Studies on the [2,3]-Meisenheimer Rearrangement of 2-Vinylazetidine *N*-Oxides

Ryuji YONEDA, Lisa ARAKI, Shinya HARUSAWA, and Takushi KURIHARA*

Osaka University of Pharmaceutical Sciences, 4–20–1, Nasahara, Takatsuki, Osaka 569–1094, Japan.
Received Nobember 28, 1997; accepted January 19, 1998

Oxidation of 2-vinylazetidine 6a with *m*-chloroperbenzoic acid (*m*CPBA) in methylene dichloride (CH_2Cl_2) gave a mixture of dihydro-7*H*-[1,2]oxazepine 9a and the nitrone 10a. It was clarified that the former was obtained *via* the [2,3]-Meisenheimer rearrangement of the corresponding *cis*-*N*-oxide A, and the latter was formed by successive oxidation of the isoxazolidine 11 formed *via* the [1,2]-Meisenheimer rearrangement of the corresponding *trans*-*N*-oxide B.

Key words Meisenheimer rearrangement; tertiary amine *N*-oxide; 2-vinylazetidine; [1,2]oxazepine; *m*-chloroperbenzoic acid

The thermal [1,2]- and [2,3]-rearrangements of tertiary amine *N*-oxides bearing benzyl or allyl groups are known collectively as the Meisenheimer rearrangement.[1] The [1,2]-Meisenheimer rearrangement of nitrogen heterocycle *N*-oxides has been extensively investigated for the preparation of 1,2-oxaza derivatives. However, few studies on the [2,3]-Meisenheimer rearrangement of cyclic amine *N*-oxides have so far been reported.[1,2]

Recently, we reported[3] a novel ring expansion of 2-vinylhexahydroazetopyridoindoles **1** to the 1,2-oxazepinopyridoindoles **3** *via* the [2,3]-Meisenheimer rearrangement of the corresponding *N*-oxides **2** under very mild reaction conditions (Chart 1). In order to demonstrate the synthetic utility of this method, we synthesized 12-carbaeudistomins **4**.[4] Racemic 6-methoxy-12-carbaeudistomin **4** (R=OMe) showed similar activity against influenza virus to that of natural (−)-debromoeudistomin K **5**.[5] As a continuation of our work on the [2,3]-Meisenheimer rearrangement, we were interested in the *m*-chloroperbenzoic acid (*m*CPBA) oxidation of 2-vinylazetidines **6** lacking the indole moiety of **1**.

The new azetidines **6a—d** were synthesized by Swern oxidation of the known azetidinemethanol **7**[6] followed by the Horner–Emmons or Wittig olefination of the resulting aldehyde **8** in 35—65% yields as shown in Chart 2. Compound **6e** (see Chart 4) was prepared by the reported method.[7]

When a CH_2Cl_2 solution of *m*CPBA (1.0 eq) was added to a CH_2Cl_2 solution of **6a** in the presence of $NaHCO_3$ at room temperature (Chart 3), the reaction proceeded to give two products [**9a** (42%), **10a** (15%)], with recovery (29%) of the starting material **6a** (Table 1). Use of 2.0 eq of *m*CPBA resulted in lower yields of **9a** and **10a**, though the starting material disappeared. The less polar product **9a** [MS *m/z*: 239 (M^+), ^{1}H-NMR δ 5.72 (br d, J=12.5 Hz, 6-H), 5.85 (m, 5-H)] was assigned as methyl 2-

