Pergamon

Tetrahedron Letters, Vol. 38, No. 41, pp. 7199-7202, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)01714-0

(Arene)tricarbonylchromium Complexes in Radical Reactions: Samarium(II) Iodide-Mediated Coupling of Chromium-Complexed Benzaldehyde or Acetophenone with Methyl Acrylate

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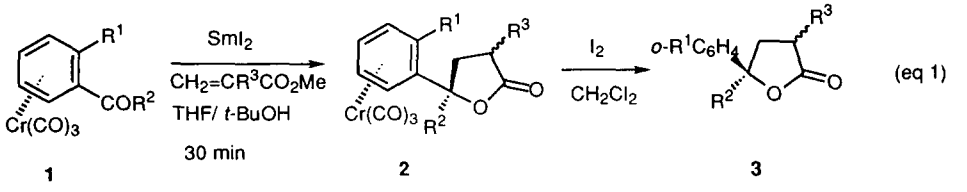
Abstract: Planar chiral tricarbonylchromium complexes of *ortho*-substituted benzaldehydes or acetophenones were coupled with methyl acrylate in the presence of samarium(II) iodide to give stereoselectively γ-butyrolactones in good yields. © 1997 Elsevier Science Ltd.

The asymmetric formation of a carbon-carbon bond utilizing radical intermediates remains a challenging goal in organic synthesis. In general, chiral auxiliaries have been employed for the asymmetric induction in an inter- or intramolecular radical reaction.[1,2] Lewis acids are also effective for highly asymmetric induction in the radical reaction, where the Lewis acids block one face of the radical acceptor.[1,3] The source of asymmetric induction using the chiral auxiliaries or Lewis acids is postulated to be highly stereodefined radical intermediates or alkene radical acceptor via a chelation structure of the samarium metal with oxygen or nitrogen moiety of the chiral auxiliaries or alkenes. The SmI_2-mediated reductive radical reaction of carbonyl compounds with olefins has been established as an excellent method for the synthesis of coupling products.[4,5] In this radical reaction, the acrylates derived from chiral *N*-methylephedrine were coupled with ketones in the presence of SmI_2 to afford the γ-butyrolactones through the chelated intermediate in highly enantiomeric purities.[6] We have recently reported[7] that the planar chiral (benzaldehyde)$Cr(CO)_3$ or (benzaldimine)$Cr(CO)_3$ complexes provided the corresponding *threo*-1,2-diols or 1,2-diamines mediated by SmI_2. In these reductive coupling reactions, the tricarbonylchromium-complexed benzyl radical species, generated *in situ*, is postulated to be a conformationally stable radical intermediate without C_α-C_{ipso} bond rotaton owing to an interaction of the d-orbital on the chromium with the p-orbital of the benzylic carbon. For further synthetic applications of the tricarbonylchromium-complexed benzyl radical, we wish to report the stereoselective carbon-carbon bond-forming of the planar chiral tricarbonylchromium complexes of *o*-substituted benzaldehydes or acetophenones with methyl acrylate giving enantiomerically pure γ-butyrolactones.

Typical procedure is follows: a solution of samarium(II) iodide (0.1M in THF, 9.3 mL, 0.93 mmol) was added to a solution of enantiomerically pure (+)-(*R*)-tricarbonyl(*o*-methyl acetophenone)chromium (**1**)

(R^1=R^2=Me, R^3=H) (0.37 mmol), methyl acrylate (0.44 mmol) and *t*-BuOH (0.37 mmol) in THF (1 mL), and the reaction mixture was stirred for 30 min. The mixture was quenched with saturated aqueous NH_4Cl, extracted with ether, concentrated under reduced pressure. The residue was chromatographed on silica gel (30% ethyl acetate in hexane) to afford the γ-butyrolactone chromium complex **2** (R^1=R^2=Me, R^3=H) ($[\alpha]_D^{24}$ +15.7 (*c* 0.30, $CHCl_3$)) as a single diastereomer in 75% yield. The stereochemistry was determined by X-ray analysis of the corresponding racemic compound (Fig. 1). Demetallation of **2** with I_2 in methylene chloride at room temperature gave the (+)-(*R*)-γ-butyrolactone **3** as an enantiomerically pure compound.



1 2 3 (eq 1)

Table 1. Reductive Coupling of Chromium Complexes 1 with Acrylates Mediated by SmI_2

Entry	Complex **1** R^1	R^2	Acrylate R^3	React Temp °C	Yield **2** (%)	**2** $[\alpha]_D$ ($CHCl_3$)	Yield **3** (%)	**3** $[\alpha]_D$ (MeOH)
1	OMe	H	H	−78	72	+163.0 (*c* 0.33)	91	+70.0 (*c* 0.25)
2	Me	H	H	−78	75	−102.0 (*c* 0.20)	89	+59.6 (*c* 0.23)
3	Br	H	H	0	53	−84.3 (*c* 0.24)	87	+37.5 (*c* 0.32)
4	OMe	Me	H	0	71	+219.8 (*c* 0.61)	92	+36.0 (*c* 0.25)
5	Me	Me	H	0	75	+15.7 (*c* 0.30)	91	+33.7 (*c* 0.43)
6[a]	Me	Me	Me	0	84	*b*	90	*b*

a; obtained as 5 : 1 diastereomeric mixture at the α-position of lactone carbonyl. *b*; not measured.

