direct methods and refined using the full-matrix least-squares on F^2 with all non-H atoms anisotropically defined (except the external sodium atom and the solvent molecules). For 4426 observed reflections ($I > 2\sigma(I)$) and 921 parameters, the conventional R is 0.0879 ($wR2 = 0.2670$ for 10835 independent reflections). Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-154158 (**4**) and CCDC-154159 (**8**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

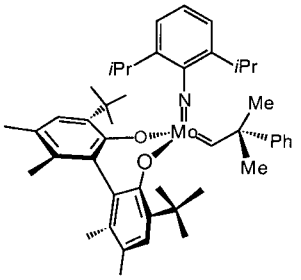
A Readily Available and User-Friendly Chiral Catalyst for Efficient Enantioselective Olefin Metathesis**

Sarah L. Aeilts, Dustin R. Cefalo, Peter J. Bonitatebus, Jr., Jeffrey H. Houser, Amir H. Hoveyda,* and Richard R. Schrock*

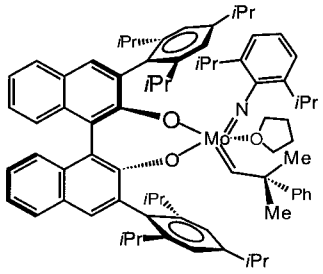
We recently reported the synthesis and utility of various Mo-based chiral catalysts that promote enantioselective olefin metathesis.[1] These complexes, represented by (*S*)-**1**[2] and (*R*)-**2**[3], are the only existing class of chiral catalysts that efficiently and selectively promote the formation of optically pure or enriched carbo- and heterocycles through asymmetric ring-closing[4] and ring-opening metathesis (ARCM and AROM, respectively).[5] One notable difference between **1** and **2** is that biphenolate **1** initiates selective ARCM of five-membered rings and binaphtholate **2** is often the catalyst of choice for the enantioselective synthesis of six-membered analogues.[3]

From a practical point of view, binaphthol-based systems (e.g., **2**) have a significant advantage: the synthesis of the optically pure diolate begins from the inexpensive and commercially available (*R*)- or (*S*)-binaphthol.[6] In contrast, access to the optically pure biphenol ligand in **1** and its derivatives requires resolution of the racemic samples by fractional crystallization of the derived phosphorus(v) mentholates.[2] We therefore judged that a chiral Mo complex that bears a "biphenol-type" ligand, but is synthesized from the readily available optically pure binaphthol, would be an important and valuable addition to this unique class of chiral catalysts. We also suspected that such a catalyst could exhibit greater generality: its reactivity and selectivity trends may overlap those exhibited by the biphenol- (e.g., **1**) *and* binaphthol-based complexes (e.g., **2**).

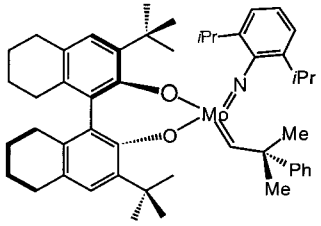
Herein, we report the synthesis, structure, and synthetic utility of chiral complex **3**, a Mo catalyst that resembles a biphenol-based catalyst (**1**) but, similar to **2**, is easily prepared from optically pure binaphthol. We demonstrate that complex **3** offers a solution to the important problem of practicality in Mo-catalyzed asymmetric olefin metathesis. The new catalyst may be prepared from commercially available starting materials and can be used in situ, without isolation, to effect enantioselective olefin metathesis.



(*S*)-**1**



(*R*)-**2**



(*R*)-**3**

Preparation of chiral catalyst **3** (Scheme 1) begins with catalytic hydrogenation of commercially available, optically pure (*R*)-**4** in the presence of PtO_2[7] under 100 psi (6.9 atm, 690 KPa) H_2 in glacial acetic acid (HOAc).[8] In a 20 g (69.9 mmol) scale reaction, the desired octahydrobinaphthol **5** is formed in >98% yield (cream-colored powder).[9] Installation of *t*Bu groups at the C2 and C2′ sites is carried out by acid-catalyzed alkylation with isobutylene, a procedure that involves the difficult separation of the desired functionalized binaphthol from adventitious oligoisobutylenes; pure dialkylated product is obtained after chromatography on silica gel in 40% yield. However, when the unpurified mixture is directly treated with 2 equivalents of KH, the derived dipotassium salt (*R*)-**6** is isolated in 85% yield. Through this procedure, oligoisobutylene impurities are removed by washing with pentane. The resulting dipotassium salt (*R*)-**6** (soon to be commercially available through Strem) does not need further purification before it is employed in the synthesis of **3**.[10]

