Mass Spectral Mechanisms. N-Alkyl-3-cyano-1,4-dihydropyridine Fragmentation. Kinetic Isotope Effects for Expulsion of Deuterium from the 4 Position and Transition from Quantal to Purely Classical Isotope Effect[1-3]

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Abstract: The mass spectra of N-alkyl-3-cyano-1,4-dihydropyridines-4-*d* show elimination of a protium or deuterium atom from the 4 position of the molecular ion as the primary decomposition process. The ratio of rate constants for loss of these hydrogen and deuterium atoms is found to be inversely related to the ionizing voltage (k_H/k_D = 1.25 − 7.8 at voltages near the appearance potential). Most of the fragments are formed from the pyridinium ions resulting from loss of a hydrogen atom from the 4 position of the dihydropyridine. Rearrangement leads to nicotinonitrilium ion (*m/e* 105). In order for N-methyl-3-cyanopyridinium ion to form *m/e* 105, it must expel methylene (CH_2) as a neutral fragment; this process is relatively unfavorable (2.8% of base peak). In the N-ethyl analog, expulsion of a thermodynamically stable ethylene molecule gives a *m/e* 105 peak which is the second most intense in the spectrum (95% of base peak). Deuterium labeling in the N-alkyl compounds methyl, ethyl, and *n*-butyl established that the hydrogen atom transferred to the ring to form the *m/e* 105 ion is preferentially from the β-carbon atom of the alkyl group, probably *via* a four-center transition state. The opening of the ring was found to occur by cleavage of the 1,2 and 5,6 bonds. Mass spectra of the N-*n*-propyl and N-*n*-pentyl analogs and of 1,4,4-trimethyl-1,4-dihydropyridine are also discussed.

Mechanisms of reactions of ions formed by electron bombardment of molecules within the mass spectrometer are diverse and interesting. We have studied the fragmentation of some N-alkyl-3-cyano-1,4-dihydropyridines for two reasons. (1) Hydrogen atom loss from the 4 position of the molecular ion should be very favorable, leading to a stable, aromatic, *even-electron* pyridinium ion. The further fragmentation of such ions should be very interesting in comparison with aromatic *radical* ions which are formed as the molecular ions from aromatic molecules. (2) The expected overwhelming predominance of hydrogen atom loss at low bombarding energy (voltage) should make it possible to determine competitive kinetic isotope effects for loss of D *vs.* H from the 4 position of a 4-monodeuterated dihydropyridine in the absence of any other appreciable fragmentations. The ion intensities under these conditions directly measure the relative rate constants k_H/k_D. Our results indicate that these assumptions are correct, and we have learned a good deal about the fragmentation mechanisms by studying specifically deuterated molecules. The isotope effects observed are interesting because they are for unimolecular loss of hydrogen atoms, in contrast to hydrogen transfers, which have been extensively studied in thermal reactions of molecules.

Results and Discussion

Fragmentation Patterns of N-Alkyl-3-cyano-1,4-dihydropyridines. At high ionizing energies, about 76 ev, the molecular dihydropyridinium ions decompose readily to form aromatized N-alkyl-3-cyanopyridinium ions by expelling a hydrogen atom, as evidenced by the strong peak intensities at M − 1 in the mass spectra of all N-alkyl-3-cyano-1,4-dihydropyridines examined. In addition, at this energy secondary fragmentation processes also become prominent. Some of these processes involve ring opening of the pyridinium ion and also of the molecular ion as part of the decomposition mechanism. It has been shown[5] that in the mass spectrum of pyridine, there is a peak corresponding to the loss of HCN molecule from the molecular ion. In the case of N-methyl-3-cyano-1,4-dihydropyridine, mol wt 120 (Figures 1 and 2), a small amount of ions is found at *m/e* 92, which could arise from the elimination of an HCN molecule from the 3 position of the pyridinium ion (*m/e* 119), as evidenced by a metastable peak at *m/e* 71.1. Unfortunately, it is not easy to ascertain whether the resulting ion remains a cyclic, pyridynium ion or becomes linear. The trideuteriomethyl analog showed that the pyridinium ion (*m/e* 122) splits out HCN molecule. The hydrogen atom in the HCN molecule seems to originate from the 2 and 4 positions, as was shown by specific deuterium labeling. In the mass spectrum of N-methyl-3-cyano-1,4-dihydropyridine-2-*d*, both *m/e* 93 and 92 peaks are present, although the peak at *m/e* 93 is about 15% more intense; the peak at *m/e* 93 could arise from a concerted elimination of H and CN from the 3 and 4 positions. The pyridinium ion also decomposes to form the 3-cyanopyridine cation (*m/e* 104) by ejecting the alkyl group.

Decomposition processes which involve ring opening produce fragments at *m/e* 78, 77, 51, and 42. The peak at *m/e* 42, $HCNCH_3^+$, could arise analogously to the

(1) Previous papers: S. J. Weininger, Vu Thi Mai, and E. R. Thornton, *J. Amer. Chem. Soc.*, **86**, 3732 (1964); E. P. Smith and E. R. Thornton, *ibid.*, **89**, 5079 (1967).

(2) Supported in part by Public Health Service Grant GM-10693.

(3) For further details, *cf.* B. J.-S. Wang, Ph.D. Dissertation in Chemistry, University of Pennsylvania, 1966; submitted to University Microfilms.

(4) Esso Fellow, 1964–1965; Allied Chemical Fellow, 1965–1966.

(5) J. Momigny, J. Urbain, and H. Wankenne, *Bull. Soc. Roy. Sci. Liege*, **34**, 337 (1965).

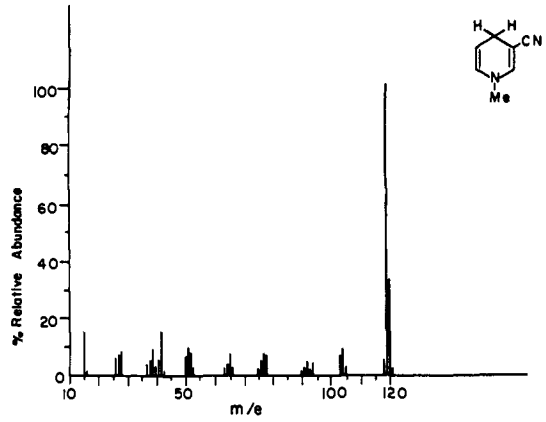


Figure 1. Mass spectrum of N-methyl-3-cyano-1,4-dihydropyridine at 76 ev.

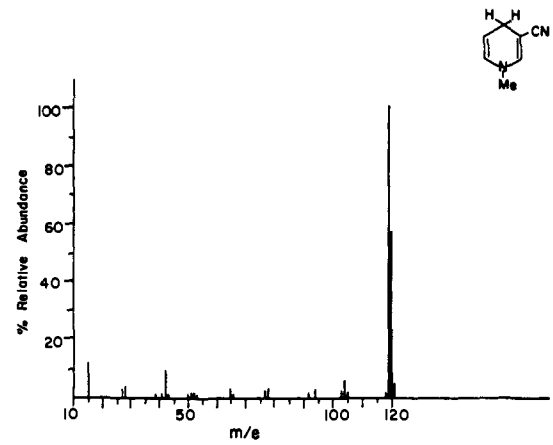


Figure 2. Mass spectrum of N-methyl-3-cyano-1,4-dihydropyridine at 15 ev + *ca.* 5.6 (correction) = 20.6 ev.

formation of the thermodynamically stable HCN molecule from the molecule ion of pyridine;[5] in the methyl-d_3 sample the corresponding peak is shifted to *m/e* 45, leaving the other fragment ions at *m/e* 78, 77, and 51. On the other hand, N-methyl-3-cyano-1,4-dihydropyridine-4-*d* yields peaks at *m/e* 79, 78, 77, 52, and 51 (loss of either H or D from the 4 position being possible) while leaving the former peak at *m/e* 42.

