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Article Enantioselective reduc

Enantioselective reduction of ketones catalyzed by rareearth metals complexed with phenoxy modified chiral prolinols

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mance of rare-earth metal amides combined with phenoxyfunctionalized chiral prolinols in the stereoselective reduction of carbonyl compounds. To our delight, a variety of simple and α , β unsaturated ketones underwent enantioselective hydroboration and subsequent hydrolysis, which gave optically active alcohols in excellent yields and high to excellent enantiomeric excesses.

Results and discussion

Best to our knowledge, the utilization of efficient metal species with chiral ligands for the purpose of stereoselective hydroboration reduction of ketones are still limited.¹⁰ In a preliminary study, the rare-earth metal-based catalytic system, 10 mol% ytterbium amide La[N(SiMe₃)₂]₃ and 20 mol% phenoxy-functionalized chiral ((S)-2,4-di-tert-butyl-6-[[2prolinol (hydroxydiphenylmethyl)pyrrolidin-1-yl]methyl]phenol) (H_2L^1) was employed in the enantioselective reduction of a simple ketone with 2 equivalent of borane. Results of the model reaction of acetophenone are summarized in Table 1. Pinacolborane, catecholborane and 9-BBN were chosen to assess the influence of borane on the reactivity and selectivity. Pinacolborane performed the best in both reactivity and selectivity, while 9-BBN showed poor reactivity, probably owing to its bulkier structure (Table 1, entries 1-3). To investigate the effects of the central metals of catalysts on the transformation, four homoleptic bis(trimethylsilyl)amides of rare-earth metal amides RE[N(SiMe₃)₂]₃ (RE = La, Yb, Nd, and Sc) were tested, all gave about 80% yields, but different enantioselectivities (Table 1, entries 3-6). Amides with central metal of moderate ionic radius, such as Yb[N(SiMe₃)₂]₃, gave higher ee value (Table 1, entry 4), while the catalysts with larger metal ionic radius (La[N(SiMe₃)₂]₃ and Nd[N(SiMe₃)₂]₃) or smaller one (Sc[N(SiMe₃)₂]₃) gave lower *ee* values (Table 1, entries 3, 5-6). This may be attributed to the size of proligand H₂L¹ matched with appropriate ionic radius of ytterbium, which is considered important in controlling the enantioselectivity in enantioselective synthesis. Since the existence of LiCl in complex [(Me₃Si)₂N]₃RE(µ-Cl)Li(THF)₃ may sometimes improve the activity of RE[N(SiMe₃)₂]₃,^{9b, 11} or produce the opposite effect,¹² a chloride-bridged "ate" complex [(Me₃Si)₂N]₃Yb(µ-Cl)Li(THF)₃ was also tested. A dramatic decrease of ee value was observed (Table 1, entry 7), which proved that the configuration around the central metal plays a key role in controlling enantioselectivity. In addition, three other phenoxy-functionalized chiral prolinols H₂L² ((S)-2,6-dicumyl-6-((2-(hydroxydiphenylmethyl)pyrrolidin-1yl)methyl)phenol), H₂L³ ((S)-2-methyl-6-((2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)methyl)phenol), and H₂L⁴ ((S)-2-butyl-6-((2-(hydroxydiphenylmethyl)pyrrolidin-1yl)methyl)phenol) were also synthesized 9b to examine the impact of the different substituents of ligands. Higher ee values were obtained when the substituents are bulky tert-butyl group at the ortho- position of the phenol hydroxyl group (Table 1, entries 4, 8-10). Screening of solvents indicated that 1,2-dimethoxyethane

(DME) gave both higher yield and enantioselectivity (Table 1, entries 10 and 11). In addition, we investigated the effects of two more chiral ligands L⁵ (commercial available prolinol) and L⁶ (pyridyl modified prolinol) on the enantioselective reduction of the model reaction. The yields of the corresponding alcohol were also high, however, *ee* values resulted lower (Table1, entries 17-

18). It suggests that phenoxy moiety in our catalytic system is essential, which is not only beneficial to stabilize the structure of chiral ytterbium catalysts, but also to enhance their enantioselectivity.

Since the combination of Yb[N(SiMe₃)₂]₃ and proligand H₂L⁴ in 1:2 molar ratio gave optimal result, we speculated that the ytterbium complex 1 [L⁴Yb(L⁴H)] may be the active species that catalyze the enantioselective reduction of acetophenone. This hypothesis was consolidated by the experiment with ytterbium complex 1, which gave the target alcohol with improved yield (95%) and *ee* value (73%) (Table 1, entry 12). Thus, the routine screening of reaction conditions, including the catalyst loading, reaction temperature, additives, solvents and concentration, were carried out using ytterbium complex 1 as the catalyst (SI Table S1) and the optimal reaction conditions were established as: 10 mol % ytterbium complex 1 as the catalyst, 2 equiv. HBpin as reductant, 50 mol% pyridine as additive in DME, at -10 °C for 8 h (Table 1, entry 16).