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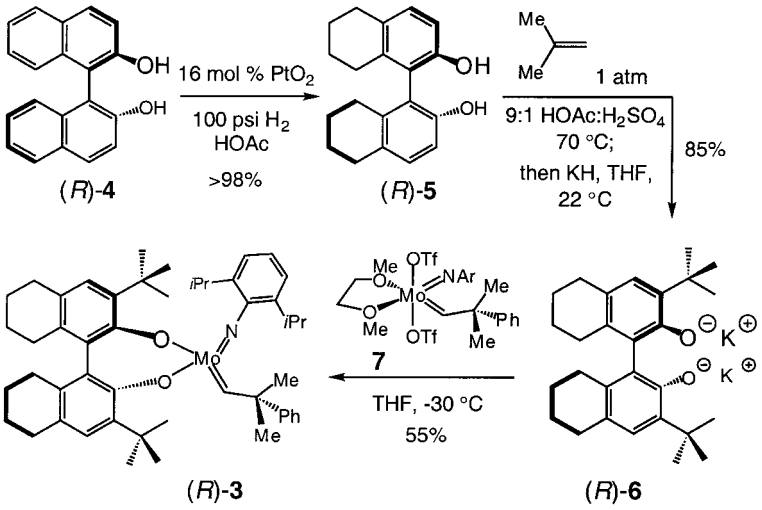


Scheme 1. Synthesis of chiral catalyst **3**.

Complex (*R*)-**3** is synthesized by treatment of (*R*)-**6** with bis(triflate) **7** at $-30\,^{\circ}C$ in THF in 55% yield as an orange solid after recrystallization from MeCN to afford (*R*)-**3**·MeCN, a complex that releases the bound solvent in vacuo, yielding analytically pure (*R*)-**3**.[11] The (*R*)-**3**·MeCN complex allows for facile isolation of the chiral catalyst, since solvent free **3** is soluble in hydrocarbons (e.g., pentane and toluene) and Et_2O and is recrystallized with difficulty even from these relatively nonpolar media. We have prepared *rac*-**3** in an analogous manner and find that it can be recrystallized far more readily (vs. (*R*)-**3**) to deliver red needles from *n*-octane.

Crystals of *rac*-**3** were suitable for X-ray crystallography (Figure 1).[12] Distances and bond angles in **1**[4b] and **3**, listed in Table 1 for comparison, indicate that the geometry of the

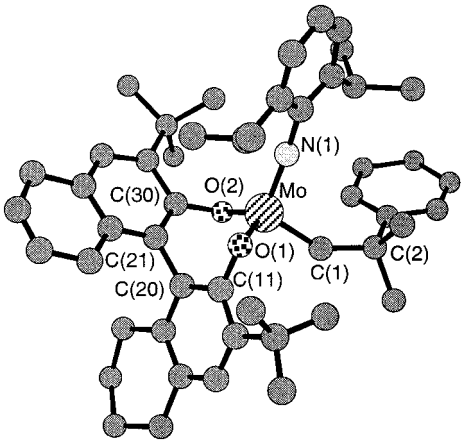


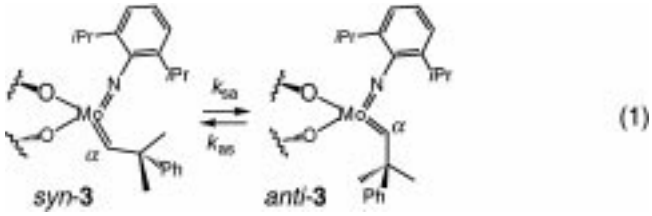
Figure 1. X-ray structure of **3**.

chiral diolate in **3** deviates significantly from that of the biphenolate in **1**. In particular, the dihedral angle C(30)-C(21)-C(20)-C(11) is smaller in **3** than in **1** (88.6° vs. 102.2°). Other structural differences between **1** and **3** include: a smaller O-Mo-O angle in **3** (119.9(5)° vs. 127.0(2)°), and larger Mo-O-C bond angles in **3** (102.8(7)° and 102.0(8)° vs. 97.1(4)° and 96.8(4)°). The above features are consistent with a greater steric repulsion between the cyclohexyl rings of the chiral diolate and the imido and alkylidene groups, as compared to the smaller Me substituents in **1**.

