**5-Fluoro-2-hydroxy-2-methylpentane.**[20] An identical procedure as described for the chloro compound was used. From 10.4 g (0.1 mol) of 5-fluoro-2-pentanone[21] there was obtained 6.8 g (57%) of the desired compound, bp 62–64° (60 mm); fluorine spectrum: $\phi$ +216.6 (m). Three grams (0.025 mol) of alcohol was shaken with 25 ml of ice-cold aqueous concentrated hydrochloric acid for 15 min. The organic material was taken up in pentane, washed with dilute sodium bicarbonate solution, dried, and distilled. There was obtained 2.6 g (74%) of the desired compound, bp 58–61° (45 mm); fluorine spectrum: $\phi$ +218.8 (m).

**2,4-Difluoro-2-methylpentane.** 5-Fluoro-2-hydroxy-2-methylpentane (6 g, 0.05 mol) was shaken with 50 ml of ice-cold concentrated aqueous hydrobromic acid for 15 min. The organic material was taken up in pentane, washed with cold dilute sodium bicarbonate, dried, and distilled. There was obtained 8.1 g (87%) of an oil, bp 49–52° (28 mm), whose nmr spectrum was consistent with that expected for 5-bromo-2-fluoro-methylpentane; fluorine spectrum: $\phi$ +218.9 (m). This material (0.044 mol) was treated with 25.4 g (0.2 mol) of argentous fluoride (Harshaw) in 50 ml of dry acetonitrile at room temperature for 2 hr. The reaction mixture was filtered and poured into 150 ml of cold water and extracted with 50 ml of pentane. The pentane extract was washed twice with 25-ml portions of water, dried, and distilled through a 6-in. microcolumn packed with glass helices. There was obtained 3.4 g of material, bp 30–32° (20 mm); fluorine spectrum: $\phi$ +218.7 (m) and +138.9 (m).

**Preparation of Ions and Nmr Studies.** Solutions of ions in antimony pentafluoride–sulfur dioxide solution were prepared as described previously.[2,3] Solutions of ions in fluorosulfuric acid–antimony pentafluoride–sulfur dioxide solution were prepared by adding *ca.* 0.15 g of precursor dropwise with vigorous stirring to 1 ml of 1:1 *M* antimony pentafluoride in fluorosulfuric acid diluted with 1 ml of sulfur dioxide at −78°.

Nmr spectra were obtained on a Varian A-56-60A nmr spectrometer with variable-temperature probe. Chemical shifts are referred to external TMS. Methanolysis was performed as described previously.[2,3]

(20) Fluorine spectra (56.4 MHz) were recorded at room temperature in $CCl_4$ with $CFCl_3$ as internal standard. Abbreviations used: t, triplet; m, multiplet.

(21) Fluorine spectrum: $\phi$ +219.7 (t) $J_{H-F}$ = 47.6 Hz; (t) $J_{H-F}$ = 25.4 Hz.

**Acknowledgment.** Support of the work by grants of the National Science Foundation and the Petroleum Research Fund administered by the American Chemical Society is gratefully acknowledged.

# Mass Spectrometry in Structural and Stereochemical Problems. CLXV.[1] A Study of Skeletal Rearrangements in $^{13}$C-Labeled Aromatic Amines[2]

**Alexander V. Robertson and Carl Djerassi**

*Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305.* *Received July 5, 1968*

**Abstract:** The mass spectra of 1-$^{13}$C-aniline, 1-$^{13}$C-acetanilide, 1-$^{13}$C-sulfanilamide, and 1-$^{13}$C-*p*-nitroaniline were examined. The fragmentations $C_6H_7N\cdot^+ \rightarrow C_5H_6\cdot^+ + HCN$ and $C_6H_6N^+ \rightarrow C_5H_5^+ + HCN$ were studied to determine the extent of any skeletal rearrangement of the $C_6H_7N$ and $C_6H_6N$ species. Careful intensity measurements under high resolution were required to separate various isobaric components of the same nominal mass. Analysis of the results reveals that for the reactions involving loss of HCN, the odd-electron species $C_6H_7N^+\cdot$ is rearranged only to a small extent, whereas the even-electron species $C_6H_6N^+$ is rearranged to a considerable extent. The rearrangement is discussed in terms of ring-expanded azepinium ions. For *p*-nitroaniline, the fragment $C_5H_6N^+$ formed by successive loss of NO· and CO from the molecular ion contains only five-sixths of the label, suggesting that the structure of the ion $C_6H_6NO^+$ from which the CO is expelled has the label uniformly randomized.

