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Ligand-Accelerated Asymmetric [1,2]-Stevens Rearrangment of Sulfur Ylides *via* Decomposition of Diazomalonates Catalyzed by Chiral Bisoxazoline/Copper Complex

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Abstract: The first example of catalytic asymmetric [1,2]-Stevens rearrangement reaction of 1,3-oxathiolanes with diazomalonates has been developed and up to 90% *ee* is achieved by the bisoxazoline **4e**/copper(II) triflate [$Cu(OTf)_2$] complex.

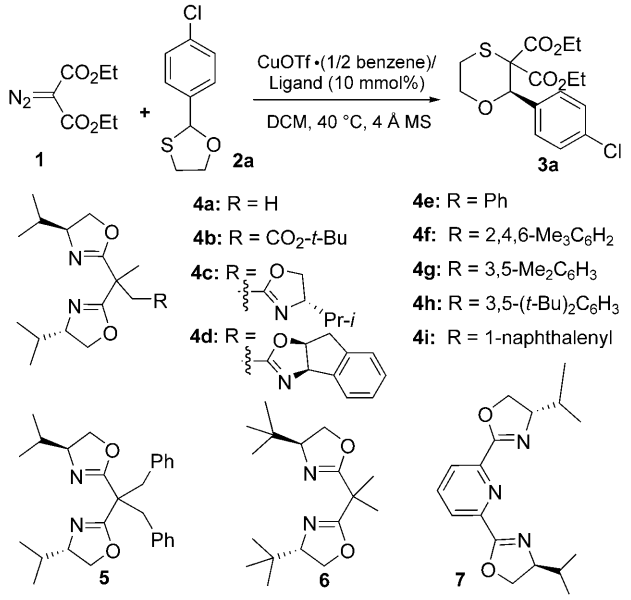
Keywords: asymmetric catalysis; bisoxazolines; Stevens rearrangement; ylides

The asymmetric rearrangement reactions[1] of sulfur ylides[2] are one of the powerful tools for the preparation of optically active sulfur compounds and are very useful in organic synthesis. Although the enantioselective [2,3]-sigmatropic rearrangements of sulfur ylides[3] and [1,2]-Stevens reactions of oxygen ylides[4] have been intensively studied, asymmetric [1,2]-Stevens rearrangements of sulfur ylides have seldom been explored. To obtain the key intermediate for the total synthesis of showdomycin, Kametani developed a substrate-controlled asymmetric [1,2]-Stevens rearrangment reaction of sulfides with diazomalonate in 1987.[4b] Aggarwal and his co-workers also observed the Stevens rearrangement product during their study on the asymmetric sulfur ylide epoxidation reaction.[5] To the best of our knowledge, there is no report on a catalytic asymmetric [1,2]-Stevens rearrangement reaction of sulfur ylides. Very recently, we explored sidearmed bisoxazoline/$Cu(OTf)_2$ as a catalyst in the asymmetric [1,2]-Stevens reaction[6] of 1,3-oxathiolane[7] with diazomalonate[8] and up to 90% *ee* was achieved. This provides the first example of a catalytic asymmetric [1,2]-Stevens rearrangement reaction of 1,3-oxathiolanes. Herein, we wish to report the results in detail.

Huang et al. found that Cu(I)-mediated decomposition of ethyl diazomalonate in the presence of dibutyl telluride could generate the corresponding telluronium ylide, which reacted with aldehydes to give alkylidenemalonates.[9] Using sulfide instead of telluride, we envisaged that it would be possible to form a chiral sulfur ylide by the reaction of diazomalonate with a sulfide in the presence of a chiral ligand/Cu(I), followed by the Stevens rearrangement to furnish optically active sulfur compounds. Initial attempts, by employing CuOTf as a catalyst in the absence of ligand and 2-(4-chlorophenyl)-1,3-oxathiolane as a substrate, failed to give the desired product even when the reaction temperature was raised to 40 °C (entry 1, Table 1). Using 15 mol% of CuOTf in combination of 10 mol% of bisoxazoline,[10] however, we were pleased to find that the [1,2]-Stevens rearrangement proceeded smoothly to afford the desired product **3** in good yield with 52% *ee* (entry 2, Table 1). This result suggested that the ligand accelerates the reaction and encouraged us to optimize the ligands to further improve the yield and selectivity.

