Selective Carbon-Carbon Bond Formation: Terpenylations of Amines Involving Hydrogen Transfers

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General Experimental Details:

All reactions were carried out under an inert atmosphere with standard Schlenk techniques, unless otherwise mentioned. Toluene was distilled and purified by solvent purification system equipped with a series of activated filter columns. D (+) Camphor sulfonic acid and hydroxyquinoline were purchased from commercial sources and used as received. Proton magnetic resonance (1H NMR) spectra were recorded on Bruker GPX (300 MHz, 400 MHz and 500 MHz) spectrometers and carbon magnetic resonance (13C NMR) spectra were performed at 75, 100, 125 MHz. Chemical shifts (δ) are reported in parts per million relative to residual chloroform (7.26 ppm for 1H; 77.0 ppm for 13C). Coupling constants are reported in Hertz. 1H NMR assignment abbreviations are the following: singlet (s), doublet (d), triplet (t), quartet (q), pentet (p), broad singlet (bs), doublet of doublets (dd), doublet of triplets (dt), and multiplet (m). All reagents were weighed and handled in air, and refilled with an inert atmosphere of Argon at room temperature. HRMS were recorded on a Varian MAT 311 mass spectrometer with an EI source or on ZAB Spec TOF with an ESI source.
2-Hydroxyquinoline (100 mg, 0.68 mmol) was dissolved in DCM (6 mL) in a Schlenk tube at room temperature under argon atmosphere. tBuOK (85 mg, 0.75 mmol) was then added and the mixture was stirred for one hour. [RuCl₂(p-cymene)]₂ (210 mg, 0.34 mmol, 0.5 eq) was then added and the reaction mixture stirred for 16 h. The solvent was evaporated, and the crude mixture was dissolved in 8 mL of dry dichloromethane. Filtration by canulation to remove the inorganic salts followed by concentration in vacuo afforded cat. D as a yellow solid yield (250 mg, 85%); CCDC 918329 contains the supplementary crystallographic data for this complex. ¹H NMR (400 MHz, CDCl₃): δ 7.76 (d, 1H, J = 8.90 Hz), 7.50 (d, 2H, J = 7.6 Hz), 7.38 (d, 1H, J = 8.3 Hz), 7.18-7.16 (m, 1H), 6.22 (d, 1H, J = 9.0 Hz), 5.71-5.64 (m, 2H), 5.50 (d, 1H, J = 5.5 Hz), 5.39 (d, 1H, J = 5.5 Hz), 2.92-2.89 (m, 1H), 2.31 (s, 3H), 1.22-1.19 (m, 6H); ¹³C NMR (125 MHz, CDCl₃), 175.7, 144.1, 138.4, 129.4, 127.9, 121.7, 121.2, 118.8, 113.4, 100.7, 79.1, 78.9, 79.0, 75.9, 30.9, 21.3, 21.2, 18.1.

**Figure 1.** X-Ray structure of complex cat. D
General procedure for N-alkylation of cyclic amines with terpenes (I):

Procedure I with aldehydes:
Cyclic amine (1.05 equiv.) and aldehyde (6.65 mmol, 1 equiv.) were added into a Schlenk tube under an inert atmosphere. Subsequently formic acid (1.5 equiv.) was added dropwise. Then the reaction mixture was stirred at 100 °C in neat condition for 16 h and then allowed to cool down to room temperature. The crude mixture was analyzed by GC and purified by column chromatography on silica gel (Pentane/Diethyl ether/ triethylamine) to give the desired product 3 in 68-95 % isolated yields.

Procedure II with allylic alcohols:
To a stirred solution of allylic alcohol (1.2 equiv.) in 2 mL of toluene, Cyclic amine (1 equiv., 1.05 mmol), formic acid (1.1 equiv.) and Cat. A (5 mol %) were sequentially added. Then the reaction mixture was stirred at 150 °C for 16 h. The residue was directly purified by column chromatography (Et₂O/PE) to afford the alkylated amine 3 in 52-61% isolated yields.

