25-mL portions of H_2O. The ether layer is then dried over $MgSO_4$ and stripped of solvent. The resulting mixture is then separated by silica gel chromatography by first eluting with hexane to remove the methyl phenyl selenide and then with 1:1 ether/hexane to remove the product. The combined ether/hexane solutions are dried over $MgSO_4$ and stripped of solvent to give **31**.

Physical and Spectral Data. For **4**: mp 56–58 °C; ^{1}H NMR ($CDCl_3$) 10.50–9.90 (br s, 1), 7.70–7.12 (m, 5), 3.10–270 (t, J = 6 Hz, 2), 2.52–2.13 (t, J = 6 Hz, 2), 2.01–1.60 (m, 4); IR ($CHCl_3$) 1700 cm^{-1}; mass spectrum, m/e 256, 258; precise mass calcd for $C_{11}H_{14}O_2{}^{78}Se$ m/e 256.016 65, found 256.023 62.

For **6**: yellow oil; ^{1}H NMR ($CDCl_3$) 10.37–10.10 (br s, 1), 7.70–7.12 (m, 5), 3.12–2.83 (t, J = 7 Hz, 2), 2.64–2.40 (t, J = 6 Hz, 2), 2.27–1.84 (m, 2); IR ($CHCl_3$) 1705 cm^{-1}; mass spectrum, m/e 242, 244; precise mass calcd for $C_{10}H_{12}O_2{}^{80}Se$ m/e 244.000 20, found 244.000 38.

For **8**: colorless liquid; ^{1}H NMR ($CDCl_3$) 1.20 (s, 9), 9.47 (br s, 1).

For **10**: mp 120–121 °C; ^{1}H NMR ($CDCl_3$) 10.50–10.11 (br s, 1), 8.27–7.40 (m, 5).

For **12**: mp 157–158 °C; ^{1}H NMR ($CDCl_3$) 7.08–6.47 (m, 3), 3.75 (s, 3), 2.94–1.52 (m, 11), 1.66 (s, 3), 1.13 (s, 3).

For **14**: colorless liquid; ^{1}H NMR ($CDCl_3$) 11.00 (br s, 1), 2.54–2.20 (t, J = 6 Hz, 2), 1.94–1.15 (m, 4), 1.10–0.78 (t, J = 6 Hz, 3).

For **16**: colorless liquid; ^{1}H NMR ($CDCl_3$) 9.52 (br s, 1), 2.40–1.82 (m, 3), 1.13–0.88 (d, J = 6 Hz, 6).

For **19**: yellow oil; ^{1}H NMR ($CDCl_3$) 10.41 (br s, 1), 7.70–7.10 (m, 5), 5.86–5.42 (br s, 2), 3.00–2.90 (m, 2), 2.40–2.01 (m, 5), 1.45–1.25 (m, 1); IR ($CHCl_3$) 1710 cm^{-1}; mass spectrum, m/e 294, 296; precise mass calcd for $C_{14}H_{16}O_2{}^{80}Se$ m/e 296.031 52, found 296.031 40.

For **21**: yellow oil; ^{1}H NMR ($CDCl_3$) 10.30 (br s, 1), 7.70–7.12 (m, 5), 6.40–5.90 (m, 2), 3.20–2.91 (m, 4), 2.11–2.02 (m, 1), 1.43–1.11 (m, 3); IR ($CHCl_3$) 1710 cm^{-1}; mass spectrum, m/e 308, 310; precise mass calcd for $C_{15}H_{18}O_2{}^{80}Se$ m/e 310.047 17, found 310.047 03.

For **23**: mp 44–46 °C; ^{1}H NMR ($CDCl_3$) 10.05 (br s, 1), 3.08–2.92 (t, J = 6 Hz, 2), 2.06–1.41 (m, 6); IR ($CHCl_3$) 1710 cm^{-1}; mass spectrum, m/e 270, 272; precise mass calcd for $C_{12}H_{16}O_2{}^{80}Se$ m/e 272.031 52, found 272.036 49.

For **25**: mp 48–51 °C; ^{1}H NMR ($CDCl_3$) 10.20 (br s, 1), 3.58–3.16 (m, 1), 2.80–2.42 (t, J = 7 Hz, 2), 2.14–2.71 (m, 2), 1.60–1.40 (d, J = 7 Hz, 3), 7.70–7.12 (m, 5); IR 1705 cm^{-1}; mass spectrum, m/e 256, 258; precise mass calcd for $C_{11}H_{14}O_2{}^{80}Se$ m/e 258.015 85, found 258.020 03.

For **27**: yellow oil; ^{1}H NMR ($CDCl_3$) 10.23 (br s, 1), 7.65–7.00 (m, 5), 3.31–2.93 (m, 1), 2.71–2.35 (m, 2), 2.03–0.80 (m, 15); IR ($CHCl_3$) 1710 cm^{-1}; mass spectrum, m/e 326, 328; precise mass calcd for $C_{16}H_{24}O_2{}^{80}Se$ m/e 328.094 12, found 328.097 36.

For **31**: colorless liquid; ^{1}H NMR ($CDCl_3$) 7.34–6.28 (m, 5), 3.50 (br s, 1), 2.71 (s, 3).