Table 1 Screening of the reaction conditions of enantioselective reduction of acetophenone^a $\,$



Entry	Cat.(Ligand	Additive	Solvent	Т	Yield	ee
	RE=)				(°C)	(%) ^b	(%)
1 ^d	La	H_2L^1	-	THF	25	61	8
2 ^e	La	H_2L^1	-	THF	25	36	0
3	La	H_2L^1	-	THF	25	82	28
4	Yb	H_2L^1	-	THF	25	84	40
5	Nd	H_2L^1	-	THF	25	84	31
6	Sc	H_2L^1	-	THF	25	77	8
$7^{\rm f}$	Yb	H_2L^1	-	THF	25	85	9
8	Yb	H_2L^2	-	THF	25	83	12
9	Yb	H_2L^3	-	THF	25	81	56
10	Yb	H_2L^4	-	THF	25	83	60
11	Yb	H_2L^4	-	DME	25	84	68
12	1	-	-	DME	25	95	73
13	1	-	HN(TMS) ₂	DME	25	85	61
14	1	-	Et ₃ N	DME	25	75	75
15	1	-	Ру	DME	25	96	76
16	1	-	Ру	DME	-10	90	81
17	Yb	L^5	-	DME	25	86	11
18	Yb	L^6	-	DME	25	81	39

^a Reactions were performed with acetophenone (0.3 mmol) and HBpin (0.6 mmol) in 1 mL of THF for 8 h in the presence of 10 mol % catalyst and 20 mol% ligand, 0.3 equivalent of additive was added if noted. ^bIsolated yield. ^cDetermined by HPLC. ^d Catecholborane as reductant. ^c9-BBN as reductant. ^f Complex [(Me₃Si)₂N]₃Yb(μ-Cl)Li(THF)₃ was used as catalyst.

A variety of different substituted acetophenones were investigated under the optimal conditions. As expected, all the substrates underwent the enantioselective reduction smoothly with catalyst 1 in DME. The data are summarized in Table 2. Substrates with both electron-donating and electron-withdrawing groups on the phenyl rings gave the corresponding alcohol in high yields, varying from 90-99% with, however, different ee values. Those substrates bearing ortho- position substitutes gave good to excellent ee values (up to 95%) (Table 2, 4b-4f), while other aryl methyl ketones, substituted at meta- or para- positions resulted in reduced ee values (around 75%) (Table 2, 4g-4l). Diaryl ketone 3m also smoothly gave product 4m in 90% yield and 83% ee. Hence, we have realized the first case of rare-earth metal complex modified with phenoxy-functionalized chiral prolinols catalyzed enantioselective hydroboration of simple ketones, and the results are overall better than the previous ones,10a-b, 10d and comparable with that of Woodward's outcome.10c

Table 2 Scope of the substituted acetophenones^a



^aReactions were performed with ketone (0.3 mmol) and HBpin (0.6 mmol) in 1 mL of DME for 8 h using 10 mol % of catalyst [L⁴Yb(L⁴H)]; isolated yields; *ee* values were determined by HPLC.

Based on the good performance of Yb-catalyzed enantioselective hydroboration of simple ketones, a more intricate enantioselective reduction of α , β -unsaturated ketone was investigated with reductant HBpin. A commercially available chalcone was chosed as the substrate of the model reaction. After the composite tests of the catalyst species and the chiral ligands, the enantioselective hydroboration of chalcone was proved to undergo better in the presence of ytterbium complex **2** [L¹Yb(L¹H)], which gave 99% yield and 61% *ee* (Table 3, entry 10). The routine screenings of other reaction conditions, including the catalyst loading, reaction temperature, additives, solvents and concentration, were also carried out (SI Table 2). Finally, the optimal reaction conditions were established as: 10 mol % ytterbium complex **2** as the catalyst, 1.2 equiv. HBpin as reductant, 50 mol% pyridine as additive, in THF, at -40 °C for 24 h (Table 3, entry 11).

A systematic study of the substrate scope, such as chalconederived substrates bearing different substituent groups on both phenyl rings, heteroaromatic, and *endo-*, and *exo-* cyclic α , β unsaturated ketones, were then conducted. As seen from Table 4, the chiral ytterbium catalyst showed high tolerance of the various substituents. Excellent yields were observed for all the allylic alcohols, while the *ee* values changed sharply.

 Table 3 Optimization of the reaction conditions of the enantioselective reduction of chalcones^a



Entry	Cat.(RE=)	Ligand	T (°C)	Yield (%) ^b	ee (%) ^c
1 ^d	Yb	H_2L^1	25	99	7
2	Yb	H_2L^1	25	99	59
3	Y	H_2L^1	25	99	57
4	Sc	H_2L^1	25	99	13
5	Sm	H_2L^1	25	99	51
6	La	H_2L^1	25	99	49
7	Yb	H_2L^2	25	99	57
8	Yb	H_2L^3	25	99	38
9	Yb	H_2L^4	25	99	53
10	2	-	25	99	61
11 ^e	2	-	-40	99	83

^a Reactions were performed with chalcone (0.3 mmol), HBpin (0.36 mmol) in 2 mL THF. ^bIsolated yields. ^c Determined by chiral HPLC analysis. ^dComplex [(Me₃Si)₂N]₃Yb(μ -Cl)Li(THF)₃ was used as catalyst. ^cAddition of 50 mol% pyridine, 1 mL THF.

For noncyclic enones, containing either electron-donating groups, such as methyl group and methoxy group, or electronwithdrawing groups, such as halogen and nitro group, the enantioselectivities of the corresponding allylic alcohols were all good, ranging from 77% to 89% *ee* (Table 4, **6a-6k**). Heteroaromatic styryl ketone **6l**, was also converted to corresponding allylic alcohol with 89% *ee*. However, poor enantiomeric excess of the al-

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25 26 lylic alcohols from *endo*-, and *exo*- cyclic α , β -unsaturated ketones were observed (21-49%), although the yields are all quantitative (Table 4, **6m-60**). The outcomes using current chiral rare-earth metal catalysts are comparable with those of Co and Mn complexes, ^{7a-b} but slightly less than those of Ni complex system.^{7c}

Table 4 Scope of α , β -unsaturated ketones^a



^aReactions were performed with chalcone and its derivatives (0.3 mmol), HBpin (0.36 mmol), pyridine 0.15 mmol, 1 mL of THF at -40 °C for 24 h in the presence of 10 mol % of complex [L¹Yb(L¹H)]. Isolated yields. The *ee* values were determined by chiral HPLC.

