Cyclohexene. Preparative GC was used to isolate the products from cyclohexene. The major product was identified as 3-(nitromethyl)cyclohexene: NMR ($CDCl_3$) δ 5.6 (m, 2 H), 4.2 (d, 2 H), 2.9 (m, 1 H), 1.9–1.5 (m, 6 H); IR (neat) 3055, 2965, 1555, 1385 cm^{-1}. Anal. Calcd for $C_7H_{11}NO_2$: C, 59.57; H, 7.80; N, 9.93. Found: C, 59.94; H, 8.06; N, 9.96. A poorly resolved shoulder peak on the back of the major component appeared to be a nitro-containing compound, possibly 1-(nitromethyl)cyclohexene, on the basis of its weak spectra: IR (neat) 3075, 2980, 1545, 1390 cm^{-1}; NMR ($CDCl_3$) δ 5.7, 4.3, 1.9–1.6 (all poorly resolved). Another byproduct was identified as cyclohexen-3-yl acetate: NMR ($CDCl_3$) δ 5.8 (m, 2 H), 5.25 (m, 1 H), 2.0 (m, 6 H), 1.7 (s, 3 H); IR (neat) 3075, 2975, 1720, 1250, 1030 cm^{-1}.

Cyclopentene. The concentrated product mixture from the cyclopentene reaction after reactant removal contained 50% of a major component, ~10% each of three minor products, and very small amounts of other compounds. Preparative GC did not successfully separate the major components, so spectral analysis was done on the concentrated product mixture: NMR ($CDCl_3$) δ 5.9–5.7 (overlapping m), 5.05 (s, $C{=}CCH_2NO_2$) 4.4 (d, $CHCH_2NO_2$), 3.5–3.0 (overlapping m), 2.5–1.6 (overlapping m and s); IR (neat) 3470 (weak), 3090, 2880, 1785, 1730, 1550, 1380, 1240, 1200 cm^{-1}. The major product was 3-(nitromethyl)cyclopentene: mass spectrum, m/e 67 (100, $M^+ - CH_2NO_2$), 96 ($M^+ - HNO$), 68, 70, 95; NMR δ 5.8, 4.4, 1.8; IR 1550, 1380 cm^{-1} (NO_2 group). One minor product was cyclopenten-3-ol [mass spectrum, m/e 84 (M^+), 66 (100, $M^+ - 18$), 83, 67; IR 3470 cm^{-1} (O–H stretch)] while another was cyclopenten-3-yl acetate: mass spectrum, m/e 67 (100, $M^+ - CH_3CO_2$), 66 ($M^+ - CH_3CO_2H$), 83 ($M^+ - CH_3CO$), 84; IR 1730 (C=O), 1240 (CO) cm^{-1}. A minor product, not cleanly resolved by GC/MS, was likely 1-(nitromethyl)cyclopentene (NMR siglet at δ 5.05).

1-Pentene. Essentially only one product was obtained (low yield) and had a retention time fairly similar to that of the suspected acetate from cyclopentene. No nitro group stretches were observed in the IR of the concentrated product mixture.

1-Octene. A complex mixture of minor products (<1%) was found. No further efforts at product identification were attempted.

Styrene. GC analysis showed that the viscous product mixture from styrene contained relatively small amounts of a number of volatile products. NMR analysis of the product mixture showed small signals at δ 4.3 (t, $CH_2CH_2NO_2$), 2.5 (m), and 2.0 (s) in addition to signals related to the styrene structure. Though a nitromethylated styrene is implicated, the amount present was very little, as only weak nitro group stretches were observed in the IR. The high viscosity and NMR spectrum indicated some polystyrene.

