Taylor & Francis
Taylor & Francis Group

Synthetic Communications

An International Journal for Rapid Communication of Synthetic Organic Chemistry

ISSN: 0039-7911 (Print) 1532-2432 (Online) Journal homepage: http://www.tandfonline.com/loi/lsyc20

TBAI/$K_2S_2O_8$-Facilitated Reaction of Sulfonylhydrazides with Alkynes: Facile Synthesis of (E)-β-Iodovinyl Sulfones

Chuo Tong, Bing Gan, Yiyan Yan & Yuanyuan Xie

To cite this article: Chuo Tong, Bing Gan, Yiyan Yan & Yuanyuan Xie (2017): TBAI/$K_2S_2O_8$-Facilitated Reaction of Sulfonylhydrazides with Alkynes: Facile Synthesis of (E)-β-Iodovinyl Sulfones, Synthetic Communications, DOI: 10.1080/00397911.2017.1337152

To link to this article: http://dx.doi.org/10.1080/00397911.2017.1337152

TBAI/$K_2S_2O_8$-Facilitated Reaction of Sulfonylhydrazides with Alkynes: Facile Synthesis of (*E*)-β-Iodovinyl Sulfones

Chuo Tong[1], Bing Gan[1], Yiyan Yan[1], Yuanyuan Xie[1,2,]

[1]College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou, P.R. China

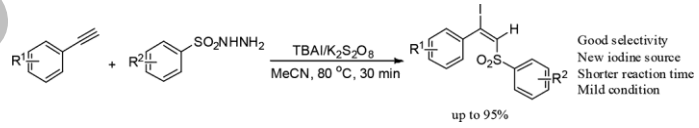
[2]Collaborative Innovation Center of Yangtze River Delta Region Green Pharmaceuticals, Zhejiang University of Technology, Hangzhou, P.R. China

Corresponding author Yuan-Yuan Xie. E-mail: xyycz@zjut.edu.cn

Abstract

An efficient and convenient approach for the construction of various (*E*)-β-iodovinyl sulfones has been developed via $K_2S_2O_8$/TBAI-facilitated reaction of sulfonylhydrazides with alkynes. The products were obtained in good to excellent yields. The salient features of this reaction are the applications of a new iodine source, environmentally benign, safer solid oxidant and shorter reaction time.

Graphical Abstract



KEYWORDS: (*E*)-β-Iodovinyl Sulfones; Sulfonylhydrazides; TBAI; $K_2S_2O_8$

INTRODUCTION

(*E*)-β-Iodovinyl sulfones are very useful synthons for the synthesis of a wide variety of structures, including sulfonylacetylenes,[1] enynes,[2] and vinyl tellurides.[3] Moreover, they have been used as a precursor for the synthesis of biologically and pharmacologically active compounds, e.g., cysteine protease inhibitors,[4] and HIV-1 inhibitors.[5] Despite the prevalence of (*E*)-β-iodovinyl sulfones, few examples for the convenient synthesis of (*E*)-β-iodovinyl sulfones were reported owing to the instability of sulfonyl iodide.[6]

Generally, (*E*)-β-iodovinyl sulfones are synthesized by cerium (IV) ammonium nitrate (CAN) or $PhI(OAc)_2$ mediated reaction of alkynes with arylsulfinates in the presence of MI (M = K or Na).[7,8] Recently, Li and co-workers reported a procedure through the tert-butyl hydroperoxide (TBHP) mediated reaction of aryl acetylenes with sulfonylhydrazides in the presence of I_2.[9] Very recently, Wang and coworkers developed a method via the direct difunctionalization of alkynes with sulfinic acids and molecular iodine in 1,2-dimethoxyethane (DME) for 12-24 h.[10] However, those procedures mentioned above suffer from certain limitations such as the use of transtion-metal catalyst, potentially dangerous oxidants and longer reaction time. The combination of tetrabutylammonium iodide (TBAI) and potassium persulfate ($K_2S_2O_8$) has been widely used as a powerful oxidation system in various coupling reactions. For example, it has been applied to complete the syntheses of oxindoles[11] and 1, 2, 3-thiadiazole.[12] Meanwhle, TBAI has been used as a source of iodine, and iodine can promote functionalization reactions of alkynes with sulfonylhydrazides.[13] Herein, we would like to report the

preparation of (*E*)-β-iodovinyl sulfones via TBAI/$K_2S_2O_8$-facilitated reaction of sulfonylhydrazides with alkynes.

