Metal-Free Synthesis of β-Bromoalkenyl Sulfides via Deoxygenative Bromination/Olefination/Sulfenylation of Ketones with Sulfonyl Hydrazides and Pyridinium Tribromide

Yishu Bao,[a] Lingyu Zhong,[a] Qiaodan Hou,[a] Qingfa Zhou,[a]* and Fulai Yang [a]*

ABSTRACT A novel metal-free method for synthesis of β-bromoalkenyl sulfides via deoxygenative bromination/olefination/sulfenylation process using commercially available ketones, sulfonyl hydrazides and pyridinium tribromide as starting materials has been developed. In this reaction, pyridinium tribromide plays the role of oxidant and substrate, wherein water and molecular nitrogen are generated as environmentally benign by-products. Preliminary investigation revealed that vinyl bromides were critical intermediate. Importmantly, this protocol not only obviates the use of alkynes and traditional sulfenylating agents, but also reveals that ketones can be used as precursors of vinyl bromides.

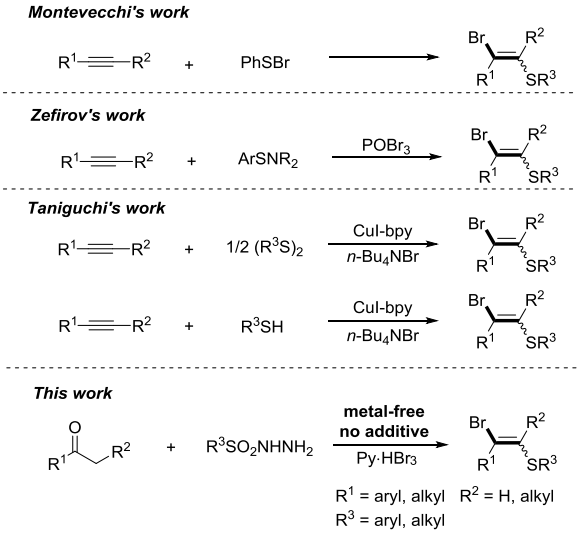
KEYWORDS Ketones, Sulfonyl hydrazides, Deoxygenative, β-Bromoalkenyl sulfides, Pyridinium tribromide

Introduction

Carbon-carbon double bond is ubiquitous structural motif because of its occurrence in a wide range of natural products, drugs, functional materials and biologically relevant molecules.[1] Consequently, developing new methodologies for rapid and efficient construction of functionalized carbon-carbon double bonds represents one of the major domains in chemical synthesis. In this context, developing effective methods to access β-haloalkenyl sulfides represents a striking research topic because they can be easily decorated into various alkenes and alkynyl sulfides due to the presence of carbon-halogen bond and carbon-sulfur bond.[2] Increasing attention has been devoted to the synthesis of β-haloalkenyl sulfides since the original work of Modena's group on the addition of sulfenyl chlorides to acetylenes.[3] Later, many similar methods were reported to synthsize β-haloalkenyl sulfides via the halothiolation of alkynes using different sulfenylating agents, such as sulfenyl halides,[4] sulfenamides,[5] disulfides,[6] thiols,[6a] sodium arenesulfinates,[7] and thiosulfate.[8] However, methods for the synthesis of β-bromoalkenyl sulfides are scarce (Scheme 1).[4c, 5, 6] Nevertheless, these strategies have some well-known disadvantages: (1) many of the sulfenylating agents are unstable to air and moisture, and prepare difficultly, or possess unpleasant smelling; (2) many of these reactions involve the use of metal catalysts[4a, 4b, 5] or excess additives,[7] which are not consistent with the concept of green chemistry. To address such issues, it is highly desirable to develop new strategies for synthesis of β-bromoalkenyl sulfides using readily accessible substrates through environmentally-friendly reaction conditions.

Sulfonyl hydrazides which are stable, commercially available and low-toxic could serve as ideal sulfenylating agents,[9] and they have been widely employed to react with ketones to deliver sulfonylhydrazones which have been one of the most important synthons for the formation of various olefins since the seminal findings of Bamford–Stevens[10] and Shapiro.[11] Inspired by this work, very recently, we developed an unprecedented protocol for the synthesis of β-iodoalkenyl sulfides using readily available ketones, sulfonyl hydrazides and iodine as starting materials.[12] This protocol obviates the need for alkynes and traditional sulfenylating agents. However, in the view of green chemistry, it also encounters disadvantages, such as the use of excess KI as additive and the requirement of 50 mol % iodine which is easy to sublimate and is environmentally-unfriendly. According to our proposed mechanism, sulfonyl hydrazides reacted with ketones to afford sulfonylhydrazones which were oxidized by iodine to afford vinyl iodides, and then vinyl iodides reacted with the in situ generated sulfenyl iodides afford β-iodoalkenyl sulfides. Encouraged by this work, we questioned whether bromides could be used to oxidize sulfonylhydrazones to give β-bromoalkenyl sulfides without additive and metal catalyst.

Scheme 1 Methods for β-Bromoalkenyl Sulfides Synthesis.



