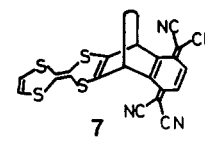
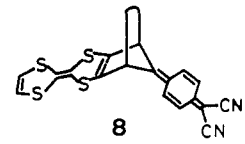
and of the magnetic circular dichroism (MCD) measurements.[19]

Perspective

Powerful donor and acceptor components incorporated in a rigid framework are expected to lead to unprecedented electronic systems with interesting properties. For the forbidden CTI, the ground-state wave function, Ψ_G, is approximated to be the ground-state configuration, Φ (DA), of the closed-shell structure or the electron-transferred configuration, Φ ($D^+ A^-$), of the open-shell structure. In the former closed-shell structure, i.e., $\Psi_G \simeq \Phi$ (DA), almost one electron transfers in the first excited state, i.e., $\Psi_E \simeq \Phi$ ($D^+ A^-$). Interesting photochemical behavior is expected from the distinct charge separation. In the latter open-shell structure, strong donor–acceptor pairs may give rise to *intra*molecular radical ion pairs in the ground states. Such electronic situations can be seen in the hypothetical molecule **7** which belongs to mode 6. On the other hand,



7



8

the unknown molecule **8** is also of interest. In contrast to **7**, CTI is allowed in **8** which belongs to mode 5. Therefore, the molecule is expected to contain a considerable contribution of the ionic structure in the closed-shell ground state in spite of a diminished amount of the orbital overlap between the components. It would obviously be of great interest to see if these predictions are realized experimentally.

Registry No. 1·BF_4^-, 63166-75-6; 2·BF_4^-, 76466-39-2; 3·BF_4^-, 73101-19-6; **4a**, 73524-84-2; **4b**, 73524-85-3; **4c**, 77493-09-5; **4d**, 77478-11-6; **4e**, 77478-12-7.

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Lithiation of α-Nitrosaminoalkyl Ethers. Synthetic Equivalents of α-Primary Amino Carbanions[1]

Joseph E. Saavedra

Basic Research Program-LBI,† Chemical Carcinogenesis Program, National Cancer Institute, Frederick Cancer Research Facility, Frederick, Maryland 21701

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Successful experiments directed toward the C-1 alkylation and hydroxyalkylation of primary amines are reported. Primary amines are converted into their *N*-nitroso-*N*-(1-methoxyethyl) derivatives, which are subsequently lithiated and condensed with various electrophiles, denitrosated, and hydrolyzed to produce the desired compounds in good to excellent yields.

Metalation of nitrosamines is a well-established method of considerable synthetic value for preparing masked α-secondary amino carbanions.[2] The metalated nitrosamine can undergo reaction with a great variety of electrophiles at the α-carbon, and the secondary amine can be regenerated by using standard procedures.[2,3]

On the other hand, umpolung reactivity for primary amines is a more complicated process. The best known method involves preparation of the corresponding isocyanide. This derivative is lithiated to react with electrophiles, followed by hydrolytic demasking to the primary amine.[4] Another method, with more limited applicability, requires oxidation of the amine to the nitro group[5] as the initial step.

One pathway by which the reactivity of a primary amine could be reversed is to convert it to a chemical specie similar to a secondary amine which can then be nitrosated. The nitrosamine would then undergo electrophilic attack at the α-carbon, and, finally, a demasking step would regenerate the primary amine (Scheme I). α-Nitrosaminoalkyl ethers are the type of compound meeting the characteristics described above. These compounds, as well as the α-acetoxy analogues, have been widely used as model

Scheme I

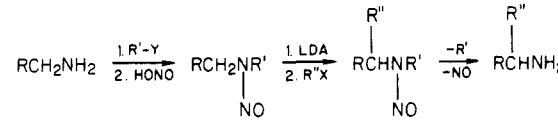

Table I. Reaction of Lithio-α-nitrosaminoalkyl Ethers with Electrophiles

nitrosamine	electrophile	product (yield, %)	primary amine (yield, %)
1	MeI	3 (80%)	$EtNH_2$·HCl (80%)
3	MeI	4 (52%)	$(Me)_2CHNH_2$·HCl (84%)
1	MeCHO	5a,b (77%)	$MeCHOHCH_2NH_2$·HCl (92%)
1	$(Me)_2CO$	6 (78%)	$(Me)_2COHCH_2NH_2$·HCl (90%)
1	BzBr	7 (86%)	$Ph(CH_2)_2NH_2$ (56%)
1	EtI	8 (55%)	$Me(CH_2)_2NH_2$·HCl (93%)
1	*n*-PrI	9 (43%)	$Me(CH_2)_3NH_2$·HCl (87%)

†Research sponsored by the National Cancer Institute, DHHS, under contract No. NO1-CO-23909 with Litton Bionetics, Inc. The contents of this publication do not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commerical products, or organizations imply endorsement by the U.S. Government.

