

This article was downloaded by:

On: 28 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713618290>

Highly Stereoselective Tandem Pummerer Reaction/ α -Hydroxy Imine Rearrangement of E.P. β -Sulfinylenamines

Pierfrancesco Bravo; Marcello Crucianelli; Alessandro Volonterio; Matteo Zanda

To cite this Article Bravo, Pierfrancesco , Crucianelli, Marcello , Volonterio, Alessandro and Zanda, Matteo(1997) 'Highly Stereoselective Tandem Pummerer Reaction/ α -Hydroxy Imine Rearrangement of E.P. β -Sulfinylenamines', *Phosphorus, Sulfur, and Silicon and the Related Elements*, 120: 1, 353 – 354

To link to this Article: DOI: 10.1080/10426509708545545

URL: <http://dx.doi.org/10.1080/10426509708545545>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Highly Stereoselective Tandem Pummerer Reaction/ α -Hydroxy Imine Rearrangement of E.P. β -Sulfinylenamines

PIERFRANCESCO BRAVO, MARCELLO CRUCIANELLI,[†]
 ALESSANDRO VOLONTERIO AND MATTEO ZANDA

C.N.R. - C.S.S.O.N. Dipartimento di Chimica del Politecnico, via Mancinelli
 7, I-20131 Milano, Italy. [†] Dipartimento di Chimica, Ingegneria Chimica e
 Materiali, Università di L'Aquila, Via Vetoio, I-67010, Italy

Abstract. The highly stereoselective tandem Pummerer reaction/ α -hydroxy imine rearrangement of E.P. α -fluoroalkyl- β -sulfinylenamines affording chiral non-racemic fluoropyruvaldehydes *N,S*-ketals is described.

The synthesis of fluorosubstituted organic fine chemicals is an important goal, owing to the outstanding chemical and biomedical properties induced by the insertion of fluorine. However, the stereoselective synthesis of fluoroorganic molecules represents a significant challenge for the chemist.

We have recently reported the synthesis of enantiomerically pure α -fluoroalkyl- β -sulfinylenamines **1**, new useful fluorinated chiral templates.¹

Treatment of **1** with trifluoroacetic anhydride, followed by addition of silica gel or of an aqueous NaHCO₃ solution, gives rise to a stereoselective tandem Pummerer reaction/arylthio group migration, producing the corresponding fluoro pyruvaldehydes *N,S*-ketals **2** in high enantiomeric excess (figure 1 and table 1).²

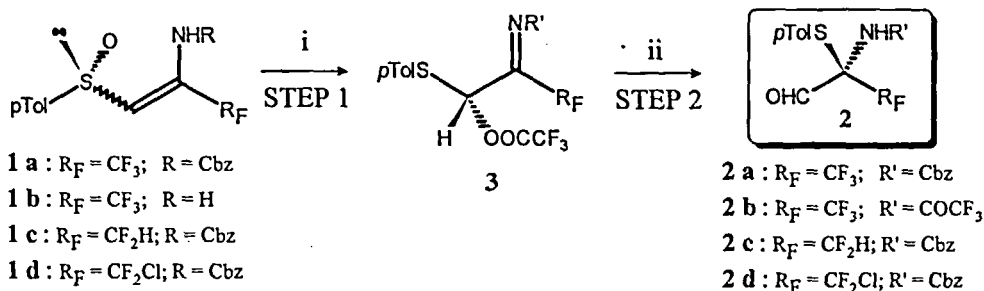


FIG. 1. Key: (i) TFAA, THF, 0°C, 1 min; (ii) NaHCO₃ 5% or SiO₂/H₂O (see table 1), 0°C, 10 min.

TABLE 1. Stereoselective formation of fluoropyruvaldehydes *N,S*-ketals **2** from sulfoxides **1**.

Enamine	R _F	Product	NaHCO ₃ 5%; e.e. (yield)	SiO ₂ then H ₂ O; e.e. (yield)
(<i>R</i>)-(Z)- 1a	CF ₃	(+)-(<i>R</i>)- 2a	68 % (85 %)	74 % (49 %)
(<i>S</i>)-(Z)- 1a	CF ₃	(-)-(<i>S</i>)- 2a	68 % (85 %)	not performed
(<i>R</i>)-(Z)- 1b	CF ₃	(+)-(<i>R</i>)- 2b	67 % (88 %)	73 % (71 %)
(<i>R</i>)-(Z)- 1c	CF ₂ H	(+)-(<i>R</i>)- 2c	42 % (86 %)	62 % (58 %)
(<i>R</i>)-(E)- 1c	CF ₂ H	(+)-(<i>R</i>)- 2c	6 % (86 %)	8 % (56 %)
(<i>R</i>)-(Z)- 1d	CF ₂ Cl	(+)-(<i>R</i>)- 2d	not performed	79 % (70 %)

The formation of the intermediate imine **3** was confirmed by performing the reaction in a NMR tube. Indeed, addition of trifluoroacetic anhydride (1 equiv) to a THF-*d*₈ solution of enamine **1**, resulted in the clean formation of **3**, stable for several days at room temperature.

In the light of these results, a reasonable mechanism for the stereoselective formation of the aldehydes **2** from **1** involves a Pummerer reaction (step 1), followed by an α -hydroxy imine rearrangement (step 2), both occurring with high stereoselection.

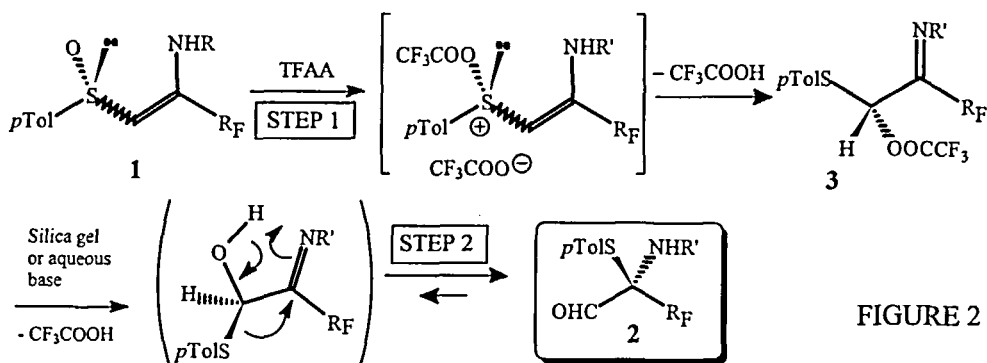
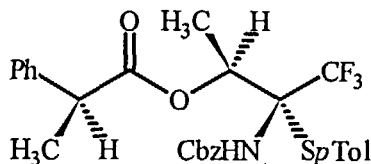


FIGURE 2

The absolute stereochemistry of the aldehydes **2** has been determined by X-ray crystallographic analysis of the enantiomerically pure molecule **4**, obtained by addition of CH₃MgCl to (*R*)-**2a** and subsequent esterification with (+)-(*S*)- α -phenylpropionic acid (figure 3).



4 FIGURE 3

REFERENCES

1. Arnone, A.; Bravo, P.; Capelli, S.; Meille, S. V.; Zanda, M.; Cavicchio, G.; Crucianelli, M., *J. Org. Chem.*, **61**, 3375 (1996).
2. Bravo, P.; Crucianelli, M.; Fronza, G.; Zanda, M., *Synlett*, 249 (1996).