Electronic Supplementary Information

Synthesis and structure of air-stable cationic organobismuth complex and its use as a highly efficient catalyst for direct diastereoselective Mannich reaction in water

Renhua Qiu, Shuangfeng Yin*, Xiaowen Zhang, Jun Xia, Xinhua Xu* and Shenglian Luo

College of Chemistry and Chemical Engineering, Hunan University, Changsha, 410082, China. Tel (Fax): +86-731-511-8161; E-mail: sfyin73@yahoo.com.cn (S. F. Yin); xhx1581@yahoo.com.cn (X. H. Xu).

Experimental

General: The chemicals were purchased from Aldrich. Co. Ltd as well as from other chemical providers and used as received unless otherwise indicated. The processor $[S(CH_2C_6H_4)_2BiCl]$ (**2**) of complex $[S(CH_2C_6H_4)_2Bi(OH_2)]^+[ClO_4]^-$ (**1**) was prepared according to the procedure described elsewhere.[1, 2] Catalyst **1** was prepared in air using THF as solvent. The direct diastereoselective Mannich reactions were carried out in various solvents. The NMR spectra were recorded at 25^{o}C using an INOVA-400M (USA) instrument calibrated using tetramethylsilane (TMS) as internal standard. Elemental analysis was performed over VARIO EL III (Germany). X-ray single crystal diffraction analysis was performed in Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences over a SMART-APEX instrument. Melting points of compounds were determined over a XT-4 micro apparatus (Beijing Tech Instrument Co. Ltd). The acidity was measured by Hammett indicator method as described previously.[3, 4] The employed indicators included dimethyl yellow (*pKa* = 3.3), methyl red (*pKa* = 4.8), neutral red (*pKa* = 6.8), bromothymol blue (*pKa* = 7.2), and thymol blue (*pKa* = 8.9). Acid and base strength was expressed in terms of Hammett acidity function (H_0) and Hammett basicity function (H_-), respectively, as scaled by *pKa* value of the indicators.

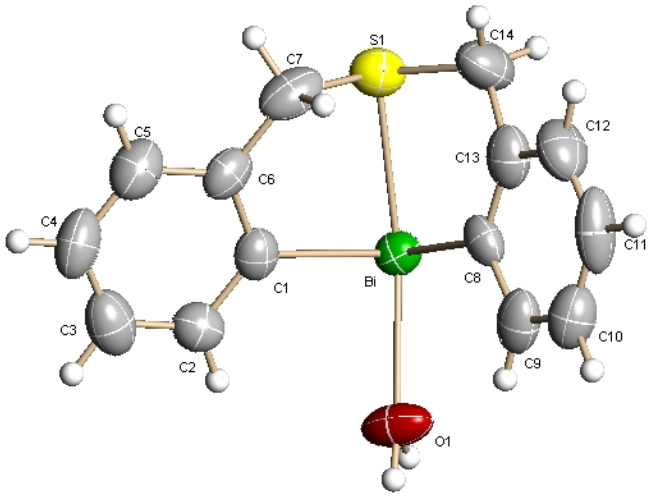
Crystal data refinements details

Data collection: Bruker *SMART*; cell refinement: Bruker *SMART*; data reduction: Bruker *SHELXTL*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: Bruker *SHELXTL*; software used to prepare material for publication: Bruker *SHELXTL*.

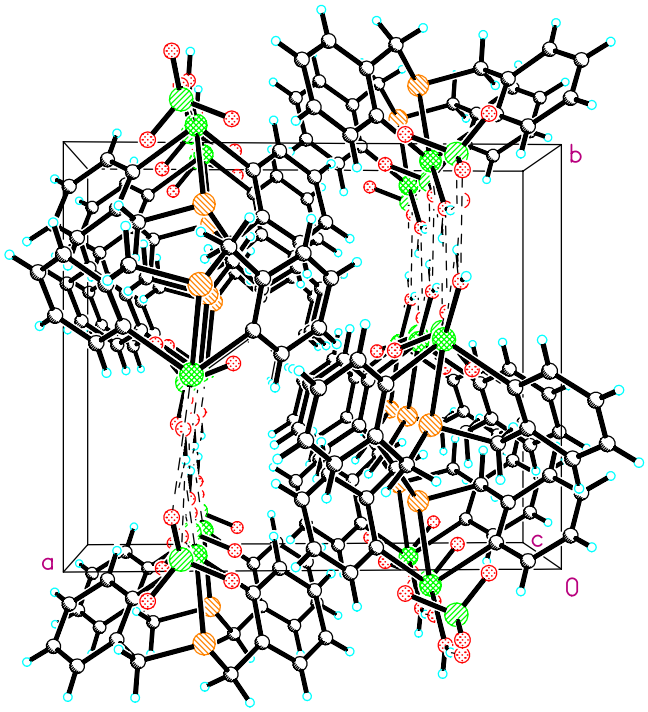
ESI-Table 1. Crystal data and structure refinement for $[S(CH_2C_6H_4)_2Bi(OH_2)]^+[ClO_4]^-$ (**1**)[a]