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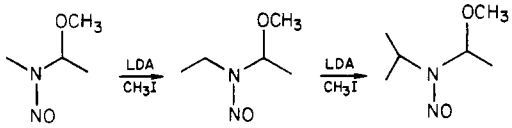
0022-3263/83/1948-2388$01.50/0

compounds in studies of nitrosamine metabolism and carcinogenesis,[6] and methods for their preparation are well established.[6,7] Lithiation occurs at the carbon α to the nitroso group on the opposite side of the ether linkage. After reaction with the electrophile has taken place, regeneration of the primary amine may be accomplished through a hydrolytic or reductive cleavage.

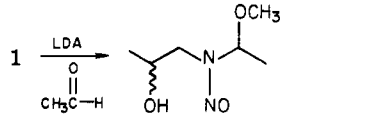
Results and Discussion

Methylamine was condensed with acetaldehyde and methanol in the presence of nitrous acid, giving *N*-nitroso-*N*-methyl-1-methoxyethylamine (**1**). This compound was also prepared in high yield upon acid-catalyzed addition of methanol to *N*-nitroso-*N*-methylvinylamine (**2**)[7a]. Metalation of **1** with lithium diisopropylamide in tetrahydrofuran at −80 °C, followed by electrophilic addition of methyl iodide gave *N*-nitroso-*N*-ethyl-1-methoxyethylamine (**3**) in 80% yield (eq 1). Methylation of



1 **3** **4** (1)

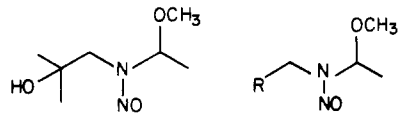
the lithio derivative of **3** gave *N*-nitroso-*N*-isopropyl-1-methoxyethylamine (**4**) in 52% yield. Additional examples of this type of reaction are included in Table I. The hydroxyalkylation of **1** with acetaldehyde as the electrophile is worth mentioning. A new asymmetric center is introduced at the β-carbon, giving a 0.98:1 mixture of the two diastereomers **5a** (less polar) and **5b** (more polar) (eq 2). These isomers are separable on silica gel and have



(2)

5a,b

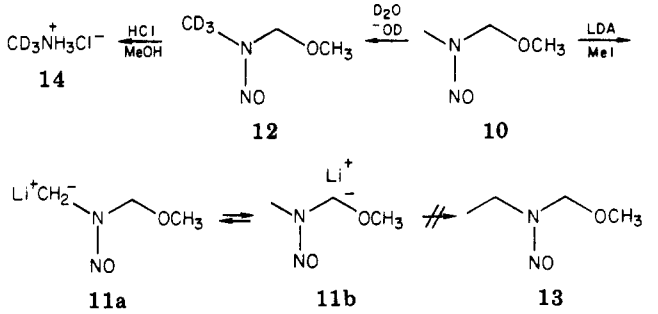
identical mass and infrared spectra, but each has a distinct NMR pattern (see Experimental Section).



6

7, R = $PhCH_2$
8, R = C_2H_5
9, R = n-C_3H_7

Scheme II



Our studies demonstrate that α-nitrosaminoalkyl ethers undergo electrophilic addition at the α-position, giving fair to excellent yields of product provided that a substituent on the ether-bearing carbon is present. Originally, *N*-nitroso-*N*-methylmethoxymethylamine (**10**) had been chosen for this investigation. This compound was prepared from methylamine, formaldehyde, and methanol in the presence of nitrous acid.[7b] The acidity of the α-hydrogens was demonstrated by the reaction of **10** with sodium deuterioxide in D_2O at 90 °C for 1 h. Complete H–D exchange occurred at the *N*-methyl group to form *N*-nitroso-*N*-methyl-d_3-methoxymethylamine (**12**) in 64% yield. This type of deuterium exchange has been reported for *N*-nitrosooxazolidines and *N*-nitrosoetrahydro-1,3-oxazines[8] which are cyclic analogues of α-nitrosaminoalkyl ethers. Metalation of **10** with lithium diisopropylamide in tetrahydrofuran at −80 °C followed by addition of iodomethane gave none of the expected *N*-nitroso-*N*-ethylmethoxymethylamine (**13**), and, furthermore, only traces of starting material were recovered. An equilibrium mixture of two lithionitrosamines, **11a,b**, may be formed followed by rapid decomposition of the unstable anion α to the ether function[9] **11b** (Scheme II).

The NMR spectrum of **1** at 25 °C disclosed that the orientation of the nitroso group was anti (*E*) to the side of the molecule bearing the methoxy group. One would, therefore, expect anion formation to take place preferentially at the α-alkyl group where a dipole-stabilized system[10,11] can occur. Proton removal on the other side of the nitrogen is a less favorable process, not only because of a reduced stability inherent to the anti anion system[12] but also because of the tertiary nature of the site and the destabilizing effect caused by the ether linkage.[9] On the basis of the NMR spectrum the unsubstituted analogue **10** also appears to exist only as the *E* rotamer at ambient temperature. However, the syn lithio anion **11a** is not formed to the exclusion of the less favored **11b**. This denotes that a substituent α to the ether oxygen is essential if clean alkylations on the opposite α-carbon are to be carried out. The next step is to investigate the regeneration of the primary amine, thus completing the cycle of reversible umpolung. Denitrosation under hydrolytic conditions[2a,3a] proved to be an effective method for converting *N*-nitroso-*N*-methylmethoxymethylamine (**10**) and its congeners to the corresponding primary amine salts. When refluxed in methanolic HCl, compounds **10** and

