 Bull. Chem. Soc. Jpn., 74, 917—925 (2001)

Mechanistic Considerations on the Oxime–Nitrone Isomerization and Intramolecular Cycloaddition Reaction of 3-(Alk-2-enylamino)propionaldehyde Oximes

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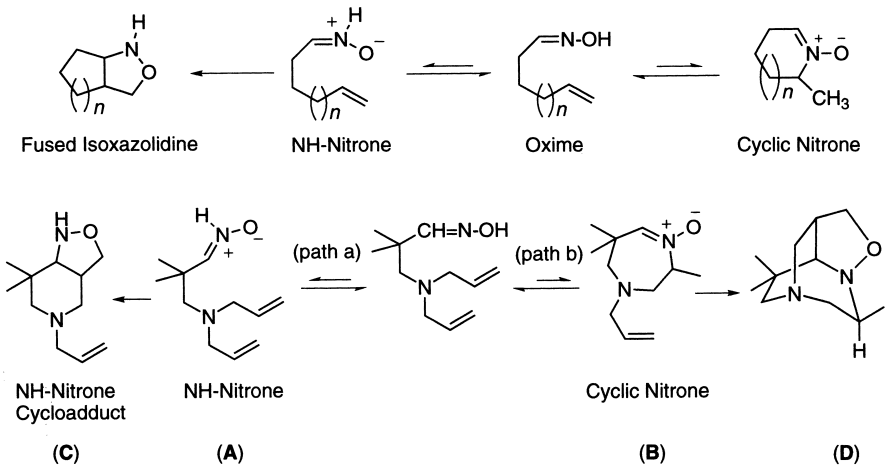
(Received October 2, 2000)

3-(Alk-2-enylamino)- and 3-(acryloylamino)-2,2-dimethylpropionaldehyde oximes underwent thermally induced 1,3-dipolar cycloaddition under mild conditions, leading to perhydroisoxazolo[4,3-*c*]pyridine derivatives. The features of the intramolecular oxime–olefin cycloaddition in this system and the roles of the geminal methyl groups at the 2-position and the alkenylamino nitrogen in the oxime–nitrone isomerization process are discussed based on kinetic studies.

Since a new concept concerning the isomerization of oxime to nitrone through the thermal 1,2-hydrogen shift was proposed by Grigg and co-workers,[1] and the existence of the resultant NH-nitrone was elucidated by forming intramolecular cycloaddition products (named the intramolecular oxime olefin cycloaddition; IOOC), extensive investigations on the synthesis of highly functionalized isoxazolidine derivatives have been developed by many groups.[2] Nevertheless, only a few reports on a further mechanistic elucidation of the oxime–nitrone isomerization have been found;[3] we have demonstrated that a facile oxime–nitrone isomerization takes place in the oximes of heterocyclic aldehydes bearing the *N*-alk-2-enylbenzylamino moiety at the adjacent position.[3a,b] The alkenylbenzylamino nitrogen in the oximes, therein, could play the role as an intramolecular catalyst in the isomerization of oxime to NH-nitrone.

In a previous paper,[4] we showed that the thermal reaction of 3-(*N*,*N*-diallylamino)-propionaldehyde oxime with more conformational flexibility in protic solvents, such as ethanol (EtOH) and butan-1-ol (*n*-BuOH), gave the cycloadduct (C) through an NH-nitrone (A) via a 1,2-H shift of the oxime (path a). On the other hand, a similar reaction in toluene afforded a tricyclic product (D) through cyclic nitrone (B) via an ene-type reaction (ATP reaction)[5] (path b) of the oxime together with the above-mentioned NH-nitrone cycloadduct (Scheme 1). The existence of equilibrium among the oxime and NH-nitrone (A) and cyclic nitrone (B) was suggested based on the effects of the utilized solvents.

In order to obtain further information on the oxime–nitrone isomerization process of this system, we examined the thermal behaviors of further 3-(alk-2-enylamino)propionaldehyde oximes.

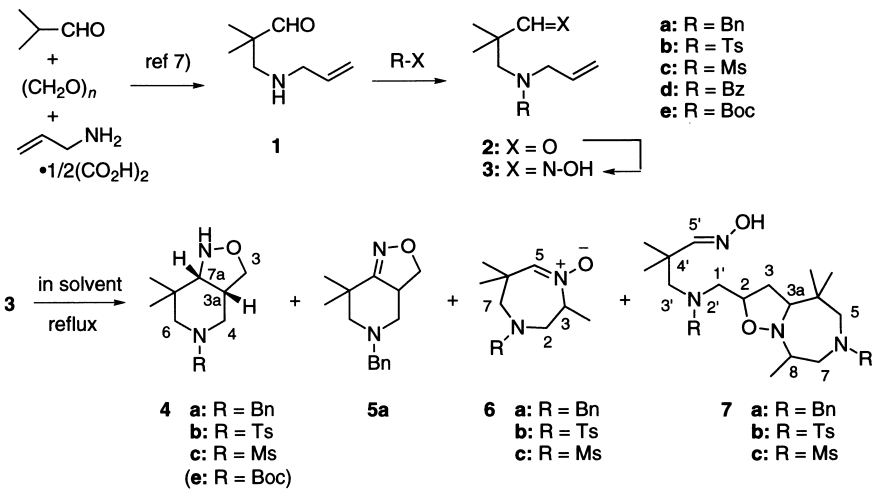


Scheme 1.

Results and Discussion

Oxime–Nitrone Isomerization and Cycloaddition Reaction. In order to elucidate the scope and features of the IOOC in the 3-(alk-2-enylamino)propionaldehyde oximes, four 3-(*N*-substituted allylamino)propionaldehyde oximes **3a–d** were prepared and their thermal behaviors in both protic and aprotic solvents examined (Scheme 2). The reaction of *N*-benzyl oxime **3a** in *n*-BuOH under reflux for 24 h gave *cis*-fused NH-nitrone cycloadduct **4a** in 78% yield.[4] A similar reaction in toluene (in 0.2 M solution) (1 M = 1 mol/dm^{-3}) under reflux for 24 h gave **4a** (42%), isoxazoline **5a** (2%), cyclic nitrone **6a** (3%), and dimeric product **7a** (44%). Isoxazoline **5a** was a secondary product from **4a** and product **7a** was formed by the dimeric cycloaddition reaction of cyclic nitrone **6a** and oxime **3a**, respectively. Product **7a** was obtained as a single isomer and the structure was deduced as being a perhydroisoxazolo[2,3-*d*][1,4]diazepine derivative from the ^{13}C NMR spectrum; the carbon signal at the lowest field (δ 74.2) among the sp^3-carbon signals was assigned to methine one (2-C) by a distortionless enhancement by a polarization transfer (DEPT) measurement. However, the stereochemistry of product **7a** could not be deduced. A similar reaction of **3a** at 0.1 M concentration afforded almost the same results, and at 0.02 M concentration an increase in the yield of cyclic nitrone **6a** and a slightly depressed formation of dimeric product **7a** were observed (Table 1, runs 3 and 4). This means that the dimeric cycloaddition reaction of cyclic nitrone **6a** with oxime **3a** proceeds easily under ordinary reaction conditions. A similar propensity with respect to the solvents utilized was observed in the reaction of *N*-tosyl **3b** and *N*-mesyl oxime **3c**; the thermal reactions of **3b** and **3c** in toluene afforded dimers **7b**,**c** as major products, while NH-nitrone cycloadducts **4b**,**c** were obtained as major products in a similar reaction in *n*-BuOH (Scheme 2 and Table 1). The reactions of *N*-benzoyl **3d** and *N*-Boc oxime **3e** were also examined in toluene and/or *n*-BuOH. However, the ^{1}H and ^{13}C NMR spectra of these products provided only very broad signals at a range of −50 to 60 °C and, unfortunately, no information on the product structures could be obtained, except for **4e**.[6]

To obtain a more precise understanding of the isomerization process of oxime to NH-nitrone, the thermal reaction of 3-(*N*-substituted cinnamylamino)propionaldehyde oximes **10a–d** was examined, in which the formation of cyclic nitrone could be interrupted owing to steric and/or electronic grounds. Oximes **13a–c**, having dipolarophile moieties activated by a single carbonyl component, were also prepared (Scheme 3). The reaction of oxime **10a**–c in EtOH or toluene under reflux for 30–36 h gave NH-nitrone cycloadducts **14a–c** in good yields (Scheme 3 and Table 2). A similar reaction of *N*-benzoyl oxime **10d** proceeded smoothly to give a single product by TLC and HPLC; however, its structural confirmation was not attained owing to signal broadening in the ^{1}H and ^{13}C NMR spectra. The reaction of oximes **13** having activated di-

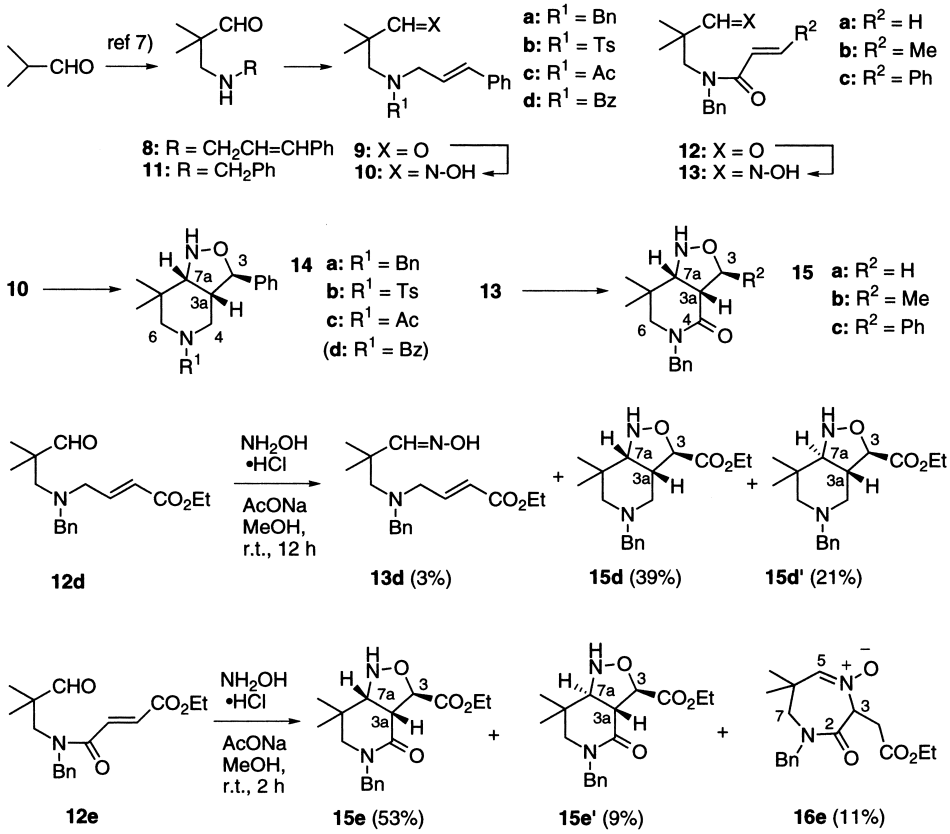


Scheme 2.

