a twisted allene structure **8**.[10] The loss of activity with increase in temperature further suggests that **8** may rapidly racemize through an intermediate or transition state that can be represented by any of the three structures **6**, **11**, or **12** or a diradical.

Finally, since concerted opening of optically active **8** to **9** should give an active hydrocarbon, **13** was allowed to react with potassium menthoxide in the absence of the furan trap. Unfortunately, **9** was formed in only very low yield (only 2–3%; probably as a result of low thermal stability during the very slow reaction with the less reactive base). However, the small amount that was formed, after isolation as its silver salt and very thorough washing to remove all traces of menthol, was indeed found to be optically active ($[\alpha]_D^{25}$ +2.2 ± 0.2°; microcell). This suggests that the allene may be the progenitor of **9**, although further work will be required before this is secure.

Acknowledgment. We gratefully acknowledge support of this work by the National Science Foundation.

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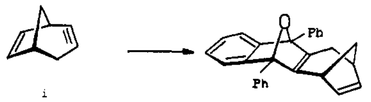
(9) Intuitively, a concerted elimination in competition with carbanion formation (without elimination) seems unlikely. However, unlike most β-eliminating systems, in this case the carbanion electrons are presumably orthogonal to the carbon–halogen bond and unlike orthogonal α-eliminating systems (such as bromoform) it is unlikely that much electron density is localized on the carbon with the leaving group. Intuition not withstanding, if this reaction does go via an allene intermediate (rather than an alkyne),[10] the results reported here require that at least a portion of the reaction go by a concerted mechanism.

(10) A possible alternative to the allene intermediate is the alkyne i. This is chiral and could therefore give active products. We feel, however, that this is unlikely for two reasons. First, despite careful searching, none of the alkyne adducts could be found and it seems unlikely that both syn and anti ii would completely tautomerize to the allene adducts. Second, in contrast to the allene,[3] the alkyne does not provide a viable mechanism for formation of **9** which is observed in the absence of trap but not in its presence.



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Enantioselective Aldol Condensations. 3. Erythro-Selective Condensations via Zirconium Enolates[1]

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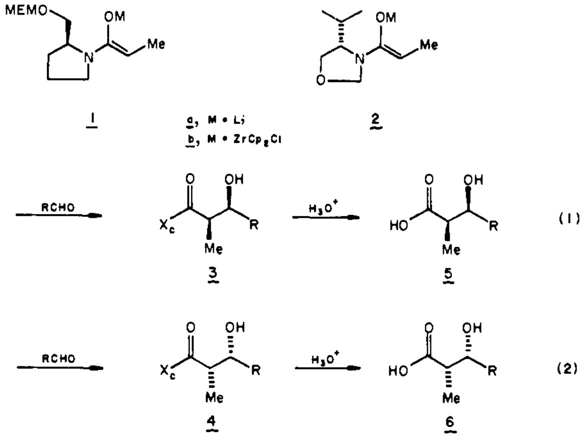
The important role that sterically demanding metal centers play in the enhancement of aldol stereoregulation has recently become apparent.[2,3] For dialkylboryl enolates kinetic aldol product stereochemistry has been shown to be strongly coupled to enolate geometry,[2] while for dicyclopentadienylchlorozirconium enolates kinetic erythro-selective condensations have been observed from either enolate geometry.[3] Recent studies from this laboratory have demonstrated that while the lithium enolates derived from prolinol amides exhibit excellent diastereoface selection (15–30) in alkylation reactions,[4] the complimentary aldol condensations were nearly stereorandom. The purpose of this communication is to report that high levels of aldol stereoregulation may be restored to the condensation process if zirconium enolates are employed and the complimentary amino acid derived amide enolates **1b** and **2b** exhibit excellent levels of asymmetric induction in the aldol process (eq 1, 2). Both of the illustrated chiral auxiliaries have been designed to incorporate a masked hydroxyl function which has been shown to assist in the acid-catalyzed amide hydrolysis vis N → O acyl transfer.[4]

Table I. Comparative Aldol Condensations of the Lithium and Zirconium Enolates **1** and **2** (eq 1, 2)[7]

enolate	metal^a	RCHO	product 3:4	distribution^b T_1:T_2	yield, %
1b	Zr	n-C_4H_9CHO	96:2	1:1	(3a) 69^c
1a	Li		39:29	15:17	
2b	Zr		1:97	1:1	(4a) 96^d
2a	Li		35:42	6:17	
1b	Zr	i-C_3H_7CHO	96:2	1.5:0.5	(3b) 77^c
1a	Li		43:36	9:12	
2b	Zr		0.5:97.5	1:1	(4b) 77^c
2a	Li		42:41	13:4	
1b	Zr	C_6H_5CHO	96:1	2:1	(3c) 71^c
1a	Li		31:33	23:13	
2b	Zr		1.5:94.5	2:2	(4c) 71^e
2a	Li		41:29	24:6	

