than the fragmentation of the carbon–halogen bonds.

Experimental Section

The four 6-halogeno-2*H*,3*H*-benzo[*b*]thiophene-2,3-diones were prepared by cyclization of the appropriate 3-halogenophenylthioacetic acid[12,13] according to the general procedure described by Werner et al.[14] and by subsequent oxidation of the 6-halogeno-3-hydroxybenzo[*b*]thiophene[14,15] by the method of El Shanta et al.:[16] 6-F, mp 108–111 °C (from methanol); 6-Cl, mp 134–135 °C (from methanol); 6-Br, mp 169–170 °C (from methanol); 6-I, mp 197–198 °C (from benzene). Satisfactory elemental analyses were obtained. Carbonyl adsorptions were recorded at 1725 cm^{-1} (CS_2). Solid potassium *tert*-butoxide and hydroxide were commercial materials while sodium *tert*-butoxide was prepared by a standard method. Reagent grade solvents were utilized without further purification with the exception of dimethyl sulfoxide which was distilled under reduced pressure from calcium hydride and stored over molecular sieves.

Radical anions, detected with a Varian E-109 spectrometer, were simply generated in capillary glass tubes by adding the solvent to the solid reagents. Degassing of the solutions resulted neither in any improvement of the quality of the ESR spectra nor in any change of the observed reactivity.

Acknowledgment. Financial support from CNR (Rome) is gratefully acknowledged.

Registry No. I (X = F), 73655-11-5; I (X = Cl), 50789-28-1; I (X = Br), 73655-14-8; I (X = I), 73655-16-0; I (X = H), 493-57-2; II (X = F) K^+, 75750-94-6; II (Y = F) Na^+, 75716-07-3; II (Y = Cl) K^+, 75716-08-4; II (Y = Br) K^+, 75716-09-5; II (Y = I) K^+, 75716-10-8.

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Gas-Phase Synthesis of Nitriles

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n-Octanenitrile is obtained in 87% yield from the copper-catalyzed, gas-phase reaction of 1-octanol with ammonia at 325 °C and 1 atm. Similar high yields of alkyl or aryl nitriles are obtained from the reaction of ammonia with primary alcohols, aldehydes, primary amines, secondary amines, and esters. The effect of reaction variables is examined: highest yields of nitriles are obtained when the reaction is carried out at ca. 300 °C and at ammonia to substrate ratios of greater than 10:1. The 15% Cu/Al_2O_3 case was examined most extensively, but vanadium, iron, and nickel also show selectivity to nitriles while manganese and antimony give only very small amounts of these products.

A number of methods have been developed for the synthesis of organic nitriles. Although it is often possible to convert a specific functional group into a nitrile group, no convenient, general method of synthesis has been reported.

Approaches to nitrile synthesis may be divided into two distinct groups. The first generally involves the use of cyanide as a nucleophile and results in the formation of an organic nitrile containing one more carbon atom than the starting material. Several modifications in this methodology have appeared recently. The reaction of potassium cyanide with alkyl halides is facilitated by the use of crown ether in acetonitrile solvent[1] or by the use of hexamethylphosphoramide solvent with or without added crown ether.[2] The reaction of *n*-alkyl bromides with sodium cyanide impregnated onto alumina allows the small-scale synthesis of aliphatic nitriles in hydrocarbon solvent,[3] and aryl nitriles are formed from the reaction of aryl halides with sodium cyanide in the presence of catalytic amounts of nickel phosphine[4] or palladium phosphine[5] complexes.