Conclusion

In summary, rare-earth metals complexed with phenoxyfunctionalized chiral prolinols were first explored in the enantioselective hydroboration of ketones by HBpin. Enantioselective reduction of simple ketones were catalyzed by catalyst **1** $[L^4Yb(L^4H)]$ and produced chiral alcohols with excellent yields (90-99%) and good to excellent *ee* values (68-95%). Meanwhile, using ytterbium catalyst **2** $[L^1Yb(L^1H)]$, chalcone derivatives of different substituents underwent enantioselective reduction to form chiral allylic alcohols quantitatively with good to high enantioselectivities (41-89% *ee*).

Experimental section

General Procedures. All reagents are commercially available, reagent grade, and used as received unless otherwise noted. The reactions involving air and water sensitive components were

performed with the standard Schlenk techniques or in the glovebox. Solvents, such as THF, DME, toluene, hexane, and so on, were degassed and distilled from sodium benzophenone ketyl before use. Analytical thin layer chromatography (TLC) was performed using F254 pre-coated silica gel plate (0.2 mm thickness). After elution, plates were detected using UV radiation (254 nm) on a UV lamp. Flash chromatography was performed using 200-300 mesh silica gel with freshly distilled solvents. Columns were typically packed as slurry and equilibrated with the appropriate solvent system prior to use. Nuclear magnetic resonance spectra were obtained on a Bruker AV-400 apparatus (CDCl3 as solvent). Chemical shifts for NMR spectra are reported as in units of parts per million (ppm) downfield from SiMe₄ (0.0) and relative to the signal of chloroform-d (7.26, singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet); or m (multiplets). High Resolution Mass (HRMS) spectra were obtained using Bruker ESI-TOF. The ee values determination was carried out using HPLC (Agilent Technologies 2000 Series) and SHIMADZU LC-20A with Daicel Chiralcel columns at 35 °C. Optical rotation was measured using an Autopol IV Polarimeter equipped with a sodium vapor lamp at 589 nm. The absolute configurations of 4a-4m were determined by comparing the specific rotation with the literature data.6a-6b The absolute configurations of 6a-60 were determined by comparing the specific rotation with the literature data.4a

General procedures of the rare-earth metal amides and complexes 1 and 2

Preparation of complexes RE[N(SiMe3)2]3

Complexes $RE[N(SiMe_3)_2]_3$ (RE = La, Nd, Sm, Yb, Y, Sc) were prepared according to the published procedures.¹³

Preparation of complex [(Me₃Si)₂N]₃Yb(µ-Cl)Li(THF)₃

Complex $[(Me_3Si)_2N]_3Yb(\mu$ -Cl)Li(THF)₃ was prepared according to the published procedures.¹⁴

Preparation of complexes 1 [L⁴Yb(L⁴H)] and 2 [L¹Yb(L¹H)]

According to our previous work,^{9b} to a THF solution of Yb[N(SiMe₃)₂]₃ (2 mmol), a THF solution of H₂L¹ (4 mmol) (H₂L¹ = (S)-2,4-di-tert-butyl-6-((2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)methyl)phenol) was added and the mixture was stirred at room temperature for 12 h. The solvent was evaporated and the mixture was crystallized in toluene. The colorless crystals **2** were obtained at room temperature after 1 or 2 days (1.38 g, yield 62% based on ytterbium).

Using a THF solution of H_2L^4 (4 mmol) ($H_2L^4 = (S)$ -2-tert-butyl-6-((2-(hydroxydiphenylmethyl)pyrrolidin-1-yl)methyl)phenol), the colorless crystals **1** were obtained at room temperature after several days (1.26 g, yield 63% based on ytterbium).

Typical procedure for the preparation of simple alcohols

Typical example for the synthesis of **4a**. Pyridine (0.15 mmol, $12 \ \mu$ L) was added to a stirred DME solution of the chiral ytterbi-

um complex 1 [L⁴Yb(L⁴H)] (0.03 mmol, 33.4 mg) under argon atmosphere. The mixture was stirred at -10 °C for 30 min. Acetophenone **3a** (0.3 mmol, 35.1 μ L) was added to the mixture for another 30 min. Pinacolborane (0.6 mmol, 87 μ L) was added in the above solution and stirred for 8 h at -10 °C. The reaction was quenched by 5% (V/V) TFA in ethyl acetate, and washed with saturated solution of sodium carbonate and extracted with ethyl acetate. The organic layer was collected and concentrated and the crude product was purified by column chromatography (ethyl acetate-petroleum ether, 1:5) to obtain the final hydrolysis product **4a**. The enantiomeric excess of alcohol **4a** was determined by chiral HPLC.

Characteristic data of simple alcohols

(*S*)-1-Phenylethan-1-ol (4a): Colorless Oil, (32.7 mg, yield 90%); $[\alpha]_D^{20} = -15.16^{\circ}$ (*c* 0.329, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.32 (m, 5H, Ph), 4.88 (q, *J* = 6.5 Hz, 1H, CH-OH), 2.11 (s, 1H, OH), 1.49 (d, *J* = 6.5 Hz, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 145.8, 128.5, 127.5, 125.4, 70.4, 25.2; 81% *ee*, HPLC: Daicel column OD-H, 98% hexanes, 2% ¹PrOH, 1.0 mL/min, 10.38 min (minor), 11.55 min (major); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₈H₁₀ONa 145.0624; found 145.0633.

