Pergamon

A Mild Aldol Reaction of Aryl Aldehydes through Palladium-Catalyzed Hydrosilation of α,β-Unsaturated Carbonyl Compounds with Trichlorosilane

Syun-ichi Kiyooka,* Atsushi Shimizu, and Seiko Torii

Department of Chemistry, Faculty of Science, Kochi University, Akebono-cho, Kochi 780-8520, Japan

Abstract: A mild aldol reaction of aryl aldehydes took place by using N,N-dimethylacrylamide and trichlorosilane with a catalytic amount of tetrakis(triphenylphosphine)palladium. A unique *anti* selectivity was observed in the reaction.

A variety of developments on aldol reaction are currently being addressed in synthetic organic chemistry. During our search for new types of aldol reaction, we envisioned the use of an intermediate formed *in situ* from metal-catalyzed hydrosilation[1] of α,β-unsaturated carbonyl compounds for realizing a formal aldol reaction. A prototype of such reaction reported by Mukaiyama is the bis(1,3-diketonato)cobalt (II) -catalyzed coupling reaction of α,β-unsaturated compounds with aldehydes by the use of phenylsilane, in which a carbon-bound cobalt enolate was assumed as the precursor for the successive coupling reaction.[2] Matsuda reported the phosphine-modified $Rh_4(CO)_{12}$-catalyzed three-components coupling of α,β-enone, aldehyde, and diethylsilane[3] and suggested an oxygen-bound rhodium enolate as a plausible intermediate in the aldol-type reaction.[4] We disclose herein a preliminary result of a mild aldol reaction of aryl aldehydes through palladium-catalyzed hydrosilation of α,β-unsaturated carbonyl compounds with trichlorosilane.
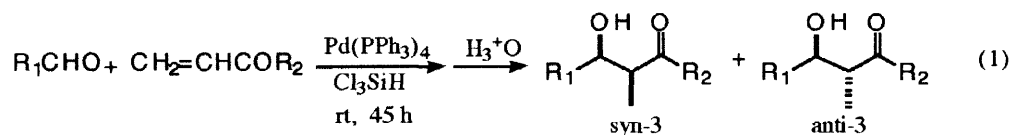
A typical procedure is as follows: A solution of tetrakis(triphenylphosphine)palladium (58 mg, 0.05 mmol) and trichlorosilane (0.13 ml, 1.3 mmol) in CH_2Cl_2 (5 ml) was stirred for 20 min at room temperature under argon and then to the solution was added aldehyde (1 mmol). After stirring for 5 min, N,N-dimethylacrylamide (110 mg, 1.1 mmol) was added. The resulting mixture was stirred for 45 h at that temperature and then quenched with 10% aqueous hydrochloric acid (1 ml). After standard workup procedure, the crude material was purified by flash column chromatography (silica-gel with a solvent system of ethyl acetate and hexanes) to isolate each *syn*- and *anti*-isomer.[5]

Reactions of aryl aldehydes with N,N-dimethylacrylamide and trichlorosilane took place very cleanly in the presence of the palladium catalyst to give the corresponding aldols (Eq. 1), as shown in Table 1. *Anti selectivity was observed in the reaction.* This finding is very striking because *syn* selectivity was reported in similar type reactions.[2,3] The reaction using *tert*-butyl acrylate resulted in low yields with normal *syn* selectivity (Entries 7, 8, and 9). Use of triethylsilane instead of trichlorosilane did not effect the reaction. This is the first example of an aldol reaction through palladium-catalyzed hydrosilation.

Table 1.   Reaction of aryl aldehydes with α,β-unsaturated carbonyl compounds
and trichlorosilane in the presence of a catalytic amount of $Pd(PPh_3)_4$ (Eq. 1)[a]

Entry	R_1CHO	R_2	Yield of 3 (%)	syn / anti
1	Benzaldehyde	$-N(CH_3)_2$	87 (3a)	32 / 68
2	1-Naphthaldehyde	$-N(CH_3)_2$	78 (3b)	24 / 76
3	p-Tolualdehyde	$-N(CH_3)_2$	72 (3c)	31 / 69
4	2-Naphthaldehyde	$-N(CH_3)_2$	93 (3d)	30 / 70
5	4-Nitrobenzaldehyde	$-N(CH_3)_2$	68 (3e)	28 / 72
6	4-Clorobenzaldehyde	$-N(CH_3)_2$	75 (3f)	36 / 64
7	Benzaldehyde	$-O^tBu$	37 (3g)	72 / 28
8	2-Naphthaldehyde	$-O^tBu$	32 (3h)	73 / 27
9	4-Phenylbenzaldehyde	$-O^tBu$	36 (3i)	62 / 38

[a] Reaction procedure is described in the text.