RESULTS AND DISCUSSION

We began investigation with a model reaction using phenylacetylene (**1a**, 0.5 mmol) and 4-methylbenzenesulfonyl hydrazide (**2a**, 0.6 mmol) with $K_2S_2O_8$ (1 mmol) as an oxidant. During early runs, taking advantage of I_2 as the source of iodine in acetonitrile (2 mL) and stirring in the sealed tube at 80 ^oC for 4 h, desired product (*E*)-β-iodovinyl sulfone (**3aa**) was isolated in 36% yield (Table 1, entry 1). When KI was evaluated, no desired product was observed (Table 1, entry 2). However, making use of TBAI in acetonitrile (2 mL) at 80 ^oC for 30 min provided the desired product in 93% yield (Table 1, entry 3). Increasing the amount of $K_2S_2O_8$ and prolonging reaction time, the yields do not fluctuate. Encouraged by this result, we briefly screened the reaction parameters, including the reaction vessel, solvents and oxidants to optimize the reaction performance. The investigation indicated that reaction in the sealed tube was improved, for avoiding the volatilization of phenylacetylene (Table 1, entry 4). Preliminary exploration found that lower yield was obtained when the reaction temperature was decreased (Table 1, entry 5). The following experimental results showed that solvent also had a significant impact on this reaction. Taking into account the solubility of $K_2S_2O_8$, a variety of polar solvents were tested, such as CH_3CN/H_2O (1:1), DMF and tetrahydrofuran (THF), unfortunately, lower yields were obtained (Table 1 entries 6-8). When the amount of TBAI was increased to 1.5 equivalents,

a relatively lower conversion was observed (Table 1 entry 9). In addition, TBHP as an oxidant also delivered corresponding product **3aa** in 88% yield (Table 1, entry 10). Thus the following conditions were found to be the optimal reaction conditions for the desired conversion: alkynes (1 mmol), sulfonylhydrazides (1.2 equiv), TBAI (1.2 equiv), and $K_2S_2O_8$ (2 equiv) were stirred in MeCN (2 mL) in a sealed tube at 80 ^oC for 30 min. The relative configuration of **3aa** was confirmed by comparison with known compound as a *trans*-form.[9], [14]

After the optimal conditions were established, we focused our attention on examining the scope and limitations of the reaction. As shown in Scheme 1, benzenesulfonyl hydrazide with electron-donating or electron-withdrawing groups on the phenyl ring, such as methyl, and Cl, reacted smoothly with phenylacetylene and gave the corresponding products (**3aa, 3ab, 3ac, 3ad**) in 91-95% yields. This indicated that substituents on the benzenesulfonyl hydrazine imposed less effect on the reaction. The results that 2-fluorophenylacetylene (**3ba, 3bb, 3bc**) in 90-93% yields and 4-ethylphenylacetylene (**3ca, 3cb, 3cc**) in 70-74% yields also conform to the above findings. Meanwhile, the steric effect of the aromatic substitution didn't play a significant role on the yield (**3ad**). In addition, phenylacetylene with the electron-withdrawing or electron-donating groups on the phenyl ring, such as F, Cl, and ethyl, also reacted smoothly with 4-methylbenzenesulfonylhydrazide to give the expected products (**3aa, 3ba, 3ca, 3da**) in 93%, 90%, 73%, 90% yields, respectively. Thus, the electron-withdrawing groups on the phenyl rings clearly favored the reaction as

compared with the electron-donating groups resulting in lower yields. However, the product of methyl propiolate was significantly reduced to only 40% yield (**3ea**). Unfortunately, none of the desired product was obtained when methanesulfonyldrazide was used as the substrate. To further confirm the configuration of the products, the olefin hydrogen of the product **3cb** was double-irradiated and found to have no NOE enhancement with any hydrogen of the product (Scheme 2). It appears that product **3** is *trans*-configuration rather than *cis*-configuration.

In order to gain a good insight into the mechanism of reaction, one control experiment was conducted. The radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) was added to the preformed solution of phenylacetylene (**1a**) and 4-methylbenzenesulfonyl hydrazide (**2a**) under the optimal conditions and the desired product **3aa** was not found (Scheme 3).

On the basis of the observations above and previous reports, [8], [9], [15], [16] we proposed a plausible mechanism for this reaction in Scheme 4. Initially, $K_2S_2O_8$ is well known to generate the sulfate radical **A** in combination with TBAI. [17] Then, the resultant radicals abstract hydrogen atoms from 4-methylbenzenssulfonylhydrazide **2a** to generate sulfonyl radical **B** with the release of molecular nitrogen.[18] Next, addition of sulfonyl radical **B** to the phenylacetylene **1a** provides the corresponding vinylsulfone free radical **C**. Finally, reaction of radical **C** with *in situ* generated molecular I_2 or iodine free radical affords

(*E*)-β-iodovinyl sulfone **3aa** (Scheme 4).[7] Therefore, it is speculated that TBAI-facilitated the reaction of sulfonylhydrazides with alkynes via radical **A**.

