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REGIOSPECIFIC REARRANGEMENT OF HYDROXYLAMINES TO SECONDARY AMINES USING DIISOBUTYLALUMINUM HYDRIDE †

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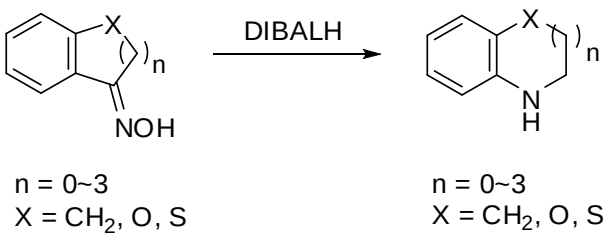
Abstract – A systematic investigation of a reductive ring-expansion reaction of *N*-monosubstituted hydroxylamines with diisobutylaluminum hydride (DIBALH) was carried out. The reaction regiospecifically provided a variety of bicyclic or tricyclic heterocycles or linear secondary amines containing nitrogen attached to an aromatic ring.

INTRODUCTION

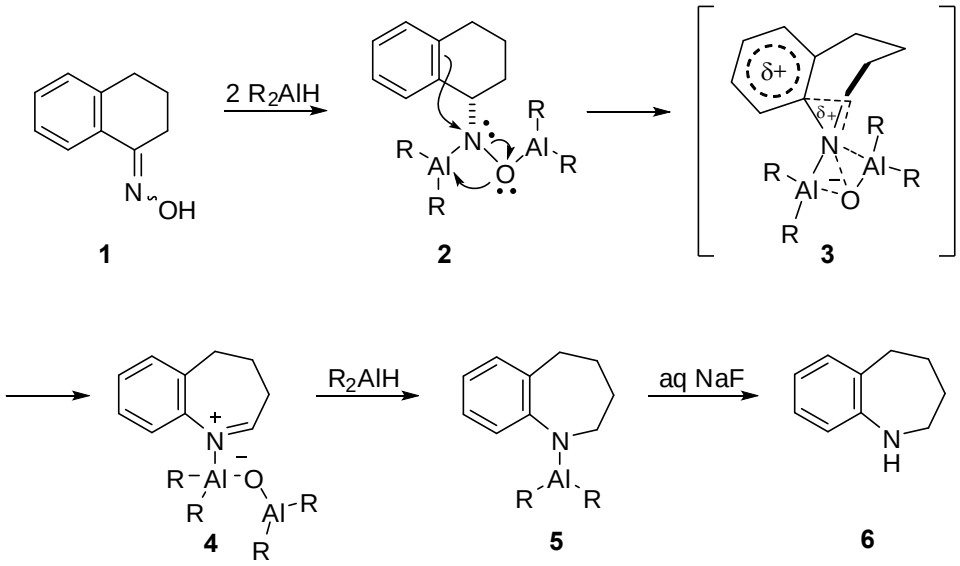
The development of synthetic methods for unsubstituted basic skeletons of heterocycles is important from the viewpoint of both synthetic chemistry and medicinal chemistry. In particular, the synthesis of bicyclic or tricyclic fused heterocycles containing nitrogen attached to an aromatic ring such as benzazepine, benzoxazine, benzoxazepine, benzthiazine, and benzthiazepine, is essential, because these skeletons often form the core structures of pharmaceuticals or clinical candidates. However, only a few straightforward and versatile synthetic procedures are available to construct the heterocyclic systems.[1]



Scheme 1. Previous Reductive Ring-Expansion Reaction of Cyclic Ketoximes using DIBALH

† This paper is dedicated to Professor Albert Eschenmoser on the occasion of his 85th birthday.

