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Cycloalkene Budding: A Unique Rearrangement Observed in the Mass Spectra of *N*,*N*-Dimethylhydrazones of Unsaturated Aldehydes

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In the course of studying the electron-ionization mass spectra of unsaturated aldehyde derivatives, we encountered a new mass spectral rearrangement and fragmentation that is both diagnostically useful and fundamentally interesting from a mechanistic viewpoint. When a double bond is present at position 5 or 6 in an unsaturated straight-chain aldehyde, under electron-ionization conditions its *N*,*N*-dimethylhydrazone undergoes an unprecedented combination of bond-making and bond-breaking reactions, for which we suggest the term "cycloalkene budding". The spectra obtained are analytically useful, since the position of the double bond can be deduced by the appearance of characteristic peaks at *m*/*z* $(M - 68)^+$ or $(M - 82)^+$, representing losses of C_5H_8 or C_6H_{10} for 5- and 6-alkenal derivatives, respectively. Although fragmentations of gas-phase ions resulting in hydrocarbon elimination, not initiated by the charged site, have been well established,[1−3] these examples have usually involved a 1,4-elimination process which is not analogous to the charge-mediated process which we now report.

The electron-ionization (EI) mass spectrum of the (*E*)-5-tetradecenal derivative depicted in Figure 1a provided us with the first example of this novel fragmentation. It shows several peaks that are generally expected in EI spectra of *N*,*N*-dimethylhydrazones.[4,5] An intense molecular ion and peaks representing losses of 15 and 44 mass units from the molecular ion are characteristic of these derivatives.[5] A peak at *m*/*z* 86 which represents a γ-hydrogen transfer by a McLafferty rearrangement (Scheme 1) is particularly prominent.

In addition to these anticipated ions, however, there is a prominant peak at *m*/*z* 184 $(M - 68)^+$ in the mass spectrum of (*E*)-5-tetradecenal dimethylhydrazone which cannot be explained by known fragmentation mechanisms. Indeed, we found this loss of 68 mass units from the molecular ion to be characteristic of dimethylhydrazones bearing a double bond at the 5 position. Mass spectral data presented in Table 1 shows that this unique loss appears in the mass spectra of derivatives of both the cis and trans isomers of 5-decenal, 5-dodecenal, 5-tetradecenal, and 5-hexadecenal. A homologous loss of 82 mass units is observed in the spectra of 6-alkenal derivatives. For example, the spectrum of (*E*)-6-tetradecenal dimethylhydrazones, illustrated in Figure 1B, shows an $(M - 82)^+$ signal at *m*/*z* 170.

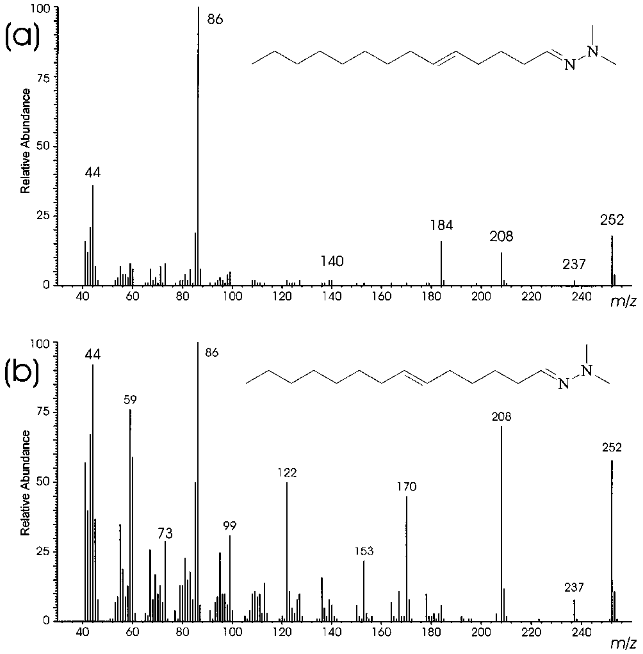

Figure 1. Electron-ionization mass spectra (70 eV) of *N*,*N*-dimethylhydrazones of (*E*)-5-tetradecenal (a), and (*E*)-6-tetradecenal (b).

The elemental composition of the *m*/*z* 184 ion observed in the spectrum of (*E*)-5-tetradecenal dimethylhydrazone was obtained by high-resolution mass spectrometry ($R = 10000$). The measured mass of 184.1931 (calculated for $C_{11}H_{24}N_2$ 184.1940) recorded for this ion established that the 68 Da loss represents a removal of C_5H_8 from the molecular ion (252.2565 observed, 252.2566 calculated). To rationalize the loss of C_5H_8 from the molecular ion, we propose an intramolecular cycloaddition followed by ring cleavage of the bicyclic intermediate, which results in the elimination of cyclopentene (Scheme 2).

