Supporting Information

**Oxa-, Thia-, Heterocycle and Carborane Analogs of SQ109: Bacterial and Protozoal Cell Growth Inhibitors**

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Figure S1. Dose-response curves for the top five *T. brucei* cell growth inhibitors and their corresponding effects on HEK293T and HepG2 cell growth.
Figure S2. A. Plot of selectivity index (HEK293T CC\textsubscript{50}/T. brucei IC\textsubscript{50}) versus log(T. brucei IC\textsubscript{50}, μg/mL). B. Plot of selectivity index (HepG2 CC\textsubscript{50}/T. brucei IC\textsubscript{50}) versus log(T. brucei IC\textsubscript{50}, μg/mL).
Figure S3. Effects of SQ109 (2) or 27 on the mitochondrial membrane potential of digitonin-permeabilized T. brucei procyclic forms. PCF trypanosomes (5 x 10⁷ cells) were added to reaction buffer (2.4 mL) containing 2 mM succinate and 5 µM safranine, and the reaction initiated by addition of 50 µM digitonin. (A, C) CaCl₂ (12 µM), EGTA (200 µM), various concentrations of SQ109 (A) or 27 (C), and 8 µM FCCP were added where indicated. (B, D) Changes in safranine fluorescence after addition of SQ109 (1-30 µM, 0.33-10 µg/mL), 27 (1-20 µM, 0.45-9.0 µg/mL) or FCCP (8 µM), as shown in (A, C), respectively. The results are means ± SD of three independent experiments.
METHODS

Cell growth inhibition assays: Cell Lines. *Mycobacterium tuberculosis* H37Rv, *Mycobacterium tuberculosis* Erdman, *Mycobacterium smegmatis* ATCC 700084, *Bacillus subtilis* subsp. *subtilis* ATCC 6051, *E. coli* ATCC 29425, and *Saccharomyces cerevisiae* ATCC 208352 were purchased from the American Type Culture Collection. *Trypanosoma brucei brucei* strain 427 (bloodstream form) was cultivated at 37 °C with a 5% CO₂ atmosphere in HMI-9 medium supplemented with 10% fetal bovine serum (FBS). *T. brucei* was subcultured every 3 or 4 d and maintained until the twentieth passage. The HEK293T, human embryonic kidney, and HepG2, the hepatocellular carcinoma cell line used in the cytotoxicity test was cultivated at 37 °C with a 5% CO₂ atmosphere in Dulbecco's modified Eagle's medium supplemented with 10% FBS.

*M. tuberculosis* H37Rv Growth Inhibition Assay. The compounds were assayed for inhibition of *M. tuberculosis* H37Rv cell growth as described previously¹.

*M. tuberculosis* Erdman Growth Inhibition Assay. The compounds were assayed for inhibition of *M. tuberculosis* Erdman cell growth as described previously².

*E. coli* ATCC 29425 Growth Inhibition Assay. IC₅₀ values for *E. coli* growth inhibition were determined by using a broth microdilution method. An overnight culture of *E. coli* was diluted 50-fold into fresh Luria–Bertani (LB) broth and incubated to an OD₆₀₀ of ~0.4. The culture was then diluted 500-fold into fresh LB medium and 100 μL inoculated into each well of a 96-well flat-bottom culture plate (Corning Inc., Corning, NY). The starting concentration of each compound was 200 μg/mL, and this was 2×serially diluted to 0.19 μg/mL. Plates were incubated for 3 h at 37 °C to midexponential phase. An MTT ((3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) cell proliferation assay (ATCC) was then carried out to obtain bacterial viability dose–response curves. Briefly, 10 μL of MTT reagent was added into each
well, followed by incubation for 2–4 h until a purple precipitate was visible. Then, 100 μL of detergent reagent was added, and the plates were incubated in the dark at 22 °C for 2 h. Absorbance was measured at 570 nm and a nonlinear regression analysis carried out using Origin 6.1 software. The average error was 11%.

**B. subtilis ATCC® 6051TM growth inhibition assay.** A 16 h culture of *B. subtilis* was diluted 50-fold into fresh Luria-Bertani (LB) broth and incubated to an OD$_{600}$ of ~ 0.4. The culture was then diluted 500-fold into fresh LB medium and 100 μL were inoculated into a 96 well flat bottom culture plate (Corning Inc., Corning, NY). The starting concentration of each compound was 0.5 μg/mL and was then serial diluted. Plates were incubated for 12-16 h at 37 °C. The absorbance was recorded at 570 nm. A non-linear regression analysis was carried out on the data obtained using Origin 6.1. The average error was 9%.

**S. cerevisiae growth inhibition assay.** The protocol was the same as with the *B. subtilis* assay protocol except that YPD medium was used and the 96-well plate was incubated for 36 h instead of 12-16 h. A non-linear regression analysis was carried out on the data obtained using Origin 6.1. The average error was 14%.

**M. smegmatis ATCC 700084 growth inhibition assay.** The protocol was the same as with the *B. subtilis* assay protocol except that 7H9/ADC (9:1) medium was used. A non-linear regression analysis was carried out on the data obtained using Origin 6.1. The average error was 9%.

**Analysis of mitochondrial membrane potential.** We monitored the mitochondrial membrane potential spectrofluorometrically using safranine as the probe$^{3,4}$. The reaction buffer contained 125 mM sucrose, 65 mM KCl, 10 mM Na-Hepes-KOH buffer, pH 7.2, 1 mM MgCl$_2$, 2.5 mM potassiumphosphate, and 5 μM safranine. *T. brucei* BSF (2 x 10$^8$ cells) were added to the
reaction buffer (2.0) containing 1 mM ATP, 200 µM EGTA and 500 µM sodium orthovanadate, and the reaction was started by addition of 40 µM digitonin. PCF (5 x 10^7 cells) were added to the reaction buffer (2.4 ml) containing 2 mM succinate and the reaction started by addition of 50 µM digitonin. Incubations were at 28 °C (PCF) or 37º C (BSF). Drugs, ADP (10 µM), oligomycin (Oligo, 2 µg/ml), CaCl_2 (12 µM), EGTA (200 µM), and FCCP (8 µM) where added where indicated. Fluorescence changes were monitored using a Hitachi 4500 spectrofluorometer (excitation wavelength = 496 nm; emission wavelength = 586 nm).

**Mammalian cell cytotoxicity assay.** For evaluation of mammalian cell cytotoxicity, HEK293T and HepG2 cells were cultured at 37 °C with 5% CO_2 in Dulbecco’s modified eagle medium containing 10% FBS. HEK293T and HepG2 cells were diluted to 8 X 10^4/mL and 4 X 10^4/mL, respectively, and were seeded in 384 well plates. The compounds at 2-fold dilution in 10-points concentration were tested and incubated for 72 h. To determine viability, 10 µL of a 280 µM solution of resazurin sodium salt (final concentration, 40 µM of resazurin) was added to each well for 5 h. To assess cell viability, resazurin reduction was measured with a Victor 3™ fluorimeter at an excitation wavelength of 530 nm and emission of 590 nm. Chloropromazine was used as a reference drug and DMSO 1% was used as a drug-negative control.

**Synthesis and Characterization of Compounds**

\[
\begin{align*}
N-(2-(((1r,3r,5r,7r)-Adamantan-2-yl)oxy)ethyl)-3-methylbut-2-en-1-amine hydrochloride (3)
\end{align*}
\]
To a suspension of NaH (washed with and dried from hexane, 368 mg, 16 mmol) in THF (30 mL) was added 2-adamantanol (1.5 g, 10 mmol) at 0 °C. Stirring was continued for 30 min at 25 °C, then allyl bromide (1.8 g, 15 mmol) was added. Stirring was continued for 3h at 25 °C, then the reaction was quenched by adding saturated aqueous NH₄Cl. Upon separation and concentration under reduced pressure using a rotary evaporator, the residue was purified by silica gel column chromatography using 5% EtOAc in hexane as eluent to afford the allyl ether (1.4 g, 75%). To a suspension of the allyl ether (1.4 g, 7.5 mmol) in MeCN/H₂O/ethyl acetate (1/2/1, 35 mL) was added NaIO₄ (8.42 g, 40 mmol), then RuCl₃·H₂O (110 mg, 0.5 mmol). After stirring for 10 h at 25 °C, ethyl acetate (40 mL) was added. Separation and concentration of the organic phase under reduced pressure gave the crude acid (1.3 g, 84%). To a solution of crude acid (210 mg, 1 mmol), isopentenylamine (102 mg, 1.2 mmol), EDCI (228 mg, 1.2 mmol) and HOAT (164 mg, 1.2 mmol) in dry THF/DMF (2 mL/2 mL) was added N-methylmorpholine (505 mg, 5 mmol) at 0 °C with stirring. Stirring was continued for 2 h at 25 °C. The reaction mixture was distributed between saturated aqueous NH₄Cl and hexane. The hexane phase was dried over anhydrous Na₂SO₄ and solvents removed under reduced pressure to give a residue. Purification of the residue with flash chromatography (SiO₂, hexane/ethyl acetate = 10/1) gave the amide (226 mg, yield: 82%). To a solution of the amide (200 mg, 0.72 mmol) in dry ethyl ether (6 mL) was added LiAlH₄ (76 mg, 2 mmol) under N₂. Stirring was continued for 10 h at reflux, the reaction flask was then cooled in an ice-bath and the reaction quenched by adding aqueous ammonium hydroxide (37%, 0.2 mL). Vigorous stirring was continued for 20 min. Upon separation and concentration under reduced pressure, the residue was purified by using silica gel column chromatography (using NH₄OH (37%)/MeOH/EtOAc = 1/5/100 as eluent) to afford the product (134 mg, 71%). The HCl salt was obtained by neutralizing the amine with HCl in toluene in quantitative yield. The purity of the
product was determined by qNMR: 98.5%. $^1$H NMR (500 MHz, chloroform-$d_1$) δ 9.31 (s, 2H), 5.38 (m, 1H), 3.77 (t, $J = 5.3$ Hz, 2H), 3.68 (m, 2H), 3.45 (s, 1H), 3.07 (m, 2H), 1.96-1.40 (m, 20H). HRMS (ESI) m/z [M + H]$^+$ calculated for [C$_{17}$H$_{30}$NO]$^+$ 264.2327, found 264.2342.