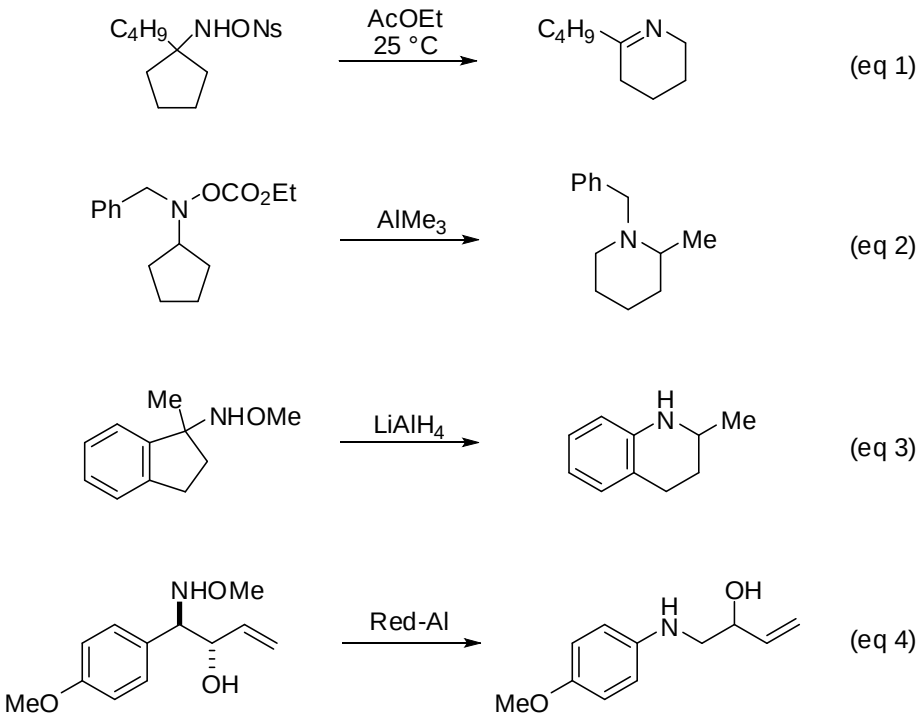
Recently, we have reported an investigation of the reductive ring expansion reaction of cyclic ketoximes fused to aromatic rings using diisobutylaluminum hydride (DIBALH) (Scheme 1).[2a,2b] The treatment of an *E*/*Z* mixture of ketoximes with 5 equiv of DIBALH furnished the corresponding ring expansion product with nitrogen attached to the aromatic ring as the sole isomer. According to preliminary results (Table 1, entry 2) showing that the treatment of the hydroxylamine with DIBALH gave the reductive ring expansion product and theoretical calculations based on the density functional theory (DFT), we proposed a reaction mechanism involving the 1,2-reduction of an oxime to hydroxylamine and a regiospecific rearrangement via a partial phenonium cation intermediate (Scheme 2).[2b]



Scheme 2. Reaction Mechanism based on DFT Calculations

It is known that hydroxylamines activated by an electron-withdrawing group on the oxygen and *O*-alkyl hydroxylamines activated by aluminum agents undergo rearrangement reactions. Hoffman described the rearrangement of *O*-arylsulfonyl hydroxylamines (Scheme 3, eq 1).[3a,b] Yamamoto and Maruoka reported a rearrangement-alkylation sequence of hydroxylamine carbonate effected by trialkylaluminum (eq 2).[3c] The reductive migration of *O*-methyl hydroxylamine with LAH was reported by Booth (eq 3),[3d] and the reaction of hydroxylamine with Red-Al was described by Naito and Miyata (eq 4).[3e-h] In contrast to these examples, no report has appeared on the reductive rearrangement of unfunctionalized hydroxylamines to the best of our knowledge.

Therefore, we carried out a systematic investigation of the rearrangement reaction of hydroxylamine. Herein, we report its scope and generality of the reaction.



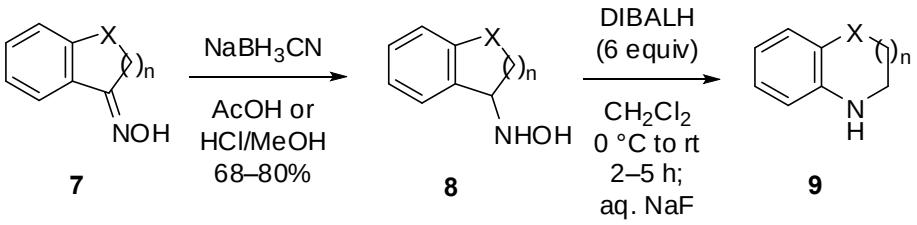
Scheme 3. Rearrangement of Hydroxylamine Derivatives

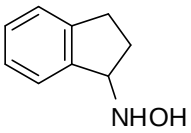
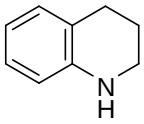
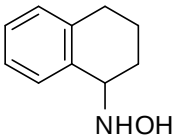
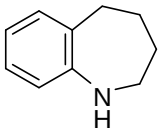
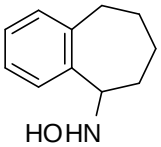
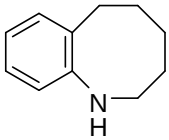
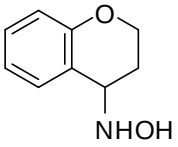
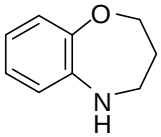
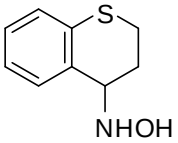
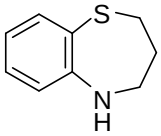
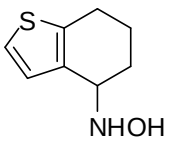
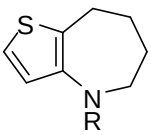
RESULTS AND DISCUSSION

