

uses would appear to be as: (a) a latentiated acidifier in spontaneous carbonation of aqueous systems; (b) a desiccant in food and drug products; (c) a reagent in synthesis of various citric acid derivatives.

(1) T. Higuchi, S. Eriksson, H. Uno, and J. Windheuser, *J. Pharm. Sci.*, 53, 280(1964).

(2) J. Robinson, A. Repta, and T. Higuchi, *ibid.*, 55, 1196(1966).

(3) A. Repta, J. Robinson, and T. Higuchi, *ibid.*, 55, 1200(1966).

A. J. REPTA

T. HIGUCHI

Department of Pharmaceutics and
Pharmaceutical Chemistry

School of Pharmacy

University of Kansas

Lawrence, KS 66044

Received January 3, 1969.

Accepted for publication January 31, 1969.

Mass Spectrometry of Lysergic Acid Diethylamide

Keyphrases ☐ Lysergic acid diethylamide—analysis ☐ Fragmentation pattern—lysergic acid diethylamide ☐ Mass spectroscopy—analysis

Sir:

The need for sensitive and specific tests for lysergic acid diethylamide (LSD), a dangerous and widely abused drug, has led to the development of analyses based on thin-layer and gas chromatographic techniques

(1-3). IR spectroscopy offers an additional criterion of identity (3, 4). The authors have found that mass spectrometry provides an unequivocal method for establishing the presence of LSD in only trace amounts. The present communication suggests the fragmentation pattern for the compound and demonstrates the forensic value of the technique.

The mass spectrum (Fig. 1A) of LSD tartrate (LSD 25 of Sandoz) closely resembles that (Fig. 1B) of the base showing that the salt dissociates readily. Fragment ions from tartaric acid appear only at low m/e values (highest m/e value: 105, base peak 76) and therefore do not interfere with the analytically significant portion of the spectrum. In both spectra the base peak is the molecular ion $M(m/e\ 323)$. The parent ion as well as the fragment ions tend to lose hydrogen atoms in order to acquire increased conjugation. Thus, small peaks are observed at $M-1$ and $M-2$, possibly due to cleavage of hydrogen atoms at C-4 and C-5. Spectra of aged samples (exposed to light and air) show small peaks at $M-3$ and $M-4$ also. Near the most prominent fragments (e.g., at $m/e\ 221, 207, 196$, and 181) clusters of peaks differing in mass number by 1 are observed. Consequently all metastable peaks, except that at $m/e\ 242.8$, were broad with maxima at the approximate m/e values shown in Scheme I.

The fragmentation of LSD appears to be directed by the amido carbonyl group and the tertiary amino group, and proceeds through characteristic α - and β -cleavages of the former and α - and C,N-bond cleavages of the latter (5). Metastable peaks for some of these transitions were located and are shown in Scheme I.

The most prominent cluster of fragment ions is in the region $m/e\ 221-223$; these ions are formed via the loss of the side chain (see Scheme I). Fragment $m/e\ 223$ yields $m/e\ 222$ and $m/e\ 221$ by H-atom loss. A broad metastable peak at $m/e\ 194$ could arise from loss of CH_3 from $m/e\ 222$ yielding the highly conjugated moiety $m/e\ 207$. Other modes of fragmentation of $m/e\ 223$ probably involve fission of the piperidine ring. α -Cleavage of the 7,8-bond with hydrogen transfer and subsequent expulsion of $\text{CH}_2=\text{N}=\text{CH}_2$ produces $m/e\ 181$ which yields the fully conjugated species $m/e\ 154$. The identities of $m/e\ 154$ and $m/e\ 167$ have been established earlier (6) by high-resolution mass spectrometry. Alternative fission of the piperidine ring may proceed via rupture of 8,9- and 7,N-bonds, the resulting ion $m/e\ 196$ yielding $m/e\ 167$ through loss of $\text{CH}_2=\text{NH}$. Minor but characteristic ions appearing