The question of whether ring opening occurs at the 1,2 bond or at the 1,6 bond is resolved by the 2-deuterio compound, the ring-nitrogen-containing fragment of which still remains at *m/e* 42, with the peak at *m/e* 78 promoted to *m/e* 79. This implies that the 1,2 bond is broken. Of course, the peak at *m/e* 42 may originate from either the parent ion or the pyridinium ion. The peak at *m/e* 78 can best be rationalized as originating from direct decomposition of the parent ion, while the peak at *m/e* 77 may contain ions from fragmentation of *m/e* 78 (loss of a hydrogen atom) and from ring opening of the pyridinium ion (the small metastable ion peak at *m/e* 14.8 (119 → 42) could explain the fragment of *m/e* 77, for if *m/e* 42 can form from *m/e* 119, then so should *m/e* 77). Further decompositions of these daughter ions are observed, as evidenced by a metastable peak found at *m/e* 33.3 (78 → 51), corresponding to the loss of a neutral HCN molecule from the fragment at *m/e* 78. One can also envision loss of a CN group from *m/e* 77 to produce the same ion at *m/e* 51.

The relatively intense methyl peak at *m/e* 15 (*m/e* 18 for the methyl-d_3 compound) probably cannot be explained by the loss of the methyl cation upon fragmentation of the pyridinium ion to form a nicotinonitrile molecule, since the charge distribution during the decomposition would very probably favor the formation of a pyridine cation over a methyl cation. Another source of the methyl cation could be the decomposition of the fragment $CH_3N{\equiv}CH^+$, eliminating a neutral HCN molecule. This process, made favorable by formation of a very stable neutral fragment, was also observed from an isomeric fragment, $CH_3C{\equiv}NH^+$, from 3,6-dimethyl-*s*-tetrazine.[6]

Another ring-opening process results in an ion at *m/e* 65. From the deuterated compounds, it was found that for the trideuteriomethyl sample the peak shifted from *m/e* 65 to 67, for the sample monodeuterated at the 2 position there was a partial increase to *m/e* 66 (about 50%), and for the sample monodeuterated at the 4 position there was also a partial increase to *m/e* 66 (about 50%). The data can best be rationalized if this ion fragment includes the ring nitrogen atom, a methylene group from the N-methyl group, and the 2, 3, and 4 skeletal carbon atoms to form conjugated ions $CH_2{=}N^+{=}C{=}C{=}CH\cdot$ and $CH_2{=}N^+{=}CHC{\equiv}C\cdot$. The formation of these ions is accompanied by a metastable ion at *m/e* 46.0 (92 → 65) and the path can be traced to the loss of an HCN molecule from $CH_2{=}N^+{=}CHCCN{=}CH\cdot$. The fragmentation pattern of the N-methyl-3-cyano-1,4-dihydropyridine is summarized in Figure 3.

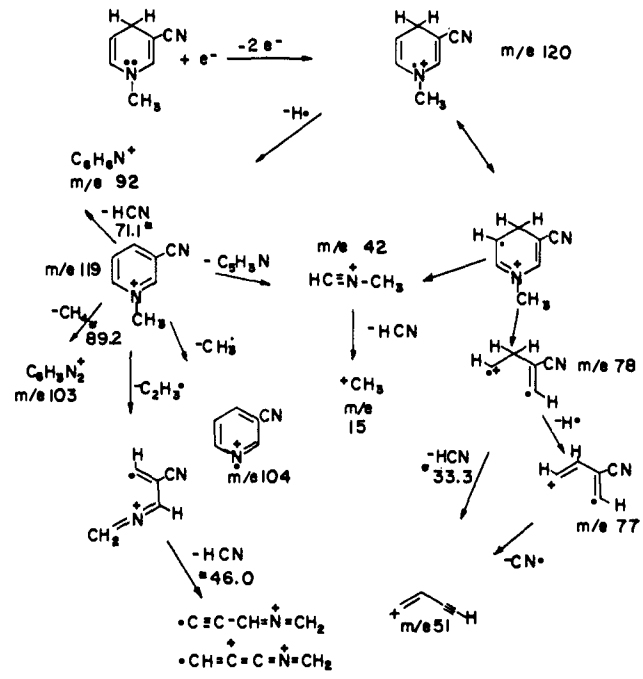


Figure 3. Mass spectral fragmentation pattern of N-methyl-3-cyano-1,4-dihydropyridine; asterisk denotes *m/e* of observed metastable peaks.

As expected, when the N-alkyl chain is longer, the possibility for it to participate in the decomposition increases. Processes which are energetically unfavorable in the N-methyl compound play an important part in the decomposition. In the spectrum of N-ethyl-3-cyano-1,4-dihydropyridine (Figure 4), the most noticeable

(6) S. J. Weininger and E. R. Thornton, *J. Amer. Chem. Soc.*, 89, 2050 (1967).

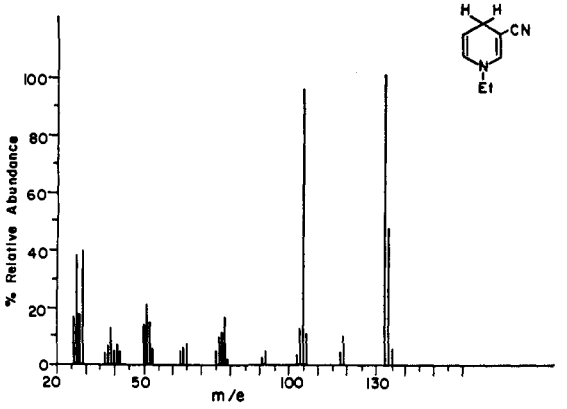


Figure 4. Mass spectrum of N-ethyl-3-cyano-1,4-dihydropyridine at 76 ev.

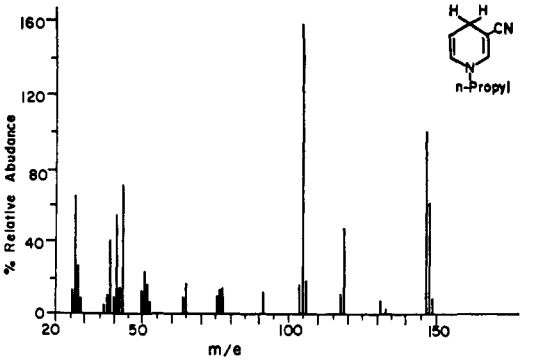


Figure 5. Mass spectrum of N-*n*-propyl-3-cyano-1,4-dihydropyridine at 76 ev.

change in the decomposition path is the ease of loss of an ethylene molecule from the N-ethyl-3-cyanopyridinium ion, with transfer of one hydrogen atom to form N-protonated 3-cyanopyridinium ion, *m/e* 105. The intensity of the latter ion is almost equal to that of the original pyridinium ion; presumably this unusually high intensity is a result of (1) the two thermodynamically stable fragments formed, ethylene and the new pyridinium ion, and (2) the stability of this new pyridinium ion to further decomposition. The primary driving force favoring this mode of decomposition for the N-ethyl compound can be traced to the stable neutral ethylene molecule formed, as compared with methylene from the N-methyl analog.

