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CROTYLZIRCONIUM DERIVATIVES AS A NEW REAGENT FOR THE THREO SELECTIVE SYNTHESIS OF β-METHYLHOMOALLYL ALCOHOLS

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Crotylzirconium derivatives, prepared from the reaction of crotylmagnesium chloride or crotyllithium with bis(cyclopentadienyl)zirconium dichloride, undergo a rapid reaction with aldehydes to afford the threo product predominantly. The ratio of Cram/anti-Cram product via this reagent is ca. 75/25 ~ 60/40.

The development of the stereoselection via enolates or allylic organometallic compounds as a basic synthetic strategy for complex acyclic molecules has seen rapid growth in the past few years. The information so far reported on the reaction of aldehydes with enolates or allylic organometallics is summarized in the Table 1.

Table 1. Erythro and Threo Selectivity in the Reaction of Aldehydes

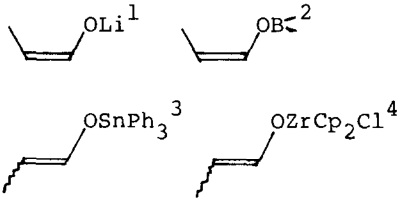
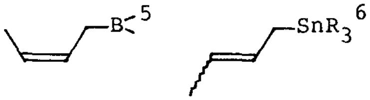
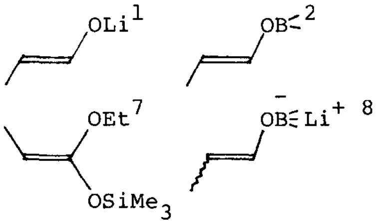
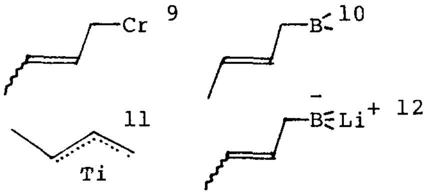
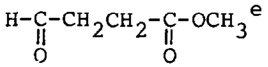
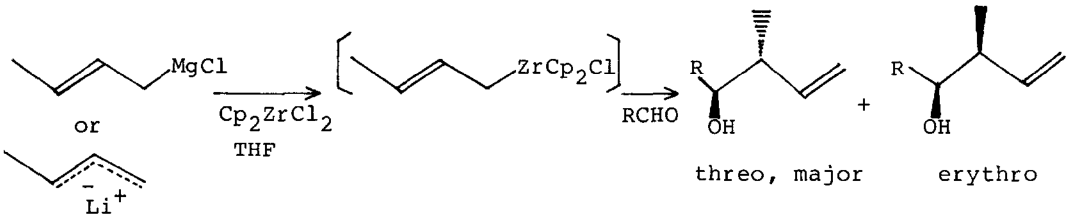
	Enolates	Allylic Organometallics
Erythro-selective		
Threo-selective		

Table 2. Reaction of Crotylzirconium Derivatives with Aldehydes[a]

Aldehyde	Threo (%)	Erythro (%)	Total yield (%)[b]
C_6H_5CHO	81	19	90
C_6H_5CHO[c]	85	15	(95)
C_6H_5CHO[d]	86	14	(90)
CH_3CHO	73	27	85
CH_3CH_2CHO	86	14	88
$(CH_3)_2CHCHO$	88	12	90
 $H-\underset{\underset{O}{\Vert}}{C}-CH_2CH_2-\underset{\underset{O}{\Vert}}{C}-OCH_3$[e]	94	6	90

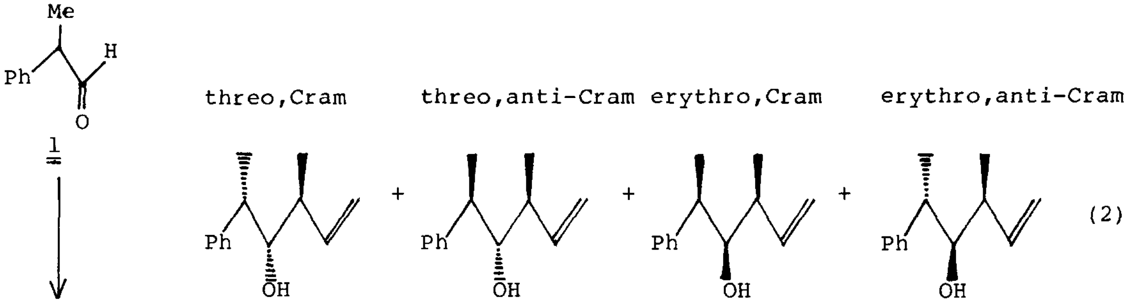
[a] All reactions were carried out on a 1 mmol scale. Aldehydes were added to a THF solution of crotylzirconium derivatives at -78°C. Normally, the reaction was quenched at -30~0°C with water. The ratio of threo/erythro was determined by ^1H NMR spectra and/or Glpc analysis. [b] Isolated yield (Glpc yield).
[c] $(Crotyl)_2ZrCp_2$ (0.5 mmol), prepared from crotylmagnesium chloride (1 mmol) and Cp_2ZrCl_2 (0.5 mmol), was treated with benzaldehyde (1 mmol). The yield was based upon the aldehyde. [d] $CrotylZrCp_2Cl$ was prepared from crotyllithium.
[e] After the allylation was completed, the reaction mixture was further treated with $BF_3 \cdot OEt_2$ to induce the lactonization. The ratio was determined by Glpc analysis of the resulting lactone.



(1)

We now wish to report that crotylzirconium derivatives, easily prepared in situ by the addition of crotylmagnesium chloride or crotyllithium to Cp_2ZrCl_2 in THF, can be added in the Table 1 as a promising candidate for the threo selective synthesis of β-methylhomoallyl alcohols (eq 1). The results are summarized in the Table 2. The stereoselectivity of the zirconium reagent from crotyllithium is to some extent higher than that from crotylmagnesium chloride, and the selectivity of the bis(crotyl)$ZrCp_2$ is slightly higher than that of crotyl$ZrCp_2Cl$. Furthermore, the reagent is chemoselective; it reacts selectively with an aldehyde in the presence of an ester group.

The relative asymmetric induction through the zirconium reagent is also investigated (eq 2).[13] The ratio of Cram/anti-Cram product is 75/25 (or 73/27) for **1** and 61/39 for **2**. Consequently, the reasonably high stereoselectivity, chemoselectivity, and operational simplicity of crotylzirconium reagents well complement the utility of other methods for threo selective synthesis of the homoallyl alcohols. Although the precise structure of crotyl$ZrCp_2Cl$ and (crotyl)$_2ZrCp_2$ is not obvious, the crotyl group of the former is presumably σ-bonded, and one of the crotyl group of the latter is probably π-bonded and the other σ-bonded.[14] Therefore, the threo selectivity is presumably a reflection of the 6-membered cyclic transition state in which the oxygen atom of aldehydes coordinates to zirconium metal.



(2)

	threo,Cram	threo,anti-Cram	erythro,Cram	erythro,anti-Cram
$\xrightarrow[92\ \%]{\text{CrotylZrCp}_2\text{Cl}}$	73	27	trace	trace
$\xrightarrow[92\ \%]{(\text{Crotyl})_2\text{ZrCp}_2}$	75	25	trace	trace

threo/erythro = ~100/~0

References and Notes

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