α-Methylstyrene. The concentrated product mixture from α-methylstyrene after reactant removal was shown by GC to consist of about 50% of a major component and 15% of a second component, with the remaining 35% being composed of a complex mixture of more than ten minor components (1–5%). Preparative GC was unsuccessful in further purifying this mixture, so it was analyzed as is by NMR and IR. The IR showed strong bands at 3025, 2975 (CH), 1740, 1240 (OAc), 1555, 1380 (NO_2), and 760, 690 cm^{-1} (monosubstitution) plus other weaker signals. The NMR ($CDCl_3$) contained prominent signals at δ 7.2–7.3 (overlapping s, aromatic), 4.3 (t, 2 H, CH_2NO_2), 2.5–2.9 (overlapping m, 4 H), 2.0 (s, 3 H, CH_3), and 1.9 (s, 3 H, acetate methyl) and other smaller complex signals at δ 5.4–5.0 (C=CH and/or $ArCH_2NO_2$), 2.9–3.3, and 1.5–1.8.

The major product was 1-nitro-3-phenyl-3-butyl acetate: mass spectrum, m/e 237 (M^+), 91 (100, $C_7H_7^+$), 131 ($M^+ - CH_3CO_2H,NO_2$), 121, 115, 105, 77, 65, 51; the major IR and NMR signals were consistent with this structure. A minor product was a nitromethylated α-methylstyrene (either nuclear or side chain); mass spectrum, m/e 177 (M^+), 117 (100, $M^+ - CH_2NO_2$), 116, 135, 102, 91, 77.

Registry No. Cyclohexene, 110-83-8; cyclopentene, 142-29-0; 1-pentene, 109-67-1; 1-octene, 111-66-0; styrene, 100-42-5; α-methylstyrene, 98-83-9; 3-(nitromethyl)cyclohex-1-ene, 85097-24-1; 3-(nitromethyl)cyclopent-1-ene, 85097-25-2; 1-nitro-3-phenyl-3-butyl acetate, 85097-26-3; manganese(III) acetate, 993-02-2; copper(II) acetate, 142-71-2; nitromethane, 75-52-5.

Regioselective Cyanation of Pyridine 1-Oxides with Trimethylsilanecarbonitrile: A Modified Reissert–Henze Reaction[1]

Wilmer K. Fife

Department of Chemistry, Indiana University—Purdue University at Indianapolis, Indianapolis, Indiana 46223

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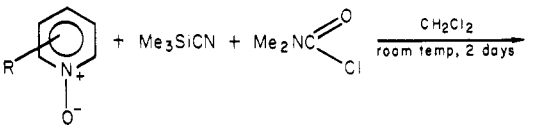
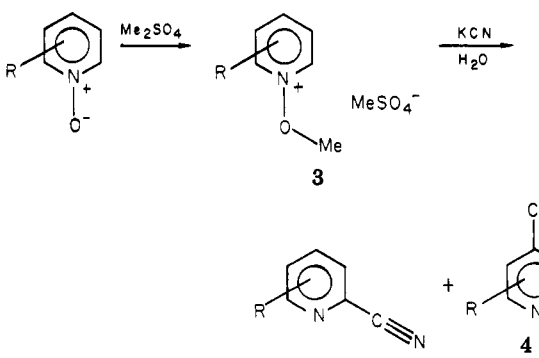
Treatment of pyridine 1-oxides **1** with equimolar quantities of trimethylsilanecarbonitrile and dimethylcarbamyl chloride in dichloromethane gives nearly quantitative yields of the corresponding 2-pyridinecarbonitriles **2** (eq 1, Table I). This new modification of the Reissert–Henze reaction[2] represents a significant improvement over previous methods for synthesis of 2-pyridinecarbonitriles, which often give low yields and cyanation at both the 2- and 4-positions of the pyridine (eq 2, Table I). It



a, R = H; **b**, R = 2-CH_3; **c**, R = 3-CH_3; **d**, R = 4-CH_3



is the first application of trimethylsilanecarbonitrile to the cyanation of pyridine 1-oxides. The use of trimethylsilanecarbonitrile in Reissert reactions of pyrimidine, quinoline, isoquinoline, and other fused, multiple-ring, nitrogen heterocycles has been reported recently.[3] It is especially noteworthy that unsubstituted, and 2- and 4-methylpyridine 1-oxides give exclusively the corresponding 2-pyridinecarbonitrile. Reaction of the 3-methyl derivative **1c** is almost as selective, producing 90% 3-methyl-2-pyridinecarbonitrile and 5% 5-methyl-2-pyridinecarbonitrile.[4]

(1) Portions of this work were reported at the American Chemical Society Central Regional Meeting, Dayton, OH, May 1981, and the 182nd American Chemical Society National Meeting, New York, Aug 1981.

