Asymmetric Normal-Electron-Demand Aza-Diels–Alder Reaction via Trienamine Catalysis

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Supplementary Information

Table of Contents

1. General methods

2. Exploration of more imine substrates in aza-Diels–Alder reaction

3. Preparation of 2-aryl-3H-indol-3-ones

4. General procedure for asymmetric Aza-Diels–Alder and reduction reactions

5. Aza-Baylis-Hillman-type pathway of simple 2,4-hexadienal or 2,4-heptadienal

6. Synthetic transformations of cycloadduct

7. Crystal data and structure refinement for enantiopure 2,4-dinitrobenzenehydrazone of aldehyde of product 4a

8. NMR spectra and HPLC chromatograms
1. General Methods

TLC was performed on glass-backed silica plates. Column chromatography was performed using silica gel (200-300 mesh) eluting with EtOAc/petroleum ether or acetone/petroleum ether. NMR spectra were recorded with tetramethylsilane as the internal standard. $^1$H NMR spectra were recorded at 400 MHz (Varian) and $^{13}$C NMR spectra were recorded at 100 MHz (Varian). Chemical shifts are reported in ppm downfield from CDCl$_3$ ($\delta = 7.26$ ppm) for $^1$H NMR and relative to the central CDCl$_3$ resonance ($\delta = 77.0$ ppm) for $^{13}$C NMR spectroscopy. Coupling constants are given in Hz. Optical rotations were measured at 589 nm at 20 ºC. Enantiomeric excess was determined by HPLC analysis on Chiralpak IA, IB, IC, AD and Chiralcel OD columns. THF was distilled from sodium. All other chemicals were used without purification as commercially available. Toluene, THF, ethyl acetate (EA), petroleum ether (PE), methylene chloride (DCM) and MeCN were freshly distilled before use. 2,4-Dienals$^1$ and secondary amine catalysts$^2$ 1 were synthesized according to the literature procedures.


2. Exploration of more imine substrates in aza-Diels–Alder reaction

![Diagram showing aza-Diels–Alder reaction with different imine substrates and results.](image-url)
3. Preparation of 2-aryl-3H-indol-3-ones

2-Aryl-3H-indol-3-ones could be conveniently prepared according to the literature procedure.3


For some selected 1H NMR data:

Red solid (m.p. = 159.9-161.2 °C); 1H NMR (400 MHz, CDCl3): δ = 8.38-8.36 (m, 1H), 7.53-7.46 (m, 3H), 7.41-7.37 (m, 2H), 7.26-7.23 (m, 1H), 7.06-7.02 (m, 1H), 2.66 (s, 3H) ppm.

Red solid (m.p. = 128.0-131.1 °C); 1H NMR (400 MHz, CDCl3): δ = 8.38 (d, J = 7.6 Hz, 2H), 7.59-7.55 (m, 1H), 7.52-7.49 (m, 3H), 7.42 (s, 1H), 7.26-7.25 (m, 1H) ppm.

Red solid (m.p. = 172.6-172.9 °C); 1H NMR (400 MHz, CDCl3): δ = 8.21-8.19 (m, 2H), 7.57-7.53 (m, 2H), 7.44-7.35 (m, 3H), 7.29-7.25 (m, 1H), 2.44 (s, 3H) ppm.

