JOC Article

Palladium-Catalyzed Enantioselective 1,3-Rearrangement of Racemic Allylic Sulfinates: Asymmetric Synthesis of Allylic Sulfones and Kinetic Resolution of an Allylic Sulfinate

Thomas Jagusch, Hans-Joachim Gais,* and Oleg Bondarev

Institut für Organische Chemie der Rheinisch-Westfälischen Technischen Hochschule (RWTH) Aachen, Prof.-Pirlet-Str. 1, 52056 Aachen, Germany

gais@rwth-aachen.de

Received November 5, 2003

Described is an asymmetric synthesis of cyclic and acyclic allylic *S*-aryl and *S*-alkyl sulfones through a highly selective palladium(0)-catalyzed 1,3-rearrangement of racemic allylic sulfinates. Treatment of racemic cyclic and acyclic allylic *S*-tolyl- and *S*-*tert*-butylsulfinates with $Pd_2(dba)_3{\cdot}CHCl_3$ as precatalyst and *N*,*N*′-(1*R*,2*R*)-1,2-cyclohexanediylbis[2-(diphenylphosphino)benzamide] as ligand for the palladium atom afforded the corresponding isomeric allylic *S*-tolyl and *S*-*tert*-butyl sulfones of 93−99% ee in 82−96% yield. The rearrangement of the allylic sulfinates most likely proceeds in an intermolecular fashion via formation of a cationic π-allylpalladium complex and the sulfinate ion. The racemic allylic sulfinates were obtained from the corresponding racemic alcohols and racemic tolylsulfinyl chloride and racemic *tert*-butylsulfinyl chloride, respectively, in high yields. Rearrangement of the racemic *tert*-butylsulfinic acid 2-cyclooct-1-enyl ester with $Pd_2(dba)_3{\cdot}CHCl_3$ and the bisphosphane was accompanied by a highly selective kinetic resolution of the substrate and gave at 50% conversion the (*R*)-configured sulfinate as mixture of the S_S and R_S diastereomers of 92% ee and 85% ee and the (*S*)-configured 3-*tert*-butylsulfonyl cyclooctene sulfone **15a** with 98% ee in almost quantitative yields.

Introduction

Enantioselective palladium-catalyzed 1,3- and 3,3-rearrangements that interchange allylic heteroatoms have, despite their considerable synthetic potential, received only little attention.[1] A notable exception is the palladium(II)-catalyzed 3,3-rearrangement of allylic imidates, which has been developed in recent years into a valuable method for the asymmetric synthesis of allylic amines.[2] We have studied recently the palladium(0)-catalyzed 1,3-rearrangement of racemic acyclic and cyclic *O*-allylic thiocarbamates and observed high enantioselectivities in their conversion to the *S*-allylic thiocarbamates[3] by using the bisphosphane **BPA**[4] as ligand for the palladium atom (Scheme 1).

This rearrangement proceeds in an intermolecular fashion through an ion-pair mechanism; that is, the racemic substrate reacts with the palladium(0) catalyst with formation of a π-allylpalladium(II) complex and the thiocarbamate ion which is subsequently alkylated by the former complex at the S-atom.[3] In continuation of our exploration of the potential of the palladium(0)-catalyzed 1,3-allylic O,S-rearrangement, we became interested in the enantioselective transposition of racemic allylic sulfinates into allylic sulfones (Scheme 2).

Allylic sulfones are important intermediates in organic synthesis because of the ability of the allylic sulfonyl group to act not only as a carbanion-stabilizer but also as a versatile nucleofuge.[5,6] Chiral nonracemic allylic

(1) (a) Kočovský, P.; Starý, I. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., de Meijere, A., Eds.; Wiley-Interscience: New York, 2002; Vol. 2, p 2011. (b) Nakamura, H.; Yamamoto, Y. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., de Meijere, A., Eds.; Wiley-Interscience: New York, 2002; Vol. 2, p 2919. (c) Nubbemeyer, U. *Synthesis* **2003**, 961. (d) Reggelin, M.; Zur, C. *Synthesis* **2000**, 1.

(2) (a) Overman, L. E.; Owen, C. E.; Pavan, M. M.; Richards, C. J. *Org. Lett*. **2003**, *5*, 1809 and previous work of this group cited therein. (b) Uozumi, Y.; Kato, K.; Hayashi, T. *Tetrahedron: Asymmetry* **1998**, *9*, 1065. (c) Jiang, Y.; Longmire, J. M.; Zhang, X. *Tetrahedron Lett*. **1999**, *40*, 1449. (d) Leung, P.-H.; Ng, K.-H.; Li, Y.; White, A. J. P.; Williams, D. J. *Chem. Commun*. **1999**, 2435. (e) Kang, J.; Yew, K. H.; Kim, T. H.; Choi, D. H. *Tetrahedron Lett*. **2002**, *43*, 9509.