$N$-$(2-(((1r,3r,5r,7r)$-Adamantan-2-yl)oxy)ethyl)$-3-methylbutan-1-amine hydrochloride (4)

To a solution of amine 3 (HCl salt, 60 mg, 0.2 mmol) in MeOH (4 mL) was added palladium on charcoal (5%, 15 mg) under N$_2$. Stirring was continued for 1 h at 22 $^\circ$C after switching the reaction atmosphere from N$_2$ to H$_2$ using a hydrogen balloon. The reaction mixture was passed through a Celite pad, then the filtrate was evaporated under reduced pressure to give the product as a white powder (55 mg, 90%). The purity of the product was determined by qNMR: 93.2%. $^1$H NMR (500 MHz, chloroform-$d_1$) δ 9.44 (s, 2H), 3.87 (t, $J = 5.2$ Hz, 2H), 3.51 (s, 1H), 3.22 (t, $J = 5.2$ Hz, 2H), 3.15 (dt, $J = 7.0$, 4.0 Hz, 2H), 2.15 – 1.33 (m, 17H), 0.94 (s, 3H), 0.93 (s, 3H). HRMS (ESI) m/z [M + H]$^+$ calculated for [C$_{17}$H$_{32}$NO]$^+$ 266.2484, found 266.2459.

$(2E,6E)-N$-$(2-(((1r,3r,5r,7r)$-Adamantan-2-yl)oxy)ethyl)$-3,7,11-trimethyldodeca-2,6,10-trien-1-amine (5)

5 was made by following the protocol used for 3. Purity of the product was determined by qNMR: 93.8%. $^1$H NMR (500 MHz, chloroform-$d_1$) δ 5.28 (m, 1H), 5.10 (m, 2H), 3.56 (t, $J = 5.2$ Hz, 2H), 3.43 (s, 1H), 3.28 (d, $J = 6.8$ Hz, 2H), 2.80 (t, $J = 5.2$ Hz, 2H), 2.11-1.45 (m, 22H), 1.65 (s, 3H), 1.65 (s, 3H), 1.0 (s, 6H). HRMS (ESI) m/z [M + H]$^+$ calculated for [C$_{27}$H$_{46}$NO]$^+$ 400.3579, found 400.3573.
N-(2-(((1r,3r,5r,7r)-Adamantan-2-yl)oxy)ethyl)-3,7,11-trimethyldodecan-1-amine hydrochloride (6)

6 was made by following the protocol used for 4. Purity of the product was determined by qNMR: 96.4%. \(^1\)H NMR (500 MHz, chloroform-\(d_1\)) \(\delta\) 9.40 (s, 2H), 3.87 (s, 2H), 3.51 (s, 2H), 3.30 – 3.05 (m, 4H), 2.05 – 0.97 (m, 31H), 0.91 (d, \(J = 6.6\) Hz, 3H), 0.87 (d, \(J = 6.6\) Hz, 6H), 0.84 (d, \(J = 6.6\) Hz, 3H). HRMS (ESI) m/z [M + H]^+ calculated for [C\(_{27}\)H\(_{52}\)NO]^+ 406.4049, found 406.4035.

(1r,3r,5r,7r)-2-(3-(((E)-3,7-Dimethylocta-2,6-dien-1-yl)amino)propyl)adamantan-2-ol (7)

To a solution of 2-adamantanone (300 mg, 2 mmol) in dry THF (7 mL) was added allylmagnesium chloride (2 M in THF, 1.1 mL) dropwise at 0 °C with stirring. Stirring was continued for 30 min at 0 °C and 30 min at 25 °C. The reaction mixture was diluted with ethyl acetate and quenched with saturated aqueous NH\(_4\)Cl. The organic phase was dried over anhydrous Na\(_2\)SO\(_4\) and evaporated under reduced pressure to give the crude olefin. To a solution of the crude olefin in dry THF (7 mL) was added 9-BBN (0.5 M in THF, 4.4 mL) dropwise. Stirring was continued for 30 min at 0 °C and 1 h at 25 °C. The reaction flask was then placed in
an ice-bath and NaOH (3N in H₂O, 3 mL) and H₂O₂ (30% in water, 0.68 mL) added, sequentially. Stirring was continued for 30 min at 0 °C and 1 h at 25 °C. The reaction mixture was then diluted with ethyl acetate and quenched with saturated aqueous Na₂S₂O₃ at 0 °C. The organic phase was dried over Na₂SO₄ and then evaporated under reduced pressure to give the crude diol.

To a solution of the crude diol in DCM (7 mL) was added Dess-Martin periodinane (848 mg) at 0 °C. Stirring was continued for 30 min at 0 °C and 1 h at 25 °C. The residue from the reduced-pressure evaporation was purified by using flash chromatography (SiO₂, hexane/ethyl acetate = 6/1) to give the hemiacetal (203 mg, 49%). To a solution of the hemiacetal (166 mg, 0.8 mmol) in dry DCM (5 mL) was added geranylamine (122 mg, 0.8 mmol) and sodium triacetoxyborohydride (424 mg, 2 mmol). Stirring was continued for 12 h at 25 °C. The reaction was quenched by adding saturated aqueous NaHCO₃ (5 mL). The organic phase was dried over anhydrous Na₂SO₄ and evaporated under reduced pressure to give a residue. Purification of the residue with flash chromatography (SiO₂, chloroform/methanol = 8/1) gave the product 7 (177 mg, 64%). Purity of the product was determined by qNMR: 93.3%. ¹H NMR (500 MHz, chloroform-d₆) 5.26 (t, J = 10.0 Hz, 1H), 5.08 (t, J = 10.0 Hz, 1H), 3.26 (d, J = 6.9 Hz, 2H), 2.69 (t, J = 6.1 Hz, 2H), 2.28 (dd, J = 11.8, 3.5 Hz, 2H), 2.09-1.51 (m, 23H), 2.64 (s, 3H), 1.60 (s, 3H).

HRMS (ESI) m/z [M + H]⁺ calculated for [C₂₃H₄₀NO]⁺ 346.3110, found 346.3113.

(E)-3,7-Dimethyl-N-2-(((1r,3r,5r,7r)-2-methyladamantan-2-yl)oxy)ethyl)-octa-2,6-dien-1-amine (8)
To a solution of 2-adamantanone (150 mg, 1 mmol) in dry THF (4 mL) was added methyl lithium (1.6 M in diethyl ether, 0.8 mL) dropwise at 0 °C, with stirring. Stirring was continued for 30 min at 0 °C and the reaction quenched by adding saturated aqueous NH₄Cl. The organic phase was separated, dried over anhydrous Na₂SO₄ and evaporated under reduced pressure to give the crude alcohol. To a solution of crude alcohol and allyl bromide (360 mg, 3 mmol) in dry DMF (3 mL) was added NaH (washed with and dried from hexane, 46 mg) at 0 °C with stirring. Stirring was continued for 1 h at 0 °C. The reaction mixture was distributed between saturated aqueous NH₄Cl and hexane. The hexane phase was separated and dried over anhydrous Na₂SO₄ then evaporated under reduced pressure to give the crude olefin. To a solution of crude olefin in ethyl acetate/MeCN and deionized water (5 mL/5 mL/5 mL) was added RuCl₃ hydrate (10 mg, 0.05 mmol) and NaIO₄ (428 mg, 2 mmol) at 0 °C. Vigorous stirring was continued for 20 min at 0 °C and for 4 h at 25 °C. The organic phase was dried over anhydrous Na₂SO₄ and evaporated under reduced pressure to give the crude acid. To a solution of the crude acid, geranylamine (153 mg, 1 mmol), EDCI (191 mg, 1 mmol) and HOAT (136 mg, 1 mmol) in dry THF/DMF (2 mL/2 mL) was added N-methylmorpholine (505 mg, 5 mmol) at 0 °C with stirring. Stirring was continued for 2 h at 25 °C. The reaction mixture was distributed between saturated aqueous NH₄Cl and hexane. The hexane phase was dried over anhydrous Na₂SO₄ and evaporated under reduced pressure to give a residue. Purification of the residue with flash chromatography (SiO₂, hexane/ethyl acetate = 10/1) gave the amide (147 mg, yield: 41%). To a solution of the amide (108 mg, 0.3 mmol) in dry diethyl ether (3 mL) was added LiAlH₄ (38 mg, 1 mmol) under N₂. Stirring was continued for 10 h at reflux, the reaction flask cooled in an ice-bath and the reaction quenched by adding aqueous ammonium hydroxide (37%, 0.2 mL). Vigorous stirring was continued for 20 min. Upon separation and concentration under reduced pressure, the residue
was purified by silica gel column chromatography (using NH₄OH (37%)/MeOH/EtOAc = 1/5/100 as eluent) to afford the product 8 (69 mg, 67%). Purity of the product was determined by qNMR: 98.9%. ¹H NMR (500 MHz, chloroform-δ) δ 5.27 (t, J = 5.9 Hz, 1H), 5.09 (t, J = 7.2 Hz, 1H), 3.45 (t, J = 5.3 Hz, 2H), 3.26 (d, J = 6.8 Hz, 2H), 2.77 (t, J = 5.3 Hz, 2H), 2.20 – 1.37 (m, 18H), 1.67 (s, 3H), 1.64 (s, 3H), 1.60 (s, 3H), 1.26 (s, 3H). HRMS (ESI) m/z [M + H]⁺ calculated for [C₂₃H₄₀NO]⁺ 346.3110, found 346.3098.

(E)-N-(2-(((1r,3r,5r,7r)-2-Isopropyl adamantanyl-2-yloxy)ethyl)-3,7-dimethylocta-2,6-dien-1-amine (9)

9 was made by following the protocol used for 8. Purity of the product was determined by qNMR: 98.2%. ¹H NMR (500 MHz, chloroform-δ) δ 5.28 ((t, J = 5.0 Hz, 1H), 5.10 (t, J = 5.0 Hz, 1H), 3.55 (t, J = 5.2 Hz, 2H), 3.43 (s, 1H), 3.26 (d, J = 6.7 Hz, 2H), 2.79 (t, J = 5.2 Hz, 2H), 2.19 – 1.35 (m, 25H), 1.68 (s, 3H), 1.64 (s, 3H), 1.60 (s, 3H). HRMS (ESI) m/z [M + H]⁺ calculated for [C₂₅H₄₄NO]⁺ 374.3423, found 374.3432.

