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Communication

Synthesis and structure of the bimetallic organoantimony catalyst and its application in diastereoselective direct Mannich reaction as facile separation catalytic system

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ABSTRACT

A bimetallic organoantimony catalyst with four Lewis/Brønsted acidic/basic sites assembled orderly was successfully synthesized and showed high catalytic efficiency. It has been applied in diastereoselective direct Mannich reaction by adding 0.1 mol% catalyst. This reaction presented unexpected facile separation ability from homogenous solution to heterogeneous solution.

1. Introduction

In recent years, the sustainable and economic chemical processes have been always concerned, the chemists were dedicated to develop the good reaction systems for molecular transformations by using abundant main-group elements [1–8]. As the fifth main-group element, antimony has attracted considerable attention and been adopted in numerous chemical synthesis, pharmaceutical and materials [9–21]. Previous studies indicated that inorganic antimony compounds are a kind of high activity Lewis acid in a wide range of organic reactions [22–28]. At the same time, a variety of organoantimony complexe also have been reported owning to its unusual catalytic activity in organic synthesis [22–28]. In previous work, Nomura and coworkers developed a kind of antimony-based organometallic complexes that could be selected as an effective catalyst for reactions such as chemical fixation of CO_2 [29–31], polymerization [32–34], esterification [35] and amidation [36,37]. Gabbaï et al. have designed a platform, a variety of inexpensive antimony halides, to realize previously inaccessible reaction such as activating the transition metals by direct interaction or anion abstraction [38–42]. Lei [25] and Xia [27] et al. have separately found a method to efficiently catalyse the direct diastereoselective Mannich reaction and allylation of aldehydes using the organoantimoy complex (5% mol catalyst loading). Considering on reducing the amount of catalyst and improving the efficiency of the catalyst, herein, we have designed and characterized bimetallic organoantimony catalysts, which displayed high catalytic efficiency in direct diastereoselective Mannich reaction (0.1% mol catalyst loading).

2. Experiment

2.1. Materials and physical measurement

All chemicals were purchased from Sigma-Aldrich. Co. Ltd unless otherwise indicated. The synthesis of Ph_2SbCl [43] and $C_8F_{17}SO_3H$ [44] are according to the literature. The preparation of catalyst was carried out under nitrogen atmosphere with freshly distilled solvents unless otherwise noted. THF and hexane were distilled from sodium/benzophenone system. Acetonitrile was distilled from CaH_2 system. The NMR spectra were recorded at 25 °C on INOVA-400 M (USA) (400 MHz to ^1H NMR and 101 MHz to ^{13}C NMR) calibrated with tetramethyl silane (TMS) as an internal reference. The abbreviations are used to describe peal patterns: singlet (s), doublet (d), triplet (t) and multiplet (m). TG-DSC analysis was performed on a HCT-1 (HENVEN, Beijing, China) instrument. Thin-layer chromatography (TLC) and column chromatography silica gel (200–300) were purchased from Anhui Liangchen Co. Ltd. X-

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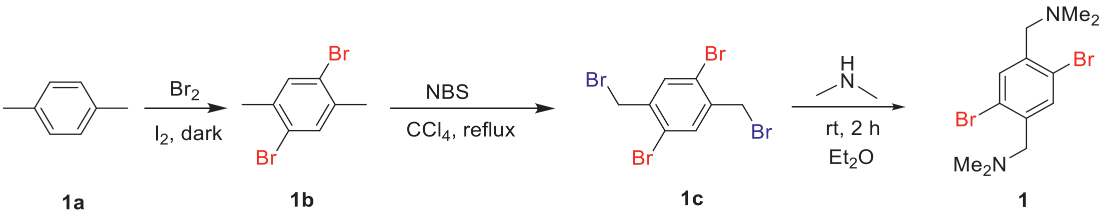


Scheme 1. Synthesis of ligand of $C_6H_2(CH_2NMe_2)_2Br_2$ (**1**).

ray single crystal diffraction analysis was performed over SMART-APEX and RASA-7A by Shanghai Institute Organic Chemistry, China Academy of Science. The acidity was measured by Hammett indicator method as described previously [45]. Acid strength was expressed in terms of Hammett acidity function (H_o) as scaled by *p*Ka value of the indicators.

