PRACTICAL USE OF

ANHYDROUS LiClO$_4$ and Mg(ClO$_4$)$_2$

IN ORGANIC SYNTHESIS

GFS
CHEMICALS ®

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FOREWORD – PERPETUATING THE TRADITION

A family-owned business can spawn a host of traditions over 73 years. Given the influence of Professor G. Frederick Smith as an educator and mentor to a broad scientific community, it's no wonder that the company he founded – now GFS Chemicals, Inc. – continues to be one of the few, truly service-oriented businesses of its kind.

The development of this monograph is consistent with Smith's own focus on research and publication. During the formative years of analytical chemistry, the promotion of interesting chemistries and reagents was always of greater import than the promotion of the company. Smith's communications even included synthetic methods for organic ligands that were very difficult to make, and which he offered for sale in the company catalog of products.

It is most fitting that one of the earliest topics of interest to Smith and his co-workers involved the behavior of perchlorate salts in organic solvents. Early on, it became apparent that the remarkable solubility (>6M) of anhydrous $LiClO_4$ in diethyl ether was an indicator of unusual chemistries to come. Although it took nearly eighty years, the role of lithium perchlorate in the promotion of key synthetic methodologies has become a major focus for organic chemists worldwide.

It is to these traditions of scientific curiosity, discovery, and communication that we commit this monograph.

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PREFACE

The study of organic reaction mechanisms took on a new focus in the 1990's as the unusual ability of lithium perchlorate to promote complex synthetic processes became apparent. Reviews published in 2000 and 2001 underscored the need for ongoing documentation of the broader implications of perchlorate-assisted methodologies. These include:

- Dramatic improvements in selectivity, yield, and operating conditions of complex reactions
- Application to a remarkably broad range of synthetic chemistries
- Achievement of results far superior to, if not impossible with, any other methodology
- Tailoring methodology to the use of Li, Mg and other perchlorate salts in various solvents
- Development of data demonstrating safety in multi-molar scale use of anhydrous $LiClO_4$
- Potential extension of technology to both organic and inorganic novel reaction processes

This document, initially prepared in 2002 through the efforts of GFS Chemicals (Columbus, OH) and the Ohio State University Department of Chemistry, is the first of a series of publications to be offered as instruction and encouragement in the safe use of perchlorate reagents to promote commercially attractive synthetic chemistries. Issues are organized according to reaction type, and will include reaction schemes, a brief description of reaction features, and appropriate references.

This and future issues will be made available through a variety of venues, including:
- Hard copies, available at trade shows, meetings, and upon request to GFS Chemicals
- GFS web site download
- Subscription to automatically receive future issues (2-3 times per year)
- Periodic compilation of sets of issues into a bound monograph available from GFS

GFS will continue to explore the commercial potential of these chemistries. In the near future, PowerPoint® technical overviews will be available for presentation to selected academic and commercial audiences. The interactive GFS web site is structured to encourage customer input in all areas of advanced technology. We look forward to your comments on this significant segment of our business.

SOME FUNDAMENTALS OF PERCHLORATE CHEMISTRY

Physical and Chemical Properties

Application of perchlorate salts to commercial processes will not be widely accepted without a greater, systematic understanding of the character and behavior of the family of materials. This is especially true of applications that involve organic media. Even the superior performance of anhydrous lithium perchlorate in key battery electrolytes has been insufficient to overcome safety concerns that appear marginal at best and, in many cases, utterly unfounded.

Lithium perchlorate is a very well characterized material. The hydrated salt is easily melted; with gradual heating it will readily lose two moles of water from the trihydrate crystal lattice. Anhydrous material is produced upon heating to around 150 deg C. Thermal decomposition at over 480 deg C produces oxygen and lithium chloride as expected.

Lithium perchlorate is also a robust salt. The production of very high purity and extremely dry lithium perchlorate can be achieved by well-established molten salt technology, producing spherical beads, about 1 mm in diameter, which are free-flowing and uniform in appearance and size.
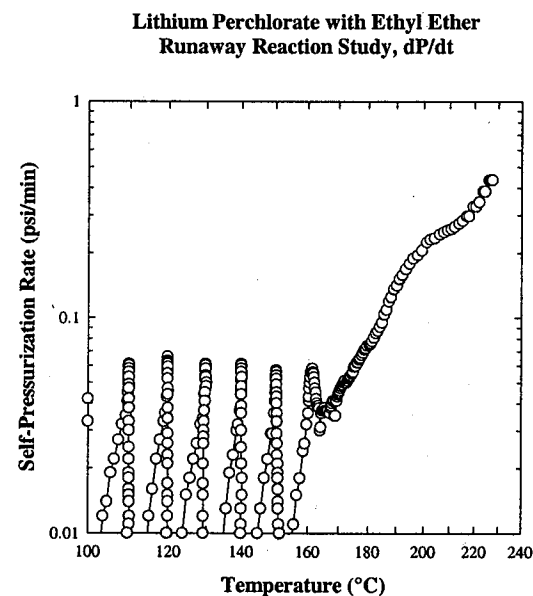
Breaking the first Cl=O bond in the perchlorate ion *at room temperature* is very difficult, the obvious rate-determining step in perchlorate ion decomposition. The easily oxidizable Cr(II) species gives no reaction with ClO_4^- in 0.001M concentrations at 25 deg C. Under similar conditions, the Ti(III) ion requires 1,470 hours to complete one-half of the redox reaction.[1] This is consistent with the observation that the oxidizing properties of perchloric acid require conditions of elevated concentration and/or temperature.

Thermodynamically, perchlorate is predicted to oxidize water and most transition metal salts (M^{2+}), as well as bromide and iodide ions. In reality, *these reactions do not occur* because they are inhibited kinetically.

All research and process development involving perchlorates must address the issue of mechanisms that might undermine the kinetic control of perchlorate reactions. This is especially true of perchlorate reactions in organic media, where oxidative conditions must be avoided under all circumstances.

One key question is whether perchlorate oxidations in organic media are governed by mechanisms similar to those that control the oxidative character of perchloric acid in water. Temperatures around 150 deg C are required to initiate the oxidation of organic substrates by sufficiently concentrated aqueous solutions of $HClO_4$.[2]

The issue of the oxidative capacity of solutions of lithium perchlorate in diethyl ether (LPDE) has been addressed by a series of experiments involving Adiabatic Calorimetry.[3] Tests run on a saturated solution sample demonstrated that temperatures in excess of 160 deg C were required to produce a self-sustaining exotherm. In addition, this exotherm was observed to proceed in a controlled fashion as the temperature was incrementally raised to over 220 deg C. These data are plotted in the graph at the right to the point where the exotherm became uncontrolled.

Lithium Perchlorate with Ethyl Ether Runaway Reaction Study, dP/dt

Tabulating the physical properties of some common perchlorate salts gives the first indication that the chemistry of lithium perchlorate merits careful examination. The property that opened the door to decades of groundbreaking research is the remarkable solubility of anhydrous lithium perchlorate in diethyl ether (Table I), which was described in the literature as early as 1923.[4]

TABLE I. Physical Properties of Selected Anhydrous Perchlorate Salts at 25 Deg C

Property	NH_4ClO_4	$LiClO_4$	$NaClO_4$	$KClO_4$	$Mg(ClO_4)_2$
Density	1.952	2.429	2.499	2.5298	2.60
Solubility (g/100g solv.)					
Water	24.922	59.71	209.6	2.062	99.601
Methanol	6.862	182.25	51.36	0.105	51.838
Ethanol	1.907	151.76	14.71	0.012	23.962
Propanol (n)	0.387	105.00	4.888	0.010	73.400
Acetone	2.260	136.52	51.745	0.155	42.888
Ethyl Acetate	0.032	95.12	9.649	0.001	70.911
Ethyl Ether	0.000	113.72	0.000	0.000	0.291

In comparison, the solubility of lithium perchlorate trihydrate in diethyl ether is reduced (compared to anhydrous material) to less than 1 gram per 100 grams of solvent.

The association between $LiClO_4$ and diethyl ether can be reliably defined as the 1:2 etherate – $LiClO_4:2Et_2O$ - at concentrations above 4.25 M. At lower concentrations, the solutions are a mixture of 1:2 and 1:1 etherates. Grieco[5] carried out much of his seminal research at concentrations of 5M LPDE, a very viscous composition. However, there will always be safety concerns regarding process R&D with any diethyl ether solution of perchlorate The next decade of research must provide assurances that lower concentrations of $LiClO_4$ (and possibly other perchlorate salts) in a variety of solvents will provide synthetic routes that are both novel and commercially useful.

Validation of the Methodology

Decades ago, many isomerizations and rearrangements were shown to be subject to the catalytic effect of perchlorates and/or perchloric acid. Mutarotation of glucose in pyridine was shown to be catalyzed by lithium perchlorate. The *cis-trans* isomerization of n-butene occurs in the presence of acidic metal salts or perchloric acid. In 1977, Pocker used solutions of lithium perchlorate in aprotic solvents to rearrange 1-phenylallyl chloride.[6] Lithium and tetrabutylammonnium perchlorates have been effective catalysts in the synthesis of ketones from organic nitriles via Grignard reactions.

The role that an organic solvent plays in a synthetic reaction is frequently linked to its polarity. If strongly ionic inorganic species are present, novel Lewis acid/base effects can be observed. Because of the remarkable solubility properties of LPDE systems, the combination of lithium perchlorate with diethyl ether (and, it is expected, with similar solvents/substrates) exhibits some of the most dramatic behavior of this kind.

However, even after the concept of reaction rate enhancement via $LiClO_4$ was elucidated in 1959,[7] it took over 25 additional years before that potential began to be fully explored in Diels-Alder and other synthetic methodologies. The Table of Contents that precedes this section illustrates the broad synthetic appeal that has been realized to date.

The cascade of research in this area in the 1990's was led by the many and diverse contributions from Grieco and co-workers, and quickly became an international focus. As a result, a remarkably wide range of synthetic systems were identified that could be dramatically enhanced by treatment with LPDE

solutions and similar reagent systems in various concentrations, usually under mild conditions.

The reaction sections of this monograph provide a summary of the most striking and opportune chemistries reported in the recent literature for perchlorate-assisted synthetic methodologies. Given the inertness of the perchlorate ion and the ability of key solvent systems to fine-tune the selectivity of "naked-ion" chemistries of Li^+ and Mg^{2+}, the potential afforded by these chemistries is truly limited only by the creativity of the synthetic chemist's imagination. Eventually, more and more guidelines will be put into place to help govern larger scale use of perchlorates.

Since the validity and value of the methodology is becoming increasingly apparent, this will encourage ongoing examination of the safety aspects of perchlorate chemistry carried out in organic media. Given appropriate controls, it is tempting to conclude that the stage has been prepared for a significant paradigm shift – the optimization and extension of novel perchlorate chemistry into successful commercial and process development.

Opportunities for Larger Scale Use of Perchlorates

Various metal perchlorate salts find application as catalysts in polymerization reactions. The polymerization of styrene and its catalysis by perchloric acid has been studied most extensively because of its considerable commercial importance. It was shown that magnesium perchlorate provides a stronger catalytic effect than potassium, ammonium or barium perchlorate.

