

Aldrichimica Acta

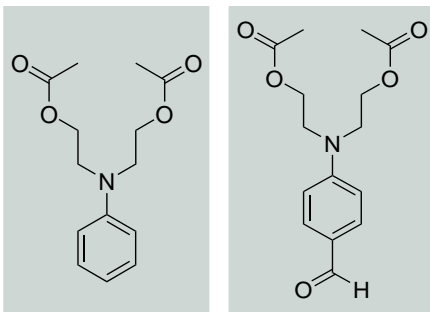
Volume 31, Number 3, 1998 (*Last issue in 1998*)



Transition-Metal-Based Lewis Acid Catalysts

New Products

Polymers with promising electro-optic features, including high second-order optical nonlinearity, good thermal and temporal stability, and low long-wavelength absorption, have been prepared from these two compounds.¹⁻³

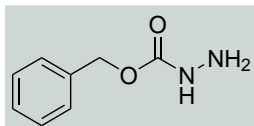


(1) Wang, P.N. et al. *Chem. Mater.* **1995**, 7, 185. (2) Zhang, Y. et al. *Polymer* **1997**, 38, 2893. (3) Sun, S.-S. et al. *Chem. Mater.* **1996**, 8, 2539.

47,797-4 N-Phenyldiethanolamine diacetate, 97%

48,488-1 4-[Bis[2-(acetoxy)ethyl]amino]benzaldehyde, 98%

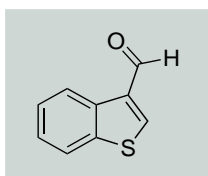
Benzyl carbamate is frequently used to prepare hydrazine-substituted compounds. Examples include azapeptides and hydrazine-substituted flavins.^{1,2}



(1) Quibell, M. et al. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2843. (2) Kim, J.-M. et al. *J. Am. Chem. Soc.* **1995**, 117, 100.

49,978-1 Benzyl carbamate, 98%

Benzo[*b*]naphtho[*d*]thiophene and [1]benzothieno[3,2-*h*]isoquinolines have been prepared from this aldehyde.^{1,2}



(1) Castle, N. et al. *J. Heterocycl. Chem.* **1981**, 18, 967. (2) Shafiee, A. et al. *ibid.* **1976**, 13, 141.

49,496-8 Thianaphthene-3-carboxaldehyde, 95%

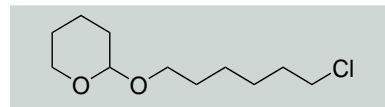


Molecular wires,¹ phenylethyne oligomers,² angular phenylenes,³ and dehydrobenzoannulenes⁴ have been prepared from these arylacetylenes.

(1) Anderson, S. et al. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2383. (2) Hsung, R.P. et al. *Organometallics* **1995**, 14, 4808. (3) Schmidt-Radde, R.H.; Vollhardt, K.P.C. *J. Am. Chem. Soc.* **1992**, 114, 9713. (4) Haley, M.M. *Synlett* **1998**, 557.

48,469-5 (2-Bromophenylethynyl)trimethylsilane, 98%

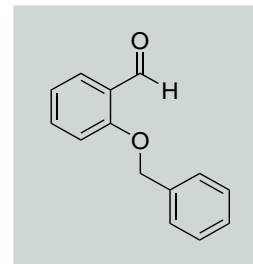
49,401-1 (4-Bromophenylethynyl)trimethylsilane, 98%



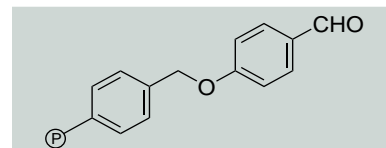
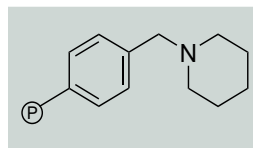
Leukotriene B₄ antagonists and blocking groups for rotaxanes have been prepared from these useful synthons.^{1,2}

(1) Chan, W.K. et al. *J. Med. Chem.* **1996**, 39, 3756. (2) Gibson, H.W. et al. *J. Org. Chem.* **1993**, 58, 3748.

49,718-5 2-(6-Chlorohexyloxy)tetrahydro-2H-pyran, 95%



49,974-9 2-Benzyloxybenzaldehyde, 98%



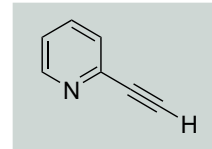
These polymer-bound reagents are used as scavengers in solid-phase organic synthesis. The polymer-bound piperidine is an acid scavenger, while the benzaldehyde is used to scavenge primary and secondary amines via formation of the imine.

Kaldor, S.W. et al. *Tetrahedron Lett.* **1996**, 37, 7193.

49,461-5 Piperidine, polymer-bound

47,208-5 4-Benzyloxybenzaldehyde, polymer-bound

Polymers with interesting electrical properties have been prepared using ethynylpyridine.^{1,2}

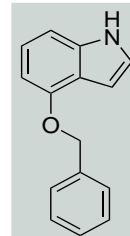


(1) Balogh, L. et al. *J. Polym. Sci., Part A: Polym. Chem.* **1998**, 36, 703. (2) Gal, Y. et al. *Bull. Korean Chem. Soc.* **1998**, 19, 22.

46,992-0 2-Ethynylpyridine, 98%

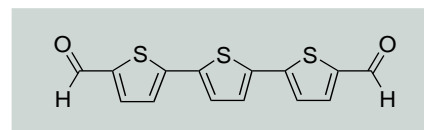
A number of heterocycles with promising pharmacological activity have been prepared from this indole.^{1,2}

(1) Chan, W.K. et al. *J. Med. Chem.* **1996**, 39, 3756. (2) Sheppard, G.S. et al. *ibid.* **1994**, 37, 2011.



24,621-2 4-Benzyloxyindole, 98%

Oligothiophenes with interesting electronic and optical properties have been prepared from this terthiophene.^{1,2}



(1) Novikova, T.S. et al. *Synth. Met.* **1996**, 83, 47. (2) Wei, Y. et al. *Chem. Mater.* **1996**, 8, 2659.

49,910-2 2,2':5',2''-Terthiophene-5,5''-dicarboxaldehyde, 97%



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About Our Cover

The *Brown Family* (oil on paper mounted on canvas, 23% x 28½ in.) by the American artist Eastman Johnson (1824–1906) represents James Brown, whose father



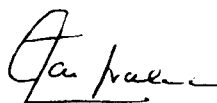
founded the international mercantile banking firm that still bears the name Brown Brothers and Company, with his wife Eliza and their grandson William in the parlor of their house on University Place in New York. It is at one time both a scene of everyday life and a group portrait, combining the two types of painting for which Johnson was best known. Signed and dated 1869, it is a record of the appearance of the home where the Browns had raised their family, commissioned from the artist in anticipation of a move further uptown to a new residence at Park Avenue and 37th Street.

The Browns are shown seated by the fire in their comfortable parlor. Young William has in-

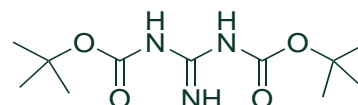
terrupted his grandfather's reading of the evening paper, causing his grandmother to look up from her knitting. The room, with its paintings and other decorative objects, carved furniture, gilded frames, heavy red draperies, carved marble mantle, green wallpaper, strapwork ornament and figured carpet, reflects the affluence and social position of the Brown family. However, the appearance of this room was criticized as garish and tasteless when the painting was first exhibited. Nevertheless, when the Browns moved to their new Park Avenue home they had this room dismantled and reinstalled there, and their son John even later moved it into his own house.

This painting is a gift of David Edward Finley and Margaret Eustis Finley to the National Gallery of Art.

“Please Bother Us.”

by 

Jai Nagarkatti, President



Dr. Ganesan Vaidyanathan of the Department of Radiology at the Duke University Medical Center kindly suggested that we offer 1,3-bis(*tert*-butoxycarbonyl)guanidine. This reagent converts bromoalkanes to guanidines using sodium hydride,¹ and alcohols to guanidines using Mitsunobu's conditions.²

(1) Vaidyanathan, G.; Zalutsky, M.R. *J. Org. Chem.* **1997**, *62*, 4867.
(2) Dodd, D.S.; Kozikowski, A.P. *Tetrahedron Lett.* **1994**, *35*, 977.

49,687-1 1,3-Bis(*tert*-butoxycarbonyl)guanidine, 98%

Naturally, we made this useful reagent. It was no bother at all, just a pleasure to be able to help.

CRC Handbook of Chemistry and Physics, CRCnetBASE 1999

David R. Lide

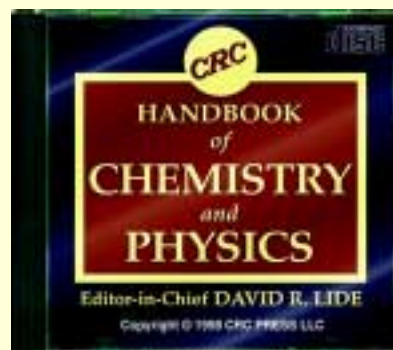
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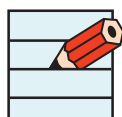
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Lab Notes

Moving Disc Filtration: Low-Temperature, Inert- Atmosphere Removal of Solvent from Low- Melting Crystals in an Ordinary, One-Neck Flask

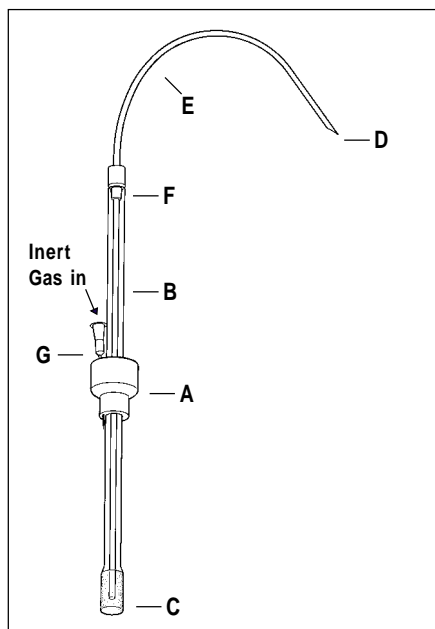
The motivation for assembling this device came from our need to rapidly and efficiently remove mother liquors from crystalline, low-melting solids under conditions which allow maintenance of a low-temperature and/or dry, inert atmosphere. For finely divided crystals containing significant amounts of entrapped liquid, suction/pressure filtration was mandated. The several devices uncovered in a literature search,¹⁻⁵ while effective, require more specialized apparatus and complicated maneuvers than does the one described herein. This device differs from others in that it allows the crystalline solid to remain in the one-neck flask in which it has crystallized, and is easily adapted to fit a range of flask sizes. Furthermore, it can be assembled almost entirely from commercially available parts.