4. General procedure for asymmetric aza-Diels–Alder and reduction reactions

The reaction was performed with 2-aryl-3H-indol-3-one 2 (0.1 mmol), 2,4-dienal 3 (0.12 mmol), catalyst 1a (0.02 mmol) and salicylic acid (0.02 mmol) in xylene (0.5 mL) at 10 °C for a specified reaction time. After completion, the DA adduct was isolated by flash chromatography, and dissolved in dichloromethane (0.5 mL). Sodium triacetoxyborohydride (0.3 mmol) were added sequentially and the resulting mixture was stirred at room temperature for 12 hours. The mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate) to afford the alcohol product 4.
4a yellow oil; 94% yield; $[\alpha]_D^{20} = -135.0$ (c = 5.5 in CHCl$_3$); 92% ee, determined by HPLC analysis [Chiralpak OD, n-hexane/i-PrOH = 70/30, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 5.84 min, t (minor) = 7.22 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.69$ (d, $J =$ 8.0 Hz, 1H), 7.58-7.54 (m, 1H), 7.35-7.21 (m, 11H), 6.82 (t, $J =$ 7.2 Hz, 1H), 6.18-6.16 (m, 1H), 5.07 (d, $J =$ 14.0, 2.8 Hz, 1H), 3.42-3.38 (m, 1H), 3.23 (dd, $J =$ 18.4, 6.0 Hz, 1H), 2.59-2.53 (m, 1H), 1.46-1.39 (m, 1H), 0.78-070 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 203.7, 162.1, 141.6, 139.5, 138.8, 137.9, 128.5, 128.0, 127.5, 127.3, 126.4, 125.6, 121.5, 117.9, 121.6, 117.7, 109.8, 67.7, 58.8, 51.7, 35.0, 28.0 ppm; ESI-HRMS: calcd. for C$_{26}$H$_{23}$NO$_2$+Na$^+$ 404.1621, found 404.1627.

4b yellow oil; 77% yield; $[\alpha]_D^{20} = -135.0$ (c = 5.5 in CHCl$_3$); 83% ee, determined by HPLC analysis [Chiralpak OD, n-hexane/i-PrOH = 70/30, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 5.14 min, t (minor) = 6.31 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$ 7.42 (t, $J =$ 8.0 Hz, 1H), 7.35-7.23 (m, 10H), 7.08 (d, $J =$ 8.4 Hz, 1H), 6.58 (d, $J =$ 6.7 Hz, 1H), 6.17 (t, $J =$ 2.8 Hz, 1H), 5.05 (d, $J =$ 7.2 Hz, 1H), 3.60-3.55 (m, 1H), 3.46-3.41 (m, 1H), 3.22 (dd, $J =$ 18.0, 6.0 Hz, 1H), 2.63-2.58 (m, 4H), 1.48-1.40 (m, 1H), 0.90-0.77 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 204.1, 162.7, 141.6, 141.2, 139.6, 139.4, 137.1, 131.3, 128.6, 128.5, 127.9, 127.5, 127.3, 126.4, 121.6, 119.6, 116.0, 106.9, 67.6, 59.1, 51.8, 35.2, 28.3, 18.5 ppm; ESI-HRMS: calcd. for C$_{27}$H$_{25}$NO$_2$+Na$^+$ 418.1778, found 418.1779.

4c yellow oil; 97% yield; $[\alpha]_D^{20} = -216.9$ (c = 12.2 in CHCl$_3$); 90% ee, determined by HPLC analysis [Chiralpak OD, n-hexane/i-PrOH = 80/20, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 20.40 min, t (minor) = 11.80 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$ 7.35-7.23 (m, 12H), 7.12 (d, $J =$ 2.4 Hz, 1H), 6.19-6.17 (m, 1H), 5.02 (d, $J =$ 10.8 Hz, 1H), 3.80 (s, 3H), 3.62-3.56 (m, 1H), 3.48-3.43 (m, 1H), 3.21 (dd, $J =$ 18.4, 6.4 Hz, 1H), 2.54 (dt, $J =$ 18.0, 2.8 Hz, 1H), 1.50-1.44 (m, 1H), 0.90-0.83 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 203.8, 158.5, 152.6, 141.8, 139.5, 139.2, 128.7, 128.6, 128.5, 127.9, 127.5, 127.1, 126.3, 121.3, 117.6, 111.5, 105.1, 68.5, 58.9, 55.8, 52.3, 34.9, 28.5 ppm; ESI-HRMS: calcd. for C$_{27}$H$_{25}$NO$_3$+Na$^+$ 434.1732, found 434.1730.
4d yellow oil; 74% yield; $[\alpha]_D^{20} = -170.6$ ($c = 10.5$ in CHCl$_3$); 85% ee, determined by HPLC analysis [Chiralpak OD, $n$-hexane/i-PrOH = 90/10, 1.0 mL/min, $\lambda$ = 254 nm, $t$ (major) = 18.09 min, $t$ (minor) = 21.40 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.64 (d, $J$ = 2.0 Hz, 1H), 7.50 (dd, $J$ = 8.8, 2.4 Hz, 1H), 7.36-7.23 (m, 11H), 6.19-6.18 (m, 1H), 5.05 (d, $J$ = 9.8 Hz, 1H), 3.54 (dt, $J$ = 10.4, 2.8 Hz, 1H), 3.46-3.41 (m, 1H), 3.24 (dd, $J$ = 19.2, 5.6 Hz, 1H), 2.54 (dt, $J$ = 18.0, 2.4 Hz, 1H), 1.47-1.40 (m, 1H), 0.78-0.72 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 202.5, 160.4, 141.5, 139.3, 138.4, 137.8, 128.7, 128.6, 128.2, 127.1, 126.4, 124.6, 123.0, 121.3, 118.6, 111.2, 68.2, 58.6, 51.8, 34.7, 28.0 ppm; ESI-HRMS: calcd. for C$_{26}$H$_{22}$ClNO$_2$+Na$^+$ 438.1231, found 438.1233.

