Table I. Flow Rates at 2.5 mmHg through Silica[a] and Preabsorbent[b]

solvent	wt of silica, g	column width, mm	column ht, mm[c]	flow rate, mL/min
petroleum ether[d]	50	32	140	5
CCl_4[e]	50	32	140	2.5
petroleum ether	25	32	70	10
CCl_4	25	32	70	4
petroleum ether	10	10	18	0.8
CCl_4	10	10	18	0.3
petroleum ether	5	10	8.5	1.1
CCl_4	5	10	8.5	0.5

[a] 10-40 μm. [b] Diatomaceous earth-weight preabsorbent is 10% that of the silica. [c] Height of sorbent only. [d] Viscosity (20 °C) = 0.3 cP. [e] Viscosity (20 °C) = 0.97 cP.

allowed to be absorbed by the preabsorbent layer (C_1), and with the system under vacuum, successive small volumes of solvent are added until the resulting narrow sample band is introduced onto the sorbent (C_2). Although best avoided, the preabsorbent and the top of the absorbent layer may run dry during sample application without adversely affecting the column. Once the sample is on the sorbent, the column and solvent reservoir can be filled with solvent as desired.

Sample Application B. For difficult separations, a glass tube having a diameter of approximately half that of the column is inserted into a one-hole rubber stopper, and one end of the tube is carefully forced through the preabsorbent layer (C_1) until contact with the sorbent is made. Diatomaceous earth is then added through the tube and compressed manually to produce a layer twice the height of the original preabsorbent layer. With the rubber stopper securely in place on the top of the column, the sample, dissolved in a minimal quantity of solvent, is applied through the glass tube, using the same method as that described in procedure A. When the narrowed sample band is on the sorbent, the glass tube is cautiously removed.

Elution. Elution is performed under vacuum. The vacuum is applied to the system until the solvent front has passed through the length of the sorbent. Stopcock G is then closed to eliminate direct exposure of the eluent to the vacuum system. To maintain a constant solvent flow rate and vacuum, stopcock G need only to be opened for short, intermittent periods (e.g., ~30 s every 5–10 min). Stopcock F is closed, affording minimal loss of eluent during these evacuation periods, and the eluent is collected in the reservoir (E) during this time. It is convenient to perform this evacuation procedure while changing fractions by rotation of the receiver head (H).

When collection flasks are filled, they are easily replaced after isolation of the receiving unit from the system. The manifold and stopcock F are closed (i.e., eluent is collected in reservoir E). The receiving unit is brought to normal pressure by the opening of stopcock G to the atmosphere. After the flasks are changed, the manifold and stopcock G are opened to the vacuum, which results in the evacuation of the receiving unit. Once the receiving unit is at sufficiently low pressure, stopcock F is opened, and the elution is continued, as described. Since the collected fractions can be evaporated quickly under reduced pressure and transferred to other flasks, only six or nine ground-glass flasks are needed for operation of the system.

Acknowledgment. The authors wish to thank D. Michaud, University of Oklahoma, for demonstrating the sintered glass Büchner funnel method to us, F. C. Morey for his expertise in making the VLC apparatus, and L. N. Lester for his helpful suggestions. N.T. is indebted to the Chemistry Department, UMO, for laboratory space and the use of their research facilities. This research was partially supported by a grant from the UMO Office of Research and Public Service.

Catalytic Reactions of Pyridine with CO and H_2O. Reduction of CO to Hydrocarbon. Applications of the Water-Gas Shift Reaction. 4[1]

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We are currently searching for homogeneous metal-cluster catalysis reactions which mimic heterogeneous catalysis reactions. In this regard, we have recently described the rhodium cluster catalyzed exchange of deuterium for hydrogen at the saturated carbons of triethylamine, which occurs concurrently with rhodium catalysis of the water–gas shift reaction.[2] This observation coupled with our continuing interest in catalysis reactions wherein H_2O serves as the source of hydrogen[1-3] prompted the investigation of a possible catalytic reaction of pyridine with CO and H_2O under conditions where homogeneous catalysis of the water–gas shift reaction is known to occur.[4]