CONCLUSIONS

In summary, we have developed an efficient and convenient protocol for the facile synthesis of (*E*)-β-iodovinyl sulfones via $K_2S_2O_8$/TBAI-facilitated reaction of sulfonylhydrazides with alkynes. An environmentally benign and safer solid oxidant is used in generating the corresponding products with good to excellent yields with shorter reaction time. Moreover, TBAI is used as a source of iodine in the preparation of (*E*)-β-iodovinyl sulfones. Further synthetic applications of this method are ongoing in our laboratory.

EXPERIMENTAL

Melting points were determined using a Büchi B-540 capillary melting point apparatus. ^{1}H NMR and ^{13}C NMR were recorded with a Varian instrument at 400 and 100 MHz, respectively, and TMS were used as internal standard. Mass spectra were measured with Thermo Finnigan LCQ-Advantage. High resolution mass spectral (HRMS) analyses were done on a Bruker micrOTOF-Q II instrument using ESI technique. All reagents were obtained from commercial sources (purity > 99%) and used without further purification except for sulfonylhydrazides. Silica gel for column chromatography was purchased from

Qingdao Haiyang Chemical Co., Ltd. Reactions were stirred using Teflon-coated magnetic stir bars.

General Procedures For The Preparation Of Sulfonylhydrazides [19]

Hydrazine monohydrate (2.5 mmol) was added dropwise to a solution of an arylsulfonyl chloride (1.0 mmol) in tetrahyrdofuran (4 mL) under nitrogen at 0°C. During the addition the mixture became brown and a white precipitate of hydrazine hydrochloride was deposited. The mixture was stirred at 0 °C for 30 min, added ethyl acetate (120 mL), and washed with saturated brine (3×10 mL). The organic layer was dried over sodium sulfate, filtered, and added slowly to stirred hexane (25 mL) over 5 min. After being stirred for 10 min, the mixture was filtered, and the collected solid was dried in vacuum. The yields for the formation of sulfonylhydrazides range from 62% to 73%.

General Procedure For The Preparation Of (*E*)-B-Iodovinyl Sulfones

Phenylacetylene **1a** (0.051 g, 0.5 mmol), 4-methylbenzenssulfonylhydrazide **2a** (0.112 g, 0.6 mmol), TBAI (0.222 g, 0.6 mmol) and $K_2S_2O_8$ (0.270 g, 1 mmol) were added to CH_3CN (2 mL) in a sealed tube with magnetic stirring at 80℃ (oil bath) for 30 min. After completion of the reaction (monitored by TLC), the sealed tube was allowed to cool to room temperature. Then, the reaction solution was filtered and removed under vacuum, and the residue was purified by column chromatography (SiO_2, petroleum ether/ethyl acetate = 1:10) to give desired product **3aa**.

SUPPLEMENTARY MATERIAL

Supplementary material includes full experimental details, ^{1}H NMR, ^{13}C NMR and Mass spectra of the product (3aa-3ea) for this article.

ACKNOWLEDGEMENTS

We are grateful to the National Natural Science Foundation of China (No. 21576239) for financial support. We thank Dr. Bin Mao for helpful discussions.

REFERENCES

[1] Shameem, M. A.; Esfandiarfard, K.; Oberg, E.; Ott, S.; Orthaber, A. *Chem. Eur. J.* **2016**, 22, 10614-10620.

[2] (a) Gu, X. X.; Xie, M. H.; Zhao, X. Y.; Sun, Y.; Zhang, W.; Xie, F. D.; Wang, S. W. *Chin. J. Chem*., **2008**, 26, 1625-1627; (b) Bates, C. G.; Saejueng, P.; Venkataraman, D. *Org. Lett*. **2004**, 6, 1441-1146.

[3] (a) Huang, X. Liang, C. G.; Xu, Qing. He, Q. W. *J. Org. Chem.* **2001**, 66, 74-81; (b) Huang, X.; Liang, C.G. *Synth. Commun.* **2000**, 30, 1903-1906.

[4] Palmer, J. P.; Rasnick, D.; Klaus, J. L.; Bromme, D. *J. Med. Chem.* **1995**, 38, 3193-3197.

[5] Meadows, D. C.; Sanchez, T.; Neamati, N.; North, T. W.; Gervay-Hugue, J. *Bioorg. Med. Chem.* **2007**, 15, 1127-1130.

