

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>

Enantioselective Reduction of 2-Ketoalkanephosphonate by Baker's Yeast

Ke Wang^a; Zuyi Li^a; Chengye Yuan^a

^a Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, China

Online publication date: 27 October 2010

To cite this Article Wang, Ke , Li, Zuyi and Yuan, Chengye(2010) 'Enantioselective Reduction of 2-Ketoalkanephosphonate by Baker's Yeast', *Phosphorus, Sulfur, and Silicon and the Related Elements*, 177: 6, 1797 — 1800

To link to this Article: DOI: 10.1080/10426500212307

URL: <http://dx.doi.org/10.1080/10426500212307>

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.



ENANTIOSELECTIVE REDUCTION OF 2-KETOALKANEPHOSPHONATE BY BAKER'S YEAST

Ke Wang, Zuyi Li, and Chengye Yuan
Shanghai Institute of Organic Chemistry, Chinese Academy
of Sciences, Shanghai, China

(Received July 29, 2001; accepted December 25, 2001)

Bioreduction of 2-oxo-3-halo (or azido) alkanephosphonates and 4-ethoxy-4,2-dioxobutanephosphonates by baker's yeast afforded 3-substituted 2-hydroxyalkanephosphonates in moderate to good yields and ee value. Moreover, a regio- and stereoselective bioreduction of 2,3-dioxoalkanephosphonates and 2,4-dioxoalkanephosphonates by baker's yeast was studied also. The resulting chiral hydroxy compounds can be used as chirons for the stereoselective synthesis of biologically active molecules.

Keywords: Baker's yeast; dicarbonyl phosphonates; monocarbonyl phosphonates

Baker's yeast (*Saccharomyces cerevisiae*) is now well recognized as a valuable stereoselective reagent in biotransformations of organic molecules.^{1–3} The asymmetric reduction of carbonyl groups with this microbiological substance has been studied extensively; nevertheless, there are only a few reports dealing with the enzymatic reduction of their phosphorus analogs, namely, β -ketoalkanephosphonates.⁴ On the other hand, chiral hydroxyalkanephosphonic acids have received much attention due to their unique physiological activities. As a part of our systematic study on the biotransformation of organicphosphorus compounds, we report in this paper the bioreductive behaviors of monocarbonyl phosphonates and dicarbonyl phosphonates.

This project was supported by the National Natural Science Foundation of China (NNSFC), grants 20072052 and 29832050.

Address correspondence to Chengye Yuan, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China.

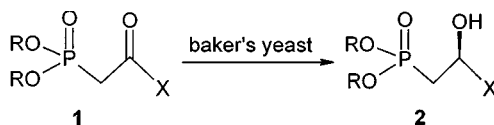


FIGURE 1

RESULTS AND DISCUSSION

Reduction of Monocarbonyl Phosphonates

Bioreduction of 3-substituted 2-oxoalkanephosphonates by baker's yeast (Figure 1 and Table I) afforded 3-substituted 2-hydroxyalkanephosphonates in moderate to good yields and *ee* value. These compounds could serve as useful chiral building blocks for the stereoselective synthesis of phosphorus analogs of biologically active molecules, including (*R*)-carnitine and (*R*)-GABOB.

Reduction of Dicarbonyl Phosphonates

The reduction of 4-alkoxy-4,2-dioxobutanephosphonate is shown in Figure 2.

2-Ketoalkanephosphonates are commonly employed as synthetic reagents, particularly in the Horner–Wadsworth–Emmons reaction. The nonracemic 3(4)-hydroxy-2-oxo-alkanephosphonates should be important as synthetic building blocks, since they are phosphorus-functionalized aldols. The Horner–Emmons olefination leading to nonracemic 1-hydroxy-4-alken-3-ones is therefore attractive. An

TABLE I Reduction of **1** with Baker's Yeast

Substrate	R	X	Time (h)	Yield (%)	<i>ee</i> (%) ^a	Configuration ^b
1a	Me	CH ₂ Cl	24	74	70	<i>R</i>
1b	Et	CH ₂ Cl	12	82	72	<i>R</i>
1c	iPr	CH ₂ Cl	24	57	13	—
1d	nBu	CH ₂ Cl	24	88	70	<i>R</i>
1e	Et	CH ₂ Br	24	35 ^c	83	<i>R</i>
1f	iPr	CH ₂ Br	24	41 ^c	52	—
1g	nBu	CH ₂ Br	24	55 ^c	87	<i>R</i>
1h	Et	CH ₂ N ₃	12	77	92	<i>S</i>
1i	Et	CF ₃	48	86	52	—
1j	Et	C ₃ F ₇	24	55	20	—

^aThe *ee* (%) was determined by the use of quinine as a chiral solvating agent.

^bThe absolute configuration was determined according to Mosher's methods.

^cThe 2-oxo-propane-phosphonate was isolated as a by-product.

