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Catalytic Asymmetric Synthesis of Chiral Allylic Amines. Evaluation of Ferrocenyloxazoline Palladacycle Catalysts and Imidate Motifs

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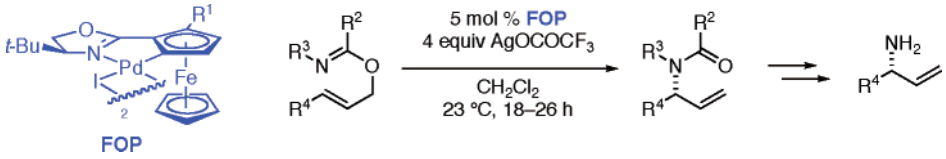


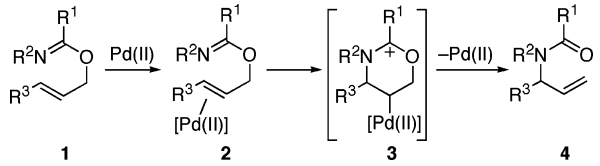
Palladium(II) catalysts based on a ferrocenyloxazoline palladacyclic (FOP) scaffold were synthesized and evaluated for the rearrangement of prochiral allylic *N*-(4-methoxyphenyl)benzimidates. When iodide-bridged dimer FOP precatalysts are activated by reaction with excess silver trifluoroacetate, the allylic rearrangement of both *E* and *Z* prochiral primary allylic *N*-(4-methoxyphenyl)-benzimidates takes place at room temperature to give the corresponding chiral allylic *N*-(4-methoxyphenyl)benzamides in high yield and good ee (typically 81−95%). Several allylic imidate motifs were evaluated also. Because the corresponding enantioenriched allylic amide products can be deprotected in good yield to give enantioenriched allylic amines, allylic *N*-aryltrifluoroacetimidates were identified as promising substrates.

Introduction

The [3,3]-rearrangement of allylic imidates is a widely used reaction for the allylic interchange of alcohol and amine functionality.[1] Complexes of soft metal salts, particularly those of mercury(II)[2] and palladium(II),[1a] catalyze the rearrangement of allylic trichloroacetimidates and allow this transformation to be carried out at temperatures much lower than those required to facilitate the rearrangement thermally.[1] Substantial evidence suggests that the catalyzed rearrangement proceeds by a cyclization-induced rearrangement mechanism, which is illustrated in Scheme 1 for a palladium(II) catalyst.[1]

Recent investigations in these laboratories have focused on the development of asymmetric palladium(II) catalysts for the addition of external (nonmetal bound) nucleophiles to prochiral alkenes.[3−5] Such asymmetric alkene activation is exemplified by the catalytic asymmetric rearrangement of *N*-arylbenzimidates **5a** to chiral *N*-arylbenzamides **6a**[3a] and the transformation of allylic alcohol **7** to *N*-sulfonyl 2-oxazolidinone **8** (Scheme 2).[5] In both cases, the catalyst was generated in situ by reaction of iodide-bridged ferrocene oxazoline palladacycle (FOP) **9a** with an excess of silver trifluoroacetate.[6]

SCHEME 1. Pd(II)-Catalyzed Allylic Imidate Rearrangement



Since our initial report of the catalytic asymmetric rearrangement of allylic *N*-arylbenzimidates using cationic Pd(diamine) complexes such as **10** and cationic Pd(bis-oxazoline) complexes,[3b] several additional chiral

(1) (a) Overman, L. E. *Acc. Chem. Res.* **1980**, *13*, 218−224. (b) Overman, L. E. *Angew. Chem., Int. Ed. Eng.* **1984**, *23*, 579−586. (c) Metz, P.; Mues, C.; Schoop, A. *Tetrahedron* **1992**, *48*, 1071−1080. (d) Schenck, T. G.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2058−2066.

(2) (a) Overman, L. E. *J. Am. Chem. Soc.* **1974**, *96*, 597−599. (b) Overman, L. E. *J. Am. Chem. Soc.* **1976**, *98*, 2901−2910.

(3) (a) Donde, Y.; Overman, L. E. *J. Am. Chem. Soc.* **1999**, *121*, 2933−2934. (b) Calter, M.; Hollis, T. K.; Overman, L. E.; Ziller, J.; Zipp, G. G. *J. Org. Chem.* **1997**, *62*, 1449−1456. (c) Hollis, T. K.; Overman, T. K. *Tetrahedron Lett.* **1997**, *38*, 8837−8840. (d) Cohen, F.; Overman, L. E. *Tetrahedron: Asymmetry* **1998**, *9*, 3213−3222.

(4) (a) Overman, L. E.; Owen, C. E.; Pavan, M. M.; Richards, C. J. *Org. Lett.* **2003**, *5*, 1809−1812. (b) Anderson, C. E.; Overman, L. E. *J. Am. Chem. Soc.* **2003**, *125*, 12412−12413. (c) Kirsch, S.; Overman, L. E.; Watson, M. P. *J. Org. Chem.* **2004**, *69*, 8101−8104.

(5) Overman, L. E.; Remarchuk, T. P. *J. Am. Chem. Soc.* **2002**, *124*, 12−13.

(6) The ferrocene moiety in the catalyst generated under these conditions has been shown recently to be a ferrecenium cation; see: Remarchuk, T. P. Ph.D. Dissertation, University of California, Irvine, 2003.

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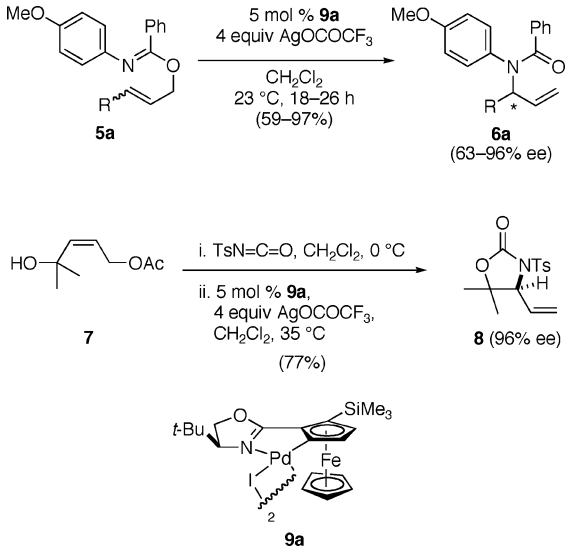
SCHEME 2. Reactions Catalyzed by FOP Complex 9a



palladium(II) catalysts have been described by our group[3,4] (complexes **12**, **14a**, and **14b**) and others[7] (complexes **11**, **13**, **16a**, and **16b**) for this transformation (Figure 1). The major reaction pathway competing with the allylic imidate rearrangement, observed with the earliest catalysts,[3b] is ionization of the allylic imidate to give an allylic cation that then loses a proton to form diene products or is trapped indiscriminately by nucleophiles in the reaction mixture. This process undoubtedly is promoted by coordination of the imidate nitrogen to the palladium catalyst.[3b,7a] Our recent work has focused on asymmetric Pd(II) catalysts that differ from the early dicationic catalysts by containing two monoanionic ligands.[3,4] Palladacyclic catalysts containing a metallocene fragment, including the FOP precatalyst **9a**[3a] and the COP catalysts **15a** and **15b**,[4] emerged from these investigations as being particularly effective. By design, these catalysts project substituents above and below the palladium(II) square plane, a topography that should be particularly effective for influencing enantioselective steps that involve square-based pyramidal intermediates or transition states.[8]

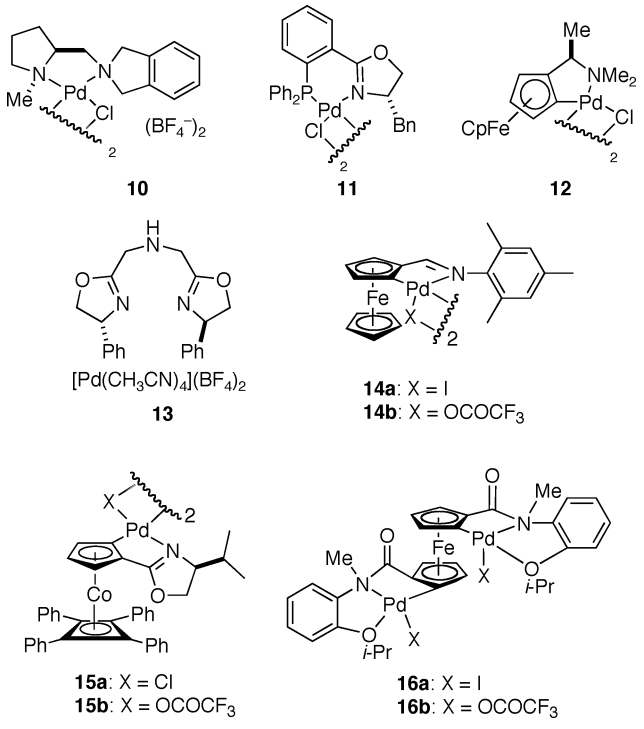


FIGURE 1. Asymmetric catalysts for the rearrangement of allylic *N*-arylbenzimidates.

