Cycloadditions

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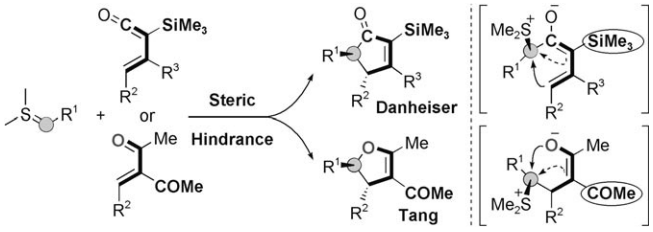
Tuning Electronic and Steric Effects: Highly Enantioselective [4+1] Pyrroline Annulation of Sulfur Ylides with α,β-Unsaturated Imines**

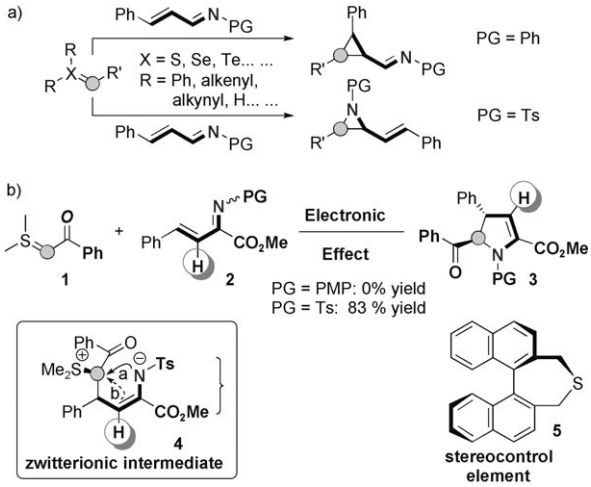
Liang-Qiu Lu, Ji-Ji Zhang, Fang Li, Ying Cheng, Jing An, Jia-Rong Chen, and Wen-Jing Xiao**

The [4+1] annulation of 1,3-conjugated systems with two-electron, one-carbon fragments presents a particularly attractive but underexploited strategy to construct naturally occurring and biologically active carbo- and heterocyclopentenes, especially asymmetrically.[1] In this context, besides carbon monoxide,[2] isocyanides,[3] nucleophilic carbenes,[4] and diazo reagents[5] used as typical one-carbon units, ylides[6] have also been gradually developed as functional units and reacted with various electron-deficient conjugated components to provide such scaffolds.[7] For example, Danheiser and co-workers have shown that sulfur ylides can be used in the [4+1] annulation of (trialkylsilyl)vinylketenes to yield cyclopentenones (Scheme 1, top).[7a] Recently, by employing a camphor-derived sulfur ylide, Tang's group developed a highly efficient method to synthesize enantiopure dihydrofuran derivatives from substituted methene-2,4-pentanediones (Scheme 1, bottom).[7c] However, as analyzed by Sun and Tang,[6c] the success of these [4+1] routes over competitive [2+1] routes is largely attributed to the steric hindrance at the reactive centers. Herein, independent of this effect, we describe an unprecedented [4+1] annulation of sulfur ylides with α,β-unsaturated imines, which allows efficient construction of pyrroline moieties with high chemo- and stereoselectivity (83–99% yields, up to >95:5 d.r., and 98% *ee*).



Scheme 1. Previous [4+1] annulations of sulfur ylides largely relied upon steric hindrance. Dashed arrows indicate the [2+1] pathway.

In spite of the remarkable significance of pyrrolines and their derivatives in enantioselective catalysis,[8] natural products, and pharmaceuticals,[9] the alternative [4+1] annulation of azadienes has been little used for their synthesis,[10] compared with the popular [3+2] approach.[11] To our knowledge, almost all previous endeavors with unstable or semi-stabilized ylides have suffered from the kinetic preference to form aziridines or cyclopropanes (Scheme 2a).[12,13] Therefore the [4+1] annulation between sulfur ylides and α,β-unsaturated imines to synthesize pyrrolines remains a stimulating challenge.



Scheme 2. a) Previously reported methods for cyclopropanes and aziridines. b) Realizing the [4+1] pyrroline annulation of sulfur ylides and α,β-unsaturated imines by tuning electronic effects. PMP = *para*-methoxyphenyl, Ts = 4-toluenesulfonyl.