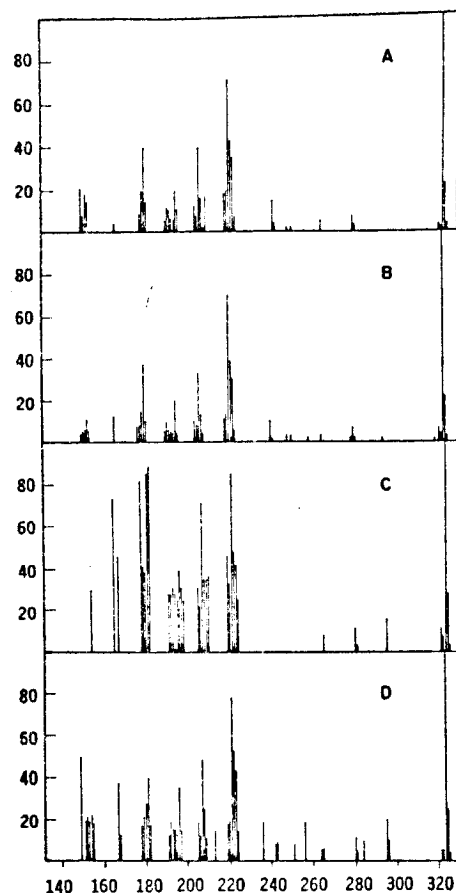
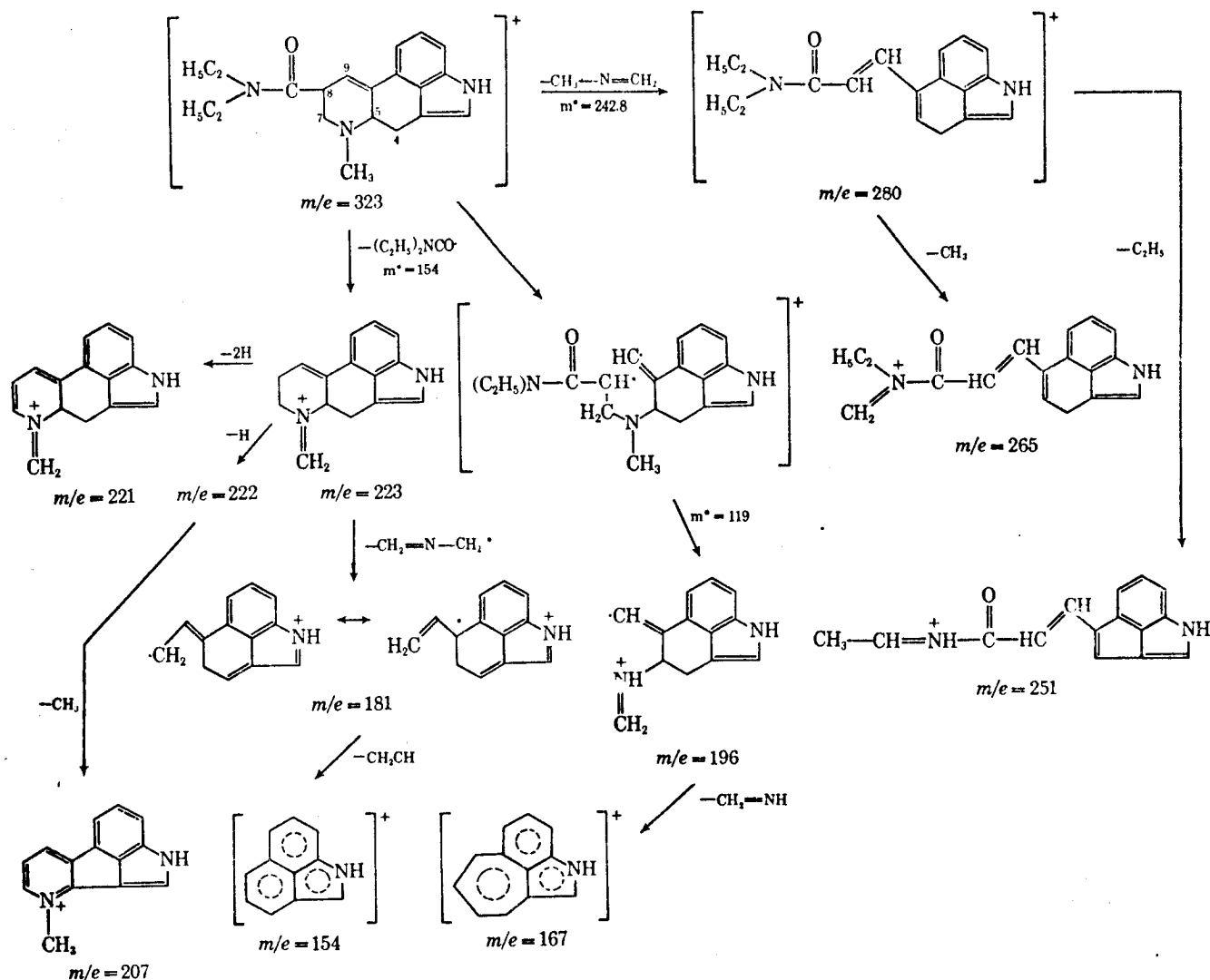


