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Chiral primary amino alcohol organobase catalysts for the asymmetric Diels–Alder reactions of anthrones with maleimides

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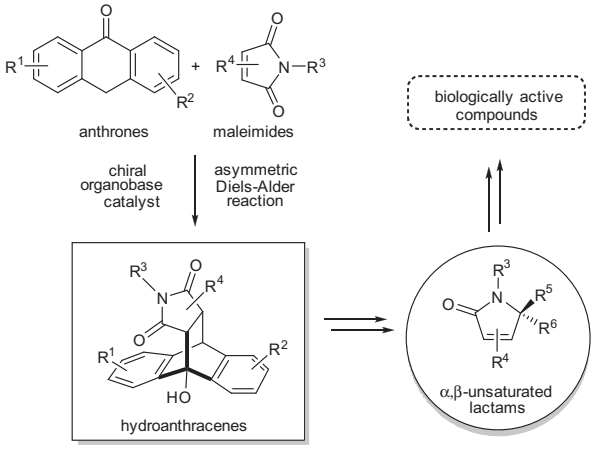
ABSTRACT

Simple chiral triethylsilyl-amino alcohol organocatalysts containing a bulky triethylsilyl group on the oxygen atom at the γ-position were designed and synthesized as new organocatalysts for enantioselective Diels–Alder reactions of anthrones with maleimides to produce chiral hydroanthracene Diels–Alder adducts in up to 99% yield and with up to 94% ee.

1. 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] The base catalyzed asymmetric Diels–Alder reaction is one of the most straightforward and atom economical method to construct chiral six-membered carbocyclic compounds in synthetic organic chemistry.[1] Among the dienes, anthrone is considered to be one of the most powerful diene components and can react with a variety of dienophiles.[2] Particularly, the Diels–Alder reaction of anthrone with *N*-substituted maleimide[3] to construct cage anthrone derivatives, which are key intermediates for the preparation of some unsaturated lactams with antipsoriatic and antiproliferative biological activities, have been studied extensively.[4] Several efficient chiral organobases, such as cinchona alkaloids,[5] pyrrolidine derivatives,[6] cyclic guanidines,[7] bisoxazolines,[8] and tertiary amine thioureas[9] have been used to promote these reactions (Scheme 1).[10] However, to the best of our knowledge, the effectiveness of primary β-amino alcohol[11] organocatalysts as organobases in this reaction has not been shown yet.

We designed a series of chiral primary amino alcohols **1a–f**, **2a–h**, and **3–5** with several substituent groups at the β-position as organobase catalysts (Scheme 2). The reaction using these designed amino alcohol catalysts might proceed through transition state **X** (Fig. 1). Thus, anionic anthracene is formed by the reaction with amino alcohol acting as a base. Next both the anionic diene and maleimide dienophile are fixed by hydrogen bondings with the ammonium alcohol and might react stereoselectively to afford the Diels–Alder adduct in good chemical yields and enantioselectivity.



Scheme 1. The asymmetric Diels–Alder reaction of anthrones with maleimides and its application.

Herein we report that a newly designed primary amino alcohol containing a bulky silyl group on the oxygen atom at the γ-position is an efficient organobase catalyst for the asymmetric Diels–Alder

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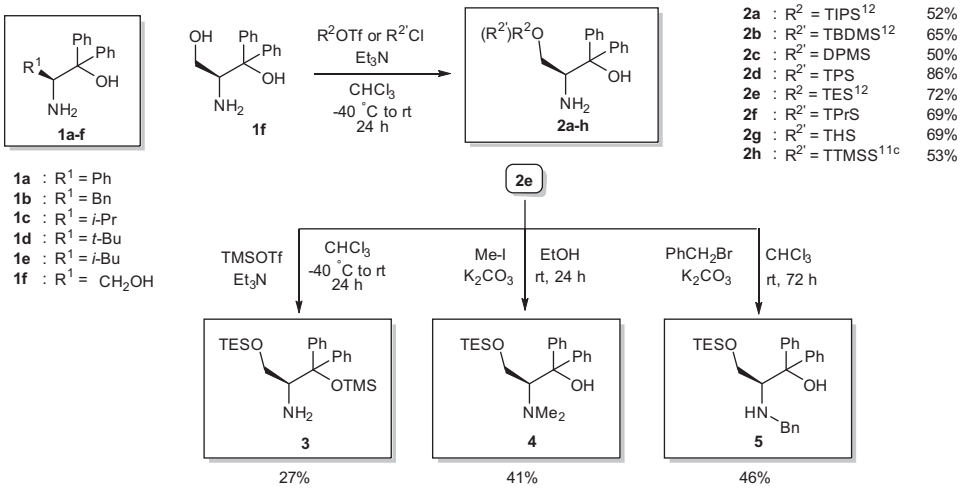


Scheme 2. Preparations of amino alcohol organocatalysts.

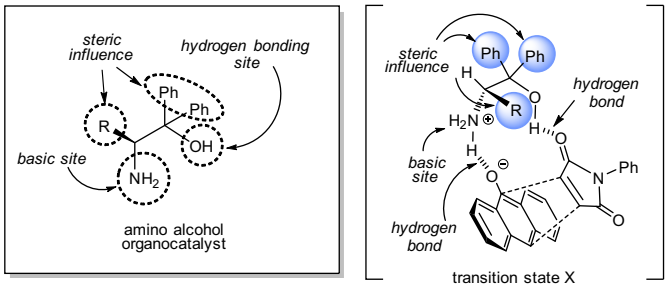


Figure 1. Concept for catalyst design.