Results and Discussion

However, the much lower reactivity of bromides might render the development of such a tandem reaction a great challenge. With commercially available acetophenone (**1a**) and *p*-toluenesulfonyl hydrazide (**2a**) as model substrates, the reaction was initially investigated (Table 1). First, the reaction was performed in *n*-hexane in the presence of 0.5 equiv Br_2, 4.0 equiv KBr at 120 °C, unfortunately, β-bromoalkenyl sulfide **3a** was obtained in 34% yield (entry 1), while a similar result was got without KBr (entry 2). Consequently, a range of other bromides were evaluated without additive KBr (entries 3-8), among which pyridinium tribromide was proved to be the optimal choice (entry 8). In addition, the effects of various solvent was also examined, but no other solvent promoted yield (entries 9-11). Further

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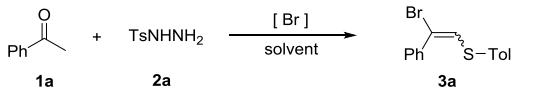
This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/cjoc.201800375

examination showed that extending the reaction time and changing the amount of bromide gave no improvements in efficiency (entries 12-14). To our delight, a satisfactory result was obtained when the ratio of **1a**, **2a** and Py·HBr_3 was adjusted to 2:4:1, which delivered **3a** in 69 % yield (entry 15). However, decreasing the temperature to 100 °C resulted in only a trace amount of the expected product (entry 16). Thus, the optimal reaction conditions were 1 equiv of **1a**, 2 equiv of **2a** and 0.5 equiv of Py·HBr_3 in *n*-hexane at 120 °C.

Table 1 Screening reaction conditions for synthesis of β-bromoalkenyl sulfides [a]



1a 2a 3a

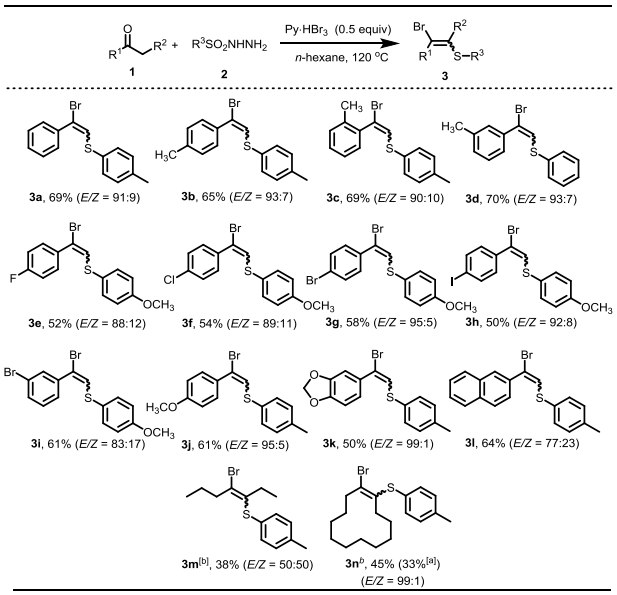
Entry	[Br]	Solvent	Yield [%][b]	*E/Z*
1[c]	Br_2[d] (0.5)	*n*-hexane	34	-
2	Br_2[d] (0.5)	*n*-hexane	32	-
3	NBS (1.0)	*n*-hexane	25	-
4	$TBABR_3$ (0.5)	*n*-hexane	31	-
5	NBP(1.0)	*n*-hexane	15	-
6	DBDHM (0.5)	*n*-hexane	26	-
7	PBr_3 (0.5)	*n*-hexane	44	-
8	Py·HBr_3 (0.5)	*n*-hexane	54	91:9
9	Py·HBr_3 (0.5)	dioxane	38	-
10	Py·HBr_3 (0.5)	toluene	33	-
11	Py·HBr_3 (0.5)	EtOH	27	-
12[e]	Py·HBr_3 (0.5)	*n*-hexane	45	-
13	Py·HBr_3 (0.4)	*n*-hexane	53	88:12
14	Py·HBr_3 (0.75)	*n*-hexane	46	-
15[f]	**Py·HBr_3 (0.5)**	***n*-hexane**	**69**	**89:11**
16[g]	Py·HBr_3 (0.5)	*n*-hexane	trace	-

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), in solvent (0.5 mL), at 120 °C (oil bath), for 3 h. [b] Yield of isolated product. [c] KBr (4 equiv) [d] 1.0 mol / L in methylene chloride. [e] 5h. [f] **2a** (0.4 mmol). [g] At 90 °C (oil bath). NBS = *N*-bromosuccinimide, $TBABr_3$ = tetrabutylammonium tribromide, NBP = *N*-bromophthalimide, Py·HBr_3 = pyridinium tribromide, DBDMH = 1,3-dibromo-5,5-dimethylhydantoin.

With the optimized reaction conditions in hand, the substrate scope of ketones was explored. As shown in table 2, a range of aryl methyl ketones reacted smoothly to afford the corresponding products in moderate to good yields with high *E/Z* selectivity (**3a-3k**). Halides including fluoro, chloro, bromo and iodo groups were successfully introduced into β-bromoalkenyl sulfides (**3e-3i**). 2-Acetonaphthone was also applied in the reaction with satisfactory yield, however, the regioselectivity was adversely affected (**3l**). To further explore scope, alkyl-substituted ketones were also evaluated. To our delight, aliphatic ketones could also afford corresponding *β*-bromoalkenyl (**3m, 3n**) in moderate yields. It is worth noting that the reactions of **1m** and **1n** required a shorter reaction time to increase the efficiency.

