

# MASS SPECTROMETRY IN STRUCTURAL AND STEREOCHEMICAL PROBLEMS—CCXXXV<sup>1</sup>

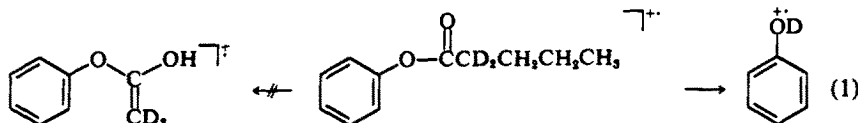
## A HIDDEN HYDROGEN REARRANGEMENT IN LONG CHAINED ANILIDES

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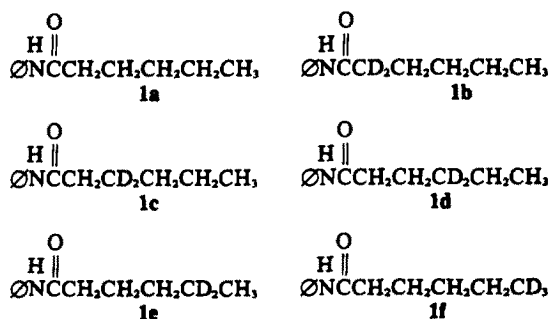
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**Abstract**—The mass spectra of deuterium labeled hexananilides show an unexpected rearrangement of a hydrogen atom from C-4 with formation of a  $C_6H_7N^{+}$  ion. The decomposition of the McLafferty rearrangement ion in these compounds is shown to involve expulsion of the elements of ethynyl alcohol rather than ketene.

Smith and Cowley have reported<sup>2</sup> that phenyl esters of long chain acids undergo specific hydrogen transfer from C-2 of the acid with formation of a  $C_6H_5O^+$  ion. On the other hand no McLafferty rearrangement was observed in these ions (Scheme 1).



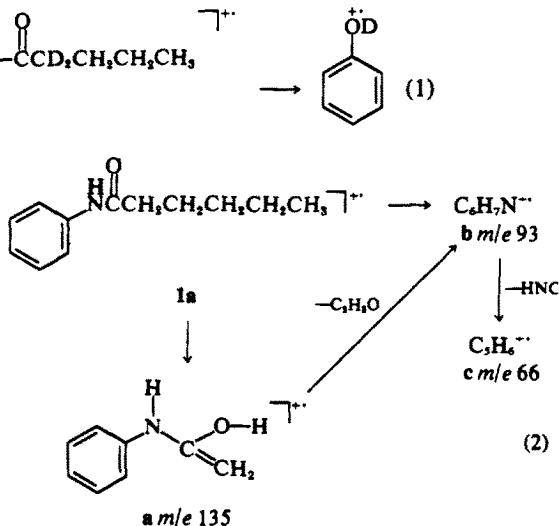
We have been interested for some time in similar reactions in acetanilide<sup>3</sup> and felt that it would be worthwhile to investigate longer chain anilides. We are now reporting the results of our study of hexananilide (1a) and its deuterium labeled analogs (1b-f) (see Table 1 for mass spectral data).



Hexananilide (1a) undergoes two main fragmentations upon electron impact: (1) McLafferty rearrangement with loss of  $C_4H_8$  and hydrogen transfer to oxygen ( $m/e$  135, a) and (2) hydrogen transfer to the aniline moiety with elimination of  $C_4H_{10}O$  ( $m/e$  93, b). The mass 135 ion fragments further by loss of  $C_2H_2O$ , which constitutes an alternate path

to the  $C_6H_7N^{+}$  ion b. The latter decomposes further by loss of HCN to form the mass 66 ion c (Scheme 2).

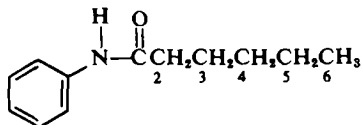
Deuterium labeling showed that the hydrogen transferred in the McLafferty rearrangement was