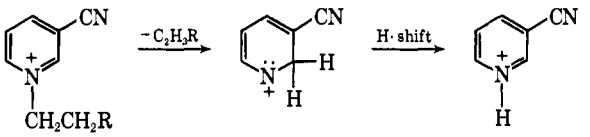
The origin of the proton transferred to form the protonated 3-cyanopyridinium ion apparently is not from any carbon atom exclusively (Table I), but the

Table I. Deuterium Transfer during the Rearrangement Decomposition of N-Alkyl-3-cyanopyridinium Ions[a,b]

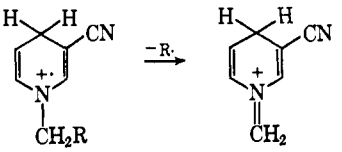
Alkyl group	Ionizing voltage	Intensity at *m/e* 105	Intensity at *m/e* 106	D transferred	D transferred, %
n-Butyl	76	68.2	1.5	...	...
n-Butyl-4,4,4-d_3	76	52.4	10.2	9.1	14.5
Ethyl	76	45.9	1.2	...	...
Ethyl-1,1-d_2	76	41.5	10.5	9.4	18.1
Ethyl-2,2,2-d_3	76	29.1	55.3	54.6	65.4
n-Butyl	15	58.4	2.1	...	...
n-Butyl-4,4,4-d_3	15	50.3	10.6	8.8	14.6
Ethyl	15	56.5	0.9	...	...
Ethyl-1,1-d_2	15	90.5	22.3	20.9	18.5
Ethyl-2,2,2-d_3	15	25.6	62.3	62.3	63.5

[a] The numbers listed in the table are arbitrary peak height units including the natural stable isotopes and are consistent only within each sample. [b] Deuterium transfer is calculated by taking the ratio of the corresponding protiated compound, *m/e* 106 over *m/e* 105, and multiplying the ratio by the intensity of the deuterated compound at *m/e* 105. This product is subtracted from the deuterated compound intensity at *m/e* 106 to obtain D transferred.

protons at the β-carbon atom seem to be predominant in the process, *i.e.*, a four-membered-ring transition state is favored over a three-membered- or six-membered-ring transition state. However, with the data available one cannot readily rule out the possible interaction of the 2 position with the hydrogen atom from the alkyl group. In any case, the final ion probably would be the stable pyridinium ion, resulting from hydrogen shift to the nitrogen atom.



Another process which is enhanced by the change of alkyl group is formation of the cross-conjugated ion at *m/e* 119. This process becomes more favored because methyl radical expulsion from the N-ethyl compound requires less energy than expulsion of a hydrogen atom from the N-methyl analog. The structural assignment is reinforced by the mass spectra of deuterated samples.



R = H, CH_3

The spectrum of N-ethyl-1,1-d_2-3-cyano-1,4-dihydropyridine shows that the corresponding peak has shifted two mass units higher, from *m/e* 119 to 121. On the other hand, the ethyl-2,2,2-d_3 analog produces a fragment at *m/e* 119 and monodeuteration at the 4 position promotes the fragment from *m/e* 119 to 120.

Similarly to the N-methyl analog, the ring-opening process at the 1,2 bond of the N-ethyl compound yields fragments at *m/e* 78, 77, and 51, along with the ion $HCN^+CH_2CH_3$. This latter ion does not have any significant intensity; however, its daughter ions, $CH_2CH_3^+$ and HCN^+, are very intense. The labeled ethyl analogs give rise to peaks at *m/e* 31 from the ethyl-1,1-d_2 sample and *m/e* 32 from the ethyl-2,2,2-d_3 sample, respectively. The formation of stable fragments is probably responsible for this decomposition.

The spectrum of N-*n*-propyl-3-cyano-1,4-dihydropyridine (Figure 5) shows essentially the same fragmentation patterns as those of the N-ethyl analog, except the relative intensities of the fragments are shifted, particularly the peaks at *m/e* 119 and at *m/e* 105. This observation seems quite reasonable, because the corresponding neutral fragments that accompany these ions are energetically more stable; for example, the neutral fragment from formation of the ion at *m/e* 119 is now an ethyl radical instead of a methyl radical and the neutral

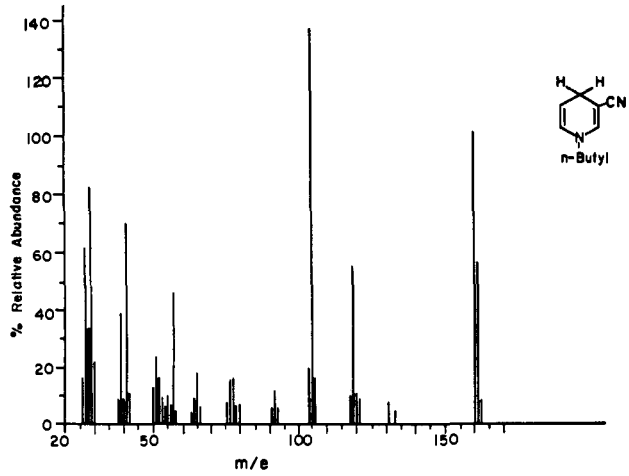


Figure 6. Mass spectrum of N-*n*-butyl-3-cyano-1,4-dihydropyridine at 76 ev.

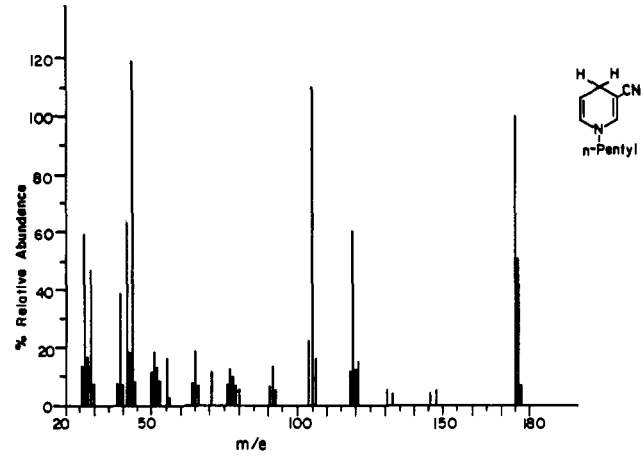
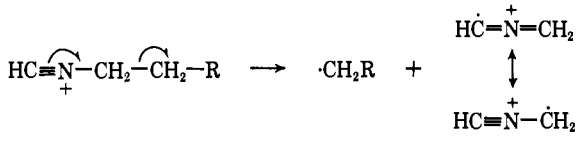


Figure 7. Mass spectrum of N-*n*-pentyl-3-cyano-1,4-dihydropyridine at 76 ev.

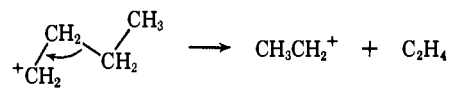
fragment from formation of the ion at *m/e* 105 is propylene instead of ethylene.

During the ring opening, the fragment containing the ring nitrogen, $HCNR^+$, may decompose to form the $CH_3CH_2CH_2^+$ and HCN^+ ions. In addition, with the chain of three carbon atoms, there is the possibility of another favorable process, cleavage of the β bond from the nitrogen atom of form a new ammonium ion. This transition is shown to be likely by the very intense peak



at *m/e* 41. Of course, part of this peak can be attributed to an alternative process where the *n*-propyl ion ejects a hydrogen molecule to form the propenium ion, CH_3-$CH{=}CH^+$. This contribution can be estimated to be minor by examining the N-*n*-butyl spectrum where the analogous *n*-butyl ion, *m/e* 57, loses a hydrogen molecule to form butenium ion, *m/e* 55, which is not at all prominent. Moreover, in the spectrum of the N-*n*-butyl analog, the peak at *m/e* 41 is again very strong, which points to a decomposition process similar to that of the N-propyl compound. In fact this peak, *m/e* 41, is observed to be very intense in every spectrum studied where the alkyl group is longer than two carbon atoms. The charge distribution in the rearrangement decomposition apparently favors overwhelmingly the localization of the charge in the ammonium fragment, as is shown by the absence of ions at *m/e* values corresponding to the alkyl fragments in each case.

In addition to the decomposition described above, the breakdown pattern for N-*n*-butyl-3-cyano-1,4-dihydropyridine (Figure 6) also shows further fragmentation of the *n*-butyl cation, *m/e* 57, to form an ethylene molecule and an ethyl cation at *m/e* 29. This hypothesis is



further verified by the presence of an intense peak at *m/e* 32 from the *n*-butyl-4,4,4-d_3 analog. For the N-*n*-pentyl compound (Figure 7), however, similar decomposition apparently leads to formation of a neutral ethylene molecule or a cyclopropane molecule, giving ions at *m/e* 43 and 29, respectively; in fact, both peaks are observed in high intensities.