First, bicyclic hydroxylamines were synthesized from readily accessible fused bicyclic ketoximes by 1,2-reduction with sodium cyanoborohydride[4] under acidic conditions; they were then subjected to reductive conditions with DIBALH (Table 1). Thus, hydroxylamines were treated with 6 equiv of DIBALH at 0 °C to room temperature. The reaction was quenched by adding NaF.[1,2] Although the theoretical amount of DIBALH was 3 equiv, we used an excess amount of the reagent to achieve complete consumption of the substrate.

The reductive rearrangement of hydroxylamines was found to be applicable to a variety of bicyclic substrates (Table 1). In all cases, the reaction gave the expected reductive ring expansion product as the sole isomer as observed in the reaction of the corresponding oximes with DIBALH.[2] Thus, the aromatic ring migrated to the nitrogen atom to form bicyclic compounds having nitrogen attached to the aromatic ring. Reactions of five- to seven-membered ring substrates **8a**, **8b**, and **8c** provided 1,2,3,4-tetrahydroquinoline **9a**, 2,3,4,5-tetrahydro-1*H*-benz[*b*]azepine **6**, and 1,2,3,4,5,6-hexahydrobenz[*b*]azocine **9c**, respectively (entries 1 to 3). In addition, the reactions were applicable to the synthesis of 2,3,4,5-tetrahydrobenzo[*b*][1,4]oxazepine **9d** and 2,3,4,5-tetrahydrobenzo[*b*][1,4]thiazepine **9e** (entries 4 and 5). Furthermore, a cyclohexyl ring fused to thiophene expanded smoothly to give 5,6,7,8-tetrahydrothieno[3,2-*b*]azepine **9f**,[1a] which was isolated as a *p*-nitrobenzoyl amide **10f** owing to the instability of **9f** (entry 6).

Table 1. Reductive Rearrangement of Hydroxylamines Derived from Bicyclic Ketoxime with DIBALH

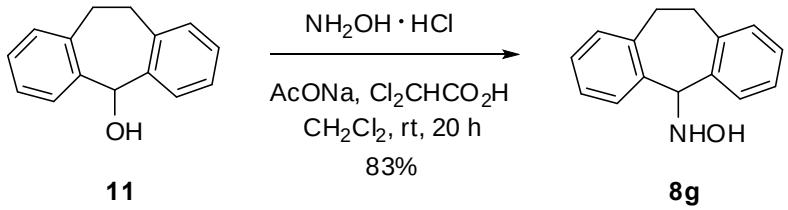


Entry	Hydroxylamine		Product		Yield (%)[a]
1		**8a**		**9a**	49
2[b]		**8b**		**6**	72
3		**8c**		**9c**	62
4		**8d**		**9d**	67
5		**8e**		**9e**	56
6		**8f**		**9f** R = H **10f** R = COC_6H_4p-NO_2	--- 67

[a]Yields are based on hydroxylamine. [b]Ref. 2b

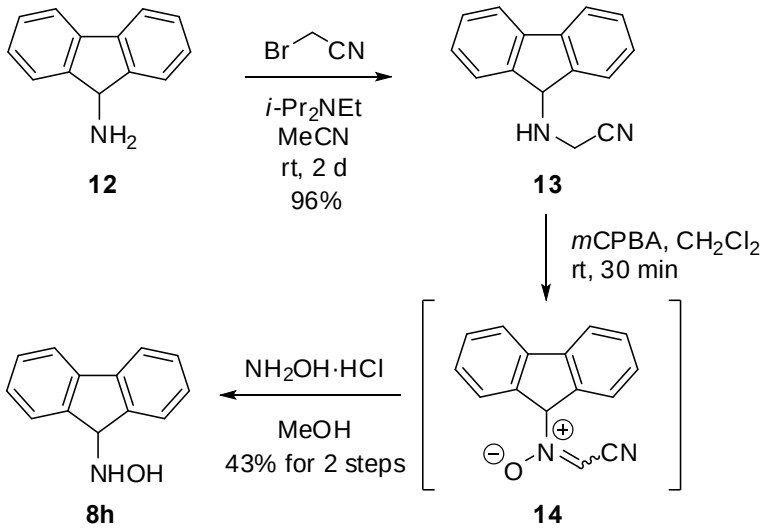
Although the reaction yields of hydroxylamines with DIBALH are slightly lower than those of the corresponding oximes with the reagent,[2b] one of the advantages of using hydroxylamine instead of an oxime as a substrate should be its broad synthetic accessibility.[5–12] Thus, in addition to the reduction of oximes, hydroxylamines can be prepared from alcohols or primary amines by substitution reactions or