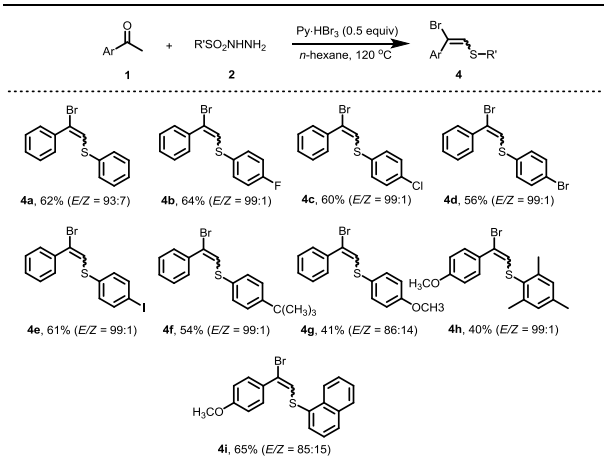
Subsequently, the reaction was further evaluated using a series of sulfonyl hydrazides (table 3). Various arylsulfonyl hydrazides with electron-donating and electron-withdrawing groups reacted with ketones to give the corresponding β-bromoalkenyl sulfides (**4a-4g**, **4i**) in moderate to good yields. Moreover, 2,4,6-trimethylbenzenesulfonoh-ydrazide (**2h**) could transformed to corresponding product **4h** with lower yields because of steric hindrance.

Table 2 caption Scope of Ketones **1** for Synthesis of β-Bromoalkenyl Sulfides 3. [a]



[a] Reaction conditions: **1** (0.2 mmol), **2** (0.4 mmol), Py·HBr_3 (0.1 mmol), in *n*-hexane (1.0 mL), at 120 °C (oil bath), for 3 h. [b] 1h.

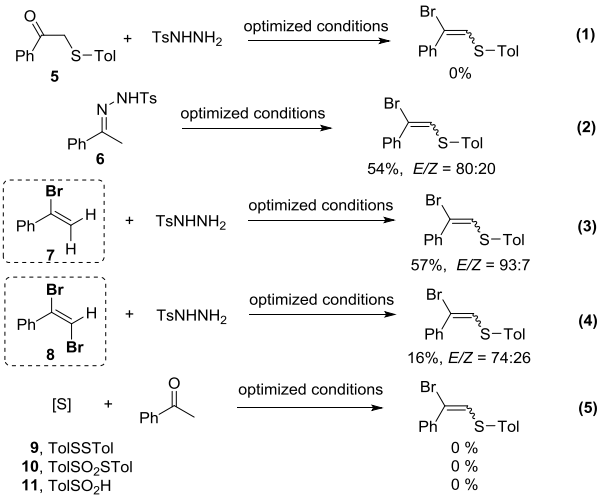
Table 3 Scope of Sulfonyl Hydrazides **2** for Synthesis of β- Bromoalkenyl Sulfides 4. [a]



[a] Reaction conditions: 1 (0.2 mmol), 2 (0.4 mmol), Py·HBr_3 (0.1 mmol), in *n*-hexane (1.0 mL), at 120 °C (oil bath), for 3 h.

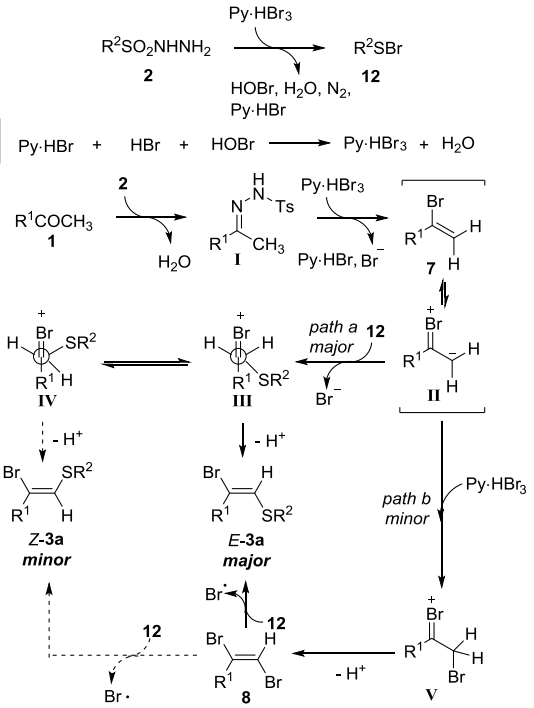
To obtain insight into a possible reaction mechanism, a series of control experiments were performed (Scheme 2). **5** and **6**, as the most possible two intermediates, were subjected to the optimized conditions, however, no desire product **3a** was found when **5** reacted with *p*-toluenesulfonyl hydrazide (**2a**), while **6** could afford desire product **3a** in 54% yield (eqns (**1**) and (**2**)). Vinyl bromide **7** and vinyl dibromide **8** which were detected to be two critical intermediates could react with *p*-toluenesulfonyl hydrazide (**2a**) to give final product **3a** in 57% and 16% yields, respectively (eqns (**3**) and (**4**)). Sulfonyl hydrazide **2a** easily decomposed upon heating to generate disulfide **9**, sulfonothioate **10** and sulfinic acid **11**.[6] Each of them was treated with **1a,** however, no desired product **3a** was obtained, which substantially elucidated the $NHNH_2$ group in the sulfonyl hydrazide was required (eqn (**5**)).

Scheme 2 Control Experiments.