4e yellow oil; 76% yield; $[\alpha]_D^{20} = -40.3$ ($c = 3.3$ in CHCl$_3$); 84% ee, determined by HPLC analysis [Chiralpak OD, $n$-hexane/i-PrOH = 90/10, 1.0 mL/min, $\lambda$ = 254 nm, $t$ (major) = 5.44 min, $t$ (minor) = 7.43 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.61 (d, $J$ = 4.4 Hz, 1H), 7.36-7.23 (m, 11H), 6.79 (dd, $J$ = 8.4, 1.6 Hz, 1H), 6.19-6.18 (m, 1H), 5.02 (d, $J$ = 9.6 Hz, 1H), 3.52 (dt, $J$ = 10.4, 3.2 Hz, 1H), 3.44-3.40 (m, 1H), 3.25 (dd, $J$ = 18.0, 5.6 Hz, 1H), 2.54 (dd, $J$ = 13.2, 3.2 Hz, 1H), 1.47-1.40 (m, 1H), 0.73-0.67 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 202.2, 162.2, 144.6, 141.4, 139.3, 138.4, 128.7, 128.6, 128.2, 127.7, 127.2, 126.5, 126.4, 121.4, 118.7, 116.2, 109.8, 68.2, 58.6, 51.8, 34.7, 28.0 ppm; ESI-HRMS: calcd. for C$_{26}$H$_{22}$ClNO$_2$+Na$^+$ 438.1231, found 438.1235.

