C–C Bond Cleavage of Cyclohexene Oxide in the Reaction with 1-Aminoindoline

Yoshimitu Kiryu, Satoshi Itoh, Kimiyoshi Kaneko, and Hajime Katayama*

Niigata College of Pharmacy, 5–13–2 Kamishin'ei-cho, Niigata 950–2081, Japan.

Received May 19, 1998; accepted August 10, 1998

The reaction of cyclohexene oxide with 1-aminoindoline under neat conditions gave a C–C bond-cleavage product of cyclohexene oxide as a dihydrazone and a 1,2-aminoalcohol-type product. No hydrazinoalcohol was obtained.

Key words 1-aminoindoline; epoxide ring opening; C–C bond cleavage; dihydrazone formation

In the course of studies on the chemistry and biological activity of pyrazolo[1,5-*a*]indole derivatives,[1] we were required to prepare 1,2-hydrazinoalcohol **5** as a potential intermediate, after oxidation to a keto-indole derivative, for the preparation of indolo[1,2-*b*]indazoles, compounds having an additional ring at the C2–C3 bond position of pyrazolo[1,5-*a*]indole. Since phenylhydrazine was reported to react with epoxide to afford the hydrazinoalcohol,[2] we examined this reaction for our purpose. When 1,2-epoxycyclohexane (**2**) (3 mol eq) was reacted with 1-aminoindoline (**1**) at 120 °C for 2 d under neat conditions, two products were obtained after chromatographic separation of the reaction product. The first product (15%) was crystalline (mp 133.0—135.0 °C) and the second (30%) was an oil. The composition of the crystalline material was $C_{22}H_{26}N_4$ by high resolution mass spectrometry (HR-MS) and elemental analysis. ^{1}H-NMR showed thirteen protons, among which signals for four aromatic protons and two triplet signals for two methylene protons suggested the presence of the indoline structure. The presence of an aldehyde hydrazone unit, *i.e.* N–N=C<u>H</u>–, was evident from the signal at δ 6.73 which appeared as a triplet (J=5.4 Hz) with small triplet coupling (J=0.8 Hz) due to the two adjacent methylene units. In the H-H correlation spectroscopy (H-H COSY) spectrum weak coupling was observed between this proton and 2-H of the indoline unit. In the phase-sensitive nuclear Overhauser and exchange spectroscopy (PNOSY), correlation between these protons was also observed. Two methylene units were detected at δ 1.68 and 2.38 as multiplets that were correlated with the hydrazone proton (δ 6.73) in the PNOSY spectrum. In the ^{13}C-NMR spectrum, eleven different carbon atoms were detected. Based on these analyses, the symmetrical structure **3** was assigned to this product (Chart 1).

This structure was confirmed by an alternative preparation starting from cyclohexene (reaction 2 in Chart 1). Dihydroxylation of cyclohexene, glycol-cleavage of the glycolic product[3] and subsequent reaction of the dialdehyde with 1-aminoindoline (**1**) yielded the dihydrazone which was identified by comparison with the sample **3** obtained above by NMR and MS spectroscopy.

The second oily product was further purified by preparative thin layer chromatography (TLC). The purified material had an OH absorption in the IR spectrum (3519 cm^{-1}). The ^{1}H-NMR spectrum supported the presence of indoline and cyclohexane rings. The configuration of the hydroxy group on the cyclohexane ring was found to be equatorial since the proton at the carbon bearing the OH group (δ 3.63) displayed td splittings (J=10.0, 6.1 Hz). The signals for the adjacent CH group bearing nitrogen were not detected because of masking by multiplet signals (δ 3.28—3.22). In the ^{13}C-NMR spectrum fourteen carbons, including six aromatic ones, were detected. As the MS spectrum showed a molecular peak (M$^+$) at m/z 217, which is 15 units (NH) less than that of the expected product **5**, the structure **4** was assigned to this oily product. When **4** was treated with carbonyldiimidazole (CDI), no cyclic carbamate **6** was formed, but carbamate **7** (M$^+$, m/z 311 in MS) having an imidazole ring was obtained in 69% yield after purification (Chart 2). Final confirmation of the adduct **4** was carried out by independent synthesis according to the pathway **2** shown in Chart 2.

