Use of Manganese (V) Nitrides as Enantioselective Nitrogen-Transfer Reagents

Thesis by
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Abstract.

Once activated, manganese(V)nitrides have been shown to efficiently transfer nitrogen to furanoid glycals. This process, followed by hydrolysis, forms the corresponding amino alcohols in high yield and diastereoselectivity. The isolation of an intermediate oxazoline and the ability to form this oxazoline from the amino alcohol was also discovered. The formation of chiral manganese nitrides is also described. After considerable experimentation, the transfer of nitrogen in these cases resulted in enantiomeric excesses of up to 92% accompanied by high yields.

Introduction.

A variety of processes involving the stereocontrolled functionalization of alkenes have been studied extensively, such as cyclopropanations, epoxidations, and dihydroxylations (Figure 1).[1,2] An area less explored is that of nitrogen transfer, despite the potential use for such a process. Thus, we sought to explore the availability of this transformation.

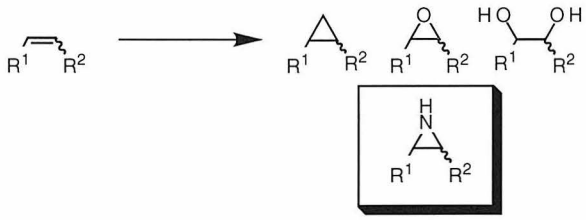

Figure 1. Functionalized systems available from olefins.

Background.

Much of the earlier work in nitrogen-transfer chemistry using free nitrenes and simple metal nitrenoids is plagued with problems ranging from low yielding reactions to the inability to control competing side reactions, such as insertion into C-H bonds and H-abstraction.[3,4]

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[1] (a) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidation of Organic Compounds,* Academic: New York, 1981. (b) *Organic Synthesis by Oxidation with Metal Compounds*; Mijs, W. J.; de Jonge, C. R. H. I., Eds. Plenum: New York, 1986. (c) Jacobsen, E. N. *Comprehensive Organometallic Chemistry II*, Abel, E. W.; Stone, F. G. A.; Wilkinson, G., Eds.; Pergamon: Oxford, U.K., 1995, Vol. 12, 1097. (d) Murahashi, S.-I.; Naota, T. In *Comprehensive Organometallic Chemistry II*, Abel, E. W.; Stone, F. G. A.; Wilkinson, G., Eds.; Pergamon: Oxford, U.K., 1995, Vol. 12, 1177.

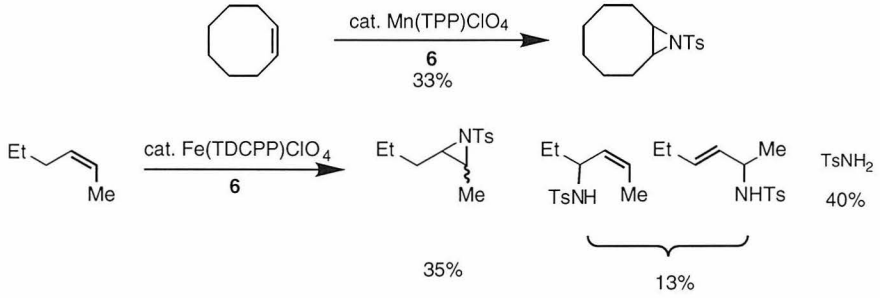
[2] (a) Jacobsen, E. N. In *Catalytic Asymmetric Synthesis*, Ojima, I., Ed.; VCH: New York, 1993, p. 159. (b) Jorgensen, K. A., *Chem. Rev.* **1989**, *89*, 431. (c) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 243, and references therein. (d) Johnson, R. A.; Sharpless, K. B. In *Catalytic Aysmmetric Synthesis*, Ojima, I., Ed.; VCH: New York, 1993, p 103. (e) Doyle, M. P. *AldrichimicaActa* **1996**, *29*, 1996. (f) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919.

[3] For earlier work with free nitrenes, see: (a) Lwowski, W.; Mattingly, T. W. *Tetrahedron Lett.* **1962**, *7*, 277. *Nitrenes*; (b) Lwowski, W., Ed.; Interscience: New York, 1970. (c) Lwowski, W.; Mattingly, T. W. *J. Am. Chem. Soc.* **1965**, *87*, 1947. (d) Lwowski, W.; Maricich, T. J. *J. Am. Chem. Soc.* **1965**, *87*, 3630.

[4] For one of the first metal-stabilized nitrenes, see: Kwart, H.; Kahn, A. A. *J. Am. Chem. Soc.* **1967,** *89*, 1951.

Mansuy has used (N-(*p*-tolylsulfonyl)imino)phenyliodinane (PhI=NTs) **6** to transfer nitrogen using manganese(III) or iron(III) complexes containing porphyrin-derived ligands (Scheme 1).[5] Although as little as 5 mol % of the catalyst is required, the use of 100 equiv of the substrate makes this methodology somewhat limited to simple inexpensive olefins. In addition, yields are relatively low (23-43%) and competing reactions are problematic.

Scheme 1.



Evans has developed a system using Cu(I) or Cu(II) salts and iodinane **6** as the nitrene source.[6] In his system, both electron-rich and electron-poor alkenes **7** undergo aziridination in yields typically ranging from 55-90% (Table 1). This process has the advantages that essentially no allylic insertion or hydrogen abstraction product is observed and that the copper catalysts required are inexpensive and commercially available. Unfortunately, the methodology requires 5 equiv of the olefin, so the yield is reported with respect to iodinane **6**.

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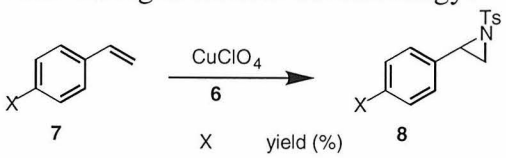
[5] (a) Mansuy, D.; Mahy, J. -P.; In *Metalloporphyrins Catalyzed Oxidations*; Montanari, F. and Casella, L., Eds.; Kluwer Academic Publishers: Dordrecht, 1994, 175. (b) Mahy, J. -P.; Bedi, G.; Battioni, P.; Mansuy, D. *New J. Chem.* **1989**, *13*, 651. (c) Mahy, J. -P.; Bedi, G.; Battioni, P.; Mansuy, D. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1517. (d) Mahy, J. -P.; Bedi, G.; Battioni, P.; Mansuy, D. *Tetrahedron Lett.* **1988**, *29*, 1927. (e) Mansuy, D.; Mahy, J. -P.; Duréault, A.; Bedi, G.; Battioni, P. *J. Chem. Soc. Chem. Commun.* **1984**, 1161.

[6] Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *114,* 2742.

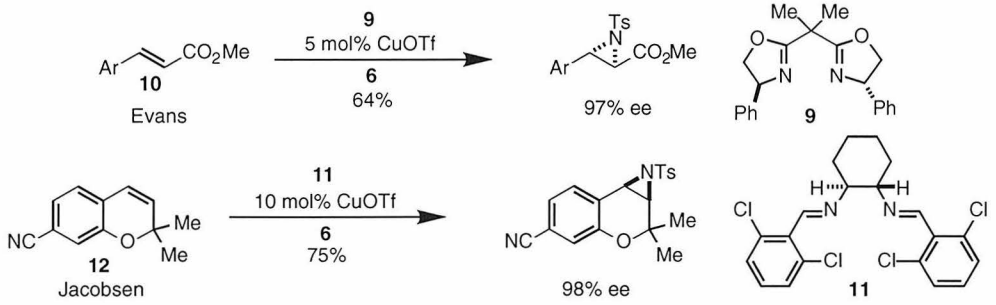
Table 1. Examples of Evans' nitrogen transfer methodology.



	X	yield (%)
8a	OMe	78
8b	Me	83
8c	Cl	90
8d	NO_2	89

Evans[7] and Jacobsen[8] simultaneously published reports of the enantioselective aziridination of olefins. Both systems use copper triflate (CuOTf) as the catalytic metal source, a chiral ligand, Ph=NTs (**6**) as the nitrene source, and the olefin as the limiting reagent (Scheme 2). Evans' methodology uses bis(oxazoline) ligand **9** and works best with cinnamic esters **10**. Other less-functionalized substrates also undergo the oxidative nitrogen-transfer reaction, but require excess olefin (5 equiv). Jacobsen's system, on the other hand, uses salen-derived ligand **11** and appears to perform the transformation optimally with styrene-derived substrates such as **12**.

Scheme 2.



Groves has developed a method of nitrogen-transfer using manganese porphyrin nitrido complexes **13**.[9] These complexes, when activated with trifluoroacetic anhydride

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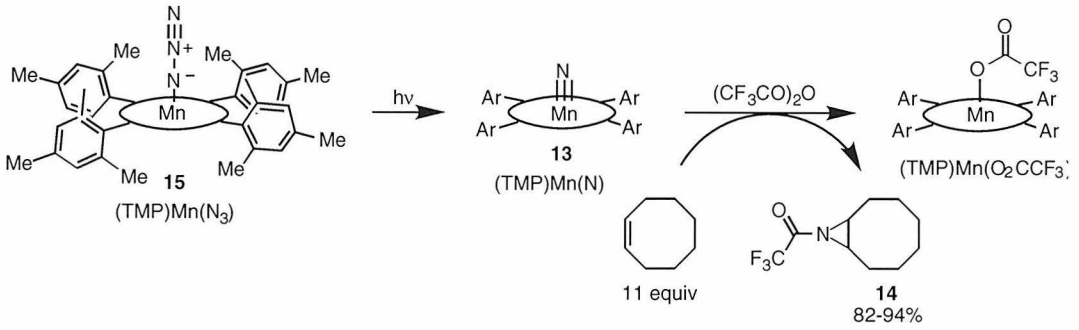
[7] Evans, D. A.; Faul, M. M.; Bilodeau, M. T.; Anderson, B. A.; Barnes, D. M. *J. Am. Chem. Soc.* **1993**, *115,* 5328.

[8] Li, Z.; Conser, K. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1993**, *115*, 5326.

[9] (a) Groves, J. T.; Takahashi, T. *J. Am. Chem. Soc.* **1983**, *105*, 2073. (b) Groves, J. T.; Takahashi, T.;

(TFAA), transfer nitrogen in good yield to cis-cyclooctene (90%) to form N-trifluoroacetyl aziridine **14** (Scheme 3).

Scheme 3.



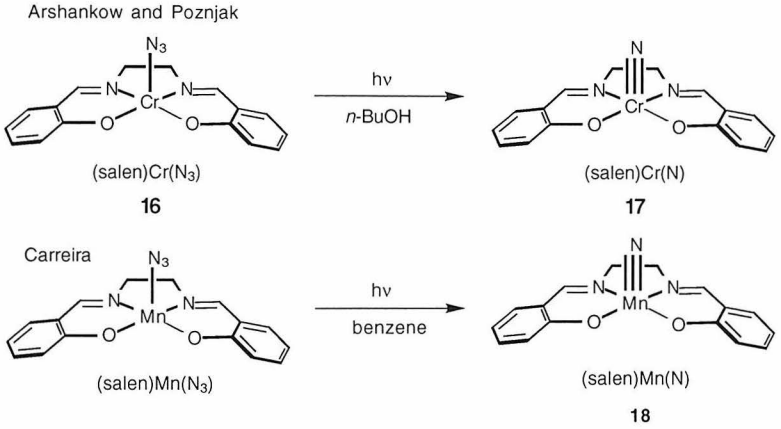
Several requirements of this process makes it impractical for multistep synthesis, however. First, the formation of the nitrido complex involves an expensive ligand (meso-tetrakis(2,4,6-trimethylphenyl)porphyrin) (TMP). In addition, generation of nitrido **13**, via photolysis of **15**, is not suitable for large-scale synthesis. Furthermore, this process requires that the olefin be used in excess (11 equiv). This may not present a problem with readily-available and inexpensive substrates, but is not ideal for most cases.