For **33**: mp 143–145 °C; ^{1}H NMR (Me_2SO-d_6 + $CDCl_3$) 10.05 (br s, 1), 8.03–7.27 (m, 6), 5.00–4.40 (overlapping dq, $J^1 = J^2$ = 7 Hz, 1), 1.65–1.40 (d, J = 7 Hz, 3).

For **35**: yellow oil; ^{1}H NMR ($CDCl_3$) 7.63–7.00 (m, 5), 3.04–2.80 (t, J = 7 Hz, 2), 2.70–2.40 (t, J = 6 Hz, 2), 2.20–1.77 (m with overlapping s, 5); IR ($CHCl_3$) 1708 cm^{-1}; mass spectrum, m/e 240, 242; precise mass calcd for $C_{11}H_{14}O^{80}Se$ m/e 242.020 96, found 242.019 48.

For **37**: yellow oil; ^{1}H NMR ($CDCl_3$) 7.60–7.15 (m, 5), 3.02–2.80 (t, J = 7 Hz, 2), 2.27–1.60 (m with overlapping s, 6); IR ($CHCl_3$) 1710 cm^{-1}; mass spectrum, m/e 254, 256; precise mass calcd for $C_{12}H_{16}O^{80}Se$ 256.036 61, found 256.043 72.

For **44**: colorless liquid; ^{1}H NMR ($CDCl_3$) 7.20 (br s, 5), 4.92–4.50 (q, J = 7 Hz, 1), 1.50–1.30 (d, J = 7 Hz, 3).

Acknowledgment. Financial support for this work was provided by grants from the National Institutes of Health and Research Corp.

Registry No. **1**, 112-29-8; **2**, 61539-89-7; **3**, 542-28-9; **4**, 66241-82-5; **5**, 96-48-0; **6**, 23768-06-1; **7**, 598-98-1; **9**, 120-51-4; **11**, 1231-74-9; **13**, 539-82-2; **15**, 659-70-1; **17**, 939-48-0; **18**, 2744-05-0; **19**, 77461-93-9; **20**, 64550-47-6; **21**, 77461-94-0; **22**, 502-44-3; **23**, 66241-83-6; **24**, 108-29-2; **52**, 66241-87-0; **26**, 706-14-9; **27**, 77461-95-1; **28**, 93-89-0; **29**, 613-93-4; **30**, 28685-60-1; **32**, 7244-67-9; **34**, 517-23-7; **35**, 66241-86-9; **36**, 1123-19-9; **37**, 77461-96-2; **38**, 93-58-3; phenyl selenide anion, 14971-39-2.

Deamination of Primary Aminoalkanols. Formation of Substituted *N*-Nitroso-1,3-oxazolidines and *N*-Nitroso-1,3-tetrahydrooxazines[1]

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The deamination of 2-amino- and 3-aminoalkanols in the presence of nitrous acid is reported. The 2-aminoalkanols generated aldehydes upon loss of nitrogen, followed by oxazolidine formation by reaction with starting material and finally nitrosation to substituted *N*-nitroso-1,3-oxazolidines. Ethanolamine gave *N*-nitroso-2-methyl-1,3-oxazolidine; 2-amino-2-methyl-1-propanol was converted to *N*-nitroso-2-isopropyl-4,4-dimethyl-1,3-oxazolidine. Deamination of 1-amino-2-propanol gave propionaldehyde, which upon further reaction produced *cis*- and *trans*-*N*-nitroso-2-ethyl-5-methyl-1,3-oxazolidines. (*E*)- and (*Z*)-*N*-nitroso-2-ethyl-4-methyl-1,3-oxazolidines were obtained from the deamination of 2-amino-1-propanol. Propionaldehyde and formaldehyde were produced by diazotiazation of 1-amino-3-propanol. Further reaction of the aldehydes with unreacted amine formed *N*-nitroso-1,3-tetrahydrooxazine and *N*-nitroso-2-ethyl-1,3-tetrahydrooxazine. Nuclear magnetic resonance and deuterium-exchange studies of these compounds are discussed.

It is well established that 2-amino- and 3-aminoalkanols can undergo a pinacolic rearrangement to aldehydes, ketones, epoxides and glycols in nitrous acid[2,3] (Scheme I). Howver, Nance et al.[4] were the first to isolate a nitrosooxazolidine from the deamination of 2-amino-1-butanol. The reaction involved the generation of butyraldehyde followed by oxazolidine formation with unreacted aminoalkanol and finally nitrosation to *N*-nitroso-2-propyl-4-ethyl-1,3-oxazolidine. When 3-aminoalkanols were deaminated, carbonyl compounds were produced,[3] but nitrosamine formation in these reaction has not been reported.

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(3) J. English, Jr., and A. D. Bliss, *J. Am. Chem. Soc.*, 78, 4057 (1956).