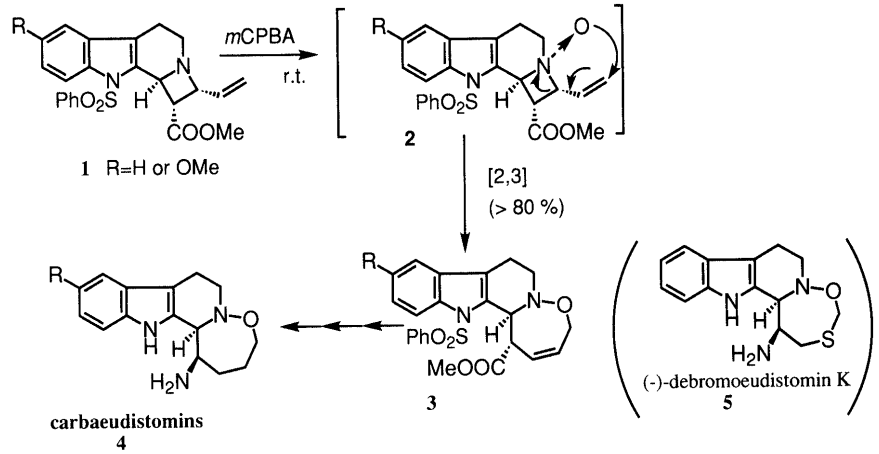


Chart 1

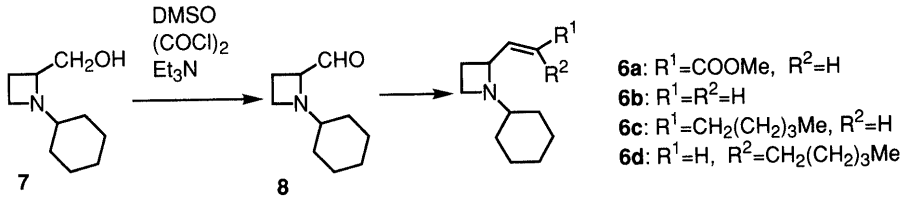


Chart 2

* To whom correspondence should be addressed.

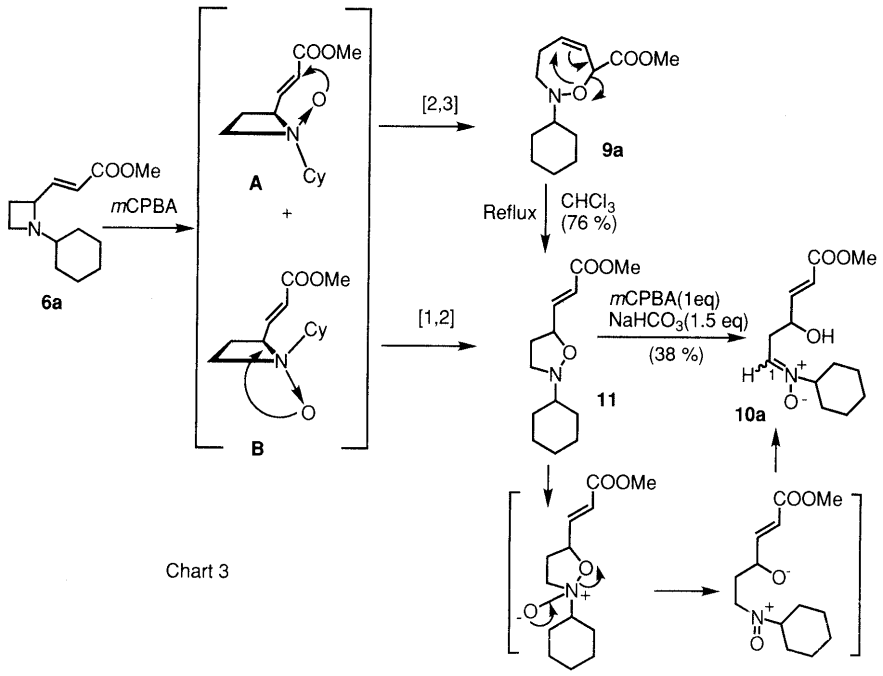
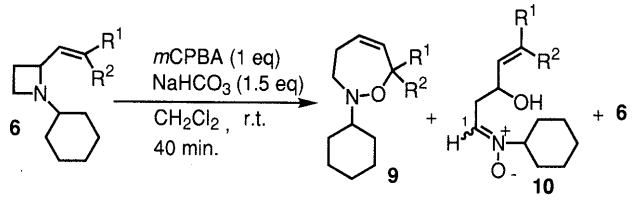


Chart 3

Chart 3

Table 1. Oxidation of the Azetidines (**6a—d**) with *m*CPBA



	R^1	R^2	Yield (%)[a] of **9**	Yield (%)[a] of **10**	Recovery of **6** yield (%)[a]
6a	COOMe	H	**9a** 42	**10a** 15	29
6b	H	H	**9b** 23	**19b** 6	22
6c	C_5H_{11}	H	**9c** 26	**10c** 5	40
6d	H	C_5H_{11}	—	**10d** 39	27

a) Isolated yield.