Recently, sidearmed bisoxazolines[11] have already proved to be excellent ligands in metal-catalyzed Friedel–Crafts,[12] Kinugasa,[13] Diels–Alder,[14] cyclopropanation,[15] 1,3-dipolar cycloaddition,[16] and asymmetric allylic substitution and oxidation.[17] Compared with the parental bisoxazolines, in some cases, these sidearmed bisoxazolines exhibited better enantiofacial control, higher reactivity, and better tolerance to impurities so that reactions could be run in an air atmosphere. Thus, we evaluated various sidearmed bisoxazolines in the aforementioned reaction. The results were summarized in Table 1. It turned out that the

Table 1. Sidearm effects in the reaction [1,2]-Stevens of 1,3-oxathiolane with diazomalonate.[a]



Entry	Ligand	Time [h]	Yield[b] [%]	*ee*[c] [%]
1	–	39	0	–
2	**4a**	39	65	52
3	**4b**	39	24	0
4	**4c**	39	44	80
5	**4d**	39	40	82
6	**4e**	11	99	80
7	**4f**	39	87	70
8	**4g**	39	99	78
9	**4h**	39	44	79
10	**4i**	39	55	78
11	**5**	39	67	73
12	**6**	39	99	6
13	**7**	39	0	–

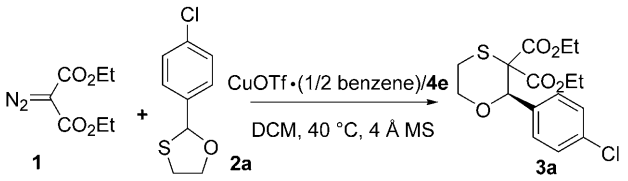
[a] *Reaction conditions:* **1** (37.2 mg, 0.2 mmol), **2a** (80.3 mg, 0.4 mmol), CuOTf·(1/2 benzene) (7.5 mg, 0.03 mmol), ligand (0.02 mmol), DCM (2.0 mL).
[b] Isolated yield.
[c] Determined by Chiral HPLC.

sidearm significantly influenced both the reactivity and enantioselectivity in this reaction. Pendant groups such as an ester group, or an oxazolinyl group obviously slowed down the reaction and only moderate yields were obtained (entries 3–5). We speculated that the diminished yields in the case of bisoxazolines **4b–d** resulted from the attenuated Lewis acidity of the copper catalyst, probably due to the coordination of the sidearm that retarded the formation of a metallocarbene intermediate. Gratifyingly, however, an oxazoline ring as the sidearm impressively increased the enantiomeric excess up to 82% *ee* (entries 4 and 5). Further studies showed that a simple phenyl group as a pendant group significantly increased the reactivity and enantioselectivity. For example, by employing ligand **4e**, the reaction could finish within 11 h and afforded the desired product in almost quantitative yield with up to 80% *ee* (entry 6). To further improve the enantioselectivity, other bisoxazolines **4f–4i** with substituted phenyl groups were designed and tested (entries 7–10). In these cases, unfortunately, slightly diminished *ee* values were observed. We also checked the effect of bisoxazolines **5** with two phenyl groups as sidearms, but it turned out to be detrimental (entry 11). Two commercially available bisoxazolines **6** and **7** were also examined in this reaction. Bisoxazoline **6** afforded excellent yield but poor enantioselectivity. 2,6-Bis[(*S*)-4,5-dihydro-4-isopropyloxazol-2-yl]-pyridine (PYBOX) did not promote the reaction at all.

