |
| TP | thymolphthalein | 11,455-3 |
| TPB | 1,1,4,4-tetraphenyl-1,3-butadiene | 17,870-5<br>18,521-3 |
| TPC | thymolphthalein complexone | 22,326-3 |
| TPCD | tetraphenylcyclopentadienone | T2,580-1 |
| TPCK | L-1-*p*-tosylamino-2-phenylethyl chloromethyl ketone | 85,725-4 |
| TPE | tetraphenylethylene | T2,620-4 |
| TPN | triphosphopyridine nucleotide, sodium salt | 85,659-2 |
| TPNH | reduced triphosphopyridine nucleotide, sodium salt | |
| TPP | tetraphenylporphyrin | 16,099-7<br>24,736-7 |
| TPP | triphenyl phosphate | 10,585-6<br>24,128-8 |
| TPP | triphenylphosphine | T8,440-9 |
| TPS- | 2,4,6-triisopropylbenzenesulfonyl- | |
| TPS | triphenylsulfonium chloride | |
| TPSCl (or TPS) | 2,4,6-triisopropylbenzenesulfonyl chloride | 11,949-0 |
| TPTZ | 2,4,6-tris(2′-pyridyl)-*s*-triazine | 15,528-4 |
| TRIAMO | triaminosilane | |
| Tricine | *N*-[tris(hydroxymethyl)methyl]glycine | 16,378-3 |
| Tr | trityl | |
| Triglyme | triethylene glycol dimethyl ether | T5,980-3 |
| TRIS | tris(hydroxymethyl)aminomethane | 15,456-3<br>T8,760-2 |
| TRITC | tetramethylrhodamine isothiocyanate | |
| TrOC | (see Tcec) | |
| Trp | tryptophan | T9,020-4 |
| TRPGDA | tripropyleneglycol diacrylate | 24,683-2 |
| Ts | tosyl (or *p*-toluenesulfonyl-) | |
| TSIM | *N*-trimethylsilylimidazole | 15,358-3 |
| TSNI | 1-(*p*-toluenesulfonyl)-4-nitroimidazole | |
| TSP | tribasic sodium phosphate | 22,200-3 |
| TSPP | tetrasodium pyrophosphate | 22,136-8 |
| TTC | 2,3,5-triphenyltetrazolium chloride | T8,485-9 |
| TTEGDA | tetraethyleneglycol diacrylate | 24,682-4 |
| TTF | tetrathiafulvalene | 18,318-0 |
| TTFA | thallium(III) trifluoroacetate | 15,053-3 |
| TTN | thallium(III) nitrate | 16,301-5 |
| Tyr (or Tyr-OH) | tyrosine | T9,040-9 |
| Tyr-OMe | tyrosine methyl ester | T9,080-8 |
| U | uracil | 13,078-8 |
| U | uridine | U288-1 |
| UDMH | *unsym*-dimethylhydrazine | D16,160-8 |
| UDP | uridine 5′-diphosphate | 85,211-2 |
| UMP | uridine 5′-monophosphate | 85,210-4 |
| UTP | uridine 5′-triphosphate | 85,213-9 |
| Val | valine | V70-5 |
| VMA | DL-4-hydroxy-3-methoxymandelic acid | 14,880-6 |
| VTC | vinyltrichlorosilane | 10,487-6 |
| VTEO | vinyltriethoxysilane | 17,556-0 |
| VTMO | vinyltrimethoxysilane | 23,576-8 |
| VTMOEO | vinyltris(2-methoxyethoxy)silane | |
| XDP | xanthosine 5′-diphosphate | |
| XMP | xanthosine 5′-monophosphate | |
| XTP | xanthosine 5′-triphosphate | |
| Xy | xylene | X104-0<br>13,490-2<br>18,556-6<br>13,444-9<br>21,473-6<br>24,045-1<br>24,764-2 |
| Z- | (see CBn) | |
| ZDBC | zinc dibutyldithiocarbamate | |
| ZDEC | zinc diethyldithiocarbamate | |
| ZDMC | zinc dimethyldithiocarbamate | |
| ZPCK | *N*-CBZ-L-phenylalanine chloromethyl ketone | 86,079-4 |

### *About the Authors*

A native of Milwaukee, Professor Guido H. Daub received the Ph.D. degree from the University of Wisconsin in 1949. He has been a member of the faculty of the University of New Mexico since 1949, attaining the rank of Associate Professor of Chemistry in 1955 and Professor of Chemistry in 1963. He was Director of the University of New Mexico Graduate Center in Los Alamos from 1958 to 1963 and Chairman of the Chemistry Department from 1970 to 1981.

Research interests include synthetic organic chemistry in the areas of polycyclic aromatic compounds, liquid scintillator solutes, UV laser dyes, labeling of compounds of physiological interest with $^{13}C$ and $^{15}N$ in strategic positions, and the $^{13}C$ labeling of the oxide carbon of arene oxides for studying their reactions by $^{13}C$ NMR.

S. Barrie Walker specializes in chemical information and is an Information Officer with the Plant Protection Division of ICI. During the 1960's he was a chemist with ICI Pharmaceuticals Division and for three years worked on the ICI CROSSBOW system, preparing an inventory of all ICI's test chemicals. He was the systems and database manager for the CAOCI project, involving work groups from many of the leading UK pharmaceutical companies (*J. Chem. Inf. Comp. Sci.* **1983**, *23*, 3-5). For many years he has taught WLN in tutorials at many UK universities on behalf of the Chemical Notation Association (UK). He is Assistant Editor of the British Crop Protection Council's publication "The Pesticide Manual," now in its seventh edition. He is currently involved in the conversion of ICI databases into MACCS (Molecular Access System from Molecular Design, Ltd. of Hayward, California).

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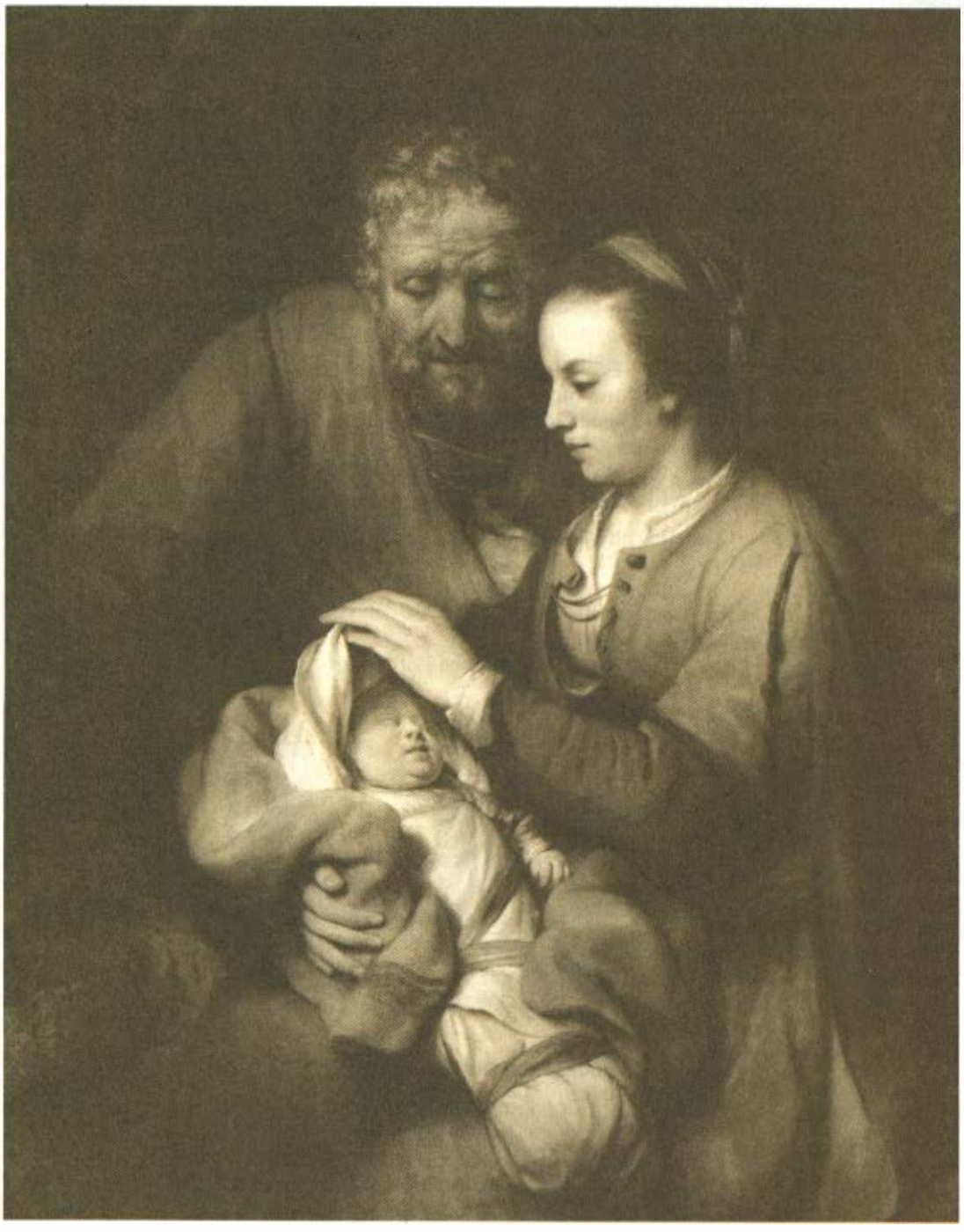
# Aldrichimica Acta

Volume 17, Number 2, 1984



## Preparative Flash-Vacuum Thermolysis. The Revival of Pyrolytic Synthesis
## Synthetic Routes to Cyclopentanoid-Fused Unnatural and Natural Products

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# Aldrichimica Acta

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# About Our Cover:

Our chemist-collector owns several works by Gerbrand van den Eeckhout, and this is his favorite. Eeckhout, who was a student of Rembrandt and became one of his good friends, was influenced by both Rembrandt's teacher, Pieter Lastman (see *Aldrichimica Acta* Vol. 8, No. 2, Fig. 1), and by Rembrandt, as in the painting on this cover.

This painting (oil on canvas, 39-½ x 33 inches, signed and dated 1652) may be a *Rest on the Flight to Egypt* in which Baroque paintings traditionally show Joseph as an old man. Here is the essence of fatherly love and pride, and equally touching is the care with which Mary handles her baby. Can you think of a more beautiful depiction of parental love?

Aert de Gelder, one of Rembrandt's last students, dealt with this same subject 30 years later in one of his masterpieces (Fig. 2) which is now in Boston. Perhaps de Gelder was influenced by Eeckhout's work, for his painting, too, depicts the parents' great care for their child. Love is infectious: we feel good all over just looking at these paintings.

Fig. 1

Fig. 2

Are you interested in our *Acta* covers? Selections from the Bader Collection, with 30 duotone reproductions, many of previous *Acta* covers, and an introduction by Professor Wolfgang Stechow is available to all chemist art-lovers.

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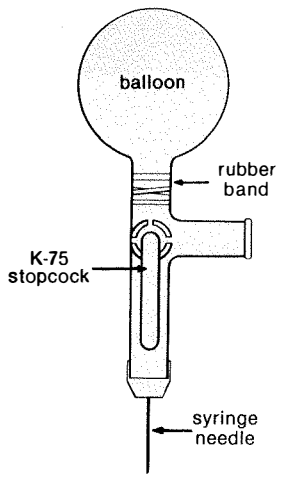
Because of the ever-increasing demand for earlier issues of the *Acta*, we now offer a collection of articles selected from volumes 1 - 15.

# Lab Notes

When conducting small- to moderate-scale hydrogenations *without elevated pressure*, it is convenient to transfer and introduce the hydrogen using an apparatus assembled from a syringe needle, a Pharmaseal® K-75 three-way stopcock, a balloon, and a rubber band (as illustrated).

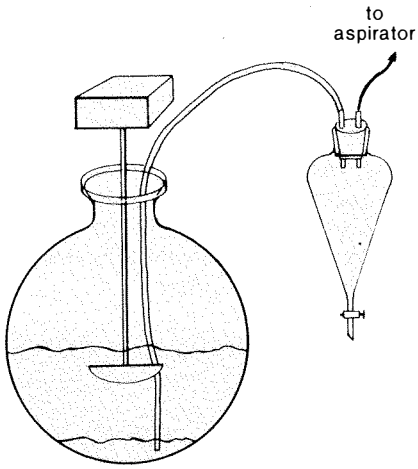
Hydrogen is introduced into the balloon (after it has been deflated completely) by attaching a piece of surgical tubing to a hydrogen tank port, inserting the needle through the tubing, then filling the balloon *under low pressure*. After the stopcock is closed, the apparatus may be easily transported to the reaction flask and connected by inserting the needle through a septum. Purging the reaction vessel and the solvent is accomplished by attaching a vacuum source to the open stopcock port with a needle-tubing connector, followed by repeated evacuation/hydrogen introduction cycles *via* the stopcock. After purging, the vacuum source may be disconnected, and the reaction left under positive pressure.

A typical balloon will hold in excess of 250cc of gas, and maintain a positive pressure overnight. Should more hydrogen be needed, the stopcock/balloon assembly is easily disconnected leaving the needle in place, and another filled unit is connected.



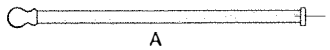

*Carl Wheeler*
*Department of Chemistry - 4630*
*Washington State University*
*Pullman, Washington 99164*

We have developed a method for thorough extraction of large volumes of aqueous solution with chloroform, which eliminates the tedious and physically exhausting use of large separatory funnels. We had 12 liters of aqueous layer which we placed in a 22-liter flask. A 300-ml portion of chloroform was added and the mixture was agitated (we used a vibromixer, but an overhead stirrer would probably work as well). Mixing was stopped and the lower layer was sucked by an aspirator into a 500-ml separatory funnel through a long plastic tube. It is not necessary to be able to see the bottom of the flask: when the aqueous layer starts coming over, stop the transfer. The chloroform layer was saved and the aqueous layer was returned to the large flask. The process can be repeated as often as necessary without ever lifting anything heavy, until it is time to deal with the chloroform layer. In our case, this amounted to a much more manageable 2 liters.

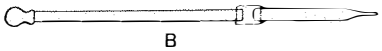



*David Reingold*
*Eaton Group*
*University of Chicago*
*Department of Chemistry*
*Chicago, Illinois 60637*

A simple modification of the applicator/-holder for the popular disposable TLC spotters has increased their utility. By replacing the 4 x 25-mm tubing with a longer one (A), TLC samples may be easily taken from reaction vessels.




An offshoot of this idea is the extension for use with Pasteur pipettes (B). Using this device, it is quite easy to apply samples to chromatography columns with minimal disruption of the bed. We have found this to be especially useful with partially filled columns, such as those encountered with flash chromatography.




*Michael Okagaki*
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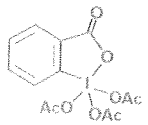
*Any interesting shortcut or laboratory hint you'd like to share with Acta readers? Send it to Aldrich (attn: Lab Notes) and if we publish it, you will receive a handsome Aldrich coffee mug as well as a copy of* **Selections from the Bader Collection**. *We reserve the right to retain all entries for consideration for future publication.*

# "Please Bother Us."

by Ofra Bader.

Recently Professor J.C. Martin suggested that we offer the periodinane,[1]




an elegant, new reagent for the oxidation of primary and secondary alcohols to aldehydes and ketones. Aldehydes are not further oxidized to acids, even with excess reagent. Other easily oxidized functional groups, such as sulfides, enol ethers and N-alkylindoles, are not affected.

Naturally, we made it; but how do you name it? The systematic name, 1,1,1-triacetoxy-2,1-benzoxiodol-3(3*H*)-one, is quite cumbersome. It is a periodinane, but some day we may want to offer others, such as $IF_5$. Perhaps *Dess-Martin periodinane* is a good name.

1) Dess, D.B.; Martin, J.C. *J. Org. Chem.* **1983**, *48*, 4155.

It was no bother at all, just a pleasure to be able to help.

# Preparative Flash-Vacuum Thermolysis.[1] The Revival of Pyrolytic Synthesis

*U.E. Wiersum*
*Akzo Research Laboratories*
*Corporate Research Department*
*Velperweg 76, 6800 AB Arnhem*
*The Netherlands*


## *I. Introduction*

Thermal or pyrolytic principles* are not generally accepted today as resources in organic synthesis.[1,2] Traditional pyrolysis reactions require prolonged exposure times at high temperatures and often give rise to low yields or tarry residues, especially when run in the molten phase.[3] These characteristics are presently still associated with pyrolysis and, despite the fact that pyrolysis has always been an organic discipline, relatively few reactions have become standard procedures in organic synthesis. Generally known examples[4] include dehydrocarbon cracking,[5] carboxylation of carboxylic acids,[6] pyrolytic elimination from alkyl halides, esters, amine oxides or xanthates,[7] Elbs cyclodehydration and dehydrocyclization reactions for preparation of aromatic systems,[8] Claisen and Cope rearrangements,[9] retro-Diels-Alder reaction,[10] and ketene formation.[11]

Since 1970 there has been increased awareness that pyrolysis reactions have a broader range of synthetic application. They can be run conveniently in the gas phase with short contact times at relatively high temperatures, and under low-pressure conditions enabling direct trapping and spectroscopic observation of highly reactive compounds.[12] This technique, known as flash-vacuum thermolysis (FVT) or flash-vacuum pyrolysis (FVP),* has disclosed many new thermal reaction principles[13] and has proved to be an excellent method for the synthesis of numerous compounds that are difficult to prepare by alternative means.[1,2,14,15]

In this review examples of all kinds are presented to illustrate the preparative scope of FVT. Besides, most of the structures obtained will tickle the imagination of the organic chemist. In this respect, the "sledgehammer approach," as FVT was classified once,[15] is obviously the best way to "shape the diamonds," taking into account the great efforts that were made to obtain some of the described compounds *via* liquid-phase reactions. An enumeration of the classes obtained by FVT, *e.g.*, carbene and nitrene rearrangement products, isoannelated heteroaromatics, quinonoid systems, cyclopentadienone-related structures, cyclobutadiene systems, acetylenes and cumulenes, small-ring compounds, sulfenic acids and silaolefins, was recently published.[1,2]

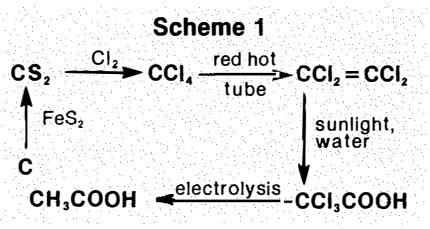
* The use of thermolysis or pyrolysis as two similar terms for the subject reactions has been adequately commented upon,[2] and is merely a matter of semantics. The symbol $\overset{\Delta}{\not}$ has been used to differentiate FVT conditions from ordinary heating, symbolized by $\Delta$.

## *II. Historical perspective*

### 1. Pyrolysis, a cornerstone in early organic chemistry

In 1845, Kolbe's use of a pyrolysis reaction — dimerization of carbon tetrachloride (Scheme 1) — to synthesize a truly organic natural product, acetic acid, in a multistep sequence directly from the inorganic elements, definitely broke the vitalist theory.[16] At that time, during the early development of organic chemistry, pyrolysis reactions like dry distillations of wood, bones, and oils, were major sources for new compounds, aromatic systems in particular.**

**Scheme 1**




These experiments prompted Kékulé's concept of the essence of aromatic structure. It was certainly inspired by Berthelot's work on thermolysis of methane and its homologs, which showed a building-up process to more complicated molecules, like benzene, styrene, naphthalene and anthracene.[3,5b] Berthelot was the first who envisaged that such synthetic transformations must be governed by coherent rules that would render a scientific basis to organic chemistry. He formulated the idea that rational synthesis would unify all organic substances.[16] The large contribution of pyrolysis experiments to the development of organic chemistry can best be judged from Hurd's classic book "The Pyrolysis of Carbon Compounds," written in 1929, which gives a comprehensive account of all pyrolytic processes at that time.[3]

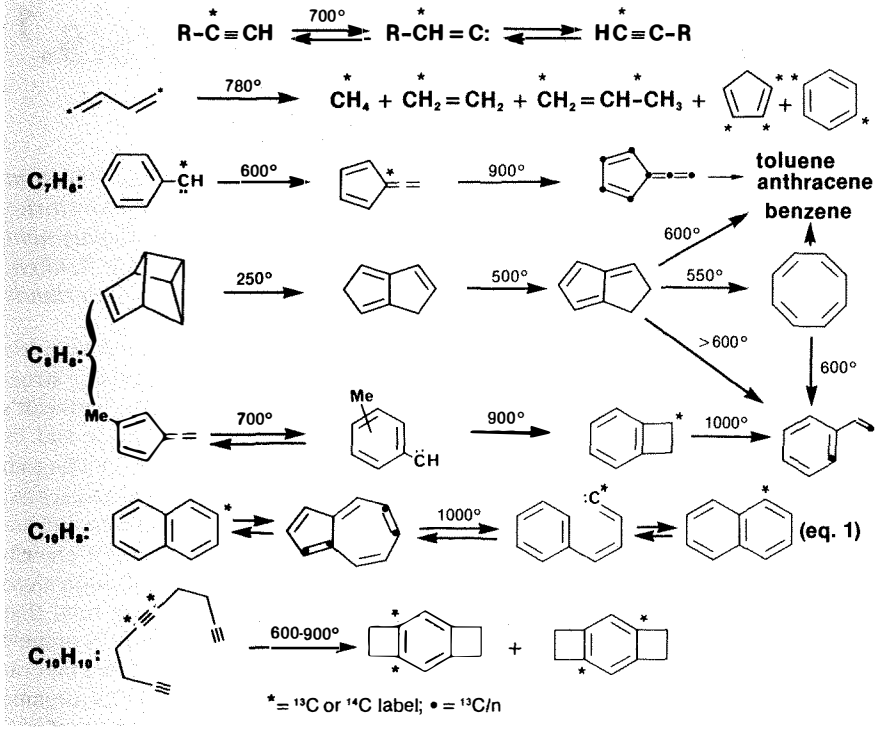
** Today this has a parallel in the pyrolytic recycling of waste polymers that gives a substantial amount of aromatics.[17]

### 2. Old surmises elaborated

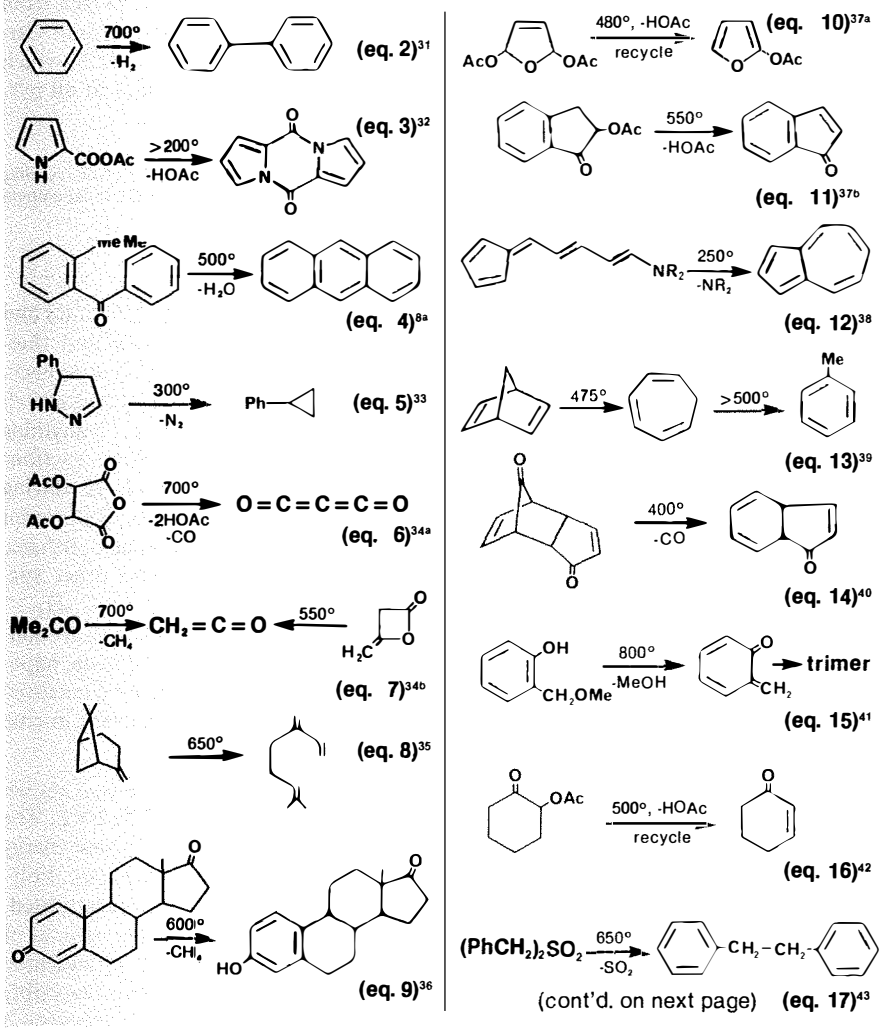
Berthelot's theory that all aromatics and heteroaromatics, *e.g.*, pyrrole and thiophene, are always built from low-molecular-weight key intermediates such as acetylene and butadiene, does not reveal anything about the complex scrambling reactions that such intermediates undergo during thermolysis. This is apparent from recent FVT work with labelled acetylenes (Scheme 2),[18] butadiene,[19] and several other species,[1,2] *e.g.*, $C_7H_6$,[15,20] $C_8H_8$,[20,21] $C_{10}H_8$,[1,22] and $C_{10}H_{10}$,[22] ultimately leading to aromatics such as benzene, toluene, styrene, naphthalene, anthracene and higher condensed heteroaromatics[5b,23,24] as they exist in coal tar.[25]

The study of reaction patterns as shown in Scheme 2 has been aided by FVT. The aromatics are the products of lowest energy in a pool of sequential intermediates. Polycyclic, highly strained, polyunsaturated, carbenoid radical and aromatic species of the same molecular formula, as indicated briefly for $C_8H_8$, do sometimes reversibly interconvert on a thermal energy surface.[1]

## Scheme 2




## Scheme 3




(cont'd. on next page)

The reversibility of the reactions explains the so-called automerization reactions[15] that some intermediates, including stable aromatics, undergo, as recently described for azulene, naphthalene (eq. 1), and benzene.[22a] Some of the intermadiates fragment, dimerize, or add to other species as well, which explains the pyrogenic build-up process.*** FVT studies with compounds that contain heteroatoms have revealed that a series of hydrocarbon intermediates, $C_mH_n$, may, especially in the cases of nitrogen and oxygen, also occur as a parallel set of heterointermediates, $C_{m-1}H_{n-1}N$ and $C_{m-1}H_{n-2}O$. For example, phenylnitrene or pyridylcarbene, $C_6H_5N$, show ring contractions like phenylcarbene in the $C_7H_6$ series,[15] while formation of dibenzo-*p*-dioxin, by dimerization of $C_6H_4O$, is similar to the formation of anthracene from $C_7H_6$.[1a] This type of work as a further extension of Berthelot's ideas, particularly pioneered by Badger[5b,23] and Fields and Meyerson,[24] has preparative implications under FVT conditions.[1,2]

*** Since almost all combustion processes involve such species, the resulting polycyclic aromatics, *e.g.*, from modern traffic and cigarette smoke, are the most prevalent carcinogens.[26] Smoke formation from burning plastics, a major threat in fires, is a similar process.[27] The same basic reactions are operative in coal pyrolysis[28] (liquefaction), an area that has gained considerable momentum because of our need for non-petroleum-based fuels, as well as in waste incinerators that belch forth toxic pyrolytic condensates, including polychlorinated dibenzo-*p*-dioxins, in their fly ash.[29]

### 3. Pre-FVT preparations fit in the new fashion

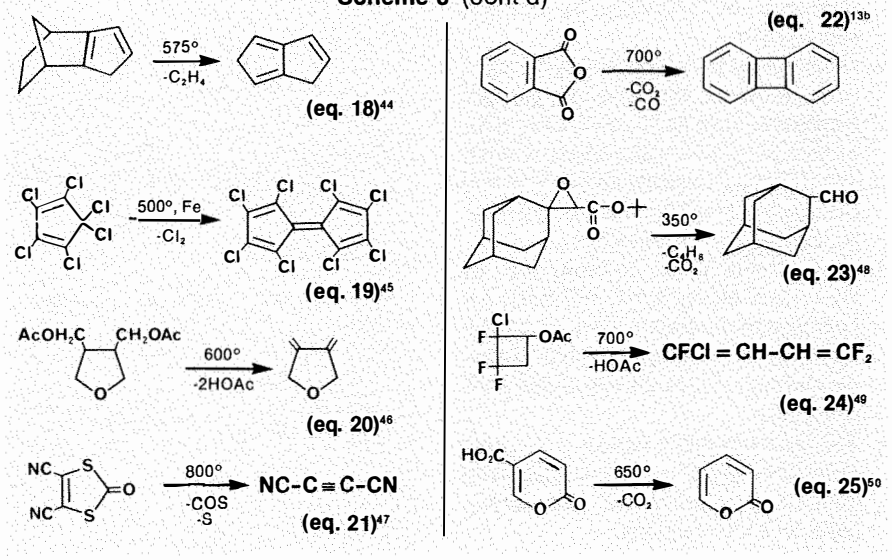
There are quite a number of useful preparations caused only by heat in the older literature, including examples in "Organic Synthesis."[3a] The index of Hurd's book[3] lists about 150 thermal preparations. A variety of examples, some already run under vacuum conditions, is shown in Scheme 3.