Ideally, a simpler ligand which would be readily made from simple starting materials could be used to form an analogous metal complex with similar reactivity. Along these lines, it was noticed that Arshankow and Poznjak prepared (salen)Cr(III)(N) **16** from the corresponding azide **17** photolytically (Scheme 4).[10]

Butler, W. M. *Inorg. Chem.* **1983**, *22*, 884.

[10] Arshankow, S. I.; Poznjak, A. L. *Z. Anorg. Allg. Chem.* **1981**, *481*, 201.

Scheme 4.



Using this report as precedent, Carreira formed (salen)Mn(N) **18** in an analogous fashion.[11] In addition, Du Bois of the Carreira group developed a large scale synthesis (20 g) of **18** using inexpensive and commercially-available chemicals (Figure 2). The nitrido derived from 2,3-diamine-2,3-dimethylbutane **19** was also synthesized in this manner. The latter metal complex has the advantage of being more soluble in common organic solvents.

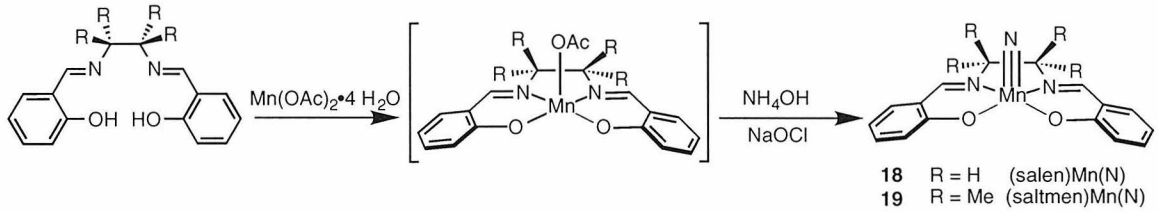


Figure 2. Carreira's synthesis of salen-derived manganese nitrides.

After extensive experimentation, it was shown that the nitrogen transfer methodology worked best with electron-rich olefins. Specifically, it was shown that nitrido complex **19**, once activated by TFAA, could transfer the N-trifluoroacetyl group

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[11] Du Bois, J.; Hong, J.; Carreira, E. M.; Day, M. W. *J. Am. Chem. Soc.* **1996**, *118*, 915.

to silyl enol ethers **20** to afford α-amino ketones **21**, presumably *via* an aziridine intermediate **22** (Figure 3).

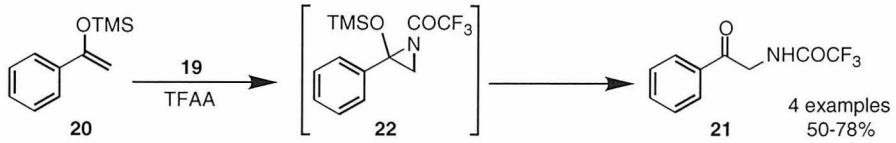

Figure 3. Carreira's formation of α-amino ketone *via* aziridination.

Searching for other substrates, glycals were considered since there are relatively few methods to obtain α-amino sugars despite the potential use of this methodology.[12] Danishefsky, Fitzsimmons, and Leblanc are key pioneers in the exploration of the conversion of carbohydrate glycals to the corresponding 2-amino alcohol products. Even these processes, however, require multiple steps. Thus, the development of a one-step nitrogen transfer process to glycals seemed worthwhile.

Results.

Noting that electron-rich substrates such as silyl enol ethers can undergo nitrogen-atom transfer with the salen-derived manganese nitrido complex,[11] we sought to determine whether glycals could undergo the analogous transformations. The goal of this particular project was to prepare furanoid glycals and determine if nitrogen could be transfered efficiently. Specifically, two glycal furanoids were prepared, each in one step from known procedures. A key intermediate to the first substrate, a dibenzyl-protected furanoid **25**, was synthesized from 2-deoxyribose as shown by Walker[13] and Yokoyama[14]

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[12] (a)Leblanc, Y.; Fitzsimmons, B. J.; Springer, J. P.; Rokach, J. *J. Am. Chem. Soc.* **1989**, *111*, 2995. (b)Leblanc, Y.; Fitzsimmons, B. J. *Tetrahedron Lett.* **1989**, *30*, 2889. (c) Leblanc, Y.; Fitzsimmons, B. J.; Chan, N.; Rokach, J. *J. Am. Chem. Soc.* **1988**, *110*, 5229. (d) Leblanc, Y.; Fitzsimmons, B. J.; Rokach, J. *J. Am. Chem. Soc.* **1987**, *109,* 285. (e) Kozlowska-Gramz, E.; Descotes, G. *Can. J. Chem.* **1982**, *60*, 558. (f) Kozlowska-Gramsz, E.; Descotes, G. *Tetrahedron Lett.* **1981**, *22*, 563. (g) Danishefsky, S. J.; Bilodeau, M. T.; *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1380. (h) Gijsen, H. J. M.; Qiao, L.; Fitz, W.; Wong, C. -H. *Chem. Rev.* **1996**, *96*, 443. (i) Danishefsky, S. J.; Roberge, J. Y.; *Pure Appl. Chem.* **1995**, *67*, 1647. (j) Banoub, J.; Boullanger, P.; Lafont, D. *Chem. Rev.* **1992**, *92*, 1167. (k) Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212.

[13] Dyson, M. R.; Coe, P. L.; Walker, R. T. *Carbohydrate Research* **1991**, *216*, 237.

(Figure 1). The desired glycal **26** was then synthesized by treatment of the pentofuranose with mesyl chloride (MsCl) and triethylamine (Et_3N) in 54% yield (Figure 4).

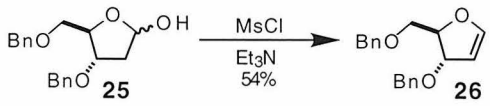

Figure 4. Formation of glycal **26**.

With the desired substrate **26** for nitrogen transfer in hand, conditions for the desired transformation were considered. The procedure used in Carreira's initial publication regarding nitrogen-atom transfer involved addition of trifluoroacetic anhydride (TFAA) at -78 °C to a solution of (saltmen)Mn(N) **19**, olefin, and pyridine followed by warming to room temperature over 3-4 h would be ideal.[15] However, attempts to employ this strategy for the furanoid system failed. It was then thought that a small concentration of the active nitrogen-atom transfer reagent combined with a relatively high concentration of substrate would be advantageous. This would keep the relative concentration of the reactive acylated nitrido low at all times. This system could be accomplished through the slow addition of the metal complex to a solution of the glycal, pyridine, and TFAA. This method, however, also failed. Control experiments suggested that neither advantitious acid resulting from the reaction of TFAA and a small amount of H_2O nor TFAA affected the glycal, even at room temperature over several hours.

We speculated that perhaps pyridine was acting as a ligand to the metal complex in addition to neutralizing any acid present. 2,6-Di-*tert*-butyl-4-methylpyridine **27**, a much more hindered base, was then employed. This procedure involved adding TFAA to a -78 °C mixture of glycal **26**, nitrido **19**, and pyridine **27** in CH_2Cl_2.followed by the gradual warming of this solution to rt over 4-5 h. After optimization, nitrogen transfer to

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[14] Yokoyama, M,; Ikuma, T.; Obara, N.; Togo, H. *J. Chem. Soc., Perkin Trans. 1*, **1990**, 3243.
[15] Du Bois, J.; Hong, J.; Carreira, E. M.; Day, M. W. *J. Am. Chem. Soc.* **1996**, *118*, 915.

a putative labile aziridine intermediate followed by hydrolysis under slightly acidic conditions yielded the resulting amino alcohol **28** in 80% yield (Figure 5).

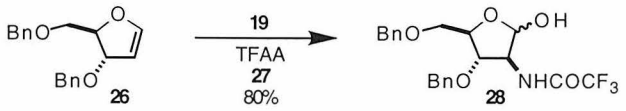


Figure 5. Formation of amino alcohol **28** from glycal **26**.

Further experimentation using less-hindered pyridines such as 2,6-lutidine never proved to be as successful. Furthermore, slow addition strategies using 2,6-di-*tert*-butyl-4-methylpyridine were also met with disappointment.

A minor product, the epimer of the 2 position, was also formed. ^{1}H NMR studies were inconclusive since lack of complete selectivity and anomerization of the alcohol led to four diastereomers. But after oxidation with pyridinium chlorochromate (PCC) in the presence of molecular sieves (96% yield), it was easily determined (^{1}H NMR) from the resulting lactone **29** that the major epimer at the 2 position was obtained in a 10:1 ratio (Figure 6).

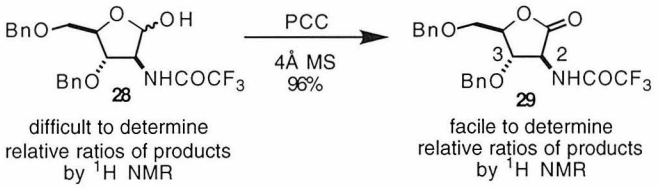


Figure 6. Oxidation of amino alcohol **26** to lactone **29**.

The diastereoselectivity is easily rationalized by sterics. The reactive metal imido species would favorably add to the side of the glycal opposite the 3-substituent. This would later be shown to be consistent in all systems studied.

Next, another glycal was sought in order to assay the generality of this method. We hoped to choose a class of substrates in which a variety of typical saccharide

protecting groups could be shown to survive the reaction conditions. Noting that Freudenberg, Wolf, Nicolaou and Ireland, in separate publications, had synthesized allylic alcohol **30** from d-mannitol,[16,17,18] it seemed reasonable to add a suitable silyl protecting group (Figure 9). This simple process would give easy access to **30**, which was then allowed to react with di-*tert*-butyldiphenylsilylchloride in DMF in the presence of imidazole to afford the silyl ether **31** in 87% yield (Figure 7).

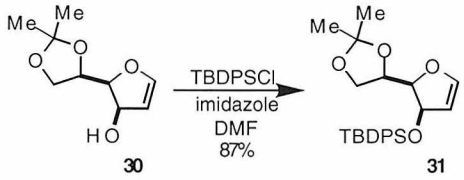
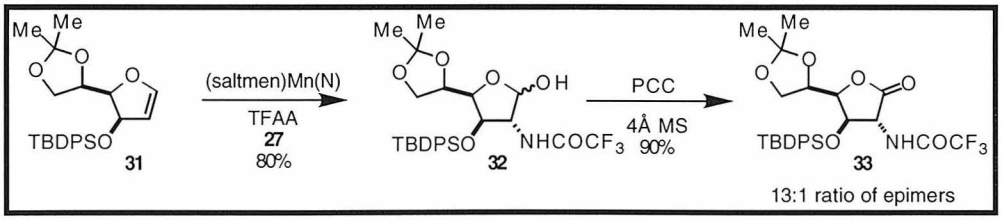


Figure 7. Formation of glycal **31**.

This substrate turned out to work as well as the previous glycal and the resulting amino alcohol **32** was obtained in 80% yield under identical conditions. Oxidation of **32** by PCC (87% yield) gives lactone **33**, which was found to have a diastereoselectivity of 13:1 (Scheme 5). Thus is was demonstrated that silyl groups, ketals, and benzyl protecting groups can all undergo the transformation.

Scheme 5.



