Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron Letters 47 (2006) 2717–2719
Tetrahedron Letters

An efficient and novel method for the synthesis of sulfinate esters under solvent-free conditions

Abdol R. Hajipour,[a,b,*] Ali R. Falahati[b] and Arnold E. Ruoho[b]

[a]*Pharmaceutical Research Laboratory, Department of Chemistry, Isfahan University of Technology, Isfahan 84156, Iran*
[b]*Department of Pharmacology, University of Wisconsin Medical School, 1300 University Avenue, Madison, WI 53706-1532, USA*

Received 21 January 2006; revised 15 February 2006; accepted 15 February 2006
Available online 3 March 2006

Abstract—The present letter describes a reliable one-stage process for the preparation of sulfinate esters from the corresponding sulfinic acid and alcohols in the presence of *N*,*N*′-dicyclohexylcarbodiimide (DCC) under solvent-free conditions.

1. Introduction

Reaction of organometallic reagent with a diastereomerically pure sulfinate ester of menthol continues to be the method that is most often employed for the preparation of optically active sulfoxides.[1] Despite recent advancement in the asymmetric oxidation of sulfides to sulfoxides,[2] the requisite sulfinate esters are generally prepared from the corresponding sulfinic acids either directly[3] or via the sulfinyl chlorides.[4] Alternatively, the sulfinyl chloride may be directly prepared from a more available disulfide, by reaction with chlorine[5] or sulfuryl chloride in the presence of acetic acid.[6] The most commonly used methods are the reaction of sulfinyl chlorides with alcohols in the presence of triethylamine or pyridine[7] and sodium sulfinates with chlorocarbonates in alcohols.[8] Other methods including alkylation of sulfinic acids are also known,[9–11] a useful one-step synthesis of alkyl *tert*-alkansulfinates was reported.[12]

Reactions under solvent-free conditions have recently attracted attention.[13–15] The advantage of these methods over conventional classical method is that they are cleaner reactions, have decreased reaction time, and easier workup. In continuation of our ongoing program to develop environmentally benign methods under solvent-free conditions,[16–19] we now wish to report a convenient one-step method for the preparation of sulfinate esters, starting from sulfinic acid and alcohols in the presence of DCC under solvent-free conditions. This method would be widely applicable as a general method for the synthesis of alkyl sulfinate esters.

2. Results and discussion

The process in its entirety involves a simple mixing of sulfinic acid and alcohols in the presence of DCC in a mortar and grinding the mixture for the time specified in Table 1 at room temperature. This method is very fast and purification of product is straightforward (Scheme 1). The diastereoselectivity of products when we use optical pure L-menthol was determined by ^{1}H NMR analysis on the crude reaction products. The diastereoselectivity was between 70:30 and 90:10; the products have been characterized by ^{1}H NMR, mass spectroscopy and CHN analysis. The products were usually isolated in excellent yield, and excellent diastereoselectivity and short reaction time (Table 1). In all cases, the major diastereomer is that with the more upfield methane, and when separation was possible, the major diastereomer in all cases proved to have a negative sign of rotation, indicating the S configuration at sulfur.[20,21]

In conclusion, the discovery of this efficient method promises to find widespread application in the preparation of chiral sulfinate esters for which the corresponding sulfinyl chlorides are thermally unstable and sensitive to moisture. This technique should allow a more rapid and complete screening of sulfur constituent effects in chiral sulfoxide chemistry than has previously been possible. This methodology is superior from the

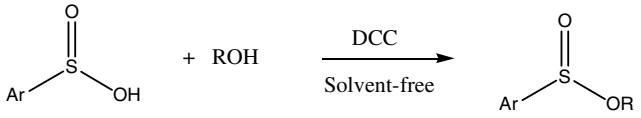
Keywords: DCC; Solvent-free; Sulfinic acid; Sulfinate esters.
* Corresponding author. Fax: +98 311 391 2350; e-mail: haji@cc.iut.ac.ir

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.02.080

Table 1. Preparation of sulfinate esters[a]

