Tetrahedron Vol. 40, No. 9, pp. 1487 to 1490, 1984
Printed in Great Britain.

0040-4020/84 $3.00 + .00

ON THE EXCHANGE OF CYANIDE WITH ACETONITRILE. A TEST OF THEORETICAL CALCULATIONS

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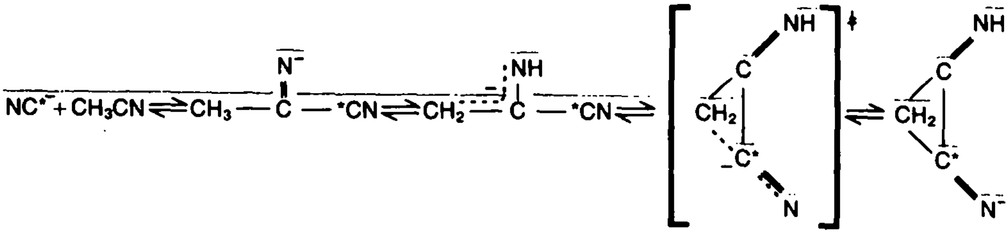
(*Received in USA* 13 *July* 1983)

Abstract - The theoretically predicted formation of an adduct between cyanide and anhydrous acetonitrile was tested experimentally; no evidence for such a complex was found. The previously reported radioactivity loss in the reactions of cyanide - ^{14}C in acetonitrile solutions was possibly due to protonation and loss of hydrogen cyanide, since no exchange between cyanide and acetonitrile was evidenced within the sensitivity limits of ^{13}C labelling. Potassium cyanide and carbonate in the presence of 18-crown-6 ether catalyze the H/D exchange between acetonitrile and trideuteroacetonitrile.

Molecular orbital calculations, both ab initio and semi-empirical, have been used to predict reaction mechanisms, especially when experimental study of the latter cannot be easily devised.[2] We have been involved in finding cases in which experiments can be devised to test predictions of calculations.[3] We report here on another application of this approach.

Semi-empirical MNDO calculations with full geometry optimization predicted[4] that cyanide (**1**) and acetonitrile (**2**) form the very stable adduct **3**, or the tautomer of the latter, **4**. The cyano and imino carbons can exchange places via the cyclic transition state **5** and intermediate **6** (equation 1)[4] This scheme was proposed to rationalize the loss of radioactivity in the product from the reaction of benzyl bromide with potassium cyanide-^{14}C in acetonitrile containing 18-crown-6 ether, reported by two of us.[5]†



(1)

1 **2** 0#   **3** −30.9#   **4** −36.6#   **5** 6.4#   **6** 1.6#

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†Noting that the errors inherent to the MNDO method, as well as neglect of solvation, affect their results, the authors in ref. 4 suggested that the calculations be used as a guide for further experiments.

#Relative energy (Kcal/mole).

The energy profile calculated for equation 1 requires that 1 and 2 be fully converted to 4 (or 3). Therefore, we searched for 3 or 4 by ^{13}C-NMR. Formation of either 3 or 4 should shift upfield the signal of 1 by about 40 ppm,[6] while the methyl signal of 2 should show a large downfield shift. We observed no change whatsoever upon adding 2 to a solution of potassium cyanide and crown ether in methanol (Table 1, entries 1-5). This could be explained by the solvation energy of 1 in methanol being greater than the exothermicity of formation of 3 and 4. (The free energy of transfer of 1 from methanol to acetonitrile is 6.3 Kcal/mole.)[7] A similar chemical shift was observed, however, for cyanide in dry acetonitrile (Table 1, entry 6). The small change for acetonitrile relative to methanol solution is in the direction opposite to the predictions for 3 and 4. Also, addition of methanol (Table 1, entries 9,10) or water (Table 1, entries 7,8) produces a small upfield shift for the cyanide signal of KCN in acetonitrile solution, instead of the large downfield shift expected for breaking the adduct (3 or 4). Finally, no chemical shift changes were noted after heating the solutions for several hours at 60-75°, indicating that 3 and 4 are not formed with a sizeable energy barrier either.