The stereochemistry of the furan-derived amino alcohol **32** was further confirmed by conversion to the corresponding glucose structure **34** following a procedure described

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16 Freudenberg, K.; Wolf, A. *Ber.* **1927**, *60*, 232.
17 Hwang, C. K.; Li, W. S.; Nicolaou, K. C. *Tetrahedron Lett.* **1984**, *25*, 2295.
18 Ireland, R. E.; Thaisrivongs, S.; Vanier, N.; Wilcox, C. S. *J. Org. Chem.* **1980**, *45*, 48. Ireland, R. E.; Wilcox, C. S.; Thaisrivongs, S. *J. Org. Chem.* **1978**, *43*, 786.

by Fitzsimmons and Leblanc involving the addition of acetyl chloride in methanol followed by acetic anhydride in pyridine.[19] Subsequent nOe experiments were consistent with the assigned structures of **28** and **32** (Figure 8).

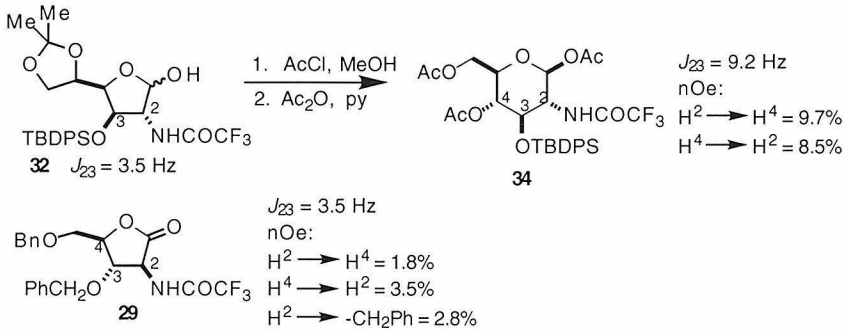

Figure 8. NOe experiments and coupling constants confirm proposed stereochemistry.

It is interesting to note that part of the workup includes the addition of 80% aq. acetic acid. Thin-layer chromatography (TLC) analysis of the reaction mixture indicates that a product of relatively high R_f value slowly decomposes to the desired amino alcohol **32**. The addition of the acetic acid greatly accelerates this transformation, allowing optimal yield of the 2-amino saccharide. In fact, TLC before the addition of acetic acid qualitatively suggests that the major product is the higher spot. Analysis of a separate reaction without the addition of acetic acid immediately followed by purification indicated that this spot corresponds to oxazoline **34**, obtained in 65% yield, which was isolated along with amino alcohol **31** in 10% yield (Figure 9).

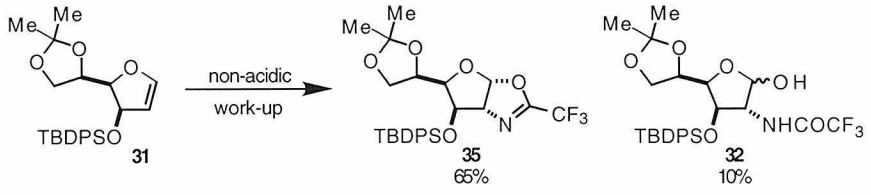

Figure 9. Non-acidic work-up allowed for the isolation of oxazoline **35**.

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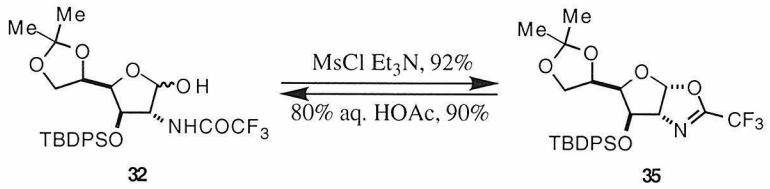
[19] Leblanc, Y.; Fitzsimmons, B. J.; Springer, J. P.; Rokach, J. *J. Am. Chem. Soc.* **1989**, *111*, 2995.

In addition, the isolated oxazoline **35**, when treated with 80% aq. acetic acid, is converted into the amino alcohol **32** in 92% yield (Figure 12). Furthermore, amino alcohol **32**, when treated with MsCl and Et_3N, reforms oxazoline **35** in 90% yield.



32 35

Figure 10. Interconversion of amino alcohol **32** and oxazoline **35**.

The formation of this type of oxazoline is well-precedented.[20] Similar oxazolines, in fact, have been used to couple in other monosaccharides to form disaccharides (Figure 11).[21]

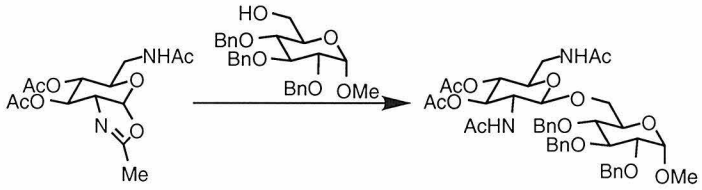


Figure 11. The use of oxazolines to couple in sugars.

Simultaneous work within the Carreira group by Du Bois showed that glycals in general are good substrates. Nine pyranoses were shown to be good nitrogen-transfer substrates, although yields and selectivity were typically slightly lower than in the furanose systems. As previously mentioned, all resulting amino alcohols **36** exhibited the 2,3-*trans* stereochemistry in the major product (Figure 12).

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[20] Pochet, S.; Kansal, V.; Destouesse, F.; Sarfati, S. R. *Tetrahedron Lett.* **1990**, *31*, 6021. Nakabayashi, S.; Warren, C. D.; Jeanloz, R. W. *Carbohydrate Research* **1988**, *174*, 279.

[21] Boldt, P. -C.; Schumacher-Wandersleb, M. H. M. G.; Peter, M. G. *Tetrahedron Lett.* **1990,** *32*, 1413.

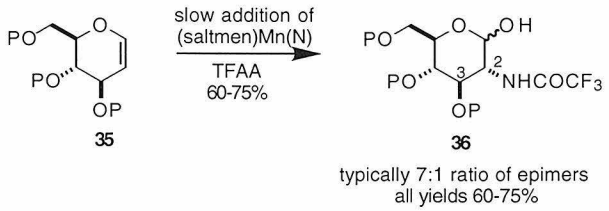

Figure 12. Nitrogen transfer to pyranose glycals.

Optimal conditions for the pyranoses were not identical to those of the furanoses. Instead, these reactions were optimized when TFAA was slowly added (over 8 h) to a solution of the glycal and (saltmen)Mn(N) in CH_2Cl_2. Under identical conditions the pyranoid glycals gave dramatically decreased yields compared to the furanoid glycals. Concurrent development suggested that systems that are more easily oxidized should be run with conditions similar to that of the furanoid glycals, whereas systems not as easily oxidized should be run with conditions similar to that of the pyranoid glycals. Franck[22] confirmed the expectations that similar furans have higher HOMO's than their pyranoid counterparts, as calculated at the AM1 level with the SPARTAN program package.[23]

In summary, two furanoid glycals **26** and **31** have been prepared and have shown to transfer nitrogen efficiently to form corresponding amino alcohols **28** and **31**. In one example, oxazoline **35** could be isolated and was shown to interconvert with the corresponding amino alcohol **32** under appropriate conditions (Scheme 6).

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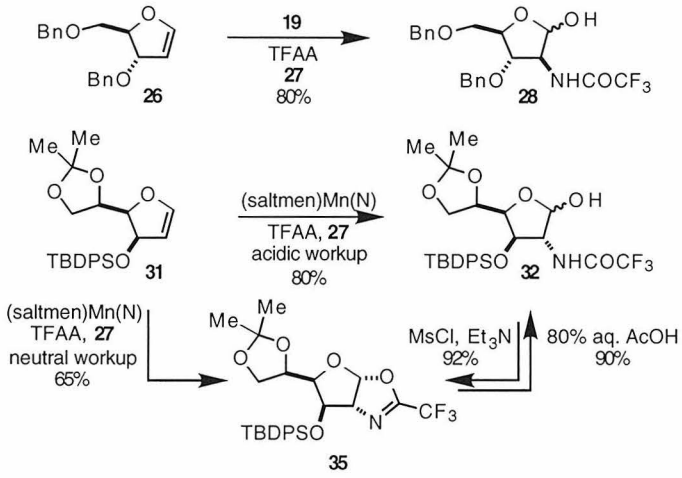
[22] Capozzi, G.; Dios, A.; Franck, R. W.; Geer, A.; Marzabadi, C.; Menichetti, S.; Nativi, C.; Tamarez, M. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 777.

[23] SPARTAN is an integrated software package for quantum chemical calculations produced by Wavefunction, Inc., Irvine, CA.

Scheme 6.



This system offers many advantages that previous nitrogen-atom transfer methodologies cannot. First of all, it allows the substrate to be the limiting reagent. This point is especially crucial when considering the transfer of nitrogen to more elaborate non-commercially available substrates. Secondly, the resulting amino alcohols are conveniently protected as the corresponding trifluoroacetamides which have been shown to be labile under mild conditions.[24] In addition, later studies with manganese nitrido complexes have been shown to transfer nitrogen with different protecting groups. With this system relatively well-developed, the enantioselective transfer of nitrogen was sought.

The enantioselective transfer of nitrogen.

With the knowledge of salen-derived manganese nitrides in hand, it seemed reasonable that chiral ligands, such as those presented by Jacobsen,[25] could chelate to manganese and assist in the transfer of nitrogen in an asymmetric fashion.

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[24] Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, John Wiley & Sons Ltd.: New York, 1991, 2nd Ed., p. 253.
[25] Li, Z.; Conser, K. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1993**, *115*, 5326.

It was difficult to pick a chiral ligand. On one hand, a known ligand that has been proven in many instances was desired. On the other hand, however, perhaps new systems with novel reactivity could be revealed.

With the knowledge of salen-derived ligands and that of 4,5-(dihydrooxazoles),[26] it seemed reasonable that the two ideas could be combined. This ligand must be easily prepared and robust, and offer the versatility necessary. 4,5-Dihydro-2-(2'-hydroxyphenyl)oxazoles **21** seemed to fit every requirement (Figure 13). Bolm has described the synthesis of a number of optically active 4,5-dihydro-2-(2'-hydroxyphenyl)oxazoles which are prepared from 2-cyanophenol and the appropriate chiral amino alcohol (both commercially available).[27] The rigorousness of the reaction conditions necessary to form these oxazolines (132 °C for 24 h) demonstrates their sturdiness. It seemed reasonable that a manganese nitrido complex with two of these ligands could be formed. It was also discovered that the phenyl ring could be easily fine-tuned to fit the desired reactivity.[28]

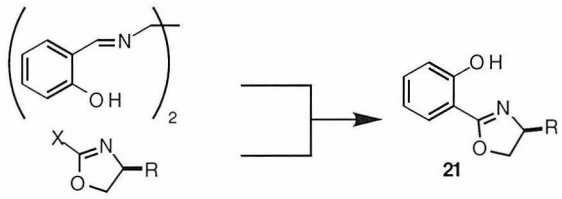

Figure 13. Combination of ligands to form 4,5-dihydro-2-(2'-hydroxyphenyl)oxazoles.

The synthesis of **21** involves heating a solution of 2-cyanophenol **22**, the appropriate chiral amino alcohol **23** (normally obtained from the reduction of an amino acid[29]) and a catalytic amount of zinc(II) chloride ($ZnCl_2$) (Figure 14).[16] Microwave

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[26] For a brief review of bis(4,5-dihydrooxazolyl) derivatives in asymmetric catalysis, see: Bolm, C. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 542.

