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CHIRAL PRIMARY AMINO SILYL ETHER ORGANOCATALYST FOR THE ENANTIOSELECTIVE DIELS-ALDER REACTION OF 1,2-DIHYDROPYRIDINES WITH ALDEHYDES

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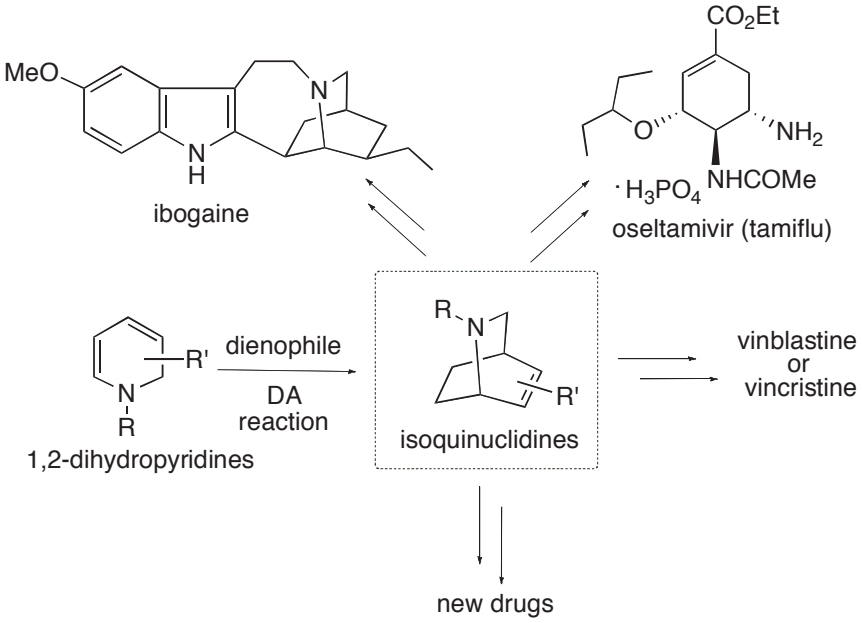
Abstract –The enantioselective Diels-Alder reactions of 1,2-dihydropyridines with acroleins using a chiral primary amino silyl ether organocatalyst afforded chiral isoquinuclidines with good chemical yields and excellent enantioselectivities (up to 70% and up to 99% ee).

INTRODUCTION

Asymmetric organocatalysis has emerged as an important and rapidly growing area of synthetic organic chemistry, and excellent covalent and non-covalent organocatalysts have been developed for use in a wide range of reactions.[1] Recently, we also developed a covalent-type oxazolidine and β-amino alcohol organocatalyst[2] that works as an efficient catalyst in the asymmetric Diels-Alder (DA) reaction of 1,2-dihydropyridines[3] with acroleins, which is an important reaction for the construction of chiral

* Dedicated to Dr. Ei-ichi Negishi on the occasion of his 77th birthday.

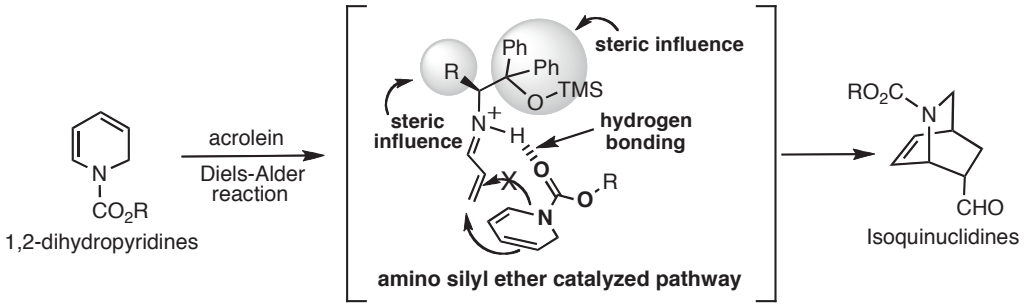
isoquinuclidines (2-azabicyclo[2.2.2]octanes). Isoquinuclidines are found widely in natural products such as iboga-type alkaloids, which have varied and interesting biological properties (Scheme 1).[4] In particular, there are the *anti*-cancer drugs, vinblastine and vincristine, which possess isoquinuclidines, with the aspidosperma portion.[5] Furthermore, it has recently been indicated that ibogaine reduces cravings for alcohol and other drugs by means of its ability to boost the levels of a growth factor known as glial cell line-derived neurotrophic factor (GDNF)[6]. Most recently it has also been shown that the isoquinuclidines can be used as the synthetic intermediates for the synthesis of oseltamivir phosphate (Tamiflu) which is an important *anti*-influenza drug.[7] Therefore, it is meaningful to establish an effective catalytic asymmetric synthetic methodology for chiral isoquinuclidines using an organocatalyst.