oxidation through the regioselective formation of nitrone in a stepwise protocol. For instance, tricyclic hydroxylamine **8g** was prepared by the reaction of alcohol **11** with hydroxylamine hydrochloride in the presence of sodium acetate and dichloroacetic acid (Scheme 4).[8a,b]



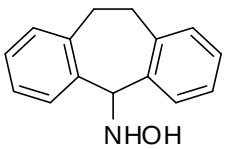
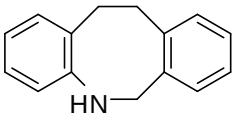
Scheme 4. Preparation of Hydroxylamine 8g by Substitution Reaction

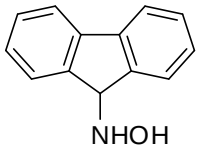
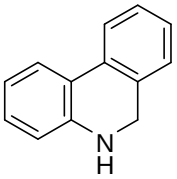
On the other hand, *N*-(9-fluorenyl)hydroxylamine **8h** was prepared from primary amine **12** by a stepwise protocol including cyanomethylation, regioselective oxidation to nitrone, and hydroxyaminolysis[7c] (Scheme 5). The reductive ring expansion reaction of tricyclic hydroxylamines **8g** and **8h** proceeded smoothly to give the corresponding secondary amines **9g** and **9h** (Table 2, entries 1 and 2).



Scheme 5. Preparation of Hydroxylamine 8h by Oxidation of Primary Amine

Table 2. DIBALH-mediated Rearrangement of Tricyclic Hydroxylamines[a]

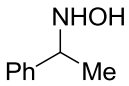
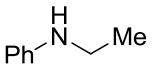
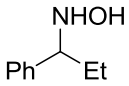
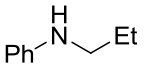
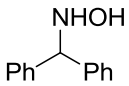
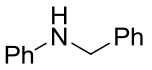
Entry	Hydroxylamine		Product		Yield (%)
1		**8g**		**9g**	69

2		**8h**		**9h**	43

[a]Hydroxylamine (1 equiv) and DIBALH (6 equiv) were used in CH_2Cl_2 at rt for 2–3 h.

Finally, we examined the reaction of linear hydroxylamines, which were easily prepared by reduction of the corresponding ketoximes (Table 3).[5] We observed the specific migration of aryl groups providing the corresponding aniline derivatives as the sole product. Thus, the reaction of *N*-(1-phenylethyl)-hydroxylamine **8i**[13] and *N*-(1-phenylpropyl)hydroxylamine **8j** afforded *N*-ethylaniline **9i** and *N*-propylaniline **9j** via specific aryl migration (entries 1 and 2). *N*-Diphenylmethanehydroxylamine **8k**[14] was also transformed into benzylaniline **9k** in high yield (entry 3). The preferential migratory aptitude of an aryl group over that of an alkyl chain of hydroxylamines was also observed in the reaction of oximes with DIBALH.[2b]

Table 3. DIBALH-mediated Rearrangement of Linear Hydroxylamines[a]

Entry	Hydroxylamine		Product		Yield (%)
1		**8i**		**9i**	55
2		**8j**		**9j**	65
3		**8k**		**9k**	84

[a]Hydroxylamine (1 equiv) and DIBALH (6 equiv) were used in CH_2Cl_2 at rt for 2–3 h.

In summary, we have established the reductive rearrangement reaction of hydroxylamines with DIBALH. A systematic investigation demonstrated that the *N*-monosubstituted hydroxylamines serve as a suitable substrate for the reductive rearrangement reaction. In addition, the reaction gave cyclic or acyclic secondary amines having nitrogen attached to the aromatic rings specifically owing to the preferential migratory aptitude of the aromatic rings. Because hydroxylamines can be easily prepared from a various precursors such as oximes,[4–6] primary amines,[7] alcohols,[8] nitroalkanes,[9,10] conjugated nitroalkenes,[11] and nitronates,[12] the rearrangement reaction of hydroxylamines with DIBALH should be useful and the resulted aromatic amines will likely find use in the field of fine and medicinal chemistry.