Assembly begins by boring a hole (cork borer) through rubber septum **A** (e.g., $\text{F}\frac{1}{2}$ 19/22, Aldrich **Z10,076-5**) to allow insertion (snug fit, inserted through the narrow end of the septum) of gas-dispersion tube **B** (**Z14,546-7**, porosity 170–220, 12mm o.d.). The length of protrusion of the fritted glass end (**C**) will be adjusted throughout the course of liquid removal. The noncoring tip **D** of an 18-inch, 12-gauge, double-ended needle (**E**) is pushed through the small end of “#3” rubber septum **F** (e.g., **Z10,072-2**), far enough to allow the flat end of the needle to reach the bottom of the inside of the gas-dispersion tube, with the #3 septum sealing the top of the gas-dispersion tube. The noncoring end of the needle is bent into a smooth $\sim 120^\circ$ arc. Syringe needle **G** (e.g., a B-D PrecisionGlide[®], **Z19,250-3**) is inserted into the well of the $\text{F}\frac{1}{2}$ 19/22 septum, until the tip emerges through the bottom of the wall on the lower end of the septum. Needle **G** is connected to a gas line (e.g., N_2 , Ar; needle-tubing connector w/male Luer Lok[®]). The apparatus is now ready to use.

The $\text{F}\frac{1}{2}$ 19/22 septum (**A**) fits snugly into a standard 50-mL Erlenmeyer flask. To adapt the apparatus to a larger flask (with or without a standard taper joint), conical neoprene rubber filter

adapters (set: **Z25,423-1**) can be nested on the flask. We have thus removed mother liquors from 50- to 500-mL Erlenmeyer flasks.

Multiple crystallizations are needed to separate (2'R)-1'-(3'-bromo-2'-methylpropyl) (1S)-10-camphorsulfonate (mp 29 °C) from its higher-melting (2'S) diastereomer. In a typical procedure, a solution of these isomers in methanol is crystallized at 0 °C. The flask, held in an ice-water bath, is fitted with the



apparatus, with the inert gas flowing gently. The gas dispersion tube is held above the liquid, and the noncoring end of the needle is inserted about 1.5 inches into a receiver flask, to accommodate spitting. The gas dispersion tube is then pushed down to make and maintain contact with the liquid (immersion is not necessary). Gas pressure forces the liquid out through the needle. When the gas dispersion tube reaches the top of the crystalline solid, it is held in contact with the solid surface; wicking action continues to drain solvent from the crystals. When an acceptable level of dryness is attained, the crystals can be rinsed with additional cold solvent. We rinse these crystals with cold ether to facilitate drying. When the crystals are sufficiently dry that they will not melt/dissolve in the remaining solvent, the flask is removed from the cold bath, and the crystal drying is completed in any of the standard ways. We normally weigh and analyze the completely dry crystals, then redissolve them in the appropriate amount of solvent for the next crystallization, all without removing them from the flask. We have handled amounts of solid from ~ 1 g to 100g in

this way, and have used bath temperatures as low as -30°C ; much lower temperatures should not be a problem.

The basic principle of this apparatus can be used in modified versions. For example, on a larger scale (larger, wider-mouth, or multiple-neck flask), the 18-inch needle can be omitted and the gas dispersion tube modified (bent at the receiver end, a larger-diameter fritted disc at the immersed end). With this modification, we have removed 1-2 liters of solvent from 200-300g of crystals in a beaker (in an ice bath) by aspirator suction, with an inert gas blanket to minimize moisture condensation. The fritted disk is easily moved around and used to tamp down the crystals while providing a wicking surface, thereby maximizing solvent removal.

- (1) Czapkiewicz, J.; Tutaj, B. A Design for Low-Temperature Filtration of Strongly Hygroscopic Crystals. *J. Chem. Educ.* **1992**, *69*, 590.
- (2) Shaw, C.F., III; Allred, A.L. Crystallization and Filtration Apparatus for Low Temperatures and Inert Atmosphere. *J. Chem. Educ.* **1970**, *47*, 164.
- (3) Giese, R. Low Temperature Recrystallization Tube. *J. Chem. Educ.* **1968**, *45*, 610.
- (4) Holah, D.G. Apparatus for Preparations and Filtrations Under Inert, Dry Conditions. *J. Chem. Educ.* **1965**, *42*, 561.
- (5) Smith, F.E. *Aldrichimica Acta* **1989**, *22*, 58, and references therein.

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Please turn to page 87 for more *Lab Notes*

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Transition-Metal-Based Lewis Acid Catalysts

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Chicago, IL 60637

Outline

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2. Background
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5. The Oxo–Ene Reaction
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7. The Mukaiyama and Sakurai Reactions
8. Mechanisms of the Mukaiyama and Sakurai Reactions
9. Concluding Remarks
10. Acknowledgments
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1. Introduction

In 1960, Yates and Eaton reported that molar equivalents of aluminum trichloride were capable of accelerating certain Diels–Alder reactions by as much as 10^5 times over the corresponding thermal reactions.¹ Whereas proton catalysis of these reactions had been reported,² the observation that Lewis acids were capable of accelerating the Diels–Alder cycloaddition was a seminal discovery which propelled the development of a variety of new reactions that relied on Lewis acid promotion. In addition to the classical Diels–Alder reaction (eq 1), these include the Mukaiyama³ (eq 2) and Sakurai⁴ (eq 3) reactions, the hetero-Diels–Alder cycloadditions⁵ (eq 4), the ene reactions⁶ (eq 5), and the nitron–olefin [3+2] additions⁷ (eq 6).

After the efficacy of aluminum trichloride was demonstrated, it was natural to investigate the halides of B(III), Sn(IV) and Ti(IV) as well as those of the lanthanides, Zn(II), and Mg(II) for Lewis acid promotion. Generally, stoichiometric or greater amounts of the Lewis acid were employed in order to achieve maximum acceleration and to compensate for the destruction of the Lewis acid by hydrolysis. Later, when these Lewis acids were modified for use in asymmetric synthesis, catalytic quantities began to be used. These modified chiral Lewis acids were usually prepared by addition of a chiral ligand to an appropriate Lewis acid precursor. Although notable successes have been reported by the use of these chiral catalysts, they present a number of disadvantages. Among these are their high sensitivity to water, the tendency of ligated

Lewis acids to scramble their ligands and to form oligomeric species. The fact that the (achiral) Lewis acid precursor is usually more catalytically active than the chiral ligated species can lead to diminution of the observed enantiomeric excess unless the chiral catalyst is completely formed. As a consequence, great care and considerable effort is required in order to exclude these complications or to identify the catalytically active species. It was for these reasons that, some years ago, we began a search for transition-metal-based Lewis acid catalysts in the expectation that structurally defined, stable catalysts would be produced.

2. Background

Soon after we began our search for suitable transition-metal-based Lewis acids, there appeared three reports on such catalysts, **1**,⁸ **2**,⁹ and **3**.¹⁰ Compound **1** is a very effective catalyst for the classical Diels–Alder reaction at low catalyst loading. However, it has a strong tendency to polymerize dienes and is moisture sensitive. Despite these problems, this was an important discovery because it indicated how a normally electron-rich metal, in this case d^6 tungsten(0), could be modified to act as a Lewis acid. The SbF_6^- ligand in **1** is very labile and is readily replaced by the carbonyl functions of dienophile aldehydes, ketones, and esters; this results in the formation of cationic adduct complexes. Further, because the coordination of the adduct is trans disposed to the NO^+ ligand, the dienophile is labile by virtue of the strong trans-effect of NO^+ . The lability of the adduct is important in catalysis because it assures that ligand dissociation will not be turnover-limiting.¹¹ Lewis acid induced activation of a substrate occurs because the Lewis acid withdraws electrons from the substrate and thereby activates it to reaction. A positively charged Lewis acid is expected to enhance the required electronic displacement over that provided by a similar neutral Lewis acid. The presence of charge in transition-metal Lewis acids may be generally necessary, at least for the classical Diels–Alder reaction, but is not sufficient to provide Lewis acidity. In the case of **1**, the electron-withdrawing π -acidic carbonyl and nitrosyl ligands are important in contributing to the tungsten Lewis acidity. Thus, we have replaced, successively, one and two of the carbonyl ligands of **1** by phosphines and



Professor Brice Bosnich (right) receiving the 1998 ACS Award in Inorganic Chemistry from Dr. Mark A. Drezdson, Manager–Techware, Sigma-Aldrich Research.

have found that the Lewis acidity, as measured by the rates of a standard Diels–Alder reaction, is progressively reduced. This is consistent with the expectation that the replacement of electron-withdrawing carbonyl ligands by electron-donating phosphines will increase the negative charge on the metal, thereby diminishing its Lewis acidity. That charge alone is not necessarily sufficient to produce Lewis acidity is demonstrated by our observation that the cationic complex $[\text{Ru}(\text{diphos})_2\text{Cl}]^+$ (diphos is $\text{Ph}_2\text{PCH}_2\text{CH}_2\text{PPh}_2$) is a very poor catalyst for most Diels–Alder reactions.

From the above discussion, it is obvious that **2** should be a powerful Lewis acid catalyst; it has two nitrosyl ligands, is dipositively charged, and has a vacant coordination position for substrate binding. This is the case,⁹ but like **1**, it suffers from being a potent catalyst for polymerizing dienes. Compound **3**, on the other hand, is expected to be electron-rich but the presence of the positive charge might provide mild Lewis acidity. It was found that **3** is a useful catalyst for the (Danishefsky) hetero-Diels–Alder reaction, but the classical Diels–Alder reaction is not catalyzed by **3**. The principal reason for the latter inactivity is that dienophiles, which are generally electron-deficient olefins, displace the ethylene ligand of **3** to form stable π -olefin complexes which do not react with dienes.