Patent literature describes processes for polymerization of isobutene with magnesium perchlorate, of THF with $Mg(ClO_4)_2$ and sulfuric acid; preparation of poly(oxymethylene) has also employed perchlorate salts as catalysts.

Major industrial operations continue to be built upon the ability of perchlorate solutions to carry out complex and demanding electromachining and electropolishing procedures. Jet engine turbine components can be crafted out of a solid block of metal using state-of-the-art computer-based technologies. These high precision machining techniques reduce surface and compositional irregularities and are conducive to brightly polished metal surfaces.

The use of non-aqueous solutions for such purposes is common because such use facilitates control of current densities, over-voltage effects, and solubilities. The perchlorate electrolyte is not readily oxidized and forms readily soluble salts with the metal ions produced by anodic reaction of the sample to be worked. Electrolytic solutions that include either perchloric acid or salts in their formulation include: acetic anhydride and perchloric acid ; acetic acid and perchloric acid; acetic acid and sodium perchlorate; ethanol and perchloric acid; methanol and perchloric acid; ethanol, ethylene glycol monobutyl ether and perchloric acid; and dimethylsulfoxide and perchloric acid.

The hazards associated with the use of perchloric acid and perchlorate salts in electropolishing baths have been given significant emphasis and reviewed by several authors. The positive safety record of numerous industries, including various long-term battery research programs, reflects the high degree of both performance and safety that can be attained in the use of perchlorates in commercial applications.

Recent work carried out at GFS has shown that the LPDE reagent can be used successfully on a multi-molar scale. The reaction of kilo quantities of isoprene and maleic anhydride in the presence of five liters of 5 M LPDE provided greater than a 90% yield of Diels-Alder product in less than two hours, with

only a slight exotherm (10-15 degrees) and modest amounts of isoprene oligimers formed:
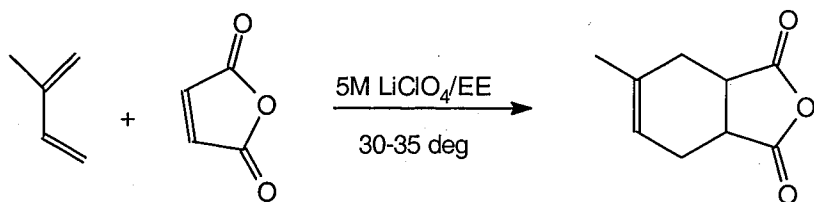
| Isoprene 8 moles | Maleic Anhyd 5 moles | LPDE 5 liters | 4-methyl-1,2,3,6- tetrahydrophthalic anhydride |

Since lithium perchlorate is the main focus of this publication, it is especially appropriate to compare its nature in the following table with that of other lithium salts considered to be key components in advanced commercial technologies such as fuel cells, battery compositions, and ionic liquids:

CRITERIA	$LiClO_4$	$LiPF_6$	$LiBF_4$	LiOTf
Manufacturing method	acid-base	high-temp corrosive	high-temp corrosive	acid-base
Production Scale	ton	multi-ton	small batch	large batch
Drying factors	dry ton lots to <200 ppm moisture	difficult to maintain <1000 ppm	very hard to remove solvent	dries to >99% purity
Material handling	free-flowing fine powder	powder may clump when wet	packed powder	powder may clump
Hydrolysis factors	minimal moisture sensitivity	corrosive hydrolysis products	corrosive hydrolysis products	moisture sensitive
Cost (for 100 grams)	$20	>$200	>$200	>$100

The commercialization of process chemistries involving lithium perchlorate will, in large part, be driven by the fact that the anhydrous salt can be economically supplied in ton lots. Most perchlorate-assisted reactions have not shown significant moisture sensitivity. With a secure line of raw material supplies, GFS can provide full and immediate support to efforts to commercialize this technology.

Additional Resources and References

Fortunately, the accelerated interest in broader perchlorate chemistries is supported by the publication of significant new resources; these include two books: 1) *Perchloric Acid and Perchlorates*, A. A. Schilt, 2nd Edition, published by GFS Chemicals, 2002; 2) *Perchlorate in the Environment*, E. Urbansky, Ed., Environmental Science Research Volume 57, Kluwer Academic/Plenum Publishers, New York. In addition, the May/June 2002 issue of the Chemical Health & Safety journal (Volume 9, No. 3) was scheduled to include a very pertinent article, Perchlorate Safety: Reconciling Inorganic and Organic Guidelines. All these texts are extensively referenced.

The issue of perchlorate fume hood decontamination was thoroughly addressed by R. J. Kelly in Chemical Health & Safety, Vol. 7, No. 3 (May/June), 2000, p.5. Additional insights on fume hood disposal are available from Mr. Marwan Bader, Oak Ridge National Lab, via e-mail: b6v@ornl.gov.

The current GFS catalog features an extensive Q&A section that addresses issues of properties and applications of perchlorates that are most frequently raised. Much of this information is also available on the GFS web site: www.gfschemicals.com .
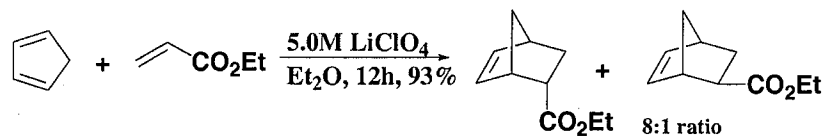
References

1. For additional examples see Espenson, J. H., in *Perchlorate in the Environment*, E. Urbansky, Ed., Environmental Science Research, Volume 57, Kluwer Academic/Plenum Publishers, New York, Chapter 1.

2. Smith, G. F., in The Wet Chemical Oxidation of Organic Compositions Employing Perchloric Acid, GFS Chemicals publ., 1965.

3. GFS data, generated by Ashland Specialty Chemical Co., Corporate Technology Services Engineering Research Group, Dublin, OH.

4. Willard, H. H., Smith, G. F., *J. Am. Chem. Soc.*, **1923**, *45*, 286.

5. Grieco, P. A., in Organic Chemistry: Its Language and Its State of Art, V. Kisaknerek, Editor, VCH, Basel, **1993**, 133.

6. Pocker, Y., Ellsworth, D. L. , *J. Amer. Chem. Soc.*, **1977**, *99*, 2276.

7. Winstein, S., Smith, S., Darwish, D., *J. Am. Chem. Soc.*, **1959**, *81*, 5511.

Reactions Promoted by Anhydrous Lithium Perchlorate

A. Intermolecular Diels-Alder Reactions

Example 1:

Features: Reaction run at ambient temperature and pressure. Stereoselectivities and yields are improved using LPDE.

Reference: *J. Am. Chem. Soc.*, **1990**, *112*, 4595.

Example 2:
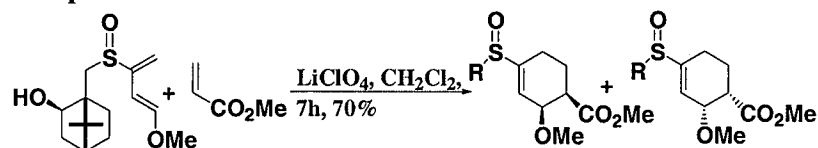
Features: Remarkable acceleration in rate of reaction and diastereofacial selectivity was observed with LPDE.

Reference: *Tetrahedron Lett.*, **1993**, *34*, 7367.

Example 3:
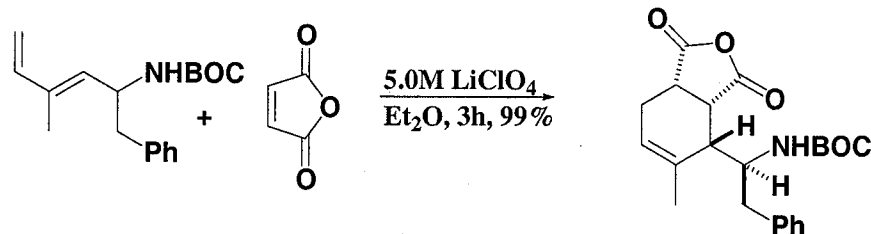
Features: Asymmetric induction in Diels-Alder cycloadditions using sulfoxides as chiral auxiliaries was studied using various Lewis acids. The best catalyst was lithium perchlorate, the use of which as a suspension in dichloromethane gave only the endo isomers in a ratio of 96:4.

Reference: *Tetrahedron Lett.*, **1993**, *34*, 6481.

Example 4:
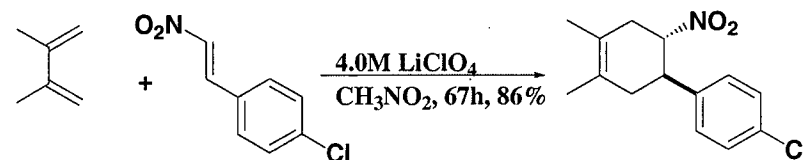
Features: Diels-Alder reaction in which nitroalkenes, acting as dienophiles, are substantially accelerated in 4M lithium perchlorate-nitromethane solutions. This acceleration is higher than that observed with 5M LPDE.

Reference: *Tetrahedron Lett.*, **1995**, *36*, 4447.

Example 5:
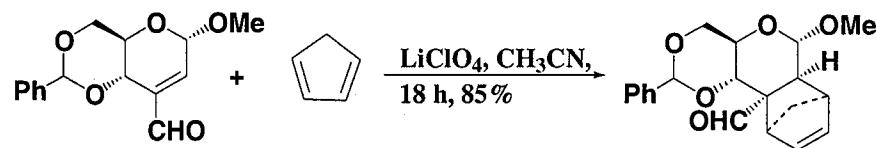
Features: A sugar-derived cyclic dienophile showed a high exo and face selectivity in the Diels-Alder reaction with cyclopentadiene using lithium perchlorate-acetonitrile as medium.

**Reference:** *Org.Lett.*, **2000**, *2*, 1073

See following references for LiClO$_4$ catalyzed Intermolecular Diels-Alder Reactions:

1.   Grieco, P. A.; Nunes, J.; Gaul, M. *J. Am. Chem. Soc.* **1990**, *112*, 4595.
2.   Forman, M.; Dailey, W.; *J. Am. Chem. Soc.*, **1991**, *113*, 2761.
3.   Lucchi, O.; Fabbri, D.; Lucchini, V. *Tetrahedron* **1992**, *48*, 1485.
4.   Adams, H.; Jones, D.; Aversa, M.; Bonaccorsi, P.; Giannetto, P. *Tetrahedron Lett.* **1993**, *34*, 6481.
5.   Grieco, P. A.; Beck, J. *Tetrahedron Lett.* **1993**, *34*, 7367.
6.   Pfizenmayer, A.; Corova, R. *Tetrahedron: Asymmetry* **1994**, *5*, 519.
7.   Chiba, K.; Tada, M. *J. Chem. Soc., Chem. Commun.* **1994**, *21*, 2485.
8.   Bains, S.; Pagni, R.; Kabalka, G.; Pala, C.; *Tetrahedron Asymm.*, **1994**, *5*, 821.
9.   Ayerbe, M.; Cossio, F. *Tetrahedron Lett.* **1995**, *36*, 4447.
10.   Heard, N. E.; Turner, J. *J. Org. Chem.* **1995**, *60*, 4302.
11.   Mayer, S.; Bunuel, E.; Cativiela, C.; Diaz-de-Villegas, M. D. *Tetrahedron* **1995**, *51*, 8923.