Under the conditions described below, pyridine reacts via several pathways to give products resulting from reduction, hydrodenitrogenation, methylation, and aminomethylation.[5]

Experimental Section

General Methods. Pyridine was purchased from Baker (100.0% purity, confirmed by NMR, GC, and GC/MS) and 2-, 3-, and 4-methylpiperidine, piperidine, 2-, 3-, and 4-methylpyridine, and 2-, 3-, and 4-formylpyridine was purchased from Aldrich. $RH_6(CO)_{16}$ was purchased from Strem Chemicals and CO from Matheson Gases. All reagents were used as received.

Product Analysis. Initial product analysis was performed by using a gas chromatograph–mass spectrometer (LKB-9000 interfaced with a PDP-12) equipped with a 40-m OV-101 capillary column. Products were identified by 70-eV fragmentation patterns, and elemental composition was confirmed by high-resolution mass spectrometry using a CEC21-110B instrument. Further confirmation was obtained by enhancing production of an identified product as described below and comparing 70-eV mass spectral fragmentation patterns of the proposed product with that of enhanced product as well as by comparing retention times on the GC/MS capillary column and the retention times of the products on a 4.0 m × 0.328 cm column packed with 5% carbowax on acid-washed Chromosorb G installed in a Hewlett-Packard Model 5711 gas chromatograph equipped with FID. ^{13}C NMR spectra were taken on an XL-100-15FT spectrometer modified for multinuclear operation. Me_4Si was used as internal standard.

Catalytic Runs. A standard run for the pyridine study requires mixing 6.0 mL (74 mmol) of pyridine, 2.0 mL (110 mmol) of H_2O, 0.1 mmol of $Rh_6(CO)_{16}$, and 1.5 mmol of *n*-butyl ether (internal standard for GC analysis) in a quartz-lined Parr general-purpose bomb reactor. The reactor, which contains the mixture and a magnetic stir bar, was sealed and degassed by three 800-psi pressurization/depressurization cycles with CO. The reactor is then charged to 800 psi of CO and heated with stirring at 150 °C for 5 h. After 5 h, the reactor is quickly cooled to 0

(1) Previous paper in this series: R. M. Laine, *Ann. N.Y. Acad. Sci.*, in press.
(2) R. M. Laine, D. W. Thomas, L. W. Cary, and S. E. Buttrill, *J. Am. Chem. Soc.*, **100**, 6527 (1978).
(3) R. M. Laine, *J. Am. Chem. Soc.*, **100**, 6451 (1978).
(4) Some work in this area has previously been reported: N. S. Imyanitov, B. E. Kuvaev and D. M. Rudkovskii, *Zh. Prikl. Khim.*, (*Leningrad*), **40**, 2821 (1967). However, under the conditions reported it is possible to hydrogenate pyridine with CO and H_2O without catalyst as described by Dr. Frank R. Mayo of this research group: *J. Org. Chem.*, 1, 496, (1936).
(5) For a description of aminomethylation, see A. F. M. Iqbal, *Helv. Chim. Acta*, **54**, 1440 (1971), and references therein.

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°C. The pressure is released and a fresh charge of CO is introduced followed by heating to 150 °C. This process is repeated every 5 h until 20 h of reaction time is reached.