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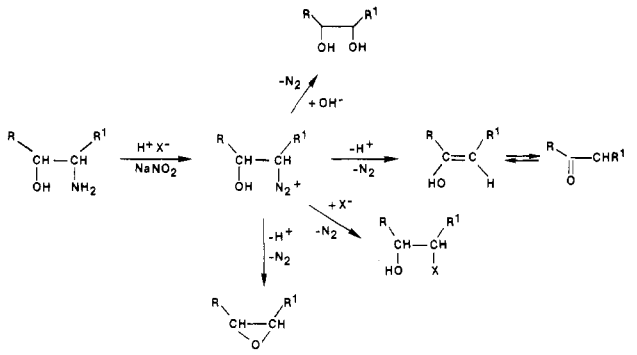
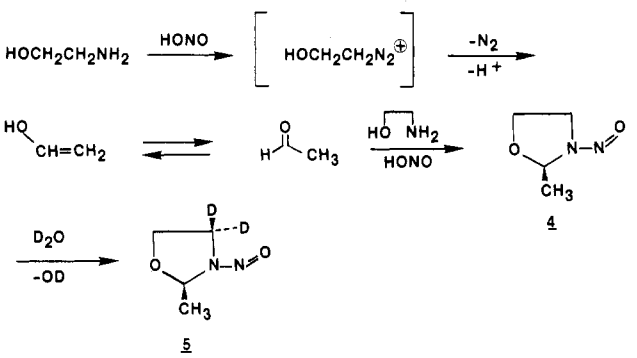
Scheme I

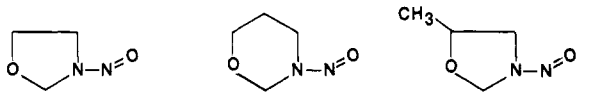


Scheme II



Synthetic methods for preparing open-chain and cyclic α-nitrosaminoalkyl ethers including *N*-nitroso-1,3-oxazolidines and *N*-nitroso-1,3-tetrahydroxazines were developed by Eiter et al.[5] They were able to introduce the desired aldehyde or ketone into the molecule without any formation of aldehydes from the parent aminoalkanol.

N-Nitroso-1,3-oxazolidine (**1**) and *N*-nitrosotetrahydro-1,3-oxazine (**2**) are strong liver carcinogens[6,7] in rats.



However, the carcinogenicity of their substituted derivatives has not been reported. Since primary aminoalkanols are widely used in industry, it is important to be aware that they may be the source of a wide variety of substituted heterocyclic nitrosamines. A recent example of this has been reported by Stephany et al.,[8] who found *N*-nitroso-5-methyl-1,3-oxazolidine (**3**) in a commercial cutting fluid.

This report describes the reaction of several aminoalkanols in the presence of excess sodium nitrite in aqueous acid solutions and the spectral properties of the products.

Results and Discussion

Ethanolamine in acid solution was nitrosated with concomitant loss of nitrogen to form acetaldehyde (Scheme II). The aldehyde condensed with excess ethanolamine and was nitrosated to form *N*-nitroso-2-methyl-1,3-oxazolidine (**4**). The nitrosamine was formed in 10–27% yield, depending on the reaction conditions (Table I).

The major product in all the reactions was **4**. Only traces of chloroethanol and ethylene glycol were detected when the reaction was carried out in hydrochloric acid; however, significant amounts of acetaldehyde were observed. In acetic acid small amounts of acetaldehyde and ethylene glycol were detected. The other possible product, ethylene oxide, was not trapped under the reaction conditions used here. At pH 5 the yield of the heterocycle was higher since the conditions favored condensation of the aldehyde with nonprotonated amine.[9] At lower pH values the amine which has not been diazotized is completely protonated and cannot condense with the aldehyde at a reasonable rate. The relative amount of free aldehyde is greater at lower pH values (Table I).

Table I. Nitrosation[a] of 0.5 M Solutions of Ethanolamine

entry	acid	pH	*T*, °C	products (% yield)[b]	% yield of **4**[c]
1	HCl	2	25	acetaldehyde (19), chloroethanol (5), ethylene glycol (3), **4** (73)	14
2	HCl	2	37	acetaldehyde (33), chloroethanol (3), ethylene glycol (3), **4** (60)	12
3	HOAc	3.5	25	acetaldehyde (14), ethylene glycol (7), **4** (73)	14
4	HOAc	3.5	37	acetaldehyde (7), ethylene glycol (6), **4** (83)	10
5	HOAc	5	25	acetaldehyde (7), ethylene glycol (4), **4** (88)	27
6	HOAc	5	37	acetaldehyde (8), ethylene glycol (2), **4** (87)	22

[a] Nitrosated with 2.5 equiv of $NaNO_2$ for 2 h. [b] Relative yields of products based on GLC analysis of the aqueous solutions. [c] Isolated yields of **4**.

The nuclear magnetic resonance spectrum of **4** indicated that the preferred orientation of the nitroso group was anti (*E*) to the 2-methyl substituent, and 94% of the mixture consisted of this isomer. The syn methyl group appeared as a doublet at δ 1.40, while the anti methyl was shifted downfield to δ 1.78. Protons at C-4 and C-5 gave a complex pattern between δ 3.42 and 4.7. The C-2 proton appeared as a quartet at δ 5.56; however, no distinction between a syn and anti proton was observed. The spectrum was simplified, and the acidity of the C-4 protons was demonstrated by the H–D exchange of **4** at 90 °C in a mixture of deuterium oxide, dimethyl-d_6 sulfoxide, and sodium deuteroxide.[10] The two protons at C-4 exchanged within 15 min to form compound **5**; the C-2 proton did not exchange, even after prolonged heating.

