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Supporting Information

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Oxazaborolidine-derived Lewis Acid Assisted Chiral Lewis Acid as a Moisture Tolerant Enantioselective Diels-Alder Catalyst

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Experimental Section

General Procedures.

All non aqueous reactions were carried out in oven- or flame-dried glassware under an atmosphere of dry nitrogen unless otherwise noted. Except as otherwise indicated, all reactions were magnetically stirred and monitored by analytical thin-layer chromatography using Merck pre-coated silica gel plates with F_{254} indicator. Visualization was accomplished by UV light (256 nm) with phosphomolybdic acid and / or iodine, or ninhydrin as an indicator. Flash column chromatography was performed according to the method of Still using silica gel 60 (mesh 230-400) supplied by E. Merck. Yields refer to chromatographically and spectrographically pure compounds, unless otherwise noted.

Commercial grade reagents and solvents were used without further purification except as indicated below. Toluene and dichloromethane (in Pure-Pac^{TM} stainless steel containers, from Aldrich) were purified by both A2 alumina and Q5 reactant using MBRAUN MB-SP series solvent purification system. Triethyl amine was stored over KOH. Ethyl acetate and DMF were dried over 4A molecular sieves. *i*PrOH was distilled from calcium hydride. 1,3-Cyclopentadiene was cracked at 170˚C and re-distilled. Methacrolein was freshly distilled from calcium hydride before use. Isoprene and 2,3-dimethyl-1,3-butadiene were distilled from calcium hydride and stored at –30 ˚C over 4A molecular sieves. Crotonaldehyde and ethyl acrylate were distilled from calcium hydride and stored at –30 ˚C. Ethyl vinyl ketone and 2-cylohexen-1-one were distilled from anhydrous magnesium sulfate. $SnCl_4$ and $TiCl_4$ were distilled and stored as a 1.0 M solution in dichloromethane in a Schlenk flask. BF_3•OEt_2 was distilled according to the literature (G. Zweifel, H. C. Brown, *Organic Reaction*. **1963,** *13*, 28.) and stored as a 1.0 M solution in

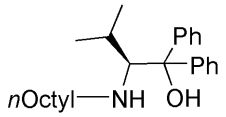
dichloromethane in a Schlenk flask. Triphenylboroxine was prepared from phenylboronic acid by heating at 150 ˚C *in vacuo* (*ca*. 2 Torr) for 15 h.

Infrared spectra were recorded as thin films on sodium chloride plates using a Nicolet 20 SXB FTIR. ^{1}H, ^{13}C, and ^{11}B NMR spectra were recorded on a Bruker Advance 400 (400 MHz ^{1}H, 100 MHz ^{13}C, 128 MHz ^{11}B) and a Bruker Advance 500 (500 MHz ^{1}H, 125 MHz ^{13}C). Chemical shift values (δ) for ^{1}H and ^{13}C NMR are reported in ppm relative to Me_4Si (δ 0.0 ppm) or residual solvent signals as an internal standard. ^{11}B NMR chemical shifts are reported as δ downfield from BF_3•OEt_2 (δ 0.0)by pre-referencing of the spectrometer. The proton spectra are reported as follows δ (multiplicity, number of protons, coupling constant *J*). Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (heptet), m (multiplet) and br (broad). Optical rotations were measured on a JASCO DIP-140 digital polarimeter. GC analysis was done with Shimadzu model 17A instrument with a flame-ionization detector and a capillary column of PEG-Ht (25 m x 0.25 mm), chiral column Chiraldex G-TA (20 m x 0.25 mm), or chiral column Chiraldex B-TA (20 m x 0.25 mm) using nitrogen as a carrier gas. Analytical HPLC was done with a chiral column (4.6 mm x 25 cm, CHIRALCEL OD-H, AD-H).

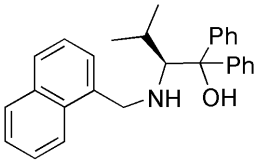
All references for supporting information can be found in the main text.

General Procedure for the Preparation of *N*-substituted Amino Alcohols.