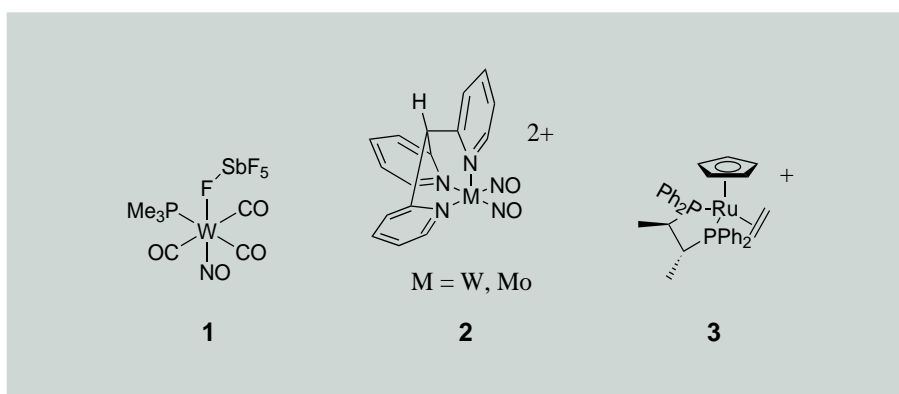
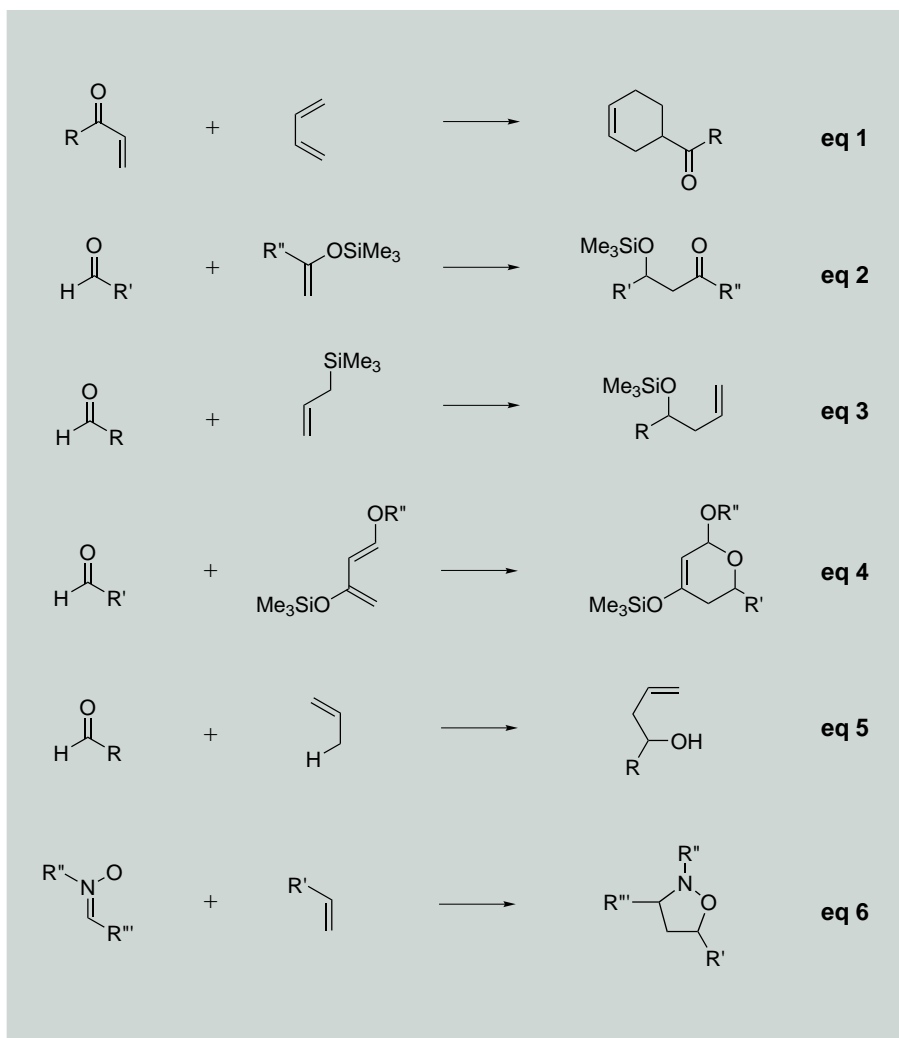
Thus, for the classical Diels–Alder reaction in particular, the problem of generating transition-metal Lewis acids resides in producing complexes where the electron density of the metal is such that diene polymerization does not

occur and where π -olefin coordination is suppressed. Tuning the Lewis acidity of the transition metal can be a fairly rational process and different reactions require varying degrees of Lewis acidity. For example, strong Lewis acids are generally required for the classical Diels–Alder reaction whereas milder Lewis acids are preferred for the Mukaiyama reaction and its variant, the (Danishefsky) hetero-Diels–Alder reaction.

3. Ruthenium and Titanium Complexes as Lewis Acids

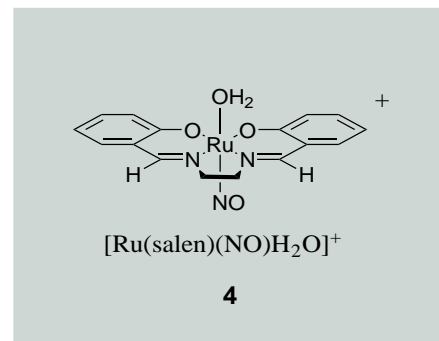
The complex $[\text{Cp}_2\text{TiCl}_2]$, where Cp is the cyclopentadienyl ligand, is a stable, robust complex which can be modified into chiral forms by appropriate substitution of the Cp ligands.¹² Although it has a vacant d orbital,¹³ it does not form Lewis acid adducts because the vacant orbital is sterically inaccessible. With sterically less demanding ligands, such as acetonitrile, this remaining orbital is employed for coordination as occurs in the complex $[\text{Cp}_2\text{Ti}(\text{NCCH}_3)_3]^{2+}$. Titanium (IV), however, is an electropositive metal and it would be expected to act as a strong Lewis acid even in the presence of the electron-donating Cp ligands provided that the chloro ligands in $[\text{Cp}_2\text{TiCl}_2]$ were replaced by readily displaceable ligands such as H_2O or the triflate anion ($\text{CF}_3\text{SO}_3^- = \text{OTf}$). The complexes $[\text{Cp}_2\text{Ti}(\text{OTf})_2]$ and $[\text{Cp}'_2\text{Ti}(\text{H}_2\text{O})_2](\text{OTf})_2$, where Cp' is the pentamethylcyclopentadienyl ligand, had already been prepared and characterized.¹⁴ Both of these complexes are soluble in weakly coordinating solvents such as methylene chloride and nitroalkanes. We found that, in these solvents, organic aldehyde and ketone ligands readily replaced the OTf or H_2O ligands, and, moreover, the exchange is rapid and reversible. The latter condition is necessary for efficient catalysis,¹¹ otherwise the catalytic turnover could be controlled by the rates of substrate coordination and dissociation. The intrinsic Lewis acidity of these titanium (IV) centers will be enhanced by the fact that the substrate adducts will carry a positive charge. Thus, the complexes $[\text{Cp}_2\text{Ti}(\text{OTf})_2]$ and $[\text{Cp}'_2\text{Ti}(\text{H}_2\text{O})_2](\text{OTf})_2$ have the necessary characteristics for catalytic Lewis acid activity. As we show presently, these complexes are efficient catalysts for the classical Diels–Alder reaction. A related zirconium (IV) complex, $[\text{Cp}_2\text{Zr}(\text{O}-t\text{-Bu})\text{THF}]^+$, was also shown to act as a catalyst for the Diels–Alder reaction.¹⁵

Unlike titanium(IV), ruthenium(II) complexes are generally electron-rich at the metal center. Ruthenium(II) complexes are usually robust, air-stable, water-insensitive, diamagnetic (d^6) octahedral compounds. These are attractive characteristics if the complexes could be modified to act as Lewis acids. For this purpose, we prepared the stable and robust



ruthenium(II) complex **4** as the weakly coordinating SbCl_6^- salt.¹⁶

The characteristics which were expected to make **4** a Lewis acid were its positive charge, the presence of the electron-withdrawing ligand NO^+ trans disposed to the H_2O ligand, and the presence of hard donor ligands such as oxygen and nitrogen. Because of the trans-disposed NO^+ ligand, the water ligand was expected to be very labile. This proved to be the case, because, in nitromethane solutions, exchange with $^{17}\text{OH}_2$ at -25°C was rapid on a ^1H NMR time scale.



Further, addition of aldehydes or ketones to these solutions led to the formation of adducts which were stable but exchanged rapidly. It is interesting to note that these adducts became more stable with an increase in temperature.

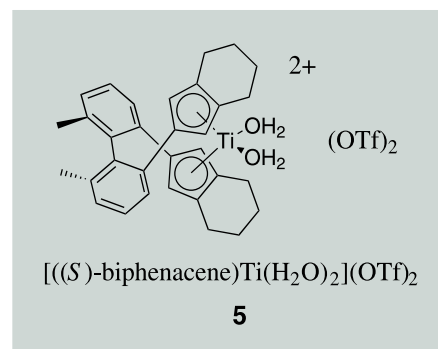
4. The Diels–Alder Reaction

Some of the results obtained using the three catalysts $[\text{Ru}(\text{salen})(\text{NO})(\text{H}_2\text{O})]^+$, $[\text{Cp}'_2\text{Ti}(\text{H}_2\text{O})_2]^{2+}$ and $[\text{Cp}_2\text{Ti}(\text{OTf})_2]$ are collected in **Table 1**. Many other dienes and aldehyde and ketone dienophiles are subject to catalysis by these complexes but the list in **Table 1** serves to exemplify the salient features. None of these three catalysts significantly accelerates the Diels–Alder reactions of α,β -unsaturated esters at these low catalyst loadings. Even at 1 mol % loadings these catalysts accelerate the reactions by a factor of 10^3 to $>10^5$ over the corresponding thermal reactions. As is nearly always observed in catalysis of the Diels–Alder reaction, the product isomer ratio is greater than in the corresponding thermal reactions. Whereas the ruthenium catalyst tends to have a lower turnover frequency, it has an advantage over

the titanium catalysts in that no polymerization of the dienes is observed. For slow reactions, which take more than 50 h for 90% completion, the titanium complexes do cause small amounts of diene polymerization.

Unlike traditional Lewis acids, neither the $[\text{Ru}(\text{salen})(\text{NO})(\text{H}_2\text{O})]^+$ nor the $[\text{Cp}'_2\text{Ti}(\text{H}_2\text{O})_2]^{2+}$ catalyst is destroyed by water. Moreover, Diels–Alder catalysis can be carried out in the presence of water. Even in the presence of a 100-fold excess of water over the catalyst concentration, only a small retardation in turnover frequency is observed. Thus, as a practical matter, these two robust, air-stable catalysts can be used at low catalyst loadings without special precautions for the Diels–Alder reaction. Although the $[\text{Cp}_2\text{Ti}(\text{OTf})_2]$ complex does undergo some hydrolysis in solution, it also can be used without special precautions for the Diels–Alder reaction. As we shall see presently, this hydrolysis is a significant feature for other reactions.

Unlike many other Lewis acid catalyzed reactions, the Diels–Alder reaction preserves the binding functionality of the dienophile in the product. In other words, for example, an aldehyde functionality in the dienophile



produces an aldehyde product. As a consequence, it might be assumed that product inhibition in catalysis would be observed because of product binding to the catalyst. Perhaps surprisingly, only weak product inhibition is observed. In the presence of a 100-fold excess of product over the catalyst, the Diels–Alder reaction proceeds only three times more slowly than in the absence of initially added product. Presumably, the greater steric bulk of the product over that of the substrate accounts, to some extent, for the mild product inhibition.