Thus, indoline and 1,2-epoxycyclohexane (**2**) were reacted in acetonitrile at room temperature for 1 h in the presence of lithium perchlorate.[4] The adduct **4** was obtained in 66% yield, which was similarly transformed to carbamate **7** and these products were compared with the materials obtained above. When similar reaction conditions were adopted to the reaction of 1-aminoindoline (**1**) and epoxide **2**, three products, **3** (14%), **4** (18%) and **5** (38%) were obtained. The structure of **3** and **4** were confirmed by comparison with the above specimens by ^{1}H-NMR spectra. The product **5** was found to be the initially desired one and its structure was supported by the following observations: (i) Composition was determined to be $C_{14}H_{20}N_2O$ by HR-MS. (ii) The shift of the C-2 signal to low magnetic field (13.6 ppm) in the ^{13}C-NMR spectrum was observed in hydrazinoalcohol **5** compared with aminoalcohol **4**. A similar shift was detected in *N*-aminoindoline (13.6 ppm). Further, the 2′-H proton of **5** in the ^{1}H-NMR spectrum appeared at higher magnetic field (δ 3.22—3.28 ppm) than that of **4** (δ 2.86—3.00 ppm). The assignments of these signals were supported by H-H COSY and C-H COSY spectra, although precise resolution was not possible. A similar shift of protons was also observed in **11b** and **11c**, *vide infra*. The stereochemistry of **5** was determined from the coupling constant of the 2′-H proton as for **4**. Thus C–C bond cleavage of epoxide was further investigated with other hydrazines (Chart 3) and the results are summarized in Table 1. For comparison, the result with **1** is included in the table.

When the aliphatic hydrazine **8a** (or **8b**) was reacted with an equivalent of epoxide **2** in the presence of excess $LiClO_4$, the adduct **11a** (or **11b**) was obtained as a sole product. The composition of the adduct was confirmed by the HR-MS

---

* To whom correspondence should be addressed.