(E)-N-(2-(((1r,3r,5r,7r)-2-Methoxy adamantan-2-yl)ethyl)-3,7-dimethylocta-2,6-dien-1-amine (10)

To a solution of 2-adamantanone (150 mg, 1 mmol) in dry THF (4 mL) was added allylmagnesium chloride (2.0 M in THF, 0.6 mL) dropwise at 0 °C with stirring. Stirring was
continued for 30 min at 0 °C and the reaction quenched by adding saturated aqueous NH₄Cl. The organic phase was separated, dried over anhydrous Na₂SO₄ and evaporated under reduced pressure to give the crude alcohol. To a solution of the crude alcohol and MeI (426 mg, 3 mmol) in dry DMF (3 mL) was added NaH (washed with and dried from hexane, 46 mg) at 0 °C with stirring. Stirring was continued for 1 h at 0 °C. The reaction mixture was distributed between saturated aqueous NH₄Cl and hexane. The hexane phase was dried over anhydrous Na₂SO₄ and evaporated under reduced pressure to give the crude olefin. To a solution of crude olefin in ethyl acetate/MeCN and deionized water (5 mL/5 mL/5 mL) was added RuCl₃ hydrate (10 mg, 0.05 mmol) and NaIO₄ (428 mg, 2 mmol) at 0 °C. Vigorous stirring was continued for 20 min at 0 °C and for 4 h at 25 °C. The organic phase was dried over anhydrous Na₂SO₄ and evaporated under reduced pressure to give the crude acid. To a solution of the crude acid, geranylamine (153 mg, 1 mmol), EDCI (191 mg, 1 mmol) and HOAT (136 mg, 1 mmol) in dry THF/DMF (2 mL/2 mL) was added N-methylmorpholine (505 mg, 5 mmol) at 0 °C with stirring. Stirring was continued for 2 h at 25 °C. The reaction mixture was distributed between saturated aqueous NH₄Cl and hexane. The hexane phase was dried over anhydrous Na₂SO₄ and evaporated under reduced pressure to give a residue. Purification of the residue with flash chromatography (SiO₂, hexane/ethyl acetate = 10/1) gave the amide (155 mg, yield: 41%). To a solution of the amide (108 mg, 0.3 mmol) in dry diethyl ether (3 mL) was added LiAlH₄ (38 mg, 1 mmol) under N₂. Stirring was continued for 10 h at reflux, the reaction flask cooled in an ice-bath and the reaction quenched by adding aqueous ammonium hydroxide (37%, 0.2 mL). Vigorous stirring was continued for 20 min. Upon separation and concentration under reduced pressure, the residue was purified by silica gel column chromatography (using NH₄OH (37%)/MeOH/EtOAc = 1/5/100 as eluent) to afford the product 10 (74 mg, 67%). Purity of the product was determined
by qNMR: 90.1%. $^1$H NMR (500 MHz, chloroform-$d_1$) δ 5.27 (t, $J = 5.3$ Hz, 1H), 5.10 (t, $J = 5.0$ Hz, 1H), 3.23 (d, $J = 6.8$ Hz, 2H), 3.16 (s, 3H), 2.63 (t, $J = 10.0$ Hz, 2H), 2.11-1.4 (m, 18H), 1.68 (s, 3H), 1.64 (s, 3H), 1.60 (s, 3H). HRMS (ESI) m/z [M + H]$^+$ calculated for [C$_{23}$H$_{40}$NO]$^+$ 346.3110, found 346.31094.

$(E)$-$N$-(3-(((1r,3r,5r,7r)-adamantan-2-yl)propyl)-3,7-dimethyl-cta-2,6-dien-1-amine (11)

11 was made following the protocol used for 10. The only modification was that hydroboration-oxidation of the olefin was carried out prior to sodium periodate oxidation. To a solution of the olefin (171 mg, 0.83 mmol) in dry THF (2 mL) was added 9-BBN (0.5 M in THF, 2 mL, 1 mmol) under N$_2$ at 0 °C. Stirring was continued for 2 h at 0 °C, then aqueous NaOH (3N, 1 mL) and H$_2$O$_2$ (30% in water, 0.18 mL, 1.66 mmol) was added, sequentially. Vigorous stirring was continued for 30 min at 0 °C and for 1 h at 25 °C, and then ethyl acetate (4 ml) and saturated aqueous Na$_2$S$_2$O$_3$ was added, with stirring. The organic phase was separated and evaporated under reduced pressure to give the crude alcohol. Purity of the product was determined by qNMR: 94.1%. $^1$H NMR (500 MHz, chloroform-$d_1$) δ 5.26 (t, $J = 5.0$ Hz, 1H), 5.10 (t, $J = 5.0$ Hz, 1H), 3.23 (d, $J = 6.8$ Hz, 2H), 3.12 (s, 3H), 2.61 (t, $J = 7.2$ Hz, 2H), 2.11-1.45 (m, 22H), 1.68 (s, 3H), 1.64 (s, 3H), 1.60 (s, 3H). HRMS (ESI) m/z [M + H]$^+$ calculated for [C$_{24}$H$_{42}$NO]$^+$ 360.3266, found 360.3253.

$N$-(2-(((1r,3r,5r,7r)-adamantan-2-yl)oxy)ethyl)-2,4-difluoroaniline (12)
12 was made by following the protocol used for 3. Purity of the product was determined by qNMR: 98.1%. ¹H NMR (500 MHz, chloroform- d$_1$) 7.76 (m, 1H), 6.93 (m, 2H), 3.7 (t, $J$ = 5.2 Hz, 2H), 3.55 (t, $J$ = 5.2 Hz, 2H), 3.40 (s, 1H) 1.92-1.41 (m, 14H). HRMS (ESI) m/z [M + H]$^+$ calculated for [C$_{18}$H$_{24}$F$_2$NO]$^+$ 308.1826, found 308.1850.

$N$-((1$r$,3$r$,5$r$,7$r$)-Adamantan-2-yl)oxy)ethyl)aniline (13)

13 was made by following the protocol used for 3. Purity of the product was determined by qNMR: 95.0%. ¹H NMR (500 MHz, chloroform- d$_1$) δ 7.62 (m, 2H), 7.39 (m, 3H), 3.71 (t, $J$ = 5.6 Hz, 2H), 3.50 (t, $J$ = 5.5 Hz, 2H), 3.36 (s, 1H), 1.96-1.39 (m, 14H). HRMS (ESI) m/z [M + H]$^+$ calculated for [C$_{18}$H$_{26}$NO]$^+$ 272.2014, found 272.2008.

$N$-((1$r$,3$r$,5$r$,7$r$)-Adamantan-2-yl)oxy)ethyl)-4-butoxyaniline (14).

14 was made by following the protocol used for 3. Purity of the product was determined by qNMR: 99.5%. ¹H NMR (500 MHz, chloroform- d$_1$) δ 6.78 (d, $J$ = 8.8 Hz, 2H), 6.62 (d, $J$ = 8.8 Hz, 2H), 3.89 (t, $J$ = 6.6 Hz, 2H), 3.64 (t, $J$ = 5.2 Hz, 2H), 3.44 (m, 1H), 3.24 (t, $J$ = 5.2 Hz, 2H), 2.07 – 1.37 (m, 18H), 0.96 (t, $J$ = 7.4 Hz, 3H). HRMS (ESI) m/z [M + H]$^+$ calculated for [C$_{22}$H$_{34}$NO]$^+$ 344.2590, found 344.2601.

$N$-((1$r$,3$r$,5$r$,7$r$)-Adamantan-2-yl)oxy)ethyl)-3-(benzyloxy)pyridin-2-amine (15).
15 was made by following the protocol used for 3. Purity of the product was determined by qNMR: 95.4%. $^1$H NMR (500 MHz, chloroform-$d_{1}$) $\delta$ 7.77 (dd, $J = 4.8, 1.6$ Hz, 1H), 7.41 – 7.33 (m, 2H), 7.24 (d, $J = 7.8$ Hz, 2H), 7.21 – 7.15 (m, 1H), 7.11 (dd, $J = 7.8, 1.7$ Hz, 1H), 6.81 (dd, $J = 7.8, 4.8$ Hz, 1H), 4.64 (s, 2H), 3.48 (dd, $J = 5.4, 4.1$ Hz, 2H), 3.44 (s, 1H), 3.37 (t, $J = 4.8$ Hz, 2H), 2.14 – 1.50 (m, 14H). HRMS (ESI) m/z [M + H]$^+$ calculated for [C$_{24}$H$_{31}$N$_2$O$_2$]$^+$ 379.2386, found 379.2389.

(E)-N-(2-(((1r,3r,5r,7r)-Adamantan-2-yl)thio)ethyl)-3,7-dimethylocta-2,6-dien-1-amine (16).

Thio-adamantanol was made according to a reported protocol$^5$. To a stirred solution of geranylamine (153 mg, 1.0 mmol) in CHCl$_3$ (3 mL), chloroacetyl chloride (167 mg, 1.5 mmol) was added drop-wise at 0 °C. Then water (2 mL) was added followed by K$_2$CO$_3$ (414 mg, 3.0 mmol). A catalytic amount of tetrabutylammonium hydrogen sulfate was added to the reaction mixture which was then stirred for 4 h. After completion of the reaction, as monitored by TLC, the organic layer was separated and dried over anhydrous Na$_2$SO$_4$ and filtered. The filtrate was concentrated under reduced pressure. The residual mass was purified by silica gel column chromatography using 25% EtOAc in hexane as eluent to afford the chloroacetamide (183 mg, 80%). To a solution of 2-(thio)adamantanol (84 mg, 0.5 mmol) in dry THF (3 mL) was added
NaH (washed with and dried from hexane, 23 mg, 1 mmol) at 0 °C with stirring. After stirring for 30 min at 22 °C, the chloroacetamide (115 mg, 0.5 mmol) was added. Stirring was continued for 12 h at 22 °C, then the reaction was quenched by adding saturated aqueous NH₄Cl. Upon separation and concentration under reduced pressure, the residue was purified by silica gel column chromatography using 25% EtOAc in hexane as eluent to afford the 2-(adamantanythio) acetamide (152 mg, 84%). To a suspension of LiAlH₄ (38 mg, 1 mmol) in dry THF (2 mL) was added 2-(adamanta-nylthio)acetamide (121 mg, 0.33 mmol) at 25 °C. Stirring was continued for 5 h at refluxing, the reaction mixture cooled in an ice-bath and quenched by adding aqueous ammonium hydroxide (37%, 0.3 mL). Vigorous stirring was continued for 20 min. Upon separation and concentration under reduced pressure, the residue was purified by silica gel column chromatography (using NH₄OH (37%)/MeOH/EtOAc = 1/5/100 as eluent) to afford the product 16 (89 mg, 78%). The HCl salt was obtained by neutralizing the amine with HCl in toluene with a quantitative yield. Purity of the product was determined by qNMR: 92.0%. ¹H NMR (500 MHz, chloroform-d₆): δ 9.60 (s, 2H), 5.41 (m, 1H), 5.04 (m, 1H), 3.65 (m, 2H), 3.02 (m, 5H), 2.26 – 1.36 (m, 27H). HRMS (ESI) m/z [M + H]⁺ calculated for [C₂₂H₃₈NS]⁺ 348.2725, found 348.2726.