Although not commonly recognized as a problem in Lewis acid catalysis, there is a possible alternative origin for the catalysis. It could be argued that the aquo groups in the catalysts, whether incorporated initially or formed subsequently by hydrolysis, are acidic and that the observed catalysis is merely the result of proton catalysis. The exclusion of Brønsted over Lewis acid catalysis is not always easy to establish. An indication that the Diels–Alder reactions by the present catalysts are due to Lewis acid promotion is the observation that the strong acid $\text{CF}_3\text{CO}_2\text{H}$, at 1 mol % loadings, does not catalyze any of the Diels–Alder reactions studied in the times for the catalyzed reactions shown in **Table 1**. The most persuasive case against proton catalysis is the observation of enantioselection by chiral modifications of the titanium catalysts. The chiral diaquo complex **5** was prepared in enantiopure forms.¹⁷ The Diels–Alder reaction (**eq 7**) was carried out in methylene chloride solution at -78°C using 2 mol % of **5**.¹⁸ The reaction was complete in 30 minutes and the enantiomeric excess (ee) of the major isomer (exo) was 75%. This result clearly indicates that the major, if not the sole, path for catalysis involves the activation of the dienophile by binding to the metal rather than the result of proton catalysis.

5. The Oxo–Ene Reaction

The ene reaction has traditionally been promoted by using stoichiometric or greater amounts of Lewis acids, although a number of catalytic systems using $\text{Zn}(\text{II})$ ¹⁹ and $\text{Ti}(\text{IV})$ ²⁰ have been reported.

Table 1. Results of Diels–Alder Catalysis at 25°C Using 1 mol % of $[\text{Ru}(\text{salen})(\text{NO})(\text{H}_2\text{O})]^+$, $[\text{Cp}'_2\text{Ti}(\text{H}_2\text{O})_2]^{2+}$, and $[\text{Cp}_2\text{Ti}(\text{OTf})_2]$.^a

	Dienophile	Diene	Time in hours for 90% yield (isomer ratio)		
			$[\text{Ru}(\text{salen})(\text{NO})(\text{H}_2\text{O})]^+{}^b$	$[\text{Cp}'_2\text{Ti}(\text{H}_2\text{O})_2]^{2+}{}^c$	$[\text{Cp}_2\text{Ti}(\text{OTf})_2]{}^c$
1			5 (99:1)	6.7(95:5)	18(87:13)
2			4.4 (98:2)	3.2 (94:6)	0.4 (97:3)
3			3 (93:7)	3.2 (91:9)	5.7 (92:8)
4			48 (70:30)	76 (75:25)	66 (80:20)
5			71 (91:9)	13 (94:6)	3.8 (92:8)
6			22 (99:1)	2.1 (95:5)	4.9 (93:7)

^a Catalyses were carried out using 2.8 M concentrations of each substrate for the ruthenium catalyst, and using 1.0 M of each substrate for the two titanium catalysts. ^b In CH_3NO_2 solutions. ^c In CH_2Cl_2 solutions.

The intermolecular ene reaction is generally restricted to electron-deficient aldehydes. We have explored a number of these reactions using the ruthenium catalyst; some of the results are collected in **Table 2**.²¹ Although catalysis is restricted to very activated carbonyl compounds, the results serve to illustrate that a d⁶ transition metal can be modified to act as a catalyst for the normally sluggish ene reaction. These reactions are not catalyzed by 2 mol% CF₃CO₂H under the same conditions, indicating that the ruthenium center is the true catalyst.

We found that 1,3-dienes, unlike mono-olefins, undergo more facile catalysis, presumably by a stepwise process involving carbenium ion intermediates (**eq 8**). A number of dienes were investigated, and all gave a mixture of the ene and hetero-Diels–Alder products presumably because of the bifurcation caused by the two putative intermediates illustrated in **eq 8**.²¹

It is probable, however, that the ruthenium catalyst will find application for the intramolecular ene reaction. An example is the clean conversion of (+)-citronellal to l-isopulegol using 1 mol % of the ruthenium catalyst in CH₃NO₂ solution at 25°C. The catalyst gives 80% yield of l-isopulegol, the rest consisting of the other (three) isomers. This transformation is used in the industrial production of l-menthol, in which zinc bromide is used as the Lewis acid in stoichiometric amounts.

6. The [3+2] Nitron–Olefin Cycloaddition

Traditionally, the [3+2] nitron–olefin cycloaddition has been carried out thermally generally using electron-rich olefins. There have been a number of reports where traditional Lewis acids have been employed,²² usually in amounts ≥ 20 mol %. The complex [Cp₂Ti(OTf)₂] seemed ideally suited for this reaction because nitrones were expected to bind strongly to the titanium center by the oxygen atom and, after reaction, the oxygen atom would become a less strongly coordinating ether (**eq 6**). Thus product inhibition was not expected to be significant.

Using nitron **6** and ethyl vinyl ether in CH₂Cl₂ solution in the presence of 4 mol % of [Cp₂Ti(OTf)₂], the reaction depicted in **eq 9** occurred rapidly at 25°C.²³

After a certain amount of experimentation, it was determined that the majority of the transformation was due to proton catalysis. It was found that very small concentrations of water, which remain even after drying the CH₂Cl₂ solvent, caused the formation of triflic acid by the process shown in **eq 10**.

The oligomeric species, “[Cp₂TiO]” is not a catalyst but HOTf is a very potent catalyst for this reaction. This hydrolysis reaction does not

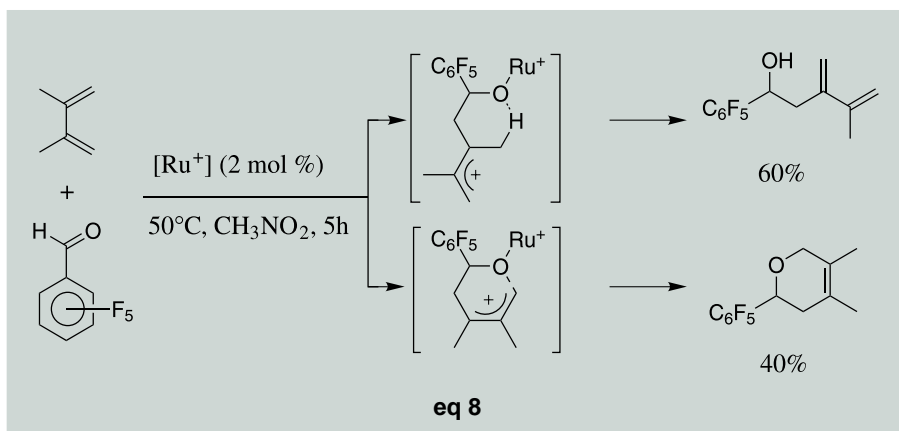
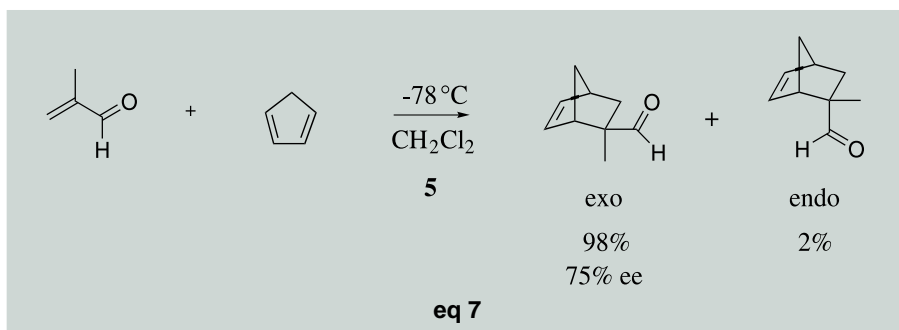


Table 2. Results of the Intermolecular Oxo–Ene Reaction Using 2 mol % of [Ru(salen)(NO)H₂O]⁺ in CH₃NO₂ Solution at 50°C.

	Enophile (0.5M)	Olefin (conc., M)	Product	t, h ^a
1				5
2				40
3				41
4				42

^a Time required for 95% reaction.

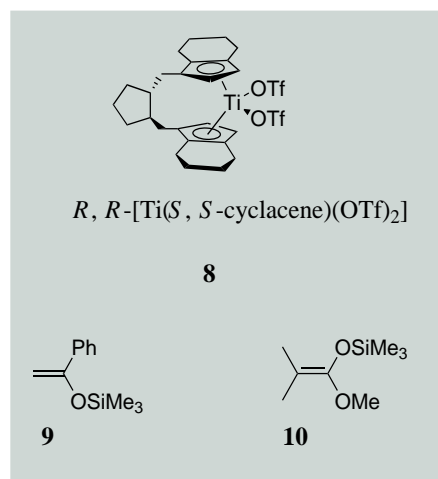
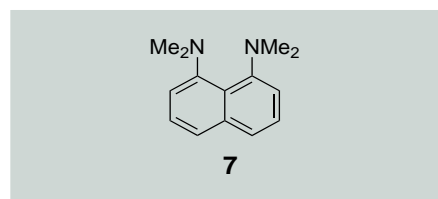
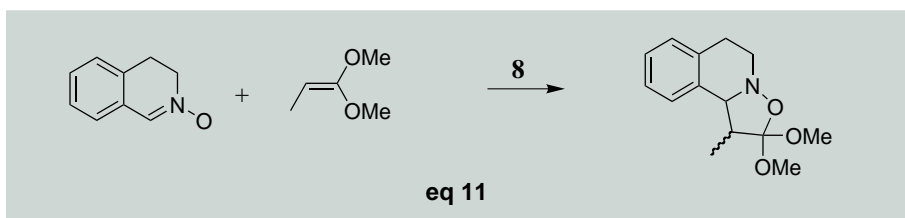
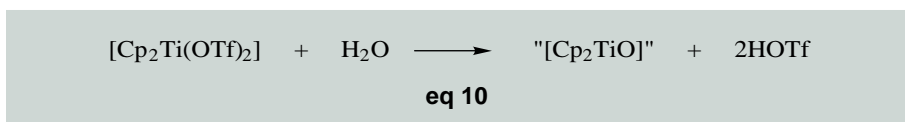
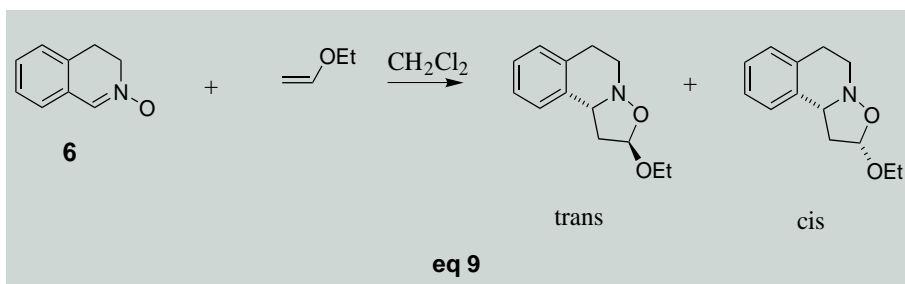


Table 3. Results of [3+2] Nitron–Olefin Cycloadditions^a

	Nitron	Olefin	t for 95% Yield (h)	Isomer Ratio (trans:cis)
1			60	75:25
2			40	88:12
3			0.3	65:30
4			0.5	32:68
5			31	17:83

^a Using 3 mol% $[\text{Cp}_2\text{Ti}(\mathbf{6})_2](\text{OTf})_2$ in the presence of 6 mol% of proton sponge in CH_2Cl_2 solutions at 25°C . Concentrations of the nitrones are ~ 0.5 M and those of the olefins are 0.6–1.0 M.

appear to interfere in the Diels–Alder reaction as we noted earlier. Proton catalysis of the nitron–olefin reaction occurs even with pyridinium triflate, and it was found necessary to use Proton-Sponge[®] **7** in order to suppress proton catalysis.