We describe here further experiments to provide more definitive information on the structure of some fragment ions in the mass spectrometer. They are based on the potential analogy between the fragmentation of toluene and the aromatic amines. The extensive labeling experiments of Meyerson and coworkers on toluene are most readily explained by a tropylium structure for the M−1 ion.[3] Rinehart's group recently established with doubly $^{13}$C-labeled toluene that the methyl carbon is inserted randomly between the ring carbons.[4] Similar ring expansions have been postulated, but rarely proven, in many other systems. The fragmentation of several $^{13}$C-labeled nitrogen heterocycles demands skeletal rearrangement, and ring expansion provides the most obvious rationalization.[5] We recently reported, in a preliminary communication, semiquantitative results of experiments to test the possibility of rearrangement, presumably to azepinium structures, of ions in the mass spectra of 1-$^{13}$C-labeled aniline, acetanilide, and sulfanilamide.[6] Independently, Rinehart and coworkers have also published similar, more accurate results on the mass spectral fragmentation of aniline-1-$^{13}$C.[7] Full details of our work, which now include a study of 1-$^{13}$C-*p*-nitroaniline, are presented below. Our present results are more accurate for experimental reasons than those of the preliminary

(1) For paper CLXIV see Y. M. Sheikh, A. M. Duffield, and C. Djerassi, *Org. Mass Spectrometry*, in press.

(2) We are indebted to the National Institutes of Health for financial support (Grant No. GM 11309), and to the Australian–American Educational Foundation for the award of a Fulbright Travel Grant (to A. V. R.).

(3) H. M. Grubb and S. Meyerson in "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Academic Press, New York, N. Y., 1963, Chapter 10.

(4) K. L. Rinehart, Jr., A. C. Buchholz, G. E. Van Lear, and H. L. Cantrill, *J. Am. Chem. Soc.*, 90, 2938 (1968).

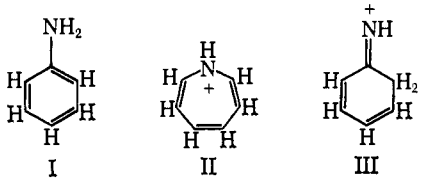
(5) M. Marx and C. Djerassi, *ibid.*, 90, 678 (1968).

(6) A. V. Robertson, M. Marx, and D. Djerassi, *Chem. Commun.*, 414 (1968).

(7) K. L. Rinehart, Jr., A. C. Bucholz, and G. E. Van Lear, *J. Am. Chem. Soc.*, 90, 1073 (1968).

account,[6] and details of the differences are included in the Experimental Section.

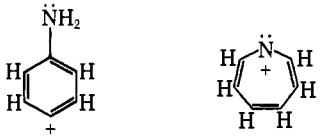
The base peak in the mass spectrum of aniline is due to the molecular ion, $C_6H_7N\cdot^+$ (*m/e* 93).[8] Structure I is the most plausible one for the unrearranged ion radical, and II is one canonical form for a ring-expanded species. The base peak in the mass spectrum of acetanilide is associated with an ion radical of identical



I II III

composition, formed by loss of ketene (observable metastable peak) from the molecular ion.[9] Depending on whether transfer of the methyl hydrogen atom proceeds through a four- or six-membered ring, the structure of the $C_6H_7N\cdot^+$ species from acetanilide could be portrayed as I or III.[10] In either event, rearrangement to II is a theoretical possibility.

The base peak for sulfanilamide is due to the molecular ion, which decomposes (observable metastable peak) to the even-electron species $C_6H_6N^+$ (*m/e* 92, 60%) by loss of $\cdot SO_2NH_2$.[11] Similarly, *p*-nitroaniline has a strong molecular ion signal (it can be the base peak, depending on the instrument used), and loss of $\cdot NO_2$ (observable metastable peak) again yields the ion of composition $C_6H_6N^+$ (40%).[12] One canonical representation of the unrearranged structure of this ion is structure IV, and of a ring-expanded form, V.