[27] (a) Bolm, C.; Weickhardt, K.; Zehnder, M.; Glasmacher, D. *Helv. Chem. Acta* **1991**, *74*, 717. (b) Bolm, C.; Weickhardt, K.; Zehnder, M.; Ranff, T. *Chem. Ber.* **1991**, *124*, 1173.

[28] Adachi, M.; Matsumara, H.; Sugasawa, T. Eur. Patent 0 257 583, 1988; *Chem. Abstr.* **1988**, *109*, 73156j

[29] A number of chiral amino alcohols can be obtained from Aldrich Chemical Co. In addition, these can be obtained by the reduction of a amino acid, see: (a) Giannis, A.; Sandhoff, K. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 218. (b) Dickman, D. A.; Myers, A. I.; Smith, G. A.; Gawley, R. E. *Org. Syn. Coll. Vol.*

irradiation was recently introduced as a substitute for heating, which drastically reduces the required time and temperature for the reaction to go to completion.[30] This latter method, however, is much less explored.

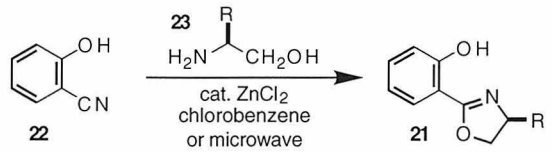

Figure 14. Bolm's method to form oxazoline **21**.

These oxazolines have been shown to form metal complexes with a variety of transition metals including titanium, zirconium, vanadium, copper, zinc, nickel, cobalt, and iron.[31] In addition, the metal complex would remain analogous to the (saltmen)Mn(N) complex in that the ligand system would be dianionic. Also, like the salen-derived ligands, both systems would incorporate the coordination to the metal via two phenolate and two imine donors. Presumably, the desired chiral manganese nitrido complexes could be prepared in a manner analogous to that of (saltmen)Mn(N) and transfer nitrogen in high enantioselectivity and yield.

Results.

Molecular models suggested that 4,5-dihydro-2-(2'-hydroxyphenyl)oxazole ligands derived from (S)-(+)-valinol and (S)-(+)-phenylglycinol would be optimal, due to the α-branch sidechain not seen in most other commerically-available chiral amino alcohols. Following the protocol described by Carreira[32], the desired oxazoline manganese nitrido complexes **24a** and **24b** could not be formed from the corresponding oxazoles **25a** and **25b** (Figure 15). It was surmised that perhaps the reaction conditions,

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VII, **1990**, 530. (c) Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1992**, *33*, 5517.
[30] Clarke, D. S.; Wood, R. *Synthetic Communications* **1996**, *26*, 1335.
[31] Cozzi, P. G.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *Inorg. Chem.* **1995**, *34*, 2921.
[32] Du Bois, J.; Hong, J.; Carreira, E. M.; Day, M. W. *J. Am. Chem. Soc.* **1996**, *118*, 915.

which included Chlorox bleach and concentrated ammonium hydroxide, were too harsh for the metal complex.

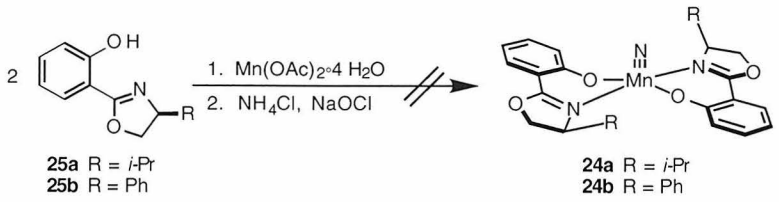

Figure 15. Formation of the desired metal complexes **24a** and **24b** did not form under conditions described by Carreira.

It had been discovered earlier that a milder method to generate the nitrido complex was available.[33] After extensive optimization, it was determined that the nitridos **24a** and **24b** were best formed when 5 equiv of NBS was added to a CH_2Cl_2 solution of $Mn(OAc)_2 \bullet 4H_2O$and NH_3 at -42 °C (Figure 16). A color change from dark green to dark purple occurred immediately upon addition of liquid ammonia, suggesting the formation of the purple nitrides **24a** and **24b**. An aqueous quench followed by filtration through celite and basic alumima followed by concentration of the organic layer afforded the desired nitrido complex in about 55% yield from either ligand **25a** or **25b** as a brownish-purple foam. The complexes could then be crystallized by vapor diffusion of hexanes into a diethyl ether solution of the complex to afford X-ray quality single crystals.

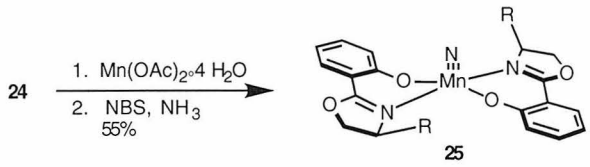

Figure 16. Formation of nitrido 25 using milder conditions.

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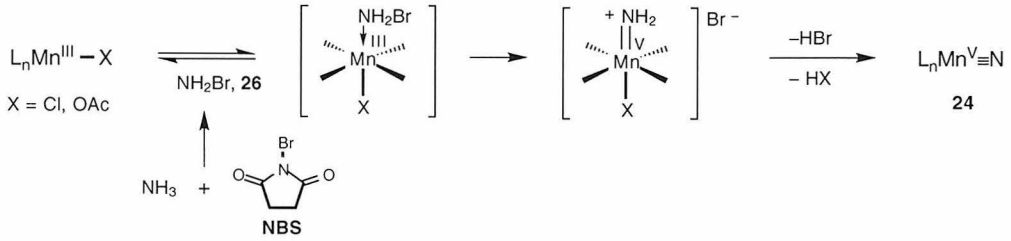
[33] Du Bois, J.; Tomooka, C. S.; Hong, J.; Carreira, E. M.; Day, M. W. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1645.

The mechanism of this reaction presumably includes the formation of bromoamine **26**, followed by coordination and deprotonation (Scheme 7). The ability to form analogous metal nitrido complexes with other halogenating agents supports this claim.[34]

Scheme 7.



We considered a number of potential sulfides as test substrates. We sought an inexpensive, commercially available chemical. In addition, since it was anticipated that steric interactions would play a major role, it was deemed necessary for one substituent to be large, and the other to be small. In addition, a nonvolatile product whose enantiomeric excess (ee) could be accurately measured was desired. Also required was the ability to adjust the electronics of the substrate if necessary. Finally, a substrate of significant value was sought. After considerable deliberation, it was determined that methyl *p*-arylsulfides **27** were suitable candidates (Scheme 8).

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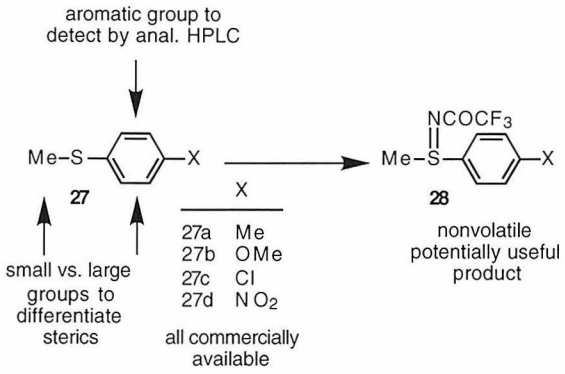
[34] In this reaction, it is conceivable that ammonia trichloride is formed. Although no accidents have occurred in our hands, it is strongly advised that appropriate protection be used.

Scheme 8.



Methyl is the smallest practical substituent available (thiols were not seriously considered since they readily react with anhydrides). *p*-Tolyl groups, meanwhile, are relatively large. Similar sulfilimines[35] have been shown not to be volatile, and it was anticipated that ee's could be determined by a UV detector in conjunction with an analytical HPLC, due to the chromophore of the aromatic ring. It was also noticed that the substituents of the aromatic portion of the substrate could easily be adjusted. For instance, *p*-methoxy, *p*-chloro, and *p*-nitro- analogs are all commercially available.

For the formation of amino alcohols, two optimal substrate-specific procedures exist. One, which works best with pyranoid glycals, involves the slow addition (over eight hours) of a CH_2Cl_2 solution of (saltmen)Mn(N) to a CH_2Cl_2 solution of substrate and distilled TFAA (5 equiv) (method A). The other procedure, which works best with furanoid glycals, involves adding all reagents at -78 °C then gradually warming the solution to room temperature over about 4-5 h (method B). Both methods were tested, as were both nitrido complexes **24a** and **24b**. Method B clearly gave superior ee's. In addition, it was discovered that use of the phenylglycinol nitride **24b** gave slightly higher ee's than **24a** (Table 2).

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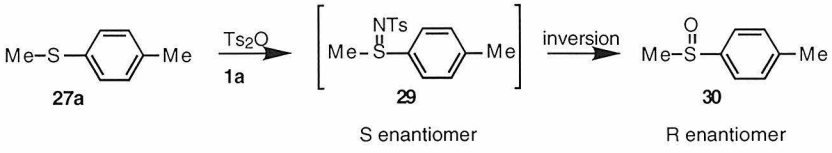
[35] Abou-Gharbia, M.; Ketcha, D. M.; Zacharias, D. E.; Swern, D. *J. Org. Chem.* **1985**, *50*, 2224.

Table 2. Enantiomeric excesses of both manganese nitrido complexes under previously described conditions.

	method	ee (%)
24a	A	55
24b	A	50
24a	**B**	**75**
24b	B	72

The absolute stereochemistry of the resulting sulfilimine was then determined. However, these sulfilimines had never been made enantioselectively, whereas the corresponding sulfoxides have been thoroughly characterized. Fortunately, it was discovered by Komatsu that salen-derived manganese nitrido complexes could be acylated by toluene sulfonic anhydride (Ts_2O).[36] Cram has showed that, in the presence of acid or base, N-tosyl sulfilimines will hydrolyze stereoselectively to the sulfoxide.[37] N-Tosyl-S-methyl-S-*p*-tolylsulfilimine **29** was presumably formed transiently, which hydrolyzed *in situ*, allowing the corresponding sulfoxide **30** to be isolated (Scheme 9). By comparing rotations with literature values, it was determined that the sulfoxide **27a** was obtained in 36% ee. More importantly, however, it was determined that the major sulfoxide obtained was the (R) enantiomer.[38] By analogy, therefore, it can be determined that the sulfilimine formed **29** was the (S) enantiomer. This designation of stereochemistry is assumed to be general and is used for all substrates.

Scheme 9.



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[36] Ando, T.; Minakata, S.; Ryu, I.; Komatsu, M. *Tetrahedron Lett.* **1998**, *39*, 309.
[37] Day, J.; Cram, D. J. *J. Am. Chem. Soc.* **1965**, *87*, 4398.
[38] Mislow, K.; Axelrod, M.; Rayner, D. R.; Gotthardt, H.; Coyne, L. M.; Hammond, G. S. *J. Am. Chem. Soc.* **1965**, *87*, 4958.

It was then thought that perhaps other parameters, such as the number of equivalents of reagents or the solvent would have a substantial effect. Running the reaction with a variable amount of **24** caused a very minimal change in ee or yield. All subsequent reactions were then run with 1.0 equiv. Solvent effects were then investigated. It was postulated that coordinating solvents could substitute trifluoroacetate as a ligand and, therefore, effect the geometry, reactivity, and electronics of the resulting imido complex. When different solvents were used, whether more polar (THF, acetonitrile, 1.0 equiv of pyridine in CH_2Cl_2) or more nonpolar (toluene), ee's were considerably lower, although yields were still high (Table 3).

Table 3. Assay of enantiomeric excesses in various solvents.

