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A novel, easy and mild preparation of sulfilimines from sulfoxides using the Burgess reagent

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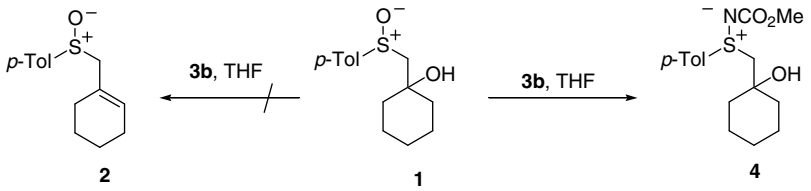
ABSTRACT

A novel preparation of sulfilimines from the corresponding sulfoxides using the Burgess reagent is described. The reaction is general to dialkyl- and aryl alkyl sulfoxides and proceeds under mild conditions in benzene. A variety of protecting groups can be introduced on the nitrogen of the sulfilimine by choosing the appropriate Burgess reagent.

Chiral sulfilimines,[1] the nitrogen analogs of sulfoxides, are an interesting class of compounds whose chemistry remains underdeveloped partly because of the limited methods available for their preparation. Chiral sulfilimines have been prepared by kinetic resolution of racemic sulfilimines,[2] from the corresponding sulfoxides,[3] and from sulfides by nitrene transfer.[4] In continuation of our interest in the chemistry of sulfilimines,[5] we sought a route to sulfilimines possessing protecting groups that are removable under mild conditions so that they would be synthetically useful as inter-[6] and intramolecular nucleophiles,[5] from the corresponding sulfoxides,[7] which are readily available. In connection with another project, to secure cyclohexene derivative **2**, we subjected tertiary alcohol **1** to treatment with the Burgess reagent[8] **3b** under standard conditions.[9] However, TLC analysis did not reveal less polar spot and further analysis indicated that we had not obtained **2** but polar sulfilimine **4** instead (Scheme 1). This discovery prompted us to examine the generality of this transformation and the results of this investigation are reported herein.

Initially, racemic methyl *p*-tolyl sulfoxide **5a** was reacted with the Burgess reagent **3a**[9f] (1 equiv) in anhydrous THF (0.2 M) at 60 °C. After 2 h, sulfilimine **6a** was isolated in 30% yield along with unreacted **5a** and methyl *p*-tolyl sulfide (**7**, Table 1).

The use of excess of **3a** (2 equiv) relative to **5a** led to the complete consumption of the latter to furnish **6a** in 72% yield along with methyl *p*-tolyl sulfide **7** in 10% yield. The reaction of **5a** with **3a** proceeded at rt in both acetonitrile and dichloromethane, with an excess of **3a** being required for completion over a 5–7 h period. Interestingly, when the reaction was carried out in benzene, conversion was observed at 0 °C and complete conversion was observed in 5 h to yield **6a** in 80% yield. The same reaction at rt was complete within 2 h affording **6a** in 85% yield. Having standardized the reaction conditions,[10] the generality of the procedure was examined employing a variety of aryl alkyl and di-alkyl sulfoxides (Table 2). A perusal of Table 2 reveals that the reaction is general, high yielding and proceeds under mild conditions. The reaction proceeds with equal facility on sulfoxides with electron



Scheme 1.

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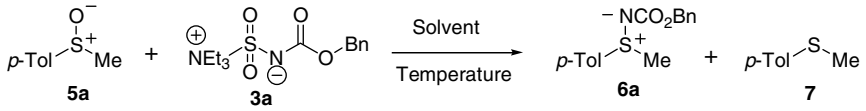
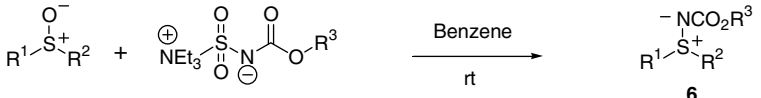
Table 1
Reaction of **5a** with **3a** in different solvents[a]