(S)-1-(o-Tolyl)ethan-1-one (4b): Colorless Oil, (38.4 mg, yield 94%); $[\alpha]_D{}^{20} = -59.65^{\circ}$ (*c* 0.56, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.50(d, *J* = 7.48Hz, 1H, Ph), 7.17(m, 3H, Ph), 5.11(q, *J* = 6.44Hz, 1H, CH-OH), 2.33(s, 3H, Ph-CH₃), 1.82(s, 1H, OH), 1.45(d, *J* = 6.4Hz, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 143.4, 133.8, 129.9, 126.7, 125.9, 124.0, 66.3, 23.4, 18.4; 94% *ee*, HPLC: Daicel column IE, 99% hexanes, 1% 'PrOH, 1.0 mL/min, 18.03 min (minor), 19.82 min (major); HRMS (ESI, positive) m/z: [M+Na]⁺ calcd. for C₉H₁₂ONa 159.0786; found 159.0793.

(S)-1-(2,6-Dimethylphenyl)ethan-1-ol (4c): white solid, mp 64-66 °C (40.5 mg, yield 90%); $[\alpha]_D^{20} = -54.7^{\circ}$ (*c* 0.11, CHCl₃);¹H NMR (400 MHz, CDCl₃) δ 7.01-7.10 (m, 3H, Ph), 5.39(q, J =6.28 Hz,1H, CH-OH), 2.48(s, 6H, CH₃-Ph), 2.10(s, 1H, OH), 1.55(d, J = 6.4Hz, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 140.1, 135.1, 128.9, 126.4, 87.1, 20.9, 20.2; 90% *ee*, HPLC: Daicel column OD-H, 99% hexanes, 1% ¹PrOH, 1.0 mL/min, 11.48 min (major), 14.02 min (minor); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₁₀H₁₄ONa 173.0937; found 173.0935

(S)-1-(2-methoxyphenyl)ethan-1-ol (4d): Colorless Oil, (41.7 mg, yield 92%); $[\alpha]_D{}^{20} = -52.08^{\circ} (c \ 0.63, \text{CHCl}_3)$; ¹H NMR (400 MHz, CDCl}3) δ 7.28-7.45 (m, 2H, Ph), 6.93-7.04 (m, 2H, Ph), 5.17(q, J = 6.32 Hz,1H, CH-OH), 3.88 (s, 1H, OH), 3.19 (s, 3H, OCH}3), 1.55(d, J = 6.4Hz, 3H); ¹³C NMR (100 MHz, CDCl}3) δ 155.9, 133.3, 127.6, 125.6, 120.3, 109.9, 85.4, 54.7, 22.8; 95% *ee*, HPLC: Daicel column OD-H, 98% hexanes, 2% 'PrOH, 1.0 mL/min, 11.53 min (minor), 12.16 min (major); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₉H₁₂O₂Na 175.0730; found 175.0335.

(S)-1-(2-Chlorophenyl)ethan-1-ol (4e): Colorless Oil, (42.6 mg, yield 92%); $[\alpha]_D^{20} = -27.45^{\circ}$ (c 0.255, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.57 (d, J = 2.96Hz, 1H, Ph), 7.31 (m, 2H, Ph), 7.18 (m, 1H, Ph), 5.26(q, 1H, CH-OH), 3.28(br, 1H, OH), 1.46(d, J = 6.42, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 142.6, 131.0, 128.3, 127.8, 126.7, 125.9, 66.3, 23.0; 90% *ee*, HPLC: Daicel column OD-H, 99% hexanes, 1% ⁱPrOH, 0.8 mL/min, 15.13 min

(minor), 15.78 min (major); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₈H₉ClONa 179.0240; found 179.0231.

(*S*)-1-(2-(Trifluoromethyl)phenyl)ethan-1-ol (4f): Colorless Oil, (54.6 mg, yield 96%); $[\alpha]_D^{20} = -49.29^{\circ}$ (*c* 0.076, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.55 (m, 1H, Ph), 7.28-7.40 (m, 2H, Ph), 7.12(m, 1H, Ph), 5.10(q, *J* = 6.28 Hz,1H, CH-OH), 3.88(s, 1H, OH), 2.96(d, *J* = 6.4Hz, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 144.7, 131.7, 128.0, 126.6, 126.2, 125.9, 125.3, 124.7, 122.8, 84.9, 24.5; 85% *ee*, Daicel column IA, 99% hexanes, 1% ⁱPrOH, 1.0 mL/min, 9.36 min (minor), 11.71 min (major); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₉H₉F₃ONa 213.0498; found 213.0503.

(*S*)-1-(3-Methoxyphenyl)ethan-1-ol (4g): Colorless Oil, (40.8 mg, yield 90%); $[\alpha]_D^{20} = -11.66^{\circ}(c \ 0.261, \text{CHCl}_3)$; ¹H NMR (400 MHz, CDCl₃) δ 7.27 (m, 1H, Ph), 6.82-6.97 (m, 3H, Ph), 4.81(q, *J* = 6.28 Hz,1H, CH-OH), 3.09(s, 1H, OH), 2.96(d, *J* = 6.4Hz, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 159.6, 147.8, 129.4, 117.8, 112.6, 111.0, 69.9, 55.0, 25.2; 78% *ee*, HPLC: Daicel column IA, 98% hexanes, 2% 'PrOH, 1.0 mL/min, 16.45 min (minor), 18.14 min (major); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₉H₁₂O₂Na 175.0730; found 175.0737.

(*S*)-1-(3-Chlorophenyl)ethan-1-ol (4h): Colorless Oil, (42.3 mg, yield 91%); $[\alpha]_D^{20} = -64.07^{\circ}$ (*c* 0.072, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.35 (s, 1H, Ph), 7.24(m, 3H, Ph), 4.84(q, *J*=6.28, 1H, CH-OH), 2.77(s, 1H, OH), 1.45(d, *J* = 6.44Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 142.6, 131.0, 128.8, 127.8, 126.7, 125.9, 66.3, 23.0; 75% *ee*, HPLC: Daicel column OJ-H, 95% hexanes, 5% ¹PrOH, 1.0 mL/min, 9.12 min (major), 10.39 min (minor); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₈H₉ClONa 179.0240; found 179.0246.

