Lithiation-Substitutions of *N*-Boc *N*-Alkyl Cyclopropylamines

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A series of lithiation-substitution reactions at the α and β positions of *N*-Boc *N*-alkyl cyclopropyl amines is reported. The cyclopropane ring is the preferred position for lithiation in the *N*-ethyl and *N*-methyl derivatives **6** and **7**, but the *N*-allyl and *N*-benzyl derivatives **8** and **9** undergo lithiation at the methylene groups. Lithiations at β positions of the cyclopropylamine ring are observed if the α-position is blocked or the β-positions are activated by phenyl substitution as shown for the reactions of **10, 15** and **21**. Both α and β lithiations can be used in lithiation-cyclization reactions to provide the bicyclic spiro or endo fused *N*-Boc amines **15, 16** and **25**. Lithiations of *N*-Boc-4-tosyloxy piperidine **30** with *s*-BuLi/(-)-sparteine followed by trimethylsilyl chloride give the *N*-Boc azabicyclo[3.1.0] hexane **32** with enantiomeric excesses which range from 18-55%. Two β-carbomethoxy substituted *N*-Boc cyclopropylamines **18** and **26** can participate in a formal [3+2] cycloaddition with tetracyanoethylene to give highly substituted cyclopentanes.
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Lithiation-substitution at the α positions of *N*-Boc derivatives of primary and secondary amines provide a key reaction in a developing strategy for regioselective, diastereoselective and enantioselective amine synthesis.[1] We now report extension of this methodology to *N*-Boc *N*-alkyl cyclopropylamines.[2] This approach allows replacement of the α and β protons of the cyclopropyl ring in the sequences shown for the conversion of **1** to **2** and **3**.
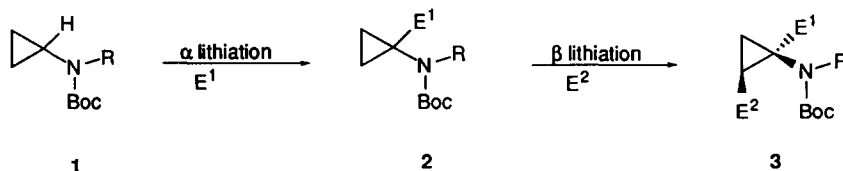

The presence of an activating group on a cyclopropyl ring enhances deprotonative lithiation. The sequence of α-lithiation-substitution of cyclopropanes has been successfully performed with carboxylate[3a-c], cyano[3d], isocyano[3e], sulfonyl[3f-g] sulfide[3h], phenyl[3i], vinyl[3j], acetylene[3k-l] and carbamate[3m] groups as activating groups. For the β-substitution of

cyclopropanes, N,N-diisopropylcarbamoyl[4a], hydroxymethyl[4b-d], and N-phenyl carbamoyl[4e] groups have been effective activating and directing groups. The combination of $sp^{2.3}$ hybridization of the C-H bond, resonance, inductive and complexing effects of the substituents can be used to rationalize the lithiations.[5] The β-lithiations proceed stereospecifically: the new substituent is introduced *cis* to the activating group, consistent with favorable organization of a transition state in which the base is delivered and the developing carbanion is stabilized by complexation of organolithium with the activating group.[6] Eaton has noted for cyclopropyl amides, that even though a thermodynamically more acidic α-proton may be available, the complex induced proximity effect can overcome the resonance and inductive effects so that the β-proton can be magnesiated preferentially.[7]

The construction of highly functionalized cyclopropanes has received substantial attention, since the cyclopropyl group is found as a structural element in a large number of naturally occurring compounds of biological importance and is a synthetically useful intermediate in organic synthesis.[8] There is recent interest in the preparation of enantioenriched cyclopropanes and methods based on catalytic activation and chiral ligands have been developed.[9] Cyclopropyl amino acids have been of special interest because of their potential in biological studies.[10]

α-Lithiation-substitution of N-Boc Cyclopropylamine

The facile α-lithiation-substitution reactions of the N-Boc cyclopropylamines **4** and **6** to give **5** and **10** respectively in good yields have been reported.[2] The lithiations of **4** and **6** provide the first cases in which formation of a dipole-stabilized carbanion occurs by deprotonation of an unstabilized formal tertiary position of a carbamate in the presence of an available secondary position. This result is different from previous observations of secondary over tertiary lithiation in unsymmetrical cyclic cases[11a] and primary over secondary deprotonation in an unsymmetrical acyclic N-Boc amine[11b].
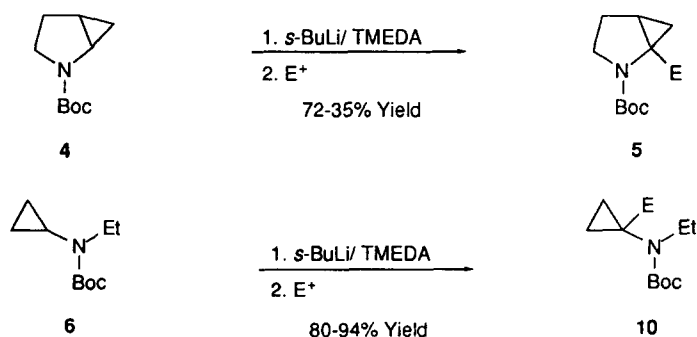
To evaluate the preferred position for α-lithiation in a competition between a cyclopropyl and selected alkyl groups, the *N*-Boc-*N*-alkyl cyclopropylamines **6-9** were investigated. The results are shown in Table 1. Lithiation of *N*-Boc-*N*-ethyl cyclopropylamine (**6**) occured at the cyclopropyl ring to give **10** regiospecifically. When *N*-Boc-*N*-methyl cyclopropylamine (**7**) was treated with *s*-BuLi/TMEDA and 1-bromo-4-chlorobutane, two regioisomers **11a** and **11b** were produced in a ratio of 1.4 : 1 in 42% yield. Compound **11a** which arises from the lithiation-substitution at the cyclopropyl tertiary position is the major product of the reaction. Because the products **11a** and **11b** could not be separated by chromatographic techniques, the ratio was determined by ¹H-NMR of the product mixture and the structural assignments to **11a** and **11b** were established by ¹H-NMR and ¹³C-NMR with comparison to authentic compound **11b** prepared independently.