Table 1. Selected bond lengths [Å] and angles [°] in chiral Mo complexes **1** and **3**.

	Complex **1**	Complex **3**
Mo-N(1)	1.738(6)	1.761(11)
Mo-C(1)	1.885(10)	1.919(13)
Mo-O(1)	1.999(5)	1.949(8)
Mo-O(2)	2.006(5)	1.980(9)
N(1)-Mo-C(1)	105.2(3)	106.0(6)
N(1)-Mo-O(1)	110.2(2)	105.9(5)
N(1)-Mo-O(2)	107.9(3)	115.0(5)
C(11)-O(1)-Mo	97.1(4)	102.8(7)
C(30)-O(2)-Mo	96.8(4)	102.0(8)
O(1)-Mo-O(2)	127.0(2)	119.9(5)
C(2)-C(1)-Mo	143.8(7)	146.4(11)
C(30)-C(21)-C(20)-C(11)	102.2(8)	88.6(15)

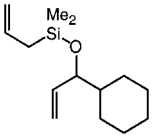
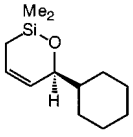
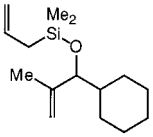
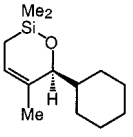
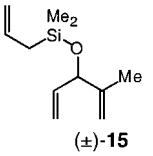
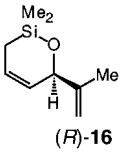
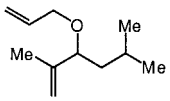
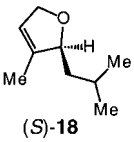
Crystals of *rac*-**3** exist as *syn*-alkylidene isomers [Eq. (1)]. Nonetheless, in the ^1H NMR spectrum of **3** (C_6D_6, 22 °C), in



addition to a resonance at $\delta = 10.97$ assigned to the alkylidene CH in the *syn* isomer (determined by ^{13}C satellite resonances), there is another resonance at $\delta = 12.76$, assigned to the alkylidene CH in the *anti* isomer. At 22 °C, the *syn*/*anti* equilibrium constant is ~13, and the *syn* and *anti* CH resonance signals sharpen when the sample is cooled to 0 °C and broaden when it is heated to 70 °C. The latter observation is consistent with interconversion of the two isomers on the NMR time scale. We have calculated a rate constant (k_{sa}, [Eq. (1)]) for *syn* to *anti* conversion by spin-saturation transfer experiments. At 20 °C, $k_{sa} = 0.21(1)\ s^{-1}$, a value that is similar in magnitude to that measured for **1** ($0.50\ s^{-1}$).[13, 14] These findings suggest that both *syn* and *anti* alkylidenes are probably accessible in solution. Therefore, it may well be the relative rates of the subsequent steps (e.g., metallacyclobutane formation) that determine the identity of the faster reacting (kinetic resolution) or major enantiomer (asymmetric synthesis).

The data summarized in Table 2 illustrate some of the unique attributes of chiral complex **3** in connection with its ability to catalyze the kinetic resolution[15] of polyenes. Catalytic ARCM in entries 1–3 indicate that **3**, similar to the biphen-based catalyst **1** but in contrast to binaptholate **2**, efficiently promotes the kinetic resolution of **11**.[16] There is no significant difference in the activity of **3** versus **1**, and the amount of dimeric side product[17] generated by **3** remains relatively small. Another example is the catalytic resolution of diene **13** in entries 4–6; although more dimer is generated than

Table 2. Mo-catalyzed kinetic resolutions through ARCM.[a]