IV V

These major ions in the fragmentation of aniline and acetanilide decompose further *via* eq 1, and of sulfanilamide and *p*-nitroaniline *via* eq 2. Expulsion of the

$$\underset{m/e\ 93}{C_6H_7N\cdot^+} \xrightarrow[*(46.8)]{-HCN} \underset{m/e\ 66}{C_5H_6\cdot^+} \quad (1)$$

$$\underset{m/e\ 92}{C_6H_6N^+} \xrightarrow[*(45.9)]{-HCN} \underset{m/e\ 65}{C_5H_5^+} \quad (2)$$

elements of HCN may be used as a probe to test for the presence or absence of rearranged species such as II or V. If C-1 of the starting amines is specifically enriched with $^{13}C$, then any rearrangements during fragmentation that yield structures with the nitrogen atom attached to two carbon atoms (*e.g.*, II and V) must necessarily have the $^{13}C$ label randomized to some extent. There is as yet no evidence on the bonding within the fragment of composition HCN in eq 1 and 2, or on the mechanism of its formation. Nevertheless, if it is assumed that the carbon atom in the HCN fragment originates entirely from a carbon atom linked to the nitrogen atom in $C_6H_7N\cdot^+$ or $C_6H_6N^+$, the following consequences are obvious for a 1-$^{13}C$ sample. Loss of label as $H^{13}CN$ would be total from an unrearranged intermediate (*e.g.*, I or IV), whereas the HCN lost from rearranged species such as II or V would remove only a portion of the $^{13}C$. The precise amount depends on the exact mechanism of the rearrangement. For example if ring expansion did occur to form II, one's first tendency would be to insert the nitrogen atom in I exclusively between C-1 and the *o*-carbon atoms, but the recent results for toluene[4] show that random insertion of the nitrogen needs to be considered. These two cases presumably represent the extremes of mechanism for hypothetical ring-expansion models. In the first case, one-half of the HCN from the ring-expanded species would be lost as $H^{13}CN$, compared with only one-sixth loss as $H^{13}CN$ in the second case.

In short, experiments with 1-$^{13}C$ aromatic amines constitute a double-labeling procedure in which one of the labels happens to be nitrogen. The logical assumption that the carbon–nitrogen link in the intermediates retains its identity in the HCN fragment is crucial to the interpretation. This assumption, previously tacit,[5-7] is emphasized here because mass spectral fragmentation of aromatic systems is an area of science in which the hazards of making reasonable assumptions based on general organic perspectives are notorious. In addition, any $^{12}C/^{13}C$ isotope effect has been ignored in the interpretations below.

Aniline, acetanilide, sulfanilamide, and *p*-nitroaniline were synthesized (see Experimental Section) with 44% excess of $^{13}C$ specifically at C-1. Mass spectra, taken on an MS-9 instrument, were complicated in the regions of interest by the presence of several isobaric components at each nominal mass. Intensity measurements were therefore made under high-resolution conditions, and the composition of all relevant ions was determined unequivocally. For easy comparison, the results are presented in the same tabular format as used by Rinehart and coworkers.[7]

The ideal experiment for ease of interpretation would be one in which the samples were 100% enriched at C-1, and lacking any natural abundance of $^{13}C$; that is, a homogeneous array of molecules in which C-1 was entirely $^{13}C$, and with only $^{12}C$ elsewhere. In that event the relative intensities of the peaks for $C_5H_6$ and $^{13}CC_4H_6$ would yield directly the loss of $H^{13}CN$ *vs.* $H^{12}CN$ from $^{13}CC_5H_7N\cdot^+$, etc. This ideal experiment cannot be executed at the moment, but the spectrum it would generate was calculated from the observed spectrum of the partly enriched compounds as follows. The intensities of the individual components in the region of interest were measured relative to the largest component there, both in the spectra of the unlabeled and the enriched samples. The various contributions due to the natural abundance of $^{13}C$ were subtracted to yield corrected spectra. Typically there was a relative intensity difference for the same component in the corrected unlabeled *vs.* the corrected labeled spectra. Now these differences are due to the fact that in the labeled sample, 44 of the C-1 atoms are $^{13}C$ for very 100 $^{12}C$ atoms there. In other words, the fraction of 1-$^{13}C$ molecules

(8) P. N. Rylander, S. Meyerson, E. L. Eliel, and J. D. McCollum, *J. Am. Chem. Soc.*, **85**, 2723 (1963); J. Momigny, *Bull. Soc. Roy. Sci. Liege*, **22**, 541 (1953).
(9) J. L. Cotter, *J. Chem. Soc.*, 5477 (1964).
(10) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, p 350.
(11) G. Spiteller and R. Kaschnitz, *Monatsh.*, **94**, 964 (1963).
(12) Reference 10, p 327.