Table 1. Thermal Reaction of Oximes **3a–c**

Run	Oxime	Solvent	Time/h	Product yield/%[a)]				Recovered oxime/%
1	**3a**	*n*-BuOH[b)]	24	**4a**/78	—	—	—	**3a**/6
2	**3a**	Toluene[c)]	24	**4a**/42	**5a**/2	**6a**/3	**7a**/44	**3a**/6
3	**3a**	Toluene[d)]	50	**4a**/36	**5a**/2	**6a**/7	**7a**/44	**3a**/3
4	**3a**	Toluene[e)]	50	**4a**/40	**5a**/6	**6a**/12	**7a**/28	**3a**/3
4	**3b**	Toluene	12	**4b**/20	—	**6b**/8	**7b**/62	**3b**/2
5	**3b**	*n*-BuOH	108	**4b**/60	—	—	**7b**/10	**3b**/27
6	**3c**	Toluene	18	**4c**/18	—	**6c**/8	**7c**/66	**3c**/2
7	**3c**	*n*-BuOH	10	**4c**/50	—	**8c**/6	**7c**/12	**3c**/12

a) Based on isolated products. b) Ref. 4. c) At 0.2 M. d) At 0.1 M. e) At 0.02 M.



Scheme 3.

Table 2. Thermal Reaction of Oximes **10** and **13**

Run	Oxime	Solvent	Time/h	Product yield/%[a)]
1	**10a**	EtOH[b)]	36	**14a**/quant
2	**10b**	Toluene	36	**14b**/92
3	**10c**	Toluene	30	**14c**/88
4	**13a**	EtOH	24	**15a**/81
5	**13a**	Benzene	30	**15a**/72
6	**13b**	EtOH	30	**15b**/82[c)]
7	**13c**	EtOH	48	**15c**/quant
8	**13c**	Benzene	48	**15c**/quant

a) Based on isolated products. b) Ref. 4. c) Oxime **13b** was recovered in 9% yield.

polarophile moieties was also examined; *N*-acryloyl-**13a**, *N*-crotonoyl-**13b**, and *N*-cinnamoyl-benzylamino oxime **13c** were easily converted to the corresponding *cis*-fused perhydroisoxazolopyridines **15a–c** in a reaction in EtOH or benzene under reflux. On the other hand, ethyl 4-[*N*-(3-hydroxyimino-2,2-dimethylpropyl)benzylamino]crotonate (**13d**) was not stable even at room temperature, and gave *cis*- and *trans*-fused NH-nitrone cycloadduct **15d** and **15d′** together with an intractable mixture of products, including a cyclic nitrone. Oxime **13e**, having a dipolarophile moiety activated by two carbonyl components, could not be isolated under the usual oximation conditions, and spontaneously cyclized to give *cis*- and *trans*-fused NH-nitrone cycloadducts, **15e** and **15e′**, and cyclic nitrone **16e** together with an intractable mixture of products, including the dimer (Scheme 3). A similar oximation of aldehyde **12e** at 0 °C for 5 h afforded almost the same results. As expected, the reaction of oximes **13**, having activated dipolarophile moieties, proceeded smoothly to give NH-nitrone cycloadducts **15**.

Oxime–Nitrone Isomerization Process. Our next concern was focused on mechanistic considerations of the IOOC in this system. Based on a previous discussion,[3] it is reasonable to assume that the oxime–nitrone isomerization process of IOOC is the rate-determining step. The rates of the conversion of oxime **10a** in several solvents were examined using an HPLC method (see Experimental section). In these cases the rates of the disappearance of oxime **10a** were first-order with respect to the oxime concentrations. Replacing dioxane with propiononitrile (EtCN) as a solvent resulted in a small increase in the reaction rates of oxime **10a**, though a similar conversion in *n*-BuOH was accelerated (11.0 times faster than in dioxane). Also, the relative rates of the conversion of oximes **10a–d** and **13c** in *n*-BuOH at 80 °C are summarized in Table 3. Therein, lowering the basicity of the alkenylamino nitrogen of the oximes by replacing the benzyl group with tosyl or acetyl resulted in a small decrease of the reaction rate, in contrast with the cases of 2-(*N*-substituted allylamino)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidine-3-carbaldehyde oximes **17**; the reaction of *N*-benzyl oxime **17a** in dioxane was 45-times faster than *N*-phenylsulfonyl oxime **17b**.[3b] Finally, the activation energy for the conversion of oxime **10a** into perhydroisoxazolopyridine **14a** in *n*-BuOH was estimated to be 115 kJ mol^{-1} from the Arrhenius plot. The activation enthalpy and entropy for the conversion at 339 K were estimated to be 71 kJ mol^{-1} and -129 J

Table 3. Rates for the Conversion of Oxime **10a–d** and **13c**

Oxime	Solvent	Temp/°C	$10^5\ k/s^{-1}$	Relative rate
10a	Dioxane[a)]	97.2	1.61	1.00
10a	Dioxane[b)]	97.2	1.64	1.02
10a	EtCN[a)]	97.2	4.26	2.64
10a	*n*-BuOH[a)]	97.2	17.7	11.0
10a	*n*-BuOH	80.1	4.00	1.00
10b	*n*-BuOH	80.1	2.78	0.675
10c	*n*-BuOH	80.1	0.648	0.162
10d	*n*-BuOH	80.1	0.637	0.159
13c	*n*-BuOH	80.1	4.38	1.10

a) Performed at 2.2×10^{-3} M. b) At 2.2×10^{-2} M.

$mol^{-1}\ K^{-1}$. The value of the activation entropy in the IOOC of **10a** was negatively larger (more than 45 J $mol^{-1}\ K^{-1}$) than those of oxime **17a** (-84 J $mol^{-1}\ K^{-1}$)[3b] and 4-(*N*-allylbenzylamino)coumarin-3-carbaldehyde oxime (**18a**) (-68 J $mol^{-1}\ K^{-1}$)[3a] (Fig. 1).

In conclusion, the reaction features of the oxime–nitrone isomerization and intramolecular cycloaddition reaction of 3-(*N*-substituted allylamino)propionaldehyde oximes **3** are summarized below; a thermal reaction of the oximes gave NH-nitrone (E) via a 1,2-H shift (path c), leading to NH-nitrone cycloadducts **4**, and cyclic nitrone (F) via an ene-type reaction (ATP reaction)[5] (path d) followed by dimerization with oxime **3** gave **7**. The existence of an equilibrium among oxime and NH-nitrone (E) and cyclic nitrone (F) is plausible. The 1,2-H shift process is known to involve an ionic species,[1] while the ATP reaction appears to be nearly concerted.[5] The former process should be accelerated by protic solvents, such as *n*-BuOH, while the latter would not be so affected by the polarity of the solvents utilized; therefore, the results of the reaction of oximes **3** demonstrated in Table 1 were explainable (Scheme 4).

The activation enthalpy in the conversion of oxime **10a** implied that the geminal methyl groups at the 2-position in **10a** should be insufficient to control its conformation necessary for the oxime–nitrone isomerization and/or the intramolecular cycloaddition step of the resulting NH-oxime. The role of the alkenylamino nitrogen in the isomerization of oxime to NH-nitrone seems to be delicate; the relative rates of the conversion of *N*-benzyl **10a**, *N*-tosyl **10b**, and *N*-acetyl oxime **10c** were 1.0, 0.68, and 0.16, respectively. The role of the alkenylamino nitrogen of oxime **10a** as an intramolecular catalyst was not very effective, as expected. We have suggested that this can be ascribed to the high conformational mobility of oxime **10a** compared with the corresponding heteocyclic aldehyde oximes, **17a** and **18a**.

Further investigations on the oxime–nitrone isomerization assisted by intramolecular interactions are in progress, and the details will be reported elsewhere.

Experimental

General. Mps were measured on a Yanagimoto micro-melting-point apparatus and are uncorrected. IR spectra were measured on a JASCO IR-Report-100 spectrophotometer from samples as KBr pellets or NaCl discs. ^{1}H NMR and ^{13}C NMR spectra were measured on a JEOL EX-270 (270 MHz for ^{1}H and 67.8 MHz for ^{13}C) spectrometer in deuteriochloroform ($CDCl_3$) solutions, unless otherwise stated. Tetramethylsilane was used as an internal standard and the *J*-values are given in Hz. The splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad signal; and ov, overlapping with each other. The mass spectra were determined on a JEOL JMS-SX102A spectrometer. Elemental analyses were performed on a Yanagimoto MT-5 CHN analyser. All non-aqueous reactions were run under a

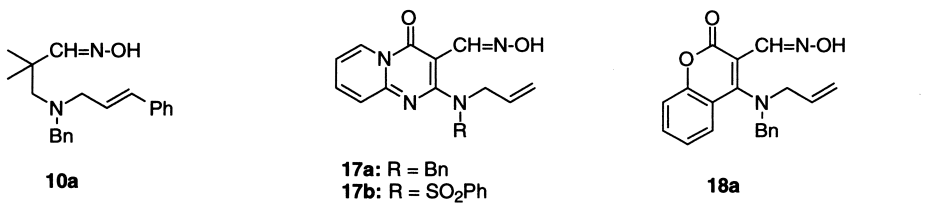
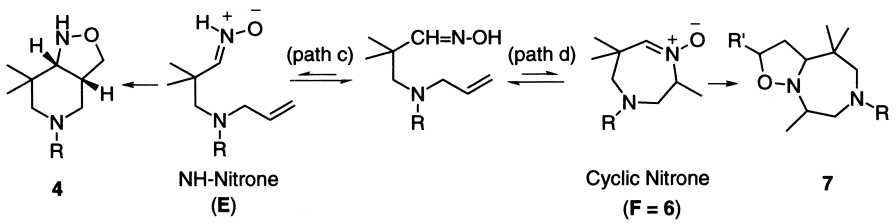


Fig. 1. Activation parameters for conversion of oxime–nitrone isomerization of **10a**, **17a**, and **18a**.