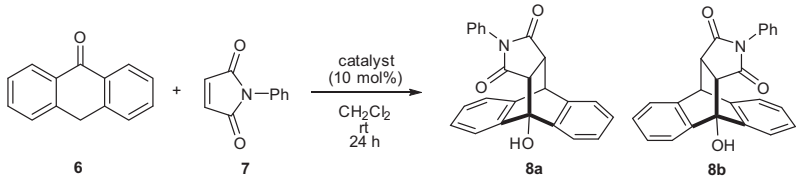
reaction of anthrone with maleimides to afford chiral hydroanthracene as a Diels–Alder adduct in good chemical yields (up to 99%) and with excellent enantioselectivity (up to 94% ee).

2. Results and discussion

Primary β-amino alcohol catalysts **1a–f**,[11] **2a–h** and **3–5** containing several substituent groups at the β-position were prepared as follows (Scheme 2). Amino alcohols **1a–f** containing aliphatic or aromatic substituent groups at the β-position were easily prepared by the well-known Grignard reaction with the corresponding α-amino acid esters. The bulkier β-amino alcohol catalysts **2a–g** containing several silyl groups on the oxygen atom at the γ-position were also easily prepared[11b] by the reactions of the amino alcohol **1f** with R^2OTf [R^2 = triisopropylsilyl (TIPS), triethylsilyl (TES)] or $R^{2'}Cl$ [$R^{2'}$ = *tert*-butyldimethylsilyl (TBDMS), diphenylmethylsilyl (DPMS), triphenylsilyl (TPS), tripropylsilyl (TPrS), trihexylsilyl (THS)] in moderate to good yields (50–86%). The bulkiest β-amino alcohol catalyst **2h** containing our explored super tris(trimethylsilyl)silyl (TTMSS) group[11c] on the oxygen atom at the γ-position was also easily obtained by the reaction of **1f** with tris(trimethylsilyl)chloride in 53% yield.[11c] In addition, catalyst **3** masked the hydroxy group at the α-position by trimethylsilyl group prepared from the reaction of **2e** with TMSOTf in 27% yield. Moreover, catalyst **4** containing the tertiary amino group was obtained by the reaction of **2e** with MeI in moderate yield (41%). Catalyst **5** containing a secondary amino group was also prepared by the reaction of **2e** with benzyl bromide in 46% yield.

We first examined the Diels–Alder reaction of anthrone **6** with *N*-phenylmaleimide **7** using the common amino alcohols **1a–f** as organobase catalysts (Table 1). The reaction of **6** (1 equiv) with **7** (1.2 equiv.) was carried out at room temperature in CH_2Cl_2 in the presence of 10 mol % of catalysts **1a–f**, respectively (entries 1–6). The obtained Diels–Alder adducts **8** (**8a** and/or **8b**) were isolated and the absolute configurations were determined on the basis of both literature values of the specific rotation and retention times on HPLC chiral column.[9] Catalysts **1a–e** did not show satisfactory catalytic activity and afforded the Diels–Alder adduct **8** in only low chemical yields (14–29%) and enantioselectivities (3–23% ee). Furthermore, amino diol catalyst **1f** afforded **8** in a good chemical yield (76%), but the enantioselectivity was low (9%). Considering the above results, we next examined the same Diels–Alder reaction using amino alcohols **2a–h** containing bulkier substituted silyl groups on the oxygen atom at the γ-position in the catalyst. The reaction of **6** (1 equiv) with **7** (1.2 equiv) was carried out at room temperature in CH_2Cl_2 in the presence of catalysts **2a–h** (10 mol %), respectively (entries 7–14). From the results of these reactions, it can be seen that all of the catalysts showed a catalytic activity and afforded the Diels–Alder adduct **8** in moderate to fairly good chemical yields (32–92%). Furthermore, enantioselectivity also increased in the reaction using almost all catalysts **2a–c**,**e–g** (32–43% ee), other than TPS-**2d** (16% ee) and TTMSS-**2h** (25% ee), although satisfactory enantioselectivities were not observed under these reaction conditions. The best chemical yield and enantioselectivity were 92% and 42% ee when using the catalyst **2e**, which has a triethylsilyl moiety on the oxygen atom at the γ-position in the molecule (entry 11). From these results, it was indicated that the use of an amino alcohol catalyst bearing a considerably bulky silyl substituent on the oxygen atom at the γ-position might not be effective for obtaining satisfactory enantioselectivity in this reaction. The same reaction using triethylsilyl-amino silyl ether catalyst **3**, in which the hydroxyl group was protected by a trimethylsilyl (TMS) group brought about a great decrease in the chemical yield and enantioselectivity (74%, 6% ee, entry 15) in comparison with the result of the reaction using the corresponding amino alcohol catalyst **2e** with a free hydroxyl group (92%, 42% ee, entry 11). This difference may be due to the loss of the ability for hydrogen bonding to maleimide dienophile **7** or the steric influence of the bulkier TMS group on the molecule, although the reasons are not clear. Furthermore, the catalytic abilities of both catalyst **4** with tertiary amino group and catalyst **5** with secondary amino group in the molecules were also examined (entries 16 and 17). However, these catalysts did not afford Diels–Alder adduct **8a** with satisfactory enantioselectivities despite having stronger basic properties than primary catalyst **2e**.