^{a} Zr refers to $ZrCp_2Cl$. ^{b} Determined by capillary GLC and standardized to base 100. T_1 and T_2 refer to the threo diastereomers. ^{c} Chromatographed to 99% of a single diastereoisomer. ^{d} Purified by molecular distillation. Diastereoisomer ratio unchanged. ^{e} Purified by recrystallization, mp 139.5-140 °C. .



The lithium enolates **1a** and **1b**, which were generated from the respective propionamides[5] and LDA (THF, 0 °C, 30 min), were transformed into the corresponding zirconium enolates **1b** and **2b** by subsequent treatment with 1.1 equiv of Cp_2ZrCl_2 (0.16 M in THF).[3a] The aldol condensations with representative aldehydes were carried out between −78 and 0 °C as previously described.[3a] Complete aldol diastereomer analysis was carried out by capillary gas chromatography on the unpurified reaction products.[6] The comparative aldol condensations of the zirconium

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(1) Presented at the 12th International Symposium on the Chemistry of Natural Products, Tenerife, Canary Islands. Evans, D. A.; Takacs, J. M.; McGee, L. R.; Ennis, M. D.; Mathre, D. J.; Bartroli, J. *Pure Appl. Chem.* **1981**, in press. Evans, D. A.; McGee, L. R. Also presented at the 2nd Chemical Conference of the North American Continent, Las Vegas, NV, Aug 28, 1980; Abstract ORGN 288.

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(5) (a) The propionamide precursor of enolate **1a** is formed by alkylation of prolinol propionamide[4a] with MEMCl.[17] After workup and bulb-to-bulb distillation [bp 110 °C (<0.001 mm)] the desired amide was obtained in an 86% yield, $[\alpha]_D$ −66.4° (c 3.79, CH_2Cl_2). (b) The propionamide precursor of enolate **2a** is formed by azeotropic removal of water from an equimolar mixture of *l*-valinol and paraformaldehyde in benzene followed by acylation with propionic anhydride. After workup and bulb-to-bulb distillation [bp 90 °C (0.01 mm)] the desired amide was obtained in an 80% yield, $[\alpha]_D$ +20.7° (c 2.34, CH_2Cl_2).

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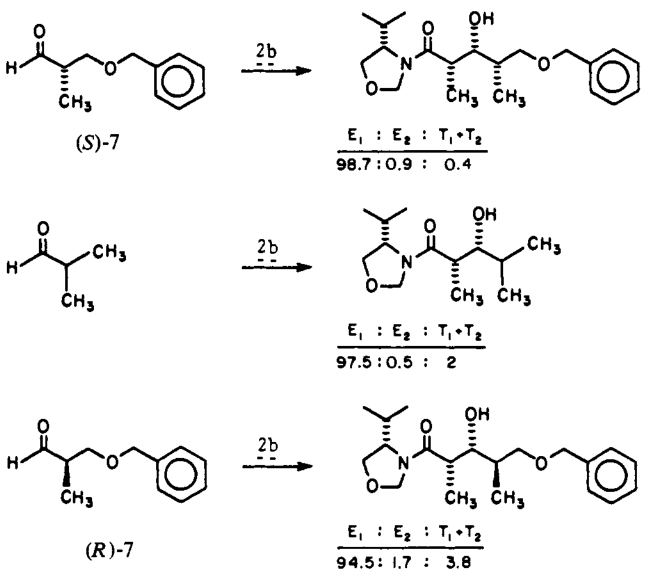
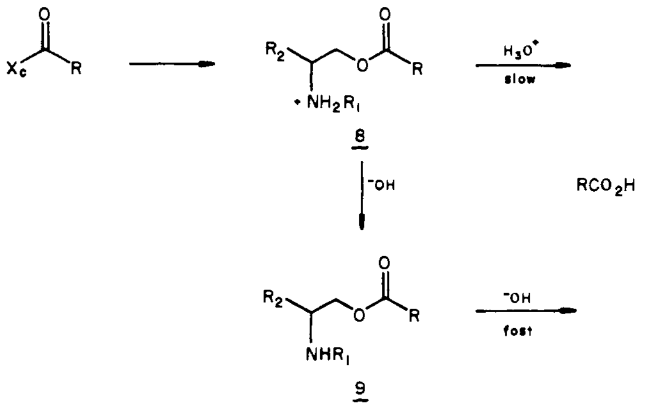
Scheme I