Scheme 4.

positive pressure of argon or nitrogen. All of solvents were dried by standard methods before use. The progress of the reactions was monitored by TLC (Silica Gel 60F-254, Merck). Chromatographic purification was performed with Wakogel C-200 (100–200 mesh, Wako Pure Chemical Industries) and/or Silica Gel 60 (230–400 mesh, Merck). The starting oximes, **3a** and **10a**, are known.[4]

Preparation of Oximes. Preparation of Oximes 3. General Procedures: A Mannich reaction of isobutyraldehyde (1.83 mL, 20 mmol), allylamine oxalate (2.67 g, 20 mmol), and 37% aqueous formaldehyde (1.58 mL, 21 mmol) in EtOH (30 mL) gave 3-allylamino-2,2-dimethylpropionaldehyde (**1**) in 56% yield, similarly to the reported method.[7] Aldehyde **1** (0.30 g, 2.1 mmol) was allowed to react with tosyl chloride (0.60 g, 3.0 mmol) in the presence of Et_3N (0.58 mL, 4.2 mmol) and DMAP (0.13 g, 1.0 mmol) in THF (10 mL) to give *N*-tosyl aldehyde **2b** (0.35 g, 64%). A mixture of *N*-tosyl aldehyde **2b** (0.74 g, 5.0 mmol) with hydroxylamine hydrochloride (0.21 g, 6.0 mmol) and sodium acetate (0.245 g, 6.0 mmol) in aqueous acetonitrile (1/3) (10 mL) was stirred at room temperature for 4 h. After evaporating the solvent, the residue was extracted between 3%-aqueous sodium hydrogencarbonate and dichloromethane. The organic layer was washed with brine, dried over anhydrous magnessium sulfate, and the precipitates were filtered off. The filtrate was evaporated to dryness and the residue was subjected to column chromatography on silica gel to give oxime **3b** (0.67 g, 86%) by elution with hexane/ethyl acetate (5/1).

2,2-Dimethyl-3-(*N*-tosylallylamino)propionaldehyde Oxime (3b). Colorless oil; IR (NaCl) 3450, 1340, 1180 cm^{-1}; ^1H NMR (270 MHz) δ 1.17 (s, 6 H, 2-Me_2), 2.43 (s, 3 H, Me), 3.22 (s, 2 H, 3-H_2), 3.84 (d, J = 6.3 Hz, >NCH_2CH=), 5.08–5.15 (ov, 2 H, =CH_2), 5.32 (m, 1 H, –CH=CH_2), 7.30, 7.70 (each br d, J = 8.3 Hz, each 2 H, ArH), 7.36 (s, 1 H, 1-H), 7.76 (br s, 1 H, OH); ^{13}C NMR (67.8 MHz) δ 21.5 (Me), 23.9 (2-Me_2), 38.7 (2-C), 51.8 (3-C), 55.0 (>NCH$_2$CH=), 120.1 (=CH_2), 127.3, 129.7, 137.2, 143.4 (Ar–C), 132.2 (–CH=CH_2), 157.6 (1-C). Found: C, 57.86; H, 7.33; N, 8.70%. Calcd. for $C_{15}H_{22}N_2O_3S$: C, 58.04; H, 7.15; N, 9.02%.

Similarly, mesylation with mesyl chloride/Et_3N–DMAP, benzoylation with benzoyl chloride/Et_3N-DMAP, and a reaction with *t*-butyl chloroformate/Et_3N–DMAP of the aldehyde gave the corresponding *N*-protected aldehydes **2c–e** in 67–88% yields, which were oximized by the usual method.

3-(*N*-Mesylallylamino)-2,2-dimethylpropionaldehyde Oxime (3c). Yield 93%; colorless needles from hexane–benzene; mp 87 °C; IR (KBr) 3325, 1320, 1170 cm^{-1}; ^1H NMR (270 MHz) δ 1.16 (s, 6 H, 2-Me_2), 2.88 (s, 3 H, SO_2Me), 3.25 (s, 2 H, 3-H_2), 3.89 (d, J = 6.6 Hz, 2 H, >NCH_2CH=), 5.26–5.33 (ov, 2 H, CH=CH_2), 5.82 (m, 1 H, –CH=CH_2), 7.38 (s, 1 H, 1-H), 7.57 (s, 1 H, OH); ^{13}C NMR (67.8 MHz) δ 23.8 (2-Me_2), 38.9 (2-C), 39.7 (SO_2Me), 51.9 (3-C), 54.7 (>NCH$_2$CH=), 120.5 (–CH=CH$_2$), 132.1 (–CH=CH_2), 157.6 (1-C). Found: C, 45.97; H, 7.90; N, 11.84%. Calcd for $C_9H_{18}N_2O_3S$: C, 46.13; H, 7.74; N, 11.96%.

3-(*N*-Benzoylallylamino)-2,2-dimethylpropionaldehyde Oxime (3d). Yield 81%; colorless needles from hexane–benzene; mp 103.5–105.5 °C; IR (KBr) 3300, 1600 cm^{-1}; ^1H NMR (270 MHz) δ 1.22 (s, 6 H, 2-Me_2), 3.56 (s, 2 H, 3-H_2), 3.90 (d, J = 4.3 Hz, 2 H, >NCH_2CH=), 5.08–5.17 (ov, 2 H, –CH=CH_2), 5.53 (m, 1 H, –CH=CH_2), 7.36 (ov, 5 H, Ph), 7.46 (s, 1 H, 1-H), 7.72 (br s, 1 H, OH); ^{13}C NMR (67.8 MHz) δ 23.9 (2-Me_2), 39.9 (2-C), 52.1 (3-C), 53.3 (>NCH$_2$CH=), 117.6 (–CH=CH$_2$), 126.4, 128.4, 129.4, 136.5 (Ph-C), 133.2 (–CH=CH_2), 157.7 (1-C), 173.2 (*C*OPh). Found: C, 69.10; H, 7.93; N, 10.63%. Calcd for $C_{15}H_{20}N_2O_2$: C, 69.20; H, 7.74; N, 10.76%.

3-(*N*-*t*-Butoxycarbonylallylamino)-2,2-dimethylpropionaldehyde Oxime (3e). Yield 86%; colorless oil; IR (NaCl) 3350, 1690 cm^{-1}. This compound was a (1:1) mixture of two atropisomers in $CDCl_3$ and gave broad signals in ^1H and ^{13}C NMR spectra. ^1H NMR (270 MHz) δ 1.11 (s, 6 H, 2-Me_2), 1.47 (s, 9 H, –CMe_2), 3.19 (br s, 2 H, 3-H_2), 3.87 (br, 2 H, >NCH_2CH=), 5.03–5.09 (ov, 2 H, –CH=CH_2), 5.73 (ov, 1H, –CH=CH_2), 7.34 (br, 1 H, 1-H), 8.39 (br, 1 H, OH); another isomer δ 1.11 (s, 6 H, 2-Me_2), 1.44 (s, 9 H, –CMe_2), 3.22 (br s, 2 H, 3-H_2), 3.79 (br, 2 H, >NCH_2CH=), 5.09 (ov, 2 H, –CH=CH_2), 5.73 (ov, 1H, –CH=CH_2), 7.38 (br, 1 H, 1-H), 8.35 (br, 1 H, OH); ^{13}C NMR (67.8 MHz) δ 23.5, 23.7 (2-Me_2), 28.0 (CMe_3), 39.4, 39.5 (2-C), 51.1, 51.7 (>NCH$_2$CH=), 55.2 (3-C), 79.7 (*C*Me$_3$), 116.0, 116.3 (–CH=CH$_2$), 133.5, 133.7 (–CH=CH_2), 157.3 (CO_2), 157.5 (1-C); Found: C, 60.63; H, 9.79; N, 10.85%. Calcd for $C_{13}H_{24}N_2O_3$: C, 60.91; H, 9.44; N, 10.93%. HRMS (EI) *m/z* 256.1783. Calcd for $C_{13}H_{24}N_2O_3$: 256.1787.

Preparation of Oximes 10. General Procedures: 3-Cinnamylamino-2,2-dimethylpropionaldehyde (**8**) was prepared using cinnamylamine oxalate in 88% yield, similarly to the method for 3-allylamino-2,2-dimethylpropionaldehyde (**1**). Tosylation, acetylation, and benzoylation of the aldehyde gave the corresponding *N*-protected aldehydes **9b–d** in 75–91% yields, which were oximized by the usual method.

3-[(*E*)-*N*-Tosylcinnamylamino]-2,2-dimethylpropionaldehyde Oxime (10b). Yield 91%; colorless prisms from hexane–benzene; mp 120–121 °C; IR (KBr) 3300, 1320, 1160 cm^{-1}; ^1H NMR (270 MHz) δ 1.17 (s, 6 H, 2-Me_2), 2.42 (s, 3 H, Me), 3.26 (s, 2 H, 3-H_2), 3.98 (d, J = 5.9 Hz, 2 H, >NCH_2CH=), 5.62 (td, J = 6.9 and 15.8 Hz, 1 H, –CH=CHPh), 6.37 (d, J = 15.8 Hz, 1 H, –CH=CHPh), 7.15–7.34 (ov, 7 H, Ar-H), 7.40 (s, 1 H, 1-H), 7.73 (br d, J = 8.3 Hz, 2 H, Ar-H), 8.34 (br s, 1 H, OH); ^{13}C NMR (67.8 MHz) δ 21.3 (Me), 23.7 (2-Me_2), 38.6 (2-C), 51.2 (>NCH$_2$CH=), 55.1 (3-C), 122.9 (–CH=CHPh), 126.3, 127.3, 128.2, 128.4, 129.6, 135.9, 137.1, 143.4 (Ph-C), 134.6 (–CH=CHPh), 157.3 (1-C). Found: C, 65.19; H, 7.07; N, 7.29%. Calcd for $C_{21}H_{26}N_2O_3S$: C, 65.26; H, 6.78; N, 7.25%.