We next screened solvents using bisoxazoline **4e**. As shown in Table 2, diethyl ether, toluene and THF all gave moderate yields and enantioselectivities. 1,1,2,2-Tetrachloroethane (TTCE) afforded the highest *ee*, but the yield was 26% even if the reaction time was prolonged to 96 h (entry 5). Although raising temperature to 50 °C increased yield, the *ee* decreased slightly (entry 6). Of the solvents examined, dichloromethane (DCM) was the optimal (entries 1–6). Varying the ratio of CuOTf and chiral ligand from 1.50/1.0 to 1.20/1.0, the yield was decreased from 99% to 79% albeit with no loss of enantiomeric excess (entries 1 and 7, Table 2).

To further improve the enantioselectivity, the effects of Lewis acids were also examined. The results are summarized in Table 3. $Cu(OAc)_2 \cdot H_2O$, $FeCl_3$,

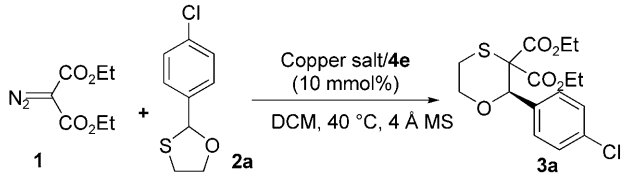
Table 2. Effects of solvents and the ratio of copper salt/**4e** on the rearrangement.[a]



Entry	Cu(I)/**4e**	Solvent	Yield[b] [%]	*ee*[c] [%]
1	1.50/1	DCM	99	80
2	1.50/1	Et_2O	58	72
3	1.50/1	Toluene	69	72
4	1.50/1	THF	83	78
5	1.50/1	TTCE	26	82
6	1.50/1	TTCE	91[d]	79
7	1.20/1	DCM	79	80

[a] *Reaction conditions:* **1** (37.2 mg, 0.2 mmol), **2a** (80.3 mg, 0.4 mmol), ligand **4e** (6.9 mg, 0.02 mmol), solvent (2.0 mL), 40 °C.
[b] Isolated yield.
[c] Determined by Chiral HPLC.
[d] 50 °C.

Table 3. Effects of copper salts on the rearrangement.[a]



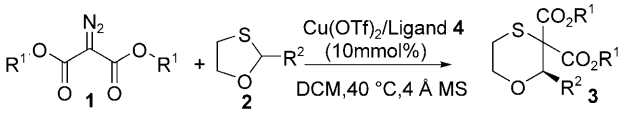
Entry	Copper salt	Yield[b] [%]	*ee*[c] [%]
1	CuOTf·(1/2 benzene)	99	80
2	CuOTf·(1/2 toulene)	49	55
3	$CuPF_6·(CH_3CN)_4$	99	36
4	$CuClO_4·(CH_3CN)_4$	60	63
5	$Cu(OTf)_2$	80	83
6	$Cu(OTf)_2$	90[d]	83
7	$Cu(SbF_6)_2$	95	71
8	$Cu(BF_4)_2$	43	10
9	$Cu(TFA)_2·(H_2O)_2$	30	3

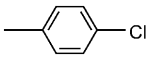
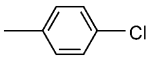
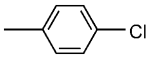
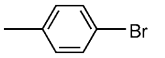
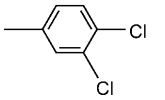
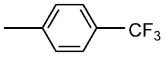
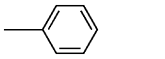
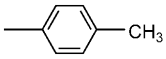
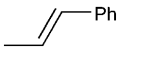
[a] *Reaction conditions:* **1** (37.2 mg, 0.2 mmol), **2a** (80.3 mg, 0.4 mmol), copper salt (0.03 mmol), ligand **4e** (6.9 mg, 0.02 mmol), DCM (2.0 mL).
[b] Isolated yield.
[c] Determined by Chiral HPLC.
[d] Reaction was run in air atmosphere.

