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Dicobalt Hexacarbonyl-Complex of Propynals in Organic Synthesis: Strong *E*-Enolate:Threo/*Z*-Enolate:Erythro Correlation in the Aldol Reaction of Cobalt-Complexed Propynals

Chisato Mukai, Kazuyoshi Nagami, and Miyoji Hanaoka*
Faculty of Pharmaceutical Sciences, Kanazawa University
Kanazawa 920, Japan

Summary: Reaction of lithium E-enolates with the cobalt-complexed propynals gave the threo isomers, whereas lithium Z-enolates afforded the erythro derivatives in a highly stereoselective manner.

In the preceding paper,[1)] we described the aldol reaction of cobalt-complexed propynals with silyl enol ethers where a high erythro stereoselectivity was observed irrespective of the geometry of the starting silyl enol ethers. Our endeavor was then focused on the direct cross aldol reaction between the cobalt-complexed propynals and lithium enolates to explore further utilities of cobalt-complexed propynals in stereoselective reactions. We report here a highly stereoselective aldol reaction of cobalt-complexed propynals with *E*-enolate and *Z*-enolate giving threo and erythro isomer, respectively.

The cobalt-complexed propynal (**1**)[1)] was exposed to lithium enolate (**2**), prepared either by direct treatment of cyclohexanone with lithium diisopropylamide[2)] or by reaction between trimethylsilyloxycyclohexene

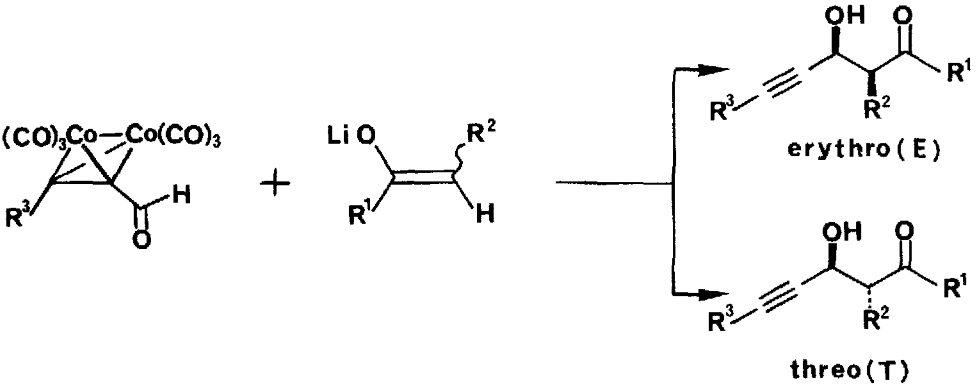
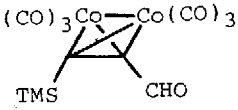
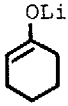
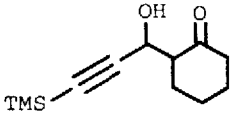
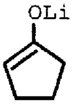
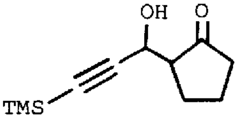
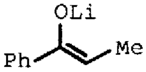
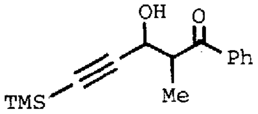
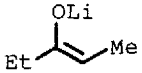
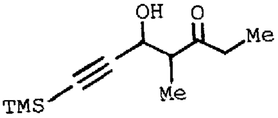
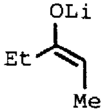
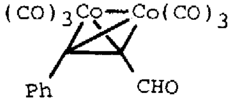
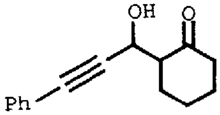
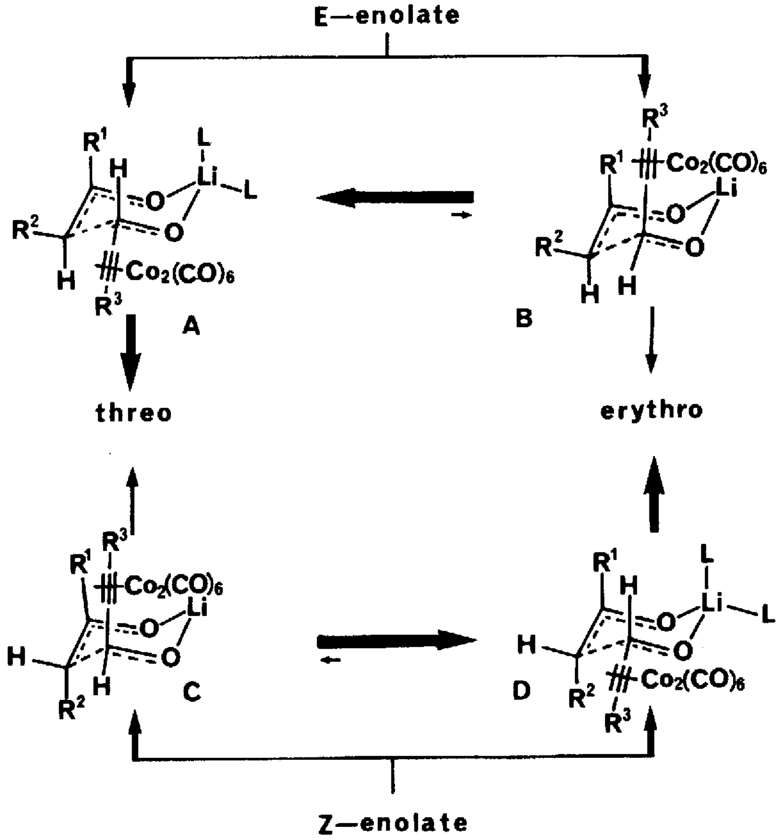