On the basis of our previous study on the chemistry of stable sulfur ylides,[14] we speculated that the electronic effect could be another potential factor by which to alter the kinetic preference. If we could extend the lifetime of the key zwitterionic intermediates, generated from the Michael addition of sulfur ylides to α,β-unsaturated imines, this would allow formation of the thermodynamic products chemoselectively. Indeed, treatment of phenylacyl sulfur ylide **1** with ester-bearing Ts-protected α,β-unsaturated imine[15] in CH_2Cl_2 at room temperature (Scheme 2b) produced the desired pyrroline-2-carboxylate in 83% yield within 0.5 hours. In contrast, no reaction occurred when the PMP-protected imine was used. According to these results, we can conclude that the introduction of electron-withdraw-

[*] L.-Q. Lu, J.-J. Zhang, Dr. F. Li, Y. Cheng, J. An, Dr. J.-R. Chen, Prof. Dr. W.-J. Xiao
Key Laboratory of Pesticide & Chemical Biology, Ministry of Education, College of Chemistry, Central China Normal University
152 Luoyu Road, Wuhan, Hubei 430079 (China)
Fax: (+86) 27-6786-2041
E-mail: wxiao@mail.ccnu.edu.cn
Homepage: http://chem-xiao.ccnu.edu.cn/

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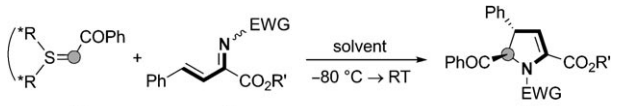
ing groups such as tosyl and ester groups is helpful in 1) stabilizing the anionic enamine intermediates and therefore leading to chemoselective pyrroline formation by attack of the nitrogen atom, and 2) it also helps to promote the Michael addition of ylides to unsaturated imines (Ts vs. PMP).

Next, we focused our attention on the asymmetric version of this novel [4+1] annulation. Atropisomeric sulfide **5** was chosen as the element of stereocontrol because of its ease of preparation from cheap and readily available starting materials (both (*S*)- and (*R*)-binol).[16] Treating sulfur ylide **1a** with imine **2** (PG = Ts) at −80 °C for 48 hours and subsequently warming to room temperature provided the desired enantioenriched [4+1] cycloadduct with an encouraging result of 93 % yield and 81 % *ee* (Table 1, entry 1). Optimization of the reaction conditions led to improved enantioselectivity. Enhancing the size of the ester (Table 1, entry 1 vs. 2), electron deficiency of the protecting group (Table 1, entry 1 vs. 3), solvent polarity (Table 1, entries 4–7), or concentration (Table 1, entry 7 vs. 8) offered no advantage. However, we found that increasing the steric bulk of the sulfonyl group substantially improved the enantioselectivity (Table 1, entries 1 and 4 vs. 9). Owing to the greater repulsive ability of the TIPBS group, a satisfactory result was finally achieved with 95 % yield, a d.r. value greater than 95:5, and 98 % *ee* under optimal reaction conditions (Table 1, entry 9).[17]

Experiments that probed the generality of this asymmetric [4+1] annulation were performed. As summarized in Table 2, the reaction displays a broad scope for sulfur ylides and excellent levels of chemo- and stereoselectivity are achieved. Sulfur ylides having electron-rich (Table 2, entries 2 and 3), electron-neutral (Table 2, entry 1), and electron-deficient substitutents (Table 2, entries 4–6) on the aryl rings all perform well, furnishing products with 88–98 % yields, d.r. values greater than 95:5, and 95–98 % *ee*. Substituents at the *ortho*, *meta*, and *para* positions on the aryl rings are tolerated (Table 2, entries 6–8). In the case of the *meta*-bromo-substituted ylide **1h**, the enantiomeric excess was at a good level although slightly decreased (Table 2, entry 8). Notably, the feasibility of this reaction could also be realized effectively for other stable sulfur ylides, such as heteroaryl- (Table 2, entry 9), alkenyl- (Table 2, entry 10), and alkylacyl-substituted (Table 2, entry 11) substrates.

