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Reactivity and Selectivity Differences between Catecholate and Catechothiolate Ru Complexes. Implications Regarding Design of Stereoselective Olefin Metathesis Catalysts

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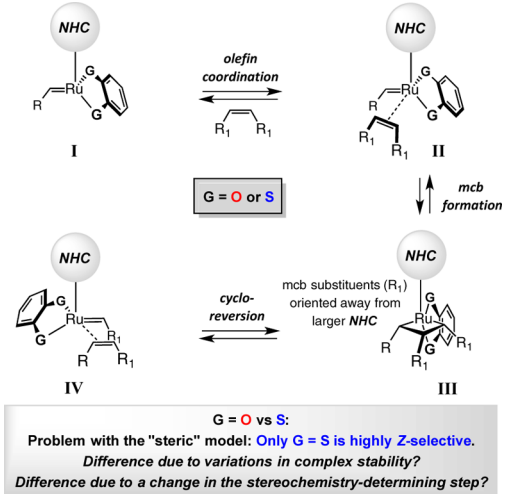
Supporting Information

ABSTRACT: The origins of the unexpected finding that Ru catechothiolate complexes, in contrast to catecholate derivatives, promote exceptional *Z*-selective olefin metathesis reactions are elucidated. We show that species containing a catechothiolate ligand, unlike catecholates, preserve their structural integrity under commonly used reaction conditions. DFT calculations indicate that, whereas alkene coordination is the stereochemistry-determining step with catecholate complexes, it is through the metallacyclobutane formation that the identity of the major isomer is determined with catechothiolate systems. The present findings suggest that previous models for *Z* selectivity, largely based on steric differences, should be altered to incorporate electronic factors as well.

Development of catalysts for stereoselective olefin metathesis (OM) is a central objective of research in chemistry. The discovery of *Z*-selective OM catalysts is a recent advance with significant implications in chemical synthesis.[1] The primary breakthrough was in connection with ring-opening/cross-metathesis (ROCM) reactions promoted by a Mo-based monopyrrolide aryloxide complex.[2] Kinetically controlled *Z* selectivity was attributed to the size difference that distinguishes the apical (imido and aryloxide) ligands of a trigonal bipyramidal intermediate; it has been proposed that the metallacyclobutane (mcb) substituents prefer to be oriented toward the more diminutive (imido) unit.[3] The latter model has led to identification of other Mo and W alkylidenes as well as Ru carbenes for *Z*-selective cross-metathesis (CM)[4] and ring-closing metathesis.[5,6] More recent investigations based on similar design principles have yielded Ru-based catechothiolates that catalyze ring-opening metathesis polymerization (ROMP) and ROCM efficiently and *Z* selectively;[7] already, in one total synthesis application, Ru dithiolates have proven superior in promoting a key *Z*-selective CM.[8] Surprisingly, the closely related Ru catecholates induce minimal stereochemical control. These latter observations indicate that steric effects alone might not be sufficient as the foundation for a reliable catalyst design template or dependable predictor of stereoselectivity.

Herein, we show that the electronic nature of the anionic groups[9] (i.e., G = O vs S in Scheme 1) is crucial to determining the effectiveness of a Ru-based *Z*-selective OM catalyst. Our studies illustrate that the bidentate heteroatomic ligands influence the extent to which a Ru diolate or dithiolate can retain its structural integrity and determine whether a complex's

Scheme 1. Stages of a Catalytic Cycle and Key Issues[a]



[a]mcb = metallacyclobutane, NHC = N-heterocyclic carbene.

decomposition leads to the formation of other reactive but non-stereoselective carbenes. The identity of the turnover-limiting step appears to be dictated by the anionic ligands as well: considerable *Z* selectivity may be induced if mcb formation (**II** → **III**) is turnover-limiting as opposed to alkene coordination (**I** → **II**). We demonstrate that it is at the stage of metallacycle generation that the size difference between the NHC and the heteroatomic ligand that is trans to it can strongly influence the stereochemical course of an OM process.