Table 1
The asymmetric Diels–Alder reaction of anthrone **6** with *N*-phenylmaleimide **7**



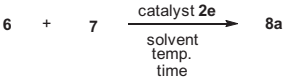
6 **7** **8a** **8b**

entry	catalyst	yield (%)[a]	ee (%)[b] 8a	ee (%)[b] 8b
1	**1a**	23	12	
2	**1b**	17	23	
3	**1c**	28	17	
4	**1d**	14		7
5	**1e**	29	3	
6	**1f**	76	9	
7	**2a**	68	34	
8	**2b**	69	42	
9	**2c**	32	32	
10	**2d**	40	16	
11	**2e**	92	42	
12	**2f**	65	43	
13	**2g**	57	41	
14	**2h**	66	25	
15	**3**	74		6
16	**4**	84		21
17	**5**	37	11	

[a]Isolated yields.[b]The ee was determined by HPLC using a Daicel AD-H column (*n*-hexane/2-propanol = 80:20).

In order to optimize the reaction conditions using the superior triethylsilyl-amino alcohol organocatalyst **2e**, we next examined the effect of the molar ratio of catalyst **2e**, the effect of the solvent, the reaction temperature, and the reaction time (Table 2). Increasing the catalytic loading of **2e** to 20 mol % resulted in a slight increase in both the chemical yield (93%) and enantioselectivity (46% ee) (entry 1) when compared to the reaction containing 10 mol % of **2e** (Table 1, entry 11). However, decreasing the catalytic loading of **2e** to 5 mol % resulted in a substantial decrease in the chemical yield (50%) and enantioselectivity (28% ee) (entry 2). To further improve the enantioselectivity, the reactions using **2e** were examined at lower temperatures of both 0 °C and −30 °C (entries 3 and 4). However, satisfactory results were not observed in terms of chemical yield and enantioselectivity under either temperature. Next, we examined the solvent effects on this reaction. Commonly used aprotic ($CHCl_3$, $ClCH_2CH_2Cl$, Et_2O, MeCN, benzene, toluene), polar aprotic (DMF, DMSO) and protic (EtOH, MeOH) solvents were screened, respectively (entries 5–14). Only $ClCH_2CH_2Cl$ afforded an excellent chemical yield (99%) (entry 6), but the other solvents gave chiral Diels–Alder adduct **8a** in moderate to good yields (60–84%) (entries 5–10). Unfortunately, no improvements in enantioselectivity were observed in these solvents in comparison with the use of CH_2Cl_2 (Table 1, entry 11). Furthermore, the reactions did not proceed when using polar aprotic (DMF, DMSO) and protic (EtOH, MeOH) solvents (entries 11–14). Under the best reaction conditions (CH_2Cl_2, **2e**: 20 mol %, rt), extending the reaction time from 24 to 48 h led to an increase in the chemical yield (98%) with 47% ee (entry 15).

Table 2
Optimization of the reaction conditions using catalyst **2e**

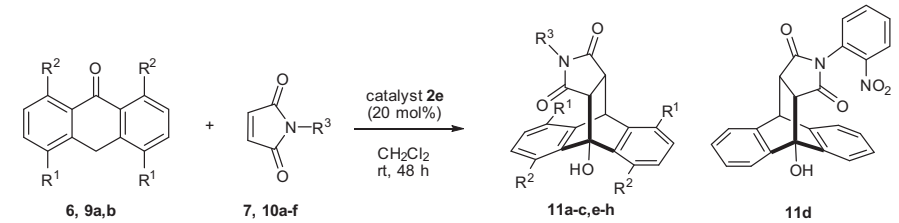


entry	**2e** (mol%)	solvent	temp. (°C)	time (h)	yield (%)[a]	ee (%)[b]
1	20	CH_2Cl_2	rt	24	93	46
2	5	CH_2Cl_2	rt	24	50	28
3	20	CH_2Cl_2	0	24	65	27
4	20	CH_2Cl_2	-30	24	24	11
5	20	$CHCl_3$	rt	24	76	43
6	20	$ClCH_2CH_2Cl$	rt	24	99	27
7	20	Et_2O	rt	24	81	10
8	20	MeCN	rt	24	60	7
9	20	benzene	rt	24	84	17
10	20	toluene	rt	24	76	18
11	20	DMF	rt	24	--	--
12	20	DMSO	rt	24	--	--
13	20	MeOH	rt	24	--	--
14	20	EtOH	rt	24	--	--
15	20	CH_2Cl_2	rt	48	98	47

[a]Isolated yields.[b]The ee was determined by HPLC using a Daicel AD-H column (*n*-hexane/2-propanol = 80:20).

Under the optimized reaction conditions, a wide range of Diels–Alder reactions with anthrones **6**, **9a**,**b**[2] and maleimides **7**, **10a**–**f**[3–9] were investigated using superior triethylsilyl-catalyst **2e** and the results are shown in Table 3. The obtained Diels–Alder adducts **11a**–**h** were isolated and their absolute configurations were determined on the basis of the literature values of the specific rotation and retention times on HPLC chiral columns.[7,9,10a] The use of *N*-methylmaleimide **10a** afforded the corresponding Diels–Alder adduct **11a**[10a] in an excellent chemical yield (97%), although the enantioselectivity was low (39% ee) (entry 1). The reaction with *N*-(4-methylphenyl)maleimide **10b** also afforded the Diels–Alder adduct **11b**[10a] in a reasonably good chemical yield (91%) and the enantioselectivity also increased to 32% ee (entry 2). Although the bulkier *N*-benzylmaleimide **10c** also did not afford the **11c**[9]