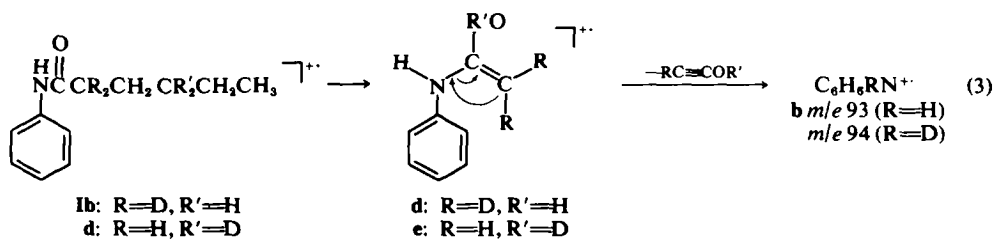
abstracted from the  $\gamma$ -position (Table 2). Metastable analysis and direct analysis of daughter ions (DAD)<sup>4</sup> showed that the McLafferty rearrangement ion underwent hydrogen transfer only from the methylene group to form b and did not involve migration of the hydrogen on oxygen (Eq 3).

The 70 eV spectrum of 2,2-d<sub>2</sub>-hexananilide showed that 92% of the hydrogen transferred is derived from the 2-position (Table 2). This decreased to 83% specificity at 15 eV and to 50% at 11 eV. No metastable peak, however, was observed for deuterium transfer. Thus the low energy mole-

Table 1. 70 eV Mass spectra of hexananilides and its deuterium labeled analogs



<i>m/e</i>	1a(d <sub>0</sub> )	1b(2,2-d <sub>2</sub> )	1c(3,3-d <sub>2</sub> )	1d(4,4-d <sub>2</sub> )	1e(5,5-d <sub>2</sub> )	1f(6,6-d <sub>2</sub> )
41	5	4	3	2	3	3
42	1	3	3	3	3	2
43	10	6	5	5	4	3
44	1	11	10	10	9	6
45	—	9	7	8	7	8
46	—	—	—	—	—	6
55	2	2	—	2	2	2
56	—	1	—	1	—	—
57	—	1	2	1	—	—
65	4	5	4	5	5	4.5
66	3	3	3	3	3	3
67	1	1	—	1	—	—
71	4	—	—	—	—	—
72	—	—	—	—	—	—
73	—	5	4	4	4	—
74	—	—	—	—	—	4
77	5	6	5	5	5	5
91	1	1	1	1	1	—
92	3	3	3	3	3	3
93	100	11	100	100	100	100
94	9	100	10	11	11	0
95	—	11	1	1	1	—
99	2	—	—	—	—	—
100	—	—	—	—	—	—
101	—	3	2	2	2	—
102	—	—	—	—	—	2
119	1	1	—	—	—	—
120	2	2	2	2	2	2
135	7	—	7	1	7	7
136	1	2	1	4	1	1
137	—	9	—	1	—	—
138	—	1	—	—	—	—
190	1	—	—	—	—	—
191	12	—	—	—	—	—
192	2	2	1	1	2	—
193	—	12	9	9	10	1
194	—	3	1	1	2	8
195	—	—	—	—	—	2



cular ions do not transfer hydrogen from the 2-position. Examination of the mass spectra of 1c-f showed that hydrogen transfer also occurred from C-4 and C-5 in molecular ions with low internal

energy and especially from those ions decomposing in the field free regions.

In light of these results, we examined the metastable transitions for the formation of the  $\text{C}_6\text{H}_6\text{O}^+$  ion

Table 2. Percent deuterium transferred in specifically labeled hexananilides\*

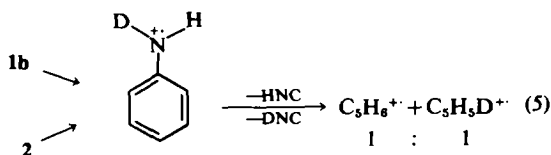
	1b(2,2-d <sub>2</sub> )	1c(3,3-d <sub>2</sub> )	1d(4,4-d <sub>2</sub> )	1e(5,5-d <sub>2</sub> )	1f(6,6,6-d <sub>2</sub> )
<i>m/e</i> 136	—	—	100	—	—
<i>m/e</i> 137	100	—	—	—	—
<i>m/e</i> 94 70 eV	92	3	4	4	2
<i>m/e</i> 94 15 eV	83.5	1	5	6	2
<i>m</i> * for M <sup>+</sup> → 94 <sup>+</sup>	—	—	√	√	—

\* Corrected for isotopic purity

from specifically labeled phenyl hexanoates, since Smith and Crowley<sup>7</sup> did not mention them in their paper. The base peaks in the mass spectra are due to hydrogen transfer from C-2 as observed for the hexananilides. We observed, however, deuterium transfer only from C-2 in the metastable transitions and in the formation of the daughter ions. Thus the amides and esters behave differently.