Scheme II



and lithium enolates derived from **1** and **2** are summarized in Table I.[7]

In all cases the lithium enolates exhibited low levels of both erythro–threo diastereoselection and enolate diastereoface selection under kinetic conditions (−78 °C, 5 s). In contrast, the zirconium enolates **1b** and **2b** afforded predominately a single aldol diastereomer for the illustrated aldehydes. The high levels of erythro diastereoselection (96–98%) noted with these enolates is in good agreement with other amide enolate condensations previously reported.[3a] Complimentary enolate diastereoface selection for **1b** and **2b** within the erythro product manifold (**3** vs. **4**) was also found to be excellent (50–200). From a mechanistic standpoint it is interesting to note that virtually no asymmetric induction was observed within the threo diastereomer manifold.

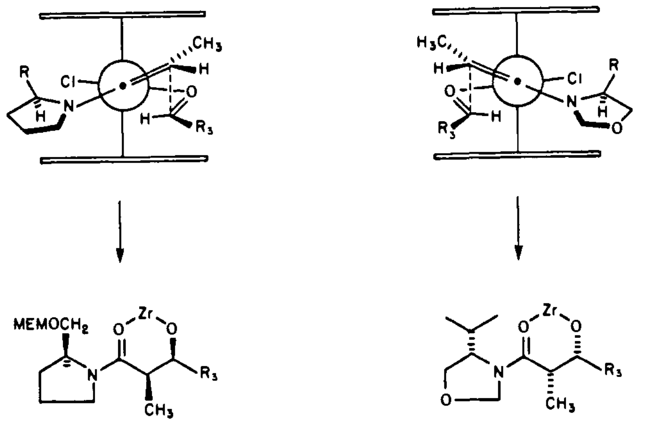
The aldol condensations of these enolates with chiral α-substituted aldehydes have also been examined. As illustrated in Scheme I, the condensation of zirconium enolate **2b** with both (*R*)-**7** and (*S*)-**7**[8] afforded comparable levels of erythro enantioselection.[7,9] Similar results were also noted in the aldol condensations between enolate **1b** and aldehydes (*R*)-**7** and (*S*)-**7**. In all of these reactions resident enolate chirality largely overrides the intrinsic Cram selectivity[10] imposed by resident chirality in the aldehyde condensation partner.[11]

Table II. Yield and Optical Rotation of Hydroxy Acids 6 and 7

acid	yield, %	$[\alpha]_D$, deg (*c*, g/100 mL)
5a	89	−13.8 (6.9, CH_2Cl_2)
6a	91	+14.9 (6.8, CH_2Cl_2)
5b	90	+9.3 (2.6, CH_2Cl_2)
6b	91	−9.7 (1.5, CH_2Cl_2)
5c	78[a]	+29.5 (3.7, $CHCl_3$)
6c	79[a]	−30.0 (3.7, $CHCl_3$)[b]

[a] Contains 3% threo from epimerization of the benzylic position. [b] $[\alpha]_D$ −29.5° (*c* 2.03, $CHCl_3$) (ref 11d).

Scheme III



The details of the acid-catalyzed hydrolysis of the aldol adducts are illustrated in Scheme II. Initial treatment of the aldol adducts **3** and **4** with 5% HCl (10 equiv H^+, 100 °C, 2 h) has been demonstrated to effect facile hydroxyl unmasking and subsequent N → O acyl transfer [12a] to give **8** followed by a much slower acid-catalyzed hydrolysis step to give the liberated erythro β-hydroxy acids.[12b] However, neutralization with aqueous sodium bicarbonate after acyl transfer resulted in the rapid liberation of the desired carboxylic acids (ca. 5 min, 25 °C). The general base-catalyzed hydrolysis of **9** is well precedented for related tertiary β-amino esters[12c] but is somewhat surprising in view of the potential competing O → N acyl transfer which has been documented for primary and secondary β-amino esters.[12d] In the absence of acid-sensitive functionality the enantiomeric erythro β-hydroxy acids **5** and **6** may be obtained in good yield without loss of stereochemistry at either stereocenter (Table II). An exception to this statement was found with the benzaldehyde adducts **5c** and **6c** where complete epimerization at the hydroxyl center was noted under the previously described hydrolysis conditions. However, if the hydrolyses of **3c** and **4c** were carried out under somewhat milder conditions (4 equiv of 5% HCl in an equal volume of dioxane, 4 h at reflux), hydroxyl epimerization was reduced to 3%. The relative stereochemical assignments for the acids **5** and **6** were determined by both ^1H and ^{13}C NMR,[13] and

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(6) Capillary gas chromatographic analyses were conducted on an Hewlett-Packard Model 5880A Level 3 Gas Chromatograph by using either a 30M × 0.32 mM fused silica WCOT SE-54 column or a 25M × 0.21 mM fused silica WCOT Carbowax column.