An alternative approach involves the conversion of an organic compound into a nitrile containing the same total number of carbon atoms. One example involves the conversion of aliphatic primary alcohols to nitriles over a fused iron catalyst[6] (eq 1). Nitriles have also been obtained from

$$n\text{-}C_4H_9OH + NH_3 \xrightarrow[320\ ^\circ C,\ 1\ atm]{\text{“Fe”}} \underset{85\%}{n\text{-}C_3H_7C{\equiv}N} \qquad (1)$$

the ammoxidation of aldehydes, ketones,[7] and benzylic or allylic methyl groups,[8] but these reactions require severe conditions (usually >400 °C). Aryl nitriles are obtained from the reaction of aryl aldehydes with ammonia and an excess of nickel peroxide.[9] Methods have also appeared for the conversion of amides to nitriles,[10] the dehydration of aldoximes,[11,12] the synthesis of nitriles from nitro compounds,[13] and the synthesis of nitriles via the reaction of sulfimide with aldehydes.[14]

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Table I. Yields of Nitriles Obtained from the Reaction of Ammonia with a Variety of Organic Compounds[a]

starting matl	product	yield, %[b]	temp, °C
benzaldehyde	benzonitrile	95	300
benzyl alcohol		96	300
benzylamine		95 (89)	300
p-methoxybenzaldehyde	*p*-methoxybenzonitrile	95	280
ethanol	acetonitrile	87	325
ethyl acetate		95[c]	325
n-butanol	butyronitrile	96	325
n-octanol	*n*-octanenitrile	90 (87)	325
n-octanal		92	325
n-octylamine		92	325
di-*n*-octylamine		95[c]	325

[a] The catalyst used was 15% Cu/Al_2O_3; NH_3/starting material ratio was ~20:1. [b] Yields were determined by GLC. Yields in parentheses are isolated yields. [c] Based on formation of 2 mol of nitrile/mol of starting material.

Each of these routes works in reasonable-to-excellent yield for a limited group of compounds. We felt that it would be possible to synthesize nitriles from the vapor-phase reaction of ammonia with a wider variety of organic compounds than allowed by many of the current methods. In addition, this approach should eliminate the need for costly solvents and minimize the workup. We present the results of this study here.

Results and Discussion

The conversion of 1-octanol to *n*-octanenitrile occurs in good yield and illustrates the general method. 1-Octanol was fed by syringe into a flowing stream of ammonia to produce a mixture containing ca. 5 mol % of octanol. This mixture was heated to 325 °C and passed through a catalyst bed containing 3 cm^3 of 15% Cu/Al_2O_3. The pressure in the system was ca. 1 atm, and the normal residence time was ca. 2 s. The product stream was cooled, collected, and analyzed. In this case, GLC analysis indicated a 90% yield of *n*-octanenitrile. *n*-Octanenitrile was isolated in 87% yield after drying and distillation of the crude product.

Similar yields of *n*-octanenitrile have been obtained from the reaction of ammonia with *n*-octanal, *n*-octylamine and di-*n*-octylamine. Other examples in Table I demonstrate the generality of this process: alkyl and aryl nitriles are prepared from a relatively wide variety of functional groups including primary alcohols, aldehydes, primary amines, secondary amines, and esters. In the case of dialkylamines and esters, 1 mol of nitrile is formed from each "half" of the molecule.

The conditions described above were the best found for nitrile preparation and resulted from a careful study of the reaction variables.

The most important variable is the reaction temperature. This is illustrated by the data in Figure 1. At 200 °C, the reaction of octanol with ammonia leads to *n*-octylamine as the major product. In agreement with predictions based on the calculated thermodynamics of the system, the product ratio changes as the temperature is increased, and octanenitrile quickly becomes the dominant species formed. Other workers have observed a similar temperature dependence in the amination of alcohols.[6] Qualitatively, although enthalpy favors the amine, entropy favors the nitrile and becomes the dominant factor above ~220 °C.

