DOI: 10.1002/adsc.201300126

Copper(I)-Catalyzed Stereoselective Synthesis of (1*E*,3*E*)-2-Sulfonyl-1,3-dienes from *N*-Propargylic Sulfonohydrazones

Yu Zhu,[a] Hai-Tao Tang,[a] and Zhuang-Ping Zhan[a,*]

[a] Department of Chemistry, College of Chemistry and Chemical Engineering, Xiamen University, Xiamen 361005, Fujian, People's Republic of China
Fax: (+86)-592-218-0318; e-mail: zpzhan@xmu.edu.cn

Received: February 7, 2013; Revised: March 18, 2013; Published online: ■■ ■■, 0000

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201300126.

Abstract: A new method for the stereoselective synthesis of highly substituted (1*E*,3*E*)-2-sulfonyl-1,3-dienes from *N*-propargylic sulfonohydrazone derivatives has been developed *via* copper(I)-catalyzed [3,3]rearrangement and highly regioselective migration of the sulfonyl group.

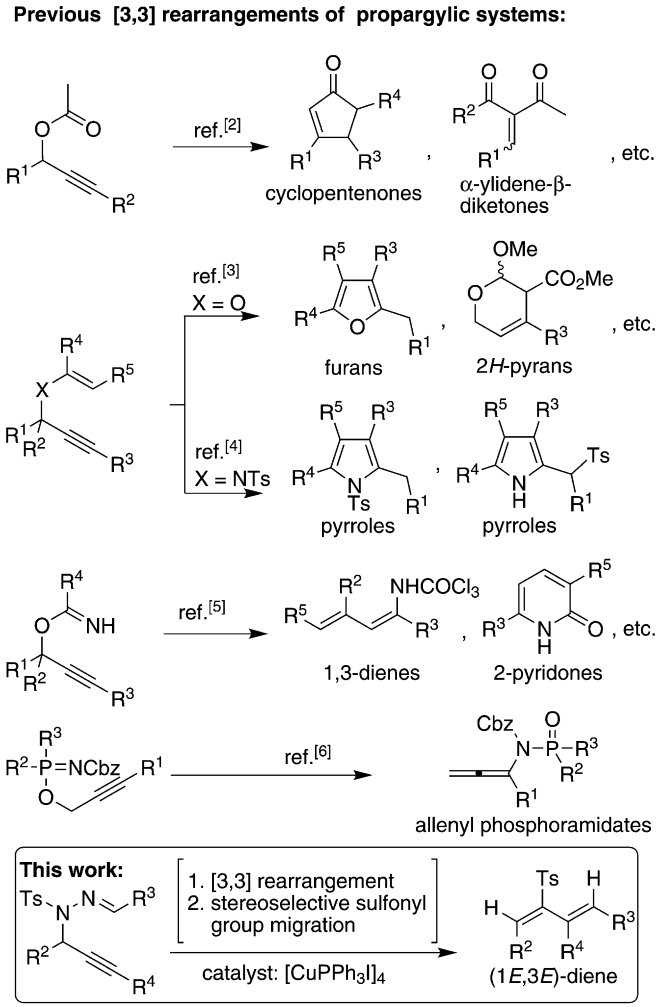
Keywords: migration of the sulfonyl group; *N*-propargylic sulfonohydrazone; [3,3] rearrangements; (1*E*,3*E*)-2-sulfonyl-1,3-dienes

Metal-catalyzed skeletal rearrangements which involve cleavage and formation of several covalent bonds have been known as an effective pathway for the construction of complex molecules. In particular, the [3,3]rearrangements of propargylic systems have been well studied (Scheme 1).[1] Propargyl carboxylates as substrates have demonstrated a diversity of the skeletal rearrangement which offers versatile entries into a range of fascinating structures.[2] The Claisen rearrangement of propargyl vinyl ethers constitutes a synthetically convenient route to β-allenic alcohols, substituted furans, 2*H*-pyrans or multifunctionalized aromatic products.[3] Similar approaches to preparing pyrrole derivatives from aza-Claisen rearrangement of *N*-propargylic enaminone derivatives have been accomplished.[4] Overman and his co-workers reported the rearrangement of propargylic trichloroacetimidates to form allenamides, 1,3-dienes and 2-pyridones (Overman rearrangement).[5] Recently, the palladium-catalyzed [3,3]rearrangement of propargylic phosphorimidates for the facile synthesis of allenyl phosphoramidates has been described by Mapp's group.[6]

To the best of our knowledge, a [3,3]rearrangement of *N*-propargylic hydrazones has not been disclosed. Herein, we report that *N*-propargylic sulfonylhydrazones **1** undergo a novel [3,3]rearrangement and stereoselective shift of the sulfonyl group[4a,7] catalyzed by copper(I) and eventually furnish (1*E*,3*E*)-2-sulfonyl-1,3-dienes **2** in moderate to good yields (Scheme 1).