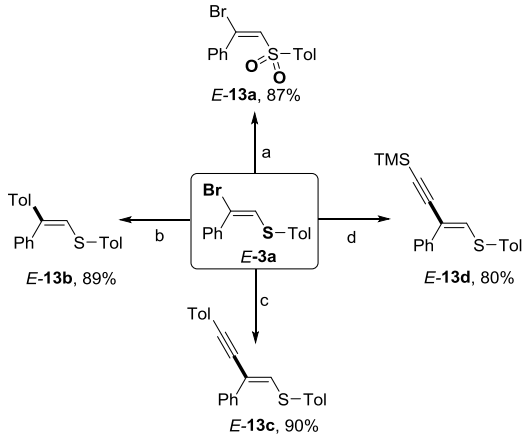
Based on the above and our previous studies,[9, 12, 13] a proposed pathway is delineated (Scheme 3). First, acetophenone (**1**) easily reacts with sulfonyl hydrazide (**2**) to give sulfonylhydrazone **I**, which is oxidized by pyridinium tribromide to affords intermediate **7**. Simultaneously, Sulfonyl hydrazide (**2**) reacts with pyridinium tribromide to yield sulfenyl bromide **12**. In the reaction process, Py.HBr_3 is converted into HBr, Py.HBr and HOBr, the three of which react to give water and regenerate Py.HBr_3 to continue the catalytic cycle, so 0.5 equiv. of Py.HBr_3 is enough in the transformation. Subsequently, intermediate **II**, isomerization of **7**, further react with **12** to give the major target product *E*-**3a** and minor product *Z*-**3a**, while a part of **II** via *path b* continue to react with bromide afford **8**, and then react with **12** to furnish *E*-**3a** and *Z*-**3a**.[5]

Scheme 3 Plausible Reaction Mechanism.



To showcase the utility of this methodology, further transformation were conducted as shown in Scheme 4. Upon treatment with *m*-CPBA, *E*-**3a** successfully converted into the corresponding oxidized products *E*-**13a** in a yield of 87%.[14] The presence of carbon–bromine bond can be subsequently used in a series of coupling reaction. *E*-**3a** via a Suzuki–Miyaura coupling furnished *E*-**13b** in an excellent yield (89%),[15] while *E*-**13c** was generated via Sonogashira–Hagihara coupling in yield of 90%.[16] Furthermore, introducing trimethylsilylacetylene to *E*-**3a** could also take place catalyzed by palladium, providing conjugated enyne *E*-**13d** in 80% yield.[17]

Scheme 4 Transformations of *E*-3a.



(a) *m*CPBA (2 equiv), CH_2Cl_2, 60 °C, 4 h. (b) *p*-$MeC_6H_4B(OH)_2$ (2 equiv), $Pd(OAc)_2$ (5 mol %), XPhos (10 mol %), K_2CO_3 (2 equiv), toluene, 110 °C, 12 h. (c) *p*-MeC_6H_4CCH (1.2 equiv), $Pd(PPh_3)_4$ (5 mol %), CuI (5 mol %), Et_3N (2 equiv), CH_3CN, 70 °C, 3 h. (d) TMSA (1.5 equiv), $PdCl_2(PPh_3)_2$ (5 mol %), CuI (10 mol %), Et_3N (1.5 equiv), PPh_3 (10 mol %), toluene, 70 °C, 2 h. Tol = *p*-tolyl. TMSA = trimethylsilylacetylene. XPhos = 2-dicyclohexylphosphino-2', 4', 6'-triisopropylbiphenyl.

Conclusions

In summary, we have developed an unprecedented metal-free reaction for synthesis of β-bromoalkenyl sulfides via deoxygenative bromination/olefin-tion/sulfenylation process using commercially available ketones, sulfonyl hydrazides and pyridinium tribromide as starting materials. In the presence of 50 mol % pyridinium tribromide, a range of arylsulfonyl hydrazides smoothly reacted with various ketones to give structurally diverse β-bromoalkenyl sulfides with high regio- and stereoselectivity. This novel methodology not only obviates the use of alkynes and traditional sulfenylating agents, but also reveals that ketones can be used as precursors of vinyl bromides. Importantly, the versatile synthetic utilize of β-bromoalkenyl sulfides revealed its great potential value in organic and medicinal chemistry.

Experimental

General Information. Reactions were monitored through thin layer chromatography (TLC) on 0.30 mm SiliCycle silica gel plates and visualized under UV light. All known compounds were identified by ^{1}H NMR, ^{13}C NMR and compared with previously reported data. NMR spectra of the new products were recorded using Bruker AC-300 or Bruker AC-500 instruments, calibrated to $CDCl_3$ as the internal reference (7.26 and 77.0 ppm for ^{1}H and ^{13}C NMR spectra, respectively). Chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz, respectively. The following abbreviations indicated the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Mass spectra were taken on a Finnigan TSQ Quantum-MS instrument in the electrospray ionization (EI), electron spray ionization (ESI) or atmospheric pressure chemical iosziaa-lion (APCI) mode.

Sulfonyl hydrazides[18] (except **2a**) and compounds **5**[18] were prepared according to literature procedures. The rest of chemical reagents were obtained from commercial suppliers.

General Procedures for the Synthesis of *β*-Bromoalkenyl Sulfides (3 or 4). To a solution of sulfonyl hydrazide **2** (0.40 mmol) in *n*-hexane (0.5 mL) was added acetophenone **1** (0.20 mmol) and pyridinium tribromide (31.98 mg, 0.10 mmol). The resulting mixture was stirred at 120 °C (oil bath) under air for 3 h, cooled to room temperature, and purified by silica gel chromatography, eluting with petroleum ether to give mainly desired product **3** or **4**.

The synthesis of *E*-13a.[14] To a solution of *E*-**3a** (61.05 mg, 0.20 mmol) in CH_2Cl_2 (1.0 mL) was added *m*CPBA (86.29 mg, 0.50 mmol). The resulting mixture was stirred at 60 °C for 4 h, cooled to room temperature, and purified by silica gel chromatography, eluting with petroleum ether/ethyl acetate (10:1), to give *E*-**13a** (58.7 mg) in 87% yield.