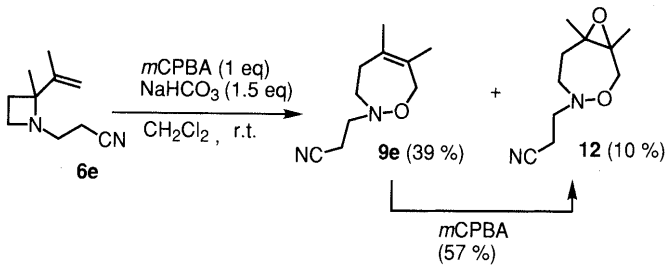


Chart 4

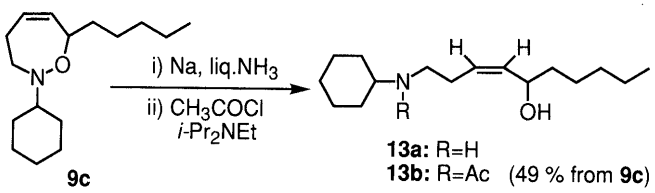


Chart 5

cyclohexyltetrahydro-1,2-oxazepine-7-carboxylate. It is noteworthy that the oxazepine **9a** was converted into the isoxazolidine **11** [MS *m/z*: 239 (M^+), ^{1}H-NMR δ 6.03 (d, J=15.2 Hz, *trans*-CH=CHCOO), 6.90 (dd, J=15.2, 5.9 Hz, *trans*-CH=CHCOO)] in 76% yield *via* [1,3]-shift[3b] under refluxing conditions in $CHCl_3$. The structure of the more polar component **10a** was determined as *N*-(3-hydroxy-5-methoxycarbonyl-4-pentenylidene)cyclohexylamine *N*-oxide[8] on the basis of spectral data, as follows. Inspection of the ^{1}H-NMR spectrum showed C1–H of nitrone moiety[9] at δ 6.90 (t, J=5.8 Hz), and two vinyl protons at δ 6.18 (dd, J=15.5, 2.5 Hz) and 6.92 (dd, J=15.5, 4.8 Hz). Examination of the MS [*m/z* 255 (M^+)] revealed the insertion of two oxygen atoms into **6a**. Oxidation of the isoxazolidine **11** with *m*CPBA in CH_2Cl_2 at room temperature afforded the nitrone **10a** in 38% yield. On the basis of these results, the reaction of **6a** with *m*CPBA was considered to proceed as follows: the [2,3]-Meisenhiemer rearrangement of the *cis*-*N*-oxide A gave the oxazepine **9a**, while the corresponding *trans*-*N*-oxide B initially gave the isoxazolidine **11** *via* the [1,2]-Meisenheimer rearrangement, followed by *N*-oxidation with ring opening, leading to **10a**, as shown in Chart 3.

Analogously, the *m*CPBA oxidation of the azetidines **6b, c** gave a mixture of oxazepines [**9b** (23%), **9c** (26%)] and nitrones [**10b** (6%), **10c** (5%)], respectively, while **6d** afforded only **10d** (39%). A different result was obtained in the case of the azetidine **6e** (Chart 4). Treatment of **6e** with *m*CPBA under ordinary conditions afforded the oxazepine **9e** (39%) and the epoxide **12** (10%). The structure of **12** was assigned on the basis of the spectroscopic data and finally by an alternative synthesis of **12** based on the oxidation of **9e** with *m*CPBA.

We also examined the utility of the oxazepines **9** thus obtained in organic synthesis. Reduction of the oxazepine **9c** with Na in liquid NH_3 at -78 °C afforded a linear

allylic alcohol **13a** [δ 5.49 (td, J=11.0, 7.9 Hz), 5.64 (dd, J=11.0, 6.8 Hz)] with retention of the (*Z*)-stereochemistry of **9c** (Chart 5). The structure of **13a** was supported by conversion into the *N*-acetate **13b**.

Experimental

IR spectra were recorded on a Shimadzu IR-435 spectrometer. ^{1}H-NMR spectra were recorded on Varian XL-300 and Varian Gemini-200 spectrometers in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard and MS on a Hitachi M-4000H instrument. All reactions were carried out in a nitrogen atmosphere. For column chromatography, FL-60D (Fuji Silysia Chemical Ltd.) was used.