We began by addressing the question of whether there are dissimilarities in the structural robustness of O- vs S-based complexes. Part of the disparity in the stability of a catecholate (e.g., **1a**) and a catechothiolate (e.g., **2**) species might arise from the difference in the lability of Ru−O vs Ru−S bonds. Comparison of the ability of **1a** and **2** to promote *Z*-selective ROCM with hydroxyl-containing substrates and styrene revealed that, whereas the reaction promoted by **1a** was efficient (Table 1, entry 1), there was <2% conversion when alcohol-containing alkenes were used (entries 2 and 3); a similar trend was observed with a cyclic alkene bearing two alcohol units (entries 4 and 5). With dithiolate **2**, on the other hand, efficient *Z*-selective reactions were observed in all cases. Exchange of the catecholate

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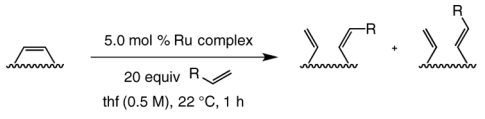
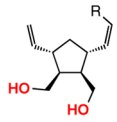
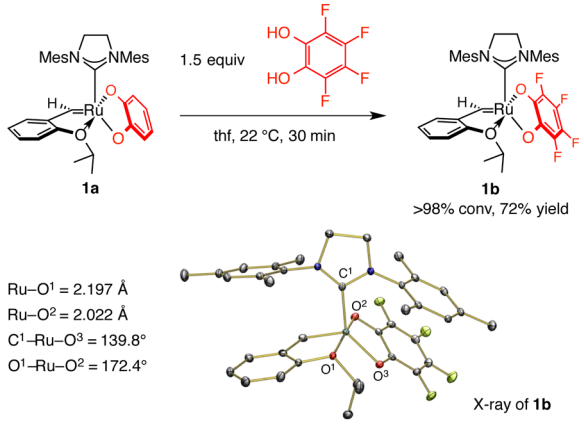
Table 1. Effect of Catalyst Structure on ROCM Reactions[a]



entry	product	R	with 1a conv (%);[b] Z:E;[b]	with 2 conv (%);[b] Z:E;[b]
1	 3	a C_6H_5	>98; 55:45[c]	>98; 97:3
2		b CH_2OH	<2; na	>98; 88:12
3		c $(CH_2)_2OH$	<2; na	>98; 87:13
4	 4	a C_6H_5	<2; na	>98; 97:3
5		b C_6H_{11}	<2; na	88; >98:2

[a]See the Supporting Information (SI) for details. [b]By analysis of ^{1}H NMR spectra of unpurified mixtures. [c]28% yield. For other yield values, see ref 7b. Mes = 2,4,6-$Me_3C_6H_2$, na = not applicable.

Scheme 2. Facile Exchange of Catecholate Ligands



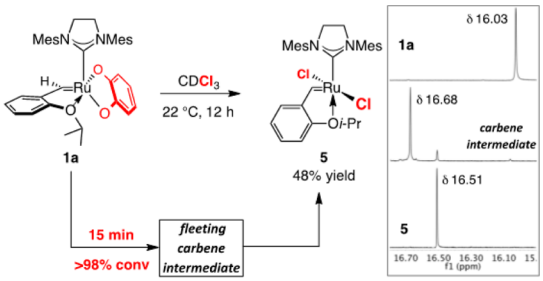
<2% exchange after 90 min when Ru dithiolate **2** is used

with aliphatic alcohols in all probability gives rise to substantial lowering of catalyst activity.[10]

Another finding corroborated the proposal that O-based ligands readily exchange with other hydroxyl groups: Conversion of catecholate **1a** to tetrafluorocatecholate **1b** resulted in a ligand substitution process that reached completion within 30 min at 22 °C (Scheme 2). In contrast, when catechothiolate complex **2** was subjected to tetrafluorocatechol, <2% transformation was detected after 90 min.

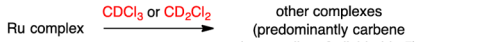
Investigating the constitutional stability of catecholate and catechothiolate complexes in commonly used chlorinated solvents was next. Our interest in this question arose from reports illustrating that ROMP with Ru diolates,[11] including closely related catecholates,[12] is especially efficient but non-stereoselective when carried out in chloroform. We wondered whether decomposition to a highly active dichloro-Ru carbene in chlorohydrocarbon media might be at least partially responsible for the aforementioned stereoselectivity difference. Indeed,

Scheme 3. Reaction of Ru Catecholate with Chloroform-*d*[a]



[a]See the SI for details.