(2) (a) Seebach, D.; Enders, D. *Angew Chem., Int. Ed. Engl.* **1975**, *14*, 15. (b) Seebach, D.; Enders, D.; Renger, B. *Chem. Ber.* **1977**, *110*, 1852. (c) Renger, B.; Seebach, D. *Ibid.* **1977**, *110*, 2334. (d) Renger, B.; Kalinowski, H.-O.; Seebach, D. *Ibid.* **1977**, *110*, 1866. (e) Wykypiel, W.; Seebach, D. *Tetrahedron Lett.* **1980**, *21*, 1927. (f) For a review on methods of reactivity umpolung see: Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.

(3) (a) Fraser, R. R.; Passannanti, S. *Synthesis* **1976**, 540. (b) Seebach, D.; Wykipiel, W. *Ibid.* **1979**, 423.

(4) Schollkopf, U. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.

(5) Kornblum, N. *Org. React.* **1962**, *12*, 101.

(6) (a) Weissler, M. "N-Nitrosamines"; Anselme, Jean-Pierre, Ed.; American Chemical Society: Washington, DC, 1979; ACS Symp. Ser. No. 101, Chapter 4 and references therein. (b) Saavedra, J. E. *J. Org. Chem.* **1979**, *44*, 4511. (c) Okada, M.; Mochizuki, M.; Anjo, T.; Sone, T.; Wakabayshi, Y.; Suzuki, E. "N-Nitroso-Compounds: Analysis, Formation and Occurrence"; IARC Scientific Publications: Lyon, France, 1980; No. 31, p 71.

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(8) Saavedra, J. E. *J. Org. Chem.* **1981**, *46*, 2610.

(9) Bordwell, F. G.; VanDerPuy, M.; Vanier, N. R. *J. Org. Chem.* **1976**, *41*, 1885.

(10) Beak, P.; Reitz, D. B. *Chem. Rev.* **1978**, *78*, 275.

(11) (a) Lyle, R. E.; Saavedra, J. E.; Lyle, G. G.; Fribush, H. M.; Marshall, J. L.; Lijinsky, W. *Tetrahedron Lett.* **1976**, 4431. (b) Fraser, R. R.; Dhawan, K. L. *J. Chem. Soc., Chem. Commun.* **1976**, 674. (c) Fraser, R. R.; Ng, L. K. *J. Am. Chem. Soc.* **1976**, *98*, 5895.

(12) Houk, K. N.; Strozier, R. W.; Rondan, N. G.; Fraser, R. R.; Chavagui-Offermanns, N. *J. Am. Chem. Soc.* **1980**, *102*, 1427.

N-nitroso-*N*-ethylmethoxymethylamine (**13**) gave methyl- and ethylamine hydrochloride, respectively, in nearly quantitative yields (eq 3 and 4). Compound **10**, although

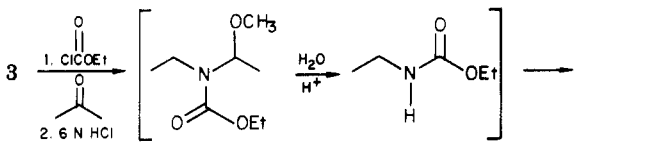
$$10 \xrightarrow[\substack{\text{MeOH}\\(97\%)}]{\text{HCl}} CH_3NH_3^+Cl^- \xleftarrow[(5\%)]{} 1 \qquad (3)$$

$$13 \xrightarrow[(99\%)]{} CH_3CH_2NH_3^+Cl^- \xleftarrow[(7\%)]{} 3 \qquad (4)$$

not useful as a synthetic equivalent of a primary amino carbanion, can be used to prepare methyl-d_3-amine hydrochloride (**14**) via acid hydrolysis of *N*-nitroso-*N*-methyl-d_3-methoxymethylamine (**12**), as shown in Scheme II. When this method for demasking was applied to the compounds substituted on the ether-bearing carbon, extremely low yields of the primary amine salts were obtained. Methylamine hydrochloride was isolated in 5% yield from **1**, and ethylamine hydrochloride was obtained in 7% yield from **3**.

Hydrogenolysis of **1** and **3** on an aluminum–nickel catalyst[3b] by utilizing the method of Lunn et al.[13] was investigated. The α-nitrosaminoalkyl ether **1** was converted within 30 min to methylethylamine in 89% yield, and the ethyl analogue **3** gave diethylamine in 86% yield; however, neither compound gave significant amounts of the primary amines.