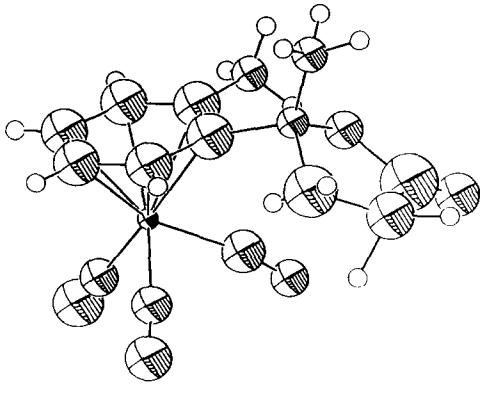


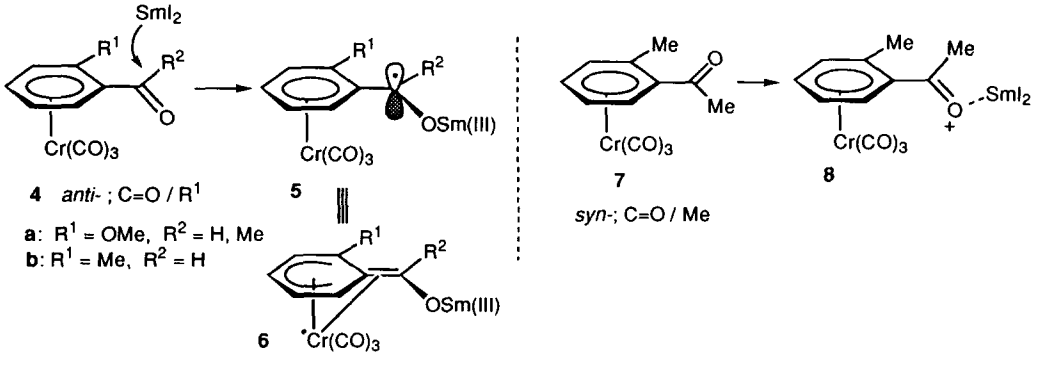
Fig. 1. Crystal structure of 2 (R^1=R^2=Me, R^3=H)

Other reaction results are summarized in Table 1. (−)-(*R*)-Tricarbonyl(*o*-methoxy acetophenone)-chromium (**1**) (R^1=OMe, R^2=Me, R^3=H) provided the corresponding (γ-butyrolactone)$Cr(CO)_3$ with the (*R*)-configuration at the benzylic position without formation of diastereoisomeric complex under similar reaction conditions (entry 4). Similarly, (*o*-substituted benzaldehyde)$Cr(CO)_3$ complexes were coupled with methyl acrylate at lower reaction temperature to afford the corresponding tricarbonylchromium complexes of γ-butyrolactones as a single compound, respectively (entries 1~3). Methyl methacrylate provided the coupling product as a diastereomeric mixture at the α-position of lactone carbonyl by the reaction with (*o*-methyl acetophenone)chromium (entry 5).

However, the reductive coupling with methyl crotonate instead of acrylate gave unsatisfactory results due to, probably, steric hindrance. Thus, the reaction of methyl crotonate with a (*o*-anisaldehyde)$Cr(CO)_3$ complex in the presence of SmI_2 afforded a mixture of the corresponding pinacol coupling product (81%) and a benzylalcohol complex (13%) without formation of the γ-butyrolactone.

The reaction mechanism for the stereoselective radical coupling would be explained as follows (Figure 2). The carbonyl oxygen of chromium-complexed benzaldehydes or acetophenones with the electron-donationg *ortho* substituents tends usually to be an *anti*-conformation **4** to *ortho* substituents in both solid and solution states.[8,9] An *exo*-attack of samarium to the carbonyl of the *anti*-conformer in these complexes generated a kety radical intermediate **5**, which possesses a substantial exocyclic double bond character **6** with a limitation of the C_α-C_{ipso} bond rotation and is trapped with the acrylate from the *exo*-side leading to the product **2**.

Fig. 2. Plausible reaction mechanism



It is noteworthy that the stereochemistry of the chromium-complexed γ-butyrolactone obtained by coupling of (*o*-methyl acetophenone)chromium with methyl acrylate was identical with those of the coupling products derived from other chromium complexes. It is well documented that the benzylic carbonyl oxygen of (*o*-methyl acetophenone)chromium is oriented in the *syn*-conformation **7** to the *o*-methyl group due to the steric effect, and the nucleophiles such as Grignard or hydride reagents attack to the carbonyl in such *syn*-conformation from the *exo*-side giving one diastereomer predominantly.[8,9] But, in this samarium-mediated radical reaction of (*o*-methyl acetophenone)chromium, a ketyl radical intermediate seems to be generated by the *exo*-attack of SmI_2 t the carbonyl in the *anti*-conformation. Thus, the stereochemical result of the coupling product suggests that the *syn*-conformer **7** would be isomerized[10] to the *anti*-conformation **8** by the coordination of the Lewis acid (SmI_2) with carbonyl oxygen prior to one electron reduction.[11]

In conclusion, this method provides a stereoselective carbon-carbon bond forming via a tricarbonylchromium-stabilized ketyl radical without the chelated structure, and further mechanistic and synthe studies are in progress.

Acknowledgment: This research was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan. M.U. thanks Chiba-Geigy Foundation (For Japan) and The Asahi Glass Foundation for financial support.

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(*Received in Japan* 2 *July* 1997; *revised* 13 *August* 1997; *accepted* 18 *August* 1997)