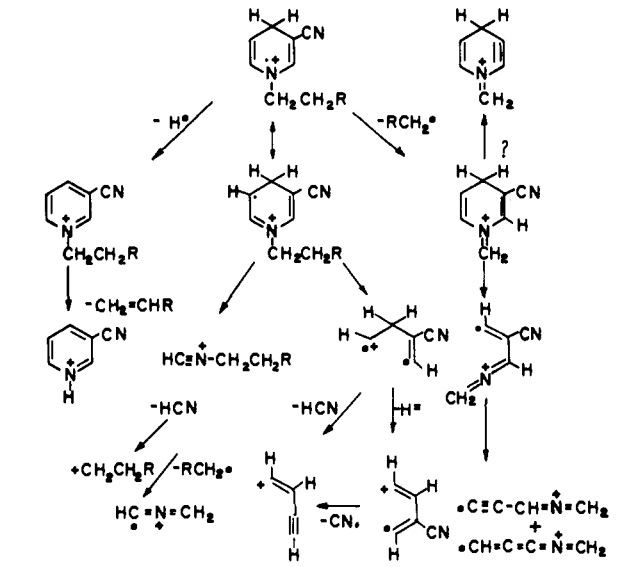
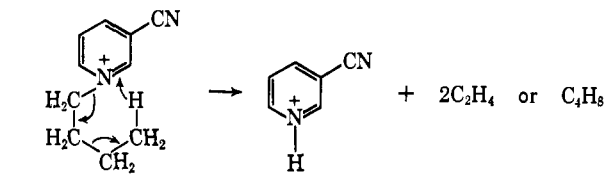


Figure 8. General fragmentation pattern for N-alkyl-3-cyano-1,4-dihydropyridines.

It is of interest to point out that in the rearrangement path involving the formation of the protonated 3-cyanopyridinium ion, the possible six-centered transition state does not play an important part in the rearrangement (see Table I).



The remaining parts of the spectra for the *n*-butyl and *n*-pentyl compounds show very similar fragmentation to that of the ethyl analog; therefore, a summary of these fragmentation mechanisms may be presented (Figure 8).

Kinetic Isotope Effects. The intramolecular competitive isotope effects for loss of H *vs.* D from the 4 positions of N-alkyl-3-cyano-1,4-dihydropyridines could be

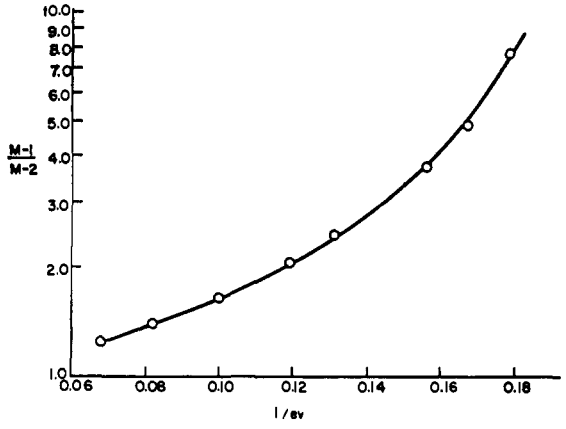
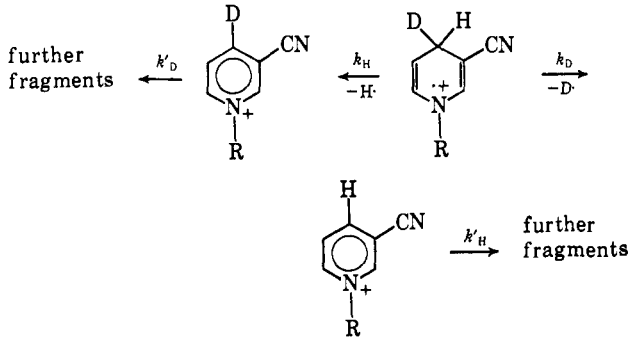


Figure 9. Dependence of isotope effect on ionizing electron energy for N-methyl-3-cyano-1,4-dihydropyridine-4-*d*.

determined directly, since the overwhelming process in the fragmentation pattern is for the molecular ion to aromatize to form a pyridinium ion by expelling a hydrogen atom (not a proton), and, furthermore, at the low ionizing voltages that are of particular interest (the appearance potential region) the aromatization becomes essentially the only process in the decomposition path of the parent ion. In the case of N-alkyl-3-cyano-1,4-dihydropyridines-4-*d*, specifically monodeuterated at the 4 position, a competitive loss of a hydrogen atom or a deuterium atom occurs. The fragmentation steps are



straight forward and without other competitive decomposition processes from the molecular ion. At low voltages, the further decompositions, k_D' and k_H', become negligible and the expression for kinetic isotope effects can be written simply as

$$k_H/k_D = (M - 1)/(M - 2) \quad (1)$$

where M − 1 is the intensity of the peak corresponding to the molecular ion minus a hydrogen atom and M − 2 is the intensity of the peak corresponding to the molecular ion minus a deuterium atom. Quantitatively, the three peaks M, M − 1, and M − 2 together constitute *ca.* 96, 98, and >99% of total ionization (% Σ_{15}) at *ca.* 13, 12, and 11 ev, respectively, for the methyl compound. We have recently observed a preliminary isotope effect of 16.5 for the N-methyl compound at *ca.* 10 ev. The ratio (M − 16)/(M − 17), for the negligible process of loss of methyl from the pyridinium ion of the N-methyl compound, is very nearly equal to the ratio (M − 1)/(M − 2) at each voltage, demonstrating that k_H' very nearly equals k_D'. The isotope effects for a series of N-alkyl-substituted (methyl, ethyl, *n*-propyl, and *n*-butyl) 1,4-dihydropyridines were determined and similar behavior was found among these homologs (Table II). The hydrogen–deuterium isotope effects were found to range from 1.25 to 7.85, depending on the bombarding electron energy. A smooth dependence of the isotope effects on the bombarding energies is shown by plotting the logarithm of the observed isotope effects *vs.* the reciprocal of the bombarding electron energies, as shown for the N-methyl compound in Figure 9.

Table II. Isotope Effects for N-Alkyl-3-cyano-1,4-dihydropyridines-4-*d* at Ionizing Voltages near the Appearance Potential[a,b]

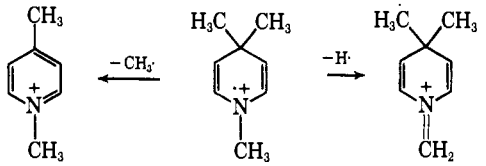
Ionizing potential, ev	Methyl	Ethyl	*n*-Propyl	*n*-Butyl
11.2	7.85	6.23	...	...
11.6	4.99	4.31	5.68	6.08
12.0	3.86 ± 0.02	3.35	4.44	4.30
13.2	2.49 ± 0.02	2.47 ± 0.05	2.64 ± 0.06	2.71 ± 0.09
14.0	2.08 ± 0.04	2.12 ± 0.06	2.24 ± 0.02	2.30 ± 0.07
15.6	1.65 ± 0.03	1.69 ± 0.02	1.84 ± 0.07	1.83 ± 0.03
17.8	1.39 ± 0.04	1.53 ± 0.07	1.68 ± 0.04	1.62 ± 0.05
20.1	1.25 ± 0.02	1.45 ± 0.05	1.56 ± 0.06	1.51 ± 0.02

[a] The ionizing voltages listed above are approximately corrected by adding 5.6 ev to the measured values (argon as internal standard). [b] The isotope effects listed above are corrected for some dideuterated species at 2 and 4 positions (for details see Experimental Section).