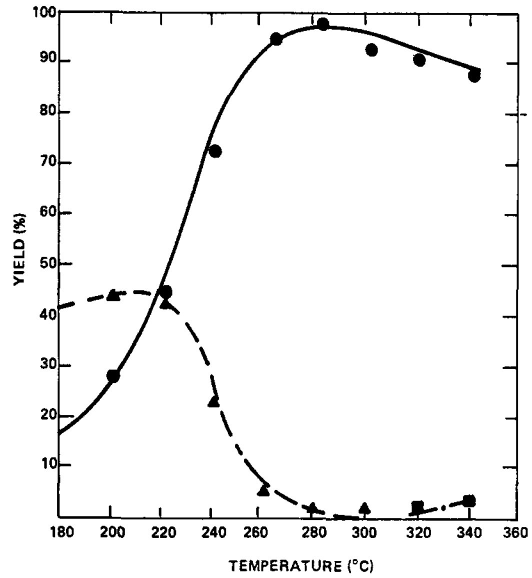
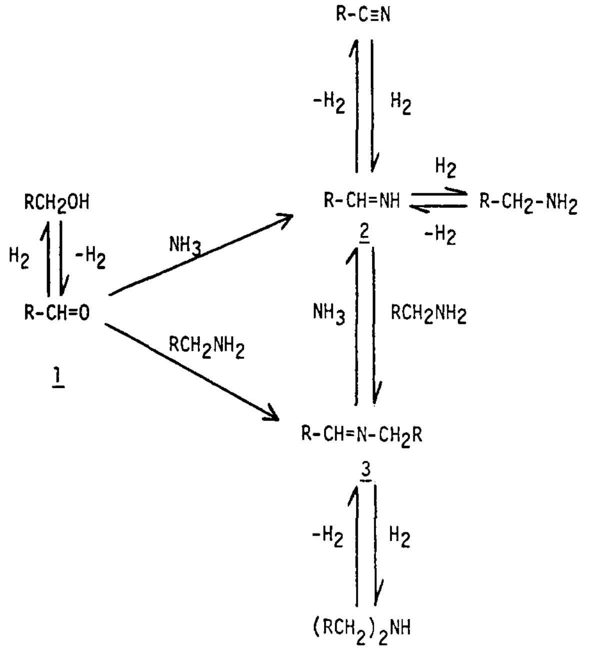


Figure 1. Product yields obtained from the reaction of 1-octanol with ammonia over 15% Cu/Al_2O_3 as a function of temperature: $NH_3/H_2/ROH$ = 20:5:1; octanenitrile, ●; octylamine, ▲; octane, ■.

Scheme I



Small amounts of octane are observed at >320 °C. Presumably, this is due to alumina-catalyzed dehydration of 1-octanol followed by metal-catalyzed hydrogenation of the olefin intermediate. Octane is not observed under these conditions when a silica support is used.

Formation of amines as the major products from the reaction of alcohols with either ammonia or low molecular weight amines is well documented and is used commercially.[15,16]

The currently accepted mechanism for this process is illustrated in Scheme I. The data in Table II demonstrate that most of these reactions are reversible.

At low temperatures, the reaction is kinetically controlled, and different product ratios are obtained from each starting material (Table II). Thermodynamic equilibrium

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Table II. Yields of Products Obtained from the Reaction of Ammonia with Octane Derivatives[a]

reaction matl[b]	temp, °C	product yields, %[b,c]			
		RCH_2OH	RCH_2NH_2	RC≡N	other[d]
RCH_2OH	185[e]	20	50	10	21
RCHO	185[e]	2	56	15	27
RCH_2NH_2	185[e]	0	70	9	20
$(RCH_2)_2NH$	185[e]	0	54	11	31
RCH_2OH	200	21	42	28	9
RCH_2NH_2	200	0	62	19	18
RCN	200	0	31	64	4
RCH_2OH	250	0	12	83	6
RCH_2NH_2	240	0	15	68	17
$(RCH_2)_2NH$	255	0	13	83	4
RCN	240	0	11	82	7

[a] Conditions, unless otherwise noted: 15% Cu/Al_2O_3 catalyst; NH_3/H_2/starting material ratio of 20:5:1; 1 atm; contact time ca. 2 s. [b] R = n-C_7H_{15}. [c] Determined by GLC. [d] Almost exclusively $(RCH_2)_2NH$. [e] NH_3/H_2/starting material ratio of 50:15:1.

is reached at ~250 °C, and above this temperature, nearly identical product ratios are obtained from the various starting materials. (See, for example, the data in Table I.)