Entry	$[S(CH_2C_6H_4)_2Bi(OH_2)]^+[ClO_4]^-$ (**1**)
Formula	$C_{14}H_{14}BiClO_5S$
Formula weight	538.74
Crystal system, space group	Monoclinic, *P*2(1)/*c*
a Å, *b* Å, *c* Å,	13.8231 (17), 11.7666 (14), 10.0447 (12)
β deg	92.639 (2)
V, Å^3	1632.0 (3)
Z, D_{calcd}, Mg m^{-3}	4, 2.193 Mg m^{-3}
μ, mm^{-1}	11.11 mm^{-1}
F(000)	1016
Crystal size, mm	0.19 × 0.17 × 0.17
θ range, deg.	4.6–52.0
Limiting indices	−17≤h≤16, −14≤k≤10, −12≤l≤12
Reflections collected/ unique	8802 / 3206, R_{int} = 0.1169
Completeness to theta =26.00	99.8%
Goodness-of-fit on F^2	1.074
Final R indices [I>2σ(I)]	R1 = 0.0572, wR2 = 0.1499
R indices (all data)	R1 = 0.0667, wR2 = 0.1545
Largest diff peak & hole /e. Å^{-3}	3.871 and -2.337

[a] Temperature: 293(2) K; Wavelength: Mo/K*α*, 0.71073 Å; Refinement method: Full-matrix least-squares on F^2; Absorption correction: Empirical; $w = 1/[\sigma^2(F_o^2) + (0.0805P)^2 + 3.7674P]$, where $P = (F_o^2 + 2F_c^2)/3$; CCDC register number: CCDC 728508.



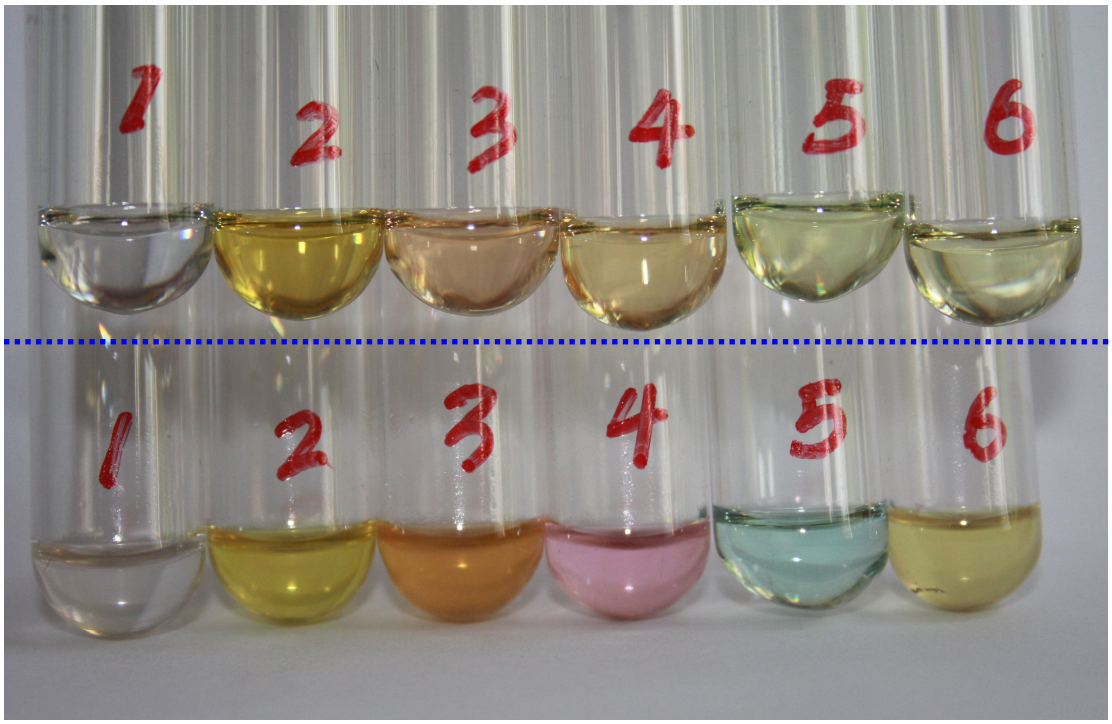
ESI-Fig. 1 An ORTEP view showing 50% probability ellipsoids of cationic organobismuth $[S(CH_2C_6H_4)_2Bi(OH_2)]^+$ of complex **1**.