Gas chromatographic analysis of the reaction solution gas yields of piperidine (7% of reacted pyridine) and piperidineformamide (14% of reacted pyridine) by comparison with the internal standard. With the isolation of **3** (see below) quantitative GC analysis of **3** (55% yield based on reacted pyridine), **4** and **5** was also possible. Product yields of **4** and **5** were obtained by difference. Thus, the standard reaction solution was jubjected to rotary evaporation to remove excess pyridine and piperidine. Further treatment by refluxing of the remaining material in 10 mL of concentrated HCl for 5 h followed by neutralization with aqueous K_2CO_3, ether extraction (two portions of 20 mL), drying over $MgSO_4$, and further rotary evaporation obtained 1.6 g of oil consisting of **3**, **4**, and **5**. Of this 1.1 g is **3** (4.0 mmol), 0.1 g is **4** (0.6 mmol), and 0.4 g is **5** (1.1 mmol). (It is assumed the GC sensitivity for **4** is essentially the same as for **3**.) The oil is treated with HCl gas, and following 2 months of standing, crystals of the dihydrochloride of **3** separated: ^{13}C NMR (Me_2SO, relative to Me_4Si) for **3**·2HCl δ 55.1 (2 C), 51.6 (4 C), 23.2 (1 C), 22.1 (6 C), 21.4 (2 C); elemental composition–high-resolution mass spectrum, calcd for $C_{15}H_{30}N_2$ m/e 238.2409, found 238.2394; major 70-eV fragments, m/e 239, 98.

Analysis for **4a,b** consists of elemental composition–high-resolution mass spectrum, calcd for $C_{16}H_{32}N_2$ m/e 252.2565, found 252.2567 ± 0.0020. Major 70-eV fragments: m/e 252, 112, 98, identical for **4a** and **4b**; for **4c** (2-methyl derivative which was not found but was made as below) m/e 252, 237, 112, 98.

Analysis for **5a–c** consists of elemental composition–high-resolution mass spectrum, calcd for $C_{21}H_{41}N_3$ m/e 335.3300, found 335.3285 ± 0.0010 for all three compounds. Major 70-eV fragments for **5a** or **5b**; m/e 335, 251, 250, 98. These are identical for **5a** and **5b**. Major 70-eV fragments for **5c**: m/e 335, 251, 237, 195, 98.

Enhanced Catalytic Formation of 3a–c. The standard reaction described above is modified by the substitution of 2.0 mL of 2-, 3-, or 4-methylpiperidine for 2.0 mL of pyridine. The reaction is carried out in a similar manner. In these reactions 20–25% of the pyridine introduced reacts. The major trimeric products, approximately 70% in all cases, are **3a**, **3b**, or **3c**, with **4a**, **4b**, or **4c** amounting to 20% based on reacted pyridine and **3** accounting for the remaining 10%. Trimeric products account for 70% of the pyridine reacted, with 20–25% forming piperidineformamide and 5–10% obtaining tetrameric derivatives such as **5**. Both **4a** and **4b** are obtained in significant quantities in these enhanced reactions. Again, the 70-eV fragmentation patterns for **4a** and **4b** are identical as are the retention times on both GC columns as described above. Thus, resolution of which isomers are present is not possible. Product **4c**, the 2-methyl derivative, also exhibits enhanced yield and has a significantly different 70-eV fragmentation from **4a** to **4b**.

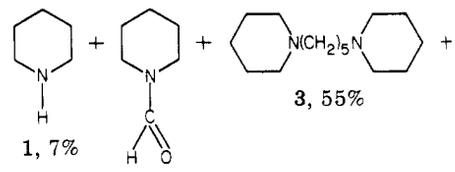
Enhanced Catalytic Formation of 5a–c. Substitution of 2.0 mL of 2-, 3-, or 4-formylpyridine for pyridine in the standard reaction results in an increase in formation of **5a**, **5b**, or **5c** as determined by GC and GC/MS analysis. Again, the 70-eV fragmentation patterns for **5a** and **5b** are identical, and differentiation between the two possible products is not possible even with GC capillary separation. **5c**, which is the major product (75% of the tetrameric products), is identifiable on the basis of 70-eV mass spectroscopy and GC retention times. As above, 20–25% of the pyridine reacts, and 30% of the reacted pyridine becomes incorporated in the formation of **5a–c**. The remainder is partitioned between **3** and **4** and a variety of new products of no consequence to the present work.