Scheme 1. Utility of isoquinuclidines

We report herein that primary amino silyl ether with CF_3CO_2H is an efficient organocatalyst for the DA reaction of 1,2-dihydropyridines with acroleins affording chiral isoquinuclidines at good chemical yields (up to 65%) and excellent enantioselectivities (up to 99% ee).

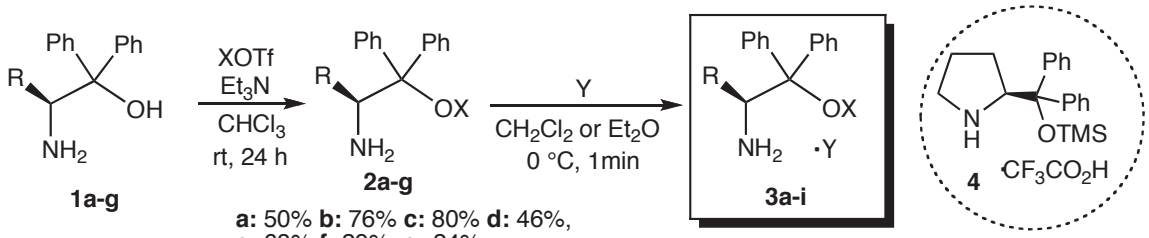
Concerning the concept for catalyst design, it is suggested that the formation of the iminium ion intermediate from the reaction of an amino silyl ether catalyst with acroleins might be able to control the attack of a diene that was fixed by the hydrogen bonding interactions between the hydrogen on the iminium ion intermediate and the carbonyl group on 1,2-dihydropyridines. And therefore, the steric influence of the bulky diphenyl silyloxy group at the 1-position and a substituent at the 2-position in the iminium ion intermediate might also effectively to afford high enantioselectivity in the reaction (Scheme 2).



Scheme 2. Function of amino silyl ether organocatalyst.

RESULTS AND DISCUSSION

Catalysts **3a-i**, respectively, were easily prepared by the reactions of the corresponding *β*-amino alcohols with XOTf (X= TMS, TES, and TIPS) followed by treatment with an organic acid (Scheme 3). Thus, the silylations of the *β*-amino alcohols **1a-g**, respectively, afforded the corresponding precursor amino silyl ethers **2a-g** in good to moderate chemical yields. The treatments of **2a-g** with YCO_2H (Y= CF_3, CCl_3, CH_3) afforded the desired amino silyl ether salt catalysts **3a-i** in quantitative yields. Proline-based amino silyl ether[8]-CF_3CO_2H salt catalyst **4** was also obtained by the treatment of the precursor proline-based amino silyl ether with CF_3CO_2H under the same reaction conditions.



2a-g

a: R = Me, X = TMS,
b: R = ^{i}Pr, X = TMS,
c: R = ^{t}Bu, X = TMS,
d: R = Ph, X = TMS,
e: R = Bn, X = TMS,
f: R = ^{t}Bu, X = TES
g: R = ^{t}Bu, X = TIPS

3a-i

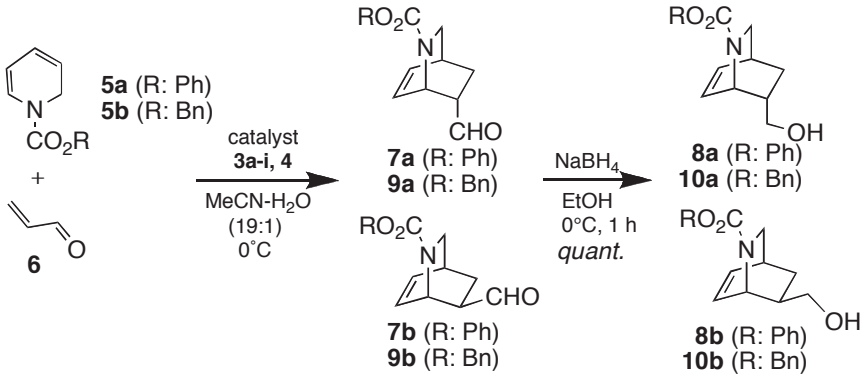
a: R = Me, X = TMS, Y = CF_3CO_2H
b: R = ^{i}Pr, X = TMS, Y = CF_3CO_2H
c: R = ^{t}Bu, X = TMS, Y = CF_3CO_2H
d: R = Ph, X = TMS, Y = CF_3CO_2H
e: R = Bn, X = TMS, Y = CF_3CO_2H
f: R = ^{t}Bu, X = TMS, Y = CH_3CO_2H
g: R = ^{t}Bu, X = TMS, Y = CCl_3CO_2H
h: R = ^{t}Bu, X = TES, Y = CF_3CO_2H
i: R = ^{t}Bu, X = TIPS, Y = CF_3CO_2H

Scheme 3. Preparations of amino silyl ethers **2a-g** and organocatalysts **3a-i**.

