pane prepared above for the 1,3-diiodo-2,2-dimethyl-propane used by these workers. The yield of acid was 22 g., b.p. 75–103° at 12 mm. (lit.[25] b.p. 105–106° at 15 mm.).

Silver 3,3-dimethylcyclobutanecarboxylate was prepared from 3,3-dimethylcyclobutanecarboxylic acid following the procedure of Cason and Way.[26] The silver salt was air dried at room temperature, and then dried at 0.5 mm. for 4 days prior to its use in the brominative decarboxylation.

3,3-Dimethylcyclobutyl Bromide from Silver 3,3-Dimethylcyclobutanecarboxylate. The procedure was modeled after that described for the preparation of cyclobutyl bromide.[26] The reaction flask was dried by distilling 50 ml. of carbon tetrachloride from it immediately before use. Bromine and carbon tetrachloride were dried by distillation from phosphorus pentoxide.

The silver salt (38.9 g., 0.17 mole) was added over the course of 1 hr. to 250 ml. of carbon tetrachloride and 28.9 g. (0.18 mole) of bromine in a 500-ml., three-necked, round-bottomed flask equipped with mechanical

(26) J. Cason and R. L. Way, *J. Org. Chem.*, 14, 31 (1949).

stirrer and thermometer and immersed in a Dry Ice–acetone bath. The salt was added through a piece of Gooch tubing connecting one inlet of the reaction flask directly to the erlenmeyer flask in which the salt had been dried. No carbon dioxide evolution was observed until the solution had been warmed briefly to +20°; after the reaction had started, the solution was cooled to 0° and the remainder of the silver salt was added. When gas evolution had ceased, the reaction mixture was allowed to stand overnight and then filtered, washed once with aqueous sodium bisulfite, once with 2 N potassium hydroxide solution, and once with water. The organic layer was dried over calcium sulfate, and the carbon tetrachloride was removed through a 10-cm. glass-helix packed column. The bromide was distilled under slightly reduced pressure through a 30-cm. Vigreux column. The product (12 g., 45%) had b.p. 132° by the capillary boiling point method. The purity of the product was approximately 95% as estimated by v.p.c. (column K, 110°). The n.m.r. and infrared spectra were consistent with the desired structure.

Anal. Calcd. for $C_6H_{11}Br$: C, 44.19; H, 6.80; Br, 49.01. Found: C, 44.13; H, 5.94; Br, 48.80.

Mass Spectrometry in Structural and Stereochemical Problems. LXXIX.[1] Aliphatic and Alicyclic Nitro Compounds[2]

R. T. Aplin,[3a] M. Fischer,[3b] D. Becher,[3c] H. Budzikiewicz, and Carl Djerassi

Contribution from the Department of Chemistry, Stanford University, Stanford, California. Received June 7, 1965

The mass spectra of several aliphatic and alicyclic nitro compounds were measured by low- and high-resolution techniques. In contrast to the results with aromatic nitro compounds, no significant amount of rearrangement to nitrites was encountered. With the exception of nitromethane, the molecular ion peak is either very small or not at all discernible. The nitro group is not a charge-stabilizing moiety (in the sense for instance that the amino group is) as is shown by the nature of the fragment ions. The loss of an NO_2 radical and the subsequent decomposition of alkyl fragments constitute one important process. Another is the loss of both oxygen atoms (apparently by the sequential elimination of an oxygen atom and of water) to yield the equivalent of nitrile species. Rearrangement of one oxygen atom with the generation of ions containing only C, H, and O is of no importance in nitroalkanes. The loss of the elements of nitrous acid and the subsequent decomposition of the resulting olefins $(M - HNO_2)^+$ represent the most significant feature of the mass spectra of tertiary nitroalkanes.

One of the most recent attempts to interpret mass spectra of structurally unknown organic compounds is the computer-aided analysis of high-resolution spectra which allows the conclusion that certain heteroatoms are located within a given number of carbon atoms.[4] This approach, however, can only be useful if no rearrangements of functional groups occur prior to fragmentation. While hydrogen shifts[5] are a well-established and virtually ubiquitous phenomenon in mass spectrometry, alkyl[6a] and aryl[6b] migrations seem to be less common. Little appears to be known about possible rearrangements of functional groups with one noticeable exception, namely, aromatic nitro compounds,[7] which upon electron impact are transformed extensively to the isomeric nitrite esters. In view of this observation, it seemed to us of interest to investigate whether aliphatic nitro compounds underwent a similar process and, if so, whether any mechanistic conclusions could be reached by high-resolution

(4) K. Biemann, *Pure Appl. Chem.*, 9, 95 (1964); see also J. W. Daly, B. Witkop, P. Bommer, and K. Biemann, *J. Am. Chem. Soc.*, 87, 124 (1965).

(5) See C. Djerassi, *Pure Appl. Chem.*, 9, 159 (1964).

(6) (a) F. Komitsky, Jr., J. E. Gurst, and C. Djerassi, *J. Am. Chem. Soc.*, 87, 1398 (1965); P. Brown, C. Djerassi, G. Schroll, H. J. Jakobsen, and S. O. Lawesson, *ibid.*, 87, 4559 (1965), and references cited therein; (b) P. Funke, K. G. Das, and A. K. Bose, *ibid.*, 86, 2527 (1964).