In the competition for deprotonation between a cyclopropyl proton and an allylic proton in **8**, the lithiation takes place at the allylic position exclusively and the reaction of the electrophile occurrs at the γ-position regiospecifically.[12] The carbon-carbon double bond is assigned the Z configuration based on the coupling constant of the adjacent olefinic protons (J = 8.5 Hz). In the competition between a cyclopropyl activated position and a benzyl activated position with *N*-Boc *N*-benzyl cyclopropylamine (**9**) and EtI, the lithiation-substitution took place at the benzylic position to generate compound **13** exclusively.
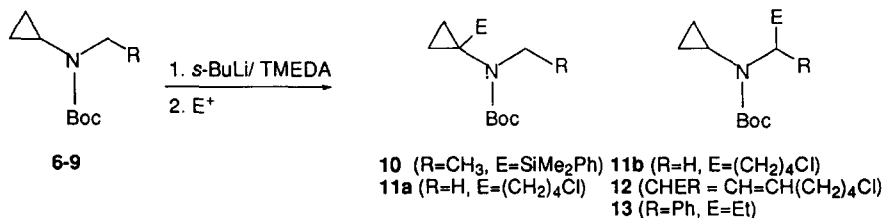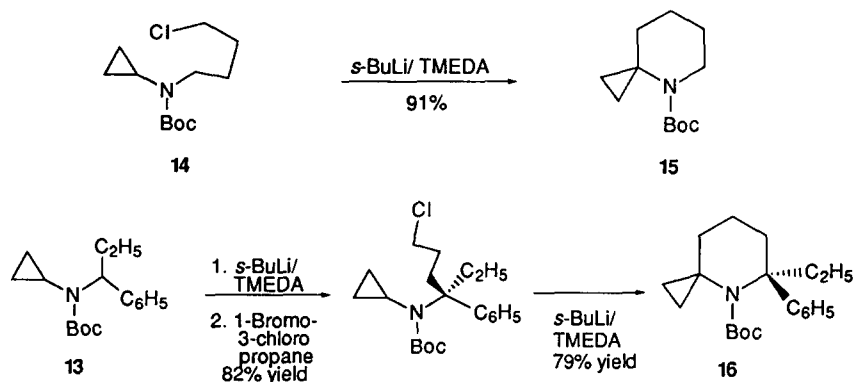

1. *s*-BuLi/ TMEDA
2. E⁺

6-9

10 (R=CH₃, E=SiMe₂Ph) **11b** (R=H, E=(CH₂)₄Cl)
11a (R=H, E=(CH₂)₄Cl) **12** (CHER = CH=CH(CH₂)₄Cl)
13 (R=Ph, E=Et)

Table 1. Regioselectivity of the Lithiation-Substitution of **6, 7, 8** and **9**

RCH₂	Reactant	E⁺	Product	yield (%)
CH₃CH₂	**6**	PhMe₂SiCl	**10**	83
CH₃	**7**	Cl(CH₂)₄Br	**11a/11b**	42 (60:40)
CH₂=CHCH₂	**8**	Cl(CH₂)₃Br	**12**	85
PhCH₂	**9**	EtI	**13**	93

A synthetic application of this methodology for the syntheses of azaspiro compounds bearing cyclopropyl rings is illustrated by the syntheses of **15** and **16**. The *N*-Boc cyclopropyl amine **14** was prepared by the reaction of *N*-Boc cyclopropylamine with 1-bromo-4-chlorobutane

and NaH. Treatment of **14** with *s*-BuLi/TMEDA in ether for 5 h at -78 °C afforded the azaspiro compound **15** in 91% yield.

When α-ethyl substituted benzyl cyclopropylamine **13** was treated with *s*-BuLi/TMEDA, the lithiation-substitution of **13** took place at the benzylic position to give the α,α-disubstituted product regiospecifically in the competition between two tertiary positions. The 5-ethyl, 5-phenyl substituted azaspiro compound **16** was obtained in 65% overall yield from **13**, when the disubstituted product was treated with *s*-BuLi/TMEDA at -78 °C for 5 h. These intramolecular cyclizations should be extendable to the preparation of other azaspiro systems.
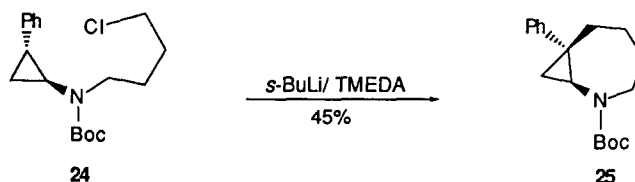

β-Lithiation-substitution of *N*-Boc Cyclopropylamine

The lithiation-substitution of the cyclopropyl ring at the β-position was investigated with the α-substituted cyclopropylamines **10**, **15**, and **19**. When **10** was treated with *s*-BuLi/TMEDA at -78 °C for 30 h followed by dimethyl carbonate, the β-position was lithiated and substituted to give **17** in moderate yield. However, when the α-substituent is Me, Et or 4-chlorobutyl, the desired product was not detected and starting material was recovered, demonstrating that the α-substituent can affect the lithiation at the β-position. We have also found that the azaspiro compound **15** can be substituted at the β-position to give **18** in 64% yield, after treatment with *s*-BuLi/TMEDA at -78 °C for 30 h followed by dimethylcarbonate. The azabicyclic compound **19** has three possible positions which can be lithiated and substituted; the α-pyrrolidine, the β-cyclopropane, and the benzylic position. When **19** was treated with *s*-BuLi/TMEDA at -78 °C for 10 h, the pyrrolidine α-position was lithiated exclusively and two diastereomers of **20** were produced in a ratio of 1.5 : 1.
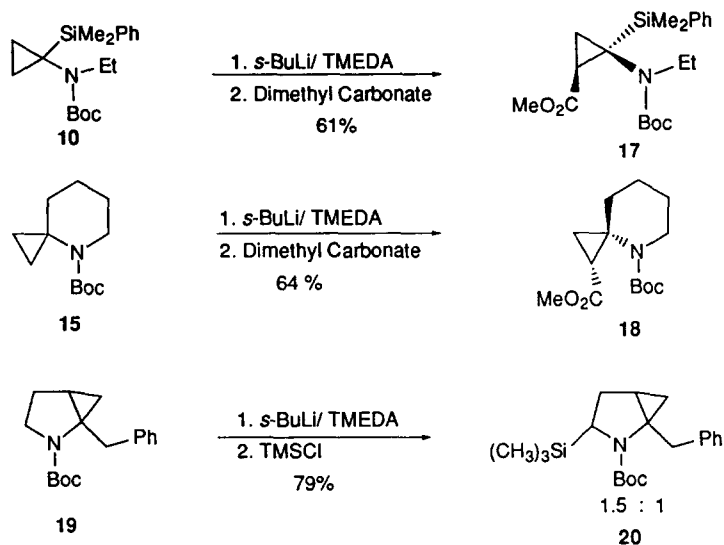
We also investigated whether a β-position could be selectively lithiated in preference to an α-position if additional activation is provided for β-lithiation by phenyl substitution. When **21** was treated with *s*-BuLi/TMEDA at -78 °C for 8 h followed by EtI, the major product **22** was obtained from the lithiation-substitution at the β-benzylic position. A minor product **23** was obtained from the lithiation-substitution of the other β-position. The phenyl group has apparently activated both β positions and products from lithiation at the α-position were not observed.[13] The regioselectivity of the lithiations was increased from 2 : 1 to 31 : 1 (**22 : 23**), when **21** was treated with *s*-BuLi/(-)-sparteine under the same reaction conditions. In an attempt to synthesize enantioenriched cyclopropylamines, **21** was treated with 0.5 equiv of *s*-BuLi/(-)-sparteine and MeI at -78° C for 4 h in THF. However, **21** was not kinetically resolved in the reaction and the racemic product **22** was obtained in 6% yield.