These reactions illustrate that the development of FVT to its present status as a method with unique preparative potential has been a gradual process. On the other hand, the initial development of FVT techniques is rooted in low-pressure/high-temperature gas-phase kinetic studies**** of organic free radicals.[13a,51] One[13c] of the modern originators[2,5b,13,51] of FVT noted that many people were using it for a long time without knowing it. New attention to old routes[53] was recently acknowledged by Brown,[2] with his estimate that Hurd's book[3] will remain relevant during the next fifty years. Most of the old pyrolysis reactions do proceed better under FVT conditions, *e.g.*, formation of pyrocoll, a cigarette smoke constituent[32] (eq. 3) *via* dimerization of azafulvenone,[1b,54] the Elbs reac-

direct trapping on IR cells[54,56] (eq. 3), photoelectron spectroscopy of 1,3-dithiol-2-ones[57] (eq. 21), and pyrolysis-mass spectrometry, *e.g.*, in aryne formation[58] (eq. 22), were developed for closer study of FVT intermediates. Although many new thermal reactions have been reported in the recent abundance of FVT articles,[1,2,12] the statement that many others are to be discovered[14a,20a] is still appropriate. However, since FVT has come to the forefront during the past decade, pyrolytic methods have regained their traditional position earned in the nineteenth century for the preparation of a multitude of structures.

**** Explicitly based on this work, a new process was developed for the manufacture of ethylene *via* selective oxidation of methane by chlorine at very high temperatures and exceedingly short contact times.[52]

**Scheme 3** (cont'd)




## *III. Selected FVT preparations*

### 1. Apparatus and generalizations

Essential to FVT reactions is that the starting compound be sublimed *in vacuo*, or sometimes in a reduced-pressure nitrogen flow,[22b] through a hot quartz tube connected to a liquid-nitrogen-cooled trap, as indicated in Fig. 1. Flow conditions may give different results, *e.g.*, recombination of reactive fragments,[1a] compared to low-pressure (<0.1mm) flash reactions. The vacuum ensures a short contact time that permits the high temperatures often required for complete, one-pass reactions. With the equipment shown, the products, free of contaminants, are collected in the trap without further experimental handling or, when not volatile, are deposited at the exit of the furnace in the bend of the quartz tube.[1a] Utilizing the same quartz tube, a trapping agent for capturing highly reactive species can be introduced (Fig. 2), or copyrolysis (Fig. 3) and recycle thermolysis experiments (Fig. 4) can be pursued.[1a]

In exploratory work, the following generalizations[1a] are helpful to judge if a compound is likely to undergo a clean rearrangement or fragmentation by FVT:

a. Multiple unsaturated and/or polycyclic structures mostly undergo either concerted or homolytic rearrangements, or retro fragmentations.
b. Heteroatoms (nitrogen, oxygen, silicon, phosphorus, sulfur, selenium) present in such systems, and polyhalogen com-

## Glassware for Flash-Vacuum Thermolysis

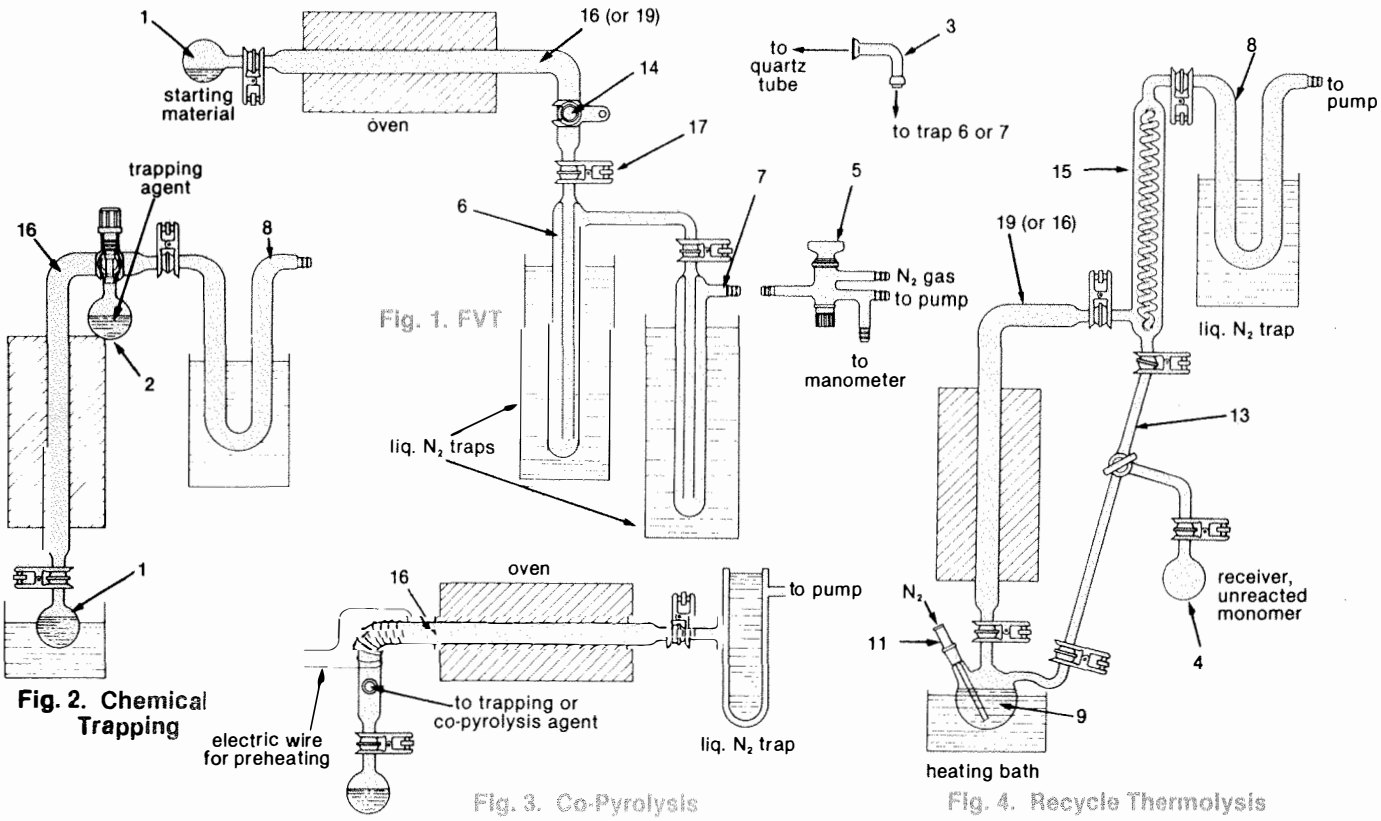



Fig. 1. FVT

Fig. 2. Chemical Trapping

Fig. 3. Co-Pyrolysis

Fig. 4. Recycle Thermolysis

pounds often engage in parallel, orbital-symmetry-controlled reaction patterns, expressed in a.

c. Compounds, preferably polycyclic and/-or unsaturated, that can lose gaseous fragments, such as $N_2$, CO, $CO_2$, $CS_2$, S, SO, $SO_2$, $CF_2$, $CH_2$, $C_2H_4$, $CH_2O$, and $(CH_3)_2CO$, usually give radical and carbene intermediates that can selectively rearrange to end-products.

d. Thermal elimination reactions (*e.g.*, of HCl, $H_2O$, HCN, ROH, RCOOH, dehydrogenation, dealkylation, dechlorination, ester, xanthogenate and sulfoxide pyrolysis) proceed nicely under FVT conditions.

e. The heteroaromatic part of a molecule frequently opens up to cumulene and quinonoid intermediates and participates in FVT reactions.

f. FVT reactions may produce a range of kinetic products of the same molecular formula, often accessible from different precursors, thus providing the intermediates that belong to the energy surface of a certain species.

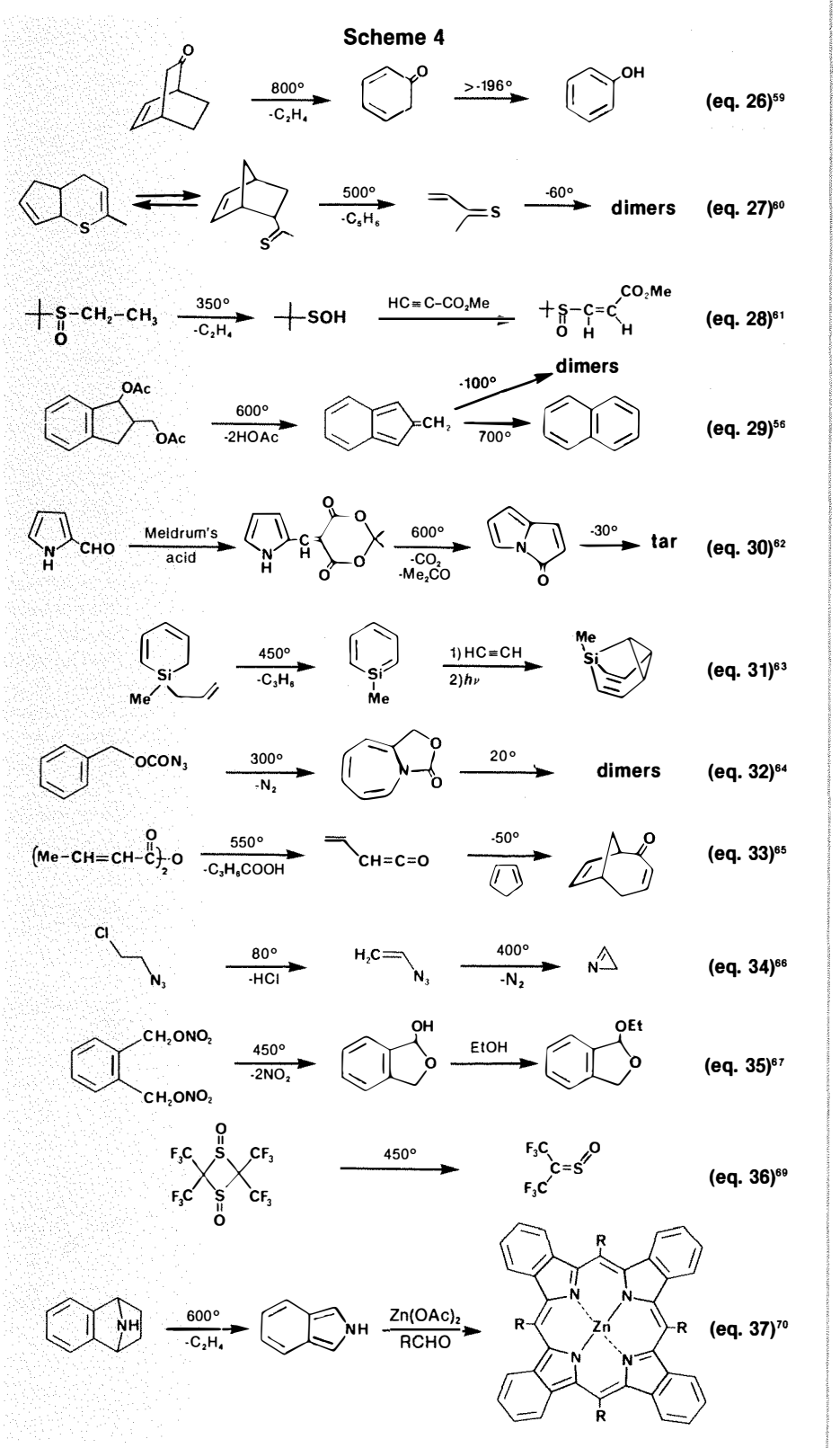
Thermal reactions like those in Scheme 3 reflect these rules. Reversibly, suitable precursors for a desired primary reactive fragment, for example, those in Scheme 2, can be formulated according to rules c and d. In the following sections, recent examples of widely diverging preparative FVT reactions illustrate the broad explorations anticipated by these rules. In addition, they are placed in a context to show some typical FVT aspects and synthetic strengths. Mechanistic rationalizations are omitted and can be found in the original papers.

## 2. Generation of labile and highly reactive compounds

Because of its intrinsic ability to trap the reaction products on a liquid-nitrogen surface, FVT is the method of choice for isolation of reactive compounds, *e.g.*, pentalene, fulvenallene, sulphene, isobenzofuran, quinodimethane, benzazete, oxetene, and many others.[1a] Scheme 4 shows some recent developments in this category. More examples appear in later schemes (*vide infra*).

The chemistry of most reactive intermediates, *e.g.*, that of pyrrolizin-3-one (eq. **30**), is largely unexplored. Their kinetic decay, *e.g.*, to keto tautomers (eq. 26), or to dimers (eqs. 27, 29 and 32) can now be studied. Synthetic use, however, looks like the most versatile option, as shown for *tert*-butylsulfenic acid (eq. 28), silatoluene [to silasemibullvalene (eq. 31)] and vinylketene (eq. 33). Phthalyl alcohol dinitrate pyrolysis (eq. 35) is a rapid method of preparation for the alkoxyphthalans, precursors to isobenzofurans.[67,68] An appealing example is isoindole[68] that, in one step, provides tetrabenzoporphyrins[70] (eq. 37).

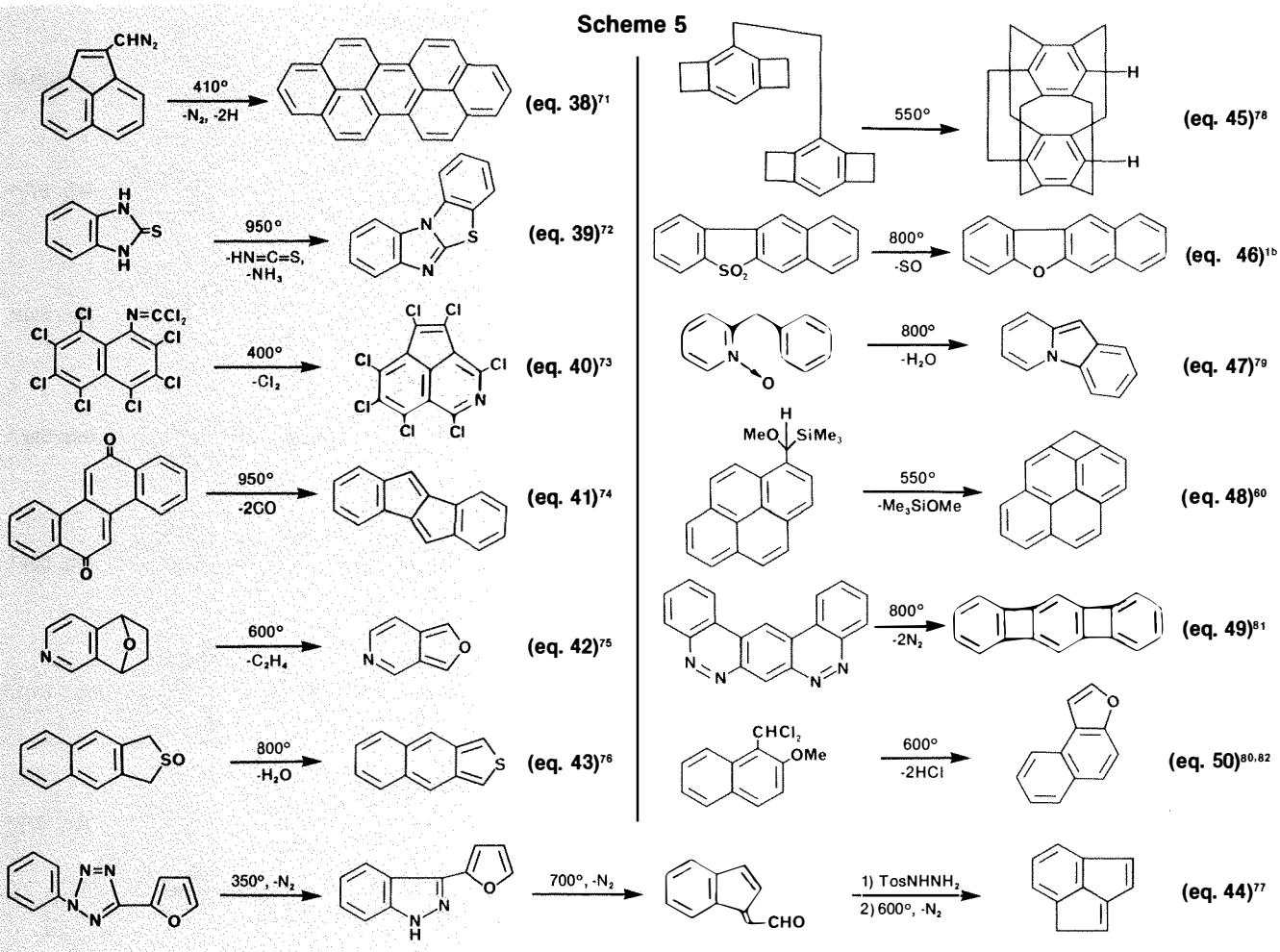
**Scheme 4**




## 3. Preparation of polycyclic aromatics and pseudoaromatics

The formation of polycyclic heteroaromatics was already associated with FVT (see II, 2) from their occurrence in coal tar.[23,25] FVT reactions are of preparative importance for an indefinite number of structures that belong to this group. The Elbs reaction, azulene and diphenylene formation (Scheme 3, eqs. 4, 12 and 22), is an example, as is the formation of isobenzofulvene and isoindole (Scheme 4, eqs. 29 and 37). Other entries to polycyclics are shown in Scheme 5.

## Scheme 5



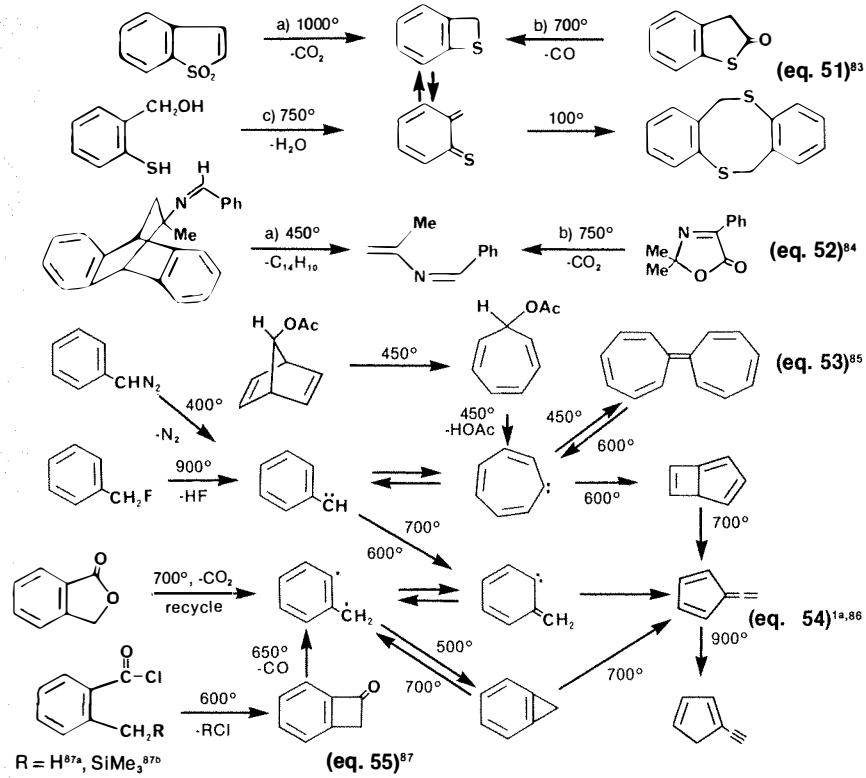

The reactions, all proceeding in fair to quantitative yields, can be run on gram scale in equipment shown in Fig. 1. FVT is often the shortest or even the only way to get to these products. Furopyridine (eq. 42) is a reagent for the preparation of condensed azaaromatics.[68] Eq. 44 shows, in a nutshell, the variety of possibilities with preparative FVT in three consecutive steps in the synthesis of a tricyclic [10] annulene system.[77] The cyclobutabibenzyl (eq. 45) for preparation of [2$_5$] (1.2.3.4.5) cyclophane was obtained *via* FVT steps as well.[78] Formation of *peri*-methanoarenes (eq. 48) involves particularly interesting rearrangements of arylcarbenes.[82]

### 4. Different structures that give the same intermediates

Certain intermediates and products have appeared to be accessible from rather different starting materials, when according to rules c and d, the same primary fragments are generated. Scheme 6 shows the formation of benzothiete[57] (eq. 51), azabutadiene (eq. 52) and $C_7H_6$ products[15] (eqs. 53, 54 and 55) *via* different routes.

Azabutadienes give further rearrangements at higher temperatures.[84a] The $C_7H_6$ species

## Scheme 6



dimerizes at lower temperature *via* cycloheptatrienylidene and is isolated as heptafulvalene[85] (eq. 53). Fulvenallene, the ultimate product of $C_7H_6$, has been obtained from at least eleven precursor compounds.[15] Its preparation from phthalide[86] (eq. 54) is an example of recycle thermolysis. Bicyclo[3.2.0]hepta-1,4,6-triene, ethynylcyclopentadiene, and benzocyclopropene are other products in the $C_7H_6$ energy surface[1a,15] (rule f). Similarly, very different starting materials yield species that constitute other energy surfaces, *e.g.*, azulene and naphthalene[1] (eqs. 1, 12, 29 and 71) of the $C_{10}H_8$ series, and benzocyclobutene[88a] (Schemes 2 and 7) of the $C_8H_8$ series.

### 5. Parallel reaction patterns with carbon- and heteroatoms

Benzo- and naphthocyclobutenones are conveniently prepared from *o*-methylaroyl chlorides[87] (eq. 55). FVT-induced 1,4-eliminations from *o*-substituted aromatics as in eqs. 15, 51c and 55, are more general, excellent preparations for a great variety of annelated four-membered ring systems (Scheme 7).

These reactions illustrate that carbon and hetero compounds often feature parallel product formation in FVT reactions (rule b) because of their predominantly nonionic, orbital-symmetry-controlled mechanisms.[93] Numerous intramolecular pericyclic reactions of acetylenic carbon and hetero compounds[94] fit into this context as well. Benzocyclobutenes and their analogs (Scheme 7) open up to their quinonoid forms[68] [*e.g.*, *o*-xylylenes (eq. 56)] which are highly reactive dienes in Diels-Alder reactions. They are frequently used in natural-product synthesis,[95] and are key intermediates in preparation of [2$_n$]cyclophanes[78,83c] (eq. 45), pyridinophanes[89] and tropoquinophanes.[96] Some members of the series, like *o*-quinone itself, *o*-quinone methide (eq. 15) and dimethylenedihydrofuran (eq. 58), exist only in the open form.[1b]

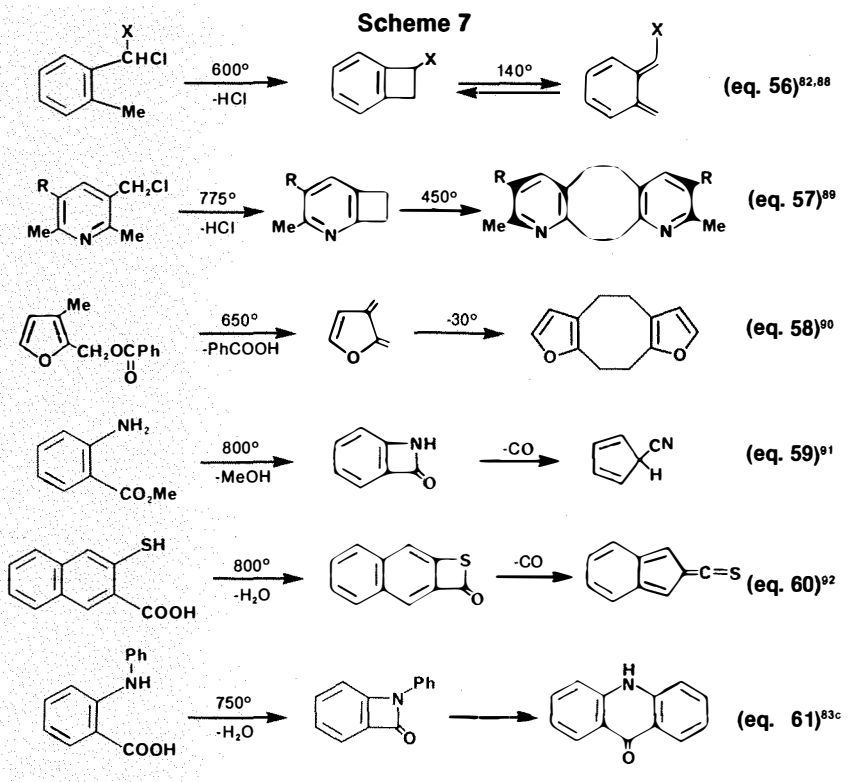
When not trapped, these systems dimerize[83c] (eqs. 51, 57 and 58) or trimerize (eq. 15). With the lactones,[92] thiolactones, and lactams, sequential decarbonylation occurs (eqs. 59 and 60), analogous to fulvenallene formation (eq. 55). Internal trapping of the primary 1,4-elimination product occurs *via* the open *o*-quinonoid form, with benzylidene derivatives being converted to anthracenes,[82] and *N*-phenylanthranilic acid to acridone (eq. 61). Likewise, the Elbs reaction (eq. 4) proceeds *via* tautomerization to the *o*-xylylene enol.[2]

### 6. Reactions with participation of aromatic rings

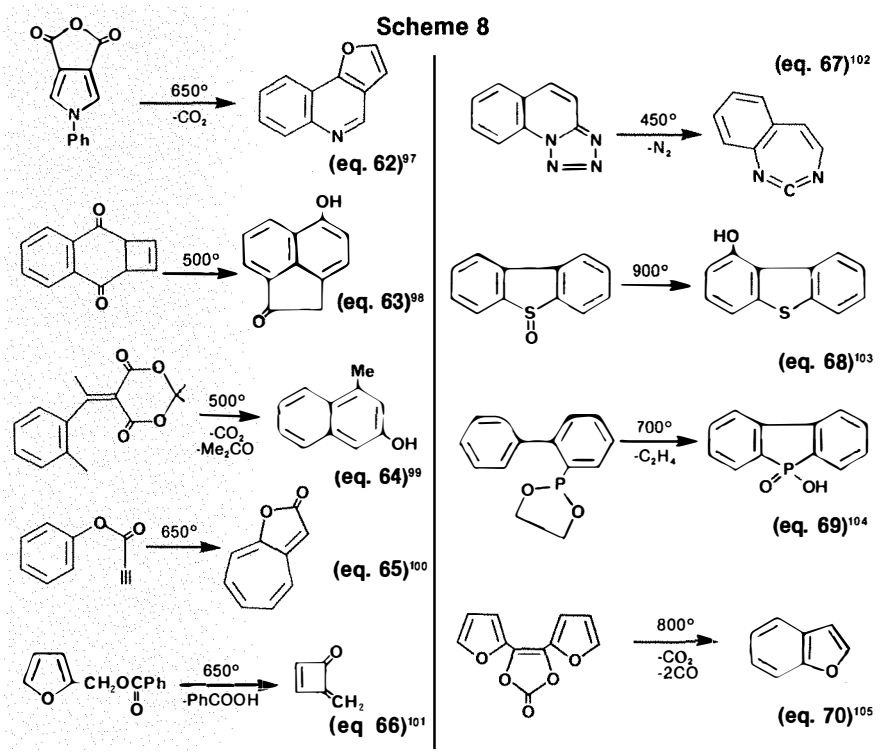
Participation of aromatic rings (rule e) as in eqs. 3, 4, 31, 32, 38, 40, 44, 47, 50, 54, 60 and 61 is very common. Some other preparations involving substitution, formation, or destruction of aromatic rings are given in Scheme 8.