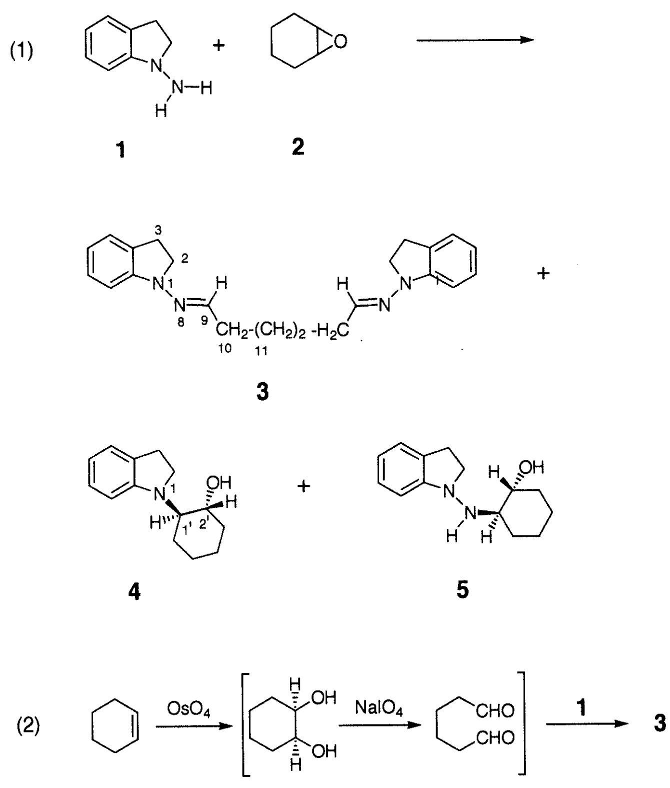

Chart 1

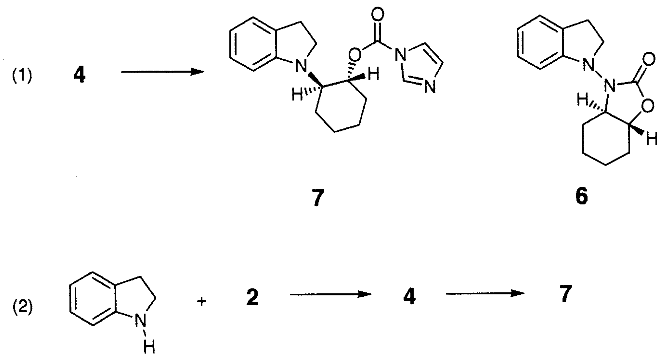

Chart 2

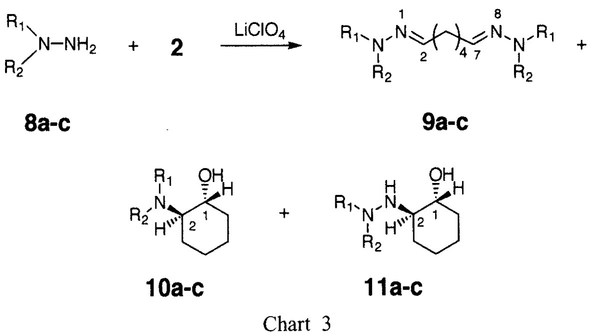

Chart 3

Table 1. Reaction of Hydrazine **8** with Epoxide **2** in the Presence of $LiClO_4$

Hydrazine	R^1	R^2	Time (h)	Product (%)		
8a	Me	Me	9	**9a**: —	**10a**: —	**11a**: 10
8b	$-(CH_2)_5-$		5	**9b**: —	**10b**: —	**11b**: 61
8c	Ph	Me	5	**9c**: 10	**10c**: 34	**11c**: 10
1			10	**3**: 14	**4**: 18	**5**: 38

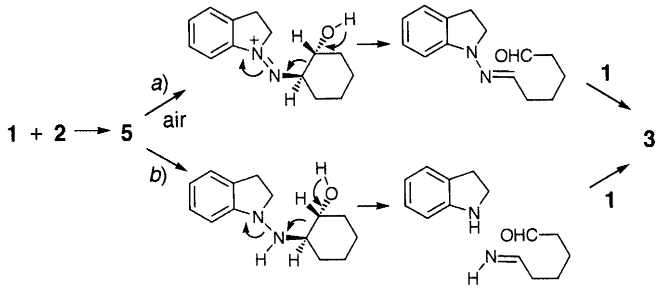

Chart 4

spectrum and the stereochemistry was determined by analysis of the ^{1}H-NMR spectrum. When a similar reaction was carried out with *N*-methyl-*N*-phenylhydrazine **8c**, three products were obtained. The first product from the column chromatography was crystalline dihydrazone **9c**, whose structure was determined by detailed analyses of the ^{1}H- and ^{13}C-NMR spectra as in the case of **3**, *vide supra*. The structures of the other two products, **10c** and **11c**, were determined similarly as described above. Since the aliphatic hydrazine reacted to give the adduct as a sole product and the product derived from the C–C bond cleavage of epoxide was only produced from the aromatic hydrazines (Table 1), the presence of an aromatic ring in the hydrazine appears to be essential for C–C bond cleavage. The yields of the cleavage product **3** and **9c** were not improved after repeating experiments.

Periodic acid is reported to open the epoxide ring and cleave the C–C bond simultaneously5) but this is a normal oxidative cleavage of the C–C bond of the glycol formed by acid-catalyzed ring opening of an epoxide. Kempmann *et al.* have reported that a 1,2-hydrazinoalcohol, after oxidation to the azoalcohol and subsequent exposure to acid, can undergo C–C bond cleavage.2) Another example of epoxide ring opening and subsequent C–C bond cleavage is the Eschenmoser fragmentation of a α,β-epoxyhydrazone which eventually gives the ethynylformyl compound.6) Selective C–C bond cleavage of epoxide without C–O opening is reported to be possible only when special structural requirements are realized, *i.e.*, the carbonyl ylide formation.7) In our reaction, the conditions are nearly neutral and no assistance of acid is involved. For the formation of dihydrazone **3**, two reaction pathways are possible starting from hydrazinoalcohol **4** which will be initially formed by the nucleophilic epoxide ring opening (Chart 4). In pathway a, air oxidation of **4** to azonium alcohol may be essential and initiate C–C bond cleavage as in the case of Kempmann *et al.*2) The second pathway b involves fragmentation possibly *via* intramolecular proton transfer. Indoline thus formed in this pathway can participate in opening the epoxide ring leading to indolinoalcohol **4**. The reaction of **8c** and **2** may take similar pathway.