4f yellow oil; 82% yield; $[\alpha]_D^{20} = -225.0$ ($c = 9.5$ in CHCl$_3$); 85% ee, determined by HPLC analysis [Chiralpak IA, $n$-hexane/i-PrOH = 80/20, 1.0 mL/min, $\lambda$ = 254 nm, $t$ (major) = 20.40 min, $t$ (minor) = 11.79 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.78 (d, $J$ = 2.4 Hz, 1H), 7.61 (dd, $J$ = 8.8, 2.0 Hz, 1H), 7.35-7.20 (m, 11H), 6.19-6.18 (m, 1H), 5.04 (d, $J$ = 11.6 Hz, 1H), 3.52-3.47 (m, 1H), 3.43-3.40 (m, 1H), 3.23 (dd, $J$ = 19.2, 6.4 Hz, 1H), 2.54 (d, $J$ = 18.0 Hz, 1H), 1.48-1.39 (m, 1H), 0.76-0.69 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 202.2, 160.6, 141.5, 140.3, 139.3, 138.4, 128.7, 128.6, 128.2, 127.8 127.2, 126.4, 121.4, 119.3, 111.6, 109.8, 68.2, 58.7, 51.8, 34.9, 28.0 ppm; ESI-HRMS: calcd. for C$_{26}$H$_{22}$BrNO$_2$+Na$^+$ 482.0727, found 4382.0733.
4g yellow oil; 69% yield; $[\alpha]_D^{20} = -32.9$ ($c = 1.6$ in CHCl$_3$); 89% ee, determined by HPLC analysis [Chiralpak OD, $n$-hexane/i-PrOH = 70/30, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 5.08 min, t (minor) = 6.90 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.69$ (d, $J = 7.2$ Hz, 1H), 7.57-7.53 (m, 1H), 7.32-7.22 (m, 6H), 7.14-7.05 (m, 4H), 6.83-6.79 (m, 1H), 6.17-6.16 (m, 1H), 5.07 (d, $J = 10.4$ Hz, 1H), 3.57-3.51 (m, 1H), 3.43-3.38 (m, 1H), 3.20 (dd, $J = 18.0$, 6.4 Hz, 1H), 2.54 (dt, $J = 18.0$, 2.4 Hz, 1H), 2.28 (s, 3H), 1.46-1.39 (m, 1H), 0.83-0.76 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 203.8$, 162.0, 141.5, 139.5, 137.8, 137.7, 135.6, 129.2, 128.5, 127.4 127.1, 126.4, 125.5, 121.5, 117.7, 117.6, 119.7, 67.5, 58.8, 51.6, 35.0, 28.1, 21.0 ppm; ESI-HRMS: calcd. for C$_{27}$H$_{25}$NO$_2$+Na$^+$ 418.1778, found 418.1784.

4h 72% yield; $[\alpha]_D^{20} = -236.4$ ($c = 9.4$ in CHCl$_3$); 87% ee, determined by HPLC analysis [Chiralpak OD, $n$-hexane/i-PrOH = 80/20, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 5.85 min, t (minor) = 7.92 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.69$ (d, $J = 7.2$ Hz, 1H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.35-7.25 (m, 6H), 7.16 (t, $J = 7.2$ Hz, 1H), 6.83-6.75 (m, 3H), 6.17-6.16 (m, 1H), 5.07 (d, $J = 10.8$ Hz, 1H), 3.59-3.54 (m, 1H), 3.46-3.41 (m, 1H), 3.23 (dd, $J = 18.4$, 6.4 Hz, 1H), 2.56 (d, $J = 18.4$ Hz, 1H), 2.04 (s, 3H), 1.47-1.40 (m, 1H), 0.84-0.77 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 203.8$, 162.1, 141.5, 139.5, 138.6, 138.2, 137.9, 128.8, 128.6 128.4, 127.8, 127.5, 126.4, 125.6, 124.3, 121.6 117.8, 117.7, 109.7, 67.7, 58.9, 51.7, 35.0, 28.1, 21.5 ppm; ESI-HRMS: calcd. for C$_{27}$H$_{25}$NO$_2$+H$^+$ 412.1907, found 412.1913.