Procedure III with alcohols:
Cyclic amine (11.7 mmol, 1 equiv.) and alcohol (1.05 equiv.) were added into the Schlenk tube under inert atmosphere. Then Catalyst A (1 mol %) was added and the reaction mixture was stirred at 140 °C in neat condition for 16 h and then allowed to cool down to room temperature. The crude mixture was analyzed by GC and purified by column chromatography on silica gel (pentane/ diethyl ether/ triethylamine) to give the desired product 3 in 54-63 % isolated yields.

Procedure IV dialkylation of piperazine with aldehydes:
Cyclic amine (11.7 mmol, 1 equiv.) and aldehyde (2 equiv.) were added into a Schlenk tube under an inert atmosphere. Subsequently formic acid (2 equiv.) was added dropwise. Then the reaction mixture was stirred at 100 °C in neat condition for 16 h and then allowed to cool down to room temperature. The crude mixture was analyzed by GC and purified by column chromatography on silica gel (Pentane/ Diethyl ether/ triethylamine) to give the desired products 3i and 3j in 49, 57 % isolated yields respectively.
General Procedure V for (β) C-H alkylation of amine (II)

Procedure V for the preparation of amines 4:
See manuscript

Procedure VI for the preparation of amines 5:
To a stirred solution of amine 3 (1 equiv., 0.44 mmol) in 1.5 mL of toluene was added aldehyde 2 (2 equiv.). Subsequently D-(+)-Camphor sulfonic acid (15 mol %) and catalyst A (3 mol %) were added and then the sealed Schlenk tube was stirred in at 150 °C (Oil bath temperature) for 18 h. After 18 h the reaction mixture was cooled down and then HCOOH (2 equiv.) was added and stirring was continued at 130 °C for 3 h. The crude mixture was directly taken for GC analysis and purified by column chromatography (Et<sub>2</sub>O/PE) to afford the triterpenylated amine 5 as colorless oil.

1-(3, 7-dimethyloct-6-en-1-yl) piperidine (3a)

Compound 3a was prepared according to general procedure I, II and III after purification through column chromatography (Et<sub>2</sub>O/PE/Et<sub>3</sub>N: 2/8/0.025) in 81%, 57% and 58% yield, respectively and spectral data are in accordance with literature<sup>1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 5.23-5.20 (m, 1H), 2.29-2.26 (m, 6H), 2.09-1.98 (m, 2H), 1.67 (s, 1H), 1.57 (s, 3H), 1.56-1.51 (m, 6H), 1.45-1.38 (m, 1H), 1.34-1.20 (m, 4H), 0.92 (d, 3H, J= 6.6 Hz); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 131.0, 124.8, 57.6, 54.7, 37.2, 33.8, 31.3, 25.9, 25.6, 25.4, 24.5, 19.7, 17.6, HRMS calculated for C<sub>15</sub>H<sub>30</sub>N<sup>+</sup>: [M+H]<sup>+</sup> 224.23783, found [M+H]<sup>+</sup> 224.2380.

2-(3, 7-dimethylene-6-en-1-yl)-1, 2, 3, 4-tetrahydroisoquinoline (3b)

Compound 3b was prepared according to general procedure \textbf{I} after purification through column chromatography (Et$_2$O/PE/Et$_3$N: 2/8/0.025) in 65 \% yield and spectral data are in accordance with literature$^2$. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.04-7.00 (m, 3H), 6.94-6.92 (m, 1H), 5.03 (t, 1H, $J$= 7.0 Hz), 3.54 (s, 2H), 2.83 (t, 2H, $J$= 5.8 Hz), 2.66-2.63 (m, 2H), 2.46-2.41 (m, 2H), 1.96-1.88 (m, 2H), 1.61 (s, 3H), 1.53 (s, 3H), 1.46-1.42 (m, 1H), 1.34-1.25 (m, 2H), 1.17-1.08 (m, 2H), 0.85 (d, 3H, $J$= 6.5 Hz); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 134.8, 134.3, 131.1, 128.6, 126.5, 126.0, 125.5, 124.8, 56.5, 56.3, 51.0, 37.2, 34.2, 31.1, 29.1, 25.7, 25.5, 19.7, 17.6, HRMS calculated for C$_{19}$H$_{30}$N$: [M+H]$^+$ 272.23783, found [M+H]$^+$ 272.2376.