ESI-Fig. 2 An ORTEP view showing 50% probability ellipsoids of crystal cell of $[S(CH_2C_6H_4)_2Bi(OH_2)]^+$ $[ClO_4]^-$ (**1**).

Acidity and basicity measurement

The acidity was measured by Hammett indicator method as described previously.[3, 4] Benzene was chosen as solvent and dehydrated over 3A zeolite prior to use. The indicators used in this study are listed in Table 1, together with their color and pKa values. The employed indicators included dimethyl yellow (*pKa* = 3.3), methyl red (*pKa* = 4.8), neutral red (*pKa* = 6.8), bromothymol blue (*pKa* = 7.2), and thymol blue (*pKa* = 8.9). Each indicator was dissolved in benzene to generate a solution of 0.1 wt%. Acid and base strength was expressed in terms of Hammett acidity function (H_0) and Hammett basicity function (H_-), respectively, which was scaled by *pKa* value of the indicators. The procedure for determining the acidity and basicity of complex **1** is as follows: 5 mg complex **1** was dissolved in 0.5 ml benzene in a test tube (10ml), followed by sonication till the complex was completely dissolved in the solvent. Then one drop of the indicator was added to the solution by an 1 ml plastic syringe, and acidity or basicity strength was estimated according to color change as shown in the following figure (ESI-Fig. 3).



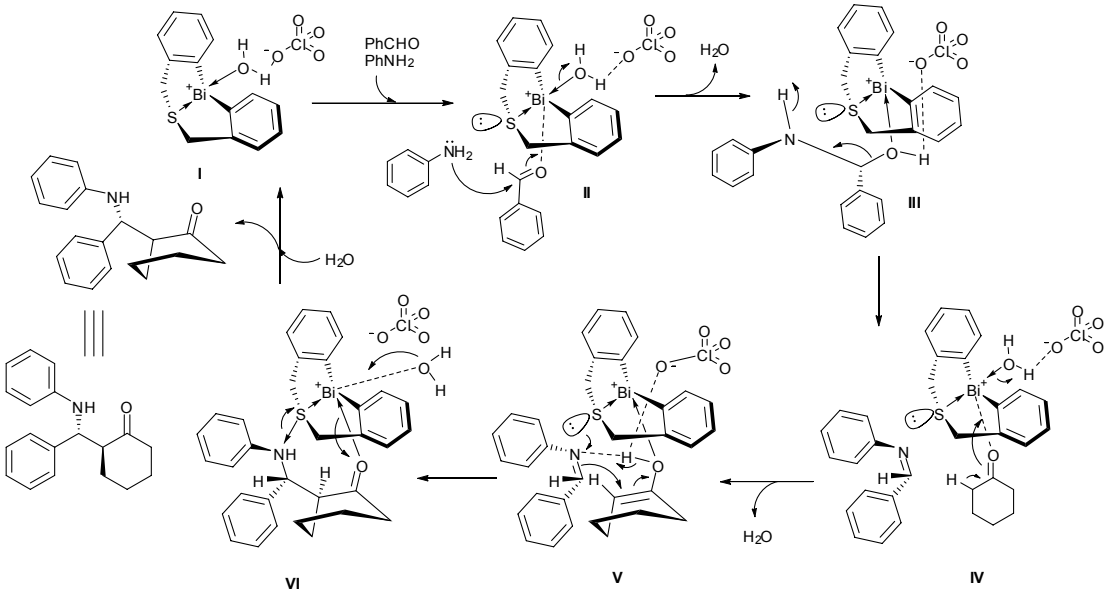
ESI-Fig. 3 The upper samples show the indicators dissolved in benzene (1. benzene; 2. dimethyl yellow; 3. methyl red; 4. neutral red; 5. bromothymol blue; 6. thymol blue); the lower samples show complex (**1**) dissolved in benzene solution after addition of different indicators (1. blank [complex (**1**) dissolved in benzene]; 2. dimethyl yellow; 3. methyl red; 4. neutral red; 5. bromothymol blue; 6. thymol blue).

