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Supported Chiral Mo-Based Complexes as Efficient Catalysts for Enantioselective Olefin Metathesis

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Abstract: Syntheses and catalytic activities of seven new polymer-supported chiral Mo-based complexes are disclosed. Four of the complexes are polystyrene-based, and three involve polynorbornene supports. Studies concerning the ability of the polymer-bound chiral complexes to promote an assortment of asymmetric ring-closing (ARCM) and ring-opening (AROM) metathesis reactions are detailed. In many instances, levels of reactivity and enantioselectivity are competitive with those of the analogous homogeneous catalysts. The positive effect of lower cross-linking within the polymer backbone on reaction efficiency and asymmetric induction is detailed. The optically enriched products obtained through the use of the supported complexes, after simple filtration and removal of the supported Mo catalysts, contain significantly lower levels of metal impurities as compared to products synthesized with the corresponding homogeneous catalysts.

Introduction

Since the emergence of catalytic olefin metathesis[1] as an indispensable method in organic synthesis, the design and development of supported metathesis catalysts has been the focus of investigations in a number of laboratories.[2] The aims of such studies have been manifold. In addition to the requirement for ease of preparation and handling, the most desirable supported metathesis catalysts are those that promote transformations with efficiencies that are similar (or higher) to those of the related homogeneous complexes. Other attractive attributes include the ability to recover and recycle the catalyst, low levels of metal residue in the unpurified products, and substrate generality.

A critical area of research that has received relatively scant attention is the development of supported optically pure catalysts for enantioselective olefin metathesis. The availability of supported optically pure complexes would allow for the effective and practical synthesis of optically enriched small organic molecules that can be used in the preparation of biologically active agents.[3] The synthesis of a library of drug-like molecules[4] in the nonracemic form would be facilitated if highly efficient, enantioselective, readily retrievable, and recyclable supported chiral catalysts that effect asymmetric ring-closing (ARCM) and ring-opening (AROM) metathesis reactions were available.

Research in these laboratories during the past several years has involved the design and development of chiral catalysts for enantioselective olefin metathesis.[5,6] A representative number of Mo-based chiral metathesis catalysts have resulted from these studies (Chart 1).[1n] (The absolute configuration of the biphenoxides or binaphtholates employed varies from catalyst to catalyst; for convenience and clarity, only the (*S*) antipodes are illustrated.) These chiral complexes have allowed us to develop

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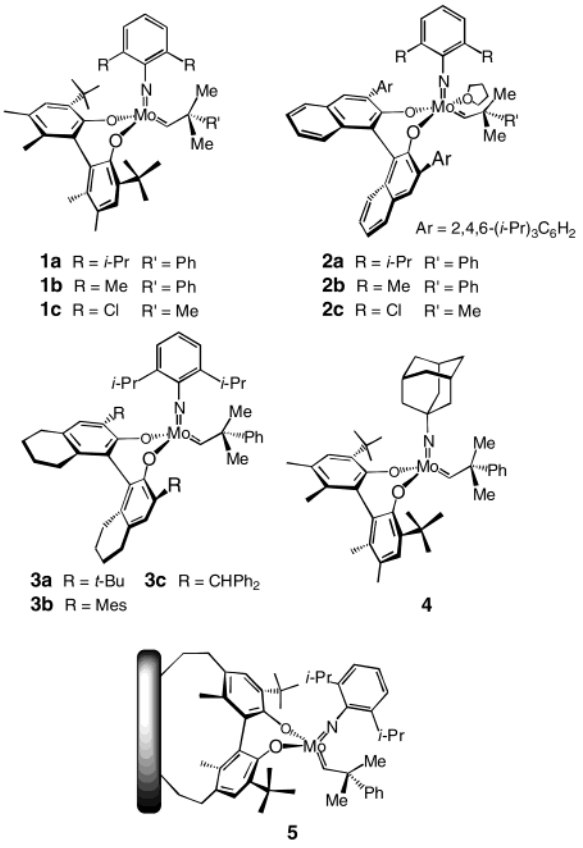
(1) For reviews on catalytic olefin metathesis, see: (a) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446−452. (b) Schmalz, H.-G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1833−1836. (c) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036−2056. (d) Ivin, K. J.; Mol, J. C. *Olefin Metathesis and Metathesis Polymerization*; Academic Press: San Diego, 1997. (e) Furstner, A. *Top. Catal.* **1997**, *4*, 285−299. (f) *Alkene Metathesis in Organic Synthesis*; Furstner, A., Ed.; Springer: Berlin, 1998. (g) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 371−388. (h) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413−4450. (i) Randall, M. L.; Snapper, M. L. *Strem Chem.* **1998**, *17*, 1−9. (j) Phillips, A. J.; Abell, A. D. *Aldrichchimica Acta* **1999**, *32*, 75−89. (k) Wright, D. L. *Curr. Org. Chem.* **1999**, *3*, 211−240. (l) Furstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012−3043. (m) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18−29. (n) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *38*, 4555−4708. (o) *Handbook of Olefin Metathesis*; Grubbs, R. H., Ed.; VCH−Wiley: Weinheim, 2003.

(2) For representative recent examples, see: (a) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168−8179. (b) Yao, Q. *Angew. Chem., Int. Ed.* **2000**, *39*, 3896−3898. (c) Kingsbury, J. S.; Garber, S. B.; Giftos, J. M.; Gray, B. L.; Okamoto, M. M.; Farrer, R. A.; Fourkas, J. T.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 4251−4255. (d) Grela, K.; Trynowski, M.; Bieniek, M. *Tetrahedron Lett.* **2002**, *43*, 9055−9059. (e) Dowden, J.; Savovic, J. *Chem. Commun.* **2001**, 37−38. (f) Connon, S. J.; Dunne, A. M.; Blechert, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 3835−3838. (g) Audic, N.; Clavier, H.; Mauduit, M.; Guillemin, J.-C. *J. Am. Chem. Soc.* **2003**, *125*, 9248−9249. (h) Varray, S.; Lazaro, R.; Martinez, J.; Lamaty, F. *Organometallics* **2003**, *22*, 2426−2435. (i) Yao, Q.; Zhang, Y. *J. Am. Chem. Soc.* **2004**, *126*, 74−75. (j) Kingsbury, J. S.; Hoveyda, A. H. In *Polymeric Materials in Organic Synthesis and Catalysis*; Buchmeiser, M. R., Ed.; Wiley-VCH: Weinheim, Germany, 2003; pp 467−502. (k) Buchmeiser, M. R. *Chem. Rev.* **2000**, *100*, 1565−1604. (l) Buchmeiser, M. R. *New J. Chem.* **2004**, *28*, 549−557. For a general review of supported chiral catalysts and their utility in enantioselective synthesis, see: (m) Brase, S.; Lauterwasser, F.; Ziegert, R. E. *Adv. Synth. Catal.* **2003**, *345*, 869−929.

