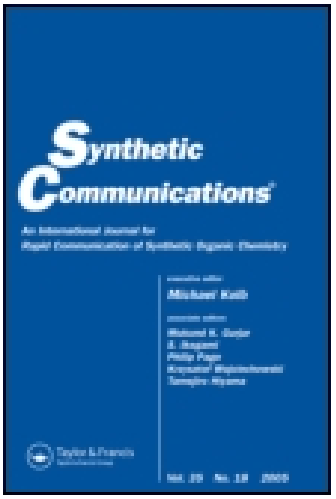

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SYNTHESIS OF VICINAL DIAMINO-*ENDO, CIS*-NORBORNENE DERIVATIVES

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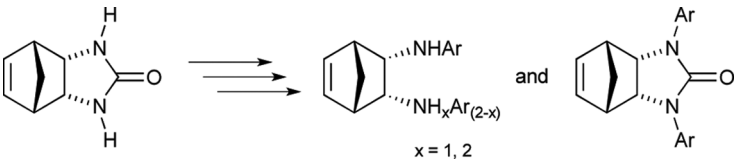
GRAPHICAL ABSTRACT



Abstract *The synthesis of 2,3-disubstituted-*endo,cis-*norborn-5-ene derivatives is described. Cyclic ureas and* cis *vicinal diamines substituted with* p-*tolyl and perfluorophenyl rings were prepared. The use of potassium carbonate as an innocuous CO source for the formation of a cyclic urea was demonstrated.*

Keywords Bicyclic compound; cyclic urea; *endo*-substituted norbornene; vicinal diamine

INTRODUCTION

Werner's pioneering work on cobalt(III) ammine chloride complexes laid the ground for our understanding of today's coordination chemistry.[1] A wide range of molecules containing nitrogen atoms is used nowadays as ancillary ligands to tailor the reactivity of transition-metal complexes. Several multidentate anionic nitrogenous ligands have been used in transition-metal complexes that exhibit high catalytic activities in a wide range of transformations, from nitrogen fixation[2] and oxygen activation[3] to olefin metathesis[4] and polymerization of vinyl monomers[5] and lactides.[6]

However, very little work has been reported on the synthesis of vicinal *cis* diamino bicyclic compounds.[7,8] Furthermore, in cases where amine substituents are *cis* to each other, the exo-configuration is always isolated.[9] We thus became interested in developing new synthetic methodologies to prepare vicinal diamino-*endo,cis*-norbornane and norbornene derivatives for possible use as ligands for transition metals. We herein report our work on the synthesis of several new compounds of this class.

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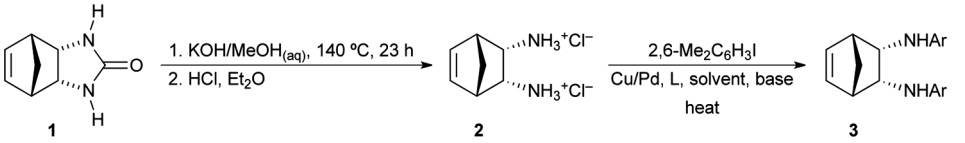


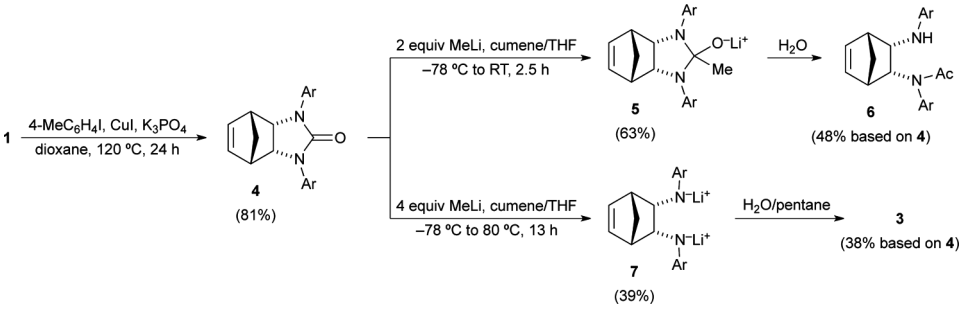
Scheme 1. Attempted C–N cross-coupling reactions with **2**.