In conclusion our observations above constitute a novel example of C–C bond cleavage of an epoxide ring in the reaction of 1,2-epoxycyclohexane **2** with aromatic hydrazines **1** and **8c** under neutral conditions.

Experimental

Melting points (mp) were determined on Yanaco micro-melting point apparatus without correction. IR spectra (KBr pellet unless stated otherwise) were measured on a Perkin-Elmer FT-IR 1720. ^{1}H- and ^{13}C-NMR were obtained at ambient temperature (25—27 °C) with a JEOL JNM-FT 200 and

JNM-ALPHA 400 in $CDCl_3$ unless otherwise specified, with tetramethylsilane as an internal standard. MS and HR-MS were recorded on Hitachi RMU-7MG and the figures in parentheses indicate the relative intensities. Anhydrous tetrahydrofuran (THF) was prepared by distilling in the presence of ketyl radical and dry acetonitrile by distilling with calcium hydride.

Reaction of 1,2-Epoxycyclohexane (2) with 1-Aminoindoline (1) a) Neat Reaction: A mixture of **1** (1.39 g, 10 mmol) and **2** (3 ml, 30 mmol) was heated at 100 °C for 2 h, then at 120 °C for 1 d. After brief evaporation with a Kugelrohr distillation apparatus at ca. 60 °C under water-aspiration, the residue (3.07 g)was subjected to flash column chromatography (silica gel 150 g, hexane–ethyl acetate 4 : 1). Fractionation gave the first eluate, which was crystallized (CH_2Cl_2–*iso*-Pr_2O) to give **3** (258 mg), and the second eluate (0.65 g). Dihydrazone **3**, yellow needles, mp 133.0—135.0 °C (EtOAc). MS *m/z*: 346 (M^+, 19.6), 344 (7.6), 227 (13.5), 213 (13.0), 212 (50.4), 134 (10.0), 119 (38.0), 118 (100), 117 (42.0), 116 (14.1), 96 (12.2), 91 (51.2), 90 (12.7), 89 (13.2). HR-MS. Calcd for $C_{22}H_{26}N_4$: 346.2211. Found: 346.2183. IR cm^{-1}: 1606, 1591, 1489, 1463, 1402, 752. ^{1}H-NMR δ: 1.68 (2H, m, 11-H), 2.38 (2H, m, 10-H), 3.11 (2H, t, J=8.3 Hz, 3-H), 3.61 (2H, t with broadening, J=8.3 Hz, 2-H), 6.73 (1H, tt, J=5.4, 0.8 Hz, 9-H), 6.75 (1H, td, J=7.3, 1.2 Hz, 5-H), 7.05 (1H, dm, J=7.8 Hz, 7-H), 7.08 (1H, dm, J=7.3 Hz, 4-H), 7.117 (1H, tm, J=7.6 Hz, 6-H). ^{13}C-NMR δ: 27.1 (C-11), 27.2 (C-3), 32.7 (C-10), 48.8 (C-2), 108.8 (C-7), 119.5 (C-5), 124.6 (C-4), 126.8 (C-4a), 127.7 (C-6), 137.8 (C-9), 149.1 (C-7a). *Anal.* Calcd for $C_{22}H_{26}N_4$: C, 76.27; H, 7.56; N, 16.17. Found: C, 76.21; H, 7.60; N, 16.15. Preparative TLC of the second eluate (silica gel, ethyl acetate–hexane 1 : 4 and CH_2Cl_2) gave a pure sample of **4** as an oil, MS *m/z*: 217 (M^+, 75.0), 158 (100), 145 (18.6), 132 (42.6), 118 (15.0), 91 (6.4); IR ($CHCl_3$) cm^{-1}: 3519, 1606, 1488, 1386, 1264, 1237, 1072. ^{1}H-NMR δ: 1.26—1.4 (4H, m), 1.69—1.71 (1H, m), 1.77—1.79 (2H, m), 2.17—2.22 (1H, m), 2.97 (2H, dd, J=10.0, 6.1 Hz, 3-H_2), 3.22—3.28 (1H, m, 1′-H), 3.28—3.33 (1H, m, 2-H), 3.46 (1H, dt, J=8.3, 6.4 Hz, 2-H), 3.63 (1H, td, J=10.0, 4.4 Hz, 2′-H), 6.53 (1H, d, J=7.8 Hz, 7-H), 6.67 (1H, t, J=7.5 Hz, 5-H), 7.06 (1H, t, J=7.5 Hz, 6-H), 7.08 (1H, d, J=7.3 Hz, 4-H); ^{13}C-NMR δ: 23.7, 24.2, 25.2, 28.4, 33.4, 46.5, 61.7, 70.5, 107.5, 118.0, 124.6, 127.3, 130.4, 151.2.