12. Yang, T. K.; Chu, H.Y.; Lee, D. S.; Jiang, Y. Z.; Chou, T. S. *Tetrahedron Lett.,* **1996**, *37*, 4537.
13. Crisp, G. T.; Gebauer, M. G.; *J. Org. Chem.* **1996**, *61*, 8425.
14. Adams, H.; Anderson, J. C.; Bell, R.; Neville Jones, D.; Peel, M. R.; Tomkinson, Nicholas, C. *J. Chem. Soc. Perkins Trans. 1* **1998**, 3967.
15. Chapuis, C.; Kucharska, A.; Rzepecki, P.; Jurczak, J.; *Helv. Chim. Acta*, **1998**, *81*, 2314.
16. Chiba, K.; Jinno, M.; Kuramoto, R.; Tada, M. *Tetrahedron Lett.,* **1998**, *39*, 5527.
17. Earle, M.; McCormac, Seddon, K.; *Green. Chem.*; **1999**, *1*, 23.
18. Shanmugasundaram, M.; Raghunathan, R.; *Tetrahedron*, **2000**, *56*, 5241.
19. Pellegrinet, S. C, Spanevello, *Org. Lett.,* **2000**, *2*, 1073.

B. Intramolecular Diels-Alder Reactions
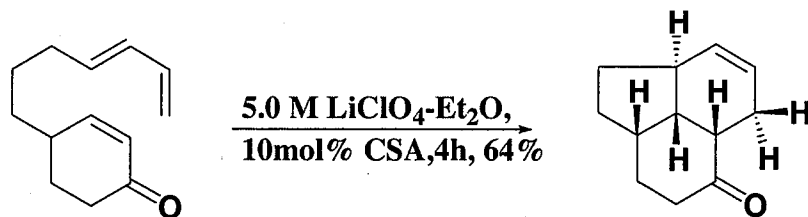
Example 1:

Features: Use of 10 mol% camphorsulfonic acid in 5.0 M lithium perchlorate-diethyl ether for intramolecular Diels-Alder reactions of conformationally restricted substrates.

Reference: *Tetrahedron Lett.,* **1994**, *35*, 6783

Example 2:

n=1,2
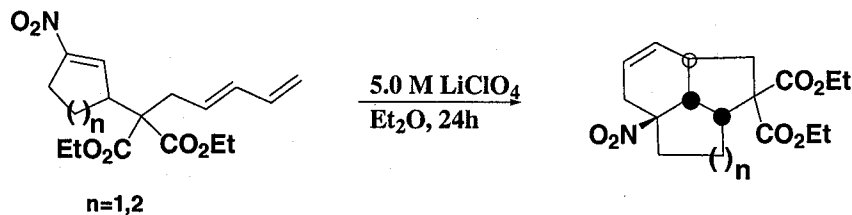
Features: The reaction takes place at room temperature in the presence of LPDE and is remarkably selective. The mild Diels-Alder reaction proceeds exclusively via an anti transition state controlled by electronic and steric effects. Use of other Lewis acid TiCl$_2$ gave polymerized products.

Reference: *Syn Lett.,* **1994**, **647**

Example 3:
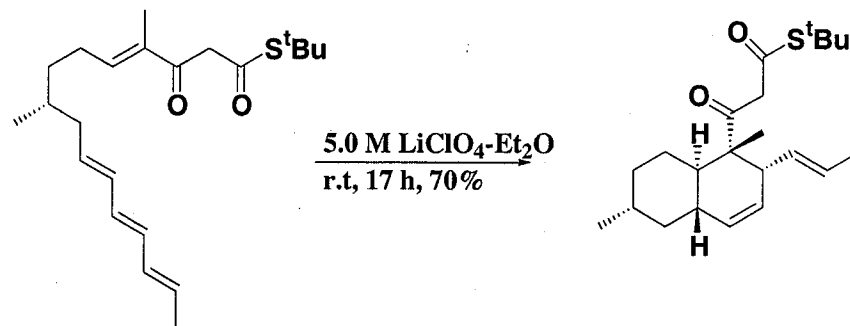
Features: Stereoselective synthesis of the natural product Equisetin, a potent inhibitor of HIV-1 integrase enzyme, has been achieved using lithium perchlorate mediated intramolecular Diels-Alder reaction of a fully conjugated *E,E,E*-triene with a trisubstituted γ,δ-unsaturated β-ketothioester.

Reference: *Org.Lett.,* **2000**, *2*, 3611.

See following references for LiClO$_4$ catalyzed Intramolecular Diels-Alder Reactions:

1. Grieco, P. A.; Handy, S.; Beck, J. *Tetrahedron Lett.* **1994**, *35*, 2663.
2. Grieco, P. A.; Beck, J.; Handy, S.; Saito, N.; Daeuble, J. *Tetrahedron Lett.* **1994**, *35*, 6783.
3. Guy, A.; Serva, L. *Synlett* **1994**, *8*, 647.
4. Grieco, P.A.; Kaufman, M. D. *J. Org. Chem.* **1999**, *64*, 2590.
5. Grieco, P.A.; Kaufman, M. D. *J. Org. Chem.* **1999**, *64*, 6041.
6. Greico, P. A.; Kaufman, M. D. *J. Org. Chem.* **1999**, *64*, 7586.
7. Greico, P. A.; Kaufman, M. D. *Tetrahedron Lett.,* **1999**, *40*, 1265.
8. Burke, L. T.; Dixon, D. J.; Ley, S. V.; Rodriguez, F.; *Org. Lett.,* **2000**, *2*, 3611.
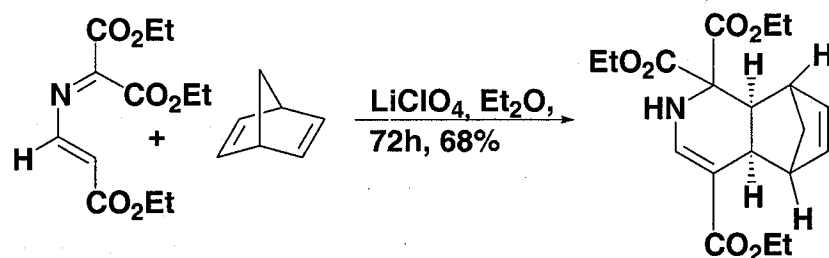
C. Hetero- and Ionic Diels-Alder Reactions

Example 1:
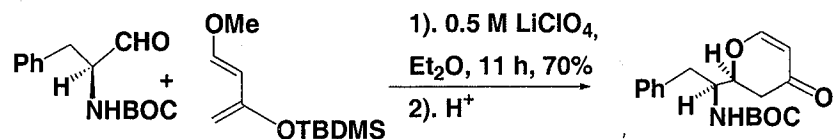
Features: Lithium perchlorate in diethyl ether catalyzes the cyclocondensation of N-BOC protected α-amino aldehydes with Danishefsky's diene providing, after exposure to acid, dihydropyrones possessing the *threo* configuration.

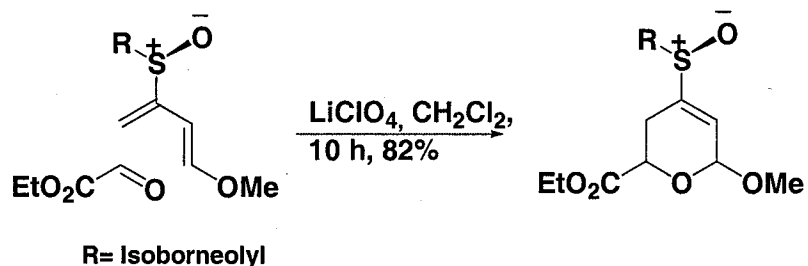**Reference:** *Tetrahedron Lett.,* **1993**, *34*, 5567.

Example 2:

Features: This is the first example of rate-enhancement in Diels-Alder reactions of electron-poor azadienes by perchlorates in nonaqueous solvents.

Reference: *J. Org. Chem.,* **1995**, *60*, 2384

Example 3.

R= Isoborneolyl

Features: This is an example of hetero-D-A cycloaddition of isoborneol-substituted butadiene with ethyl glyoxalate. LiClO$_4$ was found to be most effective catalyst in enhancing facial diasteroselectivity.

Reference: *Tetrahedron Asymm.,* **1997**, *8*, 2989

See following references for LiClO$_4$ catalyzed Hetero- and Ionic Diels-Alder Reactions:

1.   Desimoni, G.; Faita, G.; Righetti, P.; Tacconi, G.; *Tetrahedron,* **1991**, *47*, 8399.
2.   Grieco, P. A; Moher, E. *Tetrahedron Lett.* **1993**, *34*, 5567.
3.   Reetz, M.; Gansaeuer, A. *Tetrahedron* **1993**, *49*, 6025.
4.   Grieco, P. A.; Collins, J. L. Handy, S. T. *Synlett.* **1995**, *11*, 1155.
5.   Palcios, F.; Perez de Heredia, I.; Rubiales, G. *J. Org. Chem.* **1995**, *60*, 2384.
6.   Desimoni, G.; Faita, G.; Righetti, P. *Tetrahedron Lett.* **1995**. *36*, 2855.
7.   Grieco, P. A; Kaufman, M.; Daeuble, J.; Saito, N. *J. Am. Chem. Soc.* **1996**, *118*, 2095.
8.   Aversa, M. C.; Baratucci, A.: Bonaccorsi, P.; Bruno, G.; Giannetto, P.; Panzalorto. M. *Tetrahedron: Asymmetry* **1997**, *8*, 2989.
9.   Kumareswaran, R.; Vankar, P. S.; Reddy, M. V. R.; Pitre, S. V.; Roy, R.; Vankar, Y. D.; *Tetrahedron,* **1999**, *55*, 1099.
10.   Yadav, J. S.; Reddy, B. V. S.; Srinivas, R.; Madhuri, Ch.; Ramalingam.; *Synlett.,* **2001**, 240.
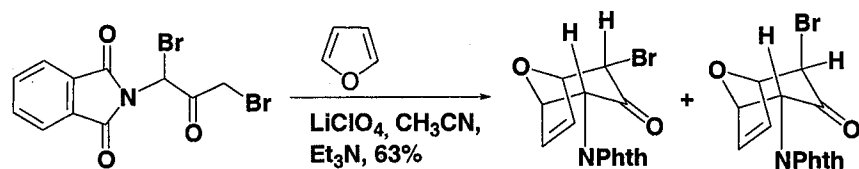
D. Cycloaddition Reactions:

Example 1.
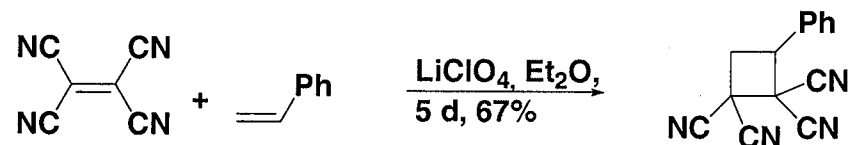
Features: Strong Lewis acids EtAlCl$_2$ and Et$_{1.5}$AlCl$_{1.5}$ give unidentified products. With mild Lewis acid LiClO$_4$ cyclobutane compounds are stable and do not undergo further reaction.