N-(2-(((1r,3r,5r,7r)-Adamantan-2-yl)thio)ethyl)-3,7-dimethyloctan-1-amine (17).

To a solution of the unsaturated amine 16 (30 mg) in methanol (2 mL) was added palladium on charcoal (10%, 30 mg) under N₂. Stirring was continued for 1 h at 25 °C after switching the reaction atmosphere from N₂ to H₂ using a hydrogen balloon. Filtration and evaporation gave the product 17 (25 mg, 83%). Purity of the product was determined by qNMR: 97.9%. ¹H NMR (500
MHz, chloroform-\textit{d}_1): 3.04 (s, 1H), 2.80 (t, \textit{J} = 6.5 Hz, 2H), 2.69 (t, \textit{J} = 6.5 Hz, 2H), 2.62 (m, 2H), 2.16 (d, \textit{J} = 12.7 Hz, 2H), 2.13 (s, 1H), 1.96-1.10 (m, 24H), 0.88-0.86 (m, 9H). HRMS (ESI) m/z [M + H]^{+} calculated for [C_{22}H_{42}NS]^{+} 352.3038, found 352.3030.

**N-(2-(((1r,3r,5r,7r)-Adamantan-2-yl)sulfonyl)ethyl)-3,7-dimethyloctan-1-amine (18).**

![Chemical structure of 18](image)

To a solution of the thioether 17 (50 mg, 0.14 mmol) in HOAc (1 mL) was added H_{2}O_{2} (30\% in water, 79 mg) at 0 °C with stirring, then ethyl acetate (5 mL) and water (5 mL) was added. Stirring was continued for 12 h at 25 °C. Solid NaHCO_{3} was added in portion until no bubbling was observed. The ethyl acetate phase was separated, washed with saturated aqueous Na_{2}S_{2}O_{3}, dried over anhydrous Na_{2}SO_{4}, and then evaporated under reduced pressure to give a residue. Purification of the residue with flash chromatography (SiO_{2}, chloroform/MeOH = 6/1) gave the product 18 (30 mg, yield: 57\%). Purity of the product was determined by qNMR: 98.7\%. $^1$H NMR (500 MHz, chloroform-\textit{d}_1) δ 3.28 (s, 1H), 3.14 (s, 4H), 2.62 (m, 2H), 2.53 (d, \textit{J} = 3.8 Hz, 2H), 2.46 (dd, \textit{J} = 13.3, 3.2 Hz, 2H), 1.96 (dt, \textit{J} = 11.5, 3.1 Hz, 4H), 1.83 – 1.02 (m, 18H), 0.86 (m, 9H). HRMS (ESI) m/z [M + H]^{+} calculated for [C_{22}H_{42}NO_{2}S]^{+} 384.2936, found 384.2936.

**1-((2-(((1r,3r,5r,7r)-Adamantan-2-yl)oxy)ethyl)-4-hexyl-1H-1,2,3-triazole (19).**

![Chemical structure of 19](image)

A mixture of 2-adamantyl bromide (215 mg, 1 mmol), Ag_{2}SO_{4} (310 mg, 1 mmol) and ethylene...
glycol (1 ml) was heated for 1.5 h at 90 °C. The reaction mixture was then distributed between ethyl acetate and water. The ethyl acetate phase was separated and dried over anhydrous Na₂SO₄ then evaporated under reduced pressure to give a residue. Purification of the residue with flash chromatography (SiO₂, hexane/ethyl acetate = 6/1) gave the alcohol product (110 mg, yield: 56%). To a solution of the alcohol (98 mg, 0.5 mmol) in dry DCM (3 mL) was added Ph₃P (183 mg, 0.7 mmol) and CBr₄ (232 mg, 0.7 mmol) at 0 °C with stirring. Stirring was continued for 30 min at 0 °C and 2 h at 25 °C. The reaction mixture was then concentrated and purified by using flash chromatography (SiO₂, hexane/ethyl acetate = 20/1) to give the bromide product (117 mg, yield: 91%). A mixture of the bromide product (103 mg, 0.4 mmol), NaN₃ (65 mg, 1 mmol) and DMF (1.5 mL) was heated for 1 h at 80 °C. The reaction mixture was then distributed between hexane and water. The hexane phase was separated and dried over anhydrous Na₂SO₄, then evaporated under reduced pressure to give the azide (83 mg, yield 95%). A mixture of the azide (44 mg, 0.2 mmol), CuI (7 mg, 0.04 mmol), 1-octyne (22 mg, 0.2 mmol) and sodium ascorbate (98 mg, 0.5 mmol) in H₂O/DCM (1 mL/2 mL) was then stirred for 12 h at 25 °C. The organic phase was concentrated and purified by using flash chromatography (SiO₂, hexane/ethyl acetate = 8/1) to give the product 19 (48 mg, yield: 72%). The HCl salt was obtained by neutralizing the triazole with HCl in toluene with quantitative yield. Purity of the product was determined by qNMR: 99.5%. ¹H NMR (500 MHz, chloroform-d₁) δ 7.58 (s, 1H), 4.57 (t, J = 4.9 Hz, 2H), 3.80 ((t, J = 4.9 Hz, 3H), 3.41 (s, 1H), 2.80 (t, J = 7.7 Hz, 2H), 2.02 – 1.22 (m, 22H), 0.88 ((t, J = 5.0 Hz, 3H). HRMS (ESI) m/z [M + H]⁺ calculated for [C₂₀H₃₄N₃O⁺] 332.2702, found 332.2698.

1-(2-(((1r,3r,5r,7r)-Adamantan-2-yl)oxy)ethyl)-4-(((1r,3r,5r,7r)-adaman-ntan-2-yl)oxy)methyl)-1H-1,2,3-triazole hydrochloride (20).
20 was made by following the protocol used for 19. Purity of the product was determined by qNMR: 95.9%. \(^1\)H NMR (500 MHz, chloroform-\(d_1\)) \(\delta\) 7.89 (s, 1H), 4.77 (s, 2H), 4.61 (t, \(J = 5.0\) Hz, 2H), 3.82 (t, \(J = 4.9\) Hz, 2H), 3.59 (s, 1H), 3.42 (s, 1H), 2.23 – 1.34 (m, 28H). HRMS (ESI) m/z [M + H]\(^+\) calculated for \([C_{25}H_{38}N_3O_2]\)\(^+\) 412.2964, found 412.2961.

\(N\)-(2-(((1r,3r,5r,7r)-Adamantan-2-yl)oxy)ethyl)-4-heptyl-4,5-dihydro-1H-imidazol-2-amine hydroiodide (21).

To a solution of 1,2-nonanediol (320 mg, 2 mmol) in dry DCM (6 mL) was added pyridine (480 mg, 6 mmol) and MsCl (342 mg, 3 mmol) at 0 °C with stirring. Stirring was continued for 1 h at 0 °C then the reaction was quenched by adding saturated aqueous NaHCO\(_3\). The DCM phase was separated and concentrated to give the crude dimesylate. A mixture of the the crude dimesylate and NaN\(_3\) (260 mg, 4 mmol) in DMF (4 mL) was heated at 80 °C for 2 h. The resulting mixture was distributed between hexane and water. The hexane phase was separated and dried over anhydrous Na\(_2\)SO\(_4\) and solvents removed under reduced pressure to give the diazide. A mixture of diazide and PtO\(_2\) (40 mg, 0.1 mmol) in MeOH (4 mL) was stirred under H\(_2\) for 2 h at 25 °C. Filtration and evaporation gave the diamine (227 mg, 72%). To a solution of the diamine (227 mg, 1.44 mmol) in dry DCM was added 1,1'-thiocarboxyldiimidazole (356 mg, 2 mmol) at 0 °C. Stirring was continued for 2 h at 25 °C. The reaction mixture was purified by using flash
chromatography (SiO$_2$, hexane/ethyl acetate = 6/1) to give the thiourea (216 mg, yield: 75%). A solution of the thiourea (216 mg, 1.08 mmol) and MeI (426 mg, 3 mmol) in methanol (4 mL) was refluxed for 4h. The solution was evaporated to give methylthioimidazole which was used in the next step. The amine (38 mg, 0.2 mmol) and methylthioimidazole (69 mg, 0.2 mmol) were refluxed in isopropanol (2 mL) for 2 h. The reaction mixture was concentrated and purified with flash chromatography (SiO$_2$, CHCl$_3$/MeOH/ Et$_3$N = 100/10/5) to give 21 (64 mg). The HCl salt of 21 was obtained by neutralizing it with HCl in toluene. Purity of the product was determined by qNMR: 95.6%. $^1$H NMR (500 MHz, chloroform-d$_j$) $\delta$ 8.99 (s, 1H), 8.42 (d, 1H), 7.05 (d, 1H), 4.51 – 3.80 (m, 2H), 3.74 – 3.57 (m, 2H), 3.53 (s, 1H), 3.49 – 3.10 (m, 3H), 2.09 – 1.66 (m, 11H), 1.62 – 1.15 (m, 15H), 0.89 (t, $J = 5.0$ Hz, 1H). HRMS (ESI) m/z [M + H]$^+$ calculated for [C$_{22}$H$_{40}$N$_3$O]$^+$ 362.3171, found 362.3171.

3-(2-(((1r,3r,5r,7r)-Adamantan-2-yl)oxy)ethyl)-1-((E)-3,7-dimethylocta-2,6-dien-1-yl)-1H-imidazol-3-ium methanesulfonate (22).