27a **24b** **28a**

Solvent	ee (%)
CH_2Cl_2	75
toluene	38
tetrahydrofuran	16
acetonitrile	66
pyridine (1.0 eq in CH_2Cl_2)	52

We considered at this point variation of the choice of ligand. Since oxazoline ligands **25** held considerable promise, minimal adjustments such as slight variations of the aromatic ring were desired. We sought analogs of 25 which were derived from commercially available starting materials or were otherwise easily accessible by our route.

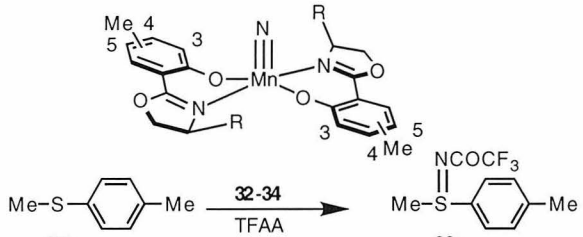
Forunately, a patent describes the ortho-cyanation of phenols **29** (Scheme 10).[39] This allows easy access to various 2-cyanophenols **30**. This procedure is not perfect, however, as functional groups that react with $AlCl_3$, BCl_3, and/or methyl thiocyanate (such as methoxy groups) or are electron-withdrawing prevent formation of the desired 2-

[39] Kabushiki, S. S.; Makoto, A.; Hiromu, M.; Tsutomu, S. European Patent 0 257 583, 1988; *Chem. Abstr.* **1988**, *109*, 73160.

cyanophenol. In addition, functional groups incompatible with strongly acidic or basic conditions are not tolerated under the reaction conditions. On the other hand, this reaction is regiospecific, owing to the proposed imine intermediate **31**, which has been isolated by addition of a weak base ($NaHCO_3$) instead of NaOH and HCl.

Scheme 10.

Noting that starting materials *o*-, *m*-, and *p*-cresol are inexpensive and readily available, the ortho-cyanation reaction formed the desired cyanophenols, which were then converted to the corresponding oxazolines and nitrido complexes. These were then assayed for enantioselectivity (Table 4).



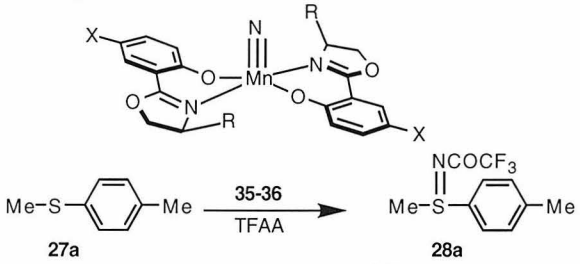
	pos. of methyl	R	ee (%) of **28a**
32a	3	*i*-Pr	59
32b	3	Ph	47
33a	4	*i*-Pr	66
33b	4	Ph	70
34a	5	*i*-Pr	54
34b	**5**	**Ph**	**80**

Table 4. Enantiomeric excesses using monomethylated nitrido complexes.

Enantiomeric excesses using the corresponding nitrido complexes for the most part were disappointingly lower than those of the parent complexes. One result, however, looked promising. Using nitrido **34b**, an 80% ee was determined.

At this point, it seemed necessary to persue this lead. Although the patent described only the syntheses of mono- and di-methylated 2-cyanophenols as well as mono- and dichloro-2-cyanophenols, there was no reason to believe that other alkyl, or even aromatic groups could not be tolerated. It was decided that perhaps the size of the group at the 5 position plays a key role in the enantioselective process. Using commercially-available 4-*tert*-butylphenol and 4-phenylphenol as starting materials, the corresponding nitridos were prepared, and ee's were assayed in their subsequent N-transfer reactions (Table 5). Surprisingly, ee's were somewhat lower. Consistent with previous results, assays using the valinol-derived nitrido complexes remained about 5% lower in ee than the corresponding phenylglycinol-derived nitridos.

Table 5. Ligands containing bulkier substituents at the 5 position were tested.



	X	R	ee (%) of **28a**
35a	*t*-Bu	*i*-Pr	59
35b	Ph	Ph	47
36a	*t*-Bu	*i*-Pr	66
36b	Ph	Ph	70
34b	**Me**	**Ph**	**80**

The Pfaltz group has used a similar class of ligands to enantioselectively hydrogenate an imine.[40] It was determined that the best ee's and yields were obtained using the ligand derived from 2,4-dimethylphenol. Once again, the appropriate phenol was commercially available and the corresponding nitrido complex was formed. In this case, the phenylglycinol-derived complex resulted in a 91% ee - by far the best to date (Table 6). In addition, the yield (95%) was equally as impressive.

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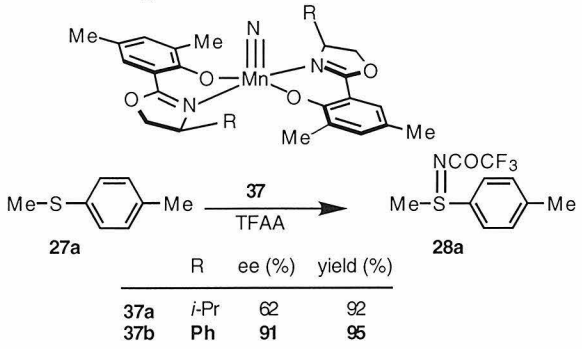
[40] Koch, G. Ph.D. Thesis, Institut fur Organische Chemie, Universitat Basel, 1996.

Table 6. Enantiomeric excesses greater than 90% were realized for the first time.



	R	ee (%)	yield (%)
37a	*i*-Pr	62	92
37b	**Ph**	**91**	**95**

We next considered the generality of the transformation for more highly-substituted sulfides. Ethyl phenyl sulfide **38** was arbitrarily chosen. Reactions run under identical conditions to that of the initial substrate resulted in the desired sulfilimine **39** in 82% ee, but when run at -78 °C for 36 h, the ee increased to 90% (Figure 17).

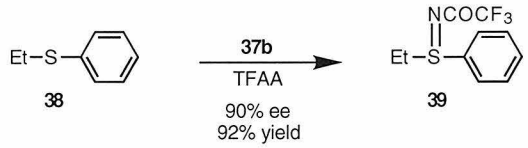
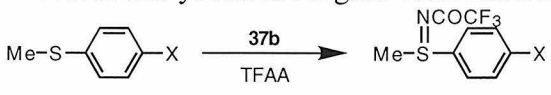


Figure 17. Ethyl phenylsulfide undergoes the oxidation reaction with high ee and yield.

Electronics of the sulfide were then investigated. It seemed reasonable to persue the role of the π stacking interactions. Methyl *p*-methoxyphenylsulfilimine was obtained in 92% ee, whereas the *p*-chloro and *p*-nitro derivatives were obtained in 83% and 33%, ee respectively (Table 7). The yields of all substrates ranged from good to excellent. The ability to transfer nitrogen to methyl aryl sulfides with either eletron-rich or electron-poor substitutents suggest that this type of reaction is general.

Table 7. Enantiomeric excesses and yields are higher with electron-rich sulfides.



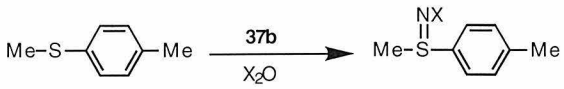
27 **28**

	X	ee (%)	yield (%)
28a	Me	91	95
28b	MeO	92	95
28c	Cl	83	93
28d	NO_2	33	80

Given that tosyl anhydride could activate the nitrido complexes, it seemed reasonable to activate nitrido **37b** with other activating agents. Electrophiles such as methyl triflate, ethyl chloroformate, methyl triflate, acetic anhydride, and chloroacetic anhydride all failed to activate the nitrido. In fact, in one case it was shown that 80% of the nitrido could be recovered. When more reactive anhydrides such as dichloroacetic anhydride and trichloroacetic anhydride were used, however, product formation of sulfilimines **40** and **41** occurred. Although ee's were not as high as with TFAA, the products were still obtained in good ee and in excellent yield (Table 8). In addition, it was interesting to note that the ee's go up with the smaller acyl group on the nitrogen. Electronegativity data is inconsistent with an an electronic argument.

Table 8. Studies showed that enantiomeric excesses increased with decreasing size of the

acyl group X.



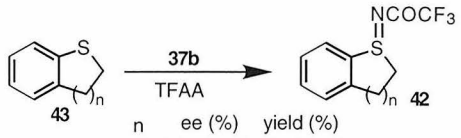
27a **28a, 40, 41**

	X	yield (%)	ee (%)	size	electronegativity
28a	CF_3	95	91	smallest	most electronegative
40	$CHCl_2$	91	86		least electronegative
41	CCl_3	90	83	largest	

We next considered cyclic sulfides. Although still obtained in excellent yields, the resulting sulfilimines **42a** and **42b** of 2,3-dihydrobenzothiophene **43a** and

thiochromane **43b** gave substantially lower ee's (46% and 50%, respectively) (Table 9).[41] It was thought that perhaps this inability of the aromatic ring to freely rotate was directly responsible for these lower ee's. We speculated that the lack of rotation of the aromatic group makes the aromatic group effectively much smaller.

Table 9. Although enantiomeric excesses were low for cyclic sulfilimines, yields remained high.



	n	ee (%)	yield (%)
42a	1	46	87
42b	2	50	91

A separate class of substrate, dialkyl sulfides, was then investigated. Systems most similar to those that worked well were sought. Specifically, methyl isopropylsulfide **44a** and cyclohexyl methylsulfide **44b** were run under identical conditions as before. Although ee's could not be obtained by HPLC with a UV detector, it is interesting to note that these systems also gave good yields of the isopropyl **45a** and cyclohexyl **45b** sulfilimines, 81% and 75%, respectively (Table 9).

Table 9. Dialkyl sulfides also undergo nitrogen transfer in good yields.

	R	Yield (%)
45a	*i*-Pr	84
45b	cyclohexyl	79

Having demonstrated that the oxazoline-derived nitrido efficiently transfers nitrogen to sulfides, we sought to optimize the conditions. The first variation involves

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[41] For the synthesis of 2,3-dihydrobenzothiophene, see: Fricke, R.; Spilker, G. *Ber.* **1925**, *58*, 1589. For the synthesis of thiochromane, see: Truce, W. E.; Milionis, J. P. *J. Am. Chem. Soc.* **1952**, *74*, 974.

looking at the concentration effect. The formation of aza-bridged products of manganese nitrides has been reported (Figure 18).[42,43] The dilution of solution, therefore, would disfavor any interaction between acylated nitrido complexes. Typically, the reaction was performed at 0.05 M. However, reactions were then run at up to four times as concentrated and twice as dilute with no significant change in either yield or ee.

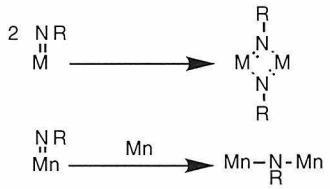

Figure 18. Transition metals have been known to undergo aza-bridging.

Temperature effects were also investigated. To this end, three experiments were conducted. The first involved the warming of the reaction at a faster rate (over about 30 min). This resulted in a slightly lower ee (88%). The addition of TFAA at the somewhat warmer temperature of -53 °C resulted in an even lower ee (83%) not surprisingly. Finally, when the reaction was kept at -78 °C for 3 h, or even 36 h, ee's failed to improve.

Stoichiometry could also play a key role in the asymmetric induction of sulfilimines. We wondered if the Lewis acidity of TFAA plays an important role. Specifically, TFAA could coordinate to a number of electron rich sites, including the imido nitrogen, the amide oxygen, or even part of the ligand itself. The standard protocol involves the addition of 5 equiv of TFAA. Variations ranging from 1.2 equiv to 20 equiv of TFAA were employed. However, no increase in ee was observed and, in fact, a lower ee and lower yield was observed when using 1.2 equiv. It is also conceivable that TFA plays an important role. Although TFAA is purified before use, advantitious water would quickly form TFA. To this end, 1.0 equiv of TFA was deliberately added to the reaction

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[42] Odom, A. L.; Cummins, C. C. *Organometallics,* **1996**, *15*, 898.