Additionally, a series of ester-bearing unsaturated imines proved to be suitable for this reaction as highlighted in Table 3. The electronic nature of aromatic substrates (Table 3, entries 1–6) has little effect on the yield and generally,

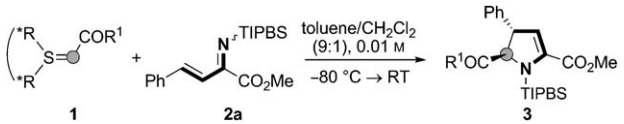
Table 1: Optimization of reaction conditions for asymmetric [4+1] annulation.[a]



Entry	R′	PG	Solvent	Yield [%][b]	*ee* [%][c]
1	Me	Ts	toluene/CH_2Cl_2 (4:1)	93	81
2	*i*Pr	Ts	toluene/CH_2Cl_2 (4:1)	70	81
3	Me	Ns	toluene/CH_2Cl_2 (4:1)	82	83
4	Me	TMBS	toluene/CH_2Cl_2 (4:1)	88	85
5	Me	TMBS	toluene	86	86
6	Me	TMBS	CH_2Cl_2	87	33
7	Me	TMBS	toluene/CH_2Cl_2 (9:1)	95	87
8[d]	Me	TMBS	toluene/CH_2Cl_2 (9:1)	85	82
9[e]	Me	TIPBS	toluene/CH_2Cl_2 (9:1)	95	98

[a] Conditions: **1a** (0.25 mmol), **2** (0.20 mmol), and solvent (20 mL), 48 h. [b] Yield of isolated product. [c] Determined by HPLC analysis using a chiral stationary phase. [d] 4 mL solvent. [e] Ylide **1a** was reduced to 1.1 equiv of imine **2** and d.r. > 95:5, determined by ^{1}H NMR methods. EWG = electron-withdrawing group, Ns = 4-nitrobenzenesulfonyl, TMBS = 2,4,6-trimethylbenzenesulfonyl, TIPBS = 2,4,6-triisopropylbenzenesulfonyl.

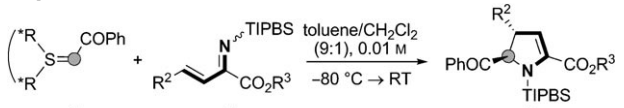
Table 2: Investigating the scope of sulfur ylides in asymmetric [4+1] annulation.[a]



Entry	**1**, R^1	**3**	Yield [%][b]	d.r.[c]	*ee* [%][d]
1	**1a**, Ph	**3a**[e]	95	> 95:5	98
2	**1b**, *p*-$MeOC_6H_4$	**3b**	88	> 95:5	97
3	**1c**, *p*-MeC_6H_4	**3c**	98	> 95:5	96
4	**1d**, *p*-FC_6H_4	**3d**	90	> 95:5	98
5	**1e**, *p*-ClC_6H_4	**3e**	95	> 95:5	95
6	**1f**, *p*-BrC_6H_4	**3f**	93	> 95:5	97
7	**1g**, *o*-BrC_6H_4	**3g**	85	> 95:5	97
8	**1h**, *m*-BrC_6H_4	**3h**	91	> 95:5	90
9	**1i**, thiophen-2-yl	**3i**	96	> 95:5	98
10	**1j**, Ph-CH=CH	**3j**	99	> 95:5	82
11	**1k**, $PhCH_2CH_2$	**3k**	83	> 95:5	88

[a] Conditions: **1** (0.22 mmol), **2** (0.20 mmol), and toluene/CH_2Cl_2 (9:1, 20 mL), 48 h. [b] Yield of isolated product. [c] Determined by ^{1}H NMR methods. [d] Determined by HPLC analysis using a chiral stationary phase. [e] The absolute configuration of product **3a** was established by X-ray analysis.

Table 3: Investigating the scope of unsaturated imines in asymmetric [4+1] annulation.[a]