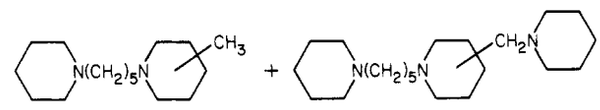
Catalytic Reactions with Diethylethanolamine. A 6.0-mL (51 mmol) sample of diethylethanolamine is substituted for pyridine in the standard reaction mixture and treated similarly. After 20 h of reaction time, GC analysis shows 10 mol of triethylamine have formed per mole of added $Rh_6(CO)_{16}$.

Silylation with $CF_3C(O)N[Si(CH_3)_3]_2$. Treatment of the standard reaction solution after 20 h reaction time with 0.5 mL of $CF_3C(O)N[Si(CH_3)_3]_2$ via standard techniques results in the silylation of two minor products **7a** and/or **7b** and 5-(*N*-piperidinyl)-1-pentanol, allowing their detection by GC/MS. The products amount to less than 2% of the total reaction products.

Results and Discussion

In a typical reaction, 6.0 mL (74 mmol) of pyridine, 2.0 mL (110 mmol) of H_2O, 0.1 mmol $Rh_6(CO)_{16}$, and 1.5 mmol of *n*-butyl ether as internal standard, are heated to 150 °C under 800 psi of CO for 20 h. The reaction gases and mixture are analyzed every 5 h, and a new charge of CO is introduced. Normally 30–35% of the pyridine reacts to produce:

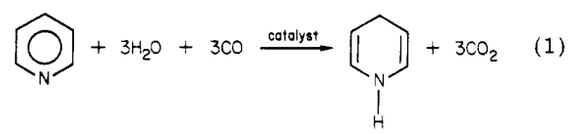




4a, 4-methyl
b, 3-methyl
6%

5a, 4-piperidinomethyl
5b, 3-piperidinomethyl
5c, 2-piperidinomethyl
18%

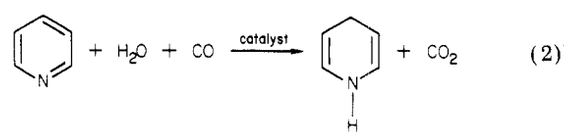
Thus, piperidine (**1**) accounts for 7% of the reacted pyridine and is simply the product of pyridine reduction (eq 1).



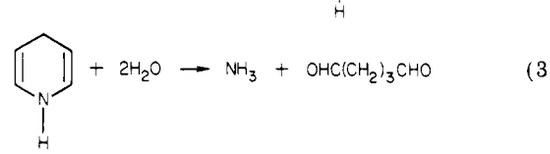
(1)

Piperidineformamide (**2**) accounts for 14% of the reacted pyridine and results from the well-documented transition metal catalyzed insertion of CO into N–H bonds.[6]

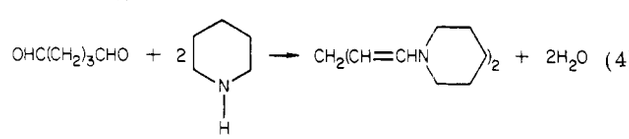
The formation of **3–5** is not as easily explained. The pentamethylene linkages derive from the extrusion of NH_3 from pyridine—hydrodenitrogenation. The exact route by which this occurs is not obvious. A likely derivation of **3** is shown in eq 2–5.



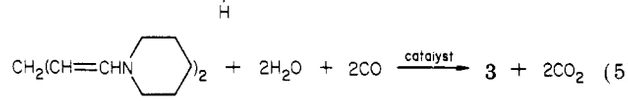
(2)[7]



(3)



(4)



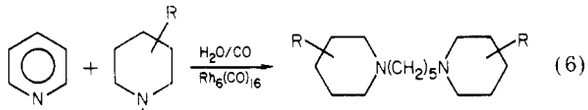
(5)

When 2.0 mL of 2-, 3-, or 4-methylpiperidine is substituted for 2.0 mL of pyridine in the original reaction, the major product obtained is the corresponding dimethylated

(6) (a) B. D. Dombek and R. J. Angelici, *J. Catal.*, **48**, 433 (1977); (b) B. D. Dombek and R. J. Angelici, *J. Organomet. Chem.*, **134**, 203 (1977); (c) G. L. Rempel, W. K. Teo, B. R. James, and D. V. Plackett, *Adv. Chem. Ser.*, **no. 132**, 166 (1974).