Reference: *J. Org. Chem.,* **1994**, *59*, 5424

Example 2.

Features: The nitrogen-substituted oxallyl cation can be generated from the dibromide using LiClO$_4$/CH$_3$CN/Et$_3$N. These cations were found to undergo [4+2] cycloaddition reactions with furan and cyclopentadiene. The diastereo- and regioselectivities in these reactions were found to be influenced in a positive manner by the presence of Li$^+$.
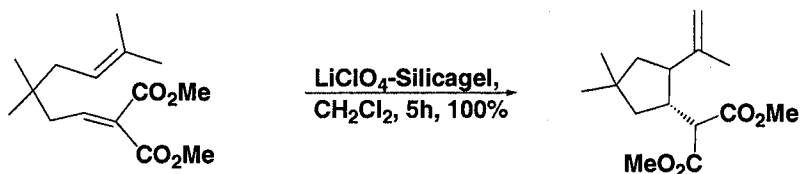
Reference: *J. Org. Chem.*, **1996**, *61*, **1478**

Example 3.
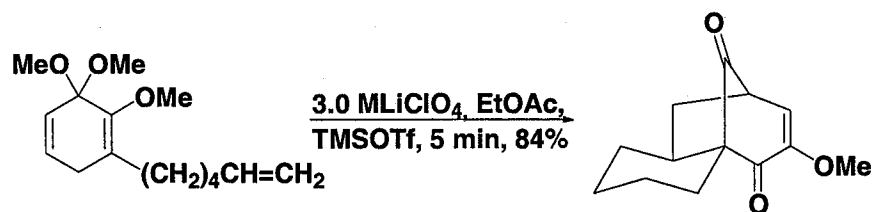
Features: 3.0M LiClO$_4$-EtOAc/TMSOTf reagent system was found to be effective for promoting intramolecular cationic [5+2] cycloaddition reactions. This methodology has been used in formal synthesis of the angular triquinane isocomene.

Reference: *Tetrahedron*, **1997**, *53*, **8975.**

Example 4.

Features: LiClO$_4$-supported silica gel is an effective catalytic system for promoting ene cyclizations of activated 1,6 and 1,7-dienes. LP-SG dramatically accelerates these reactions and provides a mild, effective and recyclable catalyst for intramolecular ene reactions.

Reference: *Synlett.*, **1996, 87.**

See following references for LiClO$_4$ catalyzed Hetero- and Ionic Diels-Alder Reactions:

1. Fohlisch, B.; Herrscher, I., *Chem. Ber.* **1986**, *119*, 524.
2. Srisiri, W.; Padias, A.; Hall Jr., H. *J. Org. Chem.* **1994**, *59*, 5424.
3. Walters, M. A.; Arcand H. R. *J. Org. Chem.* **1996**, *61*, 1478.
4. Collins, J. L.; Grieco, P. A.; Walter, J. K. *Tetrahedron Lett.*, **1997**, *38*, 1321.
5. Grieco, P. A.; Walter, J. K. *Tetrahedron*, **1997**, *53*, 8975.
6. Cho, S. Y.; Lee, J. C.; Cha, J. K., *J. Org. Chem.* **1999**, *64*, 3394.
7. Chiba, K.; Fukuda, M.; Kim, S.; Kitano, Y.; Tada, M.; *J. Org. Chem.* **1999**, *64*, 7654.
8. Sarkar, T. K.; Nandy, S. K.; Ghorai, B. K.; Mukherjee, B.; *Synlett.*, **1996**, 97.
9. Lecea, B.; Arrietia, A.; Arrastia, I.; Cossio, F. P.; *J. Org. Chem.* **1998**, *63*, 5216.
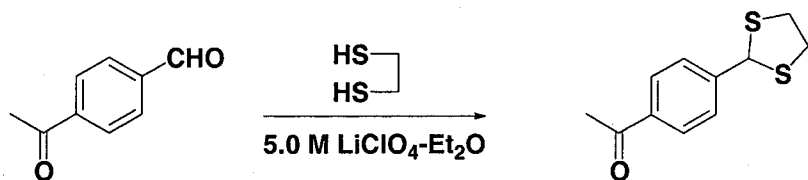
E. Addition and Substitution Reactions:

Example 1.
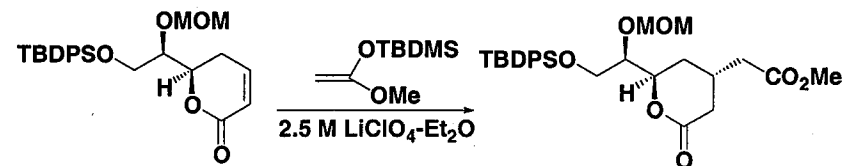
Features: Silyl ketene acetals add in a conjugate fashion to highly functionalized, hindered α,β-unsaturated carbonyl systems in the presence of LiClO$_4$ at atmospheric pressure, thus obviating the need for ultra high pressure.

**Reference:** *Tetrahedron Lett.*, **1991**, *32*, **4665.**

Example 2.

Features: Aldehydes and acetals were efficiently converted to acyclic and cyclic dithioacetals in 5.0 M LPDE medium at ambient temperature in high yields. The chemoselective dithioacetalization of aldehydes in the presence of ketones was observed. This method offers a convenient, efficient and neutral medium for the protection of aldehydes to dithioacetals.
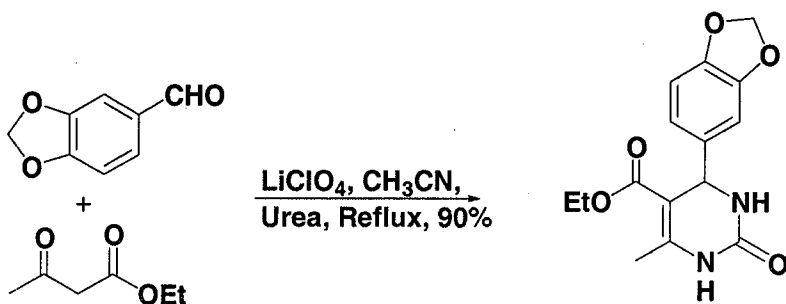
Reference: *J. Org. Chem.*, 1994, *59*, 4665.

Example 3.
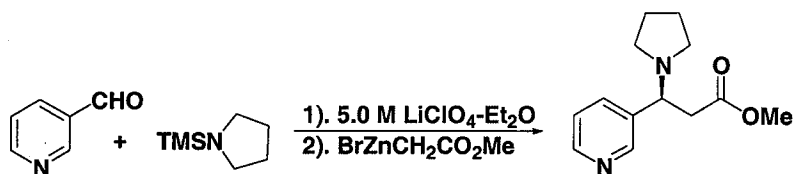
Features: Treatment of aldehydes with silylated dialkyl amines in the presence of LPDE presumably gives the imines, which on treatment with RZnBr produces *N,N*-dialkylamino esters in short time and in good to moderate yields.
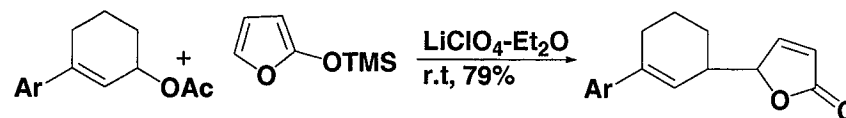
Reference: *J. Chem. Soc. Perkin Trans 1.*, 1997, 1983.

Example 4.

Features: LiClO$_4$ catalyzes three component condensation of β-keto ester, aldehyde and urea. This provides an efficient protocol for Biginelli reactions, affording the corresponding dihydropyrimidinones in high yields.
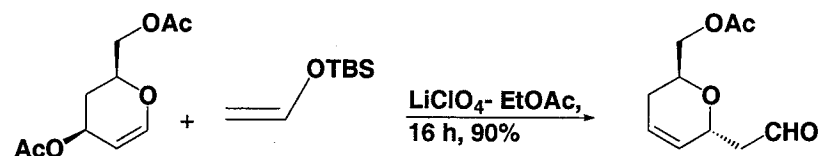
Reference: *Synthesis.*, 2001, 1341.

Example 5.

Features: LPDE promoted substitution reaction allows convenient access to γ,δ-unsaturated esters, ketones and aldehydes. The efficiency of this method for carbon-carbon bond formation makes it a good alternative to transition metal-catalyzed processes.

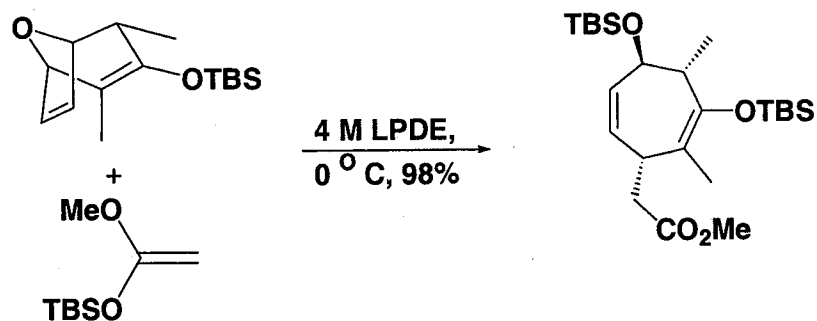**Reference:** *J. Org. Chem.*, 1992, *57*, 2986.

Example 6.

Features: LiClO$_4$-EtOAc catalyzes a highly stereoselective carbon Ferrier-type reaction between glucal and the t-butyldimethylsilyl enol ether of acetaldehyde. Use of conventional Lewis acids such as MgBr$_2$, ZnCl$_2$ gave substantial amounts of undesired oligomer.

Reference: *Tetrahedron Lett.*, 1998, *39*, 1275.

Example 7.

Features: Readily available strained bicyclic molecules such as 8-oxabicyclo-[3.2.1]octadienes and octenes react with silyl ketene acetals in 4.0-5.0 M LPDE to give highly functionalized cycloheptadienes that can be further reacted as part of the synthesis of natural products.

Reference: *Org. Lett.,* 2001, *3,* 481.