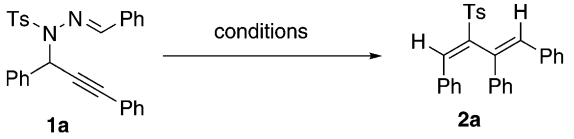
The 2-sulfonyl-1,3-dienes have been deemed to be versatile synthons in organic transformations. The 2-sulfonyl-1,3-diene moiety offers a handle for transformation into various other skeletons *via* Diels–Alder reactions[8] or Michael additions.[9] Moreover, epoxidation of either double bond of 2-sulfonyl-1,3-dienes leads to synthetically useful epoxy sulfones.[10] However, the stereocontrolled synthesis of 1,3-diene sulfones has rarely aroused extensive attention. The previous procedures for the synthesis of 2-sulfonyl-1,3-dienes involved reagents such as Hg,[11] Se,[12] thiophenol[13] organic tin[14] or strong base.[15] These processes have drawbacks with regard to convenient synthesis and disadvantageous effects on the environment.

On the basis of work that has been previously carried out in our laboratory,[16] *N*-propargylic sulfonohydrazones **1** could be easily prepared through $FeCl_3$-catalyzed nucleophilic substitution of propargylic acetates with hydrazones in a single synthetic step, all of which are easily accessible. In the initial study, we decided to investigate the reaction conditions in order to improve the yield using **1a** as the reactant (Table 1). The reaction was smoothly catalyzed by CuI and CuCl in toluene and the desired product **2a** was isolated in 78% and 60% yields, respectively (Table 1, entries 1 and 2). Gratifyingly, the reaction rate increased dramatically catalyzed by 5 mol% $[CuPPh_3I]_4$ and a higher yield was achieved (Table 1, entry 4). When $Cu(PPh_3)_3I$ was utilized under the same conditions, the reaction proceeded slowly to afford **2a** in 60% yield (Table 1, entry 5). The Lewis acid $Cu(OTf)_2$ failed to promote this transformation (Table 1, entry 3). The reaction took place in a less effective manner when using solvents such as CH_3CN (20%),THF (0) and DMF (0) (Table 1, entries 6, 7



Scheme 1. Rearrangements of the propargylic system.

Table 1. Optimization of the reaction conditions.[a]



Entry	Catalyst	Solvent	Time [h]	Yield[b]
1	20 mol% CuI	PhMe	12	78%
2	20 mol% CuCl	PhMe	12	60%
3	20 mol% $Cu(OTf)_2$	PhMe	12	complex
4	5 mol% $[Cu(PPh_3)I]_4$	PhMe	6	85%
5	20 mol% $Cu(PPh_3)_3I$	PhMe	8	60%
6	5 mol% $[Cu(PPh_3)I]_4$	CH_3CN	15	20%
7	5 mol% $[Cu(PPh_3)I]_4$	THF	12	n.r.[c]
8	5 mol% $[Cu(PPh_3)I]_4$	DMF	12	n.r.[d]
9	–	PhMe	12	n.r.

[a] *Conditions:* **1a** (234 mg, 0.5 mmol), solvent (2 mL), reflux.
[b] Isolated yields.
[c] n.r. = no reaction.
[d] The reaction was performed below 120 °C.

and 8). Absence of the catalyst led to complete recovery of **1a** (Table 1, entry 9).