FVT of both the Meldrum's acid derivative (eq. 64) and the propargyl ester (eq. 65) proceeds *via* internal trapping of transient methyleneketenes.[2] Methylenecyclobutenone (eq. 66) and the cyclic carbodiimide (eq. 67) are highly reactive intermediates that polymerize and dimerize on warming the cold trap. The preparation of 5-hydroxydibenzophosphole-5-oxide (eq. 69) involves intramolecular trapping of a highly reactive phosphonobenzene intermediate, a species that was also trapped by leaking methanol vapor into the pyrolysis tube (Fig. 2). The quantitative formation of benzofuran (eq. 70), like that of the

**Scheme 7**




**Scheme 8**



aldehyde in eq. 44 and methylenecyclobutenone (eq. 66), must proceed *via* a furylcarbeneallenylketene intermediate[101] that further decarbonylates.

### 7. Fragmentation *via* tautomers

In quite a few cases, a fragmentation pattern as expressed by rules c and d cannot be predicted at first glance from the structure of the precursor chemical, since equilibration to isomers or tautomers (rules a and b) occurs prior to decomposition. Loss of water in the Elbs reaction (eq. 4), in Cava's sulfoxide dehydration[68] (eq. 43), and from pyridine N-oxides (eq. 47), may proceed *via* a primary enolization step. A thio-Claisen rearrangement precedes retro-Diels-Alder reaction (eq. 27), while indazoles equilibrate before loss of $N_2$ (eq. 44) and sulfonesultine rearrangement[1b] explains elimination of SO (eq. 46). More examples are collected in Scheme 9.

In some cases, isomeric products can be isolated (eqs. 71, 74 and 76) and then fragmented at higher temperatures. Unstable valence tautomers of phenols or other thermodynamically less stable products occurring on energy surfaces usually obtained from designed precursors (eqs. 26, 29, 53 and 71), can sometimes be prepared directly by FVT of their stable forms (eqs. 73 and 74). A Claisen rearrangement[94] is the primary step in the decarbonylation, with scrambling of the nitrogen label of propargyl 4-pyridyl ether (eq. 72). Scrambling of the functional-group atoms as in eqs. 75, 76, 77 and 78 is typical of the whole group of carboxylic acid derivatives: anhydrides[2] (eqs. 6, 22 and 33), carbonates (eq. 70), amides and esters[112] and their thio analogs[112] (eqs. 21 and 51). Isonitrile-nitrile rearrangement is the nitrogen equivalent of the acetylene-vinylidenecarbene equilibration (Scheme 2). Trimethylsilyl groups (eq. 80) are being utilized as protecting and leaving groups in FVT synthesis.[114a,b] Allenyl ketones rearrange into furans.[114c]

### 8. Strategic applications of thermolabile groups

Among the reaction principles most frequently applied in synthetic schemes are the long known thermal eliminations,[7] often from acetates (eqs. 10, 11, 16, 20, 29 and 58) and retro-Diels-Alder cleavages of cyclopentadiene and anthracene derivatives[14c] (eqs. 27, 52a, 85 and 88).

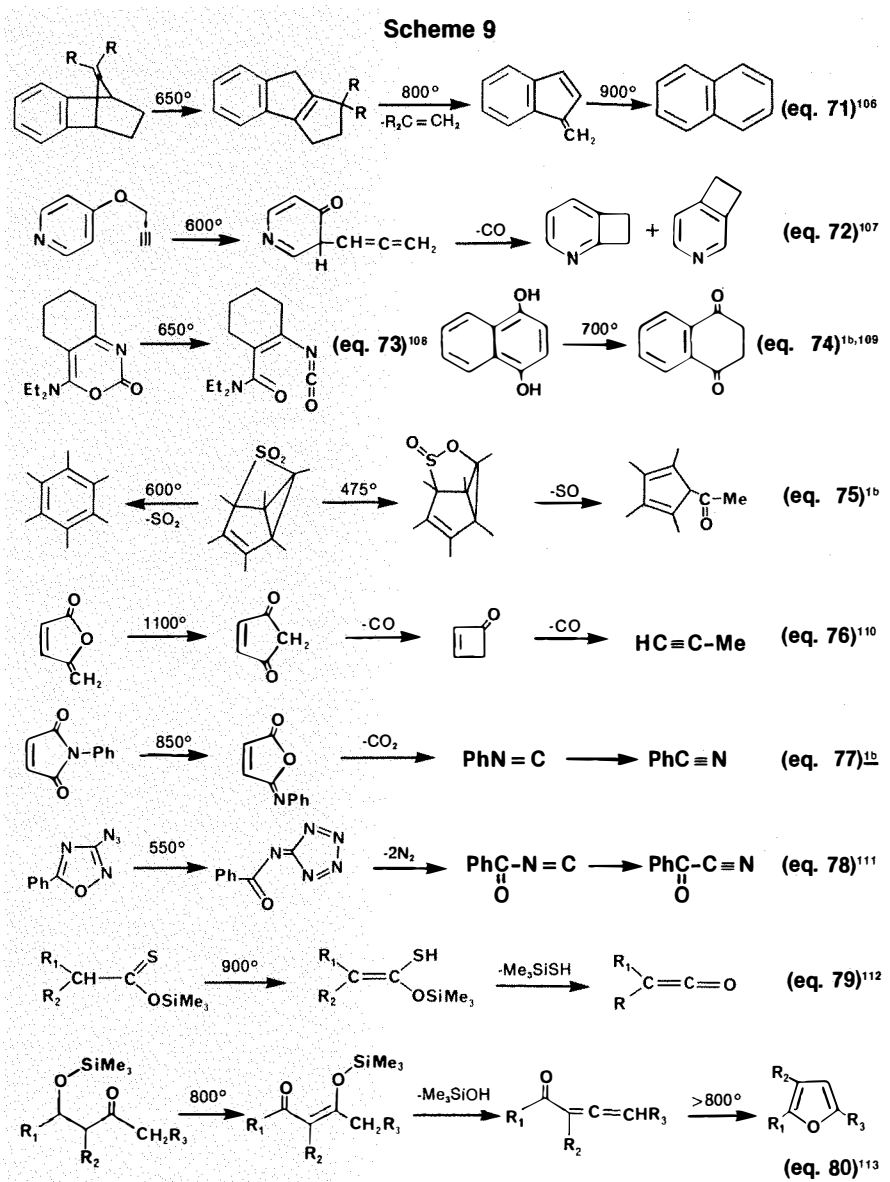
Other notable examples of broadly applicable thermolabile groups are the anions of tosylhydrazones[115] (eqs. 38 and 44), Meldrum's acid derivatives (eqs. 30 and 64), and oxazolones[102b] (eq. 52b) for the generation of carbene and nitrene intermediates.[20] The rapid development of cyclophane synthesis[78,83c] (eq. 45) utilizing sulfone pyrolysis[14d] (eq. 17) and the benzocyclobutene-*o*-quinodimethane equilibrium (eq. 56) illustrates the sometimes rather unpredictable preparative potential of FVT reactions. The reactions in Scheme 10 illustrate some other methodical FVT preparations.

The classic dimerization of carbon tetrachloride (Scheme 1) has been applied (eq. 81) to other dimerizations and co-dimerizations.[1a] Co-pyrolysis with haloforms and tetrahaloethylenes leads to insertion reactions with dichloro- and difluorocarbene.[125] The trimethylsilyl group was used as a protecting group (eq. 82) in preparation of cyclopentenone synthons[126] (eq. 85). Tosylhydrazones (eq. 83) are used for synthesis of strained olefins and anti-Bredt compounds.[120,127] Like other isonitriles and acetylenes, highly reactive organic fulminates (eq. 84) were obtained from isoxazolone cleavage, which is very much related to fragmentation of Meldrum's acid derivatives (eqs. 86 and 87). N-Acylimines were generated *in situ via* FVT, to be internally trapped in Diels-Alder (eq. 88) or ene cyclizations (eq. 89). The cycloreversion reaction in eq. 90 suggests a potential route for preparation of dodecahedrane.[123a] Cleavage of the labile peroxide bond has appeared to be selective under FVT conditions (eq. 91).

### 9. FVT steps in natural-product synthesis

The application of a pyrolytic step as in Scheme 1 has been used by many in natural-product synthesis. The retro-cleavage in eq. 90 is the key step for construction of the skeleton of the marine product capnellene, occurring in soft coral.[123b] FVT of 1,5-dimethyl-6,7-dioxabicyclo-[3.2.1]octane, a cyclic peroxide (eq. 91), gives access to the pheromone frontalin.[124]

**Scheme 9**



Relatively small molecules like pheromones[128] or fragrance substances are well suited to FVT because of their intrinsic volatility, but steroids[1a] and alkaloids[129] can also be flashed without difficulty. The reaction in eq. 9 for making 19-norsteroids is a commercial process. FVT principles have been applied for a long time to terpenes in the fragrance industry[130] and commercially used for supplying starting materials like myrcene from β-pinene (eq. 8). Scheme 11 shows some examples for further assessment of the possibilities with FVT reactions in natural-product synthesis.

Use of FVT in the synthesis of natural products does not necessarily mean that the product is formed in the final step as in eqs. 96 and 97. The sequence to the marine sesquiterpene sinularene (eq. 93) includes two acetate eliminations within fourteen steps.

Three essentially different approaches can be distinguished concerning application of FVT steps in total synthesis:

i) Reactive intermediates generated by separate FVT reactions are used as synthons to build up a structure.

ii) A desired functionality is generated in a system *via* a thermal reaction principle, sometimes with the intention to trap it in subsequent intramolecular cyclizations.

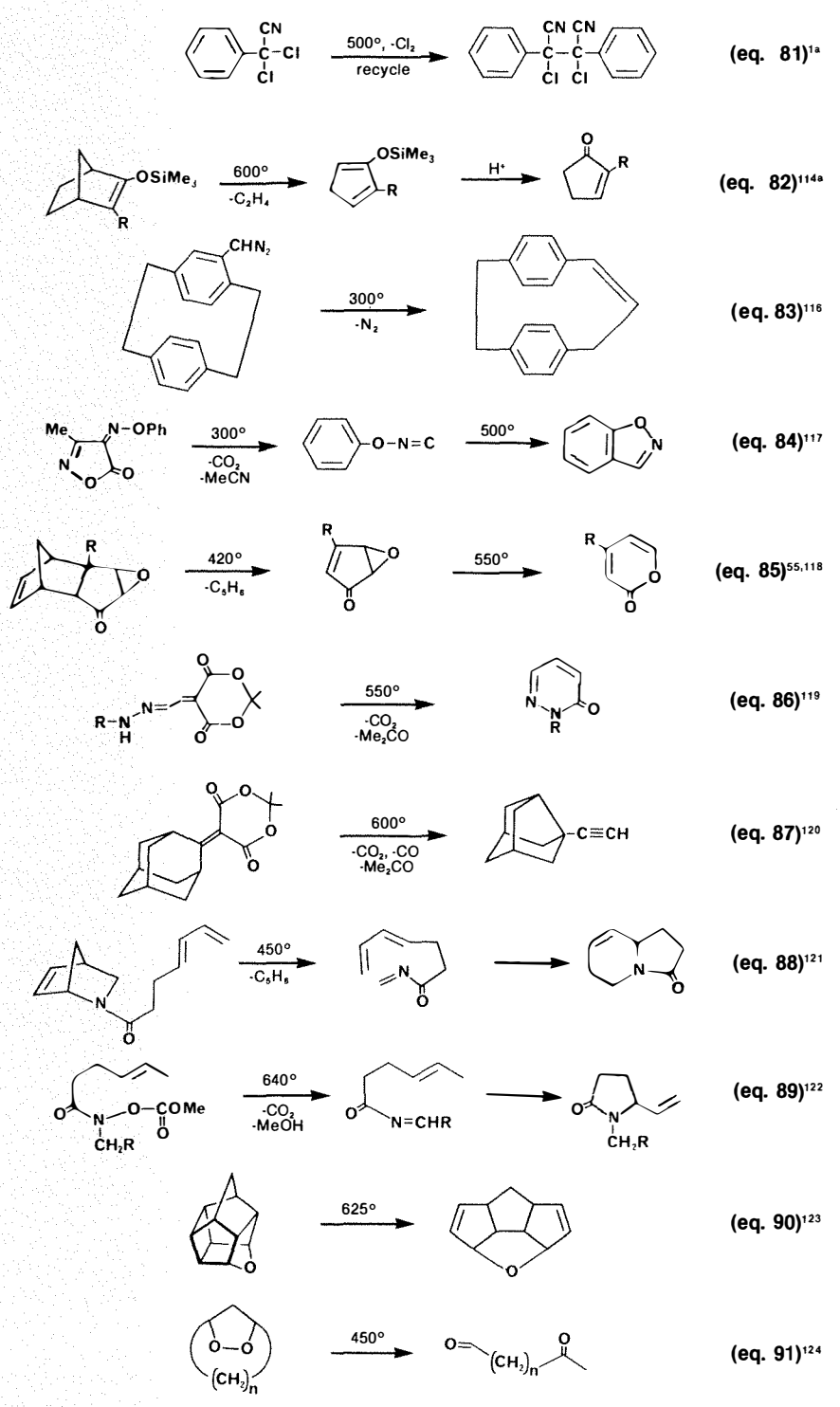
iii) A molecule is modified with a thermolabile group to enable certain synthetic transformations after which the modified system is regenerated by flashing off the protective group.

Synthesis of daunomycinone (eq. 92) *via* isobenzofuran[67,68] generated *via* α-pyrone (eqs. 25 and 85) is a type i reaction. A wide range of reactive intermediates (*vide supra*), in addition to long known examples such as carbon suboxide and ketene[34] (eqs. 6 and 7), have now become available for synthetic exploration.

The steroid and terpene routes in eqs. 94 and 95 are, like reactions in Scheme 8, and 88 and 89, type ii examples with internal trapping. This principle is widely applied with *o*-quinodimethanes[68] (eq. 94) and alternatively with isobenzofurans[137] for construction of polycyclic natural products.[95b] The hetero analogs in Scheme 7 are likewise suited as intermediates in similar sequences.[95b]

The preparation of the antibiotic pentenomycin (eq. 96) illustrates the idea[128] formulated in approach iii, although strict differentiation between ii and iii is not always possible, as can be seen from the elegant and rapid preparation of long-chain insect pheromones (eq. 97), with simultaneous cleavage of the protecting group and generation of the diene part.

**Scheme 10**




## IV. Conclusion

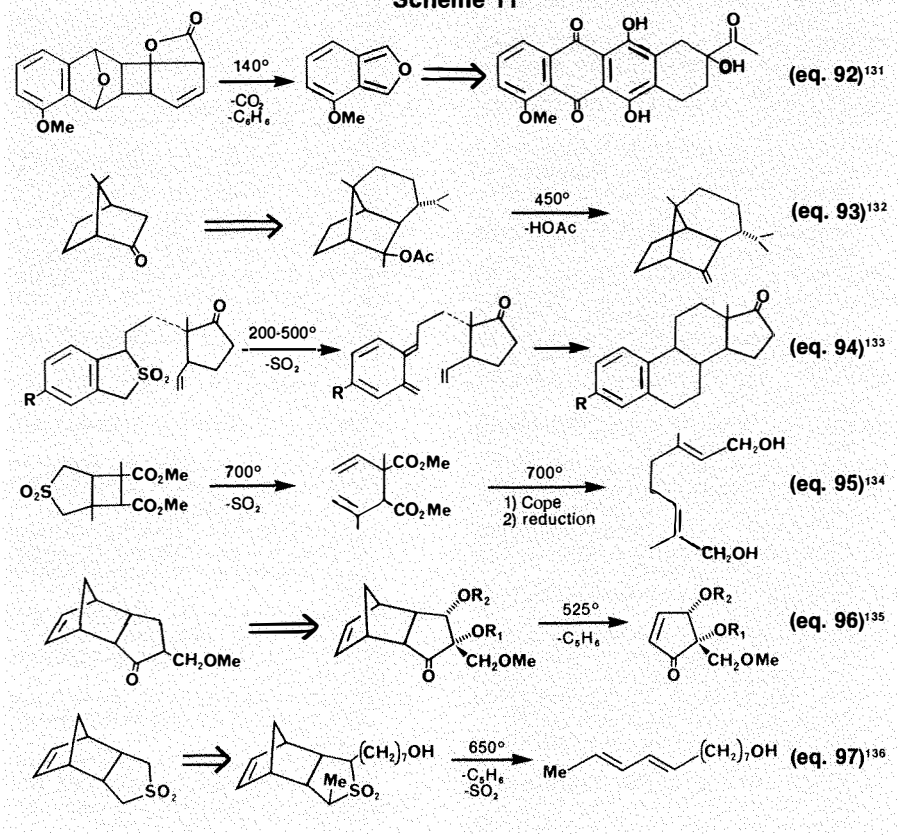
Gas-phase reactions, in the modern form of FVT, have been rediscovered and revalued for their unique synthetic strength and experimental simplicity. A main charm of FVT is that highly reactive intermediates, worthy for the fundamental understanding of the reactivity of organic structures, can be isolated. They are widely applicable in synthesis as well, although this develops only gradually. Fulveneallene (eq. 54), for example, has hardly been used, and benzazete was used as synthon only ten years after it was first generated.[138] The intrinsic pyrolytic build-up of non-volatile condensates in combustion processes proceeds *via* reactive intermediates. Therefore, FVT offers a means for studying reaction steps in

such areas, including incineration or recycling of waste materials.

In this review, typical FVT preparations were collected and classified with the aim to promote synthetic application. A certain similarity in reaction patterns between carbon and hetero compounds unifies different classes in these primarily non-ionic gas-phase reactions. FVT is mechanistically related to mass spectrometry[139] and plasma chemistry.[140] Synthetic use of FVT is sometimes only routinely mentioned,[141] and therefore hard to spot, in the rapidly growing stream of FVT publications. Thus, it becomes exceedingly difficult to assimilate and generalize all the work, although this will remain essential in order to get FVT more involved in organic chemistry.

Nevertheless, FVT is still in the exploratory phase and chemists who engage in it will discover new reactions. Application of these results to synthetic goals will broaden the scope and make it even more challenging.

**Scheme 11**





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### *About the Author*

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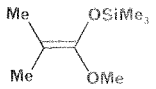
At the AKZO Corporate Research Department, Dr. Wiersum did pioneering work in the area of flash-vacuum thermolysis, with special emphasis on synthetic utility. His research activities include radical chemistry to study polymer-degradation mechanisms in relation to polymer additives as flame retardants, polymerization initiators, antioxidants, and poly(propylene) degradants.

## *Catalyst for Group-Transfer Polymerization*




**Methyl trimethylsilyl dimethylketene acetal** {[(1-methoxy-2-methyl-1-propenyl)-oxy]trimethylsilane, MTDA} has a history of interesting organic-chemical applications. For example, MCPBA oxidation followed by desilylation yields methyl $\alpha$-hydroxyisobutyrate,[1] while singlet oxygenation and desilylation give the $\alpha$-hydroperoxy ester.[2] **MTDA** also undergoes $\alpha$-tertiary alkylation under mild conditions (*tert*-alkyl chloride, zinc chloride catalyst, $CH_2Cl_2$).[3]

Undoubtedly the most exciting chemistry of **MTDA** is its use in a recently revealed technique termed Group-Transfer Polymerization (GTP),[4] widely reported in the chemical news.[5] GTP of $\alpha,\beta$-unsaturated carbonyl compounds (*e.g.*, methyl methacrylate) with **MTDA** yields a "living polymer." The molecular weight of the polymer is controlled by the **MTDA**/monomer ratio, and the molecular weight distribution falls within a narrow range. GTP with **MTDA** represents a major breakthrough in polymer science.[5]

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# Synthetic Routes to Cyclopentanoid-Fused Unnatural and Natural Products

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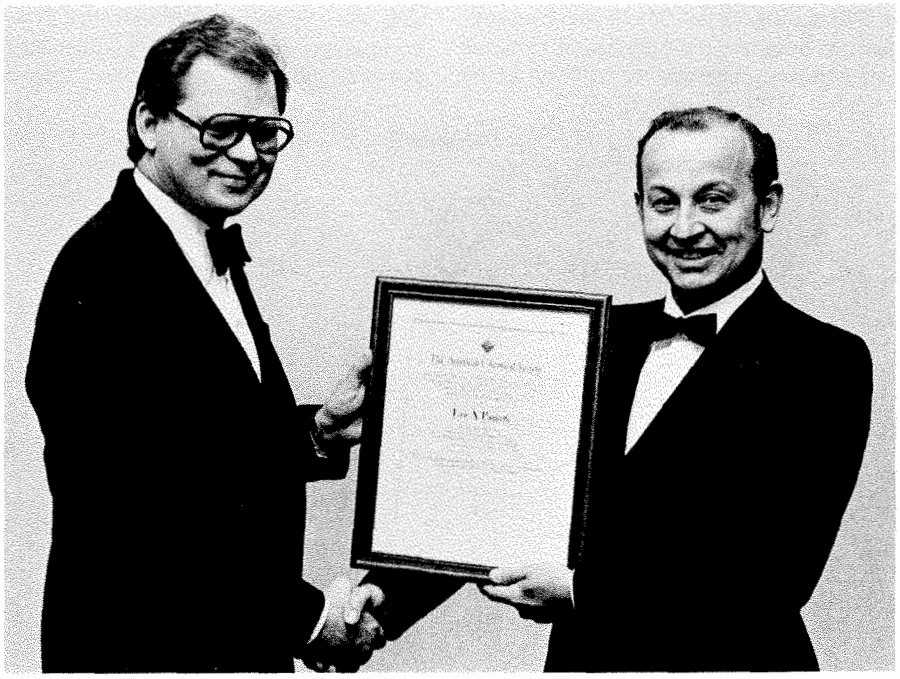
Some time ago, we pinpointed as synthetic goals a wide range of di-, tri-, and higher cyclopentanoid hydrocarbons of theoretical interest. In setting these targets, our objectives were to expand the reach of organic methodology and to achieve understanding of the chemical and physical properties of unusual molecular constructs and $\pi$ networks (in polyunsaturated systems). As results began to emerge from these investigations, it gradually became clear that an increasing number of fascinating new natural products featuring fused five-membered rings were being isolated world-wide from terrestrial and marine sources. The simultaneous pursuit of these targets proved equally tantalizing, especially because the necessary prospect of developing "state-of-the-art" synthetic ventures was perceived in both arenas. As matters have turned out, the protocols successfully devised by us in the unnatural and natural product fields show little, if any, formal similarity. Moreover, the considerable ingenuity displayed by the many other investigators involved in parallel endeavors is testimony to the rich harvest of new reactions that the recent effort in polyquinane chemistry[1] has brought forward. As the present article unfolds, a selection of achievements realized by my students will be outlined with special emphasis given to the key strategy elements deployed.

## Molecules of Theoretical Interest

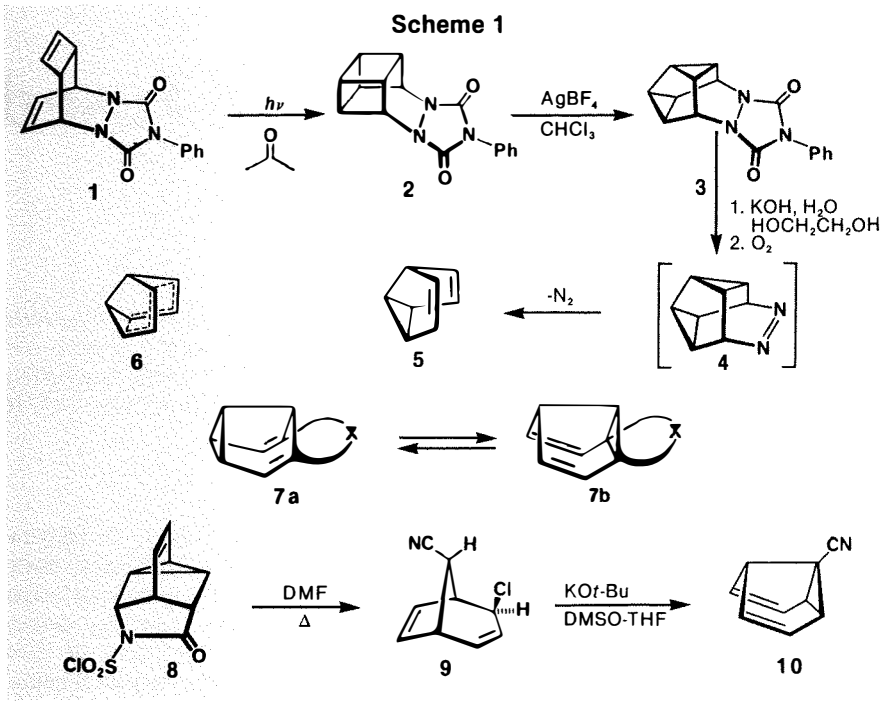
The strain imposed on the divinylcyclopropane substructure in semibullvalene (**5**) is such that the activation energy to degenerate Cope rearrangement is quite low (5.5 kcal/mol).[2] With the advent of molecular orbital calculations signaling the unusual possibility of attaining a delocalized ground state species (**6**) upon proper substitution of its nucleus,[3] a convenient procedure for gaining access to semibullvalenes on a preparative scale was sought. The best existing method at the time involved photorearrangement of barrelene[4] and was not of sufficiently broad scope. The prior elusiveness of these systems was obviated by taking advantage of the facile Ag(I)-promoted valence isomerization of cubane derivatives, a remarkably general process previously uncovered in this laboratory.[5] To arrive at the parent hydrocarbon, *N*-phenyltriazolinedione was added to cyclooctatetraene dibromide and the Diels-Alder adduct was debrominated to give **1** (Scheme 1). Following triplet-sensitized photocyclization to **2**, access to **3** was gained by exposure to $AgBF_4$ in chloroform.[6] The sequence was completed by saponification and air oxidation. The azo compound so formed (**4**) spontaneously decomposes to **5**.