b) Reaction in the Presence of $LiClO_4$: A mixture of hydrazine **1** (252 mg, 1.88 mmol) and 1,2-epoxycyclohexane (**2**) (0.19 ml, 1.88 mmol) in dry acetonitrile (0.5 ml) containing lithium perchlorate (210 mg, 1.98 mmol) was refluxed for 10 h under dry nitrogen. The reaction mixture was poured into aqueous 10% Na_2CO_3 solution and extracted with CH_2Cl_2. The extracts were washed (saturated brine), dried (anhydrous Na_2SO_4) and evaporated in vacuo to give the crude product which was purified by column chromatography (silica gel 20 g, hexane–CH_2Cl_2 2 : 3 to CH_2Cl_2 only), yielding the products **3** (14%), **4** (18%) and **5** (38%). Product **3** and **4** were identified by comparison with the samples obtained above by ^{1}H-NMR spectra. Hydrazinoalcohol **5**, MS *m/z*: 232 (M^+, 100), 133 (98.1), 118 (85.1), 91 (39.5), 85 (68.7), 82 (53.4). HR-MS: Calcd for $C_{14}H_{20}N_2O$: 232.1576. Found: 232.1571. IR ($CHCl_3$) cm^{-1}: 3387, 1607, 1486, 1255, 1044. ^{1}H-NMR δ: 1.23—1.37 (4H, m), 1.72—1.74 (2H, m), 1.82—1.85 (1H, m), 1.98—2.04 (1H, m), 2.86—3.00 (3H, m, 1′-H, 3-H_2), 3.15 (1H, dd, J=17.6, 8.5 Hz, 2-H), 3.58—3.64 (1H, m, 2′-H), 3.75 (1H, td, J=8.3, 5.4 Hz, 2-H), 4.18 (1H, br s, OH), 6.85 (1H, t, J=7.3 Hz, 5-H), 7.00 (1H, d, J=7.8 Hz, 7-H), 7.11 (1H, d, J=8.0 Hz, 4-H), 7.15 (1H, t, J=7.6 Hz, 6-H). ^{13}C-NMR δ: 24.0, 24.5, 28.0 (C-3), 29.7, 33.3, 58.8 (C-2), 62.4 (C-1′), 75.6 (C-2′), 111.1 (C-7), 121.0 (C-5), 124.6 (C-4), 127.4 (C-6), 128.5 (C-3a), 153.2 (C-7a).

Alternative Preparation of 3 A solution of cyclohexene (0.1 ml, 1 mmol) and 4% osmium tetroxide (0.3 ml, 5 mol %) in a mixture of ether and water (1 : 1, 6 ml) was stirred vigorously, and to this solution sodium periodate (432 mg, 2 mmol) was added gradually over a period of 1 h. The resulting solution was stirred at room temperature for 2 h. The solution was diluted with ethyl acetate and the organic phase was collected. Washing (saturated brine), drying (anhydrous sodium sulfate) and concentration of the organic extracts gave a liquid product (*ca.* 0.5 ml) which was immediately dissolved in ethyl acetate (2.5 ml) and treated with a solution of 1-aminoindoline (**1**) (228 mg, 1.7 mmol) in ethyl acetate (1 ml). After 0.5 h, the solution was concentrated *in vacuo*, and the residue was chromatographed (silica gel, ethyl acetate–hexane 1 : 9 to 1 : 2). The dihydrazone was obtained as yellow needles (162 mg, 46%), mp 134—135 °C (*iso*-Pr_2O) which were identical with the above sample of **3** by comparison of mp, MS, ^{1}H-NMR and ^{13}C-NMR spectra. The hydrazine **1** (966 mg, 29%) was also recovered from the column.