To broaden the scope of this reaction, we carried out the reaction of the *N*-propargylic sulfonohydrazone derivatives (summarized in Table 2) under the optimized conditions. The substrates **1a** (R^1 = 4-MeC_6H_4) and **1c** ($R^1 = C_6H_5$) gave the desired results, providing 2-sulfonylbuta-1,3-dienes **2a** and **2c** in 85% and 87% yields, respectively (Table 2, entries 1 and 3). The electron-deficient sulfonohydrazone **1b** (R^1 = 4-BrC_6H_4) reacted smoothly affording the product **2b** in 91% yield (Table 2, entry 2). The electron-donating sulfonohydrazone **1d** (R^1 = 4-$MeOC_6H_4$) was also successfully employed in the reaction to give product **2d** in 65% yield (Table 2, entry 4). Obviously, electron-poor sulfonohydrazones provided the desired products in higher yields than electron-rich sulfonohydrazones. The substrates **1e**, **1n** and **1o** bearing a fused ring or thiophene moiety were also suitable for the transformations (entries 5, 14 and 15). Electron-neutral, electron-deficient, and electron-rich aromatic groups (R^2 and R^3) on **1** were all well tolerated, and the desired products (**2f–2l**) were obtained in moderate to good yields (75–92%, Table 2, entries 6–12). The reaction of **1m** (R^3 = 2-OHC_6H_4) containing a weakly acidic hydroxy group also afforded **2m** in moderate yield (Table 2, entry 13). Additionally, internal alkynes **1p** and **1q** ($R^4 = n$-C_4H_9 and cyclopropanyl) readily underwent this tandem reaction to afford substituted alkenes **2p** and **2q** in moderate yields (Table 2, entries 16 and 17). Methylsulfonylhydrazone **1r** (R^1 = Me) also afforded the corresponding migration product in low yield (Table 2, entry 18). However, the results suggested that reactants **1s** (R^4 = H) and **1t** (R^2 = H) failed to form 2-sulfonyl-1, 3-dienes (Table 2, entries 19 and 20). The reaction of acetohydrazone **1u** and methoxycarbonylhydrazone **1v** did

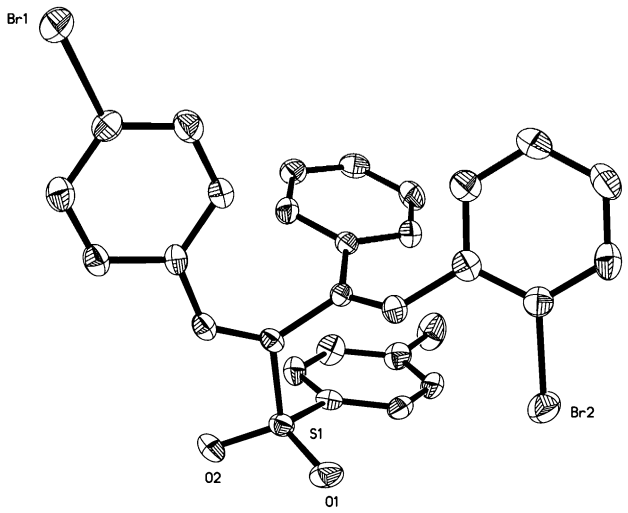
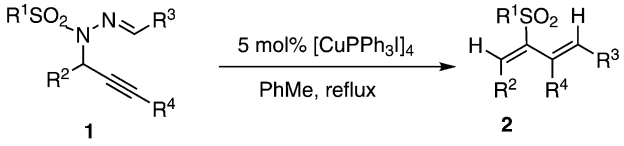


Figure 1. X-ray structure of **2i**.

Table 2. Copper(I)-catalyzed formation of 2-sulfonyl-1,3-dienes.[a]