EXPERIMENTAL

General

Column chromatography was performed on silica gel 60N (Kanto, 63-210 μm) and flash column chromatography was performed on silica gel 60N (40-60 μm) using the indicated solvents. Reactions and chromatography fractions were monitored by employing pre-coated silica gel 60 F_{254} plates (0.25 mm). All melting points were uncorrected. IR spectra were measured with a FT-IR spectrometer and were reported in wave numbers (cm^{-1}). NMR spectra were recorded on 400 MHz or 500 MHz spectrometers with tetramethylsilane (0 ppm) or chloroform (7.24 ppm) as the internal standard. Chemical shifts were reported in δ (ppm downfield from tetramethylsilane). Coupling constants were reported in Hz. Mass spectra were obtained using following ionization techniques: electron impact (EI), fast atom bombardment (FAB).

General synthetic procedure of hydroxylamines

From representative oxime derivatives: *N*-4-chromanylhydroxylamine (8d): To a stirred solution of chroman-4-one oxime (326 mg, 2.00 mmol) in MeOH (4.0 mL) was added $NaBH_3CN$ (624 mg, 9.93 mmol) at rt and added hydrogen chloride in MeOH (1.0 M, 6.0 mL) at 0 ºC. After stirring for 1.5 h at rt, the reaction was quenched with saturated aqueous $NaHCO_3$. The reaction mixture was extracted with EtOAc, and the combined extracts were washed with brine, dried over anhydrous Na_2SO_4, concentrated under reduced pressure. The residue was purified by recrystallization (from EtOAc/*n*-hexane) to give hydroxylamine **8d** (226 mg, 68%) as colorless needles: mp 142-144 °C; IR (KBr) 3258, 3175, 2887, 1491, 1229, 770 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (1H, dd, *J* = 8.8, 1.6 Hz), 7.19 (1H, ddd, *J* = 8.8, 6.8, 1.6 Hz), 6.89 (1H, ddd, *J* = 8.8, 6.8, 0.8 Hz), 6.84 (1H, dd, *J* = 8.8, 0.8 Hz), 5.86 (1H, br s), 5.25 (1H, br s), 4.28-4.21 (2H, m), 4.10 (1H, dd, *J* = 3.6, 3.6 Hz), 2.22 (1H, ddd, *J* = 14.8, 6.8, 3.6 Hz), 2.10-1.97 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 130.3, 129.5, 120.3, 119.7, 117.2, 62.0, 54.9, 25.2; LRMS (EI) *m/z* 165 (M^+); HRMS *m/z* Calcd for $C_9H_{11}NO_2$ (M^+) 165.0790, found 165.0778.

From alcohol derivatives: Preparation of 10,11-dihydro-5-hydroxyamino-5*H*-dibenzo[*a*,*d*]-cyclopentane (8g): To a stirred solution of dibenzosuberone (1.00 g, 4.80 mmol) in MeOH (12.0 mL) was added $NaBH_4$ (545 mg, 14.4 mmol) potionwise at 0 °C. After stirring for 10 min at the same temperature, the reaction was quenched with saturated aqueous NH_4Cl and the mixture was extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, *n*-hexane:EtOAc = 85:15) to afford alcohol **11** (1.00 g, quant.) as a colorless oil: IR (neat) 3317, 1483, 1456, 1030 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (2H, d, *J* = 8.0 Hz), 7.22-7.13 (6H, m), 5.96-5.95 (1H, m), 3.47-3.38 (2H, m), 3.15-3.06 (2H, m), 2.24 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 138.9, 130.2, 127.9, 127.0, 126.2, 76.6, 32.4; LRMS (EI) *m/z* 210 (M^+); HRMS *m/z* Calcd for $C_{15}H_{14}O$