It had been documented by Eiter et al.[14] that *N*-nitroso-1,3-oxazolidines and *N*-nitrosotetrahydro-1,3-oxazines react with halogen compounds such as phosgene, ethyl chloroformate, etc. under anhydrous conditions to give N-substituted 1,3-oxazolidines or *N*-substituted tetrahydro-1,3-oxazines and nitrosyl chloride. a modification of the above reaction was our preferred method for the regeneration of primary amines from the corresponding α-nitrosaminoalkyl ether substituted on the ether-bearing carbon. The demasking step involved the reaction of the α-nitrosaminoalkyl ether, i.e., **3**, with ethyl chloroformate in refluxing acetone under nonanhydrous conditions to give *N*-ethylurethane (eq 5). The acetone was removed, and,



$CH_3CH_2\overset{+}{N}H_3Cl^-$ (5)

without further purification, the carbamate was hydrolyzed to ethylamine hydrochloride in 80% yield from **3**. The yields of the primary amines or their corresponding hydrochloride salts obtained by this method are listed in Table I.

Conclusions

A method for umpolung reactivity of primary amines has been developed. Primary amines can be readily converted to α-nitrosaminoalkyl ethers, nitroso compounds which possess several interesting features. Protons α to the nitroso group on the opposite side of the ether linkage are acidic, making this site reactive toward electrophiles. Since the N–C–O linkage on the other side of the molecule is, effectively, a masked carbonyl group, it is possible to regenerate the primary amine.

Warning! Most N-nitroso compounds produce cancer in experimental animals and should be handled with due caution.

Experimental Section

Proton magnetic resonance spectra were measured on a Varian XL-100 or a Perkin-Elmer R-12B spectrometer with $CDCl_3$ or D_2O as the solvent. The IR spectra were obtained on a Perkin-Elmer 467 spectrometer. Low-resolution mass spectra were taken on a Finnigan 330 mass spectrometer equipped with a Finnigan 6000 MS data system. High-resolution spectra were obtained from a VG Micromass ZAB-2F mass spectrometer equipped with a VG 2000 data system. 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-FFF-1BP-coated GasChrom Q glass column and a 2.5-m, 10% Carbowax 20M + 2% KOH on 80/100 Chromosorb W glass column (Applied Science Division) were used. Melting points were determined on an Electrothermal capillary melting point apparatus and were not corrected. The starting materials 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.

***N*-Nitroso-*N*-methyl-1-methoxyethylamine (1).** To 80 mL (1.04 mol) of methylamine (40% aqueous solution) were added 250 mL of water and 200 mL of methanol. The solution was cooled to 0 °C and made acidic to pH 5 by the addition of 200 mL of glacial acetic acid. To the resulting solution was added dropwise 44 g (1 mol) of acetaldehyde. Solid sodium nitrite (138 g, 2 mol) was added in small lots, and the reaction temperature not allowed to go above 5 °C. The reaction mixture was stirred overnight at 4 °C. The cold solution was neutralized with potassium carbonate and extracted with methylene chloride. The organic layer was washed with water, dried over anhydrous sodium sulfate, and filtered through anhydrous magnesium sulfate. The solvent was removed on a rotary evaporator and the residue vacuum distilled to give 38.9 g (33%) of *N*-nitroso-*N*-methyl-1-methoxyethylamine (**1**): bp 45 °C (0.3 mmHg); NMR ($CDCl_3$) δ 1.56 (d, 3 H), 2.96 (s, 3 H), 3.26 (s, 3 H), 5.84 (q, 1 H); only the rotamer where the nitroso function was syn (*Z*) to the *N*-methyl group was present; IR (film) 2990, 2940, 1470, 1450, 1360, 1020 cm^{-1}; MS, *m/z* (relative intensity) 118 (M^+, 17.7), 89 (5), 87 (28), 60 (4), 59 (100), 58 (11.4), 57 (18.6), 56 (20), 45 (5), 43 (8), 42 (17); exact mass (M^+) 118.0752, required for $C_4H_{10}N_2O_2$ (M^+) 118.072.

***N*-Nitroso-*N*-ethyl-1-methoxyethylamine (3).** A solution of 1.65 mL (11.7 mmol) of diisopropylamine in 12 mL of anhydrous THF was cooled to 0 °C under nitrogen. A 1.5 M hexane solution of *n*-butyllithium (7.8 mL, 11.7 mmol) was added and stirred for 5 min. The resulting lithium diisopropylamide (LDA) solution was cooled to −80 °C. A 1 M solution of 1.15 g (9.7 mmol) of *N*-nitroso-*N*-methyl-1-methoxy-ethylamine (**1**) in THF was injected into the LDA solution and the lithio anion allowed to form in 5 min. Methyl iodide (1.25 mL, 20 mmol) was added and the reaction mixture stirred at −80 °C under nitrogen for 30 min. The reaction was quenched with 0.5 mL of methanol and the mixture warmed to room temperature. The solvent was evaporated, and the residual paste was extracted with methylene chloride and washed with a saturated ammonium chloride solution. The organic layer 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 residue was vacuum distilled to give 1.02 g (80%) of *N*-nitroso-*N*-ethyl-1-methoxyethylamine (**3**): bp 49–50 °C (2.5 mmHg); NMR ($CDCl_3$) δ 1.11 (t, 3 H), 1.58 (d, 3 H), 3.24 (s, 3 H), 3.52 (q, 2 H), 5.80 (q, 1 H); IR (film), 2995, 2945, 2840, 1472, 1385, 1370, 1210, 1100, 1065, 1035, 870, 820, 685 cm^{-1}; MS, *m/z* (relative intensity) 132 (M^+, 1), 101 (6), 100 (3), 85 (3), 72 (3.4), 71 (11.4), 70 (7.8), 59 (100), 58 (11.4), 57 (10), 56 (45); exact mass (M^+) 132.0906, required for $C_5H_{12}N_2O_2$ (M^+) 132.088.