**Table I.** Mass Spectral Peaks for Aniline-1-$^{13}$C (High Resolution)

| *m/e* | Composition | Rel abundance[a–c] | Abundance ratios |
|---|---|---|---|
| 65 | $C_4H_3N$ | 0.037 (0.060) | |
| | $C_5H_5$ | 0.519 (0.480) | (i) $C_5H_5/(C_5H_5 + {}^{13}CC_4H_5) = 0.85$ |
| 66[d] | $^{13}CC_3H_3N$ | 0.066 | (ii) $^{13}CC_3H_3N/(C_4H_3N + {}^{13}CC_3H_3N) = 0.64$ |
| | $C_4H_4N$ | 0.018 (0.057) | |
| | $^{13}CC_4H_5$ | 0.092 | |
| | $C_5H_6$ | 1.000 (1.000) | (iii) $C_5H_6/(C_5H_6 + {}^{13}CC_4H_6) = 0.92$ |
| 67 | $^{13}CC_3H_4N$ | 0.059 | (iv) $^{13}CC_3H_4N/(C_4H_4N + {}^{13}CC_3H_4N) = 0.78$ |
| | $C_4H_5N$ | 0.020 (0.077) | |
| | $^{13}CC_4H_6$ | 0.088 | |
| 68 | $^{13}CC_3H_5N$ | 0.072 | (v) $^{13}CC_3H_5N/(C_4H_5N + {}^{13}CC_3H_5N) = 0.88$ |

[a] Abundance of $C_5H_6$ defined as 1.000. [b] Corrected for naturally abundant $^{13}C$, and extrapolated to 100% specific enrichment; see text. [c] Values in parentheses are for unlabeled aniline, corrected for natural $^{13}C$. [d] At low resolution the *m/e* 66 signal was 28% as intense as the base peak (*m/e* 93) for the unlabeled sample, and 40% for the labeled sample.

**Table II.** Mass Spectral Peaks for Acetanilide-1-$^{13}$C (High Resolution)

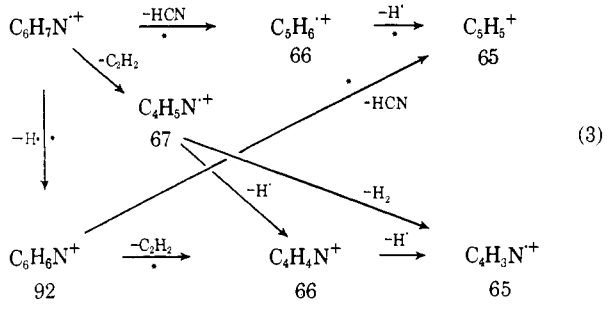
| *m/e* | Composition | Rel abundance[a–c] | Abundance ratios |
|---|---|---|---|
| 65 | $C_4H_3N$ | 0.065 (0.055) | |
| | $C_5H_5$ | 0.934 (0.770) | (i) $C_5H_5/(C_5H_5 + {}^{13}CC_4H_5) = 0.87$ |
| 66[d] | $^{13}CC_3H_3N$ | 0.059 | (ii) $^{13}CC_3H_3N/(C_4H_3N + {}^{13}CC_3H_3N) = 0.48$ |
| | $C_4H_4N$ | 0.013 (0.033) | |
| | $^{13}CC_4H_5$ | 0.141 | |
| | $C_5H_6$ | 1.000 (1.000) | (iii) $C_5H_6/(C_5H_6 + {}^{13}CC_4H_6) = 0.96$ |
| 67 | $^{13}CC_3H_4N$ | 0.033 | (iv) $^{13}CC_3H_4N/(C_4H_4N + {}^{13}CC_3H_4N) = 0.72$ |
| | $C_4H_5N$ | 0.017 (0.050) | |
| | $^{13}CC_4H_6$ | 0.043 | |
| 68 | $^{13}CC_3H_5N$ | 0.049 | (v) $^{13}CC_3H_5N/(C_4H_5N + {}^{13}CC_3H_5N) = 0.75$ |