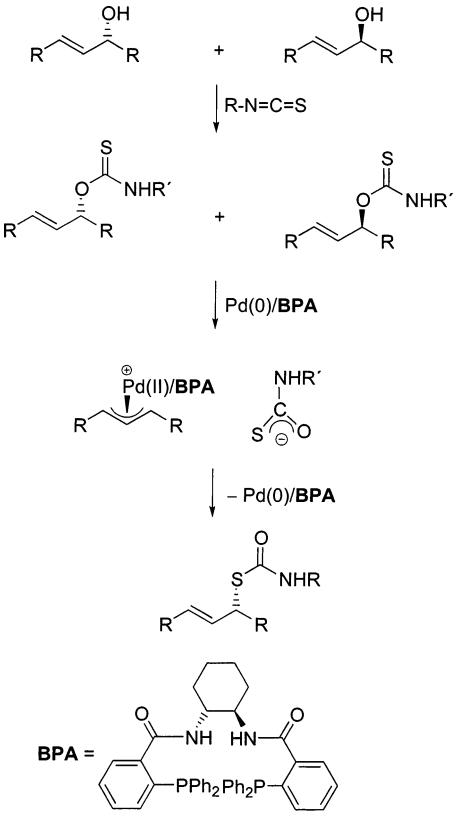
(3) (a) Böhme, A.; Gais, H.-J. *Tetrahedron: Asymmetry* **1999**, *10*, 2511. (b) Gais, H.-J.; Böhme, A. *J. Org. Chem*. **2002**, *67*, 1153.

(4) (a) Trost, B. M.; Van Vranken, D. L. *J. Am. Chem. Soc*. **1992**, *114*, 9327. (b) Sesay, S. J.; Williams, J. M. J. *Adv. Asymetric Synth*. **1998**, *3*, 235. (c) Heumann, A. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 1998; Vol. 1, p 251. (d) Trost, B. M.; Lee, C. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH: Weinheim, 2000; p 593. (e) Acemoglu, L.; Williams, J. M. J. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., de Meijere, A., Eds.; Wiley-Interscience: New York, 2002; Vol. 2, p 1945. (f) Butts, C. P.; Crosby, J.; Lloyd-Jones, G. C.; Stephen, S. C. *Chem. Commun*. **1999**, 1707. (g) Fairlamb, I. J. S.; Lloyd-Jones, G. C. *Chem. Commun*. **2000**, 2447.

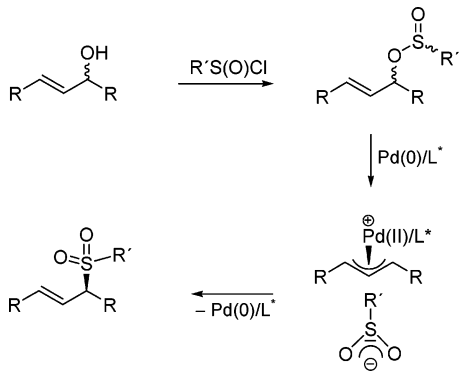
(5) For reviews, see: (a) Biellman, J.-F.; Ducep, J.-B. *Org. React*. **1982**, *27*, 1. (b) Oae, S.; Uchida, Y. In *The Chemistry of Sulfones and Sulfoxides;* Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; Wiley: New York, 1988; p 583. (c) Ogura, K. In *Comprehensive Organic Synthesis*; Schreiber, S. L., Ed.; Pergamon: Oxford, 1991; Vol. 1, p 505. (d) Krief, A. In *Comprehensive Organic Synthesis*; Pattenden, G., Ed.; Pergamon: Oxford, 1991; Vol. 3, p 85. (e) Yamamoto, Y. In *Comprehensive Organic Synthesis;* Heathcock, C. H., Ed.; Pergamon: Oxford, 1991; Vol. 3, p 55. (f) Simpkins, N. S. *Sulphones in Organic Synthesis*, Pergamon: Oxford, 1993**.** (g) Braun, M. In *Stereoselective Synthesis (Houben-Weyl)*; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, 1995; Vol. E21b, p 1713. (h) Pyne, S. In *Stereoselective Synthesis (Houben-Weyl)*; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, 1995; Vol. E21b, p 2068.

10.1021/jo030340d CCC: $27.50
Published on Web 03/19/2004

SCHEME 1. Enantioselective Palladium-Catalyzed 1,3-Rearrangement of Allylic Thiocarbamates



SCHEME 2. Enantioselective Palladium-Catalyzed 1,3-Rearrangement of Allylic Sulfinates (L* = Chiral Ligand)



sulfones could perhaps make interesting starting materials for the stereoselective allylic alkylation of organometallic compounds[7] and for the synthesis of chiral nonracemic allylic α-sulfonyl carbanions.[8] Although the palladium(0)-catalyzed allylic alkylation of sulfinate ions with racemic allylic carbonates already provides an excellent means for the asymmetric synthesis of allylic sulfones,[9,10] the allylic sulfinate to sulfone rearrangement could be a valuable supplement because for the following reasons. While arylsulfinate salts are easily prepared,[11] alkylsulfinate salts are less readily accessible and alkylsulfinic acids tend to be unstable.[12] A further limitation of the allylic alkylation of sulfinate salts can arise because of the necessity to use water as a cosolvent. It was recently observed that racemic allylic carbonates, which are normally preferred over acetates because of their higher reactivity, can suffer in the presence of water a facile palladium(0)-catalyzed "hydrolysis" to the corresponding optically active allylic alcohols.[13] Of advantage to the 1,3-rearrangement route to allylic sulfones would be that (1) racemic allylic sulfinates are readily available from the corresponding racemic allylic alcohols and sulfinyl chlorides,[14] (2) alkyl as well as arylsulfinyl chlorides are both easily accessible from disulfides or thiols and sulfuryl chloride,[15] (3) no external nucleophile would be required, and (4) the thermal rearrangement of allylic sulfinates takes only place at high temperatures.[14,16] Surprisingly, despite these promising prospects only a very few studies of the enantioselective palladium(0)-catalyzed rearrangement of the sulfinates of achiral or racemic allylic alcohols have been described. In an early investigation, Hiroi et al. observed that the tolylsulfinates of some achiral acyclic allylic alcohols suffered in the presence of $Pd(PPh_3)_4$ as precatalyst and (4*R*,5*R*)-4,5-bis-(diphenylphosphinomethyl)-2,2-dimethyl-1,3-diotolane ((−)-DIOP) as ligand a facile rearrangement with formation of the corresponding optically active allylic sulfones together with the isomeric achiral allylic sulfones.[17] However, this first-generation ligand generally provides only low enantioselectivities in palladium(0)-catalyzed allylic substitution.[4c−e,18] In a more recent investigation of the rearrangement of racemic cyclohexenyl tolylsulfinate, an axially chiral P,N-ligand was used