Table 3
The asymmetric Diels–Alder reaction of anthrones **6**, **9a**,**b** with maleimides **7**, **10a**–**f** using catalyst **2e**



6, 9a,b **7, 10a-f** **11a-c,e-h** **11d**

6 : $R^1 = R^2 = H$
9a : R^1 = Cl, R^2 = H
9b : R^1 = H, R^2 = Cl

7 : R^3 = Ph
10a : R^3 = Me
10b : R^3 = 4-Me-Ph
10c : R^3 = Bn
10d : R^3 = 2-NO_2-Ph
10e : R^3 = 3-NO_2-Ph
10f : R^3 = 4-NO_2-Ph

11a : $R^1 = R^2$ = H, R^3 = Me
11b : $R^1 = R^2$ = H, R^3 = 4-Me-Ph
11c : $R^1 = R^2$ = H, R^3 = Bn
11d : $R^1 = R^2$ = H, R^3 = 2-NO_2-Ph
11e : $R^1 = R^2$ = H, R^3 = 3-NO_2-Ph
11f : $R^1 = R^2$ = H, R^3 = 4-NO_2-Ph
11g : R^1 = Cl, R^2 = H, R^3 = Ph
11h : R^1 = H, R^2 = Cl, R^3 = Ph

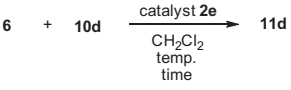
entry	diene	dienophile	Diels-Alder adduct	yield (%)[a]	ee (%)[b] 11a-c,e-h	ee (%)[b] 11d
1	**6**	**10a**	**11a**	97	39	
2	**6**	**10b**	**11b**	91	32	
3	**6**	**10c**	**11c**	93	46	
4	**6**	**10d**	**11d**	97		66
5	**6**	**10e**	**11e**	97	32	
6	**6**	**10f**	**11f**	95	35	
7	**9a**	**7**	**11g**	98	25	
8	**9b**	**7**	**11h**	98	38	

[a]Isolated yields.[b]The ee was determined by HPLC using a Daicel AD-H column (*n*-hexane/2-propanol = 80:20).

in a satisfactorily enantioselectivity (46% ee), the chemical yield was reasonably good (93%) (entry 3). Based on the results of the reaction using maleimides **7**, **10a**–**c**, the Diels–Alder reaction of **6** with *N*-(2-nitrophenyl)maleimide **10d** with a polar and bulkier strong electron-withdrawing nitro group at the 2-position on the phenyl group using triethylsilyl catalyst-**2e** (20 mol %) was examined at rt for 48 h (entry 4). The reaction proceeded smoothly and afforded the Diels–Alder adduct **11d**[7] in an excellent chemical yield (97%) and with better enantioselectivity (66% ee) in comparison to the result obtained using other maleimides **7**, **10a**–**c** (entry 4). However, the reactions using both *N*-(3-nitrophenyl)maleimide **10e** and *N*-(4-nitrophenyl)maleimide **10f** also afforded the corresponding Diels–Alder adducts **11e**[10a],**f**[10a] respectively, in excellent chemical yields (**11e**: 97%, **11f**: 95%), but satisfactory enantioselectivities (**11e**: 32% ee, **11f**: 35% ee) were not obtained under the optimized reaction conditions (entries 5, 6). Furthermore, the reactions of dichloroanthrones **9a**,**b** with **7** were also examined in the same reaction conditions (entries 7 and 8). Although, that reactions also afforded the corresponding Diels–Alder adducts **11g**,[10a]**h**[10a] in excellent chemical yields (**11g**: 98%, **11h**: 98%), satisfactory enantioselectivities were not obtained (**11g**: 25% ee, **11h**: 38% ee).

To further improve the enantioselectivity in the reaction of **6** with **10d** using **2e**, we next examined the effect of the molar ratio of catalyst **2e**, the reaction temperature and the reaction time (Table 4). The reaction was examined at lower temperatures of both 0 °C and −20 °C (entries 1 and 2). The best enantioselectivity (94% ee) with a good chemical yield (65%) were obtained when the reaction was carried out at 0 °C (entry 1). However, when the reaction was carried out at −20 °C, it led to a decrease in both the chemical yield and the enantioselectivity (21%, 86% ee) (entry 2). Furthermore, the decrease in the catalytic loading of **2e** to 10 mol % and 5 mol %, respectively, resulted in a significant