$Fe(ClO_4)_3·(H_2O)_9$, $Zn(ClO_4)_2·(H_2O)_6$ and $Co(ClO_4)_2·(H_2O)_6$ failed to promote the reaction under the same reaction conditions. CuOTf·(1/2 toluene) was less enantioselective and less reactive than CuOTf·(1/2 benzene) (entry 2, Table 2). Other Cu(I) salts with different counter anions, such as $CuPF_6·(CH_3CN)_4$ and $CuClO_4·(CH_3CN)_4$, worked smoothly but gave lower enantioselectivities than CuOTf·(1/2 benzene). In a previous study on the application of pseudo C_3-symmetric trisoxazolines in asymmetric synthesis,[11–17] we developed the first example of a Cu(II)-catalyzed asymmetric Kinugasa reaction,[12] in which Cu(II) was proven to give better *ee*s than the corresponding Cu(I). Thus, Cu(II) salts were tested. To our delight, $Cu(OTf)_2$ in combination with bisoxazoline **4e** proved to be more enantioselective and up to 83% *ee* could be achieved. Noticeably, the reaction could be carried out in an air atmosphere without loss of reactivity and enantioselectivity, which can greatly simplify the experimental procedure (entry 6). $Cu(BF_4)_2$ and $Cu(TFA)_2·(H_2O)_2$ gave low yields with low *ee*s (entries 8 and 9).

On the basis of the systematic study of the effects of ligands, solvents, and Lewis acids on the reaction, we evaluated the generality of the current reaction by investigating various 1,3-oxathiolanes (2.0 equivalents) in CH_2Cl_2 at 40 °C in the presence of 4 Å molecular sieves and 10 mol% of the bisoxazoline **4e**/$Cu(OTf)_2$ complex. As shown in Table 4, the ester groups of diazomalonates proved to influence the enantioselectivities (entries 1–3). Compared with methyl and ethyl diazomalonates, benzyl diazomalonate gave the best result, and 88% *ee* was obtained. Substituent R^2 on 1,3-oxathiolane has a slight effect on the yields and strong effect on the enantioselectivities. For instance, when R^2 was either an electron-donating or an electron-withdrawing substituted phenyl group, the reactions gave the desired products in high yields (81–98%, entries 3–8). For enantiofacial selectivities, 1,3-oxathiolanes with a benzene ring bearing electron-withdrawing groups such as a halogen and a CF_3 could furnish the corresponding 1,4-oxathianes with high *ee*s (entries 3–7). However, an electron-donating group on the benzene ring decreased the selectivity greatly (entry 8). Noticeably, there are two possible reactions for substrate **2i**: [1,2]-Stevens rearrangement and [2,3]-sigmatropic rearrangement. In the present conditions, fortunately, only the [1,2]-shift product was obtained in good yield with up to 38% *ee* (entry 9). By employing ethyl diazoacteate and ethyl

Table 4. Reaction of diazomalonates with 1,3-oxathiolanes.[a,19]

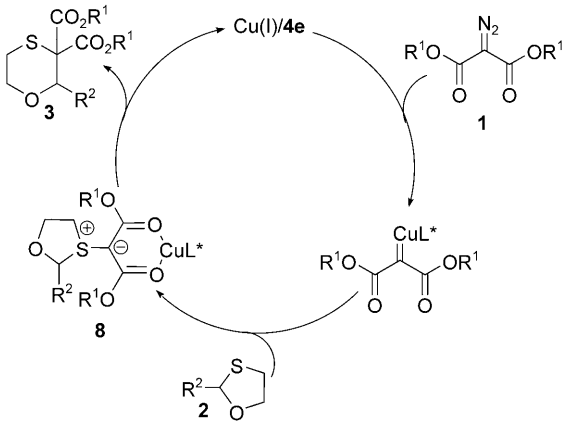


Entry	R^1	Substrate No.	R	Product	Yield[b,c] [%]	*ee*[c,d] [%]
1	Me	**2a**		**3a**	94 (85)	78 (78)
2	Et	**2b**		**3b**	80 (73)	83 (80)
3	Bn	**2c**		**3c**	97 (98)	88 (86)
4	Bn	**2d**		**3d**	90 (81)	90 (85)[e]
5	Bn	**2e**		**3e**	95 (84)	83 (80)
6	Bn	**2f**		**3f**	98 (91)	89 (86)
7	Bn	**2g**		**3g**	(90)	(80)
8	Bn	**2h**		**3h**	(85)	(52)
9	Bn	**2i**		**3i**	66 (90)	23 (38)