(6) For recent examples, see: (a) Miyaoka, H.; Isaji, Y.; Mitome, H.; Yamada, Y. *Tetrahedron* **2002**, *59*, 61. (b) Chenevert, R.; Courchenese, R. G. *Tetrahedron Lett.* **2002**, *43*, 7971. (c) Kinoshita, M.; Mahisa, O.; Nakamura, D.; Akita, H. *Chem. Pharm. Bull.* **2002**, *50*, 930. (d) Vaz, B.; Alvarez, R.; de Lera, A. R. *J. Org. Chem.* **2002**, *67*, 5040. (e) Scheidt, K. A.; Bannister, T. D.; Tasaka, A.; Wendt, M. D.; Savall, B. M.; Fegley, G. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 6981. (f) Barrero, A. F.; Cuerva, J. M.; Alvarez-Manzaneda, E. J.; Oltra, J. E.; Chahboun, R. *Tetrahedron Lett.* **2002**, *43*, 2793. (g) Furuichi, N.; Hara, H.; Osaki, T.; Mori, H.; Katsumura, S. *Angew. Chem.* **2002**, *114*, 1065; *Angew. Chem., Int. Ed.* **2002**, *41*, 1023. (h) Kim, G. T.; Wenz, M.; Park, J. I.; Hasserodt, J.; Janda, K. D. *Bioorg. Med. Chem.* **2002**, *10*, 1249. (i) Cao, P.-X. *Tetrahedron* **2002**, *58*, 1301.

(7) (a) Trost, B. M.; Ghardiri, M. R. *J. Am. Chem. Soc.* **1986**, *108*, 1098. (b) Trost, B. M.; Merlic, C. A. *J. Am. Chem. Soc.* **1988**, *110*, 5216.

(8) (a) Gais, H.-J.; Vollhardt, J.; Lindner, H. J. *Angew. Chem.* **1986**, *98*, 916; *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 939. (b) Gais, H.-J.; Hellmann, G. *J. Am. Chem. Soc.* **1992**, *114*, 4439. (c) Gais, H.-J.; van Gumpel, M.; Raabe, G.; Müller, J.; Braun, S.; Lindner, H. J.; Rohs, S.; Runsink, J. *Eur. J. Org. Chem.* **1999**, 1627. (d) Piffl, M.; Weston, J.; Anders, E. *Eur. J. Org. Chem.* **2000**, *16*, 2851. (e) Gais, H.-J.; van Gumpel, M.; Schleusner, M.; Raabe, G.; Runsink, J.; Vermeeren, C. *Eur. J. Org. Chem.* **2001**, 4275.

(9) (a) Eichelmann, H.; Gais, H.-J. *Tetrahedron: Asymmetry* **1995**, *6*, 643. (b) Eichelmann, H. Ph.D. Thesis, RWTH Aachen 1997. (c) Gais, H.-J.; Eichelmann, H.; Spalthoff, N.; Gerhards, F.; Frank, M.; Raabe, G. *Tetrahedron: Asymmetry* **1998**, *9*, 235. (d) Gais, H.-J.; Spalthoff, N.; Jagusch, T.; Frank, M.; Raabe, G. *Tetrahedron Lett.* **2000**, *41*, 3809. (e) Gais, H.-J.; Jagusch, T.; Spalthoff, N.; Gerhards, F.; Frank, M.; Raabe, G. *Chem. Eur. J.* **2003**, *9*, 4202.

(10) (a) Trost, B. M.; Organ, M. G.; O'Doherty, G. A. *J. Am. Chem. Soc.* **1995**, *117*, 9662. (b) Trost, B. M.; Krische, M. J.; Radinov, R.; Zanoni, G. *J. Am. Chem. Soc.* **1996**, *118*, 6297. (c) Trost, B. M.; Krueger, A. C.; Bunt, R. C.; Zambrano, J. *J. Am. Chem. Soc.* **1996**, *118*, 6520.

(11) Baskin, J. M.; Wang, Z. *Tetrahedron Lett.* **2002**, *43*, 8479.

(12) Pinnick, H. W.; Reynolds, M. A. *J. Org. Chem.* **1979**, *44*, 160.

(13) Lüssem, B. J.; Gais, H.-J. *J. Am. Chem. Soc.* **2003**, *125*, 6066.

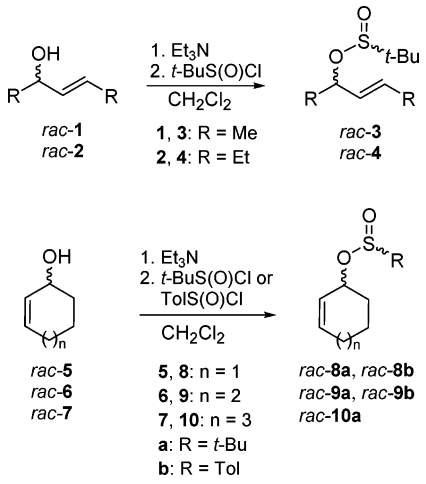
(14) Knight, D. J.; Whitham, G. H.; Williams, J. G.; Hibbs, D.; Hursthouse, M. B. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2149.