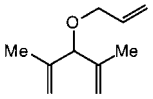
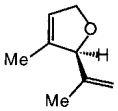
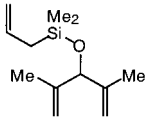
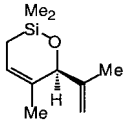
Entry	Substrate	Product[b]	Catalyst	Time	Conv [%][c]	Dimer [%]	k_{rel}[d]
1	 (±)-**11**	 (*S*)-**12**	**1**	2 min	52	< 2	> 25
2			**2**	5 min	63	< 2	3.0
3			**3**	2 min	58	7	> 25
4	 (±)-**13**	 (*S*)-**14**	**1**	1 h	54	47	< 2.0
5			**2**	1 h	60	8	> 25
6			**3**	1 h	65	45	> 25
7	 (±)-**15**	 (*R*)-**16**	**1**	5 min	51	< 2	2.0
8			**2**	30 min	41	< 2	5.0
9			**3**	5 min	42	18	20
10	 (±)-**17**	 (*S*)-**18**	**1**	5 min	59	< 2	11
11			**2**	6 h	44	< 2	< 2.0
12			**3**	1 h	58	< 2	23

[a] Conditions: 5 mol % catalyst, Ar atmosphere, C_6H_6. [b] Identity of products shown is for reactions promoted with catalysts **2** and **3** ((*R*)-binaphtholates); the opposite isomer is generated with **1** ((*S*)-biphenolate). [c] Conversion determined by analysis of the 400 MHz ^{1}H NMR spectrum of the unpurified mixture. [d] Enantioselectivity determined by gas-liquid chromatography (GLC) analysis (CHIRALDEX-GTA by Alltech) in comparison with authentic racemic material. Relative rate determined based on the recovered substrate (see ref. [16]).

in reactions involving diene **11**, complex **3** provides similar levels of selectivity observed with binaphthol **2** but not **1**. In the catalytic resolution of **15** (entries 7–9), **3** affords larger amounts of the dimeric product. It is however only catalyst **3** that initiates a resolution with $k_{rel} = 20$ (entry 9); biphenolate **1** or binaphtholate **2** fail to deliver substantial levels of enantioselection (entries 7 and 8). Entries 10–12 provide an example of a catalytic kinetic resolution of a 1,6-diene, a class of substrates for which complex **1** is particularly well suited.[4a] Complex **3** catalyzes ARCM even more efficiently and enantioselectively than **1**. The above data collectively illustrate that the more readily available **3** promotes catalytic ARCM with similar or higher levels of selectivity than **1**.

The data in Table 3 showcase representative catalytic asymmetric desymmetrization processes involving catalysts **1**–**3**. With triene **19** as the substrate, catalyst **3** is more efficient than **1** and affords the desired compound **20** with similar levels of selectivity as with **1** and **2**. In the case of the catalytic ARCM of silyl triene **21**, another representative of a class of substrates for which **2** is most suitable,[3] catalyst **3** not only performs far more efficiently and selectively than **1**, it delivers (*R*)-**22** in 96 % *ee* and 54 % isolated yield. The catalytic ARCM effected by **3** (entry 6) remains synthetically useful, but is less efficient and selective than that effected with **2** as the catalyst (entry 5). Nevertheless, the outcome shown in entry 6 of Table 3 is delivered by a catalytic system (**3**) that

Table 3. Enantioselective desymmetrization through Mo-catalyzed ARCM.[a]

Entry	Substrate	Product[b]	Catalyst	Time [h]	*T* [°C]	Conv [%][c]	Dimer [%]	Yield [%][d]	*ee* [%][e]
1	 **19**	 (*S*)-**20**	**1**	6	22	52	< 2	86	93
2			**2**	1	22	63	< 2	72	90
3			**3**	1	22	58	7	81	92
4	 **21**	 (*S*)-**22**	**1**	24	22	50	32	17	65
5			**2**	3	60	> 98	< 2	98	> 98
6			**3**	3	80	69	11	54	96

[a]–[c] See Table 1. [d] Yields of isolated products after silica gel chromatography. [e] Enantioselectivity determined by GLC analysis (CHIRALDEX-GTA by Alltech) in comparison with authentic racemic material.