4i yellow oil; 84% yield; $[\alpha]_D^{20} = -151$ ($c = 5.4$ in CHCl$_3$); 91% ee, determined by HPLC analysis [Chiralpak OD, $n$-hexane/i-PrOH = 80/20, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 15.56 min, t (minor) = 13.48 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.69$ (d, $J = 8.0$ Hz, 1H), 7.56 (t, $J = 7.6$ Hz, 1H), 7.35-7.24 (m, 6H), 7.16 (d, $J = 8.8$ Hz, 2H), 6.83-6.75 (m, 3H), 6.17-6.16 (m, 1H), 5.06 (d, $J = 6.8$ Hz, 1H), 3.76 (s, 1H), 3.57-3.52 (m, 1H), 3.45-3.43 (m, 1H), 3.18 (dd, $J = 18.0$, 6.0 Hz, 1H), 2.54 (d, $J = 18.0$ Hz, 1H), 1.47-1.41 (m, 1H), 0.85-0.78 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 203.9$, 161.9, 159.2, 141.6, 140.0, 137.9, 130.7, 128.6, 128.5, 127.5, 126.5, 125.6, 124.3, 121.5, 117.8, 117.6, 113.9, 109.7, 67.3, 58.9, 55.2, 51.6, 35.0, 28.3 ppm; ESI-HRMS: calcd. for C$_{27}$H$_{25}$NO$_3$+H$^+$ 414.1907, found 412.1913.
**4j** yellow oil; 82% yield; $[\alpha]_{D}^{20} = -170.6$ ($c = 10.5$ in CHCl$_3$); 84% ee, determined by HPLC analysis [Chiralpak OD, $n$-hexane/i-PrOH = 80/20, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 6.90 min, t (minor) = 10/15 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$ 7.68 (d, $J = 4.0$ Hz, 1H), 7.61-7.56 (m, 1H), 7.36-7.19 (m, 10H), 6.85 (t, $J = 7.6$ Hz, 1H), 6.16-6.15 (m, 1H), 5.08 (d, $J = 7.2$ Hz, 1H), 3.57-3.53 (m, 1H), 3.48-3.43 (m, 1H), 3.17 (dd, $J = 15.6$, 2.4 Hz, 1H), 2.60-2.55 (m, 1H), 1.51-1.43 (m, 1H), 0.87-0.77 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 203.1, 162.2, 141.9, 139.4, 138.1, 137.6, 133.9, 128.8, 128.6, 127.7, 126.4 125.7, 121.1, 118.3, 117.6, 110.0, 67.2, 58.8, 51.8, 35.2, 28.2 ppm; ESI-HRMS: calcd. for C$_{26}$H$_{22}$ClNO$_2$+H$^+$ 416.1412, found 416.1411.

**4k** yellow oil; 72% yield; $[\alpha]_{D}^{20} = -394$ ($c = 13$ in CHCl$_3$); 90% ee, determined by HPLC analysis [Chiralpak AD, $n$-hexane/i-PrOH = 80/20, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 8.83 min, t (minor) = 13.47 min] $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$ 7.66 (d, $J = 7.6$ Hz, 1H), 7.54-7.49 (m, 1H), 7.26-7.24 (m, 3H), 7.19-7.17 (m, 2H), 7.09 (d, $J = 8.4$ Hz, 1H), 6.78 (t, $J = 7.2$ Hz, 1H), 5.75 (d, $J = 4.0$ Hz, 1H), 4.30 (d, $J = 11.6$ Hz, 1H), 3.60-3.52 (m, 2H), 3.03 (dd, $J = 17.6$, 6.0 Hz, 1H), 2.34 (dd, $J = 17.6$, 6.0 Hz, 1H), 1.75-1.69 (m, 4H), 0.81-0.73 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 203.9, 161.8, 138.8, 137.7, 135.9, 128.5, 127.9, 127.5, 125.6, 118.6, 117.6, 117.5, 109.5, 67.9, 59.0, 53.9, 34.4, 27.6, 21.1 ppm; ESI-HRMS: calcd. for C$_{21}$H$_{21}$NO$_2$+Na$^+$ 342.1465, found 342.1471.