In eq 1 it is assumed that the hydrogen atom expelled from the molecular ion would originate solely from the 4 position. This is reasonable because, by considering the energy requirements, the formation of an aromatic pyridinium ion, if not the exclusive process, must be overwhelmingly favored over the removal of a hydrogen atom from other positions of the ring to form a 1,4-dihydropyridinium ion. In addition, the breaking of a tetrahedral, sp^3, carbon–hydrogen bond is favored over the breaking of a trigonal, sp^2, carbon–hydrogen bond by[7] about 4–8 kcal mole^{-1}. Setting aside the possible contribution from the alkyl protons for the moment, it is expected that when the ionization voltage is decreased, the contribution from the ring protons will decrease accordingly. As a result the corresponding ratio of M − 1 to M − 2 will also decrease. However, the opposite trend is observed at the lower ionizing energies, which would mean that (1) the contribution of the ring protons to the hydrogen atom loss is negligible, (2) the contribution from the actual isotope effect is increasing as the ionizing energy decreases, while the decreasing contribution from loss of ring protons is more than offset by the increase of the actual isotope effect, or (3) there is further loss of a hydrogen atom from the pyridinium ion to form a M − 2 fragment which could contribute to a damping effect on the isotope effect at the higher ionizing energies, and this damping effect decreases at lower ionizing voltages. A number of experiments were performed to examine the possibility of ring hydrogen atom contamination in the isotope effect measurements. A great deal of effort was made to synthesize N-methyl-3-cyano-1,4-dihydropyridine-4,4-d_2 by the reduction of the salt in D_2O and the oxidation of the product with chloranil. Five such redox cycles were carried out, but afforded no higher than 85% deuteration at the 4 position; therefore, this method (observing

(7) B. E. Knox and H. B. Palmer, *Chem. Rev.*, **61**, 247 (1961).

only M − D fragments from the dihydropyridine-4,4-d_2) was abandoned. The mass spectra of 1,4,4-trimethyl-1,4-dihydropyridine were taken at 76 ev and at low ionizing voltages and showed that the predominant process is the loss of a methyl radical to form the corresponding pyridinium ion at *m/e* 108, while the loss of a hydrogen atom to give *m/e* 122 (M − 1) was very small and disappeared completely at about 14.5–15.5 ev. Even in this case, the loss of a hydrogen atom would probably occur at the N-methyl group to produce the cross-conjugated, even-electron ion shown. Loss of a vinyl proton would probably require even higher bombarding energies.



m/e 108 *m/e* 122

In the system studied, the cyano group at the 3 position conceivably might facilitate the loss of the neighboring hydrogen atom at the 2 position. This was shown to be unlikely by deuterium labeling at the 2 position; the mass spectrum of this sample showed essentially no M − 2 (no loss of deuterium atom) at 76 ev. Furthermore, possibility 3 is shown to be a small contribution by the observation of essentially no M − 3 peak for samples deuterated at the 2 or 4 position (for the N-methyl-4-*d* compound, (M − 3)/(M − 1) is *ca.* 0.03 at *ca.* 25 ev, falling to zero before *ca.* 16 ev); similarly, there was negligible M − 2 contribution for the undeuterated N-methyl compound (for example, (M − 2)/(M − 1) is *ca.* 0.02 at *ca.* 20 ev, falling to zero before *ca.* 14 ev).

In order to show that the alkyl groups do not contribute to the loss of a hydrogen atom in the M − 1 measurements, a series of deuterated alkyl groups was incorporated into the 1,4-dihydropyridines. In the N-methyl-3-cyano-1,4-dihydropyridine system, the methyl group was replaced by a methyl-d_3 group. At both 76 and 13.5 ev there was essentially no contribution from loss of a deuterium atom (the small amount of M − 2 peak, 2–3% of the M − 1 peak, at 76 ev was not observed at 13.5 ev, which indicates that the peak may originate from the M − H_2 fragmentation which is observed in the protiated analog). Deuterium labeling was also carried out for the ethyl homolog, both methylene-d_2 and methyl-d_3, along with the terminal methyl-d_3 *n*-butyl homolog. It was found that there is no appreciable loss of the deuterium (M − 2) from any of the labeled positions at 76 or 15 ev.

Another source of extraneous hydrogen atoms might be the isomerization of the N-alkyl-3-cyano-1,4-dihydropyridine-4-*d* to either the 1,2- or the 1,6-dihydropyridine, or a mixture of both isomers. Since the mobility of a proton (*i.e.*, the hydrogen atom at the 4 position) is greater than that of a deuteron, one would expect a greater probability of forming the protiated methylene (CH_2) isomer; the rearranged species would produce too high an apparent isotope effect (too much hydrogen atom loss). As the voltage was decreased, the (M − 1)/(M − 2) ratio could conceivably change in such a way that the loss of a hydrogen atom xceeded the loss of a deuterium atom by severalfold. The dihydropyridine could isomerize either (1) by thermal excitation or (2) by electronic excitation during the ionization process.

Considering first thermal isomerization, the N-alkyl-3-cyano-1,4-dihydropyridines-4-*d* are stable at least at their boiling points (about 100° at 0.02 mm, 140° at 11 mm). In addition, a sample of N-methyl-3-cyano-1,4-dihydropyridine-2-*d* was heated at 140–150° for 30 min in an evacuated sealed tube and no change in its nmr and mass spectra was found. The isotope effects for N-methyl-3-cyano-1,4-dihydropyridine-4-*d* were measured at different inlet temperatures, 65–180°, and there was no dependence of their values on temperature. As for electronic excitation induced isomerization, if the process did occur, one would expect it to decrease with the electron bombarding energy. As a result one would expect a lower observed isotope effect. It is found that the observed trend of the isotope effects is just the opposite (high isotope effect at lower ionizing voltages). Furthermore, the mass spectrum of N-methyl-3-cyano-1,4-dihydropyridine-2-*d* yielded essentially no M − 2 peak. This at least rules out isomerization to the 1,2-dihydro isomer, which should be at least as likely as isomerization to the 1,6-dihydro isomer.

The foregoing evidence indicates strongly that the observed isotope effects actually result from the competitive rates of loss of a hydrogen atom or a deuterium atom from the 4 position.

For methane-*d*, the isotope effect (statistically corrected) is about 1.4 at 15 ev, but is approximately constant at 2.5 from 22 to 55 ev.[8–12] Isotope effects in McLafferty rearrangements are also reported to be independent of ionizing voltage.[13] A number of other studies of mass spectra of deuterated molecules exist, *e.g.*, ref 9–12 and 14–17, mostly, however, around 70 ev.

The quasi-equilibrium theory of mass spectra[18] provides two factors contributing to a competitive isotope effect such as for loss of H *vs.* D: (1) the activation energy (different for H than for D loss because of zero-point energy differences between the respective activated complexes) and (2) the density of energy levels above the zero-point levels of the respective activated complexes. For molecular ions of energy *E*, these two factors should determine the probability of loss of H *vs.* D. However, upon electron impact, molecular ions of a variety of energies will be produced, so that the probability of loss

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(11) V. H. Dibeler and F. L. Mohler, *J. Res. Nat. Bur. Stand.*, **45**, 441 (1950).
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(14) J. Delfosse and J. A. Hipple, *Phys. Rev.*, **54**, 1060 (1938).
(15) V. H. Dibeler and R. B. Bernstein, *J. Chem. Phys.*, **19**, 404 (1951).
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(17) Reviews: M. Corval and M. R. Viallard, *Bull. Soc. Chim. Fr.*, 3710 (1966); P. Natalis, *Bull. Soc. Chim. Belges*, 73, 389 (1964).
(18) H. M. Rosenstock, M. B. Wallenstein, A. L. Wahrhaftig, and H. Eyring, *Proc. Nat. Acad. Sci. U. S.*, **38**, 667 (1952); H. M. Rosenstock and M. Krauss in "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Academic Press Inc., New York, N. Y., 1963, Chapter 1.

