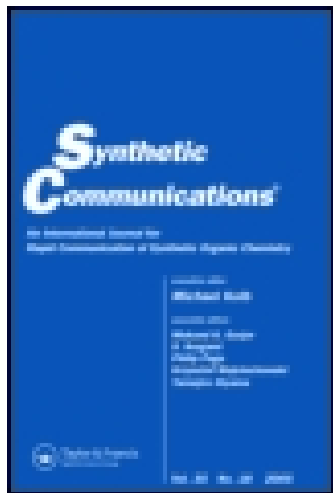




Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for
authors and subscription information:

<http://www.tandfonline.com/loi/lsyc20>

An Efficient Method for the Reduction of Cephalosporin Sulfoxides

Neera Tewari^a, Yatendra Kumar^a, Rajesh
Kumar Thaper^a & Jag Mohan Khanna^a

^a Ranbaxy Research Laboratories, Plot No.
20, Sector-18, Udyog Vihar, Gurgaon, 122001,
Haryana, India

Published online: 21 Aug 2006.

To cite this article: Neera Tewari, Yatendra Kumar, Rajesh Kumar Thaper & Jag Mohan Khanna (1996) An Efficient Method for the Reduction of Cephalosporin Sulfoxides, *Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry*, 26:6, 1169-1173, DOI: [10.1080/00397919608003725](http://dx.doi.org/10.1080/00397919608003725)

To link to this article: <http://dx.doi.org/10.1080/00397919608003725>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis.

The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

AN EFFICIENT METHOD FOR THE REDUCTION OF CEPHALOSPORIN SULFOXIDES

Neera Tewari, Yatendra Kumar, Rajesh K. Thaper, Jag Mohan Khanna*
Ranbaxy Research Laboratories, Plot No.20, Sector-18, Udyog Vihar,
Gurgaon-122001 (Haryana), India

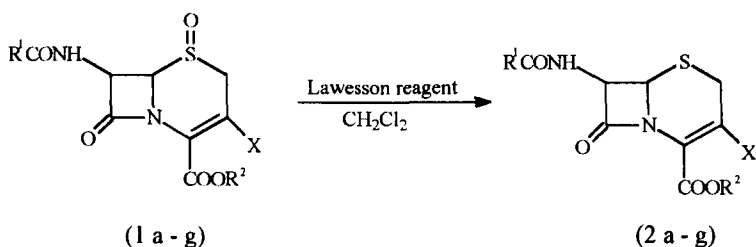
Abstract : An efficient and convenient method for the reduction of cephalosporin sulfoxides to their corresponding sulfides by Lawesson reagent is reported.

The reduction of cephalosporin sulfoxides (1) to their corresponding sulfides (2) is important owing to the biological activity associated with latter. β -Lactam sulfoxides, finding application as intermediates for antibiotics like Cefaclor, Cefroxidine, etc., need to be reduced to their corresponding sulfides at some stage of the process. Despite numerous methods¹ available for the reduction of sulfoxides, only a few are suitable for reduction of Cephalosporin sulfoxides. The problems associated with common methods are the use of DMF or DMAc as solvents, longer reaction times where the yields are mainly dependent on the dryness and purity of solvents^{2,3}. In a hunt for new deoxygenation methods for cephalosporins sulfoxides, we

* To whom correspondence should be addressed

found Lawesson reagent^{4,5} to be an excellent reducing agent. To the best of our knowledge use of this reagent as reducing agent in cephalosporin chemistry has not been reported earlier.

In this paper we describe the use of Lawesson reagent for the easy and convenient conversion of cepham / cephem sulfoxides to their corresponding cephem sulfides. The deoxygenation using this reagent is fast, clean and good yielding and the product obtained needs no further purification by chromatography.



Scheme 1

About 1.2 to 1.5 mol. eq. of reagent is needed for the reaction which goes to completion in 15-30 min time.

The results of this finding are summarised in the table.

Hydroxy compounds (2f) and (2g) were synthesized from exomethylene sulfoxides (1a) and (1b) respectively by an efficient single pot method involving ozonolysis followed by insitu deoxygenation with Lawesson reagent and isolation as acetic acid solvates.