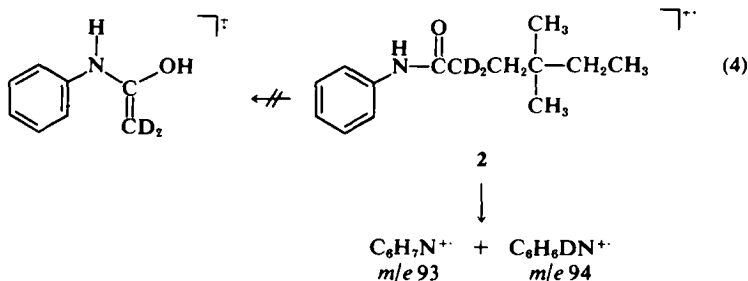
Since the McLafferty rearrangement ion in 1b also gives rise to the mass 94 ions, the possibility should be considered that the mass 94 daughter ions being observed in the spectra arose primarily through this reaction rather than from the molecular ion while the metastable transitions were indicative of the operation of the one-step process. To examine this possibility 2,2-dideuterio-4,4-dimethylhexananilide (2) was prepared and its mass spectrum examined. No McLafferty rearrangement was observed in this compound, but predominant deuterium transfer was still observed (82% at 70 eV, 77% at 15 eV) (Eq 4). The metastable transi-

form an aniline ion (Eq 5).<sup>3</sup>



It has been observed that if two fragmentations compete, the fragmentation occurring through the more loosely bound transition state will decrease relative to the other as the ionizing energy is decreased.<sup>3</sup> Since hydrogen transfer from C-2 occurs through a 4-membered transition state, this eliminates the possibility of hydrogen transfer to the aromatic ring from C-3 or C-4 through 8- or 9-membered transition states.

An alternative mechanism which is consistent with the kinetic data involves bonding between the CO carbon and C-4 or C-5 occurring simultaneously with hydrogen transfer from C-4 or C-5 to nitrogen



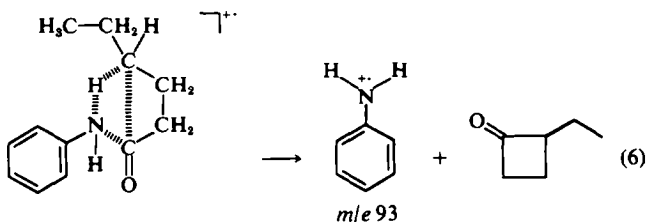
tions, however, still indicated only hydrogen transfer. The secondary decomposition of the McLafferty rearrangement ion to form C<sub>6</sub>H<sub>7</sub>N<sup>+</sup> does not interfere with our results indicating hydrogen transfer from C-2 at high internal energies and hydrogen transfer from C-4 and C-5 at low internal energies.

The C<sub>6</sub>H<sub>6</sub>DN<sup>+</sup> ion resulting from deuterium transfer from C-2 in 1b and 2 was observed to lose HNC and DNC in a 1:1 ratio in the first and second field free regions and from the DADI spectra of 1b. This is consistent only with deuterium transfer to nitrogen through a 4-membered transition state to

(Eq 6). A lower frequency factor is expected for a bicyclic transition state than for a 4-membered transition state.\* The cycloalkanone neutral formed in the reaction is also expected to be thermodynamically more stable than the ketene neutral which is consistent with the lower activation energy observed for hydrogen transfer from C-4 and C-5.

The reason for the nonobservance of this bicyclic rearrangement in the phenyl hexanoate, however, is not obvious based on this mechanism. One major difference between phenyl hexanoate and hexananilide which may or may not be related to the above discussion is the ratio of simple cleavage ions (*m/e* 43, 55, 71, 77 and 99) to rearrangement ions (*m/e* 135 and 93 in hexananilide and *m/e* 94 in

\* Inspection of molecular models of the two transition states shows that the bicyclic transition state is more tightly bound than is the 4-membered transition state.



phenylhexanoate). This ratio is 23:100 at 70 eV and 7/100 at 15 eV for hexananilide but is 240240:100 at 70 eV and 146:100 at 15 eV for phenylhexanoate.