(15) (a) Prinzbach, H.; Netscher, T. *Synthesis* **1987**, 683. (b) Hermann, R.; Youn, J.-H. *Tetrahedron Lett.* **1986**, *27*, 1493. (c) Hermann, R.; Youn, J.-H. *Synthesis* **1987**, 72. (d) Sharpless, K. B.; Liu, H.; Gontcharov, A. V. *Org. Lett.* **1999**, *1*, 783.

(16) Hiroi, K.; Makino, K. *Chem. Pharm. Bull.* **1987**, *36*, 1727.

(17) (a) Hiroi, K.; Makino, K. *Chem. Lett.* **1986**, 617. (b) Hiroi, K.; Makino, K. *Chem. Pharm. Bull.* **1988**, *36*, 1744.

SCHEME 3. Synthesis of Racemic Allylic Sulfinates



for the palladium atom. However, the corresponding allylic sulfone was formed with a disappointingly low enantioselectivity.[19]

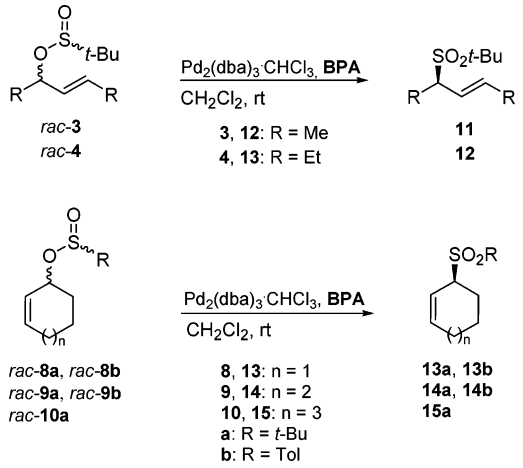
In this paper, we describe the highly enantioselective palladium(0)-catalyzed rearrangement of racemic cyclic and acyclic allylic *S*-aryl- and *S*-alkylsulfinates by using ligand **BPA** and the observation of the kinetic resolution of an allylic sulfinate.

Results and Discussion

Synthesis of Racemic Allylic Sulfinates. The racemic acyclic allylic *tert*-butylsulfinates *rac*-**3** and *rac*-**4** were obtained as mixtures of two diastereomers in a ratio of 1:1 (^{1}H NMR, GC) from the racemic allylic alcohols *rac*-**1** and *rac*-**2**, respectively, and racemic 2-*tert*-butylsulfinyl chloride[15a,d] in CH_2Cl_2 at −10 °C in the presence of NEt_3 in 82% and 92% yield, respectively (Scheme 3).

Similiary, the racemic cyclic allylic *tert*-butyl- and tolylsulfinates *rac*-**8a**, *rac*-**8b** *rac*-**9a**, *rac*-**9b**, and *rac*-**10a**, respectively, were prepared as mixtures of two diastereomers in ratios of 1:1 (GC), 1:1 (^{1}H NMR), 1.2:1 (GC), 1:1 (^{1}H NMR), and 1.3:1 (^{1}H NMR, GC, HPLC), respectively, from the corresponding allylic alcohols *rac*-**5**, *rac*-**6**, and *rac*-**7** and racemic *tert*-butylsulfinyl chloride and tolylsulfinyl chloride[15b] in CH_2Cl_2 at −10 °C in 86%, 85%, 87%, 96%, and 90% yield, respectively. Fortunately, sulfinates *rac*-**3**, *rac*-**4**, *rac*-**8a**, *rac*-**8b**, *rac*-**9a**, *rac*-**9b**, and *rac*-**10a** were stable, and at room temperature no thermal rearrangement[16] to the corresponding racemic sulfones occurred.

SCHEME 4. Palladium-Catalyzed Enantioselective 1,3-Rearrangement of Cyclic and Acyclic Allylic Sulfinates



Palladium-Catalyzed Rearrangement. The chiral bisphosphane **BPA**[4] was selected as ligand for the palladium atom because of the high enantioselectivities which had been recorded previously in the allylic alkylation of tolyl- and *tert*-butylsulfinate ions with racemic cyclic and acyclic allylic carbonates.[9,10] Furthermore, the choice of **BPA** would allow for a direct comparison of the enantioselectivities of the rearrangement of the allylic sulfinates with those of the substitution of the corresponding allylic carbonates or acetates with external sulfinate ions. The $Pd_2(dba)_3{\cdot}CHCl_3$[20] complex was used as precatalyst and CH_2Cl_2 as solvent for the rearrangement reactions of the allylic sulfinates. Besides the variations of the carbon skeleton, the substituent at the S-atom of the racemic allylic sulfinates was varied in order to see whether both aryl- and alkylsulfinates are amendable to a highly selective rearrangement. To avoid regioselectivity problems, only substrates with a symmetrically substituted carbon skeleton were studied.