Proposed mechanism related to catalysis by cationic organobismuth complex 1: According to the findings reported so far[5, 6], the mechanism of the direct Mannich reaction of benzaldehyde, aniline and cyclohexanone catalyzed by cationic organobismuth complex **1(I)** in water can be postulated (Scheme 1). When solid **I** is added to the reaction solution, there is immediate hydration of bismuth cationic groups. At this stage, there is frequent intra-molecular and intermolecular exchange of water with reaction substrates. The carbonyl oxygen atom of benzaldehyde coordinates with the bismuth cations and is activated; and there is the formation of intermediate **II**. Then aniline (nucleophile) attacks the activated carbonyl group of benzaldehyde to produce the desired intermediate enmine **IV** (with the release of a water molecule).

Meanwhile, the carbonyl oxygen atom of cyclohexanone coordinates with the bismuth cation and is activated, forming cyclohex-1-enol intermediate **V**. The key factor of this mechanism is "coordinated attack": first the nitrogen atom of enmine accepts the lone pair electrons of sulphur atom, the π-electrons of the activated and unstabilized enamine are then transferred to

the activated cyclohex-1-enol, forming a new carbon-carbon bond via *si*-face of double bond plane. With the redistribution of π-electrons of activated cyclohex-1-enol, there is the formation of cyclohexanone, and the hydrogen atom is transferred to the nitrogen atom. It is worth pointing out that all the electron-transfer processes happen simultaneously and it is impossible for the substrates to choose other positions for the occurance of side reactions such as aldol addition and condensation. After this step, the *anti*-diastereoselective Mannich adducts are formed.

The catalyst **I** is renewed with the intake of one water molecule. At the present stage of investigation, we are still not sure of the transient intermediates that are possibly formed during the reaction. Further work is still being conducted for clarification of this aspect.



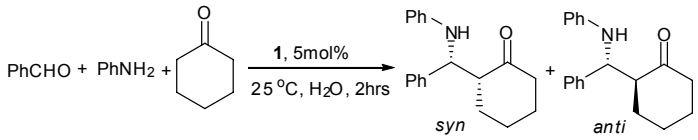
ESI-Scheme 1 A proposed mechanism on direct Mannich reaction of benzaldehyde, aniline and cyclohexanone catalyzed by cationic organobismuth complex **1**.

Typical procedure for direct diastereoselective Mannich reaction: To a 25 mL round bottomed flask was added catalyst **1** (46 mg, 0.05 mmol), PhCHO (106 mg, 1.0 mmol), $PhNH_2$ (93 mg, 1.0 mmol), cyclohexanone (108 mg, 1.0 mmol) and H_2O (2.0 mL). Then the mixture was stirred for 2 hrs under TLC analysis until the PhCHO and $PhNH_2$ as well as the intermediate (E)-N-benzylideneaniline (obtained form PhCHO and $PhNH_2$) was completely consumed. Then the solvents of the resulted mixture were removed by vacuum evaporation, and the residue was dissolved in Et_2O and the mixture was subject to filtration. After vaporization of the collected filtrate at room temperature, colorless crystals suitable for direct ^1H NMR analysis were obtained. The other procedure is described as follows: the mixture was extracted with Et_2O (10 mL×3), and the resulted residue was subject to column chromatograph (PE/EA=5/1). Yield, 276 mg, 99%; mp 172-173 ^oC (lit.: 170-172 ^oC); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.65-1.74 (2H, m, CH_2 of Cy),

1.82-1.94 (4H, m, $(CH_2)_2$ of Cy), 2.30-2.37 (1H, m, one of proton of CH_2 in Cy), 2.37-2.46 (1H, m, one of proton of CH_2 in Cy), 2.75-2.79 (1H, m, one of proton of Cy), 4.62 (0.95 H, d, J = 7.2 Hz, CH, *anti*-isomer), 4.78 (0.05 H, d, J = 4.8 Hz, CH, *syn*-isomer), 6.55 (2H, d, J = 8.0 Hz, Ph), 6.63 (1H, t, J = 7.6 Hz, Ph), 7.06 (2H, t, J = 8.4 Hz, Ph), 7.23 (1H, t, J = 7.2 Hz, Ph), 7.30 (2H, t, J = 7.2 Hz, Ph), 7.36 (2H, t, J = 7.2 Hz, Ph); δ_C (100 MHz; $CDCl_3$; Me_4Si) 23.62, 27.87, 31.27, 41.76, 57.41, 58.05, 113.66, 117.58, 127.16, 127.16, 127.25, 128.45, 129.04, 141.59, 147.07, 212.87. All the adduct products of direct diastereoselective Mannich reaction were characterized based on detail comparison of ^1H and ^{13}C NMR spectra data.[7-13]