of H *vs.* D will be an average. Very little is known about the energy distribution to be expected upon impact by electrons of a certain voltage and, at high voltages, an exceedingly simplified type of distribution has been assumed in making calculations; the results are not very sensitive to changes in the assumed distribution.[18] In contrast, at voltages approaching the appearance potential, it may be expected that the energy distribution will change greatly with electron bombarding energy. Qualitatively, the quasi-equilibrium theory predicts that, if the molecular ions are produced with energies only slightly above the activation energies for loss of H and of D, the first factor—the zero-point energy difference between activated complexes—will determine the isotope effect. Since the activated complex for loss of H still has a full complement of D zero-point energy, while the activated complex for loss of D still has a full complement of H zero-point energy, the activation energy for loss of H will be lower and loss of H will be preferred. The ratio k_H/k_D would then be expected to increase as the average energy of molecular ions (E_{av}) decreased, until it became very large when E_{av} became less than the activation energy for loss of D. Presumably, the lower the electron bombarding energy, the lower E_{av} would be. As E_{av} increased, effect 2 should begin to determine the isotope effect, and since D vibrational levels are about 1.4 times more closely spaced than H vibrational levels, the loss of H should be favored by about 1.4 (since, for loss of H, one degree of freedom of H motion is the reaction coordinate motion, leaving three D and two H degrees of freedom; for loss of D, three H and two D degrees of freedom remain). If the reaction coordinate involved motion of atoms other than the one being ejected, the high E_{av} limit should give an effect between 1.4 and 1.0.

The discussion in the previous paragraph assumes that the translational–rotational contribution is negligible,[18] which is probably so for an intramolecular isotope effect in a large ion; the translational energy level contribution to an intramolecular isotope effect is precisely unity, and the products of the moments of inertia of the activated complexes for loss of H and of D must have a ratio very near unity, since these two activated complexes differ in geometry only by interchange of D and H between nearly equivalent positions, with several heavy atoms retaining identical relative geometry in both. The general theory of isotope effects[19] indicates that the high E_{av} limit should be simply the ratio of imaginary frequencies, $\nu^{\ddagger}_{1L}/\nu^{\ddagger}_{2L}$, for reaction coordinate motion. This limit occurs since the isotopic ratio of translational and rotational energy level densities can be shown, through the Redlich–Teller product rule, to equal $\nu^{\ddagger}_{1L}/\nu^{\ddagger}_{2L}$ multiplied by the inverse of the isotopic ratio of vibrational energy level densities.

Since the zero-point energy gives a purely quantum mechanical contribution to the isotope effect, and the $\nu^{\ddagger}_{1L}/\nu^{\ddagger}_{2L}$ factor is a purely classical contribution, it appears that we have observed a transition from largely quantal isotope effects at low ionizing voltages to almost purely classical isotope effects at high ionizing voltages. The latter effects should be *ca.* 1.41, since $\nu^{\ddagger}_{1L}/\nu^{\ddagger}_{2L}$ for reaction coordinates involving motion of essentially only H ($\nu^{\ddagger}_{1L}$) or D ($\nu^{\ddagger}_{2L}$) should be equal to $(m_H/m_D)^{-1/2}$.

Though we have not attempted to make calculations for dihydropyridines, a calculation of the ratio C_2D^+/C_2H^+ in the 70-ev mass spectrum of C_2HD predicts 1.44 whereas the observed effect is 1.92.[17,20] It is difficult to understand why this and several other[9-16] effects are so large, especially because the effects for dihydropyridines appear to approach the expected value of *ca.* 1.4.

Two other factors may be entering: the energy distribution, and its dependence on bombarding electron voltage, may be different for different molecular structures; also, the quasi-equilibrium assumption is certainly not valid at very low E_{av},[18] in which case reactions of the molecular ion may depend on its exact vibronic state immediately after collision with the bombarding electron. Failure of the quasi-equilibrium assumption may not have a large effect on isotope effects, however, since the subsequent fragmentation will still be determined by competition and thus by the same two basic factors which determine quasi-equilibrium rates. If some of the molecular ion's excitation energy were localized in bonds other than the CH and CD bonds, the observed isotope effect should be greater than expected from quasi-equilibrium.

It seems highly probable that the isotope effect for methane-*d* would become large at voltages sufficiently near the apparenace potential of CH_3^+.[21] Since the effect appears to be going through a minimum,[21] there may be a complex dependence of molecular ion energy distribution upon bombarding electron voltage.

It will be noted (Table II) that the isotope effects for all dihydropyridines are fairly close to 1.41 at higher voltages, except in the case of N-methyl-3-cyano-1,4-dihydropyridine-4-*d*. We cannot be certain whether the effects for the N-methyl compound are really below 1.41, because the corrections for dideuterated compound are fairly large. Though we have no reason to question our correction procedure, it does turn out that, after correction for natural isotope abundance only, the isotope effect is, for example, 1.65 at 20.1 ev; possibly we have over-corrected for the presence of dideuterated compound.

Experimental Section

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected except where noted. Boiling points are uncorrected. Analyses were performed by Micro-Analysis, Inc., Wilmington, Del. Gas chromatography was carried out with an Aerograph Autoprep Model A-700 with an aluminum column (1 cm × 6 m) packed with 20% SF-96 silicone oil on firebrick. Nmr spectra were obtained with a Varian Associates Model HA-60 instrument. All nmr spectra reported are proton spectra and chemical shifts are in parts per million relative to internal tetramethylsilane. Infrared spectra were obtained with Perkin-Elmer 521 and Infracord spectrophotometers. Ultraviolet spectra were obtained with a Perkin-Elmer Uv-Vis-Cord, Model 202. Deuterium oxide was transferred with syringes from a stopcocked ampoule and all reaction vessels were dried in an oven at 200° for at least 4 hr prior to use.

N-Methyl-3-cyanopyridinium iodide was prepared according to a modification of the procedure of Schenker and Druey.[22] Nico-

(19) J. Bigeleisen and M. Wolfsberg, *Advan. Chem. Phys.*, 1, 15 (1958); J. Bigeleisen and M. Goeppert-Mayer, *J. Chem. Phys.*, 15, 261 (1947).

(20) P. C. Haarhoff, *Mol. Phys.*, 8, 49 (1964).

(21) Preliminary experiments indicate that this is so (P. Chen, University of Pennsylvania). Further experiments with dihydropyridines and deuterated methanes are being undertaken with a precise, magnetically scanning instrument.

(22) K. Schenker and J. Druey, *Helv. Chim. Acta*, 42, 1960 (1959).

tinonitrile (Matheson Coleman and Bell, 7.5 g, 0.072 mol) and methyl iodide (14.2 g, 0.1 mol) were dissolved in ethyl acetate (50 ml) in a sealed 20-cm test tube and heated on the steam bath 3 hr. The tube was cooled in ice before it was opened and the salt was further precipitated from the slurry of crystals by addition of ether, yielding yellow crystals (16.2 g, 92.7%). Recrystallization from absolute ethanol gave bright yellow needles, mp 198–199° dec (lit.[22] mp 198° dec). This modified procedure was employed in all subsequent pyridinium salt preparations, except that longer heating times were required.

N-Ethyl-3-cyanopyridinium iodide (15 hr heating) gave bright yellow needles, mp 193–194° dec.

Anal. Calcd for $C_8H_9N_2I$: C, 37.01; H, 3.50. Found: C, 37.01; H, 3.75.

N-*n*-Propyl-3-cyanopyridinium iodide (16 hr heating) gave bright yellow needles, mp 160–161° dec.

Anal. Calcd for $C_9H_{11}N_2I$: C, 39.42; H, 4.05. Found: C, 39.38; H, 4.10.

N-*n*-Butyl-3-cyanopyridinium iodide (36 hr heating) gave long yellow needles, mp 137–138.5° dec.