The palladium catalyzed rearrangement of the racemic acyclic *S*-*tert*-butylsulfinates *rac*-**3** und *rac*-**4** proceeded quantitatively at room temperature and gave the allylic sulfones **11** and **12** of 93% ee and 97% ee, respectively, in high yields (Scheme 4, Table 1, entries 1 and 2).[21] To achieve a complete conversion of the heptenylsulfinate *rac*-**4**, a higher amount of the catalyst was required. Similarly effective was the palladium catalyzed rearrangement of the *S*-*tert*-butyl-substituted cyclohexenyl- and cycloheptenylsulfinates *rac*-**8a** and *rac*-**9a**, respectively, which gave the allylic sulfones **13a** and **14a**, respectively, with 95% ee and 98% ee, respectively, in high yields (entries 3 and 5). The rearrangement is not restricted to allylic *S*-*tert*-butylsulfinates. Treatment of the racemic cyclic *S*-tolylsulfinates *rac*-**8b** and *rac*-**9b** with 2 mol % of $Pd_2(dba)_3{\cdot}CHCl_3$ and 6 mol % of ligand **BPA** at room temperature furnished the allylic *S*-tolyl sulfones **13b** and **14b**, respectively, each with 99% ee in high yields

(18) It was reported that treatment of (±)-4-methylbenzenesulfinic acid (*E*)-2-butenyl ester with 0.15 equiv of $Pd(PPh_3)_4$ in the presence of 0.60 equiv of (−)-DIOP in THF and that of acetic acid (*E*)-2-butenyl ester with *p*-$TsSO_2Na$ in the presence of 0.15 equiv of $Pd(PPh_3)_4$ and 0.60 equiv of (−)-DIOP in THF both gave a mixture of the corresponding achiral sulfone and (−)-1-(but-3-ene-2-sulfonyl)-4-methylbenzene with 88.0% ee and 87.0% ee, respectively.[17] Determination of the ee values of the sulfone was done on the basis of its optical rotation. In our hands, treatment of acetic acid (*E*)-2-butenyl ester with *p*-$TsSO_2$-Na in the presence of 0.15 equiv of $Pd(PPh_3)_4$ and 0.60 equiv of (−)-DIOP in THF afforded a mixture of the corresponding achiral sulfone, the corresponding sulfinate, and (−)-1-(but-3-ene-2-sulfonyl)-4-methylbenzene of only 14% ee.[9a,b] Determination of the ee value of the sulfone was done by GC (Lipodex-E) of the mixture. Identification of the peaks of the chiral sulfone in the GC chromatogram was made by co-injection with the racemic sulfone.

(19) Valk, J. M.; Claridge, T. D. W.; Brown, J. M. *Tetrahedron: Asymmetry* **1995**, *6*, 2597.

(20) Ukai, T.; Kawazura, H.; Ishii, Y. *J. Organomet. Chem.* **1974**, *65*, 253.

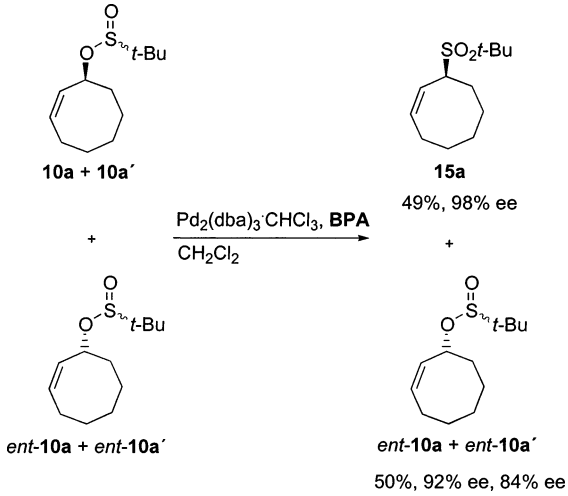
(21) Treatment of *rac*-**3** with 0.15 equiv of $Pd(PPh_3)_4$ in the presence of 0.60 equiv of (−)-DIOP in THF gave sulfone **11** as an *E*/*Z* mixture in a ratio of 9:1 in 90% yield. Sulfones *E*-**11** and *Z*-**11** were of 11% and 17% ee, respectively (GC, Lipodex-E: 15 m, 0.25 mm, 100 kPa H_2; t_R (*E*-**11**) = 24.3 and 28.5 min; t_R (*Z*-**11**) = 25.2 and 30.2 min) (Jagusch, T. Ph.D. Thesis, RWTH Aachen 2003).

TABLE 1. Palladium-Catalyzed Enantioselective Rearrangement of Racemic Allylic Sulfinates

entry	sulfinate[a]	Pd/**BPA** (mol %)	*t* (h)	sulfone	yield (%)	ee (%)
1	*rac*-**3**	4/6	15	**11**	86	93[b]
2	*rac*-**4**	12/19	24	**12**	84	97[b]
3	*rac*-**8a**	4/6	3.5	**13a**	92	95[c]
4	*rac*-**8b**	4/6	15	**13b**	96	99[d]
5	*rac*-**9a**	4/6	19.5	**14a**	82	98[b]
6	*rac*-**9b**	4/6	24	**14b**	87	99[d]
7	*rac*-**10a**	4/6	144	**15a**[e]	49	98[b]
8	*rac*-**10a**	12/19	16	**15a**	84	98[b]

[a] Mixture of two diastereomers. [b] Determined by GC on a chiral stationary phase containing column. [c] Determined by ^{1}H NMR spectroscopy in the presence of a chiral shift reagent. [d] Determined by HPLC on a chiral stationary phase containing column. [e] Besides **15a**, a mixture of *ent*-**10a** and *ent*-**10a′** of 92% ee and 85% ee was isolated in 50% yield.