See following references for LiClO$_4$ Catalyzed Addition and Substitution reactions:

1. Grieco, P. A.; Cooke, R.; Henry, K.; VanderRoest J. M. *Tetrahedron Lett.,* **1991,** *32,* 4665.
2. Grieco, P. A.; Collins, J.; Henry, K. *Tetrahedron Lett.* **1992,** *33,* 4735.
3. Pearson, W. H.; Schkeryantz, J. M.; *J. Org. Chem.* **1992,** *57,* 2986.
4. Saraswathy, V.; Sankararaman, S. *J. Org. Chem.* **1994,** *59,* 4665.
5. Otera, J.; Fujita, Y.; Fukuzumi, S.; Hirai, K.; Gu, J.; Nakai, T. *Tetrahedron Lett.* **1995,** *36,* 95.
6. Saraswathy, V. G.; Sankararaman, S. *J. Org. Chem.* **1995,** *60,* 5024.
7. Saraswathy, V.; Sankaraman, S. *J. Chem. Soc. Perkin. Trans.1,* **1996,** 29.
8. Hatanaka, M. Ishida, A.; Tanaka, Y.; Ueda, I. *Tetrahedron Lett.* **1996,** *37,* 401.
9. Saida, M. R.; Khalaji, H. R.; Ipaktschi, J. *J. Chem. Soc., Perkins Trans. 1* **1997,** 1983.
10. Martin, S. F.; Bur, S. K.; *Tetrahedron Lett.,* **1997,** *38,* 7641
11. Grieco, P. A; Speake, J. D.; *Tetrahedron Lett.* **1998,** *39,* 1275.
12. Heydari, A.; Karimian, A.; Ipaktschi, J.; *Tetrahedron Lett.,* **1998,** *39,* 6729.
13. Sankararaman, S.; Sudha, R. *J. Org. Chem.* **1999,** *64,* 2155.
14. Tietze, L. F.; Weigand, B.; Wulff, C.; *Synthesis,* **2000,** 69.
15. Dixon, D. J.; Foster, A. C.; Ley, S. V.; *Org. Lett.;* **2000,** 2, 123.
16. Nakada, M.; Takano, M.; Iwata, Y.; *Chem. Pharm. Bull.;* **2000,** *48,* 1581.
17. Naimi-jamal, M.; Ipaktschi, J.; Saidi, M. R.; *Eur. J. Org. Chem.;* **2000,** 1735.
18. Saidi, M. R.; Reza, N.; *Synth.Commun.;* **2000,** *30,* 3849.
19. Hunt, K. W.; Grieco, P. A.; *Org. Lett.;* **2001,** *3,* 481.
20. Yadav, J. S.; Reddy, B. V. S.; Srinivas, R.; Venugopal, T.; Ramalingam, T.; *Synthesis,* **2001,** 1341.
21. Yadav, J. S.; Reddy, B. V. S.; Murthy, C. V. S.; Kumar, G. M.; Madan, Ch.; *Synthesis,* **2001,** 783.
22. Mojtahedi, M. M.; Saidi, M. R.; Shirzi, J. S.; Bolourtchian, M.; *Synth. Commun.;* **2001,** *31,* 3587.
23. Hunt, K. W.; Grieco, P. A.; *Org. Lett.;* **2002,** *4,* 245.
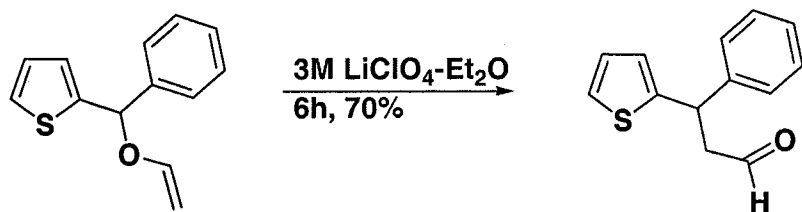
F. Rearrangement Reactions:

Example 1.
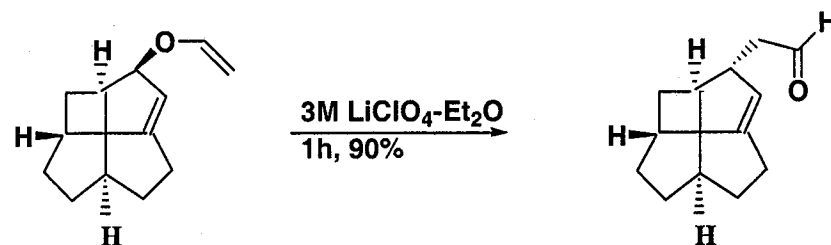
Features: 0.2 M solutions of several allyl vinyl ethers in 3.0 M LPDE were shown to undergo exclusive [1,3] sigmatropic rearrangement after one hour at ambient temperature, giving rise to corresponding aldehydes in excellent yields (72-94%).

Reference: *J. Am. Chem. Soc.,* 1991, *113,* 5488.

Example 2.

3M LiClO$_4$-Et$_2$O
6h, 70%

Features: Benzyl and naphthylmethyl vinyl ethers are inert in LPDE medium, whereas heteroaromatic methyl vinyl ethers, viz. 2-furyl and 2-thienylmethyl vinyl ethers, undergo formal [1,3] rearrangement in LPDE medium. This provides a simple, mild route for the synthesis of γ-heteroaryl propanals.

Reference: *Tetrahedron Lett.,* **1995**, *36*, 9527.

Example 3.

LiClO$_4$-toluene
Reflux, 100%
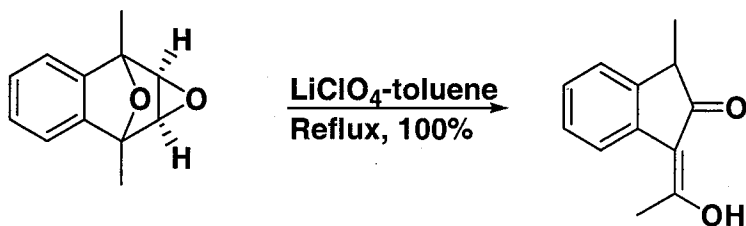
Features: LiClO$_4$ promotes carbocation-driven ring contracting rearrangements of epoxides derived from Diels-Alder adducts of benzynes and furans. The unprecedented transformation provides moderate to excellent yields of novel α-formyl and α-acyl-2-indanones.

Reference: *Tetrahedron Lett.,* **1991**, *32*, 851.

**Example 4.**

LiClO$_4$-Et$_2$O,
2 h, 83%
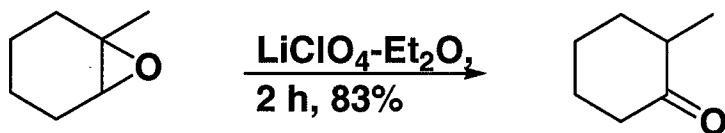
Features: LiClO$_4$ is found to be an effective mild catalyst for conversion of epoxides to carbonyl compounds. Many epoxides were rearranged with 5.0M LPDE to products with high chemo- and regioselectivities.

Reference: *Tetrahedron Lett.,* **1991**, *32*, 851.

See following references for LiClO$_4$ catalyzed rearrangement reactions:

1. Grieco, P.; Clark, J.; Jagoe, C. *J. Am. Chem. Soc.* **1991**, *113*, 5488.
2. French, L.; Fenion, E.; Edward, E.; Charlton, T. *Tetrahedron Lett.* **1991**, *32*, 851.
3. Grieco, P.; Collins, J. L.; Henry Jr. K. J, *Tetrahedron Lett.* **1992**, *33*, 4735.
4. Palani, N.; Balasubramanian, K. K. *Tetrahedron Lett.* **1995**, *36*, 9527.
5. Sudha, R.; Narasimhan, K.M.; Saraswathy, V.G.; Sankararaman, S. *J. Org. Chem*, **1996**, *61*, 1877.
6. Mitamura, S.; Ishikawa, K.; Nakagawa, T.; Nomoto, H.; *Jpn. Kokai Tokkyo Koho* **2001**, 6pp.JP 2001233818 A2 20010828.

G. Glycosylation Reactions:

CH$_2$Cl$_2$, 1M LiClO$_4$,
CsF, M.Sieves
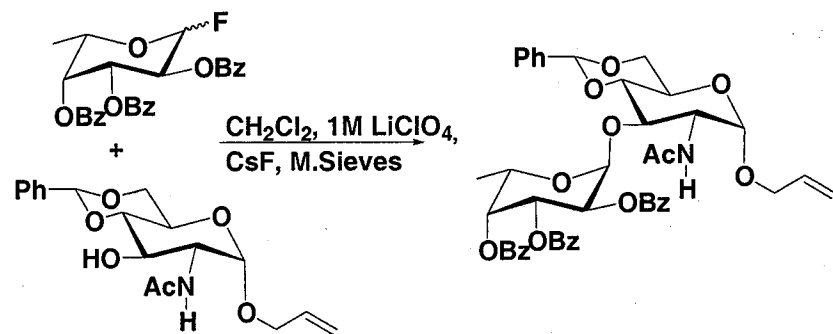
Features: Glycosyl donors (fucosyl fluoride and trichloroacetamidate) are activated under neutral conditions in 1M solutions of CH$_2$Cl$_2$ or ether to react with mono- and disaccharides to give fucosyl glycosides in high yields and high regioselectivity.
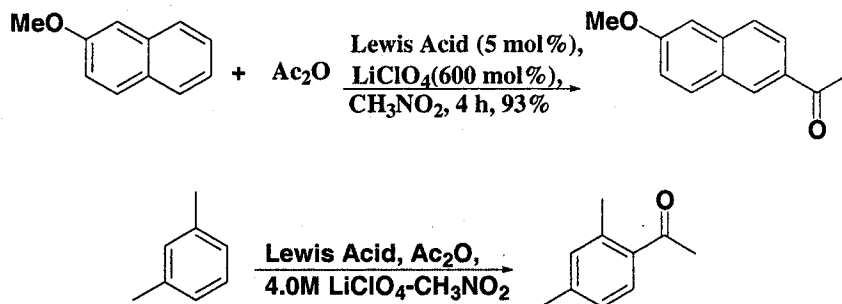
Reference: *Tetrahedron Lett.,* **1995**, *36*, 3843.

See following references for LiClO$_4$ Catalyzed Glycosylation Reactions:

1. Waldmann, H.; Bohm, G.; Schmid, H.; Rottele, H. *Angew Chem.Int.Ed.Engl.* **1994**, *33*, 1944.
2. Bohm, G.; Waldmann, H. *Tetrahedron Lett.* **1995**, *36*, 3843.
3. Uchiro, H.; Mukaiyama, T. *Chem.Lett.*, **1996**, 271.
4. Boehm, G.; Waldmann, H.; *Liebigs Ann.*, **1996**, 613.
5. Mukaiyama, T.; Takeuchi, K.; Higuchi, S.; Uchiro, H. *Chem.Lett.* **1996**, 1123.
6. Uchiro, H.; Miyazaki, K.; Mukaiyama, T. *Chem. Lett.* **1997**, 403.

7. Schene, H.; Waldman, H.; *Chem. Commun.*, **1998**, 2759.
8. Babu, B. S.; Balasubramanian, K. K.; *Carbohydr. Lett.*, **1999**, *3*, 339.
9. Gupta, A.; Vankar, Y.D. *Tetrahedron*, **2000**, *56*, 8525.

H. Friedel-Crafts Acylation Reactions:

References: *Tetrahedron Lett.*, **1995**, 36, 409-412. *Tetrahedron*, **2000**, *56*, 6463.

Features: In the presence of a catalytic amount of a metal triflate such as $Sb(OTf)_3$ or $Ga(OTf)_3$, 2-methoxynaphthalene reacted with acetic anhydride in $LiClO_4-CH_3NO_2$ to afford 2-acetyl-6-methoxynaphthalene, a well known intermediate for the synthesis of the anti-inflammatory drug naproxen, in high yield.

See following references for LiClO$_4$ Catalyzed Friedel-Crafts Reactions:

1. Hachiya, I.; Moriwaki, M.; Kobayashi, S.; *Tetrahedron Lett.*; **1995**, *36*, 409.
2. Frost, C. G.; Hartley, J. P.; Proc. ECSOC-3, Proc. EC SOC-4, 1999, **2000**, 955.
3. Kobayashi, S.; Komoto, I.; *Tetrahedron.*; **2000**, *56*, 6463.
4. Chapman, C. J.; Frost, C. G.; Hartley, J. P.; Whittle, A. J.; *Tetrahedron Lett.*, **2001**, *42*, 773.