Anal. Calcd for $C_{10}H_{13}N_2I$: C, 41.66; H, 4.55. Found: C, 41.47; H, 4.62

N-*n*-Pentyl-3-cyanopyridinium iodide (36 hr heating) gave bright yellow crystals, mp 153.5–154.5° dec.

Anal. Calcd for $C_{11}H_{15}N_2I$: C, 43.70; H, 5.00. Found: C, 43.42; H, 4.93.

N-Methyl-3-cyano-1,4-dihydropyridine was prepared according to the procedure of Schenker and Druey.[22] N-Methyl-3-cyanopyridinium iodide (25.0 g, 0.10 mol) in 150 ml of water was placed in a 500-ml two-necked flask equipped with a magnetic stirring bar and a dropping funnel. To this flask was added dropwise with rapid stirring a solution of sodium carbonate (16.0 g, 0.15 mol) and sodium dithionite (26 g, 0.15 mol) in 150 ml of water. After the addition was complete, the mixture was stirred for an additional 30 min. The solution was cooled in ice, causing an oily layer to appear above the aqueous phase, and was extracted with chloroform five times (30 ml each). The combined chloroform solutions were dried over sodium sulfate. Subsequent removal of the solvent on a rotary evaporator at room temperature afforded a reddish oil (5.1 g, 43%). Vacuum distillation, bp 138–140° (11 mm), produced a bright yellow oil (4.0 g) which crystallized when cooled in ice. The oil and the crystals were found to be sensitive to oxygen, turning to a reddish brown oil. When sealed in a glass tube filled with dry nitrogen, the compound was found to be stable.

The infrared spectrum, including the fingerprint region, and the ultraviolet spectrum were identical with those reported in the literature.[22]

The nmr spectrum in deuteriochloroform showed five different absorptions, at δ 2.90, 3.07, 4.61, 5.62, and 6.42, with electronic integration giving ratios of 5.1 (δ 2.90, 3.07):1.0:1.0:1.0, respectively. The splitting pattern, as well as the chemical shifts, indicate that the absorptions are for methyl, 4, 5, 6, and 2 protons, respectively. This spectrum was similar to that reported for N-methyl-1,4-dihydronicotinamide.[23]

A higher yield of the dihydropyridine could be obtained by adding sodium dithionite and sodium carbonate directly to the aqueous solution of the pyridinium salt. For example, the pyridinium iodide (0.55 g, 0.002 mol) was dissolved in 15 ml of water and to this solution was added a dry mixture of sodium dithionite (1.0 g, 0.005 mol) and sodium carbonate (0.5 g, 0.003 mol). The solution was stirred with a magnetic bar for 1 hr, followed by extraction with chloroform. Vacuum distillation of the reddish oil afforded 0.16 g (59%) of a bright yellow oil which exhibited infrared and nmr absorption spectra identical with those of the authentic N-methyl-3-cyano-1,4-dihydropyridine.

N-Ethyl-3-cyano-1,4-dihydropyridine was prepared by the reduction of the corresponding pyridinium salt with dithionite. N-Ethyl-3-cyanopyridinium iodide (0.5 g, 0.002 mol) was dissolved in 15 ml of water and to the solution was added a mixture of sodium dithionite (1.0 g, 0.005 mol) and sodium carbonate (0.5 g, 0.003 mol). The mixture was stirred vigorously with a magnetic bar for 2 hr. Subsequently, the solution was extracted three times with chloroform (10 ml each) and the combined solutions were dried over sodium sulfate and then evaporated. Vacuum distillation of the residual red oil afforded a bright yellow oil, bp 74.5–75.5° (0.026 mm), n^{25}D 1.5490.

Anal. Calcd for $C_8H_{10}N_2$: C, 71.64; H, 7.46; N, 20.89. Found: C, 71.39; H, 7.51; N, 20.56.

The infrared spectrum exhibited functional group absorptions at 3030 w, 2950, 2800 s, 2160 vs, 1660 s, and 1580 cm^{-1} s. The nmr spectrum showed six types of protons, at δ 1.11, 3.01, 3.20, 4.65, 5.86, 6.71. Electronic integration gave area ratios of 3.1:4.2:1.0:1.0:1.0, respectively.

This same procedure was used for preparation of the following three higher homologs.

N-*n*-Propyl-3-cyano-1,4-dihydropyridine was a yellow-orange oil (yield, 75%), bp 67–69° (0.023 mm), n^{25}D 1.5411.

Anal. Calcd for $C_9H_{12}N_2$: C, 72.97; H, 8.11; N, 18.92. Found: C, 73.07; H, 8.07; N, 18.81.

The infrared spectrum exhibited functional group absorptions at 3030 m, 2950, 2850 s, 2190 vs, 1670 vs, and 1600 cm^{-1} vs. The nmr spectrum showed seven types of proton absorptions, at δ 1.03, 1.56, 3.07, 4.70, 5.94, 6.77. Electronic integration gave area ratios of 3.2:2.1:4.2 (for peaks at δ 3.17 and 3.07):1.0:1.0:1.0, respectively.

N-*n*-Butyl-3-cyano-1,4-dihydropyridine was a yellow-orange oil (yield, 83%), bp 93.5–94.5° (0.020 mm), n^{25}D 1.5341. (The oil crystallized quickly in the receiver.)

Anal. Calcd for $C_{10}H_{14}N_2$: C, 74.07; H, 8.64; N, 17.28. Found: C, 73.72; H, 8.58; N, 17.42.

The infrared spectrum exhibited functional group absorptions at 3010 w, 2900, 2830 vs, 2180 vs, 1670 s, and 1600 cm^{-1} vs. The nmr spectrum showed seven types of proton absorptions, at δ 0.94, 1.43, 3.06, 3.14, 4.65, 5.89, 6.70. Electronic integration gave area ratios of 7.6 (for peaks at δ 0.94 and 1.43):4.2 (for peaks at δ 3.06 and 3.14):1.0:1.0:1.0, respectively.

N-*n*-Pentyl-3-cyano-1,4-dihydropyridine was a yellow-orange oil (yield, 76%), bp 97–99° (0.020 mm), n^{25}D 1.5273.

Anal. Calcd for $C_{11}H_{16}N_2$: C, 75.00; H, 9.09; N, 15.91. Found: C, 75.03; H, 9.16; N, 15.82.

The nmr spectrum of the sample showed seven types of proton absorptions at δ 0.94, 1.41, 3.06, 3.16, 4.80, 5.94, 6.65. Electronic integration gave area ratios of 9.2 (for peaks at δ 0.94 and 1.41):4.1 (for peaks at δ 3.06, 3.16):1.0:1.0:1.0, respectively.

N-Methyl-3-cyano-1,4-dihydropyridine-4-*d* was prepared by the reduction of the corresponding pyridinium iodide in deuterium oxide. N-Methyl-3-cyanopyridinium iodide (0.5 g) was dissolved in 15 ml of deuterium oxide in a 50-ml erlenmeyer flask equipped with a drying tube. A vacuum-dried mixture of sodium dithionite (2.0 g) and sodium carbonate (1.0 g) was added to the solution, which was stirred vigorously with a magnetic stirrer. Then the flask was immersed partially into an oil bath at 60° and allowed to stir for 1 hr. The extraction was accomplished by adding 10 ml of chloroform to the stirring solution for 2 min, then allowing the phases to separate. The chloroform in the lower phase was pipetted from the solution. This extraction was performed three times and the combined chloroform solutions were dried over sodium sulfate. After evaporating the solvent on a rotary evaporator, the red residue was vacuum distilled, giving a yellow oil (0.10 g, 41%) showing in its nmr spectrum a reduction of the peak area at δ 3.07 from a relative ratio of 5.1 protons to 4.2 protons. Furthermore, the triplet of doublets at δ 4.61 became a doublet of doublets, indicating that only one proton at the 4 position is coupled with the 5 proton. Slight deuteration at the 2 position was observed, as evidenced by the smaller peak area (0.93 proton) under the peak at δ 6.42. A mass spectrum of this yellow oil showed the molecular ion at *m/e* 121.