Table 1. Reaction of Cobalt-Complexed Propynals and Uncomplexed Propynals with Lithium Enolates

entry	aldehyde	enolate	product[a]	yield %[b] (erythro:threo)[c]
1	 **1**	 **2**	 **3**	59 (2 :>98)
2	TMS—≡—CHO **4**	**2**	**3**	51 (54 : 46)
3	**1**	 **5**	 **6**	60 (20 : 80)
4	**4**	**5**	**6**	64 (40 : 60)
5	**1**	 **7**[d]	 **8**	60 (>98: 2)
6	**4**	**7**	**8**	72 (67 : 33)
7	**1**	 **9**[d]	 **10**	79 (84 : 16)
8	**1**	 **11**[d]	**10**	84 (39 : 61)
9	 **12**	**2**	 **13**	57 (2 :>98)
10	Ph—≡—CHO **14**	**2**	**13**	77 (50 : 50)

[a] Stereochemical assignment was made by careful analysis of coupling constant[7)] of propargyl proton in each isomer in 400-MHz ^{1}H NMR; 3**E** : 4.76 ppm, J=2.9 Hz, 3**T** : 4.58 ppm, J=7.8 Hz, 6**E** : 4.65 ppm, J=4.0 Hz, 6**T** : 4.59 ppm, J=7.8 Hz, 8**E** : 4.83 ppm, J=4.1 Hz, 8**T** : 4.70 ppm, J=7.5Hz, 10**E** : 4.63 ppm J=4.6 Hz, 10**T** : 4.47 ppm, J=7.6Hz, 13**E** : 4.97 ppm, J=3.4 Hz, 13**T** : 4.82 ppm, J=8.2Hz. [b] Yields of pure products isolated, after treatment with CAN, by flash chromatography. [c] Determined by 400-MHz ^{1}H NMR unless otherwise stated. [d] Prepared with MeLi and silyl enol ethers[3)] (**7** : E/Z=2/>98, **9** : E/Z=18/82, **11** : E/Z=79:21). The ratios of **E** and **Z** were unambiguously determined by ^{1}H NMR spectrum.

and methyllithium,[3)] in dry tetrahydrofuran at -78°C to give, after decomplexation with cerium ammonium nitrate,[4)] the aldol product (**3**) in 59% yield. ^{1}H NMR spectrum of **3** showed that **3** is made up of only the threo isomer (**3T**; 4.58 ppm, J=7.8 Hz; >98%).[5)] Results obtained under the same condition were summarized in Table 1. Similar high threo selectivity was observed in the reaction between the cyclic enolates (E-enolate) with the cobalt-complexed propynals (entry 3 and 9[5)]), although the diastereoselectivity is somewhat low in the case of the lithium enolate (**5**) of cyclopentanone compared to other cases. It is noteworthy that no characteristic diastereoselectivity was virtually detected in the reaction of the uncomplexed propynals (**4** and **14**)(entry 2,4, and 10). On the other hand, the Z-enolate (**7**) was treated with **1** to give rise to the erythro isomer (**8E**; >98%)[6)] exclusively in 60% yield, while the uncomplexed propynal (**4**) afforded a 67:33 mixture of **8E** and **8T**.



These results strongly suggest that the aldol reaction of cobalt-complexed propynals with lithium enolates must proceed *via* the six-membered chair-like transition state⁷⁾ in contrast to Lewis acid catalyzed reaction of the cobalt-complexed propynals.¹⁾ The largest cobalt complex moiety should be equatorial (conformer A and D) and prevent an interconversion to a possible other conformer (B or C) having axial cobalt-complexed triple bond. However, the naked triple bond might not be large enough to be frozen into an equatorial position and resulted in fairly low diastereoselectivity. In the cases of the lithium enolates (**9** and **11**) derived from diethyl ketone, the ratios of *erythro* and *threo* isomers in **10** also completely reflect those of *E* and *Z* geometry in the starting enolates (entry 7 and 8).

Application of this highly stereoselective aldol reaction to a synthesis of natural products is in progress in our laboratory.

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5) No *erythro* isomer could virtually be detected by ^{1}H NMR spectrum.
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7) Excellent reviews: (a) Mukaiyama,T. *Org. Reac.* **1982**, 28, 203. (b) Evans,D.A.; Nelson,J.V.; Taber,T.R. *Top. Stereochem.* **1982**, 13, 1. (c) Heathcock,C.H. *Asymmetric Synthesis*; Academic: New York, **1984**, vol.3, p.111. (d) Bartlett,P.A. *Tetrahedron* **1980**, 36, 2. (e) Seebach,D.; Prelog,V. *Angew. Chem. Int. Ed. Engl.* **1982**, 21, 654. (f) Masamune,S.; Choy,W.; Peterson,J.S.; Sita,L.R. *Angew. Chem. Int.* Ed. Engl. **1985**, 24, 1.

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