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Stereoselective synthesis of Mannich-type products having a terminal olefin by use of benzaldiminetricarbonylchromium derivatives

Kaori Ishimaru* and Takakazu Kojima

Department of Chemistry, The National Defense Academy, Hashirimizu 1-10-20, Yokosuka 239-8686, Japan

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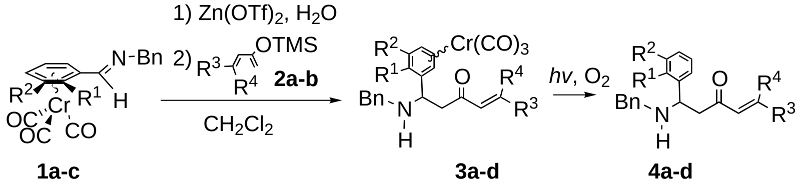
Abstract—Mannich-type products having a terminal olefin were obtained with high facial selectivities by reaction of benzaldiminetricarbonylchromium derivatives with 2-silyloxy-1,3-butadienes under mild conditions. The reaction by using the chiral chromium complex was also achieved to give the corresponding chiral Mannich-type product. © 2001 Elsevier Science Ltd. All rights reserved.

Mannich or Mannich-type reactions have been widely known and used for the synthesis of β-aminoketones.[1] In spite of many reports on the stereoselective reactions with enolates,[2] the reaction of aldimines with 2-silyloxy-1,3-butadienes in the presence of Lewis acid usually gave [4+2]-type cycloadducts.[3] The isolation of the Mannich-type products has been reported; however, substituents of aldimines or dienes must be chosen carefully.[4] Recently, we have developed a general synthetic method for pharmaceutically attractive Mannich-type products having a terminal olefin[5] by the reaction of aromatic and aliphatic aldimines with 2-silyloxy-1,3-butadienes in the presence of zinc triflate and water.[6] Herein, we describe the first stereoselective reaction of benzaldiminetricarbonylchromium derivatives with 2-silyloxy-1,3-butadienes in the presence of zinc triflate and water.

Benzaldiminetricarbonylchromium complexes **1** were prepared as previously described,[7] and the reaction of **1a** with **2a** (1.2 equiv. to **1a**) was carried out in the presence of zinc triflate (2 equiv. to **1a**) and water (3 equiv. to **1a**) in dichloromethane under similar conditions, as we described before (Scheme 1).[6] After the reaction mixture was quenched by aqueous $NaHCO_3$ and dichloromethane, only one diastereomer was observed in the ^1H NMR (500 MHz) spectrum of the crude product. Removal of the tricarbonylchromium moiety of the isolated complex **3a** by air and sunlight in dichloromethane or ether was unsuccessful; however, the reaction mixture of **1a** and **2a** in the presence of zinc triflate and water without work-up was exposed to air and sunlight to afford the corresponding Mannich-type product **4a** in 62% isolated yield. Under similar conditions, the reactions of various aldimine complexes



1a : R^1= OMe, R^2= H
1b : R^1= H, R^2= Me
1c : R^1= Me, R^2= H

2a : R^3= Ph, R^4= H
2b : R^3= Me, R^4= Me

Scheme 1.

Keywords: stereocontrol; imines; dienes; Mannich reactions.

* Corresponding author. Tel.: +81-468-41-3810 ext. 3580; fax: +81-468-44-5901; e-mail: kaoriisi@nda.ac.jp

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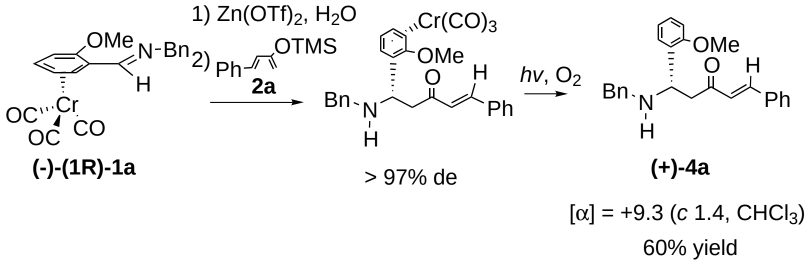
Table 1. Preparation of Mannich-type products

Complex	Diene	Conditions	De of **3** (%)[a]	Product	Yield (%)[b]
1a	**2a**	rt, 12 h	>97	**4a**	62
1b	**2a**	rt, 12 h	>97	**4b**	59
1c	**2a**	rt, 12 h	>97	**4c**	67
1a	**2b**	rt, 12 h	>97	**4d**	60

[a] De was measured by ^{1}H NMR.

