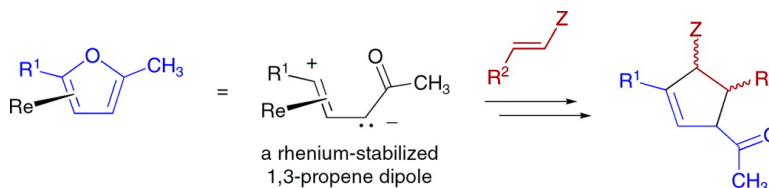


Rhenium-Promoted Diastereo- and Enantioselective Cyclopentannulation Reactions: Furans as 1,3-Propene Dipoles

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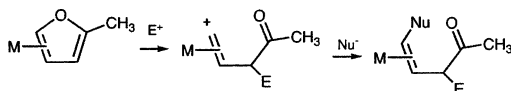
Rhenium-Promoted Diastereo- and Enantioselective Cyclopentannulation Reactions: Furans as 1,3-Propene Dipoles

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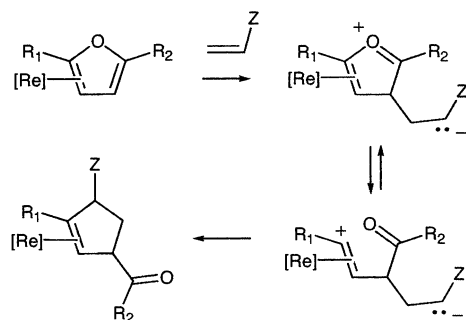
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Furans hold a prominent position among aromatic heterocycles as versatile synthons for more complex heterocyclic systems.^{1,2} Herein, we wish to report a new manifold of furan reactivity, as promoted by a transition-metal π base. When furan is dihapto-coordinated to the $\{\text{TpRe}(\text{CO})(\text{MeIm})\}^{3,4}$ (MeIm = 1-methylimidazole; Tp = hydridotris(pyrazolyl)borate) fragment, it becomes highly susceptible to the addition of electrophiles at the uncoordinated β -position. The resulting 3H-furanium species features a labile C–O bond which readily cleaves to form the functional equivalent of a vinyl cation, stabilized by the metal.⁵ In this regard, the coordinated furan takes on the role of a 1,3-propene dipole.



We first encountered this mode of reactivity for dihapto-coordinated furans during an investigation of osmium(II)-furan complexes.^{6,7} When the complex $[\text{Os}(\text{NH}_3)_5(\eta^2\text{-furan})]^{2+}$ was reacted with various aldehydes under Lewis-acidic conditions, dihydrofuran complexes were recovered in which the aldehyde was incorporated into a newly formed dihydrofuran ring.⁸ In a similar fashion, we envisioned a reaction in which an electron-deficient alkene replaced the aldehyde as the electrophile, thereby forming the cyclopentene ring-system, a structural feature ubiquitous in natural products.^{9,10} Although this goal was never realized using osmium as the promoter,⁷ the more electron-rich rhenium π base (vide supra) effects the novel cyclopentannulation reaction shown in Scheme 1, often with excellent control of the associated stereochemistry.

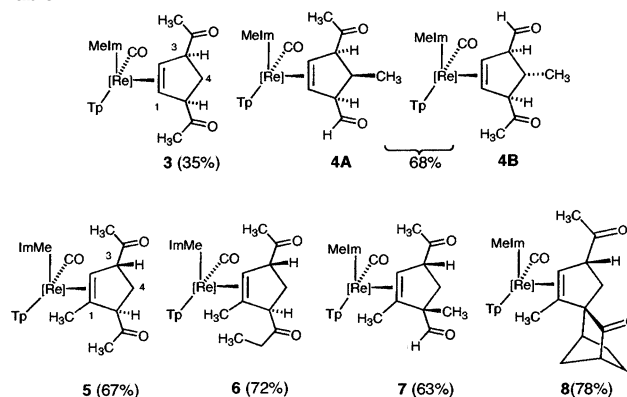
Scheme 1. A Rhenium-Promoted Cyclopentannulation Reaction



When the 2-methylfuran complex $\text{TpRe}(\text{CO})(\text{MeIm})(\eta^2\text{-2-methylfuran})$ (**1**) is dissolved in CH_2Cl_2 and treated with methyl vinyl ketone (MVK) in the presence of $\text{BF}_3\cdot\text{OEt}_2$ at -40°C , the bisacetylcyclopentene complex **3** is isolated (35%) as a single diastereomer (Table 1).

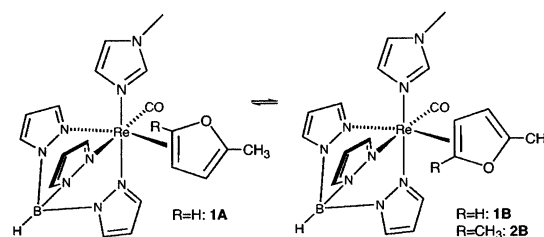
NOE and coupling data indicate that the two acetyl groups are anti to the rhenium. The cyclopentene ligand of **3** is a meso compound; thus only one coordination diastereomer is possible.

Table 1



However, when this reaction is repeated with crotonaldehyde, two diastereomers were recovered in a 1:1 ratio. Given the position of the acetyl group relative to the rhenium ligand set, this outcome indicates that the two products (**4A** and **4B**; 68%) were each derived from a different coordination isomer of the starting furan complex **1** (originally present in a 1.4:1 ratio). Mixtures of diastereomers were likewise obtained for reactions of **1** with 2-cyclopenten-1-one and methacrolein in moderate yields.