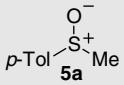
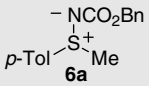
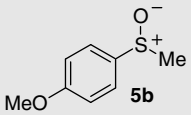
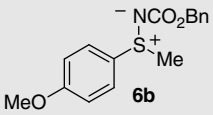
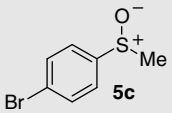
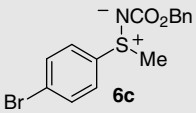
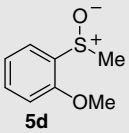
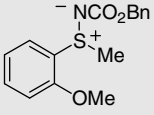
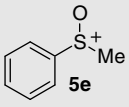
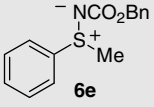
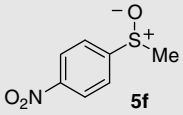
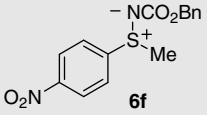
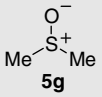
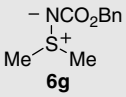
Entry	Equiv of **3a**	Solvent	Temp in °C (Time in h)	Yield[b] (%)
1	1	THF	rt	No Rxn
2	1	THF	60 (2)	30[c]
3	2	THF	60 (1.5)	72[d]
4	1	CH_3CN	rt (6)	32[c]
5	2	CH_3CN	rt (5)	68[d]
6	1	CH_2Cl_2	rt (7)	30[c]
7	2	CH_2Cl_2	rt (6)	65[d]
8	1	PhH	0 to rt (7)	30[c]
9	2	PhH	0 to rt (5)	80
10	2	PhH	rt (2)	85

[a] All reactions were run using 0.5 mmol of **5a**, 0.2 M in solvent.
[b] Isolated yield.
[c] Starting material ca. 60% was recovered.
[d] 10–15% of sulfide **7** was isolated.

Table 2
Reaction of sulfoxides with Burgess reagents

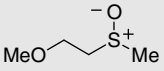
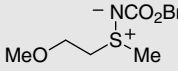
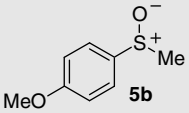
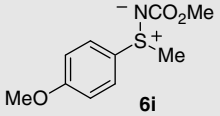
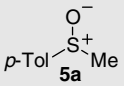
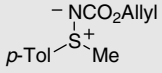
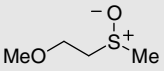
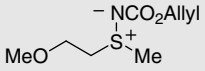
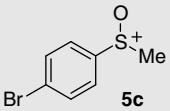
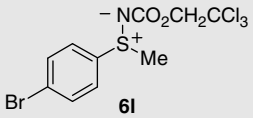


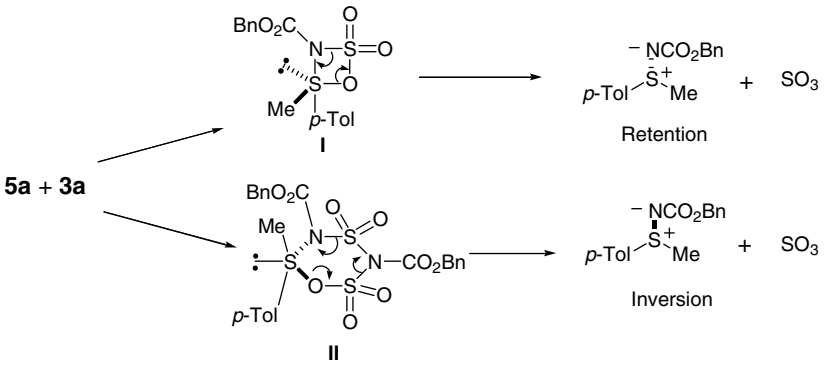
3a, R^3 = Bn; **3b**, R^3 = Me
3c, R^3 = Allyl; **3d**, R^3 = CH_2CCl_3