Demasking of 3 to Ethylamine Hydrochloride. A solution of 1 g (7.6 mol) of N-nitroso-*N*-ethyl-1-methoxyethylamine (**3**) in 10 mL of nonanhydrous acetone was refluxed for 1 h with 0.8 mL (10 mmol) of ethyl chloroformate. The progress of the reaction

(13) Lunn, G.; Sansone, E. B.; Keefer, L. K. *Food Cosmet. Toxicol.* **1981**, *19*, 493.
(14) Hebenbrock, K.-F.; Eiter, K. *Justus Liebigs Ann. Chem.* **1972**, *765*, 78.

was followed by GLC for the appearance of *N*-ethylurethane. The reaction mixture was cooled to room temperature and the acetone removed under a stream of nitrogen. The residue was taken up in 10 mL of 6 N HCl and refluxed for 2 h. The solution was cooled to 0 °C, made basic by addition of aqueous sodium hydroxide, and distilled into a receiver containing 5 mL of 12 N hydrochloric acid at 0 °C. The distillate was evaporated on a rotary evaporator, and the last traces of moisture were removed under high vacuum to give (499 mg (80%) of ethylamine hydrochloride: mp 106 °C (lit[15] mp 110 °C); benzamide, mp 70–71 °C (lit.[16] mp 71 °C).

Preparation and Demasking of *N*-Nitroso-*N*-isopropyl-1-methoxyethylamine (4). A solution of lithium diisopropylamide in 15 mL of THF was prepared from 0.995 mL (7 mmol) of diisopropylamine and 4.7 mL of 1.5 M *n*-butyllithium as described above. A 1 M solution of 620 mg (4.7 mmol) of **3** in THF was added to the LDA solution at −80 °C and stirred under nitrogen for 5 min. Methyl iodide (0.935 mL, 10 mmol) was added and the mixture stirred at −80 °C for 30 min. The reaction mixture was worked up as described above and vacuum distilled to give 357 mg (52%) of **4**: bp 50–52 °C (2 mmHg); NMR ($CDCl_3$) δ 1.26 (d, 1.1 H), 1.50 (d, 1.9 H), 1.32 (d, 3.8 H), 1.62 (d, 2.2 H), 3.19 (s, 1.1 H), 3.32 (d, 1.9 H), 4.16 (m, 1 H), 5.74 (q, 0.6 H), 6.06 (q, 0.4 H), the NMR spectra indicated a mixture of 62% *E* rotamer (N=O is anti to the methoxy group) and 38% *Z* rotamer; IR (film) 2965, 2880, 1470, 1384, 1366, 1248, 1100, 1040, 870 cm^{-1}; MS, *m/z* (relative intensity) 146 (M^+, 6.1), 116 (1.7), 115 (24.3), 113 (94), 111 (38), 110 (3.9), 96 (100), 87 (33), 86 (25.6), 85 (55), 81 (62); exact mass (M^+) 146.1053, required for $C_6H_{14}N_2O_4$ (M^+) 146.103.

A solution of 126 mg (0.86 mmol) of **4** in acetone was treated with ethyl chloroformate followed by acid hydrolysis as described above to give 69 mg (84%) of isopropylamine hydrochloride: mp 154 °C (lit.[17a] mp 153–155 °C); NMR (D_2O) δ 1.28 (d, 6 H), 3.50 (m, 1 H).

***N*-Nitroso-*N*-(2-hydroxypropyl)-1-methoxyethylamine (5a,b).** The lithio anion of **1** (3.21 g, 0.027 mol) in 27 mL of THF was prepared as described above. To this solution at −80 °C was added 2.8 mL (0.05 mol) of acetaldehyde, and the mixture was stirred under nitrogen for 15 min and worked up as described above. The residual oil was vacuum distilled to give 3.36 g (77%) of the diastereomeric mixture **5a,b**, bp 98 °C (0.5 mmHg). GLC analysis of the mixture on an 8% HI-EFF-1BP column at 120 °C gave a 0.98:1 ratio of **5a/5b**. The mixture was separated preparatively on silical gel, eluted with methylene chloride and 7.1 methylene chloride/acetone. The less polar isomer **5a** exhibited the following spectral properties: IR (film) 3445, 2980, 2940, 2840, 1465, 1386, 1365, 1250, 1100, 1060, 1305 cm^{-1}; NMR ($CDCl_3$) δ 1.20 (d, 3 H), 1.64 (d, 3 H), 3.35 (s, 3 H), 3.95–4.06 (m, 3 H), 3.85 (s, 1 H), 5.87 (q, 1 H); MS, *m/z* (relative intensity) 131 (M^+ − 31, 1), 100 (3.1), 86 (2.1), 60 (3.7), 59 (100), 57 (6.4), 56 (36.7). The more polar disastereomer **5b** gave practically identical signals in the infrared and mass spectrometers: NMR ($CDCl_3$) δ 1.15 (d, 3 H), 1.62 (d, 3 H), 2.86 (s, 1 H), 3.31 (s, 3 H), 3.45–4.15 (m, 3 H), 5.82 (q, 1 H).