## I. Epoxide and Aziridine Ring Opening Reactions:
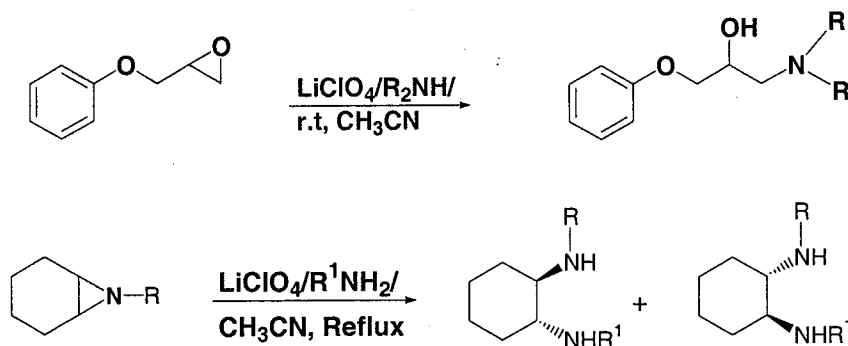
Features: $LiClO_4$ in acetonitrile was found to be the preferred medium for nucleophilic opening of epoxides with cyanides, azides, amines, alcohols and thiols to give corresponding β-hydroxy nitriles, azides, amines, alcohols and thiols in high yield. The ring opening of aziridines is completely stereoselective, giving only *trans* products in good yield.

See following references for LiClO$_4$ Catalyzed Epoxide and Aziridine Ring Opening Reactions:

1. Chini, M.; Crotti, P.; Macchia, F. *Tetrahedron Lett.*, **1990**, *31*, 5641.
2. Chini, M.; Crotti, P.; Macchia, F. *Tetrahedron Lett.*, **1990**, *31*, 4661.
3. Chini, M.; Crotti, P.; Favero, L.; Macchia, F. *Tetrahedron Lett.*, **1991**, *32*, 4475.
4. Chini, M.; Crotti, P.; Gardelli, C. Macchia, F. *Syn Lett.*, **1992**, 673.
5. Chini, M.; Crotti, P.; Giovani, E.; Macchia, F.; Pineschi, M. *Syn Lett.*, **1992**, 303.
6. Chini, M.; Crotti, P.; Gardelli, C.; Macchia, F. *Tetrahedron.*, **1992**, *48*, 3805.
7. Rosse, G.; Quertani, F.; Schroeder, H.; *J. Comb. Chem.*; **1999**, *1*, 397.
8. Fernandez-megia, E.; Montaos, M. A.; Sardina, F. J.; *J. Org. Chem.* **2000**, *65*, 6780 (aziridine formation reaction)
9. Anaya de parrodi, C.; Quintero, L.; Juaristi, E.; *Synth. Commun.* **2001**, *31*, 3295 (aziridine opening reactions).
10. Pousset, C.; Haddad, M.; Larcheveque, M.; *Tetrahedron*, **2001**, *57*, 7163.
11. Vega-Perez, J. M.; Candela, J. I.; Romero, I.; Blanco, E.; Iglesias-Guerra, F.; *Eur. J. Org. Chem.*, **2001**, 3949.
12. Yadav, J. S.; Reddy, B. V. S.; Jyothirmai, B.; Murthy, M. S. R.; *Synlett.*, **2002**, 53.
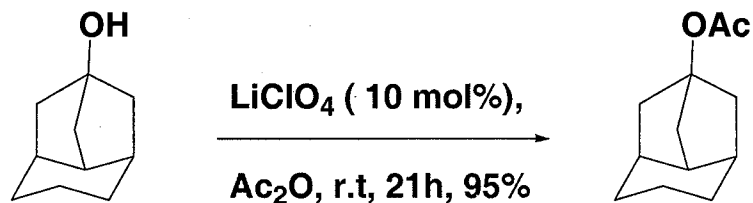
J. Baylis-Hillman Reaction
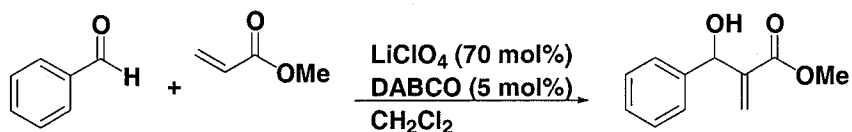
Features: With the use of LiClO$_4$ and catalytic amounts of DABCO, remarkable acceleration in coupling of α,β-unsaturated carbonyl compounds with aldehydes was observed, giving adducts in moderate to good yields.

Reference:

Kawamura, M.; Kobayashi, S.; *Tetrahedron Lett.*, **1999**, *40*, 1539.

K. Acetylation of Alcohols:

Features: LiClO$_4$ is a very efficient and versatile catalyst for acetylation of alcohols and phenols. The advantage of the method is that even hindered alcohols (e.g. adamantol) can be acylated in high yield under typical reaction conditions.
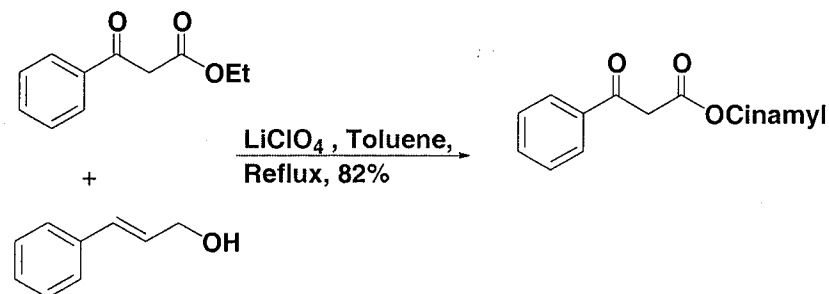
Reference:

Nakae, Y.; Kusaki, I.; Sato, T.; *Synlett.*, **2001**, 1584.

For Deacetylation using LiClO$_4$-Et$_3$N see

Hu, Y.; Bai, D.; *Tetrahedron Lett.*, **1998**, *39*, 2375.

## L. Trans Esterification of β-keto esters:

Features: LiClO$_4$ is also a very efficient catalyst for trans-esterification of several β-keto esters, essentially under neutral conditions.

Reference:

Bandgar, B. P.; Sadavarte, V. S.; Uppalla, L. S.; *Synlett*, **2001**, 1338.

M. Protection of Hydroxyl Group

Features: Alcohols and phenols can be silylated with HMDS under microwave (MW) irradiation without solvent using LiClO$_4$ as a neutral catalyst. Chemoselective silylation of benzylic alcohol was achieved in the presence of a phenol group as well as a primary amine.
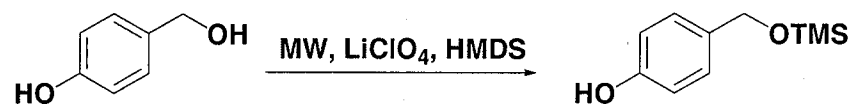
Reference: Bandgar, B. P.; Kasture, S. P.; *Monatsh. Chem.,* **2001**, 1101.

N. Deoxygenation of Allylic Alcohols and Acetates:
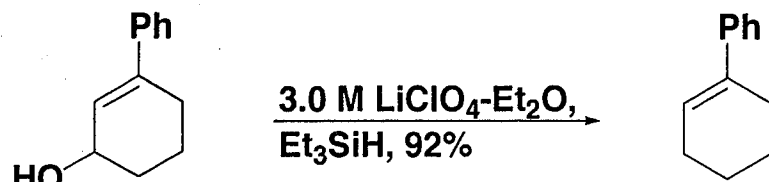
Features: The allylic deoxygenation for cyclohexenyl alcohols and acetates can be conveniently carried out using triethyl silane in presence of LPDE. Unlike other methods it does not require expensive transition metal catalysis. A variety of functional groups such as esters, ketals are unaffected.

**Reference:** Wustrow, D. J.; Smith III, W. J.; Wise, L. D.; *Tetrahedron Lett.*; **1994**, *35*, 61.

O. Reviews and Recent Publications on Lithium Perchlorate in Organic Reactions:

1. Grieco, P. A.; *Aldrichimica Acta*, **1991**, *24*, 59.
2. Waldman, H.; *Angew. Chem. Int. Ed. Eng.*, **1991**, *30*, 1306.
3. Grieco, P. A.; Organic Chemistry in Lithium Perchlorate/Diethyl Ether. In *Organic Chemistry: Its language and its State of the Art*; Kisakurek, V., Ed.; Basel, **1993**, 133.
4. Flohr, A; Waldman, H.; *J. Prakt. Chem.*, **1995**, *33*, 609.
5. Long, J. R.; G.I.T. Laboratory Journal, **2000**, *4*, 222.
6. Kumar, A.; *J. Chem. Eng. Data*, **2000**, 630.
7. Sankararaman, S.; Nesakumar, J. E.; *Eur. J. Org. Chem*, **2000**, 2003.
8. Kumar, A.; *Chem. Rev.*, **2001**, *101*, 1.

Reactions Promoted by Anhydrous Magnesium Perchlorate

A. Diels-Alder Reactions

Example 1:

100%
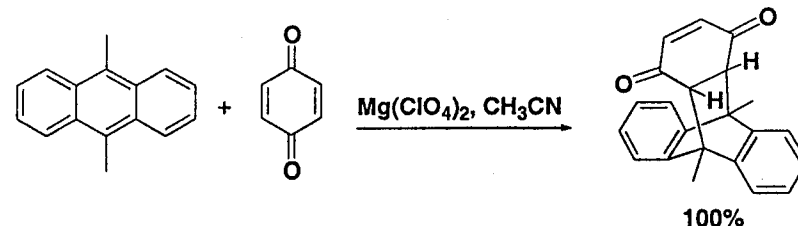
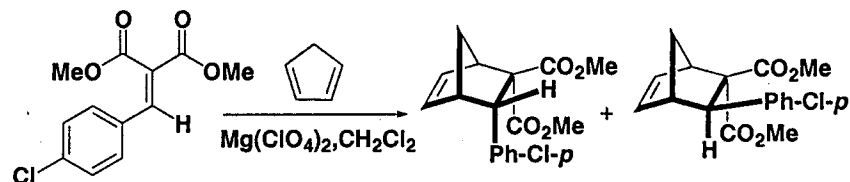**Features:** Diels-Alder reactions of anthracene derivatives with *p*-benzoquinone (regarded as weak dienophile) proceed very efficiently in the presence of $Mg(ClO_4)_2$ in acetonitrile via Mg^{2+}-catalyzed electron transfer from anthracene to *p*-benzoquinone derivatives.

Reference: *J. Am. Chem. Soc.*, **1993**, 115, 11600.

Example 2:

Features: The D-A reaction of 2-arylidene-malonic acid dimethyl ester and cyclopentadiene in an acetone solution of lithium perchlorate at room temperature over 15 days gave an 80% yield of cycloadducts. When the reaction was performed in dichloromethane with 0.5 eq. of MP, a quantitative yield of adducts was obtained within 30 min. The rate acceleration of the Diels-Alder reaction depends upon the organic solvent and the metal cation. Among inorganic perchlorates $Mg(ClO_4)_2$ is found to be the most active cation and sodium is the least active one.

