BISMUTH TRICHLORIDE AS A NEW EFFICIENT CATALYST IN THE ALDOL REACTION

Hidenori Ohki, Makoto Wada,[★] and Kin-ya Akiba[★] Department of Chemistry, Faculty of Science, Hiroshima University Higashisenda-machi, Hiroshima 730, Japan

Abstract: In the presence of a catalytic amount of bismuth trichloride (5 mol%), silyl enol ethers react with aldehydes at room temperature to give the corresponding aldols in good yields.

Among group VB elements, bismuth can be expected to play some role for organic synthesis according to its enhanced metallic character. To our knowlege, however, organic synthesis, especially carbon-carbon bond forming reaction by using bismuth element has been scarcely studied.¹⁾ Recently, we discovered the first example of chemoselective metallic bismuth.²⁾ and bismuth(III) chloride (BiCl₃)-metallic zinc-,³⁾ -metallic iron-,³⁾ or -metallic aluminium⁴⁾-mediated allylation of aldehydes with allylic halides to homoallylic alcohols. In relation to organic synthesis by using bismuth element, herewith, we wish to communicate the first example of BiCl₃ (5 mol%) promoted aldol reaction between silyl enol ethers and aldehydes in CH₂Cl₂ at room temperature. The overall scheme is shown below.

Scheme 1

$$\begin{array}{c} OSi \equiv \\ R^{1} \swarrow R^{2} + R^{3}CHO \xrightarrow{BiCl_{3}(5mol^{6})} CH_{2}Cl_{2}, r.t.} \begin{pmatrix} R^{1} \swarrow OSi \equiv \\ R^{2} & R^{3} \end{pmatrix} \xrightarrow{MeOH/1NHCl} R^{1} \xrightarrow{OOH} R^{3} \\ R^{2} & 3 \end{pmatrix} \xrightarrow{MeOH/1NHCl} R^{1} \xrightarrow{OOH} R^{3} \\ R^{2} & 4 \end{pmatrix}$$

The reaction between 1-trimethylsiloxy-1-cyclohexene (1c) and benzaldehyde in the presence of BiCl₃ (5 mol%) in CDCl₃ at room temperature was monitored by ¹H NMR spectroscopy. The NMR signals at 0.17 ppm (s, $O-Si\underline{Me}_3$), 4.87 ppm (t, vinyl-<u>H</u>), and 10.00 ppm (s, aldehyde-<u>H</u>) disappeared within 1 h, and new signals appeared at -0.02 ppm (s, $O-Si\underline{Me}_3$ of the threo product), 0.03 ppm (s, $O-Si\underline{Me}_3$ of the erythro product), 5.10 ppm (d, $O-C\underline{H}$ of the threo product, J=7.91 Hz), and 5.37 ppm (d, $O-C\underline{H}$ of the erythro product, J=3.95 Hz). The above results illustrate that the silyl enol ether 1c reacts with benzaldehyde smoothly under the influence of a catalytic amount (5 mol%) of BiCl₃, giving the aldol silyl ether.

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Entry	Silyl Enol Ether	Receptor	Reaction Time	Product ^{a)}	Yield(%) ^{b)}
1		PhCHO	25 min	Ph	h 94
2	0Si€	сн ₃ (сн ₂) ₂ сно	40 min	Ph OH	85
3	Ph 1ª	PhCOCH ₃	6 h		n ⁶⁵
4		PhCOCH ₃	11 h		h ^{73°)}
5	QSi€	PhCHO	50 min	Ph Ph	95(56:44) ^{d)}
6	Ph 1b	PhCOCH ₃	40 h	Ph Ph	22 ^{e)}
7	OSi€ 1c	РҺСНО	1 h	Ph	84(25:75) ^{d)}
8	Ph mosis OMe 1d	E PhCHO	1 h	[≥] SiO O Ph OM Ph OH O Ph OH O Ph OM	e ₄₀ e),f) e ^{32^{e),f)}}
9	OSi∈ Ph∕ 1a	CH3CH(OEt)2	6 h	Ph OEt	41
10	OSi∉ Ph 1a	сн ₃ сн=снсно	15 min	Ph & OH Ph & L &	₆₈ g) H 31 ^{g)}
11	OSi€ Ph 1ª	Ph CH3	3 h	Phere	74