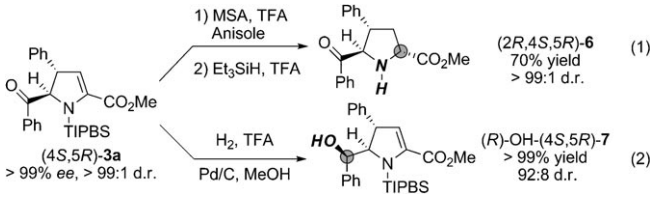


Entry	**2**, R^2	**3**	Yield [%][b]	d.r.[c]	*ee* [%][d]
1	**2a**, Ph	**3a**	95	> 95:5	98
2	**2b**, *p*-$MeOC_6H_4$	**3l**	91	> 95:5	97
3	**2c**, *p*-MeC_6H_4	**3m**	92	> 95:5	98
4	**2d**, *p*-FC_6H_4	**3n**	99	> 95:5	95
5	**2e**, *p*-ClC_6H_4	**3o**	96	> 95:5	95
6	**2f**, *p*-BrC_6H_4	**3p**	91	> 95:5	94
7	**2g**, *o*-FC_6H_4	**3q**	94	> 95:5	86
8	**2h**, *m*-BrC_6H_4	**3r**	89	> 95:5	90
9	**2i**, furan-2-yl	**3s**	95	> 95:5	95
10	**2j**, Ph-CH=CH	**3t**	96	> 95:5	93
11[e]	**2a**, Ph	**3a**	93	> 95:5	96

[a] Conditions: **1a** (0.22 mmol), **2** (0.20 mmol), and toluene/CH_2Cl_2 (9:1, 20 mL), 48 h; entries 1–8 and entry 11: R^3 = Me; entries 9 and 10: R^3 = Et. [b] Yield of isolated product. [c] Determined by ^{1}H NMR methods. [d] Determined by chiral HPLC analysis. [e] Gram scale: **1a** (2.5 mmol, 1.08 g), **2a** (2.5 mmol, 1.14 g).

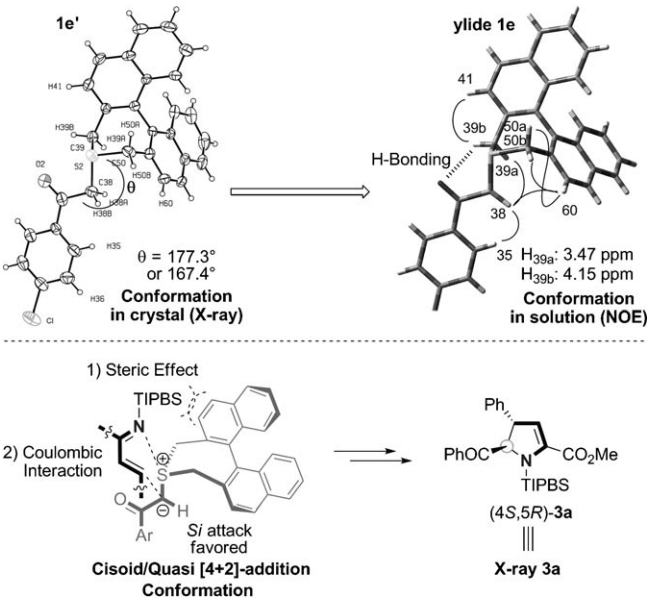
excellent stereoselectivity was achieved (91–99% yields, >95:5 d.r., 94–98% *ee*). In exploring another dimension by varying the position of the substitution on the aryls rings appended to the imines (Table 3, entries 7 and 8), good results were still achieved (89% yield, >95:5 d.r., ≥86% *ee*). Furthermore, the heteroaryl- and alkenyl-substituted unsaturated imines can also be employed in this annulation, with excellent yields and high levels of stereoselectivity being achieved (Table 3, entries 9 and 10).[18] Importantly, the reaction can be carried out on the gram scale without obvious loss in the reaction efficiency (Table 3, entry 11), and with essentially quantitatively recovered sulfide **5** (95% yield).

In addition, the resultant [4+1] cycloadducts could be applied to the synthesis of important building blocks. For instance, two-step deprotection/reduction operations for optically pure **3a** delivered the 4,5-substituted proline ester **6** as a single isomer [Eq. (1); MSA = methanesulfonic acid, TFA = trifluoroacetic acid]. Moreover, the functional group introduced together with the one-carbon unit could be effectively transformed into other moieties. As illustrated in Equation (2), the carbonyl group in **3a** was reduced to a hydroxy group through the acid-assisted Pd-catalyzed hydrogenation with excellent yield and significant diastereoselectivity (>99% yield and 92:8 d.r.).