This strategy is amenable to the preparation of many (though not all) monosubstituted semibullvalenes[7] (in optically active form if desired[8]) and 2,8-bridged derivatives such as **7**.[9,10] When none of these substances gave evidence of neutral homoaromaticity, attention was directed to preparation of the 1(5)-cyano derivative (**10**) which had escaped us so far. The serviceable route which was devised took advantage of the skeletal reorganization that occurs on uniparticulate electrophilic[11] additions to barrelene. When chlorosulfonyl isocyanate is involved, **8** results. Heating **8** to 75-95 °C in dimethylformamide provided **9** which was readily cyclized in strong base.[12] The beautifully crystalline **10** was analyzed by X-ray methods and shown to



*Professor Leo A. Paquette (right) receiving the A.C.S. Award for Creative Work in Synthetic Organic Chemistry, sponsored by Aldrich, from Dr. Irwin Klundt, vice-president of Aldrich.*

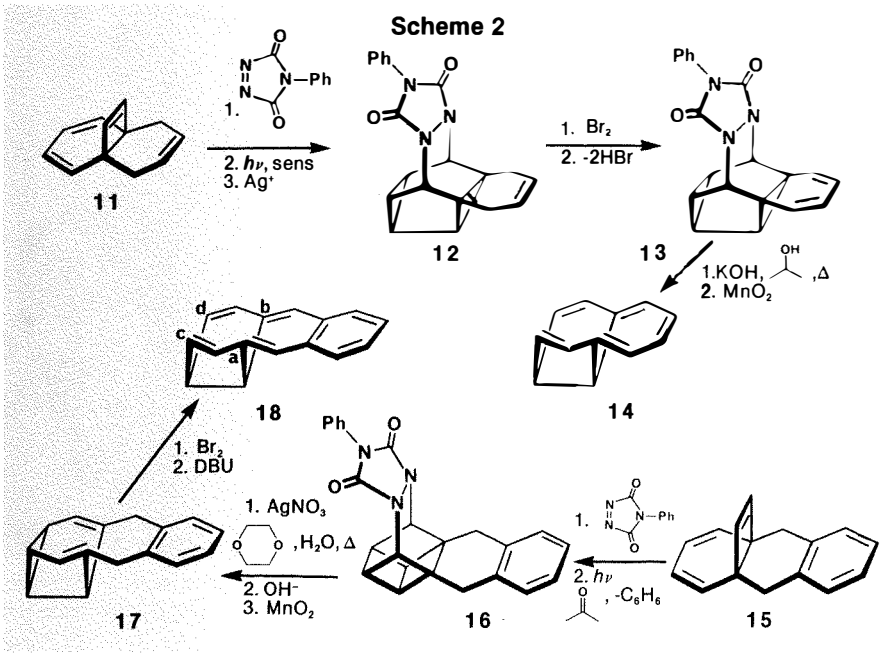
**Scheme 1**



consist wholly of the indicated tautomer.[12,13] Reduction of the activation energy of a Cope rearrangement to a negative value has yet to be realized.[14]

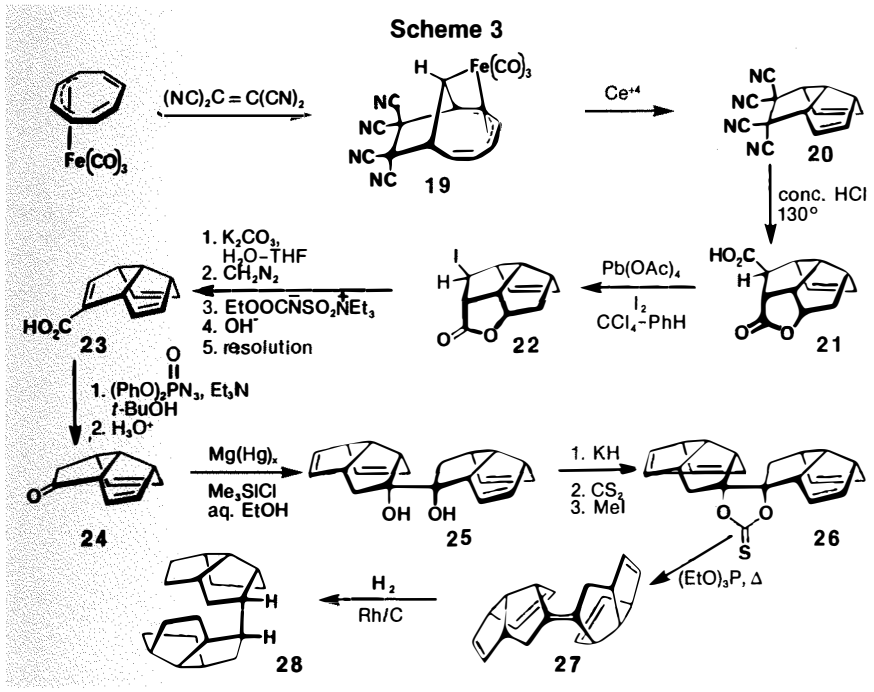
The reaction sequences in Scheme 1 are illustrations of the principle that prearrangement of carbon-carbon bonds followed by their controlled intramolecular translocation can lead expeditiously to new structural networks. Through proper selection of substrate frameworks, it has proven possible to utilize this methodology for inspection of those delicate factors responsible for homoaromatic character (Scheme 2). Following Diels-Alder addition of *N*-phenyltriazolinedione to propellatetraene **11** and subsequent conversion to **12** by photochemical [2+2] cyclization and Ag(I)-induced isomerization, a bromination-dehydrobromination sequence was used to generate **13**. Removal of the urazole ring as before was accompanied by electrocyclization and formation of the bishomo[10]annulene **14** known as elassovalene.[15] In order to confirm the conclusion arrived at on the basis of extensive spectral evidence that **14** possesses some degree of homoaromatic character in its bridged cycloheptatriene unit, the crystalline benzo derivative **18** was comparably synthesized and subjected to X-ray analysis.[16] By this means, it proved possible to demonstrate that the internuclear distance *a-b* (2.44 Å) and the enforced p orbital cant at these centers are adequate to foster a non-negligible level of interaction. On the other hand, the gap between carbon atoms *c* and *d* (2.54 Å) is too large to expect meaningful orbital overlap. Prior to this study, the attitude was pervasive that related molecules, 1,6-methano[10]annulene being the most widely known, did not enjoy homoconjugation in the central portion of their structures. In the intervening years, we have been pleased to see that our viewpoint has been generally adopted.[17]

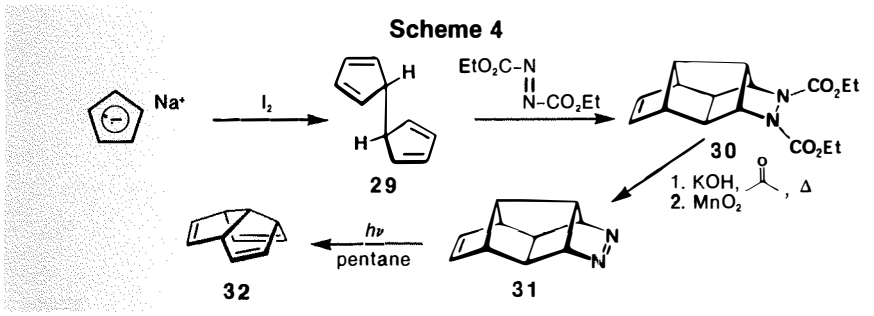
**Scheme 2**

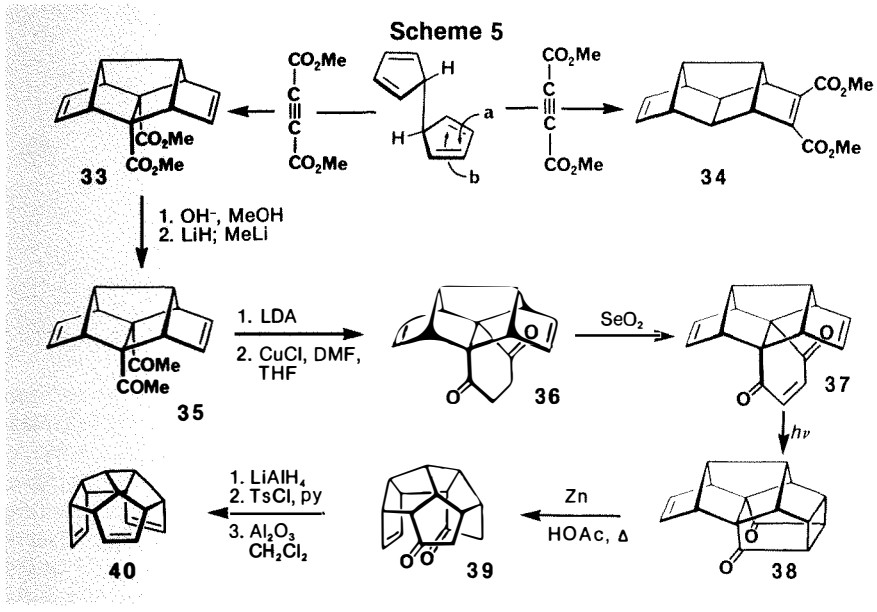


During an examination of the response of cyclooctatetraeneiron tricarbonyl derivatives to electron-deficient dienophiles of various types,[18] we noted that tetracyanoethylene acted in a unique fashion to deliver $\sigma,\pi$-bonded complexes such as **19** (Scheme 3).[19] When it was discovered that ceric ion oxidation of **19** gave **20**, its subsequent conversion to triquinacene-2-carboxylic acid (**23**) was developed.[20] Our interest in **23** was fueled by its ease of resolvability and ready conversion to (+)-2,3-dihydrotriquinacen-2-one (**24**) of assignable absolute configuration.[21] With the availability of (+)-**24**, it was possible to contemplate the dimerization of two triquinacene halves as a prelude to dodecahedrane construction. Pinacolic reduction of the enantiomerically pure ketone proceeded expectedly with *exo,exo* carbon-carbon bond formation to deliver necessarily the single diastereomeric diol **25**.[22] Conversion of **25** to its thionocarbonate and treatment with hot triethyl phosphite set the stage for exhaustive catalytic hydrogenation and isolation of *dl*-bivalvane (**28**). Alternative two-fold dehydration of **25** with phosphorus oxychloride in pyridine furnished *dl*-bistriquinacene.[23] For all practical purposes, any expectation that **28** might be coaxed into five-fold dehydrogenation was dismissed upon X-ray analysis.[24] In the solid state, the two structural halves are positioned as remotely from each other as possible to avoid non-bonded steric interactions. For comparison, the conformation provided in the illustrated formula is maximally congested.

During the period of our interest in triquinacene chemistry, we took pause to determine whether the unusual cup-shaped geometry of this triene, with its p$\pi$ orbitals projected toward the center of the concave face, would give rise to measurable homoaromaticity. X-ray studies conducted on **32** at 90K showed the non-bonded sp$^2$ centers to be separated by 2.533 Å, a gap seemingly prohibitive of homoconjugative interaction.[25] While photoelectron spectroscopic data ($\beta$ = 0.35-0.4 eV) proved inconclu-




sive,[26] circular dichroism measurements on (+)-(1*R*,4*S*,7*R*,10*S*)-(2-$^1$H)-triquinacene and (–)-(1*S*)-2-methyltriquinacene were consistent only with a simple independent-systems model wherein no electron exchange between the three olefinic chromophores was assumed.[27]

This series of experiments provided the impetus for the design of a more spherical molecule having an improved geometric arrangement for effective cyclic six-electron pp-$\pi$ overlap. The highly convex topology of $C_{16}$-hexaquinacene (**40**) with its three symmetry planes intersecting a threefold rotation axis was considered unrivaled. The efficient synthesis of this rather esoteric hydrocarbon that was ultimately realized had its genesis in a four-step conversion of sodium cyclopentadienide to triquinacene which was being developed at roughly the same time (Scheme 4). The observation that $C_5H_5^-$ could be dimerized to thermally sensitive 9,10-dihydrofulvalene (**29**) with iodine had previously been made.[28] Subsequent addition of diethyl azodicarboxylate triggered the all-important domino Diels-Alder sequence wherein four new $\sigma$ bonds are formed to produce **30**.[29] Following successful reduction to practice of this novel polycondensation concept, it proved an easy matter to achieve conversion to **31**. Irradiation of this azo compound through Pyrex provided triquinacene as the end result of tandem nitrogen extrusion and cleavage of a central C-C bond.

In a generalized sense, the domino Diels-Alder reaction involves initial intermolecular [4 + 2] cycloaddition of a dienophile to a 1,3-diene moiety, subsequent involvement of the newly formed olefinic center in intramolecular [4 + 2] bonding, and continuation of this sequence if structurally permissible.[30,31] A related cyclocondensation pathway requires that the dienophile be originally acetylenic and proceeds by capture of this reagent between the two diene components. Two-stage cyclizations of this type have been termed pincer Diels-Alder reactions.[29b,30,32] In the specific case involving **29** and dimethyl acetylenedicarboxylate, attack along the *a* coordinate ultimately provides "pincer" product **33** while use of reaction coordinate *b* affords "domino" product **34** (Scheme 5).[29b,30] The formation of these diesters in approximately equal amounts suggests that initial $\pi$ complexation may offset the steric impedance to dienophile approach from the *a* direction.

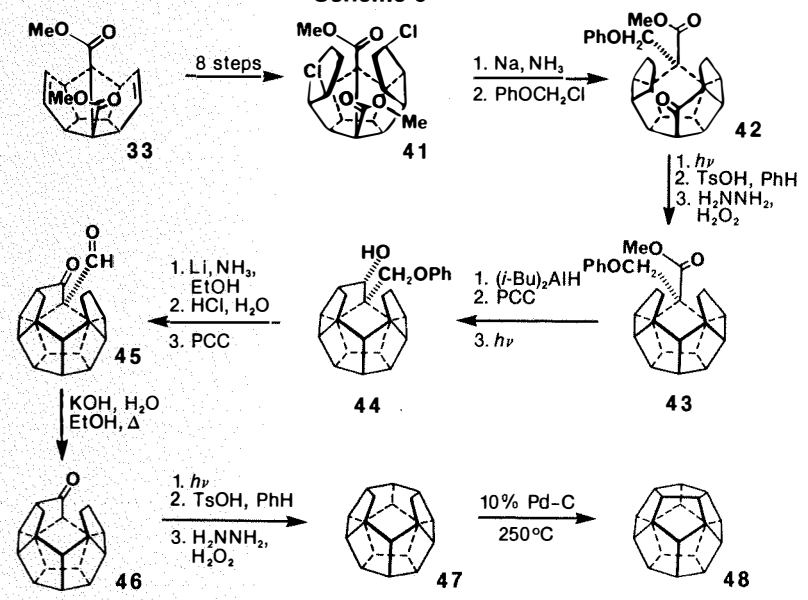
Although **33** is hexacyclic, its five-membered rings are not properly arrayed relative to those in **40**, and some level of structural reorganization becomes necessary. Also, two additional carbon atoms must be inserted before the two systems can be related. These goals were realized by conventional formation of diketone **35** followed by cuprous chloride-promoted coupling of its dienolate.[33] In order to set the stage for more considerable operations, two additional changes were now effected. First, **36** was oxidized with selenium dioxide to **37**. Next, this trienedione was energized photochemically and converted to **38**. Once cyclobutane ring formation had occurred (note that $C_{2v}$ symmetry of **37** causes the two excited-state bonding options to deliver

a single caged diketone), two strained σ bonds become properly disposed in a geometric sense for stereoelectronically facilitated reductive cleavage. As a direct result of this near ideal alignment, heating **38** with zinc in acetic acid cleanly delivered **39**. This product already adopts the spherical contour and C-C connectivities of our target molecule into which it was transformed in three laboratory steps. Disappointingly, however, X-ray crystal structure analysis and the electronic properties of **40** have ruled out the presence of homoaromatic character in this triene.[34]

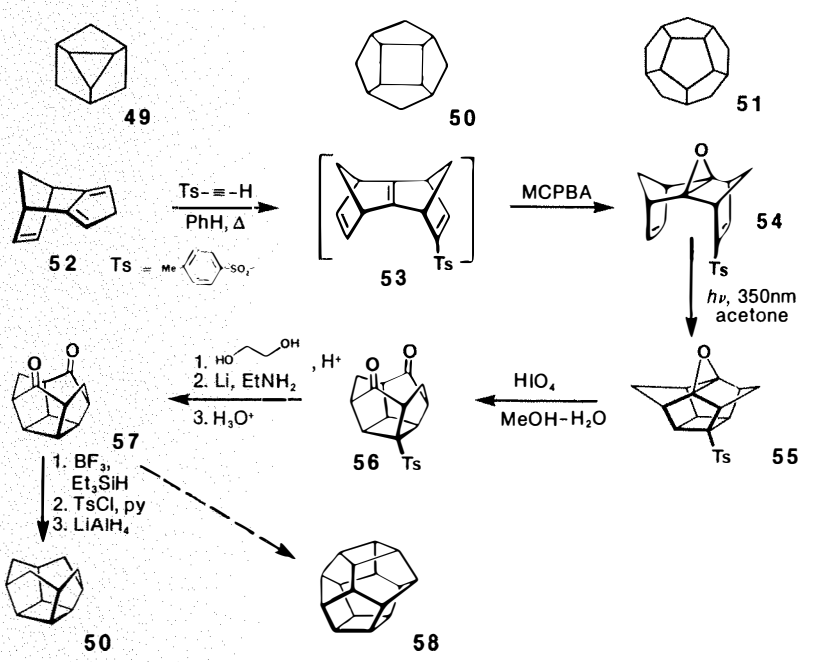
It will not be lost upon the reader that diester **33**, viewed from a different perspective (Scheme 6), can be considered to be a potential "cornerstone" precursor to the long-sought dodecahedrane molecule.[35] In point of fact, sequential application to **33** of Trost's spiroalkylation methodology,[36] Eaton's acid-catalyzed spirolactone rearrangement sequence,[37] and bislactone cleavage with methanolic hydrogen chloride gave the pivotal dichloro diester **41**.[38] We were now especially interested in resolving the question of how best to coax **41** into framework C-C bond formation. The most formidable component of this objective was the implementation of synthetic maneuvers that would lead to products substantially more strained than their precursors. We did not doubt that dodecahedrane lies in an energy well. However, its mono-, di-, and tri-*seco* derivatives do embody impressively high levels of non-bonded steric strain.

Under the influence of sodium in liquid ammonia, **41** experiences a splendid reduction-alkylation sequence to generate a dienolate,[39] treatment of which with one equivalent of chloromethyl phenyl ether yields **42**.[40] In this way, the *endo* orientation of the ester carbonyl carbon was guaranteed. Since we had earlier established the inefficacy of $S_N1$ and $S_N2$ processes with such molecules, the use of free-radical-mediated bond formation was mandated. Thus, light-induced ring closure at the ketone site in **42** (ester groups are generally not photoactivated), dehydration of the resulting tertiary alcohol, and diimide reduction delivered tri-*seco* ester **43**. While this intermediate clearly possesses many of the desirable structural features being sought, its opposed methylene groups remain unfunctionalized. After some preliminary studies, the decision was made to defer this potentially complex issue to a later stage. Following reduction of **43** to the aldehyde level, photocyclization was effected as before. Sequential Birch reduction, acid hydrolysis, and pyridinium chlorochromate oxidation of **44** made keto aldehyde **45** cleanly available. With arrival at **45**, the acquisition of hydrocarbon **47** was made possible by retro-Claisen cleavage and three-step interlacing of the penultimate bond. The final step was accomplished by catalytic dehydrogenation at elevated temperature.[40] Scheme 6 is noteworthy because of the central position played by homo-Norrish excited-state reactions in the cumulative elaboration of a fused polycyclopentanoid assembly.

**Scheme 6**




**Scheme 7**




The unusual hemispherical topologies of certain $(CH)_{2n}$ polyhedral systems such as **49-51** are also aesthetically appealing. Several years ago, Nickon[41] and Garratt[42] succeeded in devising routes to [3]peristylane (**49**), and Eaton's group was responsible for the design of an elegant pathway to [5]peristylane (**51**).[43] The challenge of preparing the third member of this set has recently been met.[44] Admittedly, it was our special familiarity with the intricacies of π-facial stereoselective Diels-Alder additions to tricyclo[5.2.1.$0^{2,6}$]deca-2,5,8-triene (**52**) that dictated our approach. As with other dienophiles,[45] **52** entered into bonding with *p*-toluenesulfonylacetylene essentially completely from the below-plane direction (Scheme 7). Direct epoxidation of **53** delivered **54**, photocyclization of which in

acetone solution with 350-nm light proceeded efficiently. The action of periodic acid on **55** gave **56** and marked arrival at the [4]-peristylane framework. Following conversion to diketone **57**, its anticipated pouch-shaped ground-state conformation was confirmed by X-ray analysis.[46] The relative proximity of the carbonyl groups necessitated that stepwise reduction be employed to arrive at **50**.[44] Possible schemes for converting **57** into the spherical hydrocarbon **51** are currently under investigation.

## Molecules of Natural Origin

One need only survey the recent developments in terpene chemistry to recognize that nature has seen fit to incorporate carbocyclic five-membered rings into many of its end products. Gymnomitrol (**59**),[47,48] quadrone (**60**),[49,50] retigeranic acid (**61**),[51] pleuromutilin (**62**),[52,53] ingenol (**63**),[54] and ginkgolide A (**64**)[55] constitute representative examples (Scheme 8). In certain cases, the structural complexity arises from the manner in which various rings are interlocked. In others, such as **62**, where seven of the eight stereogenic centers reside on the medium ring, stereochemical complexity is most telling.

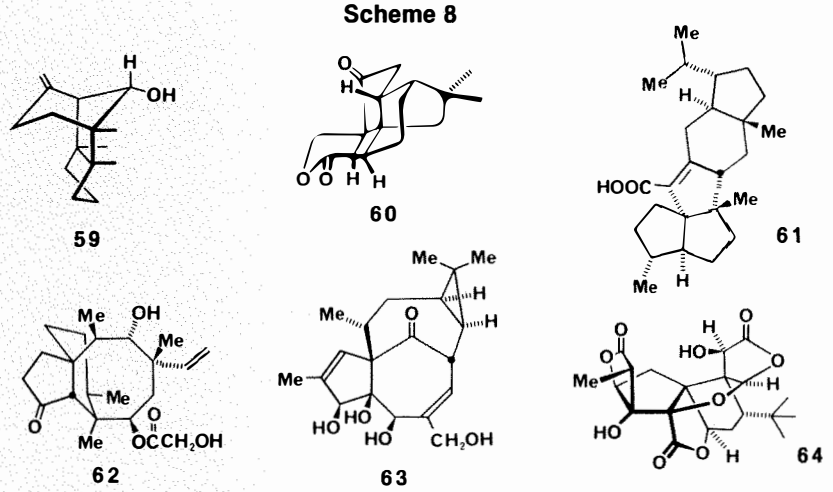
Our own approach to the architectural problems posed by these and related molecules has been to focus on potentially general methods of bond construction while simultaneously overcoming obstacles as they surface. The four major thrusts to be exemplified are: (a) five-ring annulation; (b) oxyanionic chemistry; (c) Claisen rearrangement methodology; and finally (d) photo-induced bond switching.

As a means of setting the stage for the elaboration of isocomene (**70**),[56] one of the several interesting triquinanes recently isolated,[1] we chose to add the Grignard reagent of β-bromopropionaldehyde ethylene ketal to **65** in Marfat-Helquist fashion[57] (Scheme 9). The ultimate intent was to effect intramolecular Prins closure within unsaturated aldehyde **67**. Because this expectation was efficiently realized, we made the decision to utilize a comparable strategy for arrival at pentalenene (**76**).[58] However, the improved receptiveness of **71** to the conjugate addition of lithium bis(3-butenyl)cuprate prompted initial introduction of the four-carbon chain and its later segmentation by ozonolysis (Scheme 10). As before, installation of the third five-membered ring (**73** → **74**) proceeded with exceptional regiochemical control to produce only the internal double-bond isomer.

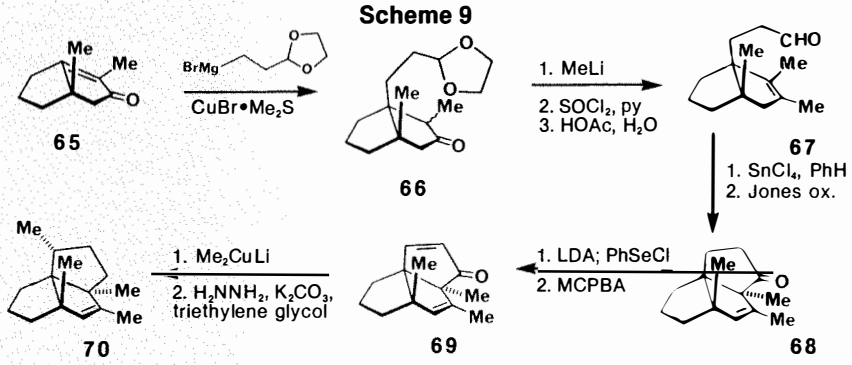
On the companion front, our total synthesis of **76** was designed to resolve questions surrounding the stereodisposition of the secondary methyl group. Biogenetic considerations require that the configuration at this site be fixed under kinetically controlled conditions.[59] However, knowledge of the more stable configuration about this center was lacking. The combined weight of several experiments showed the β-methyl configuration as in **75** to be sterically most comfortable. In fact, only through use of the sterically bulky reagent combination $(C_2H_5)_3SiH/(Ph_3P)_3RhCl$ was kinetic control observed not to strictly parallel thermodynamic control.[58] The proposed biosynthesis was thereby lent considerable credence.