RESULTS AND DISCUSSION

Compounds **1** and **2** were prepared from hydantoin using previously reported methods.[7,10,11] Attempts to prepare the bisarylamine derivative **3** through C–N cross-coupling reactions between **2** and 2-iodo-1,3-dimethylbenzene were unsuccessful (Scheme 1). All combinations of either palladium or copper with different amine or phosphine coordinating ligands, in different solvents at elevated temperatures, always led to mixtures of several compounds that could not be isolated and characterized.[12]

We therefore decided to explore the arylation of **1** as substrate using standard C–N cross-coupling reaction conditions[13] and subsequently ring-open the cyclic urea **4** under conditions[8] similar to those employed for the synthesis of **2**. Reaction of **1** with 4-iodotoluene in the presence of potassium phosphate as a base with a catalytic amount of copper(I) iodide and *trans*-1,2-diaminocyclohexane in dioxane at 125 °C generated **4** in 81% yield (Scheme 2).

Multiple attempts to hydrolyze **4** into **3** under conditions analogous to those used for the ring opening of cyclic urea **1** were unsuccessful.[7] The starting substrate was quantitatively recovered when reacted with lithium methoxide in methanol,[14] potassium hydroxide in methanol at 150 °C for 3 days in a pressure tube,[7] potassium *tert*-butoxide in water–dimethylsulfoxide (DMSO) and concentrated HCl with microwave irradiation.[15] In analogy to the ring opening of perimidin-2-ones,[16] addition of 2 equiv MeLi to **4** generated the lithium salt of the methylated compound **5** in 63% yield (Scheme 2). An aqueous workup yielded the ring-opened monoacetylated product **6** in 48% yield, possibly through decomposition of the putative highly unstable hydroxyethyl-1,1-diamine. Addition of 4 equiv MeLi to **4** led to the formation of the dilithium salt **7** in 39% yield. Attempts to purify **7** using nonanhydrous



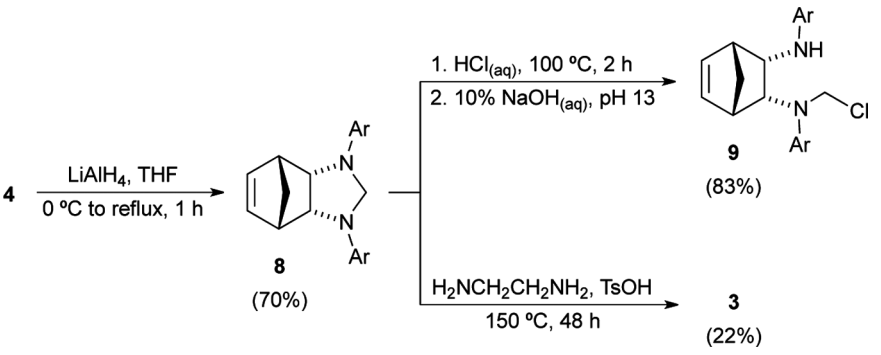
Scheme 2. Ring opening of cyclic urea **4**.

pentane led to its rapid hydrolysis to the diamine **3** in 38% yield (based on the starting material **4**) with the characteristic broad ^{1}H NMR resonance for N*H*Ar at 3.58 ppm (in C_6D_6) integrating to two protons and the broad N–H IR stretching frequency at 3380 cm^{-1}.

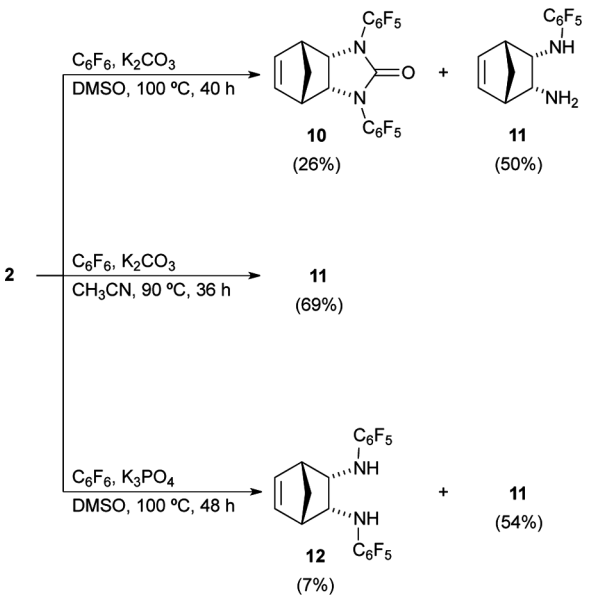
Considering the relatively poor isolated yield of **3** through this approach, activation of the ring by means of reducing the cyclic urea **4** into the corresponding cyclic diamine **8** was explored (Scheme 3). Martens has in fact demonstrated that such cyclic diamines undergo ring opening significantly more easily than cyclic ureas.[14] Reduction of **4** with lithium aluminum hydride in tetrahydrofuran (THF) gave **8** as a white crystalline solid. While reaction of **4** with hydrochloric acid did not open the cyclic urea, that of **8** gave the unexpected unsymmetrical compound **9** in excellent yield, demonstrating the enhanced reactivity of the reduced cyclic diamine. The desired product **3** was successfully obtained by transamination of **8** with ethylene diamine in the presence of catalytic *p*-toluenesulfonic acid, with imidazolidine as by-product, albeit in the poor overall yield of 15% based on **4**.