As regards the mechanism, oxidative-addition of trichlorosilane is presumed to be the first step in the catalytic hydrosilation. After the α,β-carbonyl compound is coordinated to the palladium intermediate, hydride migratory insertion takes place. However, the following steps are not clear. From the viewpoint of the selectivity observed, we consider that the reaction differs from the case of palladium enolates. The reductive-elimination may occur to give trichlorosilyl enol compounds, followed by an aldol reaction assisted by the trichlorosilyl moiety, related to the recent results reported by Denmark.[6]

Work is under way to improve the reaction conditions because reaction with aliphatic aldehydes did not proceed.

References and Notes

1. Rhodium-catalyzed hydrosilation of α,β-unsaturated carbonyl compounds to give silyl ketene acetals and silyl enol ethers: (a) Ojima, I.; Kogure, T.; Nagai, Y. *Tetrahedron Lett.* **1972**, 5035 - 5038. (b) Revis, A.; Hilty, T. K. *J. Org. Chem.* **1990**, 55, 2972 - 2973.

2. Isayama, S.; Mukaiyama, T. *Chem. Lett.* **1989**, 2005 - 2008.

3. Matsuda, I.; Takahashi, K.; Sato, S. *Tetrahedron Lett.* **1990**, 31, 5331 - 5334.

4. (a) Sato, S.; Matsuda, I.; Izumi, Y. *Tetrahedron Lett.* **1986**, 27, 5517 - 5520. (b) Slough, G. A. ; Bergman, R. G.; Heathcock, C. H. *J. Am. Chem. Soc.* **1989**, 111, 938 - 949.

5. The stereochemistry of syn- and anti-isomers was assigned by using their ^1H vicinal coupling constants and ^{13}C chemical shifts of carbinol carbon in comparison with the reported data ((a) Heathcock, C. H.; Buse C. T.; Kleschick, W. A.; Pirrung M. C.; Sohn, J. E., Lampe, J. *J. Org. Chem.* **1980**, 45, 1066 - 1081. (b) Heathcock, C. H.; Pirrung, M. C. ; Sohn, J. E. *Ibid.* **1979**, 44, 4294 - 4299. (c) Mulzer, J.; Zippel, M.; Brüntrup, G.; Segner, J.; Finke, J. *Liebigs Ann. Chem.* **1980**, 1108 - 1134.), as listed below: syn-3a (2.7 Hz, 73.1 ppm), anti-3a (5.8 Hz, 76.3 ppm); syn-3b (2.0 Hz, 69.5 ppm), anti-3b (5.1 Hz, 73.3 ppm); syn-3c (2.2 Hz, 73.0 ppm), anti-3c (5.8 Hz, 76.5 ppm); syn-3d (2.0 Hz, 73.2 ppm), anti-3d (6.1 Hz, 76.6 ppm); syn-3e (2.0 Hz, 72.5 ppm), anti-3e (6.8 Hz, 75.7 ppm); syn-3f (1.7 Hz, 72.6 ppm), anti-3f (7.1 Hz, 75.9 ppm); syn-3g (4.12 Hz, 73.8 ppm), anti-3g (7.6 Hz, 76.3 ppm); syn-3h (4.12 Hz, 73.7 ppm), anti-3h (8.0 Hz, 76.5 ppm); syn-3i (4.12 Hz, 73.6 ppm), anti-3i (7.8 Hz, 76.1 ppm).

6. Denmark, S. E.; Winter, S. B. D.; Su, X.; Wong, K. -T. *J. Am. Chem. Soc.* **1996**, 118, 7404 - 74 (b) Denmark, S. E.; Wong, K. -T.; Stavenger, R. A. *Ibid.* **1997**, 119, 2333 - 2334.