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Asymmetric lithiation of 2-alkynyl aryl sulfides—Enantio- and diastereoselective formation of allenyl aryl sulfides and their application in nickel-catalyzed cross-coupling reactions

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Abstract—The enantio- and diastereoselective synthesis of allenyl aryl sulfides by asymmetric lithiation of 2-alkynyl (2-hetero)aryl sulfides is described. A dynamic thermodynamic resolution by selective crystallization of the intermediate lithium complexes derived from deprotonation, applying a bis(oxazoline) ligand, was achieved to give enantioselectivities up to 85% ee. Subsequent stereospecific nickel-catalyzed cross-coupling reactions with arylzinc reagents established a versatile access to threefold carbon-substituted allenes.

Asymmetric synthesis is pervaded by the chemistry of chiral organolithiums; especially lithiated α-hetero-substituted reagents and intermediates became essential tools in enantioselective synthesis.[1] Among these, α-thio-substituted carbanions were often the matter of mechanistic interest but of little synthetic significance.[2–5] Possibly, because chiral α-hetero-carbanions are predominantly generated by asymmetric deprotonation pathways requiring a configurationally stable lithium species, whereas α-thio-carbanions are known to racemize rapidly even at temperatures below −78 °C.[6] Only a few α-thio-substituted organolithium compounds show considerable configurational stability; they are all derived from dipole stabilized secondary *S*-organyl thiocarbamates.[7] The first highly enantioselective reaction of a configurationally labile, non-dipole stabilized α-thio-organolithium intermediate was demonstrated by Toru and co-workers.[8] They reported the asymmetric substitution of α-lithiated benzyl aryl sulfides applying bis(oxazoline)s as external chiral ligands. A high level of asymmetric induction was achieved in the post-deprotonation step by dynamic thermodynamic resolution of the intermediate lithium bis(oxazoline) complex or by dynamic kinetic resolution upon the reaction with electrophiles, respectively.[9,10] They also expanded this method successfully to the enantioselective lithiation and substitution of allyl aryl sulfides.[11] However, since the work of Nakai,[12] asymmetric induction arising from complexation with chiral bis(oxazoline) ligands became an efficient method for enantioselective synthesis utilizing configurationally labile lithium-carbanions.[13,14]

In a corporation of the Toru and the Hoppe group, we became interested in the asymmetric lithiation of 2-alkynyl aryl sulfides: propargylic lithium-carbanions are formidable precursors for titanium-mediated synthesis of allenes demonstrated in recent example.[15,16] Enantioenriched 4-hydroxyallenes **2** were isolated in good yields and with excellent diastereomeric ratios after (−)-sparteine-mediated, asymmetric deprotonation of **1**, transmetallation with $ClTi(OiPr)_3$, and subsequent suprafacial addition to aldehydes (Scheme 1).

The synthesis of optically active allenyl aryl sulfides provides the special attraction that sulfides serve well as electrophilic reagents in transition-metal cross-coupling reactions.[17,18] Hence, herein we report an access to

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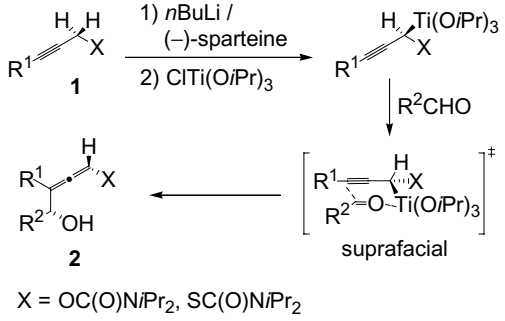
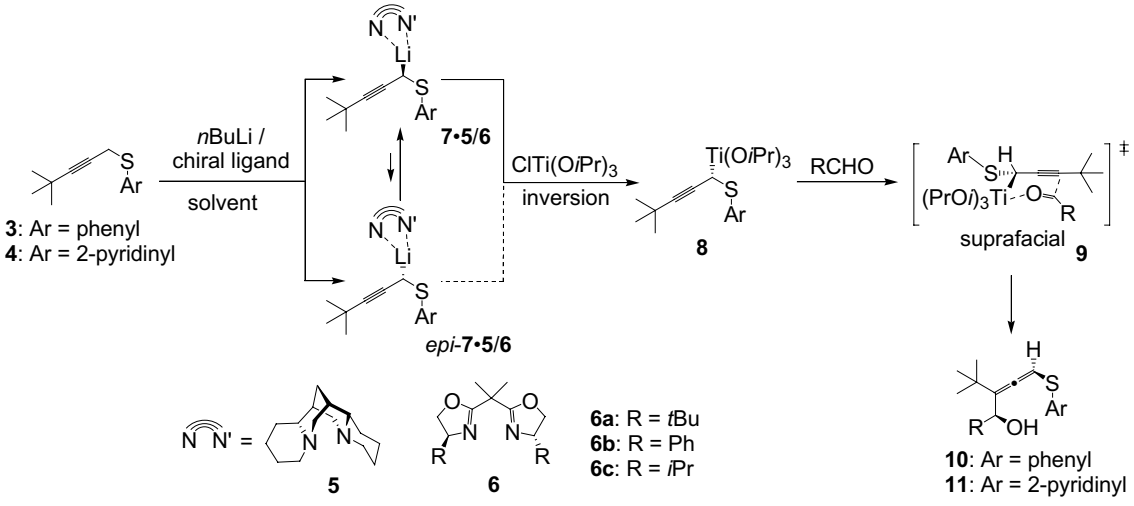