[6] (a) Truce, W. E.; Wolf, D. C. *J.Org. Chem*. **1971**, 36, 1727-1732; (b) Truce, W. E.; Heuring, D. L.; Wolf, G. C. *J. Org. Chem.* **1975**, 39, 238-244.

[7] (a) Nair, V.; Augustine, A.; Geroge, T. G.; Nair, L. G. *Tetrahedron Lett.* **2001**, 42, 6763-6765; (b) Nair, V.; Augustine, A.; Suja, T. D. *Synthesis.* **2002**, 15, 2259-2265.

[8] Katrun, P.; Chiampanichay, S.; Korworpan, K.; Pohmakotr, M.; Pohmakotr, M.; Reutrakul, V.; Jaipetch, T. *Eur. J. Org. Chem.* **2010**, 29, 5633-5641.

[9] Li, X. Q.; Xu, X. S.; Shi, X. H. *Tetrahedron. Lett*. **2013**, 54, 3071-3074.

[10] Wei, W.; Wen, J. W.; Yang, D.S.; Jing, H. J.; You, J. M.; Wang, Hua. *RSC Adv.* **2015**, 5, 4416-4419

[11] Ji, P. Y.; Zhang, M. Z.; Xu, J. W., Liu, Y. F.; Guo, C. C. *J. Org. Chem.* **2016**, 81, 5181-5189.

[12] Chen, J. F.; Jiang, Y.; Yu, J. T.; Cheng, J. *J. Org. Chem.* **2016**, 81, 271-275.

[13] (a) Wei, W.; Wen, J. W.; Yang, D. S.; Guo, M. Y.; Wang, Y. Y.; You, J. M.; Wang, H. *Chem. Commun.* **2015**, 51, 768-771; (b) Wen, J. W.; Wei, W.; Xue, S. N.; Yang, D. S.; Lou, Y.; Gao, C. Y.; Wang, H. *J. Org. Chem.* **2015**, 80, 4966-2972.

[14] Wan, J. P.; Hu, D. Q.; Bai, F.C.; Wei, L.; Liu, Y. Y. *RSC Adv.* **2016**, 6, 73132-73135.

[15] Yogesh, S.; Manjunath, L.; Kandikere, R. P. *J. Org. Chem.* **2014**, 79, 3856-3865.

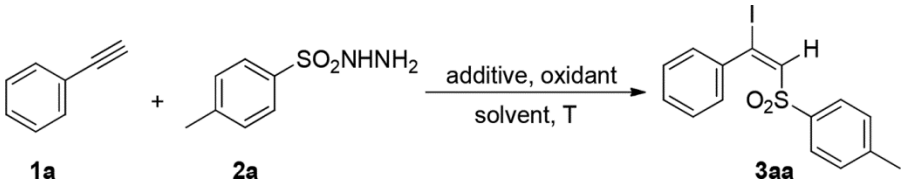
[16] Kiyokawa, K.; Kosaka, T.; Minakata, S. *Org. Lett.* **2013**, 15, 4858-4861.

[17] Ji, P. Y.; Zhong, M. Z.; Xu, J. W.; Gu, C. C. *J. Org. Chem.* **2016**, 81, 5181-5190.

[18] Li, X.; Xu, X.; Hu, P.; Xiao, X.; Zhou, C. *J. Org. Chem.* **2013**, 78, 7343-7348.

[19] Liu, C.; Ding, L.H.; Guo, G.; Liu, W. W. *Org. Biomol. Chem.* **2016**, 14, 2824-2827.

Table 1 Optimization of the reaction conditions[a]



1a **2a** **3aa**

Entry	Additive(equiv.)	Oxidant	Solvent	Temp.(^{o}C)	Yield(%)[b]
1[c]	I_2 (0.5)	$K_2S_2O_8$	MeCN	80	36
2[c]	KI (1.2)	$K_2S_2O_8$	MeCN	80	N.R.
3	TBAI (1.2)	$K_2S_2O_8$	MeCN	80	93
4[d]	TBAI (1.2)	$K_2S_2O_8$	MeCN	80	85
5	TBAI (1.2)	$K_2S_2O_8$	MeCN	60	61
6[e]	TBAI (1.2)	$K_2S_2O_8$	MeCN/H_2O	80	80
7	TBAI (1.2)	$K_2S_2O_8$	THF	80	65
8	TBAI (1.2)	$K_2S_2O_8$	DMF	80	53
9	TBAI (1.5)	$K_2S_2O_8$	MeCN	80	88
10	TBAI (1.2)	TBHP	MeCN	80	88

[a]Reaction conditions: phenylacetylene **1a** (0.5 mmol), 4-methylbenzenesulfonyl hydrazide **2a** (0.6 mmol), oxidants (1 mmol), and solvent (2 mL) were stirred in a sealed tube at 60-80 ^{o}C for 30 min unless noted.