1-(3, 7-dimethylene-6-en-1-yl)azepane (3c)

Compound 3c was prepared according to general procedure \textbf{I}, \textbf{II} and \textbf{III} after purification through column chromatography (Et$_2$O/PE/Et$_3$N: 2/8/0.025) in 68\%, 61\%, 63\% yield, respectively. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 5.11 (t, 1H, $J$= 7.0Hz), 2.63 (t, 4H, $J$= 5.6Hz), 2.54-2.42 (m, 2H), 2.04-1.95 (m, 2H), 1.69 (s, 3H), 1.65-1.61 (m, 4H), 1.61-1.60 (m, 6H), 1.53-1.45 (m, 2H), 1.37-1.29 (m, 2H), 1.26, 1.13 (m, 2H), 0.90 (d, 3H, $J$= 6.5 Hz); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 130.1, 124.9, 56.4, 55.6, 37.2, 34.4, 31.1, 27.9, 27.0, 25.7, 25.5, 19.7, 17.6; GC-MS m/z (%): 237 (M$^+$, 3\%), 152 (16\%), 112 (81\%); HRMS calculated for C$_{16}$H$_{32}$N$: [M+H]$^+$ 238.25348, found [M+H]$^+$ 238.2537.

4-(3,7-dimethyloct-6-en-1-yl)morpholine (3d)

Compound 3d was prepared according to general procedure I after purification through column chromatography (Et₂O/PE/Et₃N: 2/80.025) in 79% yield. ¹H NMR (400 MHz, CDCl₃): δ 5.02 (t, 1H, J = 7.0 Hz), 3.64 (t, 4H, J = 4.5 Hz), 2.40-2.36 (m, 4H), 2.29-2.22 (m, 2H), 1.94-1.86 (m, 2H), 1.61 (s, 3H), 1.53 (s, 3H), 1.47-1.34 (m, 2H), 1.30-1.19 (m, 2H), 1.14-1.05 (m, 1H), 0.82 (d, 3H, J = 6.4 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 131.1, 124.7, 67.0, 57.2, 53.9, 37.2, 33.5, 31.0, 25.7, 25.4, 19.6, 17.6. HRMS calculated for C₁₄H₂₈NO⁺: [M+H]⁺ 226.21709 found [M+H]⁺ 226.2169

1-(3,7-dimethyloct-6-en-1-yl) pyrrolidine (3e)

Compound 3e was prepared according to general procedure I, III after purification through column chromatography (Et₂O/PE/Et₃N: 2/80.025) in 62, 54% yield. ¹H NMR (400 MHz, CDCl₃): δ 5.02 (t, 1H, J = 6.6 Hz), 2.42-2.32 (m, 6H), 1.94-1.84 (m, 2H), 1.71-1.70 (m, 4H), 1.61 (s, 3H), 1.53 (s, 3H), 1.50-1.35 (m, 2H), 1.30-1.21(m, 2H), 1.14-1.05 (m, 1H), 0.82 (d, 3H, J = 6.4 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 131.0, 124.8, 37.2, 36.0, 31.1, 25.6, 25.4, 23.3, 19.7, 17.6, 54.6, 54.2, HRMS calculated for C₁₄H₂₈N⁺: [M+H]⁺ 210.22218, found [M+H]⁺ 210.2220
1-((2,6,6-trimethylcyclohexa-1,3-dien-1-yl)methyl) piperidine (3f)

![Image of compound 3f]