Scheme 1. Stereoselective synthesis of allenyl carbamates **2**.

enantioenriched allenyl aryl sulfides by asymmetric lithiation in the presence of bis(oxazoline) ligands and, moreover, we present first results concerning the nickel-catalyzed coupling reactions with organozinc reagents to form threefold carbon-substituted allenes.[19,20]

Our initial studies focused on 2-alkynyl phenyl sulfide **3**.[21] Lithiation with 1.2 equiv of *n*-butyllithium (*n*BuLi) in toluene or diethyl ether in the presence of 1.3 equiv of chiral bis(oxazoline) **6a** proceeded smoothly within 60 min at −78 °C. Subsequent transmetallation to titanium by adding 3 equiv of $ClTi(OiPr)_3$ or $ClTi(NEt_2)_3$, respectively, and reaction with 2-naphthaldehyde regioselectively gave the 4-hydroxy allene **10** (Ar = phenyl, R = 2-naphthyl) in good yield but in low enantioselectivities and without any diastereoselectivity (Scheme 2, Table 1, entries 1 and 2). The phenyl moiety seems to be not suitable for a diastereoselective hydroxyalkylation presumably due to the lack of chelating properties leading to an incomplete lithium-titanium exchange or a less defined reaction pathway than the Zimmerman–Traxler-type transition state **9** proposed for the addition to carbonyl compounds. Better results were achieved utilizing 2-pyridinyl propargyl sulfides **4**.[21] Upon deprotonation with *n*BuLi at −78 °C and addition of 2 equiv $ClTi(OiPr)_3$ a transmetallation time of only 5–10 min was sufficient to get the diastereomerically pure allene **11b** (Ar = 2-pyridinyl, R = 2-naphthyl) in reasonable yields. Regarding the enantioselectivity of this reaction, again only slightly enantioenriched products were obtained. Upon deprotonation in diethyl ether in the presence of bis(oxazoline) ligand **6a**, the enantiomeric excess increased slightly with prolongation of the deprotonation time, but never exceeded 20% ee (entries 3–5). Higher temperatures, meaning heating–cooling procedures, had no impact on the enantiomeric excess, whereas reaction at −96 °C resulted in a significantly lower selectivity giving *ent*-**11b** with only 1% ee (entries 6 and 7). Change of solvents did not improve the enantioselectivity (entries 8 and 9). Using bis(oxazoline) **5b**, the chemical stability of the intermediate lithium complexes **7·6b** decreased. Only lithiation at −78 °C in diethyl ether as well as in toluene containing 2 equiv of diethyl ether was possible. But the outcome of the reactions was comparable to that obtained with **6a**. However, in this case the opposite enantiomer of *ent*-**11b** was formed with 13% and 16% ee, respectively (entries 10 and 11). Reactions in the presence of (−)-sparteine (**2**) in diethyl ether or toluene gave the 4-hydroxy allenes *ent*-**11b** in moderate enantiomeric excesses as well (entries 12–15).

Gaining poor stereoselection within deprotonation in solution we went for a last chance finding conditions for an asymmetric transformation of the second kind of the diastereomeric lithium complexes **7·5/6** by selective crystallization.[16,22,23] Upon deprotonation in *n*-hexane precipitation of the lithium complexes **7·5/6** was observed. Efforts towards the optimization achieving a selective crystallization utilizing (−)-sparteine (**5**), bis(oxazoline) **6b** or **6c** were unsuccessful (entries 20–22). In the presence of bis(oxazoline) **6a** a selective crystallization occurred upon the deprotonation at −50 °C (entry 17). Transmetallation with $ClTi(OiPr)_3$ and trapping with 2-naphthaldehyde at −78 °C gave allene **11b** in 73% yield and 77% ee. Surprisingly, the opposite enantiomer was formed compared to reaction in diethyl ether or toluene. The best result was obtained for the



Scheme 2. Asymmetric lithiation of **3** and **4**: enantio- and diastereoselective synthesis of allenyl aryl sulfides **10** and **11** (Only the major enantiomer of **8** is depicted.).