[b] Isolated yield.



Scheme 2.

1 with dienes **2** were carried out (Table 1).[8] High diastereoselectivities were observed in all cases, and all reactions proceeded at room temperature. Interestingly, the reaction using the chromium complex having a substituent at *meta* position **1b** gave high facial selectivity because coordination of the bulky polymeric zinc triflate to the complex would stabilize the conformation of the complex.[9] The reaction with 2-silyloxy-1,3-butadiene having various substituents at the 4-position proceeded; however, the reaction with the diene having no substituents at the 4-position gave a cycloadduct and decomposed products.

Next, (–)-(1*R*)-**1a** was prepared as described in the literature,[7] and the reaction with **2a** yielded the chiral Mannich-type chromium complex **3a**, which was converted to the corresponding Mannich-type product (+)-**4a** (Scheme 2).[10] Because of the instability of the Mannich-type products having a terminal olefin, attempts to determine the enantiopurity of (+)-**4a** by chiral columns or shift reagents were unsuccessful. However, >97% de of **3a** would indicate that the product (+)-**4a** was enantiomerically pure, because racemization would not occur when removing the tricarbonylchromium moiety.

Fig. 1 shows a possible mechanism of the reaction. When the reaction of **1a** with **2a** was quenched at 1 min, aldimine complex **1a**, Mannich-type product **3a** (δ 2.9–3.0, m, CH$_2$), and cycloadduct **5a** (δ 2.4–2.5, m, CH$_2$) were observed in the ^{1}H NMR spectrum of the crude product, indicating that the reaction proceeded by way of a cycloadduct as in the case of aldimine.[6] Thus, the mechanism showed that C–N bond cleavage of both secondary and tertiary amines occurred.

General procedure for preparing Mannich-type products **4**: To a stirred solution of chromium complex **1** (0.5 mmol), zinc triflate (0.36 g, 1 mmol), and water (1.5 mmol) in dichloromethane (5 mL) was added 2-silyloxy-1,3-butadiene **2** (0.6 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h in the dark (the de was determined after the reaction mixture was quenched with aqueous NaHCO$_3$ and dichloromethane, but the isolated mixture was not used for the deprotection of Cr(CO)$_3$), dichloromethane (20 mL) was added, and the mixture was exposed to air and sunlight for 0.5–1 h. The solvent was evaporated and ether (15 mL) was added to the mixture. The precipitates were filtered off and the solvent was evaporated to give the crude product which was purified by short flash column chromatography on SiO$_2$ (*n*-hexane/EtOAc = 3/1). Isolated yields were measured without isolation of **3**.

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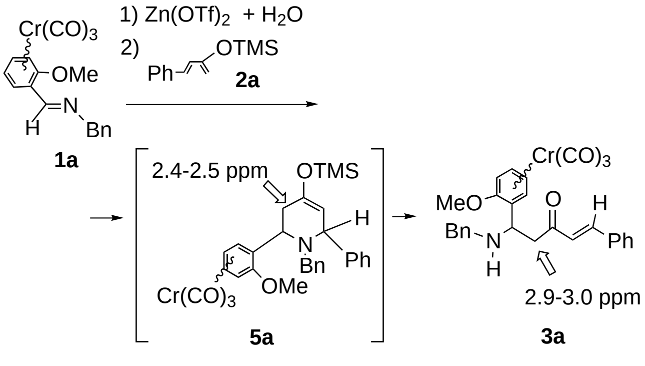

Figure 1.

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