Carbamate 7 Under dry nitrogen, CDI (153 mg, 1.5 eq) was added to a solution of **4** (146 mg, 0.63 mmol) in dry THF (15 ml) and the solution was stirred at room temperature for 4 h. For completion of reaction, additional CDI (155 mg, total 308 mg, 3 eq) and stirring overnight were required. The solution was poured into water and extracted with ether. The extracts were washed (saturated brine), dried (anhydrous sodium sulfate) and evaporated to give the crude product (210 mg). Column chromatography (silica gel, ethyl acetate–hexane 1 : 2) yielded the carbamate **7** (145 mg, 69%) as an oil, MS *m/z*: 311 (M^+, 63.1), 267 (12.7), 216 (7.2), 199 (7.1), 171 (4.2), 158 (75.0), 145 (15.0), 132 (13.5), 118 (11.4), 82 (100); IR ($CHCl_3$) cm^{-1}: 1757, 1607, 1490, 1395, 1322, 1292, 1282, 1243, 1181, 1097, 1006, 669. ^{1}H-NMR δ: 1.37—1.46 (2H, m), 1.54—1.68 (2H, m), 1.86—1.89 (2H, m), 1.94 (1H, td, J=13.4, 3.2 Hz), 2.27—2.30 (1H, m), 2.91 (2H, t, J=8.6 Hz, 3-H_2), 3.41 (1H, dd, J=13.7, 8.3 Hz, 2-H), 3.45 (1H, dd, J=13.7, 8.6 Hz, 2-H), 3.67 (1H, ddd, J=11.7, 10.5, 3.9 Hz, 1′-H), 5.13 (1H, td, J=10.5, 4.6 Hz, 2′-H), 6.45 (1H, d, J=7.8 Hz, 7-H), 6.51 (1H, t, J=7.3 Hz, 5-H), 6.99—6.93 (3H, m, Ar-H+Imd-H), 7.14 (1H, s, Imd-H), 7.88 (1H, s, Imd-H); ^{13}C-NMR δ: 151.0, 148.0, 136.9, 129.5, 129.0, 127.0, 124.5, 117.1, 117.0, 106.0, 77.3, 57.6, 46.0, 31.5, 28.1, 27.8, 24.8, 24.1.

Alternative Preparation of 4 and 7 a) Indoline (1 ml, 8.9 mmol) was added to a solution of 1,2-epoxycyclohexane (**2**) (1 ml, 9.9 mmol) in dry acetonitrile (2 ml) containing lithium perchlorate (1.064 g, 10 mmol) under dry nitrogen and the resulting mixture was stirred at ambient temperature for 1 h. The solution was poured into water and extraction with ether gave crude product (1.56 g) which was purified by column chromatography (silica gel, ethyl acetate–hexane 1 : 4), yielding an oil (1.27 g, 66%). This product was identical with **4** obtained above by ^{1}H-NMR spectral comparison. b) The above oil **4** (75.9 mg, 0.35 mmol) and CDI were reacted in dry THF at ambient temperature as described above. CDI was added in two portions (70 mg+225 mg, 1.39 mmol) at an interval of 4.5 h and the reaction was continued for 2 d. Purification of the crude product (120 mg) by preparative TLC (silica gel, ethyl acetate–hexane 1 : 2) gave an oil (89 mg, 83%) which was identified with the carbamate **7** by ^{1}H-NMR spectral comparison.