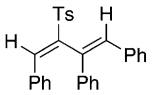
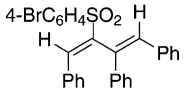
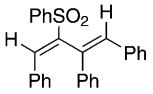
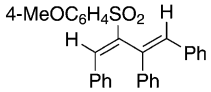
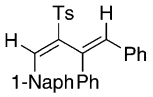
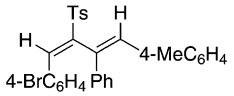
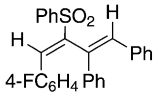
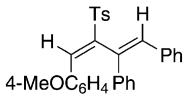
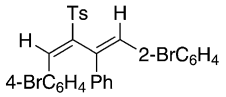
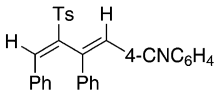
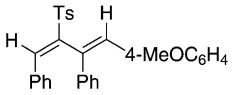
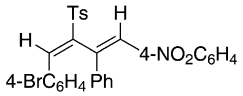
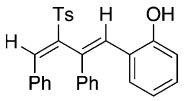
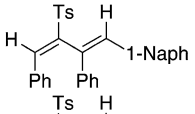
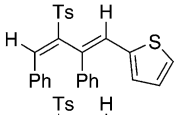
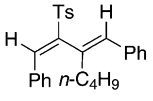
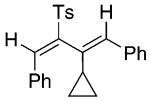
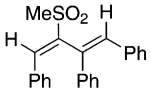
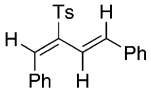
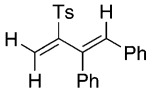
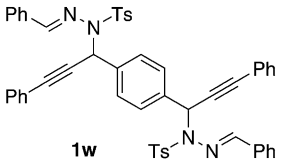
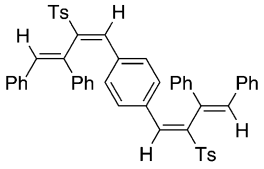
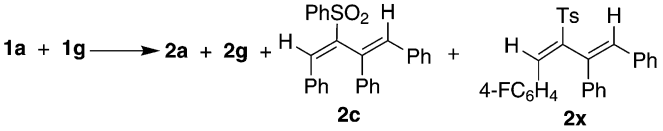
Entry	Substrates **1**: R^1; R^2; R^3; R^4	Products **2**	Yield[b]
1	**1a**: 4-MeC_6H_4; C_6H_5; C_6H_5; C_6H_5		85% (**2a**)
2	**1b**: 4-BrC_6H_4; C_6H_5; C_6H_5; C_6H_5		91% (**2b**)
3	**1c**: C_6H_5; C_6H_5; C_6H_5; C_6H_5		87% (**2c**)
4	**1d**: 4-MeOC_6H_4; C_6H_5; C_6H_5; C_6H_5		65% (**2d**)
5	**1e**: 4-MeC_6H_4; 1-naphthyl; C_6H_5; C_6H_5		60% (**2e**)
6	**1f**: 4-MeC_6H_4; 4-BrC_6H_4; 4-MeC_6H_4; C_6H_5		82% (**2f**)
7	**1g**: C_6H_5; 4-FC_6H_4; C_6H_5; C_6H_5		87% (**2g**)
8	**1h**: 4-MeC_6H_4; 4-MeOC_6H_4; C_6H_5; C_6H_5		92% (**2h**)
9	**1i**: 4-MeC_6H_4; 4-BrC_6H_4; 2-BrC_6H_4; C_6H_5		82% (**2i**)
10	**1j**: 4-MeC_6H_4; C_6H_5; 4-CNC_6H_4; C_6H_5		85% (**2j**)
11	**1k**: 4-MeC_6H_4; C_6H_5; 4-MeOC_6H_4; C_6H_5		75% (**2k**)
12	**1l**: 4-MeC_6H_4; 4-BrC_6H_4; 4-$NO_2C_6H_4$; C_6H_5		79% (**2l**)
13	**1m**: 4-MeC_6H_4; C_6H_5; 1-naphthyl; C_6H_5		65% (**2m**)
14	**1n**: 4-MeC_6H_4; C_6H_5; 1-naphthyl; C_6H_5		68% (**2n**)
15	**1o**:4-MeC_6H_4; C_6H_5; 2-thiophenyl; C_6H_5		51% (**2o**)
16	**1p**: 4-MeC_6H_4; C_6H_5; C_6H_5; n-C_4H_9		67% (**2p**)

Table 2. (Continued)

Entry	Substrates **1**: R^1; R^2; R^3; R^4	Products **2**	Yield[b]
17	**1q**: 4-MeC_6H_4; C_6H_5; C_6H_5; cyclopropanyl		55% (**2q**)
18	**1r**: Me; C_6H_5; C_6H_5; C_6H_5		48% (**2r**)
19	**1s**: 4-MeC_6H_4; C_6H_5; C_6H_5; H		complex
20	**1t**: 4-MeC_6H_4; H; C_6H_5; C_6H_5		n.r.[c]
21	 **1w**		75%[d] (**2w**)

[a] Conditions: substrates **1** (0.5 mmol), PhMe (2 mL), $[CuPPh_3I]_4$ (46 mg, 0.025 mmol), reflux.
[b] Isolated yields.
[c] n.r. = no reaction.
[d] $[CuPPh_3I]_4$ (91 mg, 0.05 mmol).

