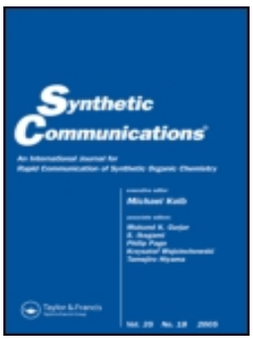

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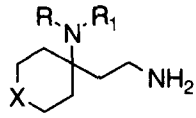
SYNTHESIS OF NOVEL RESTRICTED DIAMINES; 2-(1-AMINOCYCLOALKAN-1-YL)ETHYLAMINES

Takeshi Suzuki,* Naoki Imanishi, Hirotsune Itahana, Susumu Watanuki, Mitsuaki Ohta, and Toshiyasu Mase

Chemistry Laboratories, Institute for Drug Discovery Research,
Yamanouchi Pharmaceutical Co., Ltd.
21 Miyukigaoka Tsukuba Ibaraki 305, Japan

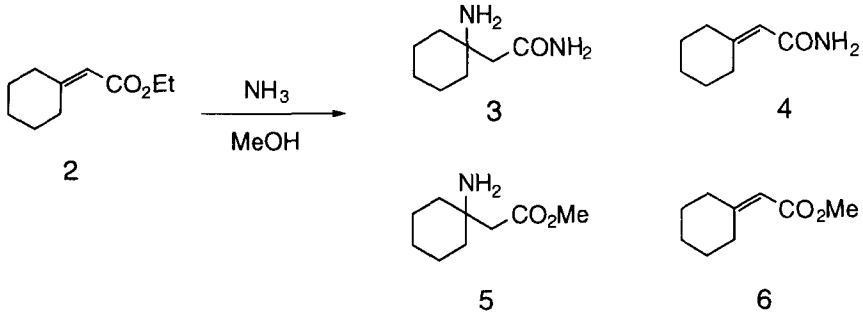
Abstract: Novel restricted diamines, 2-(1-aminocycloalkan-1-yl)ethylamines **1**,were prepared by using Michael addition of ethyl cyclohexylideneacetate **2** and cycloalkylideneacetonitriles **7** with amines. In Michael addition, ester **2** needed high reaction temperature and gave several products, whereas **7** reacted smoothly and gave 2-(1-amino-1-cyclohexyl)acetonitriles **8** in good yield (NH_3 85%, $MeNH_2$ 89%, $EtNH_2$ 80%) and were easily converted to diamines **1**.

In the area of medicinal chemistry, structurally restricted compounds are ordinarily synthesized considering the interaction between drugs and receptors or enzymes. The restricted structures are commonly formed by a direct cyclization; however, it is also possible to make that ones indirectly by the effect of the repulsion of neighboring substituents. In this paper, we report the effective synthetic methods for novel diamines **1** having restricted conformations by the latter method.



1

Regarding introduction methods of a C-2 unit for 1-aminocycloalkan-1-yl derivatives, only two methods have been reported as followings. One is the way going through β-lactams by (2+2) cycloaddition with methylenecycloalkane and chlorosulfonylisocyanate.[1-5] Another is the way using Michael addition of cycloalkylideneacetates with ammonia,[6] and they reported that (1-amino-1-cyclopentyl)acetamide was obtained from ethyl cyclopentylacetate in 40% yield.[6]



2 3 4 5 6

Chart 1

We planned to examine Michael addition of cycloalkylideneacetate in more detail by using ethyl cyclohexylideneacetate. Consequently, we found that this reaction proceeded at high temperature and gave the desired compound **3** in variable yield due to the sensitivity to the reaction conditions (temperature, reaction time, and reaction scale). In principal, it gave four products **3**, **4**, **5**, and **6** (Table 1, run 1). But product ratio of them was changed by reaction conditions (run 1 - 3). That is, longer-time reaction slightly raised the yield of **3** with a further increased yield of **4** (run 2). In an