Anal. (for **5ab** as a mixture) Calcd for $C_6H_{14}N_2O_3$: C, 44.43; H, 8.70, N, 17.27. Found: C, 44.52; H, 8.66; N, 17.31.

A solution of 214 mg (1.32 mmol) of **5a,b** in 10 mL of acetone was added to 0.312 mL (4 mmol) of ethyl chloroformate and refluxed for 1 h followed by acid hydrolysis as described above to give 135 mg (92%) of 1-amino-2-propanol hydrochloride: mp. 69–70 °C (lit.[17b] mp 72.5–74 °C); NMR (D_2O) δ 1.24 (d, 3 H), 3.05 (m, 2 H), 4.0 (m, 1 H).

***N*-Nitroso-*N*-(2-hydroxy-2-methylpropyl)-1-methoxyethylamine (6).** The anion of **1** (1.054 g, 0.0089 mol) in 9 mL of THF was formed with LDA at −80 °C as described above. To this solution was added 1.41 mL (10 mmol) of anhydrous acetone, and the mixture was stirred at −80 °C under nitrogen for 1 min and worked up as described above. The crude product was vacuum distilled to give 1.22 g (78%) of **6**: bp 68 °C (0.15 mmHg); IR (film) 3440, 2970, 2935, 1460, 1380, 1360, 1210, 1135, 1005 cm^{-1}; ($CDCl_3$) δ 1.00 (2, 3 H) and 1.22 (s, 3 H), corresponding to the geminal dimethyls, 1.64 (d, 3 H), 3.40 (s, 3 H), 5.86 (q, 1 H), 3.68 (br, 1 H); due to the hindered rotation of the geminal dimethyls exerted by the nitroso group interaction, the α-methylene appeared as an AX system, 3.10 (d, 1 H, *J* = 14.4 Hz), 4.28 (d, 1 H, *J* = 14.4 Hz); MS, *m/z* (relative intensity) 176 (M^+, 0.06), 145 (M^+ − 31, 2.3), 114 (2.5), 100 (2.8), 73 (6), 59 (100), 57 (12.2), 56 (32.6), 43 (15.1). Anal. Calcd for $C_7H_{16}N_2O_3$: C, 47.71; H, 9.15; N, 15.90. Found: C, 47.93; H, 9.43; N, 16.14.

A solution of 221 mg (1.25 mmol) of **6** in 6 mL of acetone was converted to 2-(aminomethyl)-2-propanol hydrochloride in 90% yield by using the ethyl chloroformate method described above: mp 54–56 °C; NMR (D_2O) δ 1.35 (s, 6 H), 2.66 (s, 2 H).

***N*-Nitroso-*N*-(phenylethyl)-1-methoxyethylamine (7).** To the lithio anion of **1** in 30 mL of THF at −80 °C was added 2.34 mL (23 mol) of benzyl bromide. After 30 min at −80 °C the reaction mixture was quenched and worked up as described above to yield 3.12 g of a crude product mixture. The mixture was purified on dry-packed silica gel, eluted with 9:1 hexane/acetone, to give 2.7 g (86%) of **7**: IR (film) 3040, 2945, 1606, 1470, 1455, 1360, 1255, 1100, 1060, 855, 700 cm^{-1}; NMR ($CDCl_3$), only the *E* rotamer is observed, δ 1,56 (d, 3 H), 2.84 (m, 2 H), 3.24 (s, 3 H), 3.64 (m, 2 H), 5.84 (q, 1 H), 7.29 (s, 5 H); MS, *m/z* (relative intensity) 208 (M^+, 0.6), 178 (0.7), 177 (5), 149 (3.2), 146 (2.7), 132 (3.4), 105 (47.3), 104 (31.4), 91 (46.9), 77 (12), 65 (10), 60 (14), 59 (100), 56 (71.5), 51 (8.3); exact mass (M^+) 208.1199, required for $C_{11}H_{16}N_2O_2$ 208.119.

To a solution of 1.223 g (5.88 mmol) of **7** in 20 mL of acetone was added 0.625 mL (8 mmol) of ethyl chloroformate. The reaction was carried out as described above for demasking **3**. In this case, the free base and not the hydrochloride salt was isolated in 56% yield: bp 132–135 °C (130 mmHg) [lit.[18] 92–93 °C (19 mmHg)]; NMR ($CDCl_3$) δ 2.18 (s, 2 H), 2.56–3.07 (m, 4 H), 7.23 (s, 5 H); benzamide, mp 113–116 °C (lit.[16] mp 116 °C).