Similarly, the accurate mass of the *m*/*z* 170 ion observed in the spectrum of 6-tetradecenal dimethylhydrazone is 170.1778 ($R = 10000$; calculated for $C_{10}H_{22}N_2$, 170.1783). This observation established that the 82 Da loss represents a loss of C_6H_{10} from the molecular ion, which can be rationalized analogously as a cyclohexene extrusion (Scheme 3).

To test this hypothesis, several deuterium labeled 5- and 6-alkenals capable of providing diagnostically useful results were synthesized. The mass spectra of the dimethylhydrazones of (*E*)-5-[1-$^2H_1$]tetradecenal and (*E*)-6-[1-$^2H_1$]tetradecenal showed the expected rearrangement peaks still at *m*/*z* 184 and 170, respectively (Figure 2, parts a and c), confirming that the C-1 deuterium atom is lost as anticipated. Further support for the proposed fragmentation was provided by the mass spectrum of derivative of (*Z*)-5-[5,6-$^2H_2$]tetradecenal (Figure 2b). In this spectrum, a peak was observed at *m*/*z* 185, corresponding to a 69-Da loss from the molecular ion. According to the proposed mechanism, the C-5 deuterium

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Scheme 1. McLafferty Rearrangement of an N,N-Dimethylhydrazone

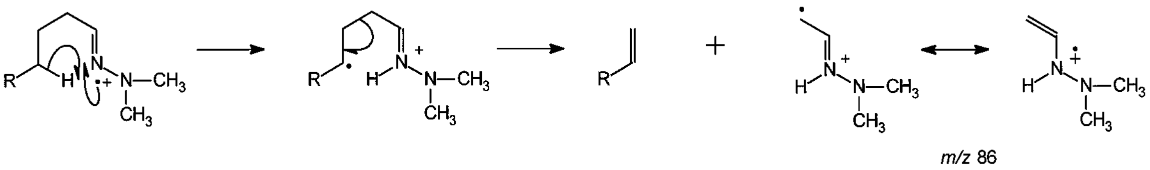
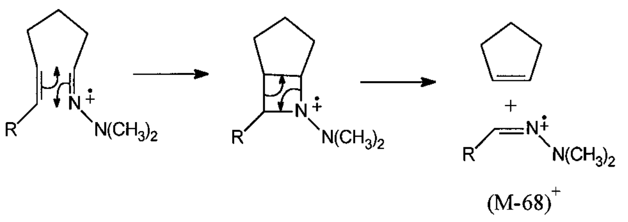


Table 1. Electron-Ionization Mass Spectra (70 eV) of N,N-Dimethylhydrazones of Some 5- and 6-Alkenals