Table 2. Stability of Ru Carbenes in Chlorinated Solvents[a]



entry	Ru complex	with $CDCl_3$ temp (°C); time	with $CDCl_3$ conv (%)[b]	with CD_2Cl_2 temp (°C); time (h)	with CD_2Cl_2 conv (%)[b]
1	catecholate **1a**	22; 10 min	97	50; 24	82
2	F_4-catecholate **1b**	22; 10 min	16	50; 24	29
3	catecholate·pyr **1c**	22; 12 h	11	50; 24	20

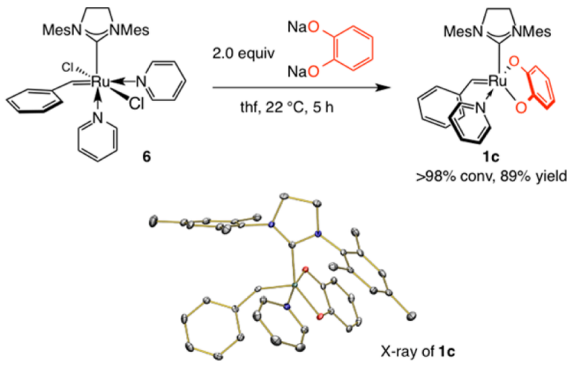
[a]See the SI for details.

ROMP of norbornene in the presence of **1a** or dichloride **5** in $CHCl_3$ proceeded with identical stereoselectivities (~55:45 *Z*:*E*).[13] The aforementioned hypothesis is further supported by a recent disclosure indicating that a Ru complex containing two carboxylic ester ligands is transformed, albeit slowly, to the derived dichloride species upon exposure to dichloromethane (12%, "overnight").[14]

In the event, subjection of Ru catecholate **1a** to $CDCl_3$[15] led to complete disappearance of the initial carbene signal at δ 16.03 within 15 min at ambient temperature (Scheme 3). The fleeting carbene (δ 16.68), the precise identity of which is the subject of ongoing investigations, was then converted to Ru dichloride complex **5** (δ 16.51),[16] which was isolated in 48% yield after silica gel chromatography.

The data provided in Table 2 offer additional insight regarding comparative reactivity of Ru catecholates in chloroform. Carbene **1a** underwent 97% conv in 10 min (entry 1), and after 15 min dichloride **5** was detected spectroscopically; on the contrary, F_4-catecholate **1b** reacted at a noticeably slower rate (16% in 10 min; entry 2). Similar increase in stability was observed with pyridine complex **1c**, synthesized via bis-pyridyl species **6** (Scheme 4): there was no more than 11% conv after 12 h (entry 3, Table 2).

Scheme 4. Preparation and X-ray Structure of Pyridine Adduct



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Decomposition in CD_2Cl_2 demanded elevated temperatures, conditions under which Ru catecholates have been used to promote OM;[12b] specifically, there was 82% conversion at 50 °C, affording 27% **5** (<2% conv at 22 °C). Spectroscopic analysis indicated that treatment of catechothiolate **2** with $CDCl_3$ (22 °C) or CD_2Cl_2 (50 °C) leads to decomposition as well (~50% in $CDCl_3$, 1.0 h, 22 °C; <10% in CD_2Cl_2, 24 h, 50 °C), but Ru dichloride **5** was not discernible (<2% by 400 MHz ^{1}H NMR).

The disparity in the rate of reactions carried out with catecholates **1a**−**1c** in chlorinated hydrocarbons might be caused by the less facile dissociation of the chelating O*i*-Pr and pyridine ligands, respectively. The tetrafluoroaryl unit enhances Ru Lewis acidity to reinforce (*i*-Pr)O→Ru chelation in **1b**, whereas dissociation in **1c**[17] has probably a higher barrier due to firmer (pyr)N→Ru binding. These data provide an explanation for the diminished OM activity when catecholates that contain electron-withdrawing groups are used;[12b] in the presence of **1b** there is <2% conv for the ROCM shown in entry 5, Table 1 (1 h).