We first examined the DA reaction of common 1-phenoxycarbonyl-1,2-dihydropyridine **5a** with acrolein **6**. The reaction of **5a** (1 equiv) with **6** (3 equiv) was carried out at 0 °C in CH_3CN-H_2O (19:1)[2] in the presence of 10 mol% of catalysts **3a-i** to give the DA adduct **7**, and its chemical and optical yields were determined by conversion to the alcohol **8**. The results are summarized in Table 1. The reaction catalyzed

by 2-methyl-1-OTMS **3a** gave the DA adduct **7** in low chemical yield and with moderate enantioselectivity (entry 1). The use of 2-isopropyl-1-OTMS **3b** brought about an increase in both chemical yield (53%) and enantioselectivity (*endo*-**7a**: 91% ee) (entry 2). Bulkier 2-*tert*-butyl-1-OTMS catalyst **3c** gave the *endo*-DA adduct **7a** in good chemical yield (55%) and with excellent enantioselectivity (95% ee) (entry 3). In contrast, the catalytic activity of sterically crowded 2-phenyl-1-OTMS **3d** was low and those reactions proceeded slightly with *exo*-DA adduct **3b** (entry 4). On the other hand, more sterical larger 2-benzyl-1-OTMS **3e** showed a high level of catalytic activity to afford the *endo*-DA adduct **7a** at 56% and 85% ee (entry 5), although the reasons for this are unclear. Furthermore, the use of 2-*tert*-butyl-1-OTMS catalyst **3f** with CH_3CO_2H did not show the catalytic activity in the reaction (entry 6). In addition, the activity of 2-*tert*-butyl-1-OTMS catalyst **3f** with CCl_3CO_2H was also examined, but the chemical yield was not satisfactory, although the *endo*-DA adduct **7a** was obtained with good enantioselectivity (entry 7). We next examined the efficiencies of the catalysts **3h,i** having bulkier OTES and OTIPS at the 1-position on amino silyl ether (entries 8,9).

Table 1. Enantioselective DA reaction of **5** with **6** using catalysts **3** or **4**.