2 : 1 (TMEDA)
2 : 1 (none)
9 : 1 (none in ether)
31 : 1 (sparteine)
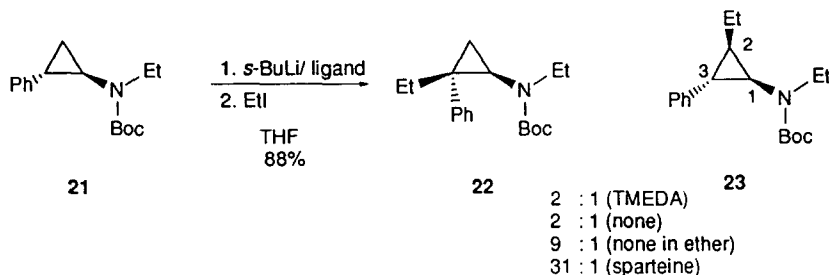
The lithiation-substitution reactions of **21** proceeds with high stereoselectivity; the new substituent is introduced *cis* to the activating group.[4] The geometry of **22** was deduced from NOE experiments which showed an enhancement of signal intensity of aromatic protons on irradiation of the methylene proton which is *cis* to the α-proton. The *cis* proton is assigned by the coupling constants with the α-proton. The geometry of 2-ethyl-3-phenyl cyclopropylamine (**23**) was inferred from a coupling constant of $J_{1,2} = 7.1$ Hz, between the C_1 proton and the C_2 proton, which indicates their *cis* relationship.[14]


In an application of this methodology to the syntheses of azabicyclic compound, the intramolecular lithiation-substitution cyclization reaction of compound **24** produced the azabicyclo [5.1.0] fused ring compound **25** in 45% yield. The other product of the reaction of **24** was the olefin resulting from HCl elimination from the chlorobutyl group. An attempt to make the corresponding piperidine by reaction of *N*-Boc 3-chloropropyl phenylcyclopropyl amine with *s*-BuLi/TMEDA at -78 °C for 9 h, gave only the elimination product.

[3+2] Cycloaddition of a *N*-Boc β-carbomethoxy Cyclopropylamine

The introduction of an CO_2Me to the β position of an *N*-Boc cyclopropyl amine offered an opportunity to asses the products as synthetic equivalents for an all carbon 1,3-dipole. When **21** was treated with *s*-BuLi at -78 °C for 8 h in ether followed by dimethyl carbonate, the 2-carboxymethyl-2-phenyl cyclopropylamine **26** was obtained in 81% yield. Compound **26** as a vicinally electron donor-acceptor activated cyclopropyl ring compound can be envisioned to undergo a ring opening to give the reactive intermediate **27** which could participate in [3+2] cycloaddition.[15]
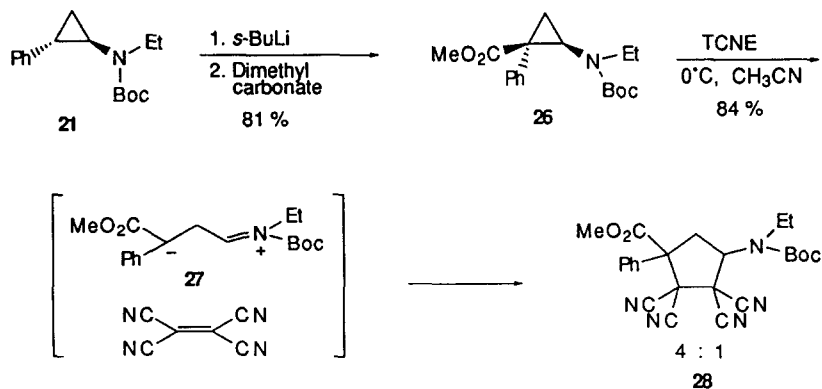
To test this possibility, tetracyanoethylene (TCNE) was allowed to react with **26**. The products of a formal [3+2] cycloaddition were obtained as two diastereomers of **28** in a ratio of 4 : 1 in 84% yield. We also found that **18** which does not bear a phenyl group produces the cyclopentane derivative **29** stereospecifically in the reaction with TCNE in high yield. However, the silyl substituted compound **17** did not give the corresponding product in a reaction with TCNE.
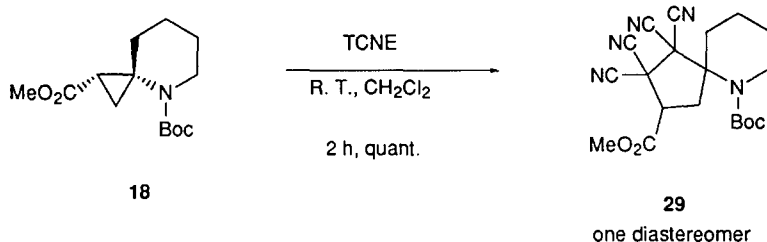
In an effort to broaden the synthetic utility of this cycloaddition, the donor-acceptor activated cyclopropane **26** was treated with the less activated electrophiles; fumaronitrile, dimethyl maleate, and acrylonitrile respectively. The reactions did not produce cyclopentane derivatives even at reflux and starting materials were recovered.

Asymmetric Synthesis of *N*-Boc Azabicyclic[3.1.0]hexane

In previous work,[2] we reported 2-azabicyclo [3.1.0] hexane **32** was readily formed by treatment of *N*-Boc-4-chloropiperidine with 2.2 equiv of *s*-BuLi/TMEDA for 8 h at -78 °C followed by TMSCl. The 2-azabicyclo[3.1.0]ring system is closely related to derivatives of

aminocyclopropanecarboxylic acids and to the indolizidine-pyrrolizidine alkaloid ring systems.
A facile preparation of enantioenriched compounds would be of interest.[10,16]   In order to
investigate the possibility, s-BuLi/(-)-sparteine[17] was used to induce asymmetry.   Reaction of
N-Boc-4-chloropiperidine with s-BuLi/(-)-sparteine gave 32 in 71% yield in racemic form.   The
leaving group effect on the enantioselectivity of the intramolecular cyclization was studied.   The
tosylate 30 and nosylate 31 which have better and bulkier leaving groups at 4-position than the
chloride give better enantiomeric excesses than the chloride.   Treatment of N-Boc-4-tosyloxy
piperidine 30 with 2.2 equiv of s-BuLi/(-)-sparteine at -78 °C for 4 h in diethyl ether followed by
addition of TMSCl gives enantioenriched 32 in good yield with moderate enantiomeric excess
(55% ee) as shown in Table 2.   The enantioenrichment of 32 was determined by conversion of
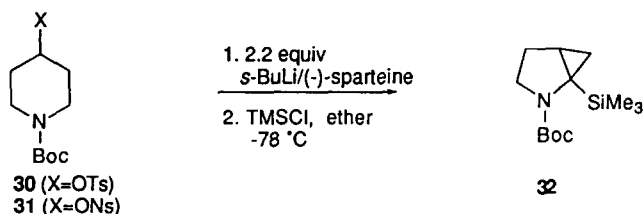the product to the corresponding 3,5-dinitrobenzamide with analysis by CSP-HPLC.

Table 2. Enantioselectivity in the Lithiation-cyclizations of 30 and 31.