autoclave for 3 days, **4** was obtained as a major product (run 3). Basis on the result that α,β-unsaturated amide **4** itself did not react with ammonia in methanol at 150 ℃ at all, a mechanism to afford these products was supposed as following. At first, **2** or **6** can be converted faster into **5** by Michael addition than into **4** by amidation of the ester. Subsequently, **5** may be amidated with ammonia to generate **3**. Whereas deamination of **3** gradually and irreversibly proceeded to generate α,β-unsaturated amide **4**. As a result, shorter-time reaction left α,β-unsaturated ester **6** and intermediate **5**, whereas longer-time reaction increased the yield of by-product **4**. It seemed to make difficult to control a yield of **3** at a high level.

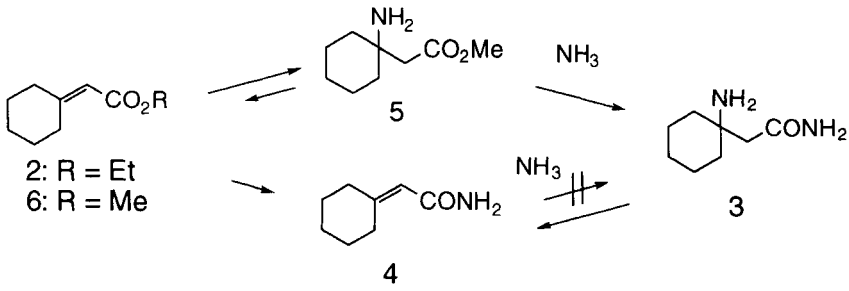


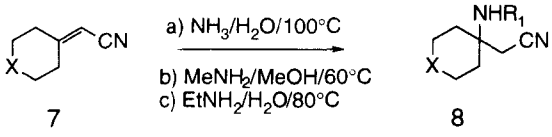
Chart 2

Table 1. Michael addition of ethyl cyclohexylideneacetate with ammonia

Run	Reaction condition	3	4	5	6
1	NH_3, MeOH,140°C, 13h (0.84g, 5mmol)(in sealed tube)	52%	6%	30%	12%
2	NH_3, MeOH,140°C, 3days (0.84g, 5mmol)(in sealed tube)	54~74%	13~28%	trace	
3	NH_3, MeOH,135°C, 3days (6.25g, 37mmol) (in Autoclave)	35%	53%		

Then we selected more activated cycloalkylideneacetonitriles as a Michael acceptor. The reaction of **7** with 29% aqueous ammonia proceeded smoothly at 100 ℃ and

gave **8a** without by-products, which was at least a 50℃ lower temperature than that for **2**. In addition, **7** was also reacted with 40% methylamine in methanol at 60℃ and 70% ethylamine in water at 80℃.



7 8

	R_1	X	yield
8a	H	CH_2	85%
8b	Me	CH_2	89%
8c	Et	CH_2	80%
8d	Me	—	87%
8e	Me	O	84%
8f	Me	S	86%
8g	Me	NMe	80%