The synthesis of highly electron-deficient perfluoroaryl derivatives was explored via electrophilic nucleophilic substitution of **2** (Scheme 4). Reaction of the hydrochloride salt **2** with hexafluorobenzene at 100 °C for 40 h in anhydrous DMSO and potassium carbonate as a base, like that reported for the synthesis of tris(aminoalkyl)amines,[17] surprisingly yielded a mixture of compounds containing the cyclic urea **10**, with the inorganic carbonate as the carbonyl source, and the unsymmetrical monoarylated compound **11**. This is, to the best of our knowledge, the first report of such reactions where an inorganic carbonate is used in lieu of phosgene or other organic carbonates to form a cyclic urea from a vicinal diamine.

The ^{1}H and ^{13}C NMR spectral and high-resolution mass-spectrometry (HRMS) data for **10** are consistent with the proposed structure. Interestingly, the ^{19}F NMR spectrum shows four broad resonances at −141.7, −145.6, −161.3, and −162.0 ppm, assigned to the *ortho*- and *meta*-fluorine nuclei, with the *para*-fluorine nucleus resonating at −154.8 ppm as a sharp triplet ($^3J_{FF} = 22.1$ Hz). The broad resonances for the *ortho*- and *meta*-fluorine are due to hindered rotation about the N–C_{ipso} bond, possibly from weak C–F ··· carbonyl interactions.[17] In contrast to that observed for **10**, the ^{19}F NMR spectrum of the unsymmetrical **11** showed three



Scheme 3. Ring opening of **8**.



Scheme 4. Formation of derivatives with perfluorinated phenyl rings.

sharp resonances at −161.5 (d), −162.5 (t), and −175.0 (t) ppm in a 2:2:1 ratio, for the *ortho*-, *meta*- and *para*-fluorine, respectively, as determined by ^{19}F–^{19}F 2D correlation spectroscopy (COSY) NMR. The sharp resonances are expected considering the absence of any possible C–F···carbonyl interactions. The ^{1}H NMR spectrum of **11** shows all the expected resonances, while none of the resonances in the aromatic region are observed on the ^{13}C NMR spectrum because of the relatively poor solubility of the compound and coupling to ^{19}F nuclei.

Interestingly, reaction of **2** with hexafluorobenzene in acetonitrile at 90 °C with K_2CO_3 as the base led to the isolation of **11** in 69% yield, with no spectroscopic evidence for the formation of either **10** or the diperfluorophenyl analog **12** (Scheme 4). The latter was successfully isolated as a minor component from the reaction of **2** with hexafluorobenzene in DMSO at 100 °C with K_3PO_4 as the base. Performing the reaction at 100 °C, 140 °C, and 160 °C in sealed tubes over several days led to more unidentified side products with no higher conversion to **12**. The ^{1}H NMR shows six distinctive resonances with the aminic protons observed at 3.33 ppm as a broad singlet with a relative integration of two. Similar to that observed for **11**, the ^{19}F NMR spectrum shows three sharp resonances at −159.4 (d), −163.7 (t), and −170.4 (t) ppm in a relative integration of 2:2:1, assigned to the *ortho*-, *meta*- and *para*-fluorine nuclei, respectively, with no evidence of hindered rotation.

In conclusion, we have developed methodologies to prepare a variety of previously unreported 2,3-disubstituted-*endo,cis*-norborn-5-enes, including some unique fluorinated derivatives. The use of sodium carbonate as a CO source in the formation of **10** has also been demonstrated.

EXPERIMENTAL

Melting points of the solid samples were recorded on a Fisher-Johns melting-point apparatus and are uncorrected. Air-sensitive NMR samples were prepared under nitrogen in 5 mm Wilmad 507-PP J. Young valve NMR tubes. Otherwise standard NMR tubes were used. ^{1}H, ^{13}C, and ^{19}F spectra were acquired on Bruker AV 300 or Bruker AV 400 spectrometers at room temperature. ^{1}H spectra were referenced internally to residual protio-solvent and ^{13}C resonances were referenced internally to the deuterated solvent resonances and are reported relative to tetramethylsilane $\delta = 0$ ppm. *J* coupling constants are reported in hertz (Hz). ^{19}F spectra were referenced externally to trifluorotoluene. ^{1}H and ^{13}C assignments were confirmed by J-modulated spin-echo (JMOD) and other two-dimensional ^{1}H-^{1}H, ^{13}C-^{1}H, and ^{19}F-^{19}F correlation NMR experiments. Infrared samples (IR) were prepared as Nujol mulls or KBr pellets, and the spectra were recorded on a Thermo Genesis II FTIR spectrometer. Data are quoted in wavenumbers (cm^{-1}) with following abbreviations: strong (s), medium (m), and broad (br). High-resolution mass spectra (HRMS) were recorded on QSTAR Elite, a hybrid quadrupole time-of-flight mass spectrometer (QqTOF) from Sciex, MDS Analytical Technologies.