Reactant	Solvent	Ligand	Yield (%)	% ee
30	ether	(-)-sparteine	77	55
30	ether, -100° C	(-)-sparteine	41	58
30	ether:pentane (1:1)	(-)-sparteine	51	47
30	t-BuOMe	(-)-sparteine	63	44
30	THF	(-)-sparteine	81	18
30	ether	33	32	-47
30	ether	34	28	-3
31	ether	(-)-sparteine	43	42

(-)-sparteine   33   34
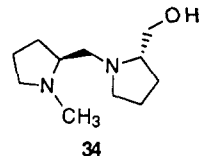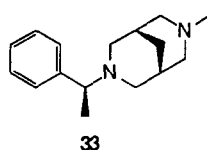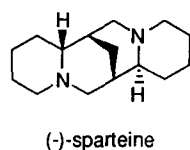
As shown in Table 2, the reaction of tosylate **30** was carried out in several different solvents under the same reaction conditions as the reaction in ether. The enantiomeric excess was 47% ee in 1:1 mixture of ether and *n*-pentane, 44% ee in *t*-BuOMe, and 18% ee in THF. In a search for new ligands which would give high enantioselectivity and be readily available in both enantiomeric forms, the bispidine ligand **33** and the diamino alcohol **34** were investigated.[18] Use of **33** as a ligand for the reaction of **30** in ether provided **32** with -47% ee and use of **34** for the reaction of **30** provided racemic **32**. The increased enantioselectivities of the 4-arenesulfonate sustituted *N*-Boc piperidines compared to 4-chloro *N*-Boc piperidine may be attributed to the increased conformational rigidity of **30** and **31** due to the diaxial interactions and/or to the increased reaction rate due to the better leaving group abilities in **30** and **31**.

In summary the *N*-Boc group is effective as an activating and directing group for the α and β lithiations substitutions of *N*-Boc cyclopropanes. In competition with an ethyl or methyl group, the cyclopropyl group is the preferred position for α-lithiation of *N*-Boc-*N*-alkyl cyclopropylamine. In the β lithiation-substitutions, the reactions proceed stereospecifically with the new substituent introduced *cis* to the Boc group. Bicyclic *N*-Boc cyclopropyl amines in which the cyclopropyl ring is spiro or endo fused can be prepared by this methodology. A formal [3+2] cycloaddition is demonstrated with two β-carbomethoxy *N*-Boc cyclopropyl amines and tetracyanoethylene but the reaction could not be generalized. Asymmetric synthesis of *N*-Boc azabicyclic[3.1.0]hexane can be carried out with *s*-BuLi/(-)-sparteine and *N*-Boc-4-tosyloxy piperidine.

EXPERIMENTAL

General All reagents and solvents were obtained from commercial sources and used without further purification, unless mentioned otherwise. (-)-Sparteine, TMEDA, and CH_3CN were distilled from calcium hydride under a nitrogen atmosphere. THF, diethyl ether, *t*-BuOMe, and *n*-pentane were distilled from sodium and benzophenone under a nitrogen atmosphere.

General Procedure for the Preparation of *N*-Boc-*N*-alkyl-cyclopropylamines 7, 8, 9, 14, 21 and 24.

To a solution of cyclopropylamine(1.0 equiv) in methylene chloride at 0° C was added dropwise a solution of 1.1 equiv of $(Boc)_2O$ in methylene chloride. After stirring the mixture for 1 h at room temperature, the methylene chloride was removed and the residue was taken up in hot hexane. Cooling provided *N*-Boc-cyclopropylamine as white crystals. The resulting crystals were dissolved in THF and slowly added to the solution of NaH and methyl iodide (allyl bromide, benzyl bromide, or 1-bromo-4-chlorobutane) in THF at 0° C. After stirring the mixture for 10 h at room temperature, the mixture was dissolved in water at 0° C, extracted with ether

and dried over MgSO4. Concentration of the ether extracts gave a yellow oil that was purified by flash chromatography.

N-Boc-N-methyl-cyclopropylamines (7)

From N-Boc cyclopropylamine (1.0 equiv) and methyl iodide (1.2 equiv), 2.6 g (95%) of 7 was obtained as a colorless oil. ^1H NMR (CDCl3, 300 MHz) δ 2.76 (s, 3H, N-CH3), 2.43 (m, 1H, N-CH), 1.39 (s, 9H), 0.65-0.52 (m, 4H, (CH2)2) ; ^{13}C NMR (CDCl3, 75 MHz) δ 156.9, 79.1, 34.6, 30.2, 28.3, 7.7; EIMS (70eV) m/z (relative intensity) 171 (4, M+), 156 (4), 115 (95), 98 (51), 71 (100), 57 (100); HRMS Calcd for $C_9H_{17}NO_2$: 171.1259 Found: 171.1259.

N-Boc-N-allyl-cyclopropylamines (8)

From N-Boc cyclopropylamine (1.0 equiv) and allyl bromide (1.2 equiv), 2.1 g (87%) of 8 was obtained as a colorless oil. ^1H NMR (CDCl3, 300 MHz) δ 5.78-5.73 (m, 1H, CH=CH2), 5.09-5.03 9m, 2H, CH=CH2), 3.77 (m, 2H, CH2CH=CH2), 2.49 (m, 1H), 1.42 (s, 9H, C(CH3)3), 0.70-0.56 (m, 4H, (CH2)2) ; ^{13}C NMR (CDCl3, 75 MHz) δ 156.5, 134.5, 115.4, 79.3, 50.5, 29.1, 28.3, 7.7; CIMS (70eV) m/z (relative intensity) 198 (M++1); HRMS Calcd for $C_{11}H_{20}NO_2$ (M++1): 198.1494, Found: 198.1489.

N-Boc-N-benzyl-cyclopropylamines (9)

From N-Boc cyclopropylamine (1.0 equiv) and benzyl bromide (1.2 equiv), 1.2 g (82%) of 9 was obtained as a colorless oil. ^1H NMR (CDCl3, 300 MHz) δ 7.30-7.19 (m, 5H, Ph), 4.41 (s, 2H, CH2Ph), 2.44 (m, 1H, N-CH), 1.44 (s, 9H), 0.66 (m, 4H, (CH2)2) ; ^{13}C NMR (CDCl3, 75 MHz) δ 156.6, 138.7, 128.2, 127.1, 126.7, 79.4, 51.3, 29.1, 28.2, 7.9; EIMS (70eV) m/z (relative intensity) 247 (1, M+), 191 (19), 174 (21), 156 (63), 132 (12), 112 (64), 91 (100), 84 (100), 70 (100), 57 (100); HRMS Calcd for $C_{12}H_{22}NO_2Cl$: 247.1339 Found: 247.1339.

N-Boc-N-4-chlorobutyl-cyclopropylamines (14)

From N-Boc cyclopropylamine (1.0 equiv) and 1-bromo-4-chloro-butane (1.2 equiv), 1.0 g (81%) of 14 was obtained as a colorless oil. ^1H NMR (CDCl3, 300 MHz) δ 3.56 (t, J = 6.0 Hz, 2H), 3.23 (t, J = 7.0 Hz, 2H), 2.48 (m, 1H, CH(CH2)2), 1.74 (m, 4H, CH(CH2)2), 1.45 (s, 9H), 0.73 (m, 2H), 0.58 (m, 2H); ^{13}C NMR (CDCl3, 75 MHz) δ 156.7, 79.4, 46.5, 44.7, 29.9, 28.6, 28.4, 25.7, 8.0; EIMS (70eV) m/z (relative intensity) 247 (1, M+), 191 (12), 146 (56), 132 (28), 91 (82), 57 (100); HRMS Calcd for $C_{15}H_{21}NO_2$: 247.1572 Found: 247.1572.