[a–c] As for Table I. [d] At low resolution the *m/e* 66 signal was 11% as intense as the base peak (*m/e* 93) for the unlabeled sample and 16% for the labeled sample.

in the total aggregate was 44/144, that is 30.5%. Multiplication of the above differences by 100/30.5 then extrapolated them to the case where all of the sample molecules have $^{13}C$ at C-1. Algebraic addition of this extrapolated difference for each component and the intensity of the corresponding component in the corrected unlabeled spectrum then yielded the relative abundances desired from the ideal experiment above. It is these calculated relative abundances for 100% specific enrichment, and corrected for natural $^{13}C$, that are listed in Tables I–IV. The form of the abundance ratios used in the tables is such that any species that had lost nitrogen *and* all of the $^{13}C$, or retained nitrogen *and* all of the $^{13}C$ would produce a value of 1.00. Footnote *d* in each of the tables permits an estimate of the intensities relative to the base peak of each spectrum. It will be noted that many of the peaks, especially those containing nitrogen, are extremely small in an absolute sense. Experimental errors in obtaining accurate intensity measurements on such small components are relatively greater and are magnified threefold by the extrapolation from 30.5 to 100% enrichment during the calculation. The second decimal place in the abundance ratios for these peaks therefore has dubious significance, although it is meaningful in the values from the major hydrocarbon peaks.

The results in Table I are in broad agreement with those of Rinehart, *et al.*,[7] for aniline-1-$^{13}C$. They used a CEC 21-110B instrument, and any discrepancies are presumably due to the source conditions in the different instruments of the two groups. The main interest is in ratio iii, which shows that 92% (*cf.* 93% in ref 7) of the HCN in eq 1 was lost as $H^{13}CN$. The 8% lost as $H^{12}CN$ can only arise from a rearranged molecular ion. If the rearrangement is to the azepinium species II, the 8% represents one-half to five-sixths of the total rearrangement, depending on the mechanism of nitrogen insertion between the two extreme models described above (*i.e.*, insertion between C-1 and the *o*-carbons or randomization throughout the ring as in toluene[4]).

Reaction scheme 3 shows fragmentation pathways that are possible, and most have been confirmed by metastable and/or labeling evidence.[7,8] Apart from




(3)

consideration of HCN losses, valuable structural information is available from the reactions proceeding with expulsion of acetylene (*m/e* 93 → *m/e* 67 and *m/e* 92 → *m/e* 66). Acetylene ejection is a sensitive test for a rearranged precursor, since it is impossible to expel labeled acetylene from an unrearranged species and yield a nitrogen-containing ion. Some 12% of $C_4H_5N$ and 22% of $C_4H_4N$ (ratios v and iv in Table I) are formed from the labeled *m/e* 93 and 92 species, which must imply rearrangement. Its extent again depends on the model hypothesis chosen for a rearranged ion. As Rinehart, *et al.*, have pointed out,[7] statistical loss of acetylene from azepinium-2-$^{13}C$ would give four-fifths $^{13}CC_2H_5N$ and one-fifth $C_4H_5N$; if the rearrangement gave instead uniformly labeled azepinium-

**Table III.** Mass Spectral Peaks for Sulfanilamide-1-$^{13}$C (High Resolution)

| *m/e* | Composition | Rel abundance[a–c] | Abundance ratios |
|---|---|---|---|
| 63 | $C_5H_3$ | 0.208 (0.182) | (i) $C_5H_3/(C_5H_3 + {}^{13}CC_4H_3) = 0.89$ |
| 64 | $C_4H_2N$ | 0.011 (0.021) | |
| | $^{13}CC_4H_3$ | 0.026 | |
| | $C_5H_4$ | 0.144 (0.118) | (ii) $C_5H_4/(C_5H_4 + {}^{13}CC_4H_4) = 0.76$ |
| 65[d] | $^{13}CC_3H_2N$ | 0.020 | (iii) $^{13}CC_3H_2N/(C_4H_2N + {}^{13}CC_3H_2N) = 0.64$ |
| | $C_4H_3N$ | 0.023 (0.066) | |
| | $^{13}CC_4H_4$ | 0.046 | |
| | $C_5H_5$ | 1.000 (1.000) | (iv) $C_5H_5/(C_5H_5 + {}^{13}CC_4H_5) = 0.75$ |
| 66 | $^{13}CC_3H_3N$ | 0.059 | (v) $^{13}CC_3H_3N/(C_4H_3N + {}^{13}CC_3H_3N) = 0.72$ |
| | $C_4H_4N$ | 0.048 (0.074) | |
| | $^{13}CC_4H_5$ | 0.328 | |
| 67 | $^{13}CC_3H_4N$ | 0.075 | (vi) $^{13}CC_3H_4N/(C_4H_4N + {}^{13}CC_3H_4N) = 0.61$ |