To a solution of aldehyde (6 mmol) in MeOH (50 ml) was added a powder of (*S*)-(-)-2-amino-3-methyl-1, 1'-diphenyl-1-butanol (5 mmol), and AcOH (7.5 mmol, 434 μl) at 0 °C. After being stirred for 15 min at this temperature, a powder of $NaBH_3CN$ was added. The resulting reaction mixture was allowed to warm to room temperature, and stirred for 16 h. The solvent was then evaporated *in vacuo*, and the residue was treated with *sat*.$NaHCO_3$ *aq*.. The aqueous layer was extracted with $CHCl_3$ three times, and the combined organic extracts were dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (Hexane / AcOEt as eluent) to give the corresponding *N*-substituted amino alcohols.



(2*S*)-3-Methyl-2-[(octyl)-amino]-1,1'-diphenyl-butan-1-ol. (81% yield, as a clear oil.) $[\alpha]_D^{29}$-39.9° (c = 1.10, $CHCl_3$); R_f 0.4 (EtOAc/Hexanes, 1:9); FTIR (neat) υ_{max} 3349, 2926, 2855, 1490, 1449, 1370, 1177, 1131, 746 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 7.65 (d, *J*= 8.0Hz, 2H), 7.53 (d, *J*= 8.0Hz, 2H), 7.30-7.25 (m, 4H), 7.17-7.14 (m, 2H), 5.43 (bs, 1H), 3.49 (d, *J*= 0.9Hz, 1H), 2.48-2.42 (m, 1H), 2.11-1.96 (m, 2H), 1.30-1.14 (m, 12H), 1.02 (d, *J*= 7.0Hz, 3H), 0.88 (t, *J*= 6.8Hz, 3H), 0.65 (d, *J*= 6.9Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.07 (C), 145.67 (C), 128.01 (CH), 127.91 (CH), 126.44 (CH), 126.29 (CH), 126.20 (CH), 126.10 (CH), 78.45 (C), 68.86 (CH), 50.86 (CH_2), 31.95, 30.71, 29.43, 29.34, 28.89, 27.11, 23.00, 22.78, 15.93 (CH_3), 14.24 (CH_3). MS (CI) Exact Mass Calcd for $C_{25}H_{37}NO$ $(M+H)^+$: 367.4. Found 367.4.

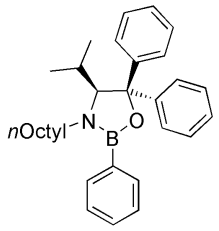


(2*S*)-3-Methyl-2-[(1-napthyl)-amino]-1,1'-diphenyl-butan-1-ol. (88% yield) white solid (recrystallized from dichloromethane/hexanes): mp 110-113 °C; $[\alpha]_D^{29}$-60.9° (c = 1.10, $CHCl_3$); R_f 0.4 (EtOAc/Hexanes, 1:9); FTIR ($CHCl_3$) υ_{max} 3348, 3057, 2957, 2870, 1510, 1449, 1393, 1370, 1330, 1217, 1177, 1086, 801, 780 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 7.88 (d, *J*= 7.5Hz, 2H), 7.79 (d, *J*= 8.0Hz, 1H), 7.73 (d, *J*= 8.2Hz, 1H), 7.61 (d, *J*= 7.4Hz, 2H), 7.51 (d, *J*= 8.3Hz, 1H), 7.44-7.19 (m, 9H), 7.15 (t, *J*= 7.3Hz, 1H), 4.88 (brs, 1H), 3.85 (s, 2H), 3.81 (d, *J*= 2.1Hz, 1H), 2.06-2.00 (m, 1H), 1.34 (brs, 1H), 0.99 (d, *J*= 7.0Hz, 3H), 0.69 (d, *J*= 6.9Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.46 (C), 145.43 (C), 136.09 (C), 133.94 (C), 131.92 (C), 128.62 (CH), 128.28 (CH), 128.10 (CH), 126.75 (CH), 126.74 (CH), 126.36 (CH), 126.29 (CH), 126.23 (CH), 125.83 (CH), 125.78 (CH), 125.45 (CH), 124.33 (CH), 79.07 (C), 69.33 (CH), 53.69 (CH_2), 29.07 (CH), 22.71 (CH_3), 16.06 (CH_3). MS (CI) Exact Mass Calcd for $C_{28}H_{29}NO$ $(M+H)^+$: 395.3. Found 395.3.