(2) (a) Ochiai, E. "Aromatic Amine Oxides"; Elsevier: Amsterdam, 1976; p 269. (b) Katritzky, A. R.; Lagowski, J. M. "Chemistry of the Heterocyclic N-Oxides"; Academic Press: London, 1971; p 300. (c) Abramovitch, R. A.; Smith, E. M. *Chem. Heterocycl. Compd.* **1974**, *14*, 114–117.

(3) (a) Ruchirawat, S.; Phadungkul, N.; Chuankamnerdkarn, M.; Thebtaranonth, C. *Heterocycles* **1977**, *6*, 43–46. (b) Bhahacharjee, D.; Popp, F. D. *J. Heterocycl. Chem.* **1980**, *17*, 1207–1212. (c) Veeraragharan, S.; Bhahacharjee, D.; Popp, F. D. *Ibid.* **1981**, *18*, 443.

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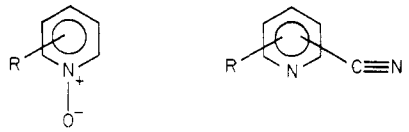
Table I. Cyanation of Pyridine 1-Oxides with Trimethylsilanecarbonitrile and Dimethylcarbamyl Chloride[a, b]



		2-C≡N (%)[c]	4-C≡N (%)[c]
R = H	R = H	94[d] (49)	0 (32)
2-Me	6-Me	~100 (48)	0 (10)
3-Me	3-Me	90 (36)	0 (6)
3-Me	5-Me	5[e] (6)	
4-Me	4-Me	~100 (40)	
2,6-Me_2	2,6-Me_2		0 (40)

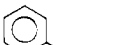
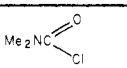
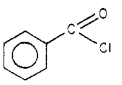
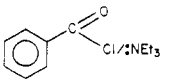
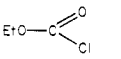
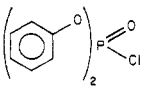
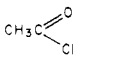
[a] Method A. [b] Yields are based on isolated, recrystallized products and VPC analysis (Carbowax 20 M, 5%, on Chromosorb W) of filtrates from recrystallizations, unless otherwise noted. Yields given in parentheses are values reported by: Feely, W. E.; Beavers, E. M. *J. Am. Chem. Soc.* **1959**, *81*, 4004–4007. [c] All products gave melting points and/or IR and NMR spectra that were in excellent agreement with literature data. [d] Yield based on VPC analysis (Carbowax 20 M 5%, on Chromosorb W) of crude product. [e] Yield based on VPC analysis (25 M fused silica capillary column with OV-1 coating) of filtrate from recrystallization.

Comparison of several acyl chlorides as catalysts for the reaction (Table II) indicates the particular effectiveness of dimethylcarbamyl chloride in bringing about cyanation. Benzoyl chloride and trimethylsilanecarbonitrile in 2- and 5-fold excess, respectively, also effect quantitative cyanation of pyridine 1-oxide at the 2-position. An excess of reagents is required for cyanation in the presence of benzoyl chloride and perhaps several other acyl chlorides due to side reactions that form acyl cyanides[5] and acid anhydrides.[6] Repeated efforts to obtain cyanation of pyridine 1-oxide under the usual or modified Reissert conditions gave only 4% 2-pyridinecarbonitrile at best. The particular effectiveness of trimethylsilanecarbonitrile as a cyanating agent is probably due to two factors: its solubility in organic solvents and its relatively slow reaction with acyl halides to produce acyl cyanides and subsequent related compounds.