General Procedure for the Reaction of Hydrazine 8 with Epoxide 2 in the Presence of $LiClO_4$ Hydrazine **8** (5 mmol) was added to a solution of 1,2-epoxycyclohexane (**2**) (5 mmol) in dry acetonitrile (1 ml) containing lithium perchlorate (5 mmol) under dry nitrogen and the resulting mixture was heated to reflux until the disappearance of **8** was noted. The solution was poured into aqueous 10% Na_2CO_3 solution and extracted with CH_2Cl_2, to yield crude product which was purified by column chromatography.

***trans*-2-(*N′*,*N*-Dimethylhydrazino)cyclohexanol (11a)**: MS *m/z*: 158 (M^+, 70.1), 143 (3.9), 138 (5.8), 114 (20.3), 99 (16.3), 86 (12.2), 80 (9.0), 67 (6.1), 58 (100), 43 (22.6). HR-MS: Calcd for $C_8H_{18}N_2O$: 158.1419. Found: 158.1411. IR ($CHCl_3$) cm^{-1}: 3313, 1670, 1451, 1240, 1071, 668. ^{1}H-NMR δ: 0.95—1.05 (1H, m), 1.12—1.23 (3H, m), 1.39—1.45 (1H, m), 1.60—1.62 (2H, m), 1.83—1.89 (1H, m), 2.41 (6H, s, NMe_2), 2.58 (1H, ddd, J=11.2, 8.3, 3.9 Hz, 2-H), 3.43 (1H, ddd, J=10.5, 8.3, 4.9 Hz, 1-H). ^{13}C-NMR d: 23.6 , 24.4 , 29.0, 33.0, 47.5 (2×C, NMe_2), 59.1 (C-2), 77.4 (C-1).

***trans*-2-Piperidinoamino cyclohexanol (11b)**: White needles, mp 72—73 °C (hexane), MS *m/z*: 198 (M^+, 100), 178 (6.1), 139 (15.5), 125 (11.3), 114 (11.7), 99 (90.3), 84 (78.9), 53 (30.2). HR-MS: Calcd for $C_{11}H_{22}N_2O$: 198.1732. Found: 198.1714. IR cm^{-1}: 3210, 2927, 1451, 1138, 1071, 1037, 862. ^{1}H-NMR δ: 1.04—1.69 (14H, m), 1.93—1.95 (1H, m), 2.56 (3H, br), 2.74 (1H, ddd, J=11.7, 8.4, 3.9 Hz, 2-H), 3.47—3.53 (1H, m, 1-H). ^{13}C-NMR δ: 23.57, 23.64 (2×C), 24.5, 26.0 (2×C), 29.0, 33.0 (2×C), 58.5 (C-2), 77.2 (C-1).

Hexanedial,bis(*N′*-methyl-*N′*-phenyl hydrazone) (9c): White needles, mp 63—64 °C (hexane), MS *m/z*: 322 (M^+, 66.4), 215 (14.9), 201 (88.4), 159 (11.9), 133 (10.5), 122 (17.3), 107 (100), 95 (10.9), 76 (70.9). HR-MS: Calcd for $C_{20}H_{26}N_4$: 322.2157. Found: 322.2174. IR cm^{-1}: 1695, 1504, 1327, 1113, 756. ^{1}H-NMR δ: 1.66—1.69 (4H, m), 2.40—2.45 (4H, m), 3.21 (6H, s, NMe_2), 6.82—6.87 (4H, m, 2-H, 7-H, 2×*p*-H), 7.21—7.28 (8H, m). ^{13}C-NMR δ: 27.2 (2×C), 32.8 (2×C), 33.0 (NMe_2), 114.8 (4×C-*o*), 119.7 (2 x C-*p*), 128.9 (4×C-*m*), 135.6 (C-2, 7), 148.3 (2×C-*ipso*).