Methyl 1-Cyclohexyl-2-azetidinepropenoate (6a) A solution of dimethylsulfoxide (DMSO) (0.64 ml, 9.0 mmol) in CH_2Cl_2 (2 ml) was added to a solution of oxalyl chloride (0.59 ml, 6.75 mmol) in CH_2Cl_2 (14 ml) at −78 °C, and the whole was stirred for 15 min. A solution of **7** (761 mg, 4.5 mmol) in CH_2Cl_2 (4 ml) was added at −78 °C, and the reaction mixture was stirred for 20 min. Et_3N (3.15 ml, 22.5 mmol) was added at this temperature and the whole reaction was stirred for 25 min at 0 °C. The reaction was quenched by the addition of water and diluted with CH_2Cl_2. The organic layer was washed with water and brine, dried over Na_2SO_4, and evaporated to give the aldehyde **8**. A solution of the crude **8** and methyl (triphenylphosphoranylidene)acetate (1.95 g, 5.9 mmol) in benzene (30 ml) was refluxed for 15 h. The reaction mixture was then diluted with hexane, and the resulting insoluble precipitate was filtered through a Celite pad and washed with hexane. The combined hexane solution was evaporated *in vacuo*, and the residue was purified by column chromatography (35% EtOAc in hexane) to give **6a** (546 mg, 76%) as an oil. IR (neat) cm^{-1}: 1710 ($COOCH_3$). ^{1}H-NMR δ: 0.81—2.21 (m, 13H, cyclohexyl-H, 3-H), 2.82 (q, 1H, J=8.2 Hz, 4-H_a), 3.34 (m, 1H, 4-H_b), 3.67 (m, 1H, 2-H), 3.69 (s, 3H, CH_3), 5.95 (d, 1H, J=15.7 Hz, CHCOO), 7.04 (dd, 1H, J=15.6, 6.2 Hz, CH=CCOO). MS *m/z*: 223 (M$^+$). HR-MS Calcd for $C_{13}H_{21}NO_2$: 223.1571. Found: 223.1564.

1-Cyclohexyl-2-vinylazetidine (6b) A 0.5 M toluene solution of $(TMS)_2NK$ (22.4 ml, 11.2 mmol) was added to a solution of methyltriphenylphosphonium bromide (4.04 g, 11.2 mmol) in tetrahydrofuran (THF) (40 ml) with stirring at −20 °C. After 20 min, a solution of the crude aldehyde **8**, prepared from the alcohol **7** (761 mg, 4.5 mmol), in THF (5 ml) was added to the reaction mixture, and the whole was stirred for 40 min. The reaction mixture was quenched with water, and extracted with Et_2O. The extract was washed with brine, and dried over $MgSO_4$. After evaporation of the solvent under reduced pressure, the residue was purified by column chromatography (30% EtOAc in hexane) to give **6b** (319 mg, 43%) as an oil. ^{1}H-NMR δ: 0.76—1.86 (m, 11H, cyclohexyl-H), 1.97 (m, 2H, 3-H_2), 2.68 (q, 1H, J=7.3 Hz, 4-H_a), 3.23 (td, 1H, J=7.3, 3.2 Hz, 4-H_b), 3.47 (q, 1H, J=7.0 Hz, 2-H), 4.90 (d, 1H, J=9.5 Hz, *cis*-C=CH), 5.03 (d, 1H, J=17.0 Hz, *trans*-C=CH), 5.95 (ddd, 1H, J=17.0, 9.5, 7.0 Hz, CH=CH_2). MS *m/z*: 165 (M$^+$). HR-MS Calcd for $C_{11}H_{19}N$: 165.1517. Found: 165.1513.

(*E*)-1-Cyclohexyl-2-(1-heptenyl)azetidine (6c) A 1.03 M cyclohexane–Et_2O solution of PhLi (4.65 ml, 4.79 mmol) was added to a suspension of hexyltriphenylphosphonium bromide (2.05 g, 4.79 mmol) in THF (20 ml) at 0 °C, and the suspension was stirred for 2.5 h. It was then cooled to −78 °C, and a solution of the crude aldehyde **8**, prepared from the alcohol **7** (551 mg, 3.26 mmol), in THF (20 ml) was added dropwise. The whole was stirred for 20 min at −78 °C, then the solution was warmed to −30 °C, and an additional portion of PhLi (1.03 M cyclohexane–Et_2O solution, 4.65 ml, 4.79 mmol) was added. The mixture was stirred for 5 min, and then MeOH (0.65 ml, 16 mmol) was added, followed by phosphate buffer (6.5 ml, pH 7). The whole was warmed to room temperature over 2 h and then poured into water. The mixture was extracted with ether and the extract was washed with water and brine, and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the residue was diluted with hexane, and the resulting insoluble precipitate was filtered through a Celite pad and washed with hexane. The combined hexane solution was evaporated *in vacuo*, and the residue was purified by column chromatography to give **6c** (274 mg, 35%) as an oil from the first fraction eluted with 35% EtOAc in hexane. ^{1}H-NMR δ: 0.81—2.15 [m, 24H, cyclohexyl-H, $CH_3(CH_2)_4$, 3-H], 2.72 (q, 1H, J=7.3 Hz, 4-H_a), 3.28 (t, 1H, J=7.3 Hz, 4-H_b), 3.50 (q, 1H, J=7.3 Hz, 2-H), 5.49 (dt, 1H, J=15.2, 7.3 Hz, NCC=CH), 5.63 (dd, 1H, J=15.2, 7.3 Hz, NCCH=). MS *m/z*: 235 (M$^+$). HR-MS Calcd for $C_{16}H_{29}N$: 235.2299. Found: 235.2290.