**Reference:** *Tetrahedron.*, **1997**, 39, 13495.

Example 3:
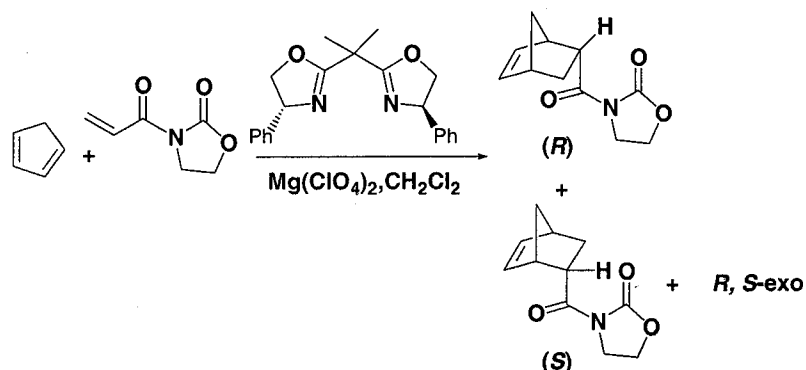
Features: Magnesium perchlorate catalyzes the asymmetric D-A reaction between cyclopentadiene and acryloyl oxazolidine to give the *endo* adduct as main product in 98% yield (*endo:exo* 93:7). A significant enantioselectivity was observed in the presence of chiral bis(oxazoline) ligand (*S* isomer in 68-70% ee).

Reference: *Tetrahedron,* **1997, 53, 7671.**

Example 4:
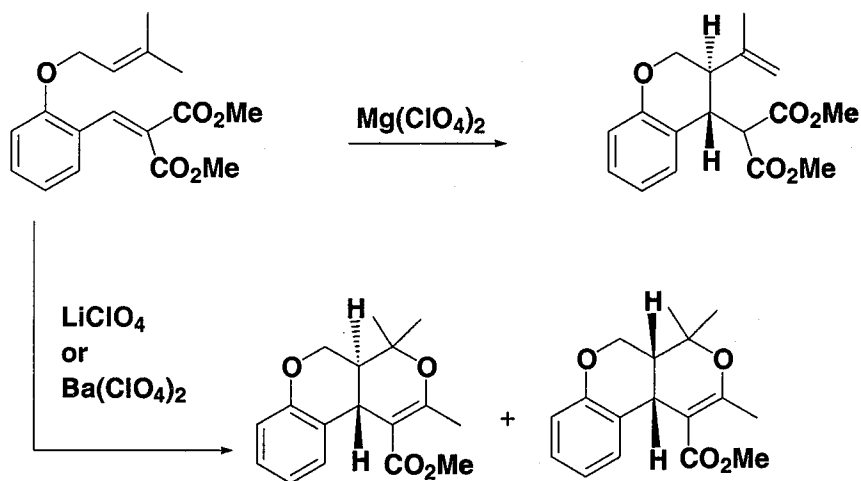
Features: Under thermal conditions and with Lithium perchlorate and Barium perchlorate at room temperature, the heterodienic cycloaddition

preferentially occurred. With Magnesium perchlorate, chemoselectivity was greatly altered in that the heterodienic adducts were minor products and the *trans*-ene product was obtained in 93% yield.

Reference: *Tetrahedron,* **1996, 52, 12009.**

See following references for Mg(ClO₄)₂ catalyzed Diels-Alder Reactions:

1. Casachi, A.; Desimoni, G.; Faita, G.; Invernezzi, A. G.; Lanati, S.; Righetti, P.; *J. Am. Chem. Soc.,* **1993,** *115,* 8002.
2. Fukuzumi, S.; Okamoto, T.; *J. Am. Chem. Soc.,* **1993,** *115,* 11600.
3. Mizuno, K.; Nire, K.; Sugita, H.; Otsuji, Y.; *Tetrahedron Lett.* **1993,** *34,* 6563.
4. Takemoto, Y.; Ueda, S.; Takeuchi, J.; Nakamoto, T.; Iwata, C.; Ohishi, H.; Hirofumi, S.; Sakaguchi, K.; Kusunoki, M.; *Chem. Pharm. Bull.,* **1995,** *43,* 559.
5. Faita, G.; Righetti, P.; *Tetrahedron,* **1995,** *51,* 9091.
6. Desimoni, G.; Faita, G.; Righetti, P.; *Tetrahedron Lett.,* **1996,** *37,* 3027.
7. Desimoni, G.; Faita, G.; Righetti, P.; Tacconi, G.; *Tetrahedron,* **1996,** *52,* 12009.
8. Desimoni, G.; Faita, G.; Righetti, P.; Sardone, N.; *Tetrahedron,* **1996,** *52,* 12019.
9. Desimoni, G.; Faita, G.; Invernezzi, A. G.; Righetti, P.; *Tetrahedron,* **1997,** *53,* 7671.
10. Desimoni, G.; Faita, G.; Mella, M.; Ricci, M.; Righetti, P.; *Tetrahedron,* **1997,** *53,* 13495.
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15. Crosignani, S.; Desimoni, G.; Faita, G.; Giuseppe, M.; Righetti, P.; *Tetrahedron,* **1998,** *54,* 15721.
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## B. Addition and Substitution Reactions:

Example 1:
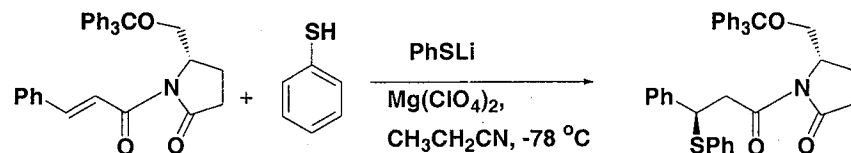
Features: Magnesium perchlorate catalyzes highly diastereoselective 1,4 Michael addition of thiophenol to cinnamoyl-butyrolactam. Highly stereoselective addition of thiophenol to other chiral olefins confirmed the general applicability of these conditions. The products were converted to the corresponding ethyl β-(phenylthio)carboxylates of high ee by treatment with saturated HCl-EtOH.

**Reference:** *J. Org. Chem.*, **1995**, *60*, 6188.

Example 2:
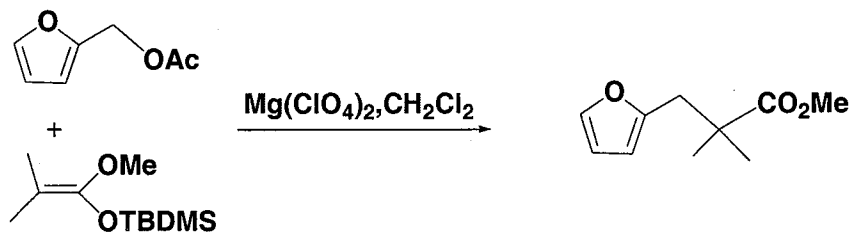
Features: Magnesium perchlorate and Magnesium triflimide are found to be efficient catalysts for the nucleophilic substitution of allylic and benzylic acetates. Reaction of 0.1 M solution of the allylic acetate in CH_2Cl_2 containing 2.0 equiv. of silyl ketene acetal with 10 mol% $Mg(ClO_4)_2$ gives the substituted product in 99% yield.

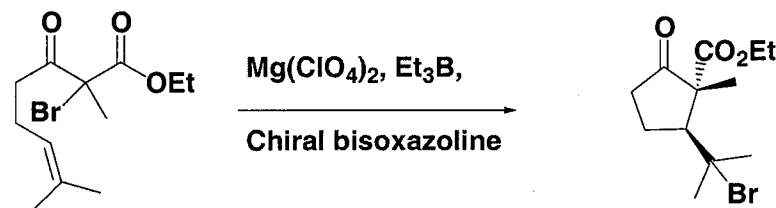**Reference:** *Tetrahedron Lett.*, **1997**, *38*, 2645.

Example 3:
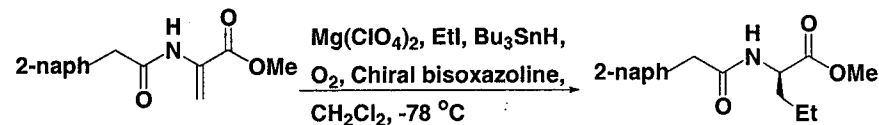
Example 4:

Features: A chiral Lewis acid derived from Magnesium perchlorate and a chiral bisoxazoline catalyzes conjugate radical addition to dehydroalanines followed by enantioselective proton transfer to provide α-amino acids in moderate to excellent yields.

Reference: *Angew. Chem. Int. Ed.*, **2001**, *40*, 1295.

Features: A chiral Lewis acid derived from Magnesium perchlorate and a chiral bisoxazoline catalyzes atom transfer cyclization reactions. In the presence of chiral ligands, the reactions catalyzed by $Yb(OTf)_3$ in ether were found to be very slow and only racemic cyclization products were obtained. However, the $Mg(ClO_4)_2$/CH_2Cl_2 and $Mg(ClO_4)_2$/toluene systems were found to be very effective in terms of stereoselectivities and yields.

Reference: *J. Am. Chem. Soc.*, **2001**, *123*, 8612.

Example 5:
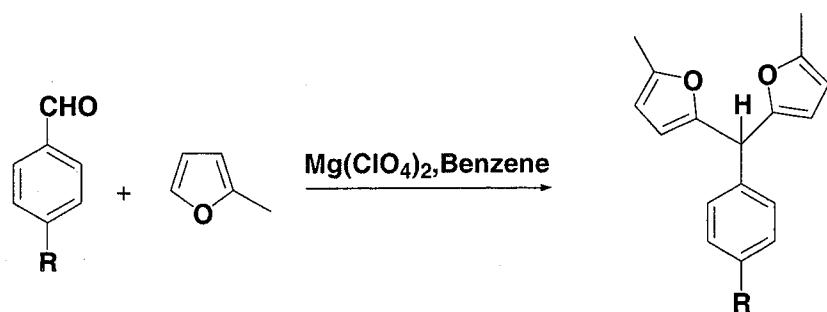
Features: Magnesium perchlorate catalyzes the condensation reaction between several aromatic aldehydes and 2-methyl furan in benzene to give benzylidene bismethylfurans in moderate to good yield.

**Reference:** *Khim. Geterotsikl. Soedin.,* **1991, 1277.**

See following references for Mg(ClO₄)₂ catalyzed Addition and Substitution Reactions:

1. Butin A. V.; Kul'nevich, V. G.; Krasnodarsk, P.; *Khim. Geterotsikl. Soedin.,* **1991,** 1277.
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22. Yang, D.; Gu, S.; Yan, Y.; Zhu, N-Y.; Cheung, K-K.; *J. Am. Chem. Soc.,* **2001,** *123,* 8612.
23. Fukuzumi, S.; Fujii, Y.; Suenobu, T.; *J. Am. Chem. Soc.,* **2001,** *123,* 10191.