At this point, we turned our attention to the 2,5-dimethylfuran complex **2**,¹¹ a species that exists as only one coordination diastereomer (**2B**):



When a CH_2Cl_2 solution of **2B** was treated with MVK ($\text{BF}_3\cdot\text{OEt}_2/-40^\circ\text{C}$), the corresponding bisacetylmethylcyclopentene complex **5** was isolated in 67% yield as a single isomer. In contrast to **3**, this cyclopentene was asymmetric, and yet only one diastereomer was recovered. Surprisingly, coupling data indicate that the two acetyl groups in **5** are now trans to each other. In a similar manner, reactions with ethyl vinyl ketone, methacrolein, and exo-methylene norbornanone (Table 1) give high yields of **6**, **7**, and **8**, respectively, with complete stereocontrol.¹² An ORTEP drawing from the X-ray structure determination of compound **8** appears in Figure 1. In contrast to **3** and **4**, all complexes derived from complex **2B** (**5**–**8**) have the carbonyl derived from the original furan (attached to C3 of the cyclopentene ligand) syn to the rhenium.¹³

The carbonyl originating from the Michael acceptor adopts an anti relationship to the metal for all examples where C5 of the

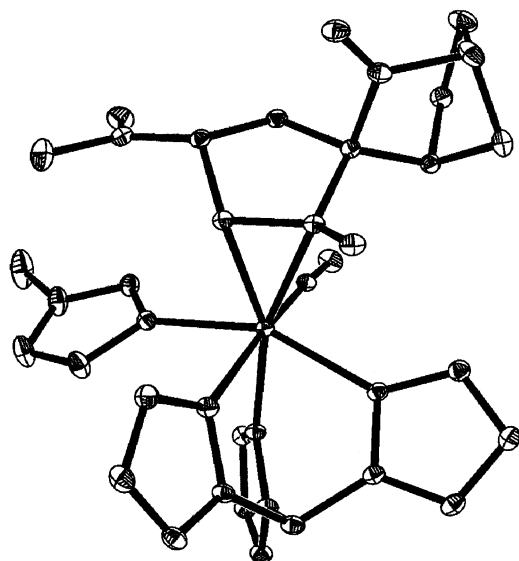
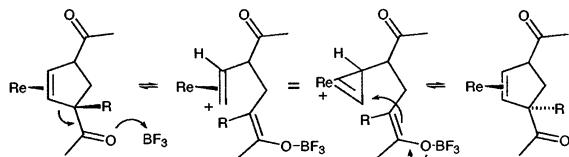


Figure 1. ORTEP drawing of compound **8** (30% ellipsoids; racemic).

cyclopentene ligand is a methine carbon. The stereochemistry of the cyclopentene ring is likely to be under thermodynamic control, given the presence of the Lewis acid. In addition to the standard carbonyl/enol tautomerization that operates under acidic conditions, an additional mechanism is accessible according to the law of microscopic reversibility that involves the cleavage of the bond between an allylic and vinylic carbon:

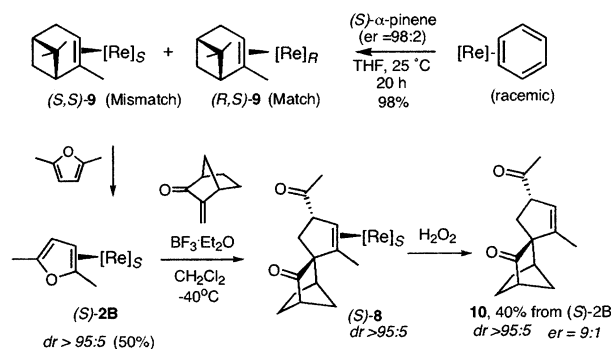


Recovery of the cyclopentene ligands from **5**, **6**, and **8** was accomplished by oxidation of the rhenium. Treatment of these complexes with H_2O_2 , Ag^+ , or, in the case of **8**, even air afforded the free organics in yields ranging from 63% (isolated) to >95% (NMR).¹⁴

The present rhenium system has been resolved previously through the use of α -pinene.¹⁵ The two coordination diastereomers formed during complexation of the pinene vary considerably in stability. When (*S*)- α -pinene was used, the mismatched form (*S,S*)-**9** readily undergoes substitution with 2,5-dimethylfuran to afford (*S*)-**2B**. This resolved furan complex was treated with *exo*-methylene norbornane and oxidatively decomplexed, and the tricyclic dione **10** was isolated (40% from (*S*)-**2B**; 63% from (*S*)-**8**; racemic). HPLC analysis using a chiral column determined that **10** was prepared with an *er* of 9:1 (Scheme 2).

In summary, rhenium(I) serves to first activate the furan toward Michael addition, then to stabilize the 3H-furanium intermediate

Scheme 2. Enantioenriched Preparation of Cyclopentannulation Product **10**



such that cyclization can occur, and finally to set both the relative and the absolute stereocenters of the cyclopentene products. The full scope of the reaction of furan complexes with Michael acceptors will be reported in due course.

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Supporting Information Available: Experimental procedures, full characterizations, and crystallographic details (PDF and CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (12) In all cases, the crude mixture contains a component that does not elute and shows no features in the NMR. We attribute any unaccounted for mass to these paramagnetic decomposition products.
- (13) A reaction of **2B** with cyclopent-2-enone generated an inseparable mixture of isomers. However, a significant component of this mixture shows a doublet ($J = 9.0$ Hz) at δ 3.11 ppm for H1 of the product, data most consistent with a compound having a C5 acetyl group syn to the metal, as is the case for compounds **5–8**.
- (14) The dihydrofuran ligands liberated from compounds **5** and **6** are easily lost to evaporation; thus yields were determined by NMR using an internal standard.
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