The second eluate with the same solvent gave **6d** (16 mg, 2.1%), which was identical with an authentic sample of **6d**, based on a comparison of their ^{1}H-NMR spectra.

(*Z*)-1-Cyclohexyl-2-(1-heptenyl)azetidine (6d) The same procedure as described for the preparation of **6b** provided a crude product from **7** (519 mg, 3.07 mmol), hexyltriphenylphosphonium bromide (3.29 g, 7.71 mmol), and $(TMS)_2NK$ (0.5 M toluene solution, 15.3 ml, 7.64 mmol). This was purified by column chromatography (30% EtOAc in hexane) to give **6d** (446 mg, 65%) as an oil. ^{1}H-NMR δ: 0.78—2.10 [m, 24H, cyclohexyl-H, $CH_3(CH_2)_4$, 3-H], 2.73 (dt, 1H, J=10.3, 7.6 Hz, 4-H_a), 3.29 (t, 1H, J=7.6 Hz, 4-H_b), 3.82 (q, 1H, J=10.2 Hz, 2-H), 5.26 (td, 1H, J=10.2, 7.5 Hz, NCC=CH), 5.61 (t, 1H, J=10.2 Hz, NCCH=). MS *m/z*: 235 (M$^+$). HR-MS Calcd for $C_{16}H_{29}N$: 235.2299. Found: 235.2305.

General Procedure for *m*CPBA Oxidation of Azetidines (6a—d): Methyl 2-Cyclohexyl-2,3,4,7-tetrahydro-1,2-oxazepine-7-carboxylate (9a) and *N*-(5-Methoxycarbonyl-3-hydroxy-4-pentenylidene)cyclohexylamine *N*-Oxide (10a) A solution of 80% *m*CPBA (86 mg, 0.5 mmol) in CH_2Cl_2 (2 ml) was added dropwise to a mixture of **6a** (112 mg, 0.5 mmol) and $NaHCO_3$ (67 mg, 0.8 mmol) in CH_2Cl_2 (2 ml) under ice cooling. The reaction mixture was stirred at room temperature for 40 min, then diluted with CH_2Cl_2 (50 ml). The solution was washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography to give **9a** (50 mg, 42%) as an oil from the first fraction eluted with 15% EtOAc in hexane. IR (neat) cm^{-1}: 1760 ($COOCH_3$). ^{1}H-NMR δ: 1.07—2.39 (m, 11H, cyclohexyl-H, 4-H_a), 2.40—2.76 (m, 2H, NCH, 4-H_b), 2.97, 3.18 (each dt, each 1H, J=12.0, 6.0 Hz, 3-H_2), 3.77 (s, 3H, $COOCH_3$), 4.94 (br s, 1H, 7-H), 5.72 (br d, 1H, J=12.5 Hz, 6-H), 5.85 (m, 1H, 5-H). MS *m/z*: 239 (M$^+$). HR-MS Calcd for $C_{13}H_{21}NO_3$: 239.1520. Found: 239.1511.

The second eluate (EtOAc) gave the starting material **6a** (31 mg, 29% recovery).