C. Rearrangement Reactions:

Example 1:

$$\text{Mg(ClO}_4)_2, \text{IDBA,} \quad \text{CH}_3\text{CN, H}_2\text{O}$$

IBDA= Iodobenzene acetate
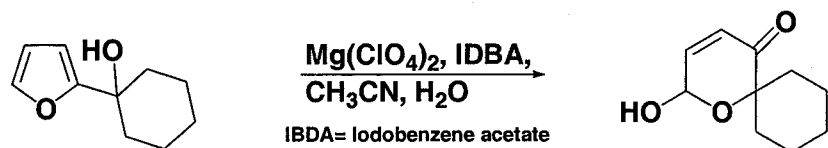
Features: The binary reagent $\text{PhI(OAc)}_2\text{-Mg(ClO}_4)_2$ is found to be very efficient for the conversion of furan alcohols to pyranones in high yield. The addition of salts such as $\text{Mg(ClO}_4)_2$, KBF_4 and methyl-viologen to a pH 7 buffered solution of 1:1 acetonitrile-water considerably enhanced the efficiency of ring enlargement of furan alcohol to pyranone. The best result was obtained by using $\text{Mg(ClO}_4)_2$, considering relative cost as well.

Reference: De Mico, A.; Margarita, R.; Pinacatelli, G.; *Tetrahedron Lett.*, 1995, 36, 3553.

Example 2:

$$\text{Mg(ClO}_4)_2, \text{CH}_3\text{NO}_2$$
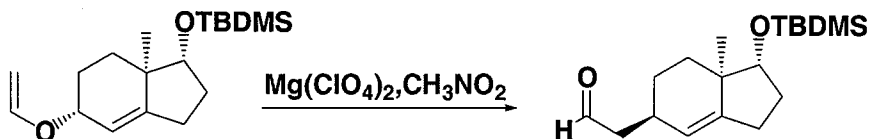
Features: Treatment of allylic ether with catalytic amount of LiClO_4 in nitromethane promotes a [1,3] sigmatropic rearrangement, giving a poor yield of the corresponding aldehyde. The yield of aldehyde was greatly improved to 83% by substituting $\text{Mg(ClO}_4)_2$ for LiClO_4. The aldehyde formed in this rearrangement reaction is a key intermediate in the synthesis of the natural product Coraxeniolide-A.
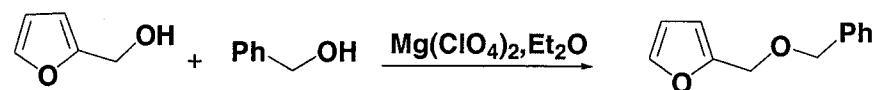
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1,2 acyl migration: Bach, R. D.; Domagala, J. M.; *J. Org. Chem.*, 1984, *49*, 1984.
Photoisomerization: Mizuno, K.; Nire, K.; Sugita, H.; Maeda, H.; *Tetrahedron Lett.*, 2001, *42*, 2689.

D. Synthesis of Mixed Allylic Ethers:

$$\text{Mg(ClO}_4)_2, \text{Et}_2\text{O}$$

Features: Magnesium perchlorate acts as a mild Lewis acid to convert acid sensitive furanyl alcohols into the corresponding unsymmetrical ethers via a cross-coupling reaction. Primary, secondary and tertiary alcohols undergo alkylation with primary allylic alcohols in good to quantitative yield.

Reference: De Mico, A.; Margarita, R.; Pinacatelli, G.; *Tetrahedron Lett.*, 1995, 36, 2679. See also for Acylation of furan derivatives, Patsenkar, L. D.; Lokshin, A. I.; Drushlyak, T. G.; Baumer, V. N.; *Chem. Heterocycl. Compd.* 1993, 33, 1266.

E. Glycosylation:

$$\text{Mg(ClO}_4)_2\text{- N-PSP,} \quad \text{Et}_2\text{O, 93\%}$$

N-PSP = *N*-phenylselenophthalimide
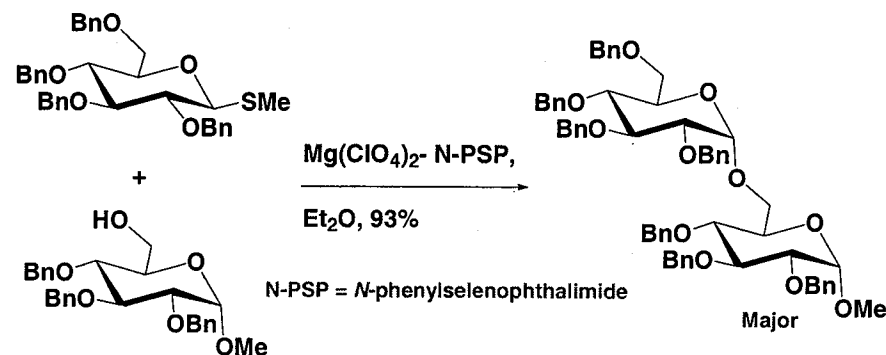
Features: Among many strong acid salts tested, only magnesium perchlorate can promote glycosylation in combination with N-PSP. Highly α-selective glycosylation was achieved using this combination. These reagents are expected to be advantageous for application to solid-phase

synthesis of oligosaccharides, since the selective glycosylation is effected at room temperature .

Reference: Fukase, K.; Nakai, Y.; Kanoh, T.; Kusumoto, S.; *Synlett.*, **1998**, 84.

## F. Epoxide or Aziridine Ring Opening Reactions:
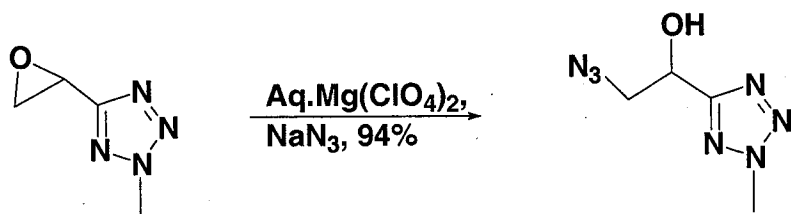
Features: Aqueous Magnesium perchlorate catalyzes nucleophilic opening of epoxide to azido alcohol in 94% yield. The azido alcohol was converted into an aziridine which is an important pharmaceutical intermediate.

Reference: Shchetinina, T. V.; Petrov, V. V.; Bratilov, S. B.; *Zh. Org. Khim.*, **1993**, 29, 2331.

See also following references for related ring opening reactions

1.   Chini, M.; Crotti, P.; Macchia, F.; *Tetrahedron Lett.*, **1990**, *31*, 4661.
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8.   Colombini, M.; Crotti, P.; Di Bussolo, V.; Favero, L.; Gardelli, C.; Macchia, F.; Pineschi, M.; *Tetrahedron.*, **1995**, *51*, 8089.
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10.   Wang, Y.; Wos, J. A.; Dirr, M. J.; Soper, D. L.; deLong, M. A.; Mieling, G. E.; Biswant, A.; Suchanek, E. G.; Taylor, C. J.; *J. Med. Chem.*, **2000**, *43*, 945.

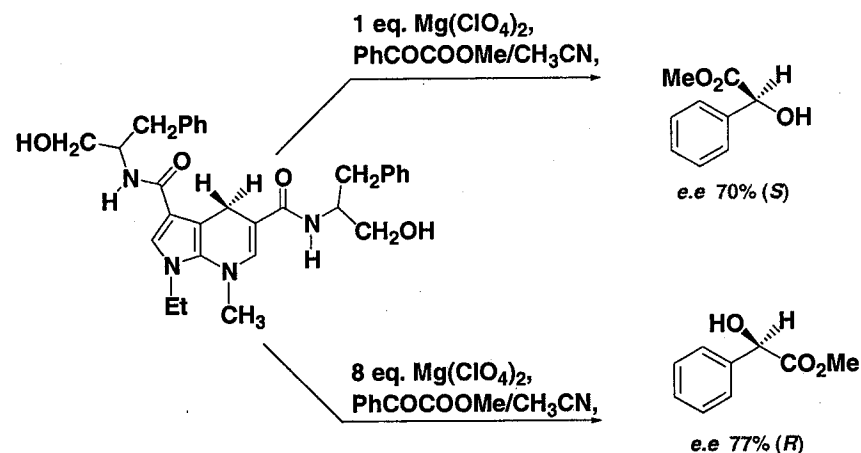## G. Deprotection of BOC-Protected Amides and Carbamates:
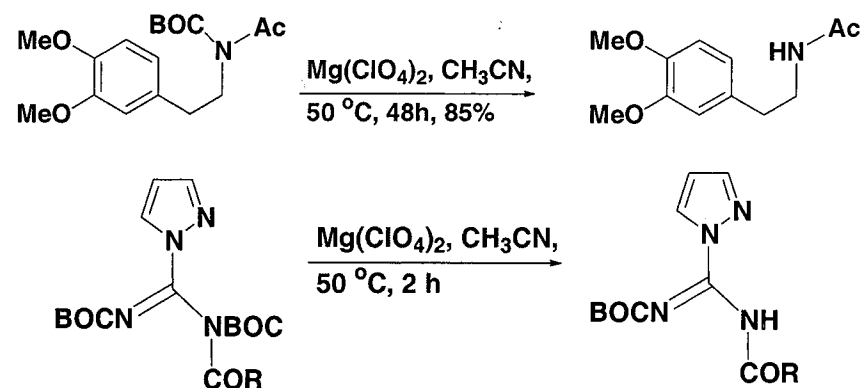
Features: BOC protected amides and carbamates undergo selective deprotection by treatment with catalytic amounts of Magnesium perchlorate in acetonitrile. This mild procedure is highly specific for compounds of BOC protected carbamates and amides and leaves simple BOC-protected amines untouched.

References: Stafford, J. A.; Brackeen, M. F.; Karnewsky, D. S.; Valvano, N. L.; *Tetrahedron Lett.,* **1993**, 34, 7873 and Dowle, M. D.; Howes, P. D.; Robinson, J. E.; Trivedi, N., PCT Int.Appl.(2000), 27pp. CODEN: PIXXD2 WO 0078723 A1 20001228. Patent number: WO 2000078723.

See also for deprotection of Cpoc and Ddz groups,Wildeman, D.; Drewello, M.; Fisher, G.; Schutkowski, M.; *Chem. Commun.*, **1999**, 1809.

H. Asymmetric Reduction Reactions:

1 eq. Mg(ClO₄)₂, PhCOCOOMe/CH₃CN,

MeO₂C H OH

e.e 70% (*S*)

8 eq. Mg(ClO₄)₂, PhCOCOOMe/CH₃CN,

HO H CO₂Me

e.e 77% (*R*)

Features: Stereoselective reduction of methyl benzoylformate using NADH models is found to be dependent on magnesium ion concentration. Methyl mandelate is obtained in good enantiomeric excesses with either (*S*) or (*R*) configuration simply by changing the magnesium ion concentration (noted above).

Reference: Leroy, C.; Levacher, V.; Dupas, G.; Queguiner, G.; Bourguignon, J.; *Tetrahedron Asymm.,* **1997, 8, 3309.**

See also for following references for related reactions

1. Brussee, J.; Benthem, R. A. T. M.; Kruse, C. G.; Van Der Gen A.; *Tetrahedron Asymm.,* **1990,** *3,* 163.
2. Konopikova, M.; Fiesera, L.; Pronayova, N.; *Liebigs. Ann. Chem,* **1993,** *10,* 1047.
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8. *Tetrahedron Lett.,* **2001,** 42, 4613.