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Dicobalt Hexacarbonyl-Complex of Propynals in Organic Synthesis: Erythro-Selective Aldol Reaction of Cobalt-Complexed Propynals with Silyl Enol Ethers

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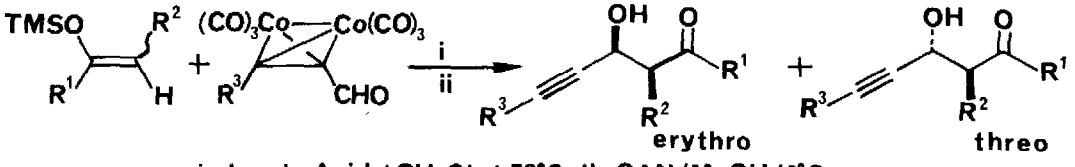
Summary: The aldol reaction of cobalt-propynal complexes with several trimethylsilyl enol ethers provided predominantly the erythro derivatives regardless of the stereochemistry of the starting silyl enol ethers.

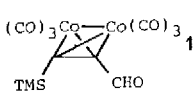
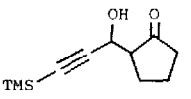
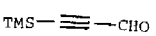
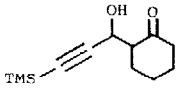
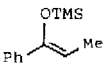
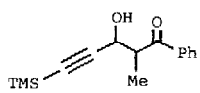
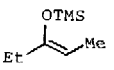
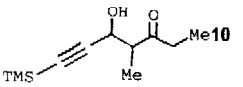
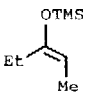
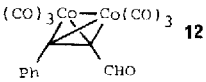
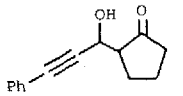
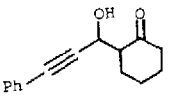
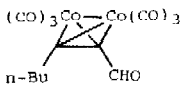
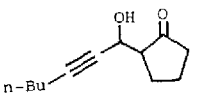
The aldol condensation[1] has been well recognized as one of the most reliable methods for the stereoselective creation of β-hydroxycarbonyl functionalities in conformationally non-rigid complex molecules such as polyether antibiotics and macrolides.[1] The enantioselective as well as diastereoselective issues[1a-c] for the aldol-type reactions have already been well solved for the last few decades. Unfortunately few information,[2] however, on the aldol process of propynal derivatives involving stereoselectivity has so far been available in spite of recent great interest in the synthesis of antitumor antibiotics, esperamicin[3] and neocarzinostatin chromophore.[4] Disclosed herein is the first example of diastereoselective aldol condensation of the cobalt-complexed propynals with silyl enol ethers,[5] where a high erythro-selectivity[7] was observed regardless of the stereochemistry of silyl enol ethers.



i : Lewis Acid / CH_2Cl_2 / -78°C ii : CAN/MeOH/0°C

The cobalt-complexed propynals, prepared in high yield (87-88%) by simple treatment of propynals with dicobaltoctacarbonyl,[5a,8,9] were exposed to silyl enol ethers in the presence of Lewis acid. Decomplexation of the resulted products with cerium ammonium nitrate (CAN)[5a,8a,b] produced the corresponding propargyl alcohols. Several representative results obtained under the standard condition were summarized in Table 1.

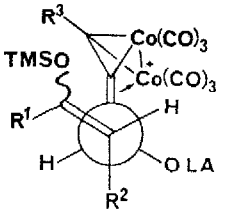
Table 1. Reaction of Cobalt-Complexed Propynals and Uncomplexed Propynals with Silyl Enol Ethers

entry	aldehyde	silyl enol ether	Lewis Acid[a]	product[b]	yield %[c] (erythro:threo)[d]
1	 **1**	 **2**	A	 **3**	90 (87:13)
2	1	2	B	3	76 (91: 9)
3		2	A	3	90 (40:60)
4	1	 **5**	A	 **6**	91 (70:30)[e]
5	1	 **7**[f]	A	 **8**	73 (91: 9)
6	1	 **9**[g]	A	 **10**	63 (91: 9)
7	1	 **11**[h]	A	**10**	75 (94: 6)
8	 **12**	2	B	 **13**	68 (88:13)
9	12	5	A	 **14**	67 (88:12)
10	 **15**	2	A	 **16**	90 (87:13)[i]

[a] A : $BF_3 \cdot OEt_2$, B : $EtAlCl_2$. [b] Stereochemical assignment was made by careful analysis of coupling constant[1] of propargyl proton in each isomer in 400-MHz ^1H NMR. [c] Yields of pure products isolated, after treatment with CAN, by flash chromatography. [d] Determined by 400-MHz ^1H NMR unless otherwise stated. [e] Ratio of each pure isomer of the cobalt-complexed products isolated by flash chromatography. [f] A mixture of E and Z isomer (E/Z=2/>98). See ref. 14. [g] A mixture of E and Z isomers (E/Z=18/82). See ref. 14. [h] A mixture of E and Z (E/Z=79/21). See ref. 15. [i] Determined by gas chromatography.

The data in Table 1 permit to mention that a high erythro-selectivity could be attained irrespective of the geometry of the starting silyl enol ethers (entry 6 and 7). Even in the case of cyclic silyl enol ethers (2 and 5) in which no isomerization could be anticipated, the erythro derivatives (e.g. entry 1,8,9) were predominantly formed. Therefore, it is not necessary either to pay special attention to preparation of Z-enol ethers or to convert once the silyl enol ethers into other metal enolates[7] in order to get erythro derivatives selectively in this procedure. Although the simplest propynal, 2-propyn-1-one decomposes under the standard condition, it is indeed not the serious drawback to this aldol reaction since the trimethylsilyl group can serve as a surrogate[10] for the ethynylic hydrogen. We examined several Lewis acids such as $BF_3 \cdot OEt_2$, $EtAlCl_2$, $TiCl_4$, and TMSOTf, and found out that the erythro/threo ratio of the condensation product was principally insensitive to the identity of Lewis acid employed.[5] The utility of the present reaction is enormously enhanced from the easy elaboration[11] of the triple bond to various functionalities. The present erythro-selectivity is very remarkable because no characteristic stereoselectivity was observed in the aldol reaction of uncomplexed propynals.

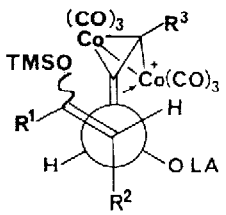
The mechanism for the erythro-selectivity has not yet been clarified. The fluxional behavior[5,6,12] of the possible cationic intermediates would make understanding the stereochemical outcome of the erythro-selectivity more difficult. However, it could be tentatively rationalized in terms of the modified synclinal transition state[13] where the hydrogen on the double bond of a silyl enol ether would be placed in the most sterically demanding position (**A-D**)[5] proposed previously in the reaction between the cobalt-complexed propargyl methyl ether derivative and a silyl enol ether. More detailed works on the present erythro-selective reaction and its scope are under active investigation.



A, B

anti cobalt cation : E-enol

: Z-enol



C, D

syn cobalt cation : E-enol

: Z-enol

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