We then established that a Ru catecholate, handled with care to safeguard its structural integrity, still does not promote OM stereoselectively. This conclusion was based on the following data: (1) ROMP reactions with **1a** in CH_2Cl_2 are non-selective at 22 °C, conditions under which Ru dichloride **5** does not form (cf. Table 2). (2) With a sample of **1a**, prepared while rigorously avoiding adverse conditions, ROMP of norbornene in thf remained minimally stereoselective (~55:45 *Z*:*E*).

It is unlikely that the change in stereoselectivity between catecholates and catechothiolates is rooted in steric effects (cf. Scheme 1). Stereoselectivity variations probably originate from electronic factors as well as alterations in the kinetics of the catalytic cycle.[18] To probe further, we examined the ROCM of norbornene and propene by DFT calculations (Figure 1).[13] Regardless of the identity of the bidentate ligand, the routes leading to the *Z* isomer were found to be energetically favored. As expected, O- and S-based ligands possess the necessary geometric (bidentate) and size requirements (smaller than NHC) for promoting *Z*-selective transformations (compare $ts1_{Z\text{-}O}$ vs $ts1_{E\text{-}O}$ and $ts1_{Z\text{-}S}$ vs $ts1_{E\text{-}S}$, Figure 1).

Nevertheless, the pathways involving the two catalyst systems have several distinguishing features: (1) The sequence leading to the *Z* isomer is energetically more demanding for the dithiolate (blue) relative to the catecholate complex (red). More notably, $mcb_{Z\text{-}O}$ derived from the catecholate is ~16 kcal/mol lower in energy than $mcb_{Z\text{-}S}$ (+5.4 vs −10.1 kcal/mol). (2) While olefin coordination (ts0) is the highest energy point along the catecholate route, in the case of the Ru catechothiolate, mcb formation ($ts1_{Z\text{-}S}$) is turnover-limiting (i.e., alkene association is reversible).[19] Such energetic differences offer a rationale for the lack of *Z* selectivity with the O-based systems: Stereochemical differentiation through formation of a metal−olefin complex is less likely, particularly in an early (substrate-like) transitions state (14e → pc, red curve in Figure 1), since the more loosely associated substrate is too distal for steric interactions to be influential (average C−Ru distance of 3.57 Å in $ts0_{Z\text{-}O}$ and $ts0_{E\text{-}O}$; see Figure 1). The extensively formed bonds of a mcb, or the more closely associated substrate in a late (product-like) transition state for olefin coordination (average C−Ru distance of 3.00 Å in $ts0_{Z\text{-}S}$ and $ts0_{E\text{-}S}$; see Figure 1), would exhibit stronger sensitivity to steric effects, favoring an all-syn metallacycle.

The more exothermic Ru−alkene coordination with the catecholate complex might be the result of two factors. One might arise from diminished σ-donation by the dioxygen ligand, enhancing Ru Lewis acidity and strengthening olefin complex-

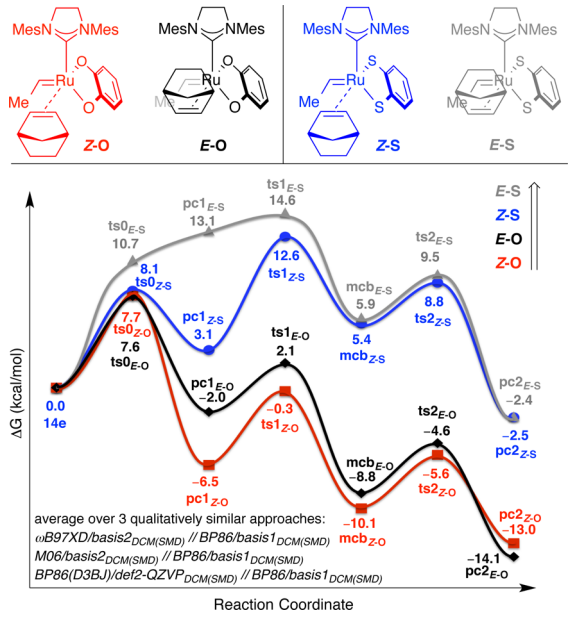
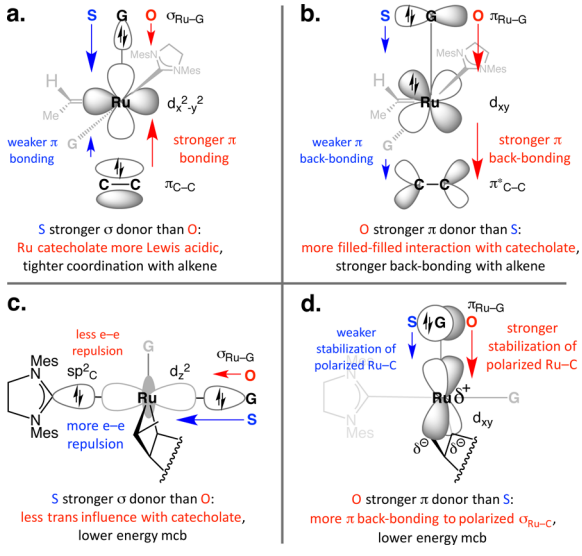