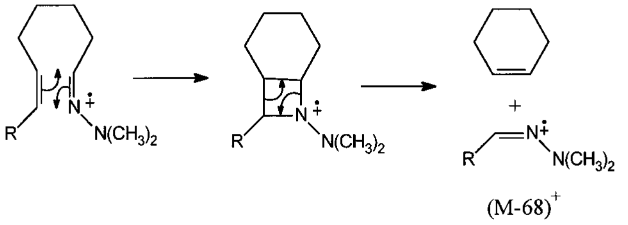
derivatized aldehyde	key fragment ions (*m*/*z*, %)
(*Z*)-5-decenal	196 (M^+, 7), 181(0.5), 152 ($M^+ - 44$, 5), **128 ($M^+ - 68$,** 10), 86(100), 44(63)
(*E*)-5-decenal	196 (M^+, 10), 181(0.5), 152 ($M^+ - 44$, 8), **128 ($M^+ - 68$,** 12), 86(100), 44(60)
(*Z*)-5-dodecenal	224 (M^+, 9), 209(2), 180 ($M^+ - 44$, 7), **156 ($M^+ - 68$,** 13), 86(100), 44(88)
(*E*)-5-dodecenal	224 (M^+, 25), 209(2), 180 ($M^+ - 44$, 12), **156 ($M^+ - 68$,** 20), 86(100), 44(50)
(Z)-5-tetradecenal	252 (M^+, 6), 237(1), 208 ($M^+ - 44$, 6), **184 ($M^+ - 68$,** 8), 86(100), 44(40)
(*E*)-5-tetradecenal	252^a (M^+, 20), 237(2), 208^b ($M^+ - 44$, 12), **184^c ($M^+ - 68$,** 18), 86(100), 44(50)
(*Z*)-5-hexadecenal	280 (M^+, 6), 265(0.5), 236 ($M^+ - 44$, 6), **212 ($M^+ - 68$,** 8), 86(100), 44(35)
(*E*)-5-hexadecenal	280 (M^+, 8), 265(0.5), 236 ($M^+ - 44$, 10), **212 ($M^+ - 68$,** 10), 86(100), 44(45)
(*Z*)-6-decenal	196 (M^+, 18), 181(2), 152 ($M^+ - 44$, 20), **114 ($M^+ - 82$,** 28),122(15), 86(72), 44(93)
(*E*)-6-decenal	196 (M^+, 15), 181(2), 152 ($M^+ - 44$, 18), **114 ($M^+ - 82$,** 28),122(15), 86(70), 44(100)
(*Z*)-6-dodecenal	224 (M^+, 18), 209(5), 180 ($M^+ - 44$, 20), **142 ($M^+ - 82$,** 25),122(21), 86(96), 44(100)
(*E*)-6-dodecenal	224 (M^+, 70), 209(10), 180 ($M^+ - 44$, 55), **142 ($M^+ - 82$,** 50),122(30), 86(85), 44(100)
(*Z*)-6-tetradecenal	252 (M^+, 15), 237(4), 208 ($M^+ - 44$, 26), **170 ($M^+ - 82$**, 24),122(24), 86(100), 44(100)
(*E*)-6-tetradecenal	252^d (M^+, 62), 237(9), 208^e ($M^+ - 44$, 75), **170^f ($M^+ - 82$**, 50),122^g(50), 86(100), 44(100)
(*Z*)-6-hexadecenal	280 (M^+, 16), 265(2), 236 ($M^+ - 44$, 29), **198 ($M^+ - 82$,** 18),122(22), 86(100), 44(100)
(*E*)-6-hexadecenal	280 (M^+, 18), 265(2), 236 ($M^+ - 44$, 30), **198 ($M^+ - 82$,** 20),122(25), 86(100), 44(100)

High-resolution data: ^{a} 252.2565 (calcd for $C_{16}H_{32}N_2$ 252.2565), ^{b} 208.2057 (calcd for $C_{14}H_{26}N$ 208.2065), ^{c} 184.1931 (calcd for $C_{11}H_{24}N_2$ 184.1939), ^{d} 252.2553 (calcd for $C_{16}H_{32}N_2$ 252.2565, ^{e} 208.2053 (calcd for $C_{14}H_{26}N$ 208.2065), ^{f} 170.1778 (calcd for $C_{10}H_{22}N_2$ 170.1783), ^{g} 122.0969 (calcd for $C_8H_{12}N_1$ 122.0970).

Scheme 2. Proposed Mechanism for C_5H_8 Loss



Scheme 3. Proposed Mechanism for C_6H_{10} Loss



atom should be eliminated in monodeuteriocyclopentene but the C-6 deuterium should be retained in the remaining cation radical. Interestingly, these fragmentations appear to be unique to the mass spectra of aldehyde *N*,*N*-dimethylhydrazones. For example, the mass spectrum of the dimethylhydrazone of 6-undecen-2-one failed to show an 82 Da loss (of 1-methylcyclopentene). Furthermore, loss of 68 and 82 mass units could not be observed in the spectra of either the parent 5- or 6-alkenals, or of their methoximes.

From the data provided, it is clear that losses of 68 and 82 mass units from the molecular ion are common features of the mass spectra of derivatives of 5- and 6-alkenals, respectively (although the spectrum illustrated in Figure 1B shows a weak ion at *m*/*z* 184, the presence of such a nonprominent ion does not interefere with the structural deductions). This can be a diagnostically useful observation, since the derivatization procedure is simple, and only a few nanograms of the aldehyde