(S)-1-(4-Chlorophenyl)ethan-1-one (4i): Colorless Oil, (43.8 mg, yield 94%); $[\alpha]_D^{20} = -21.23^{\circ}$ (c 0.529, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.29(m, 4H, Ph), 7.80(q, J = 6.36Hz, CH-OH), 3.58(br, 1H, OH), 1.44(d, J = 6.48Hz, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 143.8, 132.4, 128.0, 126.4, 69.0, 24.7; 77% ee, HPLC: Daicel column OD-H, 99% hexanes, 1% 'PrOH, 1.0 mL/min, 14.71 min (minor), 15.22 min (major); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₈H₉ClONa 179.0240; found 179.0233.

(*S*)-1-(4-Bromophenyl)ethan-1-one (4j): Colorless Oil, (57.5 mg, yield 96%); ¹H NMR (400 MHz, CDCl₃): δ 7.41 (d, J = 8.44 Hz, 2H, Ph), 7.13 (d, J = 8.40 Hz, 2H, Ph), 4.70 (q, J = 6.08 Hz, 1H, CH-OH), 4.0 (s, 1H, OH), 1.37 (d, J = 6.56 Hz, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 144.3, 130.9, 126., 120.5, 68.9, 24.7; 72% ee, HPLC: Daicel column OD-H, 98% hexanes, 2% PrOH, 1.0 mL/min, 12.46 min (minor), 13.21 min (major); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₈H₉BrONa 222.9729; found 222.9723.

(*S*)-1-(4-Nitrophenyl)ethan-1-one (4k): Yellow Oil, (49.5mg, yield 99%); $[\alpha]_D^{20} = -22.83^{\circ}$ (*c* 0.46, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 8.06(d, *J* = 8.8Hz, 2H, Ph), 7.44(d, J = 8.8Hz, 2H, Ph), 4.92(q, J = 6.28Hz, 1H, CH-OH), 2.65(br, 1H, OH), 1.41(d, *J* = 6.52Hz, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 152.9, 146.4, 125.6, 123.1, 68.7, 24.8; 76% *ee*, HPLC: Daicel column IA, 98% hexanes, 2% ¹PrOH, 1.0 mL/min, 16.77 min (minor), 17.18 min (major); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₈H₉NO₃Na 190.0480; found 190.0471.

(S)-1-(p-Tolyl)ethan-1-one (41): Colorless Oil, (37.5 mg, yield 92%); $[\alpha]_D^{20} = -39.47^{\circ}$ (*c* 0.14, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.26(m, 4H, Ph), 4.85(q, J = 6.36Hz, 1H, CH-OH),

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2.41(s, 3H, Ph-CH₃), 1.5(d, J =7.2Hz, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 142.7, 136.3, 128.6, 125.0, 69.5, 24.7, 20.7; 68% ee, HPLC: Daicel column OJ-H, 95% hexanes, 5% PrOH, 1.0 mL/min, 11.14 min (major), 13.07 min (minor); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₉H₁₂ONa 159.0786; found 159.0783.

(S)-Phenyl-(o-tolyl)methanol (4m): White solid, mp 88-90 °C, (53.4 mg, yield 90%); $[\alpha]_D^{20} = -12.7^{\circ}$ (*c* 0.68, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.54-7.56 (m, 2H, Ph), 7.17-7.36(m, 6H, Ph), 6.02(s, 1H, CH-OH), 2.30(s, 1H, OH), 2.28(s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 142.4, 141.0, 134.9, 130.1, 128.0, 127.1, 127.0, 126.7,125.8, 125.6, 72.8, 18.9; 83% *ee*, HPLC: Daicel column OJ-H, 95% hexanes, 5% ⁱPrOH, 1.0 mL/min, 22.42 min (major), 23.73 min (minor); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₁₄H₁₄ONa 221.0937; found 221.0945.

Typical procedure for the preparation of allylic alcohols

Typical example for the synthesis of **6a**. Pyridine (0.15 mmol, 12 μ L) was added to a stirred THF solution of the chiral ytterbium complex **2** [L¹Yb(L¹H)] (0.03 mmol, 33.4 mg) under argon atmosphere. The mixture was stirred at -40 °C for 30 min. Then, pinacolborane (0.36 mmol, 52 μ L) was added in the above solution for another 30 min. Chalcone **5a** (0.3 mmol, 58.3 μ L) was added to the mixture and stirred for further 24 h. The reaction was quenched with water, some silica-gel powder was added to organic phase, which was concentrated to dry. The crude product was purified by column chromatography (ethyl acetate-petroleum ether, 1:10) to obtain the final hydrolysis product **6a**. The enantiomeric excess of allylic alcohol **6a** was determined by chiral HPLC.

Characteristic data of allylic alcohols

(*S*,*E*)-1,3-Diphenylprop-2-en-1-ol (6a): White Solid, mp 56-58 °C, (62.8 mg, yield 99%); $[\alpha]_D^{20} = -20^\circ$ (*c* 0.4, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.31 (m, 6H, Ph), 7.22 (m, 3H, Ph), 7.15 (m, 1H, Ph), 6.61 (d, 1H, *J* = 15.84 Hz, CH=CH), 6.31 (dd, *J*₁ = 15.84 Hz, *J*₂ = 6.60 Hz,1H, CH=CH), 5.30 (d, *J* = 6.36 Hz, 1H, CH), 2.04 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl₃): δ 142.9, 136.7, 131.7, 130.7, 126.8, 128.7, 128.0, 127.9, 126.8, 126.5. 83% *ee*, HPLC: OD-H, 90% hexanes, 10% /PrOH, 1.0 mL/min, 13.4 min (major), 16.8 min (minor); HRMS (ESI, positive) m/z: [M+Na]⁺ calcd. for Cl₃H₁4ONa 233.0942; found 233.0946.