[a] *Reaction conditions:* **1** (0.2 mmol), **2** (0.4 mmol), $Cu(OTf)_2$ (10.9 mg, 0.03 mmol), ligand **4e** (6.9 mg, 0.02 mmol), DCM (2.0 mL).
[b] Isolated yield.
[c] The data in parenthesis were obtained using ligand **4g** (0.02 mmol).
[d] Determined by chiral HPLC.
[e] The absolute configuration of product **3d** was determined to be *R* by X-ray crystallography.[20]

α-phenyldiazoacetate instead of ethyl diazomalonates the reaction worked well to give the desired products but the diastereoselectivity was very poor.[18]

A possible mechanism for this asymmetric rearrangement is proposed as shown in Scheme 1. The



Scheme 1. Possible mechanism of the rearrangement.

copper complex decomposes diazomalonate and then reacts with oxathiolane to generate chiral sulfur ylide **8** in which BOX/Cu(I)[21] coordinates to the malonate. The ylide undergoes a Stevens rearrangement to give the desired product **3** and regenerate the catalyst. A clear mechanism must await further investigation.

In summary, we have developed the first example of catalytic asymmetric [1,2]-Stevens rearrangement reaction of sulfur ylides. The current reaction can be run in an air atmosphere when the $Cu(OTf)_2$/**4e** complex is used as the catalyst. Thus, it provides an easy access to optically active 1,4-oxathianes in high yields with good to high enantioselectivities under mild conditions. Studies on the further improvement of enantioselectivity and understanding of the mechanism are in progress in our laboratory.

Experimental Section

All reactions were carried out under a nitrogen atmosphere unless otherwise mentioned. Dichloromethane was distilled over calcium hydride. All the other solvents were purified according to the standard methods before use. All diazomalonates and 1,3-oxathiolanes were synthesized by known procedures.[22] Powdered MS 4 Å was preactivated at 250 °C under vacuum prior to use.

General Procedure for the Enantioselective [1,2]-Stevens Rearrangement (3d as Example)

A mixture of $Cu(OTf)_2$ (10.9 mg, 0.03 mmol, 15 mol%) and the ligand **4e** (6.9 mg, 0.02 mmol, 10 mol%) in CH_2Cl_2 (2 mL) was stirred at room temperature for 2 h under a nitrogen atmosphere. The resulting solution was then transferred to diazomalonate (62 mg, 0.20 mmol) *via* a syringe, followed by addition of 1,3-oxathiolane **2d** (98 mg, 0.40 mmol) and MS 4 Å (250 mg). The mixture was further stirred at 40 °C. When the reaction was complete (monitored by TLC), the reaction mixture was filtered through a thin pad of silica gel (300–400 mesh), washed with CH_2Cl_2 (50 mL). The filtrate was concentrated under reduced pressure, and the residue was purified by flash chromatography to afford the product **3d** as a colorless oil; yield: 90%; *ee* 90%. $[\alpha]_D^{20}$: −43.6° (*c* 1.00, $CDCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.23 (m, 10H), 7.14 (d, *J* = 6.9 Hz, 2H), 6.98 (d, *J* = 6.9 Hz, 2H), 5.24 (s, 1H), 5.13–5.00 (m, 3H), 4.87 (d, *J* = 12.6 Hz), 4.34 (dt, *J* = 12.0, 3.3 Hz, 1H), 3.90 (dt, *J* = 13.2, 12.0 Hz, 1H), 3.53 (td, *J* = 13.2, 3.3 Hz 1H), 2.49 (d, *J* = 12.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.25, 166.65, 137.23, 134.54, 134.43, 130.69, 129.86, 128.86, 128.44, 128.40, 128.35, 128.28, 128.12, 128.02, 127.83, 122.29, 81.25, 68.34, 67.78, 67.60, 56.50, 25.91; IR (thin film): ν = 1731, 1488, 1455, 1242, 1225, 1181, 1100, 1011, 749, 696 cm^{-1}; LR-MS-ESI: *m*/*z* = 551 ([M + Na]$^+$); HR-MS-ESI: *m*/*z* = 549.0348 [M + Na]$^+$, calcd. for $C_{26}H_{23}O_5BrS$ + Na: 549.0342. The *ee* was determined by HPLC analysis using a Chiralpak AD-H column (150 mm) with hexane/*i*-PrOH 95/5 as eluent, 254 nm, 0.7 mL min^{-1}, t_{R1} = 18.96 min (minor), t_{R2} = 26.13 min (major).

