Table IV. ^{13}C NMR and ^{1}H NMR Spectral Data for 2,5-Dibromo-3-(trimethylsilyl)thiophene 7a Obtained by Independent Synthesis[a]

		^{13}C NMR		
compd	carbon	δ (ppm)	(increment values)[b] δ (ppm)	(ref 8) δ (ppm)
7a	C_2	117.8	(117.8)	(116.5)
	C_3	142.5	(144.5)	(137.4)
	C_4	135.2	(134.7)	(134.4)
	C_5	111.1	(112.1)	(116.5)
	C_6	-0.9	-	(-0.8)
compd	hydrogen	^{1}H NMR: δ (ppm)		(ref 8)
7a	H_4	6.83		(7.00)
	CH_3	0.34		(0.33)

[a] Reference 10. [b] Reference 11.

An unequivocal result was obtained by independent synthesis of 3-bromo-2-(trimethylsilyl)thiophene (11) (Scheme IV),[14] which was identical in physical and spectroscopical properties with compound A.

As a final synthetic proof for the wrong substitution pattern **7a–d** given in the literature we have prepared the postulated 2,5-dibromo-3-(trimethylsilyl)thiophene (**7a**) within a preliminary experiment (Scheme V) via a new pathway: by reacting 3-(trimethylsilyl)thiophene (**10**) with 2 equiv of LDA and 2 equiv of BrCN at -80 °C a 2:1 mixture of 2-bromo-4-(trimethylsilyl)thiophene (**12**) and the target compound **7a**, which could be isolated and purified by Kugelrohr distillation, was obtained.[15]

The spectroscopic shift values for **7a** are completely different from those published by Zimmer (Tables IV and I) who obviously also has obtained the rearranged 3,5-dibromo-2-(trimethylsilyl)thiophene (**8**). Therefore it can be stated without any doubt that interaction of one equivalent of LDA in THF/-78 °C with 2,5-dibromothiophene leads—via BCHD mechanism and upon quenching with any electrophile—only to products with a 3,5-dibromo pattern.

We are currently optimizing the synthesis of the new compound **7a** and investigating the dependence of the BCHD mechanism on various reaction parameters.

Acknowledgment. We are dedicating this paper to our Head, Prof. Dr. Fritz Sauter, on the occasion of his 60th birthday.

(14) 2,3-Bromothiophene (1) was reacted with 1 equiv of BuLi in dry Et_2O at -80 °C (similar to: Seconi, G.; Eaborn, C.; Stamper, J. G. *J. Organomet. Chem.* **1981**, *204*, 153) to form via metal–halogen exchange (3-bromo-2-thienyl)lithium. Subsequent quenching with TMSCl afforded product 11 in high yield (87% upon distillation) and without any side products. ^{1}H NMR ($CDCl_3$): δ 7.44 (d, 1 H, J_{AB} = 4.9 Hz), 7.09 (d, J_{AB} = 4.9 Hz), 0.40 (s, 9 H).

(15) To a stirred solution of 12.9 mmol of diisopropylamide in dry tetrahydrofuran (THF) at -80 °C was added 1 g (6.4 mmol) of **10** in 10 mL of dry THF rapidly. After being stirred for 30 min at -80 °C, a solution of 1.35 g (12.8 mmol) of cyano bromide in 10 mL of dry THF was added dropwise. Stirring was continued for 15 min, and then the solution was hydrolyzed. The organic phase was separated and dried (anhydrous Na_2SO_4), and the THF was evaporated. The resulting brown residue was distilled in vacuum. Fraction I: bp 150 °C (80 mm); yield 0.8 g (53%); no further purification; ^{1}H NMR ($CDCl_3$) δ 7.30 (d, 1 H, J_{AB} = 1.2 Hz), 7.08 (d, 1 H, J_{AB} = 1.2 Hz), 0.26 (s, 9 H); ^{13}C NMR ($CDCl_3$) -0.9 (q), 112.5 (s, C_2), 132.7 (d, C_5), 133.8 (d, C_3), 142.9 (s, C_4). Fraction II: distilled twice; bp 150 °C (20 mm); yield 0.5 g (25%) of **7a**; spectroscopic data see Table IV. Anal. Calcd for $C_7H_{10}Br_2SSi$: C, 26.77; H, 3.21. Found: C, 27.02; H, 3.21.

[2,3] Wittig Rearrangement of Nonracemic Propargyloxyacetic Acids and Esters. Synthesis of Optically Active 2,5-Dihydrofurans

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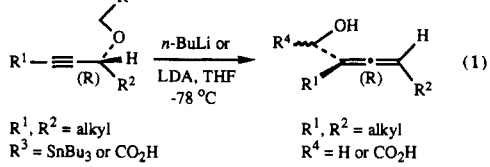
Received March 1, 1990

Summary: Optically active propargyloxyacetic acids **4**, available in ca. 90% ee through reduction of alkynones **2** with Chirald–$LiAlH_4$ followed by alkylation with chloroacetic acid, undergo highly stereoselective [2,3] rearrangement upon treatment with LDA in THF at -78 °C to afford α-(*S*)-hydroxy-β-(*R*)-allenic acids with complete transfer of chirality and >90% diastereoselectivity. The diastereomeric methyl ester derivatives **5a** and **13** cyclize stereospecifically to trans and cis 1,5-dihydrofurans upon treatment with $AgNO_3$–$CaCO_3$, PhSeCl, or NBS.