Consistent with the sequence of equilibria outlined in Scheme I, the molar ratio of hydrogen, ammonia, and starting material is also important in determining the products obtained (Table III). For the reaction of 1-octanol with ammonia, low hydrogen ratios result in maximum yields of nitrile, high ammonia/substrate ratios favor monoalkylamine formation, and low ammonia/substrate ratios favor dialkylamine formation. Similar trends have been qualitatively observed in other systems and appear to be general. Since hydrogen is detrimental to nitrile synthesis, no hydrogen was used in the preparative runs. Also, since a high ammonia to substrate ratio gave the best results, this ratio was maintained at ≥20:1 for the preparative work.

The mechanism outlined in Scheme I contains two different types of reactions: dehydrogenation and net nucleophilic addition to unsaturated intermediates, e.g., 1 and 3. An effective catalyst should be able to facilitate both processes.

A number of catalysts were screened for nitrile synthesis. Table IV presents a summary of the data. In general, the catalysts were examined over a temperature range of 200–340 °C. The data in Table IV present the maximum yield of nitrile obtained over each catalyst and the minimum temperature at which that yield was obtained. The ammonia/hydrogen/substrate ratio was maintained at 20:5:1.

This work was intended to show whether other supported catalysts would perform as well as 15% Cu/Al_2O_3 and whether they might, in addition, allow the use of lower metal loadings or low reaction temperatures or both. From the data, it appears that effective catalysts could be prepared from vanadium, iron, and nickel as well as copper, but none of these systems appears to offer significant improvement.

For the copper/alumina system, a large decrease in reaction temperature is observed on increase of the metal loading from 5% to 15%. A further increase to 30% results in only a minor additional decrease in the optimal reaction temperature.

It is interesting that manganese and antimony displayed very minor activity for nitrile formation. Reaction of 1-octanol over these catalysts resulted in relatively clean formation of mixtures of *n*-octylamine and di-*n*-octylamine. Apparently, the manganese and antimony systems facilitate nucleophilic addition to an imine-type intermediate more efficiently than they catalyze the corresponding dehydrogenation.

Our results suggest that although many metals exhibit catalytic activity for producing nitriles, careful control of metal loading and choice of support must be exercised to obtained optimum nitrile yields. Although we have not investigated catalyst stability with extended runs, we have observed no significant activity decline with 15% Cu/Al_2O_3 over a period of several days.

Some limitations to this process have been identified. Neopentyl glycol, tetrahydrofuran, ethylene glycol, *N,N*-dimethylethanolamine, and 1,3-propanediol were not converted into mono- or dinitriles under any conditions studied. In each case, a complex product mixture was obtained, and no more than minor amounts of nitrile products could be found.

Halides also present difficulties. Reaction of benzyl chloride with ammonia over fresh 15% Cu/Al_2O_3 catalyst at 300 °C produced a 60% yield of benzonitrile. Other products included bibenzyl (35%) and toluene (10%); but deactivation of the catalyst was rapid, possibly due to the poisoning effect of chlorine on copper or formation of NH_4Cl which may have clogged the pores of the supported catalyst.

o-Chlorobenzaldehyde reacted with ammonia over 15% Cu/Al_2O_3 at 320 °C to give *o*-chlorobenzonitrile in only 25% yield. This may have been due to steric problems. (*o*-Chlorotoluene was recovered unchanged under these conditions.)

In conclusion, we have demonstrated that the vapor-phase reaction of ammonia with primary alcohols, esters, amines, and aldehydes can produce nitriles in very good yield. The reaction can be used for the synthesis of both aryl and aliphatic nitriles, does not use a solvent, and requires only a minor workup. The reaction is sensitive to the presence of additional functional groups and works best for relatively simple systems. All reaction conditions are important, but careful control of temperature and substrate/ammonia mole ratio is essential.