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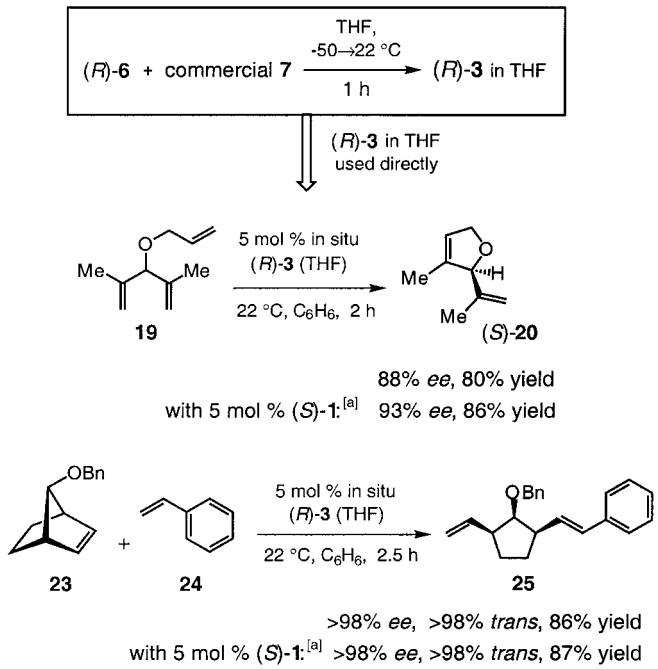
can perform as well or better in cases where catalyst **2** is entirely ineffective (see entries 1–3 and 10–12, Table 2).

Not only is catalyst **3** more easily prepared than **1**, more importantly, as illustrated in Scheme 2, a solution of this chiral complex, obtained by the reaction of commercially available



Scheme 2. In situ preparation and utility of chiral metathesis catalyst **3**. [a] Reactions were promoted by (*S*)-**1** to afford the enantiomers of the products shown.

reagents bis(potassium salt) **6** (Strem) and Mo triflate **7** (Strem), can be directly used to promote enantioselective metathesis (see the Experimental Section for procedure). Regarding the in situ catalyst preparation and use, it must be noted that: 1) similar levels of reactivity and selectivity are obtained with in situ **3** as with isolated and purified **1** or **3** (see Scheme 2),[18] 2) asymmetric olefin metatheses proceed with equal efficiency and selectivity with the same stock solutions of (*R*)-**6** and **7** after two weeks, 3) the use of a glove box, Schlenck equipment, or vacuum lines is not necessary (even with the two-week old solutions). These findings demonstrate that chiral catalyst **3** is highly user-friendly. An efficient and active catalyst solution can be accessed by the pre-mixing of a readily available salt ((R)-**6**) and a commercially available Mo triflate (**7**); this active catalyst can be used directly, without further purification, in a typical fume hood (under N_2). Noteworthy is that the formation of **25** (Scheme 2) cannot be effected by the new generation of imidazolinium-based Ru catalysts (5 mol % or one equivalent catalyst at 22 or 75 °C).[19] That is, in addition to being easy to use (commonly a Ru catalyst trademark), chiral Mo-based complexes disclosed herein offer reactivity and selectivity levels that remain unavailable with Ru-based complexes.

In summary, we disclose the synthesis, structure, and synthetic utility of a Mo-based chiral metathesis catalyst that is prepared more easily and efficiently than **1**, can be used in situ in a regular fume hood (vs. a dry box), and without the need for Schlenck or other specialty glassware. Catalyst **3** promotes ARCM reactions with equal or higher levels of efficiency and selectivity than **1**. Moreover, since **3** shares certain structural features with binaptholate **2**, it may also be employed to effect asymmetric olefin metatheses that are typically best performed by the latter complex. The advent of chiral catalyst **3** elevates the status of Mo-catalyzed asymmetric olefin metathesis to a practical as well as efficient and unique method for the synthesis of optically enriched or pure organic molecules.

