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Observation and Interpretation of an Apparent Inverse Secondary Isotope Effect on the Electron Impact-induced Loss of a Methyl Radical from Methyl Isobutyrate

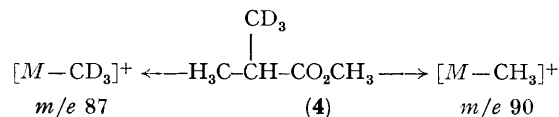
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Summary The loss of $\text{CD}_3\cdot$ from the molecular ion of methyl [$^2\text{H}_3$]isobutyrate (**4**) is 2.2 times faster than the loss of $\text{CH}_3\cdot$ at 70 eV; the unusual direction and magnitude of the isotope effect are explained by a two-step mechanism, in which a rate-determining hydrogen or deuterium atom transfer precedes the loss of $\text{CD}_3\cdot$ or $\text{CH}_3\cdot$,

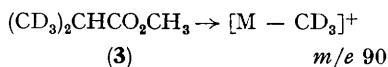
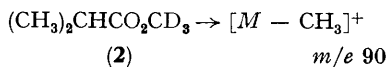
$[\text{M} - \text{CH}_3]^+ : [\text{M} - \text{CD}_3]^+$ is 0.46:1 for the ions formed at 70 eV in the ion source, and 0.36:1 for ions formed by metastable transitions in the first field-free region of a normal geometry double focusing mass spectrometer (Varian 711).

METHYL ISOBUTYRATE (**1**) gives rise to a relatively abundant $[\text{M} - \text{CH}_3]^+$ ion at m/e 87 under electron impact (30% of the most abundant ion at 70 eV, $[\text{M} - \text{CH}_3]^+ : [\text{M}^+] = 2.3 : 1$).¹ The origin of the leaving methyl radical from the isopropyl group is confirmed by the finding that [$^2\text{H}_3$]-methyl isobutyrate (**2**) retains the three deuterium atoms in the m/e 90 $[\text{M} - \text{CH}_3]^+$ ion, and methyl [$^2\text{H}_6$]isobutyrate (**3**) loses only a trideuteriomethyl radical.



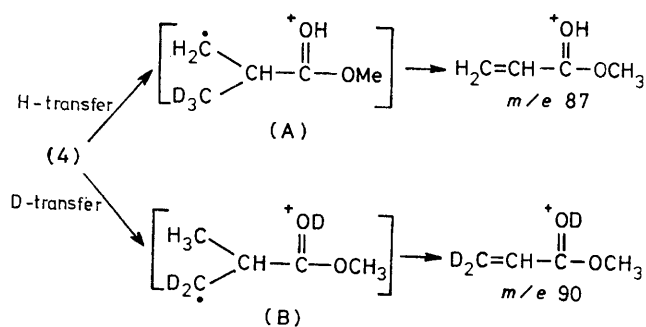
The above values found for the isotope effect for the loss of a methyl radical from (**4**) are surprising both in the direction of the effect and its magnitude. The ratio $k_{\text{H}} : k_{\text{D}}$ is generally greater than unity in mass spectral fragmentations,² while in the present case the loss of $\text{CH}_3\cdot$ radical is slower than that of $\text{CD}_3\cdot$.[†] Furthermore, secondary isotope effects are usually smaller than the values found in this work.²⁻⁴

The unusual features of this apparent large inverse isotope effect are consistent with the two-step mechanism shown in the Scheme for (**4**). The first step in this fragmentation is the transfer of a hydrogen or deuterium atom from the CH_3 or CD_3 group towards the carbonyl oxygen. The radical site at C-3 in the resulting intermediates (A) and (B) facilitates the C-C bond cleavage which leads to the $[\text{M} - \text{methyl}]^+$ ions at m/e 87 and 90.



The mass spectrum of methyl [$^2\text{H}_3$]isobutyrate (**4**) provides an opportunity to investigate the competition between the loss of $\text{CH}_3\cdot$ and $\text{CD}_3\cdot$ radicals from the molecular ion, since the ratio of abundances $[\text{M} - \text{CH}_3]^+ : [\text{M} - \text{CD}_3]^+$ is a direct measure of the isotope effect $k_{\text{H}} : k_{\text{D}}$. This ratio

[†] An inverse secondary isotope effect on the ion abundance ratio $[\text{M} - \text{I}]^+ : [\text{M}]^+$ has been recently reported for certain iodides (ref. 3).