(*S,E*)-3-(4-Methoxyphenyl)-1-phenylprop-2-en-1-ol(6b): Colorless Oil, (71.7 mg, yield 99%); $[\alpha]_D^{20} = -11^{\circ}$ (*c* 0.4, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.44 (m, 2H, Ph), 7.32 (m, 5H, Ph), 6.87 (m, 2H, Ph), 6.61 (m, 1H, CH=CH), 6.23 (m, 1H, CH=CH), 5.37 (d, *J* = 6.72 Hz, 0.5H, CH), 5.09 (m, 0.5H, CH), 3.81 (m, 3H, CH₃), 1.86 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl₃): δ 159.3, 136.9, 133.5, 130.9, 129.6, 128.6, 128.5, 128.0, 127.8, 127.7, 127.2, 127.2, 128.7, 114.1, 78.8, 55.4; 83% *ee*, HPLC: OD-H, 90% hexanes, 10% ^{*i*}PrOH, 1.0 mL/min, 15.1 min (minor), 17.1 min (major); HRMS (ESI, positive) m/z: [M+Na]⁺ calcd. for C₁₆H₁₆O₂Na 263.1048; found 263.1047.

(*S*, *E*)-3-(2-Methoxyphenyl)-1-phenylprop-2-en-1-ol (6c): Colorless Oil, (72 mg, yield 99%); $[\alpha]_D{}^{20} = -11^{\circ}$ (*c* 0.4, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.32 (m, 2H, Ph), 7.22 (m, 2H, Ph), 7.20 (m, 1H, Ph), 7.12 (m, 1H, Ph), 6.89 (m, 1H, Ph), 6.82 (m, 1H, Ph), 6.71 (m, 1H, Ph), 6.54 (d, *J* = 15.80 Hz, 1H, CH=CH), 6.25 (dd, *J*₁ = 15.80 Hz, *J*₂ = 6.68 Hz, 1H, CH=CH), 5.26 (d, *J* = 6.44 Hz, 1H, CH), 3.69 (s, 3H, CH₃), 2.12 (s, 1H, OH); ¹³C NMR

(100 MHz, CDCl₃): δ 159.9, 142.9, 141.2, 138.1, 132.0, 130.5, 129.7, 128.7, 127.9, 127.2, 126.5, 119.5, 113.6, 111.9, 75.1, 55.3; 83% ee, HPLC: OD-H, 90% hexanes, 10% PrOH, 1.0 mL/min, 9.7 min (major), 10.6 min (minor); HRMS (ESI, positive) m/z: [M+Na]⁺ calcd. for C₁₆H₁₆O₂Na 263.1048; found 263.1052.

(*S*, *E*)-1-Phenyl-3-(p-tolyl)prop-2-en-1-ol (6d): Colorless Oil, (66.6 mg, yield 99%); $[\alpha]_D^{20} = -23^{\circ}(c \ 0.2, CHCl_3)$; ¹H NMR (400 MHz, CDCl_3): δ 7.44 (m, 2H, Ph), 7.39 (m, 2H, Ph), 7.29 (m, 3H, Ph), 7.12 (m, 2H, Ph), 6.64 (d, *J* = 15.84 Hz, 1H, CH=CH), 6.36 (dd, *J*₁ = 15.84 Hz, *J*₂ = 6.60 Hz, 1H, CH=CH), 5.37 (d, *J* = 6.54 Hz, 1H, CH), 2.35 (s, 3H, CH_3), 2.16 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl_3): δ 141.6, 138.4, 137.7, 137.5, 136.9, 134.0, 131.6, 131.4, 130.7, 129.4, 128.6, 127.7, 127.2, 126.7, 75.4, 21.4; 79% *ee*, HPLC: OD-H, 90% hexanes, 10% 'PrOH, 1.0 mL/min, 10.0 min (minor), 12.7 min (major); HRMS (ESI, positive) m/z: [M+Na]⁺ calcd. for C₁₆H₁₆ONa 247.1099; found 247.1108.

(*S*, *E*)-3-(4-Fluorophenyl)-1-phenylprop-2-en-1-ol (6e): White solid, mp 68-70 °C, (68 mg, yield 99%); $[\alpha]_D^{20} = +16^{\circ}$ (*c* 0.3, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.25 (m, 4H, Ph), 7.20 (m, 2H, Ph), 7.14 (m, 1H, Ph), 6.93 (m, 2H, Ph), 6.52 (d, *J* = 15.84 Hz, 1H, CH=CH), 6.24 (dd, *J*₁ = 15.84 Hz, *J*₂ = 6.56 Hz, 1H, CH=CH), 5.24 (d, *J* = 6.52 Hz, 1H, CH), 2.18 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl₃): δ 161.2, 136.5, 131.9, 131.5, 130.9, 130.0, 128.8, 128.2, 128.1, 127.2, 127.2, 126.8, 115.7, 115.5, 74.6; 79% *ee*, HPLC: OD-H, 90% hexanes, 10% /PrOH, 1.0 mL/min, 12.2 min (major), 17.4 min (minor); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₁₅H₁₃FONa 251.0848; found 251.0858.