a) All the products gave satisfactory IR and ^{1}H NMR spectra, and some products were also identified by comparison with authentic samples. b) Isolated yields are given. c) 20 mol% BiCl₃ was used. d) The ratio of erythro:threo determined by ^{1}H NMR. e) The ratio of diastereomers was not determined. f) The reaction mixture was treated with H₂O instead of MeOH/1N HCl for the workup. g) A mixture of 1,2-addition and 1,4-addition products. A typical experimental procedure to obtain an aldol is as follows. In a 25 ml flask under nitrogen atmosphere, were placed BiCl₃ (0.05 mmol) and dry CH_2Cl_2 (3 ml). Then, benzaldehyde (1.1 mmol) and 1-phenyl-1-trimethyl-siloxyethylene (1.0 mmol) were added sequentially at room temperature, and the reaction mixture was stirred for 25 min at this temperature. The resulting reaction mixture was treated with $CH_3OH/1N$ HCl (10/1, 0.1 ml), then H_2O (10 ml) was added and the product was extracted with CH_2Cl_2 (10 ml x 3). After drying the CH_2Cl_2 layer over anhydrous MgSO₄, the solvent was evaporated <u>in vacuo</u>. The crude product was purified on thin-layer chromatography with hexane:ethyl acetate=8:1 as eluent to afford the corresponding aldol in 94% yield. Typical results are summarized in Table 1 although the optimum conditions are not surveyed.

Silyl enol ethers of acetophenone, propiophenone, cyclohexanone, and methyl phenylacetate could be used. Both an aromatic aldehyde and an aliphatic aldehyde are usable to obtain aldols in good yields and an aldehyde serves naturally as a better receptor than a ketone (entries 3, 4, and 6). The silyl enol ether <u>la</u>/acetaldehyde dimethyl acetal reaction gave the aldol-type product in 41% yield which is not the optimum one (entry 9). When crotonaldehyde was used, 1,2-addition product and 1,4-addition product were formed (entry 10). Noteworthy is the fact that 1,5-dicarbonyl compound, the Michael adduct, was obtained in good yield by the reaction of <u>la</u> with benzalacetone (entry 11).

The aldol reaction is one of the standard tools for creating new carbon-carbon bonds, and numerous methods have been developed⁵⁾ including the catalytic aldol reaction by the aid of TBAF (tetrabutylammonium fluoride),⁶⁾ TAS-F [tris(diethylamino)sulfonium(TAS) difluorotrimethylsiliconate],⁷⁾ trityl perchlorate,⁸⁾ etc.,⁹⁾ which are expensive or not commercially available. Concerning the cross-aldol reaction using silyl enol ethers, the TiCl₄-promoted reaction (Mukaiyama's method) is the first example, and the reaction has been carried out using an equimolar amount of TiCl₄ in most cases to obtain the aldols in good yields.¹⁰⁾ In this connection, we found that the expected aldol was only in 35% yield, when the silyl enol ether 1a was reacted with benzaldehyde at room temperature in CH₂Cl₂ under the influence of a catalytic amount (5 mol%) of TiCl₄.

Finally, it should be stressed that cheap and commercially available $BiCl_3$ is a new efficient catalyst of the cross-aldol reaction between silvl enol ethers and aldehydes under extremely mild conditions (room temperature and weak acidic $(BiCl_3$ is a weak Lewis acid)). In this reaction, the aldol products were obtained in good yields, however, low diastereoselectivity was realized. Further studies towards diastereoselective aldol reaction as well as clarification of mechanism and other synthetic reactions utilizing the unique characteristics of BiCl₂ are now in progress in our laboratory.

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