To better understand the stereoinduction in this asymmetric [4+1] annulation, we additionally collected and analyzed data on the conformations of these ylides in solution. In view of the open character (Scheme 3, top: arylacyl group away from atropisomeric backbone) and near coplanarity ($\theta = 177.3°$ or 167.4°) in the single crystal of **1e′**,[19] we supposed a comformer of ylide **1e** as shown in Scheme 3 (top, right). The NOE effects and the presence of an intramolecular hydrogen bond for the ylide **1e** in solution strongly supports the above proposal. On the basis of this fundamental assumption, we rationalized the important effects responsible for the stereochemical course as follows (Scheme 3, bottom): 1) the unsaturated imines attack the exposed *Si* face of chiral ylides to avoid the steric repulsion between the TIPBS group in the imine and the naphthalenyl ring in the chiral backbone; 2) this process possibly adopted the cisoid/quasi [4+2]-addition conformation because of favorable Coulombic interactions between the negatively charged N atoms of the unsaturated imines and positively charged S atoms of the stable ylides.[20] The configuration of cycloadduct **3a** was confirmed by X-ray diffraction analysis.

In summary, we have successfully developed a novel [4+1] annulation of stable sulfur ylides with ester-bearing unsaturated imines by manipulating the electronic effects. The low cost, ready availability, and recoverability of the binol-derived



Scheme 3. Rationalizing the origin of stereoselectivity based on conformational analysis of chiral ylides. ClO_4^- counterion omitted for clarity in X-ray crystallographic structure. Thermal ellipsoids are drawn at 30% probability. θ = dihedral angle ($\theta = C_{37}$-C_{38}-S_2-C_{50}, θ was different in dimer).

sulfide lead to an asymmetric process that conveniently provides chiral pyrroline-2-carboxylates with good to excellent results (83–99% yields, up to 98% *ee*, >95:5 d.r.). Although detailed investigations of the reaction mechanism and stereochemistry with Gaussian calculations are ongoing, we have rationalized the origin of stereoinduction based on a conformational analysis of chiral ylides; the high stereoselectivity is attributed to steric effects and possible Coulombic interactions. What is more promising is that this work could open up new opportunities for selectively constructing other carbon- and heterocycles beyond traditional small rings.

Experimental Section

Representative procedure: Unsaturated imine **2a** (0.2 mmol) and toluene/CH_2Cl_2 (9:1, 20 mL) were added to a 50 mL flask equipped with a magnetic stir bar. After the solution had been stirred at −80 °C for 0.5 h, chiral sulfur ylide **1a** (0.22 mmol) was introduced and the mixture stirred for 48 h at the same temperature. The reaction mixture was then slowly warmed to room temperature. Upon completion of the reaction, as monitored by TLC, the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel [silica: 200–300; eluant: petroleum ether/ethyl acetate (5:1→3:1)] to provide pure product **3a** in 95% yield. Diastereomeric ratio: >95:5 as determined by ^{1}H NMR analysis of the reaction mixture. Enantiomeric excess: 98% as determined by HPLC analysis (Daicel Chirapak OD-H, *n*-hexane/isopropyl alcohol = 95:5, flow rate 0.7 mL min^{-1}, $T = 25$ °C, 254 nm): $t_R = 7.51$ min (major), $t_R = 9.26$ min (minor). $[\alpha]_D^{33} = -93$ deg cm^3 g^{-1} dm^{-1} ($c = 1.2$ g cm^{-3}, $CHCl_3$).

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[1] a) R. W. Coscia, T. H. Lambert, *J. Am. Chem. Soc.* **2009**, *131*, 2496; b) R. A. Widenhoefer, *Angew. Chem.* **2009**, *121*, 7084; *Angew. Chem. Int. Ed.* **2009**, *48*, 6950.

[2] For selected examples with carbon monoxide as a one-carbon unit in [4+1] annulations, see: a) B. E. Eaton, B. Rollman, J. A. Kaduk, *J. Am. Chem. Soc.* **1992**, *114*, 6245; b) T. Mandai, J. Tsuji, Y. Tsujiguchi, S. Saito, *J. Am. Chem. Soc.* **1993**, *115*, 5865; c) M. S. Sigman, C. E. Kerr, B. E. Eaton, *J. Am. Chem. Soc.* **1993**, *115*, 7545; d) M. S. Sigman, B. E. Eaton, *J. Org. Chem.* **1994**, *59*, 7488; e) M. Murakami, K. Itami, Y. Ito, *Angew. Chem.* **1995**, *107*, 2943; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2691; f) M. S. Sigman, B. E. Eaton, J. D. Heise, C. P. Kubiak, *Organometallics* **1996**, *15*, 2829; g) M. S. Sigman, B. E. Eaton, *J. Am. Chem. Soc.* **1996**, *118*, 11783.