(*S*, *E*)-3-(4-Chlorophenyl)-1-phenylprop-2-en-1-ol (6f): White Solid, mp 72-74 °C, (73 mg, yield 99%); $[\alpha]_D^{20} = -25^{\circ}$ (*c* 0.2, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.30 (m, 4H, Ph), 7.19 (m, 5H, Ph), 6.52 (d, *J* = 15.88 Hz, 1H, CH=CH), 6.27 (dd, *J*₁ = 15.84 Hz, *J*₂ = 6.32 Hz, 1H, CH=CH), 5.26 (d, *J* = 6.24 Hz, 1H, CH), 2.10 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl₃): δ 141.0, 139.8, 135.2, 133.6, 132.3, 131.1, 130.0, 128.89, 128.82, 128.5, 128.0, 127.2, 126.8, 126.5, 75.1; 81% *ee*, HPLC: OD-H, 90% hexanes, 10% 'PrOH, 1.0 mL/min, 10.9 min (minor), 14.4 min (major); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₁₅H₁₃CIONa 267.0553; found 267.0558.

(*S*, *E*)-3-(4-Nitrophenyl)-1-phenylprop-2-en-1-ol (6g): Yellow Oil, (76 mg, yield 99%); $[\alpha]_D^{20} = -41^{\circ}$ (*c* 0.3, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 8.16 (m, 2H, Ph), 7.50 (m, 2H, Ph), 7.41 (m, 4H, Ph), 7.25 (m, 1H, Ph), 6.79 (d, *J* = 15.88 Hz, 1H, CH=CH), 6.56 (dd, *J*₁ = 15.88 Hz, *J*₂ = 5.76 Hz, 1H, CH=CH), 5.43 (d, *J* = 5.68 Hz, 1H, CH), 2.19 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl₃): δ 147.0, 143.3, 142.2, 136.4, 135.0, 129.0, 128.9, 128.5, 128.3, 127.9, 127.4, 127.2, 126.5, 124.0, 74.6; 77% *ee*, HPLC: OD-H, 90% hexanes, 10% 'PrOH, 1.0 mL/min, 21.6 min (minor), 23.1 min (major); HRMS (ESI, positive) m/z: [M+Na]⁺ calcd. for C₁₅H₁₃NO₃Na 278.0793; found 278.0792.

(*S*, *E*)-1-(4-Chlorophenyl)-3-phenylprop-2-en-1-ol (6h): White Solid, mp 64-66 °C, (72.8 mg, yield 99%); $[\alpha]_D^{20} = -8^{\circ}$ (*c* 0.2, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.23 (m, 8H, Ph), 7.16 (m, 1H, Ph), 6.52 (d, *J* = 15.84 Hz, 1H, CH=CH), 6.22 (dd, *J*₁ = 15.80 Hz, *J*₂ = 6.64 Hz, 1H, CH=CH), 5.21 (d, *J* = 6.64 Hz, 1H, CH), 2.27 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl₃): δ 141.3, 136.4, 133.6, 132.2, 131.2, 130.2, 128.9, 128.88, 128.81, 128.5, 128.1, 128.0, 127.8, 126.8, 74.6; 82% *ee*, HPLC: OD-H, 90% hexanes, 10% 'PrOH, 1.0 mL/min, 13.4 min (major), 19.0 min (minor); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₁₅H₁₃CIONa 267.0553; found 267.0558. (*S*, *E*)-1-(4-Bromophenyl)-3-phenylprop-2-en-1-ol (6i): White Soild, mp 68-70 °C, (86 mg, yield 99%); $[\alpha]_D^{20} = -10^\circ$ (*c* 0.2, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.39 (m, 2H, Ph), 7.22 (m, 7H, Ph), 6.59 (d, *J* = 15.80 Hz, 1H, CH=CH), 6.21 (dd, *J*₁ = 15.80 Hz, *J*₂ = 6.64 Hz, 1H, CH=CH), 5.25 (d, *J* = 6.48 Hz, 1H, CH), 2.11 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl₃): δ 141.8, 136.3, 132.2, 131.9, 131.8, 131.2, 130.3, 129.6, 128.9, 128.8, 128.3, 128.2, 126.8, 121.7, 74.6; 83% *ee*, HPLC: OD-H, 90% hexanes, 10% ⁱPrOH, 1.0 mL/min, 14.2 min (major), 20.3 min (minor); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₁₅H₁₃BrONa 311.0047; found 311.0056.

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(*S*, *E*)-1-(4-Methoxyphenyl)-3-phenylprop-2-en-1-ol (6j): White Solid, mp 103-105 °C, (71.6 mg, yield 99%); $[\alpha]_D^{20} = -10^{\circ}$ (*c* 0.2, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.39 (m, 7H, Ph), 6.93 (m, 2H, Ph), 6.56 (m, 1H, CH=CH), 6.22 (m, 1H, CH=CH), 5.04 (m, 1H, CH), 3.80 (m, 3H, CH₃), 1.29 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl₃): δ 137.6, 133.8, 131.4, 131.3, 130.6, 130.5, 129.2, 128.5, 127.6, 127.1, 127.0, 126.6, 126.5, 126.3, 75.2, 21.1; 81% *ee*, HPLC: OD-H, 90% hexanes, 10% 'PrOH, 1.0 mL/min, 17.5 min (major), 23.5 min (minor); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₁₆H₁₆O₂Na 263.1048; found 263.1045.