The arrangements of the methyl groups and double bond in silphinene (**82**)[60] and silphiperfolene (**88**)[60] differ so extensively from those in **70** and **76** as to require a radically altered annulation protocol. Fortunately, it was a simple matter to profit from controlled aldol reactions in these examples. The conversions of **77** → **78** and **83** → **84** typify this annulation sequence (Scheme 11).[61,62] Dehydration of the cyclized aldols was most satisfactorily achieved through pyrolysis of their *p*-tolyl thionocarbonate derivative.[63] Following this highly successful installation of ring C in **79**, silphinene's secondary methyl group was set into the β configuration by gaining access to epoxide **80** and exposing this substance overnight to boron trifluoride etherate in benzene at room temperature. Given the α orientation

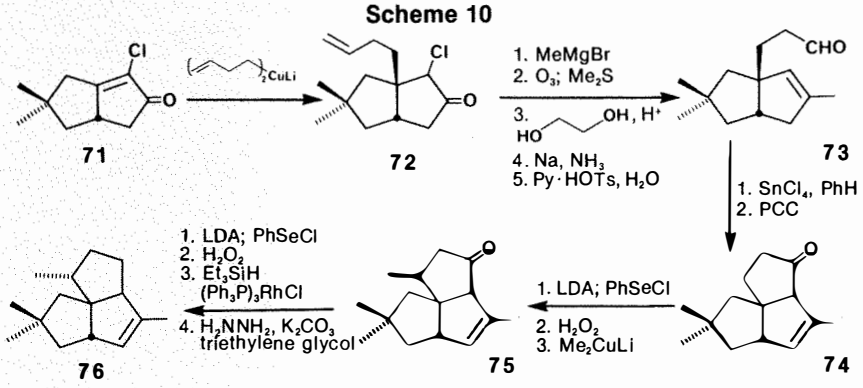
**Scheme 8**

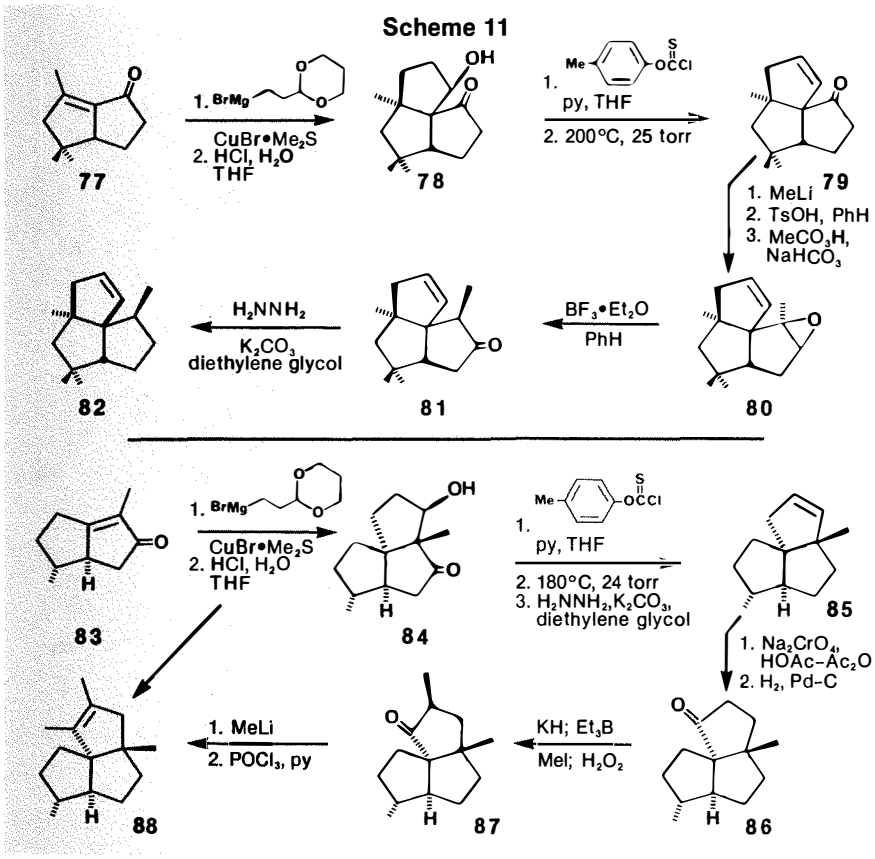


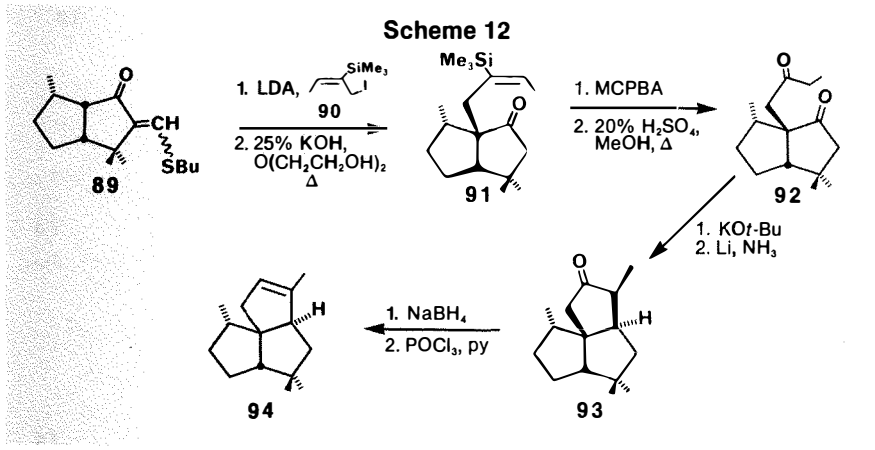

**Scheme 9**

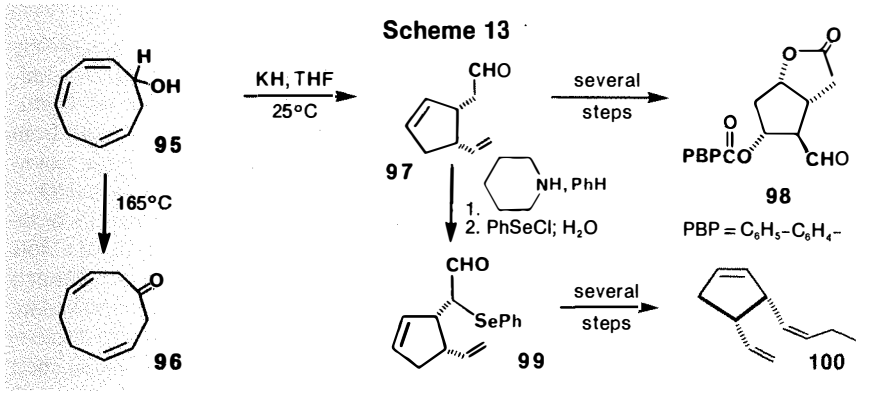



**Scheme 10**





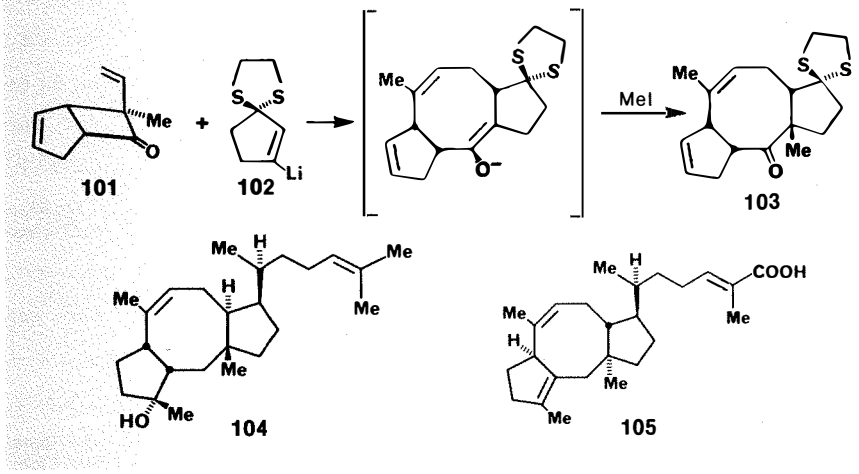

of the oxiranyl hydrogen which must undergo the 1,2 shift and the in-plane nature of this migration, the methyl-substituted carbon necessarily experiences inversion of configuration. The ensuing Wolff-Kishner reduction of **81** did not cause epimerization.[61] By contrast, introduction of the remaining functionality in silphiperfolene intermediate **85** began by allylic oxidation with sodium chromate and reduction of the conjugated double bond. Subsequent monomethylation was most efficiently achieved by condensation of the potassium enoxyborate[64] with methyl iodide. Methyllithium addition and regiospecific dehydration completed the sequence and gave **88**.[62]

Senoxydene, a related sesquiterpene hydrocarbon isolated from *Senecio oxyodontus*, was formulated as **94** on spectroscopic grounds.[65] Careful retrosynthetic analysis suggested that this target might be best reached by a new cyclopentane annulation scheme involving the electrophilic vinyl silane **90** (Scheme 12). In particular, this reagent was expected to allow expedient regiospecific installation of the C-ring endocyclic double bond and associated methyl group. We were pleased to discover that **89** could be sequentially alkylated with **90**, epoxidized, and hydrolyzed to deliver **92**.[65] With this sequence completed, we were now possessed of the further advantage that this diketone could be cyclized and reduced conventionally. Once **94** had been reached, it became abundantly clear that senoxydene had been incorrectly formulated, a fact later confirmed independently by Ito and his coworkers.[66] The proper structure of senoxydene is yet to be determined.

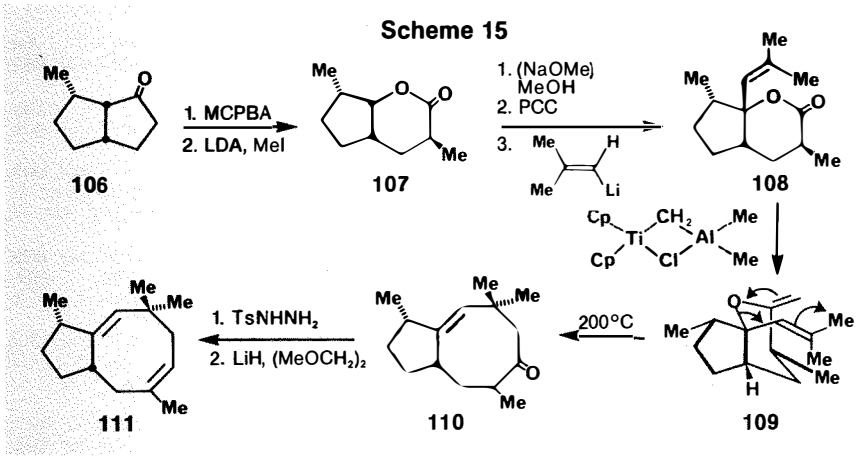
Evans had previously demonstrated that a highly ionized alkoxide substituent can substantially accelerate oxy-Cope rearrangements.[67] In our hands, it proved possible to override the normal predilection of neutral **95** for thermal isomerization to **96** *via* [1,5]hydrogen sigmatropy by conversion to the potassium alkoxide that rapidly gives only **97** at room temperature (Scheme 13).[68] This most effective mechanistic crossover provided a substrate which could be used (in combination with resolution of the derived diacid) in the development of expedient routes to the important prostaglandin intermediate **98**[69] and the powerful algal sperm attractant multifidene **(100)**[70] in optically active form.

It is worthwhile to point out the advantages of oxyanionic rearrangement chemistry in the development of efficient and regiospecific pathways to more intricate cyclopentanoid-fused natural products. In the light of experience already available, nucleophilic addition to bicyclic ketone **101** of vinyllithium reagent **102** was expected to occur from the *exo* face. The resulting alkoxide is set to experience low-energy [3,3] sigmatropic carbon shift. In fact, this isomerization cannot be interrupted (Scheme 14). If methyl iodide is introduced at this point, the single ketone **103** is isolated in 71% yield.[71] The relationship of

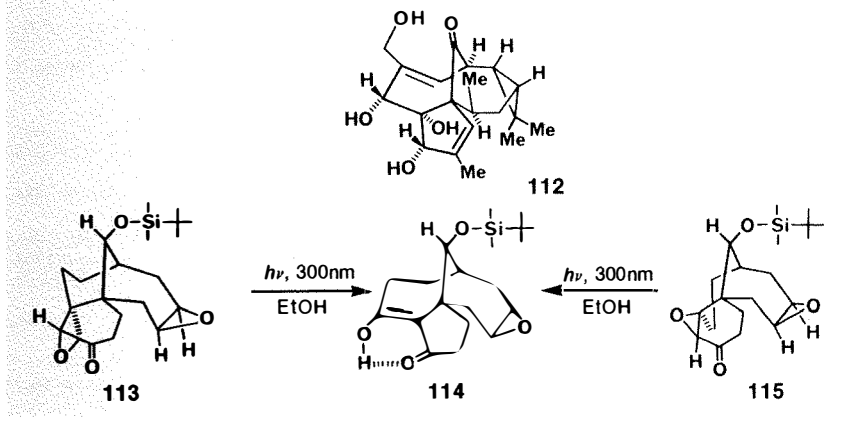
**Scheme 14**




**Scheme 15**




**Scheme 16**




of **103** to sesterterpenes such as ophiobolin **F (104)**[72] and albolic acid **(105)**[73] is self-apparent. Not only is the fundamental 5-8-5 carbocyclic framework rapidly elaborated, but the product already contains an appropriately positioned cyclooctenyl double bond and associated methyl group. Furthermore, the angular methyl substituent finds itself in an all-*cis*-fused stereochemical arrangement with an incipient carbonyl group in ring C to allow for requisite epimerization of the $\alpha$ proton and side-chain installation.

In 1979, the isolation from the soft coral *Capnella imbricata* of the biogenetically important fused 5,8-membered hydrocarbon designated as precapnelladiene **(111)** was reported.[74] In spite of the numerous investigations since that time,[75] synthesis of this sesquiterpene had not previously been accomplished. Our own examination of this uncommon framework suggested that a single operation was needed to make the ring system readily available. That necessary step was the intramolecular Claisen rearrangement within **109**, a transformation that should occur readily because of the location of the interactive groups on the open convex face (Scheme 15). Preparation of the precursor lactone **(108)** was accomplished in five steps from the known ketone **106.**[76] Upon treatment of **108** with the Tebbe reagent,[77] almost quantitative conversion to **109** was realized. The ensuing thermal isomerization to **110** was equally efficient. Now, when the tosylhydrazone of **110** was suitably decomposed, precapnelladiene was indeed isolated.[78]

The approaches to **103** and **111** just described provide the basis for general schemes by which unsaturated medium-sized rings can be annealed to preexisting smaller rings. We have observed in the context of a projected synthesis of isoingenol **(112)** that a similar end result can be achieved by a mild photochemical rearrangement pathway.[79] For example, irradiation of either **113** or **115** (the isomerization is independent of epoxy ketone stereochemistry) with 300nm light in ethanol solution provided **114** (Scheme 16).[80] Because the photoproduct is an enolic 1,3-diketone, adequate oxygen functionality is considered present for ultimate introduction of the remaining pendant groups. These ramifications are currently under active investigation.

In summary, much has been learned about expedient methods for constructing polycyclic molecules, particularly those containing two or more cyclopentanoid units. Until recently, organic chemists had not ventured deeply into this area of research. Great strides have been made in the past few years. Nevertheless, I am firmly convinced that the explosive growth period has just begun and that ingenious new advances will continue to be made in the years immediately ahead.


## Acknowledgement

The achievements discussed herein have been made possible by the expert laboratory effort and intellectual input of a number of outstanding graduate students and postdoctoral colleagues. Their names appear prominently in the references. All-important financial support was provided by grants from the National Science Foundation, National Institutes of Health, and Eli Lilly Company.



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## About the Author

Professor Leo A. Paquette received the B.S. degree from Holy Cross College in 1956 and the Ph.D. degree from the Massachusetts Institute of Technology in 1959. After serving as a Research Associate at The Upjohn Company from 1959 to 1963, he joined the faculty of The Ohio State University as Assistant Professor, and was Professor of Chemistry there from 1969 to 1981. He holds the title Kimberly Professor of Chemistry since 1981.

Dr. Paquette has been a Visiting Professor at Michigan State University (1968), the University of Iowa (1970), the University of Colorado (1974), the University of California at Santa Barbara (1975), the University of Gröningen (1975), Texas A&M University (1979), and Northwestern University (1981). He has served in an advisory capacity on the Chemistry Division Advisory Committee of the National Science Foundation and the Medicinal Chemistry B Study Section of the National Institutes of Health, and has been a member of the editorial boards of the *Journal of Organic Chemistry*, *Mechanisms of Reactions of Sulfur Compounds*, and *Chemical Reviews*. Currently, he is a member of the editorial boards of *Organic Reactions*, *Synthetic Communications*, and *Current Abstracts of Chemistry and Index Chemicus*. During 1984, he served as chairman of the Columbus Section of the American Chemical Society.

He was named a Fellow of the Alfred P. Sloan Foundation in 1965. Honors by the American Chemical Society include Morley Medalist of the Cleveland Section in 1971, the Columbus Section Award in 1979, and the Award for Creative Work in Synthetic Organic Chemistry in 1984. He was the holder of a Guggenheim Fellowship during the 1976-77 academic year and was elected to the National Academy of Sciences in 1983. In 1980, The Ohio State University awarded him its prestigious Senior Research Award, and in 1984 he was presented an honorary degree by his *Alma Mater*. He was the Chairman of the Gordon Conference on Heterocyclic Compounds in 1969, and has been a Plenary Lecturer at numerous conferences in the U.S. and abroad. He is the author of 550 research papers in organic chemistry and has more than 40 patents to his credit.

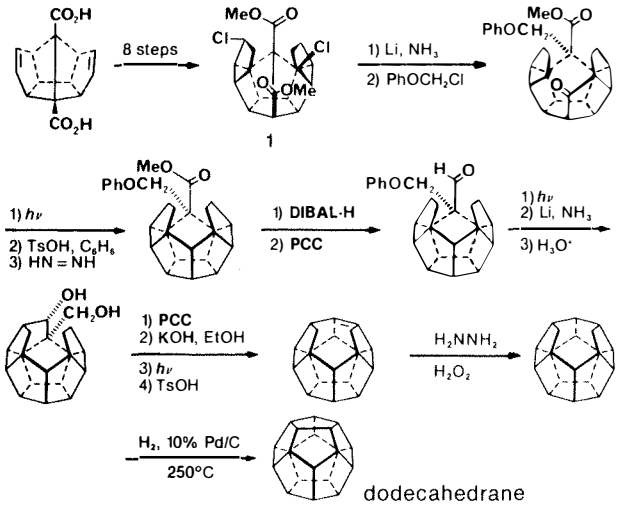
# Award-Winning Chemistry

## 1984 – Professor Leo A. Paquette

Leo A. Paquette, Kimberly Professor of Chemistry at The Ohio State University, is the recipient of the 1984 ACS Award for Creative Work in Synthetic Organic Chemistry, sponsored by Aldrich. Professor Paquette's research interests include the construction of theoretically interesting organic molecules of unusual structure, the synthesis of naturally occurring polycyclopentanoid metabolites, and the formulation of new synthetic methodology based on silicon chemistry.* The following highlight some recently reported examples of his synthetic work.

### *Dodecahedrane synthesis*

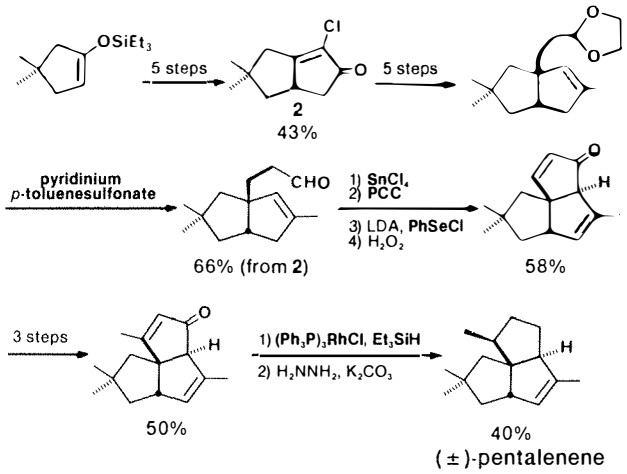
Probably the crowning achievement to over twenty years of Paquette's synthetic work was realized with the total synthesis of dodecahedrane,[1] the organic chemist's transliteration of the most complex of the five regular polyhedra described in Plato's *Timaeus*.[2] Both monomethyl-[3] and 1,16-dimethyldodecahedrane[2] have also been prepared in Professor Paquette's laboratory from intermediate **1**.




### *(±)-Pentalenene synthesis*

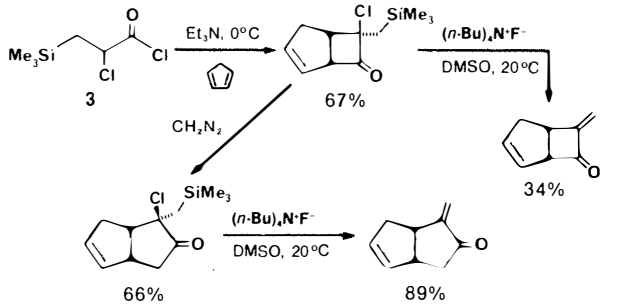
In recent years Professor Paquette has reported the synthesis of several racemic sesquiterpenoid metabolites possessing a tricyclo[6.3.0.0$^{1,5}$]undecane skeleton (*e.g.*, (±)-isocomene,[4] -silphinene,[5] -retigeranic acid,[6] -pentalenolactone E methyl ester[7]) *via* efficient stereocontrolled routes, as exemplified by his synthesis of (±)-pentalenene.[8]

*See *Aldrichimica Acta*, this issue, p 43.




### *Silicon strategy*

Paquette has recently demonstrated that chloro[(trimethylsilyl)methyl]ketene, readily available from the α-chloro acid chloride **3**, is a viable intermediate for the construction of α-methylenecyclobutanones and -cyclopentanones.[9]





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# About Our Cover:

Most readers of the *Aldrichimica Acta* know by now that our chemist-collector looks for paintings depicting episodes from the book of Tobias. One of the most dramatic of these episodes is the actual catching of the fish which was instrumental in warding off the demon that had beset Sarah, Tobias' fiancée, and in curing Tobias' father of his blindness.

The painting has a rather strange, recent history. It belonged for many years to the Los Angeles County Museum of Art, where it was attributed to Domenico Fetti, the great early-17th-century Italian artist. Connoisseurship of Fetti's works is difficult because he repeated his own compositions and was so admired that many artists copied his work. Two other versions of this composition are known, one in Dresden (Fig. 1) and one in Verona. Perhaps thinking their painting also a copy, the Museum sold it recently at an auction in Los Angeles. Subsequent cleaning has revealed many details which are different from the other versions, so our chemist believes that it may also be autograph.

The triangular composition with the fish's head at its focal point is tremendously dramatic. You can feel Tobias straining to hold the fish, and even the dog — the first friendly dog in the Bible — shares the excitement. The drama greatly impressed other artists. Note, for instance, Giovanni Antonio Guardi's depiction, now in Cleveland (Fig. 2), clearly based on Fetti's composition.

This depiction of the exciting moment when Tobias catches the magic fish seems fitting for the cover of the *Acta* in which Prof. Deslongchamps suggests how a young researcher might well choose a project which will shape his future.

Fig. 1

The Cleveland Museum of Art,
Mr. and Mrs. William H. Marlatt Fund
Fig. 2

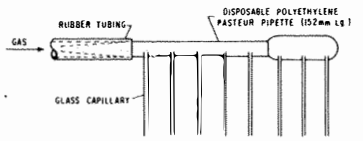
### *Pictures from the Age of Rembrandt*

Twenty-five paintings that have been reproduced on our *Acta* covers, and six that have been on our catalog covers are among thirty-six paintings in an exhibition of Dutch paintings at Queen's University in Kingston, Ontario. The fully illustrated catalog written by Professor David McTavish contains a wealth of art-historical information — enough for several evenings of relaxed enjoyment — probably the best value in art-history anywhere.

Are you interested in our *Acta* covers? ***Selections from the Bader Collection***, with 30 duotone reproductions, many of previous *Acta* covers, and an introduction by Professor Wolfgang Stechow is available to all chemist art-lovers.

# Lab Notes

An inexpensive (<$0.10) manifold for simultaneously delivering gas to a number of relatively small receptacles can be constructed in about 10 minutes from common laboratory equipment. A disposable polyethylene Pasteur pipette (length 152mm, diameter 7.5mm or length 184mm, diameter 4.5mm) is punctured along one seam with the tip of an 18-gauge hypodermic syringe needle from the bulb end to just before the tapered-end portion. The holes are then enlarged slightly by pushing the plunger from a 100-μl syringe into them. Melting-point capillaries (0.9-1.1mm i.d. x 100mm) cut to any desired length are forced into the holes to complete the manifold.




*Daniel P. Schwartz*
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Everyone, at one time or another, has had to deal with a small spillage of mercury from a manometer or a mercury seal. The normal spillage-disposal techniques have drawbacks: forming the amalgam with zinc dust or Mercurisorb is messy and the mercury is lost; sucking up the droplets with a vacuum-assisted aspirator is clumsy and requires special equipment.

I have found a quick, simple and safe way to handle such spillage. A small piece of solid carbon dioxide is placed on the surface of the mercury which very quickly freezes (m.p. -38 °C) and can then be transferred with tweezers to a suitable container for reuse.

*Stephen Mann*
*Marconi Research Centre*
*Great Baddow*
*Chelmsford, Essex*
*England*

Many recorders employ pens with capillary tips and ink reservoirs. These capillary tips tend to become clogged especially after prolonged periods of non-use.

We have found that, alternatively, fiber-tipped pens can be used, attached to either the existing pen holder, or an easily made adapter. In cases where the whole length of the fiber-tipped pen cannot be used because of space considerations, the pen (the body of which is generally plastic) can be cut to fit, as long as a sufficient length of fiber wick is left. This has the advantage that ink can be added to the wick and the pen used as long as the tip remains sharp.

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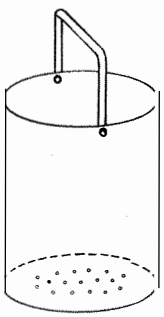
The use of highly corrosive cleaning agents, such as potassium dichromate/sulfuric acid, suffers from several drawbacks. One obvious problem is safety. If a gloved hand is used to insert and retrieve objects, there is the danger of acid burns as a result of pinhole leaks or the tearing of a glove on a sharp object. The use of tongs is less hazardous, but introduces a new problem. Have you ever attempted to retrieve a glass stopper from the bottom of a murky dichromate cleaning solution with a pair of tongs? At best it is a very frustrating endeavor.

We have devised a simple solution to this problem. Articles to be cleaned are placed in a polyethylene basket which is lowered into the dichromate cleaning solution. When cleaning is completed the basket is removed from the solution and taken to a sink where the excess cleaning solution is washed off. The entire cleaning process is accomplished without ever having to place a gloved hand in the cleaning solution, and even very small objects are readily retrievable.



A polyethylene basket can be constructed from a one-gallon micro cleaning-solution bottle. The top of the bottle is cut off about 18cm from the bottom and a number of ¼-inch holes are drilled in the bottom. A handle is fashioned from a 2 x 30cm strip of polyethylene cut from the discarded top of the bottle. A ¼-inch hole is drilled in each end of the handle and two ¼-inch holes are drilled along the top edge of the basket. The handle is riveted to the basket using 1-cm lengths of ¼-inch polyethylene tubing. The ends of the polyethylene tubing are softened with a soldering gun or other hot object and flared to rivet the handle to the basket.

The basket will fit into a 4-liter Pyrex® beaker. We have used such a basket in a potassium dichromate/sulfuric acid cleaning solution for the past six months without any noticeable deterioration of the basket.

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# "Please Bother Us."

by Aldrich

Recently Dr. Richard Jackson at Cambridge University suggested that we offer diallyl carbonate used in the elegant preparation[1] of α,β-unsaturated ketones and aldehydes from the corresponding saturated carbonyl compounds. The preparations proceed *via* the silyl enol ethers treated with diallyl carbonate and catalytic amounts of a palladium-phosphine complex, the components of which we supply also.

1) Tsuji, J. *et al. Tetrahedron Lett.* **1983**, *24*, 5635.

It was no bother at all, just a pleasure to be able to help.

# The Concept Of Strategy In Organic Synthesis

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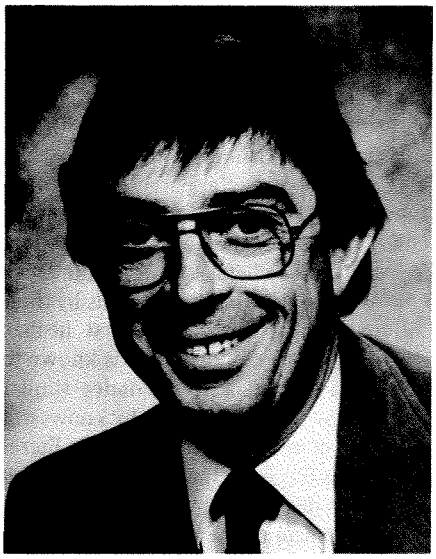


The progress made by organic chemists in the area of synthesis can be considered phenomenal, especially in the last twenty years. Almost all of the non-natural products which have been imagined by organic chemists have been prepared in the laboratory; the cage compounds tetrabutyltetrahedrane,[1] cubane,[2] twistane,[3] and dodecahedrane[4] are typical examples. Furthermore, the most important representatives of each class of natural products have all been synthesized, some of them several times, using different reactions or strategies. These natural substances include the terpenes (mono- to triterpenes), the steroids, the lipids (fatty acids, arachidonic acids and prostaglandins), the carbohydrates, and various antibiotics such as the β-lactams, the macrolides and the polyethers. The very large and rich family, the alkaloids, must also be included. Finally, those natural products considered to possess the most complex structures, *e.g.*, **vitamin $B_{12}$**,[5,6,7] **have been successfully synthesized.**

When one considers the scope of the progress already made in organic synthesis, one begins to understand why it might be difficult to decide what to do next in this field. This is especially true for those who are trying to be or to remain at the forefront of research in the area of synthesis. However, this conclusion does not mean that research in organic synthesis is dead. Indeed, this is not possible, because in synthesis, it is the chemist himself who sets his own limits, who decides on his next targets.