Table 1. Investigations of the enantioselective lithiation of **3** and **4** and titanium-mediated addition to 2-naphthaldehyde (R = 2-naphthyl)

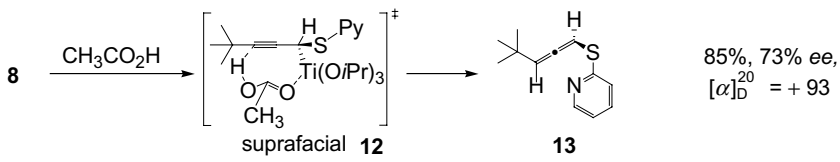
Entry	Sulfide	Ligand	Solvent	$T_{deprot.}$ (°C) ($t_{deprot.}$ (min))	Product	Yield (%)	dr[a]	ee[b] (%)
1	**3**	**6a**	Diethyl ether	−78 (60)	**10**	91	53:47	13
2[c]	**3**	**5**	Toluene	−78 (60)	**10**	63	62:38	15
3	**4**	**6a**	Diethyl ether	−78 (30)	*ent*-**11b**	67	⩾95:5	13
4	**4**	**6a**	Diethyl ether	−78 (90)	*ent*-**11b**	83	⩾95:5	19
5	**4**	**6a**	Diethyl ether	−78 (240)	*ent*-**11b**	65	⩾95:5	19
6	**4**	**6a**	Diethyl ether	−78 (30), −40 (60), −78 (30)	*ent*-**11b**	56	⩾95:5	19
7	**4**	**6a**	Diethyl ether	−96 (90)	*ent*-**11b**	79	⩾95:5	1
8	**4**	**6a**	Toluene	−78 (90)	*ent*-**11b**	62	⩾95:5	2
9	**4**	**6a**	Toluene	−78 (30), −55 (60), −78 (30)	*ent*-**11b**	75	⩾95:5	4
10	**4**	**6b**	Diethyl ether	−78 (90)	**11b**	41	⩾95:5	13
11	**4**	**6b**	Toluene[d]	−78 (60)	**11b**	64	⩾95:5	16
12	**4**	**5**	Diethyl ether	−78 (120)	*ent*-**11b**	72	⩾95:5	3
13	**4**	**5**	Diethyl ether	−78 (30), −40 (60), −78 (30)	*ent*-**11b**	76	⩾95:5	16
14	**4**	**5**	Toluene	−78 (60)	*ent*-**11b**	72	⩾95:5	11
15	**4**	**5**	Toluene	−78 (30), −30 (60), −78 (30)	*ent*-**11b**	66	⩾95:5	7
16	**4**	**6a**	Hexane	−78 (60)	*ent*-**11b**	79	⩾95:5	15
17	**4**	**6a**	Hexane	−50 (60), −78 (10)	**11b**	73	⩾95:5	77
18	**4**	**6a**	Hexane	−50 (120), −96 (10)	**11b**	69	⩾95:5	85
19[e]	**4**	**6a**	Hexane	−50 (120), −96 (10)	**11b**	61	⩾95:5	84
20	**4**	**6b**	Hexane	−50 (60), −78 (10)	**11b**	—[f]	—	—
21	**4**	**6c**	Hexane	−50 (60), −78 (10)	**11b**	58	⩾95:5	16
22	**4**	**5**	Hexane	−40 (120), −78 (15)	*ent*-**11b**	88	⩾95:5	4

[a] Determined by ^{1}H NMR analysis of the crude product.
[b] Determined by HPLC on chiral phase (Chiralcel® OD-H).
[c] $ClTi(NEt_2)_3$ was used instead of $ClTi(OiPr)_3$.
[d] Contains 2 equiv of Et_2O.
[e] Transmetallation with $ClTi(OiPr)_3$ for 2 h.
[f] Only decomposition was observed.

deprotonation and crystallization in *n*-hexane at −50 °C in the presence of ligand **6a** (Table 1, entry 18). Subsequent reaction with $ClTi(OiPr)_3$ at −96 °C and final addition of 2-naphthaldehyde afforded the diastereomerically pure allene **11b** in 69% yield and 85% ee. Trapping titanate **7** with acetic acid at 96 °C gave allene **13** in 85% yield and 73% ee (Scheme 3). Within this reaction, a variety of other aromatic and aliphatic aldehydes beside 2-naphthaldehyde were used successfully (Table 2, entries 1, 3–5). Unfortunately, efforts to extend this methodology to 2-alkynyl 2-pyridinyl sulfides **14** and **15** failed (Fig. 1). Only decomposition products were obtained from the trimethylsilyl-substituted propargyl sulfide **14** whereas reactions of **15** led to the corresponding allenyl sulfide with poor enantioselectivities.

The *aR*,*S*-configuration of allenes **11** was concluded from an X-ray crystal structure analysis with anomalous dispersion of **11a** (Fig. 2).[24,25]

Considering Zimmerman–Traxler-type transition state **9** and therefore a suprafacial addition to aldehydes, the corresponding titanate has to be *S*-configured. Consequently, allene **13** is formed with *aS*-configuration assuming transition state **12**. The lithium-titanium exchange has been proven for the analogous *S*-2-alkynyl thiocarbamates and other related allyllithium compounds to proceed with stereoinversion.[16b,22,26] Accepting this to hold true for lithiated 2-alkynyl 2-pyridinyl sulfides, the *R*-configuration can be assigned to the precipitating intermediate lithium species **7**·**6a**. Hence, the favoured diastereomer upon the deprotonation in solution is (*S*)-**7**·**6a**. The intermediate lithium complexes **7**·**6a** are prone to epimerize rather slowly in solution at −78 °C. Dissolution of the precipitate after selective crystallization in toluene and stirring for 1 h at −78 °C before trapping with $ClTi(OiPr)_3$ and 2-naphthaldehyde gave allene **11b** in 67% yield with 14% ee. But still the opposite enantiomer to that found for deprotonation in solution was obtained. Regarding the transmetallation step itself, no hints could be found pointing towards a dynamic kinetic resolution.[27] Thus, the origin of stereoselection is due to a dynamic thermodynamic resolution by selective crystallization: At −50 °C, epimerization is rapid enough for the selective and complete crystallization of the *R*-configured diastereomeric lithium complex (*R*)-**7**·**6a**. Surprisingly, the intermediate titanate **7** racemized slowly at −78 °C.[28] Prolongation

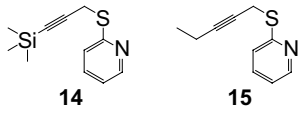


Scheme 3. Enantioselective synthesis of **11**.