2.2. Synthesis and spectral data of precursor of 1 (Scheme 1)

2.2.1. Synthesis of p-$C_6H_2(CH_3)_2Br_2$ (1b)

ao a 250 mL round flask was added 1,4-dimethylbenzene (**1a**) (73.9 mL, 600 mmol), then the initiator of I_2 was added and followed with liquid bromine (66.0 mL,1280 mmol) by drop at 0 °C. The resulting mixture was stirred in the absence of light for 8 h at 0 °C to RT. After that, the mixture was washed with saturated NaOH solution. Next, it was filtrated and the crude white solid product was obtained. The pure white powder was obtained after recrystallisation in anhydrous EtOH solution (yield 80%). mp:71–72 °C; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 7.4$ (2H, s), 2.3 (6H, s) ;^{13}C NMR ($CDCl_3$, 100 MHz, TMS); $\delta = 137.2$, 135.9, 122.9, 23.1.

2.2.2. Synthesis of $C_6H_2(CH_2Br)_2Br_2$ (1c)

To a two-necked round flask was added compound **1b** (52.7 g, 200 mmol), NBS (71.2 g, 400 mmol), 1,1′- azobis (cyanocyclohexane) (0.1 g). After vacuum and refunding nitrogen for three times, the CCl_4 (800 mL) was added. After the resulting mixture was stirred at RT for 1 hour, it was elevated to refluxing until the **1b** was consumed and monitored by TLC analysis. Then the resulting mixture was filtrated at room temperature and washed with CH_2Cl_2. The combined CH_2Cl_2 layer was washed with brine for 3 times and filtrated, dried with anhydrous Na_2SO_4, evaporated and recrystallized in anhydrous EtOH. The white needles solid product was obtained (yield 43%). mp:156–158 °C; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 7.7$ (2H, s),4.5 (4H, s);^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 138.0$, 134.3, 122.3, 30.5.

2.2.3. Synthesis of $C_6H_2(CH_2NMe_2)_2Br_2$ (1)

To a 250 mL two-necked round flask was added compound **1c** (8.435 g, 20.0 mmol). After vacuum and refunding nitrogen for 3 times, then the Me_2NH in ether solution (100 mL, 320 mmol) was added and stirred for 4 h at RT. Then washed with water and dried with Na_2SO_4, filtrated and evaporated. The resulted residue was recrystallized in petroleum ether and the white solid was hence obtained (yield 81%). mp:74–75 °C; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 7.6$ (2H, s), 3.5 (4H, s), 2.3 (12H, s), ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 138.5$, 134.4, 134.1, 123.3, 62.5, 45.5, 45.4.

2.3. Synthesis and spectral data of precursor of 2–4 (Scheme 2)

2.3.1. Synthesis of catalyst $C_6H_2(CH_2NMe_2SbPh_2)_2$ (2)

To a 50 mL tube was added compound **1** (0.631 g, 1.803 mmol), after vacuum and refunding nitrogen for 3 times, 10 mL anhydrous Et_2O was added, until the compound **1** was completely dissolved in Et_2O. The solution was setting in −60 °C and the 2.4 M *n*-BuLi (1.58 mL, 3.787 mmol) in hexane was dropping added with syringe. Then the mixture was stirred at −60 °C for 1 hour and then the reacting temperature was gradually increased to RT and stirred for another 1 hour. The resulted mixture was setting in −80 °C bath and was added with Ph_2SbCl (3.787 mmol) in Et_2O (8 mL) solution. After that, the mixture was stirred at −80 °C for 1 hour and then the reacting temperature was gradually increased to RT and stirred for another 1 hour. The final obtained mixture was evaporated and extracted with CH_2Cl_2 and evaporated again. The resulted residue was subjected to column chromatograph on silica gel (PE/EA = 20/1), and 111 mg white solid as pure product was obtained (yield 9%). mp:224–227 °C; ^1H NMR ($CDCl_3$, 400 MHz, TMS): δ_H (400 MHz; $CDCl_3$; TMS) 7.43 (10H, t, $J = 3.6$ Hz, one Ph of Ph_2Sb), 7.26 (10H, t, $J = 2.0$ Hz, another Ph of Ph_2Sb), 7.02 (2H, s, Ar*H*), 3.24(4H, s, $2CH_2$), 1.81(12H, s, $2NMe_2$); δ_C (100 MHz; $CDCl_3$; TMS) 143.6, 142.3, 140.7, 136.6, 136.1, 128.3, 127.6, 64.9, 43.7.