Entry	Burgess reagent	Sulfoxide	Sulfilimine	Yield (%)
1	**3a**	 **5a**	 **6a**	85
2	**3a**	 **5b**	 **6b**	80
3	**3a**	 **5c**	 **6c**	82
4	**3a**	 **5d**	 **6d**	70
5	**3a**	 **5e**	 **6e**	85
6	**3a**	 **5f**	 **6f**	82
7	**3a**	 **5g**	 **6g**	90

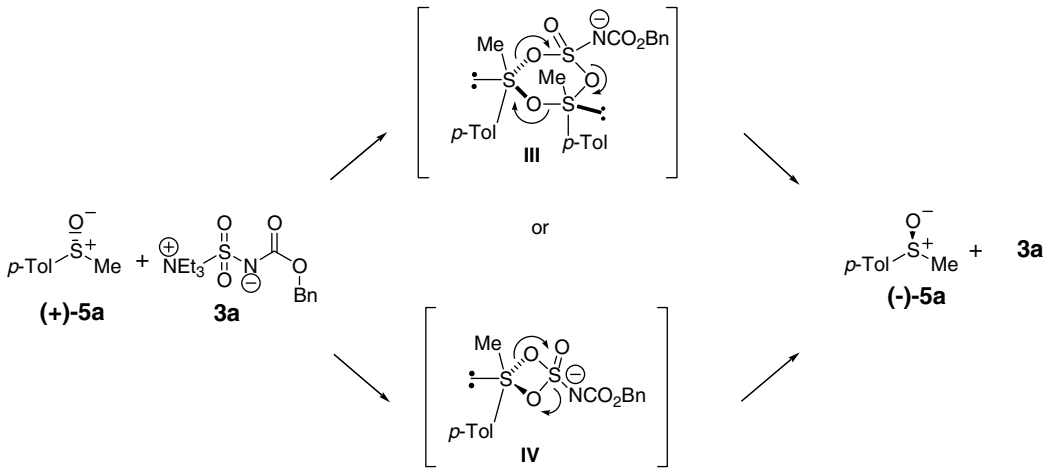
(*continued on next page*)

Table 2 (*continued*)

Entry	Burgess reagent	Sulfoxide	Sulfilimine	Yield (%)
8	**3a**	 **5h**	 **6h**	70
9	**3b**	 **5b**	 **6i**	78
10	**3c**	 **5a**	 **6j**	85
11	**3c**	 **5h**	 **6k**	76
12	**3d**	 **5c**	 **6l**	70



Scheme 2.



Scheme 3.

donating (entries 2, 4 and 9), electron withdrawing substituents (entries 3, 6 and 12) and an *o*-substituted sulfoxide (entry 4). Also the reaction was general for a variety of Burgess reagents **3a–d**[9f] thus furnishing sulfilimines with different protecting groups.

The reaction probably proceeds via intermediates **I** and/or **II** (indicated for one of the enantiomers) to afford **6a** with retention or inversion of the sulfur configuration, respectively (Scheme 2).

There are less than a handful of reports on the stereospecific transformation of chiral sulfoxides to chiral sulfilimines.[11] In an effort to prepare enantiopure sulfilimines, optically pure (+)-**5a**[12] was reacted with **3a** under standard conditions in benzene at 0 °C to rt, only to obtain racemic **6a**. Chiral HPLC[13] after 30 min revealed the presence of 20% and 28% yields of (+)- and (−)-**5a**, respectively, along with 17% and 22% yields of enantiomers of **6a**. Chiral HPLC after 1 h revealed the presence of both enantiomers of **6a** in equimolar quantity (32% each) along with enantiomers of **5a** in equal amounts (11% each). It can be inferred that (+)-**5a** is epimerized by **3a** faster than its reaction with **3a** to afford **6a**. The outcome of the reaction (+)-**5a** with **3a** in other solvents such as dichloromethane, acetonitrile and THF was no better. A mechanism explaining the racemization of (+)-**5a** by **3a**, through the intermediacy of intermediates **III** and/or **IV**, yielding (−)-**5a** and regenerating **3a** is depicted in Scheme 3.