N-Boc-N-ethyl-2-phenyl cyclopropylamine (21)

From N-Boc trans 2-phenylcyclopropyl amine (1.0 equiv) and ethyl iodide (1.2 equiv), 21 was obtained in 89% yield. ^1H NMR (CDCl3, 300 MHz) δ 7.29-7.10 (m, 5H), 3.41-3.25 (m, 2H, NCH2), 2.72 (m, 1H), 2.10 (m, 1H), 1.43 (s, 9H), 1.24 (m, 2H, NCHCH2), 1.13 (t, J = 7.0 Hz, 3H, NCH2CH3); ^{13}C NMR (CDCl3, 75 MHz) δ 156.3, 141.0, 128.2, 126.0, 125.8, 79.4, 42.0, 38.0, 28.4, 26.2, 17.4, 13.5; EIMS (70eV) m/z (relative intensity) 261 (7, M+), 205 (19),

160 (16), 132 (12), 116 (31), 90 (19), 70 (27), 57 (100). HRMS Calcd for $C_{16}H_{23}NO_2$: 261.1729, Found: 261.1721.

N-Boc-*N*-(4-chlorobutyl) 2-phenyl cyclopropylamine (24)

From *N*-Boc *trans* 2-phenylcyclopropyl amine (1.0 equiv) and 1-bromo-4-chlorobutane (1.2 equiv), **24** was obtained in 80% yield. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.29-7.10 (m, 5H, Ph), 3.55 (t, J = 6.0 Hz, 2H, ClC$\underline{H}_2$), 3.37 (m, 2H, NC$\underline{H}_a$Hb), 3.26 (m, 2H, NCH$_a\underline{H}_b$), 2.69 (m, 1H), 2.10 (m, 1H), 1.75 (m, 4H), 1.42 (s, 9H), 1.25 (m, 2H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 156.4, 140.8, 128.2, 126.0, 125.9, 79.6, 46.2, 44.6, 38.3, 29.8, 28.4, 26.3, 25.6, 17.3; EIMS (70eV) m/z (relative intensity) 323 (4, M$^+$), 267 (44), 250 (8), 222 (29), 152 (47), 146 (66), 132 (100), 116 (100), 93 (98), 57 (100); HRMS Calcd for $C_{18}H_{26}NO_2Cl$: 323.1652, Found: 323.1655.

General Procedure for the Lithiation-Substitution reaction of *N*-Boc Cyclopropanes.

Intermolecular reactions of *N*-Boc *N*-Alkyl Cyclopropylamines

To TMEDA (1.2 equiv.) in THF (*ca.* 4 mL/mmol) at -78 °C was added *sec*-BuLi (1.2 equiv.). The mixture was stirred for 15 min and then *N*-Boc *N*-alkyl cyclopropylamine (1.0 equiv.) in THF (*ca.* 2 mL/mmol) was added to the solution slowly. The resulting mixture was stirred at-78 °C for 5-10 h (for **10** and **15**, 30 h), treated with electrophile (1.2 equiv.) in THF (*ca.* 1 mL/mmol), and then allowed to slowly warm to room temperature (*ca.* 3 h). The mixture was dissolved in water and extracted with ether and the organic layer was dried over MgSO$_4$ and concentrated to give a crude product which was purified by flash column chromatography on silica gel to give the product.

Intramolecular cyclization reactions of *N*-Boc *N*-Alkyl Cyclopropylamines

To TMEDA (1.2 equiv.) in THF(*ca.* 10 mL/mmol) at -78 °C was added *sec*-BuLi (1.2 equiv.). The mixture was stirred for 15 min and then starting material (1.0 equiv.) in THF (*ca.* 4 mL/mmol) was added to the solution slowly. The resulting mixture was stirred at -78 °C for 5-10 h, and then allowed to slowly warm to room temperature (*ca.* 3 h). The mixture was dissolved in water and extracted with ether and the organic layer was dried over MgSO$_4$ and concentrated to give a crude product which was purified by flash column chromatography on silica gel to give the product.

N-Boc *N*-ethyl-1-dimethylphenylsilyl cyclopropylamine (10)

From 284 mg of **6**, 406 mg (83%) of **10** was obtained as a colorless oil. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.50-7.33 (m, 5H, Ph), 3.01-2.98 (m, 2H, NC$\underline{H}_2$), 1.44 (s, 9H), 1.04 (m, 3H, NCH$_2$C$\underline{H}_3$), 0.85 (brs, 2H), 0.66 (brs, 2H), 0.34 (s, 6H, Si(C$\underline{H}_3$)$_2$); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 156.2, 134.0, 129.2, 129.0, 127.7, 79.0, 45.1, 29.3, 28.5, 15.4, 12.8, -3.6; EIMS (70eV) m/z (relative intensity) 319 (1, M$^+$), 304 (1), 262 (29), 248 925), 218 935), 190 (29), 172 (18), 135 (100), 105 (13), 57 (100). HRMS Calcd for $C_{18}H_{29}NO_2Si$: 319.1968, Found: 319.1968.

N-Boc N-5-chloropentyl cyclopropylamine (11a) and N-Boc N-methyl-1-(4-chlorobutyl) cyclopropylamine (11b)

From 171 mg of **7**, the mixture of **11a** and **11b** was obtained as 110 mg of a colorless oil in 42% yield. **(11b)** ^{1}H NMR (CDCl$_3$, 300 MHz) δ 3.54 (t, J = 6.6 Hz, 2H), 3.21 (t, J = 7.0 Hz, 2H), 2.49 (m, 1H, N-C$\underline{H}$), 1.80 (m, 2H), 1.58 (m, 2H), 1.46 (s, 9H), 0.74 (m, 2H), 0.58 (m, 2H) ; ^{13}C NMR (CDCl$_3$, 75 MHz) δ 156.4, 78.9, 46.9, 44.6, 32.0, 28.3, 28.2, 27.3, 23.9, 7.8; EIMS (70eV) m/z (relative intensity) 261 (1, M$^+$), 176 (10), 170 (11), 165 (5), 132 (10), 126 (10), 84 (17), 70 (27), 57 (100). **(11a)** ^{1}H NMR (CDCl$_3$, 300 MHz) δ 3.35 (t, J = 6.6 Hz, 2H), 2.84 (s, 3H), 1.9-1.4 (m, 6H), 1.46 (s, 9H), 0.83 (br, 2H), 0.66 (br, 2H); EIMS (70eV) m/z (relative intensity) 261 (1, M$^+$), 226 (6), 204 (11), 188 (22), 176 (12), 170 (68), 160 (10), 132 (15), 112 (14), 98 (26), 68 (10), 57 (100).

N-Boc-N-(6-chloro-cis-1-hexene) cyclopropylamine (12).

From 400 mg (2.0 mmol) of **8**, 464 mg of **12** was obtained as a colorless oil in 85% yield. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 5.93 (d, J = 8.5 Hz, 1H), 4.96 (q, 1H), 3.53 (t, J = 6.6 Hz, 2H), 2.73 (m, 1H), 2.14 (q, 2H), 1.79 (m, 2H), 1.53 (m, 2H), 1.47 (s, 9H), 0.79 (m, 2H), 0.60 (m, 2H) ; ^{13}C NMR (CDCl$_3$, 75 MHz) δ 155.1, 126.8, 121.7, 80.1, 44.8, 32.2, 30.0, 28.3, 26.5, 26.4, 8.7; CIMS m/z 274 (M$^+$+1); HRMS Calcd for C$_{14}$H$_{24}$NO$_2$Cl: 274.1574, Found: 274.1555.