210.1045, Found 210.1048. To a stirred solution of dichloroacetic acid (4.75 mL, 57.6 mmol), sodium acetate (394 mg, 4.80 mmol) in CH_2Cl_2 (5.0 mL) was added hydroxylamine hydrochloride (1.33 g, 19.2 mmol) at rt and stirred for 1 h. To a stirred suspension was added dropwise alcohol **11** (1.00 g, 4.80 mmol) in CH_2Cl_2 (5.0 mL) at rt. After stirring for 20 h at the same temperature, the reaction was quenched with saturated aqueous $NaHCO_3$ at 0 °C and the mixture was extracted with CH_2Cl_2. The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, *n*-hexane:EtOAc = 85:15) to afford hydroxylamine **8g** (899 mg, 83%) as a colorless oil: IR (neat) 3528, 3260, 3061, 3018, 2928, 2887, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (2H, d, *J* = 7.2 Hz), 7.22-7.13 (6H, m), 5.05 (1H, s), 4.21 (1H, br s), 3.71-3.63 (2H, m), 2.91-2.83 (2H, m) (one proton signal was missing owing to exchanging to deuterium); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1, 136.8, 131.3, 130.4, 128.2, 126.0, 74.6, 32.7; LRMS (EI) *m/z* 193 [$(M-NHOH)^+$]; HRMS *m/z* Calcd for $C_{15}H_{13}$ [$(M-NHOH)^+$] 193.1018, Found 193.1022.

From amine derivatives: *N*-(9*H*-fluoren-9-yl)hydroxylamine (8h): To a stirred solution of *N*-(9*H*-fluoren-9-yl)amine **12** (739.5 mg, 4.08 mmol) in MeCN (8.2 mL) and *i*-Pr_2NEt (1.42 mL, 8.16 mmol) was added bromoacetonitrile (313 μL, 4.49 mmol) dropwise over 15 min. The reaction mixture was stirred at rt for 2 days and evaporated, diluted with CH_2Cl_2. The organic layer was washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4 to give the residue, which was purified by flash column chromatography (SiO_2, *n*-hexane:EtOAc = 3:1) to afford 2-(9*H*-fluoren-9-yl)aminoacetonitrile **13** (858 mg, 95%). To a stirred solution of **13** (192 mg, 873 μmol) in CH_2Cl_2 (2.7 mL) was added *m*-chloroperbenzoic acid (471 mg, 2.10 mmol) in portions over 15 min at 0 °C. Stirring was continued at rt for 20 min and the reaction mixture was quenched with aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$, then extracted with CH_2Cl_2. The combined extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure to give nitrone **14**. To a stirred solution of **14** in MeOH (3.5 mL) was added hydroxylamine hydrochloride (303 mg, 4.35 mmol). The mixture was heated at 60 °C for 2.5 h. Then the reaction mixture was diluted with CH_2Cl_2 (6.0 mL) and filtered. The filtrate was washed with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, CH_2Cl_2:MeOH = 50:1), followed by preparative TLC (SiO_2, CH_2Cl_2:MeOH = 50:1) to afford compound **8h** (83.8 mg, 49% for 2 steps): colorless powder; IR (neat) 3140, 2897, 1448, 1402, 1290, 1063, 1026, 1018, 910, 737, 681 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.75-7.67 (4H, m), 7.40 (2H, dd, *J* = 7.5, 7.5 Hz), 7.34-7.28 (2H, m), 6.08 (1H, brs), 5.10 (1H, s) (one proton signal was missing owing to exchanging to deuterium); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9, 141.1, 128.7, 127.4, 125.6, 120.0, 67.3; LRMS (EI) *m/z* 197 (M^+); HRMS (EI) *m/z* Calcd for $C_{13}H_{11}NO$ (M^+) 197.0841, Found 197.0830.

2-(9*H*-Fluoren-9-ylamino)acetonitrile (13): yellow powder; IR (neat) 3329, 3065, 2249, 1448, 1296, 1200, 743, 667 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70 (2H, d, *J* = 7.0 Hz), 7.58 (2H, d, *J* = 7.0 Hz), 7.41 (2H, dd, *J* = 7.5, 7.0 Hz), 7.36 (2H, ddd, *J* = 7.5, 7.0, 1.2 Hz), 5.02 (1H, s), 3.22 (2H, s), 2.27 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.0, 141.0, 128.9, 127.6, 125.0, 120.2, 118.2, 62.5, 31.9; LRMS (EI) *m/z* 220 (M^+); HRMS (EI) *m/z* Calcd for $C_{15}H_{12}N_2$ (M^+) 220.1000, Found 220.1000.

2-(9*H*-Fluoren-9-ylimino)acetonitrile *N*-oxide (14): Trituration with EtOAc, *n*-hexane and $CHCl_3$ afforded pure nitrone. colorless powder; IR (KBr) 3096, 2932, 2220, 1541, 1448, 1429, 1275, 1182, 1157, 966, 750, 725, 694 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.75 (2H, d, *J* = 7.5 Hz), 7.71 (2H, dd, *J* = 8.0, 1.0 Hz), 7.54 (2H, dd, *J* = 7.5, 7.5 Hz), 7.41 (2H, ddd, *J* = 8.0, 7.5, 1.0 Hz), 6.40 (1H, s), 5.93 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.2, 137.8, 131.0, 128.8, 125.9, 120.8, 112.1, 104.2, 80.7; LRMS (FAB) *m/z* 235 ($[M+H]^+$); HRMS (FAB) *m/z* Calcd for $C_{15}H_{11}N_2O$ ($[M+H]^+$) 235.0871, Found 235.0874.