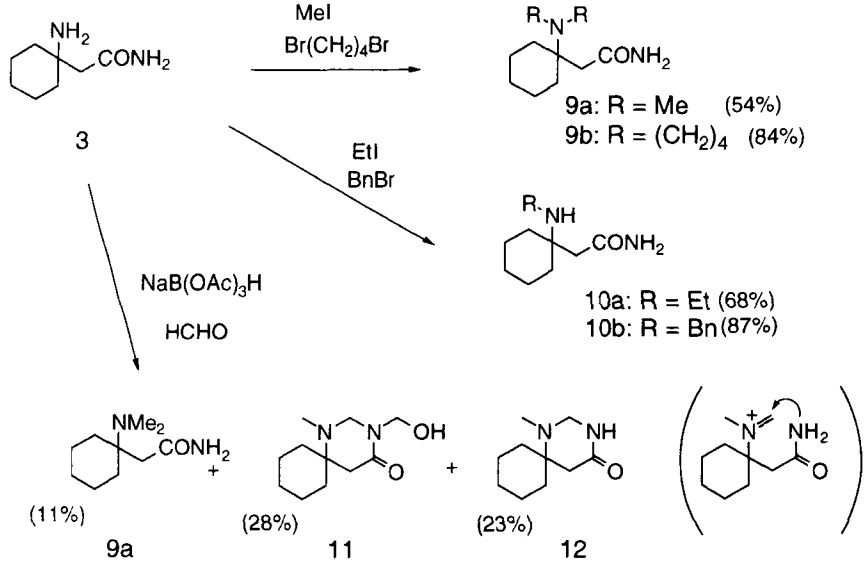
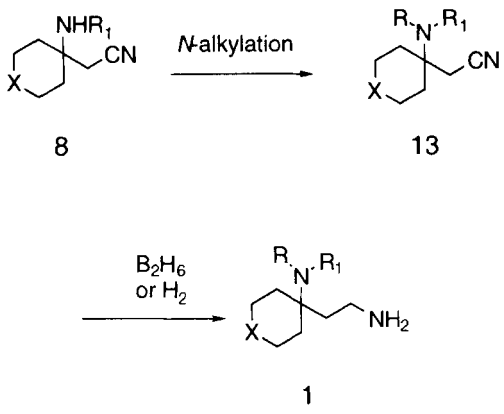


Chart 3

In *N*-alkylation, aminoamide **3** and aminonitrile **8** have steric hindrances around the amine, so they were slower than ordinary amines. They easily gave *N*,*N*-dialkylated

compound with iodomethane and alkylenedihalide, but they resisted second *N*-alkylation with iodoethane or benzylbromide, and predominantly gave monoalkylated amines even when using an excess amount. Whereas aminoamide easily cyclized to gave **11**, **12** as major products by reductive amination with formamide.



	R	R_1	X
1a	H	H	CH_2
1b	H	Me	CH_2
1c	H	Et	CH_2
1d	Me	Me	CH_2
1e	$-(CH_2)_4-$		CH_2
1f	Me	Me	—
1g	Me	Me	O
1h	Me	Me	S
1i	Me	Me	NMe

Chart 4

A series of diamines **1** were easily prepared from **8** by *N*-alkylation and reduction in good yield. In comparing with α,β-unsaturated ester, selection of α,β-unsaturated nitrile **7** as a starting material to obtain 2-(1-amino-1-cycloalkan-1-yl)ethylamine derivatives resulted in getting four advantages; 1) shortening the reaction steps to prepare diamines, 2) decreasing the reaction temperature without by-products, 3) improving treatment of intermediates **13** in organic solvents (intermediate **3** is water-soluble). 4) protecting the side chain's amine from cyclization. This method could be applied to a variety of cycloalkylideneacetonitrile derivatives having heteroatoms or other sized rings in the molecule. In addition, this method made large scale preparations feasible for **1**.

In conclusion, we demonstrated Michael addition on ethyl cyclohexylideneacetate and

cyloalkylideneacetonitrile derivatives and found the latter was an effective synthetic method for the preparation of novel restricted 2-(1-aminocycloalkan-1-yl)ethylamines.

EXPERIMENTAL

All melting points were determined on a Yanaco MP-500D melting point apparatus and are uncorrected. ^{1}H-NMR spectra were measured with a JEOL FX90Q, a FX100, a FX270 or FX400 spectrometer; chemical shifts are recorded in δ units using tetramethylsilane as an internal standard, and the following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double doublet, dt = double triplet, br = broad, br s = broad singlet, br d = broad doublet, br t = broad triplet. Mass spectra were recorded with a Hitachi M-80 electron impact (EI) or a JEOL JMD-DX300 (FAB) spectrometer. Elemental analyses were performed with a Yanaco MT-5. All organic solvents were dried over anhydrous magnesium sulfate and concentrated with a rotary evaporator under reduced pressure.