Diazotization of 2-amino-2-methyl-1-propanol (**6**) led to the formation of isobutyraldehyde upon loss of nitrogen. Condensation of the aldehyde with excess amine **6** followed by nitrosation gave a yield of up to 16% of *N*-nitroso-2-isopropyl-4,4-dimethyl-1,3-oxazolidine (**7**).

The nuclear magnetic resonance spectrum of **7** could be divided into two sets of signals for two different rotamers. The isomer in which the nitroso group was syn (*Z*) to the isopropyl group accounted for 83% of the mixture. As was the case with substituted 1,3-dioxalanes[11] and 1,3-dithi-

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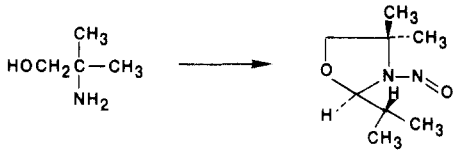
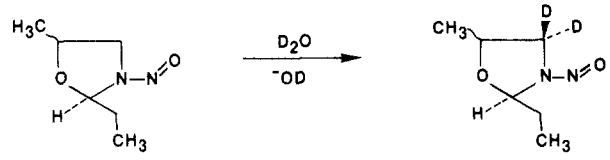


6 7

anes,[12] the nitrosooxazolidine **7** had to adjust its conformation to the steric requirements of the substituents, the nitroso group being an added steric factor. The methyl groups at C-4 were not equivalent, being in two slightly different magnetic environments, δ 1.64 and 1.67 for the *Z* rotamer and δ 1.45 and 1.51 for the *E* isomer. The isopropyl group assumed a pseudoequatorial orientation to minimize the 1,3-transannular interactions.[11] The nitroso group forces the two isopropyl methyl groups into a fixed rotational conformation; thus the two groups are not equivalent. This was evident from the presence of two doublets for the *E* and two doublets for the *Z* isomers.

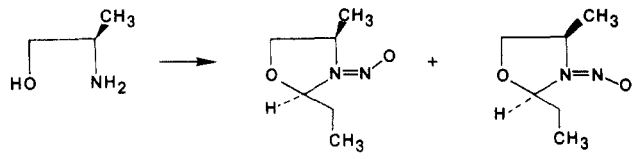
The reaction of 1-amino-2-propanol (**8**) with sodium nitrite at pH 4.5 gave propionaldehyde upon rearrangement and loss of nitrogen (Scheme III). Further reaction of the aldehyde with excess **8** followed by nitrosation gave a 13% yield of *cis*- and *trans*-*N*-nitroso-2-ethyl-5-methyl-1,3-oxazolidines (**9a,b**). The two isomers were obtained in a 1.2:1 ratio of cis to trans. Separation of the two isomers was accomplished by dry column chromatography on silica gel (activity III) eluted with 9:1 hexane–THF. Only a trace of nitrosamine **10**, derived from acetone and the amino alcohol **8**, was detected on GLC.

The assignment of the cis and trans sterochemistry was based on their nuclear magnetic resonance spectra and a comparison with those of *cis*- and *trans*-2,4-disubstituted-dioxalanes.[11] The cis isomer **9a** shows an upfield chemical shift for the C-2 proton (δ 5.48) and a downfield chemical shift for the C-5 methyl substituent (δ 1.42). The trans isomer **9b** shows a downfield shift for the C-2 proton (δ 5.77) and an upfield shift for the C-5 substituent (δ 1.32). The cis and the trans isomer exist almost exclusively as their *E* rotamers. Complete deuterium exchange took place at C-4 to form **11** when the isomeric mixture **9** was heated in D_2O/OD at 90 °C. The ratio of cis to trans isomers remained constant. The C-2 proton did not exchange.



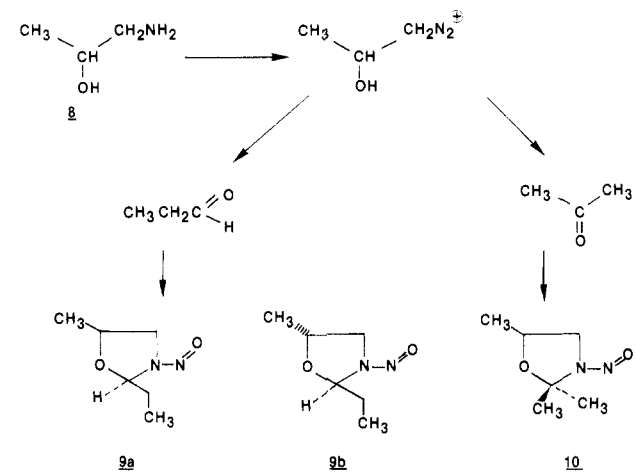
9 11

Treatment of *dl*-2-amino-1-propanol (**12**) with sodium nitrite at pH 4 gave (*E*)- and (*Z*)-*N*-nitroso-2-ethyl-4-methyl-1,3-oxazolidines (**13a,b**) in up to 22% yield. The ratio of the *E* and *Z* isomers was 2.8:1.