The synthesis of *E*-13b.[15] Under argon atmosphere, to a solution of *E*-**3a** (61.05 mg, 0.20 mmol) in anhydrous toluene (2.0 mL) was added 4-methylphenylboronic acid (54.38 mg, 0.40 mmol), K_2CO_3 (55.28 mg, 0.40 mmol), XPhos (8.49 mg, 0.02 mmol) and $Pd(OAc)_2$ (2.24 mg, 0.01 mmol). The reaction mixture was heated at 110 °C for 12 h, cooled to room temperature. The product was extracted with ethyl acetate (10 mL) three times. The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. Concentration in vacuo followed concentration in vacuo followed by silica gel chromatography, eluting with petroleum ether, to give *E*-**13b** (56.3 mg) in 89% yield.

The synthesis of *E*-13c.[16] Under argon atmosphere, to a solution of *E*-**3a** (70.45 mg, 0.20 mmol) in anhydrous CH_3CN (1.0 mL) was added 4-methylphenylacetylene (27.88 mg, 0.24 mmol), Et_3N (40.48 mg, 0.40 mmol), CuI (1.90 mg, 0.01 mmol) and $Pd(PPh_3)_4$ (11.56 mg, 0.01 mmol). The reaction mixture was heated at 70 °C for 3 h, cooled to room temperature. The product was extracted with ethyl acetate (10 mL) three times. The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. Concentration in vacuo followed concentration in vacuo followed by silica gel chromatography, eluting with petroleum ether, to give *E*-**13c** (61.3 mg) in 90% yield.

The synthesis of *E*-13d.[17] To a solution of *E*-**3a** (70.45 mg, 0.20 mmol) in anhydrous toluene (1.0 mL) was added trimethylsilylacetylene (29.47 mg, 0.30 mmol), Et_3N (30.36 mg, 0.30 mmol), CuI (3.80 mg, 0.02 mmol) and $PdCl_2(PPh_3)_2$ (7.02 mg, 0.01 mmol). The reaction mixture was heated at 70 °C for 2 h, cooled to room temperature. The product was extracted with ethyl acetate (10 mL) three times. The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. Concentration in vacuo followed concentration in vacuo followed by silica gel chromatography, eluting with petroleum ether to give *E*-**13d** (51.6 mg) in 80% yield.

(*E*)-(2-bromo-2-phenylvinyl)(*p*-tolyl)sulfane (*E*-**3a**), light yellow oil (69%, 42.1 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.8 Hz, 2H), 7.42–7.27 (m, 5H), 7.14 (d, *J* = 7.8 Hz, 2H), 6.86 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7, 131.4, 130.8, 130.34, 130.0, 129.0, 129.0, 128.2, 127.2, 116.1, 21.2; HRMS (EI) m/z calcd. for $C_{15}H_{13}BrS$ (M) 303.9921, found 303.9926.

(*E*)-(2-bromo-2-(*p*-tolyl)vinyl)(*p*-tolyl)sulfane (*E*-**3b**), light yellow oil (65%, 41.5 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 6.81 (s, 1H), 2.37 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 136.6, 133.8, 130.6, 129.3, 129.0, 127.9, 127.8, 125.4, 115.7, 20.3, 20.0; HRMS (EI) m/z calcd. for $C_{16}H_{15}BrS$ (M) 318.0078, found 318.0075.

(*E*)-(2-bromo-2-(*o*-tolyl)vinyl)(*p*-tolyl)sulfane (*E*-**3c**), light yellow oil (69%, 44.1 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26–7.23 (m, 6H), 7.12 (d, *J* = 7.2 Hz, 2H), 6.86 (s, 1H), 2.39 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 137.4, 136.2, 131.0, 130.5, 130.0, 129.4, 129.1, 128.3, 126.2, 115.8, 21.1, 19.4; HRMS (APCI) m/z calcd. for $C_{16}H_{16}BrS^+$ $(M+H)^+$ 319.0151, found 319.0150.

(*E*)-(2-bromo-2-(*m*-tolyl)vinyl)(*p*-tolyl)sulfane (*E*-**3d**), light yellow oil (70%, 44.7 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (d, *J* = 5.7 Hz, 2H), 7.28 (t, *J* = 7.8 Hz, 3H), 7.14 (d, *J* = 7.5 Hz, 3H), 6.84 (s, 1H), 2.39 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 137.7, 137.5, 131.5, 130.3, 130.0, 129.9, 129.6, 128.1, 127.0, 126.1, 116.3, 21.5, 21.2; HRMS (APCI) m/z calcd. for $C_{16}H_{16}BrS^+$ $(M+H)^+$ 319.0151, found 319.0158.

(*E*)-(2-bromo-2-(4-fluorophenyl)vinyl)(4-methoxyphenyl) sulfane (*E*-**3e**), light yellow oil (52%, 35.3 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58–7.53 (m, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.08 (t, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.1 Hz, 2H), 6.79 (s, 1H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.5 (d, *J* = 248.18 Hz), 159.8, 134.8, 133.7, 133.0, 131.0 (d, *J* = 8.4 Hz), 128.6, 125.0, 115.2 (d, *J* = 21.8 Hz), 113.6, 55.4; HRMS (APCI) m/z calcd. for $C_{15}H_{13}BrFOS^+$ $(M+H)^+$ 338.9849, found 338.9848.