Figure 1. Energy diagram for ROCM of norbornene and propene with Ru complexes **1a** and **2**. 14e = 14-electron complex, pc = π complex, ts = transition state, mcb = metallacyclobutane. See the SI for details.

Scheme 5. Electronic Basis for Stereoselectivity Differences between Catecholate and Catechothiolate Ru Complexes



ation (Scheme 5a). The other is the stronger π-donating ability of the O-based unit,[20] leading to e−e repulsion with the d_{xy} electrons and more efficient back-donation into the alkene π^* orbital (more efficient olefin binding; Scheme 5b). The significantly lower energy of catecholate mcb might be linked to a stronger destabilizing repulsive interaction between the NHC and its trans sulfide group (vs the weaker σ-donating O-based anion (Scheme 5c). It is equally feasible that the stronger π-donating oxygen ligand can better accommodate the polarized Ru−C bonds of the mcb intermediate by means of hyper-conjugative stabilization (Scheme 5d).

Natural bond orbital analysis, performed on a model system, supports the above picture.[13] Variation of the natural charge in the 14e complexes points to higher Ru Lewis acidity in the catecholate species (+0.465 vs −0.327). These studies show that

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because of stronger π donation by the O-based ligand, the nonbonding d_{xy} and d_{xz} orbitals are raised in energy (on average) by +0.13 eV (vs catechothiolate). The latter type of electronic repulsion involving the oxygen atom syn to the NHC is alleviated by conversion of the 14e complex to the mcb, leading to significant shortening (−0.078 Å) and lowering of the energy of the Ru−O σ bond (−3.53 eV); such changes are less consequential in the catechothiolate system (−0.025 Å and −2.69 eV, respectively). The larger trans influence in the S-based mcb (Scheme 5c) is manifested by a significantly elongated Ru−C^{NHC} σ bond (2.120 vs 2.054 Å), which is destabilized by 0.92 eV relative to the 14e complex (vs 0.51 eV in Ru catecholate). Finally, charge decomposition analysis performed on the olefin π-complexes predicts a larger degree of π(C═C)→Ru donation (0.591 electron) as well as Ru→π^*(C═C) back-donation (0.275 electron) in the case of the catecholate species (vs 0.552 and 0.245 electron in the catechothiolate).

The investigations described here elucidate a number of the less appreciated attributes of Ru complexes arising from the replacement of the chloride ligands in the parent systems—a strategy that is commonly adopted in catalyst development initiatives.[2c,4d,e,f,5d,7,21] The lessons learned from the present studies are expected to be essential in future efforts in designing stereoselective OM catalysts.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures, spectral and analytical data for all products, crystallographic data, and calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(19) The calculated difference between $ts0_{Z\text{-}O}$ and $ts1_{Z\text{-}S}$ points to a larger rate difference than the 1−2 order of magnitude estimated for ROMP reactions promoted by O- and S-based complexes. This discrepancy is likely because, in the transformations catalyzed by a catecholate complex, it is the ligand dissociation step (e.g., $pc1_{Z\text{-}O}$ ($mcb_{Z\text{-}O}$) → $ts0_{Z\text{-}O}$) that becomes rate limiting. See the SI for a detailed analysis and discussion.

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