12 13a 13b

Scheme III



8 9a 9b 10

The *E* rotamer **13a** (the nitroso oxygen is trans to the ether linkage) exhibited a chemical shifts for the C-2 proton at δ 5.54. The methyl at C-4 in **13a** appeared as a doublet at δ 1.25. An upfield shift at δ 5.28 for the C-2 proton and a downfield shift for the C-4 methyl at δ 1.57 were observed for the *Z* isomer **13b**.

From the work of English et al.[3] it is possible to predict that upon deamination 3-aminopropanol (**14**) will undergo ring cleavage to ethylene and formaldehyde (Scheme IV). Any formaldehyde formed would then condense with excess **14**, and the intermediate would nitrosate to form *N*-nitroso-1,3-tetrahydrooxazine (**15**). In fact, **15** was detected by GLC only as a minor product (<1%). The major product was *N*-nitroso-2-ethyl-1,3-tetrahydrooxazine (**16**).

A more favorable pathway after nitrosation involved a hydroxyalkyl migration to form a secondary diazonium ion intermediate, **14a**, which, upon loss of nitrogen, gave propionaldehyde. Further reaction of the aldehyde with excess 1,3-aminopropanol gave **16**. Deuteration of **16**, under the conditions described above, gave *N*-nitroso-2-ethyl-1,3-tetrahydrooxazine-*4,4*-d_2 (**17**). No H–D exchange at C-2 took place.

No clear conformational picture has emerged from this study for the substituted 1,3-oxazolidines. However, the NMR studies indicate that the 1,3-tetrahydrooxazines have conformational requirements similar to those of the six-membered-ring nitrosamines. Well-defined α-axial and α-equatorial protons are observed.[13] There is one common property of the five- and six-membered rings. The nitroso group prefers an orientation which is trans to the ether linkage. This is also observed in *N*-nitrosoalkyl α-methylenealkyl ethers.[14] Nuclear magnetic resonance studies are currently underway to determine the exact conformation of the five-membered rings.

Overall, this study clearly indicates that substituted nitrosooxazolidine and nitrosotetrahydrooxazines are readily formed from primary aminoalkanols. The search for compounds of this type in the environment has, however, not been pursued. This is due, in part, to our limited knowledge of their chemistry. Most of the nitrosamines described in this report have mutagenic activity,[15] and some have been shown to be carcinogenic in rats.[6,7]

Experimental Section

Proton magnetic resonance spectra were measured on a Varian

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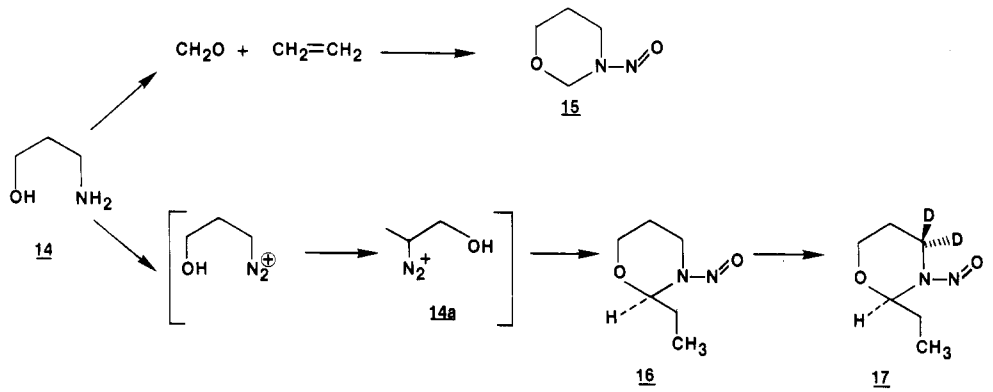
Scheme IV



XL-100 spectrometer with $CDCl_3$, containing 0.5% tetramethylsilane as an internal standard, as the solvent. The IR spectra were obtained on a Perkin-Elmer 467 spectrometer. Mass spectra were taken on a Finnigan 3300 mass spectrometer equipped with a Finnigan 6000 MS data system. Ultraviolet spectra were run as ethanolic or aqueous solutions on a Beckman Acta MVI spectrophotometer. Gas chromatographic analyses were carried out on a Shimadzu Model 4BM gas chromatograph equipped with a Hewlett-Packard 18652A A/D converter coupled to the recorder of a flame-ionization detector. A 2.5-m, 8% HI-EFF-1BP coated on Gas Chrom Q column was used (Applied Science Laboratories, Inc.). The starting materials used were obtained from Aldrich Chemical Co. Silica gel 60 (70–230 mesh, E. Merck) was used for dry-column separations. Elemental analyses were done at Galbraith Laboratories, Inc.