In this paper, we describe in full detail the synthesis and evaluation of FOP precatalysts **9a** and **40** (Scheme 5), the first precatalysts reported that, when activated, achieved >90% ees in the production of chiral allylic amides from prochiral allylic imidates.[3a] We also describe the synthesis and evaluation of a small library of other FOP catalysts that vary in both the relative orientation of the chiral oxazoline and CpFe fragments and in the 3 substituent of the palladated cyclopentadienyl ring. Studies aimed at identifying imidates other than allylic *N*-arylbenzimidates that rearrange in high yields and high enantioselectivities, and whose allylic amide products are deprotected efficiently to form the corresponding allylic amines, are reported also.

Results

A. Synthesis of Ferrocenyl Oxazoline Palladacycles. Ferrocenyl oxazoline palladacycles **9a**, **23**, and **24** were prepared from the known enantioenriched ferrocenyl oxazoline **17** (Scheme 3).[9] Ortholithiation of ferrocene **17** with *s*-BuLi, followed by quenching of the resulting lithium reagent with either chlorotrimethylsilane or chlorotriethylsilane, provided disubstituted ferrocenes **18** and **19** in 70% and 77% yield, respectively. In both cases, diastereoselection was observed to be greater than 20:1.[9] The minor diastereomer formed in each case could be removed by recrystallization from hexanes to provide chiral ferrocenes **18** and **19** as single diastereomers. Ortholithiation of diastereomerically pure ferrocenes **18** and **19** with *t*-BuLi, followed by reaction of the resulting lithium intermediates with diiodoethane, provided iodides **20** and **21** in 70% and 95% yield, respectively.[10,11] Removal of the TMS group of ferrocene **20** occurred in high yield upon reaction with TBAF in refluxing THF. In this way, access to disubstituted ferrocenyl iodide **22** was achieved. Subsequent reaction of iodides **20**, **21**, and **22** with 1 equiv of $Pd_2(dba)_3 \cdot CHCl_3$ at room temperature provided iodide-bridged dimers **9a**,

(7) (a) Uozumi, Y.; Kato, K.; Hayashi, T. *Tetrahedron: Asymmetry* **1998**, *9*, 1065−1072. (b) Jiang, Y.; Longmire, J. M.; Zhang, X. *Tetrahedron Lett.* **1999**, *40*, 1449−1450. (c) Leung, P,-H.; Ng, K.-H.; Li, Y.; White, A. J. P.; Williams, D. J. *Chem. Commun.* **1999**, 2435−2436. (d) Kang, J.; Yew, K. H.; Kim, T. H.; Choi, D. H. *Tetrahedron Lett.* **2002**, *43*, 9509−9512. (e) Kang, J.; Kim, T. H.; Yew, K. H.; Lee, W. K. *Tetrahedron: Asymmetry* **2003**, *14*, 415−418.

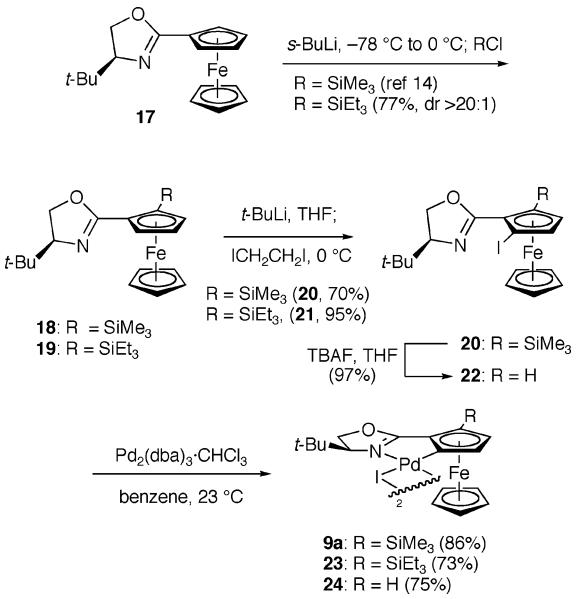
(8) For a brief discussion of catalyst design and a review of our early work in this area, see: Hollis, T. K.; Overman, L. E. *J. Organomet. Chem.* **1999**, *576*, 290−299.

(9) Sammakia, T.; Latham, H. A.; Schaad, D. R. *J. Org. Chem.* **1995**, *60*, 10−11.

(10) These conditions are adapted from the following: Rebiere, F.; Samuel, O.; Kagan, H. B. *Tetrahedron Lett.* **1990**, *31*, 3121−3124.

(11) A slight deficiency of *t*-BuLi was employed in these reactions to minimize the formation of side products resulting from lithiation of both Cp ligands of the ferrocene.

SCHEME 3. Synthesis of FOP Complexes



23, and **24** in 86%, 73%, and 75% yields, respectively;[12] complexes **9a** and **23** have the S,S_p configuration and **24** has the S,R_p configuration.[13] These complexes are air-stable and can be purified by column chromatography on silica gel or florisil. The ^{1}H NMR spectra of these palladacyclic complexes show that they exist in solution as a *cis/trans* mixture about the Pd square planes (Figure 2); a single C_1 symmetric isomer is ruled out because the

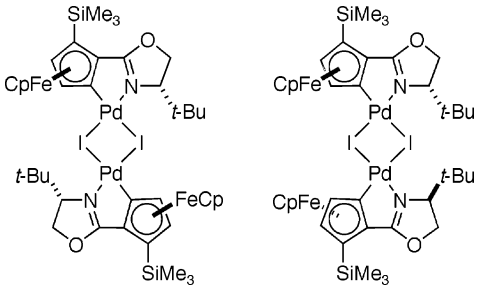


FIGURE 2. Isomers about the palladium square plane of iodide-bridged dimer **9a**.

signals for the two isomers do not occur in a 1:1 ratio. Alternate approaches to this family of catalysts involving direct cyclopalladation or transmetalation were less successful, presumably because the Pd(II) salts employed in these procedures promoted oxidative decomposition of the ferrocene unit.[14]

A collection of additional ferrocenyl oxazoline palladacyclic complexes were synthesized from (S_p)-2-[(4*S*)-4,5-dihydro-*tert*-butyl-2-oxazolyl]-1-iodoferrocene **25** (Scheme

SCHEME 4. Synthesis of Aryl-Substituted FOP Complexes

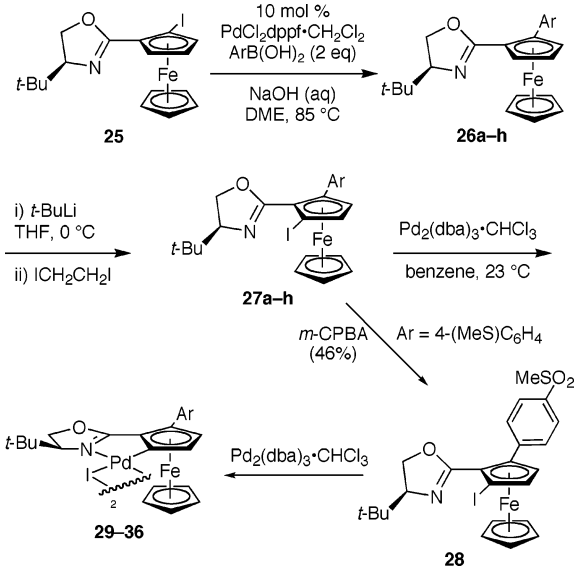


TABLE 1. Synthesis of Arylpalladacycles 29–36

entry	aryl (Ar)	**26a–h**, yield (%)	**27a–h**, yield (%)	**29–36**, yield (%)
1	Ph	**a**, 84	**a**, 78	**29**, 81
2	4-MeOC$_6$H$_4$	**b**, 88	**b**, 73	**30**, 90
3	4-CF$_3$C$_6$H$_4$	**c**, 33[a]	**c**, 57	**31**, 89
4	2,6-(MeO)$_2$C$_6$H$_3$	**d**, 20	**d**, 61	**32**, 90
5	1-C$_{10}$H$_7$	**e**, 92	**e**, 66	**33**, 98
6	2-MeC$_6$H$_4$	**f**, 89	**f**, 74	**34**, 81
7	2-MeOC$_6$H$_4$	**g**, 83	**g**, 80	**35**, 90
8	4-MeSC$_6$H$_4$	**h**, 76	**h**, 80	**36**, 79[b]

[a] Suzuki coupling required 4 equiv of 4-trifluoromethylphenylboronic acid. [b] Ar = 4-MeSO$_2$C$_6$H$_4$ (see Scheme 4).