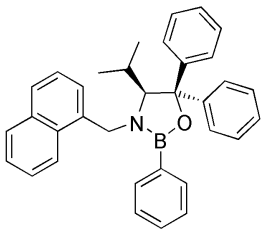
General Procedure for the Preparation of Oxazaborolidine 1a, and 1b.

A single-neck, 100 ml round-bottom flask , charged with amino alcohol (0.303 mmol), triphenylboroxine (0.101 mmol), and dry toluene (10 ml)(to avoid bumping, a few boiling stones were added), was placed into a microwave oven (Sunbeam, 600W, 2450 MHz) and heated for *ca.*10min (the time to evaporate to a volume of *ca.* 1 ml). Then, a 3-neck stopcock was quickly placed under N_2, and cooled to room temperature. Dry toluene (10 ml) was re-charged, and this operation was repeated 4 times.

The resulting residue was further concentrated to remove toluene (*ca.* 0.2 Torr, at 100 °C, 60 min.) to give corresponding oxazaborolidines as clear oil. Oxazaborolidines were used as a 0.1- 0.2 M solution in toluene (for **1a**) or in dichloromethane (for **1b**) for Diels-Alder Reactions, and stored in a Schlenk flask under nitrogen atmosphere at -20 °C.



(99%, as a colorless oil) ^{1}H NMR (500MHz, $CDCl_3$) δ; 7.83-7.81 (m, 2H), 7.75 (d, *J*= 7.9Hz, 2H), 7.57 (d, *J*= 7.7Hz, 2H), 7.42-7.39 (m, 3H), 7.29 (t, *J*= 7.8Hz, 2H), 7.25 (t, *J*= 8.0Hz, 2H), 7.19-7.13 (m, 2H), 4.27 (d, *J*= 1.4Hz, 1H), 3.48-3.42 (m, 1H), 3.17-3.12 (m, 1H), 1.89-1.84 (m, 1H), 1.35-1.30 (m, 1H), 1.22-1.16 (m, 3H), 1.09 (d, *J*= 7.3Hz, 3H), 1.09-0.90 (m, 7H), 0.84 (t, *J*= 7.3Hz, 3H), 0.77-0.76 (m, 1H), 0.71 (d, *J*= 6.7Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.46 (C), 143.30 (C), 134.24 (CH), 129.79 (C), 128.04 (CH), 127.88 (CH), 127.79 (CH), 126.87 (CH), 126.76 (CH), 126.44 (CH), 125.39 (CH), 89.55 (C), 70.52 (CH), 45.76 (CH_2), 31.92, 30.54, 29.43, 29.27, 26.46, 23.32, 22.76, 16.05 (CH_3), 14.25 (CH_3). ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.00.

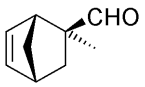


(99% yield, as a clear oil.) ^{1}H NMR (400MHz, $CDCl_3$) δ; 7.93-7.90 (m, 2H), 7.75 (d, *J*= 8.2Hz, 1H), 7.69 (d, *J*= 8.2Hz, 1H), 7.52-7.44 (m, 6H), 7.32-6.92 (m, 12H), 5.23 (d, *J*=

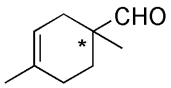
15.6Hz, 1H), 4.78 (d, *J*= 15.6Hz, 1H), 4.11 (d, *J*= 1.3Hz, 1H), 1.94-1.87 (m, 1H), 1.18 (d, *J*= 7.4Hz, 3H), 0.87 (d, *J*= 6.7Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.59 (C), 143.12 (C), 134.18 (CH), 133.88 (C), 133.79 (C), 131.65 (C), 130.16 (C), 129.16 (C), 128.47 (CH), 128.36 (CH), 128.12 (CH), 127.77 (CH), 127.73 (CH), 126.65 (CH), 126.44 (CH), 126.04 (CH), 125.75 (CH), 125.47 (CH), 125.44 (CH), 125.10 (CH), 125.05 (CH), 123.15 (CH), 90.05 (C), 69.93 (CH), 47.08 (CH_2), 30.30 (CH), 23.72 (CH_3), 16.60 (CH_3). ^{11}B NMR (128 MHz, $CDCl_3$) δ 31.65.