The third eluate (50% MeOH in EtOAc) gave **10a** (18 mg, 15%) as an oil. IR (neat) cm^{-1}: 3600 (OH), 1720 ($COOCH_3$). ^{1}H-NMR δ: 1.08—2.10 (m, 11H, cyclohexyl-H, OH), 2.62—3.02 (m, 2H, 2-H_2), 3.72 (m, 1H, CHN), 3.74 (s, 3H, $COOCH_3$), 4.67 (m, 1H, 3-H), 6.18 (dd, 1H, J=15.5, 2.5 Hz, 5-H), 6.90 (t, 1H, J=5.8 Hz, 1-H), 6.92 (dd, 1H, J=15.5, 4.8 Hz, 4-H). MS *m/z*: 255 (M$^+$). HR-MS Calcd for $C_{13}H_{21}NO_4$: 255.1469. Found: 255.1476.

Compound **10a** was alternatively synthesized as follows. The same procedure as described for the general procedure provided a crude product from **11** (46 mg, 0.2 mmol), 80% *m*CPBA (33 mg, 0.2 mmol), and $NaHCO_3$ (24 mg, 0.3 mmol), and this was purified by column chromatography to give **10a** (19 mg, 38%), which was identical with an authentic sample of **10a**, based on comparison of their ^{1}H-NMR spectra.

Similar treatments of the azetidines (**6b—d**) gave oxazepines (**9b, c**) and nitrones (**10b—d**).

2-Cyclohexyl-2,3,4,7-tetrahydro-1,2-oxazepine (**9b**): ^{1}H-NMR δ: 1.02—2.04 (m, 10H, cyclohexyl-H), 2.40 (m, 2H, 4-H_2), 2.53 (m, 1H, NCH), 3.05 (t, 2H, J=6.4 Hz, 3-H_2), 4.33 (br s, 2H, 7-H_2), 5.52—5.65 (m, 1H, 6-H), 5.65—5.79 (m, 1H, 5-H). MS *m/z*: 188 (M$^+$). HR-MS Calcd for $C_{11}H_{19}NO$: 181.1466. Found: 181.1468.

N-(3-Hydroxy-4-pentenylidene)cyclohexylamine *N*-Oxide (**10b**): IR (neat) cm^{-1}: 3420 (OH). ^{1}H-NMR δ: 1.00—2.04 (m, 11H, cyclohexyl-H, OH), 2.53—2.83 (m, 2H, 2-H_2), 3.62 (m, 1H, NCH), 4.38 (m, 1H, 3-H), 5.05 (d, 1H, J=10.8 Hz, 5-H_a), 5.24 (d, 1H, J=16.4 Hz, 5-H_b), 5.82 (ddd, 1H, J=16.4, 10.8, 5.7 Hz, 4-H), 6.86 (t, 1H, J=5.7 Hz 1-H). SI-MS *m/z*: 198 (M$^+$ + 1). HR-MS Calcd for $C_{11}H_{20}NO_2$: 198.1493. Found: 198.1492 (M$^+$ + 1).

2-Cyclohexyl-7-pentyl-2,3,4,7-tetrahydro-1,2-oxazepine (**9c**): ^{1}H-NMR δ: 0.88 (t, 3H, J=7.5 Hz, CH_3), 1.05—2.25 [m, 19H, $(CH_2)_4$, cyclohexyl-H, 4-H_a], 2.47—2.65 (m, 2H, CHN, 4-H_b), 2.86 (dt, 1H, J=12.8, 6.4 Hz, 3-H_a), 3.13 (dt, 1H, J=12.8, 7.0 Hz, 3-H_b), 4.25 (br s, 1H, 7-H), 5.45 (br d, 1H, J=11.3 Hz, 6-H), 5.63 (m, 1H, 5-H). MS *m/z*: 251 (M$^+$). HR-MS Calcd for $C_{16}H_{29}NO$: 251.2248. Found: 251.2246.

(*E*)-*N*-(3-Hydroxy-4-decenylidene)cyclohexylamine *N*-Oxide (**10c**): IR (neat) cm^{-1}: 3300 (OH). ^{1}H-NMR δ: 0.85 (t, 3H, J=7.5 Hz, CH_3), 1.00—2.20 [m, 18H, $(CH_2)_4$, cyclohexyl-H], 2.72 (m, 2H, 2-H_2), 3.68 (m, 1H, CHN), 4.38 (m, 1H, 3-H), 5.47 (dd, 1H, J=15.4, 6.3 Hz, 4-H), 5.70 (dt, 1H, J=15.4, 6.6 Hz, 5-H), 6.90 (t, 1H, J=5.7 Hz, 1-H). SI-MS *m/z*: 268 (M$^+$ + 1). HR-MS Calcd for $C_{16}H_{30}NO_2$: 268.2275. Found: 268.2261 (M$^+$ + 1).