#### EXPERIMENTAL

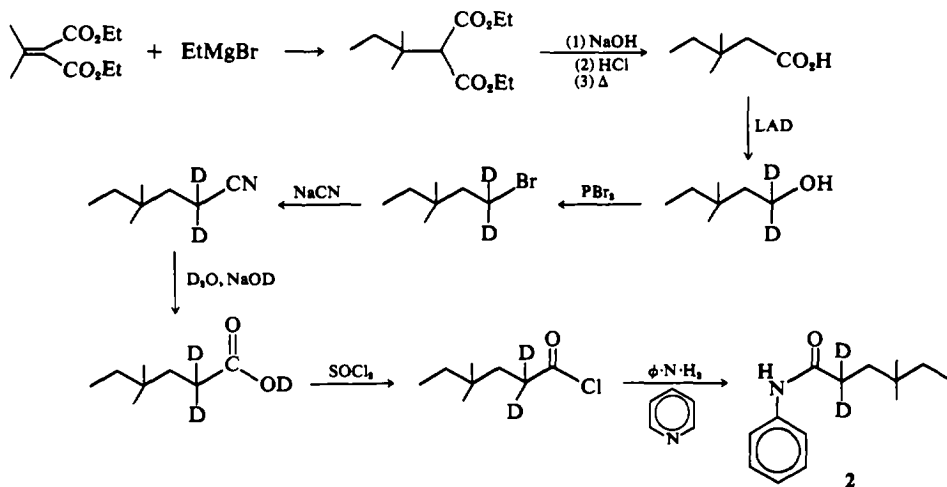
The mass spectra were run on an AEI MS-9 mass spectrometer utilizing a direct probe. Metastable peaks in the first field free region were determined on a Varian MAT 711 spectrometer utilizing the Barber-Elliott technique.<sup>6</sup> DADI spectra were kindly provided by Dr. K. H. Maurer and U. Rapp, Varian MAT, Bremen, Germany.

The labeled hexanoic acids were kindly donated by Dr. R. J. Liedtke.

The hexananilides **1a-f** were prepared by treatment of

by treatment with PBr<sub>3</sub>. The bromide was reacted with NaCN in DMF to yield the nitrile. 2,2-Dideuterio-4,4-dimethylhexanenitrile was hydrolyzed with 40% NaOD in D<sub>2</sub>O. Acidification of the mixture, extraction with ether, drying over Na<sub>2</sub>SO<sub>4</sub> and removal of the ether yielded 2,2-dideuterio-4,4-dimethylhexanoic acid. The acid chloride was prepared by heating the crude acid with SOCl<sub>2</sub> and was reacted with aniline in pyridine. The 2,2-dideuterio-4,4-dimethylhexananilide thus prepared was purified by GLC. (3% OV-25 on chromosorb-W).

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the appropriate acid chloride with aniline in pyridine. The compounds were purified by GLC. Phenyl hexanoate and its labeled analogs were prepared by treatment of the appropriate acid chloride with phenol. The compounds were purified by GLC. The following reaction sequence was used in the preparation of 2,2-dideuterio-4,4-dimethylhexananilide,<sup>7</sup> (2).

**2,2-Dideuterio-4,4-dimethylhexananilide.** EtMgBr (0.1M) was added to a soln of diethyl isopropylidene malonate (0.1M) in ether containing cuprous chloride (1.2 g).<sup>8</sup> The soln was refluxed for 2 h and saturated ammonium chloride was added. The solvent was removed *in vacuo* and the crude product was hydrolyzed with KOH aq. The soln was acidified and extracted with ether. The ether layer was dried over Na<sub>2</sub>SO<sub>4</sub> and the ether removed. The crude diacid was heated at 180° for 1 h and the product distilled b<sub>p</sub> 88–92° (unlabeled b<sub>700</sub> 201–202°)<sup>7</sup> to yield 3,3-dimethylpentanoic acid.<sup>7</sup> Reduction of the acid with LAD yielded 1,1-dideuterio-3,3-dimethylpentanol which was transformed into the bromide

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- <sup>6</sup>Varian MAT 711 instruction manual
- <sup>7</sup>See L. Schmerling, *J. Am. Chem. Soc.* **67**, 1152 (1945) for the unlabeled 4,4-dimethylhexananilide
- <sup>8</sup>M. S. Newman and N. Gill, *J. Org. Chem.* **31**, 3860 (1966)