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Studies on Diastereoselectivity of the Cobalt(I) Catalyzed Cycloisomerization of Substituted ε-Acetylenic β-Ketoester.

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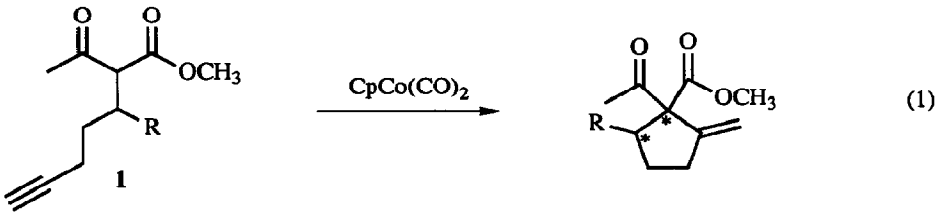
Abstract : Cobalt (I) catalyzed cycloisomerization of a ε-acetylenic β'-alkyl β-ketoester led to highly functionalized methylenecyclopentanes with stereocontrol of two contiguous centers. The level of diastereoselectivity is moderate to high (de = 12-92 %).

As part of our program designed to develop the rapid and diastereoselective construction of the basic skeletons of polycyclic natural diterpenes,[1] we have recently disclosed a new and efficient cobalt(I) catalyzed cycloisomerization of ε-acetylenic β-ketoesters leading to functionalized methylenecyclopentanes.[2]

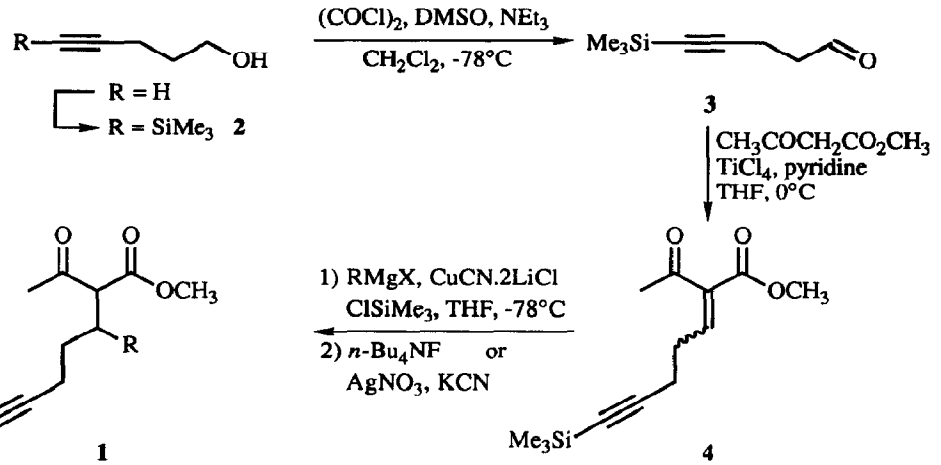
The possibility to extend this reaction to β'-substituted acetylenic ketoesters **1** appeared very attractive for several reasons, not the least of which would be the stereocontrol over two contiguous stereogenic centers[3] as well as a diastereoselective entry into highly substituted methylenecyclopentanes [eq. (1)].



(1)

Moreover, the β-ketoester moiety, through its enol tautomer, should be the reactive intermediate in the annelation process[4] and the presence of substituents in the β' position could control the transformation of keto-enol prochiral group into a new stereogenic center. Herein, we report the synthesis and the cobalt (I) catalyzed cyclization of the ε-acetylenic β'-substituted β-ketoesters **1**. Their straightforward preparation is outlined in Scheme 1.

Pentyn-1-ol was quantitatively protected as its silylated derivative **2** by using a standard procedure.[5] Swern oxidation[6] provided quantitatively the aldehyde **3**. Knoevenagel condensation[7] of **3** with methyl acetoacetate led to the unsaturated ε-acetylenic β-ketoester **4** in 90 % yield as a 1 : 1 mixture of *E* and *Z* isomers. The Nakamura procedure[8] by using a stoechiometric amount of copper (I) source allowed the formation of the 1,4- adducts. Removal of the trimethylsilyl groups from the crude mixture by using tetrabutylammonium fluoride or silver nitrate in the presence of potassium cyanide[9] achieved the preparation of the desired ketoesters **1**[10] as a 1:1 mixture of diastereomers in 65 to 70 % yield.