(3) (a) Hoveyda, A. H.; Schrock, R. R. *Chem.-Eur. J.* **2001**, *7*, 945−950. (b) Reference 1n.

(4) (a) Schreiber, S. L. *Science* **2000**, *287*, 1964−1969. (b) Schreiber, S. L. *Science* **2003**, *302*, 613−618.

Chart 1. Representative Chiral Mo Catalysts for Olefin Metathesis



a variety of efficient catalytic enantioselective methods that deliver synthetically versatile organic molecules that cannot be readily prepared by alternative catalytic or noncatalytic protocols.[5e−g,6] Moreover, the utility of these chiral catalysts has been demonstrated through application to the synthesis of medicinally important agents.[1n,5d,6d]

A more recent focus of our studies has been to introduce more practical protocols through which chiral Mo complexes can be utilized in enantioselective organic synthesis.[7] One aspect of this initiative relates to the synthesis and study of supported variants of homogeneous enantiomerically pure Mo complexes (e.g., **1**−**4** in Chart 1). It was in this context that we recently reported the synthesis, characterization, and catalytic activity of the first supported catalyst for asymmetric olefin metathesis (**5**, Chart 1).[8] Polystyrene-supported catalyst **5**, the structure of which is based on **1a**,[5a] the first effective asymmetric catalyst to emerge from our studies, promotes C−C bond-forming reactions with synthetically useful levels of reactivity and enantioselectivity. Supported Mo complex **5** can be recycled without notable reduction in efficiency and affords products that contain significantly less Mo impurity than those delivered by **1a**.[8]

A critical concept that continues to serve as a driving force in our studies is that the availability of a class of chiral catalysts is necessary if an optimal range of substrates can be subjected to enantioselective metathesis, allowing access to as wide of a variety of optically enriched products as possible.[9] Indeed, our investigations have consistently indicated that the chiral complexes shown in Chart 1 are complementary in their ability to provide the highest possible levels of efficiency and asymmetric induction in different catalytic ARCM and AROM reactions.[3] Through exploitation of the modular character of Mo-based catalysts, where substitution of sterically and electronically altered chiral diolates and/or imido groups can lead to a variety of chiral complexes that exhibit disparate reactivity and selectivity profiles, we have been able to address a number of problems in asymmetric organic synthesis. The above considerations dictate that a class of supported chiral metathesis catalysts must be made accessible if the full potential of the Mo-catalyzed enantioselective transformations is to be realized.[3]

In this Article, we provide details of the syntheses and catalytic activities of seven new supported chiral Mo-based complexes. Together with the previously reported **5** (Chart 1), the complexes discussed here constitute a small collection of supported chiral catalysts that can be employed to promote a significant range of efficient ARCM and AROM transformations. As is detailed below, certain complexes are attached to polystyrene supports, and others are polynorbornene bound. The effect of variations in support structure, as well as the influence of different levels of cross-linking, on the performance of catalysts are discussed. Issues of recyclability and levels of Mo contamination in unpurified products are addressed as well.

Results and Discussion

1. Chiral Biphenolate Complexes Bound to a Polystyrene Support. As was mentioned above, various Mo-based catalysts complement one another and can promote different enantioselective reactions efficiently.[3] Certain ARCM and AROM reactions promoted by homogeneous complexes **1c** (Chart 1) and **4** thus proceed with significantly higher enantioselectivities and/or yields than **1a** or its supported variant **5**. To address this issue, we synthesized polystyrene-supported catalysts **6** and **7** through procedures related to those developed previously in these laboratories. Catalysts **6** and **7** were isolated as red-brown

(5) Mo-catalyzed ARCM, see: (a) Alexander, J. B.; La, D. S.; Cefalo, D. R.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1998**, *120*, 4041−4142. (b) La, D. S.; Alexander, J. B.; Cefalo, D. R.; Graf, D. D.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1998**, *120*, 9720−9721. (c) Weatherhead, G. S.; Houser, J. H.; Ford, J. G.; Jamieson, J. Y.; Schrock, R. R.; Hoveyda, A. H. *Tetrahedron Lett.* **2000**, *41*, 9553−9559. (d) Cefalo, D. R.; Kiely, A. F.; Wuchrer, M.; Jamieson, J. Y.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2001**, *123*, 3139−3140. (e) Kiely, A. F.; Jernelius, J. A.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 2868−2869. (f) Dolman, S. J.; Sattely, E. S.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **2002**, *124*, 6991−6997. (g) Teng, X.; Cefalo, D. R.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 10779−10784. (h) Dolman, S. J.; Schrock, R. R.; Hoveyda, A. H. *Org. Lett.* **2003**, *5*, 4899−4902. Ru-catalyzed ARCM, see: (i) Seiders, T. J.; Ward, D. W.; Grubbs, R. H. *Org. Lett.* **2001**, *3*, 3225−3228. (j) VanVeldhuizen, J. J.; Gillingham, D. G.; Garber, S. B.; Kataoka, O.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 12502−12508.

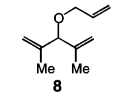
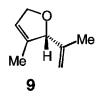
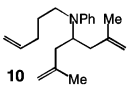
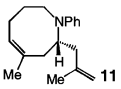
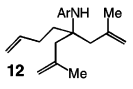
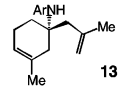
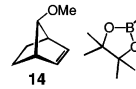
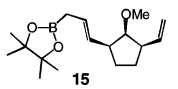
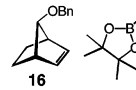
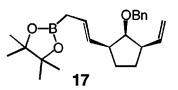
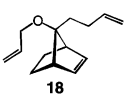
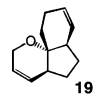
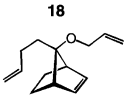
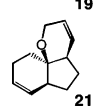
(6) For Mo-catalyzed AROM, see: (a) La, D. S.; Ford, J. G.; Sattely, E. S.; Bonitatebus, P. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999**, *121*, 11603−11604. (b) La, D. S.; Sattely, E. S.; Ford, J. G.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2001**, *123*, 7767−7778. (c) Weatherhead, G. S.; Ford, J. G.; Alexanian, E. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 1828−1829. (d) Tsang, W. C. P.; Jernelius, J. A.; Cortez, G. A.; Weatherhead, G. S.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 2591−2596. (e) Weatherhead, G. S.; Cortez, G. A.; Schrock, R. R.; Hoveyda, A. H. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5805−5809. For Ru-catalyzed AROM, see: (f) Van Veldhuizen, J. J.; Garber, S. B.; Kingsbury, J. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 4954−4955.