4).[4a,15] Coupling eight commercially available arylboronic acids with iodide **25** in the presence of PdCl$_2$dppf·CH$_2$Cl$_2$ (10 mol %) and aqueous NaOH in DME at 85 °C provided the aryl ferrocenyl oxazoline complexes **26a–h** (Scheme 4, Table 1).[16] The steric environment presented by the boronic acids affected the efficiency of these cross coupling reactions. For example, aryl boronic acids containing one ortho substituent coupled with iodide **25** in good to excellent yields (entries 5–7, 83–92%). Conversely, coupling of 2,6-dimethoxyphenylboronic acid with iodide **25** was inefficient, occurring in only 20% yield (entry 4); in this case, longer reaction times did not improve the yield of the cross-coupled product **26d**, with iodide **25** being recovered. Arylboronic acids containing an electron-releasing substituent coupled in good yields (entries 2, 6–8; 76–89%), whereas arylboronic acids containing electron-withdrawing groups coupled poorly or not at all. In the case of (4-trifluoromethyl)phenylboronic acid, 4 equiv of the arylboronic acid was required to realize even a low yield of the coupled product **26c** (entry 3, 33%).[17] Other electron-deficient aryl boronic

(12) For other examples using oxidative addition for the synthesis of palladacycles, see: (a) Denmark, S. E.; Stavenger, R. A.; Faucher, A.-M.; Edwards, J. P. *J. Org. Chem.* **1997**, *62*, 3375–3389. (b) Mateo, C.; Cardenas, D. J.; Fernandez-Rivas, C.; Echavarren, A. M. *Chem. Eur. J.* **1996**, *2*, 1596–1606.

(13) We use the descriptors for planer chirality in π-complexes codified by Schlögl: (a) Schlögl, T. *Top. Stereochem.* **1967**, *1*, 39–91. These differ from the descriptors based on CIP rules: (b) Chan, R. S.; Ingold, C. K.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385–414, which are occasionally used in the current literature.

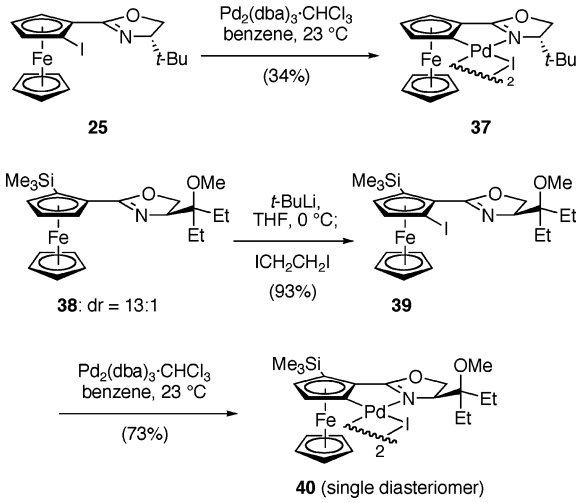
(14) For a review of palladacycle synthesis, see: Canty, A. J. In *Comprehensive Organometallic Chemistry II*; Pergamon: Oxford, New York, 1995; Vol. 9, pp 242–248.

(15) Bolm, C.; Muñiz-Fernández, K.; Seger, A.; Raabe, G.; Günther, K. *J. Org. Chem.* **1998**, *63*, 7860–7867.

(16) These conditions are adapted from Knapp, R.; Rehahn, M. *J. Organomet. Chem.* **1993**, *452*, 235–240.

(17) The monosubtituted ferrocenyl complex resulting from reduction of the iodide and the biaryl resulting from homo-coupling of the boronic acid comprised the remainder of the mass.

SCHEME 5. Synthesis of Additional FOP Complexes



acids, such as pentafluorophenylboronic acid, did not couple with iodide **25** to any detectable extent.

To complete the syntheses of the palladacyclic catalysts, ferrocenyl oxazolines **26a**−**h** were ortholithiated with *t*-BuLi, followed by quenching of the lithium intermediates with diiodoethane to provide ferrocenyl iodides **27a**−**h** in moderate to good yields (57−80%, Table 1). At this point, it was possible to access an additional FOP catalyst having an electron-deficient aryl substituent by oxidation of methyl sulfide **27h** with *m*-CPBA to provide sulfone **28** in 46% yield. Reaction of ferrocenyl iodides **27a**−**g** and **28** with 1 equiv of $Pd_2(dba)_3$·$CHCl_3$ in benzene at room temperature then provided the palladacyclic dimers **29**−**36** having the S,R_p configuration, in high yields (79−98%, Table 1).

Two additional FOP precatalysts were synthesized using an analogous sequence of transformations (Scheme 5). Synthesis of the palladacycle of (S,S_p)-**37**, in which the *tert*-butyl and ferrocene moieties occupy space on the same face of the Pd(II) square plane, was realized in 34% yield by direct reaction of iodide **25** with $Pd_2(dba)_3$·$CHCl_3$. In addition, substitution of a 1-methoxy-1-ethylpropyl group for the *t*-Bu group of ferrocene **18** allowed for the preparation of "pseudo"-enantiomeric FOP complex (S,R_p)-**40**. Complex **40** was prepared by reaction of known ferrocenyl complex **38**[9] (a 13:1 mixture of diastereomers about the ferrocene stereocenter) with *t*-BuLi followed by quenching of the resulting anion with diiodoethane. Subsequent reaction of iodide **39** with $Pd_2(dba)_3$·$CHCl_3$ yielded FOP precatalyst **40** as a mixture of iodide-bridged dimers (as observed by ^{1}H NMR analysis) in 68% yield over the two steps. Each of these palladacycles, including those containing aryl substituents on the functionalized cyclopentadienyl ring, exhibited ^{1}H NMR spectra consistent with them existing in solution as mixtures of *cis*/*trans* isomers about the Pd(II) square planes.

The structures of complexes **9a** and **40** were established by X-ray crystallography;[18] representations of these X-ray models are shown in Figure 3. In both

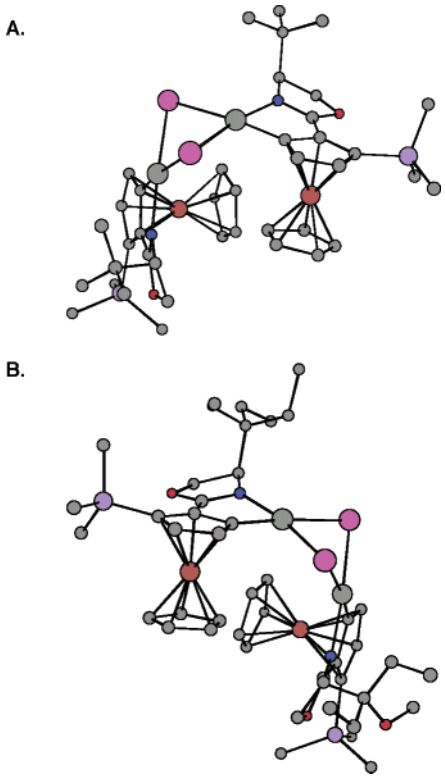


FIGURE 3. X-ray models of complexes **9a** (A) and **40** (B).

instances, the *trans* isomer preferentially crystallized. A search of the Cambridge Structure Database (CSD v5.25) shows these to be the first single-crystal X-ray structures of ferrocenyl palladacycle dimers in which the bridging atom is iodide; the majority of related structures are chloride-bridged dimers.[19] The *trans* isomers of complexes **9a** and **40** are C_2 symmetric in the solid state. The four-membered ring, containing the Pd and I atoms, is puckered, placing both FeCp fragments on the concave face, typical of halide-bridged ferrocenyl palladacycles. The degree of puckering about the central four-membered ring in these iodide-bridged dimers, measured as the dihedral angle between the two Pd(II) square planes (64.5° for **9a** and 66.7° for **40**), is greater than that previously observed (4.3−52.1°) in five-membered ring chloride- or bromide-bridged ferrocenyl palladacyclic dimers.[19] This conformation places the FeCp fragment and the 4 substituent of the oxazoline ring on opposite sides, nearly perpendicular, to the palladium square plane.