(*E*)-(2-bromo-2-(4-chlorophenyl)vinyl)(4-methoxyphenyl) sulfane (*E*-**3f**), light yellow oil (54%, 38.4 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 9.0 Hz, 2H), 7.35–7.31 (m, 4H), 6.88 (d, *J* = 2.4 Hz, 2H), 6.81 (s, 1H), 3.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.9, 136.0, 134.7, 133.1, 130.4, 129.3, 128.4, 125.0, 115.0, 113.3, 55.4; HRMS (APCI) m/z calcd. for $C_{15}H_{13}BrClOS^+$ $(M+H)^+$ 354.9554, found 354.9556.

(*E*)-(2-bromo-2-(4-bromophenyl)vinyl)(4-methoxyphenyl) sulfane (*E*-**3g**), light yellow oil (58%, 46.4 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56–7.46 (m, 2H), 7.44 (d, *J* = 7.8 Hz, 2H), 7.35 (d, *J* = 7.8 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.82 (s, 1H), 3.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.9, 136.5, 133.1, 131.4, 130.6, 129.4, 124.9, 122.9, 115.0, 113.3, 55.4; HRMS (APCI) m/z calcd. for $C_{15}H_{13}Br_2OS^+$ $(M+H)^+$ 398.9048, found 398.9050.

(*E*)-(2-bromo-2-(4-iodophenyl)vinyl)(4-methoxyphenyl) sulfane (*E*-**3h**), light yellow oil (50%, 44.7 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.36–7.30 (m, 4H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.81 (s, 1H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 137.3, 137.0, 133.1, 130.7, 129.5, 114.9, 114.9, 113.3, 94.8, 55.5; HRMS (APCI) m/z calcd. for $C_{15}H_{13}BrIOS^+$ $(M+H)^+$ 446.8910, found 446.8913.

(*E*)-(2-bromo-2-(3-bromophenyl)vinyl)(*p*-tolyl)sulfane (*E*-**3i**), light yellow oil (61%, 48.8 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.52–7.44 (m, 2H), 7.36 (d, *J* = 7.8 Hz, 2H), 7.20–7.23 (m, 1H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.84 (s, 1H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 139.4, 133.2, 132.0, 131.9, 130.2, 129.7, 127.6, 124.8, 122.2, 114.9, 112.3, 55.5; HRMS (APCI) m/z calcd. for $C_{15}H_{13}Br_2OS^+$ $(M+H)^+$ 398.9048, found 398.9041.

(*E*)-(2-bromo-2-(4-methoxyphenyl)vinyl)(*p*-tolyl)sulfane (*E*-**3j**), light yellow oil (61%, 40.9 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.78 (s, 1H), 3.83 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.9, 137.5, 131.6, 130.6, 130.2, 130.0, 125.7, 116.7, 113.8, 113.5, 55.3, 21.0; HRMS (EI) m/z calcd. for $C_{16}H_{15}BrOS$ (M) 334.0027, found 334.0037.

(*E*)-5-(1-bromo-2-(*p*-tolylthio)vinyl)benzo[*d*][1,3]dioxole (*E*-**3k**), light yellow oil (50%, 34.9 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.26 (m, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 7.07–7.04 (m, 2H), 6.86–6.77 (m, 1H), 6.77 (s, 1H), 6.00 (s, 2H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.1, 147.4, 137.7, 131.4, 131.4, 130.3, 130.0, 126.6, 123.4, 115.7, 109.5, 107.8, 101.5, 21.1; HRMS (APCI) m/z calcd. for $C_{16}H_{14}BrO_2S^+$ $(M+H)^+$ 348.9892, found 348.9894.

(*E*)-(2-bromo-2-(naphthalen-2-yl)vinyl)(*p*-tolyl)sulfane (*E*-**3l**), light yellow oil (64%, 45.5 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.89–7.82 (m, 3H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.53–7.49 (m, 2H), 7.31 (d, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 6.94 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.7, 134.9, 133.3, 132.6, 131.4, 130.4, 130.0, 128.7, 128.4, 128.0, 127.7, 127.6, 127.0, 126.6, 126.3, 116.2, 21.1; HRMS (EI) m/z calcd. for $C_{19}H_{15}BrS$ (M) 354.0078, found 354.0071.

(4-bromohept-3-en-3-yl)(*p*-tolyl)sulfane (**3m**), colorless oil (38%, 22.7 mg); ^{1}H NMR (300 MHz, $CDCl_3$) (*E*-**3m**) δ 7.17–7.13 (m, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 2.96–2.88 (m, 2H), 2.42–2.32 (m, 2H), 2.32

(s, 3H), 1.68–1.58 (m, 1H), 1.52 (s, 1H), 0.93 (t, *J* = 7.5 Hz, 3H), 0.86 (t, *J* = 7.5 Hz, 3H); ^{1}H NMR (300 MHz, $CDCl_3$) (***Z*-3m**) δ 7.17–7.13 (m, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 2.96–2.88 (m, 2H), 2.42–2.32 (m, 2H), 2.32 (s, 3H), 1.68–1.58 (m, 1H), 1.52 (s, 1H), 1.14 (t, *J* = 7.5 Hz, 3H), 1.03 (t, *J* = 7.5 Hz, 3H); HRMS (APCI) m/z calcd. for $C_{14}H_{20}BrS^+$ $(M+H)^+$ 299.0464, found 299.0468.