General procedure for the Preparation and Use of Chiral LLA Catalysts for Diels-Alder reactions.

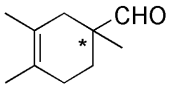
To a dried Schlenk flask was charged CH_2Cl_2 (5 ml), and a 0.2 M solution of oxazaborolidine **1b** in CH_2Cl_2 (50 μl, 10 μmol) under N_2 atmosphere. After being cooled to -78 °C, a 0.2 M solution of $SnCl_4$ in CH_2Cl_2 (50 μl, 10 μmol) was added dropwise. The resulting pale yellow solution was stirred for 15 min at this temperature. To this mixture was added freshly distilled methacrolein (83 μl, 1 mmol) dropwise, and after 1-2min, cyclopentadiene (1:1 (v/v) solution in CH_2Cl_2, pre-cooled at -78 °C, 850 μl) was added dropwise over 3 min via syringe. The reaction mixture was stirred for 2 h at -78 °C and then quenched by addition of 7 μl of Et_3N (*ca*. 5 equiv. for catalyst) at –78 ˚C. The reaction mixture was allowed to warm to room temperature slowly, and the solvent was removed *in vacuo* (ice bath). The crude product was purified by silica gel chromatography (pentane-ether as eluent) to give **2a** in >99% yield.



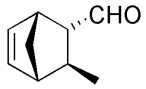
(*1R, 2S, 4R*)-Bicyclo[2,2,1]hept-5-ene-2-methyl-2-carboxaldehyde (2a). The physical and spectral data were identical to those previously reported for this compound.[14a] Diastereoselectivity (*exo-endo* ratio) was determined by ^{1}H NMR analysis of the crude mixture: δ9.69 (s, 1H, *exo*), 9.38 (s, 1H, *endo*). Enantioselectivity was determined by acetalization with (-)-(*2R, 4R*)-2,4-pentanediol and GC analysis.[16a,b] The absolute configuration was established by comparison of optical rotation values in the literature.[14b]



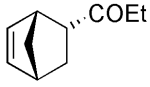
1,4-Dimethylcyclohex-3-ene-1-carboxaldehyde (3a). The physical and spectral data were identical to those previously reported for this compound.[14h,i] Enantioselectivity was determined by acetalization with (-)-(*2R, 4R*)-2,4-pentanediol and GC analysis.[5d] The absolute configuration was not determined.



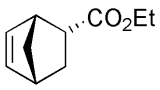
1,3,4-Trimethyl-3-cyclohexen-1-carboxyaldehyde (4a). The physical and spectral data were identical to those previously reported for this compound.[14i] Enantioselectivity was determined by acetalization with (-)-(*2R, 4R*)-2,4-pentanediol and GC analysis.[5d, 16b] The absolute configuration was not determined.



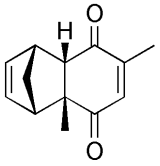
(*1S, 2S, 3R, 4S*)- 3-Methylbicyclo [2,2,1]oct-5-ene-2-carboxyaldehyde (2b). The physical and spectral data were identical to those previously reported for this compound.[5d,14b] Diastereoselectivity (*exo-endo* ratio) was determined by ^{1}H NMR analysis of the crude mixture: δ9.78 (d, *J*= 3.2Hz, 1H, *exo*), 9.37 (d, *J*= 3.2Hz, 1H, *endo*). Enantioselectivity was determined by acetalization with (-)-(*2R, 4R*)-2,4-pentanediol and GC analysis.[5d] The absolute configuration was established by comparison with authentic material prepared independently. [15a]



1-[(*1R, 2R, 4R*)-Bicyclo[2,2,1]hept-5-en-2-yl]-propan-1-one (2c). The physical and spectral data were identical to those previously reported for this compound.[4b,14c] Diastereoselectivity (*exo-endo* ratio) and enantioselectivity were determined by GC analysis using Chiraldex G-TA (20m x 0.25 mm, 100 °C, 80 kPa); t_R = 4.1 min (*exo*, major), 4.3 min (*exo*, minor), 5.1 min (*endo*, major), 5.5 min (*endo*, minor). The absolute configuration was established by comparison with optical rotation values.[4b]