**4l** yellow oil; 81% yield; $[\alpha]_{D}^{20} = -102$ ($c = 3$ in CHCl$_3$); 92% ee, determined by HPLC analysis [Chiralpak OD, $n$-hexane/i-PrOH = 70/30, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 4.31 min, t (minor) = 4.63 min] $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$ 7.66 (d, $J = 7.6$ Hz, 1H), 7.53-7.17 (m, 5H), 7.10 (d, $J = 6.4$ Hz, 1H), 6.78 (t, $J = 7.2$ Hz, 1H), 5.76-5.74 (m, 1H), 4.38 (d, $J = 11.2$ Hz, 1H), 3.61-4.00 (m, 2H), 3.05 (dd, $J = 17.2$, 4.2 Hz, 1H), 2.40-2.35 (m, 1H), 2.14-1.98 (m, 2H), 1.73-1.66 (m, 1H), 1.26 (t, $J = 6.4$ Hz, 3H), 0.80-0.73 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 204.0, 161.9, 141.6, 139.0, 137.7, 128.5, 127.9, 127.4, 125.6, 117.6, 117.6, 109.6, 68.2, 59.1, 52.6, 34.3, 27.6, 26.9, 12.2 ppm; ESI-HRMS: calcd. for C$_{22}$H$_{23}$NO$_2$+Na$^+$ 356.1621, found 3356.1625.
4m yellow oil; 69% yield; $[\alpha]_D^{20} = -70$ ($c = 4.5$ in CHCl$_3$); 80% ee, determined by HPLC analysis [Chiralpak AD, $n$-hexane/i-PrOH = 80/20, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 10.28 min, t (minor) = 13.25 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.65 (d, $J = 7.6$ Hz, 1H), 7.54-7.40 (m, 1H), 7.26-7.25 (m,3H), 7.14-7.08 (m, 2H), 6.79 (t, $J = 7.2$ Hz, 1H), 5.46 (d, $J = 1.2$ Hz, 1H), 4.44-4.43 (m, 1H), 3.65-3.60 (m, 2H), 2.90 (d, $J = 17.2$ Hz, 1H), 2.23 (d, $J = 16.8$ Hz, 1H), 1.9 (s, 3H), 1.51-1.44 (m, 1H), 1.20-1.14 (m, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 203.2, 161.7, 138.7, 137.8, 130.4, 128.5, 127.8, 126.9, 126.9, 125.6, 123.6, 117.8, 117.5, 109.5, 68.9, 59.0, 50.8, 37.6, 32.2, 23.3 ppm; ESI-HRMS: calcd. for C$_{21}$H$_{21}$NO$_2$+Na$^+$ 342.1465, found 342.1470.

4n yellow oil; 77% yield; $[\alpha]_D^{20} = -150.5$ ($c = 6.5$ in CHCl$_3$); 71% ee, determined by HPLC analysis [Chiralpak OD, $n$-hexane/i-PrOH = 70/30, 1.0 mL/min, $\lambda = 254$ nm, t (major) = 4.73 min, t (minor) = 5.53 min]; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.54-7.48 (m, 2H), 7.41-7.38 (m, 2H), 7.32-7.14 (m, 9H), 6.74 (t, $J = 7.2$ Hz, 1H), 5.91 (d, $J = 7.6$ Hz, 1H), 5.15 (d, $J = 8.0$ Hz, 1H), 3.56-3.48 (m, 2H), 3.35-3.29 (m, 1H), 2.66-2.58 (m, 1H), 2.01-2.00 (m, 1H), 1.14 (d, $J = 7.2$ Hz, 3H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 200.4, 158.9, 141.8, 140.2, 139.9, 137.1, 128.6, 128.6, 127.9, 127.7, 127.4, 126.5, 125.6, 125.5, 121.3, 117.5, 110.3, 59.7, 52.9, 36.2, 36.1, 29.7, 15.8 ppm; ESI-HRMS: calcd. for C$_{27}$H$_{25}$NO$_2$+Na$^+$ 418.1778, found 418.1781.

5. Aza-Baylis-Hillman-type pathway of simple 2,4-hexadienal or 2,4-heptadienal

2-Phenyl-$3H$-indol-3-ones 2a was tested in the reactions of simple 2,4-hexadienal or 2,4-heptadienal in xylene. The desired aza-Diels–Alder cycloadducts were not obtained, but the aza-Baylis–Hillman-type products 8 were observed at lower -20 °C but with yield. The isolated products are not very stable.
6. Synthetic transformations of cycloadduct