[3] For a representative example with isocyanides as one-carbon units in [4+1] annulations, see: M. Oshita, K. Yamashita, M. Tobisu, N. Chatani, *J. Am. Chem. Soc.* **2005**, *127*, 761.

[4] For selected examples with nucleophilic carbenes as one-carbon units in [4+1] annulations, see: a) J. H. Rigby, W. Dong, *Org. Lett.* **2002**, *2*, 1673; b) C. Spino, H. Rezaei, K. Dupont-Gaudet, F. Bélanger, *J. Am. Chem. Soc.* **2004**, *126*, 9926; c) L. Boisvert, F. Beaumier, C. Spino, *Org. Lett.* **2007**, *9*, 5361.

[5] For selected examples with diazo reagents as one-carbon units in [4+1] annulations, see: a) A. M. Dalton, Y. Zhang, C. P. Davie, R. L. Danheiser, *Org. Lett.* **2002**, *4*, 2465; b) L.-B. Zhao, Z.-H. Guan, Y. Han, Y.-X. Xie, S. He, Y.-M. Liang, *J. Org. Chem.* **2007**, *72*, 10276; c) M. W. Giese, W. H. Moser, *Org. Lett.* **2008**, *10*, 4215. Some other metal reagents were also used as one-carbon units in [4+1] annulations, such as Fischer alkoxy(alkenyl)carbene and α-benzotriazolyl organolithium compounds: d) J. Barluenga, S. López, J. Flórez, *Angew. Chem.* **2003**, *115*, 241; *Angew. Chem. Int. Ed.* **2003**, *42*, 231; e) C. P. Davie, R. L. Danheiser, *Angew. Chem.* **2005**, *117*, 6017; *Angew. Chem. Int. Ed.* **2005**, *44*, 5867.

[6] For recent reviews, see: a) V. K. Aggarwal, C. L. Winn, *Acc. Chem. Res.* **2004**, *37*, 611; b) E. M. McGarrigle, E. L. Myers, O. Illa, M. A. Shaw, S. L. Riches, V. K. Aggarwal, *Chem. Rev.* **2007**, *107*, 5841; c) X.-L. Sun, Y. Tang, *Acc. Chem. Res.* **2008**, *41*, 937.

[7] a) J. L. Loebach, D. M. Bennett, R. L. Danheiser, *J. Am. Chem. Soc.* **1998**, *120*, 9690; b) Z. Yang, M. Fan, R. Mu, W. Liu. Y. Liang, *Tetrahedron* **2005**, *61*, 9140; c) J.-C. Zheng, C.-Y. Zhu, X.-L. Sun, Y. Tang, L.-X. Dai, *J. Org. Chem.* **2008**, *73*, 6909; d) C.-Y. Zhu, X.-M. Deng, X.-L. Sun, J.-C. Zheng, Y. Tang, *Chem. Commun.* **2008**, 738; e) C.-Y. Zhu, X.-L. Sun, X.-M. Deng, J.-C. Zheng, Y. Tang, *Tetrahedron* **2008**, *64*, 5583, and references therein.

[8] For selected reviews, see: a) A. Erkkilä, I. Majander, P. M. Phihko, *Chem. Rev.* **2007**, *107*, 5416; b) S. Mukherjee, J. W. Yang, S. Hoffmann, B. List, *Chem. Rev.* **2007**, *107*, 5471.

[9] a) D. O'Hagan, *Nat. Prod. Rep.* **2000**, *17*, 435; b) D. Enders, C. Thiebes, *Pure Appl. Chem.* **2001**, *73*, 573.

[10] Only one example was reported by Murai and co-workers in 1999 regarding a Ru-catalyzed carbonylative [4+1] annulations using α,β-unsaturated imines. Please see T. Morimoto, N. Chatani, S. Murai, *J. Am. Chem. Soc.* **1999**, *121*, 1758.

[11] For selected reviews, see: a) I. Coldham, R. Hufton, *Chem. Rev.* **2005**, *105*, 2765; b) G. Pandey, P. Banerjee, S. R. Gadre, *Chem. Rev.* **2006**, *106*, 4484.