Figure 1—Mass spectra (70 ev.) of LSD. Instrument, Perkin-Elmer RMU6D equipped with MG150A direct inlet; source temperature, 190°; inlet block temperature, 300°. Samples: A, LSD tartrate (5 mcg.); B, LSD base; C, sugar cube scraping (about 2 mg.); D, sugar cube extract.



Scheme 1—Fragmentation of LSD under Electron Impact

at m/e 280, 265, and 251 may be considered to arise from the parent ion through loss of $\text{CH}_3\text{N}=\text{CH}_2$ to yield m/e 280; loss of CH_3 from m/e 280 yields m/e 265 and loss of CH_3CH_2 yields m/e 251.

These observations agree with data of Barber *et al.* (6) who reported some features of the mass spectra of ergot alkaloids and related substances. Production of fully conjugated ions m/e 154 and m/e 167 is common among lysergic acid derivatives (6). While this manuscript was in preparation, Bellman (7) reported the spectra of some lysergic acid derivatives and explained the formation of several ions but did not record metastable peaks for the proposed fragmentation processes.

LSD is well-characterized by the three prominent peaks m/e 323 (M), m/e 221 (70% of M), and m/e 207 (40% of M). The technique should prove of special value to the forensic chemist since spectra can be obtained without any special processing of the sample. The sensitivity of the method is well exemplified by Spectrum A which was obtained from a 5-mcg. sample of the pure tartrate. Smaller quantities could easily be identified with a more sensitive detector than that on the instrument used in this work. Figure 1, C and D show the mass spectra of scrapings and a chloroform-methanol (9 : 1) extract of an LSD-impregnated sugar

cube seized by officers of the Food and Drug Directorate.

- (1) K. Genest and C. G. Farmilo, *J. Pharm. Pharmacol.*, **16**, 250(1964).
- (2) C. Radecka and I. C. Nigam, *J. Pharm. Sci.*, **55**, 1861(1966).
- (3) M. Lerner, *Bull. Narcotics, U. N. Dept. Social Affairs*, **19**, 42(1967).
- (4) F. Troxler and A. Hofmann, *Helv. Chim. Acta*, **40**, 1706 (1957).
- (5) H. Budzikiewicz, C. Djerassi, and D. H. Williams, in "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, San Francisco, Calif., 1964, pp. 66, 83.
- (6) M. Barber, J. A. Weisbach, B. Douglas, and G. O. Dudek, *Chem. Ind.*, 1965, 1072.
- (7) S. W. Bellman, *J. Assoc. Offic. Anal. Chemists*, **51**, 164(1968).

ISHWAR C. NIGAM*
 JOHN L. HOLMES†
 Research Laboratories
 Food & Drug Directorate
 Ottawa, Ontario, Canada

Received March 18, 1968.

Accepted for publication December 17, 1968.

* Deceased.

† Present address: Chemistry Department, University of Ottawa, Ottawa, Ontario, Canada. To whom all correspondence should be addressed.