***trans*-2-(*N*-Methyl-*N*-phenylamino)cyclohexanol (10c)**: MS *m/z*: 205 (M^+, 51.7), 146 (100), 132 (17.8), 120 (22.3), 107 (8.4), 91 (6.5), 75 (9.3), 69 (5.7), 41 (5.4). HR-MS: Calcd for $C_{13}H_{19}NO$: 205.1467. Found: 205.1472. IR ($CHCl_3$) cm^{-1}: 3524, 1598, 1499, 1451, 1296, 1137, 1071, 997, 669. ^{1}H-NMR δ: 1.24—1.30 (2H, m), 1.35—1.46 (2H, m), 1.68—1.78 (3H, m), 2.17—2.22 (1H, m), 2.76 (3H, s, NMe), 3.40 (1H, ddd, J=11.7, 9.8, 3.4 Hz, 2-H), 3.66 (1H, td, J=9.8, 4.4 Hz, 1-H), 6.80 (1H, t, J=7.3 Hz, *p*-H), 6.93 (2H, d, J=8.5 Hz, *o*-H), 7.22—7.26 (2H, m, *m*-H). ^{13}C-NMR δ: 24.3, 25.4 , 26.0, 31.1 (NMe), 33.4, 67.0 (C-2), 70.0 (C-1), 115.6 (2×C-*o*), 118.6 (C-*p*), 129.1 (2×C-*m*), 151.3 (C-*ipso*).

***trans*-2-(*N′*-Methyl-*N′*-phenyl hydrazino)cyclohexanol (11c)**: Light brown needles, mp 70.5—71.5 °C (hexane). MS *m/z*: 220 (M^+, 100), 132 (4.6), 121 (76.1), 108 (30.5), 92 (5.0), 76 (37.4). HR-MS: Calcd for $C_{13}H_{20}N_2O$: 220.1576. Found: 220.1577. IR cm^{-1}: 3431, 1605, 1510, 1456, 1197, 1043, 822, 748, 692. ^{1}H-NMR δ: 1.17—1.30 (4H, m), 1.66—1.72 (2H, m), 1.74—1.78 (1H, m), 1.93—1.97 (1H, m), 2.80—2.86 (1H, m, 2-H), 3.03 (3H, s, NMe), 3.59 (1H, td, J=9.8, 4.4 Hz, 1-H), 6.84 (1H, t, J=7.3 Hz, *p*-H), 7.10 (2H, d, J=7.8 Hz, *o*-H), 7.22—7.26 (2H, m, *m*-H). ^{13}C-NMR δ: 24.1, 24.3, 29.5, 33.7, 41.1 (NMe), 61.0 (C-2), 75.3 (C-1), 115.0 (2×C-*o*), 119.9 (C-*p*), 128.9 (2×C-*m*), 151.0 (C-*ipso*).

Acknowledgments We are grateful to Dr. A. Kato in our institution for MS measurements.

References and Notes

1) *a*) Katayama H., Tagawa N., Kawada Y., Shiobara K., Kaneko K., Honda Y., Kondo N., Ikeda Y., *Chem. Pharm. Bull.*, **45**, 143 (1997); *b*) Katayama H., Kato O., Kaneko K., *ibid.*, **44**, 109 (1996); *c*) Shen J.-K., Katayama H., *ibid.*, **42**, 214 (1994).
2) Kempmann A., Zander D., Pfeil E., *Chem. Ber.* **101**, 3037—3046 (1968).
3) Pappo, R., Allen Jr, D. S., *J. Org. Chem.*, **21**, 478—479 (1956).
4) A similar epoxide ring opening in the presence of the Lewis acid Yb(OTf)$_3$ has been reported: Meguro M., Asao N., Yamamoto Y., *J. Chem. Soc.*, *Perkin Trans.* **1**, 2597 (1994).
5) Nagarkatti J. P., Ashley R., *Tetrahedron Lett.*, 4599 (1973).
6) *a*) Felix, R., Eschenmoser, A., *Org. Synth.*, **55**, 52—56 (1976); *b*) March J., "Advanced Organic Chemistry," 3rd Ed., Wiley Interscience, New York, 1985, p. 929.
7) *a*) Huisgen R., "1,3-Dipolar Cycloaddition," Vol. **1**, ed. by A. Padwa, John-Wiley & Sons, New York, 1984, Chap. 1, p. 23; *b*) Linn, W. J., Benson, R. E., *J. Am. Chem. Soc.*, **87**, 3657 (1965); Linn, W. J., ibid., **87**, 3665 (1965).