N-Boc-N-(1-phenpropyl)-cyclopropylamine (13)

From 111 mg of **9**, 118 mg (93%) of **13** was obtained as a colorless oil. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.30-7.21 (m, 5H, Ph), 4.92 (t, J = 7.8 Hz, 1H, C$\underline{H}$-Ph), 2.31 (m, 1H, N-C$\underline{H}$(CH$_2$)$_2$), 2.13 (m, 2H, CH-C$\underline{H}_2$), 1.44 (s, 9H, C(CH$_3$)$_3$), 1.00 (t, J = 7.3 Hz, 3H, CH$_2$C$\underline{H}_3$), 0.56 (m, 4H, CH(CH$_2$)$_2$); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 157.3, 142.2, 127.9, 127.1, 126.6, 79.4, 62.1, 28.3, 27.8, 24.1, 11.4, 7.9, 7.1; EIMS (70eV) m/z (relative intensity) 275 (1, M$^+$), 219 (6), 190 (2), 174 (42), 146 (12), 119 (27), 91 (71), 57 (100). Anal. Calcd for C$_{17}$H$_{25}$NO$_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 73.82; H, 9.40; N, 5.48.

N-Boc-4-azaspiro[2.5]octane (15).

From 594 mg (2.4 mmol) of **14**, 461 mg of **15** was obtained as a colorless oil in 91% yield. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 3.41 (t, J = 5.3 Hz, 2H), 1.71 (m, 2H), 1.51 (m, 2H), 1.45 (s, 9H), 1.40 (m, 2H), 0.84 (br, 2H), 0.58 (br, 2H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 156.0, 79.1, 46.7, 38.6, 32.6, 28.4, 25.3, 24.1, 14.3; EIMS (70eV) m/z (relative intensity) 211 (3, M$^+$), 155 (24), 138 (12), 111 (19), 110 (73), 96 (15), 82 (21), 57 (100); HRMS Calcd for C$_{12}$H$_{21}$NO$_2$: 211.1572, Found: 211.1576.

N-Boc-4-aza-5-ethyl-5-phenyl spiro[2.5]octane (16).

From 500 mg (1.8 mmol) of **13**, 518 mg of N-Boc-N-(1-ethyl-1-phenyl-4-chlorobutyl) cyclopropylamine was obtained as a colorless oil in 82% yield. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.30-7.15 (m, 5H), 3.52 (t, J = 6.4 Hz, 2H), 2.59 (m, 1H), 2.56 (m, 1H), 2.41 (m, 1H), 2.10 (m,

1H), 1.99 (m, 1H), 1.67 (m, 1H), 1.50 (m, 1H), 1.04 (s, 9H), 0.97 (m, 2H), 0.76 (m, 1H), 0.70 (t, J = 7.4 Hz, 3H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 157.2, 149.2, 127.8, 125.9, 125.3, 67.8, 45.6, 32.1, 28.48, 28.41, 27.9, 27.8, 11.2, 10.9, 8.9 ; EIMS (70eV) m/z (relative intensity) 322 (1, M$^+$-Et), 295 (2), 266 (2), 250 (1), 222 (6), 197 (23), 195 (71), 153 (15), 132 (6), 117 (20), 105 (48), 101 (38), 91 (100), 57 (100).

From 32 mg (0.09 mmol) of *N*-Boc-*N*-(1-ethyl-1-phenyl-4-chlorobutyl) cyclopropyl amine, 22 mg of **16** was obtained as a colorless oil in 79% yield. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.36-7.15 (m, 5H), 2.41 (m, 2H), 2.02 (m, 2H), 1.68 (m, 2H), 1.56 (m, 1H), 1.35 (m, 1H), 1.2 (m, 2H), 1.19 (s, 9H), 0.84 (t, J = 7.4 Hz, 3H), 0.63 (m, 2H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 155.9, 148.4, 127.5, 125.7, 125.6, 66.5, 35.5, 33.8, 33.0, 31.4, 28.2, 17.3, 17.2, 14.4, 9.88; EIMS (70eV) m/z (relative intensity) 315 (6, M$^+$), 259 (22), 242 (10), 230 (27), 200 (16), 186 (88), 145 (12), 117 (15), 91 (22), 57 (100). HRMS Calcd for C$_{20}$H$_{29}$NO$_2$: 315.2198, Found: 315.2198.

N-Boc-*N*-ethyl-1-dimethylphenylsilyl-2-carboxymethyl cyclopropylamine (17).

From 95 mg (0.30 mmol) of **10**, 69 mg of **17** was obtained as a colorless oil in 61% yield. ^{1}H NMR (two rotomers, CDCl$_3$, 300 MHz) δ 7.52-7.35 (m, 5H), 3.66, 3.60 (s, 1H), 3.40, 3.17 (m, 1H), 2.94 (m, 1H), 1.94, 1.83 (t, J = 6.9 Hz, J = 6.3 Hz, 1H), 1.59, 1.54 (t, J = 5.6 Hz, J = 5.8 Hz, 1H), 1.41, 1.40 (s, 9H), 1.16, 1.10 (t, J = 7.0 Hz, J = 7.0 Hz, 3H), 0.99 (dd, J = 5.3 Hz, 8.1 Hz, 1H), 0.42 (s, 3H), 0.36, 0.34 (s, 3H); ^{13}C NMR (two rotomers CDCl$_3$, 75 MHz) δ (171.18, 171.00), (155.66, 155.21), (136.20, 135.77), (134.11, 133.97), (129.61, 129.42), (127.99, 127.83), (79.78, 78.90), (51.85, 51.44), (45.35, 44.73), (38.93, 38.61), (28.22, 28.15), (26.99, 26.45), (18.84, 17.81), (14.86, 14.27), (-3.60, -3.64), (-3.80, -3.90); EIMS (70eV) m/z (relative intensity) 320 (1, M$^+$-*t*-Bu), 276 (92, M$^+$-Boc), 244 (11), 190 (33), 172 (81), 144 (16), 135 (100), 105 (17), 89 (15), 57 (95); CIMS m/z 378 (M$^+$+1); HRMS Calcd for C$_{20}$H$_{31}$NO$_4$Si (M$^+$+1) : 378.2101, Found: 378.2090.

N-Boc-1-carboxymethyl-4-azaspiro[2.5]octane (18)

From 229 mg (1.08 mmol) of **15**, 189 mg of **18** was obtained as a colorless oil in 64% yield. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 4.06 (br, 1H), 3.64 (s, 3H, CO$_2$Me), 2.36 (br, 1H), 2.08-1.01 (m, 7H), 1.42 (s, 9H, C(CH$_3$)$_3$), 0.85 (m, 2H, CH$_2$CN); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 170.8, 154.9, 79.5, 51.6, (47.6, 46.9), 45.4, (34.4, 33.4), 30.2, (28.3, 28.1), 26.3, (25.3, 24.6), 23.9; EIMS (70eV) m/z (relative intensity) 269 (1, M$^+$), 212 (12), 182 (14), 169 (93), 154 (96), 110 (100), 57 (100); HRMS Calcd for C$_{14}$H$_{23}$NO$_4$: 269.1627, Found: 269.1626.