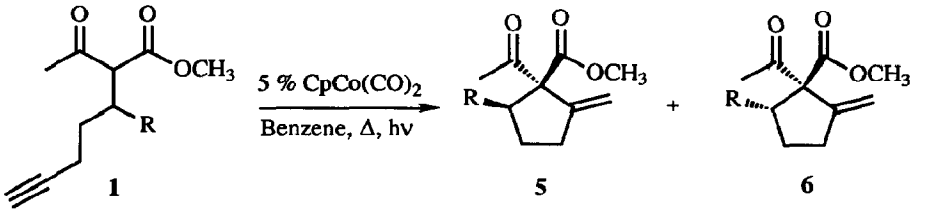


1a R = Ph ; **1b** R = Me ; **1c** R = *n*-Bu ; **1d** R = *i*-Pr ; **1e** R = CH_2-$SiMe_3$; **1f** R = *t*-Bu

Scheme 1

Exposure of **1** to a catalytic amount of (η^5-cyclopentadienyl) cobalt dicarbonyl $Cp(Co(CO)_2$ in refluxing benzene and under irradiation furnished the cycloadducts **5** and **6**[10,11] with moderate to high level of diastereoselectivity[12] as described in Table 1.

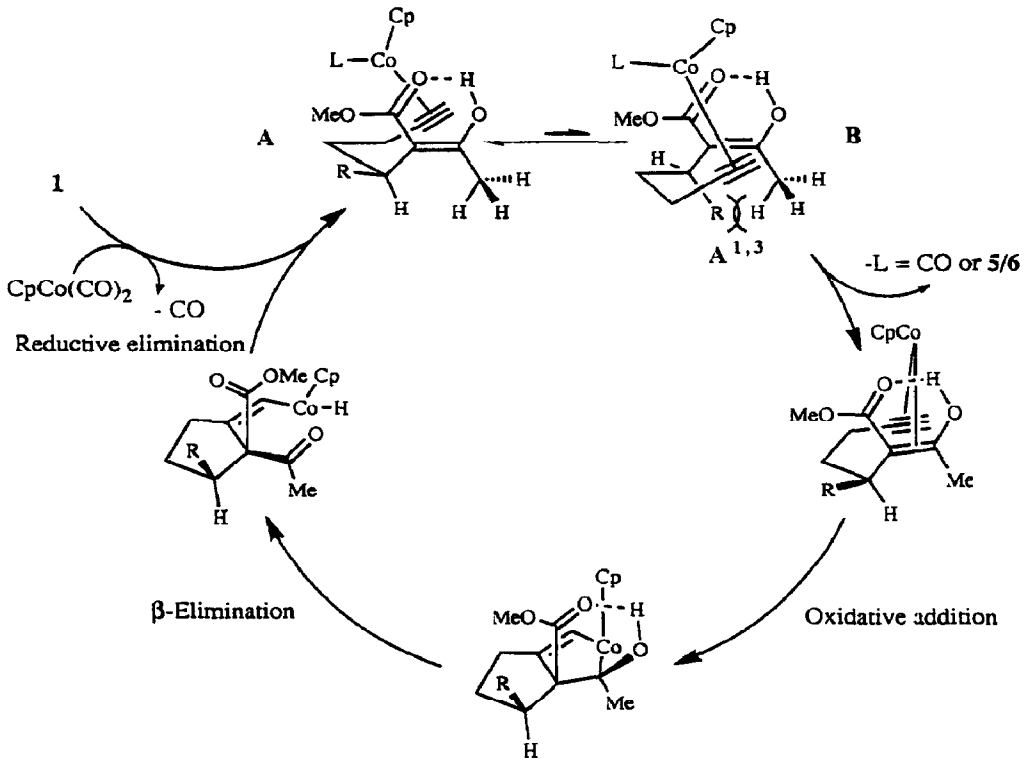
Table 1 : Cycloisomerization of **1** with $CpCo(CO)_2$



Entry	R	Yield %[a]	5/6[b]	de %
1a	Ph	69	56/44	12
1b	Me	69	77/23	54
1c	*n*-Bu	74	89/11	78
1d	*i*-Pr	52	87/13	74
1e	CH_2-$SiMe_3$	72	85/15	70
1f	*t*-Bu	64	96/4	92

(a) *Isolated yield as a mixture of 5 and 6* (b) *Ratio calculated by ^{1}H-NMR based on the integration of the CH_3 of the ester groups*

The diastereoselectivities observed could be reasonably explained by the conformational rigidity of the enol-yne cobalt (I) complex which is the effective participant of the cyclization. In fact, the process of the complexation entailes the coplanarity of the double bond of the enol and the triple bond creating an allylic 1,3-strain between the methyl group of the enol and the bulky substituent in β' (rotamer **B**) (Scheme 2).