Compound 3f was prepared according to general procedure I after purification through column chromatography (Et₂O/PE/Et₃N: 2/8/0.025) in 73% yield. ¹H NMR (400 MHz, CD₂Cl₂): δ 5.69-5.67 (m, 1H), 5.64-5.59 (m, 1H), 2.86 (s, 2H), 2.30-2.23 (m, 4H), 1.89 (d, 2H, J=5.27Hz), 1.66 (s, 3H), 1.44-1.38 (m, 4H), 1.32-1.31 (m, 2H), 0.96 (s,6H); ¹³C NMR (75 MHz, CD₂Cl₂): δ 135.9, 130.1, 128.0, 125.5, 57.0, 54.5, 40.9, 33.9, 26.7, 26.3, 25.1, 18.5, HRMS calculated for C₁₅H₂₆N⁺: [M+H]⁺ 220.20653, found [M+H]⁺ 220.2066

1-(((1R)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)methyl) piperidine (3g)

![Image of compound 3g]

Compound 3g was prepared according to general procedure I after purification through column chromatography (Et₂O/PE/Et₃N: 2/8/0.025) in 86% yield. ¹H NMR (400 MHz, CDCl₃): δ 5.29-5.26 (m, 1H), 2.77 (d, 1H, J= 13.4 Hz), 2.65 (d, 1H, J= 13.3 Hz), 2.31-2.11 (m, 8H), 2.04-2.00 (m, 1H), 1.51-1.45 (m, 4H), 1.36-1.32(m, 2H), 1.20 (s, 3H), 1.05 (d, 1H, J= 8.5 Hz), 0.75 (s, 3H) ; ¹³C NMR (100 MHz, CDCl₃): δ 145.7, 119.3, 65.2, 54.8, 44.5, 40.9, 37.9, 31.7, 31.3, 26.2, 25.9, 24.5, 21.0; HRMS calculated for C₁₅H₂₈N⁺: [M+H]⁺220.20653, found [M+H]⁺ 220.2064. [α]D²⁰ = - 4.5 (c 1, CH₂Cl₂)
(S)-1-((4-(prop-1-en-2-yl)cyclohex-1-en-1-yl)methyl)piperidine (3h)

Compound 3h was prepared according to general procedure I after purification through column chromatography (Et₂O/PE/Et₃N: 2/8/0.025) in 62% yield. ¹H NMR (400 MHz, CDCl₃): δ 5.00-5.47 (m, 1H), 4.63 (s, 2H), 2.70-2.66 (m, 2H), 2.29-2.19 (m, 4H), 2.06-1.96 (m, 4H), 1.90-1.85 (m, 1H), 1.76-1.71 (m, 1H), 1.66 (s, 3H), 1.51-1.45 (m, 5H), 1.38-1.32 (m, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 150.1, 135.1, 123.5, 108.4, 66.3, 54.6, 41.3, 30.7, 27.8, 27.8, 27.8, 26.0, 24.5, 20.7. HRMS calculated for C₁₅H₂₆N⁺: [M+H]^+ 220.20653, found [M+H]^+ 220.2067.

αD 20 = -6.0 (c 1, CH₂Cl₂)

1,4-bis(((1R)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)methyl)piperazine (3i)

Compound 3i was prepared according to general procedure IV after purification through column chromatography (Et₂O/PE: 2/8) in 49% yield. ¹H NMR (400 MHz, CDCl₃): δ 5.28 (m, 2H), 2.82 (d, 2H, J = 12.7Hz), 2.68 (d, 2H, J = 13.3 Hz), 2.32-2.27 (m, 6H), 2.18-2.10 (m, 6H), 2.01-1.99 (m, 2H), 1.50 (s, 12H), 1.20 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 145.4, 119.7, 77.2, 64.5, 53.4, 44.4, 40.9, 37.9, 31.7, 31.3, 26.2, 21.0; HRMS calculated for C₂₄H₃₉N₂⁺: [M+H]^+ 355.31132, found [M+H]^+ 355.3111. [α]D⁰ = -0.5 (c 1, CH₂Cl₂)
1, 4-bis (3, 7-dimethyloct-6-en-1-yl) piperazine (3j)