Experimental Section

(*R*)-**6**:[20] Diol (*R*)-**5** (7.0 g, 23.8 mmol) was placed in a 88 mL pressure vessel and sulfuric acid (7 mL) and glacial acetic acid (63 mL) were added. The vessel was flushed with isobutylene and pressurized to 1 atm. The mixture is heated to 70°C and allowed to stir for 14 h, at which time pressure was released, water (35 mL) added, and the biphasic mixture washed with Et_2O (2 × 20 mL). Organic layers were washed with a saturated solution of $NaHCO_3$ (2 × 20 mL), and dried over $MgSO_4$. Solvent removal in vacuo left behind a tan liquid; subsequent vacuum distillation (85 °C, 0.03 mm Hg) partially removed adventitious isobutylenes to afford impure (*R*)-**5** as a brown solid. The solid was dissolved in THF (20 mL) and KH (1.91 g, 47.6 mmol) added slowly in portions (22 °C, within 20 min). The resulting mixture was stirred for 1 h at 22 °C, then diluted with Et_2O (10 mL) and THF (5 mL), and filtered through Celite. Removal of the volatiles in vacuo produced a brown solid, which was washed with pentane (4 × 10 mL) and dried in vacuo to yield 9.80 g of (*R*)-**6** as cream-colored powder (20.3 mmol, 85 % yield). This material was used directly in the synthesis of **3**, described below.

(*R*)-**3**: Diolate (*R*)-**6** (500 mg, 1.04 mmol) was dissolved in cold (−30 °C) THF (10 mL at −30 °C) and added to a stirred solution of **7** (820 mg, 1.04 mmol) in cold THF (25 mL at −30 °C). The solution was warmed to 22 °C and the mixture stirred for 0.5 h. Volatiles were removed in vacuo to afford a brown solid. The product was taken up in pentane (20 mL) and filtered. The pentane was subsequently removed in vacuo to give the unpurified product as a dark orange powder. Precipitation from MeCN delivered **3**·MeCN as an orange solid (1.67 g, 55 % yield), which was later freed of acetonitrile in vacuo. ^{1}H NMR (C_6D_6): δ = 12.76 (s, 0.08 H, MoCH *anti*), 10.97 (s, 0.92 H, $^1J_{C,H}$ = 120, MoCH *syn*), 7.46 (d, $^3J_{H,H}$ = 7.0, 2 H, neophyl *o*-H), 7.39 (s, 1 H, aromatic H), 7.20 (t, $^3J_{H,H}$ = 7.5, 2 H, neophyl H), 7.12 (s, 1 H, aromatic H), 7.04 (t, $^3J_{H,H}$ = 7.5, 1 H, neophyl *p*-H), 6.93 (s, 3 H, imido aromatic H), 3.67 (sept, $^3J_{H,H}$ = 6.6, 2 H, C*H*(CH_3)$_2$), 2.69 (t, $^3J_{H,H}$ = 5.5, 2 H, cyclohexyl H), 2.60 (qt, $^3J_{H,H}$ = 2.3, 3 H, cyclohexyl H), 2.50 (dt, $^3J_{H,H}$ = 1.8, 1 H, cyclohexyl H), 2.30 (dt, $^3J_{H,H}$ = 1.8, 1 H, cyclohexyl H), 2.00 (m, 2 H, cyclohexyl H), 1.87 (s, 3 H, C(CH_3)$_2$Ph), 1.62 (s, 9 H, *t*Bu), 1.55 (s, 9 H, *t*Bu), 1.53 (m, 8 H, cyclohexyl H), 1.15 (d, $^3J_{H,H}$ = 6.5, 6 H, CH(CH_3)$_2$), 1.11 (s, 3 H, C(CH_3)$_2$Ph), 0.93 (d, $^3J_{H,H}$ = 7.0, 6 H, CH(CH_3)$_2$); ^{13}C NMR (C_6D_6): δ = 275.9, 155.1, 154.4, 153.8, 151.5, 146.6, 140.2, 138.3, 136.5, 135.8, 132.2, 131.7, 131.6, 130.5, 128.8, 128.6, 128.6, 127.8, 127.8, 126.3, 123.7, 53.5, 36.0, 35.7, 30.7, 30.5, 29.2, 28.1, 27.8, 23.9, 23.8, 23.6, 33.4, 33.0, 30.8, 30.4, 24.7, 24.6, 23.5; elemental analysis calcd (%) for $C_{50}H_{65}MoNO_2$: C 74.32, H 8.11, N 1.73; found: C 74.22, H 8.04, N 1.70.