Entry	Ar	R	Reaction time (min)	Yield (%)
1	p-$CH_3C_6H_4$	CH_3	2	85
2	p-$CH_3C_6H_4$	CH_3CH_2	4	95
3	p-$CH_3C_6H_4$	$CH_3(CH_2)_2$	4	95
4	p-$CH_3C_6H_4$	$CH_3(CH_2)_3$	4	90
5	p-$CH_3C_6H_4$	$CH_3CH(CH_3)CH_2$	5	85
6	p-$CH_3C_6H_4$	$CH_3(CH_2)_2CH(CH_3)$	5	98
7	p-$CH_3C_6H_4$	Cyclohexyl	10	90
8	p-$CH_3C_6H_4$	$C_6H_5CH_2$	5	95
9	p-$CH_3C_6H_4$	$C_6H_5CH_2CH_2$	10	89
10	p-$CH_3C_6H_4$	L-Menthyl	8	95
11	p-$CH_3C_6H_4$	$ClCH_2CH_2$	4	85
12	p-$CH_3C_6H_4$	$CH_3(CH_2)_6CH_2$	4	98
13	p-$CH_3C_6H_4$	1-Adamantanyl	10	87
14	p-$CH_3C_6H_4$	$(CH_3)_3C$	12	64
15	p-$CH_3C_6H_4$	$C_6H_5(CH_2)_4$	5	88
16	p-$CH_3C_6H_4$	p-$MeOC_6H_4CH_2$	5	85
17	p-$CH_3C_6H_4$	m-$MeOC_6H_4CH_2$	8	80
18	p-$CH_3C_6H_4$	p-$ClC_6H_4CH_2$	6	88
19	C_6H_5	Me	6	86
20	P-$MeOC_6H_4$	L-Menthyl	10	89
21	P-ClC_6H_4	L-Menthyl	12	92
22	P-^{t}BuC_6H_4	L-Menthyl	15	87

[a] All products were identified by spectroscopy data (IR, NMR, mass and CHN analysis).[17–20,22,23]



Scheme 1.

point of view of yield, diastereoselectivity, lower reaction time and the easier workup to the reported methods.

Acknowledgements

We gratefully acknowledge the funding support received for this project from the Isfahan University of Technology (IUT), IR Iran (A.R.H.) and Grants GM 033138, MH 065503, NS 033650 (A.E.R.) from the National Institutes of Health, USA. Further financial support from Center of Excellency in Chemistry Research (IUT) is gratefully acknowledged.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.02.080.