Nowadays, for synthetic chemists interested in making fundamental contributions to their field of research, the choice of a given target *is not* what should be considered as the most important decision; the choice of a specific target is simply an excuse to put in practice a new strategy or to demonstrate the value of, either a new reaction, or a new set of reaction conditions. Also, when one chooses a very difficult target with these principles in mind, it creates a "*must*" to innovate in order to succeed. In other words, since the researcher has put himself in a situation that organic chemists have not faced before, his chances of discovering something new and original are then quite high.

The preceding suggests that what is most important is not the choice of a given target, but *how* the goal is going to be achieved. In other words, it is the chemistry that one discovers along the way that is the important parameter, not the fact that one succeeds in the synthesis of a given compound, natural or non-natural. Indeed, when peers eventually have to evaluate one's work, either on a short-term or even more so on a long-term basis, it is only the value of the chemistry which will count.[8]

Progress in organic synthesis is being made currently through discoveries in three different areas: (a) new chemical reactions, (b) new reaction conditions, and (c) development of new strategies. It is easy to understand that discoveries made in the first two areas will have a direct impact on the field of organic synthesis. Indeed, we can readily foresee that the discovery of a new chemical reaction will be of great importance for synthesis. This is especially true when this new reaction allows the realization of a chemical transformation which was not previously possible. It is also true that the report of improved conditions to carry out a known reaction can be a very valuable contribution, especially for a reaction which was previously considered to be purely of theoretical interest.

It is important to point out here that it is extremely difficult to plan the discovery of "truly" new chemical reactions and that most of them are usually discovered by accident. On the other hand, it is relatively easy to develop new reaction conditions for a known chemical process. For example, several new types of aldol condensation have been reported recently.[9] With these new reaction conditions (*e.g.*, enol boronate,[10] or zirconium enolate[11]), higher chemo-, regio-, diastereo-, and enantioselectivity[12] are being achieved; a better control is thus obtained. As a result, these new synthetic methods are important contributions to progress in the field of organic synthesis.

The chances of discovering new reactions or of developing new reaction conditions are greatly dependent upon the present state of chemical knowledge which can be either theoretical or experimental in nature. For instance, theoretical advances of the following types are extremely valuable: (a) elucidation of the reaction mechanism for a series of chemical processes, (b) the development of a new theory which leads to

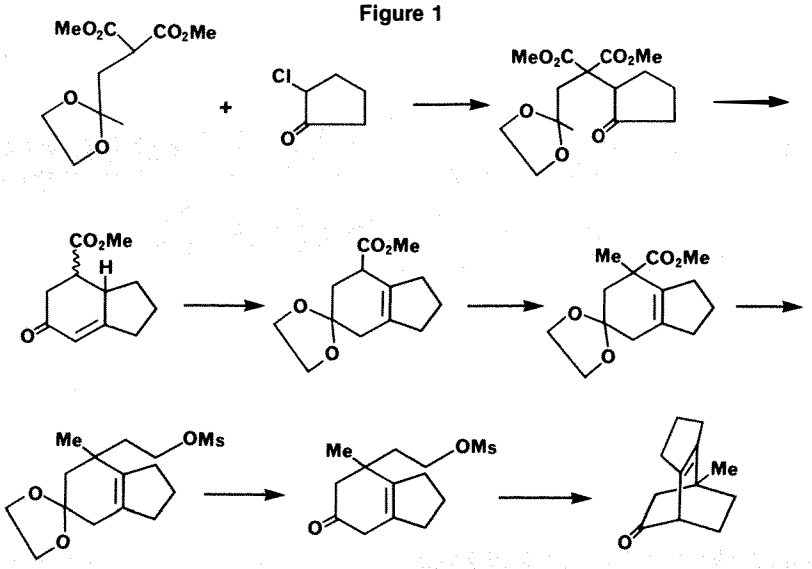
a precise knowledge of the stereochemistry of the transition states of chemical reactions, (c) new findings concerning cations, anions and solvents, and (d) development of new organic bases (*e.g.*, acid "sponges" and LDA). This is also true with experimental breakthroughs; they can be either new and more powerful techniques of purification (*e.g.*, chromatography) or new analytical tools (*e.g.*, $^{13}C$ and high resolution proton NMR spectroscopy and X-ray analysis). Also they can simply be due to a new reaction vessel, or a new tool or gadget which allows one to carry out a reaction under conditions (temperature, pressure, anhydrous conditions, size of scale, etc.) not previously facile.

As mentioned earlier, the development of new strategies is the third manner by which progress is made in organic synthesis. The next step would be to try to define strategy in order to recognize the present advances in this area. This should then prove valuable in our efforts to foresee future developments.

Strategy can be defined simply as a plan by which a particular compound is being constructed. Generally speaking, the synthetic plan will contain the following elements: it normally starts with small molecules which contain specific functional groups. The functional groups of these starting materials are then used to create at least one desired chemical bond (usually a carbon-carbon bond, but it can be also C-N, C-O, C-S bond, etc.). At the same time, a new set of functional groups is generated which can be used to create other important chemical bonds. In many instances, functional-group transformations are necessary before trying to make a new chemical bond. On other occasions, it is necessary to momentarily protect some functional groups at different stages of the synthesis so that others can be transformed specifically by an external reagent, or simply allowed to react in a specific manner. Fig. 1 describes a specific example taken from this laboratory.[13]

A good plan should contain the smallest number of the above chemical operations (*i.e.*, minimum bond-forming processes, functional-group transformations, protection and deprotection) so that it can lead to the final product in a minimum number of steps. Then a good overall yield should be obtained if high control is achieved for each chemical transformation. This means that the plan should allow very high stereochemical control as well as more-or-less complete chemo- and regioselectivity for each chemical reaction.

Figure 1




The synthetic strategy developed depends on how the chemist analyzes the target molecule and uses his imagination to circumvent the inherent difficulties. Generally speaking, if the chemist takes the view that the target molecule is very complex, the probability that he will imagine a complex solution is relatively high. If, on the contrary, the chemist takes the attitude that the target molecule is not so complex, he might come up with a very simple solution. Normally, we have the tendency to look at things in a complex manner first, then to simplify them as time goes on. This is generally true when we compare the first and the last published synthetic routes for a given substance (steroid syntheses are good examples).

At first, for a given target molecule, we try to solve, *one at a time*, all the difficulties that have to be surmounted according to the analysis that has been made. Very often, we overestimate some difficulties and sometimes we imagine others. Generally, progress in strategy is being made when an idea is found which can solve more than one difficulty at a time. Indeed, in very ingenious schemes, the plan is very simple and the apparent difficulties are often solved in one or two operations. Normally, when a chemist reports an elegant new strategy, his peers are immediately struck by the beauty and simplicity of the plan and their first reaction is that they wish that they had thought of it themselves and wonder why it had not been imagined before. In other words, there is progress in synthetic strategy only if the new plans become shorter and shorter or simpler and simpler; this is by no means an easy task.

Above all, a good strategy is a matter of control. Control is the regio- and stereocontrolled reaction of a reagent with one functional group selectively over others, which may include "apparently" identical functional groups within the same molecule. This raises the following question: What does the chemist do to obtain such control? I believe that he proceeds by three different general approaches. First, he may use a chemical reaction which is known to give high stereoselectivity under similar conditions. The chemist usually knows this either from several examples in the literature or, better, from the stereochemical information derived from a detailed study of the mechanism of the reaction. Secondly, the chemist may use a chemical reaction which is known not to be easily controlled, and then proceed to modify the experimental conditions hoping that he will obtain the desired stereochemical control. He may have good scientific reasons to proceed that way, or may do it simply because he is an experimentalist and has faith that he will succeed. Thirdly, the chemist may use well known general chemical reactions which do not normally provide selectivity, but because of a very specific tactic employed by the investigator, the reaction is observed to be completely stereocontrolled.

There are numerous examples of the first two approaches in the literature and there is no need here to discuss them further. In the third approach, the chemist has found ways by which a reagent is allowed to attack one specific functional group in a stereocontrolled manner. Thus, the chemist has tactics which he uses to restrict the approach of a reagent toward a substrate.

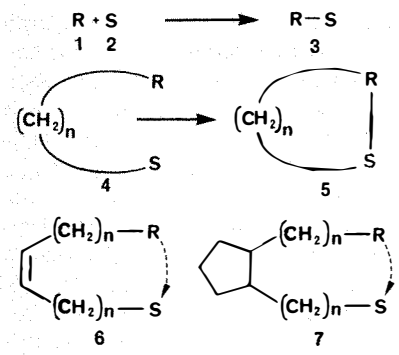
Generally, this kind of stereochemical restriction can be attained in two different

ways. First, a plan is devised such that as many as possible of the intermediate products of the synthesis are highly dissymmetric, if possible having a rigid conformation, and ideally with the desired absolute configuration. This is an intermolecular approach which is very valuable because, with dissymmetrical molecules, the chemist is convinced that he can achieve a high degree of chemo-, regio- and stereochemical control with simple reagents. I like to refer to this approach as being the "highly dissymmetrical intermolecular approach." The chemist also knows that in some cases, in order to obtain the desired product, he may need thermodynamically rather than kinetically controlled conditions for a given reaction. On other occasions, he may find it very useful to take into consideration various symmetry elements (for examples, see refs. 4 and 14).

The second manner to impose stereochemical restriction on the approach of a reagent toward a substrate's reactive center is to find a situation where the substrate and the reagent are tied together. Such a situation occurs when the chemist decides to use an intramolecular rather than an intermolecular process. I would like to point out immediately that the intramolecular approach is a strategy which is not what it may appear to be on the basis of a superficial analysis, *i.e.*, only advantageous from an entropy point of view. On the contrary, I believe that this approach to the development of new synthetic strategies is extremely rich. I am also convinced that its potential has been barely exploited and that its impact on the future of organic synthesis will be far more important than we can presently anticipate.

It is easy to understand that there is a much higher chance of obtaining a greater control on the approach of a reagent toward a substrate in an intramolecular process (**4** → **5**, Fig. 2) in comparison with

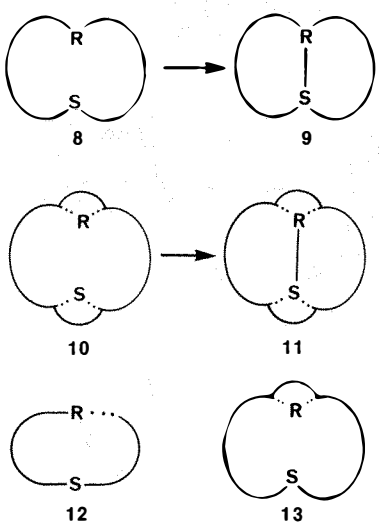
**Figure 2**




an intermolecular process (**1** + **2** → **3**). Indeed, there is a severe degree of conformational restriction in the intramolecular process which is totally absent in the intermolecular process. The only requirement of the intramolecular process is that the length of the chain which joins the two reactive centers must be appropriate, *i.e.*, it must lead to a ring which is easily formed (usually 3- to 6-membered). Additional parameters which tend to increase conformational restriction and favor the internal process will automatically further disfavor intermolecular competing processes. Conformational rigidity within the sidechain brought about by the presence of a *cis*-double bond (**6**) or of a ring (**7**) are good examples of these additional parameters which should facilitate internal cyclization.

An even higher degree of stereochemical control for the approach of a reagent toward a substrate's reactive center can be envisaged if the substrate and the reagent are held together by two chains (**8** → **9**, Fig. 3). Thus, there are different levels of intramolecular processes which can be imagined and which have an increasing degree of

**Figure 3**




stereochemical restriction. For the sake of convenience, I would like to describe here the internal process having one chain (*i.e.*, **4** → **5**) as an intramolecular process of level 1 and that with two chains (*i.e.*, **8** → **9**) as an intramolecular process of level 2 (thus, a level 2 intramolecular reaction is equivalent to a transannular reaction).

The ultimate degree in stereochemical restriction occurs when the reagent and the substrate are held rigidly in space in an appropriate relative orientation for the desired reaction to take place. It can be envisioned that, under such conditions, the anticipated chemical reaction should occur readily, and that such a situation will be observed with a sophisticated level 2 intramolecular process.

It is important to point out immediately that this process is equivalent to that which is observed with an enzymic reaction where both reactants are brought together in a specific three-dimensional orientation. The only difference is that in **8** → **9** the reagent and the substrate reactive centers are both covalently bonded to the core, whereas with an enzyme, at least one of the reactants is linked to the enzyme by weak chemical bonds (*e.g.*, hydrophobic interaction, hydrogen bonding or ionic bonds with anions or cations). Thus, the enzymic situation can be represented by drawings **10** → **11** where the non-covalent bonds which attract the reagent and the substrate are represented by dotted lines.

We can immediately see from this comparison that the long-term goal of developing synthetic strategies based on sophisticated levels of the intramolecular process will be ultimately the development of man-designed artificial enzymes which will be used for most synthetic reactions. Organic chemists should apply themselves to exploring intramolecular processes of level 1 and level 2 having covalent bonds. Then, as a second step, they should examine intramolecular processes having various degrees of non-covalently bonded substrates and/or reagents which are described by drawings **12** and **13.** This type of research activity has already started in several laboratories where a serious effort is being made to discover host molecules which can attract smaller molecules by weak chemical bonds in order to mimic enzymes.[15]

Another consequence of synthetic plans based on level 2 intramolecular processes is that, by necessity, this strategy requires the utilization of medium and large rings. However, before discussing the consequences of this important observation, we will first examine precise examples of intramolecular synthetic strategies. There are numerous examples of the level 1 internal process from which I have selected a few. We will then see that there are very few examples of the level 2 internal process.

Baldwin and Lusch[16] have recently studied the internal aldol condensation of triketones under basic conditions (KOH/MeOH). For example, they found that the aliphatic triketone **14** (Fig. 4) gave a good yield of the two isomeric products **15** and **16** in a 85:15 ratio. Thus, although there are theoretically 8 possible aldol condensation products, only two compounds are produced and one of them is highly favored. Very recently, Valenta and co-

Figure 4

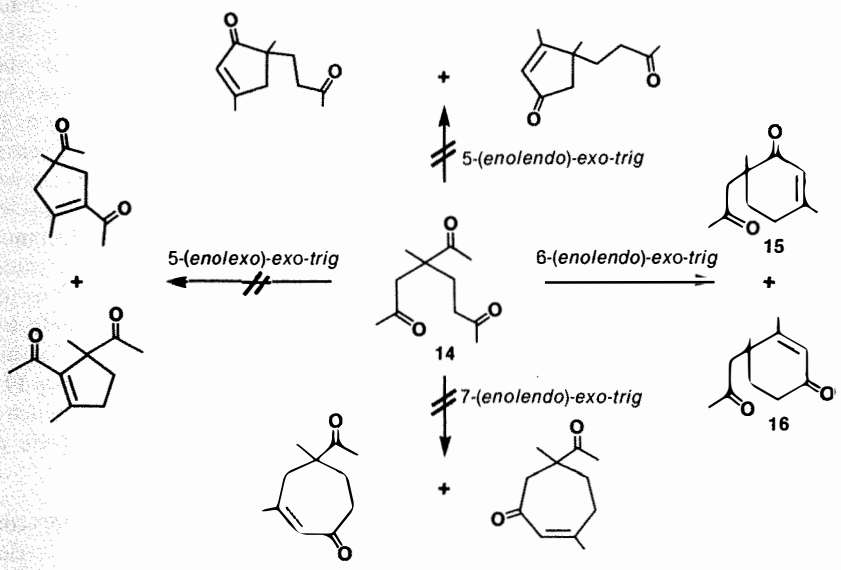



Figure 5

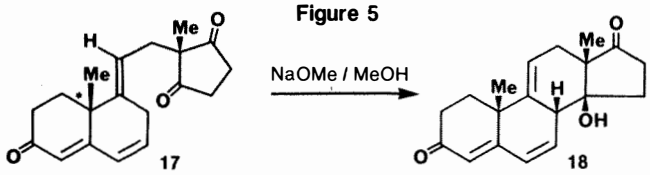



Figure 6

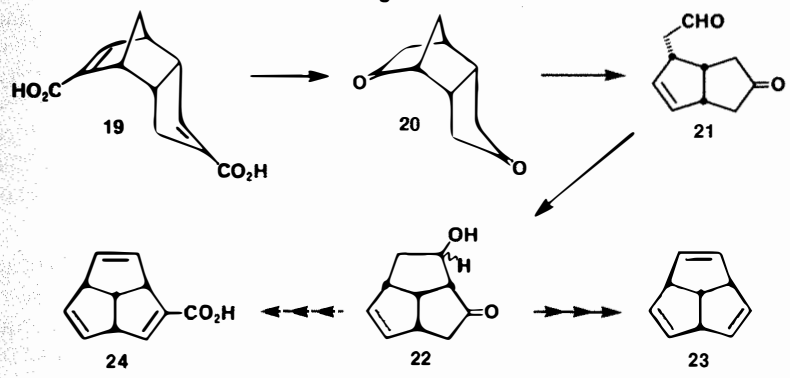
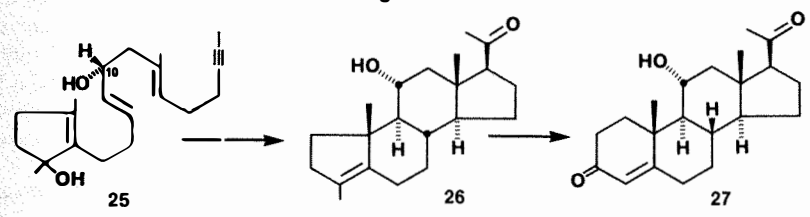



Figure 7




workers[17] reported that the treatment of tricyclic triketone **17** (Fig. 5) with sodium methoxide in methanol gave the 14$\beta$-hydroxy diketone steroid derivative **18** in 30% yield. Again, there are 8 possible theoretical tetracyclic internal aldol products and only one is observed! These investigations demonstrate clearly the discriminating power of the level 1 intramolecular aldol condensation process.

Figure 6 describes our strategy[18] for the synthesis of the triquinacene skeleton. The key tricyclic diketone **20** was obtained by appropriate functional-group transformation of the readily available Thiele's acid (**19**). The next step is the photochemically induced ring fragmentation of **20** into **21**. This is followed by an internal aldol condensation to give a good yield of the isomeric aldol products **22**, which were transformed into triquinacene (**23**) and triquinacenecarboxylic acid (**24**) by convenient functional-group transformations. The level 1 intramolecular aldol process **21** → **22** was highly favored over other internal or intermolecular processes. It is also interesting to point out that the conversion **20** → **21** is the reverse of a level 1 intramolecular condensation, indicating that such a process can be used with advantage in both directions in synthetic planning.

One of the most spectacular cases of level 1 intramolecular processes is the total synthesis of steroids by the so-called biomimetic polyene cyclization method pioneered and developed by Johnson and collaborators.[19] Figure 7 describes a specific example.[20] The acid-catalyzed cyclization of optically active monocyclic compound **25** gave optically active tetracyclic product **26** with essentially the same optical purity. Compound **26** was then converted into 11$\alpha$-hydroxyprogesterone (**27**) using straightforward functional-group transformation methodology. In this rather remarkable steroid synthesis, the single key step, **25** → **26**, is the result of three consecutive level 1 intramolecular processes and it expresses, at its best, the power of this intramolecular approach.

The synthesis of epihinesol (**33**) carried out in our laboratory[21] is another example which is interesting to examine from the point of view of strategy (Fig. 8). The first key step, the cyclization of diazoketone **28** to give cyclopropyl ketone **29**, is a level 1 intramolecular process. The next operation is the conversion of **29** into **30**, first by carbomethoxylation [NaH, $CO(OMe)_2$] followed by reduction ($NaBH_4$, MeOH). Since compound **29** is a highly dissymmetrical molecule, the conversion **29** → **30** was easily carried out with a high degree of stereochemical control by utilizing an intermolecular approach with simple reagents. Indeed, this transformation constitutes a good example of this approach. The next key step is the conversion of **30** into **32** which very likely takes place *via* the acid-catalyzed cyclopropane ring opening of intermediate **31** as shown. The ring opening of intermediate **31** is the reverse of an intramolecular process which can be classified as a level 2 type since **32** → **31** can be considered a transannular process. The synthesis of epihinesol (**33**) was then completed *via* appropriate functional-group transformations.

Figure 8

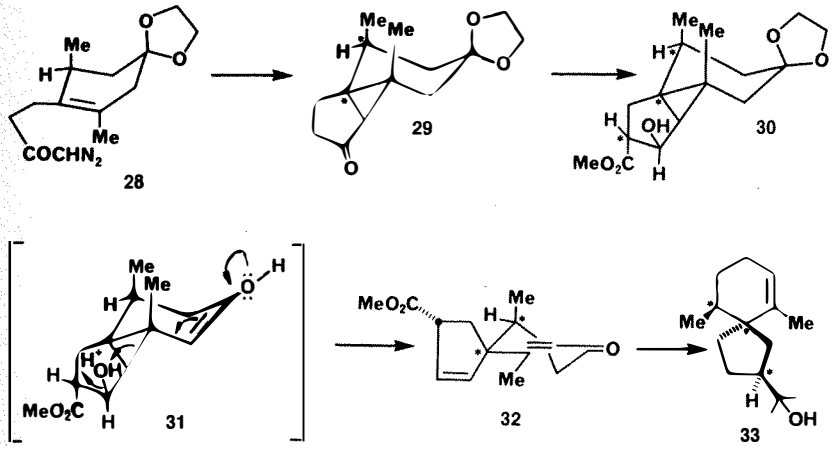


Figure 9

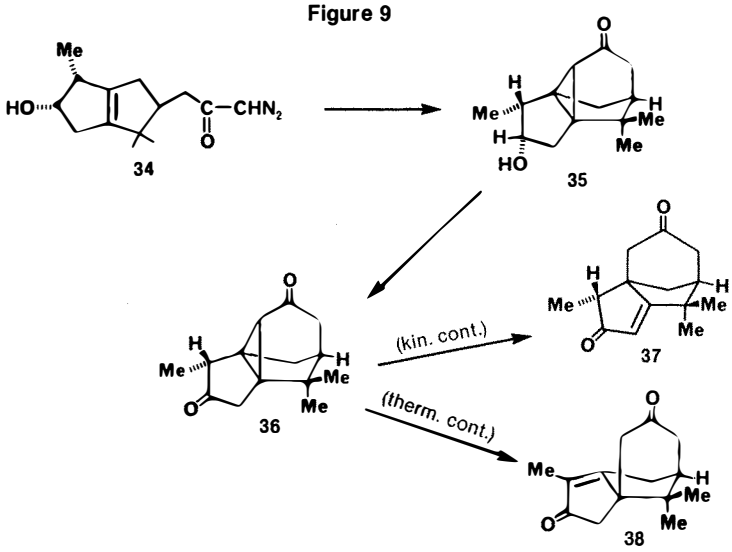
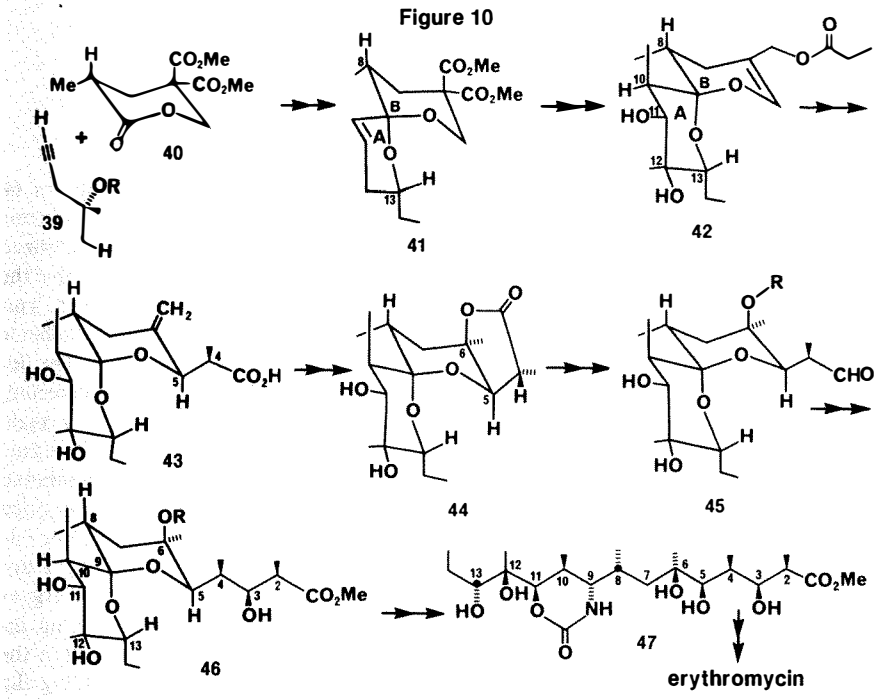


Figure 10



A similar approach[22] used for the synthesis of the cedrene and patchoulene skeleton is described in Fig. 9. First, a level 1 type intramolecular process converted diazoketone **34** into **35**, which was then oxidized to diketone **36.** Then, the reverse of a level 2 type intramolecular process takes place to give the cedrene skeleton **(37)** when **36** was treated for 20min. with sodium methoxide (3 equiv.) in methanol. When compound **37** (or compound **36)** was treated under the same conditions for 12h. the new compound **38**, having the patchoulene skeleton, was produced in high yield. This work shows the reversibility of the Michael reaction and illustrates the uses of both kinetic **(36 → 37)** and thermodynamic **(36 → 38)** control in synthesis.