The sequences illustrated in Schemes 3−5 are sufficiently efficient to conveniently provide palladacyclic complexes **9a**, **29**−**36**, and **40** in multigram quantities.

(18) The authors have deposited coordinates for these compounds with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

(19) For X-ray crystallography of chloride-bridged ferrocenyl palladacycles, see: (a) Dunina, V. V.; Gorunova, O. N.; Livantsov, M. V.; Grishin, Y., K.; Kuz'mina, L. G.; Kataeva, N. A.; Churakov, A. V. *Tetrahedron: Asymmetry* **2000**, *11*, 3967−3984. (b) Zhao, G.; Yang, Q. C-.; Mak, T. C. W. *Organometallics* **1999**, *18*, 3623−3636. (c) Zhao, G.; Wang, Q. G-.; Mak, T. C. W. *Tetrahedron: Asymmetry* **1998**, *9*, 1557−1561. (d) Wu, Y. J.; Cui, X. L.; Du, C. X.; Wang, W. L.; Guo, R. Y.; Chen, R. F. *J. Chem. Soc., Dalton Trans.* **1998**, 3727−3730. (e) Zhao, G.; Wang, Q. G-.; Mak, T. C. W. *Polyhedron* **1998**, *18*, 577−584. (f) López, C.; Bosque, R.; Solans, X.; Font-Bardia, M. *Tetrahedron: Asymmetry* **1996**, *7*, 2527−2530. (g) Reference 3d. For bromide-bridged ferrocenyl palladacycles, see: (h) Zhao, G.; Wang, Q. C-.; Mak, T. C. W. *J. Chem. Soc., Dalton Trans.* **1998**, 3785−3789. (i) Reference 19b.

SCHEME 6. Rearrangement of *N*-(4-Trifluoromethylphenyl)benzimidates

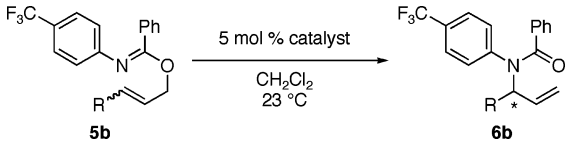


TABLE 2. Rearrangement of Imidate 5b to Amide 6b (R = *n*-Pr)[a]

entry	precatalyst	imidate stereoisomer	time	yield (%)	ee (%)/conf[b]
1	**9a**	*Z*	3 d	67	91/*R*
2	**9a**	*E*	2 d	57	79/*S*
3	**23**	*Z*	6 d	89	90/*R*
4	**23**	*E*	63 h	76	76/*S*
5	**24**	*Z*	2 d	15	49/*R*
6	**24**	*E*	2 d	77	69/*S*
7	**37**	*Z*	3 d	28	53/*R*
8	**37**	*E*	2 d	86	8/*S*
9	**40**	*Z*	6 d	81	92/*S*
10	**40**	*E*	3 d	95	72/*R*

[a] Conditions: 5 mol % of the precatalyst was preactivated by reaction with 4 equiv of Ag ($OCOCF_3$) in CH_2Cl_2 (0.1 M in substrate). [b] For determination of absolute configuration, see ref 4.

Moreover, the presence of crystalline intermediates allows for diastereomerically pure intermediates to be isolated by simple recrystallization, thus negating the need for chromatographic purification of such species. For example, palladacycle **40** was recrystallized from benzene/hexanes after its preparation, removing the minor diastereomer generated during the installation of the TMS group. All of the arylferrocenyl palladacycles, as well as **37**, were obtained as single stereoisomers by recrystallization of iodide **25** from hexanes after its preparation from ferrocene **17**.

B. Evaluation of FOP Catalysts for the Asymmetric Rearrangement of Various Allylic *N*-Arylbenzimidates. An initial evaluation of FOP catalysts examined the rearrangement of both (*E*) and (*Z*)-2-hexenyl *N*-(4-trifluoromethylphenyl)benzimidates **5b** (R = *n*-Pr) with catalysts derived from complexes **9a**, **23**, **24**, **37**, and **40** (Scheme 6). In this initial survey, the iodide-bridged dimer precatalysts (5 mol % relative to substrates) were activated by reaction with 4 equiv of silver trifluoroacetate in CH_2Cl_2 at room temperature for 3 h. The results of these experiments are summarized in Table 2. Similar levels of enantioselectivity in forming allylic amide **6b** were observed with cationic catalysts generated from **9a**, **23**, and **40**; as expected, the last of these delivered the opposite enantiomer compared to catalysts formed from **9a** and **23** (entries 1−4, 9, and 10). The catalyst formed from **37**, in which the *t*-Bu group and CpFe fragment are oriented on the same face of the palladium square plane (S_P configuration of the ferrocene moiety), rearranged allylic imidate (*E*)-**5b** (R = *n*-Pr) in acceptable 86% yield but with low enantioselection, providing **6b** in only 8% ee (entry 8). This same catalyst provided amide **6b** (R = *n*-Pr) in 28% yield and 53% ee from the corresponding *Z*-configured allylic imidate (entry 7). The catalyst derived from **24**, a diastereomer of **37** having the opposite R_p configuration, rearranged allylic imidate (*E*)-**5b** (R = *n*-Pr) in acceptable 77% yield, providing **6b** in 69% ee (entry 6). The catalyst derived from **24** also rearranged allylic imidate (*Z*)-**5b** (R = *n*-Pr) in low 15% yield, providing **6b** in 49% ee (entry 5).

SCHEME 7. Synthesis of a FOP Chloride Complex

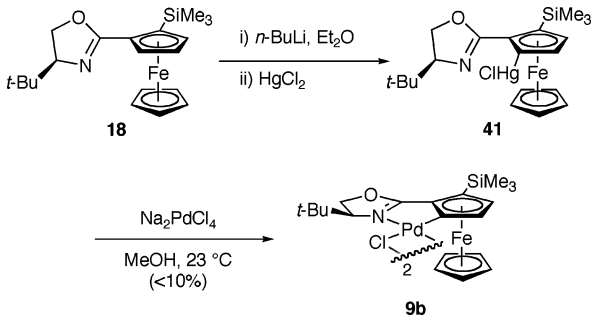


TABLE 3. Effect of the Silver Salt in Activation of FOP Precatalyst 9a for the Rearrangement of Allylic Imidate 5a[a]

entry	silver salt	imidate stereoisomer	R	time	yield (%)	ee (%)/conf[b]
1	$AgOCOCF_3$	*Z*	*n*-Pr	18 h	83	91/*R*
2	AgOTs	*Z*	*n*-Pr	2 d	83	88/*R*
3	AgONs	*Z*	*n*-Pr	2 d	67	89/*R*
4	$AgOCOCF_3$	*E*	*i*-Bu	25 h	97	84/*S*
5	$AgOCOCF_3$	*Z*	*i*-Bu	25 h	89	96/*R*
6	$AgOCOCF_3$	*Z*	$CH_2C_6H_{11}$[c]	26 h	87	90/*R*
7	$AgOCOCF_3$	*Z*	Bn	23 h	85	88/*R*
8	$AgOCOCF_3$	*E*	Ph	26 h	59	63/*R*

[a] Conditions: 5 mol % of **9a** was preactivated by reaction with 4 equiv of the silver salt in CH_2Cl_2 (0.1 M in substrate) at room temperature. [b] For determination of absolute configuration, see ref 4. [c] C_6H_{11} = cyclohexyl.

