Published in final edited form as:

Org Biomol Chem. 2018 May 15; 16(19): 3605–3609. doi:10.1039/c8ob00745d.

Efficient synthesis of 3-sulfolenes from allylic alcohols and 1,3-dienes enabled by sodium metabisulfite as a sulfur dioxide equivalent

Hang T. Dang, Vu T. Nguyen, Viet D. Nguyen, Hadi D. Arman, and Oleg V. Larionov

Department of Chemistry, The University of Texas at San Antonio, San Antonio, Texas 78249, United States

Abstract

We present herein an efficient and practical method for a gram scale synthesis of 3-sulfolenes using sodium metabisulfite as a safe, inexpensive, and easy to handle sulfur dioxide equivalent. Diversely-substituted 3-sulfolenes can be prepared by reacting a variety of 1,3-dienes or allylic alcohols with sodium metabisulfite in aqueous hexafluoroisopropanol (HFIP) or in aqueous methanol in the presence of potassium hydrogen sulfate. Advantageously, the method enables conversion of allylic alcohols directly to 3-sulfolenes, by-passing intermediate 1,3-dienes.

Five-membered sulfur heterocycles play important roles in organic synthesis,¹ medicinal chemistry,² and materials science.³ 3-Sulfolenes⁴ are key intermediates in the synthesis of sulfolanes,⁵ polycyclic heterocycles,^[1c] conjugated unsaturated compounds,⁶ as well as in natural product synthesis (Figure 1).⁷ The synthesis of 3-sulfolenes typically involves reactions with excess sulfur dioxide. Sulfur dioxide is a toxic gas,⁸ and synthetic manipulations with sulfur dioxide require high pressure equipment. In addition, measurement of exact quantities of sulfur dioxide is not practical, and variabilities in quantities of sulfur dioxide used and in reaction pressures may lead to inconsistent product yields and purities. These limitations have inspired a search for reagents that can serve as practical and safe sulfur dioxide equivalents.⁹ DABCO-bis(sulfur dioxide) (DABSO) is a solid and bench stable reagent that has recently been introduced by Willis as a convenient sulfur dioxide equivalent for the synthesis of sulfinates, sulfonamides, sulfones, and 3-sulfolenes.¹⁰ Although DABSO has a number of synthetic advantages as a sulfur dioxide equivalent, it may be expensive for some applications, and the synthesis of 3-sulfolenes using DABSO requires large excess (6 equiv.) of 1,3-diene.^{10a} Alternatively, use of excess boron trifluoride diethyl ether complex as an additive is necessary to sequester the Lewis basic DABCO that inhibits the cheletropic reaction with 1,3-dienes.^{10c} Sodium and potassium metabisulfites have recently been used as sulfur dioxide equivalents for the synthesis of sulfones and sulfonamides.¹¹ Metabisulfites are bench stable, inexpensive, solid salts with one of the highest SO₂ equivalent contents (65.4% for Na₂S₂O₅).¹² We reasoned that sodium metabisulfite can produce sulfur dioxide in situ that will then undergo the

Correspondence to: Oleg V. Larionov.

Conflicts of interest

There are no conflicts to declare.

cheletropic reaction with 1,3-dienes. In our search for appropriate reaction conditions we were guided by the studies by Faita,¹³ Vogel, and Sordo¹⁴ on the influence of solvents, as well as Brønsted and Lewis acids on the rates and the equilibrium constants of the cheletropic reaction of 1,3-dienes with sulfur dioxide.

It is known that the rate of the cheletropic cycloaddition reaction increases in more polar solvents (e.g., $k = 49 \times 10^{-5} \text{ M}^{-1} \text{ sec}^{-1}$ in CH_3OH , $E_T(30) = 55.5$; $k = 0.93 \times 10^{-5} \text{ M}^{-1} \text{ sec}^{-1}$ in C_6H_6 , $E_T(30) = 34.5$). Conversely, the rate of the cycloelimination decreases in more polar solvents (e.g., $k = 1.7 \times 10^{-5} \text{ M}^{-1} \text{ sec}^{-1}$ in CH_3OH , $E_T(30) = 55.5$; $k = 4.55 \times 10^{-5} \text{ M}^{-1} \text{ sec}^{-1}$ in C_6H_6 , $E_T(30) = 34.5$).¹³ Thus, formation of 3-sulfolenes proceeds faster and is more complete in solvents of higher polarity. On the other hand, experimental and computational studies showed that the cheletropic reaction can be accelerated by Brønsted and Lewis acids.¹⁴