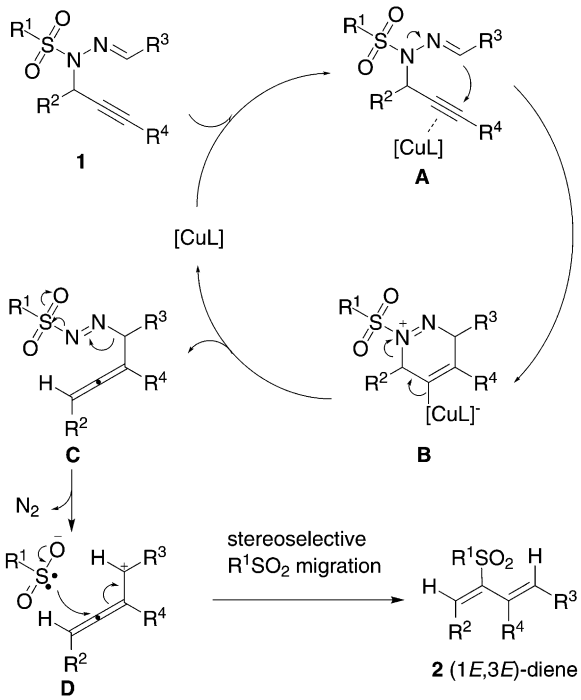


Scheme 2. Crossover experiment of **1a** and **1g**.

not occur under normal conditions.[17] Notably, starting from **1w**, we could finally obtain a symmetrical oligomer **2w** containing two 2-sulfonylbuta-1,3-diene moieties. The structure of product **2i** was unambiguously demonstrated by X-ray diffraction analysis (Figure 1, also see the Supporting Information).[18]

In order to figure out whether the migration of the sulfonyl group occurred in an intramolecular or intermolecular pathway, we performed a crossover experiment between equimolar amounts of **1a** and **1g** yielding the corresponding products **2a** and **2g** in 48% and 33% yields, respectively, and the crossover products **2c** and **2x** in 42% and 47% yields, respectively (Scheme 2, determined by HPLC). This result clearly indicated that migration of the sulfonyl group proceeds in an intermolecular manner. It was noteworthy that the sulfonyl groups were introducted to the sp^2-carbon straightforwardly with excellent stereoselectivity. The migration was triggered most likely by the release of nitrogen.

As a working hypothesis, we proposed the following mechanism based on our observation for the formation of (1*E*,3*E*)-2-sulfonyl-1,3-dienes (Scheme 3).



Scheme 3. Proposed mechanism.

First, a 6-*endo-dig* addition of sulfonohydrazone onto the copper(I)-alkyne complex **A** resulted in the formation of intermediate **B**, which collapsed into the allenic intermediate **C**. The unstable intermediate **C** decomposed to nitrogen and ion pairs **D**. Then, a nucleo-

philic attack of the tosyl anion to the central *sp* carbon atom of the hypothetical allenic moiety carbon followed by electron transfer gave the product **2**. As we surmised, no (1*E*,3*Z*)-2-sulfonyl-1,3-dienes were observed due to the sterically hindered effect between the tosyl anion and R^3. Intermolecular trapping with external nucleophiles such as ethanol and aniline has been tested. The desired product was not obtained.

In summary, a facile approach for the stereoselective synthesis of highly substituted (1*E*,3*E*)-2-sulfonyl-1,3-dienes from *N*-propargylic sulfonohydrazone derivatives has been developed. A key feature of the rearrangement was that it allowed the straightforward introduction of sulfonyl groups to alkene units. Studies aiming at exploring mechanistic aspects of this reaction and developing further transformations of *N*-propargylic sulfonohydrazone derivatives are ongoing.

Experimental Section

General Procedure for Synthesis of *N*-Propargylic Hydrazones

To a solution of propargylic acetate (5 mmol) and hydrazone (6 mmol) in CH_3CN (20 mL), $FeCl_3$ (0.5 mmol) was added and the mixture was stirred at room temperature. When the reaction was completed (monitored by TLC), the solvent was removed under vacuum, and then the residue was further purified by silica gel column chromatography (petroleum ether and ethyl acetate) to afford the desired *N*-propargylic hydrazones.