Table III. Effect of the Ammonia/Hydrogen Ratios on the Reaction of 1-Octanol with Ammonia over 15% Cu/Al_2O_3

$NH_3/H_2/RCH_2OH$ molar ratio	temp, °C	product yield, %[a,b]			
		RCH_2OH	RCH_2NH_2	RC≡N	$(RCH_2)_2NH$
20:5:1	220	2	43	45	9
15:10:1	220	2	50	28	18
10:15:1	220	0	49	12	40
5:20:1	220	0	41	5	54
20:5:1	250	0	12	83	6
15:10:1	250	0	25	72	3
10:15:1	250	0	41	46	13
5:20:1	250	0	37	28	36

[a] Determined by GLC. [b] R = n-C_7H_{15}.

Table IV. Effect of Catalyst on the Efficiency of Production of *n*-Octanenitrile from 1-Octanol

catalyst	temp, °C	yield of RC≡N, %
5% V/Al_2O_3	340	25
5% Mn/5-Å sieves	340	0
5% Mn/Al_2O_3	340	0
5% Fe/Al_2O_3	340	13
5% Fe/C	340	52
5% Fe/SiO_2	340	0
5% Ni/C	275	71
4% Ni/4-Å sieves	280	63
5% Cu/Al_2O_3	340	9
15% Cu/Al_2O_3	280	97
30% Cu/Al_2O_3	260	96
5% Sn/Al_2O_3	340	4
5% Sb/Al_2O_3	340	<1
5% Sb/C	340	<1
5% Sb/5-Å sieves	340	<1
15% Sb/Al_2O_3	340	8
5% Cu, 5% Ni/Al_2O_3	280	85
5% Cu, 5% Zn/Al_2O_3	300	97
6% Cu, 5% Mn/Al_2O_3	350	71

Experimental Section

All chemicals were reagent grade and were used without further purification. The alumina catalyst support was Cyanamid HCFX γ-Al_2O_3 in the form of 0.050-in. TRILOBE extrudates. It was calcined at 600 °C for at least 1 h prior to use. Physical properties: surface area 304 m^2/g (N_2 BET area); pore volume 0.64 cm^3/g. The carbon is a Cyanamid proprietary material with a surface area of 550 m^2/g and a pore volume of 0.85 cm^3/g. Grade 01 silica was obtained from Davison: pore volume 0.43 cm^3/g; surface area 695 m^2/g. Molecular sieves were obtained from Linde (4 Å) or Aldrich (5 Å).

NMR spectra were obtained on a Varian A-60 or EM-360A nuclear magnetic resonance spectrometer. Analytical gas chromatography was carried out on a Hewlett-Packard 5750 instrument with a flame-ionization detector, complete with a Hewlett-Packard 7128A recorder with disk integration, or a Hewlett-Packard 7128A instrument with a flame ionization detector, complete with an HP-7127A recorder with electronic integration. All GLC analyses were carried out on a 1.3 m × 6.5 mm glass column packed with 28% Pennwalt 223 plus 4% KOH on Gas Chrom R (Applied Science Laboratories).

Reactor. The reactor consisted of a 13 mm (o.d.) × 270 mm Pyrex glass tube terminating in a 10/30 ground-glass joint. A coarse-fritted glass disk was located 30–40 mm above this joint. A side arm (9 mm o.d. × 25 mm) was located 25 mm from the top of the tube for the introduction of the various reactants. The top of the tube was fitted with a rubber serum cap penetrated by a 3-mm (o.d.) Pyrex glass thermowell. A chromel–alumel thermocouple (Omega Engineering Inc.) was adjusted so that its tip was located in the center of the catalyst bed.

The reactor was placed in a tube furnace with a 2 × 22 cm core. The position of the tube was adjusted so that the catalyst bed was located at the center of the furnace.