A mixture of 2-adamantyl bromide (215 mg, 1 mmol), Ag$_2$SO$_4$ (310 mg, 1 mmol) and ethylele glycol (1 mL) was heated for 1.5 h at 90 °C. The reaction mixture was distributed between ethyl acetate and water. The ethyl acetate phase was separated and dried over anhydrous Na$_2$SO$_4$ and solvents removed under reduced pressure to give the residue. Purification of the residue with flash chromatography (SiO$_2$, hexane/ethyl acetate = 6/1) gave the alcohol product (110 mg, yield: 56%). To a solution of the alcohol (110 mg, 0.56 mmol) in dry CH$_2$Cl$_2$ (3 mL) was added
pyridine (158 mg, 2 mmol) and MsCl (91 mg, 0.8 mmol) at 0 °C with stirring. After stirring was continued for 2 h at 0 °C, all volatile components was removed under reduced pressure. The residue was purified by using flash chromatography (silica gel, hexane/ethyl acetate = 10/1) to give mesylate (146 mg, 95%). A mixture of the mesylate (27 mg, 0.1 mmol) and geranylimidazole (20 mg, 0.1 mmol) in MeCN (2 mL) was refluxed for 5 h. Evaporation gave a quantitative yield of the product 22. Purity of the product was determined by qNMR: 91.7%. ¹H NMR (500 MHz, chloroform-d₁) δ 9.96 (s, 1H), 7.47 (s, 1H), 7.08 (s, 1H), 5.37 (m, 1H), 5.03 (m, 1H), 4.88 (d, J = 7.5 Hz, 2H), 4.56 (m, 2H), 3.80 (m, 2H), 3.44 (s, 1H), 2.79 (s, 3H), 2.36 – 1.26 (m, 18H), 1.79 (s, 3H), 1.68 (s, 3H), 1.60 (s, 3H). HRMS (ESI) m/z [M]+ calculated for [C₂₅H₃₉N₂O]+ 383.3062, found 383.3066.

1-(2-(((1r,3r,5r,7r)-Adamantan-2-yl)oxy)ethyl)-3-hexylpyridin-1-ium methanesulfonate (23).

made by following to the protocol used for 22. Purity of the product was determined by qNMR: 96.11%. ¹H NMR (500 MHz, chloroform-d₁) δ 8.98 (m, 1H), 8.74 (s, 1H), 8.24 (d, J = 7.9, Hz, 1H), 7.99 (dd, J = 8.0, 6.0 Hz, 1H), 4.91 (t, J = 5.5 Hz, 2H), 3.91 (J = 5.5 Hz, 2H), 3.42 (s, 1H), 2.85 (t, J = 7.5 Hz, 2H), 2.75 (s, 3H), 2.03 – 1.11 (m, 22H), 0.90 (m, 3H). HRMS (ESI) m/z [M]+ calculated for [C₂₃H₃₆NO]+ 342.2797, found 342.2785.

1-((1r,3r,5r,7r)-Adamantan-2-yl)-3-(((E)-3,7-dimethylocta-2,6-dien-1-yl)-1H-imidazol-3-ium bromide (24).
1-(1-Adamantyl)-1H-imidazole was made according to a reported protocol. A mixture of adamantly-imidazole (40 mg, 0.2 mmol) and geranyl bromide (44 mg, 0.2 mmol) in DCM (0.5 mL) was stirred for 12 h at 25 °C. The solid resulting from evaporation was thoroughly washed with hexane to give the product (50 mg, yield: 59%). Purity of the product was determined by qNMR: 91.7%). 1H NMR (500 MHz, Chloroform-d) δ 10.65 (s, 1H), 5.40 (t, J = 7.7 Hz, 1H), 5.17 (d, J = 7.6 Hz, 2H), 5.04 (s, 1H), 4.39 (s, 2H), 2.73 (s, 3H). HRMS (ESI) m/z [M]+ calculated for [C23H35N2O]+ 339.2800, found 339.2797.

1-(((1r,3r,5r,7r)-Adamantan-2-yl)methyl)-3-octyl-1H-imidazol-3-ium bromide (25).

To a solution of methyleneadamantane7 (296 mg, 2 mmol) in dry THF was added 9-BBN (0.5 M in THF, 4.4 mL) dropwise. Stirring was continued for 30 min at 0 °C and 1 h at 25 °C. The reaction flask was cooled in an ice-bath. To the resulting reaction mixture was added NaOH (3N in H2O, 3 mL) and H2O2 (30% in water, 0.68 mL). Stirring was continued for 30 min at 0 °C and 1 h at 25 °C. The reaction mixture was diluted with ethyl acetate and quenched with saturated aqueous Na2SO3 at 0 °C. The organic phase was dried over Na2SO4 and solvents removed under reduced pressure to give the crude hydroxymethyladamantane. To a solution of the 2-hydroxymethyladamantane in DCM (6 mL) was added Ph3P (524 mg, 2 mmol) and CBr4 (662 mg, 2 mmol) at 0 °C with stirring. Stirring was continued for 30 min at 0 °C and for 2 h at 25 °C. The reaction mixture was concentrated and purified by using flash chromatography (SiO2, hexane/ethyl acetate = 20/1) to give the bromide product (274 mg, yield: 61%). To a solution of
imidazole (134 mg, 2 mmol) in dry THF (7 mL) was added NaH (washed with hexane, 58 mg, 2.5 mmol) at 0 °C with stirring. Stirring was continued for 20 min at 25 °C and 30 min at 50 °C. To the resulting solution was added bromomethyladamantane (229 mg, 1 mmol) at 25 °C, with stirring. Stirring was continued for 24 h at 50 °C. The reaction mixture was diluted with ethyl acetate and quenched with saturated aqueous NH₄Cl. The organic phase was separated and concentrated to give a residue. The residue was purified by using flash chromatography (SiO₂, ethyl acetate, 140 mg, 65%) to give the adamantanylmethylimidazole. A solution of adamantanylmethylimidazole (44 mg, 0.2 mmol) in octyl bromide (0.2 mL) was stirred for 4 h at 80 °C. To the reaction mixture was added 4 mL of hexane and the resulting precipitate was washed with hexane, three times, to give the product 25 (46 mg, yield: 56%). Purity of the product was determined by qNMR: 91.5%. ¹H NMR (500 MHz, Chloroform-dı) δ 10.76 (s, 1H), 7.22 (s, 1H), 7.18 (s, 1H), 4.48 (d, J = 8.1 Hz, 2H), 4.38 (t, J = 7.5 Hz, 2H), 2.25 (t, J = 8.2 Hz, 1H), 2.10 – 1.07 (m, 26H), 0.87 (t, J = 6.9 Hz, 3H). HRMS (ESI) m/z [M]+ calculated for [C₂₂H₃₇N₂]+ 329.2957, found 329.2947.

1-(((1r,3r,5r,7r)-Adamantan-2-yl)methyl)-3-(3-phenoxybenzyl)-1H-imidazol-3-ium bromide (26).

26 was made by following the protocol used for 25. Purity of the product was determined by qNMR: 99.1%. ¹H NMR (500 MHz, chloroform-dlı) δ 10.86 (s, 1H), 7.39 – 7.31 (m, 3H), 7.24 – 7.19 (m, 1H), 7.19 – 7.10 (m, 3H), 7.04 – 6.92 (m, 4H), 5.64 (s, 2H), 4.41 (d, J = 8.0 Hz, 2H), 2.24 (t, J = 8.1 Hz, 1H), 2.02 – 1.57 (m, 14H). HRMS (ESI) m/z [M]+ calculated for [C₂₇H₃₁N₂O]+ 399.2436, found 399.2430.
1-(2-((3r,5r,7r)-Adamantan-1-yl)ethyl)-3-((E)-3,7-dimethylocta-2,6-dien-1-yl)-1H-imidazol-3-ium bromide (27).

27 was made by following the protocol used for 25 using 1-(1-hydroxy-ethyl) adamantane as the starting material which is commercial available. Purity of the product was determined by qNMR: 91.9%. 

$^1$H NMR (500 MHz, chloroform-$d_1$) δ 10.67 (s, 1H), 7.24 (s, 1H), 7.18 (s, 1H), 5.50 – 5.28 (m, 1H), 5.03 (m, 1H), 5.01 (d, $J = 7.5$ Hz, 2H), 4.49 – 4.19 (m, 2H), 2.17 – 1.22 (m, 21H), 1.60 (s, 3H), 1.57 (s, 6H). HRMS (ESI) m/z [M]$^+$ calculated for [C$_{25}$H$_{39}$N$_2$]$^+$ 367.3113, found 367.3128.

1-(2-((3r,5r,7r)-Adamantan-1-yl)ethyl)-3-octyl-1H-imidazol-3-ium bromide (28).

28 was made by following the protocol used for 25 using 1-(1-hydroxy-ethyl) adamantane as the starting material. Purity of the product was determined by qNMR: 98.1%. 

$^1$H NMR (500 MHz, chloroform-$d_1$) δ 10.80 (s, 1H), 7.21 (m, 2H), 4.36 (m, 4H), 2.18 – 1.80 (m, 5H), 1.83 – 1.59 (m, 12H), 1.43 – 1.10 (m, 10H), 0.87 (t, $J = 6.8$ Hz, 3H). HRMS (ESI) m/z [M]$^+$ calculated for [C$_{23}$H$_{39}$N$_2$]$^+$ 343.3113, found 343.3111.

1-(2-((3r,5r,7r)-Adamantan-1-yl)ethyl)-3-(3-phenoxybenzyl)-1H-imidazol-3-ium bromide (29).
29 was made by following the protocol used for 26 using 1-(1-hydroxy-ethyl) adamantane as starting material. Purity of the product was determined by qNMR: 91.0%. $^1$H NMR (500 MHz, chloroform-$d_1$) $\delta$ 10.83 (t, $J = 1.6$ Hz, 1H), 7.42 – 7.28 (m, 3H), 7.25 – 7.10 (m, 4H), 7.06 – 6.90 (m, 4H), 5.63 (s, 2H), 4.38 – 4.16 (m, 2H), 2.17 – 1.44 (m, 17H). HRMS (ESI) m/z [M]$^+$ calculated for [C$_{28}$H$_{33}$N$_2$O]$^+$ 413.2595, found 413.2595.

1-(3-((3r,5r,7r)-Adamantan-1-yl)propyl)-3-((E)-3,7-dimethylocta-2,6-dien-1-yl)-1H-imidazol-3-ium bromide (30).

30 was made by following the protocol used for 25 using 1-(3-hydroxy-propyl) adamantane$^8$ as starting material. Purity of the product was determined by qNMR: 90.9%. $^1$H NMR (500 MHz, chloroform-$d_1$) $\delta$ 10.61 (s, 1H), 7.21 (s, 1H), 7.16 (s, 1H), 5.38 (m, 1H), 5.03 (t, m, 1H), 5.01 (d, $J = 10.0$ Hz, 2H), 4.30 (t, $J = 7.5$ Hz, 2H), 1.52 (m, 23H), 1.60 (s, 3), 1.44 (s, 6H). HRMS (ESI) m/z [M]$^+$ calculated for [C$_{26}$H$_{41}$N$_2$]$^+$ 381.3270, found 381.3267.