Table 4
Optimization of the reaction conditions using catalyst **2e**

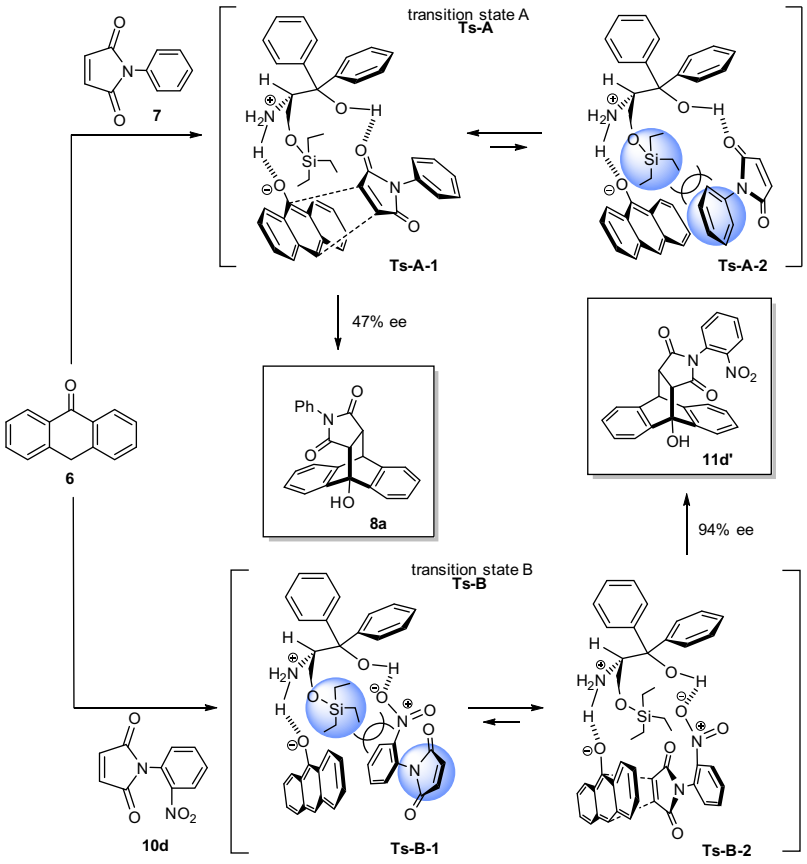


entry	**2e** (mol%)	temp. (°C)	time (h)	yield (%)[a]	ee (%)[b]
1	20	0	48	65	94
2	20	-20	48	21	86
3	10	0	48	39	91
4	5	0	48	24	89
5	20	0	72	83	94

[a]Isolated yields.[b]The ee was determined by HPLC using a Daicel AD-H column (*n*-hexane/2-propanol = 80:20).

decrease in the chemical yield (10 mol %: 39%, 5 mol %: 24%), respectively, although those enantioselectivities were good (10 mol %: 91% ee, 5 mol %: 89% ee) (entries 3 and 4). In the reaction using catalyst **2e** (20 mol %), extending the reaction time from 48 to 72 h led to an increase in their chemical yield (83%) with 94% ee (entry 5).

Based on the observed enantiopurities (Diels–Alder adduct **8a**: 47% ee, Table 2, entry 15, Diels–Alder adduct **11d**: 94% ee, Table 4, entry 5) of optically active Diels–Alder adducts **8a** and **11d**, which were obtained from the reactions of **6** with **7**, or with **10d**, the models of the enantioselective reaction courses were proposed as follows (Scheme 3). The reaction of **6** with **7** afforded the Diels–Alder adduct **8a**, which might go through transition state **Ts-A-1** since it has less steric interaction between the triethylsilyl group on the ammonium alcohol and maleimide **7** than that of the transition state **Ts-A-2** in **Ts-A**. Thus, in **Ts-A-1**, the diene and the dienophile are fixed by the two hydrogen bonding interactions



Scheme 3. Plausible reaction courses.

between the ammonium site on the ammonium alcohol intermediate and the oxygen atom on the anionic anthracene **6**, and between the hydroxy group on the ammonium alcohol intermediate and the carbonyl group on maleimide **7**, and then, might react stereoselectively from the one reaction site (i.e. **Ts-A-1**). On the other hand, the reaction of **6** with **10d** affording Diels–Alder adduct **11d** might go through the different transition state **Ts–B**, since the reaction proceeded with high enantioselectivity (94% ee) and the obtained Diels–Alder adduct **11d** have an opposite absolute stereochemistry in comparison with the reactions using other anthrones **6**,**9a**,**b** and maleimides **7**, **10a**–**c**,**e**,**f**. Thus, the reaction proceeded through transition state **Ts-B-2** in which the diene and dienophile were fixed by two hydrogen bonding interactions between the ammonium site, the hydroxy site of the ammonium alcohol and the anionic oxygen atom on anthrone **6**, or the strong ionic nitro group on maleimide **10d**. Also, **Ts-B-2** shows less steric interaction between the triethylsilyl group on the ammonium alcohol and the maleimide part in dienophile **10d** when compared with **Ts-B-1**, although the reason is not clear.

3. Conclusion

In conclusion, we have developed new chiral amino alcohols **2a**–**h**, **3**–**5** bearing silyl groups on oxygen atom at the γ-position. The catalysts were easily prepared from the condensation of inexpensive and commercially available chiral amino alcohols in two or three steps. The Diels–Alder reactions of anthrones with *N*-substituted maleimides using the explored catalysts were examined. In these catalysts, triethylsilyl-amino alcohol catalyst **2e** provided the corresponding hydroanthracene Diels–Alder adducts **11d** in reasonably good chemical yields (up to 97%) and with moderate enantioselectivity (up to 94% ee). Further studies, including catalyst design modifications and mechanistic investigations, are currently in progress.

4. Experimental

4.1. General

All reactions were carried out under an argon atmosphere in flame-dried glassware with magnetic stirring. Thin layer chromatography (TLC) was performed on silica gel 60 F_{254} and analytes were detected using UV light (254 nm) and iodine vapor. Column chromatography was carried out on silica gel 60N (40–100 μm) and preparative TLC was carried out on silica gel 60 F_{254}. Melting points were measured using a micro-melting point apparatus. Infrared (IR) spectra were measured with a FT/IR spectrophotometer (JASCO FT/IR-400). ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were measured in $CDCl_3$ on a JEOL JNM-ECA 500 spectrometer. ^{1}H NMR data are reported as follows: chemical shifts in ppm from tetramethylsilane (0.0 ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = double-doublet, m = multiplet and br = broad), coupling constants (Hz), and assignment. ^{13}C NMR spectra were measured with complete proton decoupling. Chemical shifts are reported in ppm from the residual solvent as an internal standard ($CDCl_3$; 77.16 ppm). High performance liquid chromatography (HPLC) was performed using the chiral columns AD-H 4.6 mm × 25 cm column. Optical rotations were measured with JASCO DIP-360 digital polarimeter. HRMS spectra were measured by EI using sector instruments on Hitachi RMG-6MG and JEOL-JNM-DX 303 spectrometers.