Compounds 3j were prepared according to general procedure IV after purification through column chromatography (Et₂O/PE/Et₃N: 2/8/0.025) in 57% yield as a diastereoisomeric mixture. ¹H NMR (400 MHz, CDCl₃): δ 5.01 (t, 2H, J= 7.0Hz), 2.52-2.20 (m, 12H), 1.93-1.83 (m, 4H), 1.61 (s, 6H), 1.52 (s, 6H), 1.48-1.41 (m, 2H), 1.39-1.32 (m, 2H), 1.29-1.20 (m, 4H), 1.13-1.04 (m, 2H), 0.82, 1.13(d, 6H, J=6.52Hz), ¹³C NMR (100 MHz, CDCl₃): δ 131.1, 124.8, 56.8, 53.4, 37.2, 33.8, 31.2, 25.7, 25.4, 19.7, 17.6, HRMS calculated for C₂₄H₄₇N₂⁺: [M+H]⁺ 363.37392, found [M+H]⁺ 363.3741

1-(3, 7, 11, 15-tetramethylhexadecyl) piperidine (3k)

Compounds 3k were prepared according to general procedure II after purification through column chromatography (Et₂O/PE:0.5/9.5) in 52% yield as mixture of stereoisomers. ¹H NMR (500 MHz, CDCl₃): δ 2.43-2.23 (m, 6H), 1.62-1.56 (m, 4H), 1.45-1.37 (m, 5H), 1.32-1.21 (m, 12H), 1.17-1.09 (m, 9H), 0.88 (d, 9H, J=6.6Hz), 0.86 (d, 6H, J= 7.2Hz); ¹³C NMR (125 MHz, CDCl₃): δ 57.9, 57.7, 54.7, 54.6, 54.5, 39.3, 37.5, 37.5, 37.4, 37.3, 37.3, 37.2, 34.1, 34.0, 32.7, 32.7, 31.7, 31.6, 27.9, 26.0, 24.7, 24.5, 24.4, 24.3, 22.7, 22.6, 19.9, 19.8, 19.7, 19.7, 19.6. HRMS calculated for C₂₅H₅₂N⁺: [M⁺H]⁺ 366.40998, found [M⁺H]⁺ 366.40997.
1, 3-bis(3,7-dimethyloct-6-en-1-yl)piperidine (4a)

Compounds 4a were prepared according to general procedure V after purification through column chromatography (Et₂O/PE/Et₃N: 1/9/0.025) in 80 % yield as a mixture of stereoisomers. ¹H NMR (400 MHz, CDCl₃):  δ 5.02 (t, 2H, J = 6.5 Hz), 2.85-2.80 (m, 2H), 2.26-2.20 (m, 2H), 1.98-1.82 (m, 4H), 1.69-1.66(m, 1H), 1.61 (s, 6H), 1.53 (s, 6H), 1.52-1.44 (m, 4H), 1.34-1.18 (m, 8H), 1.13-1.00 (m, 6H), 0.81 (d, 3H, J = 6.5 Hz), 0.78 (d, 3H, J = 6.3 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 131.0, 130.9, 125.0, 124.8, 61.0, 60.9, 60.7, 57.5, 54.6, 54.4, 37.2, 37.0, 37.0, 36.4, 36.4, 34.0, 33.9, 33.8, 32.6, 32.5, 32.1, 32.0, 31.3, 31.3, 31.1, 25.7, 25.5, 25.5, 19.7, 19.5, 19.5, 17.6; HRMS calculated for C₂₅H₄₈N⁺: [M+H]⁺ 362.37868, found [M+H]⁺ 362.3784.