Representative procedure for in situ use of catalyst **3**: Solutions of (*R*)-**6** (48.3 mg, 0.100 mmol, 1 mL THF) and **7** (79.2 mg, 0.100 mmol, 1 mL THF) were prepared and cooled to −50 °C (under N_2). Subsequently, 100 µL (0.01 mmol) of each solution was withdrawn, mixed in a flask cooled to −50 °C, and then warmed to 22 °C (1 h). At this point, a solution of **19** (34.4 mg, 0.2 mmol, corresponding to 5 mol % loading of in situ **3**) in C_6H_6 (2 mL) was added and the mixture stirred for 2 h at 22 °C (95 % conv). Typical work up,[3] followed by chromatography on silica gel affords (*S*)-**20** in 88 % *ee* and 80 % yield.

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[1] For a brief overview of catalytic asymmetric olefin metathesis, see: a) A. H. Hoveyda, R. R. Schrock, *Chem. Eur. J.* **2001**, *7*, 945–950. For a recent general review on catalytic metathesis, see: b) A. Fürstner,

Angew. Chem. **2000**, *112*, 3140 – 3172; *Angew. Chem. Int. Ed.* **2000**, *39*, 3012 – 3043.
[2] B. Alexander, D. S. La, D. R. Cefalo, A. H. Hoveyda, R. R. Schrock, *J. Am. Chem. Soc.* **1998**, *120*, 4041 – 4042.
[3] S. Zhu, D. R. Cefalo, D. S. La, J. Y. Jamieson, W. M. Davis, A. H. Hoveyda, R. R. Schrock, *J. Am. Chem. Soc.* **1999**, *121*, 8251 – 8259.
[4] a) D. S. La, J. B. Alexander, D. R. Cefalo, D. D. Graf, A. H. Hoveyda, R. R. Schrock, *J. Am. Chem. Soc.* **1998**, *120*, 9720 – 9721; b) J. B. Alexander, R. R. Schrock, W. M. Davis, K. C. Hultzsch, A. H. Hoveyda, J. H. Houser, *Organometallics* **2000**, *19*, 3700 – 3715; c) G. S. Weatherhead, J. H. Houser, J. G. Ford, J. Y. Jamieson, R. R. Schrock, A. H. Hoveyda, *Tetrahedron Lett.* **2000**, *41*, 9553 – 9559.
[5] a) D. S. La, J. G. Ford, E. S. Sattely, P. J. Bonitatebus, Jr., R. R. Schrock, A. H. Hoveyda, *J. Am. Chem. Soc.* **1999**, *121*, 11 603 – 11 604; b) G. S. Weatherhead, J. G. Ford, E. J. Alexanian, R. R. Schrock, A. H. Hoveyda, *J. Am. Chem. Soc.* **2000**, *122*, 1828 – 1829; c) D. R. Cefalo, A. F. Kiely, M. Wuchrer, J. Y. Jamieson, R. R. Schrock, A. H. Hoveyda, *J. Am. Chem. Soc.* **2001**, *123*, in press.
[6] Optically pure binaphthol (both antipodes) is commercially available from Kankyo Kagaku Center Co., Ltd. at approximately one U.S. dollar per gram.
[7] The PtO_2 catalyst was recovered and reused in three additional 20 g scale reactions without significant loss of activity. For the original hydrogenation procedure, see: D. S. Lingenfelter, R. C. Helgeson, D. J. Cram, *J. Org. Chem.* **1981**, *46*, 393 – 406.
[8] Catalytic hydrogenation under lower pressures of H_2 are significantly slower (e.g., consumption of **4** after one week at 45 psi (310 kPa, 3 atm)) and some partially hydrogenated product is often present.
[9] Optically pure **5** is available from Kankyo Kagaku Center, but at nearly ten times the cost of (*R*)- or (*S*)-**4**.
[10] To establish the enantiopurity of dialkylation product (*R*)-**6** and its corresponding diol, the derived mentholate phosphate was prepared and its ^{31}P NMR spectrum was compared to that of a sample of *rac*-phosphate. The spectrum of a racemic sample exhibits two resonances at $\delta = 144.4$ and 139.2 (1:1 ratio); that of (*R*)-phosphate contains a single resonance at $\delta = 144.9$. Oxidation to the corresponding phosphonate and comparison of its ^{31}P NMR spectrum to that of the corresponding racemic mixture was carried out as well ($\delta = -4.9$ and -3.3 for the *rac* sample and -4.9 for the (*R*)-isomer).
[11] Protonated (*R*)-**6** may also be treated with two equivalents of benzyl potassium and one equivalent of Mo triflate **7** (22 °C, THF) to afford optically pure (*R*)-**3** in 41 % isolated yield after purification.
[12] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-155703. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).
[13] Values for k_{sa} (determined at 10 °C intervals from 0 to 30 °C) were used to establish the activation parameters for **3** from an Eyring plot ($R^2 = 0.994$); these calculations give $\Delta H^{\ddagger} = 15.7(0.9)$ kcal mol^{-1} and $\Delta S^{\ddagger} = -8(3)$ kcal K^{-1} mol^{-1}).
[14] The variable temperature ^1H NMR spectra of **3** with one equivalent of MeCN indicates the presence of all four possible **3**·MeCN diastereomers (−60 °C). There is a notable downfield shift of the alkylidene H resonance of the less Lewis acidic *syn* isomer as the temperature is lowered, indicating the weaker association of *syn* **3** with MeCN. The more Lewis acidic *anti* isomers require a higher temperature (~0 °C) for the same process to occur.
[15] For a comprehensive review of metal-catalyzed kinetic resolutions, see: A. H. Hoveyda, M. T. Didiuk, *Curr. Org. Chem.* **1998**, *2*, 537 – 574.
[16] Relative rates are calculated based on the equation reported by Kagan, see: K. B. Kagan, J. C. Fiaud, *Top. Stereochem.* **1988**, *18*, 249 – 330.
[17] By dimeric product we mean the material obtained by catalytic intermolecular cross-coupling of two substrate molecules through their terminal alkenes.
[18] The reaction times with in situ **3** are longer (e.g., 2 h vs. 1 h for formation of (*R*)-**20**) because of the presence of the Lewis basic solvent THF. Typically the final ratio of THF:C_6H_6 is ~1:10.
[19] Treatment of **23** and the derived methoxymethyl (MOM) ether of **23** with styrene in the presence of 5 – 100 mol % of imidazolinium-containing Ru catalysts of Grubbs or Hoveyda at 22 or 75 °C (CH_2Cl_2 and $CHCl_3$) results in < 5 % conversion after 12 h. See: a) M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, *Org. Lett.* **1999**, *1*, 953 – 956; b) S. B. Garber, J. S. Kingsbury, B. L. Gray, A. H. Hoveyda, *J. Am. Chem. Soc.* **2000**, *122*, 8168 – 8179.
[20] This protocol is based on an original procedure by Koenigs and Carl, see: W. Koenigs, R. W. Carl, *Chem. Ber.* **1891**, *24*, 3889 – 3900.