Table 2. Stereoselective synthesis of allenyl 2-pyridinyl sulfides **11**

Entry	R	Product	Yield (%)	dr[a]	ee[b] (%)	$[\alpha]_D^{20c}$
1	Phenyl	**11a**	69	⩾95:5	80	+609
2	2-Naphthtyl	**11b**	73	⩾95:5	85	+752
3[d]	2-Furyl	**11c**	72	⩾95:5	81	+505
4[c]	Methyl	**11d**	70	⩾95:5	84	+147
5	Isopropyl	**11e**	66	⩾95:5	79	+78

[a] Determined by ^{1}H NMR analysis of the crude product.
[b] Determined by HPLC on chiral phase (Chiralcel® OD-H, ChiraGrom types 1 and 2).
[c] $CHCl_3$, $c = 0.98$–1.10.
[d] $ClTi(NEt_2)_3$ was used instead of $ClTi(OiPr)_3$.



14 **15**

Figure 1. 2-Alkynyl 2-pyridinyl sulfides **14** and **15**.

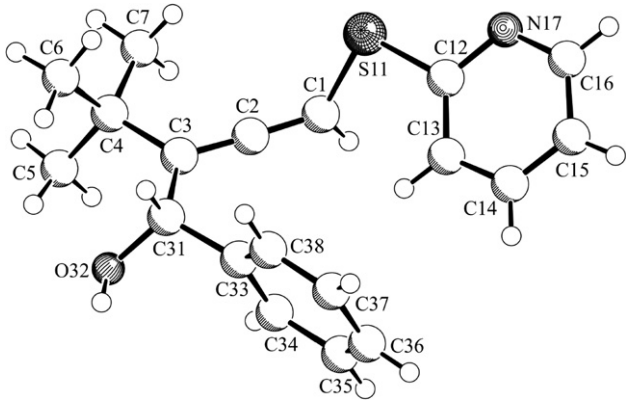


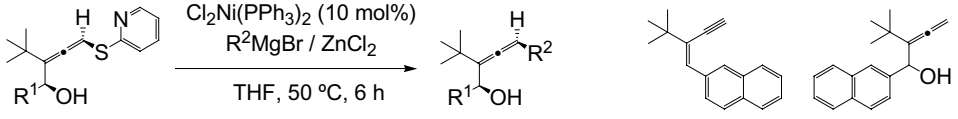
Figure 2. X-ray crystal structure analysis of **9ba**.

of transmetallation time at −78 °C to 2 h led to a dramatic decrease in enantioselectivity; the enantiomeric excess of **11b** dropped to 17%. This enantiomerization had no influence on reactions in diethyl ether or toluene,[29] but obviously affected the enantioselectivity upon selective crystallization (Table 1, entries 17 and 18). However, at −96 °C the titanate showed complete configurational stability.

With the enantioenriched and diastereomerically pure allenyl 2-pyridinyl sulfides **11** in hand, we now investigated their utility as halide equivalents in nickel-catalyzed coupling reactions (Table 3).[30] Initial attempts employing **11b** and Grignard reagents in toluene at 90 °C or THF at 50 °C in the presence of 10 mol % $Cl_2Ni(PPh_3)_2$ provided enyne **17** as the major product.[31] Reasonable improvements were achieved using the corresponding zinc compounds accessible by transmetallation of the Grignard reagents with $ZnCl_2$.[32] Reaction of **11b** with 4 equiv of phenylzinc chloride in THF at 50 °C for 6 h gave the desired coupling product **16aa** within 6 h in 77% yield, isolated as single diastereomer (entry 1).[33] A screening of other nickel catalysts confirmed $Cl_2Ni(PPh_3)_2$ to give the best results (entries 2 and 3).