(7) 1,4-Hydrogenation as shown in (3) may be the result of 1,2-hydrogenation followed by catalytic isomerization; it provides a reasonable route to a species readily hydrolyzed to glutaraldehyde.

derivative (eq 6). Products **5a–c** become negligible in



(6)

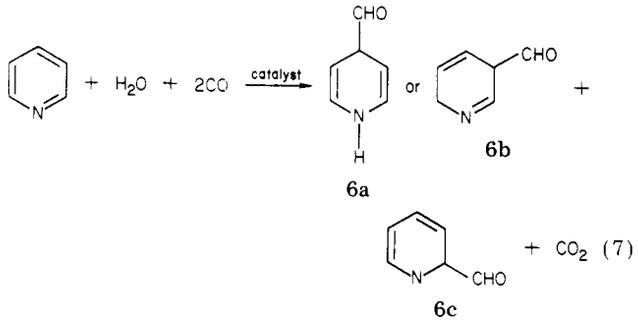
3, R = H
3a, R = 4-methyl
b, R = 3-methyl
c, R = 2-methyl

these reactions. These results strongly support the reaction pathway proposed (eq 2–5). Additional support is obtained when the reaction solution is treated with $CF_3(CO)N[Si(CH_3)_3]_2$ which allows the detection by GC/MS of small amounts (<1%) of 5-(*N*-piperidinyl)-1-pentanol as its silyl derivative. This product should form from intermediates in reaction 5, thus providing evidence for the intermediacy of glutaraldehyde.

In the standard reaction mixture the product **4** is either the 4-methyl (**4a**) or 3-methyl (**4b**) (but not the 2-methyl) analogue of **3** or a mixture of the two. A mixture of the authentic 3- and 4-methyl derivatives is inseparable by capillary GC methods, and their mass spectra are identical. The methyl groups do not derive from impurities in the starting pyridine which is obtained from Baker (100.0% purity). Purity was confirmed by GC/MS and GC and NMR spectroscopy. Therefore, the methyl groups (and the methylene groups of **5a–c**) derive from CO via a number of reductive steps requiring CO and H_2O. This represents one of the very few examples of homogeneous catalytic reduction of CO to a nonoxygenated species.[8] The average yield of **4** is 0.6 mmol which corresponds to 6 mol of product/mol of $Rh_6(CO)_{16}$ added.

Blank reactions run with 0.6 mmol of rhodium metal obtained no products which correspond to those found by using $Rh_6(CO)_{16}$. In the $Rh_6(CO)_{16}$ catalyst solutions, no particulate metal is observed at any time during the reaction. Thus, it appears that the reaction is homogeneously catalyzed.

A probable pathway for formation of **4** is via hydroformylation[3] of pyridine during the course of pyridine reduction. The initial step is hydroformylation (eq 7).

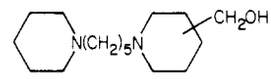


(7)

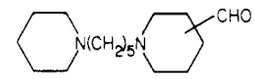
6a **6b** **6c**

The hydroformylation product can undergo a variety of reactions including hydrodenitrogenation, ring reduction and/or aldehyde reduction, and condensation and reduction. Ring opening does occur, and trace quantities of the chain methylated forms of **3** are observed by GC/MS. We have no direct evidence for single ring reduced versions of **6a–c**; however, we have observed some **7** after silylation of the reaction mixture.