[a] Abundance of $C_5H_5$ defined as 1.000. [b,c] As for Table I. [d] At low resolution the *m/e* signal was 46% as intense as the base peak (*m/e* 172) for the unlabeled sample and 54% for the labeled sample.

**Table IV.** Mass Spectral Peaks for *p*-Nitroaniline-1-$^{13}$C (High Resolution)

| *m/e* | Composition | Rel abundance[a–c] | Abundance ratios |
|---|---|---|---|
| 63 | $C_5H_3$ | 0.160 (0.160) | (i) $C_5H_3/(C_5H_3 + {}^{13}CC_4H_3) = 0.80$ |
| 64 | $C_4H_2N$ | 0.002 (0.025) | |
| | $^{13}CC_4H_3$ | 0.039 | |
| | $C_5H_4$ | 0.100 (0.100) | (ii) $C_5H_4/(C_5H_4 + {}^{13}CC_4H_4) = 0.77$ |
| 65[d] | $^{13}CC_3H_2N$ | 0.023 | (iii) $^{13}CC_3H_2N/(C_4H_2N + {}^{13}CC_3H_2N) = 0.92$ |
| | $C_4H_3N$ | 0.017 (0.060) | |
| | $^{13}CC_4H_4$ | 0.030 | |
| | $C_5H_5$ | 1.000 (1.000) | (iv) $C_5H_5/(C_5H_5 + {}^{13}CC_4H_5) = 0.74$ |
| 66 | $^{13}CC_3H_3N$ | 0.062 | (v) $^{13}CC_3H_3N/(C_4H_3N + {}^{13}CC_3H_3N) = 0.79$ |
| | $C_4H_4N$ | 0.055 (0.075) | |
| | $^{13}CC_4H_5$ | 0.345 | |
| 67 | $^{13}CC_3H_4N$ | 0.072 | (vi) $^{13}CC_3H_4N/(C_4H_4N + {}^{13}CC_3H_4N) = 0.57$ |

[a–c] As for Table III. [d] At low resolution the *m/e* 65 signal was 64% as intense as the base peak (*m/e* 128) for the unlabeled sample and 96% for the labeled sample.

$^{13}$C, the result would be two-thirds $^{13}CC_3H_5N$ and one-third $C_4H_5N$. Clearly the *m/e* 92 even-electron species that loses acetylene is much more rearranged than its odd-electron *m/e* 93 counterpart. Any difference between the abundance ratios for ions differing only by hydrogen (*e.g.*, $C_4H_4N$ and $C_4H_5N$; ratios iv and v) demands an alternative origin for the low mass ion, in addition to hydrogen loss from the high mass ion, and such pathways are available in reaction scheme 3.

The pattern in Table II is very similar to that in Table I, and all the metastable peaks observed for aniline in scheme 3 were also observed for acetanilide. Ratio iii shows that only 4% of $N^{12}CN$ was lost from 100% enriched sample, and so the species $C_6H_7N\cdot^+$ in this reaction is almost entirely unrearranged. On the other hand, the value for ratio v would indicate that the species of identical composition which loses acetylene is very largely rearranged. These conclusions are not incompatible, since the precursor ions could easily be isomeric, the one for the acetylene reaction being rearranged, and the one for the HCN reaction being unrearranged. Again, ratio iv implies that the precursor $C_6H_6N^+$ of $C_4H_4N^+$ is essentially rearranged. It should also be noted that the intensities relative to the base peak are much smaller in Table II than for Table I, with corresponding reservations about the accuracy of the measurements for the very small components.