As changing the ferrocenyl silyl substituent from $SiMe_3$ to $SiEt_3$ did not significantly affect enantioselectivity, FOP precatalyst iodide-bridged dimer **9a** and its chloride congener **9b** were chosen for further studies. The latter complex was prepared from the corresponding (chloromercuric)ferrocenyl complex **41** by transmetalation with sodium tetrachloropalladate (Scheme 7). The iodide-bridged dimer **9a** itself was a poor catalyst for the rearrangement of **5a**, providing allylic amide **6a** in only 20% yield and 41% ee after 5 days. The chloride congener **9b** rearranged imidate **5b** at a slow rate, providing **6b** in <10% yield after 3 days; however, the product was 79% ee. We initially investigated activation of **9a** with other silver salts (Table 3), surveying catalytic efficacy in the asymmetric rearrangement of (*Z*)-2-hexenyl *N*-(4-methoxyphenyl)benzimidate (**5a**, R = *n*-Pr). Catalysts generated using silver tosylate or silver *p*-nitrophenylsulfonate behaved similarly to the catalyst generated with silver trifluoroacetate**.** The reaction of **9a** with silver triflate resulted in decomposition of the complex.

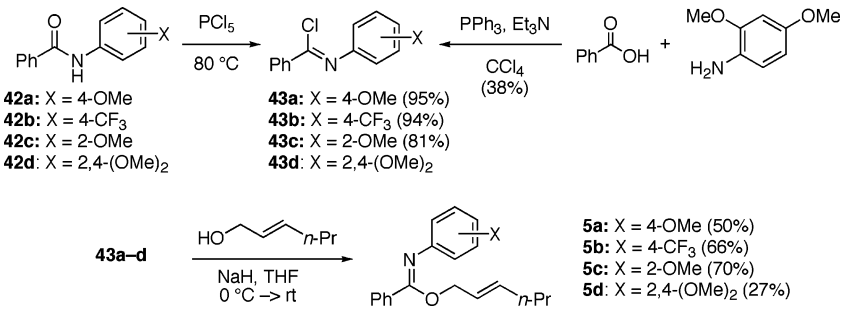
As there appeared to be no advantage to using silver salts other than $AgOCOCF_3$, the rearrangements of five additional allylic *N*-(4-methoxyphenyl)benzimidates **5a** were examined using the catalyst generated from the reaction of **9a** with this silver salt (Table 3). The rearrangement was found to be tolerant to incorporation of branched alkyl groups or a Bn group at C4 of the allylic imidate, providing rearranged allylic amides **6a** in good yields (85−97%) and high enantiomeric excesses (84−96% ee, entries 4−7). As had been observed previously,[3a] a *Z* allylic imidate rearranged with a higher level of enantioinduction (entry 5) than the corresponding *E*

TABLE 4. Rearrangement of Allylic *N*-(4-Methoxyphenyl)benzimidates 5a to Allylic *N*-(4-Methoxyphenyl)benzamides 6a with Catalysts Generated from Various FOP Precatalysts[a]

		R = (*E*)-*n*-Pr		R = (*Z*)-*n*-Pr		R = (*E*)-*i*-Bu		R = (*Z*)-*i*-Bu	
precatalyst	ferrocenyl C3	yield of **6a**, %	ee %/ conf[b]	yield of **6a**, %	ee %/ conf[b]	yield of **6a**, %	ee %/ conf[b]	yield of **6a**, %	ee %/ conf[b]
9a	TMS	93	83/*S*	83	91/*R*	97	84/*S*	89	96/*R*
24	H	70	81/*S*	20	56/*R*				
29	Ph	77	83/*S*	71	90/*R*	80	81/*S*	71	91/*R*
30	4-$MeOC_6H_4$	95	88/*S*	70	88/*R*	80	82/*S*	71	88/*R*
31	4-$CF_3C_6H_4$	85	82/*S*	84	91/*R*	85	83/*S*	70	94/*R*
32	2,6-$(MeO)_2C_6H_3$	95	88/*S*	70	94/*R*	80	86/*S*	85	91/*R*
33	1-$C_{10}H_7$	77	85/*S*	77	93/*R*	71	84/*S*	72	90/*R*
34	2-MeC_6H_4	71	87/*S*	70	91/*R*	78	85/*S*	75	85/*R*
35	2-$MeOC_6H_4$	91	84/*S*	82	93/*R*	83	87/*S*	83	92/*R*
36	4-$MeSO_2C_6H_4$	83	81/*S*	77	91/*R*	70	80/*S*	78	95/*R*

[a] Conditions: 5 mol % of **9** was preactivated by reaction with 4 equiv of $Ag(OCOCF_3)$ in CH_2Cl_2 (0.1 M in substrate) at room temperature for 3 h. [b] For determination of absolute configuration, see ref 4.

SCHEME 8. Synthesis of *N*-Arylbenzimidates



configured imidate (entry 4). The rearrangement of the allylic imidate derived from cinnamyl alcohol **5a** (R = Ph) was less efficient, providing the allylically transposed amide in lower overall yield and enantioselectivity (entry 8). The lowered yield and enantioselectivity observed in this case likely results from the competitive ionization-recombination pathway, which would proceed via a stabilized aryl-substituted allyl cation intermediate.

With the goal of improving the yield and enantioselectivity of the rearrangement of *N*-arylbenzimidates, the panel of arylferrocenyl palladacyclic FOP catalysts was evaluated. The catalytic asymmetric rearrangement of four allylic *N*-(4-methoxyphenyl)benzimidates **5a** [R = (*E*)-*n*-Pr, (*Z*)-*n*-Pr, (*E*)-*i*-Bu, and (*Z*)-*i*-Bu] was studied with catalysts generated by pretreatment of complexes **9a**, **29**−**36**, and **24** with 4 equiv of silver trifluoroacetate in CH_2Cl_2 at room temperature for 3 h; in each case, 5 mol % of the iodide-bridged dimer was employed. Filtration through Celite under an inert atmosphere removed any precipitated silver salt and provided the active catalysts. The appropriate imidate was then added to the activated catalyst solution, and the reaction was carried out at room temperature for a set time of 24 h.

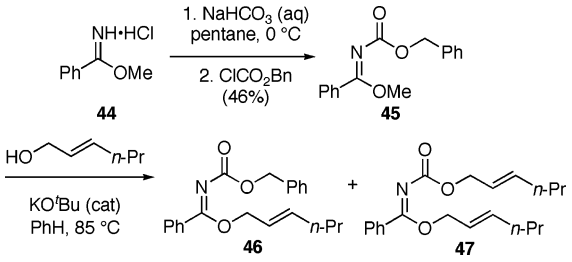
The results from rearrangement of these four *N*-(4-methoxyphenyl)benzimidates **5a** with this series of catalysts are summarized in Table 4. With the exception of the rearrangement of (*Z*)-2-hexenyl *N*-(4-methoxyphenyl)-benzimidate **5a** (R^1 = (*Z*)-*n*-Pr) with the catalyst formed from **24** (R^2 = H), the enantiomeric excess of the resulting *N*-(4-methoxyphenyl)benzamides **6a** was only slightly impacted by the substituent present on the ferrocenyl ring. The isolated yields of the allylic benzamide products changed somewhat more than the enantiomeric excess as this substituent was varied. Overall, the TMS-substituted precatalyst **9a** provided enantioselectivities comparable to or better than those achieved with the arylferrocenyl catalysts. As such, precatalyst **9a** was again chosen for further studies, this time with the goal of identifying new allylic imidate motifs that would provide allylic amide products upon rearrangement that would be more amenable to cleavage, thus providing an improved route to chiral allylic amines of high enantiopurity.