2.3.2. Synthesis of $[C_6H_2(CH_2NHMe_2SbPh_2)_2]^{2+}[OSO_2C_8F_{17}]^{2-}$ (3)

To a 50 mL tube was added (0.2052 g, 0.276 mmol) and $C_8F_{17}SO_3H$ (0.2765 g, 0.552 mmol). After vacuum and refunding nitrogen for 3 times, the mixture was added anhydrous THF (5 mL) and anhydrous CH_3CN (5 mL) and stirred at RT for 2 h. The resulting mixture was evaporated and the white solid was hence obtained (yield 95%). mp:150–151 °C; δ_H (400 MHz; $CDCl_3$; TMS) 9.451 (2H, s, Ar*H*), 7.37–7.40 (20H, s, 2(Ph_2Sb)), 4.20 (4H, d, $J = 3.6$ Hz, $2CH_2$), 2.64 (12H, d, $J = 4.8$ Hz, $2NMe_2$); δ_C (100 MHz; $CDCl_3$; TMS) 145.3, 140.8, 136.3, 136.1, 130.9, 129.6, 129.6, 113.9, 110.9, 110.3, 108.2, 68.2, 62.9, 43.2, 30.4, 19.5, 14.1. Elemental Analysis calculation (%) for $C_{52}H_{40}F_{34}N_2O_6S_2Sb_2$: C, 35.84; H, 2.31; found: C, 35.91; H, 2.26.

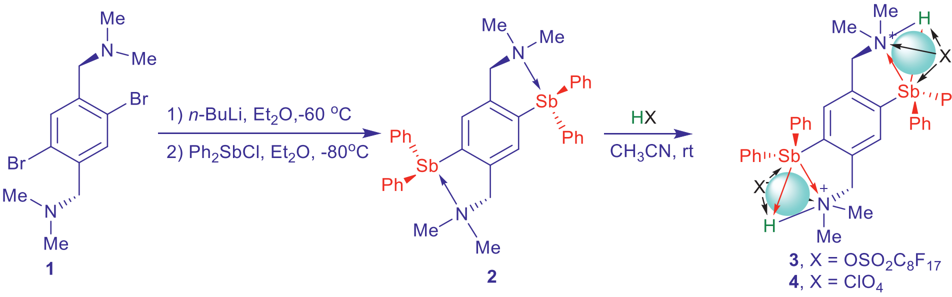
2.3.3. Synthesis of $[C_6H_2(CH_2NHMe_2SbPh_2)_2]^{2+}[ClO_4]^{2-}$ (4)

To a 50 mL tube was added complex **2** (0.2052 g, 0.276 mmol) and $HClO_4$ (0.055 g, 0.552 mmol). After three cycles of vacuum-and-nitrogen purging, the mixture was added anhydrous THF (5 mL) and anhydrous CH_3CN (5 mL), and the resulted mixture was stirred at RT for 2 h. The resulted mixture was subject to evaporation to afford the formation of a white solid (yield 94%). mp > 300 °C; δ_H (400 MHz; acetone-d_6; TMS) 7.67 (2H, s, Ar*H*), 7.39–7.51 (20H, s, 2(Ph_2Sb)), 4.71 (4H, s, $2CH_2$), 2.92 (12H, s, $2NMe_2$). Elemental Analysis calculation (%) for $C_{36}H_{40}Cl_2N_2O_8Sb_2$: C, 45.85; H, 4.27; found: C, 45.89; H, 4.20.

3. Results and discussion

3.1. Physicochemical properties

The complexes **2** – **4** remain intact in the open air for a test period of one year. The Lewis acidity of complexes **2** – **4** as estimated by the Hammett indicator method are $6.8 < H_o < 7.2$, $4.8 < H_o < 6.8$ and $4.8 < H_o < 6.8$ (H_o is Hammett acidity function), respectively (detail procedure see SI), indicating that there is increase of Lewis acidity with the incorporation of HX. According to the colour change of indicators, complex **3** is in fact higher than complex **4** in Lewis acidity, in agreement with the fact that $C_8F_{17}SO_3^-$ is higher than ClO_4^- in electron-withdrawing ability. The TG-DSC result shows that complex **3** is thermal stable up to 150 °C (Fig. 1).



Scheme 2. Synthesis of organoantimony complexes **2**–**4**.

Table 1
Crystallographic data of complex **2** and **4**.