We were therefore particularly interested in investigating the effect of hexafluoroisopropanol (HFIP) on the efficiency of the cheletropic reaction with sodium metabisulfite as a sulfur dioxide precursor. Hexafluoroisopropanol is one of the most polar ($E_T(30) = 65.3$)¹⁵ and acidic ($\text{p}K_a = 9.3$)¹⁶ common organic solvents. These properties, in addition to the high ionizing power ($Y_{\text{OTs}} = 3.79$),¹⁷ very low nucleophilicity ($N_{\text{OTs}} = -4.23$)¹⁸ and high hydrogen bond donor abilities ($\alpha = 1.96$)¹⁹ have made HFIP the solvent of choice for a number of recently developed synthetic methods.²⁰

Indeed, optimization studies for the reaction of diene **1** with sodium metabisulfite showed that HFIP is superior to other less polar solvents (e.g., entries 1 and 2, Table 1). The optimal ratio of HFIP and water was found to be 4 : 1. In this solvent mixture, sulfolene **2** was formed in 20% yield at 80 °C (entry 3). The yield improved to 50% at 100 °C (entry 4) with 2 equiv. of sodium metabisulfite. When the amount of sodium metabisulfite was increased to 5 equiv., complete conversion was observed, and sulfolene **2** was isolated in 97% yield (entry 7). In addition, to aqueous HFIP, we found that potassium hydrogen sulfate in aqueous methanol promoted the efficient conversion of diene **1** to sulfolene **2** in the presence of sodium metabisulfite (entries 9 and 10).

In this case, the lower $\text{p}K_a$ of bisulfate ($\text{p}K_a = 1.99$ in water)²¹ can promote formation of sulfur dioxide in situ, while the increased polarity and acidity of the solution may accelerate the cheletropic reaction.

We next studied the scope of the method under both conditions, i.e., in HFIP/ H_2O , and with KHSO_4 in $\text{CH}_3\text{OH}/\text{H}_2\text{O}$ (Table 2). A number of substituted 1,3-dienes were subjected to the reaction with sodium metabisulfite.

In general, most of the sulfolenes were obtained in good to excellent yields in HFIP and with KHSO_4 in methanol (e.g., sulfolenes **2-6**). Myrcene-derived sulfolene **7**-disubstituted product **8** were also obtained in good yields. Only in the case of sulfolene **9** was a significant difference in the two protocols observed. While little product was formed in HFIP/ H_2O , sulfolene **9** was formed in 81% yield on small scale, and in 75% yield on gram (3.2 g) scale in methanol and with KHSO_4 . 2,3-Disubstituted sulfolenes **10** and **11** were produced in good yields as well. In addition, the tetrasubstituted sulfolenes **12** and **13** were readily

accessed using both reaction conditions. Furthermore, the acid-sensitive benzylic alcohol functionality was not affected during the synthesis of sulfolenes **14** and **15**. Similarly, the myrcene-derived diol sulfolene **16** was readily prepared in 73% (in HFIP/H₂O) and 77% (in CH₃OH/H₂O with KHSO₄). In none of the cases was polymerization of the 1,3-dienes or isomerization to 2-sulfolenes observed. The reaction can also be readily carried out on gram scales. For example, sulfolenes **2-4**, **7-10**, as well as **12** and **13** were prepared in gram quantities (1–4.7 g), and both reaction conditions are equally amenable to scale up.

The structure of sulfolene **15** was confirmed by single crystal X-Ray crystallographic analysis.

Due to the relatively low boiling point of HFIP (58.6 °C), it can be easily recovered by distillation and reused for the synthesis of sulfolenes. For example, a synthesis of sulfolene **3** was repeated consecutively three times using recycled HFIP without any noticeable deterioration of yields.

The metabisulfite-mediated sulfolene synthesis proceeds with better yields and produces lower headspace pressure than the protocol that is based on the use of condensed sulfur dioxide generated ex situ. For example, the headspace pressure was 18 psi under the HFIP/H₂O conditions, and 10 psi using the CH₃OH/H₂O with KHSO₄ conditions. In both cases the yield of sulfolene **7** was >75%. When sulfur dioxide was generated ex situ by reacting sodium metabisulfite (10 equiv.) with 12M hydrochloric acid (20 equiv.), the headspace pressure was 32 psi, while the yield of sulfolene **7** was only 48% with methanol as a reaction solvent.