Michael addition of ethyl cyclohexylideneacetate (2) with ammonia

a) A solution of ethyl cyclohexylideneacetate **2** (0.84 g, 5.0 mol) in saturated ammonia-methanol (30 ml) was heated at 140℃ in a sealed tube for 13 h. The reaction mixture was concentrated. The residue was chromatographed on silica gel to afford **6** (eluting with AcOEt-hexane (1:1), 90 mg, 12%), **4** (eluting with AcOEt, 40 mg, 6%), **5** (eluting with $CHCl_3$-MeOH (10:1), 305 mg, 30%), and **3** (eluting with $CHCl_3$-MeOH- aq. ammonia (100:15:2), 413 mg, 52%). **6**: ^{1}H-NMR ($CDCl_3$) δ: 1.40-1.80 (6H, m), 1.80-2.35 (2H, m), 2.70-3.05 (2H, m), 3.67 (3H, s), 5.50-5.70 (1H, m). **4**: ^{1}H-NMR ($CDCl_3$) δ: 1.35-1.80 (6H, m), 1.80-2.30 (2H, m), 2.65-2.95 (2H, m), 5.50-5.70 (1H, m). EI-MS m/z: 171 (M^+). **5**: ^{1}H-NMR ($CDCl_3$) δ: 1.25-1.70 (10H, m), 1.73 (2H, s), 2.41 (2H, s), 3.68 (3H, s). **3**: mp 80-82℃, ^{1}H-NMR ($CDCl_3$) δ: 1.30-1.70 (10H, m), 1.72 (2H, s), 2.26 (2H, s), 6.35 (1H, br), 7.92 (1H, br). EI-MS m/z: 156 (M^+). *Anal.* Calcd for $C_8H_6N_2O$: C, 61.51; H, 10.32; N, 17.93. Found: C, 61.31; H, 10.17; N, 17.61.

b) A solution of ethyl cyclohexylideneacetate **2** (0.84 g, 5.0 mol) in saturated ammonia-methanol (30 ml) was heated at 140℃ in a sealed tube for 3 days. The

reaction mixture was concentrated. To the residue AcOEt was added and extracted with diluted HCl. The aqueous layer was made alkaline with K_2CO_3 and concentrated. Methanol was added to the residue and the precipitate was removed by filtration. The filtrate was concentrated and the residue was chromatographed on silica gel eluting with $CHCl_3$-MeOH-ammonia aq(100:15:2) to afford **3** as white crystals (0.57 g, 74 %). **4** was obtained from the previous AcOEt layer (90 mg, 13%).

c)Comound **2** (6.25 g, 37.2 mmol) was reacted in satulated ammonia-methanol (250 ml) at 135℃ in an autoclave for 3 days. Compounds **3** (2.48 g, 35%) and **4** (2.74 g, 53%) were obtained.

2-(1-Amino-1-cyclohexyl)acetonitrile (8a)

A solution of cyclohexylideneacetonitrile **7** (0.36 g, 3.0 mmol) in 29% aqueous ammonia (15ml) and methanol (5 ml) was heated at 100℃ in a sealed tube for 20 h. The reaction mixture was concentrated, and the residue was chromatographed on silica gel eluting with $CHCl_3$-MeOH (10:1) to afford **8a** as a colorless oil (0.35 g, 85 %). ^{1}H-NMR ($CDCl_3$) δ: 1.30-1.80 (10H, m), 2.16 (2H, br s), 2.49 (2H, s). HR-MS (EI) calcd for $C_8H_{14}N_2$ (M^+) 138.1157, found 138.1161.