[43] μ–Oxo bridged Mn dimers have been characterized in reactions with PhI=O, see: (a) Smegal, J. A.; Schardt, B. C.; Hill, C. L. *J. Am. Chem. Soc.* **1983**, *105*, 3510. (b) Smegal, J. A.; Hill, C. L. *J. Am. Chem. Soc.* **1983**, *105*, 3515.

mixture just before the addition of TFAA. Once again, however, no change in yield or ee was observed. This result suggests that this reaction is not acid-sensitive, which is encouraging, but gave very little insight on the mechanism of this reaction. We also investigated the use of a basic amine additive Many common bases, however, could also act as ligands. To help avoid this problem, a hindered base, 2,6-di-*tert*-butyl-4-methylpyridine was employed. When 1.0 equiv of the base was added in otherwise identical conditions, a lower ee was obtained. This unexpected result suggests that either acid is catalyzing an enantioselective reaction, or that 2,6-di-*tert*-butyl-4-methylpyridine is, in fact, acting as a ligand in the coordination of the metal.

It appears that optimal conditions for nitrogen transfer to sulfides include the addition of 5 equiv of TFAA to a precooled solution of 1.0 equiv of the desired sulfide, and 1.0 equiv of the nitrido derived from 2,4-dimethylphenol in a solution of dichloromethane. Allowing the reaction to warm to rt over 4-5 h followed by work-up and purification allows formation of the sulfilimine in optimal yield and ee. This process has many advantages over other metal-mediated nitrogen transfer processes. One is the ability to add only one equivalent of substrate to obtain optimal yields. Most other processes[44,45,46,47,48]require anything from 5.0 equiv to a gross excess of substrate, using the nitogen source as the limiting reagent. This is not a problem when the starting materials are inexpensive and readily available, but this could present an enormous problem if the substrate is valuable. In addition, this methodology offers the advantage of requiring only one equivalent of manganese nitrido **37b**. Also interesting to note is the amount of variables under which this system can tolerate and still work optimally. For

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[44] Groves' method uses 11 equiv, see: Groves, J. T.; Takahashi, T. *J. Am. Chem. Soc.* **1983**, *105*, 2074.
[45] Mansuy's method uses 20-100 equiv, see: Mansuy, D.; Mahy, J-. P.; Dureault, A.; Bedi, G.; Battioni, P. *J. Chem. Soc. Chem. Commun.* **1984**, 1161. Mahy, J-. P.; Bedi, G.; Battioni, P.; Mansuy, D. *J. Chem. Soc. Perkin Trans. II* **1988**, 1517.
[46] Evans' method uses 5 equiv, see: Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 2742. Evans, D. A.,; Faul, M. M.; Bilodeau, M. T.; Anderson, B. A.; Barnes, D. M. *J. Am. Chem. Soc.* **1993**, *115*, 5328.
[47] Katsuki's method uses at least 10 equiv, see: Nishikori, H.; Katsuki, T. *Tetrahedron Lett.* **1996**, *37*, 9245. Noda, K.; Hosoya, N.; Irie, R.; Ito, Y.; Katuski, T. *Synlett* **1993**, 469.
[48] Pérez, P. J.; Brookhart, M.; Templeton, J. L. *Organometallics*, **1993**, *12*, 261.

instance, variation in the amount of any reagent or solvent, or the addition of acid has virtually no effect. Finally, the protecting group can be varied. Specifically, three protecting groups have been shown not only to be compatible with this system, but also to undergo the desired reaction in high yield and enantiomeric excess.

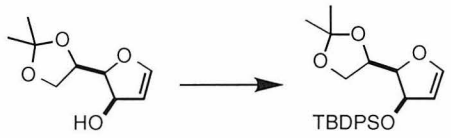
Experimental.

General methods. All reagents were commercially obtained and purified prior to use. Air and moisture-sensitive liquids and solutions were transferred via syringe. Organic solutions were concentrated by rotary evaporation below 35 °C using a water aspirator. Dichloromethane was distilled from calcium hydride prior to use. Trifluoroacetic anhydride was distilled at 39.5 °C, 1 atm prior to use. Chromatographic purification of products was accomplished using forced-flow chromatography on Baker 7024–R silica gel or by Chromatotron. Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60F plates (230-400 mesh). Visualization of the developed chromatogram was performed by either fluorescence quenching, or by staining with aqueous ceric ammonium molybdate (CAM), aqueous potassium permanganate, or ethanolic *p*-anisaldehyde.

NMR spectra were recorded on either a Delta 400 operating at 400 and 100 MHz or a General Electric 300 operating at 300 and 75 MHz, for ^{1}H and ^{13}C, respectively (as indicated). Spectra are referenced internally to residual protio solvent signals. Data for ^{1}H are reported as follows: chemical shift (d ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet), integration, and coupling constant (Hz). Data for ^{13}C are reported in terms of chemical shift. Infrared spectra were recorded on a Perkin–Elmer Paragon 1000 with samples prepared as either thin films on NaCl salt plates or as a KBr pellet (as indicated) and reported in cm^{-1}. Combustion analysis was performed by the analytical laboratory at the California Institute of Technology. High resolution mass spectra were obtained from the UC Irvine Mass Spectral facility. X–ray crystal structures were solved at the Beckman Institute Center for X–ray Crystallography.

25 26

Glycal 26. A solution of **25** (4.7 mmol, 1.0 equiv), triethylamine (6.6 mL, 10 equiv), and MsCl (0.55 mL, 1.50 equiv) in 60 mL of CH_2Cl_2 was stirred under reflux conditions for 12 h. The reaction mixture was allowed to cool to room temperature and was then poured into 5% aq. $NaHCO_3$ (100 mL). The aqueous layer was separated and extracted with diethyl ether (3 x 20 mL), and the combined organic extracts were washed with brine (20 mL) and dried (Na_2SO_4). Concentration of the filtrate under reduced pressure afforded a yellow residue, which was purified by chromatography on silica gel and concentrated to afford **26** as a colorless syrup (54%): TLC R_f = 0.30 (10:1 Hexanes/EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ 7.39-7.27 (m, 10H), 6.59 (d, 1H, J = 3.0 Hz), 5.17 (t, 1H, J = 2.4 Hz), 4.64 (m, 2H), 4.58 (d, 2H, J = 4.5 Hz), 4.52 (d, 2H, J = 0.6 Hz), 3.56-3.39 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 138.5, 138.1, 128.7, 128.6, 128.1, 128.0, 127.9, 127.7, 100.8, 85.0, 82.9, 73.6, 70.1, 69.8 ppm; IR (thin film) ν 1612, 1454, 1364, 1147, 1074, 734, 696 cm^{-1}; HRMS (FAB^+) calcd for $C_{19}H_{20}O_3$ 297.1490, found 297.1485 (MH^+).



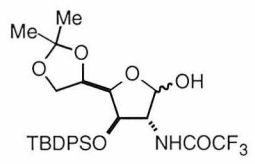
30 31

Glycal 31. A solution of **30** (4.2 mmol, 1.0 equiv), imidazole (9.2 mmol, 2.2 equiv), and TBDPSCl (5.0 mmol, 1.2 equiv) in DMF (20 mL) was stirred for 8 h. The solution was then poured into 5% $NaHCO_3$ (40 mL) and diethyl ether (20 mL). The aqueous layer was separated and extracted with diethyl ether (3 x 20 mL), and the combined organic extracts were washed with brine (2 x 20 mL) and dried (Na_2SO_4). Concentration of the filtrate under reduced pressure afforded a pale yellow residue, which was purified by chromatography on silica gel and concentrated to afford **31** as a colorless syrup (1.55 g,

87%): TLC R_f = 0.35 (20:1 Hexanes/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78-7.70 (m, 4H), 7.49-7.40 (m, 6H), 6.50 (d, 1H, *J* = 2.7 Hz), 5.01 (d, 1H, *J* = 6.9 Hz), 4.74-4.69 (m, 2H), 4.35 (t, 1H, *J* = 6.0 Hz), 4.34-4.12 (m, 2H), 1.54 (s, 3H), 1.44 (s, 3H), 1.11 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.2, 135.9, 135.8, 134.0, 133.1, 129.8, 129.7, 127.6, 127.5, 108.6, 104.6, 84.7, 74.1, 73.1, 66.0, 26.9, 26.5, 25.0, 19.1 ppm; IR (thin film) ν 1610, 1428, 1370, 1149, 1105, 1068, 738, 702 cm^{-1}; HRMS (FAB^+) calcd for $C_{25}H_{32}SiO_4$ 423.1991, found 423.1984 (MH^+).

General procedure for the preparation of 2–amino sugars from furanoid glycals: A solution of glycal (0.40 mmol), (saltmen)Mn(N) (0.80 mmol, 2.0 equiv), and 2,6–di–*tert*–butyl–4–methylpyridine (1.20 mmol, 3.0 equiv) in 4.0 mL of CH_2Cl_2 was cooled to -78 °C. Distilled TFAA (0.96 mmol, 2.4 equiv) was then added dropwise to the dark green solution. The solution was allowed to warm slowly from -78 °C to 23 °C over a 5–6 h period. During this time, the reaction mixture turned dark brown. Silica gel (200 mg), Celite (200 mg), and *n*-pentane (5 mL) were added along with 80% aq. AcOH (0.3 mL). The dark brown slurry was stirred at 23 °C for 5 h before being filtered through a 20 x 100 mm plug of silica gel using Et_2O (60 mL) as eluent. Addition of cyclohexane (10 mL) followed by concentration of the filtrate under reduced pressure afforded a yellow residue, which was purified by chromatography on silica gel.

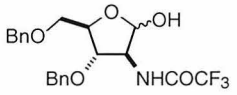
Physical data for 2–amino sugars.



32

Amino alcohol 32. TLC R_f = 0.38 (2:1 Hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.80-7.73 (m), 7.72-7.63 (m), 7.48-7.36 (m), 6.28 (d, -NH major, *J* = 2.4 Hz), 5.92 (d, -

NH minor, J = 3.3 Hz), 5.51 (dd, major, J = 4.5, 3.3 Hz), 5.09 (d, J = 10.5), 4.57 (t, J = 2.4 Hz), 4.50-4.44 (m), 4.34 (dd, major, J = 12.3, 6.6 Hz), 4.25-4.18 (m, major), 4.16-4.09 (m, major), 4.06-3.95 (m, major), 3.94-3.90 (m, major) 3.35 (br s, 1H), 3.33 (br s, 1H), 1.40 (s), 1.38 (s, major), 1.29 (s), 1.27 (s, major), 1.12 (s), 1.08 (s, major) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.0 (q, $J_{C\text{-}F}$ = 37.1 Hz), 136.3, 136.2, 136.0, 139.5, 132.6, 132.4, 132.1, 131.3, 130.6, 130.4, 130.3, 128.2, 128.0, 127.9, 127.8, 115.4 (q, $J_{C\text{-}F}$ = 285.9 Hz), 109.0, 101.1, 94.3, 83.4, 79.2, 76.7, 76.0, 75.8, 73.6, 73.2, 67.5, 66.1, 62.0, 60.1, 27.0, 26.9, 26.8, 26.3, 25.1, 25.0, 19.3, 15.3 ppm; IR (thin film) ν 3301, 1718, 1210, 1164, 1114, 1062, 702 cm^{-1}; HRMS (FAB$^+$) calcd for $C_{27}H_{34}SiNO_6F_3$ 553.2107, found 576.2016 (MNa^+).