Starting Materials, Reagents, and Solvents

Pentane, C_6D_6, and tetrahydrofuran (THF) were dried by refluxing over Na and benzophenone. They were distilled, degassed, and stored under nitrogen over a potassium mirror or stored in the glove box over activated 4-Å molecular sieves. Dimethylformamide (DMF) was dried over activated 4-Å molecular sieves and degassed prior to use. *cis-endo*-Bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic anhydride, hexafluorobenzene, and hydantoin were purchased from TCI America and were used as received. *endo*-3,5-Diacetyl-3,5-diazatricyclo[5.2.1.0]dec-8-en-4-one was synthesized according to literature procedures.[10,11]

Experimental Procedures

1,3-Diacetyl-1,3-dihydroimidazol-2-one. The procedure for the acetylation of 1,3-dihydroimidazol-2-one was improved significantly from that reported in the literature.[7] 1,3-Dihydroimidazol-2-one (10.1 g, 119 mmol) was stirred with acetic anhydride (70.2 g, 685 mmol) at reflux for 90 min. The reaction mixture was then cooled to room temperature and concentrated to dryness to get a light yellow solid. The residue was recrystallized from dichloromethane to get 1,3-diacetyl-1,3-dihydro-imidazol-2-one (19.1 g, 113 mmol, 95%) as a white crystalline solid. The spectroscopic data are consistent with those reported by Groaz et al.[7]

***endo*-3,5-Diazatricyclo[5.2.1.0]dec-8-en-4-one (1).** Compound **1** was prepared by the following modification of a literature procedure.[7,10,11] *endo*-3,5-Diacetyl-3,5-diazatricyclo[5.2.1.0]dec-8-en-4-one (3.07 g, 13.1 mmol) was suspended in methanol (10 mL) and 50% aqueous KOH (37 mL) and heated at reflux for 4.5 h. The resulting slurry was cooled to room temperature and filtered, and the solid was washed (5×15 mL) with water and dried to provide a brown solid (1.30 g). This solid was extracted with chloroform (5×15 mL), and the combined

washes were neutralized with 3 N HCl. The product was extracted with chloroform. The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to get 3,5-diazatricyclo[5.2.1.0]dec-8-en-4-one (**1**) (250 mg, 16.3 mmol) as a crystalline white powder. The filtrate was partially concentrated to 40 mL, extracted with chloroform (5×20 mL), neutralized with 3 N HCl and extracted again with chloroform (4×20 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to give additional desired product **1** as a crystalline white powder (1.40 g, 93.2 mmol). The combined yield was 1.65 g, 110 mmol, 84%. Mp 225–228 °C; IR(ν_{max}, Nujol): 3201(b), 2946 (m), 2854 (m), and 1691 (s); ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.16 (s, 2H, olefinic), 4.68 (bs, 2H, N*H*), 4.13 (s, 2H, C*H*N), 3.02 (s, 2H, bridgehead), 1.57 (d, $J = 9.3$, 1H, apical), 1.20 (d, $J = 9.3$, 1H, apical); ^{13}C NMR ($CDCl_3$): δ 163.9 (*C*=O), 134.7 (olefinic), 57.0 (bridgehead), 46.6 (apical), 44.4 (*C*CN); HRMS-ESI ($M + H^+$) m/z: calcd. for $C_8H_{10}N_2O$, 151.0871; obsd., 151.0870.

***cis-endo*-N,N′-Di(*p*-tolyl)bicyclo[2.2.1]hept-5-ene-2,3-diamine (3).** MeLi (1 M in cumene/THF, 12 mL, 12.0 mmol) was slowly added to a solution of **4** (1.01 g, 3.05 mmol) in dry THF (20 mL) under nitrogen at −78 °C. The solution was stirred at low temperature for 25 min and slowly warmed to room temperature over 30 min. It was then refluxed at 80 °C for 12 h. After cooling to room temperature, all volatiles were removed under reduced pressure to get a dark brown solid.