***N*-Nitroso-*N*-propyl-1-methoxyethylamine (8).** Ethyl iodide (1.36 mL 17 mmol) was added to 1.04 g (8.8 mmol) of the lithio anion of **1** at −80 °C and allowed to react for 1 h. It was worked up as described above. The crude **8** was contaminated with **1**. The contaminant was removed on dry-packed silica gel eluted with 10:1 petroleum ether/acetone, followed by vacuum distillation to give 707 mg (55%) of pure **8**: bp 54–55 °C (2.3 mmHg); IR (film) 2970, 2935, 1470, 1385, 1340, 1260, 1075, 1045, 880 cm^{-1}; NMR ($CDCl_3$) δ 0.85 (t, 3 H), 1.25–1.50 (m, 2 H), 1.55 (q, 2 H); MS, *m/z* (relative intensity) 146 (M^+, 0.4), 116 (2.7), 115 (4.3), 84 (2.5), 70 (6.3), 60 (4), 59 (100), 58 (3.7), 56 (19.9), 43 (27.7), 41 (14), 30 (17.6), 29 (17.2); exact mass (M^+) 146.1057, required for $C_6H_{14}N_2O_2$ (M^+) 146.103.

n-Propylamine hydrochloride was formed in 93% yield upon treatment of **8** with ethyl chloroformate, followed by acid hydrolysis as described above: NMR (D_2O) δ 1.0 (t, 3 H), 1.65 (p, 2 H), 3.02 (t, 2 H); benzamide, mp 82–83 °C (lit.[16] mp 84 °C).

***N*-Nitroso-*N*-butyl-1-methoxyethylamine (9).** The lithio anion of **1** (196 mg, 1.66 mmol) was added to 0.39 mL (4 mmol) of *n*-propyl iodide and stirred at −80 °C for 30 min. An additional 0.2 mL (2 mmol) of *n*-propyl iodide was then added and stirred for a further 30 min. The reaction mixture was worked up as described above. The crude product was chromatographed through dry-packed silica gel, eluted with 10:1 petroleum ether/acetone, to remove unreacted **1**. The product was vacuum distilled to give 114 mg (43%) of **9**: bp 48 °C (0.2 mmHg); IR (film), 2955, 2870, 1462, 1380, 1355, 1242, 1133, 1090, 1055, 1040, 845 cm^{-1}; NMR ($CDCl_3$), δ 0.90 (t, 3 H), 1.57 (d, 3 H), 3.25 (s, 3 H), 3.46 (t, 2 H), 5.80 (q, 1 H); MS, *m/z* (relative intensity) 160 (M^+, 0.4), 126 (4), 98 (1.6), 84 (9.3), 59 (100), 57 (7.5), 56 (10.6), 43 (70), 41 (11.5); exact mass (M^+) 160.1212, required for $C_7H_{16}N_2O_2$ (M^+) 160.119. A solution of **9** in 3 mL of acetone was refluxed with a slight excess of ethyl chloroformate followed by acid hydrolysis and worked up as described above to give 61 mg (87%) of *n*-butylamine hydrochloride, mp 192–195 °C (lit.[17c] mp 195 °C).

***N*-Nitroso-*N*-methyl-d_3-methoxymethylamine (12).** A partial solution of *N*-nitroso-*N*-methylmethoxymethylamine (**10**)[6b]

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(17) (a) "Dictionary of Organic Compounds"; 5th Ed.; Chapman and Hall: New York, 1982; Vol 5, p 4792. (b) *Ibid*, Vol. 1, p 322. (c) *Ibid.*, Vol. 1, p 918. (d) *Ibid.*, Vol. 4, p 2723. (e) *Ibid.*, Vol. 2, p 1799.
(18) Robinson, J. C., Jr.; Synder, H. R. "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. III, p 720.

in 50 mL of 1 N sodium deuteroxide in D_2O was heated at reflux for 1 h. The solution was cooled to 25 °C, extracted with methylene chloride, dried over anhydrous sodium sulfate, and filtered through a layer of anhydrous magnesium sulfate. The solvent was evaporated and the residue vacuum distilled to give 3.43 g (64%) of **12**: bp 37–38 °C (0.3 mmHg); NMR ($CDCl_3$) δ 3.34 (s, 3 H), 5.51 (s, 2 H); IR (film) 2940, 2825, 2240, 2190, 2110, 1454, 1386, 1345, 1235, 1090, 920, 822, 700 cm^{-1}; MS, *m/z* (relative intensity) 108 (M^+ + 1, 0.3), 107 (M^+ 3), 106 (0.5), 88 (2.1), 84 (19), 76 (8.6), 51 (17), 49 (50.6), 48 (7), 47 (12), 46 (39), 45 (100), 44 (28).