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4.2. General procedure for the preparation of amino alcohol organocatalysts 2a–g

To a solution of amino alcohol **1f** (1 mmol) in CH_2Cl_2 (15 mL) were added substituted silyl trifluoromethane sulfonates (1 mmol) or substituted silyl chlorides (1 mmol) and Et_3N (1.2 mmol) at −40 °C under argon. The mixture was stirred for 24 h at room temperature. The reaction mixture was quenched with H_2O and extracted with $CHCl_3$. The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4 and evaporated to give crude products **2a**–**g**. The residue was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate = 4:1) to give products **2a**–**g** (**2a**: 208 mg, 52%; **2b**: 232 mg, 65%; **2c**: 220 mg, 50%; **2d**: 431 mg, 86%; **2e**: 185 mg, 72%; **2f**: 275 mg, 69%; **2g**: 363 mg, 69%).

4.2.1. (*S*)-2-Amino-1,1-diphenyl-3-(triisopropyllsilyloxy)propanol 2a

Colorless oil; $[\alpha]_D^{24} = -57.1$ (*c* 0.63, EtOH); IR (neat) cm^{-1}: 2942, 2889, 1449, 1248; ^1H NMR ($CDCl_3$) δ: 7.60–7.59 (m, 2H), 7.51–7.47 (m, 2H), 7.34–7.14 (m, 6H), 3.95–3.93 (dd, J = 5.8 Hz, J = 3.8 Hz, 1H), 3.71–3.65 (m, 2H), 1.00–0.98 (m, 21H); ^{13}C NMR ($CDCl_3$) δ: 146.1, 145.0, 128.5, 128.2, 126.7, 126.6, 125.6, 125.1, 79.1, 64.8, 57.4, 17.9, 11.7. EI-MS *m*/*z*: 399 (M^+); HRMS (EI) calcd for $C_{24}H_{37}NO_2Si$ (M^+): 399.2594, found: 399.2589.

4.2.2. (*S*)-2-Amino-1,1-diphenyl-3-(*tert*-butyldimethylsilyloxy)propanol 2b

White solid (Et_2O/hexane); mp 49–51 °C; $[\alpha]_D^{22} = -51.1$ (*c* 0.45, EtOH); IR (neat) cm^{-1}: 2951, 2882, 1468, 1307; ^1H NMR ($CDCl_3$) δ: 7.59–7.57 (m, 2H), 7.50–7.48 (m, 2H), 7.34–7.15 (m, 6H), 3.92–3.90 (t, J = 4.6 Hz, 1H), 3.59–3.58 (d, J = 4.6 Hz 2H), 0.86 (s, 9H), −0.02 (s, 3H), −0.05 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 146.0, 145.1, 128.5, 128.2, 126.7, 126.6, 125.5, 125.3, 125.1, 79.3, 64.6, 57.1, 25.8, 18.1, −5.6, −5.1; EI-MS *m*/*z*: 358 $(M+H)^+$; HRMS (EI) calcd for $C_{21}H_{31}NO_2Si$ $(M+H)^+$: 358.2202, found: 358.2202.

4.2.3. (*S*)-2-Amino-1,1-diphenyl-3-(diphenylmethylsilyloxy)propanol 2c

White solid (Et_2O/hexane); mp 89–90 °C; $[\alpha]_D^{20} = -64.8$ (*c* 1.05, $CHCl_3$); IR (neat) cm^{-1}: 2948, 2885, 1428, 1255; ^1H NMR ($CDCl_3$) δ: 7.55–7.12 (m, 20H), 4.00–3.97 (m, 1H), 3.68–3.66 (m, 1H), 0.57 (s, 3H); ^{13}C NMR ($CDCl_3$) δ: 146.4, 146.3, 146.2, 144.5, 135.3, 135.2, 134.3, 130.1, 129.9, 128.5, 128.2, 128.0, 126.8, 126.6, 125.6, 125.1, 78.5, 64.7, 60.5, 57.6, 55.7, −3.3; EI-MS *m*/*z*: 440 $(M+H)^+$; HRMS (EI) calcd for $C_{28}H_{30}NO_2Si$ $(M+H)^+$: 440.2046, found: 440.2054.

4.2.4. (*S*)-2-Amino-1,1-diphenyl-3-(triphenylsilyloxy)propanol 2d

White solid (Et_2O/pentane); mp 91–92 °C; $[\alpha]_D^{22} = -55.8$ (*c* 0.52, $CHCl_3$); IR (neat) cm^{-1}: 2951, 2882, 1468, 1307; ^1H NMR ($CDCl_3$) δ: 7.53–7.50 (m, 8H), 7.46–7.43 (m, 3H), 7.37–7.35 (m, 6H), 7.30–7.27 (m, 4H), 7.18–7.14 (m, 3H), 7.11–7.08 (m, 1H), 4.68 (s, 1H), 4.02–3.98 (dd, J = 6.5 Hz, J = 3.5 Hz, 1H), 3.80–3.75 (m, 2H); ^{13}C NMR ($CDCl_3$) δ: 146.3, 144.1, 135.3, 133.5, 130.2, 128.4, 128.1, 128.0, 126.7, 126.5, 125.5, 125.0, 78.2, 65.0, 57.7; EI-MS *m*/*z*: 501 (M^+); HRMS (EI) calcd for $C_{33}H_{31}NO_2Si$ (M^+): 501.2124, found: 501.2123.

