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DIASTEREOSELECTIVE ADDITION OF 2-BUTENYLMETAL "ATE" COMPLEXES TO AROMATIC KETONES MEDIATED BY $Cr(CO)_3$ COMPLEXATION

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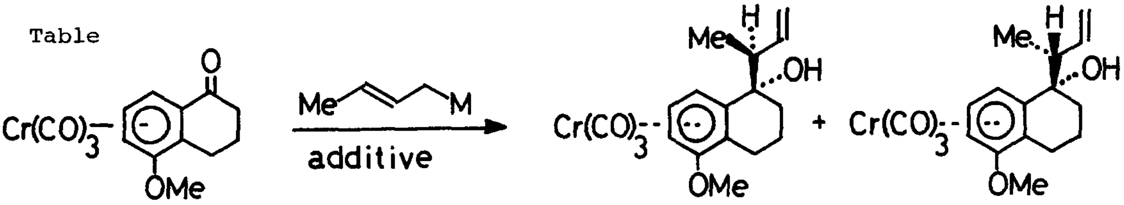
Summary: The reaction of 2-butenylmagnesium chloride with chromium complexes of aromatic ketones in the presence of trialkylaluminum produces predominantly the anti-adducts. The resulting benzylic hydroxyl group of the adducts is stereospecifically substituted with some nucleophiles.

In the last decade, considerable attention has been focused on stereoselective carbon-carbon bond forming process in acyclic and other conformationally flexible molecules$^{1)}$, particularly by the aldol addition$^{2)}$ and the related reactions of 2-butenylmetal reagents$^{3)}$ with carbonyl compounds. Generally, high diastereoselectivity has been achieved in these reactions with *aldehydes*, while much less selectivity is known about the reactions with *ketones*, because there is less difference in the steric bulkiness of both groups attached to the ketone carbonyl. In order to obtain high selectivity with *ketones*, it would be necessary to modify one substituent of the carbonyl group to a sterically more bulky group, e.g. by temporary complexation with transition metal. On the basis of this concept, we report herein the high degree of diastereoselectivity in the reaction of chromium complexes of aromatic ketones with 2-butenylmetal reagents, and stereospecific construction of adjacent two chiral centers by substitution of the benzylic hydroxyl group with some nucleophiles.

1-Tetralone derivatives usually gave no satisfactory diastereoselectivity with 2-butenyltitanium reagents[4]. Therefore, we firstly investigated the reactions of tricarbonyl(5-methoxy-1-tetralone)chromium (1) with some 2-butenylmetal reagents, directing toward the synthesis of natural products such as dihydroxyserrulatic acid[5]. The reaction was conducted under usual conditions described in the previous papers[6] and the results are summarized in Table. The reaction[7] of 2-butenyl-magnesium chloride or lithium with the complex 1 in the presence of 1 eq of trialkylaluminums gave an exo-attack[8], and anti-adduct[9] 2 with high diastereoselectivity without formation of regioisomer by α-attack of the crotyl group. Addition of triethylaluminum showed particularly high selectivity (entries 3,7). The chromium complexes of acetophenone, propiophenone and isobutyrophenone also gave the anti-adduct[9] 5 predominantly with Et_3Al and 2-butenylmagnesium chloride (entries 8,10,11).

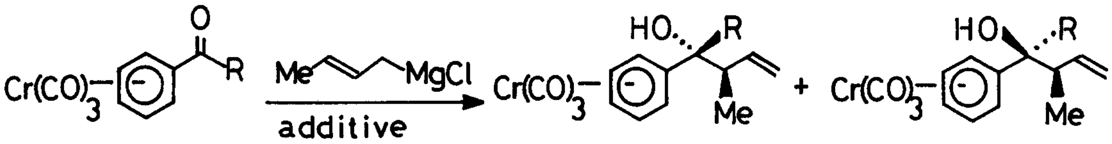
Table



1 2 3

entry	M	additive	ratio of 2 and 3	yield (%)
1	MgCl	none	50 : 50	75
2	MgCl	Me_3Al	80 : 20	75
3	MgCl	Et_3Al	93 : 7	73
4	MgCl	$(i\text{-}Bu)_3Al$	85 : 15	65
5	MgCl	Et_3B	28 : 72	30*
6	MgCl	$(i\text{-}PrO)_4Ti$	64 : 36	30*
7	Li	Et_3Al	94 : 6	60

* The starting chromium complex 1 was recovered as major product.

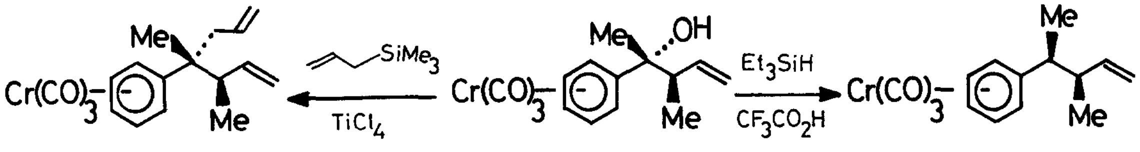


4 5 6

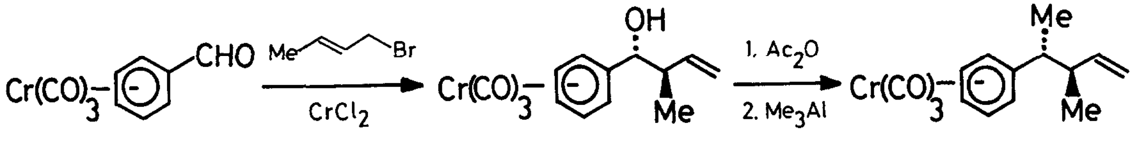
entry	R	additive	ratio of 5 and 6	yield (%)
8	Me	Et_3Al	89 : 11	95
9	Me	Et_3B	33 : 67	70
10	Et	Et_3Al	85 : 15	96
11	$CHMe_2$	Et_3Al	84 : 16	65
12	H	Et_3Al	50 : 50	90

The steric bulkiness of alkyl group (R) does not exert a strong influence upon the selectivity. This reaction presumably proceeds via a six-membered chair transition state[3,4], in which the smaller group of the ketone function occupies a pseudo-axial position and the double bond of the aluminum "ate" complex exists as E-form. Interestingly, the use of triethylborane produced predominantly the other stereoisomer, syn-adducts (entries 5,9). In contrast to the *ketones*, the chromium complex of benzaldehyde offered no selectivity with aluminum "ate" complex (entry 12). However, 2-butenylchromium(II)[10] gave exclusively anti-adduct 10 in 99% diastereoselectivity.

The resulting benzylic hydroxyl group of the chromium complexes could be further substituted with some nucleophiles to lead the useful compounds, because the benzylic carbonium ions is extremely stabilized by $Cr(CO)_3$ complexation. For example, ionic hydrogenolysis[11] of the complex 7 afforded stereospecifically the syn-compound 8 with stereochemical retention[12] at the benzylic position. On the other hand, treatment of acetate of the complex 10 with Me_3Al[11] gave the other diastereomer, anti-compound 11. The quarternary chiral center (e.g. 9) was also stereospecifically created by the reaction with allyl trimethylsilane in the presence of $TiCl_4$. The present work provides a new method for stereoselective construction[13] of both stereoisomers, in which two adjacent chiral centers are fully occupied by alkyl substituents without hetero-atom. Further investigations of the diastereoselectivity in other metal complexes of the various ketones are in progress.



9 63% 7 63% 8



93% (99% ds.) 10 68% 11

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