N-Ethyl-, N-*n*-propyl-, N-*n*-butyl-, and N-*n*-pentyl-3-cyano-1,4-dihydropyridines-4-*d*, prepared by the method used for the N-methyl compound, had the nmr and mass spectra expected by analogy with the N-methyl compound.

N-Methyl-3-cyanopyridinium-2-*d* iodide was prepared by the deuterium exchange of the undeuterated salt in deuterium oxide, catalyzed by base. N-Methyl-3-cyanopyridinium iodide (2.5 g) was dissolved in deuterium oxide (20 ml) in a 50-ml round-bottom flask and to this solution was added anhydrous sodium carbonate (2.5 g). The mixture was swirled to achieve a homogeneous solution, then heated on the steam bath for exactly 10 sec followed by immediate quenching of the exchange by immersing the flask into liquid nitrogen. The resulting solid was subjected to high vacuum freeze-drying for 16 hr. The powder was stored in a desiccator for direct reduction to dihydropyridine without purification of the salt. The nmr spectrum of the dihydropyridine indicated almost complete absence of the 2 proton on the ring at δ 6.62 and electronic integration showed that the isotopic purity for the 2 proton was greater than 90%. The mass spectrum of the oil revealed the

(23) R. F. Hutton and F. H. Westheimer, *Tetrahedron*, 3, 73 (1958).

isotopic purity to be about 94%. A sample of this oil was sealed under high vacuum (10^{-6} mm) and heated in an oil bath at 140–150° for 30 min. The resulting oil showed no change of peak area or splitting pattern in the nmr spectrum.

Dihydropyridines with Deuterium-Labeled N-Alkyl Groups. N-Alkyl-labeled dihydropyridines were prepared from pyridinium iodides or bromides by reaction of nicotinonitrile with the following alkyl halides:[3] methyl-d_3 iodide (Merck Sharp and Dohme, 99.8% pure by mass spectrometry); ethyl-2,2,2-d_3 bromide, prepared by reduction of acetic acid-d_4 (Merck Sharp and Dohme) with lithium aluminum hydride and conversion of the resulting alcohol to bromide using concentrated hydrobromic and sulfuric acids; ethyl-1,1-d_2 bromide, prepared by reduction of phenyl acetate with lithium aluminum deuteride[24] and conversion of the resulting alcohol to bromide using concentrated hydrobromic and sulfuric acids; *n*-butyl-4,4,4-d_3 bromide, prepared by addition of ethylene oxide to the Grignard reagent of ethyl-2,2,2-d_3 bromide[25] and conversion of the resulting alcohol to bromide using concentrated hydrobromic and sulfuric acids. The N-ethyl compounds were made by distilling ethyl bromide directly from the acid mixture, as it formed, into a vessel containing ethyl acetate and nicotinonitrile.

1,4,4-Trimethyl-1,4-dihydropyridine was prepared by the procedure of Kosower and Sorensen,[26] starting with 3,3-dimethylglutaric anhydride.

N-Methyl-3,4-dicyano-1,4-dihydropyridine was prepared by addition of cyanide ion to the corresponding pyridinium ion. The infrared spectrum showed absorptions at 3030 w, 2950 s, 2220 vs, 1690 s, and 1600 cm^{-1} s, very similar to the spectrum of N-methyl-3-cyano-1,4-dihydropyridine. The nmr spectrum of the solid showed absorptions at δ 3.05, 4.51, 4.79, 6.08, 6.89.

Anal. Calcd for $C_8H_7N_3$: C, 66.18; H, 4.87; N, 28.95. Found: C, 66.09; H, 4.92; N, 29.03.

This compound was found to be sensitive to oxygen and base. Repeated efforts to make a mass spectral study of the solid, using the heated inlet, resulted in a very complex spectrum which showed no resemblance to that expected.

Mass Spectra. Most mass spectra were obtained with a Consolidated Electrodynamics Corp. Model 21-130 cycloidal-focusing mass spectrometer modified to give unit resolution to *m/e* 285. Most solids and high-boiling liquids were introduced by a CEC all-glass inlet system, at 180°. The metastable ion spectra and low voltage % Σ_{15} values were obtained with a more sensitive, magnetic-scanning Hitachi Perkin-Elmer Model RMU-6D mass spectrometer.[27] Isotope effects were quite similar using the CEC (Table II) or the Hitachi instrument.

For quantitative measurements on the N-alkyl-1,4-dihydropyridines the ^{13}C abundances were estimated by obtaining empirically (M + 1)/M ratios of the alkyl halide and of the nicotinonitrile separately; the sum of these two ratios was used as the true isotope abundance for the sample.

As a result of partial deuteration at the 2 position of the N-alkyl-3-cyano-1,4-dihydropyridines-4-*d*, it was necessary to make corrections in order to obtain quantitative measurements of the loss of hydrogen *vs.* deuterium from the 4 position. The assumption is made that the monodeuterio and dideuterio species behave similarly in the mass spectrometer, *i.e.*, that loss of H· or D· at the 4 position is not affected by the deuterium at the 2 position. Therefore, the "parent minus H" peak may receive a contribution from the dideuterated species (from loss of a deuterium atom). The correction of such errors may be made as follows: P′ = observed peak height at "parent + 1" *m/e*, consisting of dideuterated molecules M′ and isotope of M; P = observed peak height at parent *m/e*, consisting of parent ion M, isotope of M − 1 ion, M′ − 1 ion, and isotope of M′ − 2 ion (negligible compared with the contributions of other ions); P − 1 = observed peak height at "parent − 1" *m/e*, consisting of M − 1 ion, M′ − 2 ion, and isotope of M − 2 ion; P − 2 = observed peak height at M − 2 *m/e*, consisting of only M − 2 ions; I = isotope ratio obtained from the empirical method described above, I(P − 2) = isotopic contribution to P − 1; (P − 1) − I(P − 2) = A ions from M − 1 and M′ − 2; P − $I(A)$ = B ions from M and M′ − 1; P′ − $I(B)$ = C the amount of M′; $(A/B)C$ = [(M − 1) + (M′ − 2)](M′)/[(M) + (M′ − 1)].

Assuming that M′ − 2 and M′ − 1 are relatively small, the expression is approximately $(A/B)C$ = (M − 1)M′/M an approximate amount of ions due to (M′ − 1) at P; $B - (A/B)C$ = approximate amount of ions due to M at P; $(P - 2)/(B - AC/B)$ = the ratio of (M − 2) to M; $[(P - 2)/(B - AC/B)]C$ = approximate contribution of (M′ − 2) to the peak (P − 1); or (M − 1) = $A - C[(P - 2)/(B - AC/B)]$; (M − 2) = (P − 2).

The ratio obtained, in principle, could be iterated to achieve a converged value (when P is larger than P − 1); for example, in the spectrum for N-methyl-3-cyano-1,4-dihydropyridine-4-*d* the following values are obtained at 13.2 ev: P′ = 22.60, P = 93.70, (P − 1) = 45.44, (P − 2) = 16.42, and I = 0.093. Substituting into the above equations, one obtains A = 43.90, B = 89.63, C = 14.32; the value for (M − 1) is calculated to be 41.05, and the corresponding isotope effect, (M − 1)/(M − 2), to be 2.502. The new value of (M − 1) can then be resubstituted into the equations, and iteration gives a new isotope effect, 2.493. Since the first correction is already within experimental error, the isotope effects reported in Table II were not iterated.

The ionizing voltage is only the apparent voltage measured from the external circuits without taking into account the contribution of the repeller and the ion field effects. The true values are probably 5.6 ± 0.4 ev higher (based on argon ionization potential as an internal standard); 5.6 ev has therefore been added to each ionizing voltage reported in Table II. High voltage spectra are reported for *uncorrected*, nominal 76 ev, since it is not clear whether the low voltage correction would also apply at high voltage.

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