2-(1-Methylamino-1-cyclohexyl)acetonitrile (8b)

A solution of cyclohexylideneacetonitrile **7** (10.94 g, 90.3 mmol) in 40% methylamine-methanol (55 ml) was heated at 60℃ in a sealed tube for 18 h. The reaction mixture was concentrated and the residue was diluted with AcOEt and extracted with dil. HCl. The aqueous layer was made alkaline with K_2CO_3 and extracted with AcOEt. The organic layer was washed with brine, dried, and concentrated to afford **8b** as a colorless oil (12.20 g, 89%). ^{1}H-NMR ($CDCl_3$) δ: 1.00-1.90 (10H, m), 2.31 (3H, s), 2.50 (2H, s). HR-MS (EI) calcd for $C_9H_{16}N_2$ (M^+) 152.1313, found 152.1314.

2-(1-Ethylamino-1-cyclohexyl)acetonitrile (8c)

A solution of cyclohexylideneacetonitrile **7** (0.36 g, 3.0 mmol) in 70% ethylamine-H_2O (5 ml) was heated at 80℃ in a sealed tube for 20 h. The reaction mixture was concentrated and the residue was diluted with AcOEt and extracted with dil. HCl. The aqueous layer was made alkaline with K_2CO_3 and extracted with AcOEt. The organic layer was washed with brine, dried and concentrated. The residue was chromatographed on silica gel eluting with AcOEt to afford **8c** as a colorless oil (0.40

g, 80%). ^{1}H-NMR ($CDCl_3$) δ: 1.12 (3H, t, J = 7 Hz), 1.20-1.85 (10H, m), 2.46 (2H, s), 2.53 (2H, q, J = 7 Hz). HR-MS (EI) calcd for $C_{10}H_{18}N_2$ (M^+) 166.1470, found 166.1473.

2-(1-Methylamino-1-cyclopentyl)acetonitrile (8d)

Yield 0.48 g (87%) as an oil. **8d** (HCl salt): mp 126-127℃ (EtOH-AcOEt). ^{1}H-NMR (DMSO-*d6*) δ: 1.55-2.15 (8H, m), 2.51 (2H, s), 3.31 (3H, s). GC-MS *m/z*: 138 (M^+). *Anal.* Calcd for $C_8H_{14}N_2 \cdot HCl$: C, 55.01; H, 8.66; Cl, 20.30; N, 16.04. Found: C, 54.73; H, 8.61; Cl, 20.57; N, 16.27.

2-(4-Methylamino-4-tetrahydropyranyl)acetonitrile (8e)

Yield 0.52 g (84%) as an oil. **8e** (HCl salt): mp 219-220℃ (EtOH-AcOEt). ^{1}H-NMR (DMSO-*d6*) δ: 1.65-2.20 (4H, m), 2.57 (2H, s), 3.40 (3H, s), 3.50-4.05 (4H, m). GC-MS *m/z*: 154 (M^+). *Anal.* Calcd for $C_8H_{14}N_2O \cdot HCl \cdot 0.1H_2O$: C, 49.92; H, 7.96; Cl, 18.42; N, 14.55. Found: C, 49.77; H, 4.98; Cl, 18.65; N, 14.74.

2-(4-Methylamino-4-tetrahydrothiopyranyl)acetonitrile (8f)

Yield 1.87 g (86%) as an oil. ^{1}H-NMR ($CDCl_3$) δ: 1.50-2.50 (6H, m), 2.29 (3H, s), 2.43 (2H, s), 2.87-3.18 (2H, m). HR-MS (EI) calcd for $C_8H_{14}N_2S$ (M^+) 170.0878, found 180.0886.

2-(4-Methylamino-1-methyl-4-piperidyl)acetonitrile (8g)

Yield 0.54 g (80%) as an oil. **8g** (2HCl salt): mp 233-234℃ (EtOH-AcOEt). ^{1}H-NMR (DMSO-*d6*) δ: 1.90-2.40 (4H, m), 2..56 (2H, s), 2.75 (3H, s), 3.15-3.85 (7H, m). GC-MS m/z: 167 (M^+). *Anal.* Calcd for $C_9H_{17}N_3 \cdot 2HCl \cdot 0.1H_2O$: C, 44.67; H, 8.00; Cl, 29.30; N, 17.37. Found: C, 44.61; H, 8.04; Cl, 29.49; N, 17.64.