(7) Aeilts, S. L.; Cefalo, D. R.; Bonitatebus, P. J.; Houser, J. H.; Hoveyda, A. H.; Schrock, R. R. *Angew. Chem., Int. Ed.* **2001**, *40*, 1452−1456.

(8) Hultzsch, K. C.; Jernelius, J. A.; Hoveyda, A. H.; Schrock, R. R. *Angew. Chem., Int. Ed.* **2002**, *41*, 589−593.

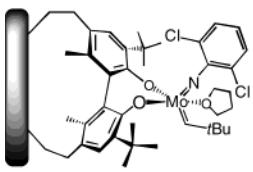
(9) For a detailed discussion regarding catalyst diversity versus specificity, see: Hoveyda, A. H. In *Handbook of Combinatorial Chemistry*; Nicolaou, K. C., Hanko, R., Hartwig, W., Eds.; Wiley-VCH: Weinheim, 2002; pp 991−1016.

Table 1. Catalytic Enantioselective Olefin Metathesis Promoted by Polystyrene-Supported Biphenol-Based Chiral Mo Complexes[a]

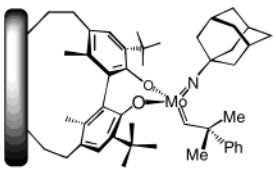
			with unbound catalyst			*with supported catalyst*		
entry	substrate	product	cat.	conv (%);[b] time (h)	yield (%);[c] ee (%)[d]	cat.	conv (%);[b] time (h)	yield (%);[c] ee (%)[d]
1	 **8**	 **9**	**1c**	>98; 1	95; 90	**6**	>98; 1	91; 81
2	 **10**	 **11**	**1c**	98; 0.5	98; 98	**6**	74; 5	60; 95
3[e]	 **12**	 **13**	**1c**	98; 0.5	91; 62	**6**	76; 20	76; 54
4	 **14**	 **15**	**4**	>98; 3	74; 90[f]	**7**	>98; 3	61; 95[f]
5	 **16**	 **17**	**4**	>98; 3	78; 94[g]	**7**	>98; 3	73; 98[g]
6	 **18**	 **19**	**4**	98; 3	80; 96[h]	**7**	98; 12	55; 88[h]
7	 **20**	 **21**	**4**	>98; 3	90; 72[i]	**7**	95; 12	85; 74[i]

[a] Conditions: 5 mol % catalyst, 22 °C, C_6H_6, under N_2 or Ar atm. The % cross-linking in **6** and **7** was 2.4%. The products are drawn with arbitrary configurations. [b] Conversion determined by ^{1}H NMR analysis. [c] Isolated yields after purification. [d] Enantioselectivities determined by chiral GLC or HPLC analysis (entries 1, 6, 7 with CDGTA column (GLC); entry 4 with chiral CD-BPH column (GLC); entries 2, 3 with Chiralcel OD column (HPLC); and entry 5 with Chiralpak AD column (HPLC)). [e] Ar = *o*-(OMe)C_6H_4. [f] Trans:cis ratio of 6:1 with **4** versus 4:1 with **7**. [g] Trans:cis ratio of 13:1 with **4** versus 10:1 with **7**. [h] 20% RCM to achiral seven-membered ring ether with **4** versus 40% with **7**. See text for details. [i] <2% RCM to achiral seven-membered ring ether with **4** versus 11% with **7**. See text for details.

powders in yields similar to those reported for **5** (~40% overall yield for seven steps from the requisite optically pure biphenol).[8] The percent cross-linking in the polymer backbone was estimated on the basis of the mol % of cross-linking agents (ligand plus divinylbenzene) employed in the synthesis of the polystyrene support.



6



7

The results of catalytic enantioselective metathesis reactions promoted by **6**[10] and **7** are depicted in Table 1; also illustrated are the outcomes of reactions initiated under identical conditions in the presence of homogeneous Mo complexes **1c** and **4** (left column). As the data in Table 1 indicate, **6** and **7** efficiently catalyze different ARCM (entries 1−3), AROM/CM (entries 4, 5; CM = cross metathesis), and AROM/RCM reactions (entries 6, 7). In all cases, reactions in the presence of the homogeneous complexes proceed to >90% conversion in a shorter period of time than those carried out with **6** and **7**; in two cases (entries 2, 3), transformations with **6** and **7** do not occur beyond 76% conversion.

Optical purities of products from transformations in the presence of **1c** and **4** versus those obtained through reactions initiated by **6** and **7** are comparable. However, there are examples (e.g., entries 1, 2) where, although generated in appreciable enantiopurity (81−91% ee), products derived from reactions with supported catalysts **6** and **7** are formed with lower asymmetric induction as compared to products from reactions that employ homogeneous catalysts **1c** and **4**. There are also instances (entries 4 and 5, Table 1) where supported catalyst **7** delivers AROM/CM products **15** and **17** in higher ee (95 and 98% ee, respectively) than products obtained with homogeneous catalyst **4** (90 and 94% ee). Despite such variations, the findings summarized in Table 1 illustrate that polystyrene-bound catalysts **6** and **7** promote enantioselective olefin metathesis with appreciable efficiency to afford products with levels of enantiopurity similar to those obtained with homogeneous catalysts **1c** and **4**.

Several additional points regarding the catalytic asymmetric transformations shown in Table 1 deserve mention:

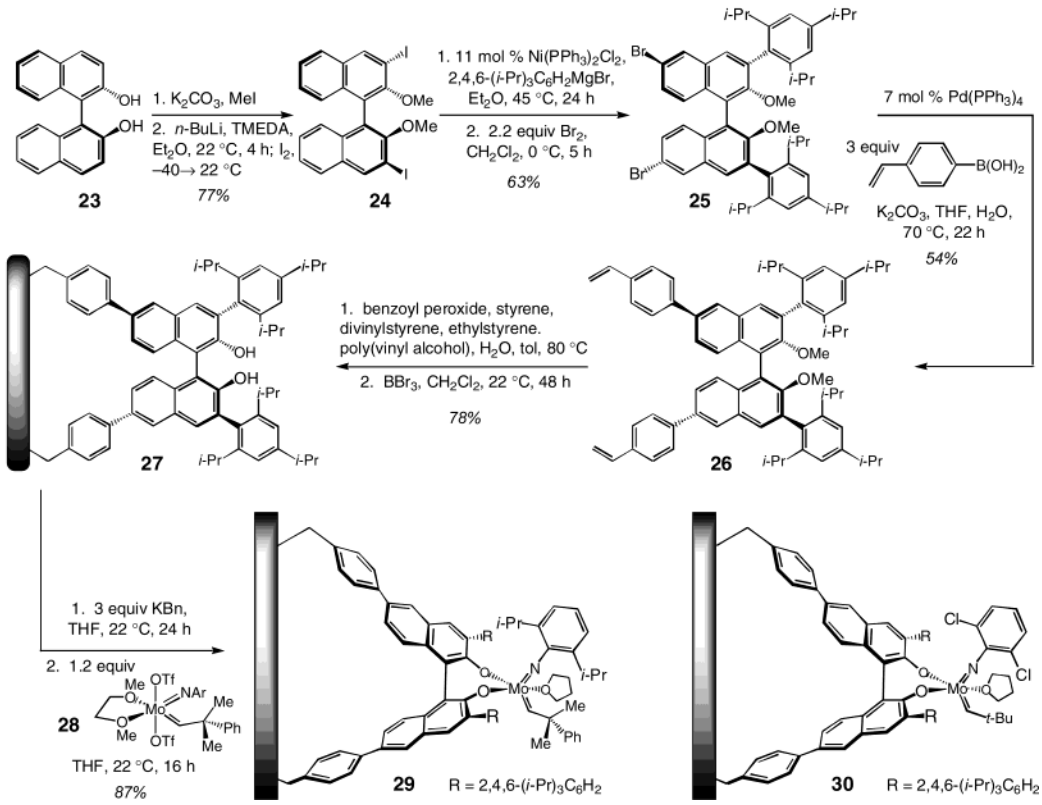
(1) Representative unpurified mixtures from which supported catalyst had been removed (simple filtration) were analyzed through ICP-MS analysis (for % Mo). In an unpurified sample of **11**, formed through catalysis with **6**, <1% Mo is present as contamination (by weight vs total amount introduced to the reaction initially). Such a degree of contamination is lower than that found in ARCM products formed when polystyrene-bound complex **5** is used (~5%).[8] In contrast, products obtained from **7** contain higher amounts of metal impurity. Thus, ICP-MS analysis of samples from reactions in entries 5−7 of Table 1 indicated 22%, 18%, and 38% Mo contamination. It is difficult to establish what processes (e.g., catalyst decomposition or hydrolysis by adventitious moisture) lead to the higher amounts of Mo residues in the above samples. However, a relevant feature of **1c** and its supported version **6** is that the metal center is more exposed and electrophilic than the transition metal center in the related 2,6-dimethylphenylimido or 2,6-diisopropylphenylimido complexes.

(2) The homogeneous Mo complex **4** and its supported variant **7** give rise to products in similar levels of stereoselectivity for the transformations shown in entries 4, 5 (trans:cis ratios of 6−4:1 for the formation of **15** and 13−10:1 for **17**). In the AROM/RCM processes illustrated in entries 6, 7 of Table 1, where achiral seven-membered ring ethers such as **22** (formed in reactions of **18**) are also generated, similar levels of selectivity are observed with homogeneous and analogous supported complexes. Thus, **22** is formed in 20% and 40% yields in the catalytic metatheses promoted by **4** and **7**, respectively (entry

22

(10) The structure of **6** is presented as a THF complex, because the corresponding homogeneous system is isolated as such (Schrock, R. R.; Jamieson, J. Y.; Dolman, S. J.; Miller, S. A.; Bonitatebus, P. J.; Hoveyda, A. H. *Organometallics* **2002**, *21*, 409−417). However, we have no proof that the supported complex also bears a THF ligand. The same applies to complexes **30** (Scheme 1) and **54** (Scheme 2).

Scheme 1. Preparation of Polystyrene-Supported Binaphthol-Based Chiral Mo Complexes



6); in the transformations depicted in entry 7 of Table 1, <2% (with **4**) and 11% (with **11**) of the corresponding achiral product are formed, respectively.

(3) Attempts to recycle the supported chiral catalysts led us to establish that reactions with recycled catalysts take place with excellent levels of enantioselectivity; however, the transformations proceed at decreasing rates. As an example, when the catalyst used (**7**) in the AROM/CM process shown in entry 5 of Table 1 was isolated through filtration (under inert atm) and resubjected to the same reaction conditions, 65% conversion was observed in 3 h, affording allylboronate **17** in 55% isolated yield and 98% ee (trans:cis ratio of 10:1).

2. Chiral Binaphtholate Complexes Bound to a Polystyrene Support. Catalytic activity and levels of asymmetric induction observed in reactions of binaphthol-based chiral Mo complexes (e.g., **2** in Chart 1) often complement the corresponding biphenol-based systems **1**.[3,11] Accordingly, we prepared polystyrene-supported Mo complexes **29** and **30** (Scheme 1) and examined their ability to promote enantioselective metathesis reactions that have been shown to be particularly suitable for catalysis by complexes **2**.

2a. Synthesis. Polystyrene-supported chiral Mo complexes **29** and **30** were prepared according to the route shown in Scheme 1. Commercially available optically pure binaphthol **23** was first converted to the derived bis(methyl ether), which was then induced to undergo regioselective iodination to afford **24** in 77% overall yield (for two steps). Subsequent Ni-catalyzed cross coupling of the aryl iodide with 2,4,6-(*i*-Pr)$_3C_6H_2MgBr$ in the presence of 11 mol % $(PPh_3)_2NiCl_2$,[11,12] followed by regioselective bromination, delivered dibromide **25** in 63% isolated yield. Pd-catalyzed coupling of **25** with *p*-vinylphenylboronic acid in the presence of 7 mol % $Pd(PPh_3)_4$ resulted in the formation of **26** in 54% yield after silica gel chromatography.[13] Bis(styrene) **26** was copolymerized in the presence of styrene and divinylbenzene (e.g., mol ratios 0.48 **26**, 33.6 styrene, and 1.48 divinylbenzene yield 5.5% cross-linked polymer), followed by removal of the methyl ether protecting groups with BBr_3 to afford supported chiral ligand **27** in 78% yield (two steps) as an off-white powder.