Complex	**2**	**4**
Formula	C_{36} H_{38} N_2 Sb_2	C_{36} H_{40} Cl_2 N_2 O_8 Sb_2
CCDC No.	951,219	951,218
Formula weight	742.18	943.13
Crystal system, space group	Monoclinic, P2(1)/n	Monoclinic, P2(1)/n
a Å	15.5729(11)	13.3543(8)
b Å	6.3228(5)	12.4528(7)
c Å	17.5148(13)	11.8911(7)
α, deg	90	90
β, deg	108.005(2)	105.6520(10)
γ, deg	90	90
V, Å^3	1640.1(2)	1904.14
Z, D_x, Mg cm^{-3}	2, 1.503	4, 1.503
μ, mm^{-1}	1. 673	1. 611
$F(000)$	740	940
Crystal size, mm	0.257 × 0.136 × 0.127	0.30 × 0.20 × 0.15
θ range for data collection, deg	1.53~26.00	2.28~30.53
Limiting indices	$-18 \leq h \leq 19$, $-7 \leq k \leq 7$, $-18 \leq l \leq 21$	$-19 \leq h \leq 19$, $-9 \leq k \leq 17$, $-16 \leq l \leq 16$
Reflections collected/unique	9415 / 3222, $R_{int} = 0.0273$	5813 / 5276, $R_{int} = 0.0178$
Goodness of fit on F^2	1.052	0.994
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0280$, $wR_2 = 0.0660$	$R_1 = 0.00176$, $wR_2 = 0.0441$
R indices (all data)	$R_1 = 0.0343$, $wR_2 = 0.0693$	$R_1 = 0.00210$, $wR_2 = 0.00463$
Largest diff peak and hole	0.439 and −0.317	0.485 and −0.555

Note: w (for **2**) = $1/[\sigma^2(F_o^2) + (0.090P)^2]$, where $P = (F_o^2 + 2F_c^2)/3$; w (for **4**) = $1/[\sigma^2(F_o^2) + (0.0218\ P)^2 + 1.1062P]$ where $P = (F_o^2 + 2F_c^2)/3$.

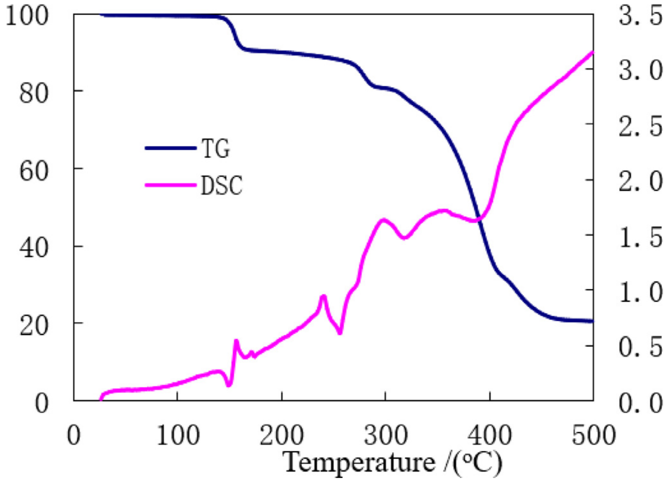


Fig. 1. TG-DSC curve of complex **3** in nitrogen flow (5 °C/min); Left: (TG/%), Right: (DSC, mg/mW).

3.2. *X-ray structure of complexes (2 and 4)*

The ORTEP views of complex **2** and **4** are shown in Fig 2. The complexes of **2** and **4** were crystallized by CH_2Cl_2 and confirmed by a single-crystal X-ray diffraction. The essential bond parameters were given in Table 1-3. The complex **3** failed to obtain a single-crystal owing to the long flexible chain of C_8F_{17} group. Complex **2** and **4** were crystallized in monoclinic space group $P2_1$/n. One can see that the complex **2** rotates around the symmetric axis of Sb(1)-Sb(1A). The N(1)-Sb(1) distance is 2.942(3) Å, as shown in the X-ray structure (Fig 2, left), which is slightly longer than the sum of the covalent radii (2.11 Å) [46], shorter than the sum of the van der Waals radii of nitrogen and antimony atoms (3.74 Å) [47], illustrating that coordinated bond exists between the nitrogen and antimony atoms. Upon reaction of complex **2** with $HClO_4$, there is elongation of N(1)-Sb(1) distance from 2.942(3) Å to 3.685(1) Å (Fig 2, right) resulting from the protonation of N(1), closing to the boundary of VDW radii (3.74 Å). This inferred that the coordination exists between two atoms is small, even can be neglected.