Data of hydroxylamines

***N*-(1-Indanyl)hydroxylamine (8a)**: colorless powder; IR (KBr) 3155, 2941, 2882, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (1H, d, *J* = 7.6 Hz), 7.24-7.14 (3H, m), 4.50 (1H, dd, *J* = 7.2, 4.0 Hz), 3.06-2.99 (1H, m), 2.87-2.80 (1H, m), 2.32-2.23 (1H, m), 2.10-2.01 (1H, m) (two proton signals were missing owing to exchanging to deuterium); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 141.6, 128.2, 126.3, 125.1, 124.9, 67.1, 30.4, 29.7; LRMS (EI) *m/z* 149 (M^+); HRMS (EI) *m/z* Calcd for $C_9H_{11}NO$ (M^+) 149.0841, Found 149.0836.

1,2,3,4-Tetrahydro-*N*-hydroxyl-1-naphthaleneamine (8b): colorless powder; IR (KBr) 3155, 2941, 2882, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (1H, dd, *J* = 6.4, 2.0 Hz), 7.25-7.09 (3H, m), 4.09 (1H, dd, *J* = 4.0, 4.0 Hz), 2.84-2.68 (2H, m), 2.25-2.20 (1H, m), 1.95-1.89 (1H, m), 1.85-1.75 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 134.3, 129.6, 129.2, 127.4, 125.8, 59.3, 29.4, 25.8, 18.3; LRMS (EI) *m/z* 163 (M^+); HRMS (EI) *m/z* Calcd for $C_{10}H_{13}NO$ (M^+) 163.0997, found 163.1015.

***N*-(6,7,8,9-Tetrahydro-5*H*-benzocyclohepten-5-yl)hydroxylamine (8c)**: colorless powder; IR (KBr) 3269, 2914, 1450, 1442, 1364, 1040, 905, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.06 (4H, m), 5.79 (2H, br s), 4.22 (1H, d, *J* = 8.4 Hz), 2.93 (1H, dd, *J* = 13.6, 10.0 Hz), 2.81-2.72 (1H, m), 2.02-1.85 (2H, m), 1.83-1.65 (3H, m), 1.63-1.50 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 141.1, 129.8, 127.0, 126.3, 126.1, 65.8, 35.6, 31.1, 27.7, 27.7; LRMS (EI) *m/z* 160 ($[M–OH]^+$); HRMS *m/z* Calcd for $C_{11}H_{14}N([M–OH]^+)$ 160.1126, Found 160.1101.

***N*-(Thiochroman-4-yl)hydroxylamine (8e)**: colorless powder; IR (KBr) 3254, 3167, 2885, 1587, 1562, 1475, 1441, 1408, 1034, 945, 887, 750 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25-7.00 (4H, m), 5.43 (1H, br s), 4.14 (1H, dd, *J* = 3.5, 3.5 Hz), 3.33 (1H, ddd, *J* = 13, 12, 3.5 Hz), 2.81 (1H, dd, *J* = 13, 4.0, 3.5 Hz), 2.60 (1H, dddd, *J* = 14, 4.0, 3.5, 3.5 Hz), 1.95 (1H, dddd, *J* = 14, 12, 3.5, 3.5 Hz) (one proton signal was missing owing to exchanging to deuterium); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.5, 131.4, 130.4, 128.3,

126.8, 124.0, 58.4, 24.4, 21.5; LRMS (EI) *m/z* 181 (M^+); HRMS (EI) *m/z* Calcd for $C_9H_{11}NOS$ (M^+) 181.0561, Found 181.0562.

***N*-(4,5,6,7-Tetrahydrobenzo[*b*]thiophen-4-yl)hydroxylamine (8f)**: colorless powder; IR (KBr) 3155, 2941, 2882, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.08 (1H, d, *J* = 5.6 Hz), 7.00 (1H, d, *J* = 5.6 Hz), 4.12 (1H, dd, *J* = 4.8, 4.8 Hz), 2.83 (1H, ddd, *J* = 16.4, 5.2, 5.2 Hz), 2.77-2.69 (1H, m), 2.08-1.80 (4H, m) (two proton signals were missing owing to exchanging to deuterium); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 133.7, 127.0, 122.3, 57.0, 26.1, 25.1, 19.8; LRMS (EI) *m/z* 169 (M^+); HRMS (EI) *m/z* Calcd for $C_8H_{11}NOS$ (M^+) 169.0561, Found 169.0567.