(7) Satisfactory combustion analysis and spectral data were obtained on all new compounds reported.

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(9) The absolute stereochemical assignment of the adduct derived from **2b** and (*R*)-**7** was determined by hydrolysis, reduction, and conversion to the *meso*-tribenzyl ether.

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(13) Heathcock, C. H.; Pirrung, M. C.; Sohn, J. E. *J. Org. Chem.* **1979**, *44*, 4294–4299.

the absolute stereochemical assignments were determined by deoxygenation[14] of the aldol adducts **3a** and **3b** and subsequent correlation with the α-methyl-substituted carboxylic acids of known absolute configuration.

It is clear that the erythro specificity of zirconium enolates is due to steric interactions in the transition state between the substituents on the enolate and the bulky cyclopentadienyl ligands of the metal.[1,15] One possible model for these interactions is shown in Scheme III. We speculate that the interaction of the cis-methyl group of the enolate with the cyclopentadienyl ligands and the influence of the side arm of the chiral pyrrolidyl ring generate a chiral pocket on the metal into which the aldehyde must fit in order for bond formation to occur. The absolute configuration of all products so far determined is consistent with this conjecture. The absolute requirement of a *Z*-substituent, such as methyl or *n*-alkyl, on the chiral enolate has been demonstrated, and the analogous acetate enolates lacking this substituent exhibit virtually no aldol diastereoface selection. Related trends have been noted in this laboratory for chiral boron enolates.[16]

Acknowledgment. This research has been supported by the National Institutes of Health.

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(14) Via the Bu_3SnH reduction of the methyldithiocarbonate derivative. Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1*, **1975**, 1574-1585.

(15) $(n\text{-}C_3H_7O)_4Zr$, $(i\text{-}C_3H_7O)_4Zr$, $(n\text{-}C_3H_7O)_4Ti$, $(i\text{-}C_3H_7O)_4Ti$, and $CpTiCl_3$ all exhibit much lower levels of diastereoselection with achiral amide enolates and benzaldehyde.

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Electronic States of 2-Methylenecyclopentane-1,3-diyl and Trimethylenemethane

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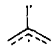
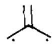
The nature of open-shell systems, such as diradicals, are important in understanding a variety of chemical processes. These systems are being widely studied by both theory[1] and experiment.[2,3] One of the best studied diradicals is trimethylenemethane (TMM) for which a number of low-lying electronic states are known (see Table I). The energy differences between the triplet ground state **1** and various excited singlet states are of great interest.[4-27] The generally accepted theoretical value for the energy difference between **1** and **2** is ~14 kcal/mol while that between **2** and **4** is 2-3 kcal/mol, with **2** being more stable. Recent experimental work has suggested, contrary to theoretical predictions, that the singlet-triplet splitting is quite small, falling between 1 and 4 kcal/mol.[26,27] This experimental work was done on a system with the TMM moiety incorporated in a five-membered ring (**5**). We

Table I. Energies for the Electronic States of Trimethylenemethane and 2-methylenecyclopentane-1,3-diyl

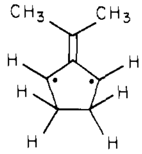
Trimethylmethane[a]

state		SOGVB	MCSCF
$^3A_2'$ (1)		0.0	0.0
$^1B_1$ (2)	 [b]	15.2	15.2
$^1A_1$ (3)		29.0	21.2
$^1B_2$ (4)	[c] 	22.1	22.1

2-Methylenecyclopentane-1,3-diyl[d]

state	MCSCF/SOGVB
$^3B_2$	0.0
$^1A'$ (C_s)	10.3
$^1B_1$	15.5
$^1A_1$	18.7
$^1B_2$	23.9

[a] Energies in kcal/mol relative to the triplet state, E (MCSCF) = -153.03095 au = E (SOGVB). [b] Orthogonal unique CH_2 group. [c] Planar unique CH_2 group. [d] Energies in kcal/mol relative to the triplet state, E (SOGVB) = -229.04382 au.



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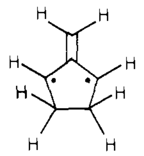

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