General Procedure for the Synthesis of (1*E*,3*E*)-1,3-Dienes

$[CuPPh_3I]_4$ (5 mol%), propargylic hydrazone **1** (0.5 mmol) was suspended in anhydrous toluene (2 mL) in a 10-mL Schlenk tube under nitrogen. The resulting solution was stirred at reflux until reaction was completed (monitored by TLC). After cooling to room temperature, the solvent was removed under vacuum. The residue was purified by column chromatography (petroleum ether:ethyl acetate = 20:1).

Acknowledgements

Financial support from National Natural Science Foundation of China (No. 21072159 and 21272190) and PCSIRT in University is gratefully acknowledged.

References

[1] For recent reviews, see: a) A. M. M. Castro, *Chem. Rev.* **2004**, *104*, 2939–3002; b) L. Zhang, J. Sun, S. A. Kozmin, *Adv. Synth. Catal.* **2006**, *348*, 2271–2296; c) S. Wang, G. Zhang, L. Zhang, *Synlett* **2010**, 692–706; d) K. Majumdar, T. Bhattacharyya, B. Chattopadhyay, B. Sinha, *Synthesis* **2009**, 2117–2142; e) K. C. Majumdar, *Synlett* **2008**, 2400–2411.

[2] For selected examples see: a) L. Zhang, S. Wang, *J. Am. Chem. Soc.* **2006**, *128*, 1442–1443; b) A. Buzas, F. Gagosz, *J. Am. Chem. Soc.* **2006**, *128*, 12614–12615; c) N. Marion, S. Díez-González, P. de Frémont, A. R. Noble, S. P. Nolan, *Angew. Chem.* **2006**, *118*, 3729–3732; *Angew. Chem. Int. Ed.* **2006**, *45*, 3647–3650; d) L. Zhang, *J. Am. Chem. Soc.* **2005**, *127*, 16804–16805; e) S. Wang, L. Zhang, *J. Am. Chem. Soc.* **2006**, *128*, 8414–8415; f) D. Garayalde, E. Gómez-Bengoa, X. Huang, A. Goeke, C. Nevado, *J. Am. Chem. Soc.* **2010**, *132*, 4720–4730; g) N. Marion, G. Lemière, A. Correa, C. Costabile, R. S. Ramón, X. Moreau, P. de Frémont, R. Dahmane, A. Hours, D. Lesage, *Chem. Eur. J.* **2009**, *15*, 3243–3260.

[3] For selected examples see: a) B. D. Sherry, F. D. Toste, *J. Am. Chem. Soc.* **2004**, *126*, 15978–15979; b) D. Tejedor, L. Cotos, F. García-Tellado, *Org. Lett.* **2011**, *13*, 4422–4425; c) M. H. Suhre, M. Reif, S. F. Kirsch, *Org. Lett.* **2005**, *7*, 3925–3927; d) H. Cao, H. Jiang, W. Yao, X. Liu, *Org. Lett.* **2009**, *11*, 1931–1933; e) H. Jiang, W. Yao, H. Cao, H. Huang, D. Cao, *J. Org. Chem.* **2010**, *75*, 5347–5350; f) E. Matoušová, A. Růžička, J. Kuneš, J. Králová, M. Pour, *Chem. Commun.* **2011**, *47*, 9390–9392; g) D. Tejedor, G. Méndez-Abt, L. Cotos, M. A. Ramirez, F. García-Tellado, *Chem. Eur. J.* **2011**, *17*, 3318–3321; h) D. Tejedor, G. Méndez-Abt, L. Cotos, F. García-Tellado, *Chem. Soc. Rev.* **2013**, *42*, 458–471; i) Z.-B. Zhu, S. F. Kirsch, *Chem. Commun.* **2013**, *49*, 2272–2283; j) H. Cao, H. Jiang, R. Mai, S. Zhu, C. Qi, *Adv. Synth. Catal.* **2009**, ***##351##352***, 143–152.

[4] a) X. Xin, D. Wang, X. Li, B. Wan, *Angew. Chem.* **2012**, *124*, 1725–1729; *Angew. Chem. Int. Ed.* **2012**, *51*, 1693–1697; b) A. Saito, T. Konishi, Y. Hanzawa, *Org. Lett.* **2010**, *12*, 372–374; c) P. Novák, R. Pohl, M. Kotora, M. Hocek, *Org. Lett.* **2006**, *8*, 2151–2153; d) K. Komeyama, M. Miyagi, K. Takaki, *Chem. Lett.* **2009**, *38*, 224–225.