The high specificity of the reaction and failure to cyanate 2,6-dimethylpyridine 1-oxide (Table I) suggest a reaction pathway that includes either intramolecular delivery of cyanide ion to the 2-position or intramolecular removal of proton from the tetracoordinate carbon formed by addition of cyanide ion or both (Scheme I). The near failure of the cyanation reaction with benzoyl chloride and cyanide ion for all pyridine 1-oxides tried except the 4-chloro-[7] and 2-, 3-, and 4-trifluoromethyl[8] derivatives strongly implicates a novel method for delivery of cyanide in this reaction.

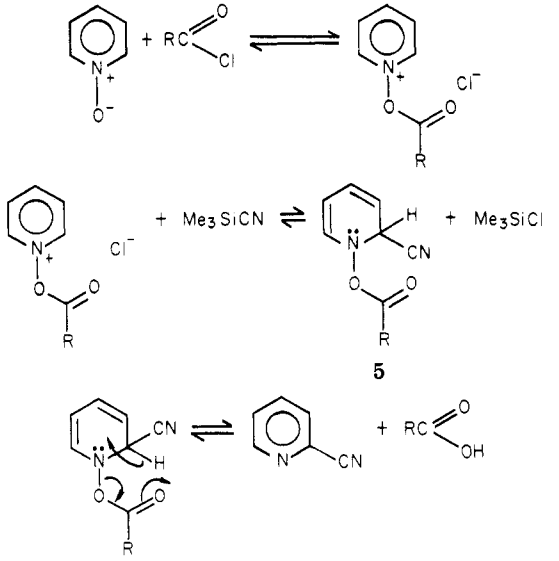
The literature contains ample precedent for all steps illustrated in Scheme I with the exception of the one in which cyanide becomes attached to the 2-position of the pyridinium ring. Experiments in which the progress of

Table II. Comparison of Acyl Chlorides as Catalysts for Reaction of Pyridine 1-Oxide with Trimethylsilanecarbonitrile[a]

acyl chloride	method	time	
	A, B, C, D	2–3 days	95
	A, B, C, D	1 day	30 (~100)[b]
	A, B, C, D	1 day	50[c]
	A, C	1 day	40
	A, C	2 days	27[d]
	C	20 min	trace (<10)[e]

[a] Reaction mixtures contained equimolar amounts of pyridine 1-oxide, trimethylsilanecarbonitrile, and acyl chloride in dichloromethane at room temperature unless otherwise noted. [b] Essentially quantitative yields of 2-pyridinecarbonitrile are obtained when pyridine 1-oxide is treated with 2 and 5 M excess of benzoyl chloride and trimethylsilanecarbonitrile, respectively. [c] These reaction mixtures contained 1 equiv of triethylamine and were treated in the manner described for related experiments. [d] S. Harusawa et al. (ref 10) report conversion of pyridine 1-oxide to 2-pyridinecarbonitrile in 24.5% yield with diethyl phosphorocyanidate. [e] The reaction mixture separates to form two liquid phases, which contain a complex mixture of products after 20–30 min.

Scheme I



5

(4) Preliminary results suggest that cyanation occurs preferentially at the 2-position of other 3-substituted pyridine 1-oxides. The variable preference for reaction at the 2- and 6-positions of different pyridine derivatives with substituents at the 3-position is well documented in a variety of reactions. See, for example: (a) ref 2c, pp 149–161. (b) Abramovitch, R. A.; Vinutha, A. R. *J. Chem. Soc. C* **1969**, 2104–2107. (c) Abramovitch, R. A.; Rogers, R. B. *J. Org. Chem.* **1974**, *39*, 1802–1807. (d) Nakanishi, M.; Yatabe, M.; Hamana, M. *Heterocycles* **1975**, *3*, 287–291. (e) Abramovitch, R. A.; Grins, G.; Rogers, R. B.; Shinkai, I. *J. Am. Chem. Soc.* **1976**, *98*, 5671–5677.

(5) (a) Groutas, W. C.; Felker, D. *Synthesis* **1980**, 861–868. (b) Koenig, K. E.; Wever, W. P. *Tetrahedron Lett.* **1975**, 2275–2278. (c) Herrmann, K.; Simchen, G. *Synthesis* **1979**, 204–205.