We recently disclosed a new application of the [2,3] Wittig rearrangement in which nonracemic propargyl (tributylstannyl)methyl ethers and α-(propargyloxy)acetic acids afford optically active allenylcarbinols and α-hydroxy-β-allenic carboxylic acids with complete chirality transfer (eq 1).[1] Additional studies have now shown that such rearrangements of the acetic acid and related acetic ester systems are highly diastereoselective as well. Furthermore, the derived α-hydroxy ester products are readily and stereospecifically converted to 2,5-dihydrofurans.



The (propargyloxy)acetic acids **4** utilized in this preliminary study were prepared along the lines of our previous report as outlined in Scheme I.[1] Reduction of the alkynones **2** with Chirald–$LiAlH_4$[2] afforded propargylic alcohols **3** of ca. 90% ee as judged by ^{1}H NMR analysis of the *O*-methyl mandelates.[3] Base treatment of acid **4a** with 2.5 equiv of LDA in THF at -78 °C followed by esterification led to the allenic ester **5a** as a 93:7 mixture of diastereomers in 80% yield. Acid **4b** was similarly converted to ester **5b** as a 91:9 mixture of diastereomers in 48% yield along with an equal amount of elimination product **6b** (1:1 *E*:*Z*). The configuration of **5a** was ascertained by ^{1}H NMR analysis of the *O*-methylmandelates

(1) Marshall, J. A.; Robinson, E. D.; Zapata, A. *J. Org. Chem.* **1989**, *54*, 5854.

(2) Aldrich Chemical Co. Chirald is a trade name for Darvon alcohol. Cf. Yamaguchi, S.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 1870.

(3) Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovic, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. D. *J. Org. Chem.* **1986**, *51*, 2370.

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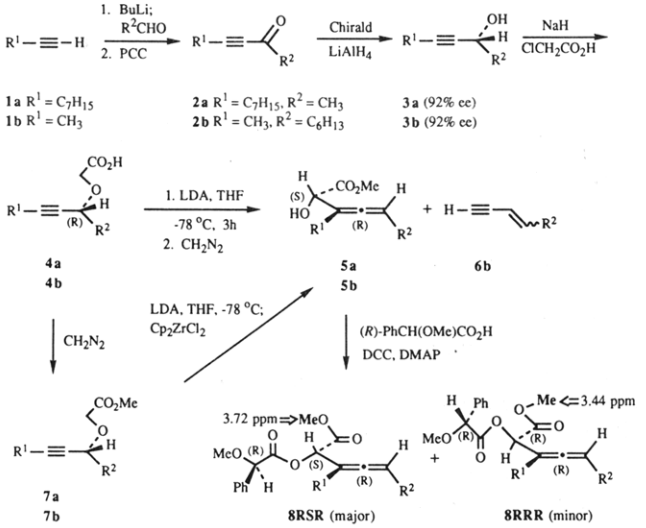
Scheme I



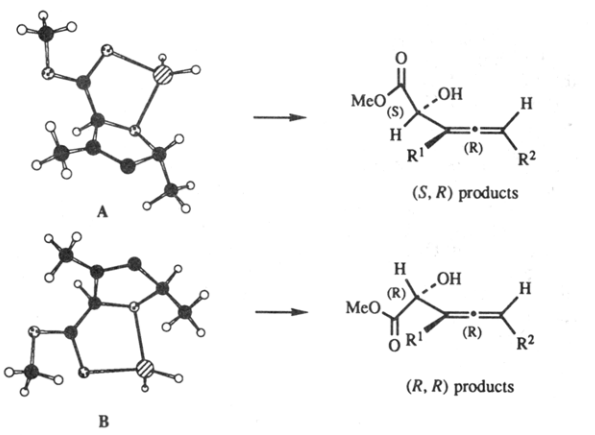


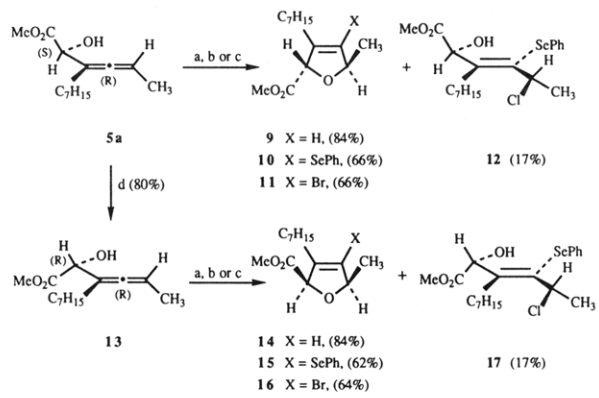
Figure 1. Chem 3D representations of diastereomeric [2,3] Wittig transition states involving chelated Zr enolates derived from methyl (*R*)-(propargyloxy)acetates (e.g. **7**, $R^1 = R^2 = CH_3$). Cp ligands are omitted for clarity.