3-[(*E*)-*N*-Acetylcinnamylamino]-2,2-dimethylpropionaldehyde Oxime (10c). Yield 78%; colorless prisms from EtOH; mp 140–141 °C; IR (KBr) 3250, 1620 cm^{-1}. This compound was a (4:1) mixture of two atropisomers in $CDCl_3$. ^1H NMR (270 MHz) major isomer: δ 1.15 (s, 6 H, 2-Me_2), 2.15 (s, 3 H, COMe), 3.45 (s, 2 H, 3-H_2), 4.09 (br d, J = 5.0 Hz, 2 H, >NCH_2CH=), 6.08 (td, J = 5.0 and 15.8 Hz, 1 H, –CH=CHPh), 6.40 (d, J = 15.8 Hz, 1 H, –CH=CHPh), 7.26–7.52 (ov, 7 H, Ph and 1-H, and OH); minor isomer (assigned signals) δ 1.18 (s, 2-Me_2), 2.15 (s, COMe), 3.35 (s, 3-H_2), 4.18 (d, J = 6.3 Hz, >NCH_2CH=); ^{13}C NMR (67.8 MHz) δ 21.8, 22.2 (COMe), 23.8, 24.2 (2-Me_2), 39.2, 39.6 (2-C), 48.8, 52.2 (>NCH$_2$CH=), 53.9, 56.3 (3-C), 123.9, 124.4 (–CH=CHPh), 126.4, 127.7, 128.0, 128.5, 128.7, 128.8, 136.0 (Ph-C), 131.7, 133.0 (–CH=CHPh), 157.0, 157.1 (1-C), 172.0 (*C*OMe). Found: C, 69.89; H, 8.11; N, 10.09%. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.04; 8.08; 10.21%.

3-[(*E*)-*N*-Benzoylcinnamylamino]-2,2-dimethylpropionaldehyde Oxime (10d). Yield 68%; colorless oil; IR (NaCl) 3320, 1620 cm^{-1}; ^1H NMR (270 MHz) δ 1.24 (s, 6 H, 2-Me_2), 3.63 (s, 2 H, 3-H_2), 4.07 (d, J = 5.0 Hz, 2 H, >NCH_2CH=), 5.93 (dt, J = 15.8 and 5.6 Hz, 1 H, –CH=CH–Ph), 6.34 (d, J = 15.8 Hz, 1 H, –CH=CH–Ph), 7.22–7.39 (ov, 10 H, Ph), 7.49 (s, 1 H, 1-H); ^{13}C NMR (67.8 MHz) δ 23.9 (2-Me_2), 39.9 (2-C), 52.0 (3-C), 52.9 (>NCH$_2$CH=), 124.4 (>NCH$_2$$C$H=), 126.4, 126.5, 128.0, 128.4,

128.6, 129.5, 136,6 (Ph-C), 132.8 (=*C*HPh), 157.9 (1-C), 173.2 (*C*OPh). Found: C, 75.21; H, 7.40; N, 8.22%. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33%.

Preparation of Oximes 13. General Procedures: 3-Benzylamino-2,2-dimethylpropionaldehyde (**11**) was similarly prepared using benzylamine oxalate in 75% yield. The reaction of the aldehyde with acryloyl chloride, crotonoyl chloride, cinnamoyl chloride, ethyl (*E*)-3-chloroformylacrylate gave the corresponding 3-[*N*-(3-substituted propenoyl)benzylamino]-2,2-dimethylpropionaldehydes **12a-c** and **12e** in 70–89% yields, which were oximized by the usual method. Ethyl 4-[*N*-(2-formyl-2-methylpropyl)benzylamino]crotonate (**12d**) was obtained by an ordinary Mannich reaction of isobutyraldehyde using ethyl 4-benzylaminocrotonate hydrochloride.

3-(*N*-Acryloylbenzylamino)-2,2-dimethylpropionaldehyde Oxime (13a). Yield 72%; colorless oil; IR (NaCl) 3250, 1640 cm^{-1}. This compound was a (4:1) mixture of two atropisomers in $CDCl_3$. ^1H NMR (270 MHz) major isomer δ 1.09 (s, 6 H, 2-Me_2), 3.43 (s, 2 H, 3-H_2), 4.58 (s, 2 H, CH_2Ph), 5.56 (dd, J = 2.3 and 7.9 Hz, 1 H, –CH=CH_2), 6.25–6.32 (ov, 2 H, =CH_2), 7.02–7.35 (ov, 6 H, Ph and 1-H), 8.21 (br, 1 H, OH); minor isomer (assigned signals) δ 1.09 (s, 2-Me_2), 3.28 (s, 3-H_2), 4.67 (s, CH_2Ph), 5.69 (br, –CH=CH_2), 6.46 (ov, =CH_2), 8.49 (br, OH); ^{13}C NMR (67.8 MHz) δ 24.2, 24.4 (2-Me_2), 39.5, 40.0 (2-C), 53.0, 54.1 (*C*H_2Ph), 54.7, 55.0 (3-C), 126.4, 127.6, 127.9, 128.2, 128.4, 128.6, 136.6, 137.0, 137.2 (Ph-C), 128.8, 129.0 (–CH=*C*H_2), 156.8, 157.7 (1-C), 167.8, 168.4 (CO). Found: C, 60.44; H, 7.70; N, 10.91%. Calcd for $C_{15}H_{20}N_2O_2$: C, 60.10; H, 7.94; N, 10.56%. HRMS (EI) *m/z* 260.1514. Calcd for $C_{15}H_{20}N_2O_2$: 260.1525.

3-(*N*-Crotonoylbenzylamino)-2,2-dimethylpropionaldehyde Oxime (13b). Yield 68%; colorless oil; IR (NaCl) 3230, 1650 cm^{-1}. This compound was a (4:1) mixture of two atropisomers in $CDCl_3$. ^1H NMR (270 MHz) major isomer δ 1.15 (s, 6 H, 2-Me_2), 1.79 (dd, J = 1.3 and 6.9 Hz, =CH*Me*), 3.48 (s, 2 H, 3-H_2), 4.64 (s, 2 H, CH_2Ph), 6.23 (qd, J = 1.3 and 4.9 Hz, 1 H, –CH=CHMe), 6.96 (m, 1 H, =CHMe), 7.10–7.42 (ov, 6 H, Ph and OH), 8.74 (s, 1 H, 1-H); minor isomer (assigned signals) δ 1.90 (dd, J = 1.3 and 7.1 Hz, =CH*Me*), 3.34 (s, 3-H_2), 4.74 (s, CH_2Ph), 6.30 (m, –CH=CH-Me); ^{13}C NMR (67.8 MHz) δ 18.1, 18.2 (=CH*Me*), 23.8, 24.0 (2-Me_2), 39.2, 39.6 (2-C), 49.7, 52.5 (*C*H_2Ph), 54.2, 54.8 (3-C), 121.5, 121.7 (–*C*H=CHMe), 126.2, 127.5, 127.9, 128.5, 128.8, 136.7, 136.9 (Ph-C), 137.2, 142.8 (–CH=*C*HMe), 156.4, 157.3 (1-C), 167.8, 168.3 (CO). Found: C, 70.55; H, 8.19; N, 10.00%. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.96; H, 8.46; N, 9.88%. HRMS (EI) *m/z* 274.1672. Calcd for $C_{16}H_{22}N_2O_2$: 274.1682.

3-[(*E*)-*N*-Cinnamoylbenzylamino]-2,2-dimethylpropionaldehyde Oxime (13c). Yield 74%; colorless prisms from hexane–benzene; mp 112–114 °C; IR (NaCl) 3230, 1640 cm^{-1}. This compound was a (3:1) mixture of two atropisomers in $CDCl_3$. ^1H NMR (270 MHz) major isomer δ 1.18 (6 H, s, 2-Me_2), 3.56 (s, 2 H, 3-H_2), 4.72 (s, 2 H, CH_2Ph), 6.80 (d, J = 15.5 Hz, 1 H, –CH=CHPh), 7.14–7.59 (ov, 11 H, Ph and 1-H), 7.73 (d, J = 15.5 Hz, 1 H, =CHPh), 8.35 (br, 1 H, OH); minor isomer (assigned signals) δ 3.44 (s, 3-H_2), 4.79 (s, CH_2Ph), 6.92 (d, J = 15.5 Hz, –CH=CHPh), 7.79 (d, J = 15.5 Hz, =CHPh), 8.43 (br, OH); ^{13}C NMR (67.8 MHz) δ 24.2, 24.5 (2-Me_2), 39.6, 40.1 (2-C), 50.5, 53.1 (*C*H_2Ph), 55.0, 55.4 (3-C), 117.6, 117.7 (6-C), 126.6–130.0 (Ph-C), 137.2, 137.4 (Ph-C), 143.7, 143.8 (=*C*HPh), 156.8, 156.9 (1-C), 167.9, 168.4 (CO). Found: C, 75.07; H, 7.29; N, 8.22%. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33%.

Ethyl 4-[*N*-(2-Formyl-2-methylpropyl)benzylamino]crotonate (12d). Colorless oil; IR (NaCl) 1720 cm^{-1}; ^1H NMR (270 MHz) δ 1.05 (s, 6 H, 2-Me_2), 1.27 (t, J = 7.2 Hz, CH_2CH_3), 2.69 (s, 2 H, 3-H_2), 3.18 (dd, J = 1.3 and 5.9 Hz, 2 H, >NCH_2CH=), 3.59 (s, 2 H, CH_2Ph), 4.19 (q, J = 7.2 Hz, 2 H, C$H_2$$CH_3$), 5.96 (td, J = 1.3 and 15.8 Hz, 1 H, =C$H$$CO_2$Et), 6.92 (td, J = 5.9 and 15.8 Hz, 1 H, >NCH_2CH=), 7.23–7.31 (ov, 5 H, Ph), 9.42 (s, 1 H, 1-H); ^{13}C NMR (67.8 Hz) δ 14.2 (CH_2*C*H_3), 20.4 (2-Me_2), 47.9 (2-C), 55.8 (*C*H_2Ph), 60.0 (5-C), 60.3 (*C*$H_2$$CH_3$), 60.8 (3-C), 123.3 (>$NCH_2$*C*H=), 127.1, 128.1, 128.7, 138.6 (Ph-C), 145.2 (=*C*HCO_2Et), 166.0 (CO_2), 206 (1-C). Found: C, 70.99; H, 8.23; N, 4.39%. Calcd for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62%.