Nitrous Acid Deamination of Ethanolamine. A solution of 500 mg (8.2 mmol) of ethanolamine in 16 mL of water was acidified with acetic acid or hydrochloric acid to the desired pH (see Table I). To the solution was added 4.6 mL of a 3.6 M aqueous sodium nitrite solution. The reaction mixture was shaken at the temperature and for the time indicated in Table I. The product was extracted into methylene chloride, washed with 5% sodium bicarbonate, and dried over anhydrous sodium sulfate. The solution was filtered through a layer of anhydrous magnesium sulfate and the solvent removed on a rotary evaporator to give *N*-nitroso-2-methyl-1,3-oxazolidine (**4**) in 10–27% yield: bp 81 °C (5 mmHg) [lit.[5] bp 48 °C (0.01 mmHg)]; IR (film) 2990, 2940, 2880, 1425, 1400, 1310, 1275, 1175, 865 cm^{-1}; UV (H_2O) λ_{max} 344 (ϵ 86); NMR ($CDCl_3$) δ 1.39 (d, 0.13 H, *syn*-CH_3), 1.76 (d, 2.87 H, *anti*-CH_3), 3.42–4.70 (m, 4 H), 5.58 (q, 1 H); mass spectrum, *m/z* (relative intensity) 116 (12.3), 101 (3), 85 (1.5), 72 (35), 56 (32), 55 (12), 43 (100), 30 (55).

H–D Exchange of *N*-Nitroso-2-methyl-1,3-oxazolidine (4). To a solution of 100 mg (0.86 mmol) of **4** in 0.5 mL of dimethyl-d_6 sulfoxide was added 0.5 mL of 40% sodium deuteroxide in D_2O. The mixture was then heated at 90 °C for 30 min and then cooled to 25 °C and diluted with 1 mL of water. The product was extracted into dichloromethane and washed three times with water. The organic layer was dried over anhydrous sodium sulfate, filtered and evaporated to give 97 mg of product: NMR ($CDCl_3$) δ 1.40 (d, 0.24 H, *syn*-CH_3), 1.78 (d, 2.76 H, *anti*-CH_3), 4.12 (q, 2 H, AB q), 5.55 (q, 1 H); mass spectrum, *m/z* (relative intensity) 118 (M^+, 5.97), 103 (1.7), 86 (6.7), 84 (17.7), 74 (15.1), 66 (20.4), 58 (14.7), 57 (9.7), 44 (51.4), 43 (58.3).

Deamination of 2-Amino-2-methyl-1-propanol (6). To a 0.5 M aqueous solution of 500 mg (5.6 mmol) of **6** was added 2 mL of acetic acid. Then, 4.7 mL of 3.6 M aqueous sodium nitrite was added to the solution (pH 4), and the mixture allowed to stand at 25 °C for 2 h. The solution was made basic by the addition of solid sodium carbonate. The product was extracted into methylene chloride. The solution was washed with 5% hydrochloric acid and then 5% sodium bicarbonate and dried over anhydrous sodium sulfate. The solvent was removed on a rotary evaporator, and the residual oil vacuum distilled to give 151 mg (16%) of *N*-nitroso-2-isopropyl-4,4-dimethyl-1,3-oxazolidine (**7**). At pH 4.7 the yield of **7** was 12%: bp 45 °C (0.2 mmHg) [lit.[5] bp 70 °C (0.3 mmHg)]; IR (film) 2975, 2880, 1465, 1420, 1370, 1260, 1105, 1060, 950 cm^{-1}; UV (EtOH) λ_{max} 357 (ϵ 74); NMR ($CDCl_3$) for isopropyl methyls δ 0.84 (d, 2.5 H, syn), 0.95 (d, 0.5 H, anti), 0.99 (d, 2.5 H, syn), 1.17 (d, 0.5 H, anti); for geminal methyls δ 1.45 (s, 0.5 H, syn), 1.51 (s, 0.5 H, syn), 1.64 (s, 2.5 H, anti), 1.67 (s, 2.5 H, anti), 3.66–4.03 (m, 2 H), 5.25 (d, 0.83 H), 5.42 (d, 0.16 H, anti); mass spectrum, *m/z* (relative intensity) 172 (19), 142 (4), 129 (49), 112 (7), 100 (28), 71 (47), 56 (100), 41 (59), 30 (22).

Deamination of 1-Amino-2-propanol (8). To a solution of 0.594 mL (9.9 mmol) of glacial acetic acid and 500 mg (6.6 mmol) of **8** in 13 mL of water (pH 4.7) was added 4.6 mL of 3.6 M aqueous sodium nitrite. The solution was stirred at 25 °C for 2 h. Solid sodium carbonate was added until the solution was basic; it was then extracted with methylene chloride. The organic layer was back-washed with 5% HCl and dried over anhydrous potassium carbonate. Evaporation of the solvent gave 125 mg of a yellow oil. GLC analysis of the product indicated the presence of a 1.2:1 mixture of a *N*-nitroso-*cis*-2-ethyl-5-methyl-1,3-oxazolidine (**9a**) and the trans isomer **9b**. A small amount of *N*-nitroso-2,2-dimethyl-1,3-oxazolidine (**10**) was also detected on GLC. The yield of **9a,b** based on 1-amino-2-propanol (**8**) was 13%, whereas the yield of **10** was only 0.2%. The chromatographic and spectral properties of these compounds were identical with authentic samples prepared as described below.