8RSR (93%) and **8RRR** (7%).[3] The ester OCH_3 signal of the latter showed significant shielding, as expected for the **RRR** diastereomer.

Formation of the elimination product **6b** was significantly diminished when the [2,3] rearrangement was conducted on the Zr complex of the enolate of methyl ester **7b**.[4] Hydroxy ester **5b** was thus secured as the sole diastereoisomer in 45% yield accompanied by only 5% of **6b** and a number of unidentified byproducts. Likewise, ester **7a** rearranged to hydroxy ester **5a**, a single diastereomer, in 57% yield. The remarkable diastereoselectivity of these rearrangements is consistent with steric interactions involving R^2 in the diastereomeric chelated bicyclo[3.3.0] transition states A and B (Figure 1). Transition state B leading to the *R,R* allenic ester is disfavored by steric interactions between R_2 (CH_3) and the ligands on Zr.

With a view toward applying these results to the synthesis of hydrofuran subunits of natural products,[5] we examined the cyclization of allenylcarbinol **5a** under several conditions to evaluate efficiency and stereoselectivity (Scheme II). Best results were obtained with $AgNO_3$–$CaCO_3$ in aqueous acetone,[6] whereupon the *trans*-2,5-dihydrofuran **9** was obtained as the sole product in 84% yield. Upon treatment with PhSeCl in CH_2Cl_2,[7] allenylcarbinol **5a** afforded a single selenophenyl dihydrofuran (**10**) in 66% yield along with 17% of the presumed (*E*)-allylic alcohol **12** (one isomer). The ratio of these two products may reflect the relative preference for *si* vs *re* attack on the allenic double bond by the PhSe moiety.[7] Cyclization of allenylcarbinol **5a** could also be effected by NBS to give the bromodihydrofuran **11** in 66% yield.[8]

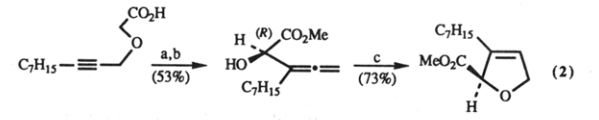
Scheme II[a]



[a] (a) $AgNO_3$, $CaCO_3$, Me_2CO–H_2O, room temperature, 48 h; (b) PhSeCl, CH_2Cl_2, room temperature, 5 min; (c) NBS, CH_2Cl_2, room temperature, 48 h; (d) Ph_3P, DEAD, $PhCO_2H$ (90%); K_2CO_3, MeOH (89%).

To confirm the diastereomeric purity of the cyclization products **9**–**11** and to develop a route to *cis*-2,5-dihydrofurans, we carried out a Mitsunobu inversion of alcohol **5a**[9] and performed analogous cyclizations on the diastereomer **13**. The 2,5-dihydrofurans **14**–**16** were thus obtained as single diastereoisomers.

In a further extension of our preliminary studies on the asymmetric synthesis of allenylcarbinols, we employed the chiral amide base lithium (*S,S*)-bis(α-phenylethyl)amide,[10] to effect [2,3] Wittig rearrangement of the achiral primary (propargyloxy)acetic acid (**18**) (eq 2). Esterification of the



(a) (*S,S*)-PhCH(Me)NHCH(Me)Ph, BuLi, THF, −78 °C; (b) CH_2N_2; (c) 1 equiv of $AgNO_3$, Me_2CO–H_2O (3:2), reflux

crude product afforded an optically active hydroxy ester enriched in the *R* enantiomer **19** (33% ee) according to ^1H NMR analysis of the *O*-methylmandelate.[3] This result is noteworthy as [2,3] Wittig rearrangement of prochiral acyclic propargylic allylic ethers with this base affords only racemic products.[10] Alcohol **19** was readily converted to the 2,5-dihydrofuran **20**.

Acknowledgment. Support for this work was provided by research grants from the National Science Foundation (CHE-8912745) and the National Institutes of Health (2 RO1 GM 29475).

(4) Cf. Kuroda, S.; Sakaguchi, S.; Ikegami, S.; Harramoto, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1988**, *29*, 4763. Uchikawa, M.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 4581.

(5) Cf. Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309. Mulholland, R. L., Jr.; Chamberlin, A. R. *J. Org. Chem.* **1988**, *53*, 1082.

(6) The conditions of Olsson, L.-I.; Claesson, A. *Synthesis* **1979**, 743.

(7) Cf. Beaulieu, P. L.; Morisset, V. M.; Garratt, D. G. *Tetrahedron Lett.* **1980**, *21*, 129.

(8) For a mechanistically oriented study on the addition of bromine to optically active allenes, see: Waters, W. L.; Linn, W. S.; Caserio, M. C. *J. Am. Chem. Soc.* **1968**, *90*, 6741.

(9) Mitsunobu, O. *Synthesis* **1981**, 1.

(10) Marshall, J. A.; Lebreton, J. *J. Am. Chem. Soc.* **1988**, *110*, 2925.