Typical procedure for direct diastereoselective Mannich reaction catalyzed by recovered catalyst 1: To a 100 mL round bottomed flask was added catalyst **1** (0.46 g, 0.5 mmol), PhCHO (1.06 g, 10.0 mmol), $PhNH_2$ (0.93 g, 10.0 mmol), cyclohexanone (1.08 g, 10.0 mmol) and H_2O (20.0 mL). Then the mixture was stirred for 2 hrs under TLC analysis until the PhCHO and $PhNH_2$ as well as the intermediate (*E*)-N-benzylideneaniline (obtained form PhCHO and $PhNH_2$) was completely consumed. The mixture was extracted with CH_2Cl_2; the CH_2Cl_2 portions were combined and subject to evaporation in vacuum to give a solid substance. Then Et_2O was added to the solid substance. Since the Mannich adduct has good solubility in Et_2O while the catalyst is indissoluble in Et_2O, it is easy to separate the catalyst and adducts by simple filtration. The related results are depicted in ESI-Table 1.

ESI-Table 1 Direct Mannich reaction of benzaldehyde, aniline and cyclohexanone over recovered catalyst **1**[a]



Recycle time	Yield of products (%) [b]	*syn/anti* [c]	Yield of recovered cat. (%) [b]
1	98	5/95	99
2	95	6/94	97
3	97	3/97	97
4	95	7/93	95
5	94	9/91	96
6	96	5/95	95
7	95	7/93	93
8	98	10/90	93
9	93	9/91	94
10	94	10/90	92

[a] PhCHO, 10.0 mmol; $PhNH_2$, 10.0 mmol; cyclohexanone, 10.0 mmol; **1**, 0.5 mmol; 25 °C. [b] Isolated yield. [c] Determined by ^1H NMR.

References

1. X.-W. Zhang, J. Xia, H.-W. Yan, S.-L. Luo, S.-F. Yin, C.-T. Au and W.-Y. Wong, *J. Organomet. Chem.*, 2009, DOI:10.1016/ j.jorganchem.2009.1005.1003.

2. T. Kotani, D. Nagai, K. Asahi, H. Suzuki, F. Yamao, N. Kataoka and T. Yagura, *Antimicrob. Agents Chemother.*, 2005, **49**, 2729-2734.
3. H. A. Benesi, *J. Am. Chem. Soc.*, 1956, **78**, 5490-5494.
4. H. A. Benesi, *J. Phys. Chem.*, 1957, **61**, 970-973.
5. E. J. Sorensen and G. M. Sammis, *Science*, 2004, **305**, 1725-1726.
6. B. List and J. W. Yang, *Science*, 2006, **313**, 1584-1586.
7. H. Wu, X.-m. Chen, Y. Wan, L. Ye, H.-Q. Xin, H.-H. Xu, C.-H. Yue, L.-L. Pang, R. Ma and D.-Q. Shi, *Tetrahedron Lett.*, 2009, **50**, 1062-1065.
8. J. S. Yadav, B. V. S. Reddy, K. S. Shankar, K. Premalatha and T. Swamy, *Lett. Org. Chem.*, 2008, **5**, 353-359.
9. Q.-X. Guo, H. Liu, C. Guo, S.-W. Luo, Y. Gu and L.-Z. Gong, *J. Am. Chem. Soc.*, 2007, **129**, 3790-3791.
10. M. A. Bigdeli, F. Nemati and G. H. Mahdavinia, *Tetrahedron Lett.*, 2007, **48**, 6801-6804.
11. Y. Gu, C. Ogawa, J. Kobayashi, Y. Mori and S. Kobayashi, *Angew. Chem. Int. Ed.*, 2006, **45**, 7217-7220.
12. B. Eftekhari-Sis, A. Abdollahifar, M. M. Hashemi and M. Zirak, *Eur. J. Org. Chem.*, 2006, **22**, 5152-5157.
13. A. Yanagisawa, H. Saito, M. Harada and T. Arai, *Adv. Syn. Catal.*, 2005, **347**, 1517-1522.