Salt 5 (0.04 mmol, 16 mg), K₂CO₃ (0.04 mmol, 5.5 mg), 18-crown-6 (0.04 mmol, 10 mg) were added to a solution of aldehyde of 4a (0.2 mmol, 76 mg) in toluene (0.5 mL), and the mixture was stirred at room temperature under O₂ atmosphere. After 8 hours, the solvent was concentrated and the residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate) to afford hemiacetal 6 as a yellow oil; (48.3 mg, 61% yield); [α]$_D^{20}$ = -135.0 ($c$ = 3.2 in CHCl₃); 92% ee, determined by HPLC analysis [Chiralpak IC, $n$-hexane/i-PrOH = 70/30, 1.0 mL/min, λ = 254 nm, t (major) = 6.26 min, t (minor) = 10.89 min]; $^1$H NMR (400 MHz, CDCl₃): δ = 7.68 (t, $J$ = 3.6 Hz, 1H), 7.57 (t, $J$ = 7.2 Hz, 1H), 7.35-7.26 (m, 11H), 6.86 (t, $J$ = 7.2 Hz, 1H), 6.22-6.20 (m, 1H), 5.33 (d, $J$ = 10.0 Hz, 1H), 3.24 (dd, $J$ = 18.8, 2.8 Hz, 1H), 2.61 (d, $J$ = 18.0 Hz, 1H), 2.16 (dd, $J$ = 16.8, 2.8 Hz, 1H), 1.83 (dd, $J$ = 16.4, 10.8 Hz, 1H) ppm; $^{13}$C NMR (100 MHz, CDCl₃): δ = 203.0, 176.1, 160.1, 140.0, 138.5, 138.2, 137.6, 128.8, 128.3, 128.0, 127.4, 127.3, 126.4, 125.6, 122.6, 118.6, 118.0, 110.7, 67.9, 52.5, 37.4, 28.1 ppm; ESI-HRMS: calcd. for C$_{26}$H$_{21}$NO$_3$+Na$^+$ 418.1414, found 418.1418.

Salt 5 (0.04 mmol, 16 mg), NaOAc (0.04 mmol, 3.3 mg) were added to a solution of aldehyde of 4a (0.2 mmol, 76 mg) in DCM (0.5 mL), and the mixture was stirred at room temperature under Ar atmosphere. After 8 hours, the solvent was concentrated and the residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate) to afford 7 as a yellow oil; (55 mg, 72% yield); [α]$_D^{20}$ = -155.0 ($c$ = 3.5 in CHCl₃); 92% ee, determined by HPLC analysis [Chiralpak AD, $n$-hexane/i-PrOH = 60/40, 1.0 mL/min, λ = 254 nm, t (major) = 7.50 min, t (minor) = 11.07 min]; $^1$H NMR (400 MHz, CDCl₃): δ = 7.63-7.55 (m, 3H), 7.55-7.50 (m, 2H), 7.50-7.24 (m, 11H), 6.95-6.78...
(m, 8H), 6.63-6.54 (m, 4H), 6.30-6.25 (m, 2H), 5.19 (d, \(J = 9.6\) Hz, 1H), 5.06 (d, \(J = 10.4\) Hz, 1H), 3.57-3.55 (m, 2H), 3.12 (td, \(J = 17.6, 6.4\) Hz, 2H), 2.59-2.49 (m, 2H), 1.59-1.51 (m, 1H), 1.29-1.22 (m, 1H), 0.78 (t, \(J = 12.0\) Hz, 1H), 0.11-0.05 (m, 1H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 209.5, 203.6, 203.0, 161.8, 161.1, 140.2, 139.6, 139.1, 138.6, 138.2, 138.0, 137.8, 137.2, 129.0, 128.8, 128.3, 128.0, 127.9, 127.9, 126.9, 126.6, 126.0, 125.7, 125.4, 122.3, 121.5, 118.5, 118.3, 117.9, 117.6, 116.1, 110.5, 73.0, 67.5, 67.0, 51.6, 49.7, 39.9, 28.0, 27.9 ppm; ESI-HRMS: calcd. for \(\text{C}_{52}\text{H}_{42}\text{N}_{2}\text{O}_{4}^+\text{Na}^+\) 781.3038, found 781.3043.