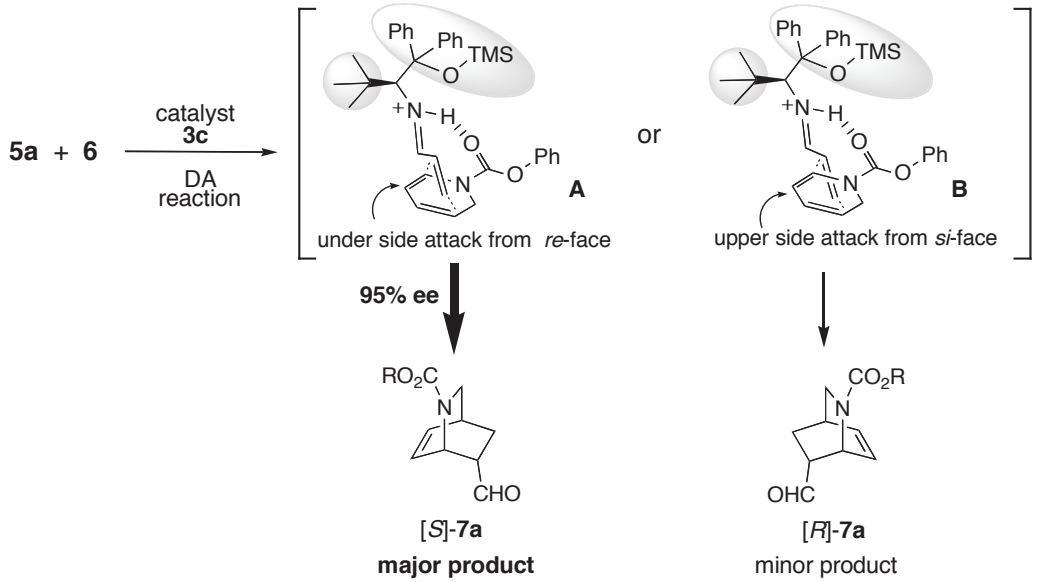


Entry	Catalyst (mol %)	Diene	Time (h)	Yield (%)[a]	*endo*/*exo*[b] (**7a**/**7b** or **9a**/**9b**)	DA adduct	*endo*-**7a**,**9a** ee (%)[c]
1	**3a** (10)	**5a**	24	24	13:1	**7a**	62 (*S*)
2	**3b** (10)	**5a**	24	53	20:1	**7a**	91 (*S*)
3	**3c** (10)	**5a**	24	55	*endo* only	**7a**	95 (*S*)
4	**3d** (10)	**5a**	24	7	6:1	**7a**	13 (*S*)
5	**3e** (10)	**5a**	24	56	20:1	**7a**	85 (*S*)
6	**3f** (10)	**5a**	24	nd	---	**---**	---
7	**3g** (10)	**5a**	24	17	15 : 1	**7a**	92 (*S*)
8	**3h** (10)	**5a**	24	22	8:1	**7a**	89 (*S*)
9	**3i** (10)	**5a**	24	18	6:1	**7a**	85 (*S*)
10	**4** (10)	**5a**	24	11	4:1	**7a**	69 (*R*)
11	**3c** (5)	**5a**	24	40	*endo* only	**7a**	92 (*S*)
12	**3c** (2.5)	**5a**	24	20	4:1	**7a**	90 (*S*)
13	**3c** (10)	**5a**	48	70	*endo* only	**7a**	95 (*S*)
14	**3c** (10)	**5b**	48	68	*endo* only	**9a**	96 (*S*)

[a] Isolated yields.[b]The *endo*/*exo* ratio was determined by ^{1}H NMR.[c]The ee of the *endo* and *exo* isomers were determined by chiral HPLC using a Daicel AD-H column (hexane/2-propanol : 85/15).

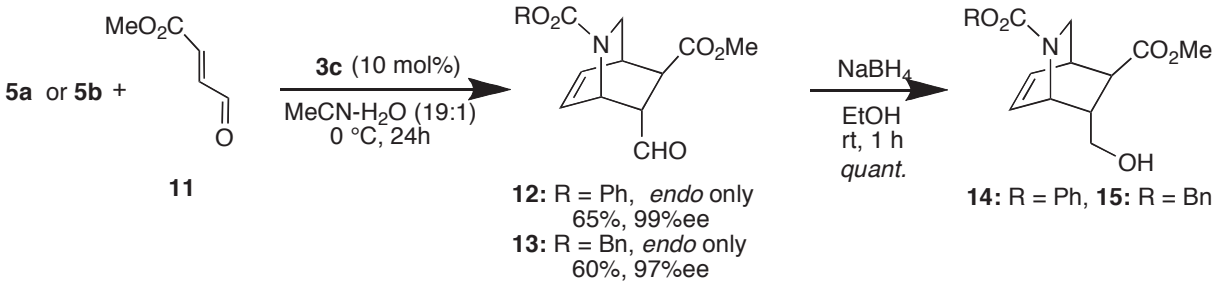
Although these catalysts **3h,i** brought about fairly good asymmetric inductions, the chemical yields were poor. The catalytic activity of common proline-based organocatalyst **4** with CF_3CO_2H in this reaction was also tested. However the catalyst did not afford a better result than did primary amino silyl ether **3c** (entry 10). The above results indicate that primary amino silyl ether was the efficient catalyst in this DA reaction. These results indicate that the existence of the OTMS group as a trisubstituted silyloxy group at the 1-position on amino silyl ether is important for obtaining a satisfactory enantioselectivity and chemical yield. To optimize the reaction conditions using superior catalysts **3c**, we next examined the effect of reducing the molar ratio of **3c**. Although the reaction mixtures containing 5 mol% of **3c** afforded fairly good enantioselectivity (*endo*-**7a**: 92% ee), the chemical yield decreased to 40% (entry 11). Lower catalytic loading to 2.5 mol% greatly decreased the chemical yield (20%) (entry 12). A dramatic increase in chemical yield to 70% was achieved with excellent enantioselectivity (95% ee), when the reaction time was changed from 24 h to 48 h (entry 13). Similarly, synthetically useful 1,2-dihydropyridine **5b** was also examined using superior catalyst **3c** and dienophile **6** (Scheme 14). The reaction was carried out at 0 °C for 24 h in the presence of 10 mol% of the best catalyst **3c** to give the corresponding *endo*-DA adduct **9a**. The chemical and optical yields of the DA adduct **9** were determined by converting to the alcohol **10**. As a result, good chemical yield and enantioselectivity (68%, 96% ee) were obtained using catalyst **3c**. These results indicated that 5-*tert*-butyl-1-OTMS catalyst **3c** with CF_3CO_2H were the most effective in the DA reactions of dienes **5a,b** with **6** to afford the DA adducts **7a, 9a,** respectively, with good chemical yields and excellent enantioselectivities (**7a:** 70%, 95% ee, **9a:** 68%, 96% ee). However, the best catalyst **3c** did not afford a better result than our corresponding previously reported *β*-amino alcohol organocatalyst **1c** with CF_3CO_2H[2a] in the same DA reaction. It might be reason that bulkier trimethylsilyloxy group on **3c** was act negatively for obtaining the DA adducts **7a** or **9a** with an excellent chemical yield and enantioselectivity.