(*S*, *E*)-3-(4-Isopropylphenyl)-1-(p-tolyl)prop-2-en-1-ol (6k): White Solid, mp 77-79 °C, (79.2 mg, yield 99%); $[\alpha]_D^{20} = +20^{\circ}$ (*c* 0.2, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.33 (m, 5H, Ph), 7.20 (m, 4H, Ph), 6.69 (d, *J* = 15.84 Hz, 1H, CH=CH), 6.34 (dd, *J*₁ = 15.80 Hz, *J*₂ = 6.48 Hz, 1H, CH=CH), 5.34 (d, *J* = 6.40 Hz, 1H, CH), 2.91 (s, 1H, CH), 2.37 (s, 3H, CH₃), 2.12 (s, 1H, OH), 1.26 (m, 6H, CH₃); ¹³C NMR (100 MHz, CDCl₃): δ 148.7, 138.9, 138.6, 137.6, 137.3, 134.5, 134.1, 131.3, 129.9, 129.3, 127.2, 127.2, 126.7, 126.7, 79.1, 34.0, 24.1, 21.3; 87% *ee*, HPLC: OD-H, 90% hexanes, 10% ⁴PrOH, 1.0 mL/min, 8.9 min (minor), 9.8 min (major); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₁₉H₂₂ONa 289.1568; found 289.1570.

(*S*, *E*)-3-Phenyl-1-(thiophen-2-yl)prop-2-en-1-ol (6l): White Solid, mp 50-52 °C, (63.7 mg, yield 99%); $[\alpha]_D^{20} = -20^{\circ}$ (*c* 0.2, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.32 (m, 2H, Ph), 7.23 (m, 2H, Ph), 7.15 (m, 1H, Ph), 6.94 (m, 1H, Ph), 6.90 (m, 1H, Ph), 6.61 (d, *J* = 15.80 Hz, 1H, CH=CH), 6.34 (dd, *J*₁ = 15.76 Hz, *J*₂ = 6.48 Hz, 1H, CH=CH), 5.51 (d, *J* = 6.36 Hz, 1H, CH), 2.25 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl₃): δ 145.0, 141.9, 136.4, 132.6, 129.1, 128.8, 128.1, 127.4, 126.9, 126.3, 125.8, 125.3, 75.4; 89% *ee*, HPLC: OD-H, 90% hexanes, 10% 'PrOH, 1.0 mL/min, 10.9 min (major), 14.4 min (minor); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₁₃H₁₂OSNa 239.0507; found 239.0518.

(*R*)-3,4,5,6-Tetrahydro-[1,1'-biphenyl]-3-ol (6m): White Solid, mp 52-54 °C, (52 mg, yield 99%); $[\alpha]_D^{20} = +6^{\circ} (c \ 0.2, CHCl_3)$; ¹H NMR (400 MHz, CDCl_3): δ 7.39 (m, 2H, Ph), 7.31 (m, 2H, Ph), 7.25 (m, 1H, Ph), 6.12 (m, 1H, CH=CH), 4.38 (m, 1H, CH), 2.37 (m, 2H, CH₂, OH), 1.92 (m, 2H, CH₂), 1.71 (m, 3H, CH₂); ¹³C NMR (100 MHz, CDCl_3): δ 141.5, 140.2, 128.4, 127.6, 126.7, 125.5, 66.5, 31.8, 27.6, 19.6; 41% *ee*, HPLC: OD-H, 90% hexanes, 10% [/]PrOH, 1.0 mL/min, 7.6 min (minor), 15.5 min (major); HRMS (ESI, positive) m/z: [M+ Na]⁺ calcd. for C₁₂H₁₄ONa 197.0942; found 197.0951.

(*R*, *E*)-2-(4-Methylbenzylidene)-2,3-dihydro-1H-inden-1-ol (6n): Colorless Oil, (70 mg, yield 99%); $[\alpha]_D^{20} = +16^{\circ}$ (c = 0.2, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.49 (m, 1H, Ph), 7.26 (m, 5H, Ph), 7.16 (m, 2H, Ph), 6.80 (m, 1H, CH=CH), 5.75 (m, 1H, CH), 3.92 (m, 1H, CH₂), 3.77 (m, 1H, CH₂), 2.35 (s, 3H, CH₃), 2.06 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl₃): δ 143.8, 143.3, 141.2, 137.0, 134.5, 129.3, 129.2, 128.9, 128.7, 127.3, 127.0, 126.3, 125.1, 124.9, 78.5, 35.7, 21.4; 49% *ee*, HPLC: OD-H, 90% hexanes, 10% ⁱPrOH, 1.0 mL/min, 7.8 min (major), 9.1 min (minor); HRMS (ESI, positive) m/z: $[M+ Na]^+$ calcd. for $C_{17}H_{16}ONa$ 259.1099; found 259.1104.

(*R*, *E*)-2-(4-Fluorobenzylidene)-1,2,3,4-tetrahydronaphthalen-1-ol (60): Yellow Oil, (69.7 mg, yield 99%); $[\alpha]D^{20} = +12^{\circ}$ (*c* 0.2, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.44 (m, 1H, Ph), 7.22 (m, 4H, Ph), 7.14 (m, 1H, Ph), 6.99 (m, 2H, Ph), 6.67 (s, 1H, CH=CH), 5.15 (s, 1H, CH), 2.98 (s, 1H, CH₂), 2.74 (m, 3H, CH₂), 2.12 (s, 1H, OH); ¹³C NMR (100 MHz, CDCl₃): δ 162.9, 140.9, 138.8, 137.4, 133.4, 130.5, 130.4, 128.4, 128.0, 127.8, 126.7, 124.4, 115.4, 115.2, 73.9, 29.8, 24.2; 21% ee, HPLC: AD-H, 90% hexanes, 10% 'PrOH, 1.0 mL/min, 20.8 min (major), 23.0 min (minor); HRMS (ESI, positive) m/z: [M+Na]⁺ calcd. for C_{17H15}FONa 277.1005; found 277.1010.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Tables of screening of the reaction conditions, NMR and HPLC spectra of compounds

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