Acknowledgements

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References

[1] For reviews on asymmetric ylide rearrangement reactions, please see: a) T. Ye, M. A. Mckervey, *Chem. Rev.* **1994**, *94*, 1091–1160; b) M. P. Doyle, D. C. Forbes, *Chem. Rev.* **1998**, *98*, 911–936; c) D. M. Hodgson, F. Y. T. M. Pierard, P. A. Stupple, *Chem. Soc. Rev.* **2001**, *30*, 50–61.

[2] For reviews on asymmetric sulfur ylide reactions, please see: a) A. Padwa, S. F. Hornbuckle, *Chem. Rev.* **1991**, *91*, 263–309; b) A.-H. Li, L.-X. Dai, V. K. Aggarwal, *Chem. Rev.* **1997**, *97*, 2341–2372; c) V. K. Aggarwal, C. L. Winn, *Acc. Chem. Res.* **2004**, *37*, 611–620; d) X.-L. Sun, Y. Tang, *Acc. Chem. Res.* **2008**, *41*, 937–948. For selected recent asymmetric reactions of sulfur ylides, please see: e) V. K. Aggarwal, M. Ferrara, C. J. O'Brien, A. Thompson, R. V. H. Jones, R. Fieldhouse, *J. Chem. Soc., Perkin Trans. 1* **2001**, 1635–1643; f) V. K. Aggarwal, E. Alonson, G. Hynd, K. M. Lydon, M. J. Palmer, M. Porcelloni, J. R. Studley, *Angew. Chem.* **2001**, *113*, 1479–1482; *Angew. Chem. Int. Ed.* **2001**, *40*, 1430–1433; g) S. Ye, Z.-Z. Huang, C.-A. Xia, Y. Tang, L.-X. Dai, *J. Am. Chem. Soc.* **2002**, *124*, 2432–2433; h) V. K. Aggarwal, J. L. Vasse, *Org. Lett.* **2003**, *5*, 3987–3990; i) X.-M. Deng, P. Cai, S. Ye, X.-L. Sun, W.-

W. Liao, Y. Tang, Y.-D. Wu, L.-X. Dai, *J. Am. Chem. Soc.* **2006**, *128*, 9730–9740; j) V. K. Aggarwal, J. P. H. Charmant, P. H. Jonathan, D. Fuentes, J. N. Harvey, G. Hynd, D. Ohara, W. Picoul, R. Robiette, C. Smith, J.-L. Vasse, C. L. Winn, *J. Am. Chem. Soc.* **2006**, *128*, 2105–2114; k) Q.-G. Wang, X.-M. Deng, B.-H. Zhu, L.-W. Ye, X.-L. Sun, C.-Y. Li, C.-Y. Zhu, Q. Shen, Y. Tang, *J. Am. Chem. Soc.* **2008**, *130*, 5408–5409.

[3] a) B. M. Trost, R. F. Hammen, *J. Am. Chem. Soc.* **1973**, *95*, 962–964; b) Y. Nishibayashi, K. Ohe, S. Uemura, *J. Chem. Soc., Chem. Commun.* **1995**, 1245–1246; c) D. W. McMillen, N. Vargar, B. A. Reed, C. King, *J. Org. Chem.* **2000**, *65*, 2532–2536; d) Z.-H. Qu, Z.-H. Ma, W.-F. Shi, X.-L. Jin, J.-B. Wang, *J. Org. Chem.* **2002**, *67*, 5621–5625; e) X.-M. Zhang, M. Ma, J.-B. Wang, *Tetrahedron: Asymmetry* **2003**, *14*, 891–895; f) M. Ma, L. Peng, X. Zhang, J.-B. Wang, *J. Am. Chem. Soc.* **2005**, *127*, 15016–15017.