***N*-(1-Phenylethyl)hydroxylamine (8i)**: colorless powder; IR (neat) 3252, 1499, 1452, 988, 760, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.26 (5H, m), 4.11 (1H, q, *J* = 6.8 Hz), 1.38 (3H, d, *J* = 6.8 Hz) (two proton signals were missing owing to exchanging to deuterium); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.3, 128.5, 127.6, 127.1, 61.8, 19.4; LRMS (EI) *m/z* 137 (M^+); HRMS (EI) *m/z* Calcd for $C_8H_{11}NO$ (M^+) 137.0841, Found 137.0858.

***N*-(1-Phenylpropyl)hydroxylamine (8j)**: colorless powder; IR (KBr) 3265, 3144, 2864, 1495, 1452, 1346, 1026, 758, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.24 (5H, m), 3.82 (1H, dd, *J* = 8.8, 5.6 Hz), 1.93-1.81 (1H, m), 1.68-1.55 (1H, m), 0.81 (3H, t, *J* = 7.6 Hz) (two proton signals were missing owing to exchanging to deuterium); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 128.4, 127.8, 127.6, 68.7, 26.2, 10.5; LRMS (EI) *m/z* 151 (M^+); HRMS (EI) *m/z* Calcd for $C_9H_{13}NO$ (M^+) 151.0997, Found 151.1023.

Diphenylmethylhydroxylamine (8k): colorless powder; IR (KBr) 3252, 3084, 3028, 2880, 1493, 1450, 1429, 1085, 1034, 1022, 894, 752, 698, 636 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52-7.20 (10H, m), 5.17 (1H, br s) (two proton signals were missing owing to exchanging to deuterium); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 128.5, 127.7, 127.5, 70.6; LRMS (EI) *m/z* 199 (M^+); HRMS (EI) *m/z* Calcd for $C_{13}H_{13}NO$ (M^+) 199.0997, Found 199.0992.

General procedure for rearrangement reaction of hydroxylamines with DIBALH

5,6,11,12-Tetrahydrodibenz[*b*,*f*]azocine (9g): To a stirred solution of hydroxylamine **8g** (68.9 mg, 0.306 mmol) in CH_2Cl_2 (3.1 mL), DIBALH (1.79 mL, 1.83 mmol, 1.02 M in *n*-hexane) was added dropwise at 0 °C under an argon atmosphere. Stirring was continued for 3.5 h at 0 °C. NaF powder (385 mg, 9.18 mmol) and water (100 μL) were added at 0 °C, and the resulting mixture was stirred for 30 min at the same temperature. Then the reaction mixture was filtered through a Celite pad. The filter cake was washed with CH_2Cl_2 and Et_2O, and the combined organic solutions were evaporated under reduced pressure. The residue was purified by preparative TLC (SiO_2, *n*-hexane:EtOAc = 9:1) yielded **9g** (44.4 mg, 69%):[2b] colorless crystals; mp 128-130 °C; IR (KBr) 3364, 2924, 1603, 1477 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.10-7.05 (3H, m), 7.02 (1H, dd, *J* = 8.0, 1.6 Hz), 6.97 (1H, dd, *J* = 7.6, 1.6 Hz), 6.89 (1H, ddd, *J* = 8.0, 7.6, 1.6 Hz), 6.68 (1H, ddd, *J* = 7.6, 7.6, 1.6 Hz), 6.49 (1H, dd, *J* = 8.0, 1.6 Hz), 4.42 (2H, s),

3.93 (1H, br s), 3.29 (2H, t, J = 7.2 Hz), 3.17 (2H, t, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 140.6, 137.3, 131.1, 130.3, 129.5, 129.3, 127.3, 126.8, 126.5, 120.0, 119.0, 51.8, 35.5, 32.5; LRMS (EI) *m/z* 209 (M^+); HRMS (EI) *m/z* Calcd for $C_{15}H_{15}N$ (M^+) 209.1204, Found 209.1179.

Similarly, the rearrangement reactions of hydroxylamines **8a-f** or **8h-k**[5-12] with DIBALH were carried out to afford compounds **6**, **9a**, **9c-e**, **9h-k**, or **10f**,[15] which were identified with those of the literatures reported previously.

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