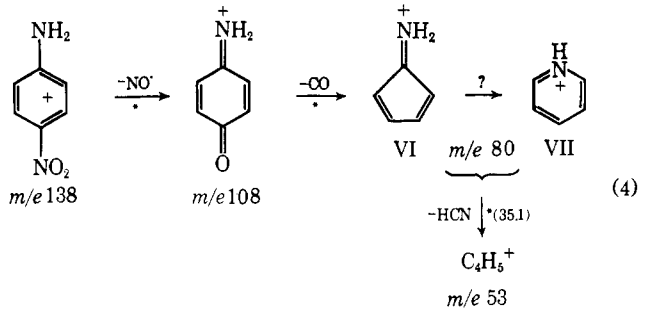
No metastable evidence to confirm possible pathways to fragments in Table III was observable except for eq 2. Nevertheless the formation of all the ions shown, and the variation between certain of the abundance ratios, demands a scheme as complex as (3), but with one less hydrogen throughout. The most important feature is ratio iv, indicating 25% loss of $H^{12}CN$ from the labeled precursor. On the basis of V as the rearranged species, it would constitute between 30 and 50% of the $C_6H_6N^+$ ions depending on whether the nitrogen was inserted in the sequence IV → V in a random or specific manner.

The results in Table IV parallel those for sulfanilamide (Table III) very closely. Again the metastable peak for eq 2 was the only one observable for the region of interest. Ratio iv is almost identical with that for sulfanilamide.

For the four compounds studied here, the general conclusion from the major fragmentation is that the odd-electron ions $C_6H_7\cdot N^+$ from aniline and acetanilide are very largely unrearranged, whereas the even-electron ions $C_6H_6N^+$ from sulfanilamide and *p*-nitroaniline are rearranged to a considerable extent. In the toluene spectrum, the tropylium ion $C_7H_7^+$ is of course even electron in character.

In the 1-$^{13}$C-*p*-nitroaniline spectrum, it was possible to examine another potential ring-expansion process (eq 4). The pathway shown[13] is confirmed by metastable peaks for each step. The structure of the *m/e* 80 fragment, formed from *m/e* 108 by loss of CO, is a natural question. Two proposed alternatives are VI and VII. The rearrangement from VI to VII can be tested by the loss of HCN as above, to form $C_4H_5^+$. Both peaks are relatively small; in our low-resolution spectra of unlabeled *p*-nitroaniline, *m/e* 80 was 9% and *m/e* 53 was 5%. High-resolution intensity mea-

(13) For leading references, see ref 10, p 326.




(4)

surements were again necessary to separate isobaric components.

It had been anticipated that no loss of $^{13}C$ would occur between the molecular ion and the $C_5H_6N^+$ ion of mass 80. In fact, the enrichment decreased from 44% excess $^{13}C$ to 36% excess $^{13}C$. That is, within experimental error, about one-sixth of the label had been expelled as $^{13}CO$. One explanation is that the carbon atoms in the *m/e* 108 precursor are already uniformly randomized, so that it is not meaningful to write structures such as VI and VII. Nevertheless the abundance ratio (calculated as above) for $C_4H_5/(C_4H_5 + {}^{13}CC_3H_5) = 0.88$, which indicates that $H^{12}CN$ loss from a calculated 100% enriched species was 12%. Interpretation of this value in terms of evidence for specific rearrangement models is not profitable in the absence of further information about the structure of the *m/e* 80 ion, and the location of its label.

## Experimental Section

**Syntheses with $^{13}C$.** Aniline-1-$^{13}C$, containing 44% excess $^{13}C$, was prepared from commercial[14] sodium acetate-1-$^{13}C$ following the method used for the synthesis of aniline-1-$^{14}C$.[15,16] This route proceeds *via* the pathway: sodium acetate, ethyl acetate, 1-methylcyclohexanol, 1-methylcyclohexene,[17] toluene, benzoic acid, and aniline. Difficulty was encountered in the dehydrogenation of labeled 1-methylcyclohexene to toluene, where the original method made use of an industrial catalyst at 450°.[15] This problem has also been reported by others.[18] In model experiments, an alternative procedure at lower temperature was developed using dehydrogenation over palladium on charcoal in the presence of maleic acid as a hydrogen acceptor[19] to inhibit disproportionation of the methylcyclohexene which would generate methylcyclohexane as well as toluene. When pure unlabeled 1-methylcyclohexene (0.97 g) was heated under reflux at 120° (oil bath) with intimately mixed 30% palladium on charcoal (0.30 g) and powdered, dry maleic acid (5.0 g), analysis of the liquid phase after 4 hr by gas chromatography showed less than 1% starting material, only 2% methylcyclohexane, and 97% toluene. However, when the $^{13}C$-labeled 1-methylcyclohexene was subjected to similar treatment, no dehydrogenation occurred, presumably because of catalyst poisoning by unidentified trace impurities. The reisolated labeled compound was therefore detoxified by being shaken (15 min) at room temperature with a small amount of 30% palladium on charcoal which was centrifuged off before repeating the dehydrogenation reaction. Dehydrogenation then proceeded, but required 28 hr. These manipulations with such volatile compounds reduced the actual yield of toluene--1-$^{13}C$ in this synthetic step to 40%.