4.2.5. (*S*)-2-Amino-1,1-diphenyl-3-(triethylsilyloxy)propanol 2e

Colorless oil; $[\alpha]_D^{24} = -63.4$ (*c* 0.55, EtOH); IR (neat) cm^{-1}: 2911, 2876, 1449, 1269; ^1H NMR ($CDCl_3$) δ: 7.60–7.58 (m, 2H), 7.50–7.49 (m, 2H), 7.34–7.15 (m, 6H), 3.94–3.93 (t, J = 4.3 Hz, 1H), 3.60–3.59 (m, 2H), 0.91–0.88 (t, J = 8.0 Hz, 9H), 0.56–0.51 (q, J = 8.0 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ: 146.1, 145.0, 128.5, 128.2, 126.7, 126.5, 125.5, 125.1, 79.1, 64.1, 57.2, 6.64, 4.12; EI-MS *m*/*z*: 358 $(M+H)^+$; HRMS (EI) calcd for $C_{21}H_{32}NO_2Si$ $(M+H)^+$: 358.2202, found: 358.2202. Anal. Calcd for ($C_{21}H_{31}NO_2Si$): C, 70.54; H, 8.74; N, 3.92; Found: C, 70.61; H, 8.70; N, 3.87.

4.2.6. (*S*)-2-Amino-1,1-diphenyl-3-(tripropylsilyloxy)propanol 2f

Colorless oil; $[\alpha]_D^{22} = -77.5$ (*c* 1.02, $CHCl_3$); IR (neat) cm^{-1}: 2953, 2867, 1449, 1204; ^1H NMR ($CDCl_3$) δ: 7.59–7.57 (m, 2H), 7.49–7.48 (m, 2H), 7.33–7.14 (m, 6H), 3.91–3.89 (t, J = 4.6 Hz, 1H), 3.57–3.56 (m, 2H), 1.32–1.24 (m, 6H), 0.92–0.89 (t, J = 7.2 Hz, 9H), 0.52–0.50 (m, 6H); ^{13}C NMR ($CDCl_3$) δ: 146.2, 145.1, 128.5, 128.2, 126.7, 126.5, 125.6, 125.1, 79.2, 64.2, 57.3, 18.4, 16.7, 16.1; EI-MS *m*/*z*: 400 $(M+H)^+$; HRMS (EI) calcd for $C_{24}H_{38}NO_2Si$ $(M+H)^+$: 400.2672, found: 400.2675. Anal. Calcd for ($C_{24}H_{37}NO_2Si$): C, 72.13; H, 9.33; N, 3.50; Found: C, 72.19; H, 9.24; N, 3.42.

4.2.7. (*S*)-2-Amino-1,1-diphenyl-3-(trihexylsilyloxy)propanol 2g

Colorless oil; $[\alpha]_D^{24} = -49.6$ (*c* 1.27, $CHCl_3$); IR (neat) cm^{-1}: 2920, 2854, 1449, 1181; ^1H NMR ($CDCl_3$) δ: 7.59–7.57 (m, 2H), 7.49–7.46 (m, 2H), 7.36–7.14 (m, 6H), 3.93–3.90 (m, 1H), 3.55–3.54 (m, 2H), 1.33–1.21 (m, 24H), 0.89–0.86 (t, J = 6.9 Hz, 9H), 0.51–0.48 (m, 6H); ^{13}C NMR ($CDCl_3$) δ: 146.2, 145.0, 128.5, 128.2, 126.7, 126.5, 125.6, 125.1, 79.1, 64.1, 57.3, 33.3, 31.6, 31.5, 23.1, 23.0, 22.6, 15.1, 14.2, 13.3; EI-MS *m*/*z*: 526 $(M+H)^+$; HRMS (EI) calcd for $C_{33}H_{56}NO_2Si$ $(M+H)^+$: 526.4080, found: 526.4074.

4.3. Preparation of amino alcohol catalyst 3

A solution of amino alcohol **2e** (358 mg, 1 mmol) in CH_2Cl_2 (15 mL) was cooled down to −40 °C. To the solution were added Et_3N (166 μL, 1.2 mmol) and trimethylsilyl trifluoromethanesulfonate (217 μL, 1.2 mmol) and the reaction mixture was stirred at room temperature for 24 h. The solution was quenched with water and extracted with $CHCl_3$. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and filtered. The filtrate was concentrated under reduced pressure to give a residue. The residue was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate = 4:1) to afford **3** (116 mg, 27%).

4.3.1. (*S*)-1,1-Diphenyl-3-(triethylsilyloxy)-1-(trimethylsilyloxy)propane-2-amine 3

Colorless oil; $[\alpha]_D^{19} = -43.8$ (*c* 1.05, $CHCl_3$); IR (neat) cm^{-1}: 2953, 2876, 1248; ^1H NMR ($CDCl_3$) δ: 7.43–7.42 (m, 2H), 7.35–7.34 (m, 2H), 7.30–7.21 (m, 6H), 3.88–3.85 (m, 1H), 3.73–3.71 (m, 1H), 3.00–2.96 (t, J = 9.5 Hz, 9H), 0.54–0.49 (m, 6H), −0.11 (s, 9H); ^{13}C NMR ($CDCl_3$) δ: 144.7, 144.2, 128.1, 128.0, 127.8, 127.5, 127.2, 127.0, 82.6, 64.8, 59.2, 6.8, 4.4, 2.1; EI-MS *m*/*z*: 430 $(M+H)^+$; HRMS (EI) calcd for $C_{24}H_{40}NO_2Si_2$ $(M+H)^+$: 430.2598, found: 430.2612.