In the presence of the proton sponge, the titanium complex acts as a catalyst. It was found more convenient to use the nitron adduct $[\text{Cp}_2\text{Ti}(\mathbf{6})_2](\text{OTf})_2$ rather than $[\text{Cp}_2\text{Ti}(\text{OTf})_2]$ as the catalyst. The bisnitron adduct is readily prepared as stable crystals and its X-ray crystal

structure is shown in **Figure 1**. In CH_2Cl_2 solutions, the catalyst exists as the bisnitron complex and, under catalytic conditions where an excess of nitron is present for the majority of catalysis, it is probable that the bisnitron complex is the catalytically active species.

Some of the results are collected in **Table 3**. The rates of the cycloadditions depend on both the nature of the nitron and olefin—the cyclic nitron and the more electron-rich olefins are associated with faster rates. Compared to the corresponding thermal reactions, the dimethyl vinyl ethers react catalytically at least 10^4 times faster, whereas the monoethers are catalyzed about 10^3 times faster than the corresponding thermal reactions. Of course, the catalytic turnover rate can be increased by increasing the catalyst concentration.

Given the strong proton catalysis observed for these reactions, it was useful to demonstrate that enantioselectivity could be observed. For this purpose, we employed the chiral catalyst R,R -[Ti(*S,S*)-cyclocene](OTf)₂ (**8**)²³ in the presence of a proton sponge in CH_2Cl_2 solutions at 25°C (**eq 11**). The major (trans) isomer of the product was isolated and found to have an ee of 14% suggesting that catalysis involves binding of the nitron to the titanium center.

7. The Mukaiyama and Sakurai Reactions

Using a variety of aldehydes and ketones and silyl enol ether **9**, or ketene acetal **10**, the ruthenium catalyst was found to promote the Mukaiyama reaction (**eq 2**) at very low catalyst loadings, even as low as 0.1 mol%.²⁴ Although

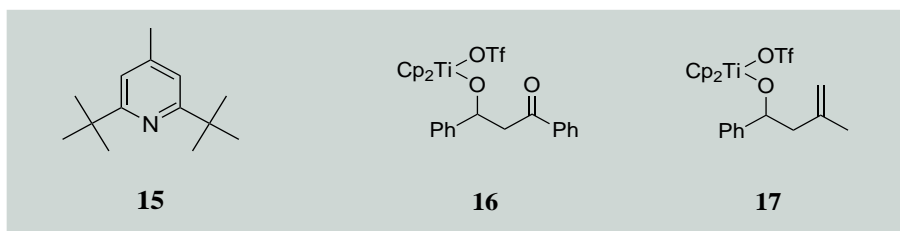
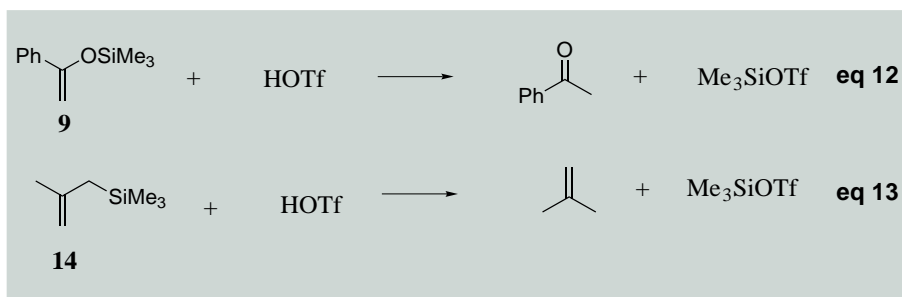
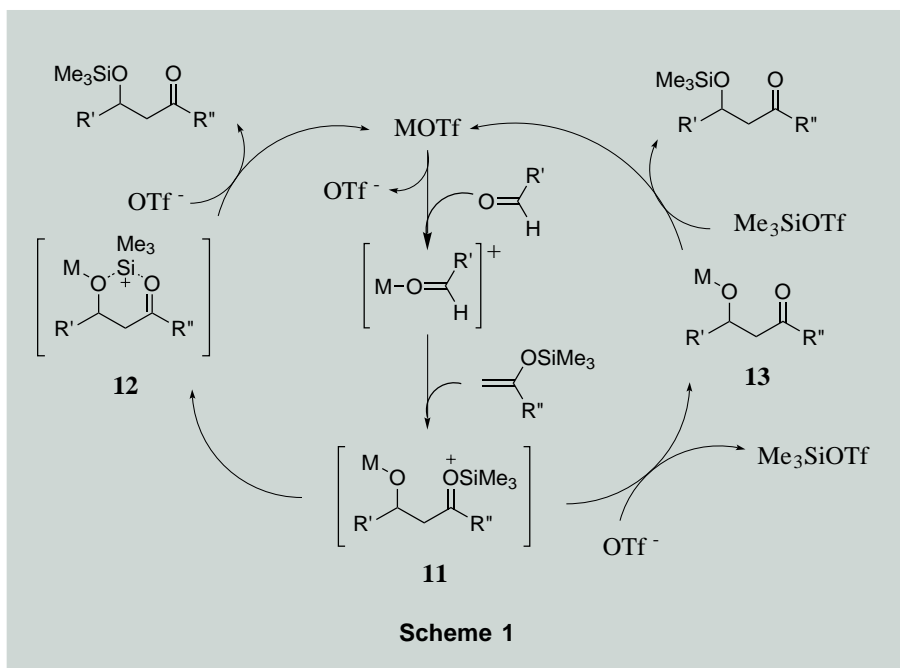
it is not clear that the ruthenium complex is the real catalyst, the complex appears to undergo reduction by the vinyl ethers or vinyl acetals. The reduction is evidenced by a sudden color change in solution but the apparent reduction is unpredictable, occurring sometimes after 20 turnovers and at other occasions after 100 or more turnovers. Because of this and other reasons, the ruthenium complex is not a useful catalyst for this reaction and suggests that the Mukaiyama reaction may require oxidatively stable transition-metal Lewis acids. One would anticipate that the $[\text{Cp}_2\text{Ti}(\text{OTf})_2]$ complex would be less likely to reduce during Mukaiyama catalysis. This proved to be the case and the titanium complex was found to catalyze the condensation of a variety of aldehydes and ketones with the olefins, **9** and **10**.²⁵ Similarly, this same complex catalyzed the Sakurai coupling (eq 3) of a variety of allylic silanes with aldehydes, ketones, acetals, ketals, and orthoesters.²⁶ We do not provide tables of these results because the $[\text{Cp}_2\text{Ti}(\text{OTf})_2]$ complex is not the primary catalyst in any of these coupling reactions. In order to show how this conclusion was reached, it is necessary to understand the mechanism of these two reactions.

8. Mechanisms of the Mukaiyama and Sakurai Reactions

The Lewis acid catalyzed Mukaiyama reaction is generally assumed to proceed by the mechanism outlined in **Scheme 1**.

The aldehyde binds to the metal by displacement of the triflate ligand. The enol ether then attacks the bound, activated aldehyde to give the intermediate, **11**. It is the fate of this intermediate which determines if the catalysis proceeds by the expected path. If the trimethylsilyl group is transferred by way of an intermediate resembling **12**, the product will form and the catalyst (MOTf) will be regenerated. On the other hand, the trimethylsilyl group in **11** could be captured by triflate ion to give intermediate **13**. Were the Me_3SiOTf to capture the aldolate, **13**, the product would also be formed by an intermolecular pathway. Trimethylsilyl triflate, however, is known to be a very powerful catalyst for the Mukaiyama reaction²⁷ and the question arises as to whether the rate of capture of the enolate, **13**, by trimethylsilyl triflate will be faster than trimethylsilyl triflate catalysis. A similar scheme can be proposed for the Sakurai reaction.

An extensive investigation of the mechanism of $[\text{Cp}_2\text{Ti}(\text{OTf})_2]$ catalysis in CH_2Cl_2 solutions of both the Mukaiyama and Sakurai reactions revealed a number of disconcerting features of these catalyses which appear to have general applicability. Addition of the enol ether, **9**, or the allylic silane, **14**, to a CH_2Cl_2 solution of $[\text{Cp}_2\text{Ti}(\text{OTf})_2]$ leads to the immediate formation of trimethylsilyl triflate. It



was shown that all of the Mukaiyama and Sakurai reactions proceed by the Me_3SiOTf path. The formation of Me_3SiOTf has its origins in the formation of HOTf by the hydrolysis reaction shown in eq 10.