2-(1-Dimethylamino-1-cyclohexyl)acetamide (9a)

Iodomethane (55.0 g, 0.39 mmol) was added dropwise to a suspension of 2-(1-amino-1-cyclohexyl)acetamide **3** (30.3 g, 0.19 mmol) and powdered K_2CO_3 (53.5 g, 0.39 mmol) in CH_3CN (500 ml) maintained at 10℃ and stirred for 5 h. The reaction mixture was filtered and concentrated. The residue was diluted with water and extracted with AcOEt. The extract was washed with brine, dried, and concentrated to afford crude **9a** (29.5g). The residue was recrystallized from AcOEt-hexane to afford **9a** as a white solid (18.8 g, 54%). mp 252-255℃ (AcOEt-n-hexane). ^{1}H-NMR ($CDCl_3$) δ: 1.30-1.80 (10H, m), 2.32 (6H, s), 2.53 (2H, s). EI-

MS *m/z*: 184 (M^+). *Anal.* Calcd for $C_{10}H_{20}N_2O$: C, 65.18; H, 10.94; N, 15.20. Found: C, 65.13; H, 10.95; N, 14.91.

2-[1-(1-Pyrrolidinyl)-1-cyclohexyl]acetamide (9b)

1,4-Dibromobutane (0.2 ml, 1.67 mmol) was added dropwise to a stirred suspension of 2-(1-amino-1-cyclohexyl)acetamide hydrochloride **3** (0.30 g, 1.56 mmol), powdered K_2CO_3 (0.75 g, 5.42 mmol) and sodium iodide (0.5 g, 3.3 mmol) in dimethylformamide (5 ml) at room temperature and stirred for 3 h. The reaction mixture was filtered and concentrated. The residue was diluted with water and extracted with $CHCl_3$-MeOH (10:1). The extract was washed with brine, dried, and concentrated. The residue was chromatographed on silica gel eluting with $CHCl_3$-MeOH-aq. ammonia (100:10:1) to afford **9b** as a colorless oil (0.28 g, 84%). ^{1}H-NMR ($CDCl_3$) δ: 1.00-2.00 (14H, m), 2.53 (2H, s), 2.60-3.00 (4H, m), 5.45 (1H, br s), 8.78 (1H, br s). EI-MS *m/z*: 210 (M^+).

2-(1-Ethylamino-1-cyclohexyl)acetamide (10a)

A suspension of 2-(1-amino-1-cyclohexyl)acetamide **3** (0.10 g, 0.64 mmol), iodoethane (0.30 g, 1.92 mmol) and K_2CO_3 (0.33 g)in acetonitrile (5 ml) was heated at 70℃ for 4 h. The reaction mixture was filtered and concentrated. The residue was chromatographed on silica gel eluting with $CHCl_3$-MeOH-aq. NH_3 (100:10:0.5) to afford **10a** as a white solid (80 mg, 68%). mp 80-82℃, ^{1}H-NMR ($CDCl_3$) δ: 1.11 (3H, t, J = 7 Hz), 1.20-1.75 (10H, m), 2.29 (2H, s), 2.56 (2H, q, J = 7 Hz), 5.25 (1H, br), 8.85 (1H, br). GC-MS *m/z*: 184 (M^+).