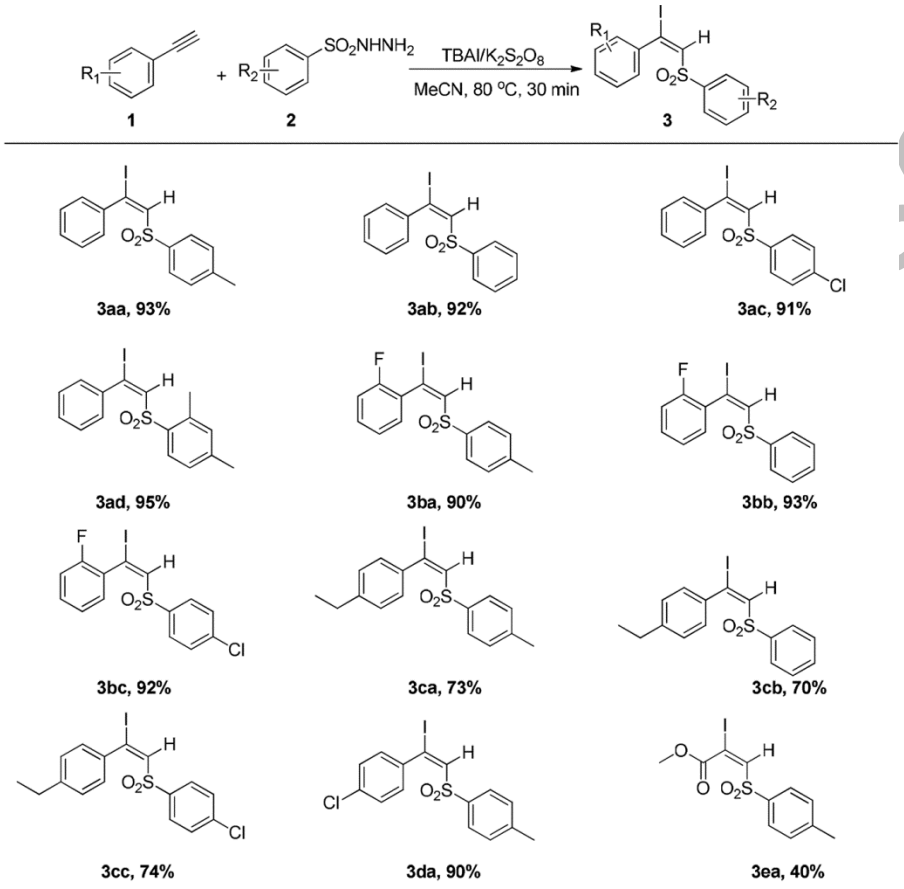
[b]Isolated yields were determined based on **1a**.

[c]Reaction time is 4h.

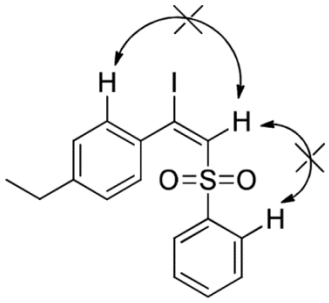
[d]Reaction in the bottle.

[e]MeCN/H_2O = 1/1 (v/v).

Scheme 1. Reaction of various alkynes with sulfonylhydrazid; [a]Reaction conditions: alkynes **1** (0.5 mmol), sulfonylhydrazides **2** (0.6 mmol), $K_2S_2O_8$ (1 mmol), TBAI (0.6 mmol) and MeCN (2 mL) were stirred in a sealed tube at 80 ^oC for 30 min; [b]Isolated yields were determined based on **1**.

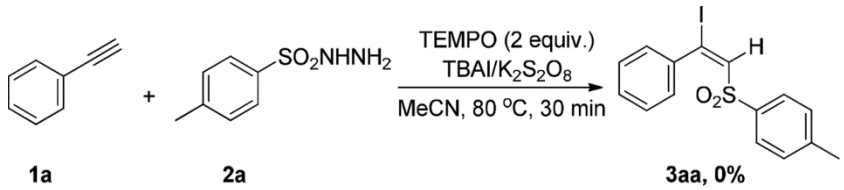


Scheme 2. The *trans*-configuration of **3cb**



3cb

Scheme 3. Preliminary mechanistic studies



1a **2a** **3aa, 0%**

Scheme 4. Plausible mechanism