***N*-Nitroso-2-ethyl-5-methyl-1,3-oxazolidine (9a,b).** A solution of 7.5 g (0.1 mol) of 1-amino-2-propanol (**8**) in 20 mL of water and 20 mL of glacial acetic acid was cooled to 0 °C. A partial solution of 11 mL (0.15 mol) of propionaldehyde and 20 mL of water was added dropwise. To the cold reaction mixture was added 14 g (0.2 mol) of sodium nitrite in small lots over a period of 30 min. The mixture was stirred at 0 °C overnight and then neutralized by the slow addition of potassium hydroxide pellets. The product was extracted into methylene chloride and washed with 5% HCl and 5% sodium bicarbonate. The solution was dried over anhydrous sodium sulfate and filtered through a layer of anhydrous magnesium sulfate, and the solvent was removed on a rotary evaporator. The crude product was vacuum distilled to give 8 g (56%) of **9a** and **9b** in a 1.2:1 ratio: bp 44–45 °C (0.25 mmHg); IR (film) 2975, 2955, 2880, 1455, 1425, 1390, 1310, 1265, 1120 cm^{-1}; UV (EtOH) λ_{max} 342 (ϵ 83).

Anal. Calcd for $C_6H_{12}N_2O_2$: C, 49.98; H, 8.39; N, 19.43. Found: C, 50.20; H, 8.65; N, 19.16.

Separation of **9a** and **9b** was accomplished on silica gel (activity III) eluted with 9:1 hexane–THF: NMR ($CDCl_3$) for **9a** with only the *E* rotamer present δ 1.04 (t, 3 H), 1.42 (d, 3 H), 2.21 (m, 2 H), 3.0 (q, 1 H, α-H at C-4), 3.97 (m, 1 H, α-H at C-4), 4.40 (m, 1 H), 5.48 (t, 1 H); mass spectrum, *m/z* (relative intensity) 144 (7), 115 (46), 84 (26), 59 (19), 41 (60), 30 (100); NMR ($CDCl_3$) for **9b** with only the *E* rotamer present δ 1.06 (t, 3 H), 1.34 (d, 3 H), 2.21 (m, 2 H), 3.56 (q, 1 H, α-H at C-4), 3.78 (q, 1 H, α-H at C-4), 4.44 (q, 1 H), 5.79 (t, 1 H); mass spectrum, *m/z* (relative intensity) 144 (16), 115 (92), 84 (62), 59 (68), 41 (35), 30 (100).

H–D Exchange of 9a,b. This reaction was carried out as described previously for compound **4**. The 1.2:1 isomer ratio remained constant. The NMR spectrum gave signals at δ 5.79 and 5.48, indicating that the methine protons at C-2 had not exchanged. The signals corresponding to the α-protons in both isomers were no longer present: NMR ($CDCl_3$) δ 1.04 (t, 1.65 H), 1.06 (t, 1.35 H), 1.42 (d, 1.65 H), 1.34 (d, 1.35 H), 2.0–2.4 (m, 2

H), 4.16 (q, 0.55 H), 4.30 (q, 0.45 H), 5.48 (q, 0.55 H), 5.79 (q, 0.45 H); mass spectrum, m/z (relative intensity) 146 (2), 117 (13), 84 (60), 66 (100), 59 (23), 43 (22).

N-Nitroso-2,2,5-trimethyl-1,3-oxazolidine (10). To a solution of 7.5 g (0.1 mol) of 1-amino-2-propanol (8) in 20 mL of water and 20 mL of glacial acetic acid was added 11 mL of acetone. The solution was cooled to 0 °C and 14 g (0.2 mol) of sodium nitrite in 25 mL of water was added dropwise. The solution was stirred at 0 °C overnight, made basic by the addition of potassium hydroxide pellets, and extracted with methylene chloride. The organic layer was washed with 5% hydrochloric acid and 5% sodium bicarbonate and dried over anhydrous sodium sulfate, and the solvent was removed on a rotary evaporator. The residual oil was vacuum distilled to give 1.6 g (11%) of **10**, which was contaminated with **9a** and **9b**: bp 64 °C (0.2 mmHg); IR (film) 2980, 2930, 1455, 1425, 1380, 1300, 1175, 1065, 985 cm^{-1}; NMR ($CDCl_3$) δ 1.4 (d, 3 H), 1.69 (s, 3 H), 1.84 (s, 3 H), 3.11 (m, 1 H), 4.06 (m, 1 H), 4.40 (m, 1 H), signals corresponding to **9a** and **9b** contaminants are not included here. The GLC retention time of compound **10** corresponds to that of the minor component obtained in the deamination reaction of 1-amino-2-propanol (8).

Deamination of 2-Amino-1-propanol (12). To a 0.5 M solution of 447 mg (4 mmol) of 2-amino-1-propanol hydrochloride in water was added enough 10% HCl to increase the acidity to pH 4. To the solution was added 3.3 mL of 3.6 M aqueous sodium nitrite. The mixture was stirred at 25° C for 2 h. The solution was extracted with methylene chloride, washed with 5% sodium bicarbonate, and dried over anhydrous sodium sulfate, and the solvent evaporated under vacuum. The residue was vacuum distilled to give an average yield of 96 mg (16%) of (*E*)- and (*Z*)-*N*-nitroso-2-ethyl-4-methyl-1,3-oxazolidines (**13a,b**) in a 2.8:1 ratio: bp 98 °C (2 mmHg); UV (EtOH) λ_{max} 361 (ϵ 80); mass spectrum, m/z (relative intensity) 144 (5), 115 (16), 98 (19), 84 (54), 70 (30), 59 (100), 43 (28), 30 (21); NMR ($CDCl_3$) δ 0.99 (t, 0.8 H), δ 1.06 (t, 2.2 H, CH_3, *E* rotamer), 1.59 (d, 0.8 H, CH_3, *Z* rotamer), 2.0–2.42 (m, 2 H), 3.8–4.1 (m, 2 H), 4.46 (sextet, 0.74 H), 4.84 (sextet, 0.26 H), 5.28 (q, 0.26 H, OCHN, *Z* rotamer), 5.54 (t, 0.74 H, *E* rotamer).