Based on both the high enantiopurity (95% ee) of the chiral DA adduct (7*S*)-**7a** that was obtained from the reaction of diene **5a** with dienophile **6** and Isihara's detail study[9] for an amino organocatalized DA reaction mechanism, a model of the enantioselective reaction was proposed as follows (Scheme 4). Thus, the reaction might be through the transition state **A** that was fixed by the hydrogen bonding interactions between the hydrogen on the iminium ion intermediate and the carbonyl group on 1,2-dihydropyridines. Then the diene might attack from the *re*-face of the olefin part on the iminium ion intermediate rather than the sterically crowded *si*-face that was masked by the combination of the bulky diphenyl trimethylsilyloxy group at the 1-position and the *tert*-butyl group at the 2-position in the iminium ion intermediate (transition state **B**).



Scheme 4. Prausible reaction course for DA reaction of **5a** with **6** using catalyst **3c**.

The effectiveness of superior 2-*tert*-butyl-1-OTMS catalyst **3c** was then evaluated in the DA reaction using acrolein derivative **11** (Scheme 5). The reactions of dienes **5a** or **5b** with dienophile **11** were carried out at 0 °C in the presence of 10 mol% of superior catalyst **3c** to give the DA adducts **12** or **13**. The chemical and optical yields of **12** or **13** were determined by conversion to alcohols **14** or **15**, respectively. In both reactions, catalyst **3c** showed satisfactory asymmetric catalytic activity and the desired DA adducts **12** or **13** were obtained in good chemical yields and with excellent enantioselectivities (**12**: 65%, 99% ee, **13**: 60%, 97% ee).



Scheme 5. Enantioselective DA reactions of **5a** or **5b** with **11** using catalyst **3c**.

In conclusion, new amino silyl ether organocatalyst **3** was explored. Catalyst **3** was easily prepared in two steps. Organocatalyst **3c**, in particular, showed efficient asymmetric catalytic activity in the Diels-Alder reactions of 1,2-dihydropyridines **5a,b** with acroleins **6, 11** to afford the chiral isoquinuclidines **7, 9, 12, 23**, respectively. Further studies are in progress to examine the scope and limitations of this organocatalyst for the catalytic asymmetric version of the DA reactions of 1,2-dihydropyridines.

EXPERIMENTAL

IR spectra were measured with a PERKIN ELMER 1725X spectrophotometer. ^{1}H-NMR spectra were recorded on a JEOL JNM-GSX 400 and a JEOL JNM-LA 600 spectrometers with TMS as an internal standard. MS were taken on a Hitachi RMG-6MG and a JEOL-JNM-DX 303 spectrometers. Optical rotations was measured with a JASCO-DIP-370 digital polarimeter.

General procedure for the preparation of amino silyl ethers 2b,c,f,g

To a solution of amino alcohols **1a-e** (2.0 mmol) in CH_2Cl_2 (30 mL) were added trisubstituted silyl trifluoromethanesulfonates (2.4 mmol) and Et_3N (2.4 mmol) at -30 °C. The mixture was stirred for 24 min at room temperature. Water (10 mL) was added, the aqueous layer was extracted with $CHCl_3$ (2 x 30 mL) and organic phases were dried over $MgSO_4$ and evaporated to give a crude products **2a-g**. The residue was purified by column chromatography (SiO_2, $CHCl_3$) to give a pure products **2a-g** (**a**: 299 mg, 50%, **b**: 498 mg, 76%, **c**: 546 mg, 80%, **d**: 333 mg, 46%, **e**: 511 mg, 68%, **f**: 223 mg, 29%, **g**: 204 mg, 24%).

(*S*)-3-Methyl-1,1-diphenyl-1-(trimethylsilyloxy)butan-2-amine (2b)

Colorless oil. $[\alpha]_D^{25}$ 129.99 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 699, 836, 1069, 1250, 1493, 2954; ^{1}H-NMR ($CDCl_3$) δ: 7.44-7.26 (m, 10H, Ph), 3.57 (s, 1H, NCH), 1.92 (s, 1H, $CH(CH_3)_2$), 1.03 (d, J = 6.9 Hz, 6H, $CH(CH_3)_2$), 0.17 (d, J = 6.9 Hz, 6H, $CH(CH_3)_2$), -0.18 (s, 9H, $Si(CH_3)_3$); ^{13}C-NMR ($CDCl_3$) δ:128.7, 128.6, 127.7, 127.5, 127.1, 84.5, 61.5, 27.0, 23.6, 15.8, 1.8 ; *Anal.* Calcd for $C_{20}H_{29}NOSi$: C, 73.34; H, 8.92; N, 4.28. Found: C, 73.15; H, 9.10; N, 4.16. EI-MS m/z: 327 (M^+).