N-Boc-1-benzyl-3-trimethylsilyl-2-azabicyclo[3.1.0]hexane (20).

From 36 mg (0.13 mmol) of **19**, 26 mg of **20-major** was obtained as a colorless oil in 57% yield. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.26-7.12 (m, 5H), 3.42 (d, J = 13.2 Hz, 1H), 3.40(t, J = 7.9 Hz, 1H), 3.14 (d, J = 13.2 Hz, 1H), 1.95 (dd, J = 7.8 Hz, 4.2 Hz, 1H), 1.53 (s, 9H), 1.5 (1H), 1.26 (m, 1H), 0.80 (dd, J = 5.1 Hz, 8.7 Hz, 3H), 0.51 (t, J = 5.0 Hz, 1H), -0.07 (s, 9H);

^{13}C NMR (CDCl$_3$, 75 MHz) δ 157.3, 138.5, 130.1, 128.1, 126.2, 79.3, 53.1, 49.4, 44.6, 38.7, 28.6, 23.5, -3.1; EIMS (70eV) m/z (relative intensity) 345 (1, M$^+$), 288 (20), 274(20), 244 (32), 230 (15), 198 (15), 172 (68), 154 (28), 91 (29), 73 (68), 57 (100), and 10 mg of **20-minor** was obtained as a colorless oil in 22% yield. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.30-7.14 (m, 5H), 3.58 (d, J = 13.9 Hz, 1H), 3.04 (dd, J = 8.4 Hz, 11.1 Hz, 1H), 2.55 (d, J = 13.9 Hz, 1H), 2.03 (m, 1H), 1.52 (s, 9H), 1.5 (1H), 0.99 (dd, J = 5.0 Hz, 8.5 Hz, 1H), 0.60 (t, J = 4.6 Hz, 1H), -0.03 (s, 9H); EIMS (70eV) m/z (relative intensity) 345 (1, M$^+$), 288 (25), 274 (43), 244 (35), 230 (21), 198 (19), 172 (69), 154 (30), 113 (16), 91 (34), 73 (70), 57 (100). HRMS Calcd for C$_{20}$H$_{30}$NO$_2$Si: 344.2046, Found: 344.2042.

N-Boc-N-ethyl-2-ethyl-2-phenyl cyclopropylamine (22).

From 88 mg (0.34 mmol) of **21**, 61 mg of **22** was obtained as a pale yellow oil in 62% yield. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.47-7.16 (m, 5H), 3.57 (m, 1H), 3.11 (m, 1H), 2.78 (dd, J = 8.0 Hz, 5.1 Hz, 1H), 1.88 (m, 1H), 1.52 (s, 9H), 1.32 (m, 1H), 1.24 (dd, J = 8.2 Hz, 6.0 Hz, 1H), 1.13 (t, J = 7.3 Hz, 3H), 0.86 (t, J = 7.3 Hz, 3H), 0.75 (dd, J = 6.0 Hz, 5.2 Hz, 1H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 157.0, 144.3, 129.1, 128.0, 126.1, 79.7, 42.7, 42.0, 34.8, 28.6, 26.4, 16.9, 13.6, 11.2; EIMS (70eV) m/z (relative intensity) 233 (7, M$^+$-t-Bu), 204 (6), 188 (7, M$^+$-Boc), 160 (45), 144 (82), 133 (20), 117 (11), 115 (15), 91 (17), 57 (100), 56 (56); HRMS Calcd for C$_{18}$H$_{27}$NO$_2$: 289.2042, Found: 289.2043.

N-Boc-N-ethyl-2-ethyl-3-phenyl cyclopropylamine (23).

From 88 mg (0.34 mmol) of **21**, 26 mg of **23** was obtained as a pale yellow oil in 26% yield. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.30-7.10 (m, 5H), 3.50 (m, 1H), 3.21 (m, 1H), 2.91 (dd, J = 7.1 Hz, 4.1 Hz, 1H), 1.78 (m, 1H), 1.75 (t, J = 4.8 Hz, 1H), 1.47 (s, 9H), 1.36 (1H), 1.2 (1H), 1.11 (t, J = 6.8 Hz, 3H), 1.06 (t, J = 7.1 Hz, 3H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 156.6, 141.7, 128.3, 126.2, 125.8, 79.4, 43.1, 42.8, 32.9, 29.6, 28.4, 21.2, 13.9, 13.4; EIMS (70eV) m/z (relative intensity) 289 (1, M$^+$), 260 (3), 233 (61), 204 (62), 188 (22), 160 (100), 144 (51), 133 (34), 117 (20), 115 (20), 91 (19), 57 (83), 56 (33); HRMS Calcd for C$_{18}$H$_{27}$NO$_2$: 289.2042, Found: 289.2043.

N-Boc-7-phenyl-2-azabicyclo[5.1.0]octane (25).

From 143 mg (0.30 mmol) of **24**, 39 mg of **25** was obtained as a pale yellow oil in 45% yield. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.32-7.17 (m, 5H), 4.05 (br, 1H), 3.06 (br, 1H), 2.89 (t, J = 6.0 Hz, 1H), 2.42 (br, 1H), 1.75 (br, 1H), 1.58 (m, 4H), 1.48 (s, 9H), 1.4 (1H), 1.3 (1H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ (APT) 158.8, 144.8 (+), 128.5 (-), 128.3 (-), 126.1 (-), 79.3 (+), 49.9 (+), 41.6 (-), 37.3 (+), 32.5 (+), 30.1 (+), 28.6 (-), 26.8 (+), 24.6 (+); EIMS (70eV) m/z (relative intensity) 287 (3, M$^+$), 231 (65), 186 (53), 170 (32), 158 (10), 144 (21), 129 (16), 117 (17), 115 (18), 91 (28), 57 (100); HRMS Calcd for C$_{18}$H$_{25}$NO$_2$: 287.1885, Found: 287.1888.

N-Boc-N-ethyl-2-carboxymethyl-2-phenyl cyclopropylamine (26).

From 363 mg (1.4 mmol) of **21**, 362 mg of **26** was obtained as a colorless oil in 81% yield. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.61-7.25 (m, 5H), 3.58 (s, 3H), 3.34-3.09 (m, 3H), 2.06 (t, J = 5.2 Hz, 1H), 1.49 (s, 10H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 170.9, 155.9, 139.2, 130.4, 128.0, 127.2, 79.5, 52.2, 44.1, 42.2, 37.9, 28.4, 20.6, 13.5; EIMS (70eV) m/z (relative intensity) 319 (2, M$^+$), 263 (23), 219 (73), 204 (68), 190 (38), 187 (48), 160 (40), 158 (45), 115 (18), 103 (27), 70 (10), 57 (100); HRMS Calcd for C$_{18}$H$_{25}$NO$_4$: 319.1783, Found: 319.1777.