[5] a) L. E. Overman, L. A. Clizbe, R. L. Freerks, C. K. Marlowe, *J. Am. Chem. Soc.* **1981**, *103*, 2807–2815; b) L. E. Overman, S. Tsuboi, J. P. Roos, G. F. Taylor, *J. Am. Chem. Soc.* **1980**, *102*, 747–754.

[6] A. M. Danowitz, C. E. Taylor, T. M. Shrikian, A. K. Mapp, *Org. Lett.* **2010**, *12*, 2574–2577.

[7] For selected examples of sulfonyl group migration see: a) M. Kimura, Y. Horino, M. Mori, Y. Tamaru, *Chem. Eur. J.* **2007**, *13*, 9686–9702; b) Y. T. Lee, Y. K. Chung, *J. Org. Chem.* **2008**, *73*, 4698–4701; c) Z. Jiang, P. Lu, Y. Wang, *Org. Lett.* **2012**, *14*, 6266–6269.

[8] For selected examples see: a) R. Fernandez de La Pradilla, C. Montero, M. Tortosa, A. Viso, *Chem. Eur. J.* **2005**, *11*, 5136–5145; b) R. Fernandez de La Pradilla, C. Montero, A. Viso, *Chem. Commun.* **1998**, 409–410; c) R. Fernandez de La Pradilla, I. Colomer, A. Viso, *Org. Lett.* **2012**, *14*, 3068–3071; d) J. E. Bäckvall, N. A. Plobeck, *J. Org. Chem.* **1990**, *55*, 4528–4531.

[9] For selected examples see: a) V. Sikervar, P. L. Fuchs, *Org. Lett.* **2012**, *14*, 2922–2924; b) K. Deng, J. Chalker, A. Yang, T. Cohen, *Org. Lett.* **2005**, *7*, 3637–3640; c) J. Evarts, E. Torres, P. L. Fuchs, *J. Am. Chem. Soc.* **2002**,

124, 11093–11101; d) J. J. Murphy, A. Quintard, P. McArdle, A. Alexakis, J. C. Stephens, *Angew. Chem.* **2011**, *123*, 5201–5204; *Angew. Chem. Int. Ed.* **2011**, *50*, 5095–5098.

[10] For selected examples see: a) E. Torres, Y. Chen, I. C. Kim, P. Fuchs, *Angew. Chem.* **2003**, *115*, 3232–3239; *Angew. Chem. Int. Ed.* **2003**, *42*, 3124–3131; b) A. El-Awa, X. M. du Jourdin, P. L. Fuchs, *J. Am. Chem. Soc.* **2007**, *129*, 9086–9093; c) G. R. Ebrahimian, X. M. du Jourdin, P. L. Fuchs, *Org. Lett.* **2012**, *14*, 2630–2633.

[11] O. S. Andell, J. E. Bäckvall, *Tetrahedron Lett.* **1985**, *26*, 4555–4558.

[12] a) J. E. Bäckvall, C. Nájera, M. Yus, *Tetrahedron Lett.* **1988**, *29*, 1445–1448; b) T. G. Back, E. K. Y. Lai, K. Muralidharan, *Tetrahedron Lett.* **1989**, *30*, 6481–6482.

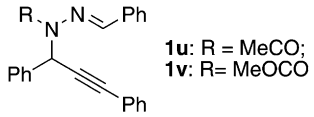
[13] J. E. Bäckvall, A. Ericsson, *J. Org. Chem.* **1994**, *59*, 5850–5851.

[14] M. Z. Cai, G. Q. Chen, W. Y. Hao, D. Wang, *J. Organomet. Chem.* **2007**, *692*, 1125–1130.

[15] T. Cuvigny, C. H. Du Penhoat, M. Julia, *Tetrahedron* **1987**, *43*, 859–872.

[16] Z. Zhan, J. Yu, H. Liu, Y. Cui, R. Yang, W. Yang, J. Li, *J. Org. Chem.* **2006**, *71*, 8298–8301.

[17] The structures of **1v** and **1u** are as follows:



1u: R = MeCO;
1v: R= MeOCO

[18] CCDC 921250 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.