2-(1-Benzylamino-1-cyclohexyl)acetamide hydrochloride(10b)

A suspension of 2-(1-amino-1-cyclohexyl)acetamide **3** (0.10 g, 0.64 mmol), bromobenzyl (0.24 g, 1.41 mmol) and K_2CO_3 (0.33 g) in acetonitrile(5 ml) was heated at 70℃ for 4 h. The reaction mixture was filtered and concentrated. The residue was chromatographed on silica gel eluting with $CHCl_3$-MeOH (100:10) to afford the free base of **10b** as a colorless oil (137 mg, 87%) and 2-(1-dibenzylamino-1-cyclohexyl)acetamide (18 mg, 8%) as a colorless oil. It was then converted to monohydrochloride salt of **10b** as a white solid . **10b** (HCl salt): mp 80-82℃ (EtOH-AcOEt), ^{1}H-NMR (DMSO-*d6*) δ: 1.10-1.25 (1H, m), 1.35-1.50 (2H, m), 1.60-1.90 (7H, m), 2.87 (2H, s), 4.15-4.20 (2H, m), 7.35-7.50 (3H, m), 7.59 (1H,

brs), 8.12 (1H, br s), 9.15 (2H, br s). GC-MS *m/z*: 246 (M^+). *Anal.* Calcd for $C_{15}H_{22}N_2O \cdot HCl \cdot 0.8H_2O$: C, 60.62; H, 8.34; Cl, 11.93; N, 9.43. Found: C, 60.54; H, 8.42; Cl, 12.06; N, 9.52.

Reductive N-alkylation of 2-(1-Amino-1-cyclohexyl)acetamide (3)

Sodium triacetoxyborohydride (1.26 g, 6.0 mmol) was added to an emulsion of 2-(1-amino-1-cyclohexyl)acetamide **3** (308 mg, 2.0 mmol) in 30% formamide (2 ml) and dichloromethane (10 ml) and stirred at room temperature for 1h. The reaction mixture was concentrated, and the residue was chromatographed on silica gel eluting with $CHCl_3$-MeOH (10:1) to afford a mixture of 1-methyl-1,3-diazaspiro[5.5]undecan-4-one **11**, **12** and **9a**. This solution was concentrated and the residue was chromatographed on silica gel eluting with AcOEt to afford **11** as a oil (120mg, 28%), eluting with $CHCl_3$-MeOH (10:1) to afford **12** as a solid (85 mg, 23%) and eluting with $CHCl_3$-MeOH-aq. NH_3 (100:15:2) to afford **9a** as a solid (40 mg, 11%). **11** (HCl salt): mp 141-142℃ (EtOH-AcOEt). ^{1}H-NMR (DMSO-*d6*) δ: 1.10-2.05 (10H,m), 2.79 (5H, s), 4.45-5.50 (4H, m),12.09 (1H, br). FAB-MS *m/z*: 213 (M^++1). *Anal.* Calcd for $C_{11}H_{20}N_2O_2 \cdot HCl \cdot 0.15H_2O$: C, 52.54 H, 8.54; Cl, 14.10; N, 11.14. Found: C, 52.51; H, 8.29; Cl, 14.18; N, 11.08. **12**: mp 102-104℃ (hexane-AcOEt). ^{1}H-NMR (DMSO-*d6*) δ: 1.20-1.70 (10H,m), 1.99 (2H, s), 2.31 (3H, s), 4.04 (2H, s), 7.43 (1H, br s). FAB-MS *m/z*: 183 (M^++1). *Anal.* Calcd for $C_{10}H_{18}N_2O \cdot 0.1H_2O$: C, 65.25 H, 9.97; N, 15.22. Found: C, 65.19; H, 9.71; N, 15.07.

2-(1-Dimethylamino-1-cyclohexyl)acetonitrile (13)

Sodium cyanoborohydride (2.40 g, 63.4 mmol) was added portionwise to an emulsion of 2-(1-methylamino-1-cyclohexyl)acetonitrile **8b** (8.92 g, 58.7 mmol), acetic acid (10 ml), and 30% formaldehyde solution (10 ml) in CH_2Cl_2 (100 ml) at 0℃, and the reaction mixture was stirred at room temperature for 4 h. The reaction mixture was made alkaline with aqueous K_2CO_3 and extracted with $CHCl_3$-MeOH (10:1). The organic layer was washed with brine, dried, and concentrated to afford **13** as a colorless oil (9.06 g, 93%).