C. Development of More Useful Imidates for the Synthesis of Chiral Nonracemic Allylic Amines from Allylic Alcohols.

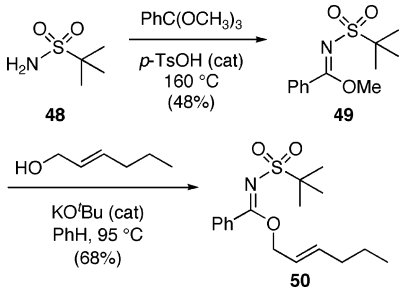
C.1. Synthesis of Protected Allylic Imidates. The search for new imidate motifs with more suitable nitrogen protecting groups began by expanding our suite of *N*-arylbenzimidates to include *N*-(2-methoxyphenyl)-benzimidates **5c** and *N*-(2,4-dimethoxyphenyl)benzimidates **5d**, with the anticipation that these aryl groups would be more easily removed from the resulting amide under oxidative conditions. The synthesis of (2-methoxyphenyl)benzimidates **5c** was achieved in a manner analogous to the preparation of *N*-(4-methoxyphenyl)-benzimidates **5a** and *N*-(4-trifluoromethylphenyl)benzimidates **5b** (Scheme 8).[3a] Reaction of benzamides **42a**−**c** with PCl_5 gave the imidoyl chlorides **43a**−**c** in good yields (81−95%). This procedure, however, failed to provide useful quantities of *N*-(2,4-dimethoxyphenyl)benzimidoyl chloride **43d**. Imidoyl chloride **43d** was accessed, albeit in low yield (38%), by reaction of benzoic acid and 2,4-dimethoxyaniline in the presence of triphenylphosphine and triethylamine in refluxing carbon tetrachloride.[20]

(20) Tamura, K.; Mizukami, H.; Maeda, K.; Watanabe, H.; Uneyama, K. *J. Org. Chem.* **1993**, *58*, 32−35.

SCHEME 9. Synthesis of *N*-Benzyloxycarbonylbenzimidate 46



SCHEME 10. Synthesis of *N-tert*-Butylsulfonylbenzimidate 50



Treatment of imidoyl chlorides **43a**−**d** with the sodium or lithium salt of (*E*)-2-hexen-1-ol in THF provided the allylic *N*-arylbenzimidates **5a**−**d** in variable yields (27−81%).

Examination of other classes of nitrogen protecting groups began with the synthesis of an allylic imidate having nitrogen protected with a benzyloxycarbonyl group. Methyl benzimidate hydrochloride[21] **44** was first treated with cold aqueous $NaHCO_3$ and pentane to provide the free base, which was allowed to directly react with benzyl chloroformate and K_2CO_3 to provide the Cbz-protected methyl benzimidate **45** in 46% yield (Scheme 9). Alkoxide exchange with (*E*)-2-hexen-1-ol in the presence of catalytic potassium *tert*-butoxide in benzene at 85 °C then gave allylic imidate **46** in 53% yield. At the elevated temperatures required for this transformation, alkoxide exchange was complicated by competitive substitution at the carbamate center to provide byproduct **47**.

An allylic benzimidate having a *tert*-butylsulfonamide (BUS) nitrogen protecting group was synthesized by the sequence summarized in Scheme 10. Initially the BUS-protected methyl benzimidate **49** was formed by reaction of *tert*-butylsulfonamide **48** and trimethyl orthobenzoate in the presence of catalytic *p*-toluenesulfonic acid at 160 °C.[22] Using this procedure, BUS-protected methyl benzimidate **49** was prepared in 48% yield. Alkoxide exchange upon reaction of methyl benzimidate **49** in the presence of (*E*)-2-hexen-1-ol and potassium *tert*-butoxide delivered the BUS-protected allylic imidate **50** in 68% yield.

Finally, *N*-aryltrifluoroacetimidate **52a** was synthesized with the expectation that the acyl group of the allylic trifluoroacetamide product would be readily removed by hydrolysis. Using the procedure of Tamura, *p*-anisidine and trifluoroacetic acid were condensed with triphenylphosphine, triethylamine, and carbon tetrachloride at reflux to provide imidoyl chloride **51** in 90% yield.[20] As in the synthesis of allylic benzimidates, treatment of imidoyl chloride **51** with the sodium salt of (*E*)-2-hexen-1-ol in THF provided allylic *N*-(4-methoxyphenyl)trifluoroacetimidate **52a** in 88% yield (Scheme 11).

SCHEME 11. Synthesis of *N*-(4-Methoxyphenyl)trifluoroacetimidates 52a

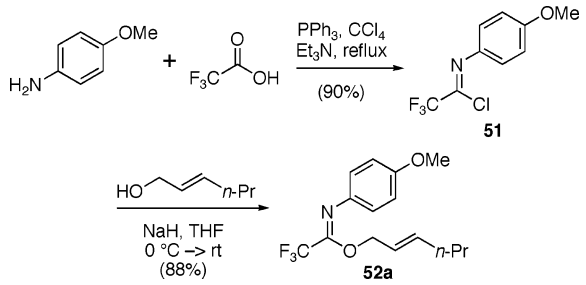


TABLE 5. Rearrangement of Allylic (*E*)-Hexenyl Imidates 5a−d, 46, 50, and 52a with the FOP Catalyst Generated from 9a[a]

entry	imidate	yield of allylamide (%)	% ee/conf[c]
1	**5a**	67	79/*S*
2	**5b**	83	83/*S*
3	**5c**	75	80/*S*
4	**5d**	76	83/*S*
5	**46**	68	5/*S*
6	**50**	no reaction	n/a
7	**52a** (R = *n*-Pr, *E*)	88[b]	76/*S*

[a] Conditions: 5 mol % of **9a** was preactivated by reaction with 4 equiv of Ag ($OCOCF_3$) in CH_2Cl_2 (0.1 M in substrate) at room temperature for 24 h. [b] 7.5 mol % of **9a** and 20 mol % 1,8-bis(dimethylamino)naphthalene. [c] Determined by chiral HPLC after cleavage of the trifluoroacetate group; absolute configuration established by correlation with products reported in ref 4.[33]

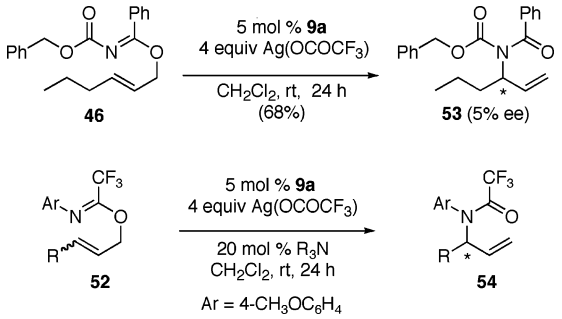
C.2. Evaluation of Substituted Allylic Imidates in the Asymmetric Allylic Imidate Rearrangement with FOP Precatalyst 9a. Catalytic asymmetric rearrangements of allylic imidates **5a**−**d**, **46**, **50**, and **52a** with the FOP catalyst generated from **9a** by reaction with 4 equiv of silver trifluoroacetate were examined (Table 5). Each imidate was then exposed to 5 mol % of the catalyst, and the reaction was maintained for 24 h at room temperature prior to analysis. In the case of trifluoroacetimidate **52a**, the catalyst loading was 7.5 mol %, and 20 mol % of 1,8-bis(dimethylamino)naphthalene was added to prevent competitive decomposition of this acid-sensitive trifluoroacetimidate.

Allylic *N*-arylbenzimidates **5a**−**d** (entries 1−4) rearranged to the corresponding allylic amides in similar yields (67−83%), with enantioselectivities ranging from 79% to 83% ee. The absolute configuration of benzamides **6c** and **6d** were assigned by analogy to those previously determined by chemical correlation of *N*-(4-methoxyphenyl)benzamide **6a** (R = Me) with (*R*)-*N*-benzoylalanine methyl ester.[3a] The Cbz-protected allylic imidate **46** rearranged to give the desired allylic amide **53** in 68% yield; however, the product was nearly racemic (Scheme 12; Table 5, entry 5). The BUS-protected allylic imidate **50** failed to rearrange under these conditions and was

(21) Casy, G.; Patterson, J. W.; Taylor, R. J. K. *Org. Synth.* **1988**, *67*, 193−197.

(22) (a) For use of the BUS group to protect amines, see: Sun, P.; Weinreb, S. M.; Shang, M. *J. Org. Chem.* **1997**, *62*, 8604−8608. (b) For synthesis of *tert*-butylsulfonamide, see: Cogan, D. A.; Liu, G.; Kim, K.; Backes, B. J.; Ellman, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 8011−8019.

SCHEME 12. Rearrangement of Cbz-Protected Benzimidates and *N*-Aryl Trifluoroacetimidates



recovered unchanged from the reaction mixture (entry 6). The allylic *N*-(4-methoxyphenyl)trifluoroacetimidate **52a** (R = *n*-Pr) was more promising, providing the corresponding allylic *N*-(4-methoxyphenyl)trifluoroacetamide **54a** (R = *n*-Pr) in 88% yield and 76% ee (entry 7).