The labeled aniline was isolated as its hydrochloride[18] (mp 196–198°), from which 1-$^{13}C$-acetanilide (mp 113–114°), 1-$^{13}C$-sulfanilimide (mp 161–162°), and 1-$^{13}C$-*p*-nitroaniline (mp 147–148°) were prepared by established procedures.[20–22]

**Mass Spectrometry.** Mass spectra were recorded by Mr. R. Ross on an A.E.I. MS-9 instrument at 70 eV. Aniline hydrochloride, acetanilide, and *p*-nitroaniline were admitted from the heated inlet system at 170°, and sulfanilimide required the direct insertion probe for volatility reasons. Spectra of aniline and its hydrochloride were identical above *m/e* 40. The ion chamber was operated with a tungsten filament as the only heat source, using 500- and 100-μA trap currents for high- and low-resolution work, respectively, which produce source temperatures of 250 and 200°. The 500-μA trap current markedly increases sensitivity and therefore the accuracy with which relative intensities can be measured. Our preliminary experiments[6] were performed at 100-μA trap current, and all samples were admitted *via* the probe, resulting in greater source-pressure variation and correspondingly less accurate intensity measurements, especially for the relatively volatile aniline and acetanilide samples. At high resolution (at least 1 in 20,000), the mass regions of interest (*e.g.*, *m/e* 63–68, 90–95) were recorded directly on chart paper (speed 0.6 in./sec) using Decrease Scan rate 2 and Bandwidth 3 control settings. Ion compositions were identified by mass matching; confirmatory evidence was available from the natural $^{13}C$-satellite intensities in the unlabeled samples, and also from the relative mass defects (Tables I–IV list compositions in order of increasing mass). Relative intensity measurements were averages of three to six scans, and were confirmed by making individual Collector Meter readings for each component (without alteration of the electron-multiplier gain through the group of peaks being examined). Confirmatory evidence for the relative intensity measurements was obtained from very low-resolution spectra (source slit 0.003 in., collector slit 0.01 in.) in which the peaks were flat topped so that signal height was the sum of the isobaric components. Measurement of the labeling enrichment was obtained more straightforwardly under high-resolution conditions since in several cases the calculations from low-resolution spectra were complicated by satellite contributions from peaks of next lower mass number. Found (by either method) for all molecular ions and $C_6H_7N$ and $C_6H_6N$ fragments, 44 ± 1% excess $^{13}C$.

(14) Schwarz Bioresearch, Inc.
(15) M. Fields, M. A. Leaffer, S. Rothchild, and J. Rohan, *J. Am. Chem. Soc.*, **74**, 5498 (1952).
(16) M. Fields, S. Rothchild, and M. A. Leaffer, *ibid.*, **74**, 2435 (1952).
(17) We are indebted to Dr. M. Marx, who performed the synthetic sequence as far as 1-methylcyclohexene-1-$^{13}C$.
(18) A. Rieker, K. Scheffler, and E. Mueller, *Ann. Chem.*, **670**, 23 (1963).
(19) E. A. Braude, R. P. Linstead, and P. W. D. Mitchell, *J. Chem. Soc.*, 3578 (1954).
(20) N. E. Searle and H. E. Cupery, *J. Org. Chem.*, **19**, 1622 (1954).
(21) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1957, p 152.
(22) A. I. Vogel, "Practical Organic Chemistry," 3rd ed, Longmans, Green and Co. Ltd., London, 1957, p 581.