Under these conditions, cross-coupling reactions of allenyl sulfides **11a** and **11e** with arylzinc reagents afforded the trisubstituted allenes **16ba** and **16bb** stereospecifically in 68% and 60% yields with 79% and 78% ee, respectively (entries 4 and 5). Employing alkylzinc

Table 3. Nickel-catalyzed cross-coupling reactions of **11**



11 **16** **17** **18**

Entry	Sulfide	ee (%) sulfide	Ni-catalyst	R^1	R^2	Product	Yield (%)	dr[a]	ee[b] (%)	$[\alpha]_D^{20c}$
1	**11b**	*rac*	$Cl_2Ni(PPh_3)_2$	2-Naphthyl	Phenyl	**16aa**	77	⩾95:5	*rac*	—
2	**11b**	*rac*	$Cl_2Ni(dppe)$	2-Naphthyl	Phenyl	**16aa**	43[d]	⩾95:5	*rac*	—
3	**11b**	*rac*	$Cl_2Ni(dppp)$	2-Naphthyl	Phenyl	**16aa**	54[e]	⩾95:5	*rac*	—
4	**11a**	80	$Cl_2Ni(PPh_3)_2$	Phenyl	Phenyl	**16ba**	68	⩾95:5	79	+51
5	**11e**	79	$Cl_2Ni(PPh_3)_2$	Isopropyl	4-Biphenyl	**16bb**	60	⩾95:5	78	−16
5	**11b**	*rac*	$Cl_2Ni(PPh_3)_2$	2-Naphthyl	*n*-Butyl (H)	**18**	29[f]	—	*rac*	—

[a] Determined by ^{1}H NMR analysis of the isolated product.
[b] Determined by HPLC on chiral phase (Chiracel® OD-H, ChiraGrom type 2).
[c] $CHCl_3$, $c = 0.68$–1.14.
[d] 20% of starting material recovered.
[e] 17% of starting material recovered.
[f] 38% of starting material recovered.

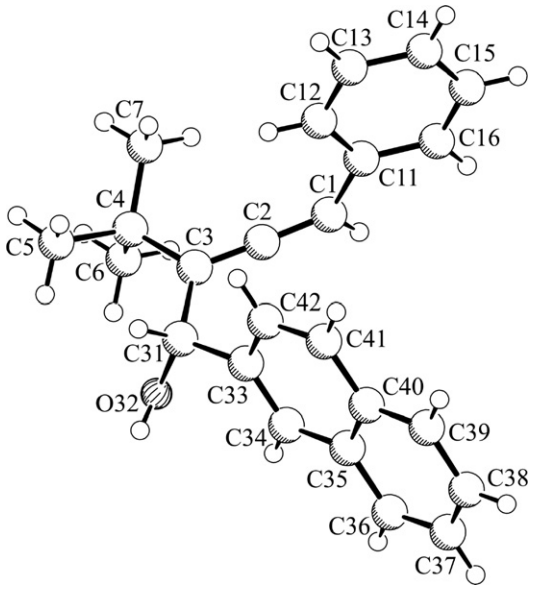


Figure 3. X-ray crystal structure analysis of **16aa**.

reagents generated in situ from *n*-butylmagnesium chloride/$ZnCl_2$, the unsubstituted allene **18** derived from a β-hydride elimination could be obtained (entry 6). Suitable crystals for X-ray crystal structure analysis were obtained from **16aa** (Fig. 3).[34] The relative configuration of the coupling products was established to be *syn*, showing that the coupling proceeds with retention of configuration with respect to the axial chiral allene moiety.

In summary, we presented a novel method for the synthesis of enantioenriched, diastereomerically pure allenyl 2-pyridinyl sulfides **11** by asymmetric lithiation utilizing chiral bis(oxazoline) ligand **6a** and subsequent titanium-mediated hydroxyalkylation of 2-alkynyl 2-pyridinyl sulfide **4**. Besides the elucidation of the stereochemistry, the enantiodetermining step was identified to be a dynamic thermodynamic resolution by selective crystallization of one of the intermediate diastereomeric lithium complexes. Moreover, the first application of allenyl 2-pyridinyl sulfides in a highly stereospecific nickel-catalyzed cross-coupling reaction with arylzinc reagents was elaborated to give enantioenriched, diastereomerically pure, threefold carbon-substituted allenes **16**.

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Supplementary data

Detailed experimental procedures for the synthesis of **11** by selective crystallization, subsequent nickel-catalyzed cross-coupling reaction and spectroscopic data for **11**, **13** and **16**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.10.037.