3.3. *Catalytic activities of complexes 2 to 4 in the Mannich reaction*

The Mannich reaction is one of the most useful approaches to synthesize nitrogen-containing compounds, as well as an effective method for the construction of $C - C$ bond [25,48–50]. In our previous works, our group have developed several efficient catalysts for such reactions, but the catalyst loading is still as high as 5 mol% [25,51–53]. Now, the complex **3** was used to catalyse the three-component (aldehyde, amine and ketone) direct diastereoselective Mannich reaction in assessing the catalytic activity. Noting that, the catalyst loading could be reduced to 0.1 mol% (shown as Table 4).

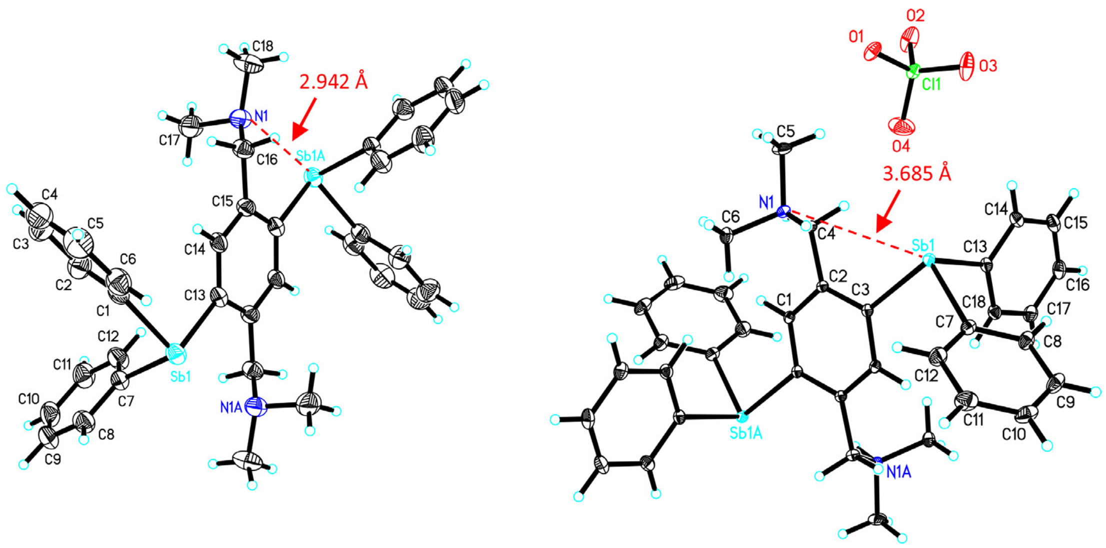


Fig. 2. The ORTEP views of complex **2** (left) and **4** (right).

Table 2
Selected bond lengths (Å) and angles (°) of complex **2**.

Selected bond lengths and angles	(Å) or (°)	Selected bond lengths and angles	(Å) or (°)
Sb(1)-C(7)	2.142(3)	C(1)-C(2)	1.380(5)
Sb(1)-C(13)	2.161(3)	C(2)-C(3)	1.383(5)
Sb(1)-C(1)	2.168(3)	C(3)-C(4)	1.351(5)
Sb(1)-N(1)	2.942(5)	C(13)-C(14)	1.382(7)
N(1)-C(17)	1.499(7)	C(13)-C(15A)	1.385(7)
N(1)-C(16)	1.388(6)	C(14)-C(15)	1.365(9)
C(7)-Sb(1)-C(13)	98.40(10)	C(2)-C(1)-C(6)	117.4(3)
C(7)-Sb(1)-C(1)	93.57(11)	C(2)-C(1)-Sb(1)	124.9(2)
C(13)-Sb(1)-C(1)	95.36(11)	C(6)-C(1)-Sb(1)	117.6(3)
C(16)-N(1)-C(18)	115.2(5)	C(14)-C(15)-C(13A)	118.6(6)
C(16)-N(1)-C(17)	112.0(5)	C(14)-C(15)-C(16)	119.1(6)
C(18)-N(1)-C(17)	108.2(5)	C(13A)-C(15)-C(16)	122.2(5)

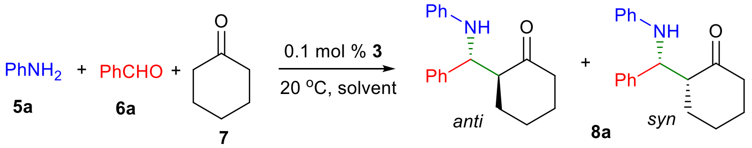
Table 3
Selected bond length (Å) and angles (°) of complex **4**.

