## [2,3]-WITTIG REARRANGEMENT OF ALLYLIC GLYCOLATE ESTERS VIA BORON AND TIN ENOLATES

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Abstract: Wittig rearrangement of allylic glycolate esters via boron and tin enolates gave diastereoselectivities as high as 99.5 : 0.5. Tin enolates were more stereoselective than boron enolates.

The [2,3]-Wittig rearrangement is a highly useful transformation for acyclic diastereoselective reactions. In recent years considerable attention has been focused on aspects which lead to milder reaction conditions and improved stereoselectivities.<sup>2</sup> A variety of functional groups have been investigated in this Investigations involving the highly useful ester functionality have been context. limited, due to its low reactivity.<sup>3</sup> This problem has been overcome by Nakai and Mikami by using 20% HMPA/THF as the solvent system.<sup>4</sup> The enolate of an  $\alpha$ -allyloxy ester has two possible modes of sigmatropic rearrangement available (Scheme 1). It has been shown when M=Li or SiMe3 a [2,3]-Wittig rearrangement occurs, the latter requiring a catalytic amount of TMSOTf.4,5,6 Our initial investigation into the asymmetric Wittig rearrangement focused on the rearrangement with other types of enolates. We report here our results with boron and tin enolates.<sup>7</sup> To the best of our knowledge, this is the first reported [2,3]-Wittig rearrangement via boron enclates and the first systematic study of tin enolates.8



The rearrangement substrates 1-8 were prepared in a straightforward manner as exemplified by equation 1 (43-77%).<sup>5</sup> The [2,3]-Wittig rearrangements proceeded by generating the enolate with diisopropylethylamine in the presence of dibutylboron triflate or tin triflate at -78°C followed by warming to ambient temperature (equation 2).<sup>9,10</sup> The results are summarized in the Table. The products were formed exclusively from Wittig rearrangements with no [3,3]-rearrangements being observed. The stereochemistry was assigned by comparing the products of substrates 1 and 2 to authentic samples derived from the method of Nakai.4,11

	$CH_{3} \rightarrow OH \qquad CI \frown CO_{2}$ $H_{3} \rightarrow OH \qquad 10 eq. NaH THF, reflux$ $CH_{3}, K_{2}CO_{3} \qquad CH_{3} \rightarrow OH$ $DMF, 20^{\circ}C$	$H \qquad CH_3 \qquad O \qquad CO_2CH_3$ $1,77\%$	,CO₂H	(1)
	R i-Pr <sub>2</sub> NEt, -78 to 25°C	HO CO <sub>2</sub> CH <sub>3</sub> + R' <b>a</b>		O₂CH₃ (2)
<u>Table</u> entry	e: Diastereoselectivity of Wittig Rea substrate	arrangement <sup>1</sup> Lewis acid	<u>a:b</u>	isolated vield(%)
1 2 3	CH <sub>3</sub> O CO <sub>2</sub> CH <sub>3</sub> 1	Sn(OTf)₂ n-Bu₂BOTf n-Bu₂BOTf	0.5 : 99.5 8 : 92 8 : 92	40 55 <sub>2</sub> 50 <sup>2</sup>
4 5 6	CH <sub>3</sub> 0 CO <sub>2</sub> CH <sub>3</sub> 2	Sn(OTf)₂ n-Bu₂BOTf n-Bu₂BOTf	85 : 15 70 : 30 69 : 31	10 54 66 <sup>2</sup>
7 8	Сн <sub>3</sub> Сн <sub>3</sub> СН <sub>3</sub> З	Sn(OTf)₂ n-Bu₂BOTf	-	37 decomposition
9 10		Sn(OTf)₂ n-Bu₂BOTf	-	traces 55
11	PhOCO <sub>2</sub> CH <sub>3</sub> 5	n-Bu <sub>2</sub> BOTf	20 : 80	55
12	CH <sub>3</sub>	n-Bu <sub>2</sub> BOTf	26 : 74	53
13		n-Bu <sub>2</sub> BOTf	53 : 47	60
14	о <sup>со2</sup> сн <sup>3</sup> В	n-Bu <sub>2</sub> BOTf	48 : 52	59

1) Unless otherwise noted  $CH_2Cl_2$  was the reaction solvent. 2) Hexanes was the reaction solvent.

Excellent diastereoselectivities (0.5 : 99.5 to 8 : 92) were observed with substrate 1, having an E-olefin, whether boron or tin enolates were used (entries 1-3). Lower stereoselectivities (85 : 15 to 69 : 31) were observed with Z-substrate 2 (entries 4-6). This is unusual in that most [2,3]-Wittig rearrangements involving Z-olefins exhibit higher diastereoselectivities.<sup>2</sup> The tin enolates were more selective than the boron enolates (entries 1, 2, 4, and 5). As expected, the reactions were solvent independent (entries 2, 3, 5, and 6). The rearrangement involving a tertiary allylic ether gave a low yield with tin triflate and decomposition with dibutylboron triflate (entries 7 and 8).<sup>12</sup> The disubstituted substrates at the proximal and distal carbon of the olefin gave 55% and 53% yield (entries 10 and 12) with a ratio of 26 : 74 in the latter. The phenyl-substituted olefin gave a ratio of 20 : 80 (entry 11). When the olefins were in an endocyclic position of a 5- or 6-membered ring low stereoselectivities were obtained (entries 12 and 14).

The rate of rearrangement was measured qualitatively by monitoring the reaction with <sup>1</sup>H NMR. A solution of diisopropylethylamine and di-n-butylboron triflate was chilled to -60°C and substrate 1 was added. The sample in the NMR probe was warmed to -30°C and a <sup>1</sup>H NMR spectra were recorded at intermediate temperature and time during this period. Monitoring the disappearance of the olefin resonance peaks of the substrate and the appearance of the terminal olefin peaks of the product revealed that  $t_{1/2}$  of the rearrangement was <20 min at -30°C.

An inherent limitation of the [2,3]-Wittig rearrangement with lithium enolates is the range of applicable substrates. It was of interest to compare this limitation with boron enolates. For example, the lithium dianion of substrate **9** (R=H) undergoes a [2,3]-Wittig rearrangement and a [1,2]-shift in a 67:33 ratio (equation 3).<sup>2</sup> Treatment of **10** with dibutylboron triflate and diisopropylethylamine under the standard conditions led to an identical ratio of [2,3]-Wittig rearrangement and [1,2]shift in 71% yield. The diastereomeric ratio was the same as that of entry 14 in the table. The lithium enolate and the boron enolate gave the same amount of the undesired [1,2]-shift.<sup>13</sup>



The stereochemical outcome of the [2,3]-Wittig rearrangement depend on the carbanion structure<sup>2</sup> and in the case of esters, the anionic carbon has a high sp<sup>2</sup>-character. Inspection of molecular models shows two possible transition states for each olefin geometry which satisfy the stereoelectronic requirements of the rearrangement. The major isomer appears to come from the synclinal transition state. It is not clear as to the reason for this at this time.



## **References and Notes:**

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- 11. It has been assumed the substrate 3-8 rearrange in the same manner as 1 and 2.
- 12. For [2,3]-Wittig rearrangement of tertiary allylic ethers of oxazolines see: Wittman, M. D.; Kallmerten, J. J. Org. Chem. **1988**, *53*, 4631-4633.
- 13 The substrate **10** (R=CH<sub>3</sub>) was prepared by LiAlD<sub>4</sub> reduction of cyclohexenone to give 1-deutriocyclohex-2-en-1-ol (76%) followed by the method outlined in equation 1 (52%).

(Received in USA 23 April 1991)