C.3. Deprotection of Enantioenriched Allylic Amides and Exploration of Scope. Cleavage of the nitrogen substituents of the enantioenriched allylic amides synthesized by the reactions reported in Table 5 was examined next. The *N*-(2,4-dimethoxyphenyl)benzamide derived from imidate **5d** (Scheme 8, Table 5, entry 4) was subjected to oxidation under a variety of conditions (ceric ammonium nitrate (CAN),[23] $AgNO_3/(NH_4)S_2O_8$,[20] and $Na_2HPO_4/K_2S_2O_8$[24]), but the dearylated amide was not obtained in greater than 30% yield. Likewise, removal of the benzoyl group by reaction of **6a** with HCl,[25] HBr/AcOH,[26] NaOEt, KO*t*-Bu/H_2O,[27] KOH/MeOH, or DIBAL-H[28] prior to dearylation was also inefficient. The crowded steric environment of benzamides **6** is likely responsible for these difficulties.[29] Similar results were obtained with *N*-(2-methoxyphenyl)benzamide **6c**. As the Cbz-protected allylic imidate **46** and BUS-protected allylic imidate **50** performed poorly in the asymmetric allylic imidate rearrangement, no attempts to deprotect the corresponding allylic amides were made. Finally, deprotection of allylic trifluoroacetamide **54a** proved facile, providing the allylic aniline **55a** in 98% yield after treatment with NaOEt in EtOH at 54 °C for 18 h (Scheme 13, R = *n*-Pr). Dearylation of **55a** with CAN in MeCN/H_2O at 0 °C gave the corresponding primary allylic amine **56a**, isolated as the maleic acid salt, in 74% yield.[4a]

Encouraged by these results, the scope of the enantioselective allylic rearrangement of allylic *N*-(4-methoxyphenyl)trifluoroacetimidates **52** was explored. The starting allylic imidates **52** were prepared in good yields (62−96%) by the procedure described in Scheme 11. The results of the rearrangement of these allylic imidates with 7.5 mol % of the FOP catalyst generated in the standard fashion from precatalyst **9a** are summarized in Table 6. Rearrangement of *E* allylic imidates containing an alkyl (entry 3) or phenethyl substituent (entry 6) at C4 took place in good yields (73% and 81%, respectively) with enantiomeric excesses of 84% ee and 73% ee, respectively. Allylic trifluoroacetimidates derived from *Z* allylic alcohols, however, gave low yields of the corresponding allylic amides, even after prolonged reaction times (entries 2 and 4). Allylic imidate **52e**, derived from cinnamyl alcohol, also rearranged in low yield and with low enantioselectivity (entry 5).

SCHEME 13. Deprotection of *N*-(4-Methoxyphenyl)trifluoroacetamides

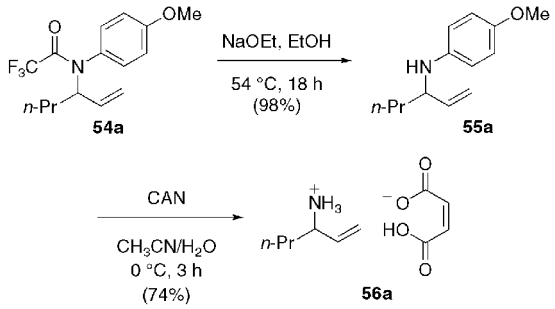


TABLE 6. Rearrangement of Allylic *N*-(4-Methoxyphenyl)trifluoroacetimidates 52 with the Catalyst Generated from FOP Precatalyst 9a[a]

entry	imidate	*E*/*Z*	R	yield (%)	% ee/conf
1	**52a**	*E*	*n*-Pr	88	76/*S*
2	**52b**	*Z*	*n*-Pr	21	87/*R*
3	**52c**	*E*	*i*-Bu	73	84/*S*
4	**52d**	*Z*	*i*-Bu	21	90/*R*
5	**52e**	*E*	Ph	46	45/*R*
6	**52f**	*E*	CH_2CH_2Ph	81	73/*S*

[a] Conditions: 7.5 mol % of **9a** was preactivated by reaction with 4 equiv of $Ag(OCOCF_3)$ and 20 mol % 1,8-bis(dimethylamino)-naphthalene in CH_2Cl_2 (0.2 M in substrate) at room temperature for 24 h.

TABLE 7. Deprotection of Allylic Trifluoroacetamides 54 to Form Enantioenriched Allylic Amines 56

entry	amide	R	yield **55** (%)	yield **56** (%)
1	**54a**	*n*-Pr	98	74
2	**54c**	*i*-Bu	99	70
3	**54e**	Ph	89	70
4	**54f**	CH_2CH_2Ph	93	80

Deprotection of the allylic *N*-(4-methoxyphenyl)trifluoroacetamides **54** to form the parent allylic amines is readily accomplished (Table 7). Cleavage of the trifluoroacetate group by reaction with 3 M NaOEt in EtOH at 55 °C provided amines **54** in excellent yields (89−99%). Subsequent cleavage of the aryl group from amines **55** by reaction with CAN proceeded efficiently to provide primary amine maleic acid salts **56** in 70−80% yield.

Discussion

Catalyst Synthesis and Evaluation. Several properties of the FOP series of catalysts are apparent from

(23) Saito, S.; Hatanaka, K.; Yamamoto, H. *Org. Lett.* **2000**, *2*, 1891−1894.

(24) Fetter, J.; Lempert, K.; Gizur, T.; Nyitrai, J.; Kajtár-Peredy, M.; Simig, G.; Hornyák. G.; Doleschall, G. *J. Chem. Soc., Perkin Trans. 1* **1986**, 221−227.

(25) Hughes, P.; Clardy, J. *J. Org. Chem.* **1988**, *53*, 4793−4796.

(26) Ben-Ishai, D.; Altman, J.; Peled, N. *Tetrahedron* **1977**, *33*, 2715−2717.

(27) (a) Gassman, P. G.; Hodgson, P. K. G.; Balchunis, R. J. *J. Am. Chem. Soc.* **1976**, *98*, 1275−1276. (b) Gassman, P. G.; Schenk, W. N. *J. Org. Chem.* **1977**, *42*, 918−919.

(28) Treatment of amide **6a** with DIBAL-H resulted in inseparable mixtures (1:1 to 4:1) of the desired product and the reduced product, *N*-benzyl-*N*-(4-methoxyphenyl)−(1-propyl-allyl) amine. For procedure see: (a) Gutzwiller, J.; Uskokovic, M. *J. Am. Chem. Soc.* **1970**, *92*, 204−205. (b) Gutzwiller, J.; Uskokovic, M. *Helv. Chem. Acta* **1973**, *56*, 1494−1503. (c) Gutzwiller, J.; Pizzolato, G.; Uskokovic, M. R. *Helv. Chem. Acta* **1981**, *64*, 1663−1671.

(29) For a brief discussion of side reactions in the oxidative removal of *N*-aryl groups from amides, see: Corley, E. G.; Karady, S.; Abramson, N. L. *Tetrahedron Lett.* **1988**, *29*, 1497−1500.

this study. Whereas the synthesis of ferrocenyl oxazoline palladacycle **9a** (Scheme 2, R = $SiMe_3$) could be performed on multigram scale to provide an air-stable solid, the corresponding desilyl congener **24a** (Scheme 3, R = H) is markedly less stable, requiring storage in an oxygen-free atmosphere to prevent decomposition. Similarly, FOP complex **37** (Scheme 5) that also lacks a substituent at C3 of the palladated cyclopentadienyl ring displays similar instability. A substituent at C3 of this ring obviously increases the stability of FOP catalysts.