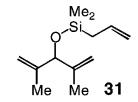
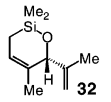
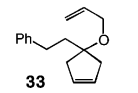
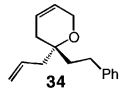
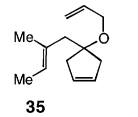
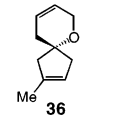
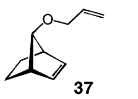
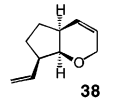
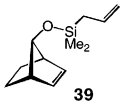
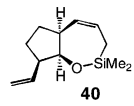
After the supported ligand was carefully dried (60 °C, 18 h), treatment with benzyl potassium at 22 °C (THF) led to the smooth formation of the bis(potassium) salt of **27** as a yellow powder. Filtration and treatment of the above-mentioned salt with Mo complex **28** afforded **29** as an orange-yellow powder in 87% overall yield. The resulting polymer was dried in vacuo (0.06 mm) for 24 h at 60 °C; elemental analysis through ICP/MS indicated 0.062 mmol/g loading, which is 53% of the theoretical loading. Supported chiral complex **30**, bearing a dichlorophenylimido ligand, was prepared through a similar procedure as a brown powder; elemental analysis indicated 97% Mo loading. On the basis of the structure of **2a**, one molecule of THF is likely bound to each transition metal center in **29** and **30**.[10] However, THF also appears to be ensconced in the polymer, because the weight of the polymer obtained is at times greater than theory, and NMR spectra of organic products obtained from reactions catalyzed by **29** or **30** clearly contain considerable amounts of additional THF.

(11) Zhu, S. S.; Cefalo, D. R.; La, D. S.; Jamieson, J. Y.; Davis, W. M.; Hoveyda, A. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1999**, *121*, 8251−8259.

(12) (a) Lingenfelter, D. S.; Helgeson, R. C.; Cram, D. J. *J. Org. Chem.* **1981**, *46*, 393−406. (b) Hu, Q. S.; Vitharana, D.; Ou, L. *Tetrahedron: Asymmetry* **1995**, *6*, 2123−2126.

(13) (a) Sellner, H.; Faber, C.; Rheiner, P. B.; Seebach, D. *Chem.-Eur. J.* **2000**, *6*, 3692−3705. (b) Hu, Q.-S.; Huang, W.-S.; Vitharna, D.; Zhang, X.-F.; Pu, L. *J. Am. Chem. Soc.* **1997**, *119*, 12454−12464.

Table 2. Catalytic Enantioselective Olefin Metathesis Promoted by Polystyrene-Supported Binaphthol-Based Chiral Mo Complex **29**[a]

			with complex ***2a***			*with supported complex* ***29***	
entry	substrate	product	mol (%); T (°C)	conv (%); time (h)	yield (%);[b] ee (%)[c]	conv (%); time (h)	yield (%);[b] ee (%)[c]
1	 **31**	 **32**	5; 60	98; 3	86; >98	>98; 3	86; >98
2	 **33**	 **34**	5; 50	98; 6	87; 91	96; 6	85; 65
3	 **35**	 **36**	9; 22	>98; 24	75; 80	85; 24	60; 98
4	 **37**	 **38**	5; 22	>98; 0.3	89; 84	70; 0.3	62; 84
5	 **39**	 **40**	5; 22	>98; 2	83; 91	>98; 2	89; 86

[a] All reactions were carried out under N_2 atm in C_6H_6, except for entry 3, where the reaction with **2a** was carried out in *i*-octane. The percent cross-linking in **29** was 3.8%. [b] Isolated yields after purification. [c] Enantioselectivities determined by chiral GLC analysis (β-dex for entries 2, 5 and CDGTA for entries 1, 3, 4).

2b. Application to Catalytic Enantioselective Synthesis. As the data shown in Table 2 indicate, supported chiral complex **29** efficiently promotes a variety of ARCM (entries 1, 2) and AROM/RCM reactions (entries 3−5). In the majority of cases, C−C bond-forming reactions are initiated with levels of efficiency (entries 1−3 and 5) similar to those promoted by chiral complex **2a**. Levels of asymmetric induction are similar in several cases. Although formation of unsaturated pyran **34** occurs with lower enantioselectivity in the presence of **29** than with **2a** as the catalyst (65% ee vs 91% ee), it is intriguing that, in one instance (entry 3), the transformation promoted by the supported catalyst provides the desired product in significantly higher enantiopurity (entry 3; 98% ee vs 80% ee). At present, we cannot offer a plausible proposal for the exact origin of such variations in enantioselectivity.

Several important issues regarding the transformations illustrated in Table 2 should be pointed out:

(1) In addition to **29**, related supported chiral complexes bearing varying degrees of cross-linking were prepared, and their catalytic activities were examined. As an example, a catalyst containing 57% cross-linking (0.29 deprotected **26**, 0.43 styrene, 0.28 divinylbenzene), isolated as a pale brown powder (82% Mo content by elemental analysis), exhibits significantly lower reactivity and selectivity (vs **29**). In the presence of the more highly cross-linked supported complex (under conditions identical to those shown for Table 2), ARCM of triene **31** proceeds to only 40% conv after 3 h to afford **32** in 88% ee (>98% conv and >98% ee with **29**). In a similar fashion, **33** → **34** occurs in only 23% conv in 6 h (vs 96% conv with **29**) to afford the desired product in 26% ee (vs 65% ee with **29**). It is likely that diffusion of substrates toward the active Mo sites is slower when the support is more rigid and less swollen (see below for additional examples).

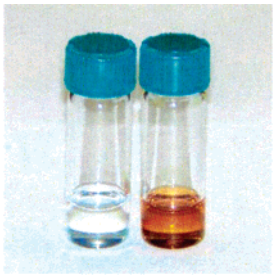


Figure 1. Sample of unpurified product mixture from a reaction (**39** → **40**, entry 5, Table 2) catalyzed by supported chiral complex **29** (left) versus a sample from the same transformation promoted by the corresponding homogeneous complex **2a**.

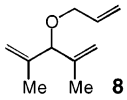
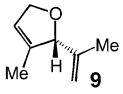
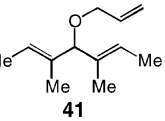
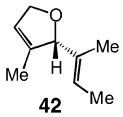
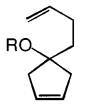
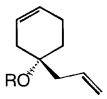
(2) Although ICP-MS analyses have not been carried out for every example in this study, the products obtained upon removal of the catalyst by filtration contain significantly lower amounts of Mo than those obtained with the homogeneous chiral complexes. Vials containing a solution of the unpurified siloxane **40** from the reaction of **29** (clear solution, left) and homogeneous complex **2a** (brown solution, right) are illustrated in Figure 1.