[4] For selected examples on asymmetric Stevens rearrangements of oxygen ylides, see: a) H. Nozaki, S. Moriuti, H. Takaya, R. Noyori, *Tetrahedron* **1968**, *24*, 3655–3669; b) T. Kametani, K. Kawamura, T. Honda, *J. Am. Chem. Soc.* **1987**, *109*, 3010–3017; c) K. Ito, M. Yoshitake, T. Katsuki, *Heterocycles* **1996**, *42*, 305; d) K. Ito, M. Yoshitake, T. Katsuki, *Chem. Lett.* **1995**, 1027–1028; e) K. Ito, T. Katsuki, *Chem. Lett.* **1994**, 1857–1860; f) M. P. Doyle, D. G. Ene, D. C. Forbes, J. S. Tedow, *Tetrahedron Lett.* **1997**, *38*, 4367–4370. For selected recent examples on the reaction of oxygen ylides: g) H. Huang, X. Guo, W. Hu, *Angew. Chem.* **2007**, *119*, 1359–1361; *Angew. Chem. Int. Ed.* **2007**, *46*, 1337–1339; h) X. Zhang, H. Huang, X. Guo, X. Guan, L. Yang, W. Hu, *Angew. Chem.* **2008**, *120*, 6749–6751; *Angew. Chem. Int. Ed.* **2008**, *47*, 6647–6649; i) W. Hu, X. Xu, J. Zhou, W.-J. Liu, H. Huang, J. Hu, L. Yang, L.-Z. Gong, *J. Am. Chem. Soc.* **2008**, *130*, 7782–7783.

[5] V. K. Aggarwal, M. Kalomiri, A. P. Thomas, *Tetrahedron: Asymmetry* **1994**, *5*, 723–730.

[6] For racemic Stevens rearrangement of sulfur ylides, please see: a) M. P. Doyle, J. H. Griffin, M. S. Chinn, D. Lrusen, *J. Org. Chem.* **1984**, *49*, 1917–1925; b) V. Nair, S. M. Nair, S. Mathai, J. Liebscher, B. Ziemer, K. Narsimulu, *Tetrahedron Lett.* **2004**, *45*, 5759–5762; c) K. K. Ellis-Holder, B. P. Peppers, A. Y. Kovalevsky, S. T. Diver, *Org. Lett.* **2006**, *8*, 2511–2514.

[7] Stevens rearrangement of 1,3-oxathiolanes: a) M. Ioannou, M. J. Porter, F. Saez, *Chem. Commun.* **2002**, 346–347; b) M. Ioannou, M. J. Porter, F. Saez, *Tetrahedron* **2005**, *61*, 43–50; c) S.-F. Zhu, C.-H. Xin, S.-Z. Zhu, *Tetrahedron* **2006**, *62*, 829–832; d) A. V. Stepakov, A. P. Molchanov, J. Magull, D. Vidovic, G. L. Starova, J. Kopf, R. Kostikov, *Tetrahedron* **2006**, *62*, 3610–3618.

[8] For diazomalonates as precursors of metal carbenes, see: a) M. P. Doyle, S. B. Davies, W. Hu, *Org. Lett.* **2000**, *2*, 1145–1147; b) R. Pellicciari, M. Marinozzi, E. Camaioni, M. C. Nunez, G. Costantino, F. Gasparini, G. Giorgi, A. Macchiarulo, N. Subramanian, *J. Org. Chem.* **2002**, *67*, 5497–5507; c) E. Roberts, J. P. Sancon, J. B. Sweeney, J. A. Workman, *Org. Lett.* **2003**, *5*, 4775–4777.

[9] Z.-L. Zhou, Y.-Z. Huang, L.-L. Shi, *Tetrahedron* **1993**, *49*, 6821–6830.