References and notes

1. (a) Anderson, K. K.; Gaffield, W.; Papanikolau, N. E.; Foleg, J. W.; Perkins, R. I. *J. Am. Chem. Soc.* **1964**, *86*, 5637; (b) Drabowicz, J.; Bujnicki, B.; Mikaasezyk, M. *J. Org. Chem.* **1982**, *47*, 3352.
2. (a) Pitchene, P.; KaganH, B. *Tetrahedron Lett.* **1984**, *23*, 1049; (b) Petchene, P.; Dunach, E.; Deshmulch, M. N.; Laynn, H. D. *J. Am. Chem. Soc.* **1984**, *106*, 8188.
3. Boar, R. B.; Puter, A. C. *Synthesis* **1982**, 584.
4. Harpp, D. N.; Friedlander, B. T.; Larsen, C.; Steliou, K.; Stockton, A. *J. Org. Chem.* **1987**, *43*, 348.
5. Douglass, I. B.; Nuton, R. V. *J. Org. Chem.* **1968**, *33*, 2104.
6. Youn, J. H.; Herrmann, R. *Synthesis* **1987**, 72.
7. Phillipe, H. *J. Chem. Soc.* **1925**, 2552.
8. Yamamoto, A.; Kobayshi, M. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1292.
9. Wilt, J. W.; Stein, R. G.; Wagner, W. J. *J. Org. Chem.* **1967**, *32*, 2097.
10. Ott, R.; Rossing, A. *Ber. Dtsch. Chem. Ges.* **1885**, *18*, 2493.
11. Kobayshi, M. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1296.
12. Mikolajczyk, M.; Darbowicz, J. *Synthesis* **1974**, 124.
13. (a) Gedye, R. J.; Westaway, K.; Ali, H.; Baldisera, L.; Laberge, L.; Rousell, J. *Tetrahedron Lett.* **1986**, *27*, 279; (b) Giguere, R. J.; Bray, T. L.; Duncan, S. M.; Majetich, G. *Tetrahedron Lett.* **1986**, *27*, 4945.
14. (a) Abramovitch, A. *Org. Prep. Proc. Int.* **1991**, *23*, 685; (b) Migos, D. M. P.; Baghurst, D. R. *Chem. Soc. Rev.* **1991**, *20*, 1; (c) Caddick, S. *Tetrahedron* **1995**, *51*, 10403.
15. Loupy, A.; Petit, A.; Ramdiani, M.; Yvanaeff, C.; Majdoub, M.; Labiad, B.; Villemin, D. *Can. J. Chem.* **1993**, *71*, 90.
16. (a) Hajipour, A. R.; Arbabian, M.; Ruoho, A. E. *J. Org. Chem.* **2002**, *67*, 8622; (b) Hajipour, A. R.; Ruoho, A. E. *Org. Prep. Proced. Int.* **2002**, *34*, 647; (c) Hajipour, A. R.; Mazloumi, G. *Synth. Commun.* **2002**, *32*, 23; (d) Hajipour, A. R.; Ruoho, A. E. *J. Chem. Res. (S)* **2002**, 547; (e) Hajipour, A. R.; Adibi, H.; Ruoho, A. E. *J. Org. Chem.* **2003**, *68*, 4553; (f) Hajipour, A. R.; Bageri, H.; Ruoho, A. E. *Bull. Korean Chem. Soc.* **2004**, *25*, 1238; (g) Hajipour, A. R.; Malakutikhah, M. *Org. Prep. Proced. Int.* **2004**, *364*, 647; (h) Hajipour, A. R.; Ruoho, A. E. *Sul. Lett.* **2002**, *25*, 151; (i) Hajipour, A. R.; Mirjalili, B. F.; Zarei, A.; Khazdooz, L.; Ruoho, A. E. *Tetrahedron Lett.* **2004**, *45*, 6607.
17. (a) Hajipour, A. R.; Mallakpour, E.; Imanzadeh, G. *J. Chem. Res.* **1999**, 228; (b) Hajipour, A. R.; Mallakpour, E.; Adibi, H. *Chem. Lett.* **2000**, 460; (c) Hajipour, A. R.; Mallakpour, E.; Afrousheh, A. *Tetrahedron* **1999**, *55*, 2311; (d) Hajipour, A. R.; Islami, F. *Ind. J. Chem.* **1999**, *38B*, 461; (e) Hajipour, A. R.; Mallakpour, E.; Imanzadeh, G. *Chem. Lett.* **1999**, 99; (f) Hajipour, A. R.; Hantehzadeh, M. *J. Org. Chem.* **1999**, *64*, 8475; (g) Hajipour, A. R.; Mallakpour, E.; Backnejad, H. *Synth. Commun.* **2000**, *30*, 3855; (h) Hajipour, A. R.; Mallakpour, E.; Afrousheh, A. *Phosphorus Sulfur Silicon* **2000**, *160*, 67; (i) Hajipour, A. R.; Mallakpour, E.; Khoee, S. *Synlett* **2000**, 740; (j) Hajipour, A. R.; Mallakpour, E.; Khoee, S. *Chem. Lett.* **2000**, 120; (k) Hajipour, A. R.; Baltork, I. M.; Nikbaghat, K.; Imanzadeh, Gh. *Synth. Commun.* **1999**, *29*, 1697.
18. (a) Hajipour, A. R.; Mahboubkhah, N. *J. Chem. Res. (S)* **1998**, 122; (b) Hajipour, A. R.; Mallakpour, E.; Adibi, H. *Chem. Lett.* **2000**, 460; (c) Hajipour, A. R.; Mallakpour, E.; Khoee, S. *Chem. Lett.* **2000**, 120; (d) Hajipour, A. R.; Mallakpour, E.; Khoee, S. *Synlett* **2000**, 740; (e) Hajipour, A. R.; Ruoho, A. E. *Org. Prep. Proced. Int.* **2005**, *37*, 298; (f) Hajipour, A. R.; Ruoho, A. E. *Org. Prep. Proced. Int.* **2005**, *37*, 279.
19. Hajipour, A. R.; Kooshki, B.; Ruoho, A. E. *Tetrahedron Lett.* **2005**, *46*, 5503.
20. Axelrod, M.; Bickar, P.; Jacobus, J.; Green, M. M.; Mislow, K. *J. Am. Chem. Soc.* **1964**, *90*, 4835.

21. Typical experimental procedure: A mortar was charged with the alcohol (1 mmol), *p*-toluenesulfinic acid (1 mmol, 0.16 g), and DCC (1 mmol, 0.21 g). The reaction mixture was ground with a pestle in the mortar for the time specified in Table 1. When TLC showed no remaining toluenesulfinic acid (EtOAc/*n*-hexane, 15:85), to the reaction mixture was added H_2O (5 ml) and extracted with ether (2×10 ml) and the combined ethereal layer was washed with saturated $NaHCO_3$, dried ($MgSO_4$) and the ether was evaporated to dryness using a rotary evaporator. The residue was purified by column chromatography using silica gel and a mixture of *n*-hexane/EtOAc (85:15) to give the pure product.
22. See Supplementary data for experimental details.
23. Klunder, J. M.; Sharpless, K. B. *J. Org. Chem.* **1987**, *52*, 2598.