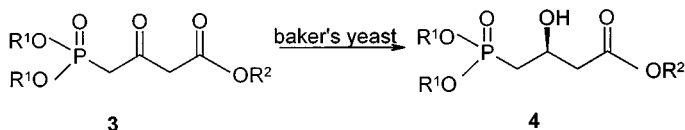


FIGURE 2 $\text{R}^1 = \text{Me, Et, } i\text{-Pr, } n\text{-Bu}$; $\text{R}^2 = \text{Me}$; yield 46–77%, *ee* 55–85%.

interesting route to a nonracemic 3(or 4)-hydroxy-2-ketophosphonate has been developed by bioreduction of dialkyl 2,3(or 4)-dioxoalkanephosphonates.

Regio- and Stereoselective Reduction of Dialkyl 2,3-Dioxoalkanephosphonates

α -Hydroxyketones are versatile chiral synthons for the construction of optical active organic compounds due to reactive functional groups: carbonyl and hydroxyl groups, which can easily be transformed to vicinal diols, amino ketones, and other functional groups. To obtain chiral α -hydroxyketones, reduction mediated by yeast is a powerful tool. In yeast reduction, two regioisomeric α -hydroxyketones are produced, and these hydroxyketones can be successively reduced to the diol. Therefore, chemical yields of the α -hydroxyketones are low. For asymmetric synthesis in such a reduction process, chemoselectivity, regioselectivity, and enantioselectivity should be taken in consideration (Figure 3).

Regio- and Stereoselective Reduction of Dialkyl 2,4-Dioxoalkanephosphonates

A series of phosphorus-based carbonyl compounds, namely, dialkyl 2,4-dioxoalkanephosphonates (**8**), was prepared by reaction of carbanion

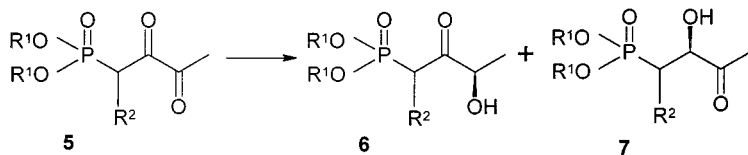


FIGURE 3

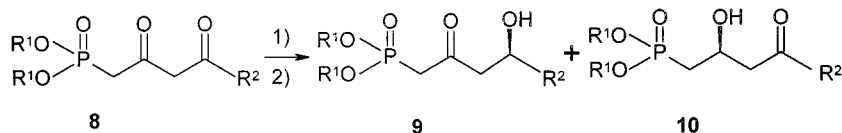


FIGURE 4 $\text{R}^1 = \text{Et, } n\text{-Bu}$; $\text{R}^2 = \text{Me, CF}_3, \text{C}_3\text{H}_7$; (1) baker's yeast; (2) yield 9/10 = 45/24 or 67%, *ee* 9 90–94%.

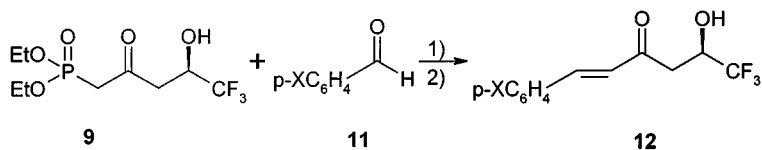


FIGURE 5 X = H, *p*-MeO, *p*-Me, *p*-Cl, *p*-Br, *p*-F, *m*-NO₂; (1) DBU, LiCl, 12–24 h, rt; (2) yield 53–72%.

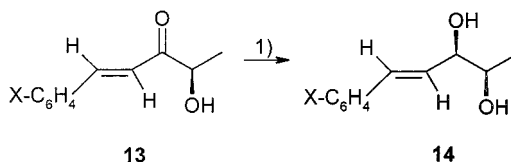


FIGURE 6 X = H, Me, MeO; (1) baker's yeast.

resulted from 2-methyl-2-oxoethanephosphonate with substituted acetates. Bioreduction of **8** by baker's yeast at 30°C for 24–48 h offered an isomeric mixture consisting of **9/10**, when R¹ is methyl, in 45/24% yield as well as 92/80% *ee* value, respectively. It is interesting to note that when R² is CF₃ or C₃F₇, a regio- and stereoselective reduction was observed. Only **9** was obtained, in 54–67% yield and 90–94% *ee* value.

The chiral 4-hydroxy-2-oxoalkylphosphonates **9** thus obtained underwent Horner–Emmons olefination as expected. Thus a series of *trans*-6,6,6-trifluoro-5-hydroxy-1-(substituted)phenyl-1-hexen-3-ones **12** was prepared by reaction of 5,5,5-trifluoro-4-hydroxy-2-oxopentane phosphonates with substituted benzaldehyde under very mild condition in 33–67% yields (Figure 5).

It is interest to note that under the Horner–Wadsworth–Emmons reaction, compound **6** gave **13** conveniently and that provided **14**, a chiral vicinal diol, upon another baker's yeast reduction (Figure 6).

REFERENCES

- [1] R. Csuk and B. I. Glanzer, *Chem. Rev.*, **91**, 49 (1991).
- [2] R. Csuk and B. I. Glanzer, In *Stereoselective Biocatalysis*, ed. R. N. Patel (Marcel Dekker, New York, 2000), p. 527.
- [3] S. Servi, *Synthesis*, **8**, 1 (1990).
- [4] E. Zymanczyk-Duda and B. Lejczak, *Tetrahedron*, **51**, 11809.