Ethyl *N*-Benzyl-*N*-(2-formyl-2-methylpropyl)fumaramate (12e). Colorless oil; IR (NaCl) 1710 cm^{-1}; ^1H NMR (270 MHz) δ 1.11 (s, 6 H, 2-Me_2), 1.27 (t, J = 7.3 Hz, 3 H, CH_2*C*H_3), 3.54 (s, 3 H, 3-H_2), 4.20 (q, J = 7.3 Hz, 2 H, C$H_2$$CH_3$), 4.65 (s, 2 H, C$H_2$Ph), 6.81 (d, J = 15.2 Hz, 1 H, –COCH=), 7.10–7.40 (ov, 6 H, Ph-H and =C$H$$CO_2$Et), 9.57 (s, 1 H, 1-H); ^{13}C NMR (67.8 MHz) δ 14.0 (CH_2*C*H_3), 20.2 (2-Me_2), 47.9 (2-C), 52.6 (3-C), 53.2 (>N*C*H_2Ph), 61.0 (*C*$H_2$$CH_3$), 126.3, 128.0, 129.0, 135.9 (Ph-C), 132.3 (–CO*C*H=), 133.1 (=*C*HCO_2Et), 165.3, 166.1 (>NCO– and CO_2), 203.2 (1-C). Found: C, 67.77; H, 7.27; N, 4.54%. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.30; N, 4.41%. HRMS (EI) *m/z* 317.1617. Calcd for $C_{18}H_{23}NO_4$: 317.1628.

Thermal Behaviors of Oximes. Thermal Reaction of Oximes 3. General Procedures: A solution of oxime **3a** (0.478 g, 2.0 mmol) in toluene (10 mL) was heated under reflux for 24 h, and the solvent was evaporated. The residue was subjected to column chromatography on silica gel to give the recovered oxime **3a** [0.029 g, 6%; hexane/ethyl acetate (5/1)], **7a** [0.210 g, 44%; hexane/ethyl acetate (4/1)], **4a**[4] [0.201 g, 42%; hexane/ethyl acetate (3/1)], **5a**[4] [0.010 g, 2%; hexane/ethyl acetate (1/1)], and **6a** (0.014 g, 3%; ethyl acetate), respectively.

1-Benzyl-3,6,6-trimethyl-2,3,6,7-tetrahydro-1*H*-1,4-diazepine 4-Oxide (6a). Colorless oil. This compound was not very stable and the structure was determined based on the spectroscopic data given below: ^1H NMR (270 MHz) δ 1.09, 1.15 (each s, each 3 H, 6-Me_2), 1.44 (d, J = 7.3 Hz, 3 H, 3-Me), 2.36, 2.43 (each d, J = 12.5 Hz, each 1 H, 7-H_2), 2.60 (dd, J = 5.9 and 13.9 Hz, 1 H, 2-H), 2.70 (1 H, dd, J = 2.3 and 13.9 Hz, 1 H, 2-H), 3.49, 3.57 (each d, J = 13.2 Hz, each 1 H, CH_2Ph), 4.16 (m, 1 H, 3-H), 6.94 (s, 1 H, 5-H) and 7.18–7.27 (ov, 5 H, Ph); ^{13}C NMR (67.8 MHz) δ 17.1 (3-Me), 26.3, 27.7 (6-Me_2), 36.7 (6-C), 59.3 (2-C), 63.9 (7-C), 66.3 (*C*H_2Ph), 70.1 (3-C), 127.4, 128.4, 128.9, 138.4 (Ph-C), 147.1 (5-C).

2-[*N*-Benzyl-*N*-(3-hydroxyimino-2,2-dimethylpropyl)aminomethyl]-4,4,8-trimethyl-6-benzyl-perhydroisoxazolo[2,3-*d*][1,4]diazepine (7a). Colorless oil; IR (NaCl) 3300 cm^{-1}; ^1H NMR (270 MHz) δ 0.69, 0.82 (each s, each 3 H, 4-Me_2), 0.99 (d, J = 6.3 Hz, 3 H, 8-Me), 1.06 (s, 6 H, 4′-Me_2), 1.59 (ddd, J = 2.7, 5.5, and 12.2 Hz, 1 H, 3-H), 2.00 (ddd, 3-H, J = 4.0, 5.9, and 12.2 Hz, 1 H, 3-H), 2.37 (s, 2 H, 3′-H_2), 2.49 (dd, J = 4.3 and 12.5 Hz, 1 H, 7-H), 3.25 (m, 1 H, 8-H), 3.54 (s, 2 H, CH_2Ph), 3.65, 3.74 (each d, J = 13.9 Hz, each 1 H, CH_2Ph), 4.02 (m, 1 H, 2-H), 7.18–7.35 (ov, 10 H, Ph), 7.38 (s, 1 H, 5′-H), 8.23 (br s, 1 H, OH); ^{13}C NMR (67.8 MHz) δ 10.7 (8-Me), 20.6, 27.3 (4-Me_2), 23.8, 24.0 (4′-Me_2), 35.8 (4-C), 36.6 (3-C), 39.0 (4′-C), 57.1 (8-C), 57.5 (1′-C), 60.8, 64.9 (*C*H_2Ph), 61.7 (3a-C), 64.8 (6-C), 70.1 (3-C), 74.6 (2-C), 126.8, 126.9, 128.0×2, 129.0, 129.2, 139.7, 140.1 (Ph-C), 158.7 (5′-C). Found: C, 73.14; H, 9.46; N, 10.99%. Calcd for $C_{30}H_{44}N_4O_2$: C, 73.13; H, 9.00; N, 11.37%. HRMS (EI) *m/z* 492.3465. Calcd for $C_{30}H_{44}N_4O_2$: 492.3465.Similarly, thermal reaction of oximes **3b**,**c** gave NH-nitrone adducts **4b**,**c**, cyclic nitrones **6b**,**c**, and dimers **7b**,**c**. 7,7-Dimethyl-5-tosylperhydroiso-

xazolo[4,3-*c*]pyridine (**4b**) was known.[4]

3,6,6-Trimethyl-1-tosyl-2,3,6,7-tetrahydro-1*H*-1,4-diazepine 4-Oxide (6b). Pale yellow oil. This compound was not very stable, and the structure was determined based on the spectroscopic data given below: ^{1}H NMR (270 MHz) δ 1.23, 1.43 (each s, each 3 H, 6-Me$_2$), 1.63 (d, J = 6.9 Hz, 3 H, 3-Me), 2.82 (s, 3 H, Me), 2.92 (d, J = 13.2 Hz, 1 H, 7-H), 3.26–3.33 (ov, 2 H, 2-H and 7-H), 3.50 (dd, J = 5.6 and 14.5 Hz, 1 H, 2-H), 4.50 (m, 1 H, 3-H), 7.00 (s, 1 H, 5-H) , 7.34, 7.64 (each br d, J = 8.3 Hz, each 2 H, Ar-H).

2-[*N*-(3-Hydroxyimino-2,2-dimethylpropyl)-*N*-tosylaminomethyl]-4,4,8-trimethyl-6-tosyl-perhydroisoxazolo[2,3-*d*]-[1,4]diazepine (7b). Colorless needles from hexane–benzene; mp 174–175 °C; IR (KBr) 3300, 1320, 1140 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.67, 0.97 (each s, each 3 H, 4-Me$_2$), 1.11, 1.13 (each s, each 3 H, 4′-Me$_2$), 1.17 (d, J = 6.3 Hz, 3 H, 8-Me), 1.65 (br q, J = 11.5 Hz, 1 H, 3-H), 1.86 (m, 1 H, 3-H), 2.35 (d, J = 13.9 Hz, 1 H, 5-H), 2.38, 2.41 (each s, each 3 H, Me×2), 2.74 (dd, J = 4.0 and 13.2 Hz, 1 H, 7-H), 3.12–3.21 (ov, 2 H, 1′-H and 3a-H), 3.28 (d, J = 13.9 Hz, 1 H, 5-H), 3.40–3.62 (ov, 5 H, 7-H$_2$, 8-H, and 3′-H$_2$), 3.65 (d, J = 14.5 Hz, 1 H, 1′-H), 7.26–7.31 (ov, 4 H, Ar-H), 7.40 (s, 1 H, 5′-H), 7.61, 7.67 (each br d, J = 8.3 Hz, each 2 H, Ar-H), 8.11 (s, 1 H, OH); ^{13}C NMR (67.8 MHz) δ 9.65 (8-Me), 19.8, 26.2 (4-Me$_2$), 21.4, 21.5 (Me×2), 23.2, 24.4 (4′-Me$_2$), 36.2 (3-C), 36.3 (4-C), 38.6 (4′-C), 50.1 (2-C), 55.5 (7-C), 55.6 (3-C), 56.7 (8-C), 61.1 (3a-C), 61.8 (6-C), 74.9 (2-C), 127.0, 127.2, 129.7, 135.7, 137.4, 143.4 (Ph-C), 157.8 (5′-C); FAB MS *m/z* (rel intensity) 621 (M$^+$ + H; base peak), 620 (48), 532 (8), 465 (26). Found: C, 57.82; H, 7.28; N, 9.02%. Calcd for $C_{30}H_{44}N_4O_6S_2$: C, 58.04; H, 7.14; N, 9.03%.