References and notes

1. For reviews, see: (a) Hoppe, D.; Hense, T. *Angew. Chem.* **1997**, *109*, 2376–2410; Hoppe, D.; Hense, T. *Angew. Chem., Int. Ed.* **1997**, *36*, 2282–2316; (b) Hoppe, D.; Marr, F.; Brüggemann, M. In *Top. Organomet. Chem.*; Hodgson, D. M., Ed.; Springer: Berlin, 2003; Vol. 5, pp 61–137; (c) Beak, P.; Johnson, T.; Kim, D.; Kim, S. In *Top. Organomet. Chem.*; Hodgson, D. M., Ed.; Springer: Berlin, 2003; Vol. 5, pp 139–176; (d) Hoppe, D.; Christoph, G. In *The Chemistry of Organolithium Compounds*; Rappoport, Z., Marek, I., Eds.; Wiley: Chichester, 2004; pp 1055–1164.
2. For review see: Toru, T.; Nakamura, S. In *Top. Organomet. Chem.*; Hodgson, D. M., Ed.; Springer: Berlin, 2003; Vol. 5, pp 177–216.
3. (a) Hoffmann, R. W.; Rühl, T.; Harbach, J. *Liebigs Ann.* **1992**, 725–730; (b) Ahlbrecht, H.; Harbach, J.; Hoffmann, R. W.; Ruhland, T. *Liebigs Ann.* **1995**, 211–216; (c) Dress, R. K.; Rölle, T.; Hoffmann, R. W. *Chem. Ber.* **1995**, *128*, 673–677; (d) Hoffmann, R. W.; Dress, R. K.; Ruhland, T.; Wenzel, A. *Chem. Ber.* **1995**, *128*, 861–870.
4. (a) Reich, H. J.; Dykstra, R. R. *Angew. Chem.* **1993**, *105*, 1489–1491; Reich, H. J.; Dykstra, R. R. *Angew. Chem., Int. Ed. Engl* **1993**, *32*, 1469–1471; (b) Reich, H. J.; Dykstra, R. R. *J. Am. Chem. Soc.* **1993**, *115*, 7041–7042; (c) Reich, H. J.; Kulicke, K. J. *J. Am. Chem. Soc.* **1995**, *117*, 6621–6622; (d) Reich, H. J.; Kulicke, K. J. *J. Am. Chem. Soc.* **1996**, *118*, 273–274.
5. Hoffmann, R. W.; Julius, M.; Chemla, F.; Ruhland, T.; Frenzen, G. *Tetrahedron* **1994**, *50*, 6049–6060.
6. Basu, A.; Thayumanavan, S. *Angew. Chem.* **2002**, *114*, 740–763; Basu, A.; Thayumanavan, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 716–738.
7. (a) Kaiser, B.; Hoppe, D. *Angew. Chem.* **1995**, *107*, 344–346; Kaiser, B.; Hoppe, D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 323–325; (b) Hoppe, D.; Kaiser, B.; Stratmann, O.; Fröhlich, R. *Angew. Chem.* **1997**, *109*, 2872–2874; Hoppe, D.; Kaiser, B.; Stratmann, O.; Fröhlich, R. *Angew. Chem., Int. Ed.* **1997**, *36*, 2784–2786; (c) Stratmann, O.; Kaiser, B.; Fröhlich, R.; Meyer, O.; Hoppe, D. *Chem. Eur. J.* **2001**, *7*, 423–435; (d) Marr, F.; Fröhlich, R.; Hoppe, D. *Org. Lett.* **1999**, *1*, 2081–2083; (e) Marr, F.; Fröhlich, R.; Wibbeling, B.; Diedrich, C.; Hoppe, D. *Eur. J. Org. Chem.* **2002**, 2970–2988.
8. (a) Nakamura, S.; Nakagawa, R.; Watanabe, Y.; Toru, T. *Angew. Chem.* **2000**, *112*, 361–363; Nakamura, S.; Nakagawa, R.; Watanabe, Y.; Toru, T. *Angew. Chem., Int. Ed.* **2000**, *39*, 353–355; (b) Nakamura, S.; Nakagawa, R.; Watanabe, Y.; Toru, T. *J. Am. Chem. Soc.* **2000**, *122*, 11340–11347; (c) Nakamura, S.; Furutani, A.; Toru, T. *Eur. J. Org. Chem.* **2002**, 1690–1695.
9. For dynamic thermodynamic resolution, see: (a) Beak, P.; Anderson, D. R.; Curtis, M. D.; Laumer, J. M.; Pippel, D. J.; Weisenburger, G. A. *Acc. Chem. Res.* **2000**, *33*, 715–727; (b) Park, Y. S.; Yum, E. K.; Basu, A.; Beak, P. *Org. Lett.* **2006**, *8*, 2667–2770; (c) Clayden, J.; Lai, L. W.; Helliwell, M. *Tetrahedron* **2004**, *60*, 4399–4412.
10. For dynamic kinetic resolution, see: (a) Noyori, R.; Tokunaga, M.; Kitamura, M. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 36–55; (b) Ward, R. S. *Tetrahedron: Asymmetry* **1995**, *6*, 1475–1490; (c) Caddick, S.; Jenkins, K. *Chem.*