1-(3-((3r,5r,7r)-Adamantan-1-yl)propyl)-3-octyl-1H-imidazol-3-ium bromide (31).

31 was made by following the protocol used for 25 using 1-(3-hydroxy-propyl) adamantaneas$^8$ starting material. Purity of the product was determined by qNMR: 97.2%. $^1$H NMR (500 MHz, chloroform-$d_1$) $\delta$ 10.76 (s, 1H), 7.22 (s, 2H), 4.36 (t, $J = 7.5$ Hz, 2H), 4.32 (t, $J = 7.5$ Hz, 2H), 2.03 – 1.17 (m, 15H), 1.12 – 1.01 (m, 2H), 0.87 (t, $J = 6.8$ Hz, 3H). HRMS (ESI) m/z [M]$^+$ calculated for [C$_{24}$H$_{41}$N$_2$]$^+$ 357.3270, found 357.3258.

1-(3-((3r,5r,7r)-Adamantan-1-yl)propyl)-3-(3-phenoxybenzyl)-1H-imidazol-3-ium bromide
32 was made by following the protocol used for 26 using 1-(3-hydroxy-propyl)adamantane\(^8\) as starting material. Purity of the product was determined by qNMR: 90.1%. \(^1\)H NMR (500 MHz, chloroform-\(d_1\)) \(\delta\) 10.90 (s, 1H), 7.35 (m, 3H), 7.24 – 7.11 (m, 3H), 6.99 (m, 5H), 5.62 (s, 2H), 4.27 (t, \(J = 7.5\) Hz, 2H), 1.96 – 1.38 (m, 17H), 1.071 (m, 2H). HRMS (ESI) m/z [M]\(^+\) calculated for [C\(_{29}\)H\(_{35}\)N\(_2\)O]\(^+\) 427.2749, found 427.2754.

1-(3-(3\(r\),5\(r\),7\(r\))-Adamantan-2-yl)propyl)-3-octyl-1H-imidazol-3-ium bromide (33)

To a solution of 2-adamantanone (5 g, 33.28 mmol) in 32 mL of methanol was added methyl 2-diethoxyphosphoacetate (9 mL, 49.68 mmol). The reaction mixture was cooled at 0 °C and into it was slowly added sodium methoxide (solution of 30% wt in methanol). The mixture was stirred overnight at room temperature. The solvent was removed under reduced pressure and the crude was treated with ethyl acetate and water. The organic layer was dried over Na\(_2\)SO\(_4\) and the solvent was removed under reduced pressure. The crude was purified by using column chromatography (silica gel, eluting with hexane/ethyl acetate 90:1) to give the unsaturated ester as a solid (6.41 g, 90%). To a solution of the unsaturated ester (6.4 g, 31.07 mmol) in methanol (100 mL) was added ammonium formiate (7.8 g, 124.33 mmol), then was added palladium on
charcoal (0.6 g, 10%) under nitrogen. The reaction mixture was stirred at room temperature for 3 h. Solvents were removed under reduced pressure. The crude was treated with water and ethyl acetate, and the organic layer was separated, dried over Na$_2$SO$_4$ and solvent removed under reduced pressure. The ester product was obtained as a colourless oil (6.2 g, 95%). To a solution of lithium aluminum hydride (1.58 g, 41.63 mmol) in anhydrous tetrahydrofuran (THF) was slowly added a solution of the ester (6.2 g, 29.76 mmol) in THF (55 mL). The reaction mixture was stirred at room temperature overnight. Then water (12 mL), sodium hydroxide 4N (12 mL) and finally water (36 mL) were added into the solution at 0 °C. The mixture was stirred for some minutes and the resulting salts were filtered through a pad of celite washing with ethyl acetate (100 mL). The crude was treated with water and CH$_2$Cl$_2$ and the organic layer was separated, dried over Na$_2$SO$_4$ and solvents removed under reduced pressure to give the alcohol product as an oil (4.83 g, 90%). To a solution of the alcohol (4.8 g, 26 mmol) in 100 mL CH$_2$Cl$_2$ was added triphenylphosphine (13.6 g, 52 mmol). The reaction mixture was stirred at room temperature while N-bromosuccinimide (NBS, 6.9 g, 39 mmol) was added in small portions. The mixture was stirred overnight and then washed with water and extracted with hexane. The organic layer was separated, dried over Na$_2$SO$_4$ and solvents removed under reduced pressure to give the bromide product as a light yellow solid (6.0 g, 95%). Imidazole (1.0 g, 15 mmol) was dissolved in THF (30 mL) and NaH (240 mg, 10 mmol) was added. The reaction mixture was stirred at room temperature for 30 minutes and then the bromide product (1.2 g, 5 mmol) was added. The reaction mixture was then heated to 80 °C and stirred overnight. The reaction was quenched with water and the mixture extracted with diethyl ether. The organic layer was separated, dried over Na$_2$SO$_4$ and solvents removed under reduced pressure. The crude product was purified by silica flash chromatography (silica gel, hexane/ethyl acetate 2:1). The imidazole product was obtained
as light yellow solid (0.6 g, 50%). The imidazole product was dissolved in 1-bromooctane and the reaction mixture stirred overnight under nitrogen at 80 °C. The reaction mixture was treated with hexane and a white precipitate formed. The mixture was centrifuged and the solution discarded. The white precipitate was washed three times with hexane and gave the product 33 as a white solid. Purity of the product was determined by qNMR: 98.9%. $^1$H NMR (500 MHz, chloroform-$d_1$) δ 10.638 (s, 1H), 7.35 (d, J = 10.5 Hz, 1H), 7.34 (d, J = 10.5 Hz 1H), 4.33 (m, 4H), 2.06 (m, 2H), 1.92-1.82 (m, 12H), 1.68 (m, 2H), 1.55 (m, 1H), 1.31-1.21 (m, 12H), 0.85 (t, J = 7.0 Hz, 3H). HRMS (ESI): m/z [M + H]$^+$ calculated for $[\text{C}_{23}\text{H}_{29}\text{N}_2]^+$ 343.3113, found 343.3119.

1-(3-((3r,5r,7r)-Adamantan-1-yl)propyl)-3-(3-phenoxybenzyl)-1H-imidazol-3-ium bromide (34).

![Image of 34](image)

34 was made by following the protocol used for 33. Purity of the product was determined by qNMR: 100%. $^1$H NMR (500 MHz, chloroform-$d_1$) δ 10.77 (s, 1H), 7.33-6.90 (m, 11H), 5.62 (s, 2H), 4.29 (t, J = 7.5 Hz, 2H), 1.92-1.82 (m, 12H), 1.68 (m, 2H), 1.55 (m, 1H). HRMS (ESI) m/z [M]$^+$ calculated for $[\text{C}_{28}\text{H}_{33}\text{N}_2\text{O}]^+$ 413.2593, found 413.2586.

1-(3-((3r,5r,7r)-Adamantan-2-yl)propyl)-3-hexyl-1H-imidazol-3-ium bromide (35)

![Image of 35](image)

35 was made by following the protocol used for 33. Purity of the product was determined by qNMR: 98.9%. $^1$H NMR (500 MHz, chloroform-$d_1$) δ 10.86 (s, 1H), 7.35 (d, J = 10.5 Hz, 1H), 7.26 (d, J = 10.5 Hz 1H), 4.37 (m, 4H), 2.06 (m, 2H), 1.92-1.82 (m, 12H), 1.68 (m, 2H), 1.55 (m,
1H), 1.31-1.21 (m, 8H), 0.85 (t, J = 7.0 Hz, 3H). HRMS (ESI): m/z [M + H]^+ calculated for [C_{21}H_{35}N_{2}]^+ 315.2830, found 315.2834.

1-(3-((3r,5r,7r)-Adamantan-2-yl)propyl)-3-decyl-1H-imidazol-3-ium bromide (36)

![Structure of 36](image)

36 was made by following the protocol used for 33. Purity of the product was determined by qNMR: 96.4%. $^1$H NMR (500 MHz, chloroform-$d_1$) δ 10.86 (s, 1H), 7.35 (d, J = 10.5 Hz, 1H), 7.26 (d, J = 10.5 Hz 1H), 4.37 (m, 4H), 2.06 (m, 2H), 1.92-1.82 (m, 12H), 1.68 (m, 2H), 1.55 (m, 1H), 1.31-1.21 (m, 16H), 0.85 (t, J = 7.0 Hz, 3H). HRMS (ESI): m/z [M + H]^+ calculated for [C_{25}H_{43}N_{2}]^+ 371.3426, found 371.3430.

1-(3-((3r,5r,7r)-Adamantan-2-yl)propyl)-3-dodecyl-1H-imidazol-3-ium bromide (37)

![Structure of 37](image)

37 was made by following the protocol used for 33. Purity of the product was determined by qNMR: 99.9%. $^1$H NMR (500 MHz, chloroform-$d_1$) δ 10.85 (s, 1H), 7.35 (d, J = 10.5 Hz, 1H), 7.26 (d, J = 10.5 Hz 1H), 4.37 (m, 4H), 2.06 (m, 2H), 1.92-1.82 (m, 12H), 1.68 (m, 2H), 1.55 (m, 1H), 1.31-1.21 (m, 20H), 0.85 (t, J = 7.0 Hz, 3H). HRMS (ESI): m/z [M + H]^+ calculated for [C_{27}H_{47}N_{2}]^+ 399.3734, found 399.3739.