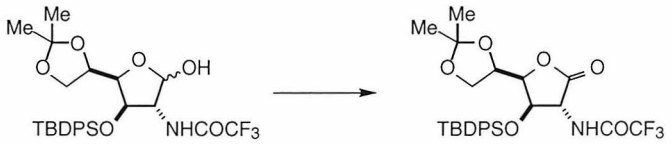
28

Amino alcohol 28. TLC R_f = 0.25 (2:1 Hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.16 (d, -NH minor, J = 7.9 Hz), 7.43-7.23 (m), 7.02 (d, -NH major, J = 7.8 Hz), 5.34 (dd, major, J = 7.5, 4.8 Hz), 5.26 (d, J = 12.0 Hz), 4.78-4.55 (m, major), 4.55-4.40 (m, major), 4.30-4.23 (m, major), 4.02 (t, major, J = 5.0 Hz), 3.97-3.82 (m), 3.64 (dd, major, J = 10.4, 2.8 Hz) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.9 (q, $J_{C\text{-}F}$ = 37.1 Hz), 137.2, 136.4, 136.2, 136.1, 128.8, 128.7, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 115.8 (q, $J_{C\text{-}F}$ = 286.0 Hz), 102.2, 96.2, 83.8, 83.2, 82.5, 82.1, 74.0, 73.8, 72.6, 72.2, 69.9, 68.7 ppm; IR (thin film) ν 3387, 3303, 1701, 1556, 1214, 1185, 1170, 699 cm^{-1}; Anal. Calcd for $C_{21}H_{22}NO_5F_3$: C, 59.29; H, 5.21; N, 3.29. Found: C, 59.49; H, 5.23; N, 3.20.

28 **29**

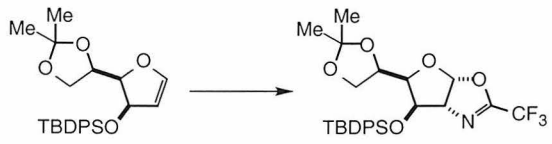
Lactone 29. A solution of **28** (0.20 mmol, 1.0 equiv), and PCC (1.00 mmol, 5.0 equiv) in 4 mL of CH_2Cl_2 was stirred at 23 °C for 1 h then filtered through a 20 mm x 20 mm

plug of silica gel using Et_2O (40 mL) as eluent. Concentration of the filtrate under reduced pressure afforded a pale yellow residue, which was purified by chromatography on silica gel and concentrated to afford **29** as a colorless syrup (96%): ^1H NMR (300 MHz, $CDCl_3$) δ 7.45-7.30 (6H, m), 7.40-7.30 (4H, m), 4.85 (1H, dd), 4.80-4.48 (6H, m), 4.15 (1H, m), 3.78 (2H, qd) ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.6, 157.1 (q, J = 38 Hz), 136.4, 136.2, 129.0, 128.8, 128.7, 128.5, 128.3, 128.2, 115.4 (q, J = 286 Hz), 82.7, 80.3, 74.4, 72.0, 69.3, 54.5 ppm; IR (thin film) ν 3306, 1718, 1212, 1165, 1114, 1063, 703 cm^{-1}; HRMS calcd for $C_{22}H_{20}F_3NO_5$ 423.1293, found 423.1262 (M^+).



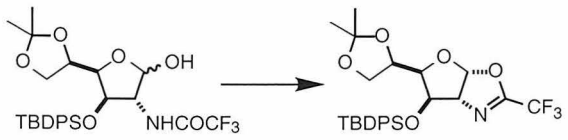
32 33

Lactone 33. A solution of **32** (0.10 mmol, 1.0 equiv), and PCC (0.50 mmol, 5.0 equiv) in 2 mL of CH_2Cl_2 was stirred at 23 °C for 5 h then filtered through a 20 mm x 20 mm plug of silica gel using Et_2O (40 mL) as eluent. Concentration of the filtrate under reduced pressure afforded a pale yellow residue, which was purified by chromatography on silica gel and concentrated to afford **33** as a colorless syrup (87%): ^1H NMR (300 MHz, $CDCl_3$) δ 7.79-7.69 (m, 4H), 7.56-7.41 (m, 6H), 6.47 (d, J=9.0 Hz, 1H), 5.69 (broad s, 1H), 4.75-4.69 (m, 2H), 4.67-4.61 (m, 1H), 4.26 (q, J=8.7, 6.0 Hz, 1H), 4.04 (q, J=8.9, 6.3 Hz, 1H), 3.77 (m, 1H), 1.51 (s, 3H), 1.43 (s, 3H), 1.39 (s, 3H), 1.27 (s, 3H), 1.13 (s, 9H), 1.06 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 156.9 (q, J=38.4 Hz, RR'CO), 136.0, 135.9, 135.8, 135.0, 133.3, 131.5, 130.8, 130.6, 128.7, 128.4, 128.1, 114.9 (q, J=285 Hz, -CF_3), 110.1, 82.6, 73.8, 73.7, 73.0, 67.0, 59.5, 26.9, 26.9, 25.5, 19.2; ^{19}F NMR (500 MHz) δ -75.3 (major), -76.2 (minor); IR (thin film) ν 3321, 1799, 1720, 1216, 1171, 1114, 1074, 703 cm^{-1}



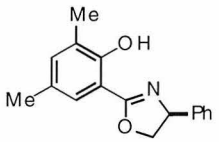
31 35

Oxazoline 35. A solution of glycal **31** (0.40 mmol), (saltmen)Mn(N) (0.80 mmol, 2.0 equiv), and 2,6–di–*tert*–butyl–4–methylpyridine (1.20 mmol, 3.0 equiv) in 4.0 mL of CH_2Cl_2 was cooled to -78 °C. Distilled TFAA (0.96 mmol, 2.4 equiv) was then added dropwise to the dark green solution. The solution was allowed to warm slowly from -78 °C to 23 °C over a 5–6 h period. During this time, the reaction mixture turned dark brown. Silica gel (200 mg), Celite (200 mg), and *n*-pentane (5 mL) were added. The dark brown slurry was stirred at 23 °C for 5 h before being filtered through a 20 x 100 mm plug of silica gel using Et_2O (60 mL) as eluent. Addition of cyclohexane (10 mL) followed by concentration of the filtrate under reduced pressure afforded a yellow residue, which was purified by chromatography on silica gel and concentrated to afford oxazoline **35** as a colorless syrup (65%), along with the ring-opened amino alcohol **32** (10%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82-7.73 (m, 4H), 7.50-7.40 (m, 6H), 6.30 (d, *J*=4.8 Hz, 1H), 4.70 (d, 1H, *J* = 2.7 Hz), 4.53 (qm, 1H, *J* = 6.0), 4.31 (ddm, 1H, *J* = 1.8 Hz) 4.23 (dd, 1H, *J* = 8.7, 6.3 Hz), 4.05 (dd, 1H, *J* = 8.6, 5.6 Hz), 3.71 (dd, 1H, *J* = 8.1, 2.7 Hz), 1.45 (s, 3H), 1.38 (s, 3H), 1.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3 (q, *J*=41 Hz), 136.1, 135.8, 133.6, 132.0, 130.3, 128.1, 127.9, 115.9 (q, *J* = 273 Hz), 109.5, 83.7, 77.7, 75.4, 71.9, 67.6, 29.8, 26.9, 26.8, 25.2, 19.4; IR (thin film) ν 1429, 1399, 1213, 1166, 1114, 1074, 932, 897, 850, 822, 740, 703, 612, 508 cm^{-1}; HRMS calcd for $C_{27}H_{33}F_3NO_5Si$ 536.2080, found 536.2082 (MH^+).

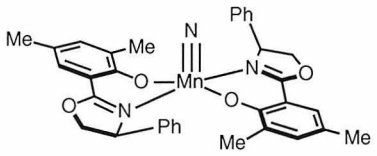


32 35

Oxazoline 35. A solution of **32** (0.05 mmol, 1.0 equiv), triethylamine (0.50 mmol, 10.0 equiv), and MsCl (0.10 mL, 2.00 equiv) in 2.5 mL of CH_2Cl_2 was stirred at 23 °C for 4 h then filtered through a 20 mm x 10 mm plug of silica gel using Et_2O (40 mL) as eluent. Concentration of the filtrate under reduced pressure afforded oxazoline **35** as a colorless syrup (90%).



(4S)-4-phenyl-4, 5-dihydro-2-(2'-hydroxy-4',6'-dimethylphenol)oxazole. TLC R_f = 0.26 (20:1 hexanes/ethyl acetate); mp = 63-64 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.15 (s, 1H, broad), 7.38-7.33 (m, 3H), 7.31-7.25 (m, 3H), 7.09 (1H, s), 5.46 (t, 1H, *J* = 9.0 Hz), 4.77 (tm, 1H, *J* = 9.0 Hz), 4.21 (td, 1H, *J* = 8.4, 1.1 Hz), 2.27 (s, 6H); ^{13}C NMR (d6-acetone, 75 MHz) δ 166.2, 156.0, 141.8, 135.2, 128.4, 127.4, 126.8, 126.2, 125.2, 125.0, 109.0, 73.7, 68.3, 19.3, 14.8 ppm; IR (thin film) ν 2909 (broad), 1635, 1602, 1477, 1369, 1272, 1195, 1126, 1020, 959, 777, 758, 698 cm^{-1}; Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.18; H, 6.41; N, 5.24. Found: C, 76.18; H, 6.60; N, 5.26.

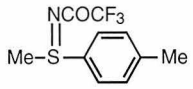


Nitrido 37b. TLC R_f = 0.35 (8:1 hexanes/ethyl acetate with slight decomposition); mp = 205-206 °C; ^{1}H NMR (d6-DMSO, 400 MHz, 19 °C) δ 7.50-7.38 (m, minor), 7.35-7.23 (m, 4H), 7.13-7.07 (m, 3H), 6.97 (s, minor), 5.45 (s, 1H, dd *J* = 9.3, 3.5 Hz), 5.35 (d, minor), 4.81 (s, 1H, *J* = 9.2 Hz), 4.74 (m, minor), 4.44 (1H, dd, *J* = 8.9, 3.5 Hz), 2.20 (s,

3H), 2.14 (s, 3H), 2.07 (s, minor), 1.90 (s, minor) ppm; ^{1}H NMR (d6-DMSO, 400 MHz, 100 °C) δ 7.37-7.23 (m, 4H), 7.17-7.07 (3H, m), 5.46 (dd, 1H, *J* = 1.8, 0.9 Hz), 4.78 (t, 1H, *J* = 9.0 Hz), 4.44 (dd, 1H, *J* = 9.0, 3.9), 2.20 (s, 3H), 2.15 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.6, 164.5, 140.2, 136.9, 128.8, 128.7, 127.9, 126.9, 125.7, 124.2; IR (thin film) ν 1625, 1601, 1562, 1469, 1435, 1317, 1262, 1249, 1210, 1145, 1046, 1020, 961, 844, 779, 749, 697 cm^{-1}.

General procedure for the transfer of nitrogen to sulfides: A solution of sulfide (1.0 equiv) and manganesenitride # (1.0 equiv) in CH_2Cl_2 (0.05 M) was cooled to -78 °C. Trifluoroacetic anhydride (5.0 equiv) was then added dropwise to the dark purple solution. The solution was allowed to warm slowly from -78 °C to 23 °C over a 4-5 h period. During this time the reaction mixture turned dark brown. Silica gel (2 g/mmol) and $NaHCO_3$ (20 equiv) were added, along with hexanes (10 mL/mmol). The dark brown slurry was stirred vigorously at 23 °C for 5 minutes before being filtered through a plug of silica gel (20 g/mmol) using Et_2O as eluent. Concentration of the filtrate under reduced pressure afforded a pale yellow residue which was purified by chromatotron.