5-Mesyl-7,7-dimethylperhydroisoxazolo[4,3-*c*]pyridine (4c). Colorless prisms from hexane–benzene; mp 168–169 °C; IR (KBr) 3200, 1320, 1160 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.00, 1.19 (each s, each 3 H, 7-Me$_2$), 2.73–2.78 (ov, 2 H, 4-H and 6-H), 2.78 (s, 3 H, SO$_2$Me), 2.88 (m, 1 H, 3a-H), 3.19 (d, J = 12.2 Hz, 1 H, 6-H), 3.26 (br s, 1 H, 7a-H), 3.71 (d, J = 7.9 Hz, 1 H, 3-H), 3.74 (m, 1 H, 4-H), 3.94 (dd, J = 4.6 and 7.9 Hz, 1 H, 3-H), 5.89 (br s, 1 H, NH); ^{13}C NMR (67.8 MHz) δ 24.6, 26.2 (7-Me$_2$), 32.6 (7-C), 34.5 (SO$_2$Me), 40.0 (3a-C), 44.6 (4-C), 51.3 (6-C), 64.8 (7a-C), 71.8 (3-C). Found: C, 45.96; H, 7.74; N, 11.91%. Calcd for $C_9H_{18}N_2O_3S$: C, 46.13; H, 7.74; N, 11.96%.

1-Mesyl-3,6,6-trimethyl-2,3,6,7-tetrahydro-1*H*-1,4-diazepine 4-Oxide (6c). Pale-yellow oil. This compound was not very stable, and the structure was determined based on the spectroscopic data given below: ^{1}H NMR (270 MHz) δ 1.27, 1.33 (each s, each 3 H, 6-Me$_2$), 1.63 (d, J = 7.3 Hz, 3 H, 3-Me), 2.85 (s, 3 H, SO$_2$Me), 3.17, 3.39 (each d, J = 13.2 Hz, each 1 H, 7-H$_2$), 3.35–3.55 (ov, 2 H, 2-H$_2$), 4.40 (m, 1 H, 3-H), 7.03 (s, 1 H, 5-H).

2-[*N*-(3-Hydroxyimino-2,2-dimethylpropyl)-*N*-mesylaminomethyl]-4,4,8-trimethyl-6-mesylperhydroisoxazolo[2,3-*d*]-[1,4]diazepine (7c). Colorless prisms from ethyl acetate; mp 188 °C; IR (KBr) 3400, 1330, 1170 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.95, 0.99 (each s, each 3 H, 4-Me$_2$), 1.14, 1.16 (each s, each 3 H, 4′-Me$_2$), 1.23 (d, J = 3.0 Hz, 3 H, 8-Me), 1.75 (ddd, J = 10.9, 11.2, and 12.5 Hz, 1 H, 3-H), 2.10 (ddd, J = 2.0, 5.6, and 12.5 Hz, 1 H, 3-H), 2.69 (d, J = 13.9 Hz, 1 H, 5-H), 2.78, 2.92 (each s, each 3 H, SO$_2$Me×2), 3.10 (dd, J = 4.0 and 12.9 Hz, 1 H, 7-H), 3.29 (dd, J = 3.3 and 11.2 Hz, 1 H, 3a-H), 3.32–3.43 (ov, 2 H, 1′-H and 5-H), 3.42 (s, 2 H, 3′-H$_2$), 3.52–3.58 (ov, 2 H, 7-H and 1′-H), 3.69 (m, 1 H, 8-H), 4.13 (m, 1 H, 2-H), 7.20 (s, 1 H, 5′-H), 7.41 (s, 1 H, OH); ^{13}C NMR (67.8 MHz) δ 9.76 (8-Me), 20.2, 26.2 (4-Me$_2$), 23.0, 24.3 (4′-Me$_2$), 35.7, 39.7 (SO$_2$Me×2), 36.0 (3-C), 36.6 (4-C), 38.6 (4′-C), 50.2 (1′-C), 54.9 (3′-C), 55.3 (7-C), 55.9 (8-C), 61.7, 61.8 (3a-C and 5-C), 74.4 (2-C), 158.0 (5′-C); FAB MS *m/z* (rel intensity) 469 (M$^+$ + H; base peak), 468 (44), 389 (26). Found: C, 45.90; H, 7.70; N, 11.83%. Calcd for $C_{18}H_{36}N_4O_6S_2$: C, 46.13; H, 7.74; N, 11.96%.

Thermal Reaction of Oximes 10 and 13. A similar reaction and work-up for oximes **10** and **13** gave NH-nitrone cycloadducts **14** and **15**, respectively; the results are summarized in Table 2. 5-Benzyl-7,7-dimethyl-3-phenylperhydroisoxazolo[4,3-*c*]pyridine (**14a**) is known.[4]

7,7-Dimethyl-5-tosyl-3-phenylperhydroisoxazolo[4,3-*c*]pyridine (14b). Colorless needles from EtOH; mp 187–188 °C; IR (KBr) 3220, 1330, 1155 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.97, 1.12 (each s, each 3 H, 7-Me$_2$), 2.45 (s, 3 H, SO$_2$Me), 2.45–2.57 (ov, 2 H, 4-H and 6-H), 2.83 (m, 1 H, 3a-H), 3.13–3.17 (ov, 2 H, 6-H and 7a-H), 3.80 (br s, 1 H, 3a-H), 5.94 (br, 1 H, NH), 7.26–7.39 (ov, 7 H, Ar-H), 7.66 (br d, J = 8.3 Hz, 2 H, Ar-H); ^{13}C NMR (67.8 MHz) δ 21.5 (Me), 24.6, 26.7 (7-Me$_2$), 32.6 (7-C), 45.6 (4-C), 47.5 (3a-C), 52.4 (6-C), 63.1 (7a-C), 83.6 (3-C), 125.0, 127.5, 127.7, 128.6, 129.8, 133.3, 140.8, 143.8 (Ph-C). Found: C, 65.08; H, 7.00; N, 7.30%. Calcd for $C_{21}H_{26}N_2O_3S$: C, 65.26; H, 6.78; N, 7.25%.

5-Acetyl-7,7-dimethyl-3-phenylperhydroisoxazolo[4,3-*c*]pyridine (14c). Colorless oil; IR (NaCl) 3200, 1630 cm^{-1}. This compound was a (4:1) mixture of two atropisomers in $CDCl_3$. ^{1}H NMR (270 MHz) major isomer δ 1.00, 1.04 (each s, each 3 H, 7-Me$_2$), 2.11 (s, 3 H, COMe), 2.68 (m, 1 H, 3a-H), 3.03 (br t, J = 13.0 Hz, 1 H, 4-H), 3.18–3.32 (ov, 4 H, 6-H$_2$, 7a-H, and NH), 4.61 (dd, J = 6.3 and 13.2 Hz, 1 H, 4-H), 4.85 (d, J = 2.0 Hz, 1 H, 3-H), 7.28–7.41 (ov, 5 H, Ph); minor isomer (assigned signals) δ 0.97, 1.02 (each s, 7-Me$_2$), 2.18 (s, COMe), 2.82 (d, J = 13.2 Hz, 6-H), 3.35 (dd, J = 11.2 and 13.9 Hz, 4-H), 3.88 (ddd, J = 1.6, 6.6, and 13.9 Hz, 4-H), 4.03 (d, J = 13.2 Hz, 6-H), 4.81 (d, J = 1.7 Hz, 3-H); ^{13}C NMR (67.8 MHz) δ 21.3, 21.4 (CO*Me*), 24.2, 24.3, 26.3 (7-Me$_2$), 32.6, 33.3 (7-C), 40.7, 45.8 (4-C), 47.1, 47.7 (3a-C), 47.9, 52.9 (6-C), 64.0, 64.7 (7a-C), 83.9, 84.1 (3-C), 125.3, 127.9, 128.7, 140.7 (Ph-C), 168.9 (*C*OMe). Found: C, 70.00; H, 8.31; N, 10.01%. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08; N, 10.21%.

5-Benzyl-7,7-dimethylperhydroisoxazolo[4,3-*c*]pyridin-4-one (15a). Colorless prisms from hexane–benzene; mp 90–91 °C; IR (KBr) 3200, 1630 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.85 (s, 6 H, 7-Me$_2$), 2.66 (dd, J = 1.3 and 12.5 Hz, 1 H, 6-H), 3.23 (d, J = 12.5 Hz, 1 H, 6-H), 3.27–3.37 (ov, 4 H, 3a-H, 6-H, 7a-H, and NH), 3.94 (br t, J = 7.8 Hz, 1 H, 3-H), 4.48 (br d, J = 7.8 Hz, 1 H, 3-H), 4.41, 4.61 (each d, J = 14.5 Hz, each 1 H, C*H*$_2$Ph), 7.17–7.28 (ov, 5 H, Ph); ^{13}C NMR (67.8 MHz) δ 23.3, 25.2 (7-Me$_2$), 33.0 (7-C), 48.9 (3a-C), 50.8 (*C*H$_2$Ph), 53.9 (6-C), 66.5 (7a-C), 77.6 (3-C), 127.6, 128.4, 128.6, 136.5 (Ph-C), 169.9 (4-CO). Found: C, 69.29; H, 8.00; N, 10.61%. Calcd for $C_{15}H_{20}N_2O_2$: C, 69.20; H, 7.74; N, 10.76%.

5-Benzyl-3,7,7-trimethylperhydroisoxazolo[4,3-*c*]pyridin-4-one (15b). Colorless prisms from hexane–benzene; mp 79–80 °C; IR (KBr) 3170, 1620 cm^{-1}; ^{1}H NMR (270 MHz) δ 0.91 (br s, 6 H, 7-Me$_2$), 1.44 (d, J = 6.3 Hz, 3 H, 3-Me), 2.73 (d, J = 12.9 Hz, 1 H, 6-H), 2.90 (dd, J = 5.3 and 8.6 Hz, 1 H, 3a-H), 3.30 (d, J = 12.9 Hz, 1 H, 6-H), 3.37 (d, J = 8.6 Hz, 1 H, 7a-H), 4.17 (br, 1 H, 3a-H), 4.49, 4.65 (each d, J = 14.5 Hz, each 1 H, C*H*$_2$Ph), 5.4–5.8 (br, 1 H, NH), 7.24–7.36 (ov, 5 H, Ph); ^{13}C NMR (67.8 MHz) δ 19.3 (3-Me), 23.0, 25.3 (7-Me$_2$), 32.2 (7-C), 50.5 (*C*H$_2$Ph), 53.6 (6-C), 54.4 (3a-C), 66.5 (7a-C), 82.6 (3-C), 127.5, 128.3, 128.5, 136.5 (Ph-C), 169.3 (4-CO). Found: C, 69.89; H, 8.41; N, 10.11%. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08; N, 10.21%.