Compounds **7a,b** must arise from the catalytic reduction of **8a,b**, and then further reduction produces **4**. Apparently, the catalyst system does not reduce **8c**. We have previously demonstrated that rhodium catalytically reduces aldehydes to alcohols with CO and H_2O;[3] however, we were previously unaware that the rhodium/CO/H_2O homogeneous catalysis system was capable of hydrogenating carbon–oxygen single bonds. Thus, to demonstrate this capability, we treated 6.0 mL (51 mmol) of diethylethanolamine as described above for pyridine with the concomitant production of 10 mol of triethylamine/mol of $Rh_6(CO)_{16}$ after 20 h.[9]



7a, 4-hydroxymethyl
b, 3-hydroxymethyl



8a, 4-formyl
b, 3-formyl
c, 2-formyl

The major product, **5**, most probably arises from intermediate formation of **8** which condenses with piperidine to form an enamine that is subsequently reduced to **5**. The major product (75% of **5**) is **5c** with either **5a** or **5b** or a mixture of **5a** and **5b** comprising the remaining portion. The reaction pathway by which the products **5a–c** are formed can be described by reactions 8–10. These reactions delineate the heretofore unexplained mechanism of the aminomethylation reaction. We believe that the aminomethylation reaction may be of considerable use to organic synthetic chemistry.[10]

$$RCH{=}CH_2 + H_2O + 2CO \rightarrow RCH_2CH_2CHO + CO_2 \quad (8)$$

$$R'CH_2CHO + R_2NH \rightarrow R'CH{=}CHNR_2 + H_2O \quad (9)$$

$$R'CH{=}CHNR_2 + H_2O + CO \xrightarrow{\text{catalyst}} R'(CH_2)_2NR_2 + CO_2 \quad (10)$$

Finally, there are several examples wherein heterogeneous catalysts convert piperidine[11,12] and pyridine[13] to **3**. The mechanism of Kindler et al. provides an alternative to the above-proposed route to **3a–c**, **4a**, and **5a–c**. If such a mechanism occurred under the catalysis conditions described here, this would then be support for modeling heterogeneous catalysis with homogeneous catalytic reactions. Unfortunately, no evidence was found for the Kindler mechanism (piperidine does not react to give **3**, **4**, or **5**), whereas the silylation products provide evidence in favor of the glutaraldehyde pathway to **3**, **4**, and **5**.[14]

Acknowledgment. We would like to thank the referees for several helpful comments. This work was supported by National Science Foundation Chemical Engineering Grant No. 77-21246.

Registry No. **1**, 110-89-4; **2**, 2591-86-8; **3**·2HCl, 71948-71-5; **3a**, 71948-72-6; **3b**, 71948-73-7; **3c**, 71948-74-8; **4a**, 71948-75-9; **4b**, 71948-76-0; **4c**, 71948-77-1; **5a**, 71948-78-2; **5b**, 71948-79-3; **5c**, 71948-80-6; **7a**, 71948-81-7; **7b**, 71948-81-7; pyridine, 110-86-1; 2-methylpyridine, 109-06-8; 3-methylpyridine, 108-99-6; 4-methylpyridine, 108-89-4; water, 7732-18-5; $Rh_6(CO)_{16}$, 54065-66-6; carbon monoxide, 630-08-0; 2-methylpiperidine, 109-05-7; 3-methylpiperidine, 626-56-2; 4-methylpiperidine, 626-58-4; 2-formylpyridine, 1121-60-4; 3-formylpyridine, 500-22-1; 4-formylpyridine, 872-85-5.

(8) See, for example, M. G. Thomas, B. F. Beier, and E. L. Muetterties, *J. Am. Chem. Soc.*, **98**, 1296 (1976).

(9) On the basis of our observations in ref 2, this reaction may be cluster catalyzed.

(10) R. M. Laine, submitted for publication.

(11) K. Kindler and D. Mathies, *Ber. Dtsch. Chem. Ges.*, **96**, 924 (1963).

(12) *Chem. Abstr.*, **54**, 19731*b* (1960).

(13) *Chem. Abstr.*, **55**, 574*f* (1961).

(14) See also F. De Angelis, I. Grgurina, and R. Nicoletti, *Synthesis*, 70 (1979).