Allylic alcohols serve as precursors to a number of 1,3-dienes.²² A method that allows for a synthesis of 3-sulfolenes directly from allylic alcohols will significantly improve the efficiency of 3-sulfolene synthesis by obviating isolation of intermediate 1,3-dienes that can be volatile and prone to polymerization. Martial and Bischoff recently showed that the DABSO/BF₃·OEt₂ system can be used to convert allylic alcohols to 3-sulfolenes.^{10c} We were therefore interested in developing a metabisulfite-based method for this transformation. Indeed, we found that a number of 3-sulfolenes, e.g., **2**, **11**, and **17-22** can be prepared from readily available allylic alcohols under modified reaction conditions in HFIP/H₂O in the presence of KHSO₄ (Table 3). Thus, sulfolenes **2** and **11** were produced from commercial allylic alcohols **23** and **24** in 86% and 63% yields, respectively. For the synthesis of sulfolenes **17-22**, alcohols **25-30** were conveniently prepared by the reaction of the corresponding ketones with vinyl- or isopropenylmagnesium bromide, and used without purification in the reaction with sodium metabisulfite. This way, sulfolenes **17-22** were prepared in >60% yield. The synthesis of sulfolene **17** was successfully carried out on a gram scale.

Conclusions

In conclusion, this paper describes the development of a simple and efficient method of preparation of 3-sulfolenes from 1,3-dienes and allylic alcohols. The reaction development was enabled by a mechanism-driven optimization of the reaction conditions. The reactions

can be carried out on gram scales with sodium metabisulfite as a bench stable and inexpensive sulfur dioxide equivalent in aqueous hexafluoroisopropanol (HFIP) or in aqueous methanol in the presence of potassium hydrogen sulfate. Advantageously, the method enables conversion of allylic alcohols directly to 3-sulfolenes, by-passing isolation of intermediate 1,3-dienes. The new method is expected to find applications in natural product synthesis, medicinal chemistry, and organic synthesis.

Experimental

General Procedure 1 (GP1) for the synthesis of sulfolenes in hexafluoroisopropanol (HFIP)

A 75 mL glass pressure vessel was charged with a 4 : 1 v/v mixture of HFIP (4 mL) and water (1 mL). The stirred mixture was degassed by bubbling argon for 5 min, then 1,3-diene (2 mmol) and sodium metabisulfite (10 mmol, 5 equiv) were added. The vessel was sealed, and the reaction mixture was stirred at 100 °C for 14 h. The reaction mixture was cooled to room temperature and concentrated under reduced pressure to remove HFIP. Ethyl acetate was added, and the solution was dried over anhydrous Na₂SO₄. The organic phase was concentrated under reduced pressure to afford the sulfolene product.

General Procedure 2 (GP2) for the synthesis of sulfolenes in methanol with KHSO₄

A 75 mL pressure vessel was charged with a 4 : 1 v/v mixture of methanol (4 mL) and water (1 mL). The stirred mixture was degassed by bubbling argon for 5 min, then KHSO₄ (4 mmol, 2 equiv.), diene (2 mmol) and sodium metabisulfite (10 mmol, 5 equiv.) were added. The vessel was sealed, and the reaction mixture was stirred at 100 °C for 14 h. The reaction mixture was cooled to room temperature and concentrated. Ethyl acetate was added, and the solution was dried over anhydrous Na₂SO₄. The organic phase was concentrated under reduced pressure to afford the sulfolene product.

General Procedure 3 (GP3) for the synthesis of allylic alcohols

To a solution of ketone (5 mmol) in tetrahydrofuran (10 mL) was added 1M vinylmagnesium bromide or isopropenylmagnesium bromide solution in THF (8 mmol, 1.6 equiv.) at 0 °C, and the reaction mixture was stirred at room temperature for 12 h. Saturated solution of ammonium chloride (3 mL) was added, and the mixture was extracted with ethyl acetate (4 × 20 mL). The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The purity of the crude allylic alcohol was assayed by means of ¹H NMR spectroscopy with 1,4-dimethoxybenzene as an internal standard, and the crude allylic alcohol was immediately used for the preparation of 3-sulfolenes (GP4).

General Procedure 4 (GP4) for the synthesis of sulfolenes from allylic alcohol

To a 48 mL pressure vessel charged with allylic alcohol (0.6–1 mmol) was added a 2 : 1 or 3 : 1 v/v mixture of degassed HFIP and water (5 mL). Sodium metabisulfite (3 mmol, 3–5 equiv.) and KHSO₄ (4 mmol, 4–7.3 equiv.) were added. The vessel was sealed, and the reaction mixture was stirred at room temperature for 15 minutes. The reaction mixture was then allowed to stir at 100 °C for 36 h. The reaction mixture was cooled to room temperature, ethyl acetate was added, and the solution was dried over anhydrous Na₂SO₄.