5-Benzyl-7,7-dimethyl-3-phenylperhydroisoxazolo[4,3-*c*]pyridin-4-one (15c). Colorless prisms from hexane–benzene; mp 98–100 °C; IR (KBr) 3160, 1620 cm^{-1}; ^1H NMR (270 MHz) δ 0.93, 0.95 (each s, each 3 H, 7-Me_2), 2.80 (d, J = 12.5 Hz, 1 H, 6-H), 3.36 (br, 1 H, 7a-H), 3.41 (d, J = 12.5 Hz, 6-H), 3.52 (br, 1 H, 3a-H), 4.52, 4.76 (each d, J = 14.5 Hz, each 1 H, CH_2Ph), 5.43 (br s, 1 H, 3-H), 5.84 (br, 1 H, NH), 7.21–7.53 (ov, 10 H, Ph); ^{13}C NMR (67.8 MHz) δ 23.2, 25.2 (7-Me_2), 32.6 (7-C), 50.9 (*C*H_2Ph), 54.0 (6-C), 55.1 (3a-C), 66.5 (7a-C), 86.7 (3-C), 125.6, 127.6, 127.9, 128.4, 128.6, 128.7, 136.6, 139.8 (Ph-C), 169.3 (4-CO). Found: C, 74.96; H, 7.38; N, 8.31%. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33%.

Oximization of Aldehydes 12d,e and IOOC Reaction of Oximes 13d,e. A solution of aldehyde **12d** (0.303 g, 1.0 mmol), hydroxylamine hydrochloride (0.035 g, 1.2 mmol), sodium acetate (0.050 g, 1.2 mmol) in MeOH (12 mL) was stirred at room temperature for 12 h. The solvent was evaporated and the residue was treated with a 3% aqueous solution of sodium hydrogencarbonate and extracted with dichloromethane (3×20 mL). The organic layer was dried and evaporated to dryness. The residue was subjected to column chromatography on silica gel to give oxime **13d** [0.010 g, 3%; hexane/ethyl acetate (4/1)] and perhydroisoxazolopyridines **15d** [0.124 g, 39%; hexane/ethyl acetate (3/1)] and **15d′** [0.067 g, 21%; hexane/ethyl acetate (3/1)], respectively.

Ethyl 4-[*N*-(3-Hydroxyimino-2,2-dimethylpropyl)benzylamino]crotonate (13d). Colorless oil. This compound was not very stable, and the structure was determined based on the spectroscopic data given below: ^1H NMR (270 MHz) δ 1.07 (s, 6 H, 2-Me_2), 1.30 (t, J = 7.2 Hz, 3 H, CH_2CH_3), 2.50 (s, 2 H, 3-H_2), 3.20 (dd, J = 1.3 and 6.3 Hz, 2 H, >N*C*H_2CH=), 3.64 (s, 2 H, CH_2Ph), 4.20 (q, J = 7.2 Hz, 2 H, C$H_2$$CH_3$), 5.93 (td, J = 1.3 and 15.7 Hz, 1 H, =C*H*CO_2Et), 6.94 (td, J = 6.3 and 15.7 Hz, 1 H, >NCH_2–C*H*=), 7.23–7.34 (ov, 5 H, Ph), 7.96 (s, 1 H, 1-H); ^{13}C NMR (67.8 MHz) δ 14.2 (CH_2*C*H_3), 23.9 (2-Me_2), 38.9 (2-C), 56.0 (*C*H_2Ph), 60.3 (5-C), 60.4 (*C*$H_2$$CH_3$), 63.9 (3-C), 123.2 (=*C*HCO_2Et), 127.1, 128.3, 128.8, 138.0 (Ph-C), 145.8 (>NCH_2*C*H=), 158.4 (1-C), 166.3 (CO_2). HRMS (EI) *m/z* 318.1942. Calcd for $C_{18}H_{26}N_2O_3$: 318.1924.

Ethyl (3*RS*,3a*RS*,7a*RS*)-5-Benzyl-7,7-dimethylperhydroisoxazolo[4,3-*c*]pyridine-3-carboxylate (15d). Colorless oil; IR (NaCl) 3200, 1740 cm^{-1}; ^1H NMR (270 MHz) δ 0.93, 1.14 (each s, each 3 H, 7-Me_2), 1.26 (t, J = 6.9 Hz, 3 H, CH_2CH_3), 2.05–2.25 (ov, 3 H, 3a-H, 4-H, and 6-H), 2.78–2.90 (ov, 2 H, 4-H and 6-H), 3.19 (s, 2 H, CH_2Ph), 4.14–4.26 (m, 2 H, C$H_2$$CH_3$), 6.13 (br, 1 H, NH), 7.42–7.33 (ov, 5 H, Ph); ^{13}C NMR (67.8 MHz) δ 14.1 (CH_2*C*H_3), 25.2, 27.9 (7-Me_2), 32.6 (7-C), 45.8 (3a-C), 53.2 (4-C), 60.6 (6-C), 61.3 (*C*H_2Ph), 62.6 (*C*$H_2$$CH_3$), 64.4 (7a-C), 80.9 (3-C), 127.0, 128.2, 128.6, 138.5 (Ph-C), 171.8 (CO_2). HRMS (EI) *m/z* 318.1924. Calcd for $C_{18}H_{26}N_2O_3$: 318.1924.

Ethyl (3*RS*,3a*RS*,7a*SR*)-5-Benzyl-7,7-dimethylperhydroisoxazolo[4,3-*c*]pyridine-3-carboxylate (15d′). Colorless oil; IR (NaCl) 3200, 1740 cm^{-1}; ^1H NMR (270 MHz) δ 1.02 (s, 6 H, 7-Me_2), 1.25 (t, J = 7.3 Hz, 3 H, CH_2CH_3), 1.82 (br d, J = 11.6 Hz, 1 H, 6-H), 2.11 (t, J = 10.6 Hz, 1 H, 4-H), 2.30 (m, 1 H, 3a-H), 2.51 (d, J = 11.6 Hz, 1 H, 6-H), 2.55 (d, J_{3a-7a} = 10.9 Hz: ax–ax *trans*, 1 H, 7a-H), 3.23 (dd, J = 3.3 and 10.6 Hz, 1 H, 4-H), 3.51, 3.57 (each d, J = 13.2 Hz, each 1 H, CH_2Ph), 4.07 (d, J_{3-3a} = 10.2 Hz: ax–ax *trans*, 1 H, 3-H), 4.12 (m, 2 H, C$H_2$$CH_3$), 5.6 (br, 1 H, NH), 7.25–7.32 (ov, 5 H, Ph); ^{13}C NMR (67.8 MHz) δ 14.1 (CH_2*C*H_3), 18.2, 27.3 (7-Me_2), 33.3 (7-C), 49.7 (3a-C), 54.9 (4-C), 61.3 (*C*$H_2$$CH_3$), 61.9 (*C*$H_2$Ph), 65.0 (6-C), 73.0 (7a-C), 79.0 (3-C), 127.1, 128.3, 128.5, 138.4 (Ph-C), 171.8 (CO_2). HRMS (EI) *m/z* 318.1934. Calcd for $C_{18}H_{26}N_2O_3$: 318.1924.

Aldehyde **12e** was oximized by similar procedures as in the preparation of oxime **13d**. Column chromatographic separation on silica gel afforded perhydroisoxazolopyridines **15e** (53%; hexane/ethyl acetate = 3/1) and **15e′** (9%; hexane/ethyl acetate = 3/1), and cyclic nitrone **16e** (11%; ethyl acetate), respectively.

Ethyl (3*RS*,3a*RS*,7a*RS*)-5-Benzyl-7,7-dimethyl-4-oxoperhydroisoxazolo[4,3-*c*]pyridine-3-carboxylate (15e). Colorless oil; IR (NaCl) 3220, 1730, 1660 cm^{-1}; ^1H NMR (270 MHz) δ 0.87, 0.92 (each s, each 3 H, 7-Me_2), 1.32 (m, 3 H, CH_2CH_3), 2.83 (d, J = 12.5 Hz, 1 H, 6-H), 3.23 (d, J = 8.3 Hz, 1 H, 7a-H), 3.56 (dd, J = 2.0 and 8.2 Hz, 1 H, 3a-H), 4.23 (m, 2 H, C$H_2$$CH_3$), 4.48, 4.70 (each d, J = 14.5 Hz, each 1 H, CH_2Ph), 4.95 (d, J = 2.0 Hz, 1 H, 3-H), 6.63 (br, 1 H, NH), 7.26–7.36 (ov, 5 H, Ph); ^{13}C NMR (67.8 Hz) δ 14.0 (CH_2*C*H_3), 22.1, 25.0 (7-Me_2), 33.1 (7-C), 51.0 (*C*H_2Ph), 52.7 (3a-C), 54.2 (6-C), 61.5 (*C*$H_2$$CH_3$), 65.6 (7a-C), 82.4 (3-C), 127.5, 128.3, 128.5, 136.2 (Ph-C), 168.0 (CO_2), 171.5 (4-CO). Found: C, 64.52; H, 7.43; N, 8.31%. Calcd for $C_{18}H_{24}N_2O_4$: C, 65.04; H, 7.28; N, 8.43. HRMS (EI) *m/z* 332.1752. Calcd for $C_{18}H_{24}N_2O_4$: 332.1737.