The hydrogen and ammonia were introduced through separate flow meters (Lab Crest) which were calibrated for the respective gases. The organic substrate was introduced by syringe by using a Harvard Apparatus compact infusion pump which was calibrated for each substrate used. (For isolated yield determinations, the amount of starting material fed into the system was determined by weight.)

A number of collection systems were used. These were usually based on a straight tube collector fitted at the top with a female 10/30 joint. The product could then be collected by bubbling the product gas through methanol or by collection in a cold trap.

Catalysts. All catalysts used were prepared by the pore volume saturation ("incipient wetness") method. Compositions are given as the percent metal on the support regardless of the form of metal present. For example, the 15% Cu/Al_2O_3 catalyst was prepared by the addition of a solution containing 14.1 g of $Cu(NO_3)_2 \cdot 3H_2O$ dissolved in 12.8 mL of water to 20.0 g of Al_2O_3. After thorough mixing, the moist solid was dried for several hours at 120 °C and then calcined for 2 h at 500 °C in flowing air.

General Reaction Procedure. In a typical run, 1-octanol was fed by syringe (0.012 g/min, 0.1 mmol/min) into a flowing stream of ammonia (45 mL/min at room temperature, 2 mmol/min) or ammonia plus H_2 (NH_3/H_2 ratio of 5, total flow 55 mL/min). The gas mixture was passed through a vaporization and preheating section packed with 3-mm glass beads into a hot zone held at 325 °C containing 3 cm^3 of 15% Cu/Al_2O_3. The product stream passed through the glass frit and was collected in methanol. The system was run for 20 min (2 mmol of octanol consumed), and then the alcoholic product solution was diluted to a total volume of 100 mL and analyzed by GLC using an external reference. Products were identified by retention time and peak enhancement with known samples.

In an alternative method, the product was collected in an ice-cooled, dry receiver flask. The crude reaction product may be analyzed by NMR and/or GLC, or it may be dried (anhydrous $MgSO_4$) and distilled to give pure nitrile.

***n*-Octanenitrile.** In the manner outlined above, 5.0 g (0.04 mol) of *n*-octanol was fed over 15% Cu/Al_2O_3 catalyst at a rate of 0.02 mL/min (0.1 mmol/min). Ammonia was introduced at 100 mL/min (4 mmol/min). The catalyst was maintained at 325 °C. The product was collected in a trap in an ice–water bath, taken up in acetone, dried (anhydrous $MgSO_4$), and distilled to yield 4.2 g (87%) of *n*-octanenitrile: NMR ($DCCl_3$) δ 2.3 (m, 2 H), 1.4 (m, 10 H), 0.9 (m, 3 H); this is identical with that of commercial material. The product contained only trace quantities of amine by GLC analysis.

Benzonitrile. Benzylamine (5.2 g, 0.05 mol) was allowed to react with ammonia under conditions identical with those above except that the catalyst was maintained at 300 °C. The product was collected at ice–water temperature, taken up in methylene chloride, dried (anhydrous $MgSO_4$), and distilled to give 4.5 g (89%) of benzonitrile. The product contained no more than trace impurities by GLC, and its NMR ($DCCl_3$) spectrum was identical with that of commercial material; δ 7.55 (m).

Acknowledgment. We thank E. Battistelli and D. Tabak for experimental assistance and Drs. A. Zweig, R. L. Potter, and R. Proverb for helpful discussions.

Registry No. Benzaldehyde, 100-52-7; benzyl alcohol, 100-51-6; benzylamine, 100-46-9; *p*-methoxybenzaldehyde, 123-11-5; ethanol, 64-17-5; ethyl acetate, 141-78-6; butanol, 71-36-3; octanol, 111-87-5; octanal, 124-13-0; octylamine, 111-86-4; dioctylamine, 1120-48-5; benzonitrile, 100-47-0; *p*-methoxybenzonitrile, 874-90-8; acetonitrile, 75-05-8; butyronitrile, 109-74-0; octanenitrile, 124-12-9; ammonia, 7664-41-7; octane, 111-65-9.