1-(2-((3r,5r,7r)-Adamantan-1-yl)ethyl)-4-octyl-1H-imidazole (38).
To a solution of dec-1-ene (5 g, 36 mmol) in DMSO (100 ml) and water (2.5 mL) was added NBS (18 g, 101 mmol) at 25 °C with stirring. Stirring was continued for 4 h at 40 °C. Water (250 mL) was added to the mixture which was then extracted with ether; the ether extracts were washed with water, dried over anhydrous Na₂SO₄ and solvents removed under reduced pressure to yield the crude bromohydrin. To a solution of the bromohydrin in acetone (25 mL) was added dropwise with stirring at 25 °C a solution of sodium dichromate (3.5 g, 12.5 mmol) in concentrated sulfuric acid (2.5 mL) plus water (15 mL). Stirring was continued for 1.5 h at 25 °C. Diethyl ether (25 mL) was added and the mixture stirred for a further 1 h. The ether layer was then separated, washed with water, dried over anhydrous Na₂SO₄ and solvents removed under reduced pressure to give 1-bromodecan-2-one (4.23 g, yield: 50%). Under N₂, the bromo-ketone (1.16 g in a minimal amount of hexane) was added to preheated formamide (10 mL, 180 °C), dropwise. The hexane rapidly evaporated and stirring was continued for 2 h at 180 °C. The reaction mixture cooled to 25 °C and then distributed between toluene and aqueous NaOH (3N). The toluene phase was separated, dried over anhydrous Na₂SO₄ and solvents removed under reduced pressure to give a residue. The residue was purified by using flash chromatography (SiO₂, ethyl acetate) to give 4-octanylimidazole (693 mg, yield: 77%). To a solution of 4-octanylimidazole (90 mg, 0.5 mmol) in dry THF (3 mL) was added NaH (washed with and dried from hexane, 16 mg, 0.7 mmol) at 0 °C, with stirring. Stirring was continued for 20 min at 25 °C and 30 min at 50 °C. To the resulting solution was added bromomethyladamantane (114 mg, 0.5
mmol) at 25 °C, with stirring. Stirring was continued for 12 h at 60 °C. The reaction mixture was diluted with ethyl acetate and quenched with saturated aqueous NH₄Cl. The organic phase was separated and concentrated to give a residue. Purification of the residue with flash chromatography (SiO₂, ethyl acetate) gave the product 38 (27 mg, yield: 16%). Purity of the product was determined by qNMR: 92.2%. ¹H NMR (500 MHz, chloroform-d) δ 7.42 (s, 1H), 6.61 (s, 1H), 3.92 – 3.82 (m, 2H), 2.54 (t, J = 7.7 Hz, 2H), 2.05 – 0.76 (m, 32H). HRMS (ESI) m/z [M + H]⁺ calculated for [C₂₃H₃₉N₂]⁺ 343.3113, found 343.3118.

1-(2-(((1r,3r,5r,7r)-Adamantan-2-yl)oxy)ethyl)-5-octyl-1H-imidazole and 1-(2-(((1r,3r,5r,7r)-adamantan-2-yl)oxy)ethyl)-4-octyl-1H-imidazole (39, as a 1/1 mixture).

39 was made by following the protocol used for 38 but using (1r,3r,5r,7r)-2-(2-bromoethoxy)adamantane as the alkylation reagent. Purity of the product was determined by qNMR: 91.5%. ¹H NMR (500 MHz, chloroform-d) δ 1/1 regioisomer: 7. 60 (s, 1H), 7.53 (s, 1H), 6.77 (s, 1H), 4.05 (t, J = 5.2 Hz, 2H), 4.02 (t, J = 5.3 Hz, 2H), 3.65 (m, 4H), 3.38 (m, 2H), 2.55 (m, 4H), 2.01 – 1.14 (m, 52H), 0.88 (m, 6H). HRMS (ESI) m/z [M + H]⁺ calculated for [C₂₃H₃₉N₂O]⁺ 359.3062, found 359.3056.

N-(((1r,3r,5r,7r)-Adamantan-2-yl)methyl)-5-octyl-4,5-dihydro-1H-imidazol-2-amine hydroiodide (40).

40 was made by following the protocol used for 21. Purity of the product was determined by
qNMR: 92.4%. $^1$H NMR (500 MHz, chloroform-$d_1$) $\delta$ 4.02-3.15 (m, 5H), 2.01-1.26 (m, 28 H), 0.88 (t, $J = 6.9$ Hz, 3H). HRMS (ESI) m/z [M + H]$^+$ calculated for [C$_{22}$H$_{40}$N$_3$]$^+$ 346.3222, found 346.3218.

$N$-($2$-($3r,5r,7r$)-Adamantan-1-yl)ethyl)-5-octyl-4,5-dihydro-$1H$-imidazol-2-amine hydroiodide (41).

41 was made by following the protocol used for 21. Purity of the product was determined by qNMR: 95.4%. $^1$H NMR (500 MHz, chloroform-$d_1$) 4.45 and 4.28 (broad, 2H), 3.75 (m, 1H), 3.57 (t, $J = 10.0$ Hz, 2H), 3.12 (t, $J = 10.0$ Hz, 2H), 2.66 and 2.56 (broad, 2H), 1.91-1.24 (m, 28H), 0.86 (m, 3H). HRMS (ESI) m/z [M + H]$^+$ calculated for [C$_{23}$H$_{42}$N$_3$]$^+$ 360.3379, found 360.3368.

$(E)$-$N$-($3$-($1'-(1',2'-Dicarbaclosododecaboranyl))propyl)-3,7-dimethylocta-2,6-dien-1-amine (42).

To a solution of o-carborane (268 mg, 2 mmol) in dry THF (6 mL, 2 mmol) was added BuLi (1.6 M in hexane, 1.25 mL, 2 mmol) at -78 $^\circ$C under N$_2$. Stirring was continued for 30 min, then trimethylene oxide (0.2 mL, 3 mmol) was added, dropwise. After stirring for 1 h at 0 $^\circ$C, the
reaction was quenched by adding saturated aqueous NH₄Cl (2 mL). The aqueous phase was extracted with ethyl acetate (3 mL x 3), then solvents were removed from the combined organic phase under reduced pressure and the residue purified by using flash chromatography (silica gel, hexane/ethyl acetate = 5/1) to give the carboranylpropyl alcohol (311 mg, 81%). To a solution of the carboranylpropyl alcohol (297 mg, 1.5 mmol) in dry CH₂Cl₂ (5 mL) was added Ph₃P (524 mg, 2 mmol) followed by NBS (356 mg, 2 mmol). After stirring for 3 h at 0 °C, all volatile components were removed under reduced pressure. The reaction residue was purified by using flash chromatography (silica gel, hexane/ethyl acetate = 15/1) to give the bromopropyl product (287 mg, 75%). To a solution of the carboranylpropyl bromide (256 mg, 1 mmol) in DMF (2 mL) was added NaN₃ (130 mg, 2 mmol), and the resulting solution was stirred for 3 h at 100 °C. The reaction mixture cooled to room temperature and distributed between ethyl acetate/water (10 mL/10 mL). The ethyl acetate phase was separated and washed with water (5 mL x 3), then solvent was removed under reduced pressure to give the crude carboranylpropyl azide. To a solution of the above crude azide in THF/H₂O (5 mL/0.5 mL) was added Ph₃P (314 mg, 1.2 mmol). Stirring was continued for 10 h at 25 °C, and then solvents were removed under reduced pressure. Flash chromatography (silica gel, CHCl₃/MeOH = 10/1) of the residue gave the carboranylpropylamine (99 mg, 52%). To a solution of the carboranylpropylamine (99 mg, 0.52 mmol) in dry CH₂Cl₂ (2 mL) was added Et₃N (0.14 mL, 1 mmol) and 2,4-dinitrobenzensulfonyl chloride (186 mg, 0.7 mmol) at 0 °C. Stirring was continued for 2 h at 0 °C and then solvents were removed under reduced pressure. Flash chromatography (silica gel, hexane/ethyl acetate = 10/1) of the residue gave carboranylpropyl dinitrobenzensulfonyl amine (120 mg, 55%). To a solution of carboranylpropyl dinitrobenzensulfonyl amine (120 mg, 0.28 mmol) in DMF (2 mL) was added geranyl bromide (73 mg, 0.34 mmol) and K₂CO₃ (47 mg, 0.34 mmol) with stirring.
Stirring was continued for 1 h at 60 °C, then the reaction mixture was cooled to room temperature. The reaction mixture was distributed between ethyl acetate/water (10 mL/10 mL) and the ethyl acetate phase was separated, dried over Na₂SO₄ and solvents removed under reduced pressure to give the crude trisubstituted amine product. To a solution of the trisubstituted amine in CH₂Cl₂ was added thioglycolic acid (26 mg, 0.28 mmol) and Et₃N (84 mg, 0.84 mmol) at 0 °C. Stirring was continued for 1 h at 25 °C. The reaction mixture was quenched with saturated aqueous NaHCO₃. The CH₂Cl₂ phase was separated, dried over Na₂SO₄ and solvents removed under reduced pressure to give the crude product 42. Flash chromatography (silica gel, CHCl₃/MeOH = 10/1) of the residue gave the desired product as a pale yellow oil (17 mg, 18%).

To a solution of amine in toluene (1 mL) was added trifluoroacetic acid (TFA) (10 mg) at 0 °C. All the volatile components were then removed to give the TFA salt of the amine in quantitative yield. Purity of the product was determined by qNMR: 96.0%. ¹H NMR (500 MHz, chloroform-d₆) δ 5.23 (m, 1H), 5.05 (m, 1H), 3.67 (s, 1H), 3.40 (d, J = 7.2 Hz, 2H), 2.74 (t, J = 6.9 Hz, 2H), 2.75-1.65 (m, 16) 2.33 (m, 2H), 1.67 (s, 6H), 1.60 (s, 3H). HRMS (ESI) m/z [M + H]⁺ calculated for [C₁₅H₃₆B₁₀N]⁺ 340.3778, found 340.3803.

1-((1'-((1',2'-Dicarbaclosododecaboranyl))ethyl)-3-pentyl-1H-imidazol-3-ium bromide (43).

To a solution of o-carborane (268 mg, 2 mmol) in dry THF (6 mL, 2 mmol) was added BuLi (1.6 M in hexane, 1.25 mL, 2 mmol) at -78 °C under N₂. Stirring was continued for 30 min, then ethylene oxide (1.2 M in THF, 2.5 mL, 3 mmol) was added dropwise. Stirring was continued for
1 h at 0 ºC, then the reaction was quenched by adding saturated aqueous NH₄Cl (2 mL). The aqueous phase was extracted with ethyl acetate (3 mL x 3) and the combined organic phase was dried over Na₂SO₄ and solvents removed under reduced pressure. The residue was purified by using flash chromatography (silica gel, hexane/ethyl acetate = 5/1) to give the carboranylethyl alcohol (303 mg, 85%). To a solution of the carboranylethyl alcohol (303 mg, 1.7 mmol) in dry CH₂Cl₂ (5 mL) was added Ph₃P (524 mg, 2 mmol) followed by NBS (356 mg, 2 mmol). Stirring was continued for 3 h at 0 ºC, then all volatile components were removed under reduced pressure. The residue was purified by flash chromatography (silica gel, hexane/ethyl acetate = 15/1) to give the bromide product (328 mg, 80%). A mixture of the carboranylethyl bromide product (33 mg, 0.1 mmol), N-pentylimidazole (14 mg, 0.1 mmol) and chloroform (0.5 mL) was heated for 3 h at 120 ºC in the sealed tube. The reaction mixture was cooled to room temperature and all volatile components removed under reduced pressure. The residue was purified by flash chromatography (silica gel, CHCl₃/MeOH = 10/1) to give the product 43 (30 mg, 65%). Purity of the product was determined by qNMR: 92.5%. ¹H NMR (500 MHz, chloroform-d₁) δ 10.60 (s, 1H), 7.52 (s, 1H), 7.20 (s, 1H), 5.11 (s, 1H), 4.58 (t, J = 10.0 Hz, 2H), 4.20 (t, J = 7.5 Hz, 2H), 3.22 (t, J = 10.0 Hz, 2H), 2.80 – 1.71 (m, 10H), 1.93 (m, 2H), 1.36 (m, 4H), 0.92 (t, J = 7.0 Hz, 3H). HRMS (ESI) m/z [M]+ calculated for [C₁₂H₂₉B₁₀N₂]⁺ 311.3261, found 311.3232.