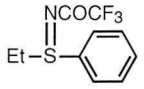
Physical data for N-trifluoroacetylated sulfilimine products:



92% yield
92% ee

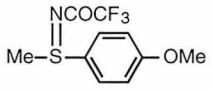
N-Trifluoroacetyl-methyl *p*-tolylsulfilimine 28a. TLC R_f = 0.34 (1:2 hexanes/EtOAc); mp = 70-72 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69 (dm, 2H, *J* = 8.4 Hz), 7.38 (d, 2H, *J* = 8.1 Hz), 2.93 (s, 3H), 2.43 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.7 (q, *J* = 37 Hz), 144.3, 131.0, 129.7, 127.1, 117.0 (q, *J* = 286 Hz), 34.7, 21.5 ppm; ^{19}F NMR ($CDCl_3$, 400 MHz) δ -73.4 ppm; IR (thin film) ν 1633, 1179, 1141, 978, 876, 810, 773

cm^{-1}; Anal. Calcd for $C_{10}H_{10}F_3NOS$: C, 48.19; H, 4.04; N, 5.62. Found: C, 47.93; H, 3.92; N, 5.90.



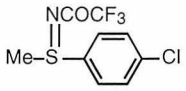
93% yield
90% ee

N-Trifluoroacetyl-ethyl phenylsulfilimine 39. TLC R_f = 0.40 (1:2 hexanes/EtOAc); mp = 62-64 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.80-7.75 (m, 2H), 7.64-7.57 (m, 3H), 3.32-3.18 (m, 2H), 1.26 (t, 3H, J = 7.5 Hz) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.7 (q, J = 37 Hz), 132.9, 130.5, 129.9, 127.3, 116.8 (q, J = 285 Hz) 43.8, 7.2 ppm; ^{19}F NMR ($CDCl_3$, 400 MHz) δ -73.4 ppm; IR (thin film) ν 1634, 1180, 1140, 882, 802, 775, 748, 688 cm^{-1}; Anal. Calcd for $C_{10}H_{10}F_3NOS$: C, 48.19; H, 4.04; N, 5.62. Found: C, 47.86; H, 4.20; N, 5.58.



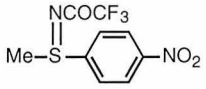
94% yield
92% ee

N-Trifluoroacetyl-methyl *p*-methoxyphenylsulfilimine 28b. TLC R_f = 0.28 (1:2 hexanes/EtOAc); mp = 80-82 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.80 (d, 2H, J = 8.7 Hz), 7.11 (d, 2H, J = 8.7 Hz), 3.92 (s, 3H), 2.98 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.3 (q, J = 38 Hz), 163.3, 129.1, 122.9, 116.7 (q, J = 286 Hz), 115.6, 55.5, 34.5 ppm; ^{19}F ($CDCl_3$, 400 MHz) δ -73.5 ppm; IR (thin film) ν 1634, 1594, 1498, 1307, 1263, 1182, 1140, 1086, 1025, 977, 876, 832, 799, 773 cm^{-1}; Anal. Calcd for $C_{10}H_{10}F_3NO_2S$: C, 45.28; H, 3.80; N, 5.28. Found: C, 45.28; H, 3.88; N, 5.22.



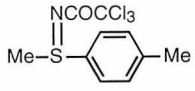
92% yield
83% ee

N-Trifluoroacetyl-methyl *p*-chlorophenylsulfilimine 28c. TLC R_f = 0.32 (1:2 hexanes/EtOAc); mp = 82-84 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.76 (dm, 2H, *J* = 8.7 Hz), 7.58 (dm, 2H, *J* = 8.7 Hz), 2.96 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.9 (q, *J* = 35 Hz), 139.9, 131.7, 130.7, 128.6, 116.9 (q, *J* = 286 Hz), 34.8 ppm; ^{19}F ($CDCl_3$, 400 MHz) δ -73.5 ppm; IR (thin film) ν 1631, 1183, 1140, 978, 824, 773 cm^{-1}; Anal. Calcd for $C_9H_7ClF_3NOS$: C, 40.09; H, 2.77; N, 5.19. Found: C, 39.94; H, 2.77; N, 5.17.



80% yield
33% ee

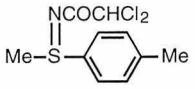
N-Trifluoroacetyl-methyl *p*-nitrophenylsulfilimine 28d. TLC R_f = 0.42 (1:2 hexanes/EtOAc); mp = 137-139 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.46 (d, 2H, *J* = 9.0 Hz), 8.03 (d, 2H, *J* = 9.0 Hz), 3.04 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.7 (q, *J* = 35 Hz), 150.6, 140.2, 128.3, 125.2, 116.9 (q, *J* = 286 Hz), 34.6 ppm; ^{19}F NMR ($CDCl_3$, 400 MHz) -73.5 δ ppm; IR (thin film) ν 1633, 1530, 1347, 1182, 1141, 978, 854, 804, 772, 744, 726, 680 cm^{-1}; Anal. Calcd for $C_{10}H_7F_3N_2O_3S$: C, 38.57; H, 2.52 N, 10.00. Found: C, 38.63 H, 2.46; N, 9.89.



94% yield
83% ee

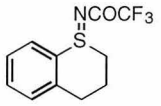
N-Trichloroacetyl-methyl *p*-tolylsulfilimine 41. TLC R_f = 0.42 (1:2 hexanes/EtOAc); mp = 103-105 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.71 (dm, 2H, *J* = 8.4 Hz), 7.38 (d, 2H, *J* = 8.2 Hz), 2.94 (s, 3H), 2.44 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.8, 144.1,

131.0, 130.3, 127.0, 95.2, 34.9, 21.6 ppm; IR (thin film) ν 1633, 1279, 978, 949, 845, 819, 796, 678 cm^{-1}; Anal. Calcd for $C_{10}H_{10}Cl_3NOS$: C, 40.22; H, 3.38; N, 4.69. Found: C, 40.32; H, 3.34; N, 4.70.



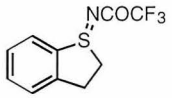
95% yield
86% ee

N-Dichloroacetyl-methyl p-tolylsulfilimine 40. TLC R_f = 0.28 (1:2 hexanes/EtOAc); mp = 82-84 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.67 (dm, 2H, *J* = 8.1 Hz), 7.37 (d, 2H, *J* = 8.1 Hz), 6.06 (br s, 1H), 2.89 (s, 3H), 2.43 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.2, 143.9, 130.9, 130.6, 127.0, 68.8, 34.9, 21.6 ppm; IR (thin film) ν 1614, 1312, 1178, 976, 945, 802, 668 cm^{-1}; Anal. Calcd for $C_{10}H_{11}Cl_2NOS$: C, 45.47; H, 4.20; N, 5.30. Found: C, 45.32; H, 3.93; N, 5.23.



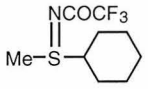
84% yield
50 % ee

S-Trifluoroacetamide thiobenzopyran 42b. TLC R_f = 0.34 (1:2 hexanes/EtOAc); mp = 100-102 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.89 (dd, 1H, *J* = 7.8, 1.2 Hz), 7.51 (td, 1H, *J* = 7.5, 1.4 Hz), 7.39 (tm, 1H, *J* = 4.4 Hz), 7.31 (dm, 1H, *J* = 7.5 Hz), 3.55 (ddd, 1H, *J* = 13.5, 5.7, 2.4 Hz), 3.25 (ddd, 1H, *J* = 14.4, 11.4, 3.0 Hz), 3.16 (td, 1H, *J* = 17.6, 4.9 Hz) 2.95 (ddd, 1H, *J* = 17.6, 10.8, 5.4), 2.76-2.61 (m, 1H), 2.28-2.17 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.3 (q, *J* = 34 Hz), 137.1, 132.8, 132.7, 131.3, 128.0, 126.5, 117.1 (q, *J* = 286 Hz), 39.2, 27.6, 15.6 ppm; ^{19}F NMR ($CDCl_3$, 400 MHz) δ -73.4 ppm; IR (thin film) ν 1633, 1179, 1139, 880, 760 cm^{-1}; Anal. Calcd for $C_{11}H_{10}F_3NOS$: C, 50.57; H, 3.86; N, 5.36. Found: C, 50.30; H, 4.01; N, 5.37.



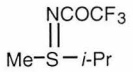
81% yield
46 % ee

S-Trifluoroacetamide benzothiophene 42a. TLC R_f = 0.32 (1:2 hexanes/EtOAc); mp = 96-97 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.01 (d, 1H, *J* = 8.0 Hz), 7.56 (t, 1H, *J* = 7.5 Hz), 7.56-7.42 (m, 2H), 3.92 (dt, 1H, *J* = 16.1, 8.4 Hz), 3.73-3.61 (m, 2H), 3.44 (ddd, 1H, *J* = 16.1, 7.3, 3.3 Hz), ^{13}C NMR (d6-acetone, 100 MHz) δ 171.4 (q, *J* = 34 Hz), 150.2, 140.4, 138.4, 133.8, 133.7, 131.8, 122.6 (q, *J* = 358 Hz), 50.2, 37.3, ppm; ^{19}F NMR ($CDCl_3$, 400 MHz) δ -73.4 ppm; IR (thin film) ν 1622, 1185, 1133, 884, 796, 764 cm^{-1}; Anal. Calcd for $C_{10}H_{18}F_3NOS$: C, 48.58; H, 3.26; N, 5.67. Found: C, 48.48; H, 3.07; N, 5.48.



79% yield

N-Trifluoroacetyl-methyl cyclohexylsulfilimine 45b. TLC R_f = 0.18 (1:2 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.18 (tt, 1H, *J* = 12.0, 6.0 Hz), 2.69 (s, 3H), 2.17 (dm, 1H, *J* = 10.8 Hz), 2.05 (dm, 1H, *J* = 12.3 Hz), 1.93 (dm, 2H, *J* = 12.0 Hz), 1.75 (dm, 1H, *J* = 9.9 Hz), 1.56-1.24 (m, 5H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.3 (q, *J* = 34 Hz), 117.1 (q, *J* = 286 Hz), 56.4, 26.7, 26.2, 25.2 ppm; ^{19}F ($CDCl_3$, 400 MHz) δ -73.6 ppm; IR (thin film) ν 1630, 1178, 1138, 967, 874, 795, 772 cm^{-1}; HRMS calcd for $C_9H_{15}F_3NOS$ (MH+) 242.0826, found 242.0821.



84% yield

N-Trifluoroacetyl-methyl isopropylsulfilimine 45a. TLC R_f = 0.14 (1:2 hexanes/ethyl acetate); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.38 (hept, 1H, *J* = 6.9 Hz), 2.62 (s, 3H), 1.37 (dd, 6H, *J* = 6.8, 3.8 Hz) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.37 (q, *J* = 34 Hz),

116.7 (q, J = 286 Hz), 47.5, 24.9, 16.1, 15.3 ppm; ^{19}F ($CDCl_3$, 400 MHz) δ -73.6 ppm; IR (thin film) ν 1634, 1184, 1139, 1070, 966, 877, 797, 773 cm^{-1}; HRMS calcd for $C_6H_{11}F_3NOS$ (MH+) 202.0513, found 202.0513.