Ethyl (3*RS*,3a*RS*,7a*SR*)-5-Benzyl-7,7-dimethyl-4-oxoperhydroisoxazolo[4,3-*c*]pyridine-3-carboxylate (15e′). Colorless oil; IR (NaCl) 3220, 1730, 1660 cm^{-1}; ^1H NMR (270 MHz) δ 1.00, 1.03 (each s, each 3 H, 7-Me_2), 1.34 (t, J = 7.3 Hz, 3 H, CH_2CH_3), 2.99 (d, J = 13.2 Hz, 1 H, 6-H), 3.07–3.17 (ov, 2 H, 3a-H and 7a-H), 3.14 (d, J = 13.2 Hz, 1 H, 6-H), 4.27 (m, 2 H, C$H_2$$CH_3$), 4.49, 4.61 (each d, J = 14.5 Hz, each 1 H, CH_2Ph), 4.74 (d, J_{3-3a} = 7.6 Hz: ax–ax *trans*, 1 H, 3-H), 5.67 (br d, J = 11.8 Hz, 1 H, NH), 7.22–7.38 (ov, 5 H, Ph); ^{13}C NMR (67.8 MHz) δ 14.1 (CH_2*C*H_3), 19.6, 28.2 (7-Me_2), 31.9 (7-C), 49.5 (*C*H_2Ph), 54.1 (3a-C), 60.3 (6-C), 61.9 (*C*$H_2$$CH_3$), 70.4, 70.6 (3-C and 7a-C), 127.8, 128.3, 128.8, 136.8 (Ph-C), 168.1 (4-CO), 171.9 (CO_2). HRMS (EI) *m/z* 332.1732. Calcd for $C_{18}H_{24}N_2O_4$: 332.1737.

1-Benzyl-3-ethoxycarbonylmethyl-6,6-trimethyl-2-oxo-2,3,6,7-tetrahydro-1*H*-1,4-diazepine 4-Oxide (16e). Colorless oil; IR (NaCl) 1740, 1650 cm^{-1}; ^1H NMR (270 MHz) δ 1.09–1.28 (ov, 9 H, 6-Me_2 and CH_2CH_3), 2.48 (dd, J = 5.3 and 16.8 Hz, 1 H, 3-C*H*HCO_2Et), 2.59 (dd, J = 8.6 and 16.8 Hz, 1 H, 3-CH*H*CO_2Et), 3.31, 3.60 (each d, J = 13.5 Hz, each 1 H, 7-H_2), 4.10 (q, J = 7.3 Hz, 2 H, C$H_2$$CH_3$), 4.35 (dd, J = 5.3 and 8.3 Hz, 1 H, 3-H), 4.65, 4.84 (each d, J = 17.5 Hz, each 1 H, CH_2Ph), 7.19–7.39 (ov, 6 H, 5-H and Ph); ^{13}C NMR (67.8 MHz) δ 14.1 (CH_2*C*H_3), 23.8, 24.0 (6-Me_2), 34.1 (6-C), 39.9 (3-*C*$H_2$$CO_2$Et), 52.6 (*C*$H_2$Ph), 54.4 (7-C), 58.4 (3-C), 61.0 (*C*$H_2$$CH_3$), 126.5, 127.8, 130.0, 136.6 (Ph-C), 157.4 (5-C), 171.0, 173.2 (2-C and CO_2). HRMS (EI) *m/z* 332.1742. Calcd for $C_{18}H_{24}N_2O_4$: 332.1737.

Kinetic Studies. General Procedures: A stirred solution of oxime **10a** (7.0 mg), naphthalene (5.5 mg) and *n*-BuOH (10 mL) in a test tube under nitrogen was inserted into one neck of a two-neck flask. A condenser was fitted to the other neck, and the flask was filled with an appropriate solvent, such as THF (bp 66.0 °C), benzene (bp 80.1 °C), propiononitrile (bp 97.2 °C), and *n*-BuOH (bp 117 °C) until the solvent was up to the solution of the test tube. The outer flask was sunk in a thermostated oil bath and heated to keep the solvent in the flask boiling. At an appropriate interval with a total of nine to fourteen data points, 0.05 mL each of the *n*-BuOH solution was withdrawn with a micro syringe through a septum rubber cap. The collected sample was immediately cooled in an ice-salt bath to stop the reaction, and was analyzed by HPLC. HPLC measurements were performed with a Hitachi L-6200 instrument using UV detector (Hitachi L-4000; 254

nm). To measure the rates of the disappearance of the oximes **10b**–d and **13c**, naphthalene was utilized as an internal standard. A Wakosil-II5C18HG (id 4.6 mm×250 mm) column was used; the flow rate of the elution was 0.8 mL min^{-1} (47 kg cm^{-2}) and the elution solvent was acetonitrile–H_2O (7:3). All rates of conversion of oximes **10** under several conditions (solvent, concentration, and temperature) were first-order with respect to the oxime concentration. The obtained rate constants [k (s^{-1})×10^5] were as below: for **10a** in *n*-BuOH, 1.63 (66 ˚C), 4.00 (80 ˚C), 17.7 (97 ˚C), and 44.6 (117 ˚C). The relative rates for the conversion of oximes **10a–d** and **13c** are summarized in Table 3.

References

1 a) R. Grigg, H. Q. N. Gunaratne, and J. Kemp, *J. Chem. Soc., Perkin Trans. 1*, **1984**, 41. b) R. Grigg, M. Jordan, and A. Tangthongkum, *J. Chem. Soc., Perkin Trans. 1,* **1984**, 47. c) R. Grigg and S. Thianpantangul, *J. Chem. Soc., Perkin Trans. 1*, **1984**, 653. Also, see: R. Grigg, *Chem. Soc. Rev.*, **16**, 89 (1987).

2 a) M. H. Norman and C. H. Heathcock, *J. Org. Chem.*, **52**, 226 (1987). b) R. Grigg, F. Heaney, J. Markandu, S. Surendrakumar, M. Thornton-Pett, and W. J. Warnock, *Tetrahedron*, **47**, 4007 (1991). c) R. Grigg, M. J. Dorrity, F. Heaney, J. F. Malone, S. Rajviroongit, V. Sridharan and S. Surendrakumar, *Tetrahedron*, **47**, 8297 (1991). d) A. Hassner and R. Maurya, *Tetrahedron Lett.*, **30**, 5803 (1989). e) A. Hassner, K. M. Lokanatha Rai, and W. Dehaen, *J. Org. Chem.*, **56**, 2775 (1991). f) A. Hassner, R. Maurga, O. Friedman, and H. E. Gottlieb, *J. Org. Chem.*, **58**, 4539 (1993). g) A. Hassner, S. Singh, R. Sharma, and R. Maurya, *Tetrahedron*, **49**, 2317 (1993). h) A. Hassner, K. M. Lokanatha Rai, and W. Dehaen, *Synth. Commun.*, **24**, 1669 (1994). i) A. Hassner, E. Falb, A. Nudelman, A. Albeck, and H. E. Gottlieb, *Tetrahedron Lett.*, **35**, 2397 (1994). j) U. Chiacchio, G. Buemi, F. Casuscelli, A. Procopio, A. Rescifina, and R. Romeo, *Tetrahedron*, **50**, 5503 (1994). k) U. Chiacchio, A. Corsaro, V. Pistarà, A. Rescifina, G. Romeo, and R. Romeo, *Tetrahedron*, **52**, 7875 (1996) and references cited therein.

3 a) M. Gotoh, T. Mizui, B. Sun, K. Hirayama, and M. Noguchi, *J. Chem. Soc., Perkin Trans. 1*, **1995**, 1857. b) M. Gotoh, B. Sun, K. Hirayama, and M. Noguchi, *Tetrahedron*, **52**, 887 (1996). c) C. O'Mahony and F. Heaney, *Chem. Commun.*, **1996**, 167; F. Heaney and C. O'Mahony, *J. Chem Soc., Perkin Trans. 1*, **1998**, 341; F. Heaney, and S. Bourke, *J. Chem Soc., Perkin Trans. 1,* **1998**, 955; F. Heaney, S. Bourke, D. Cunningham, and P. McArdle, *J. Chem. Soc., Perkin Trans. 2*, **1998**, 547. Also see Ref. 1a and 1c.

4 M. Noguchi, H. Okada, S. Nishimura, Y. Yamagata, S. Takamura, M. Tanaka, A. Kakehi, and H. Yamamoto, *J. Chem. Soc., Perkin Trans. 1*, **1999**, 185.

5 R. Grigg, J. Markandu, T. Perrior, S. Surendrakumar, and W. J. Warnock, *Tetrahedron*, **48**, 6929 (1992); R. Bishop, P. R. Brooks, and S. C. Hawkins, *Synthesis*, **1988**, 997; A. B. Holmes, A. L. Smith, S. F. Williams, L. R. Hughes, Z. Lidert, and C. Swithenbank, *J. Org. Chem.*, **56**, 1393 (1991); R. Grigg, T. R. Perrior, G. J. Sexton, S. Surendrakumar, and T. Suzuki, *J. Chem. Soc., Chem. Commun.*, **1993**, 372.

6 Reaction of oxime **3e** in *n*-BuOH under reflux for 30 h gave **4e** (40%) together with two other products. 5-*t*-Butoxycarbonyl-7,7-dimethylperhydroisoxazolo[4,3-*c*]pyridine (**4e**): Colorless prisms from hexane; mp 122–123 ˚C; IR (KBr) 3170, 1690 cm^{-1}. This compound gave broad signals in ^1H and ^{13}C NMR spectra. ^1H NMR (270 MHz) δ 0.97, 1.06 (each s, each 3 H, 7-Me_2), 1.47 (s, 9 H, –CMe_3), 2.60–2.94 (ov, 3 H, 3a-H, 4-H, and 6-H), 3.15 (br d, J = 3.6 Hz, 1 H, 7a-H), 3.5 (br, 1 H, 4-H), 3.66 (d, J = 7.6 Hz, 1 H, 3-H), 3.89 (dd, J = 5.3 and 7.6 Hz, 1 H, 3-H), 4.1 (br, 1 H, 4-H), 5.7 (br, 1 H, NH); ^{13}C NMR (67.8 MHz) δ 24.4, 24.6 (7-Me_3), 28.4 (CMe_3), 32.5 (7-C), 39.4 (3a-C), 41.9, 42.8 (4-C), 49.0, 50.1 (6-C), 66.1 (7a-C), 72.1 (3-C), 79.7 (CMe$_3$), 154.8 (CO_2). Found: C, 60.78; H, 9.76; N, 10.97%. Calcd for $C_{13}H_{24}N_2O_3$: C, 60.91; H, 9.44; N, 10.93%.

7 H. G. O. Becker, W. Ecknig, E. Fanghänel, and S. Rommel, *Wiss. Z. Techn.*, **11**, 38 (1968); *Chem. Abstr.*, **71**, 60938 (1970).