SCHEME

It is reasonable to assume that the formation of intermediate (A) or (B), which involves a rearrangement, is the rate determining step in the fragmentation. As this step involves migration of a hydrogen atom, it can be expected to exhibit a primary deuterium isotope effect. Finally, the important point in this mechanism is that the loss of $\text{CD}_3\cdot$ from (4) is preceded by a hydrogen atom transfer (via intermediate A), while the loss of $\text{CH}_3\cdot$ is preceded by a deuterium atom migration (through intermediate B). Therefore the isotope effect $k_{\text{H}}:k_{\text{D}}$ is demonstrated by the abundance

† The increase can be explained by activation energy and entropy differences (see D. H. Williams and I. Howe, 'Principles of Organic Mass Spectrometry,' McGraw-Hill, London 1972, p. 170 and references cited therein; R. G. Cooks, J. H. Beynon, R. M. Caprioli, and G. R. Lester, 'Metastable Ions,' Elsevier, Amsterdam, 1973, p. 103). Different rates of further fragmentations of the $[\text{M} - \text{CH}_3]^+$ and $[\text{M} - \text{CD}_3]^+$ ions may also play a role.

¹ A. G. Sharkey, J. L. Shultz, and R. A. Friedel, *Analyt. Chem.*, 1959, **31**, 87, report lower values for the m/e 87 ion: 15% of the most abundant ion, $[\text{M} - \text{CH}_3]^+ : [\text{M}^+] = 1.34 : 1$.

² F. H. Field and J. L. Franklin, 'Electron Impact Phenomena,' Revised edn., Academic Press, New York, 1970, p. 212, and references cited therein; F. W. McLafferty, D. J. McAdoo, J. S. Smith, and R. Kornfeld, *J. Amer. Chem. Soc.*, 1971, **93**, 3720.

³ G. Eadon and R. Zawalski, *Org. Mass Spectrom.*, 1977, **12**, 599, and references cited therein.

⁴ G. Jones and L. P. McDonnell, *J.C.S. Chem. Comm.*, 1976, **36**.

⁵ F. W. McLafferty and R. B. Fairweather, *J. Amer. Chem. Soc.*, 1968, **90**, 5915.

⁶ (a) S. Meyerson, *Internat. J. Mass Spectrom. Ion Phys.*, 1968, **1**, 309; (b) A. Mandelbaum, 'Stereochemistry—Fundamentals and Methods,' ed. H. Kagan, Georg Thieme, Stuttgart, 1977, p. 165.

⁷ R. Bar-Shai and A. Mandelbaum, Proceedings, 41st Annual Meeting, Israel Chem. Soc., October 1971, p. 194; Ref. 6b, p. 168.

ratio $[\text{M} - \text{CD}_3]^+ : [\text{M} - \text{CH}_3]^+$ rather than by its reciprocal value, and equals 2.2 for the normal and 2.8 for the metastable ions.†

Thus the mechanism suggested in the Scheme explains well the direction of the isotope effect; the magnitude of the ratio is not surprising, as it now reflects a primary isotope effect.

This mechanism finds strong support from the high intensity of the metastable transition (1.0% of the intensity of the normal peak for non-deuteriated m/e 87 ion), which suggests⁵ that the loss of the methyl radical indeed involves a rearrangement. It is also obvious that the protonated methyl acrylate structure of the $[\text{M} - \text{methyl}]^+$ ion shown in the Scheme is more stable than the alternative structure $\text{CH}_3\text{C}^+\text{HCO}_2\text{CH}_3$, with the positive charge at the α -position, which would arise by a one-step loss of the methyl radical. Hidden hydrogen transfers preceding other bond cleavages have been suggested in other fragmentation processes, e.g., the homoallylic cleavage in unsaturated esters,⁶ the elimination of methanol from dimethyl *trans*-cyclohexane-1,4-dicarboxylate,⁷ and the loss of a chlorine atom from 3-chlorobutanoates.^{6a}

The present work demonstrates that such hydrogen migrations may play an important role even in apparently simple bond cleavage processes.

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