Selected bond lengths and angles	(Å) or (°)	Selected bond lengths and angles	(Å) or (°)
Sb(1)-C(7)	2.149(1)	C(1)-C(2)	1.401(2)
Sb(1)-C(13)	2.154(1)	C(2)-C(3)	1.407(1)
Sb(1)-C(3)	2.193(1)	C(3)-C(1)	1.399(2)
Sb(1)-N(1)	3.685(5)	C(13)-C(14)	1.992(2)
N(1)-C(4)	1.509(2)	C(13)-C(18)	1.392(2)
N(1)-C(5)	1.493(2)	C(14)-C(15)	1.395(2)
C(3)-Sb(1)-C(7)	97.65(5)	C(1)-C(3)-C(2)	117.6(1)
C(3)-Sb(1)-C(13)	94.26(5)	C(1)-C(3)-Sb(1)	121.03(2)
C(13)-Sb(1)-C(7)	95.12(5)	C(2)-C(3)-Sb(1)	121.22(9)
C(4)-N(1)-C(5)	115.2(5)	C(1)-C(2)-C(3)	120.2(1)
C(4)-N(1)-C(6)	112.7(1)	C(1)-C(2)-C(4)	118.3(1)
C(5)-N(1)-C(6)	110.9(1)	C(3)-C(2)-C(4)	121.5(1)

As shown in Table 4, the poor yield and diastereoselectivity were observed when the reaction was carried out in polar solvents (entries 1 – 4, 6). When the *n*-Hexane (Table 4, entry 5) as solvent, the yield and diastereoselectivity increased up to 88% and *anti/syn* = 88/12. In short, this reaction took place in the non-polar organic solvent resulting the best yield (yield 88%, *anti/syn* = 88/12), which showed a different result comparing with previous work [25,27]. Upon investigation of the typical procedure for solubility measurement of catalyst **3**, we found that the solubility of **3** is 0.15 g/L in hexane at 20 °C (detail data see ESI). Catalyst **3** has best catalytic effect in Mannich reaction using hexane as solvent. Perhaps the catalyst **3** and raw materials have stronger polarity than hexane, which could result in stronger interaction between the catalyst and substrates and more effective precipitation of products (Fig 3, entry 5). The catalyst loadings, reaction temperature and substrate ratio were also screened as shown in Table 5–7, respectively. As shown in Table 8, complex **3** is superior to complex **4**, precursor **2** and $HO_SO_2C_8F_{17}$ as well as superior to our previous reported complex $C_6H_{11}N(C_6H_4CH_2)_2SbOSO_2C_8F_{17}$ [27] in terms of catalytic efficiency and diastereoselectivity. Therefore, the optimized reaction condition was shown as the following:1.0 equivalent of **5a**,1.2 equivalent of **6a** and 3.0 equivalent of **7** in the presence of 0.1 mol% of complex **3** at 20 °C in *n*-hexane solution for 6–24 hrs.

With the best condition in hand, we explored the scope of substrates in this catalytic system over bimetallic organoantimony catalyst **3** (Table 9). It is noted that aromatic amines with the weak electron-withdrawing inductive effect groups (*p*-Cl, *p*-Me, en-

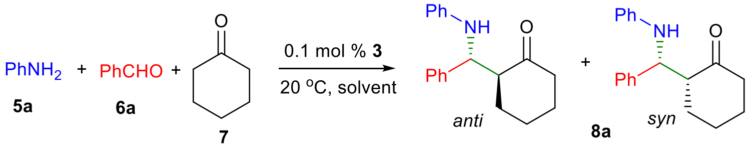
Table 4
Direct Mannich reaction of benzaldehyde, aniline and cyclohexanone in various solvents.



Entry	Solvent	Time (h)	*anti/syn*^{b}	Yield (%)^c
1	$CHCl_3$	12	81/19	79
2	CH_2Cl_2	12	82/18	78
3	THF	12	79/21	74
4	H_2O	12	76/24	84
5	Hexane	12	88/12	88
6	$[bmim]BF_4$	12	69/31	84

^{a} $PhNH_2$ (1.5 mmol), PhCHO (1.5 mmol), Cyclohexanone (4.5 mmol), Solvent (4 mL), Catalyst 3 (0.0015 mmol, 0.1 mol% based on $PhNH_2$), stirring at 20 °C for 12–18 hrs. ^{b} Determined by ^1H NMR. ^{c}GC Yield.