In the above studies (Tables 1 and 2), supported biphenolate catalysts bearing different aryl and alkylimido ligands provide reactivities and selectivities that are largely similar to those provided by the corresponding homogeneous systems. However, as the data in Table 3 demonstrate (compare with data in Table 2), with binaphtholate complexes, changing of the arylimido ligand, even though the same support is being utilized, does not necessarily lead to a bound chiral Mo complex that delivers levels of enantioselectivity competitive with those obtained through the use of their homogeneous counterparts. As shown in Table 3, although supported chiral complex **30** promotes various ARCM and AROM processes as efficiently as homogeneous system **2c** (Chart 1), the products are obtained in significantly lower optical purity. These observations suggest that additional and superior support structures are required if efficient bound variants of all chiral Mo metathesis catalysts are to become available. Nonetheless, supported catalysts represented by complexes **5** (Chart 1), **6** and **7** (Table 1), and **29** (Scheme 2) together can be used to effect nearly all Mo-catalyzed asymmetric olefin metathesis reactions reported thus far.

3. Chiral Mo Complexes Bound to Polynorbornene Supports. The polystyrene-supported catalysts described above promote various olefin metathesis reactions to afford the desired products with appreciable enantioselectivities. Nevertheless, the development of supported chiral catalysts that can be synthesized more efficiently remains an important future objective. One notable drawback of the polystyrene-supported complexes illustrated above is that the ligand is installed on the support first (e.g., Scheme 1) and the Mo complex is attached subsequently. Consequently, reactions involving any manipulation of the supported chiral ligand (e.g., demethylation, deprotonation, and treatment with Mo complex **28** in Scheme 1) cannot be monitored rigorously, and intermediates cannot be analyzed and purified. To address such complications, we have designed an alternative approach where the entire Mo complex is bound in the process of creating the polymer support.

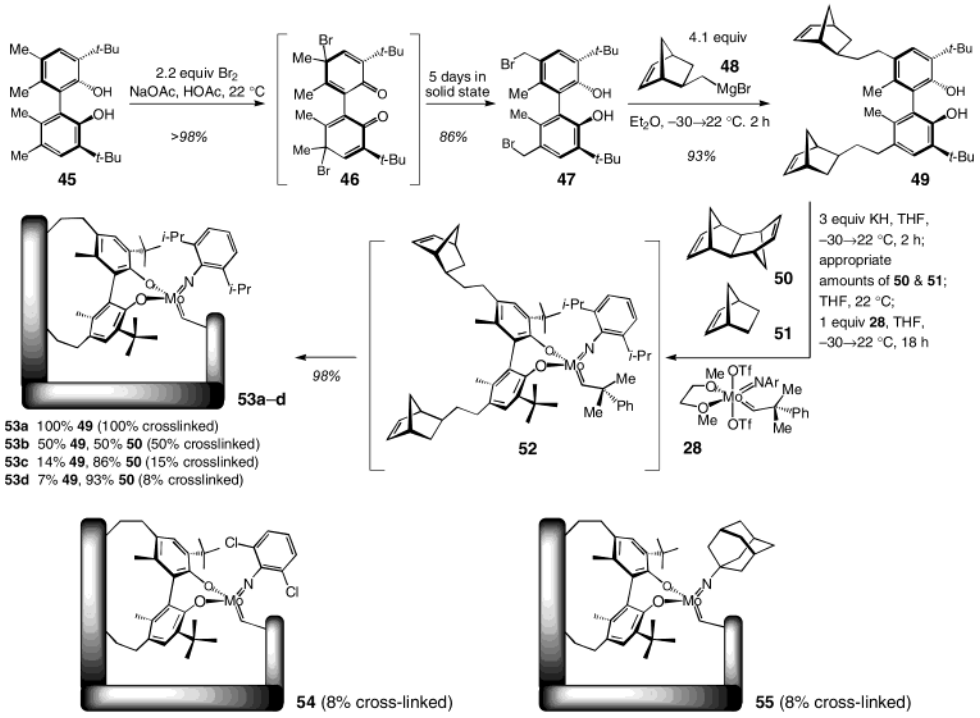
3a. Synthesis. As is illustrated in Scheme 2, treatment of optically pure biphenol **45** with Br_2 led to the formation of dibromide **46**, which after 5 days in the solid state rearranged

Table 3. Catalytic Enantioselective Olefin Metathesis Promoted by Polystyrene-Supported Binaphthol-Based Chiral Mo Complex **30**[a]

				with complex **2c**			with supported complex **30**	
entry	substrate	product		mol (%); T (°C)	conv (%); time (h)	yield (%);[b] ee (%)[c]	conv (%); time (h)	yield (%);[b] ee (%)[c]
1	 **8**	 **9**		5; 22	>98; 1	95; 86	42; 1	nd; 54
2	 **41**	 **42**		5; 22	>98; 1	95; 91	95; 1	90; 75
3	 **43**	 **44**	**a** R = Me	5; 4	98; 24	90; 90	98; 24	85; 66
4			**b** R = Bn	5; 4	98; 24	85; 85	98; 24	nd; 40

[a] All reactions were carried out under N_2 atm in C_6H_6. The % cross-linking in **30** was 3.8%. [b] Isolated yields after purification. [c] Enantioselectivities determined by chiral GLC analysis (CDGTA column). nd = not determined.

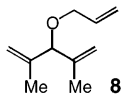
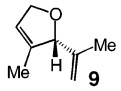
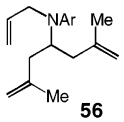
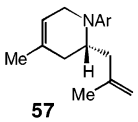
Scheme 2. Preparation of Polynorbornene-Supported Biphenol-Based Chiral Mo Complexes **53a**−**d**, **54**, and **55**



to afford bis(benzylbromide) **47** in 86% overall yield. Alkylation of **47** with alkylmagnesium bromide **48** afforded bis(norbornene) **49** in 93% isolated yield. Treatment of **49** with KH and various amounts of **50** and **51** (see below for behavior of different cross-linked polymers), followed by addition of 1 equiv of **28**, produced chiral complexes **53a**−**d**, via Mo alkylidene **52**, in near quantitative yield. All are orange-tan solids. It should be noted that, unlike alkylidene **52**, Mo complex **28** does not metathesize norbornene. Therefore, the synthesis of the polynorbornene support takes place only when one or both triflate ligands are substituted by an aryloxide ligand.