Anal. Calcd for $C_6H_{12}N_2O_2$: C, 49.98; H, 8.39; N, 19.43. Found: C, 49.94; H, 8.49; N, 19.64.

Deamination of 1-Aminopropanol (14). After a 0.5 M aqueous solution of 500 mg (6.67 mmol) of 1-amino-2-propanol (**14**) had been adjusted to pH 5 by the addition of 0.6 mL (10 mmol) of glacial acetic acid, 5.6 mL (20 mmol) of 3.6 M aqueous sodium nitrite was added, and the mixture was stirred at 25 °C for 2 h. The reaction mixture was made basic by the addition of sodium carbonate and then extracted with methylene chloride. The solution was washed with 5% hydrochloric acid and dried over anhydrous potassium carbonate. Evaporation of the solvent gave 120 mg of a yellow oil. GLC analysis indicated that two compounds were present in a 24:1 ratio. The major component was *N*-nitroso-2-ethyl-1,3-tetrahydrooxazine (**16**, 12% yield), and the minor one was *N*-nitroso-1,3-tetrahydrooxazine (**15**, 0.6% yield). The two products were identical with authentic samples of **15** and **16**.

Preparation of an Authentic Sample of N-Nitroso-2-ethyl-1,3-tetrahydrooxazine (16). This compound was prepared as described by Eiter et al.[5] in 90% yield: bp 56 °C (0.4 mmHg) [lit.[5] bp 70 °C (0.3 mmHg)]; UV (EtOH) λ_{max} 364 (ϵ 86); IR (film) 2970, 2940, 2870, 1460, 1435, 1400, 1356, 1330, 1205, 1050 cm^{-1}; NMR ($CDCl_3$) δ 1.07 (t, 3 H), 1.72 (m, 2 H), 2.21 (m, 2 H, CH_2CH_3), 3.26 (m, 1 H, syn α axial at C-4), 4.54 (m, 1 H, syn α equatorial at C-4), 3.68–δ 4.24 (m, 2 H, OCH_2), 5.23 (t, 0.9 H, anti equatorial at C-2), 5,86 (t, 0.1 H, syn equatorial); mass spectrum, m/z (relative intensity) 144 (12), 115 (56), 85 (34), 84 (20), 71 (97), 59 (43), 57 (75), 56 (40), 42 (100), 30 (36).

***N*-Nitroso-2-ethyl-1,3-tetrahydrooxazine-*4,4*-d_2 (17).** H–D exchange of **16** was carried out as described previously: NMR ($CDCl_3$) δ 1.08 (t, 3 H), 1.70 (m, 2 H), 2.23 (m, 2 H), 3.7–4.41 (m, 2 H, OCH_2), 5.24 (t, 0.9 H, anti), 5.87 (t, 0.1 H, syn); mass spectrum, m/z (relative intensity) 146 (17), 117 (79), 88 (21), 87 (43), 73 (100), 59 (55), 57 (70), 44 (91), 30 (45).

***N*-Nitroso-1,3-tetrahydrooxazine (15).** This compound was prepared as described by Eiter et al.:[5] NMR ($CDCl_3$) δ 1.72 (sextet, 2 H), 3.96 (m, 2.7 H, α-CH_2 syn at C-4 and CH_2 (C-6)), 4.44 (t, 0.3 H, anti α-CH_2 (C-4)), 5.08 (s, 0.3 H, syn), 5.42 (s, 1.7 H).

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Heterogeneous Catalysis in Organic Chemistry: Effect of Hydrogen Presaturation of the Catalyst in the Hydrogenation of Olefins

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A "time-lapse" procedure has been used to investigate the first few turnovers occurring in the hydrogenation of a double bond. Initial exposure of a platinum catalyst to either hydrogen or an olefin made no difference in the outcome of the reaction but initial treatment of a palladium catalyst with an olefin resulted in a change in its reaction characteristics. Presaturation of either the platinum or palladium catalysts with hydrogen results in the storage of a relatively large amount of hydrogen in the support by the process of spillover. By reverse spillover this hydrogen can migrate to the active sites on the catalyst and, thus, be available for reaction in the event that the site does not acquire hydrogen from the reaction medium rapidly enough.

The most common synthetic application of heterogeneous catalysis is in the hydrogenation of organic functional groups. For the most part, though, the conditions under which these hydrogenations are run are not based on any real understanding of the processes taking place on the catalyst surface. Instead, they are the result of empirical trial and error studies, or, more frequently, of conditions reportedly successful for similar reactions, or

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