2,4-bis (3,7-dimethyloct-6-en-1-yl)-1,2,3,4-tetrahydroisoquinoline (4b)

Compounds 4b were prepared according to general procedure V after purification through column chromatography (Et₂O/PE: 1/9) in 68 % yield as a mixture of stereoisomers. ¹H NMR (400 MHz, CDCl₃):  δ 7.12-6.90 (m, 4H), 5.02-5.00 (m, 2H ), 3.60-3.39 ( m, 2H), 2.74-2.69 (m, 1H), 2.57-2.36 (m, 4H), 1.94-1.89 (m,4H), 1.61(s, 6H), 1.53 (s, 6H),1.46-1.26 (m, 8H), 1.18-1.06 (m, 5H), 0.85-0.81(m, 6H); ¹³C NMR (75 MHz, CDCl₃):  δ 134.8, 134.3, 132.3, 131.1, 128.6, 126.6, 126.1, 125.5, 124.8, 56.5, 56.3, 51.0, 37.2, 34.2, 31.1, 29.1, 25.7, 25.5, 19.7, 17.6. HRMS calculated for C₂₀H₄₉N⁺: [M+H]⁺ 410.37868, found [M+H]⁺ 410.3784.
1,3-bis(3,7-dimethyloct-6-en-1-yl) pyrrolidine (4c)

Compounds 4a were prepared according to general procedure V after purification through column chromatography (Et₂O/PE/Et₃N: 1/9/0.025) in 62 % yield as a mixture of stereoisomers. ¹H NMR (400 MHz, CDCl₃): δ 5.08-5.02 (m, 2H), 2.74-2.55 (m, 2H), 2.41-2.24 (m, 4H), 1.96-1.86 (m, 6H), 1.60 (s, 6H), 1.52 (s, 6H), 1.39-1.36 (m, 1H), 1.29-1.18 (m, 8H), 1.11-0.98(m, 4H), 0.81-0.79(m,6H); ¹³C NMR (75 MHz, CDCl₃): δ 130.0, 129.9, 123.9, 123.9, 59.2, 75.1, 65.8, 56.1, 52.5, 52.3, 36.2, 36.0, 32.5, 31.4, 30.3, 30.1, 28.7, 24.7, 24.5, 18.7, 18.6, 18.5, 16.6.

2, 4-bis (3,7-dimethyloct-6-en-1-yl)morpholine (4d)

Compounds 4d were prepared according to general procedure V after purification through column chromatography (Et₂O/PE/Et₃N: 1/9/0.025) in 69% yield as a mixture of stereoisomers. ¹H NMR (400 MHz, CDCl₃): δ 5.03-5.00 (m, 2H), 3.78 (d, 1H, J= 11.0 Hz), 3.58 (t, 1H, J= 11.2 Hz), 3.40-3.34 (m, 1H), 2.71-2.62 (m, 2H), 2.26-2.23( m, 2H), 1.99-1.82 (m, 6H), 1.61 (s, 6H), 1.53 (s, 6H), 1.30-1.24 (m,7H), 1.11-1.02 (m, 5H), 0.88-0.80 (m, 6H); ¹³C NMR (75 MHz, CDCl₃): δ 130.1, 130.0, 123.9, 123.7, 75.2, 75.1, 65.8, 56.1, 52.5, 52.3, 36.2, 36.0, 32.5, 31.4, 30.3, 30.1, 28.7, 24.7, 24.5, 18.7, 18.4, 16.6. HRMS calculated for C₂₄H₄₆NO⁺: [M⁺H]⁺ 364.35794, found [M⁺H]⁺ 364.3585.
3-(3,7-dimethyloct-6-en-1-yl)-1-((2, 6, 6-trimethylcyclohexa-2,4-dien-1-yl) methyl) piperidine (4e)

See manuscript

1-(((1R, 5S)-6, 6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)methyl)-3-(3, 7-dimethyloct-6-en-1-yl)piperidine (4f)