(*Z*)-(2-bromocyclododec-1-en-1-yl)(*p*-tolyl)sulfane (*Z*-**3n**), colorless oil (45%, 33.1 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.1 Hz, 2H), 7.08 (d, *J* = 8.1 Hz, 2H), 3.64–3.54 (m, 1H), 2.99–2.89 (m, 1H), 2.47–2.37 (m, 1H), 2.31 (s, 3H), 2.12–2.02 (m, 1H), 1.78–1.56 (m, 5H), 1.36–1.26 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.4, 133.9, 133.4, 131.7, 129.8, 129.6, 38.9, 35.7, 26.3, 26.2, 25.8, 25.2, 25.1, 25.1, 25.0, 25.0, 21.0; HRMS (EI) m/z calcd. for $C_{19}H_{27}BrS$ (M) 366.1017, found 366.1015.

(*E*)-(2-bromo-2-phenylvinyl)(phenyl)sulfane (*E*-**4a**), light yellow oil (62%, 36.1 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.2 Hz, 2H), 7.42–7.28 (m, 8H), 6.90 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.6, 135.1, 129.8, 129.2, 129.0, 128.2, 127.4, 126.2, 117.4; HRMS (EI) m/z calcd. for $C_{14}H_{11}BrS$ (M) 289.9765, found 289.9757.

(*E*)-(2-bromo-2-phenylvinyl)(4-fluorophenyl)sulfane (*E*-**4b**), light yellow oil (64%, 39.6 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.5 Hz, 2H), 7.41–7.32 (m, 5H), 7.03 (t, *J* = 7.8 Hz, 2H), 6.81 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4 (d, *J* = 246.75 Hz,), 141.1, 132.4 (d, *J* = 8.18 Hz), 130.0 (d, *J* = 3.53 Hz,), 129.1, 129.0, 128.2, 126.6, 117.0,116.4 (d, *J* = 21.98 Hz); HRMS (APCI) m/z calcd. for $C_{14}H_{11}BrFS^+$ $(M+H)^+$ 308.9743, found 308.9738.

(*E*)-(2-bromo-2-phenylvinyl)(4-chlorophenyl)sulfane (*E*-**4c**), light yellow oil (60%, 39.1 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.8 Hz, 2H), 7.42–7.29 (m, 7H), 6.83 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.5, 137.4, 133.6, 131.0, 129.4, 129.2, 129.0, 128.2, 125.3, 118.5; HRMS (APCI) m/z calcd. for $C_{14}H_{11}BrClS^+$ $(M+H)^+$ 324.9448, found 324.9441.

(*E*)-(2-bromo-2-phenylvinyl)(4-bromophenyl)sulfane (*E*-**4d**), light yellow oil (56%, 41.5 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.8 Hz, 2H), 7.49–7.37 (m, 5H), 7.26 (d, *J* = 8.4 Hz, 2H), 6.86 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3, 134.2, 132.3, 131.1, 129.3, 129.0, 128.3, 125.0, 121.4, 118.7; HRMS (APCI) m/z calcd. for $C_{14}H_{11}Br_2S^+$ $(M+H)^+$ 368.8943, found 368.8945.

(*E*)-(2-bromo-2-phenylvinyl)(4-iodophenyl)sulfane (*E*-**4e**), light yellow oil (61%, 50.9 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.8 Hz, 2H), 7.52 (d, *J* = 7.5 Hz, 2H), 7.42–7.33 (m, 3H), 7.09 (d, *J* = 7.5 Hz, 2H), 6.83 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.0, 138.2, 131.6, 131.1, 129.2, 129.0, 128.2, 124.8, 119.0, 92.4; HRMS (APCI) m/z calcd. for $C_{14}H_{11}BrIS^+$ $(M+H)^+$ 416.8804, found 416.8809.

(*E*)-(2-bromo-2-phenylvinyl)(4-(*tert*-butyl)phenyl)sulfane (*E*-**4f**), light yellow oil (54%, 37.5 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.8 Hz, 2H), 7.39–7.31 (m, 7H), 6.88 (s, 1H), 1.31 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.9, 137.6, 131.4, 130.1, 129.0, 128.9, 128.1, 127.1, 126.3, 116.2, 34.6, 31.2; HRMS (APCI) m/z calcd. for $C_{18}H_{20}BrS^+$ $(M+H)^+$ 347.0464, found 347.0465.

(*E*)-(2-bromo-2-phenylvinyl)(4-methoxyphenyl)sulfane (*E*-**4g**), light yellow oil (41%, 26.3 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.5 Hz, 2H), 7.42–7.33 (m, 5H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.81 (s, 1H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 137.6, 134.8, 133.0, 129.0, 128.9, 128.4, 128.2, 125.4, 114.9, 55.4; HRMS (APCI) m/z calcd. for $C_{15}H_{14}BrOS^+$ $(M+H)^+$ 320.9943, found 320.9946.

(*E*)-(2-bromo-2-(4-methoxyphenyl)vinyl)(mesityl)sulfane (*E*-**4h**), light yellow oil (40%, 29.1 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 2H), 6.92–6.91 (m, 4H), 6.32 (s, 1H), 3.85 (s, 3H), 2.42 (s, 6H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3, 142.3, 139.0, 130.4, 130.4, 129.2, 128.1, 127.4, 114.3, 113.5, 55.3, 21.9, 21.0; HRMS (EI) m/z calcd. for $C_{18}H_{19}BrOS$ (M) 362.0340, found 362.0321.

(*E*)-(2-bromo-2-(4-methoxyphenyl)vinyl)(naphthalen-1-yl) sulfane (*E*-**4i**), light yellow oil (65%, 48.3 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82–7.75 (m, 4H), 7.56–7.40 (m, 5H), 6.95–6.88 (m, 3H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0, 133.7, 132.5, 132.3, 130.6, 129.9, 128.9, 127.9, 127.7, 127.3, 127.1, 126.8, 126.2, 124.4, 118.5, 113.5, 55.3; HRMS (EI) m/z calcd. for $C_{19}H_{15}BrOS$ (M) 370.0027, found 370.0019.

