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A Highly Erythro Selective Aldol Reaction Between Chromium-Complexed Benzaldehyde Derivatives and Cyclic Silyl Enol Ethers

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Summary:Reaction of chromium-complexed benzaldehydes having a trimethylsilyl group at the ortho position with cyclic silyl enol ethers gave, after decomplexation, the erythro products in a highly selective manner.

The synthetic potentiality of arene chromium tricarbonyl complexes[1] has been well demonstrated. Among several significant properties, Reetz[2] and Uemura[3] has independently taken advantage of the tricarbonylchromium-stabilized benzylic carbocations for a stereoselective carbon-carbon bond formation. We explore here another useful application of the stabilized benzylic carbocation of arene chromium complexes in a highly stereoselective reaction. This communication deals with the successful first example of the highly erythro selective aldol reaction of chromium-complexed benzaldehydes with cyclic silyl enol ethers[4] in the presence of Lewis acid where the ortho trimethylsilyl group in the benzaldehydes (**1**,**2**,**3**) plays a significant role to attain a high selectivity.

The chromium-complexed benzaldehyde derivatives (**1**,**2**,**3**) were prepared from the parent aldehydes[5] under the established condition.[6] The typical experimental procedure for the aldol process is exemplified by the reaction between tricarbonyl(2-trimethylsilylbenzaldehyde)chromium

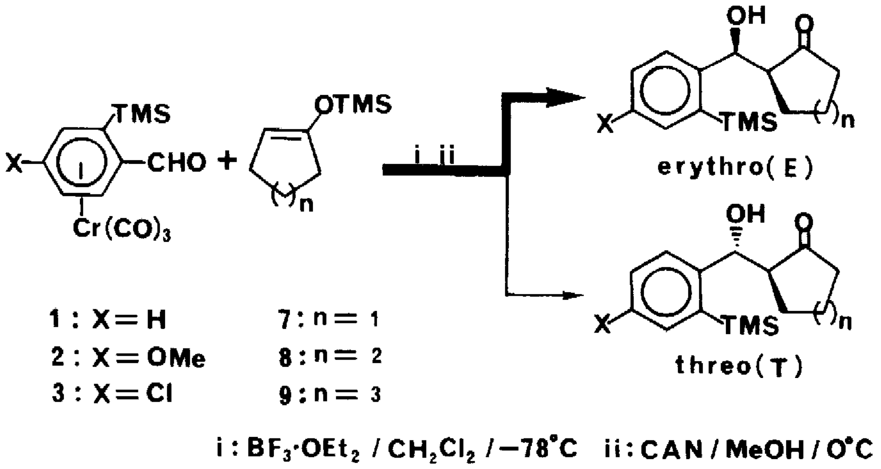
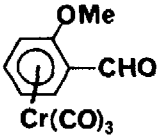
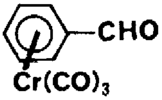
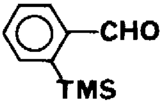


Table 1. Reaction of Chromium-Complexed and Uncomplexed Benzaldehyde Derivatives with Silyl Enol Ethers

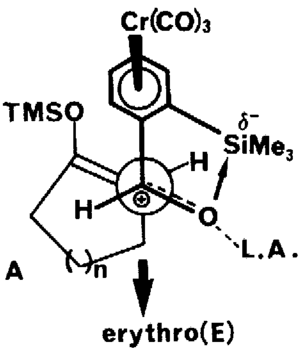
entry	aldehyde	silyl enol ether	aldol product	yield(%)[a] (E : T)[b]
1	**1**	**7**	**10**	61(96:4)[c]
2	**1**	**8**	**11**	70(90:10)
3	**1**	**9**	**12**	75(>98:2)
4	**2**	**7**	**13**	95(93:7)
5	**2**	**8**	**14**	70(97:3)
6	**2**	**9**	**15**	86(>98:2)
7	**3**	**7**	**16**	69(95:5)[c]
8	**3**	**8**	**17**	72(92:8)
9	**3**	**9**	**18**	94(95:5)
10	 **4**	**7**	**19**	84(50:50)
11	 **5**	**8**	**20**	91(47:53)
12	 **6**	**7**	**10**	63(62:38)

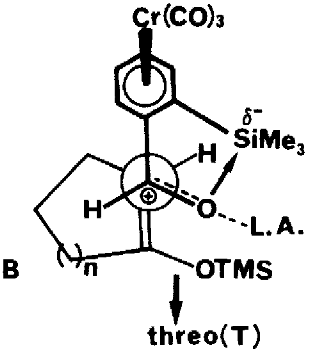
a) Yields of products isolated, after decomplexation, by flash chromatography. b) Determined by 400-MHz ^{1}H NMR spectra unless otherwise stated. c) Ratio of each pure isomer isolated by flash chromatography.