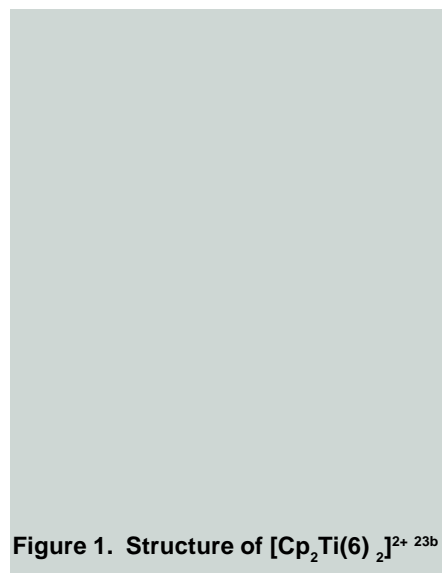
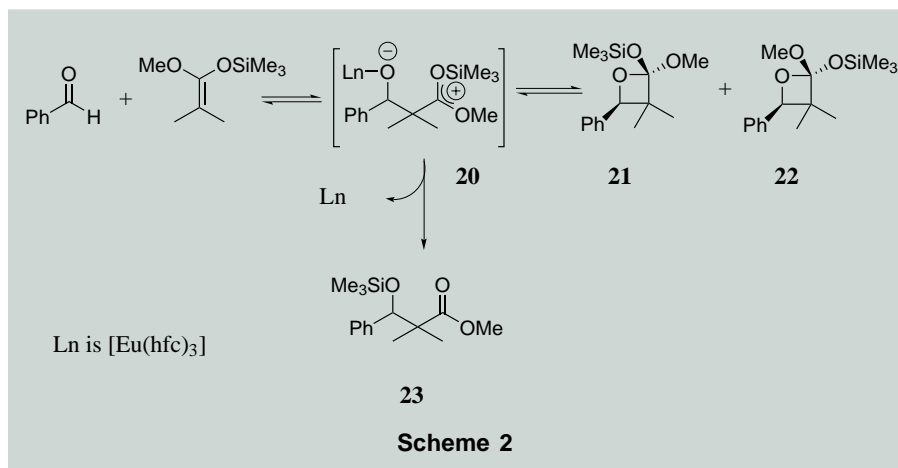
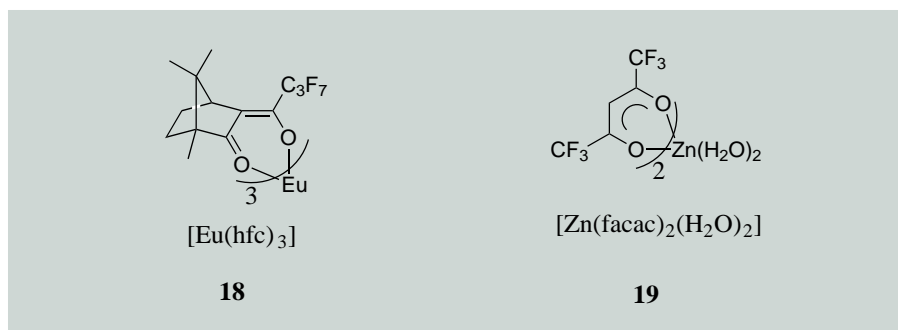
Trimethylsilyl triflate is formed by the very rapid representative reactions shown in eq 12 and eq 13.

There are two obvious ways of suppressing the formation of triflic acid. One is to thoroughly dry the solvent, but this is an impractical proposition because Me_3SiOTf is such a potent catalyst that even very small concentrations of adventitious water, as little as 10^{-5}M , are sufficient to cause rapid catalysis. The other is to take normal precautions for exclusion of water but to carry out the catalysis in the presence of a hindered base such as **15**. The protonated form of this base does not

induce the reactions shown in eq 12 and eq 13 and hence Me_3SiOTf will not form by this method.

Following the catalysis by ^1H NMR spectroscopy using $[\text{Cp}_2\text{Ti}(\text{OTf})_2]$, benzaldehyde, silyl enol ether **9**, and base **15** in CD_2Cl_2 at 25°C , revealed the formation of Me_3SiOTf and one equivalent of the aldolate, **16**. Under similar conditions, the Sakurai coupling between benzaldehyde and the allylic silane **14** also gave Me_3SiOTf and **17**.

In both cases, the aldolates, **16** and **17**, are stable in the presence of a molar equivalent of Me_3SiOTf . As a consequence, the $[\text{Cp}_2\text{Ti}(\text{OTf})_2]$ complex merely serves as an initiator for the production of the real catalyst, Me_3SiOTf . These results, namely the formation of the Me_3SiOTf catalyst either by Lewis acid hydrolysis or as a result of the formation



of a stable aldolate, are not peculiar to the present catalyst and appear to be widespread among many, but not all, reported catalysts.^{28,29}

There are, however, a number of chiral Lewis acid catalysts which act as efficient enantioselective catalysts for the Mukaiyama reaction.^{28,30,31} It is clear that these enantioselective reactions proceed via the chiral Lewis acid and not by way of the achiral, Me₃SiOTf catalyst. The question then arises as to what characteristics the Lewis acid must possess in order that the formation of Me₃SiOTf be suppressed. Inspection of **Scheme 1**

suggests that if the Lewis acid–oxygen bond of the aldolate intermediate is weak and, if no kinetic impediments exist, the probability of Me₃Si⁺ transfer, either intra- or intermolecularly, will be increased. Consequently, the probability of forming standing concentrations of Me₃SiOTf will be reduced. With these considerations in mind, we selected the two potential catalysts **18** and **19** for investigation. Both are neutral complexes and, unlike [Cp₂Ti(OTf)₂], are expected to form weak aldolate bonds. Additionally, the presence of electron-withdrawing fluorine groups in the ligands is expected to enhance the Lewis acidity of the metals. Because [Eu(hfc)₃] is expected to form 7-coordinate Lewis acid adducts and the [Zn(facac)₂(H₂O)₂] complex is expected to form 6-coordinate adducts after displacement of the water ligand, we might expect that the aldolate bonds will be especially weak in these neutral complexes. Generally, Lewis acidity decreases as the coordination number increases. Thus, both the neutral charge and the coordination number of the aldolates are expected to conspire to give weak adducts and weak aldolate metal bonds.

Using 4 mol % [Eu(hfc)₃] in benzene solution at 20°C, the reaction between benzaldehyde and the ketene acetal is represented in **Scheme 2**.³² After one hour, equilibrium between the two oxetanes, **21** and **22**, is reached using 1M solutions of each substrate. The initial kinetic ratio of oxetane isomers is 48:52, which changes to a thermodynamic ratio of 38:62. (We were unable to identify the isomers.) The equilibrium constant between the substrates and oxetanes is 3. After several hours, the Mukaiyama product, **23**, begins to appear and is completely formed irreversibly after several days. Addition of the hindered base, **15**, does not alter the rate of catalysis indicating that protons are not involved in catalysis. Using the chiral [Eu(hfc)₃] catalyst, the Mukaiyama product, **23**, was found to have an ee of 15%. As required, the oxetanes are racemic after equilibration, but if the catalysis is quenched before equilibration of the oxetanes is obtained, a small ee of 5% is found. Although these enantiomeric excesses are modest, they indicate that the lanthanide complex is involved in catalysis.

The results outlined in **Scheme 2** are significant because the aldolate, **20**, is not detected and hence its unstable Me₃Si⁺ group will not be captured by the aldehyde substrate. Rather, the aldolate collapses either to the oxetanes or to the starting substrates. For this particular case, this process occurs faster than the silyl transfer to give the Mukaiyama product. The fugacious nature of the putative intermediate and the stability of the silyl groups in oxetanes ensures that Me₃Si⁺ will not enter into the catalytic cycle. The weak aldolate bond ensures that the carbenium ion of **20** is captured rapidly but the relative rates of formation of the oxetanes and Mukaiyama product depend on both the catalyst and the substrate.³² Thus, we find that, with [Zn(facac)₂(H₂O)₂] under the same conditions and using benzaldehyde and the same ketene acetal, the formation of the Mukaiyama product occurs more quickly than in the case of the lanthanide complex. Although the oxetanes are observed, they do not achieve equilibration before the final product is formed. An extreme case is the reaction of benzaldehyde and substrate **24** using the zinc catalyst. In this case, no oxetanes are observed and only the Mukaiyama product is formed.

Although these weak Lewis acids are real catalysts for the Mukaiyama coupling reactions, they do not cause coupling of ketones with silyl ketene acetals nor coupling of silyl enol ethers with aldehydes or ketones. Further work is required to ascertain whether other Lewis acids can be devised which genuinely catalyze coupling of these less reactive substrates. For those concerned about the mechanism of enantioselection, it is clear that the origins of the chiral discrimination can be

very complex. The enantioselection will depend on the rates of equilibration of the oxetanes and on the rate of production of the Mukaiyama product. The most complicated condition is when the oxetanes are formed at a rate comparable to the rate of formation of the product.

9. Concluding Remarks

This review of our work is presented from the point of view of an inorganic chemist. Inorganic chemists tend to focus on the attributes of metal and on the mechanism of the catalysis. New transition-metal-based Lewis acids are likely to be discovered and become increasingly used. It is hoped that this review will provide some of the conceptual underpinnings for the development of new transition-metal Lewis acids.

10. Acknowledgments

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About the Author

Brice Bosnich, a native of Australia, completed his undergraduate degree at the University of Sydney and his Ph.D. at the Australian National University. He has held posts at University College, London, at the University of Toronto, and is now a professor of Chemistry at the University of Chicago. A common thread throughout his work has been an interest in inorganic stereochemistry, which has included the relationship between absolute structure and circular dichroism spectra, diastereoselective complexation, and molecular mechanics of organometallic complexes. His work in asymmetric catalysis has led him to develop new catalysts and to study their mechanisms. He is the recipient of a number of awards, including the Noranda Award of the Canadian Institute of Chemistry, the Organometallic Medal and the Nyholm Medal, both of the Royal Society of Chemistry. This review is the result of his receipt of the ACS Award in Inorganic Chemistry sponsored by Aldrich. His current interests are in cooperative bimetallic reactivity and in supramolecular recognition.