(*S*)-3,3-Dimethyl-1,1-diphenyl-1-(trimethylsilyloxy)butan-2-amine (2c)

Colorless oil. $[\alpha]_D^{26}$ 106.66 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 700, 835, 1072, 1250, 1494, 1738, 2952; ^{1}H-NMR ($CDCl_3$) δ: 7.58-7.26 (m, 10H, Ph), 3.61 (s, 1H, NCH), 0.72 (s, 9H, $C(CH_3)_3$), -0.21 (s, 9H, $Si(CH_3)_3$); ^{13}C-NMR ($CDCl_3$) δ:128.9, 128.6, 128.1, 127.5, 127.1, 126.8, 85.1, 65.1, 35.5, 28.8, 1.8; *Anal.* Calcd for $C_{21}H_{31}NOSi$: C, 73.84; H, 9.15; N, 4.10. Found: C, 73.75; H, 9.21; N, 4.02. EI-MS m/z: 342 (M^+).

(*S*)-3,3-Dimethyl-1,1-diphenyl-1-(triethylsilyloxy)butan-2-amine (2f)

Colorless oil. $[\alpha]_D^{28}$ 109.99 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 701, 850, 1069, 1230, 1494, 1738 2952; ^{1}H-NMR ($CDCl_3$) δ: 7.62-7.26 (m, 10H, Ph), 3.64 (s, 1H, NCH), 0.83 (t, J = 8.0 Hz, 9H, $Si(CH_2CH_3)_3$), 0.72 (s, 9H, $C(CH_3)_3$), 0.24 (qq, J = 7.4 Hz, J = 8.3 Hz, 6H, $Si(CH_2CH_3)_3$); ^{13}C-NMR ($CDCl_3$) δ:128.9,

128.7, 128.0, 127.7, 127.0, 126.8, 85.0, 65.5, 35.5, 28.8, 7.3, 6.0; *Anal.* Calcd for $C_{24}H_{37}NOSi$: C, 75.14; H, 9.72; N, 3.65. Found: C, 75.02; H, 9.81; N, 3.54. EI-MS m/z: 383 (M^+).

(*S*)-3,3-Dimethyl-1,1-diphenyl-1-(triisopropylsilyloxy)butan-2-amine (2g)

Colorless oil. $[\alpha]_D^{28}$ 116.66 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 704, 880, 1052, 1229, 1464, 1738, 2945; ^{1}H-NMR ($CDCl_3$) δ: 7.72-7.26 (m, 10H, Ph), 3.74 (s, 1H, NCH), 1.05 (s, 18H, $Si(CH(CH_3)_2)_3$), 0.99 (d, J = 7.4 Hz, 18H, $Si(CH(CH_3)_2)_3$), 0.90 (d, J = 7.4 Hz, 18H, $Si(CH(CH_3)_2)_3$), 0.72 (s, 9H, $C(CH_3)_3$), 0.66 (dd, J = 7.4 Hz, J = 7.7Hz, 3H, $Si(CH(CH_3)_2)_3$); ^{13}C-NMR ($CDCl_3$) δ:129.4, 129.1, 127.9, 126.8, 85.9, 66.2, 35.4, 28.9, 19.0, 14.2; *Anal.* Calcd for $C_{27}H_{43}NOSi$: C, 76.17; H, 10.18; N, 3.29. Found: C, 76.01; H, 10.29; N, 3.14. EI-MS m/z: 425 (M^+).

General procedure for the preparation of amino silyl ether・CF_3CO_2H organocatalysts 3a-i

To a CH_2Cl_2 (1.8 mL) solution of amino silyl ether **2a-g** (0.03 mmol), trifluoroacetic acid (0.036 mmol) was added at 0 °C. The resulting mixture was stirred at that temperature for 5 min. Solvent was evaporated under a reduced pressure to afford the corresponding catalyst **3a-i** as a colorless crystal in quantitative yield.

(*S*)-1,1-Diphenyl-1-(trimethylsilyloxy)propan-2-amine・CF_3CO_2H (3a)

Colorless oil. $[\alpha]_D^{28}$ 73.33 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 701, 838, 1130, 1254, 1541, 1684; ^{1}H-NMR ($CDCl_3$) δ: 7.51-7.26 (m, 10H, Ph), 4.37 (d, J = 6.9 Hz, 1H, NCH), 1.24 (d, J = 6.9 Hz, 3H, CH_3), -0.18 (s, 9H, $Si(CH_3)_3$); ^{13}C-NMR ($CDCl_3$) δ:129.0, 128.6, 128.0, 81.9, 54.9, 14.9, 1.4; *Anal.* Calcd for $C_{20}H_{26}F_3NO_3Si$: C, 58.09; H, 6.34; N, 3.39. Found: C, 57.91; H, 6.48; N, 3.22.