(**1**) and trimethylsilyloxycycloheptene (**9**)(entry 3). To a solution of **1** (58 mg; 0.185 mmol) and **9** (68 mg; 0.37 mmol) in dry CH_2Cl_2 (4 ml) was added dropwise a 1 *M* solution of $BF_3 \cdot OEt_2$ in dry CH_2Cl_2 (0.74 ml; 0.74 mmol) at -78°C under nitrogen atmosphere. After stirring for 15 min, the reaction mixture was quenched by addition of a saturated NH_4Cl solution at the same temperature. Work-up, followed by decomplexation with cerium ammonium trinitrate (CAN)$^{7)}$ in methanol at 0°C furnished, after flash chromatopraphy, the *erythro* derivative (**12E**; 40 mg) in 75% yield. Careful analysis of ^1H NMR spectrum of **12**$^{8,9)}$ indicates that this aldol reaction proceeded in a highly diastereoselective manner.$^{10)}$ In fact, no *threo* isomer could virtually be detected in its ^1H NMR spectrum. Other cyclic silyl enol ethers (**7** and **8**) also showed the similar selectivity. Several results obtained under the standard condition were summarized in Table 1.

A couple of features deserve comment. i) Uncomplexed benzaldehyde derivative (**6**) gave rise to the *erythro* derivative in moderate selectivity (entry 12), however the degree of diastereoselectivity is much lower than that of the corresponding chromium complexed aldehyde (**1**). ii) No characteristic stereoselectivity was observed when tricarbonyl(benzaldehyde)chromium (**5**) was treated with **8** (entry 11). iii) The *ortho* methoxy substituent is not adequate enough to attain a high selectivity (entry 10). 4) Changing electron density on the aromatic ring does not affect diastereoselectivity at all.

The mechanism of this highly *erythro* selective aldol reaction is not manifest yet. However, the above results suggest that both tricarbonylchromium complexation and the *ortho* trimethylsilyl group are essential for this *erythro* selective reaction. The benzylic carbocation could be generated by anchimeric assistance of the *ortho* trimethylsilyl group that can form pentacoordinated species$^{11)}$ and then stabilized by the tricarbonylchromium moiety. This cationic





intermediate[4b] should be captured by nucleophilic silyl enol ethers *via* the transition state **A** rather than **B** affording the *erythro* product.

Further application of this newly developed aldol procedure is now under active investigation.

References and Notes

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8) Stereochemical assignment was made by careful consideration of coupling constant of benzylic proton in each isomer in 400-MHz ^{1}H NMR spectrum because *erythro*-*threo* relative configuration in the aldol reaction can be conveniently assigned from the magnitude of the vicinal coulping constant.[9] For instance, **10E:** 5.59 ppm, *J*=1.5 Hz;**10T:** 4.91 ppm, *J*=9.8 Hz; **11E:** 5.63 ppm, *J*=2.0 Hz; **11T:** 5.12 ppm, *J*=9.0 Hz; **12E:** 5.38 ppm, *J*=2.7 Hz; **12T:** 5.17 ppm, *J*=9.3 Hz. **12T** was obtained nonselectively by the reaction of **6** with **9**.

9) (a) T. Mukaiyama, Org. Reac., **28**, 203 (1982); (b) D.A. Evans, J.V. Nelson, and T.R. Taber, Top. Stereochem., **13**, 1 (1982); (c) C.H. Heathcock,"Asymmetric Synthesis," Academic Press, New York, **1984**, vol. 3, p 111.

10) We isolated chromium-complexed aldol product (**21**), which was converted to **13** after decomplexation. ^{1}H NMR spectra of **21** and its *O*-acetyl derivative indicated that **21** was made up of a single isomer with respect to the aromatic ring. Therefore, we would say that this aldol reaction proceeded facial-selectively in regard to the benzene ring of the chromium-complexed benzaldehydes, although the relative stereochemistry is not elucidated yet.

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