[10] For reviews on bisoxazolines in aymmetric catalysis, please see: a) A. K. Ghosh, P. Mathivanan, J. Cappiello, *Tetrahedron: Asymmetry* **1998**, *9*, 1–45; b) K. A. Jørgensen, M. Johannsen, S. Yao, H. L. Audrain, J. Thorhauge, *Acc. Chem. Res.* **1999**, *32*, 605–613; c) J. S. Johnson, D. A. Evans, *Acc. Chem. Res.* **2000**, *33*, 325–335; d) G. Helmchen, A. Pfaltz, *Acc. Chem. Res.* **2000**, *33*, 336–345; e) O. B. Sutcliffe, M. R. Bryce, *Tetrahedron: Asymmetry* **2003**, *14*, 2297–2325; f) H. A. McManus, P. J. Guiry, *Chem. Rev.* **2004**, *104*, 4151–4202; g) G. Desimoni, G. Faita, K. A. Jørgensen, *Chem. Rev.* **2006**, *106*, 3561–3651.

[11] For reviews, see: a) J. Zhou, Y. Tang, *Chem. Soc. Rev.* **2005**, *34*, 664–676; b) L. H. Gade, S. Bellemin-Laponnaz, *Chem. Eur. J.* **2008**, *14*, 4142–4152.

[12] a) J. Zhou, Y. Tang, *J. Am. Chem. Soc.* **2002**, *124*, 9030–9031; b) J. Zhou, M.-C. Ye, Z.-Z. Huang, Y. Tang, *J. Org. Chem.* **2004**, *69*, 1309–1320; c) M.-C. Ye, B. Li, J. Zhou, X.-L. Sun, Y. Tang, *J. Org. Chem.* **2005**, *70*, 6108–6110; d) R. Rasappan, M. Hager, A. Gissibl, O. Reiser, *Org. Lett.* **2006**, *8*, 6099–6102.

[13] a) M.-C. Ye, J. Zhou, Z.-Z. Huang, Y. Tang, *Chem. Commun.* **2003**, 2554–2555; b) M.-C. Ye, J . Zhou, Y. Tang, *J. Org. Chem.* **2006**, *71*, 3576–3582.

[14] a) D. A. Evans, S. J. Miller, T. Lectka, P. Matt, *J. Am. Chem. Soc.* **1999**, *121*, 7559–7573; b) S. Barroso, G. Blay, L. Al-Midfa, M. C. Munõz, J. R. Pedro, *J. Org. Chem.* **2008**, *73*, 6389–6392.

[15] Z.-H. Xu, S.-N. Zhu, X.-L. Sun, Y. Tang, L.-X. Dai, *Chem. Commun.* **2007**, 1960–1962.

[16] a) Z.-Z. Huang, Y.-B. Kang, J. Zhou, M.-C. Ye, Y. Tang, *Org. Lett.* **2004**, *6*, 1677–1679; b) Y.-B. Kang, X.-L. Sun, Y. Tang, *Angew. Chem.* **2007**, *119*, 3992–3995; *Angew. Chem. Int. Ed.* **2007**, *46*, 3918–3921.

[17] a) M. Seitz, C. Capacchione, S. Bellemin-Laponnaz, H. Wadepohl, B. D. Warda, L. H. Gade, *Dalton Trans.* **2006**, 193–202; b) C. Foltz, M. Enders, S. Bellemin-Laponnaz, H. Wadepohl, L. H. Gade, *Chem. Eur. J.* **2007**, *13*, 5994–6008.

[18] The diastereomers cannot be separated by flash chromatography and thus the *ee*s can not be determined.

[19] No kinetic resolution was observed under the reaction conditions.

[20] CCDC 707886 (**3d**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

[21] Cu(II) can be reduced to Cu(I) by diazo compounds, see: a) R. G. Salomon, J. K. Kochi, *J. Am. Chem. Soc.* **1973**, *95*, 3300–3310; b) C. Ozen, N. S. Tuzun, *Organometallics* **2008**, *27*, 4600–4610.

[22] a) K. Kiyoshi, H. Nao, I. Shinya, S. Tsuneo, *Synlett* **2002**, 1535–1537; b) F. Kipnis, J. Ornfelt, *J. Am. Chem. Soc.* **1949**, *71*, 3554–3555.