Table 5
Effect of catalyst **3** loading on product yield[a].



Entry	mol%	Yield (%)^b
1	0	14
2	0.01	63
3	0.05	83
4	0.1	88
5	1	89

[a] $PhNH_2$ (1.5 mmol), PhCHO (1.5 mmol), Cyclohexanone (4.5 mmol), *n*-hexane (4 mL), stirring for 12 h at RT.
[b] GC yield.

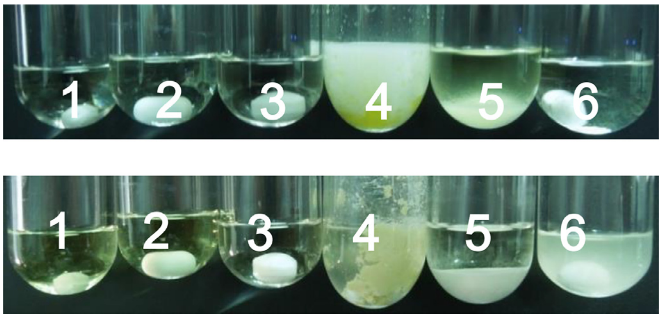


Fig. 3. Reaction-induced self-separation Mannich reaction catalysed by complex **3** in solvents corresponding to those of Table 4: Upper (beginning), lower (ending).

Table 6
Effect of reaction temperature on yield[a].

Entry	Temperature (°C)	Yield (%)^b
1	0	62
2	20	88
3	40	44
4	80	10

[a]$PhNH_2$ (1.5 mmol), PhCHO (1.5 mmol), Cyclohexanone (4.5 mmol), *n*-hexane (4 mL), Catalyst **3** (0.1 mol%), stirring for 12 h. ^{b}GC yield.

Table 7
Effect of substrate ratio on yield[a].

Entry	Ratio of $PhNH_2$: PhCHO: Cyclohexanone	Yield (%)^b
1	1:1:3	87
2	1:1.05:3	88
3	1:1.1:3	94
4	1:1.2:3	96
5	1:1.5:3	85

[a]$PhNH_2$ (1.5 mmol), PhCHO (x mmol), Cyclohexanone (4.5 mmol), *n*-hexane (4 mL), Catalyst **3** (0.1 mol%), stirring for 12 h at 20 °C.
[b] GC yield.

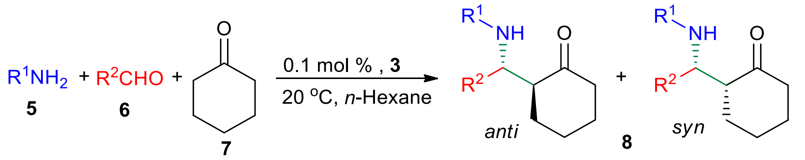
tries 2 and 9) showed higher reactivity compared to those with strong ones (*p*-NO_2, entry 4; *p*-MeO, *p*-EtO, entries 6–7). And the substrate with strong electron-donating *para*-substituent generated high diastereoselectivity with *anti/syn* ratio up to 90/10 (entry 6), implying that the formation of the (*E*)-N-benzylideneaniline intermediate played a great role on diastereoselectivity. Compared to the *para*-ones (entries 2, 4, 6, 7, 9), the *ortho*- substituted aromatic amines have a negative impact on catalytic efficiency (entries 3, 5, 8) due to steric influence. In addition, more aromatic aldehydes were explored and afforded moderate to excellent yields and diastereoselectivity (entries 10–15). It was found that the aromatic aldehydes with different functional groups exhibited distinct reactivity. An electron-withdrawing group is beneficial for product yield and diastereoselectivity (entries 10–13) due to the enhancement electrophilicity of aldehyde in favour of the formation of imine (The details of mechanism can be found in the SI). In this case, the reactivity *ortho*-CF_3-aldehydeis poor (entry 14) due to steric hindrance. 2-furylaldehyde with heterocycle provided moderate yield and diastereoselectivity (yield 79%, *anti/syn*=65/35). A series of aromatic amines (**5a-5d, 5f-5i**) and aromatic aldehydes (**6a-6 g**) could get the desired products and reaction-induced self-

Table 8
The Mannich reaction catalysed by various catalysts[a].