Table 1. Carbon-13 Spectra of Cyanide-Acetonitrile Solutions

No.	Solvent (Composition, v:v)	Crown ether/CN$^-$ (molar)	MeCN/CN$^-$ (molar)	Chemical Shifts, ppm[a] CN$^-$	CH_3-CN		MeOH	Crown Ether
1.	MeOH[b]	0	0	160.79[c]	-	-	48.27[c]	-
2.	MeOH[b]	1.2	0	160.55[d]	-	-	48.30[d]	69.75[d]
3.	MeOH[e]	-	-	-	-0.84[d,e]	116.45[d,e]	48.30[d]	-
4.	MeOH[b]	1.2	1.0	160.50[d]	0.2[d,f]	f	48.30[d]	69.75[d]
5.	MeOH[b,g]	1.2	8.5	160.75	-0.42	f	48.56	69.96
6.	CH_3CN[h,i]	1.6[j]	~160	165.25	0.46	116.99	-	69.65
7.	CH_3CN-H_2O(95:15)[k]	1.6[j]	~160	162.39[l]	0.46	117.19	-	69.65
8.	CH_3CN-H_2O(87:13)[k]	1.6[j]	~160	162.58[l]	0.59	117.64	-	69.72
9.	CH_3CN-MeOH(95:5)[k]	1.6[j]	~160	161.02[l]	0.40	116.93	48.26	69.65
10.	CH_3CN-MeOH(83:17)[k]	1.6[j]	~160	160.63[l]	0.27	116.93	48.45	69.65
11.	H_2O[m]	-	-	164.59[c]	-	-	-	-
12.	0.2 N aq. KOH[m]	-	-	165.31[c]	-	-	-	-

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[a] Measured from external (coaxial) $CDCl_3$ (central resonance taken as δ 77.00) unless otherwise stated; the signal for TMS is sometimes not separated from the acetonitrile methyl signal.

[b] 0.3M KCN

[c] From external TMS dissolved in $CDCl_3$ (δ$CDCl_3$ 77.04-77.06).

[d] From methanol (solvent) taken as δ 48.30.

[e] CH_3CN alone (1M) in methanol.

[f] The signal was too weak for accurate chemical shift determination.

[g] No changes were observed in the spectrum after heating the sample for 21 h at 65°.

[h] Estimated 0.1M KCN (weighed for 0.14M KCN; incomplete dissolution).

[i] No changes were observed in the spectrum after heating the sample for 9 h at 75°.

[j] Weighed for a 1.4 ratio (see h).

[k] Obtained from the solution in entry 6, by addition of water or methanol.

[l] Partial hydrolysis (or methanolysis) of KCN, with formation of HCN, might explain the difference from entry 6.

[m] 0.13M KCN.

In another series of experiments, we checked the exchange of cyano groups between 1 and 2, predicted by eq. 1 and reported earlier.[5] We observed no change in the ^{13}C-NMR signal intensities of solutions of potassium cyanide 90%-^{13}C and unlabeled 2 after heating for several hours (Table 1, entry 6, footnote i). Also, the ^{13}C-NMR and mass spectra of 2 distilled from the mixture showed no isotope enrichment (see Experimental Section).

The radioactivity loss observed before[5] in 1-^{14}C, and the presence of radioactivity in 2 (initially unlabeled) distilled from the reaction mixture might be due to formation of hydrogen cyanide which co-distilled with the solvent. We discovered that upon treating a mixture of 2 and 2-d_3 with potassium cyanide-crown ether under reflux, hydrogen scrambling occurred with a half-life of 2.55 h. (see Table 2, columns 2-6 and the Experimental Section). Potassium carbonate with one equivalent of crown ether catalyzes hydrogen scrambling in anhydrous acetonitrile one order of magnitude faster than 1 (Table 2, columns 7-9). For comparison, hydrogen/deuterium exchange between acetonitrile and deuterium oxide requires 12 h of reflux in the presence of calcium hydroxide[8], a much stronger base in water ($K_b = 3.74 \times 10^{-3}$)[9a] than cyanide ($K_b = 3.65 \times 10^{-7}$),[9b] or carbonate ($K_b = 3.21 \times 10^{-6}$).[9]