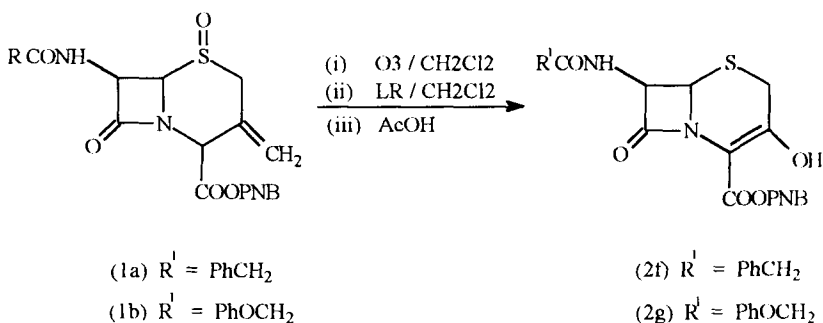
Table

Entry**	R ¹	R ²	X	Yield
2a	PhCH ₂	PNB	CH ₂	80%
2b	PhOCH ₂	PNB	CH ₂	78%
2c	PhOCH ₂	PNB	Cl	72%
2d	PhCH ₂	PNB	Cl	78%
2e	PhCH ₂	CHPh ₂	CH ₃	70%
2f*	PhCH ₂	PNB	OH	72%
2g*	PhOCH ₂	PNB	OH	80%

PNB = p-Nitrobenzyl

* isolated as acetic acid solvates

**Compounds (2 a-g) were identified by comparison of their ¹HNMR, IR spectra with those of authentic samples.



Compounds (2f) and (2g) are important as they are key intermediates in the synthesis of major antibiotics Cefaclor and Cefroxidine.

Earlier reported method for (2f) and (2g) comprises laborious two step process involving ozonolysis⁶, isolation of intermediate hydroxy sulfoxide and then its deoxygenation by PCl₃/ DMF⁷.

Experimental :

All melting points were taken on electrothermal 9300 and are uncorrected. HPLC analyses were done on Hewlet-Packard model 1090 liquid chromatograph while ¹HNMR and IR spectra were recorded on FT R-1500 and Perkin Elmer 16 PC-PT respectively. The structure of the isolated reaction products shown in table were confirmed by IR, ¹HNMR comparison with the authentic samples.

General Procedure :

The cephalosporin sulfoxide was dissolved in CH₂Cl₂ at r.t. followed by the addition of Lawesson reagent (1.2 - 1.5 mol. eq.). The contents were stirred for 15 - 30 min. at 35 - 37°C and completion of reaction was monitored by TLC. Reaction mixture was filtered and evaporated to dryness under vacuum. Addition of MeOH to the residue followed by stirring for 30 min., filtration, washing with MeOH and drying afforded pure, product.

References :

1. Trost, B.M., Fleming, I., *Comprehensive Organic Synthesis*, Vol. 8, **1991**, Pergamon Press.
2. Barton, D.H.R., Greig, D.G.T, et al., *J. Chem. Soc., Chem. Commun.*, **1970**, 1683.
3. Biggadike, K.; Humber, D.C. Laundon, B.; Lon, A.G., Ramsay, M.V.J., *Tetrahedron* **1985**, 41, 2025.

4. Ramussen, J.B., Jorgensen K.A., Lawesson S.O., *Bull. Soc. Chim. Belg.* **1978**, 87, 307.
5. Bartsch, H., Erker, T., *Tetrahedron Letts*, **1992**, 33, 199.
6. Kukolja, S., Spry, D.O., U.S. Patent 625,281, 1977; *Chem. Abstr.* **1977**, 87, 53347w.
7. Murphy, C.F., Webber, J.A., Kaiser, G.V., Heyningen, E.M.V., Wright, I.G., Cooper, R.D.G., Ger. Offen 1,940,080, 1970; *Chem. Abstr.* **1971**, 74, 22863P

(Received in The Netherlands 18 September 1995)