(*Z*)-*N*-(3-Hydroxy-4-decenylidene)cyclohexylamine *N*-Oxide (**10d**): IR (neat) cm^{-1}: 3300 (OH). ^{1}H-NMR δ: 0.90 (t, 3H, J=7.5 Hz, CH_3),

1.08—2.24 (m, 18H, $CH_2 \times 4$, cyclohexyl-H), 2.77 (m, 2H, 2-H_2), 3.71 (br t, 1H, $J=11.4$ Hz, CHN), 4.75 (td, 1H, $J=7.1$, 4.6 Hz, 3-H), 5.48 (m, 2H, 4-H, 5-H), 6.93 (t, 1H, $J=6.2$ Hz, 1-H). SI-MS *m/z*: 268 ($M^+ + 1$). HR-MS Calcd for $C_{16}H_{30}NO_2$: 268.2275. Found: 268.2276 ($M^+ + 1$).

***m*CPBA Oxidation of Azetidine (6e)** The same procedure as described for the general procedure provided a crude product from **6e** (100 mg, 0.6 mmol), 80% *m*CPBA (132 mg, 0.6 mmol), and $NaHCO_3$ (77 mg, 0.9 mmol), and this was purified by column chromatography to give 3-(5,6-dimethyl-2,3,4,7-tetrahydro-1,2-oxazepin-2-yl)propionitrile (**9e**) (43 mg, 39%) as an oil from the first fraction eluted with 30% EtOAc in hexane. IR (neat) cm^{-1}: 2250 (CN). ^{1}H-NMR δ: 1.51, 1.69 (each s, each 3H, $CH_3 \times 2$), 2.38 (t, 2H, $J=6.0$ Hz, 4-H_2), 2.60 (t, 2H, $J=6.6$ Hz, CH_2CCN), 2.88 (m, 4H, 3-H_2, CH_2CN), 4.25 (br s, 2H, 7-H_2). MS *m/z*: 180 (M^+). HR-MS Calcd for $C_{10}H_{16}N_2O$: 180.1262. Found: 180.1269.

The second eluate (60% EtOAc in hexane) gave 3-(5,6-dimethyl-5,6-epoxy-2,3,4,5,6,7-hexahydro-1,2-oxazepin-2-yl)propionitrile (**12**) (12 mg, 10%) as an oil. IR (neat) cm^{-1}: 2250 (CN). ^{1}H-NMR δ: 1.16, 1.32 (each s, each 3H, $CH_3 \times 2$), 1.70—2.98 (m, 8H, 3-H_2, 4-H_2, CH_2CH_2CN), 3.93, 4.08 (each d, each 1H, $J=14.0$ Hz, 7-H_2). MS *m/z*: 196 (M^+). HR-MS Calcd for $C_{10}H_{16}N_2O_2$: 196.1211. Found: 196.1212. This compound **12** was alternatively synthesized as follows. The general procedure provided a crude product from **9e** (43 mg, 0.24 mmol), 80% *m*CPBA (52 mg, 0.24 mmol), and $NaHCO_3$ (30 mg, 0.36 mmol), and this was purified by column chromatography to give **12** (27 mg, 57%), which was identical with an authentic sample of **12**, based on a comparison of their ^{1}H-NMR spectra.

Methyl 3-(2-Cyclohexyl-5-isoxazolidinyl)propenoate (11) A solution of **9a** (50 mg, 0.2 mmol) in $CHCl_3$ (3 ml) was refluxed for 10 h. After removal of the solvent by evaporation, the residue was purified by column chromatography (30% EtOAc in hexane) to give **11** (38 mg, 76%) as an oil. IR (neat) cm^{-1}: 1725 ($COOCH_3$). ^{1}H-NMR δ: 1.09—2.24 (m, 11H, cyclohexyl-H, 4-H_a), 2.38—2.60 (m, 3H, 3-H_2, 4-H_b), 3.26 (br s, 1H, NCH), 3.72 (s, 3H, $COOCH_3$), 4.58 (m, 1H, 5-H), 6.03 (d, 1H, $J=15.2$ Hz, CH=COO), 6.90 (dd, 1H, $J=15.2$, 5.9 Hz, CHCCOO). MS *m/z*: 239 (M^+). HR-MS Calcd for $C_{13}H_{21}NO_3$: 239.1520. Found: 239.1515.