In conclusion, we have disclosed a novel method for the preparation of a variety of sulfilimines with different protecting groups on the nitrogen, from the corresponding sulfoxides, using the appropriate Burgess reagent. Efforts to prepare optically active sulfilimines from optically active sulfoxides met with failure. Studies are in progress to prepare diastereomeric β-siloxy sulfilimines from the corresponding sulfoxides and to employ them in synthesis.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.04.152.

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9. For the use of the Burgess reagent as a source of heteroatoms in (i) the conversion of alcohols to urethanes see: (a) Wood, M. R.; Kim, J. Y.; Books, K. M. *Tetrahedron Lett.* **2002**, *43*, 3887; (b) Burgess, E. M.; Penton, H. R., Jr.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26; (c) Atkins, G. M.; Burgess, E. M. *J. Am. Chem. Soc.* **1972**, *94*, 6135; (ii) Conversion of epoxides and diols to sulfamidates see: (d) Rinner, U.; Adams, D. R.; dos Santos, M. L.; Abboud, K. A.; Hudlicky, T. *Synlett* **2003**, 1247; (e) Leisch, H.; Saxon, R.; Sullivan, B.; Hudlicky, T. *Synlett* **2006**, 445; (f) Nicolaou, K. C.; Huang, X.; Snyder, S. A.; Rao, P. B.; Bella, M.; Reddy, M. V. *Angew. Chem., Int. Ed.* **2002**, *41*, 834; (iii) Conversion of amino alcohols to sulfamides see (g) Nicolaou, K. C.; Longbottom, D. A.; Snyder, S. A.; Nalbandian, A. Z.; Huang, X. *Angew. Chem., Int. Ed.* **2002**, *41*, 3886; (iv) Epoxy alcohols to hydroxysulfamidates see: (h) Nicolaou, K. C.; Snyder, S. A.; Longbottom, D. A.; Nalbandian, A. Z.; Huang, X. *Chem. Eur. J.* **2004**, *10*, 5581; (v) Conversion of thiols to disulfides see: (i) Banfield, S. C.; Omori, A. T.; Leisch, H.; Hudlicky, T. *J. Org. Chem.* **2007**, *72*, 4989.
10. See Electronic Supplementary data.
11. For the preparation of optically active sulfilimines from sulfoxides using *N*-sulfinyl-*p*-toluenesulfonamide see: (a) Yamagishi, F. G.; Rayner, D. R.; Zwicker, E. T.; Cram, D. J. *J. Am. Chem. Soc.* **1973**, *95*, 1916; (b) Christensen, B. W. *J. Chem. Soc. D* **1971**, 597; (c) Cram, D. J.; Day, J.; Rayner, D. R.; von Schriltz, D. M.; Duchamp, D. J.; Garwood, D. C. *J. Am. Chem. Soc.* **1970**, *92*, 7369; (d) Christensen, B. W.; Kjaer, A. *Chem. Commun.* **1969**, 934; (e) Johnson, C. R.; Rigau, J. J. *J. Org. Chem.* **1968**, *33*, 4340; (f) Using *N*,*N*′-bis(*p*-toluenesulfonyl)sulfur diimide see: Ref. [11a]; Using *p*-tosyl isocyanate see: (g) Garwood, D. C.; Jones, M. R.; Cram, D. J. *J. Am. Chem. Soc.* **1973**, *95*, 1925.
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13. HPLC column conditions: Eurocel 01 chiral column, eluent: 10% IPA/90% hexane, flow rate: 1 mL/min.