(6) Pyridine 1-oxides have been shown in our laboratory to be effective catalysts for the conversion of acid chlorides to acid anhydrides. Unpublished experiments in which equimolar quantities of acyl chloride and pyridine 1-oxide in dichloromethane are treated after 2–48 h with 10% aqueous potassium carbonate give the corresponding acid anhydride in 80% yield.

(7) Ochiai, E.; Nakayama, I. *J. Pharm. Soc. Jpn.* **1945**, *65*, 7.

(8) Kokayashi, Y.; Kumadaki, I. *Chem. Pharm. Bull.* **1969**, *17*, 510–514.

reaction is directly monitored by NMR spectrometry (method C, Table II) clearly demonstrate formation of chlorotrimethylsilane along with cyanation product.[9] In addition, they show that excess dimethylcarbamyl chloride and trimethylsilanecarbonitrile are stable in the reaction mixture. The particular effectiveness of dimethylcarbamyl chloride in the reaction may be used as evidence for intramolecular proton removal as a significant step in the cyanation reaction, because proton transfer to carbamate should be favored over proton transfer to carboxylate, intermediate **5**, Scheme I. This interpretation is also consistent with results obtained by cyanation with benzoyl chloride in the presence and absence of triethylamine (Table II). Added triethylamine increases yields of cyanation product from 30% to 50% when reaction mixtures contain equimolar amounts of all reactants.

Experimental Section

All reagents used in this study were obtained from commercial sources and used without additional purification. Infrared spectra were determined on a Perkin-Elmer Model 283 spectrophotometer and NMR spectra were obtained with a Varian EM390 spectrometer. Melting points were taken (uncorrected) on a Thomas-Hoover apparatus.

Cyanation of Pyridine 1-Oxides. Method A. Reaction mixtures that contained 0.0050 mol of pyridine 1-oxide, 0.55 g (0.0055 mol) of trimethylsilanecarbonitrile, and 10 mL of dichloromethane were stirred at room temperature for 5 minutes. They were then treated with 0.0050 mol of acylating agent and stirred at room temperature for 1–5 days. Spectral evidence from method C below suggests that reactions with benzoyl chloride as acylating agent are essentially complete within 15–20 min, while those catalyzed by dimethylcarbamyl chloride require 12–15 h. Reactions run at 4 °C or reflux gave nearly the same product composition as those run at room temperature.

A solution of 10% aqueous potassium carbonate (10 mL) was added, and stirring was continued for 5–15 minutes. The organic layer was separated, and the aqueous layer was extracted twice with 5 mL of dichloromethane. The combined dichloromethane layers were dried over anhydrous potassium carbonate and rotary evaporated to obtain crude products.

The presence of 2-pyridinecarbonitrile in the crude products was confirmed by infrared (ν_{max} = 2240 cm^{-1}) and ^1H NMR ($CDCl_3$) (δ 8.5–8.7 (d, J = 4.5 Hz)) spectral analysis.

Method B. Analytical-scale experiments were carried out with 5–10 × 10^{-4} mol of reactants in 1 mL of dichloromethane. Reaction mixtures were treated with 1 mL of 10% aqueous potassium carbonate, and the organic layer was analyzed directly by VPC (Gow Mac 150 with 3-ft column, Carbowax 20 M, 5% on Chromosorb W or Varian 3700 with 25 M fused silica capillary column with OV-1 coating).

Method C. Solutions were prepared by sequential addition of 2.5 × 10^{-4} mol quantities of pyridine 1-oxide, trimethylsilanecarbonitrile, and acylating agent to 0.4 mL of chloroform-*d* that contained 1% tetramethylsilane. The final solutions were approximately 0.5 M in each reactant. NMR tubes with screw-caps and Teflon liners (Wilmad No. 507-TR) were used as reaction vessels.

Integration permitted estimation of 2-pyridinecarbonitrile and uncyanated pyridine 1-oxide. The 1-oxide appeared to be at least partially acylated in all experiments.

Method D. Analytical-scale experiments were carried out with 2.5 × 10^{-3} mol of reactants in 2.0 mL of dichloromethane. Reaction mixtures were diluted to 20.0 mL with methanol and analyzed directly by HPLC (Waters C_{18} reversed-phase column with solvent program: 90% water–10% methanol, 5 min, then 100% methanol and a flow rate of 1.0 mL/min).