SCHEME 5. Palladium-Catalyzed Kinetic Resolution of Racemic Cyclooctenylsulfinate

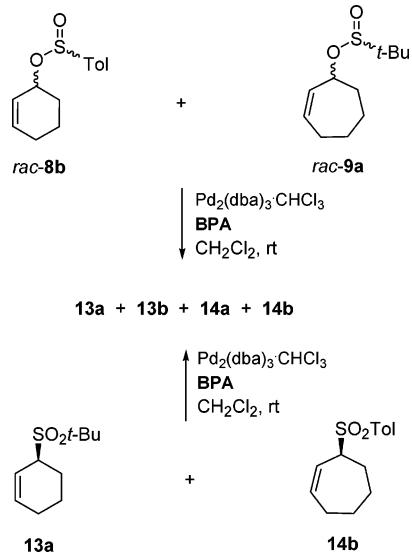


(entries 4 and 6). Thus, all rearrangements proceeded with complete conversion of the racemic substrate.

Kinetic Resolution. Interestingly, treatment of the racemic *S*-*tert*-butyl-substituted cyclooctenylsulfinates *rac*-**10a** and *rac*-**10a′** with 2 mol % of $Pd_2(dba)_3{\cdot}CHCl_3$ and 6 mol % of **BPA** gave the sulfone **15a** with 98% ee in 49% yield and the sulfinates *ent*-**10a** and *ent*-**10a′** of 92% ee and 85% ee, respectively, in 50% yield (Scheme 5) (Table 1, entry 7). The ee values and de value of *ent*-**10a** and *ent*-**10a′** were determined by GC and HPLC analyses on chiral stationary phase containing columns, which allowed a complete separation of the diastereomers and enantiomers. The palladium-catalyzed conversion of *rac*-**10a** and *rac*-**10a′** to **15a** came practically to a complete halt after 50% conversion. Thus, not only a highly selective rearrangement but also a highly selective kinetic resolution of the enantiomeric sulfinates by the chiral Pd(0)/**BPA** catalyst had occurred under these conditions. The different ee values of *ent*-**10a** and *ent*-**10a′** show that the selectivity of the kinetic resolution is also influenced to some extent by the configuration at the S-atom. Although the absolute configuration of the slower reacting diastereomeric sulfinates *ent*-**10a** and *ent*-**10a′** was not determined, we assume with some confidence that both have the *R* configuration at the C-atom.

We had previously observed that the palladium-catalyzed reaction of the racemic cyclooct-2-enyl carbonate with external lithium *tert*-butylsulfinate in the presence of **BPA** also proceeds with a highly selective kinetic resolution of the allylic carbonate, the (*R*)-configured enantiomer being the slower reacting one.[9e,22] However, in this case, a complete conversion of the slower reacting enantiomer of the racemic allylic carbonate to the sulfone **15a** was difficult to achieve and even an increase of the catalyst loading led only to partial success. In contrast, treatment of the mixture of *rac*-**10a** and *rac*-**10a′** with 6 mol % of $Pd_2(dba)_3{\cdot}CHCl_3$ and 19 mol % of ligand **BPA** led to a quantitative rearrangement of both the fast- and the slow-reacting enantiomers of the sulfinate and gave sulfone **15a** with 98% ee in 84% yield (entry 8).

SCHEME 6. Palladium-Catalyzed Rearrangement of Mixtures of Allylic Sulfinates and Allylic Sulfones



Mechanistic Considerations. A comparison between the palladium-catalyzed rearrangement of the racemic cyclic and acyclic allylic sulfinates *rac*-**3**, *rac*-**4**, *rac*-**8a**, *rac*-**8b**, *rac*-**9a**, *rac*-**9b**, and *rac*-**10a** and the palladium-catalyzed substitution of the corresponding racemic allylic carbonates with external lithium *tert*-butylsulfinate and sodium tolylsulfinate both by using phosphane **BPA** as ligand[9,10] reveals the same sense and a similar high degree of asymmetric induction in the formation of the sulfones **11**, **12**, **13a**, **13b**, **14a**, **14b**, and **15a**, respectively. These results together with those obtained previously in studies of the mechanism of the palladium(0)-catalyzed allylic sulfinate−sulfone rearrangement[4e,17] strongly suggest that the rearrangement of the allylic sulfinates also proceeds by an intermolecular ion-pair mechanism. Its key steps are (1) the reaction of both enantiomers of the racemic allylic sulfinates with the Pd(0)/**BPA** catalyst with the formation of one π-allyl-

(22) For further examples of a kinetic resolution of racemic allylic substrates in palladium(0)-catalyzed reactions with **BPA**, see: (a) Frank, M.; Gais, H.-J. *Tetrahedron: Asymmetry* **1998**, *9*, 3353. (b) Lloyd-Jones, G. C.; Stephen, S. C. *Chem. Commun.* **1998**, 2321. (c) Trost, B. M.; Hembre, E. J. *Tetrahedron Lett.* **1999**, *40*, 219. (d) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 3543. (e) Trost, B. M.; Dudash, J. Jr., Hembre, E. J. *Chem. Eur. J.* **2001**, *7*, 1619. (f) Dominguez, B.; Hodnett, N. S.; Lloyd-Jones, G. C. *Angew. Chem.* **2001**, *113*, 4419; *Angew. Chem., Int. Ed.* **2001**, *40*, 4289. (g) Lüssem, B. J.; Gais, H.-J. *J. Am. Chem. Soc.* **2003**, *125*, 6066.