This crude solid was recrystallized in nonanhydrous pentane at −78 °C. The pentane soluble part was concentrated in vacuo to get **3** as a light yellow gummy solid (350 mg, 1.15 mmol, 38%). IR (ν_{max}, KBr): 3380 (br), 2956 (m), 2915 (s), 2858 (m), 1616 (s), 1515 (s); ^{1}H NMR (300 MHz, C_6D_6): δ 6.94 (d, $J = 8.3$, 2H, aromatic C*H*CN), 6.42 (d, $J = 8.3$, 2H, aromatic C*H*CCH_3), 5.96 (s, 2H, olefinic), 3.65 (s, 2H, C*H*N), 3.58 (br s, 2H, N*H*), 2.88 (s, 2H, bridgehead), 2.16 (s, 6H, C*H*$_3$), 1.34 (d, $J = 9.1$, 1H, apical), 1.10 (d, $J = 9.1$, 1H, apical); ^{13}C NMR (C_6D_6): δ 146.1 (aromatic *C*N), 135.7 (olefinic), 130.0 (aromatic *C*CN), 126.2 (aromatic *C*CH_3), 113.7 (aromatic *C*HCCH_3), 57.7 (aliphatic *C*N), 46.9 (bridgehead), 45.0 (apical), 20.3 (CH_3); HRMS-ESI ($M + H^+$) m/z: calcd. for $C_{21}H_{24}N_2$, 305.2018; obsd., 305.2019.

Alternatively, **3** can be prepared by suspending compound **8** (90 mg, 0.28 mmol) and *p*-toluenesulfonic acid (150 mg, 0.871 mmol) in ethylenediamine (3.0 mL, 45 mmol) and heating in a stirred sealed tube at 150 °C for 48 h. The color of the reaction mixture turned dark amber. After cooling to room temperature, the reaction mixture was diluted with H_2O (10 mL) and extracted with dichloromethane (4×5 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated in vacuo to give a dark brown oil. The crude product was purified by column chromatography on silica gel (*n*-hexane–EtOAc 9:1) to give compound **3** as a light yellow oil (18 mg, 59 μmol, 22%).

***endo*-3,5-Di(*p*-tolyl)-3,5-diazatricyclo[5.2.1.0]dec-8-en-4-one (4).** Compound **1** (1.01 g, 6.60 mmol), 4-iodotoluene (4.34 g, 19.8 mmol), CuI (260 mg, 1.40 mmol, 21 mol%) and K_3PO_4 (2.84 g, 13.4 mmol) were suspended in dioxane (25 mL) and stirred for 30 min. *trans*-1,2-Diaminocyclohexane (226 μL, 204 mg, 27 mol%) was added under nitrogen with stirring and the suspension was heated at 120 °C for 24 h. The color of the reaction mixture turned from off white to dark grey. After

cooling to room temperature, the suspension was filtered through a plug of silica gel, and the solid was washed with CH_2Cl_2 (2×25 mL). The light green filtrate was concentrated to dryness in vacuo and further purified by flash chromatography over silica gel (hexane–EtOAc 5:1) to give the white crystalline product **4** (1.80 g, 5.32 mmol, 81%). Mp 175–176 °C; IR (ν_{max}, Nujol): 2944 (m), 2861 (m), and 1691 (s);^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55 (d, $J = 8.4$, 2H, aromatic C<u>H</u>CN), 7.16 (d, $J = 8.2$, 2H, aromatic C<u>H</u>CCH$_3$), 6.00 (t, $J = 1.6$, 2H, olefinic), 4.63 (t, $J = 1.3$, 2H, C<u>H</u>N), 3.40 (t, $J = 1.4$, 2H, bridgehead), 2.33 (s, 6H, C<u>H</u>$_3$), 1.70 (d, $J = 9.5$, 1H, apical), 1.42 (d, $J = 9.5$, 1H, apical); ^{13}C NMR ($CDCl_3$): δ 155.6 (<u>C</u>=O), 136.9 (Ar-<u>C</u>N), 134.3 (olefinic), 132.6 (aromatic <u>C</u>CH$_3$), 129.4 (aromatic C<u>C</u>CH$_3$), 119.3 (aromatic <u>C</u>CN), 58.3 (aliphatic <u>C</u>N), 46.2 (bridgehead), 44.4 (apical), 20.8 (<u>C</u>H$_3$); HRMS-ESI ($M + H^+$) m/z: calcd. for $C_{22}H_{22}N_2O$, 331.1810; obsd., 331.1811.