Entry	Catalyst (0.1 mol%)	Yield (%)[c]	*anti/syn*[b]
1	$[C_6H_2(CH_2NHMe_2SbPh_2)_2]^{2+}[OSO_2C_8F_{17}]^{2-}$ (**3**)	96	88/12
2	$[C_6H_2(CH_2NHMe_2SbPh_2)_2]^{2+}[ClO_4]^{2-}$ (**4**)	79	87/13
3	$C_6H_2(CH_2NMe_2SbPh_2)_2$ (**2**)	16	–
4	$HOSO_2C_8F_{17}$[d]	70	61/39
5	$C_6H_{11}N(C_6H_4CH_2)_2SbOSO_2C_8F_{17}$ [d]	66	85/15

[a] $PhNH_2$ (1.5 mmol), PhCHO (1.8 mmol), Cyclohexanone (4.5 mmol), *n*-hexane (4.0 mL), Catalyst (0.1 mol%), stirring for 12 h at 20 °C. [b] Determined by ^1H NMR. [c] Isolated yield. [d] 0.2 mol%.

Table 9
The Mannich reaction with various amines catalysed by **3**[a].



Entry	R^1	R^2	Product (**8**)	Yield (%)[c]	*anti/syn*[b]
1	Ph (**5a**)	Ph (**6a**)	**8a**	96	88/12
2	*p*-ClC_6H_4 (**5b**)	Ph (**6a**)	**8b**	95	70/30
3	*o*-ClC_6H_4 (**5c**)	Ph (**6a**)	**8c**	64	79/21
4[d]	*p*-$NO_2C_6H_4$ (**5d**)	Ph (**6a**)	**8d**	31	50/50
5[d]	*o*-$NO_2C_6H_4$ (**5e**)	Ph (**6a**)	**8e**	NR[e]	–
6	*p*-$EtOC_6H_4$ (**5f**)	Ph (**6a**)	**8f**	55	90/10
7	*p*-$MeOC_6H_4$ (**5 g**)	Ph (**6a**)	**8g**	79	85/15
8	*o*-$MeOC_6H_4$ (**5 h**)	Ph (**6a**)	**8h**	62	51/49
9	*p*-MeC_6H_4 (**5i**)	Ph (**6a**)	**8i**	94	83/17
10[f]	Ph (**5a**)	*p*-ClC_6H_4 (**6b**)	**8j**	92	69/31
11[f]	Ph (**5a**)	*p*-$CF_3C_6H_4$ (**6c**)	**8k**	95	82/18
12[f]	Ph (**5a**)	*p*-MeC_6H_4 (**6d**)	**8l**	85	68/32
13	Ph (**5a**)	*p*-$MeOC_6H_4$ (**6e**)	**8m**	79	69/31
14	Ph (**5a**)	*o*- $CF_3C_6H_4$ (**6f**)	**8n**	67	77/23
15	Ph (**5a**)	2- Furyl (**6 g**)	**8o**	79	65/35

[a] Reaction conditions: **5**, 1.5 mmol; **6**, 1.8 mmol; **7**, 4.5 mmol; *n*-Hexane, 4 mL; catalyst **3**, 0.1 mol%; 20 °C; 6–24 h. [b] Determined by ^1H NMR. [c] Isolated yield. [d] Reaction temperature, 50 °C. [e] No reaction. [f] Reaction temperature, −20 °C.

precipitation of products and catalyst **3** were observed in this reaction.

In conclusion, we successfully synthesized and characterized an air-stable bimetallic organoantimony catalyst **2**–**4**. Upon a series of research, the catalyst **3** has been applied in catalysing the three-component direct Mannich reaction with high catalytic efficiency (0.1 mol% catalyst loading) and diastereoselectivity(yield 96%, *anti/syn*=88/12) when *n*-hexane as solvent. Reaction-induced precipitation of products and catalyst were easy to be isolate at the end of the reaction. We expect with continuous effort more efficient and greener methods for exploiting more powerful organoantimony catalyst for organic synthesis.

Associated content

Detailed experimental procedures, characterization data, copies of the ^1H, ^{13}C NMR spectra.

Accession codes

CCDC 951,218 and 951,219 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.

Notes

The authors declare no competing financial interest.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2021.121820.

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