Modified Reissert Method. A mixture equimolar (2.5 × 10^{-3} mol) in pyridine 1-oxide, potassium cyanide, and triethylamine with 10 mL of anhydrous acetonitrile was stirred and treated dropwise with 1 equiv of benzoyl chloride. After 5 days of stirring at room temperature, the reaction mixture was worked up as described in method A. Chromatographic separation on Florisil gave 0.01 g (4%) of 2-pyridinecarbonitrile, identical in all respects with authentic samples.

Product Purification. The crude products obtained by method A were chromatographed over Florisil (100–200 mesh, 10 × 250 mM) with elution by the series of solvents: 5:1 hexane–dichloromethane, dichloromethane, and 10:1 dichloromethane–methanol. The side products, acyl cyanide and acid anhydride, were contained in the first fractions when present. 2-Pyridinecarbonitriles were eluted with dichloromethane, and the unreacted pyridine 1-oxides, when present, were found in the last fractions collected. It is important to note that use of alumina (Fisher neutral) as absorbent resulted in appreciable hydrolysis of the nitriles.

Final purification of solid products was accomplished by recrystallization from petroleum ether (30–60 °C)–diethyl ether mixtures.

Acknowledgment. This research was supported by a grant from Eli Lilly and Co. and the gift of starting materials from Reilly Tar & Chemical Corp. I thank R. Madadi and M. Latifi for technical assistance and Dr. E. Scriven for helpful discussions.

Registry No. **1a**, 694-59-7; **1b**, 931-19-1; **1c**, 1003-73-2; **1d**, 1003-67-4; **2a**, 100-70-9; **2c**, 20970-75-6; **2d**, 1620-76-4; 6-methyl-2-pyridinecarbonitrile, 1620-75-3; 5-methyl-2-pyridinecarbonitrile, 1620-77-5; trimethylsilanecarbonitrile, 7677-24-9; dimethylcarbamyl chloride, 79-44-7; benzoyl chloride, 98-88-4; ethyl chloroformate, 541-41-3; diphenyl phosphorochloridate, 2524-64-3.

(9) As reaction proceeds an NMR signal for chlorotrimethylsilane appears at δ 0.43 (s) and increases with time. The signal at δ 0.37 (s) for trimethylsilanecarbonitrile shows a corresponding decrease.

(10) Harusawa, S.; Hamada, Y.; Shioiri, T. *Heterocycles* **1981**, *15*, 981–984.

A Study of the Acid-Catalyzed Reaction of *N*-Bromosuccinimide in Methanol with Some α,β-Unsaturated Carbonyl Compounds

Victor L. Heasley,* Kimberley E. Wade, Thomas G. Aucoin, Daphne E. Gipe, and Dale F. Shellhamer

Department of Chemistry, Point Loma College, San Diego, California 92106

Gene E. Heasley

Department of Chemistry, Bethany Nazarene College, Bethany, Oklahoma 73008

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Recently, we attempted to prepare the methoxy bromide adduct of methyl vinyl ketone (1) by the reaction of 1 with *N*-bromosuccinimide (NBS) in methanol. This procedure has been used successfully in the synthesis of methoxy bromides from many olefins.[1,2] However, the reaction of 1 with NBS was apparently too slow and did not occur at room temperature. Attempts to increase the rate of reaction by raising the temperature of the solvent led to formation of large quantities of dibromide, presumably from decomposition of NBS.

It occurred to us that the reactivity of NBS might be enhanced by adding a catalytic amount of an acid that could bond with the nitrogen and increase the electrophilicity of the bromine. When a small amount of sulfuric acid was added, a rapid reaction did occur to give the

(1) C. Guss and R. Rosenthal, *J. Am. Chem. Soc.*, **77**, 2549 (1955).
(2) V. L. Heasley, R. A. Skidgel, G. E. Heasley, and D. Strickland, *J. Org. Chem.*, **39**, 3953 (1974).

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