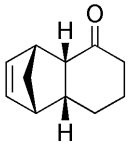


Ethyl (*1R, 2R, 4R*)-Bicyclo[2,2,1]hept-5-ene-2-carboxylate (2d). The physical and spectral data were identical to those previously reported for this compound.[4b,14d] Diastereoselectivity (*exo-endo* ratio) was determined by GC analysis. Enantioselectivity was determined by reduction with $LiAlH_4$ to the corresponding alcohol, conversion to the (*R*) – MTPA ester derivative and HPLC analysis (Daicel AD-H, hexane (99.4 %) – *i*PrOH (0.6 %), flow rate = 0.5 mL/min): t_R = 12.7 min (*endo*, minor), 13.9 min (*endo*, major). The absolute configuration was assigned by the optical rotation values of the corresponding alcohol.[15b]



(*1R, 2R, 7S, 8R*)-2,5-Dimethyl-tricyclo[6.2.1.0^{2,7}]undeca-4,9-diene-3,6-dione (2e). The physical and spectral data were identical to those previously reported for this compound.[4c, 14e]

Enantioselectivity was determined by HPLC analysis (Daicel OD-H, hexane (99.4 %)-*i*PrOH (0.6 %), flow rate = 0.5 mL/min); t_R = 28.2 min (major), 30.4 min (minor). The absolute configuration was established by comparison with optical rotation values. [4c]



(*1R, 2R, 7R, 8 S*)-Tricyclo[6.2.1.0^{2,7}]undec-9-en-3-one (2f). The physical and spectral data were identical to those previously reported for this compound.[4b,14f,g] Diastereoselectivity (*exo-endo* ratio) and enantioselectivity were determined by GC analysis using Chiraldex G-TA (20m x 0.25 mm, 100 °C, 100 kPa); t_R = 14.2 min (*exo*), 16.8 min (*exo*), 17.4 min (*endo*, major), 25.4 min (*endo*, minor). The absolute configuration was established by comparison with optical rotation values.[4b]

General procedure for Diels-Alder reactions in the presence of Lewis bases.

Method A: (Figure 2)

The use of triethylamine is representative:

To a dried Schlenk flask was charged CH_2Cl_2 (4.7 ml), and a 0.2 M solution of oxazaborolidine **1a** in toluene (250 μl, 50 μmol) under N_2 atmosphere. After being cooled to -78 °C, a 1.0 M solution of $SnCl_4$ in CH_2Cl_2 (100 μl, 100 μmol) was added dropwise. The resulting solution was stirred for 15 min at this temperature. To this mixture was added a 0.2 M solution of triethylamine in CH_2Cl_2 (250 μl, 50 μmol) dropwise. After being stirred for 5 min, freshly distilled methacrolein (83 μl, 1 mmol) was added, and after 1-2min, cyclopentadiene (1:1 (v/v) solution in CH_2Cl_2, pre-cooled at -78 °C, 850 μl) was added dropwise over 3 min via syringe. The reaction mixture was stirred for 2 h at -78 °C and then quenched by addition of 70 μl of Et_3N (*ca*. 5 equiv. for catalyst) at –78 ˚C. The same work up, followed by purifications described above provided the cycloadduct.

Method B: (in the case of water, Figure 2)

To a dried Schlenk flask was charged CH_2Cl_2 (4.7 ml), water (0.9 μl) and a 0.2 M solution of oxazaborolidine **1a** in toluene (250 μl, 50 μmol) under N_2 atmosphere. After being cooled to -78 °C (a few pieces of ice were observed at this stage), a 1.0 M solution of $SnCl_4$ in CH_2Cl_2 (50 μl, 50 μmol) was added dropwise (at this point, the reaction mixture turned into a solution). The resulting solution was stirred for 15 min at this temperature. Freshly distilled methacrolein (83 μl, 1 mmol) was added, and after 1-2min, cyclopentadiene (1:1 (v/v) solution in CH_2Cl_2, pre-cooled at -78 °C, 850 μl) was added dropwise over 3 min via syringe. The reaction mixture was stirred for 2 h and the same work-up, followed by purification by silica gel chromatography afforded the cycloadduct.