(E)-1-(-(1'-1',2'-Dicarbaclosododecaboranyl))ethyl)-3-(3,7-dimethylocta-2,6-dien-1-yl)-1H-imidazol-3-ium (44).

44 was made by following the protocol used for 43. Purity of the product was determined by
qNMR: 91.6%. \(^1\)H NMR (500 MHz, chloroform-\(d_1\)) \(\delta\) 10.32 (s, 1H), 7.49 (s, 1H), 7.14 (s, 1H), 5.37 (m, 1H), 5.09 (s, 1H), 5.04 (s, 1H), 4.81 (d, \(J = 7.5\) Hz, 2H), 4.61 – 4.49 (m, 2H), 3.27 – 3.10 (m, 2H), 2.69-1.25 (m, 14H), 1.80 (s, 3H), 1.60 (s, 3H), 1.54 (s, 3H). HRMS (ESI) m/z [M]\(^+\) calculated for \([C_{17}H_{35}B_{10}N_2]\) \(^+\) 377.3731, found 377.3772.

3-Decyl-1-((1-((1’,2’-dicarbaclosododecaboranyl))ethyl)-1\(H\)-imidazol-3-ium bromide (45).

45 was made by following the protocol used for 43. Purity of the product was determined by qNMR: 96.6%. \(^1\)H NMR (500 MHz, chloroform-\(d_1\)) \(\delta\) 10.58 (s, 1H), 7.55 (s, 1H), 7.20 (s, 1H), 5.13 (s, 1H), 4.70 – 4.45 (m, 2H), 4.19 (t, \(J = 7.5\) Hz, 2H), 3.33 – 3.03 (m, 2H), 2.75 – 1.89 (m, 10H), 1.924 (m, 2H), 1.30 - 1.25 (m, 14H), 0.88 (t, \(J = 6.8\) Hz, 3H). HRMS (ESI) m/z [M]\(^+\) calculated for \([C_{17}H_{35}B_{10}N_2]\) \(^+\) 381.4044, found 381.4071.

1-((1-((1’,2’-Dicarbaclosododecaboranyl))ethyl)-3-(3-phenoxybenzyl)-1\(H\)-imidazol-3-ium bromide (46).

46 was made by following the protocol used for 43. Purity of the product was determined by qNMR: 93.4%. \(^1\)H NMR (500 MHz, chloroform-\(d_1\)) \(\delta\) 10.62 (s, 1H), 7.51 – 6.85 (m, 11H), 5.38 (s, 2H), 5.04 (s, 1H), 4.56 (d, \(J = 3.7\) Hz, 2H), 3.21 (d, \(J = 7.9\) Hz, 2H) 2.77-1.52 (m, 10H). HRMS (ESI) m/z [M]\(^+\) calculated for \([C_{20}H_{29}B_{10}N_2O]\) \(^+\) 423.3210, found 423.3205.

1-((1-((1’,2’-Dicarbaclosododecaboranyl))ethyl)-3-octyl-1\(H\)-imidazol-3-ium bromide (47).
47 was made by following the protocol used for 43. Purity of the product was determined by 1H NMR (500 MHz, chloroform-d$_1$) δ 10.55 (s, 1H), 7.49 (d, $J = 1.6$ Hz, 1H), 7.19 (d, $J = 1.5$ Hz, 1H), 5.08 (s, 1H), 4.57 (m, 2H), 4.20 (t, $J = 7.6$ Hz, 2H), 3.20 (dd, $J = 9.8, 6.9$ Hz, 2H), 2.75 - 1.70 (m, 10H), 1.91 (m, 2H), 1.49 - 1.12 (m, 10H), 0.88 (t, $J = 6.8$ Hz, 3H). HRMS (ESI) m/z [M]$^+$ calculated for [C$_{15}$H$_{35}$B$_{10}$N$_2$]$^+$ 353.3731, found 353.3765.

1-([1'-([1',2'-Dicarbaclosododecaboranyl])ethyl]-3-dodecyl-1H-imidazol-3-ium) bromide (48).

48 was made by following the protocol used for 43. Purity of the product was determined by 1H NMR (500 MHz, chloroform-d$_1$) δ 10.72 (s, 1H), 7.36 (s, 1H), 7.17 (s, 1H), 5.10 (s, 1H), 4.68 - 4.39 (m, 2H), 4.19 (t, $J = 7.6$ Hz, 2H), 3.23 (dd, $J = 9.8, 7.1$ Hz, 2H), 2.75-1.75 (m, 10H), 1.94 (m, 2H), 1.34 - 1.25 (m, 18H), 0.88 (t, $J = 6.8$ Hz, 3H). HRMS (ESI) m/z [M]$^+$ calculated for [C$_{19}$H$_{43}$B$_{10}$N$_2$]$^+$ 409.4357, found 409.4376.

1-([1'-([1',2'-Dicarbaclosododecaboranyl])ethyl]-3-tetradecyl-1H-imidazol-3-ium) bromide (49).

49 was made by following the protocol used for 43. Purity of the product was determined by
qNMR: 92.6%. $^1$H NMR (500 MHz, chloroform-$d_1$) δ 10.56 (s, 1H), 7.48 (s, 1H), 7.19 (s, 1H), 5.10 (s, 1H), 457 (m, 2H), 4.20 (t, $J = 7.5$ Hz, 2H), 3.21 (m, 2H), 2.75-1.75 (m, 10H), 1.90 (m, 2H), (m, 22H), 0.88 (t, $J = 6.8$ Hz, 3H). HRMS (ESI) m/z [M]$^+$ calculated for [C$_{21}$H$_{47}$B$_{10}$N$_2$]$^+$ 437.4670, found 437.4689.

1-((1'-1',2'-Dicarbaclosododecaboranyl)ethyl)-3-hexadecyl-$^1$H-imidazol-3-ium bromide (50).

50 was made by following the protocol used for 43. Purity of the product was determined by qNMR: 96.1%. $^1$H NMR (500 MHz, chloroform-$d_1$) δ 10.61 (s, 1H), 7.49 (s, 1H), 7.19 (s, 1H), 5.12 (s, 1H), 4.58 (m, 2H), 4.19 (t, $J = 7.5$ Hz, 2H), 3.22 (m, 2H), 2.75 - 1.75 (m, 10H), 1.92 (m, 2 H), 2.68-1.25 (m, 26H), 0.88 (t, $J = 6.8$ Hz, 3H). HRMS (ESI) m/z [M]$^+$ calculated for [C$_{23}$H$_{51}$B$_{10}$N$_2$]$^+$ 465.4983, found 465.4977.
Figure S1. qNMR spectrum of compound 3.
Figure S2. qNMR spectrum of compound 4.
Figure S3. qNMR spectrum of compound 5.

Molecular weight: 299.66

84H-1607
Figure S4. qNMR spectrum of compound 6.
Figure S5. qNMR spectrum of compound 7.
Figure S6. qNMR spectrum of compound 8.
Figure S7. qNMR spectrum of compound 9.
Figure S8. qNMR spectrum of compound 10.
Figure S9. qNMR spectrum of compound 11.
Figure S10. qNMR spectrum of compound 12.
Figure S11. qNMR spectrum of compound 13.
Figure S12. qNMR spectrum of compound 14.
Figure S13. qNMR spectrum of compound 15.
Figure S14. qNMR spectrum of compound 16.
Figure S15. qNMR spectrum of compound 17.
Figure S16. 4NMR spectrum of compound 18.
Figure S17. qNMR spectrum of compound 19.
Figure S18. 1H NMR spectrum of compound 20.
Figure S19. qNMR spectrum of compound 21.
Figure S20. qNMR spectrum of compound 22.
Figure S21. qNMR spectrum of compound 23.
Figure S22. qNMR spectrum of compound 24.
Figure S23. qNMR spectrum of compound 25.
Figure S24. qNMR spectrum of compound 26.
Figure S25. qNMR spectrum of compound 27.
Figure S26. qNMR spectrum of compound 28.
Figure S27. 9NMR spectrum of compound 29.
Figure S28. qNMR spectrum of compound 30.
Figure S29. qNMR spectrum of compound 31.
Figure S30. qNMR spectrum of compound 32.
Figure S31. qNMR spectrum of compound 33.
Figure S32. qNMR spectrum of compound 34.
Figure S33. qNMR spectrum of compound 35.
Figure S34. qNMR spectrum of compound 36.
Figure S35. qNMR spectrum of compound 37.
Figure S36. qNMR spectrum of compound 38.
Figure S37. NMR spectrum of compound 39.
Figure S38. qNMR spectrum of compound 40.
Figure S39. qNMR spectrum of compound 41.
Figure S40. qNMR spectrum of compound 42.
Figure S41. qNMR spectrum of compound 43.
Figure S42. qNMR spectrum of compound 44.
Figure S43. qNMR spectrum of compound 45.
Figure S44. qNMR spectrum of compound 46.

Reference integral: 5.89-6.31 ppm, value = 100 (3 nuclei)

Sample integral: 2.3-4.3 ppm, value = 37.39 (2 nuclei) - purity = 94.7%
Sample integral: 4.42-4.77 ppm, value = 37.89 (2 nuclei) - purity = 94.7%

Using reference compound TMB (2.537 mg, 96.99% purity, mol weight=168.19)
Assuming sample weight 52.23 mg and mol weight 50.47
Average purity = 93.38%
Figure S45. qNMR spectrum of compound 47.
Figure S46. qNMR spectrum of compound 48.
Figure S47. qNMR spectrum of compound 49.
Figure S48. 1H NMR spectrum of compound 50.
References