palladium(II)/**BPA** complex or one set of equilibrating complexes and the sulfinate anion as internal nucleophile and (2) the substitution of the π-allylpalladium(II)/**BPA** complex by the sulfinate ion with the S-atom with formation of the allylic sulfone and the catalyst (cf. Scheme 1). Equilibrium between the allylic sulfinate and the allylic sulfone is on the side of the latter because of its greater thermodynamic stability.[23]

The formation of an ion pair and the establishment of an equilibrium is supported by the following observations. Treatment of a mixture of the cyclic sulfinates *rac*-**8b** and *rac*-**9a** with $Pd_2(dba)_3$·$CHCl_3$ and **BPA** in CH_2Cl_2 at room temperature led, according to GC analysis, to the formation of a mixture of sulfones **13a**, **13b**, **14a**, and **14b** (Scheme 6). A similar treatment of a mixture of sulfones **13a** and **14b** with $Pd_2(dba)_3$·$CHCl_3$ and **BPA** in CH_2Cl_2 at room temperature also afforded a mixture of sulfones **13a**, **13b**, **14a**, and **14b**.

Conclusion

Two complementary highly selective routes are now available for the palladium-catalyzed asymmetric synthesis of allylic sulfones from racemic allylic alcohols, the substitution of racemic allylic esters with external sulfinate ions, and the 1,3-rearrangement of racemic allylic sulfinates, which uses internal sulfinate ions. The observation of the same sense and similar degrees of asymmetric induction in both the palladium-catalyzed allylic alkylation of external sulfinate ions with allylic esters and the 1,3-rearrangement of allylic sulfinates together with results of cross-over experiments support the notion of an intermolecular ion-pair mechanism of the rearrangement. The 1,3-rearrangement route should find application especially in cases where (1) sulfinate salts are not readily accessible, (2) the necessary use of water as a cosolvent represents a problem, and (3) the high selectivity of the kinetic resolution of a racemic substrate makes a complete conversion difficult.

Experimental Section

General Procedure for the Synthesis of *O*-Allylic Sulfinates (GP1). A solution of racemic 2-methylpropane-2-sulfinyl chloride or racemic 4-methylbenzenesulfinyl chloride in CH_2Cl_2 (10 mL) was added to a solution of the racemic allylic alcohol (1 equiv) and Et_3N (1.2 equiv) in CH_2Cl_2 (10 mL) at −10 °C. The mixture was stirred at −10 °C for 2 h and then diluted with CH_2Cl_2 (10 mL). Subsequently, the mixture was successively washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl and then dried ($MgSO_4$) and concentrated in vacuo. Purification by column chromatography (pentane/ether, 2:1) gave the racemic sulfinate as a mixture of diastereomers.

2-Methylpropane-2-sulfinic Acid 2-Clooct-1-enyl Ester (*rac*-10a). Following GP1, the reaction of alcohol *rac*-**7** (1.26 g, 10 mmol) with 2-methylpropane-2-sulfinyl chloride (1.41 g, 10 mmol) gave a diastereomeric mixture (1.3:1, ^{1}H NMR; 1.3:1, GC and 1.4:1, HPLC) of the sulfinate *rac*-**10a** (2.07 g, 90%) and *rac*-**10a′** as a colorless oil: HPLC (Chiralcel OF column, *n*-heptane/EtOH, 99:1) major diastereomer t_R = 19.9 and t_R = 21.6, minor diastereomer t_R = 30.1, t_R = 34.1 min; GC (Hydrodex-β-6-TBDM) t_R (*ent*-**10a**) = 73.4, t_R (**10a**) = 74.7, t_R (*ent*-**10a′**) = 75.1, t_R (**10a′**) = 76.7 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 9H), 1.33−2.67 (m, 7H), 1.97−2.25 (m, 3H), 5.03−5.15 (m, 1H), 5.45−5.77 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6 (d), 23.3 (u), 23.5 (u), 25.7 (u), 25.8 (u), 26.4 (u), 26.5 (u), 28.7 (u), 28.8 (u), 36.1 (u), 36.7 (u), 56.9 (u), 57.1 (u), 77.2 (d), 78.4 (d), 129.5 (d), 130.6 (d), 130.9 (d), 131.2 (d); MS (CI) *m*/*z* (relative intensity) 231 [M^+ + 1] (32), 123 (100); IR (film) ν 3024 (w), 2928 (s), 2861 (s), 1475 (m), 1457 (m), 1363 (m), 1186 (w), 1128 (s), 1021 (m) cm^{-1}. Anal. Calcd for $C_{12}H_{22}O_2S$ (230.41): C, 62.58; H, 9.63. Found: C, 62.25; H, 9.72.

General Procedure for the Palladium-Catalyzed Rearrangement of Allylic Sulfinates (GP2). Ligand **BPA** and $Pd_2(dba)_3$·$CHCl_3$ were placed in a Schlenk flask, and CH_2Cl_2 (10 mL) was added at room temperature. After formation of the palladium−ligand complex, which is indicated by the development of an orange color of the solution, the allylic sulfinate (1 mmol) was added and the mixture was stirred at room temperature. After TLC indicated a complete consumption of the starting material, the mixture was quenched through addition of saturated aqueous NaCl (10 mL). The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification by chromatography (pentane/ether, 3:1) gave the pure allylic sulfone.