Methyl-d_3-amine Hydrochloride (14). A solution of 653 mg (6.1 mmol) of **12** in 12 mL of methanol at 0 °C was saturated with hydrogen chloride. The ice bath was removed, and the solution was refluxed for 2 h and then evaporated to dryness under vacuum. The residue was taken up in methanol, treated with charcoal, and filtered through Celite. Evaporation of the solvent followed by recrystallization of the residue from ethanol–acetone gave 381 mg (88%) of **14**, mp 215–220 °C. Further characterization was carried out on the *p*-toluenesulfonamide derivative: mp 74–75 °C; NMR ($CDCl_3$) δ 2.42 (s, 3 H), 4.45 (br, 1 H), 7.52 (q, 4 H); IR (solid film) 3280, 3061, 2980, 2340, 2080, 1930, 1820, 1598, 1495, 150, 1410, 1318, 1160 cm^{-1}.

Conversion of *N*-Nitroso-*N*-methylmethoxymethylamine (10) to Methylamine Hydrochloride. A solution of 615 mg (5.9 mmol) of **10** in 12 mL of methanol at 0 °C was saturated with hydrogen chloride. The solution was heated at reflux for 2 h and then evaporated to dryness on a rotary evaporator. The residue was taken up in 20% aqueous sodium hydroxide and the resulting solution distilled into a receiver containing 1 mL of 12 N hydrochloric acid. Evaporation of the solvent under vacuum gave 397 mg (97%) of methylamine hydrochloride, mp 225–227 °C (lit.[17d] 227–228 °C).

Conversion of *N*-Nitroso-*N*-ethylmethoxymethylamine (13) to Ethylamine Hydrochloride. A methanolic solution of 441 mg (3.3 mmol) of **13** was treated with hydrogen chloride as described above to give 264 mg (98%) of ethylamine hydrochloride: benzamide, mp 68–70 °C (lit.[16] benzamide mp 71 °C).

Reduction of 1 with Aluminum–Nickel Alloy. Adapting the method of Lunn et al.[13] to this type of compound, a partial solution of 122 mg (1.03 mmol) of **1** in 10 mL of 0.5 N aqueous potassium hydroxide was treated with 500 mg of aluminum–nickel catalyst and stirred at 25 °C. Aliquots of 1 μL were analyzed by direct injection into a gas–liquid chromatograph fitted with a 10% Carbowax 20M + 2% KOH column at 50 °C and a flow rate of 20 mL/min. The starting nitrosamine had completely disappeared after 1 h at 25 °C. A known amount of 1-butanol was added as an internal standard for the quantification of the flame-ionization detector peaks. The GLC analysis indicated a 91% yield of methylethylamine. The aqueous solution was distilled and the amine trapped in a receiver containing 1 mL of hydrochloric acid, giving 87 mg (89%) of methylethylamine hydrochloride: NMR (D_2O) δ 1.28 (t, 3 H), 2.26 (d, 3 H), 3.09 (q, 2 H).

Reduction of 3 with Aluminum–Nickel Alloy. This reaction was carried out on 100 mg (0.76 mmol) of **3** as described above. GLC analysis gave a quantitative yield of diethylamine. The amine was isolated as the hydrochloride in 86% yield: mp 220–225 °C (lit.[17e] mp 223.5 °C); NMR (D_2O) δ 1.3 (t), 3.09 (q).

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Photostimulated Reactions of 2-Bromopyridine and 2-Chloroquinoline with Nitrile-Stabilized Carbanions and Certain Other Nucleophiles[1a]

Marcus P. Moon,[1b] Andrew P. Komin, and James F. Wolfe*

Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, Virginia 24061

Gene F. Morris

Department of Chemistry, Western Carolina University, Cullowhee, North Carolina 28723

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Potassiophenylacetonitrile (**2**) reacts with 2-bromopyridine (**1**) and 2-chloroquinoline (**4**) via the $S_{RN}1$ mechanism when the reactants are exposed to near-UV light in liquid NH_3. Potassioacetonitrile (**6**) reacts similarly with **1** and **4** upon photostimulation; however, the photo-$S_{RN}1$ reaction with **1** is accompanied by S_NAr2 amination which becomes the major reaction in the dark or in the presence of di-*tert*-butyl nitroxide. Substrate **4** undergoes competing S_NAr2 amination with amide ion to form 2-aminoquinoline (**10**) and S_N(ANRORC) reactions with both amide ion and carbanion **6** to form 3-methylquinazoline (**11**) and 2-methyl-3-cyanoquinoline (**12**), respectively. Formation of **12** becomes the major pathway in reactions between **4** and **6** carried out in the dark. 4-Picolylpotassium (**14**) reacts with **1**, **4**, and 4-bromopyridinium chloride (**16**) under photostimulation to form the appropriate dihetarylmethanes, along with the corresponding amino heterocycles. Amination of **1**, **4**, and **16** predominates when these reactions are carried out in the dark. Ammonium thiophenoxide (**20**) undergoes a slow photo-$S_{RN}1$ reaction with **1** but fails to produce the expected 2-quinolyl phenyl sulfide with **4** after 2 h of irradiation. Potassium salts of acetylene, phenylacetylene, and phthalimide do not react with **1** or **4** after 2 h of exposure to near-UV light.

The discovery that ketone enolates displace halide from 2-chloroquinoline (**4**)[2,3] and halopyridines[4] by the $S_{RN}1$ mechanism[5] when liquid NH_3 solutions of the reactants are exposed to near-UV light prompted us to examine the

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