3b. Application to Catalytic Enantioselective Synthesis. Initially, 100% cross-linked supported complex **53a** was prepared, and its ability to promote representative enantioselective metathesis reactions was examined. As is illustrated in Table 4, these investigations indicated that **53a** is significantly less effective in promoting the ARCM of trienes **8** and **56** than the corresponding homogeneous complex **1a**. To address this complication, we decided to enhance the accessibility of the bound metal centers to substrates through the synthesis of chiral Mo complexes that have lower levels of cross-linking. Accordingly, by similar methods described above (Scheme 2), chiral complexes **53b**−**d** were prepared, and their ability to promote ARCM of **8** and **56** was investigated. As the additional data in Table 4 illustrate, as the degree of cross-linking is reduced, reaction efficiencies increase such that **53d** produces levels of reactivity nearly identical to those of the parent homogeneous complex **1a**. Thus, in the presence of 5 mol % **53d**, the ARCM of **8** and **56** proceeds to >90% conv within an hour to afford the desired nonracemic cyclic dienes in 87% and 96% ee. On

Table 4. Catalytic Enantioselective Olefin Metathesis Promoted by Various Cross-Linked-Supported Chiral Mo Complexes (**53a**−**d**)[a]

			1a	**53a** (100% x-linked)	**53b** (50% x-linked)	**53c** (15% x-linked)	**53d** (8% x-linked)
entry	substrate	product	time (h); conv (%);[b] ee (%)[c]	time (h); conv (%);[b] ee (%)[c]	time (h); conv (%);[b] ee (%)[c]	time (h); conv (%);[b] ee (%)[c]	time (h); conv (%);[b] ee (%)[c]
1	 **8**	 **9**	1; >98; 93	5; 22; 84	6; 34; 73	1; >98; 84	1; >98; 87
2[d]	 **56**	 **57**	1; >98; 98	5; 15; nd	6; 46; 73	1; >98; 95	1; 93; 96

[a] All reactions were carried out under N_2 atm in C_6H_6. [b] Conversions determined by ^1H NMR and GLC analysis. [c] Enantioselectivities determined by chiral GLC or HPLC analysis (entry 1, CDGTA (GLC); entry 2, Chiralcel OD (HPLC)). [d] Ar = *p*-BrC_6H_4.

the basis of the results obtained with chiral complex **53d** (Table 4), related dichloroarylimido complex **54** and adamantylimido complex **55** were also prepared with 8% cross-linked polynorbornene support structures.

The results of studies regarding the ability of polynorbornene-supported complexes **53d**, **54**, and **55** to initiate various catalytic ARCM and AROM processes are summarized in Table 5. Although in one case the desired product is isolated with significantly lower levels of optical purity (entry 10, Table 5) than those obtained with the homogeneous analogues, in the majority of cases the supported complexes afford reactivities and enantioselectivities similar to those of the homogeneous complexes. The above findings are particularly noteworthy because in many cases <5 mol % loading of the supported chiral complexes was used. ICP-MS analysis of representative unpurified product samples indicates low levels of Mo impurity. For example, samples of cyclic amines from reactions in entries 4 and 6 of Table 5 proved to contain only 1.5 and 5.4% Mo (by weight vs total amount introduced to the reaction initially).

As was mentioned briefly above, the increased activities of chiral complexes **53d**, **54**, and **55** could be ascribed to a higher flexibility and degree of swelling of the polynorbornene backbone as compared to polystyrene. Consequently, higher rates of diffusion of substrates to the catalyst sites are possible. There is, however, a significant disadvantage to polynorbornene-supported catalysts. As is illustrated in eq 1, "self-scavenging" through metathesis processes within the polymeric structure is able to release oligomeric pieces of the original polymeric backbone. As a result, the unpurified product mixtures from reactions shown in Table 5 contain detectable amounts of oligonorbornenes. Dichlorophenylimido complex **54** releases organic polymers upon suspension in pentane, diethyl ether, or benzene. Nonetheless, the high activity of the polynorbornene-supported catalysts, the excellent degrees of asymmetric induction observed in catalytic reactions promoted by such complexes, and the relative ease with which polymeric debris can be removed (chromatography) render the present class of chiral metathesis catalysts of notable utility in enantioselective organic and combinatorial synthesis.

It was our hope that the supported chiral complexes described here would be longer-lived than their homogeneous counterparts. However, as has been noted, activities diminish when catalysts were recycled several times, suggesting that bound catalysts still undergo decomposition. It is plausible that there remains

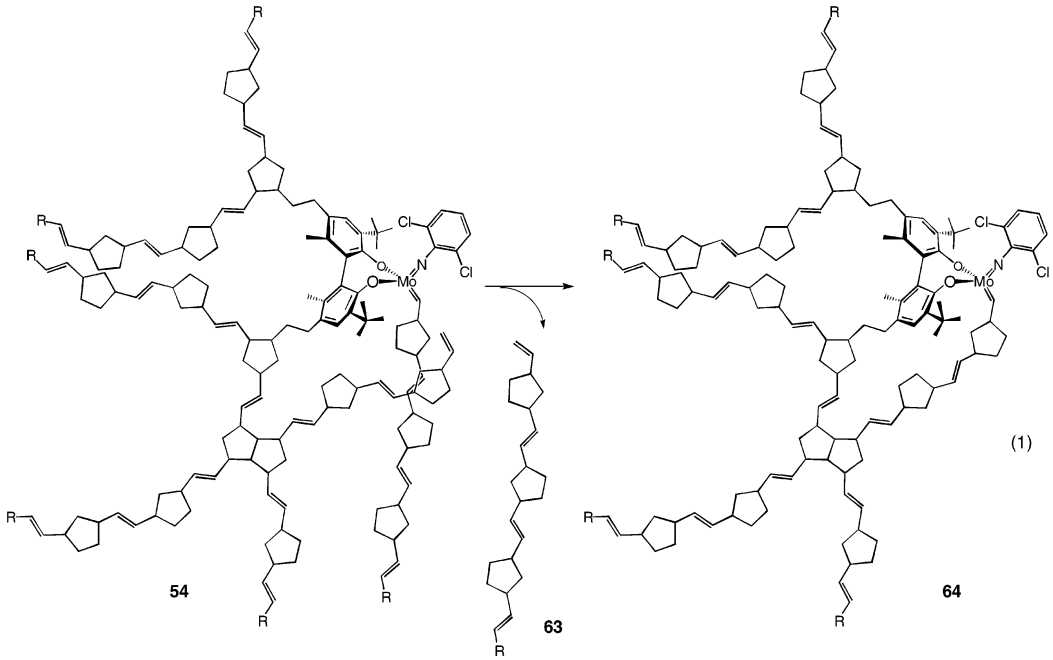
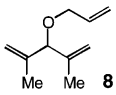
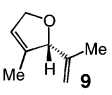
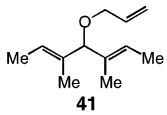
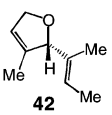
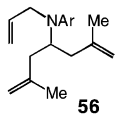
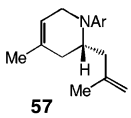
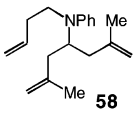
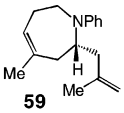
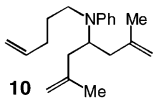
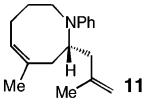
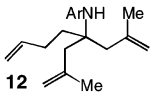
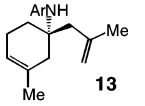
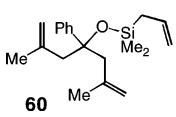
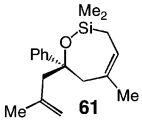
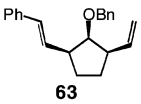
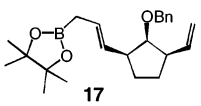