The organic phase was concentrated under reduced pressure and purified by flash chromatography (silica gel, ethyl acetate/hexane) to afford the 3-sulfolene product.

Acknowledgments

Financial support by the Welch Foundation (AX-1788), the NSF (CHE-1455061), NIGMS (SC3GM105579), and Max and Minnie Tomerlin Voelcker Fund is gratefully acknowledged.

Notes and references

1. (a) Patai, S., Rappoport, Z., editors. *The Chemistry of Functional Groups, Supplement S: The Chemistry of Sulphur-Containing Functional Groups*. Wiley; Chichester: 1993. (b) Toru, T., Bolm, C., editors. *Organosulfur Chemistry in Asymmetric Synthesis*. Wiley-VCH; Weinheim, Germany: 2008.
2. (a) Ghosh AK, Thompson WJ, Lee HY, McKee SP, Munson PM, Duong TT, Darke PL, Zugay JA, Emini EA, Schleif WA, Huff JR, Anderson PS. *J Med Chem*. 1993; 36:924–927. [PubMed: 8464047] (b) Collot M, Sendid B, Fievez A, Savaux C, Standaert-Vitse A, Tabouret M, Drucbert AS, Danze PM, Poulain D, Mallet JM. *J Med Chem*. 2008; 51:6201–6210. [PubMed: 18788729] (c) Mezler M, Geneste H, Gault L, Marek GJ. *Curr Opin Investig Drugs*. 2010; 11:833–845. (d) Brant MG, Wulff JE. *Org Lett*. 2012; 14:5876–5879. [PubMed: 23181823] (e) Ilardi EA, Vitaku E, Njardarson JT. *J Med Chem*. 2014; 57:2832–2842. [PubMed: 24102067] (f) Feng M, Tang B, Liang SH, Jiang X. *Curr Top Med Chem*. 2016; 16:1200–1216. [PubMed: 26369815]
3. (a) Barbarella G, Melucci M, Sotgiu G. *Adv Mater*. 2005; 17:1581–1593. (b) Liang Y, Yu L. *Acc Chem Res*. 2010; 43:1227–1236. [PubMed: 20853907] (c) Poirier GE. *Chem Rev*. 1997; 97:1117–1128. [PubMed: 11851444]
4. (a) Chou, T-s, Tso, H-H. *Org Prep Proc Intl*. 1989; 21:257–296. (b) Ando K, Takayama H. *Heterocycles*. 1994; 37:1417–1439. (c) Dubbaka SR, Vogel P. *Angew Chem, Int Ed*. 2005; 44:7674–7684. (d) Wang L, He W, Yu Z. *Chem Soc Rev*. 2013; 42:599–621. [PubMed: 23079733] (e) Brant MG, Wulff JE. *Synthesis*. 2016; 48:1–17.
5. (a) Zhou T, Peters B, Maldonado MF, Govender T, Andersson PG. *J Am Chem Soc*. 2012; 134:13592–13595. [PubMed: 22835144] (b) Kita Y, Hida S, Higashihara K, Jena HS, Higashida K, Mashima K. *Angew Chem, Int Ed*. 2016; 55:8299–8303. (c) Meng K, Xia JZ, Wang YZ, Zhang XH, Yang GQ, Zhang WB. *Org Chem Front*. 2017; 4:1601–1605.
6. (a) Bloch R, Hassan D, Mandard X. *Tetrahedron Lett*. 1983; 24:4691–4694. (b) Bloch R, Benecou C, Guibe-Jampel E. *Tetrahedron Lett*. 1985; 26:1301–1304.
7. (a) Martin SF, Desai SR, Philips GW, Miller AC. *J Am Chem Soc*. 1980; 102:3294–3296. (b) Nomoto T, Takayama H. *Heterocycles*. 1985; 23:2913–2916. (c) Leonard J, Hague AB, Knight JA. *Organosulfur Chem*. 1998; 2:229–292. (d) Bruyère H, Samaritani S, Ballereau S, Tomas A, Royer J. *Synlett*. 2005; 9:1421–1424.
8. Wang X-B, Du J-B, Cui H. *Life Sci*. 2014; 98:63–67. [PubMed: 24412383]
9. (a) Deeming AS, Emmett EJ, Richards-Taylor CS, Willis MC. *Synthesis*. 2014; 46:2701–2710. (b) Emmett EJ, Willis MC. *Asian J Org Chem*. 2015; 4:602–611.
10. (a) Woolven H, Gonzalez-Rodriguez C, Marco I, Thompson AL, Willis MC. *Org Lett*. 2011; 13:4876–4878. [PubMed: 21866926] (b) Emmett EJ, Willis MC. *Org Synth*. 2014; 91:125–136. (c) Martial L, Bischoff L. *Synlett*. 2015; 26:1225–1229. (d) Richards-Taylor CS, Blakemore DC, Willis MC. *Chem Sci*. 2014; 5:222–228. (e) Emmett EJ, Hayter BR, Willis MC. *Angew Chem, Int Ed*. 2014; 53:10204–10208. (f) Deeming AS, Russell CJ, Willis MC. *Angew Chem, Int Ed*. 2016; 55:747–750. (g) Deeming AS, Russell CJ, Willis MC. *Angew Chem, Int Ed*. 2015; 54:1168–1171. (h) Zheng D, Yu J, Wu J. *Angew Chem, Int Ed*. 2016; 55:11925–11929. (i) Emmett EJ, Richards-Taylor CS, Nguyen B, Garcia-Rubia A, Hayter BR, Willis MC. *Org Biomol Chem*. 2012; 10:4007–4014. [PubMed: 22407213] (j) Tsai AS, Curto JM, Roche BN, Dechert-Schmitt A-MR, Ingle GK, Mascitti V. *Org Lett*. 2016; 18:508–511. [PubMed: 26771228]
11. (a) Ye S, Wu J. *Chem Commun*. 2012; 48:10037–10039. (b) Wang M, Chen S, Jiang X. *Org Lett*. 2017; 19:4916–4919. [PubMed: 28876937] (c) Wang Y, Du B, Sha W, Mei H, Han J, Pan Y. *Org*