1-phenyl-2-(*p*-tolylthio)ethanone (**5**),[19] yellow solid, m.p. 38-39 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.5 Hz, 2H), 7.61–7.52 (m, 1H), 7.50–7.40 (m, 2H), 7.32–7.23 (m, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 4.21 (s, 2H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.2, 132.3, 130.5, 129.0, 128.8, 127.7, 127.7, 127.6, 123.3, 40.8, 20.1.

(*E*)-(1,2-dibromovinyl)benzene (**8**),[20] colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58–7.53 (m, 2H), 7.42 (m, 3H), 6.85 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.1, 129.4, 129.2, 128.2, 121.4, 103.0.

(*E*)-1-((2-bromo-2-phenylvinyl)sulfonyl)-4-methylbenzene (*E*-**13a**),[21] white solid, m.p. 97-99 °C (87%, 58.7 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.1 Hz, 2H), 7.39–7.29 (m, 5H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.13 (s, 1H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6, 138.2, 137.7, 136.2, 134.4, 130.3, 129.6, 128.6, 127.9, 127.8, 21.5.

(*E*)-(2-phenyl-2-(*p*-tolyl)vinyl)(*p*-tolyl)sulfane (*E*-**13b**), colorless oil (89%, 56.3 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–7.37 (m, 2H), 7.36–7.32 (m, 5H), 7.13 (d, *J* = 7.8 Hz, 4H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.77 (s, 1H), 2.33 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5, 139.4, 138.8, 137.0, 136.9, 133.0, 130.0, 129.9, 129.8, 129.0, 128.3, 127.7, 127.1, 124.0, 21.1, 21.1; HRMS (APCI) m/z calcd. for $C_{22}H_{21}S^+$ $(M+H)^+$ 317.1358, found 317.1356.

(*E*)-(2-phenyl-4-(*p*-tolyl)but-1-en-3-yn-1-yl)(*p*-tolyl)sulfane (*E*-**13c**), colorless oil (90%, 61.3 mg); ^{1}H NMR (300 MHz, $CDCl_3$) 7.71 (d, *J* = 7.8 Hz, 2H), 7.39 (m, 7H), 7.14 (m, 4H), 7.01 (s, 1H), 2.35 (d, *J* = 3.3 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1, 137.9, 136.8, 135.0, 131.3, 130.8, 130.0, 129.0, 128.4, 128.3, 128.2, 127.8, 120.3, 120.2, 89.7, 88.8, 21.4, 21.1; HRMS (APCI) m/z calcd. for $C_{24}H_{21}S^+$ $(M+H)^+$ 341.1358, found 341.1364.

(*E*)-trimethyl(3-phenyl-4-(*p*-tolylthio)but-3-en-1-yn-1-yl) silane (*E*-**13d**), colorless oil (80%, 51.6 mg); ^{1}H NMR (300 Hz, $CDCl_3$) δ 7.71–7.66 (m, 2H), 7.48–7.36 (m, 5H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.03 (s, 1H), 2.39 (s, 3H), 0.24 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 136.9, 131.0, 130.0, 128.4, 128.3, 128.1, 127.8, 125.3, 119.7, 105.7, 93.0, 21.1, 0.0; HRMS (APCI) m/z calcd. for $C_{20}H_{23}SSi^+$ $(M+H)^+$ 323.1284, found 323.1286.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.2018xxxxx.

Acknowledgement

The acknowledgements come at the end of an article after the conclusions and before the notes and references This work was financially supported by the National Natural Science Foundation of China (21502182, 21102179 and 21572271), Qing Lan Project of Jiangsu Province, National Found for Fostering Talents of Basic Science (J1030830), the Fundamental Research Funds for the Central Universities (3010050077) and Postgraduate Scientific Research Innovation Projects of Jiangsu Province (KYCX17_0664).

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(The following will be filled in by the editorial staff)
Manuscript received: XXXX, 2017
Revised manuscript received: XXXX, 2017
Accepted manuscript online: XXXX, 2017
Version of record online: XXXX, 2017

Entry for the Table of Contents

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Metal-Free Synthesis of β-Bromoalkenyl Sulfides via Deoxygenative Bromination/Olefination/Sulfenylation of Ketones with Sulfonyl Hydrazides and Pyridinium Tribromide

Yishu Bao,[a] Lingyu Zhong,[a] Qiaodan Hou,[a] Ruihua Shi,[a] Qingfa Zhou,[a]* and Fulai Yang[a]*

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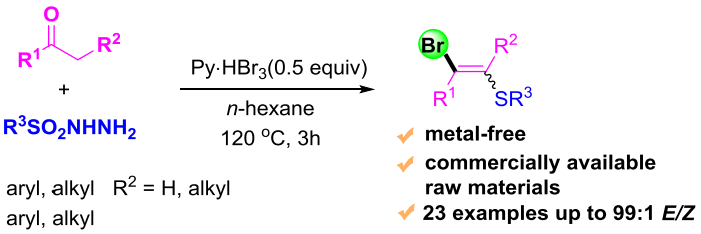

R^1 = aryl, alkyl R^2 = H, alkyl
R^3 = aryl, alkyl

A novel metal-free method for synthesis of β-bromoalkenyl sulfides via deoxygenative bromination/olefination/sulfenylation process using commercially available ketones, sulfonyl hydrazides and pyridinium tribromide as starting materials has been developed.