(*S*)-3-Methyl-1,1-diphenyl-1-(trimethylsilyloxy)butan-2-amine・CF_3CO_2H (3b)

White crystal (Et_2O). Mp 220-221 °C; $[\alpha]_D^{27}$ 113.33 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 702, 833, 1051, 1253, 1510, 1667; ^{1}H-NMR ($CDCl_3$) δ: 7.77-7.26 (m, 10H, Ph), 4.10 (d, J = 3.2 Hz, 1H, NCH), 1.97 (s, 1H, $CH(CH_3)_2$), 1.05 (d, J = 6.9Hz, 6H, $CH(CH_3)_2$), 0.45 (d, J = 6.9 Hz, 6H, $CH(CH_3)_2$), -0.20 (s, 9H, $Si(CH_3)_3$); ^{13}C-NMR ($CDCl_3$) δ:129.2, 128.9, 128.5, 82.1, 63.4, 26.6, 22.6, 17.0, 1.4; *Anal.* Calcd for $C_{22}H_{30}F_3NO_3Si$: C, 59.84; H, 6.85; N, 3.17. Found: C, 59.73; H, 6.98; N, 3.05.

(*S*)-3,3-Dimethyl-1,1-diphenyl-1-(trimethylsilyloxy)butan-2-amine・CF_3CO_2H (3c)

White crystal (Et_2O). Mp 222-223 °C; $[\alpha]_D^{24}$ 83.33 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 702, 836, 1133, 1254, 1495, 1673, 2958; ^{1}H-NMR ($CDCl_3$) δ: 7.58-7.09 (m, 10H, Ph), 4.19 (s, 1H, NCH), 0.75 (s, 9H,

$C(CH_3)_3$), -0.14 (s, 9H, $Si(CH_3)_3$); ^{13}C-NMR ($CDCl_3$) δ:129.3, 128.9, 128.7, 128.5, 128.0, 83.3, 65.2, 34.7, 28.1, 1.6; *Anal.* Calcd for $C_{23}H_{32}F_3NO_3Si$: C, 60.64; H, 7.08; N, 3.07. Found: C, 60.48; H, 7.20; N, 2.95.

(*S*)-1,2,2-Triphenyl-2-(trimethylsilyloxy)ethan-2-amine・CF_3CO_2H (3d)

White crystal (Et_2O). Mp 189-190 °C; $[\alpha]_D^{27}$ 43.33 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 697, 837, 1131, 1254, 1507, 1684; ^{1}H-NMR ($CDCl_3$) δ: 7.64-6.79 (m, 10H, Ph), 5.29 (s, 1H, NCH), -0.16 (s, 9H, $Si(CH_3)_3$); ^{13}C-NMR ($CDCl_3$) δ:129.5, 129.4, 129.2, 128.7, 128.4, 127.6, 127.5, 83.5, 62.7, 1.6; *Anal.* Calcd for $C_{25}H_{28}F_3NO_3Si$: C, 63.14; H, 5.93; N, 2.95. Found: C, 62.98; H, 6.02; N, 2.82.

(*S*)-1,1,3-Triphenyl-1-(trimethylsilyloxy)propan-2-amine・CF_3CO_2H (3e)

White crystal (Et_2O). Mp 173-174 °C; $[\alpha]_D^{28}$ 246.66 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 699, 839, 1131, 1254, 1507, 1684; ^{1}H-NMR ($CDCl_3$) δ: 7.66-7.08 (m, 10H, Ph), 4.45 (d, J = 10.9 Hz, 1H, NCH), 3.08 (d, J = 14.3 Hz, 2H, CH_2Ph), 2.45 (t, J = 14.0 Hz, 2H, CH_2Ph), -0.10 (s, 9H, $Si(CH_3)_3$); ^{13}C-NMR ($CDCl_3$) δ:129.6, 129.2, 129.0, 128.7, 128.2, 127.1, 125.6, 125.0, 81.9, 60.6, 35.1, 1.5; *Anal.* Calcd for $C_{26}H_{30}F_3NO_3Si$: C, 63.78; H, 6.18; N, 2.86. Found: C, 63.65; H, 6.29; N, 2.75.

(*S*)-3,3-Dimethyl-1,1-diphenyl-1-(trimethylsilyloxy)butan-2-amine・CH_3CO_2H (3f)

White crystal (Et_2O). Mp 167-168 °C; $[\alpha]_D^{28}$ 29.99 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 695, 837, 1074, 1179, 1541, 1698; ^{1}H-NMR ($CDCl_3$) δ: 7.67-7.11 (m, 10H, Ph), 3.67 (s, 1H, NCH), 0.72 (s, 9H, $C(CH_3)_3$), -0.32 (s, 9H, $Si(CH_3)_3$); ^{13}C-NMR ($CDCl_3$) δ:129.0, 128.5, 128.2, 127.7, 127.3, 85.0, 64.9, 35.4, 28.8, 1.8; *Anal.* Calcd for $C_{23}H_{35}NO_3Si$: C, 68.78; H, 8.78; N, 3.49. Found: C, 68.61; H, 8.92; N, 3.35.