Suzuki cross-coupling of ferrocenyl iodide **25** (Scheme 4) and aryl boronic acids proved to be a general method to incorporate aryl substituents at C3 of the palladated cyclopentadienyl ring. Electron-rich aryl boronic acids, even those having an ortho substituent, coupled with iodide **25** in high yields. More sterically hindered 2,6-disubstituted aryl boronic acids coupled in lower yield. Electron-deficient aryl boronic acids were also poor coupling partners for the cross-coupling reaction as reduction of the ferrocenyl iodide **25** and homo-coupling of the aryl boronic acid were competitive with cross-coupling.[30]

Several trends are apparent from this study of the rearrangement of allylic *N*-arylbenzimidates **5** with FOP series catalysts. First, activation of the halide-bridged dimer FOP complexes by reaction with a silver salt is required to generate kinetically competent catalysts for the rearrangement of allylic *N*-arylbenzimidates.[31] With all the catalysts examined, somewhat higher enantioselectivity was observed in the rearrangement of the *Z* stereoisomers of **5** than that realized in rearrangements of the corresponding *E* alkene isomers. In general, *Z* allylic *N*-arylbenzimidates rearranged to allylic amides more slowly than the corresponding *E* stereoisomers. The catalysts generated from silyl-containing complexes **9a** (Scheme 3, $SiMe_3$) and **23** (Scheme 3, $SiEt_3$) performed similarly, producing benzamide **6b** in >90% ee. The FOP catalysts containing electron-rich or electron-poor aryl groups, rather than silyl, at the C3 position of the cyclopalladated cyclopentadienyl ring provided quite similar results. In general, no trend in catalyst efficacy, either in terms of rate or enantioselectivity, is apparent as the substituents on the aryl ring are varied. The lower enantioselectivity observed with the catalyst formed from the unsubstituted complex **24** (Scheme 3) likely results from decomposition of this catalyst to generate a less selective catalyst as evidenced by the formation of a black precipitate and mirror on the reaction vessel during the course of the rearrangement. Rearrangements facilitated by the catalyst generated from **40** (Scheme 5) having the R_p configuration and the opposite relative configuration of the oxazoline fragment yielded the opposite enantiomer of benzamide **6b** (with similar ee) to that formed with catalysts generated from the S,S_p and S,R_p pseudo-enantiomeric complexes **9a** and **24** (Scheme 2), respectively. The catalyst generated from **37** (Scheme 5) having the S,S_p configuration gave exceptionally poor enantioselectivity in the rearrangement of (*E*)-**5b** and diminished enantioselectivity in rearranging the *Z* stereoisomer isomer compared to pseudo-diastereomeric catalysts (**9a**-(S,S_p), **23**-(S,S_p), and **40**-(S,R_p). Despite the problems of stability of the catalyst generated from **24** (the S,R_p diastereomer of **37**), this complex also gave much higher enantioselectivity in the rearrangement of (*E*)-**5b** than the catalyst generated from **37**. This decrease in enantioselectivity with the catalyst generated from **37** is consistent with our hypothesis that substituents must reside both above and below the square plane of the palladium(II) catalyst to induce high levels of enantioselectivity.[8]

Development of More Useful Imidates for the Synthesis of Chiral Nonracemic Allylic Amines from Allylic Alcohols. Replacing the aryl substituent of *N*-arylbenzimidates **5a** (Scheme 8) with common, electron-withdrawing nitrogen protecting groups produced imidates that either did not participate in the FOP-catalyzed asymmetric allylic imidate rearrangement, such as the BUS-protected benzimidate **50** (Scheme 10), or did so with low enantioselectivity, such as the Cbz-protected imidate **46** (Scheme 9). *N*-Arylbenzimidates **5b**−**d** (Scheme 8) underwent facile rearrangement to provide the corresponding *N*-arylbenzamides **6b**−**d** in good ee (Table 5); however, removal of the *N*-aryl substituent from the product allylic amides was largely unsuccessful.[29,32]

N-(4-Methoxyphenyl)trifluoroacetimidates, however, were found to be promising substrates for the catalytic asymmetric allylic imidate rearrangement with cationic FOP catalysts. These trifluoroacetimidates underwent asymmetric rearrangement with enantioselectivities somewhat less than those realized in rearrangements of comparable *N*-arylbenzimidates. However, the allylic amide products formed from the former allylic imidates have readily removed *N*-trifluoroacetyl substituents. Rearrangement of *E* allylic *N*-(4-methoxyphenyl)trifluoroacetimidates **52** (Schemes 11 and 12) took place in good yields and enantioselectivities, whereas the corresponding *Z* allylic trifluoroacetimidates rearranged only slowly, providing the rearranged allylic amides in low yield even after prolonged reaction times. Critical to obtaining good yields in the rearrangement of *E* allylic trifluoroacetimidates is the inclusion of an acid scavenger (20 mol % of 1,8-bis(dimethylamino)naphthalene) in the reaction mixture. Without such an additive, decomposition of the trifluoroacetimidate was observed. Presumably, the amine sequesters adventitious acid, thus suppressing the decomposition pathway; trace amounts of protic acid may be formed from the reaction of residual $AgOCOCF_3$ with a small amount of water under the reaction conditions.[33] The rearrangement of the cinnamyl alcohol derived allylic trifluoroacetimidate **52e** (Table 6) was also problematic, proceeding in only low yield and enantioselectivity. The inefficient rearrangement of this imidate results from a competitive ionization-recombination pathway, signaled

(30) This type of side reaction is common in cross-coupling reactions. A variety of mechanisms have been forwarded to explain results of this type; see: Nguyen, P.; Yuan, Z.; Agocs, L.; Lesley, G.; Marder, T. B. *Inorg. Chim. Acta* **1994**, *220*, 289−296 and references therein.

(31) This activation likely involves both salt metathesis, exchanging the iodide of the palladacycle for trifluoroacetate, in addition to oxidation of the ferrocene to a ferrocenium ion by the Ag(I). For studies with precatalyst **9a**, see ref 6.

(32) Oligimerization of the radical cation intermediate during oxidative dearylation has been observed in similar sterically crowded anilide systems and may account of the poor mass recovery from these experiments.[29]

(33) Anderson, C. E. Ph.D. Dissertation, University of California, Irvine, 2003.

by the presence of an amide byproduct resulting from formal [1,3]-rearrangement. This competitive reaction pathway likely results from coordination of the palladium catalyst to the imidate nitrogen, leading to the formation of a stabilized aryl-substituted allyl cation intermediate. Even in light of these limitations, *N*-aryltrifluoroacetimidates **52** remain promising motifs for the asymmetric allylic imidate rearrangement as facile hydrolysis of the trifluoroacetate moiety and subsequent dearylation of amides **54** can be accomplished to provide enantioenriched primary allylic amines **56** (Scheme 13) in good yield over the sequence.

Conclusion

Reported herein is the preparation and evaluation of a small library of ferrocene oxazoline palladacycle (FOP) complexes as asymmetric catalysts for the rearrangement of prochiral allylic imidates. The catalyst library included various members in which the C3 substituent of the palladated cyclopentadienyl ring was varied. Although substitution at the C3 position is important for catalyst stability, it has little to no effect on the efficiency or selectivity of the catalytic rearrangement. The most readily prepared of this group, the silyl FOP catalysts derived from **9** and **40**, proved to be the best catalysts for the asymmetric rearrangement of allylic *N*-arylbenzimidates and the first to realize >90% ees in the production of chiral allylic amides from prochiral allylic imidates.[3a]

In an effort to identify better imidate motifs for asymmetric allylic imidate rearrangements, several allylic imidates were prepared and evaluated. Allylic *N*-(4-methoxyphenyl)trifluoroacetimidates emerged as promising substrates as the product allylic amides can be converted to the parent allylic amines in good yields. Rearrangement of *E* allylic *N*-(4-methoxyphenyl)trifluoroacetimidates take place in good yields, although enantioselectivities were slightly less than those realized with allylic *N*-arylbenzimidates. Further studies of catalytic asymmetric rearrangements of allylic *N*-aryltrifluoroacetimidates identified catalysts related to the FOP catalysts, e.g., COP-Cl, that are highly effective, providing the first practical catalytic asymmetric method for transforming prochiral allylic trihaloacetimidates to chiral allylic amines.[4b]

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Supporting Information Available: Experimental procedures for the preparation of **5c,d**, **6c,d**, **26a**−**h**, **27a**−**c**, **27e,f**, **27h**, **29**−**36**, **43c,d**, **45**−**47**, **49**, **50**, and **53**; tabulated characterization data, copies of ^{1}H and ^{13}C NMR spectra for all new compounds, and representative HPLC traces used to determine enantiopurity; and CIF files for **9a** and **40**. This material is available free of charge via the Internet at http://pubs.acs.org.

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