Figure 10 illustrates our approach[23] toward the stereocontrolled synthesis of erythromycin. The spiro acetal **41**, which has two chiral centers ($C_8$ and $C_{13}$, erythromycin numbering system), was prepared from **39** and **40** with complete control of stereochemistry: (a) reaction of the lithium acetylide of chiral **39** with lactone **40**, (b) reduction of the triple bond to a *cis* double bond, and (c) deprotection of the secondary alcohol and acid cyclization under thermodynamically controlled conditions. The formation of the dioxaspiro acetal is necessarily a level 1 type intramolecular process and the specific production of **41** is due to the thermodynamically controlled conditions used. A detailed study[24] of the steric and stereoelectronic effects[25] of this spiro acetal system ensured that the most stable isomer must exist in the configuration and conformation shown by **41.**

The substituents at $C_{10}$, $C_{11}$, and $C_{12}$ in ring A of **42** were successively introduced using an intermolecular approach with simple reagents because the spiro compound **41** is a highly dissymmetrical molecule. Compound **41** was first transformed into the corresponding conjugated enone (C = O at $C_{12}$ by allylic oxidation), which was then treated in the following way: (a) lithium dimethylcopper 1,4-addition and reaction of the resulting enolate with dibenzoyl peroxide (benzoate formation at $C_{11}$), (b) Grignard reaction with MeMgI. The *gem*-dicarbomethoxy group of ring B was then converted into the propionate ester **42** by appropriate functional-group modifications (hydrolysis, decarboxylation, introduction of the enol ether double bond, reduction of the remaining carbomethoxy group and esterification). The resulting product **42** was then submitted to the Claisen rearrangement methodology[26] which produced the carboxylic acid **43** as the major isomer (4:1). In this important step,

two new chiral centers are produced ($C_4$ and $C_5$) with the desired configuration and it is due to a level 1 type intramolecular process (Claisen rearrangement). Similarly, the stereocontrolled introduction of the tertiary alcohol at $C_6$ is also due to the same kind of strategy: iodolactonization of **43** followed by hydrogenolysis to give lactone **44.**

It remains to transform lactone **44** into aldehyde **45** (R = $PhCH_2$) to complete the synthesis. On the other hand, aldehyde **45** was obtained by degradation of erythromycin and submitted to a condensation reaction with the zirconium enolate of methyl propionate.[11a] It gave as the major epimer (ratio 10:1), the desired aldol product **46.** It is interesting to point out that although the transformation **45** → **46** must be classified as an intermolecular reaction, the control of stereochemistry is due to a level 1 type intramolecular process! Indeed, the transition state of this reaction is very likely cyclic in nature. The difference between this internal process and others that we have analyzed so far is simply that at least one bond (to the zirconium metal) is weakly covalent in the present case. Compound **46** was then successively converted into **47**, a key intermediate in Woodward's synthesis of erythromycin.[27]

In the synthesis of twistane (**51**) described in Fig. 11,[28] the internal cyclization under basic conditions (NaH, dioxane) of keto mesylate **48** to give 4-twistanone (**50**) was found to be a very high-yield process. This result demonstrates that the enolate ion internal displacement of the mesylate group in intermediate **49** is relatively facile. In this transformation, the two reacting functional groups are easily brought into proper position to react because it is a transannular cyclization. Thus, this successful synthesis makes use of a level 2 intramolecular strategy. The power of this type of synthetic strategy was demonstrated further by the observation that the *cis*-decalindione **52** (Fig. 12) was readily converted into 8-acetoxy-4-twistanone (**55**) under acidic conditions containing an acylating agent ($BF_3$•$OEt_2$, AcOH, $Ac_2O$).[29] Indeed, this result shows that the transannular aldol condensation (**53** → **54**) takes place readily.

The synthesis of ryanodol carried out in our laboratory will now be examined.[30] The first key step is the preparation of tricyclic compound **58** (Fig. 13) from the Diels-Alder reaction of unsymmetrical diene **56** and dienophile **57.** The Diels-Alder intermolecular condensation is regarded as one of the most useful reactions by synthetic chemists. It is interesting to point out that one of the reasons that this reaction is so

**Figure 11**

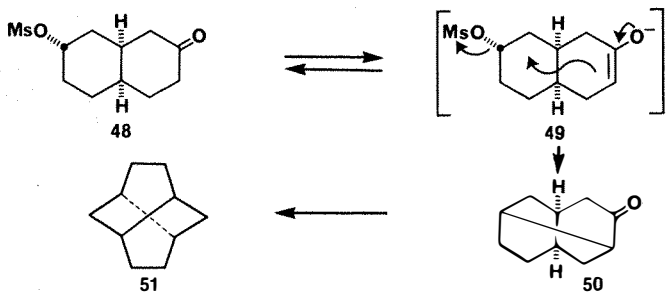



**Figure 12**

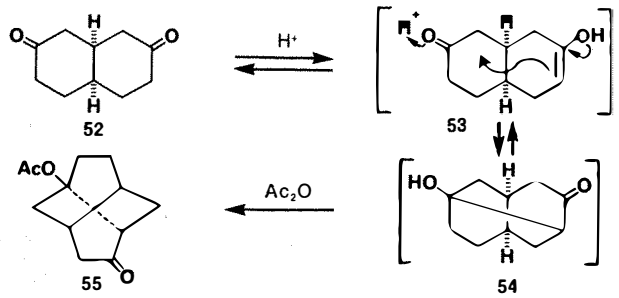
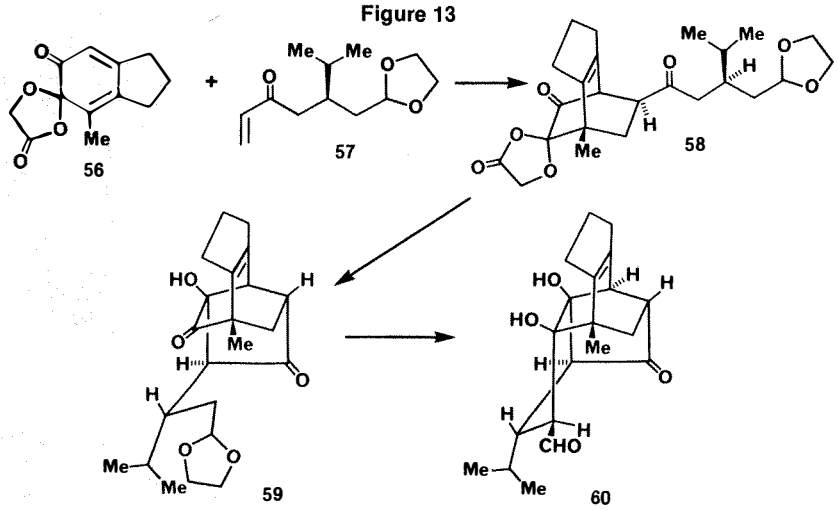



**Figure 13**




powerful is that its transition state is highly ordered. Indeed, the transition state of the Diels-Alder reaction is cyclic, and it possesses all the elements of a level 2 intramolecular process! As a result, a high degree of discrimination based on subtle steric and stereoelectronic effects occurs, and specific chemical processes are thus observed. The intramolecular version of the Diels-Alder reaction should therefore be a very powerful synthetic strategy and several recent reports show that this is indeed the case.[31]

The tricyclic compound **58** was then converted into the pentacyclic intermediate **60** *via* two consecutive level 1 type intramolecular aldol condensations (**58** → **59** → **60**) using appropriate basic and acidic conditions. The functional groups in **60** were then modified to produce the lactone product **61** (Fig. 14), which was oxidized ($O_3$, $MeCO_2Et$, *p*-TsOH; $Me_2S$) to give the aldol product **64** directly, in high yield. This very important step in the synthetic scheme merits the following comments. The intermediate diketone **62** was never detected, indicating that this compound is very readily transformed into **64.** The diketonic system in **62** is part of a nine-membered ring (a medium ring) which is maintained rigidly in space by the bridged carbocycle and the lactone ring. Thus, when the appropriate carbonyl group in **62** undergoes enolization, the enol in the resulting intermediate **63** is immediately trapped by the neighboring carbonyl group, yielding the

Figure 14

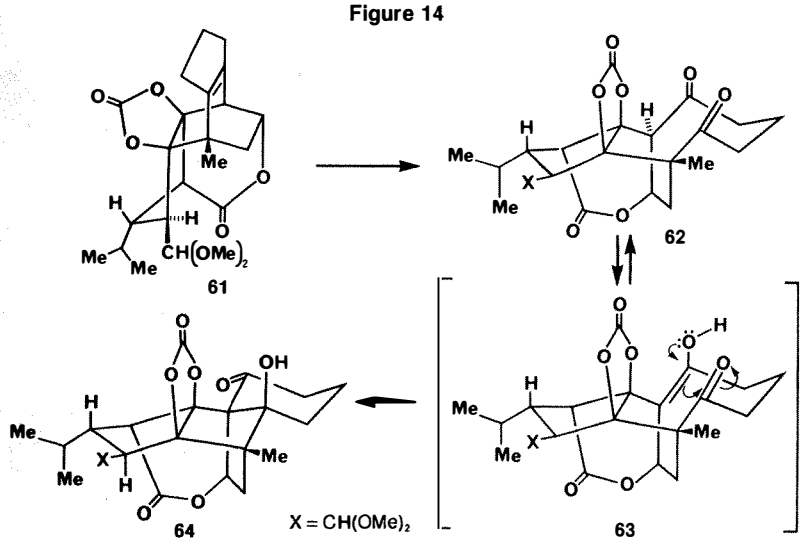



Figure 15

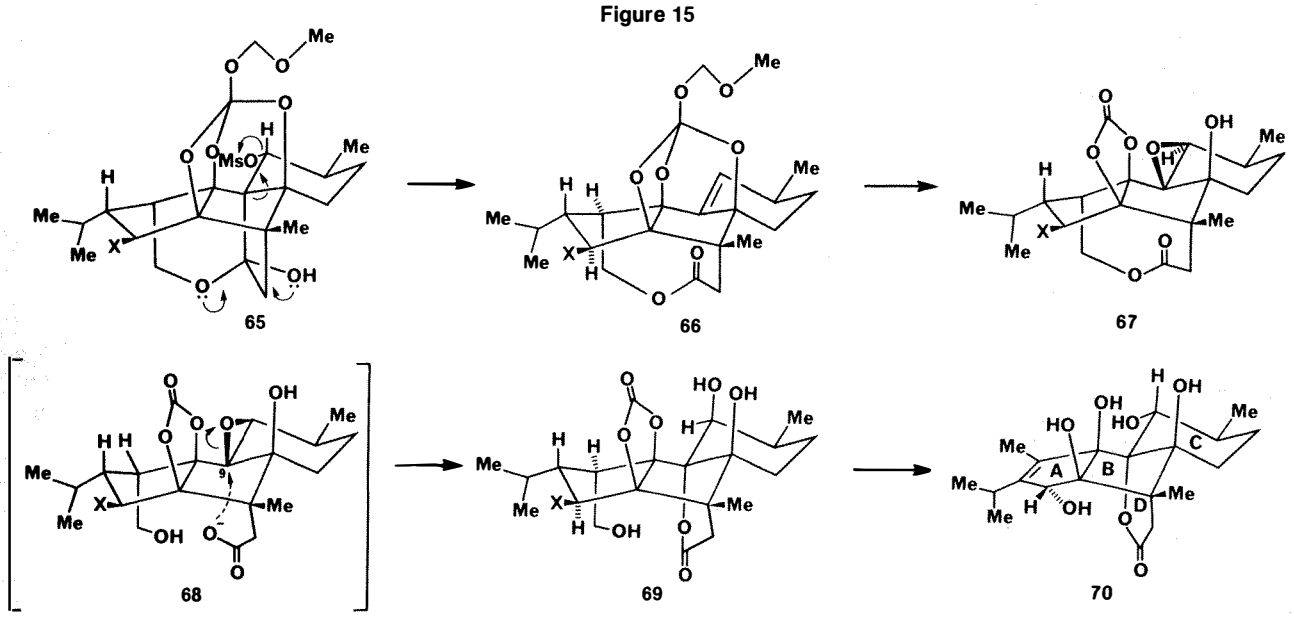
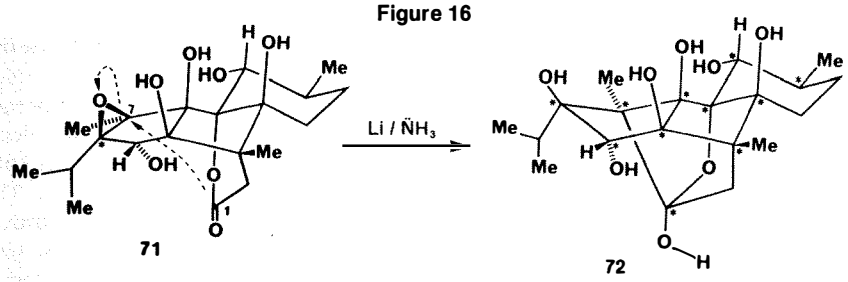



Figure 16




desired transannular aldol condensation product **64.** The great ease with which this remarkable transformation takes place is due to a level 2 type intramolecular process which contains a high degree of conformational restriction.

The aldol pentacyclic product **64** was then submitted to a series of functional-group modifications to give the hemiketal mesylate **65** (Fig. 15) which was smoothly converted ($MeSOCH_2Li$, $Me_2SO$) into the olefinic product **66** which contains a medium-ring lactone. This interesting Grob-type fragmentation[32] is the reverse of a level 2 type intramolecular process. The orthocarbonate functionality of **66** was then hydrolyzed under mild acidic conditions to the corresponding hydroxycarbonate, and the resulting product was oxidized ($CF_3CO_3H$, $Na_2HPO_4$, $ClCH_2CH_2Cl$) to the epoxide **67**; the large-ring lactone protects completely one face of the double bond, so the epoxidation of the highly dissymmetrical olefinic compound was completely stereocontrolled. Treatment of **67** under basic conditions (NaOH, DME) yielded the desired hydroxylactone **69.** This reaction takes place *via* the internal cyclization of the carboxylate ion **68.** Thus, the inverse regiospecificity observed in the epoxide opening [at the most substituted carbon ($C_9$) of the oxirane ring] is due to a level 1 type intramolecular process. Compound **69** was then converted into anhydroryanodol (**70**) through a series of relatively straightforward functional-group modifications.

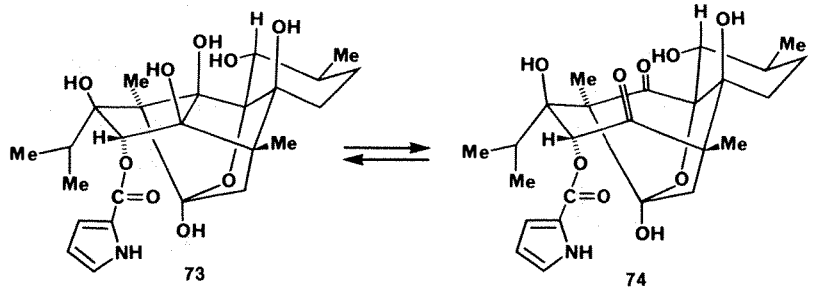
Anhydroryanodol (**70**) is a highly dissymmetrical molecule and the $\beta$-face of the tetrasubstituted double bond is less hindered than the $\alpha$-face. Accordingly, epoxidation ($CF_3CO_3H$, $Na_2HPO_4$, $ClCH_2CH_2Cl$) led to the $\beta$-epoxide **71** (Fig. 16). For the last step of the synthesis, the conversion of **71** into ryanodol (**72**), it was necessary to discover experimental conditions which would create a carbon-carbon bond between the lactone carbonyl carbon (C-1) and one carbon (C-7) of the oxirane ring (see arrow in **71**). For instance, conditions which would make the carbonyl carbon C-1 nucleophilic could be suitable. Accordingly, it was found that treatment of epoxyanhydroryanodol (**71**) with lithium in tetrahydrofuran and liquid ammonia gave ryanodol (**72**). This transannular reductive cyclization is a new reaction; the intermolecular version is not known because, in an intermolecular situation, each functional

group reacts preferentially in a separate manner under these reductive conditions. In compound **71**, the situation is totally different; the lactone and the epoxide ring are maintained in space in a rigid fashion, facing each other. So, any radical-anion-type intermediate produced by the reduction of any one of these two functional groups can be trapped by the other, generating the desired $C_1 - C_7$ bond. Thus, the success of this reaction is due to a level 2 type intramolecular strategy which contains a rather high degree of conformational rigidity.

It is interesting to realize that intramolecular processes involve generally very simple reaction conditions which can be a great advantage in synthesis. In some cases, these processes simply require either an acid or a base as catalyst; in others, an oxidizing or a reducing medium is sufficient, and sometimes only heat is necessary. In some instances, the reaction takes place even under conditions which do not appear to be very appropriate. For instance, in the course of the structural elucidation of ryanodine by chemical degradation, Wiesner and collaborators[33] observed that the *seco* derivative **74** (Fig. 17), obtained by periodate cleavage of ryanodine (**73**), gave back ryanodine in 10% yield under very unusual conditions ($H_2/PtO_2$ in AcOH) for such a process. Undoubtedly, this unexpected transformation took place because the two carbonyl groups are rigidly maintained in an ideal conformation for the reaction to take place (no doubt the yield could be increased by selecting more appropriate reductive experimental conditions). Several rather unusual transformations were also observed in the course of the synthesis of dodecahedrane,[4] and again, those were due to the very close proximity of functional groups. For instance, the last step of the synthesis (**75** → **76**, Fig. 18) in which a carbon-carbon bond was made under dehydrogenative conditions (hydrogen-presaturated - 10% Pd/C, 250°C) is noteworthy.

Baggiolini, Lee, Pizzolato and Uskokovic[34] have recently reported a new synthesis of *d*-biotin (**85**) (Fig. 19) which is very interesting from the point of view of strategy. L-Cystine dimethyl ester (**77**) was acylated to **78** which was then treated with zinc dust in acetic acid to produce the *Z*-olefinic 10-membered lactam **79** in 65% yield. The ester functional group of **79** was then modified to the corresponding nitrone (**79** → **80** → **81**) which underwent a stereocontrolled cycloaddition to yield the intermediate **82.** It remained to carry out a series of functional-group modifications to

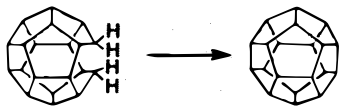
Figure 17



73 74

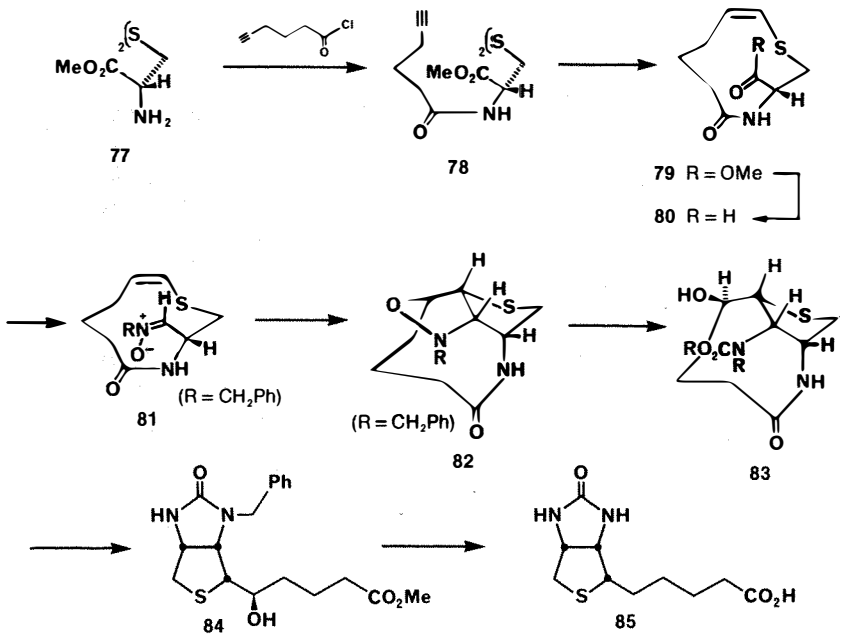
complete the synthesis: hydrogenolysis of the N-O bond (Zn dust) and acylation of the free amine (ClCOOMe, THF, $Na_2CO_3$) gave the bicyclic intermediate **83.** Treatment of **83** with barium hydroxide ($H_2O$-dioxane) gave the imidazolidinone **84** which

Figure 18



75 76

Figure 19



was transformed ($SOCl_2$, ether; $NaBH_4$, DMF; HBr, $H_2O$) into *d*-biotin (**85**).

Clearly, the key steps in this remarkable synthesis are **78** → **79** and **81** → **82.** Thus, the utilization of the medium ring and a level 2 type intramolecular cycloaddition strategy allows complete stereochemical control. Also, interestingly, intermediate **81**, which contains only one chiral center, produces **82**, which possesses four of them. It must be pointed out that earlier investigations by the same workers showed that an approach to the synthesis of *d*-biotin using a level 1 type intramolecular strategy failed because poor stereochemical control was achieved in the nitrone cycloaddition step. This work further stresses the potential of medium rings and transannular processes in synthesis.

Figure 20 describes a synthesis of the optically active sidechain of vitamin E[35] which uses a relatively classic strategy except that the use of a medium ring, the nine-membered carbonate **89**, allows complete control of the absolute configuration. The known Diels-Alder product **86** ensures complete control of the relative stereochemistry of the two secondary methyl groups of the vitamin E sidechain. Cyclopropanation ($CHBr_3$, NaOH) followed by olefin formation *via* bis-decarboxylation [$Pb(OAc)_4$, $C_5H_5N$] gave **87.** Cleavage of the olefin **87** ($O_3$, MeOH; $LiBH_4$) gave the diol **88** which was converted into the cyclic carbonate **89** ($COCl_2$, $C_5H_5N$, PhH, $CH_2Cl_2$). On reaction with optically active 1-phenylethylamine, carbonate **89** gave a mixture of optically active diastereoisomer-

ic urethanes **90A** and **90B** which were separated by chromatography. Each diastereoisomer was then converted to its corresponding allene derivative (**91A** or **91B**) and reduced catalytically (**92A** or **92B**). Appropriate functional-group modifications on **92A** and **92B** yielded the sidechain **93** having the desired absolute configuration. This synthesis shows how one can take advantage of the symmetrical properties of a medium ring in synthesis. This type of strategy based on symmetry consideration to control enantioselectivity was previously reported using a small ring.[14a]

It is also interesting to recall that in the two different routes for the synthesis of cobyric acid which led to the total synthesis of vitamin $B_{12}$,[5-7] strategies based on various levels of intramolecular processes played a major role.

For instance, in the A-B macrocyclization route (Fig. 21), level 1 type intramolecular processes were used twice (**94** → **95** and **97** → **98**; **97** was obtained from the combination of resolved **95** with chiral **96** which was prepared from camphor) to produce the pentacyclic diketone **98**, which already contains five ($C_3$-$C_7$) of the six chiral centers of the A-D subunit **104**. This subunit was obtained from the highly dissymmetrical pentacyclic diketone **98** through a

Figure 20

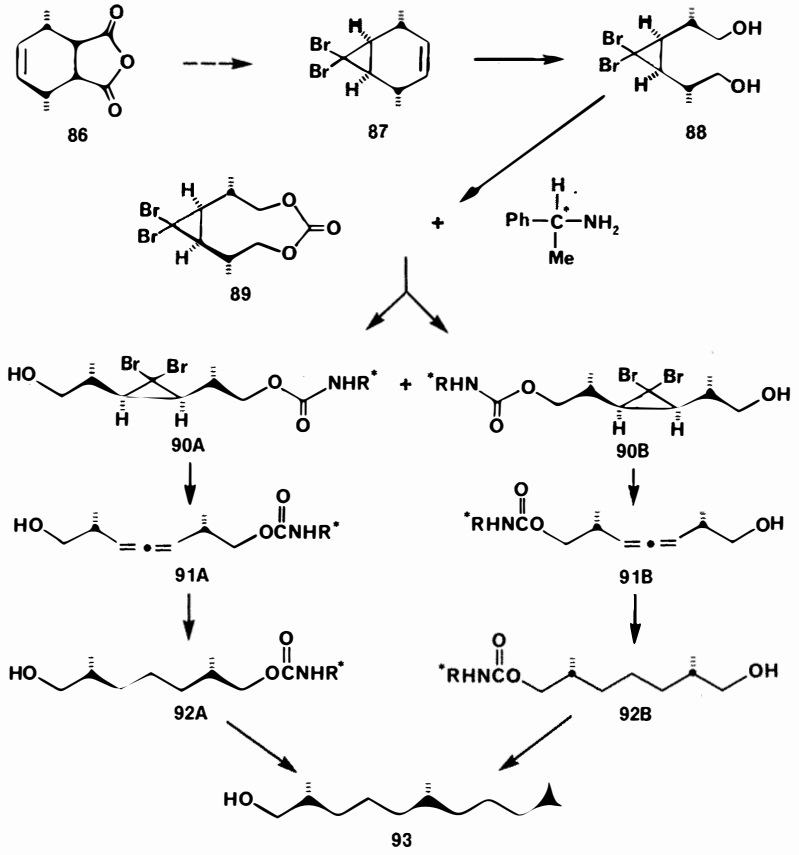
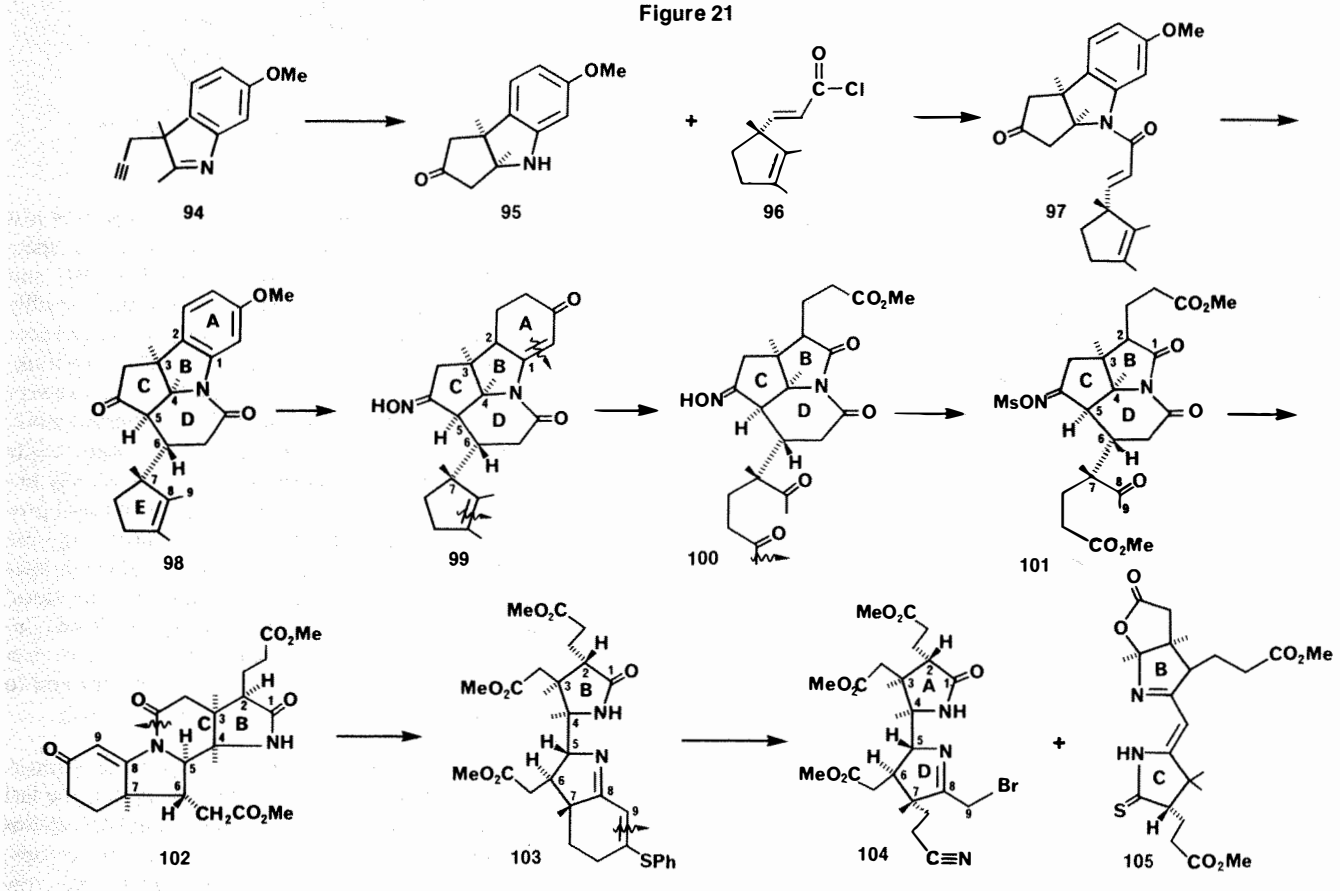



Figure 21



rather impressive series of functional-group modifications *via* the key intermediates **99-103.** The two subunits **104** and **105** were first attached by forming the thioether intermediate **106** (Fig. 22) which was then transformed into the product **107.** Thus, a weak but readily formed chemical bond, the C-S bond, was made first, which then greatly facilitated the formation of the desired carbon-carbon bond yielding **107.**

Several methods (based on the pyrrole approach to synthetic corrinoids of Johnson and co-workers[36]) were developed to effect the closure of the corrin ring system, and one specific case is described here. Functional-group modifications on compound **107** and cobalt complexation gave the new intermediate **108** in which two functional groups (imino thioester and enamine) were held together in close proximity so that the desired carbon-carbon bond formation could take place. Indeed, cyclization of **108** to give the bisnorcobyrinic acid derivative **109** (DBN, DMA, 60°) proceeded in high yield. Thus, the success of this macrocyclization is in great part due to a sophisticated level I type intramolecular process which contains a high degree of conformational restriction due to the metal complexation.