Procedure for the Synthesis of N-Boc-N-ethyl-2,2,3,3-tetracyano-4-carboxy methyl-4-phenyl cyclopentylamine (28)

To a solution of tetracyanoethylene (20 mg, 1.1 equiv) in 3 mL of CH$_3$CN was added a solution of **26** (45 mg, 0.14 mmol) in 2 mL of CH$_3$CN. The resulting reaction mixture was stirred at 0 °C for 4 h, and was then allowed to slowly warm to room temperature. Ether was added and then extracted with sat. NaCl solution. The organic layer was dried over anhydrous MgSO$_4$ and concentrated *in vacuo*. The crude product was purified by silica flash chromatography to give **28-major** (44 mg, 71% yield) and **28-minor** (8 mg, 13% yield) as a colorless oil in a ratio of 4:1. The diastereomeric ratio was determined by ^{1}H NMR of the crude products mixture. **28-major :** ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.64-7.61 (m, 2H), 7.54-7.26 (m, 3H), 5.39 (br, 1H), 3.89 (s, 3H), 3.73 (br, 1H), 3.41 (br, 1H), 3.19 (br, 1H), 2.91 (br, 1H), 1.55 (s, 9H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 167.3, 155.8, 132.8, 130.6, 129.9, 126.4, 111.4, 110.2, 110.1, 109.3, 82.9, 64.8, 62.5, 54.7, 51.6, 50.3, 40.1, 35.2, 28.2, 15.7; CIMS m/z 448 (M$^+$+1). HRMS Calcd for C$_{24}$H$_{26}$N$_5$O$_4$ (M$^+$+1): 448.1985, Found: 448.1971. **28-minor :** ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.73–7.70 (m, 2H), 7.54-7.52 (m, 3H), 5.74 (t, J = 9.8 Hz, 1H), 3.89 (s, 1H), 3.78 (br, 1H), 3.32 (m, 2H), 3.08 (br, 1H), 1.53 (s, 9H), 1.24 (t, J = 6.9 Hz, 3H).

N-Boc-1,1,2,2-tetracyano-3-carboxymethyl-6-azaspiro[4.5]decane (29)

To a solution of tetracyanoethylene (1.1 equiv) in 4 mL of CH$_3$CN was added a solution of **18** (40 mg, 0.15 mmol) in 2 mL of CH$_3$CN. The resulting reaction mixture was stirred at room temperature for 2 h. Ether was added and then extracted with sat. NaCl solution. The organic layer was dried over anhydrous MgSO$_4$ and concentrated *in vacuo*. The crude product was purified by silica flash chromatography to give 60 mg (99%) of **29** as a yellow oil. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 4.66 (br, 1H, NCH$_a$H$_b$), 4.22 (br, 1H, NCH$_a$H$_b$), 3.90 (s, 3H, CO$_2$Me), 3.49 (br, 1H), 2.40 (m, 1H), 2.28 (m, 1H), 2.13 (m, 1H), 2.00 (m, 1H), 1.75 (m, 2H), 1.59 (m, 2H), 1.48 (s, 9H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 166.7, 155.0, 110.8, 110.1, 109.9, 109.6, 82.6, 71.6, 67.0, 60.4, 53.6, 51.7, 47.5, 45.1, 28.1, 23.5, 21.0, 19.9; CIMS m/z 398 (M$^+$+1); HRMS Calcd for C$_{20}$H$_{24}$N$_5$O$_4$ (M$^+$+1): 398.1828, Found: 398.1821.

N-Boc piperidine 4-*p*-toluenesulfonate (30)

From *N*-Boc 4-hydroxy piperidine (1.0 equiv) and *p*-toluenesulfonyl chloride (1.2 equiv), **30** was obtained as a white solid in 79% yield. mp 99-100° C; ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.80 (d, J = 8.1 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 4.67 (m, 1H, C$\underline{H}$O), 3.59 (m, 2H), 3.26 (m, 2H), 2.45 (s, 3H), 1.74 (m, 4H), 1.43 (s, 9H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 154.2, 144.4, 134.0, 129.5, 127.3, 79.4, 77.7, 40.1, 31.0, 28.0, 21.3. EIMS (70eV) m/z (relative intensity) 355 (6, M$^+$), 298 (62), 282 (54), 255 (17), 238 (44), 184 (22), 173 (29), 155 (83), 126 (100), 91 (100), 57 (100). HRMS Calcd for C$_{17}$H$_{25}$NO$_5$S: 355.1453, Found: 355.1454.

N-Boc piperidine 4-*p*-nitrobenzenesulfonate (31)

From *N*-Boc 4-hydroxy piperidine (1.0 equiv) and *p*-nitrobenzenesulfonyl chloride (1.2 equiv), **31** was obtained as a yellow solid in 80% yield. mp 139-140° C; ^{1}H NMR (CDCl$_3$, 300 MHz) δ 8.35 (d, J = 8.7 Hz, 2H), 8.07 (d, J = 8.7 Hz, 2H), 4.77 (m, 1H, C$\underline{H}$O), 3.55 (m, 2H), 3.21 (m, 2H), 1.82-1.62 (m, 4H), 1.37 (s, 9H); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 154.2, 150.5, 142.8, 128.7, 124.4, 79.8, 79.7, 40.1, 31.2, 28.1. EIMS (70eV) m/z (relative intensity) 386 (3, M$^+$), 127 (53), 110 (19), 84 (63), 57 (100). HRMS Calcd for C$_{16}$H$_{22}$N$_2$O$_7$S: 386.1148, Found: 386.1146.

Procedure for the Asymmetric Synthesis of *N*-Boc-1-trimethylsilyl-2-azabicyclo[3.1.0] hexane (32).

To a solution of (-)-sparteine (0.17 mL, 2.2 equiv) in 3 mL of diethyl ether at -78 °C was added *s*-BuLi (0.75 mL, 2.2 equiv). The reaction mixture was stirred for 30 min at -78 °C and then a solution of **30** (20 mg, 0.34 mmol) in 2 mL of diethyl ether was transferred to the above solution at -78 °C. The resulting reaction mixture was stirred at -78 °C for 4 h, and then TMSCl (2.2 equiv) in 2 mL of diethyl ether was added after precooling. This mixture was then allowed to slowly warm to room temperature (3 h). Workup consisted of addition of 10 mL water, extraction of the aqueous layer with diethyl ether (3 × 5 mL), extraction of the combined diethyl ether extracts with 10 mL sat. NH$_4$Cl solution, drying over anhydrous MgSO$_4$, filtration, and concentration *in vacuo*. The crude product was further purified by chromatography to give 67 mg of **32** as a colorless oil in 77% yield. This material was identified by comparison with an authentic sample[12] by ^{1}H NMR. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 3.54 (m, 1H), 3.18 (m, 1H), 2.01 (m, 1H), 1.96 (m, 1H), 1.54 (m, 1H), 1.44 (s, 9H), 0.66 (m, 1H), 0.61 (t, J = 6.0 Hz, 1H), 0.05 (s, 9H). The enantiomeric purity of **32** was determined to be 55% ee by chiral HPLC of the 3,5-dinitrobenzoyl amide derivative on a Pirkle column packed with (*S*)-*N*-naphthylleucine[19] (2.5% v/v *iso*-propanol in hexane; a flow rate of 1.5 mL/min; and a detection wavelength of 254 nm; The major had a retention time of 14.9 min, and the minor had a retention time of 21.7 min.).

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