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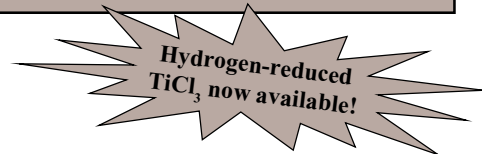
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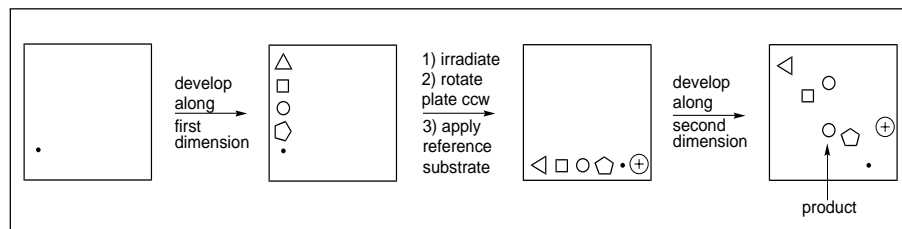
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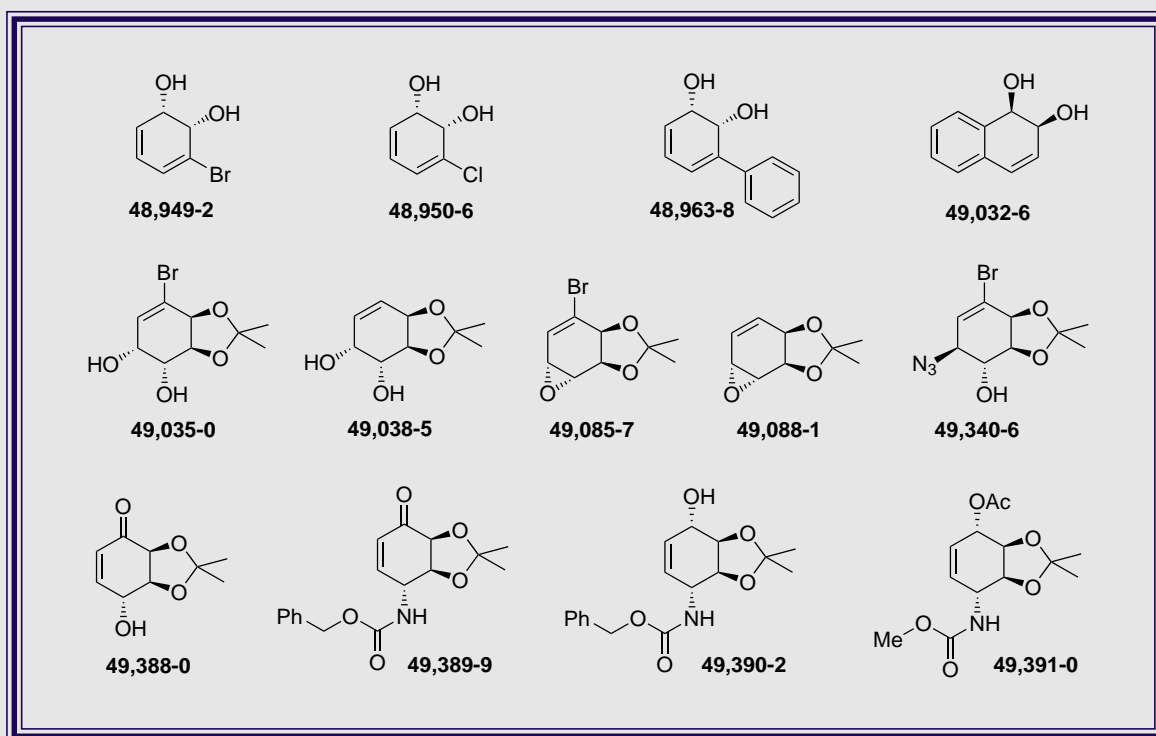
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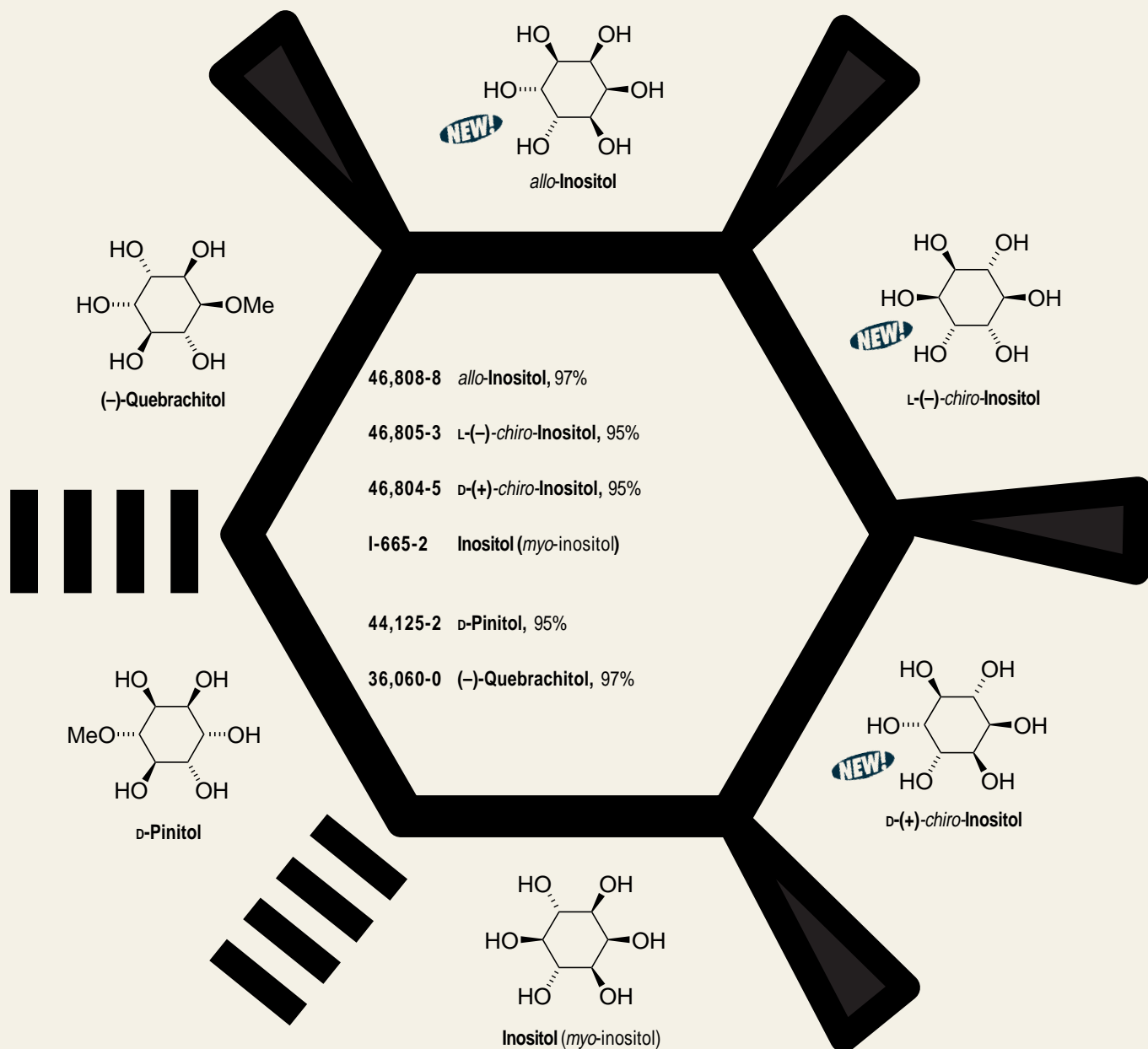
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- 49,038-5 [3*aS*-(3*αα*,4*α*,5*α*,7*αα*)]-3*a*,4,5,7*a*-Tetrahydro-2,2-dimethyl-1,3-benzodioxole-4,5-diol, 98%
- 49,085-7 [3*aS*-(3*αα*,5*αβ*,6*αβ*,6*βα*)]-4-Bromo-3*a*,5*a*,6*a*,6*b*-tetrahydro-2,2-dimethyloxireno[*e*]-1,3-benzodioxole, 98%
- 49,088-1 [3*aR*-(3*αα*,5*αβ*,6*αβ*,6*βα*)]-3*a*,5*a*,6*a*,6*b*-Tetrahydro-2,2-dimethyloxireno[*e*]-1,3-benzodioxole, 96%
- 49,340-6 [3*aS*-(3*αα*,4*α*,5*β*,7*αα*)]-5-Azido-7-bromo-3*a*,4,5,7*a*-tetrahydro-2,2-dimethyl-1,3-benzodioxol-4-ol, 99%
- 49,388-0 (3*aS*,7*R*,7*aS*)-7,7*a*-Dihydro-7-hydroxy-2,2-dimethyl-1,3-benzodioxol-4(3*aH*)-one, 98%
- 49,389-9 (3*aS*,7*R*,7*aS*)-7-(Carbobenzyloxyamino)-7,7*a*-dihydro-2,2-dimethyl-1,3-benzodioxol-4(3*aH*)-one, 98%
- 49,390-2 (3*aR*,4*S*,7*R*,7*aS*)-7-(Carbobenzyloxyamino)-3*a*,4,7,7*a*-tetrahydro-2,2-dimethyl-1,3-benzodioxol-4-ol, 98%
- 49,391-0 (3*aR*,4*S*,7*R*,7*aS*)-3*a*,4,7,7*a*-Tetrahydro-7-(methoxycarbonylamino)-2,2-dimethyl-1,3-benzodioxol-4-ol 4-acetate, 98%

Inositols

The inositols and their phosphates constitute an extremely important class of compounds. They have been used in the development of metabolically stable insulin mediators, inhibitors, and modulators of important metabolic functions such as glycolysis. Inositols are stable to degradative enzymes *in vivo* because they lack a hydrolytically labile glycosidic linkage. This feature is important for the development of metabolically stable insulin mediators.

Aldrich now offers a variety of the more rare inositols such as *D-chiro-* and *allo-*inositols; *neo-*inositol will soon be available. For more information, please call our Technical Services department at **800-231-8327** (USA).

References: (1) Potter, B.V.L. *Nat. Prod. Rep.* **1990**, 7,1. (2) Bellington, D.C. *Chem. Soc. Rev.* **1989**, 18, 83. (3) Berridge, M.J.; Irvine, R.F. *Nature* **1989**, 341, 197. (4) Hudlicky, T.; Cebulak, M. *Cyclitols and Their Derivatives. A Handbook of Physical, Spectral, and Synthetic Data*; VCH: New York, 1993. (5) Hudlicky, T. et al. *Chem. Rev.* **1996**, 96, 1195. (6) Hudlicky, T. et al. *Synthesis* **1996**, 897.



16th Herbert C. Brown Lectures in Organic Chemistry

Perspectives in Modern Synthetic Organic Chemistry

Saturday, March 27, 1999 ~ Department of Chemistry ~ Purdue University ~ West Lafayette, IN 47907

Speakers and Topics

- Professor **Alois Fürstner**; *Max Planck Institut für Kohleforschung*
Metal-Catalyzed Macrocyclization Reactions Revisited
- Professor **Yoshito Kishi**; *Harvard University*
Recent Topics in Natural Product Synthesis
- Professor **Steven V. Ley**; *University of Cambridge*
New Methods and Tools for Organic Synthesis
- Professor **Masakatsu Shibasaki**; *University of Tokyo*
Recent Developments in Multifunctional Asymmetric Catalysis

For more information, please contact:

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E-mail: chandran@chem.purdue.edu

1999 ACS Award Recipients

Aldrich, a proud sponsor of three separate ACS awards, congratulates the following 1999 recipients for their outstanding contributions to chemistry.

ACS Award for Creative Work in Synthetic Organic Chemistry: Professor **Dale L. Boger**, The Scripps Research Institute
Selected for his outstanding contributions to, among others, the total synthesis of biologically important natural products, the studies of antitumor antibiotics that derive their biological properties from binding with DNA, the development of new synthetic methodologies in heterocyclic chemistry, and the early implementation of methods to carry out solution-phase combinatorial chemistry.

ACS Award in Inorganic Chemistry: Professor **Richard D. Adams**, the University of South Carolina
Chosen in recognition of his pioneering research on the chemistry of cluster complexes (polynuclear metal complexes). This includes the preparation and characterization of novel cluster complexes, the systematic investigation of these as powerful catalysts for the transformation of small organic molecules, and the development of new forms of catalysis by metal cluster complexes.