Lithium *cis-endo*-Bicyclo[2.2.1]hept-5-ene-2,3-diamine-N,N′-(1′,1′-ethoxide) (5). MeLi 1 M solution in cumene and THF (0.62 mL, 0.62 mmol) was slowly added to a solution of substituted urea **4** (100 mg, 0.302 mmol) in dry THF (3 mL) at −78 °C under an inert atmosphere and stirred for 25 min. The solution was subsequently stirred at room temperature for 2 h. All volatiles were removed under reduced pressure to get a light yellow solid. This solid was washed with cold (−78 °C) pentane and dried to give **9** as a light yellow solid (70 mg, 0.19 mmol, 63%). ^{1}H NMR (400 MHz, C_6D_6): δ 7.55 (d, $J = 8.0$, 2H, aromatic C<u>H</u>CN), 6.80 (d, $J = 8.0$, 2H (aromatic C<u>H</u>CCH$_3$), 6.20 (s, 2H, olefinic), 3.65 (s, 2H, C<u>H</u>N), 2.90 (s, 2H, bridgehead), 2.23 (s, 6H, C<u>H</u>$_3$), 1.44 (d, $J = 9.5$, 1H, apical), 1.26 (d, $J = 9.5$, 1H, apical); ^{13}C NMR (C_6D_6): δ 144.5 (N<u>C</u>N), 137.0 (olefinic), 130.1 (aromatic <u>C</u>CH$_3$), 130.0 (aromatic <u>C</u>HCN), 119.6 (aromatic <u>C</u>CCH$_3$), 114.4 (aromatic <u>C</u>CN), 60.4 (aliphatic <u>C</u>HN), 47.5 (apical), 46.0 (bridgehead), 21.0 (p-<u>C</u>H$_3$), 20.5 (<u>C</u>H$_3$CO).

***cis-endo*-N,N′-Di(p-tolyl)-N-acetyl-bicyclo[2.2.1]hept-5-ene-2,3-diamine (6).** MeLi 1 M solution in cumene and THF (0.62 mL, 0.62 mmol) was slowly added to a solution of substituted urea **4** (100 mg, 0.302 mmol) in dry THF (3 mL) at −78 °C under an inert atmosphere and stirred for 25 min. The solution was subsequently stirred at room temperature for 2 h. The color of the solution turned from clear to light yellow. Water (2 mL) was added, and the product was extracted with $CHCl_3$ (3×7 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and filtered, and the filtrate was concentrated under reduced pressure to give **6** as an orange–brown solid (50 mg, 0.14 mmol, 48%). ^{1}H NMR (300 MHz, C_6D_6): δ 7.06, 6.81 (8H, aromatic), 5.70 (1H, aliphatic), 5.33 (1H, aliphatic), 4.83 (1H, aliphatic), 4.40 (1H, aliphatic), 3.32 (1H, N<u>H</u>), 2.9 (1H, aliphatic), 2.53 (1H, aliphatic), 2.22 (3H, C<u>H</u>$_3$), 2.03 (3H, C<u>H</u>$_3$), 1.6 (3H, C<u>H</u>$_3$), 1.25 (2H, apical).

Dilithium *cis-endo*-N,N′-Di(*p*-tolyl)bicyclo[2.2.1]hept-5-ene-2,3-diamide (7). MeLi (1 M in cumene/THF, 12.0 mL, 12.0 mmol) was slowly added to a solution of **4** (1.01 g, 3.05 mmol) in dry THF (20 mL) under nitrogen at −78 °C. The solution was stirred at a low temperature for 25 min and then slowly warmed to room temperature over 30 min. The color of the solution turned from clear to light yellow. It was then refluxed at 80 °C for 12 h. Volatiles were then removed under reduced pressure to get a dark yellow solid. This crude solid was recrystallized in dry pentane at −78 °C. The pentane-soluble part was concentrated in vacuo to get

7 as a pale yellow solid (376 mg, 1.18 mmol, 39%). ^{1}H NMR (300 MHz, C_6D_6): δ 7.31 (d, $J = 8.0$, 2H, aromatic C<u>H</u>CN), 6.79 (d, $J = 8.0$, 2H, aromatic C<u>H</u>CCH$_3$), 6.45 (s, 2H, olefinic), 3.90 (s, 2H, C<u>H</u>N), 3.00 (s, 2H, bridgehead), 2.04 (s, 6H, C<u>H</u>$_3$), 1.18 (d, $J = 9.1$, 1H, apical), 0.77 (d, $J = 9.1$, 1H, apical).