Soc. Rev. **1996**, *25*, 447–456; (d) Pellissier, H. *Tetrahedron* **2003**, *59*, 8291–8327.
11. Nakamura, S.; Kato, T.; Nishimura, H.; Toru, T. *Chirality* **2004**, *16*, 86–89.
12. (a) Komine, N.; Wang, L.-F.; Tomooka, K.; Nakai, T. *Tetrahedron Lett.* **1999**, *40*, 6809–6812; (b) Tomooka, K.; Wang, L.-F.; Komine, F.; Nakai, T. *Tetrahedron Lett.* **1999**, *40*, 6813–6816.
13. For recent examples, see: (a) Nakamura, S.; Ito, Y.; Wang, L.; Toru, T. *J. Org. Chem.* **2004**, *69*, 1581–1589; (b) Wang, L.; Nakamura, S.; Ito, Y.; Toru, T. *Tetrahedron: Asymmetry* **2004**, *15*, 3059–3072; (c) Sonawane, R. P.; Fröhlich, R.; Hoppe, D. *Adv. Synth. Catal.* **2006**, *348*, 1847–1854.
14. For the first example using catalytic amounts of bis(oxazoline) ligands, see: Nakamura, S.; Hirata, N.; Kita, T.; Yamada, R.; Nakane, D.; Shibata, N.; Toru, T. *Angew. Chem.* **2007**, *119*, 7792–7794; Nakamura, S.; Hirata, N.; Kita, T.; Yamada, R.; Nakane, D.; Shibata, N.; Toru, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 7648–7650.
15. (a) Hoppe, D.; Riemenschneider, C. *Angew. Chem.* **1983**, *95*, 64–65; Hoppe, D.; Riemenschneider, C. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 54–55; (b) Hoppe, D.; Gonschorrek, C.; Schmidt, D.; Egert, E. *Tetrahedron* **1987**, *43*, 2457–2466.
16. (a) Schultz-Fademrecht, C.; Wibbeling, B.; Fröhlich, R.; Hoppe, D. *Org. Lett.* **2001**, *3*, 1221–1224; (b) Otte, R.; Fröhlich, R.; Wibbeling, B.; Hoppe, D. *Angew. Chem.* **2005**, *117*, 5629–5633; Otte, R.; Fröhlich, R.; Wibbeling, B.; Hoppe, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 5492–5496.
17. For a review on organosulfur compounds as electrophiles in transition metal-catalyzed reactions, see: Dubbaka, S. R.; Vogel, P. *Angew. Chem.* **2005**, *117*, 7848–7859; Dubbaka, S. R.; Vogel, P. *Angew. Chem., Int. Ed.* **2005**, *117*, 7674–7684.
18. Examples for cross-coupling reactions of organyl aryl sulfides, see: (a) Okamura, H.; Miura, M.; Takei, H. *Tetrahedron Lett.* **1979**, *20*, 43–46; (b) Wenkert, E.; Ferreira, T. W.; Michelotte, E. L. *J. Chem. Soc., Chem. Commun.* **1979**, 637–638; (c) Wenkert, E.; Shepard, M. E.; McPhail, A. T. *J. Chem. Soc., Chem. Commun.* **1986**, 1390–1391; (d) Itami, K.; Mineno, M.; Muraoka, N.; Yoshida, J. *J. Am. Chem. Soc.* **2004**, *126*, 11778–11779.
19. For a recent example of enantioselective synthesis of allenes by asymmetric lithiation and substitution, see: Bou Chedid, R.; Brümmer, M.; Wibbeling, B.; Fröhlich, R.; Hoppe, D. *Angew. Chem.* **2007**, *119*, 3192–3195; Bou Chedid, R.; Brümmer, M.; Wibbeling, B.; Fröhlich, R.; Hoppe, D. *Angew. Chem., Int. Ed.* **2007**, *46*, 3131–3134.
20. For general reviews on the synthesis of allenes, see (a) Hoffmann-Röder, A.; Krause, N. *Angew. Chem.* **2002**, *114*, 3057–3059; Hoffmann-Röder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2002**, *41*, 2933–2935; (b) *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004; (c) Krause, N.; Hoffmann-Röder, A. *Tetrahedron* **2004**, *60*, 11671–11694; (d) Brummond, K. M.; DeForrest, J. E. *Synthesis* **2007**, 795–818.
21. 2-Alkynyl aryl sulfides **3a** and **3b** were prepared by alkylation of benzenethiol or pyridine-2-thiol with 1-bromo-4,4-dimethyl-pent-2-yne according to a procedure described by Rubina et al.: Rubina, K; Fleisher, M.; Abele, E.; Popelis, Y.; Lukevits, E. *Russ. J. Org. Chem.* **2003**, *39*, 963–967. 1-Bromo-4,4-dimethyl-pent-2-yne was prepared by reaction of 4,4-dimethyl-but-2-yn-1-ol with PBr_3 using a modification of the method described by Lu: Zhao, L.; Lu, X.; Xu, W. *J. Org. Chem.* **2005**, *70*, 4059–4063; For the preparation of 4,4-dimethyl-but-2-yn-1-ol, see: MacInnes, I.; Walton, J. C. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1077–1082.
22. An asymmetric transformation describes the conversion of a racemate into a pure enantiomer or into a mixture in which one enantiomer is present in excess, or of a diastereomeric mixture into a single diastereoisomer or into a mixture in which one diastereomer predominates. If the two enantiomers of a chiral substrate **A** are freely interconvertible, and if an equal amount of excess of a non-racemizing second enantiomerically pure chemical species, say (*R*)-**B**, is added to a solution of racemic **A**, then the resulting equilibrium mixture of adducts **A**·**B** will, in general, contain unequal amounts of diastereoisomers (*R*)-**A**·(*R*)-**B** and (*S*)-**A**·(*R*)-**B**. The result of this equilibration is called asymmetric transformation of the first kind. If, in such a system, the adducts differ considerably in solubility so that only one of them, say (*R*)-**A**·(*R*)-**B**, crystallizes from the solution, then the equilibration of diastereoisomers in solution and concurrent crystallization will continue so that all (or most) of the substrate A can be isolated as the crystalline diastereoisomer (*R*)-**A**·(*R*)-**B**. Such a 'crystallization-induced asymmetric transformation' is called an asymmetric transformation of the second kind. See *IUPAC Compendium of Chemical Terminology*, 2nd ed.; McNaught, A. D., Wilkinson, A., Eds.; Blackwell Science, 1997; see also (b) Harris, M. M. *Progr. Stereochem.* **1958**, *2*, 157–163.
23. For the first example of an asymmetric transformation of the second kind in lithium carbanion chemistry, see: (a) Hoppe, D.; Zschage, O. *Angew. Chem.* **1989**, *101*, 67–71; Hoppe, D.; Zschage, O. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 69–71; (b) Paulsen, H.; Graeve, C.; Hoppe, D. *Synthesis* **1996**, 141–144.
24. Data sets were collected with a Nonius KappaCCD diffractometers. Programs used: data collection COLLECT (Nonius B. V., 1998), data reduction Denzo-SMN (Otwinowski, Z.; Minor, W. *Methods in Enzymology* **1997**, *276*, 307–326), absorption correction Denzo (Otwinowski, Z.; Borek, D.; Majewski, W.; Minor, W. *Acta Crystallogr.* **2003**, *A59*, 228–234), structure solution SHELXS-97 (Sheldrick, G. M.; *Acta Crystallogr.* **1990**, *A46*, 467–473), structure refinement SHELXL-97 (Sheldrick, G. M. Universität Göttingen, 1997), graphics SCHAKAL (Keller, E. Universität Freiburg, 1997). CCDC 656888 (**11a**) and CCDC 656889 (**16aa**) contain the supplementary crystallographic data for this Letter. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44 (1223) 336 033, e-mail: deposit@ccdc.cam.ac.uk].
25. X-ray crystal structure analysis for **11a**: formula $C_{19}H_{21}NOS$, $M = 311.43$, colourless crystal $0.25 \times 0.15 \times 0.05$ mm, $a = 9.6439(2)$, $b = 9.7610(2)$, $c = 10.0250(2)$ Å, $\alpha = 111.939\ (1)°$, $\beta = 93.915(1)°$, $\gamma = 99.860(2)°$, $V = 853.35(3)$ Å^3, $\rho_{calc} = 1.212$ g cm^{-3}, $\mu = 16.80$ cm^{-1}, empirical absorption correction ($0.679 \leqslant T \leqslant 0.921$), $Z = 2$, triclinic, space group $P\bar{1}$ (No. 1), $\lambda = 1.54178$ Å, $T = 223$ K, $\omega/2\theta$ scans, 5454 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin\theta)/\lambda] = 0.60$ Å^{-1}, 3108 independent ($R_{int} = 0.038$) and 2957 observed reflections [$I \geqslant 2\ \sigma(I)$], 405 refined parameters, $R = 0.053$, $wR^2 = 0.144$, Flack parameter 0.02(2), max. residual electron density 0.24 (-0.41) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.
26. Seppi, M.; Kalkofen, R.; Reupohl, J.; Fröhlich, R.; Hoppe, D. *Angew. Chem.* **2004**, *116*, 1447–1451; Seppi, M.; Kalkofen, R.; Reupohl, J.; Fröhlich, R.; Hoppe, D. *Angew. Chem., Int. Ed.* **2004**, *43*, 1423–1427.
27. The enantioselectivity was independent of the nature of the utilized titanium reagent (Table 2, entries 3 and 4) a