2-(1-Dimethylamino-1-cyclohexyl)ethylamine dihydrochroride (1d)

A solution of 2-(1-dimethylamino-1-cyclohexyl)acetonitrile **13** (2.00 g, 12 mmol) in

EtOH (100 ml) and 4N HCl/AcOEt (6 ml) was treated with PtO_2 and hydrogenated at 4 atm and 40℃ for 15 h. The catalysts were removed by filtration, and the filtrate was concentrated. The residue was crystallized from Et_2O to afford **1** as a white solid (2.21 g, 89%). mp 252-255℃ (EtOH-AcOEt). **1d**(free base) ^{1}H-NMR ($CDCl_3$) δ: 1.20-1.80 (12H, m), 2.22 (6H, s), 2.60-2.80 (2H, m), 3.00 (2H, m). EI-MS *m/z*: 170 (M^+). bp 58.5℃ (1.2 mmHg).

2-(1-Amino-1-cyclohexyl)ethylamine (1a)

A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.20-1.80 (16H,m), 2.28 (3H,s), 2.60-2.85 (2H, m). EI-MS *m/z*: 142 (M^+). *Anal.* Calcd for $C_8H_{18}N_2$: C, 67.55 H, 12.75; N,19.69. Found: C, 67.40; H, 12.80; N, 19.40.

2-(1-Methylamino-1-cyclohexyl)ethylamine (1b)

A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.15-1.80 (15H,m), 2.28 (3H,s), 2.60-2.95 (2H, m). EI-MS *m/z*: 156 (M^+). *Anal.* Calcd for $C_9H_{20}N_2 \cdot 0.2H_2O$: C, 67.62 H,12.86; N, 17.52. Found: C, 67.48; H, 13.00; N, 17.46.

2-(1-Ethylamino-1-cyclohexyl)ethylamine (1c)

A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.09 (3H, t, J = 7Hz), 1.20-1.80 (15H,m), 2.53 (2H, q, J = 7Hz), 2.60-2.95 (2H, m). EI-MS *m/z*: 170 (M^+). *Anal.* Calcd for $C_{10}H_{22}N_2 \cdot 0.3H_2O$: C, 68.36 H, 12.96; N, 15.94. Found: C, 68.11; H, 12.88; N, 16.07.

2-(1-Pyrrolidinyl-1-cyclohexyl)ethylamine (1e)

A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.00-2.00 (18H,m), 2.45-2.88 (6H, m). FAB-MS *m/z*: 197 (M^++1).

2-(1-Dimethylamino-1-cyclopentyl)ethylamine (1f)

A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.40-1.45 (2H,m), 1.55-1.67 (6H, m), 1.73-1.78 (2H, m), 2.23 (6H, s), 2.78 (2H, t, J = 8Hz). FAB-MS *m/z*: 173 (M^++1).

2-(4-Dimethylamino-4-tetrahydropyranyl)ethylamine (1g)

A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.30-1.75 (8H,m), 2.24 (6H, s), 2.62-2.83 (2H, m), 3.48-3.96, (4H, m). FAB-MS *m/z*: 157 (M^++1).

2-(4-Dimethylamino-4-tetrahydrothiopyranyl)ethylamine (1h)

A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.35-2.00 (6H,m), 2.19 (6H, s), 2.60-3.15 (4H, m), 3.60-3.78, (2H, m). EI-MS *m/z*: 188 (M^+). *Anal.* Calcd for $C_9H_{20}N_2S$:

C, 57.40; H, 10.70; N, 14.87; S, 17.03. Found: C, 57.22; H, 10.96; N, 14.66; S, 16.80.

2-(4-Dimethylamino-4-piperidinyl)ethylamine (1i)

A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.30-1.90 (8H,m), 2.22 (6H, s), 2.27 (3H, s), 2.34-2.80 (4H, m). EI-MS *m/z*: 185 (M^+).

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