Table 2. Hydrogen Exchange Between CH_3CN and CD_3CN[a]

Base	KCN					K_2CO_3[b]		
Time (min.)	0	33	64	305	∞[c]	0	60[d]	∞[c]
CH_3CN, %	54.9	49.6	46.8	26.4	16.76	50.7	13.6	13.40
CH_2DCN, %	0.0	3.6	7.0	31.0	40.91	0.0	40.0	38.35
CHD_2CN, %	0.7	5.0	7.7	24.2	33.30	1.4	35.3	36.61
CD_3CN, %	44.4	41.8	38.4	18.4	9.03	47.9	11.1	11.65
Conversion, %[e]	0.0	10.8 ±2.8	19.2 ±2.1	74.2 ±1.1	100.0	0.0	100.4 ±2.4	100.0

[a] The molar ratio salt: crown ether: acetonitrile was 1:1:18.5; isotope distribution was determined by mass spectrometry. [b] Since one equivalent of crown ether was used in each case, an ion pair $[K^+.^-OCOO^-]$ might be the predominant species in the solution of potassium carbonate. [c] Calculated statistical label distribution. [d] Composition did not change after 300 min. total reaction time. [e] Degree of advancement toward statistical distribution.

On longer reaction time (20 h), the solutions became yellow and viscous, presumably because of acetonitrile self-condensation to 3-aminocrotononitrile and oligomers of the latter.[10] The acetonitrile oligomers are much stronger acids than 2 and protonate 1 more easily. Hydrogen cyanide thus formed co-distills with the solvent.

In conclusion, the reaction pathway predicted by equation (1)[4,5] does not operate, unless as an extremely slow process, which could be evidenced by ^{14}C-labeling, but not by ^{13}C-labeling.[11]

EXPERIMENTAL

Carbon-13 NMR analyses were performed on a JEOL FX-90Q spectrometer. Mass spectra were obtained on a CEC-103 instrument.

All reagents were opened and stored under nitrogen in a Vacuum-Atmospheres dry-box. All reactions were performed in the dry-box as well. Potassium cyanide, min. 90%-^{13}C, and acetonitrile-d_3, 99% were purchased from Merck, Sharp and Dohme; acetonitrile and 18-crown-6 ether, from Aldrich. Acetonitrile (Gold Seal) was stored over molecular sieves 3A and distilled before use.

Samples for NMR were prepared by magnetically stirring the components in the ratios shown in the tables in capped vials for 1-2 h. Traces of undissolved solids, if present, were allowed to settle and the clear solution was transferred to NMR tubes. Labeled (90%-^{13}C) KCN was used in all experiments.

The H/D exchanges and the attempted CN exchanges were performed at the boiling temperature under reflux with stirring. Solid KCN was present in all experiments. Samples were taken at the intervals shown in the text and Table 2 by distillation into a flask cooled in dry ice, and were used for NMR and MS analyses.

The attempted CN exchanges were performed in the same manner. After no increase in intensity of the CN signal for **2** was seen for experiments in entries 5 and 6 of Table 1, two more samples were prepared with $K^{13}CN$:crown ether:**2** 1:2.5:38 (A, reflux time 3 h) and 1:1.2:16.4 (B, reflux time 2 h).

The intensity of M+1 peak was used for the determination of isotope enrichment in **2** distilled from the mixture. Initial M+1: 2.65%, final: 2.70 (A) and 2.65% (B); calculated for complete scrambling: 5.04 (A), and 7.75% (B).

Sample A was also subjected to quantitative ^{13}C-NMR analysis. Seven spectra were accumulated on this sample, alternating with seven spectra of the unreacted acetonitrile. The ratio of CN to CH_3 in the integrated spectra was compared for the two samples. The result (CN/CH_3 after treatment: CN/CH_3 before) was 0.998 (average deviation 0.073).

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