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STEREOSELECTIVE SYNTHESIS OF KEY (η^6-ARENE)Cr(CO)$_3$ COMPLEXES TO ACORENONE AND ACORENONE B

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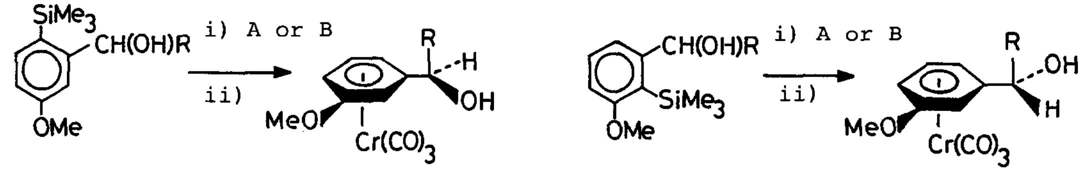
Summary: Direct diastereoselective chromium complexation of *meta*-methoxy benzylalcohol derivatives was achieved by the introduction of Me_3Si group, and the benzylic acetoxyl groups of the complexes were substituted with stereochemical retention to lead the key complexes to acorenone and acorenone B.

Diastereoselective synthesis of the chromium complexes of *ortho* - or *meta*-substituted aromatic compounds possessing chiral centers at the side chain is important for the stereoselective synthesis of fused or spiro natural products via an intramolecular nucleophilic addition of the stabilized carbanions1). The arene-$Cr(CO)_3$ unit can perform a dual purpose in stabilizing both carbanions and carbonium ions at the benzylic position2). In this communication, we disclose stereoselective synthesis of each diastereomeric chromium complexes of *meta*- methoxy benzylalcohol derivatives and further stereospecific transformation to the key chromium complexes to acorenone and acorenone B via the $Cr(CO)_3$-stabilized carbonium ions.

The synthesis of each diastereomeric chromium complexes of *meta*- methoxy benzylalcohol derivatives was achieved by the direct complexation of the compounds 1 or 2, in which the sterically bulky and easily removable trimethylsilyl group was temporarily introduced at either *ortho*-position of the hydroxyalkyl group (Scheme 1). Reaction of 6-trimethylsilyl compound 1a3) with 1 eq of $Cr(CO)_6$ in butyl ether, heptane and THF (10:1:1) at 130°C for 15-20h, followed by desilylation, gave predominantly S^*R^*-chromium complex4) 3a (mp 78°C). On the other hand, 2-trimethylsilyl compound 2a3) afforded other diastereomeric complex S^*S^*-isomer 4a (mp 66°C) under the same reaction sequences. Similarly, isopropyl compound 1b was converted into the corresponding chromium complex 3b.

Scheme 1



1 3 2 4

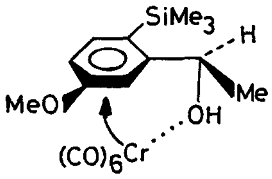
i) A; $Cr(CO)_6$, B; (naphthalene)$Cr(CO)_3$, ii) $n\text{-}Bu_4N^+F^-$

Table

Compounds	Chromium Reagents	Ratio of 3 and 4	Yield (%)
1a	A	95 : 5	66
1b	A	96 : 4	77
2a	A	2 : 98	69
1a	B	98 : 2	82
1b	B	100 : 0	85
2a	B	0 : 100	97
2b	B	0 : 100	88

a; R=Me b; $R=CHMe_2$

This direct complexation to the arene nucleus may result from same side[5)] with the benzylic hydroxyl group via an interaction of the chromium and hydroxy oxygen atom such as transition state 5, in which alkyl group should be located away from the bulky trimethylsilyl group. However, the products and ratio



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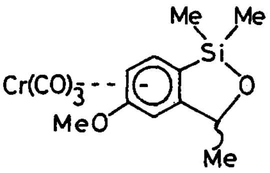
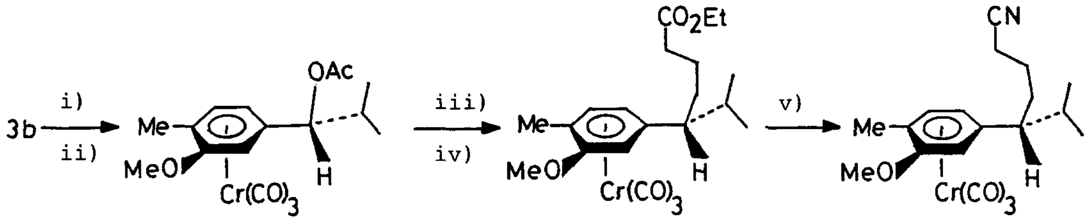


6

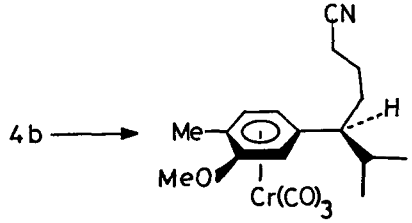
of this direct complexation depend on the reaction conditions. Reaction of excess of $Cr(CO)_6$ with 1a for 2 days gave a mixture of *exo-* and *endo-* methyl cyclic siloxane complexes 6 6) (*exo-* : *endo-* =2:3).

In order to get better stereoselectivity, kinetic complexation under milder conditions would be necessary. Thus, the compound 1a was reacted with tricarbonyl(naphthalene)chromium 7) in ether containing 1 eq of THF at 70°C for 4h, giving exclusively the S^*R^*-chromium complex 3a in better yield and selectivity (Table). More bulky isopropyl derivatives 1b and 2b gave 3b and 4b, respectively, without any diastereomeric contamination.

Since the benzylic acetoxyl group of the chromium complexes could be substituted with some nucleophiles 8) to lead carbon-carbon bond formation products, 3b and 4b were converted to the precursor of natural spiro sesquiterpenoids as follows.



7 8 9



10

i) n-BuLi/TMEDA, then 1 eq MeI/HMPA

ii) Ac_2O/pyridine,

iii) $CH_2=CHCH(SiMe_3)CO_2Et/BF_3\cdot OEt_2$,

iv) PtO_2/H_2, v) Me_2AlNH_2

Directed regioselective lithiation 9) of 3b, followed by quenching with 1 eq of MeI and subsequent acetylation, gave 4-methylated complex 7 in 80% overall yield. The compound 7 was treated with ethyl 2-trimethylsilyl-3-butenoate 10) in the presence of $BF_3\cdot OEt_2$ and hydrogenated with PtO_2 to afford 8 in 66% yield with stereochemical retention 11) at the benzylic position. Treatment of 8 with dimethylaluminum amide 12) gave nitrile chromium complex 9 in 45% yield, which was already converted to acorenone B by Semmelhack's group 13).

Similarly, the compound 4b gave the other diastereomeric complex 10, an intermediate to acorenone, by the same reaction sequences.

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3) These compounds were obtained by the reaction of RLi and the corresponding aldehydes; D. L. Comins and J. D. Brown, J. Org. Chem., 49, 1078 (1984).

4) The symbol S^*S^* or S^*R^* indicates an enantiomeric mixture of *SS*- and *RR*- or *SR*- and *RS*- diastereomers.

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6) Also, the compounds 1b, 2a and 2b gave the corresponding cyclic chromium complexes in various ratio under severe conditions with excess of $Cr(CO)_6$.

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