- Chem Front. 2017; 4:1313–1317.(d) Shavnya A, Coffey SB, Smith AC, Mascitti V. Org Lett. 2013; 15:6226–6229. [PubMed: 24256546] (e) Shavnya A, Hesp KD, Mascitti V, Smith AC. Angew Chem, Int Ed. 2015; 54:13571–13575.
12. Schroeter, LC. Sulfur dioxide; applications in foods, beverages, and pharmaceuticals. Pergamon Press, Inc.; Long Island City: 1966.
13. Desimoni G, Faita G, Garau S, Righetti P. Tetrahedron. 1996; 52:6241–6248.
14. (a) Roulet JM, Deguin B, Vogel P. J Am Chem Soc. 1994; 116:3639–3640.(b) Sudrez D, Sordo TL, Sordo JA. J Org Chem. 1995; 60:2848–2852.(c) Fernandez T, Sordo JA, Monnat F, Deguin B, Vogel P. J Am Chem Soc. 1998; 120:13276–13277.
15. Reichardt C. Chem Rev. 1994; 94:2319–2358.
16. Dyatkin BL, Mochalina EP, Knunyants IL. Tetrahedron. 1965; 21:2991–2995.
17. Bentley TW, Carter GE. J Org Chem. 1983; 48:579–584.
18. Bégué JP, Bonnet-Delpon D, Crousse B. Synlett. 2004; 1:18–29.
19. Kamlet MJ, Abboud JM, Abraham MH, Taft RW. J Org Chem. 1983; 48:2877–2887.
20. (a) Shuklov IA, Dubrovina NV, Börner A. Synthesis. 2007; 19:2925–2943.(b) Dohi T, Yamaoka N, Kita Y. Tetrahedron. 2010; 66:5775–5785.(c) Colomer I, Chamberlain AER, Haughey MB, Donohoe TJ. Nature Rev Chem. 2017; 1:0088.(d) Mfuh AM, Nguyen VT, Chhetri B, Burch JE, Doyle JD, Nesterov VN, Arman HD, Larionov OV. J Am Chem Soc. 2016; 138:8408–8411. [PubMed: 27347688] (e) Arnold AM, Pöthig A, Drees M, Gulder T. J Am Chem Soc. 2018; doi: 10.1021/jacs.8b00113
21. Perrin, DD. Ionization Constants of Inorganic Acids and Bases in Aqueous Solution. Second. Pergamon; Oxford: 1982.
22. Mehta, G., Prakash Rao, HS. Patai's Chemistry of Functional Groups. Wiley-VCH; Weinheim: 2009. Synthesis of Conjugated Dienes and Polyenes.