Herbert C. Brown Award for Creative Research in Synthetic Methods: Professor **Barry M. Trost**, Stanford University
As one of his nominating colleagues put it, Professor Trost has made "uniquely significant contributions to a broad spectrum of subjects in chemistry" and is a "pre-eminent contributor to synthetic methodology for over 33 years". Dr. Trost has fundamentally impacted such diverse research areas as the chemistry and biology of insect juvenile hormones, sulfur chemistry, the chemistry of strained rings, and transition-metal catalysis. He is credited with an impressive number of total syntheses of natural products and syntheses of important new materials such as pyraclyenes.

Congratulations to each and all!



From the
Aldrich
Bookshelf



**Asymmetric Synthesis:
Construction of Chiral Molecules
Using Amino Acids**

G.M. Coppola and H.F. Schuster, John Wiley & Sons, New York, NY, 1987, 393pp. Focuses on the use of amino acids and their second-generation derivatives to produce chiral reagents, intermediates, and final products.

Z16,762-2

Stereoselective Synthesis

R.S. Atkinson, John Wiley & Sons, New York, NY, 1995, 600pp. Covers the majority of reaction types used in modern stereoselective synthesis. Introduces a simplified classification for reactions based on the number of chiral centers.

Z26,175-0

The Logic of Chemical Synthesis

E.J. Corey and X.-M. Cheng, John Wiley & Sons, New York, NY, 1995, 436pp. Softbound. Discusses the logic underlying the analysis of complex synthetic problems.

Z27,174-8

**Molecular Spectroscopy
Workbench: Advances,
Applications, and Practical
Advice on Modern Spectroscopic
Analysis**

E.W. Ciurczak, John Wiley & Sons, New York, NY, 1998, 476pp. Compiles and updates the best articles to date from the eleven-year history of *Spectroscopy* magazine's successful "Molecular Spectroscopy Workbench" column. From the fundamentals of important techniques to novel time- and money-saving ideas, it draws from a broad spectrum of recent developments in the field of molecular spectroscopy. Includes information about near- and midrange infrared techniques, optical rotation/circular dichroism, UV/Vis and fluorescence, mass spectrometry, acousto-optic tunable filters, fiber optics, and new hardware.

Z40,865-4

**Advanced Catalysts and
Nanostructured Materials:
Modern Synthetic Methods**

W.R. Moser, Ed., Academic Press, New York, NY, 1996, 592pp. Provides a comprehensive review of the latest techniques for the preparation of advanced catalysts and solid-state materials of specific structure and morphology.

Z28,635-4

NMR Data Processing

J.C. Hoch and A.S. Stern, Wiley-Liss, New York, NY, 1996, 196pp. Complete information about how to process, present, and perform error analysis on data obtained from modern nuclear magnetic resonance (NMR) experiments. Includes extensive examples for maximum comprehension.

Z40,858-1

**Applied Homogeneous Catalysis
with Organometallic Compounds:
A Comprehensive Handbook in
Two Volumes**

B. Cornils and W.A. Herrmann, Eds., VCH Publishers, Weinheim, FRG, 1996, 1,246pp. Comprehensive treatment of one of the most important topics in organometallic chemistry. Explores both basic research and industrial applications through treatment of catalytic reactions and processes.

Z40,230-3

**The Encyclopedia of Reagents for
Organic Synthesis**

L.A. Paquette, Ed., John Wiley & Sons, New York, NY, 1995, 6234pp. Presents the facts in a "pros and cons" assessment of each reagent to give the complete picture. Where applicable, each entry includes: transformations recognized for the reagent; comparison of the specific properties of the reagent with those of other agents capable of equivalent chemistry; stereo-, regio-, and enantiocontrol qualifications.

8-volume set Z24,805-3

**Metal and Ligand Reactivity: An
Introduction to the Organic
Chemistry of Metal Complexes**

E.C. Constable, VCH Publishers, New York, NY, 1996, 308pp. Introduction to the reactions and interactions between metal ions and ligands. Provides useful information for organic synthesis.

Z28,938-8

**Purification of Laboratory
Chemicals**



4th ed., D.D. Perrin and W.L. Armarego, Eds., Butterworth, New York, NY, 1996, 450pp. Explains techniques of purification with specific methods for more than 4,000 chemicals and biochemicals.

Z28,581-1

**Asymmetric Synthetic
Methodology**

D.J. Ager and M.B. East, CRC Press, Boca Raton, FL, 1996, 483pp. Implements asymmetric synthesis in an industrial chemistry environment. Provides methodology to perform specific asymmetric transformations with emphasis on scope and limitations.

Z27,403-8

**Chiral Auxiliaries and Ligands in
Asymmetric Synthesis**

J. Seyden-Penne, John Wiley & Sons, New York, NY, 1995, 716pp. An in-depth guide for synthesis of chiral compounds in pharmaceutical and medical research. Provides an overview of the principles of physical organic chemistry governing stereoselection.

Z27,369-4

Reductions in Organic Chemistry

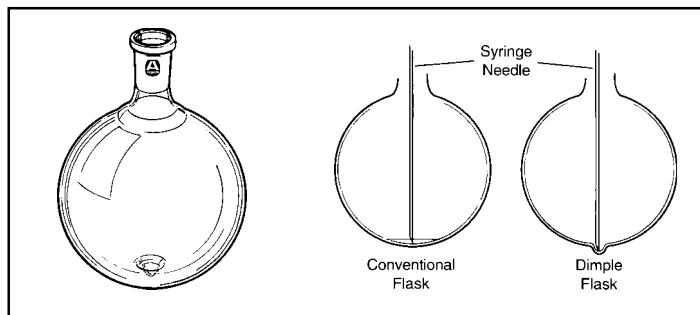
2nd ed., M. Hudlicky, American Chemical Society, Washington, DC, 1996, 429pp. A compilation of the types of reductions undergone by the various classes of organic compounds. Describes the methods, reactants, and products of reductions.

Z28,591-9

Scientific Glassware ...clearly the finest

ALDRICH DIMPLE FLASKS

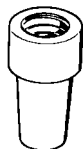
These flasks are designed to permit complete removal of liquids using noncoring type syringe needles, gauges 12 to 20, that are used for piercing rubber septa. A small indentation or "dimple" at the bottom of the flask acts as a reservoir to collect liquids which may then be drawn off via syringe. The dimple is small enough that it does not interfere with the use of egg-shaped magnetic stirring bars.



The design of these flasks was first published by Professor Brian E. Love of the East Carolina University Department of Chemistry in *Organic Preparations and Procedures International*, 1997, 29, 600-601.

Cap. (mL)	14/20 Joint Cat. No.	24/40 Joint Cat. No.
25	Z40,632-5	—
50	Z40,633-3	—
100	Z40,634-1	Z40,636-8
250	—	Z40,637-6
500	—	Z40,638-4
1,000	—	Z40,639-2

STANKOVIC TRANSFER ADAPTERS

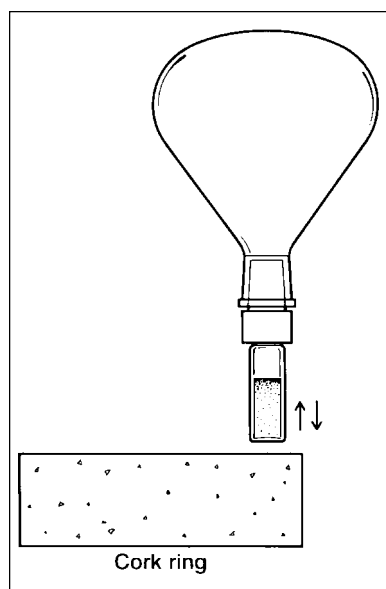


These unique adapters greatly simplify the transfer of solids from round-bottom flasks to vials. Precision-machined, chemically inert Teflon® PTFE adapters will not seize in the joint. A wide range of thread sizes are available to accommodate most sample vials including scintillation vials (22 mm threads).

- Transfers samples without exposure to air or moisture.
- Reduces sample losses due to air currents and static charge that can normally cause light solids to float or blow away when transferred open to the air.
- Excellent for transferring fluffy lyophilized samples, especially peptides.
- Transfers any freely flowing solid and eliminates the need for weighing paper or other intermediate devices.

Easy to Use:

Screw sample vial into bottle thread at top of adapter. Insert other end of adapter into flask joint. Invert assembly and gently tap* vial on a soft surface to transfer solids from flask into sample vial.

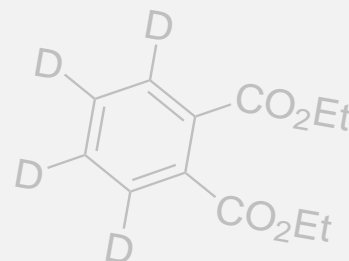
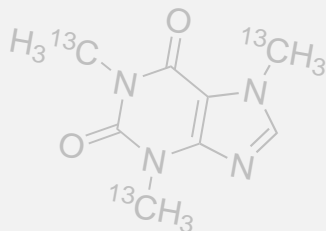


Joint	Bottle Thread	Cat. No.
14/20	13-425	Z40,646-5
	13-425	Z40,647-3
	15-425	Z40,648-1
	20-400	Z40,650-3
24/40	22mm	Z40,658-9
	13-425	Z40,651-1
	15-425	Z40,653-8
	20-400	Z40,654-6
24/29	22mm	Z40,659-7
	13-425	Z40,655-4
	15-425	Z40,656-2
	20-400	Z40,657-0
29/32	22mm	Z40,660-0

* Care must be used when tapping vial to prevent accidental breakage. Tapping on a cork ring or other soft surface is recommended.

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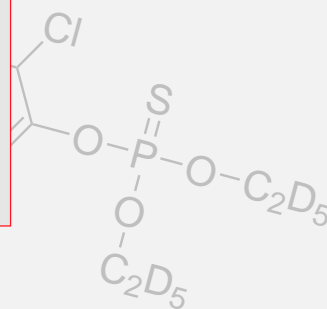
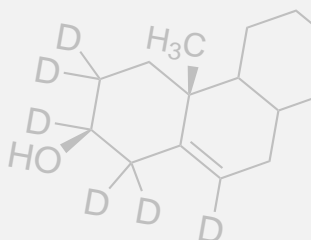
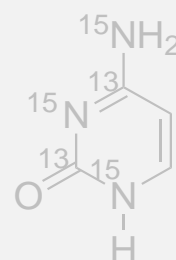
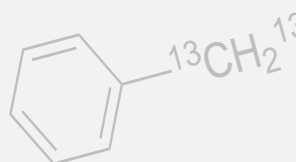
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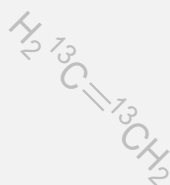
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