Table 5. Catalytic Enantioselective Olefin Metathesis Promoted by Polynorbornene-Supported Binaphthol-Based Chiral Mo Complexes **53d**, **54**, and **55**[a]

			with unbound catalyst			*with supported catalyst*		
entry	substrate	product	cat. mol (%);	conv (%); time (h)	yield (%);[b] ee (%)[c]	cat. mol (%);	conv (%); time (h)	yield (%);[b] ee (%)[c]
1	 **8**	 **9**	**1a**; 5	91; 1	85; 93	**53d**; 2.7	>98; 6	92; 87
2			**1c**; 5	>98; 1	95; 90	**54**; 2.6	>98; 1	96; 86
3	 **41**	 **42**	**1c**; 5	90; 1	86; 97	**54**; 2.5	98; 1	95; 96
4[d]	 **56**	 **57**	**1a**; 5	98; 0.5	98; 98	**53d**; 2.7	93; 2	88; 95
5	 **58**	 **59**	**1a**; 5	98; 6	95; 95	**53d**; 5	78; 6	70; 89
6	 **10**	 **11**	**1c**; 5	98; 0.5	98; 98	**54**; 5	85; 2	67;96
7[e]	 **12**	 **13**	**1c**; 5	98; 0.5	91; 62	**54**; 2.7	98; 2	76; 66
8	 **60**	 **61**	**1a**; 5	98; 2	97; 93	**53d**; 5	77; 8	62; 91
9	 **62**	 **63**	**4**; 5	98; 0.5	98; >98	**53d**; 2.7	98; 2	94; >98
10	 **16**	 **17**	**4**; 5	>98; 3	78; 90	**55**; 5	98; 12	88; 73

[a] All reactions were carried out under N_2 atm in C_6H_6. The level of cross-linking in all catalysts was 8%. [b] Isolated yields after purification. [c] Selectivities determined by chiral GLC or HPLC analysis (entries 1−3 with CDGTA column (GLC); entries 4−7 with Chiralcel OD column (HPLC); entry 8 with Chiralcel OJ column (HPLC); entry 9 with Chiralpak AD column (HPLC); and entry 10 with Chiralpak AS column (HPLC)). [d] Ar = *p*-BrC_6H_4. [e] Ar = *o*-$(OMe)C_6H_4$.

sufficient structural mobility within the low percent cross-linked polymers such that bimolecular decomposition of (especially) methylene species is feasible, particularly because the concentration of the metal centers within such a polymer is significantly higher than it would be in the related homogeneous system. Moreover, we have collected evidence suggesting that metallacyclobutane intermediates can decompose, especially in the presence of ethylene;[14] such a process might take place even at isolated metal centers of a supported system.

It should be noted that the synthesis of chiral Mo complexes attached to polymers obtained through ROMP procedures was recently reported.[15] One such complex is a polynorbornene-supported version of **1a** (i.e., a catalyst closely related to **53**), except that no additional cross-linking agent (e.g., divinylbenzene) was employed. These researchers treated **47** with a norbornylmethoxide and polymerized the resulting ligand (related to **49**) with a Ru-based metathesis catalyst. The metal was attached in a manner similar to that reported in this study. With these catalysts, observed enantioselectivities are similar to those found when the related polystyrene-based catalyst was employed.[8] Although diminution in optical purity of products was not detected, and contamination of the final product proved to be less than 5% of the total Mo introduced initially, reactivities were diminished upon recycling of the catalyst. These researchers indicate that, in contrast to what we have found here with the less sterically crowded and highly reactive catalyst systems **54** and **55**, olefins in the polymer backbone of

(14) (a) Tsang, W. C. P.; Schrock, R. R.; Hoveyda, A. H. *Organometallics* **2001**, *20*, 5658−5669. (b) Robbins, J.; Bazan, G. C.; Murdzek, J. S.; O'Regan, M. B.; Schrock, R. R. *Organometallics* **1991**, *10*, 2902−2907.

(15) (a) Buchmeiser, M. R.; Kroll, R.; Wurst, K.; Schareina, T.; Kempe, R.; Eschbaumer, C.; Schubert, U. S. *Macromol. Symp.* **2001**, *164*, 187−196. (b) Buchmeiser, M. R.; Wurst, K. *J. Am. Chem. Soc.* **1999**, *121*, 11101−11107. (c) Kroll, R.; Eschbaumer, C.; Schubert, U. S.; Buchmeiser, M. R.; Wurst, K. *Macromol. Chem. Phys.* **2001**, *202*, 645−653. (d) Kroell, R. M.; Schuler, N.; Lubbad, S.; Buchmeiser, M. R. *Chem. Commun.* **2003**, 2742−2743.

their supported complex are not attacked during catalytic metathesis reactions.

Conclusions

We have synthesized and measured the catalytic activities of seven different supported chiral Mo-based catalysts for enantioselective olefin metathesis. Together, this collection of chiral complexes offers access to a wide range of optically enriched small organic molecules that cannot be prepared easily by alternative methods and can be functionalized readily to access other chiral entities. In most cases, simple filtration of the supported catalyst affords products that contain significantly lower levels of metal impurity than products obtained with homogeneous chiral complexes. Of particular note is that in many instances activity and enantioselectivity levels are comparable to those observed with homogeneous catalysts. Also noteworthy is the facility with which the supported complexes are synthesized, particularly those that are bound to polynorbornene structures, and the dramatic effect of the levels of cross-linking on the catalytic activity and product enantiopurity.

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Supporting Information Available: Experimental procedures and spectral and analytical data for supported catalysts and representative products. This material is available free of charge via the Internet at http://www.acs.pubs.org.

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