In the second synthesis of cobyric acid, an A-D macrocyclization strategy is used (Fig. 23): the A, B, C, and D rings were first synthesized and then joined together to give an A-B-C-D intermediate which was metal complexed (*e.g.*, with $Cd^{+2}$) to yield **110.** The intermediate **110** then underwent a remarkable intramolecular photochemical process yielding the corrin **111** which was converted into bisnorcobyrinic acid derivative **109.**

The preceding analysis of specific syntheses shows the potential of strategies based on various levels of intramolecular processes. I have already mentioned that an important consequence of synthetic plans based on level 2 intramolecular processes is that, by necessity, this strategy requires the utilization of medium and large rings. *This is a rather interesting observation* because it is well known that organic chemists, at least in the last twenty years, have tried to avoid medium and large rings as much as possible. The essential reason is simply that organic chemists are not very good at constructing such rings using direct methods of cyclization. This situation explains well why there are already in the literature numerous syntheses based on an intramolecular process of level I, but very few of level 2. On the other hand, I would like to point out that a search for the development of intramolecular strategies

Figure 22

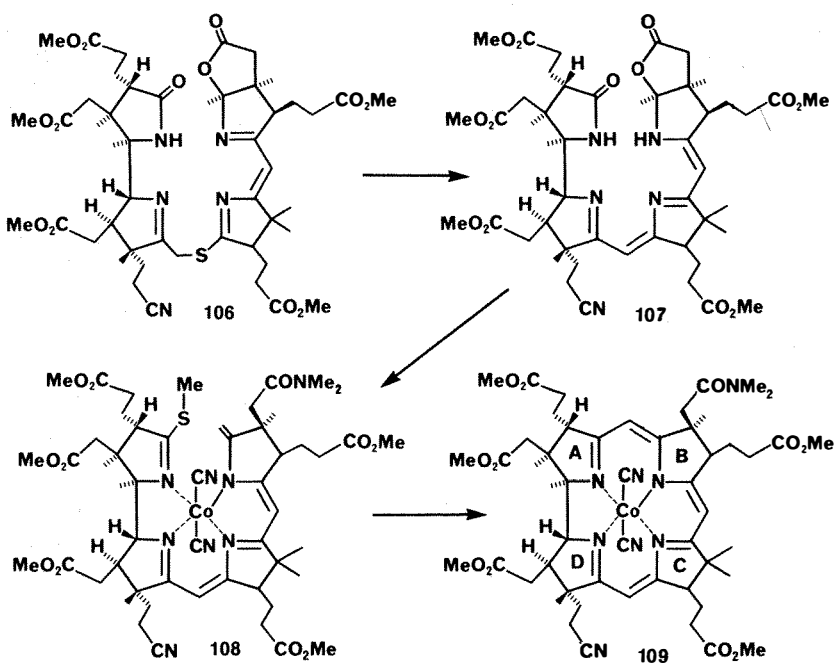
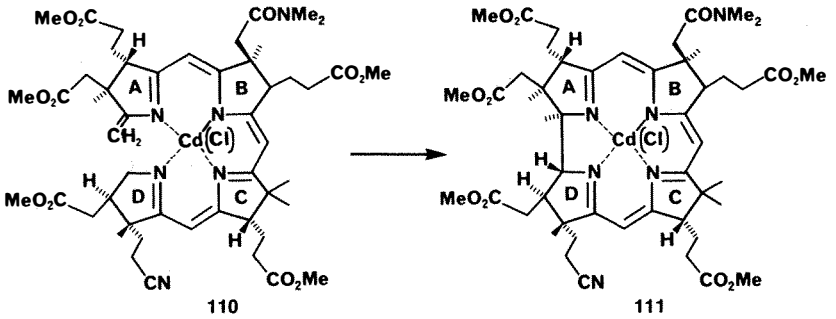



Figure 23




based on level 2 might convince organic chemists that medium and large rings can be a very exciting field which is worth exploring. A first step in this direction would therefore be the development of adequate methods to construct these types of molecules.

Interestingly, organic chemists in the past were as much interested in large and medium rings as in small rings. Indeed, in 1939, Ruzicka received the Nobel Prize for his synthesis of the macrocyclic compounds muscone and civetone.[37] Another example is Prelog, also a Nobel laureate, with his work on medium-sized carbocyclic rings.[38] However, chemists soon realized that medium and large rings were very difficult to make because yields of cyclization were in most cases very low. These compounds were also difficult to analyze from the point of view of conformation. Thus, by comparison, small rings were readily made and the conformational theory for small rings, particularly six-membered rings, was just being developed when the basic spectroscopic analytical tools (UV, IR, and especially NMR) were becoming readily available. There was also a very large variety of polycyclic natural products containing only small rings which represented very challenging synthetic targets. Furthermore, many of these compounds were easily purified and several were biologically important. By comparison, few natural products with a medium or a large ring were known (*e.g.*, germacranes and cembranes in the terpene family and a few peptides, alkaloids, and macrolides). So, it was only natural for organic chemists to neglect large- and medium-ring chemistry and to concentrate on small-ring chemistry.

It is noteworthy that synthetic chemists have very recently tackled (about the last 10 years) the synthesis of aliphatic chains containing several functional groups, substituents and chiral centers, *e.g.*, the

macrolides and the polyether antibiotics. It may be logical that it is only after mastering carbocyclic chemistry that chemists decided to develop methodologies for the stereocontrolled synthesis of aliphatic chains.[9] However, this is also due to some very practical reasons: the very recent development of powerful purification techniques like HPLC and the advent of very precise techniques of analysis like $^{13}C$ and high-resolution proton NMR spectroscopy. Indeed, with these techniques, one quickly knows if a non-crystalline acyclic substance is pure and if it has the desired structure.

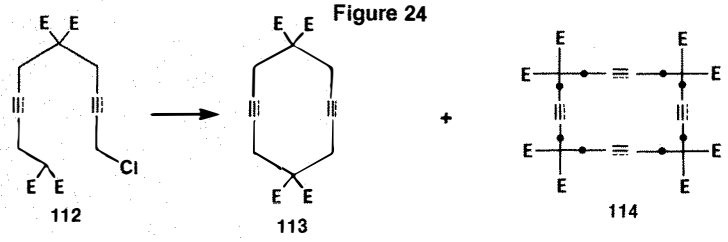
It is also interesting to point out that in the synthesis of natural products which contain a macrocyclic ring, the formation of the large ring is always left for the end of the synthesis, hoping that it will be closed without too much trouble. In other words, the large ring is rarely part of the synthetic strategy. Now that the above-mentioned powerful purification and analytical tools are at hand, it is as easy to purify and analyze medium- and large-ring compounds as it is for aliphatic chains. So, the presence of the macrocyclic ring could be regarded as a plus and new synthetic strategies based on its presence can, in principle, be imagined.

The work described in the preceding figures demonstrates that medium and large rings can be useful in synthesis. Still and co-workers have also made important contributions recently. Their chemical studies on macrocyclic lactones[39] and their successful synthesis of complex germacrane sesquiterpenes[40] have shown that (a) although theoretically medium rings can take several conformations, they normally exist in a preferred conformer, and (b) stereocontrolled reactions are observed with these medium-ring compounds. They have also shown that computer molecular modeling can be used very successfully to evaluate preferred conformations; its use on medium and large rings is equivalent to the use of Dreiding molecular models on small ring systems.

In Still's investigations, elegant but classical methodologies such as the ring-expansion method (starting with a six-membered ring) were used to construct medium rings. In the next step, I believe that organic chemists must demonstrate that *direct methods* for the synthesis of medium and large rings are possible under "standard" experimental conditions.

Generally speaking, there are two factors which influence ring closure.[41] The first is the frequency with which atoms placed at the end of a chain will come into reacting

Figure 24




E = $CO_2Me$ and —≡≡— = double bond (*cis* or *trans*) and/or triple bond

Figure 25

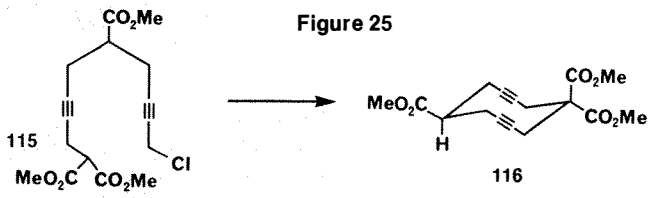



**Table 1**

| S.M. 112 | | M | Monomer 113 | Dimer 114 |
|---|---|---|---|---|
| *cis, cis** | $K_2CO_3$/acetone - 4 days | $10^{-2}$ | 84 | — |
| *cis, trans* | $K_2CO_3$/DMF-THF - 32h | $10^{-2}$ | 44 | 25 |
| *trans, trans* | $K_2CO_3$/DMF-THF - 26h | $10^{-2}$ | 10 | 42 |
| acetylene, *cis* | $K_2CO_3$/DMF-THF - 24h | $10^{-2}$ | 60 | 17 |
| | | $10^{-3}$ | 73 | 9 |
| acetylene, *trans* | $K_2CO_3$/DMF-THF - 26h | $10^{-2}$ | 17 | 35 |
| | | $10^{-3}$ | 57 | 15 |
| acetylene, acetylene** | $K_2CO_3$/DMF-THF - 12h | $10^{-2}$ | 26 | 40 |
| | | $10^{-3}$ | 39 | 12 |

*For a very similar cyclization giving a *cis-cis* monomer, see ref. 45.
**See ref. 46 for a similar cyclization.

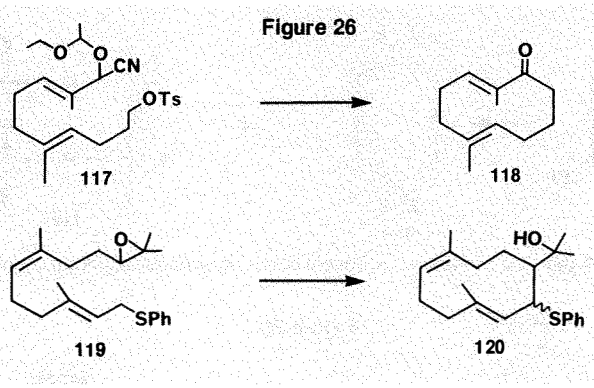
distance (entropy effect) and the second is the sum of steric and stereoelectronic interactions due to ring closure (enthalpy effect). The steric interaction can be due to Pitzer strain (imperfect staggering), Bäyer strain (deformation of bond angles), or transannular interaction due to steric crowding.

The synthesis of medium and large rings is disfavored by the entropy effect; the chain is too long and degrees of freedom are too large. The medium ring (and to some extent the large ring) is also disfavored by Pitzer strain and particularly by severe transannular steric interactions.

In some cases, Bäyer strain may also disfavor closure of medium and large rings. In principle, a very simple approach for the synthesis of medium rings is to find a device to restrict the rotational possibilities of the chain[42] and to eliminate transannular steric interaction. If both difficulties can be circumvented by using a single device, it should be possible to make medium rings *via* standard reaction conditions utilizing a very simple strategy.

A very simple device is to replace two methylene groups of a chain by a double (or a triple) bond. This, of course, has the effect of diminishing the degrees of freedom of the chain. It appeared to us that if two double (or triple) bonds are used, the degrees of freedom will be diminished considerably and if these two units are appropriately located in the chain, they should eliminate, at the same time, the transannular steric interaction! Model studies indicated that this might well be the case for the 10-membered ring system **113** having either double bonds (*cis* or *trans*) or triple bonds. We therefore studied[43] the cyclization **112** → **113** + **114** (Fig. 24) using $10^{-2}$ to $10^{-3}$ molar solutions, not high dilution. The preliminary results are indicated in Table 1. Each acyclic precursor **112** gave the cyclic monomer **113** and dimer **114**, except for the *cis-cis* acyclic case which gave only the cyclic monomer. Interestingly, all of these cyclic compounds are crystalline. In these cyclizations, two of the four carbomethoxy groups of the chain become pseudo-axial in the 10-membered ring and it must create additional steric interaction which should disfavor monomer formation. Accordingly, the cyclization of diacetylene **115** (Fig. 25) having only one carbomethoxy group in the middle of the chain, was studied,[44] and it was found to give a respectable 70% yield of monomer **116** and only 13% of the the corresponding cyclic dimer. Finally, it is also interesting to note from the above

Figure 26




results, that the dimerization process yielding the 20-membered ring always competes favorably with polymerization.

Takahashi and collaborators[47] have also recently shown that the intramolecular alkylation of cyanohydrin ethers (*cf.* **117 → 118**, Fig. 26) is an excellent general method (~80% yield) for the direct production of 2,6-cyclodecadienones. Previously, Ito and co-workers[48] had also demonstrated that the anion-induced cyclization of an epoxyphenyl sulfide (**119 → 120**) was a convenient and efficient route to macrocyclic germacradienes.

The 10-membered ring is one of the most difficult medium rings to synthesize; the above studies constitute examples[49,50] that the synthesis of medium rings by a direct method of cyclization is indeed possible. I believe that the next step is to develop various methods to construct several medium and large rings containing various functional groups. Then, as previously mentioned by Prelog,[38] "*the field of many-membered ring compounds became* [will become] *a real playground for the organic chemist.*" Indeed, I am convinced that the synthesis and the study of many-membered rings containing various functional groups is an extraordinarily rich and important domain of exploration for the organic chemist. On a short-term basis, this study should lead to the development of medium- and large-ring chemistry which is important for its own sake. Synthetically these compounds represent a real challenge, and subsequent conformational analysis studies[41,52] using NMR, X-ray and computer molecular modeling should be important and exciting. These compounds will also allow the study of transannular reactions, and are ideal for the discovery of "subtle" yet unrevealed stereoelectronic effects caused by transannular interactions.[53] Hopefully, as discussed in this article, they will also lead to new synthetic strategies for a large variety of natural products. Finally, on a long-term basis, the development of many-membered-ring chemistry appears to be a prerequisite for the eventual preparation of a large variety of molecular machines, *i.e.*, man-designed artificial enzymes. Chemists must necessarily think in terms of medium and large rings in order to attain the appropriate molecular size and the required stereochemical parameters.[15] Thus, this field of investigation should be of interest not only to chemists in particular, but also to scientists in general, because important practical applications may eventually evolve from it.


## ACKNOWLEDGEMENTS

It is with great pleasure that I acknowledge the excellent contributions of my co-workers, most of whom are cited in the references. This work was supported by the Natural Sciences and Engineering Research Council of Canada (NSERCC) and by the "Ministère de l'Éducation du Québec." Financial assistance in the form of an unrestricted grant from Merck Frosst Canada, Inc. is sincerely appreciated.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Professor Pierre Deslongchamps received the B.Sc. degree from the University of Montreal in 1959 and the Ph.D. degree from the University of New Brunswick in 1964. He did postdoctoral work with Prof. R.B. Woodward at Harvard University in 1965. He has been a member of the faculty of the Université de Sherbrooke since 1967, attaining the ranks of Associate Professor in 1968 and Professor of Chemistry in 1972.

Dr. Deslongchamps was named a Fellow of the Alfred P. Sloan Foundation in 1970, of the Guggenheim Memorial Foundation in 1979, of the Chemical Institute of Canada in 1980, and of the Royal Society of London in 1983. He has been awarded honorary doctorates from Université Pierre et Marie Curie (Paris), Bishop's University (Québec), the University of Montreal, and Laval University (Québec).

He has received numerous other awards including the Scientific Prize of Québec (1971), the E.W.R. Steacie Prize (Natural Sciences, 1974), the Médaille Vincent de l'ACFAS (1975), the Merck, Sharp, and Dohme Lectures Award (1976), and the Médaille Pariseau de l'ACFAS (1979).

He is the author of the text "Stereoelectronic Effects in Organic Chemistry" and over 65 research papers in organic chemistry, and has 8 patents to his credit. His research interests emphasize stereoelectronic effects in organic synthesis and reaction mechanisms.

# Tin Reagents for Organic Synthesis

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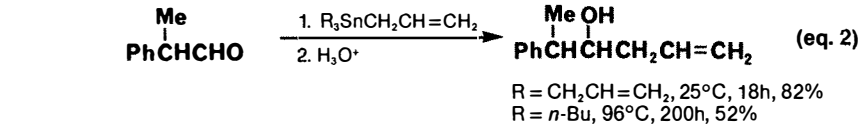
In recent years there has been considerable increase in the number of $\alpha$-organotin reagents employed in organic synthesis. In general, organotin reagents are used either as convenient precursors to alkyllithium reagents or as mild reagents for the transfer of organic moieties with displacement of, *e.g.*, halogens or acetate. Such transfer reactions generally take place under mild conditions, with retention of stereochemistry, and without attack at functional groups which react with more nucleophilic organometallic compounds, such as Grignard reagents. Aldrich offers a wide range of organotin compounds, representative synthetic uses of which are outlined below.

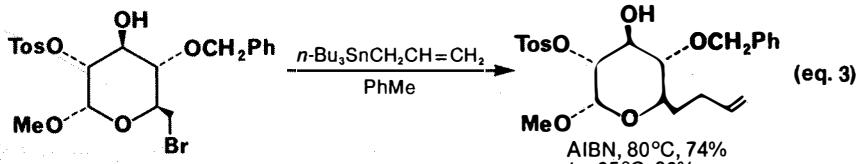
Tetraallyltin is the reagent of choice for the synthesis of allyllithium (eq. 1), either as a solid (RLi = *n*-BuLi in hexane)[1] or in solution (RLi = PhLi in $Et_2O$).[2] It has been found that tetraallyltin is more reactive than allyltributyltin in the formation of allylic alcohols from aldehydes or ketones (eq. 2).[3]

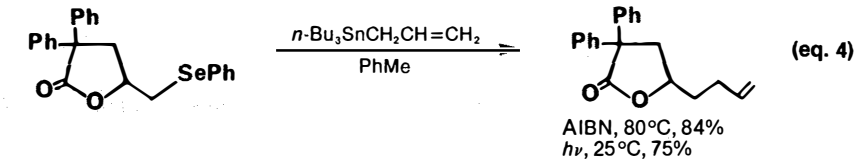
However, allyltributyltin is an effective reagent for the selective displacement of bromide (eq. 3) or selenophenoxide (eq. 4).[4]

Both tetraallyltin and allyltributyltin couple with allyl acetates in reactions catalyzed by tetrakis(triphenylphosphine)palladium(0).[5]



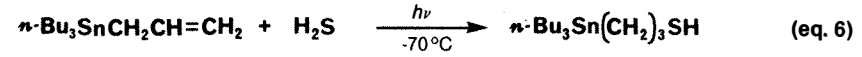



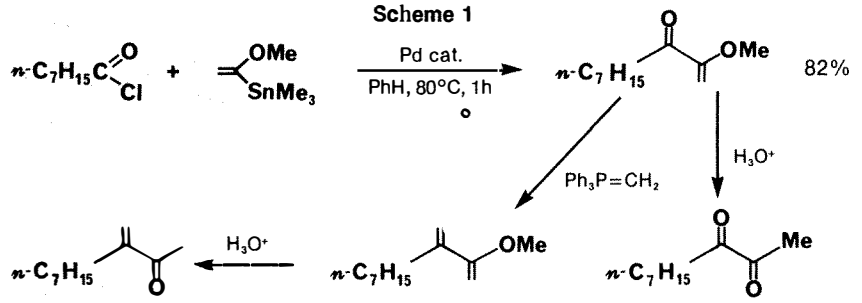



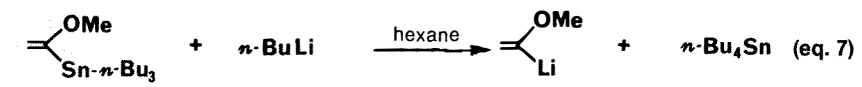


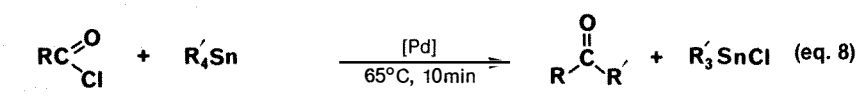





Scheme 1



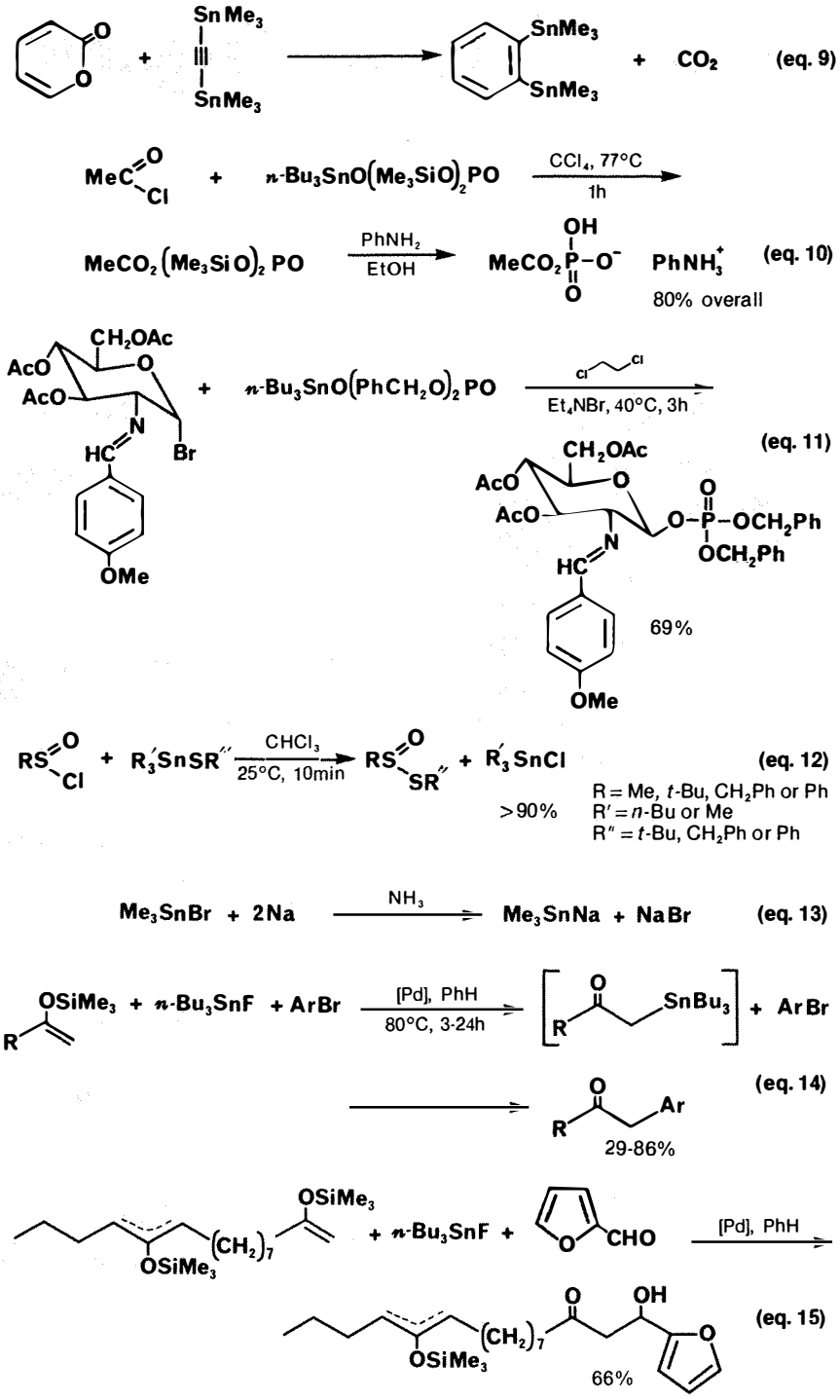
Allyltin and vinyltin compounds may undergo addition reactions at the double bond (eqs. 5 and 6).[6]

(α-Alkoxyvinyl)stannanes react directly with acyl chlorides in the presence of benzyl(chloro)bis(triphenylphosphine)palladium(II) to give α-oxygenated enones in high yield; these may be converted to other oxygenated products (Scheme 1).[7] (α-Alkoxyvinyl)stannanes are also a convenient source of pure, unsolvated (α-alkoxyvinyl)-lithium compounds (eq. 7).[8]

Ketones may be synthesized from acyl chlorides and tetraalkyltins in near quantitative yield (eq. 8).[9] Other common organometallics such as Grignard reagents or organolithium compounds are too reactive to be of use for such transformations as they react with the product. 1,2-Dichloroethane may be substituted for the more hazardous HMPA originally used as solvent.[10] α-Alkynyltributylstannanes have been found to give α-alkynyl ketones in high yield in a similar reaction.[10] Alkynyltin compounds also undergo Diels-Alder reactions (eq. 9),[11] and their use in the formation of carbon-carbon bonds has been reviewed recently.[12]

The phosphate group is found in many molecules of biological importance and may be delivered conveniently in a smooth, stoichiometric reaction by using bis(trimethylsilyl) tributyltin phosphate. The use of this reagent in the synthesis of acyl phosphates has been reported (eq. 10),[13] while similar reagents have been used in the preparation of phosphorylated sugars [14,15] *via* displacement of bromide (eq. 11).[14] Alkyltributyltin sulfides undergo reactions analogous to those outlined in eqs. 10 and 11 to give thioesters[16] and glycoside derivatives,[17] while the synthesis of thiosulfinate esters (eq. 12) has also been reported.[18]

For most reactions requiring an alkyltin halide the chlorides are used; however, for certain applications it is necessary to employ other halogenated compounds. Examples of such reactions are the metallation of alkyltin compounds (eq. 13)[19] for which the bromides are the reagents of choice, and the recently reported [20,21] use of tributyltin fluoride to generate α-stannyl ketones from silyl enol ethers. The latter reaction may be followed *in situ* by others, *e.g.*, regioselective arylation (eq. 14).[20] The desilylation of bis(silyl) enol ethers by this method has been found to be selective for the less-hindered silyl moiety (eq. 15).[21]





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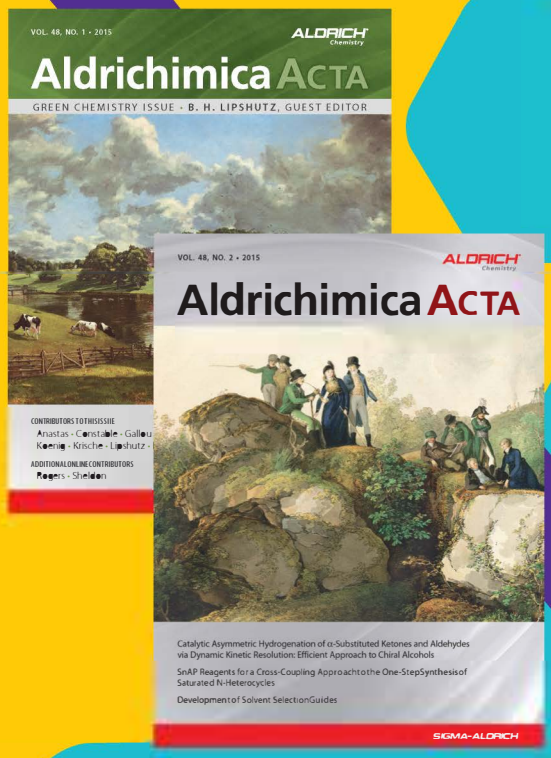


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