[12] Unstable sulfur ylides: a) D. Pearson, R. A. Field, R. A. Stockman, *Synlett* **2003**, 1985. Semi-stablized benzylic sulfonium ylide: b) 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. Semi-stablized allylic sulfonium ylides: c) A.-H. Li, L.-X. Dai, X.-L. Hou, M.-B. Chen, *J. Org. Chem.* **1996**, *61*, 4641; d) A.-H. Li, L.-X. Dai, X.-L. Hou, *J. Chem. Soc. Perkin Trans. 1* **1996**, 867; e) D. Morton, D. Pearson, R. A. Field, R. A. Stockman, *Org. Lett.* **2004**, *6*, 2377. Semi-stablized allylic tellurium ylides: f) J.-C. Zheng, W.-W. Liao, Y. Tang, X.-L. Sun, L.-X. Dai, *J. Am. Chem. Soc.* **2005**, *127*, 12222. Semi-stablized propargylic sulfonium ylides: g) A.-H. Li, Y.-G. Zhou, L.-X. Dai, X.-L. Hou, L.-J. Xia, L. Lin, *J. Org. Chem.* **1998**, *63*, 4338.

[13] Synthesis of pyrrolidines from sulfur ylides other than by [4+1] annulations: a) S. Koep, H.-J. Gais, G. Raabe, *J. Am. Chem. Soc.* **2003**, *125*, 13243; b) H.-J. Gais, L. R. Reddy, G. S. Babu, G. Raabe, *J. Am. Chem. Soc.* **2004**, *126*, 4859; c) S. K. Tiwari, H.-J. Gais, A. Lindenmaier, G. S. Babu, G. Raabe, L. R Reddy, F. Köhler, M. Günter, S. Koep, V. B. R. Iska, *J. Am. Chem. Soc.* **2006**, *128*, 7360; d) C. G. Kokotos, V. K. Aggarwal, *Chem. Commun.* **2006**, 2156; e) M. G. Unthank, N. Hussain, V. K. Aggarwal, *Angew. Chem.* **2006**, *118*, 7224; *Angew. Chem. Int. Ed.* **2006**, *45*, 7066; f) C. G. Kokotos, V. K. Aggarwal, *Org. Lett.* **2007**, *9*, 2099; g) J. M. Schomaker, S. Bhattacharjee, J. Yan, B. Borhan, *J. Am. Chem. Soc.* **2007**, *129*, 1996; h) M. G. Unthank, B. Tavassoli, V. K. Aggarwal, *Org. Lett.* **2008**, *10*, 1501.

[14] a) L.-Q. Lu, Y.-J. Cao, X-P. Liu, J. An, C.-J. Yao, Z.-H. Ming, W.-J. Xiao, *J. Am. Chem. Soc.* **2008**, *130*, 6946; b) L.-Q. Lu, F. Li, J. An, J.-J. Zhang, X.-L. An, Q.-L. Hua, W.-J. Xiao, *Angew. Chem.* **2009**, *121*, 9706; *Angew. Chem. Int. Ed.* **2009**, *48*, 9542.

[15] B. Han, Z.-Q. He, J.-L. Li, R. Li, K. Jiang, T.-Y. Liu, Y.-C. Chen, *Angew. Chem.* **2009**, *121*, 5582; *Angew. Chem. Int. Ed.* **2009**, *48*, 5474, and references therein.

[16] Y. Miyake, A. Oyamada, Y. Nishibayashi, S. Uemura, *Heteroat. Chem.* **2002**, *13*, 270.

[17] See the Supporting Information for more details.

[18] Attempts to carry out the reaction of aliphatic imines were unsuccessful. The reaction gave a complex reaction mixture under the current reaction conditions. Additional studies are ongoing in our laboratory.

[19] CCDC 764746 (**3a**) and 764745 (**1e′**) contain 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.

[20] a) V. K. Aggarwal, J. N. Harvey, J. Richardson, *J. Am. Chem. Soc.* **2002**, *124*, 5747; b) V. K. Aggarwal, E. Alonso, I. Bae, G. Hynd, K. M. Lydon, M. J. Palmer, M. Patel, M. Porcelloni, J. Richardson, R. A. Stenson, J. R. Studley, J. Vasse, C. L. Winn, *J. Am. Chem. Soc.* **2003**, *125*, 10926; c) V. K. Aggarwal, J. P. H. Charmant, D. Fuentes, J. N. Harvey, G. Hynd, D. Ohara, W. Picoul, R. Robiette, C. Smith, J. Vasse, C. L. Winn, *J. Am. Chem. Soc.* **2006**, *128*, 2105.