***endo*-3,5-Di(*p*-tolyl)-3,5-diazatricyclo[5.2.1.0]dec-8-ene (8).** A solution of *p*-tolyl substituted urea **4** (300 mg, 0.907 mmol) in dry THF (4 mL) was added to a suspension of $LiAlH_4$ (210 mg, 5.50 mmol) in dry THF (2 mL) with stirring under nitrogen at 0 °C. The suspension was warmed to room temperature and refluxed for 1 h. The color of the reaction mixture turned light grey to dark grey. The reaction mixture was cooled to room temperature. Water (2 mL), 2 M solution of aqueous NaOH (2 mL) and H_2O (2 mL) were added sequentially to quench the reaction. The reaction mixture was filtered through a small pad of Celite, and the solid was washed with diethyl ether (10 mL). The filtrate was extracted with diethyl ether (3 × 7 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated to dryness to get **8** as a white crystalline solid (200 mg, 0.632 mmol, 70%). Mp 166–168 °C; IR (ν_{max}, Nujol): 2974 (m), 2944 (m), 2880 (m), 2838 (m), 1618 (s);^{1}H NMR (300 MHz, $CDCl_3$): δ 7.15 (d, J = 8.3, 2H, aromatic C<u>H</u>CN), 6.63 (d, $J = 8.5$, 2H, aromatic C<u>H</u>CCH$_3$), 5.98 (s, 2H, olefinic), 4.70 (d, $J = 2.6$, 1H, C<u>*H*$_2$</u>N), 4.64 (d, J = 2.9, 1H C<u>*H*$_2$</u>N), 4.54 (s, 2H, N<u>*H*$_2$</u>), 3.50 (s, 2H, bridgehead), 2.33 (s, 6H, C<u>H</u>$_3$), 1.74 (d, $J = 9.3$, 1H, apical), 1.61 (d, $J = 9.2$, 1H apical); ^{13}C NMR ($CDCl_3$): δ 142.6 (aromatic <u>C</u>N), 134.6 (olefinic), 130.0 (aromatic <u>C</u>CN), 126.0 (aromatic <u>C</u>CH$_3$), 111.4 (aromatic <u>C</u>CCH$_3$), 69.4 (<u>C</u>H$_2$), 64.6 (aliphatic <u>C</u>N), 46.6 (apical), 46.0 (bridgehead), 20.3 (<u>C</u>H$_3$); HRMS-ESI ($M + H^+$) m/z: calcd. for $C_{22}H_{24}N_2$, 317.2011; obsd., 317.2012.

***cis-endo*-N-Chloromethyl-N,N′-di(*p*-tolyl)bicyclo[2.2.1]hept-5-ene-2,3-diamine (9).** Compound **8** (55 mg, 0.17 mmol) was suspended in 5 M aqueous HCl solution (5 mL) and heated to 100 °C for 2 h. After cooling to room temperature, the mixture was treated with 10% aqueous NaOH solution to approximately pH 13, and the product was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extract was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to get unsymmetrical methylated compound **9** as a brown solid (50 mg, 0.14 mmol, 83%). IR (ν_{max}, Nujol): 3398 (b), 2946 (m), 2856 (m), 1640 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 7.20, 7.04, 6.85, 6.65 (8H, aromatic), 6.35 (1H, olefinic), 6.15 (1H, olefinic), 4.37 (1H, methylene), 4.21 (1H, methylene), 4.00 (1H, C<u>H</u>N), 3.70 (1H, C<u>H</u>N), 3.07 (1H, bridgehead), 2.83 (1H, bridgehead), 2.38 (3H, C<u>H</u>$_3$), 2.22 (3H, C<u>H</u>$_3$), 1.47 (2H, apical).

***endo*-3,5-Di(perfluorophenyl)-3,5-diazatricyclo[5.2.1.0]dec-8-en-4-one (10).** Compound **2** (250 mg, 1.30 mmol) and K_2CO_3 (1.44 g, 10.4 mmol) were suspended in dry DMSO (10 mL) and stirred at 90 °C under nitrogen for 1 h. After cooling to room temperature, hexafluorobenzene (1.21 g, 6.50 mmol) was added, and the suspension was heated at 100 °C for 40 h. The color of the suspension turned to amber from beige. After cooling to room temperature, the reaction mixture was diluted with H_2O (15 mL), extracted with dichloromethane (3 × 15 mL), and washed with H_2O (2 × 10 mL). The combined organic phases were dried over anhydrous