Figure 1.
Sulfolane and 3-sulfolene in organic and medicinal chemistry.

Table 1Optimization of the 3-sulfolene synthesis from 1,3-dienes^a

Entry	Solvent (ratio)	Reagent (equiv.)	T, °C	Yield, % ^b
1	THF/H ₂ O (3 : 1)	Na ₂ S ₂ O ₅ (4)	80	3
2	HFIP/H ₂ O (3 : 1)	Na ₂ S ₂ O ₅ (4)	80	19
3	HFIP/H ₂ O (4 : 1)	Na ₂ S ₂ O ₅ (5)	80	20
4	HFIP/H ₂ O (4 : 1)	Na ₂ S ₂ O ₅ (2)	100	50
5	HFIP/H ₂ O (4 : 1)	Na ₂ S ₂ O ₅ (3)	100	60
6	HFIP/H ₂ O (4 : 1)	Na ₂ S ₂ O ₅ (4)	100	65
7 ^c	HFIP/H₂O (4 : 1)	Na₂S₂O₅ (5)	100	97
8	CH ₃ OH/H ₂ O (4 : 1)	Na ₂ S ₂ O ₅ (3) KHSO ₄ (1)	80	39
9 ^c	CH ₃ OH/H ₂ O (4 : 1)	Na ₂ S ₂ O ₅ (5) KHSO ₄ (3)	100	80
10 ^c	CH₃OH/H₂O (4 : 1)	Na₂S₂O₅ (5) KHSO₄ (2)	100	98

^aReaction conditions: 1,3-diene (2 mmol), solvent (5 mL), 16 h.^bYield was determined by ¹H NMR spectroscopy using 1,4-dimethoxybenzene as an internal standard.^cIsolated yield.

Table 2

Synthesis of 3-sulfolenes from 1,3-dienes^a

<p>2</p> <p>97% (HFIP) 2.5 g, 95% (HFIP) 98% (CH₃OH) 2.1 g, 78% (CH₃OH)</p>	<p>3</p> <p>89% (HFIP) 3.0 g, 99% (HFIP) 97% (CH₃OH)</p>	<p>4</p> <p>99% (HFIP) 2.6 g, 86% (HFIP) 75% (CH₃OH)</p>
<p>5</p> <p>91% (HFIP) 64% (CH₃OH)</p>	<p>6</p> <p>96% (HFIP) 98% (CH₃OH)</p>	<p>7</p> <p>86% (HFIP) 3.9 g, 97% (HFIP) 78% (CH₃OH)</p>
<p>8</p> <p>62% (HFIP) 1.0 g, 63% (HFIP) 84% (CH₃OH)</p>	<p>9</p> <p>81% (CH₃OH) 3.2 g, 74% (CH₃OH)</p>	<p>10</p> <p>99% (HFIP) 82% (CH₃OH) 4.7 g, 69% (CH₃OH)</p>
<p>11</p> <p>87% (HFIP) 99% (CH₃OH)</p>	<p>12</p> <p>99% (HFIP) 3.5 g, 99% 95% (CH₃OH)</p>	<p>13</p> <p>97% (HFIP) 1.6 g, 99% (HFIP) 79% (CH₃OH)</p>
<p>14</p> <p>73% (HFIP) 95% (CH₃OH)</p>	<p>15</p> <p>89% (HFIP) 57% (CH₃OH)</p>	<p>16</p> <p>73% (HFIP) 77% (CH₃OH)</p>

^aReaction conditions: HFIP: 1,3-diene (2 mmol), Na₂S₂O₅ (5 equiv.), HFIP/H₂O (4 : 1) (5 mL), 100 °C, 14 h. CH₃OH: 1,3-diene (2 mmol), Na₂S₂O₅ (5 equiv.), KHSO₄, (2 equiv.), CH₃OH/H₂O (4 : 1) (5 mL), 100 °C, 14 h.

Table 3Synthesis of 3-sulfolenes from allylic alcohols^a

Substrate	Product	Substrate	Product
 23	 2 86%	 24	 11 63%
 25	 17 83% 1.5 g, 67%	 28	 20 87%
 26	 18 74%	 29	 21 73%
 27	 19 75%	 30	 22 62%

^aReaction conditions: allylic alcohol (0.42–1 mmol), Na₂S₂O₅ (3–5.5 equiv.), KHSO₄ (4–7.3 equiv.) HFIP/H₂O (2 : 1 or 3 : 1) (5 mL), 100 °C, 36 h.