Compounds 4f were prepared according to general procedure V after purification through column chromatography (Et₂O/PE/Et₃N: 1/9/0.025) in 56% yield as a stereoisomeric mixture. ¹H NMR (400 MHz, CDCl₃): δ 5.30-5.25 (m, 1H), 5.02 (t, 1H, J = 7.0 Hz), 2.80-2.62 (m, 4H), 2.31-2.02 (m, 6H), 1.94-1.64 (m, 9H), 1.61 (s, 3H), 1.53 (s, 3H), 1.20 (s, 6H), 1.07-1.05 (m, 4H), 0.76 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): δ. 144.8, 129.9, 124.0, 118.3, 64.0, 64.0, 59.6, 53.9, 53.4, 43.4, 43.4, 39.9, 36.9, 36.0, 35.4, 33.0, 31.6, 31.5, 30.7, 30.3, 25.2, 24.7, 24.5, 20.0, 18.5, 18.5, 16.6. HRMS calculated for C₂₅H₄₄N⁺: [M+H]⁺ 358.34738, found [M+H]⁺ 385.3471
3-(3, 7-dimethyloct-6-en-1-yl)-1-(((S)-4-(prop-1-en-2-yl) cyclohex-1-en-1-yl)methyl)piperidine (4g)

Compounds 4g were prepared according to general procedure V after purification through column chromatography (Et$_2$O/PE/Et$_3$N: 1/9/0.025) in 60%, yield as a mixture of stereoisomers. $^1$H NMR (400 MHz, CDCl$_3$): δ 5.52-5.49 (m, 1H), 5.02 (t, 1H, J=6.7Hz ), 4.63 (s, 2H), 2.77-2.63 (m, 4H), 2.09-1.99 (m, 4H), 1.91-1.84( m, 4H), 1.76-1.72(m, 2H), 1.66 (s, 3H), 1.61 (s, 3H), 1.52 (s, 3H), 1.48-1.45 (m, 1H), 1.42-1.36(m, 4H), 1.28-1.18 (m, 4H), 1.11-1.03 (m, 4H), 0.78 (d, 3H, J= 6.2Hz); $^{13}$C NMR (75 MHz, CDCl$_3$): 150.1, 150.0, 135.1, 130.9, 125.0, 123.6, 123.5, 108.4, 66.3, 66.2, 66.0, 54.6, 54.4, 54.3, 41.3, 41.3, 41.2, 37.2, 37.0, 37.0, 36.3, 34.0, 33.8, 32.6, 32.5, 31.5, 31.3, 31.1, 30.7, 27.8, 27.7, 25.9, 25.7, 25.5, 25.4, 20.9, 20.8, 20.7, 19.6, 19.5, 17.6. HRMS calculated for C$_{25}$H$_{44}$N$^+$: [M+H]$^+$ 358.34738 , found [M+H]$^+$ 358.3471.

3-(((1R, 5S)-6, 6-dimethylbicyclo[3.1.1]hept-2-en-2-yl) methyl)-1-(((1S, 5R)-6, 6-dimethylbicyclo[3.1.1]hept-2-en-3-yl) methyl) piperidine (4h)

Compounds 4h were prepared according to general procedure V after purification through column chromatography (Et$_2$O/PE/Et$_3$N: 2/8/0.025) in 57% yield with a 62% diastereoisomeric excess. $^1$H NMR (400 MHz, CDCl$_3$): δ 5.28-5.26 (m, 1H), 5.10-5.05 (m, 1H), 2.81-2.61(m, 4H ), 2.29-2.25 (m, 3H), 2.20-2.19 (m, 6H), 2.08-2.00 (m, 3H), 1.76-1.70(m, 3H), 1.20-1.18 (m, 6H), 1.12-1.10(m, 2H), 1.07-1.05 (m, 2H), 0.80-0.72 (m, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): 146.5, 145.4, 119.5, 117.2, 117.2, 65.0, 61.0, 60.6, 54.8, 54.2, 46.0,
45.9, 44.6, 44.5, 42.6, 42.5, 40.9, 40.8, 37.9, 37.9, 33.8, 33.5, 31.8, 31.3, 26.3, 26.2, 25.2, 21.1, 21.0; GC-MS m/z (%): 353 (M⁺, 3.7%), 284 (7.5%), 230 (20%), 217 (30%), 85 (38%).

3-(((R)-4-(prop-1-en-2-yl) cyclohex-1-en-1-yl) methyl)-1-(((S)-4-(prop-1-en-2-yl) cyclohex-1-en-1-yl)methyl)piperidine (4i)

Compounds 4i were prepared according to general procedure V after purification through column chromatography (Et₂O/PE/Et₃N: 1/9/0.025) in 71% yield with a 5% diastereoisomeric excess. 