(*S*)-3,3-Dimethyl-1,1-diphenyl-1-(trimethylsilyloxy)butan-2-amine・CCl_3CO_2H (3g)

White crystal (Et_2O). Mp 177-178 °C; $[\alpha]_D^{29}$ 119.99 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 676, 827, 1079, 1173, 1507, 1684; ^{1}H-NMR ($CDCl_3$) δ: 7.65-7.14 (m, 10H, Ph), 4.30 (s, 1H, NCH), 0.78 (s, 9H, $C(CH_3)_3$), -0.12 (s, 9H, $Si(CH_3)_3$); ^{13}C-NMR ($CDCl_3$) δ:128.7, 128.1, 83.4, 65.3, 34.8, 28.2, 1.8; *Anal.* Calcd for $C_{23}H_{32}Cl_3NO_3Si$: C, 54.71; H, 6.39; N, 2.77. Found: C, 54.61; H, 6.47; N, 2.63.

(*S*)-3,3-Dimethyl-1,1-diphenyl-1-(triethylsilyloxy)butan-2-amine・CF_3CO_2H (3h)

Colorless oil. $[\alpha]_D^{28}$ 123.33 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 704, 832, 1133, 1243, 1507, 1684; ^{1}H-NMR ($CDCl_3$) δ: 7.51-7.26 (m, 10H, Ph), 4.23 (s, 1H, NCH), 0.77 (t, J = 7.7 Hz, 9H, $Si(CH_2CH_3)_3$), 0.75 (s, 9H, $C(CH_3)_3$), 0.26 (dt, J =7.5 Hz, J = 7.7 Hz, 6H, $Si(CH_2CH_3)_3$); ^{13}C-NMR ($CDCl_3$) δ:128.9, 128.7, 128.0,

127.7, 127.0, 126.8, 85.0, 65.5, 35.5, 28.8, 7.3, 6.0; *Anal.* Calcd for $C_{26}H_{38}F_3NO_3Si$: C, 62.75; H, 7.70; N, 2.81. Found: C, 62.63; H, 7.85; N, 2.71.

(*S*)-3,3-Dimethyl-1,1-diphenyl-1-(triisopropylsilyloxy)butan-2-amine・CF_3CO_2H (3i)

Colorless oil. $[\alpha]_D^{28}$ 143.33 (c 0.30, $CHCl_3$); IR (KBr) cm^{-1}: 706, 825, 1136, 1247, 1507, 1684; ^{1}H-NMR ($CDCl_3$) δ: 7.65-7.15 (m, 10H, Ph), 4.42 (s, 1H, NCH), 1.05 (s, 18H, $Si(CH(CH_3)_2)_3$), 0.89 (dd, J = 8.9 Hz, J = 8.0 Hz, 18H, $Si(CH(CH_3)_2)_3$), 0.73 (s, 9H, $C(CH_3)_3$), 0.60 (q, J = 7.5 Hz, 3H, $Si(CH(CH_3)_2)_3$); ^{13}C-NMR ($CDCl_3$) δ:129.4, 129.1, 128.7, 128.1, 82.7, 65.5, 34.3, 28.1, 18.7, 17.7, 13.7, 12.2; *Anal.* Calcd for $C_{29}H_{44}F_3NO_3Si$: C, 64.53; H, 8.22; N, 2.60. Found: C, 64.41; H, 8.38; N, 2.49.

General procedure for the DA reaction of 1, 2-dihydropyridine 5a,b with acrolein 6, 11 using catalyst 3c.

To a CH_3CN:H_2O (19:9, 0.5 mL) solution of catalyst **3c** (0.01 mmol) and 1,2-dihydropyridines **5a,b** (0.1 mmol), distillated acroleins **6, 11** (0.3 mmol) was added at 0 °C and the solution was stirred at 0 °C for 24 h. The reaction was quenched by water. The reaction mixture was diluted with water and extracted with Et_2O. The combined organic extracts were washed with brine, dried over Na_2SO_4, and removed under reduced pressure to give crude DA adducts **7a, 9a, 12, 13** which was used to the next reaction without purification.

To a stirred solution of products **7a, 9a, 12, 13** in EtOH (2.0 mL), $NaBH_4$ (2.0 mg, 0.05 mmol) was added and the mixture was stirred at 0 °C for 1 h. Solvent was evaporated under a reduced pressure. The reaction mixture was diluted with water and extracted with AcOEt. The combined organic extracts were washed with brine, dried over Na_2SO_4, removed under reduced pressure to give a crude DA adducts. The residue was purified by preparative TLC (SiO_2, *n*-hexane : AcOEt = 1 : 1) to afford the DA adducts **8a, 10a, 14, 15** in quantitative yield.

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