Na_2SO_4, filtered, and concentrated under reduced pressure to give a brown crude solid. It was then purified by flash chromatography over silica gel (hexane–acetone 9:1) to give **10** as a white solid (165 mg, 0.342 mmol, 26%) and **11** (180 mg, 0.625 mmol, 50%) Data for **10**: mp 118–120 °C; IR (ν_{max}, Nujol): 2950 (m), 2850 (m), 1731 (s); ^{1}H NMR (300 MHz, C_6D_6): δ 6.07 (s, 2H, olefinic), 3.93 (t, $J = 1.4$, 2H, C<u>H</u>N), 2.48 (s, 2H, bridgehead), 1.32 (d, $J = 9.6$, 1H, apical), 0.64 (d, $J = 9.6$, 1H, apical); ^{13}C NMR (C_6D_6): δ 154.9 (<u>C</u>=O), 146.2, 143.0, 139.5, 136.3 (aromatic), 134.4 (olefinic), 60.76 (<u>C</u>HNH), 45.4 (bridgehead), 44.5 (apical); ^{19}F NMR (C_6D_6): δ − 141.7, −145.6, −154.8, −161.3, −162.0; HRMS-ESI ($M + H^+$): calcd. for $C_{20}H_8F_{10}N_2O$, 483.0550; obsd., 483.0522.

***cis-endo*-N-(Perfluorophenyl)bicyclo[2.2.1]hept-5-ene-2,3-diamine (11).** Compound **2** (200 mg, 1.01 mmol) and K_2CO_3(836 mg, 6.04 mmol) were suspended in acetonitrile (5 mL) and stirred at 90 °C for 1 h. After cooling to room temperature, hexafluorobenzene (592 mg, 3.18 mmol) was added under nitrogen. The suspension was heated at 90 °C for 36 h. The color of the suspension turned to beige from off-white. After cooling to room temperature, the reaction mixture was diluted with H_2O (12 mL), extracted with dichloromethane (3 × 12 mL), and washed with H_2O (2 × 7 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a light yellow semisolid. It was then purified by flash chromatography over silica gel (hexane–EtOAc 7:1) to give **11** as a light yellow oil (199 mg, 0.685 mmol, 69%). ^{1}H NMR (400 MHz, C_6D_6): δ 5.94 (s, 1H, olefinic), 5.82 (s, 1H, olefinic), 5.02 (s, 1H, N<u>H</u>), 3.55 (s, 1H, C<u>H</u>NH), 2.98, 2.92, 2.37 (s, 3H, C<u>H</u>NH_2 and bridgehead), 1.28 (d, $J = 9.1$, 1H, apical), 0.90 (d, $J = 9.1$, 1H, apical) ppm; ^{13}C NMR (C_6D_6): δ 136.0, 135.0 (olefinic C's), 56.2 (<u>C</u>HNH), 53.0, 49.0, 48.0 (<u>C</u>HNH_2 and bridgehead C's), 45.0 (apical) ppm; resonances for C_6F_5 ring could not be assigned due to low intensity. ^{19}F NMR (C_6D_6): δ − 161.2 (d, 2 F, *ortho*), −165.5 (t, 2 F, *meta*), −174.7 (t, 1 F, *para*) ppm; HRMS-ESI ($M + H^+$) m/z: calcd. for $C_{13}H_{11}F_5N_2$, 291.0921; obsd., 291.0940.

***cis-endo*-N,N′-Di(perfluorophenyl)bicyclo[2.2.1]hept-5-ene-2,3-diamine (12).** Compound **2** (20 mg, 90 μmol) and K_3PO_4 (149 mg, 702 μmol) were suspended in DMSO (1.5 mL) and stirred at 90 °C under nitrogen for 1 h. After cooling to room temperature, hexafluorobenzene (112 mg, 0.601 mmol) was added, and the suspension was heated at 100 °C for 48 h. The color of the suspension turned to amber from beige. The reaction mixture was cooled to room temperature. Water (10 mL) was added, and the product was extracted with chloroform (3 × 5 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a yellow solid. This crude solid was then purified by flash chromatography over silica gel (hexane–EtOAc 15:1) to give **12** as a clear oil (3.00 mg, 6.60 μmol, 7%). ^{1}H NMR (300 MHz, C_6D_6): δ 5.82 (t, $J = 1.7$, 2H, olefinic), 3.68 (s, 2H, C<u>H</u>N), 3.33 (br s, 2H, N<u>H</u>), 2.62 (s, 2H, bridgehead), 1.20 (d, $J = 9.3$, 1H, apical), 0.82 (d, $J = 9.3$, 1H, apical); ^{13}C NMR (C_6D_6): δ 145.7, 143.2, 139.5, 137.0 (aromatic C's), 135.0 (olefinic), 67.5 (<u>C</u>HNH), 47.3 (bridgehead), 44.0 (apical); ^{19}F NMR (C_6D_6): δ − 159.4 (d, 4 F, *ortho*), −163.7 (t, 4 F, *meta*), −170.4 (t, 2 F, *para*); HRMS-ESI ($M + H^+$) m/z: calcd. for $C_{19}H_{10}F_{10}N_2$, 457.0763; obsd., 457.0749.

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