modified Hoffmann test (portionwise addition of $ClTi(OiPr)_3$ over a period of 10 min compared to the addition at once) showed no evidence for dynamic kinetic resolution.
28. The corresponding titanated *S*-2-alkynyl thiocarbamates and *O*-2-alkynyl carbamates **2** are configurationally stable at −78 °C.
29. Control experiments carrying out deprotonations of **4** in diethyl ether showed no dependence on the time of transmetallation. The enantiomeric excess of **11b** was not affected by reaction with $ClTi(OiPr)_3$ up to 4 h.
30. Similar attempts employing *S*-allenyl thiocarbamates **2** ($X = SC(O)NiPr_2$) from Ref. 16b failed.
31. The configuration of the double bond was determined by NOE-experiments.
32. Erdik, E. *Tetrahedron* **1987**, *43*, 2203–2212.
33. NMR analysis of the crude product gave no hints for the existence or non-existence of a second diastereomer.
34. X-ray crystal structure analysis for **16aa**: formula $C_{24}H_{24}O$, $M = 328.43$, colourless crystal $0.30 \times 0.06 \times 0.03$ mm, $a = 29.419(2)$, $b = 6.0040(4)$, $c = 21.6634(14)$ Å, $\beta = 102.200(3)°$, $V = 3740.0(4)$ Å^3, $\rho_{calc} = 1.167$ g cm^{-3}, $\mu = 5.30$ cm^{-1}, empirical absorption correction ($0.857 \leqslant T \leqslant 0.984$), $Z = 8$, monoclinic, space group $C2/c$ (No. 15), $\lambda = 1.54178$ Å, $T = 223$ K, $\omega/2\theta$ scans, 12,861 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin\theta)/\lambda] = 0.59$ Å^{-1}, 3010 independent ($R_{int} = 0.112$) and 1663 observed reflections [$I \geqslant 2\sigma(I)$], 230 refined parameters, $R = 0.073$, $wR_2 = 0.138$, residual electron density 0.22 (−0.22) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.