We tried to conduct esterification of the newly generated OH group with Mosher’s acid in order to determine its absolute configuration. Unfortunately, the corresponding ester could not be produced under diverse reaction conditions, probably due to the crowded structure and the effect of the adjacent carbonyl group.

7. Crystal data and structure refinement for enantiopure 2,4-dinitrobenzenehydrazone of aldehyde of product 4a

![Diagram of 2,4-dinitrobenzenehydrazone of aldehyde of product 4a]

Aldehyde of 4a (0.1 mmol, 91% ee), 2,4-dinitrobenzenehydrazine (0.11 mmol) and 4-toluene sulfonic acid (0.01 mmol) were stirred in EtOH (2 mL) at room temperature for 2 hour. After completion, the product was isolated by flash chromatography as a yellow solid (45.2 mg, 82% yield). The obtained 2,4-dinitrobenzenehydrazone was slowly crystallized from a solution of Et\(_2\)O/n-hexane (1:2) at room temperature to give the optically pure crystals suitable X-ray analysis. (m.p. = 194.5-196.2 °C); \([\alpha]_D^{20} = -45.0\) (c = 1.5 in CHCl\(_3\)); \(\geq 99.5\%\) ee, determined by HPLC analysis [Chiralpak AD, \(n\)-hexane/i-PrOH = 70/30, 1.0 mL/min, \(\lambda = 254\) nm, t = 15.89 min]; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 10.55\) (s, 1H), 9.09 (s, 1H), 8.23 (dd, \(J = 9.6, 2.4\) Hz, 1H), 7.74 (d, \(J = 7.6\) Hz, 1H), 7.65 (d, \(J = 9.6\) Hz, 1H), 7.62-7.58 (m, 1H), 7.39-7.26 (m, 9H), 6.90 (d, \(J = 8.4\) Hz, 1H), 6.90 (t, \(J = 7.6\) Hz, 1H), 6.65 (t, \(J = 6.4\) Hz, 1H), 6.27-6.25 (m, 1H), 5.06-5.04 (m, 1H), 4.12 (q, \(J = 7.2\) Hz, 1H), 3.30 (dd, \(J = 19.6, 6.0\) Hz, 1H), 2.60-2.56 (m, 1H), 2.43-2.37 (m, 1H), 2.21-2.14 (m, 1H) ppm; ESI-HRMS: calcd. for \(\text{C}_{32}\text{H}_{25}\text{N}_{5}\text{O}_{5}^+\text{Na}^+\) 582.1748, found 582.1755.
Based on the absolute configuration of the cycloadduct, it was found that inverted enantioselectivity was observed in comparison with our previous work (Angew. Chem., Int. Ed., 2013, 52, 948). We further checked the trienamine catalysis in literatures. In fact, the Jørgensen group reported a similar enantioselectivity in amine 1a-catalysed DA reaction of 2,4-dienals and 3-cyanochromones, though the ee values was only fair (Angew. Chem., Int. Ed., 2012, 51, 9088). We further tested our reaction with a bifunctional catalyst 1f. As outlined in the following scheme, the enantioselectivity was low but inversed in comparison with that of amine 1a, also in accordance to that observed in Jørgensen’s paper.
Therefore, as stated in Jørgensen’s paper, “the obtained results suggest that the mechanism(s) of trienamine-mediated reactions can be a rather complex issue and might be highly dependent on the structure of the starting dienal”, and the dienophiles used.

A proposed catalytic transition state was outlined in the following scheme based on the absolute configuration of cycloadduct 4a and Jørgensen’s model.

In addition, we further analyzed the structure of cycloadduct 4n. The chiral center adjacent to methyl group was established by NOE study. It was also in fine accordance to that observed in Jørgensen’s paper. The proposed transition state for the generation of aldehyde of 4n was outlined in the following scheme.
8. NMR spectra and HPLC chromatograms

2b

2e
Rac 4a

4a
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Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

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6H-H cosy

6 H-H cosy
irradiation $H_a$ at 10.26 ppm

$H_b$ signal at 7.03 ppm