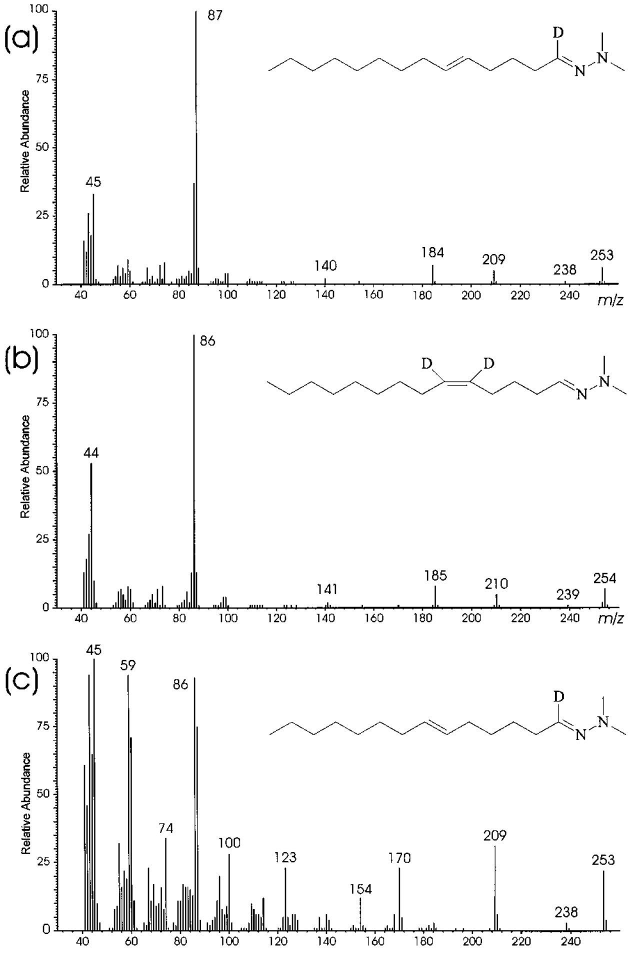


Figure 2. Electron-ionization mass spectra (70 eV) of *N*,*N*-dimethylhydrazones of (*E*)-5-[1-$^2H_1$]tetradecenal (a), (*Z*)-5-[5,6-$^2H_2$]tetradecenal (b), and (*E*)-6-[1-$^2H_1$]tetradecenal (c).

are required for analysis. Previous results have shown that *N*,*N*-dimethylhydrazone spectra are diagnostic for double bonds at the 2, 3, and 4 positions;[6] we can now add the positions 5 and 6 to this list. In addition, since these mass spectra are easily obtained by GC-MS, the determinations can be carried out without having to isolate the aldehydes in pure form. Although several microanalytical techniques are available for double bond localization.[7-9] the simple observation of cyclopentene or cyclohexene elimination may nevertheless be useful, especially since long-chain unsaturated aldehydes are encountered frequently as natural product components, for example, in plant oils or insect allomones and pheromones.

Experimental Section

Low-resolution electron-ionization (70 eV) mass spectra were obtained using a HP 5890 gas chromatograph linked to an HP 5970 mass selective detector (MSD). High-resolution mass spectrometry was performed on a Finnigan-MAT 731 instrument ($R = 10000$). All isomers of monounsaturated aldehydes were prepared from the corresponding alcohols available from the synthetic pheromone collection of the Research Institute for Plant Protection (Wageningen, The Netherlands).[10] (*Z*)-5-[1-$^2H_1$]-Tetradecenal and (*Z*)-6-[1-$^2H_1$]tetradecenal were prepared by the reduction of the corresponding nondeuterated aldehydes with $LiAlD_4$ followed by oxidation with pyridinium dichromate. (*Z*)-5-[5,6-$^2H_2$]Tetradecenal was prepared using 5-hexyn-1-ol as the starting material. After the protection of the hydroxy group of 5-hexyn-1-ol with TBDMS chloride, it was coupled with octyl bromide (BuLi/HMPT). The product was reduced with D_2/Lindlar catalyst, and after the removal of the protecting group, the alcohol was oxidized to the corresponding aldehyde with PDC. Derivatization was brought about by mixing the aldehydes with 50% *N*,*N*-dimethylhydrazine in hexane.[4]

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Additions and Corrections

Vol. 62, 1997

Takashi Takahashi,* Satoshi Tomida, Yasuharu Sakamoto, and Haruo Yamada. New Approach to the Steroid BCD-Ring Using Tandem Radical Cyclization.

Page 1912. ^{1}H NMR data of (10α,17*β*)-des-A-pregnane-5,20-dione (**4**) and (10α,17α)-des-A-pregnane-5,20-dione on page 9 of the Supporting Information are incorrect.

Supporting Information Available: A new page 9 with corrected ^{1}H NMR data (1 page). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9740195

Vol. 60, 1995

Bin Ye and Terrence R. Burke, Jr.*. A Concise Synthesis of the Differentiating Antibiotic L-Azatyrosine.

Page 2640. As pointed out by Sheldrake et al. (*J. Org. Chem.* **1997**, *62*, 3008−3009), our starting material **5** was 3-hydroxy-2-iodopyridine rather than 5-hydroxy-2-iodopyridine as we originally reported. Accordingly, compounds subsequently derived from this starting material have ring oxy substituents at the 3-position rather than the 5-position as we reported.

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