(−)-(*R*,*E*)-4-(2-Methylpropane-2-sulfonyl)-pent-2-ene (11). Following GP2, rearrangement of sulfinate *rac*-**3** (185 mg, 0.98 mmol) in the presence of **BPA** (41 mg, 0.06 mmol) and $Pd_2(dba)_3$·$CHCl_3$ (21 mg, 0.02 mmol) for 12 h gave sulfone **11** (160 mg, 86%) as a colorless oil: 93% ee (GC, Lipodex-E, t_R (**11**) = 34.1 min, t_R (*ent*-**11**) = 34.9 min); $[\alpha]_D$ = −9.4 (*c* 1.15, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 (s, 9H), 1.48 (d, *J* = 6.9 Hz, 3H), 1.75 (dd, *J* = 6.4, 1.5 Hz, 3H), 3.87 (dq, *J* = 6.4, 9.1 Hz, 1H), 5.58 (ddq, *J* = 9.2, 15.3, 1.5 Hz, 1H), 5.73(dq, *J* = 6.2, 15.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.8 (d), 17.9 (d), 24.5 (d), 58.1 (d), 61.2 (u), 127.3 (d), 130.7 (d); MS (CI) *m*/*z* (relative intensity) 191 [M^+ + 1] (3), 151 (31), 123 (100), 69 (43); IR (film) ν 3028 (w), 2978 (m), 2937 (m), 2877 (w), 1479 (m), 1451 (m), 1368 (w), 1287 (s), 1113 (s), 1012 (m) cm^{-1}. Anal. Calcd for $C_9H_{18}O_2S$ (190.29): C, 56.80; H, 9.53. Found: C, 56.77; H, 9.42.

(+)-(*S*)-3-(2-Methyl-propane-2-sulfonyl)cyclooctene (15a). Following GP2, rearrangement of sulfinate *rac*-**10a** (218 mg, 0.95 mmol) in the presence of **BPA** (135 mg, 0.19 mmol) and $Pd_2(dba)_3$·$CHCl_3$ (66 mg, 0.06 mmol) for 16 h gave sulfone **15a** (184 mg, 84%) as a colorless solid: 98% ee (GC, Hydrodex-β-6-TBDM, t_R (**15a**) = 64.5 min, t_R (*ent*-**15a**) = 65.2 min); $[\alpha]_D$ = +135.4 (*c* 0.985, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27−1.38 (m, 2H), 1.42 (s, 9H), 1.45−1.58 (m, 1H), 1.70−1.85 (m, 4H), 1.98−2.13 (m, 1H), 2.15−2.29 (m, 2H), 4.13−4.24 (m, 1H), 5.70 (m, 1H), 5.93 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1 (u), 24.3 (d), 26.8 (u), 27.3 (u), 27.3 (u), 29.2 (u), 55.2 (d), 60.9 (u), 125.2 (d), 132.5 (d); MS (CI) *m*/*z* (relative intensity) 231 [M^+ + 1] (100), 123 (72); IR (KBr) ν 3905 (w), 3631 (w), 3453 (m), 3029 (m), 2989 (s), 2930 (s), 2859 (s), 1463 (s), 1398 (w), 1367 (w), 1282 (s), 1245 (m), 1220 (w), 1194 (m), 1112 (s), 1010 (w) cm^{-1}. Anal. Calcd for $C_{12}H_{22}O_2S$ (230.406): C, 62.58; H, 9.63. Found: C, 62.49; H, 9.78.

Kinetic Resolution of 2-Methylpropane-2-sulfinic Acid 2-Clooct-1-enyl Ester (*rac*-10a and *rac*-10a′): (*S*)-3-(2-Methylpropane-2-sulfonyl)cyclooctene (15a) and (*R*)-2-Methylpropane-2-sulfinic Acid 2-Clooct-1-enyl Ester (*ent*-10a and *ent*-10a′). Following GP2, rearrangement of a diastereomeric mixture (1:1.6, ^{1}H NMR) of sulfinate *rac*-**10a** and ***ent*-10a′** (249 mg, 1.08 mmol) in the presence of **BPA** (41 mg, 0.06 mmol) and $Pd_2(dba)_3$·$CHCl_3$ (21 mg, 0.02 mmol) for 6 d gave sulfone **15a** (122 mg, 49%) as a colorless solid of 98% ee (GC, Hydrodex-β-6-TBDM, t_R (**15a**) = 64.5, t_R (*ent*-**15a**) = 65.1 min): $[\alpha]_D$ = +135.4 (*c* 0.985, CH_2Cl_2) and a mixture of sulfinates *ent*-**10a** and *ent*-**10a′** (124 mg, 50%) in a ratio of 1.6:1 (^{1}H NMR) as a colorless oil. *ent*-**10a′**: 85% ee (GC,

(23) Liebman, J. F.; Crawford, K. S. K.; Slayden, S. W. In *The Chemistry of Sulphur-Containing Functional Groups*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1993; Supplement S, p 197.

Hydrodex-β-6-TBDM, t_R (ent-**10a′**) = 75.1, t_R (**10a′**) = 76.7 min. *ent*-**10a**: 92% ee (GC, Hydrodex-β-6-TBDM, t_R (*ent*-**10a**) = 73.4, t_R (**10a**) = 74.7 min.

Acknowledgment. Financial support of this work by the Deutsche Forschungsgemeinschaft (Collaborative Research Center "Asymmetric Synthesis with Chemical and Biological Methods" SFB 380) is gratefully acknowledged. One of us (O.B.) thanks the Deutsche Akademische Austauschdienst (DAAD) for a fellowship. We thank Cornelia Vermeeren for GC and HPLC analyses.

Supporting Information Available: General experimental methods, experimental procedures, and characterization of compounds not described in the Experimental Section. This material is available free of charge via the Internet at http://pubs.acs.org.

JO030340D