Scheme 2

According to the increasing size of the β' substituent, the complex A will be favored and thus the diastereomeric excess will increase. Nevertheless, the presence of a too bulky substituent as CH_2SiMe_3 in **1e** seems to involve an antagonist 1,2 steric interaction with the ester group, decreasing the diastereomeric excess.

In summary, we have demonstrated that cobalt-catalyzed cycloisomerization could control the relative stereochemistry of two contiguous stereogenic centers. For synthetic purposes, if the ester group is bearing a chiral auxiliary the cyclization could constitute an enantioselective approach to optically pure highly functionalized methylenecyclopentanes. We are currently developping this reaction to natural product synthesis.

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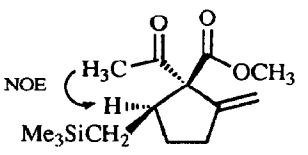
References and Notes :

(1) (a) Aubert, C. ; Gotteland, J. P. ; Malacria, M. *J. Org. Chem.* **1993**, *58*, 4298-4305.
(b) Stammler, R. ; Halvorsen, K. ; Gotteland, J. P. ; Malacria, M. *Tetrahedron Lett.* **1994**, *35*, 417-420.
(2) Stammler, R. ; Malacria, M. *Synlett* **1994**, 92.
(3) Mikami, K. ; Takahashi, K. ; Nakai, T. *Tetrahedron Lett.* **1989**, *30*, 357-360.
(4) Skeean, R. W. ; Trammell, G. L. ; White, J. D. *Tetrahedron Lett.* **1976**, 525-528.
(5) Jones, T. K. ; Denmark, S. E. *Org. Synth.* **1986**, *64*, 182-188.
(6) Mancuso, A. J. ; Huang, S. L. ; Swern, D. J. *J. Org. Chem.* **1978**, *43*, 2480-2482.
(7) Lehnert, W. *Tetrahedron Lett.* **1970**, 4723-4726.
(8) Horiguchi, Y. ; Matsuzawa, S. ; Nakamura, E. ; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 4025-4028 ; *ibid* **1986**, *27*, 4029-4032.
(9) Corey, E. J. ; Kirst, H. A. ; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 6314-6319.
(10) All compounds were fully characterized by ^{1}H and ^{13}C-NMR, infrared, mass spectroscopy and elementary analysis.
(11) **Typical procedure for the cyclization of 1a** : $CpCo(CO)_2$ (7 µL ; $5.8.10^{-2}$ mmol) was added to a boiling solution of **1a** (150 mg ; 0.58 mmol) in benzene (10 mL) degassed by three freeze-pump-thaw cycles and was irradiated (using a sun lamp). After completion of the reaction by TLC, the solvent was removed in vacuo. The residue was purified by flash chromatography (petroleum ether : ether = 7 : 3) to afford **5a** and **6a** (103.5 mg, 69 %). **5a** : ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.29-7.23 (5H, m), 5.40 (1H, dd, *J* = 2.7, 1.6 Hz), 5.36 (1H, dd, *J* = 2.7, 1.6 Hz), 4.30 (1H, dd, *J* = 9.3, 7.1 Hz), 3.21 (3H, s), 2.57-2.40 (2H, m), 2.29 (3H, s), 2.19-2.11 (2H, m) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 200.9, 170.4, 149.8, 140.9, 128.5, 128.3, 128.0, 127.4, 126.8, 113.0, 75.8, 51.9, 50.3, 33.4, 29.9, 26.8. **6a** : ^{1}H-NMR (400 MHz, $CDCl_3$) 7.21-7.14 (5H, m), 5.26 (1H, dd, *J* = 2.7, 1.6 Hz), 5.18 (1H, dd, *J* = 2.7, 1.6 Hz), 4.20 (1H, dd, *J* = 6.6, 5.5 Hz), 3.81 (3H, s), 2.76-2.63 (2H, m), 2.10-2.02 (2H, m), 1.5 (3H, s) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 204.5, 171.5, 148.9, 138.8, 128.5, 128.3, 128.0, 127.4, 126.8, 111.7, 74.6, 52.7, 51.7, 32.4, 29.9, 28.8. **5a** + **6a** : IR (neat) 2940, 2220, 1710, 1645, 1430, 1345, 900 cm^{-1} ; MS (*m/Z*) 240, 225, 215, 200, 181, 175, 155, 141, 131, 115, 103, 91, 77, 65, 51 ; Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.41 ; H, 6,98. Found : C, 74,64 ; H, 7.42.
(12) The configuration of the cyclic compounds was assigned by NOE experiments as shown below :



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