4.4. Preparation of amino alcohol catalyst 4

Amino alcohol **2e** (358 mg, 1 mmol), K_2CO_3 (276 mg, 2 mmol), and iodomethane (120 μL, 2 mmol) were stirred in EtOH (4 mL) at room temperature for 24 h. The reaction mixture was filtered with ethyl acetate. The combined organic layer was washed with water, brine, dried over anhydrous Na_2SO_4, and filtered. The filtrate was concentrated under reduced pressure to give the residue. The residue was purified by column chromatography on silica gel (*n*-hexane/ethyl acetate = 4:1) to afford **4** (152 mg, 41%).

4.4.1. *N*-Dimethyl-(*S*)-2-amino-1,1-diphenyl-3-(triethylsilyloxy)propanol 4

Colorless oil; $[\alpha]_D^{23} = -29.7$ (*c* 0.74, $CHCl_3$); IR (neat) cm^{-1}: 2953, 2875, 1447, 1234; ^1H NMR ($CDCl_3$) δ: 7.46–7.44 (m, 2H), 7.36–7.34 (m, 2H), 7.31–7.18 (m, 6H), 4.03–4.01 (m, 1H), 3.68–3.64 (m, 1H),

3.57–3.55 (m, 1H), 2.37 (s, 6H), 0.94–0.91 (t, J = 8.0 Hz, 9H), 0.58–0.53 (m, 6H); ^{13}C NMR ($CDCl_3$) δ: 146.2, 145.5, 128.0, 127.6, 127.1, 127.0, 77.6, 70.7, 61.1, 44.0, 6.8, 4.3; EI-MS m/z: 386 (M+H)$^+$; HRMS (EI) calcd for $C_{23}H_{36}NO_2Si$ (M+H)$^+$: 386.2515, found: 386.2507.

4.5. Preparation of amino alcohol catalyst 5

Amino alcohol **2e** (358 mg, 1 mmol), K_2CO_3 (332 mg, 2.4 mmol) and benzyl bromide (140 μL, 1.2 mmol) were stirred in $CHCl_3$ (10 mL) at room temperature for 72 h. The reaction mixture was then filtered with ethyl acetate. The combined organic layer was washed with water, brine, dried over anhydrous Na_2SO_4, and filtered. The filtrate was concentrated under reduced pressure to give the residue. The residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate = 4:1) to afford **5** (206 mg, 46%).

4.5.1. *N*-Benzyl-(*S*)-2-amino-1,1-diphenyl-3-(triethylsilyloxy) propanol 5

Colorless oil; $[\alpha]_D^{24} = -24.8$ (c 1.05, $CHCl_3$); IR (neat) cm^{-1}: 2954, 2875, 1449, 1238; ^{1}H NMR ($CDCl_3$) δ: 7.62–7.57 (m, 2H), 7.53–7.49 (m, 2H), 7.34–7.13 (m, 11H), 3.75–3.60 (m, 3H), 3.50–3.46 (m, 2H), 0.89–0.86 (t, J = 8.0 Hz, 9H), 0.54–0.49 (m, 6H); ^{13}C NMR ($CDCl_3$) δ: 146.6, 145.6, 128.4, 128.3, 128.1, 127.0, 126.5, 125.9, 125.5, 79.0, 63.2, 62.1, 52.4, 6.7, 4.2; EI-MS m/z: 447 (M$^+$); HRMS (EI) calcd for $C_{28}H_{37}NO_2Si$ (M$^+$): 447.2594, found: 447.2589.

4.6. General procedure for the asymmetric Diels–Alder reaction of anthrones 6 with maleimides 7

Anthrone **6** (0.10 mmol), *N*-phenylmaleimide **7** (0.12 mmol) and amino alcohol catalysts **1a**–**f**, **2a**–**h**, **3**, **4** and **5** (0.01 mmol) were stirred in CH_2Cl_2 (1 mL) at room temperature for 24 h. The reaction mixture was directly purified by preparative TLC on silica gel ($CHCl_3$) to afford Diels–Alder adducts **8**. The enantiomeric excess (ee) was determined by HPLC (DAICEL CHIRALPAK AD-H, 1.0 mL/min, n-hexane/2-propanol = 80:20). Compounds **8** were known compounds and were identified by spectroscopic data which were in good agreement with those reported.[2–9]

4.7. General procedure for the asymmetric Diels–Alder reaction of anthrones 6,9a,b, with maleimides 7,10a–f

Anthrones **6**,**9a**,**b** (0.10 mmol), maleimides **7**,**10a**–**f** (0.12 mmol) and amino alcohol catalysts **2e** (0.02 mmol) were stirred in CH_2Cl_2 (1 mL) at room temperature for 48 h. The reaction mixture was directly purified by preparative TLC on silica gel ($CHCl_3$) to afford Diels–Alder adducts **11a**–**h**. The enantiomeric excess (ee) was determined by HPLC (DAICEL CHIRALPAK AD-H, 1.0 mL/min, n-hexane/2-propanol = 80:20). Compounds **11a**–**h** were known compounds and were identified by spectroscopic data, which were in good agreement with those reported.[2–9]

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