Modular Pyridinyl Peptide Ligands in Asymmetric Catalysis: Enantioselective Synthesis of Quaternary Carbon Atoms Through Copper-Catalyzed Allylic Substitutions**

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Dedicated to Professor David A. Evans on the occasion of his 60th birthday

To develop a new transformation and achieve maximum levels of reactivity and selectivity, myriad reaction parameters must be explored and adjusted. In the context of establishing an effective catalytic enantioselective process,[1] the choice of an appropriate chiral ligand and metal salt is perhaps most crucial: a blend of mechanistic knowledge (e.g., details of coordination chemistry) and human intuition are typically used to identify a desirable metal – ligand combination. Such a task becomes significantly more facile if readily modifiable chiral ligands are at hand; depending on the nature of the metal salts involved and the type of transformation that is being developed, ligand structures may be altered so that reactivity and selectivity levels are improved. The latter approach is particularly attractive if identification of the lead candidates is accomplished through screening of ligand libraries.[2]

In the past few years we have studied and developed various peptide-based ligands that promote a range of catalytic asymmetric C–C bond-forming reactions. In all instances, optimal catalysts have been identified through examination of collections of peptide – metal complexes.[3–6] Peptidic structures represented by **I** (Figure 1) have been developed to initiate efficient and asymmetric Ti-catalyzed CN addition to epoxides[3] and imines.[4] Zr-catalyzed alkylation of imines has been demonstrated to proceed efficiently and with high asymmetric induction in the presence of ligands

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