(*Z*)-*N*-Cyclohexyl-*N*-(5-hydroxy-3-decenyl)acetamide (13b) A solution of **9c** (63 mg, 0.25 mmol) and *tert*-BuOH (22 mg, 0.3 mmol) in THF (1 ml) was added to a stirred solution of Na (23 mg, 1 mmol) in freshly distilled ammonia (10 ml) at -78 °C. The mixture was stirred for 15 min, then treated with isoprene (0.3 ml) to discharge the blue color. The ammonia was allowed to evaporate off and saturated NH_4Cl solution (0.5 ml) was added. The mixture was diluted with CH_2Cl_2 (70 ml), dried over $MgSO_4$, and evaporated to give (*Z*)-1-(cyclohexylamino)-3-decen-5-ol (**13a**). The ^{1}H-NMR spectrum of this product clearly showed it to be the (*Z*)-allyl alcohol. Selected signals were as follows: ^{1}H-NMR δ: 2.42 (m, 4H, 1-H_2, 2-H_2), 2.81 (td, 1H, $J=11.3$, 4.5 Hz, NCH), 4.27 (q, 1H, $J=6.8$ Hz, 5-H), 5.49 (dt, 1H, $J=11.0$, 7.9 Hz, 3-H), 5.64 (dd, 1H, $J=11.0$, 6.8 Hz, 4-H). Acetyl chloride (23 mg, 0.3 mmol) was added to a solution of the alcohol **13a** thus obtained and iso-$PrNEt_2$ (39 mg, 0.3 mmol) in CH_2Cl_2 (1 ml). The mixture was stirred at 0 °C for 40 min, then the reaction was quenched with cold water and the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (30% EtOAc in hexane) to give **13b** (36 mg, 49%) as an oil. IR (neat) cm^{-1}: 1625 (CON). ^{1}H-NMR δ: 0.85 (t, 3H, $J=7.5$ Hz, CH_3), 0.95—1.90 [m, 19H, cyclohexyl-H, $(CH_2)_4$, OH], 2.08 (s, 3H, $COCH_3$), 2.10—2.55 (m, 2H, 2-H_2), 3.17 (m, 2H, 1-H_2), 3.45 (m, 1H, NCH), 4.40 (m, 1H, 5-H), 5.47 (m, 2H, 3-H, 4-H). MS *m/z*: 295 (M^+). HR-MS Calcd for $C_{18}H_{33}NO_2$: 295.2510. Found: 295.2514.

References and Notes

1) For a review of the chemistry of amine *N*-oxides, see; Albini A., *Synthesis*, **1993**, 263—277.
2) a) Bailey T. S., Bremner J. B., Carver J. A., *Tetrahedron Lett.*, **34**, 3331—3334 (1993); b) Langlois Y., Gueritte F., Andriamialisoa R. Z., Langlois N., Potier P., Chiaroni A., Riche C., *Tetrahedron*, **32**, 945—949 (1976).
3) *a*) Kurihara T., Doi M., Hamaura K., Ohishi H., Harusawa S., Yoneda R., *Chem. Pharm. Bull.*, **39**, 811—813 (1991); *b*) Kurihara T., Sakamoto Y., Tsukamoto K., Ohishi H., Harusawa S., Yoneda R., *J. Chem. Soc., Perkin Trans 1*, **1993**, 81—87.
4) *a*) Kurihara T., Sakamoto Y., Matsumoto H., Kawabata N., Harusawa S., Yoneda R., *Chem. Pharm. Bull.*, **42**, 475—480 (1994); *b*) Kurihara T., Sakamoto Y., Takai M., Tsukamoto K., Sakai T., Harusawa S., Yoneda R., *ibid.*, **42**, 31—38 (1994).
5) Kurihara T., Sakamoto Y., Kimura T., Ohishi H., Harusawa S., Yoneda R., Suzutani T., Azuma M., *Chem. Pharm. Bull.*, **44**, 900—908 (1996).
6) Rodebaugh R. M., Cromwell N. H., *J. Heterocyclic Chem.*, **8**, 19—24 (1971).
7) Roberto D., Alper H., *J. Am. Chem. Soc.*, **111**, 7539—7543 (1989).
8) The geometry of the nitrone moiety remained undetermined.
9) LeBel N. A., Post M. E., Hwang D., *J. Org. Chem.*, **44**, 1814—1823 (1979).