H NMR (400 MHz, CDCl₃): δ 5.52-5.46 (m, 1H), 5.34-5.30 (m, 1H), 4.63 (s, 4H), 2.76-2.62 (m, 4H), 2.10-2.00 (m, 6H), 1.80-1.72 (m, 4H), 1.66 (s, 6H), 1.42-1.36 (m, 4H), 1.21-1.15 (m, 2H), 0.86-0.72 (m, 2H); C NMR (75 MHz, CDCl₃): 149.1, 149.1, 134.5, 120.8, 107.3, 107.4, 65.0, 134.0, 122.6, 59.5, 53.3, 41.9, 40.3, 40.2, 32.8, 29.8, 29.7, 27.7, 26.9, 26.8, 24.3, 19.7. HRMS calculated for C₂₅H₄₀N⁺: [M+H]⁺ 354.31608, found [M+H]⁺ 354.3164

2-(3, 7-dimethyloct-6-en-1-yl)-4-((4-(prop-1-en-2-yl) cyclohex-1-en-1-yl) methyl)-1, 2, 3, 4-tetrahydroisoquinoline (4j)

Compounds 4j were prepared according to general procedure V after purification through column chromatography (Et₂O/PE: 1/9) in 67% yield as a mixture of stereoisomers. H NMR (400 MHz, CDCl₃): δ 7.10-7.04 (m, 3H), 6.94-6.92 (m, 1H), 5.42-5.40 (m, 1H), 5.05-5.02 (m, 1H), 4.66 (s, 2H), 3.62-3.60 (m, 1H), 3.38-3.34 (m, 1H), 2.87-2.84 (m, 1H), 2.60-2.54 (m,
1H), 2.43-2.26 (m, 5H), 2.20-2.05 (m, 3H), 1.94-1.87 (m, 4H), 1.68 (s, 3H), 1.60 (s, 3H), 1.53 (s, 3H), 1.35-1.10 (m, 7H), 0.85-0.83 (m, 3H); 13C NMR (75 MHz, CDCl3): δ 149.0, 148.9, 138.1, 134.7, 134.5, 134.1, 130.1, 127.1, 125.3, 125.0, 124.4, 123.8, 122.0, 107.5, 56.1, 55.5, 53.6, 53.1, 43.8, 43.0, 40.3, 40.0, 36.2, 35.3, 35.0, 33.2, 29.9, 29.8, 27.8, 27.2, 26.8, 24.7, 24.5, 19.9, 19.8, 18.7, 16.6; HRMS calculated for C29H44N+: [M+H]+ 406.34738, found [M+H]+ 406.3476

1, 3, 5-tris (3,7-dimethyloct-6-en-1-yl)piperidine (5a)

Compounds 5a were prepared according to general procedure VI after purification through column chromatography (Et2O/PE: 1/9) in 53% yield as a mixture of stereoisomers. 1H NMR (400 MHz, CDCl3): δ 5.02 (t, 3H, J=6.77Hz), 2.84-2.82 (m, 2H), 2.26-1.20 (m, 2H), 1.90-1.80 (m, 6H), 1.61 (s, 9H), 1.53 (s, 9H), 1.46-1.42 (m, 4H), 1.30-1.21 (m, 12H), 1.10-1.03 (m, 9H), 0.80-0.77 (m, 9H); 13C NMR (100 MHz, CDCl3): δ. 130.0, 129.9, 124.0, 123.8, 123.9, 60.0, 60.1, 59.8, 59.7, 56.3, 37.5, 36.2, 36.0, 36.0, 35.3, 33.0, 33.0, 32.9, 31.6, 31.6, 31.2, 31.1, 30.4, 24.7, 24.5, 24.4, 18.7, 18.5, 18.5, 16.6; GC-MS m/z (%): 499 (M+, 8%), 430 (10%), 414 (37%), 374 (37%).