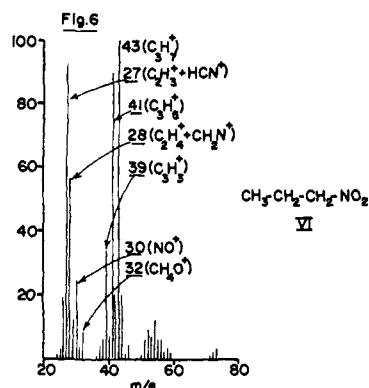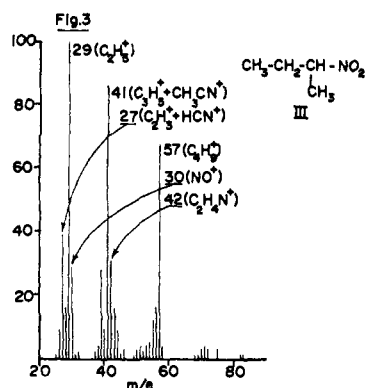(7) J. H. Beynon, R. A. Saunders, and A. E. Williams, *Ind. Chim. Belge*, 311 (1964).

Fig.1

CH$_3$-CH$_2$-CH$_2$-CH$_2$-ONO
I

27
30
43(C$_3$H$_7^+$)
60(CH$_2$=O$^+$-N=O)

Fig.2

CH$_3$-CH$_2$-CH$_2$-CH$_2$-NO$_2$
II

29(C$_2$H$_5^+$)
41(C$_3$H$_5^+$+CH$_2$CN$^+$)
27(C$_2$H$_3^+$+HCN$^+$)
57
39(C$_3$H$_3^+$)
30

Fig.3

CH$_3$-CH$_2$-CH-NO$_2$
                CH$_3$
III

29(C$_2$H$_5^+$)
41(C$_3$H$_5^+$+CH$_2$CN$^+$)
27(C$_2$H$_3^+$+HCN$^+$)
57(C$_4$H$_9^+$)
30(NO$^+$)
42(C$_2$H$_4$N$^+$)

Fig.4

CH$_3$NO$_2$
IV

30(NO$^+$)
15(CH$_3^+$)
61(M$^+$)
46(NO$_2^+$)
45(CH$_3$NO$^+$)

Fig.5

C$_2$H$_5$NO$_2$
V

29(C$_2$H$_5^+$)
27(C$_2$H$_3^+$+HCN$^+$)
41(C$_2$H$_3$N$^+$)
30(NO$^+$)
46(NO$_2^+$)
59(C$_2$H$_5$NO$^+$)
75(M$^+$)

Fig.6

CH$_3$-CH$_2$-CH$_2$-NO$_2$
VI

43(C$_3$H$_7^+$)
27(C$_2$H$_3^+$+HCN$^+$)
41(C$_3$H$_5^+$)
28(C$_2$H$_4^+$+CH$_2$N$^+$)
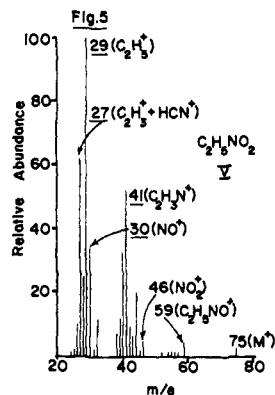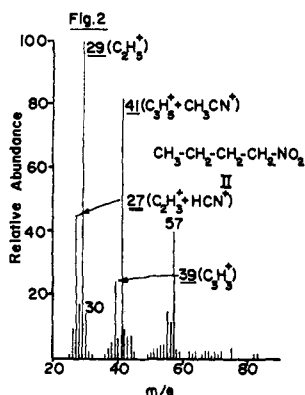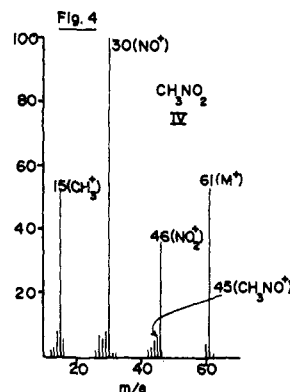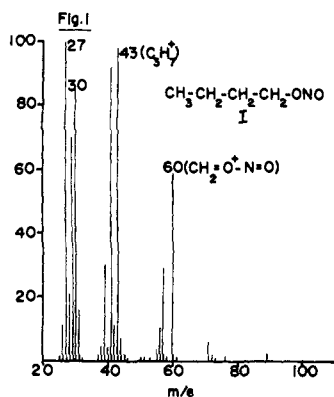39(C$_3$H$_3^+$)
30(NO$^+$)
32(CH$_4$O$^+$)

Figure 1. Mass spectrum of butyl nitrite.
Figure 2. Mass spectrum of 1-nitrobutane.
Figure 3. Mass spectrum of 2-nitrobutane.

Figure 4. Mass spectrum of nitromethane.
Figure 5. Mass spectrum of nitroethane.
Figure 6. Mass spectrum of 1-nitropropane.

mass measurements[8] as was done in the aromatic series.[7]

A comparison of the mass spectra of several nitroalkanes with those of their isomeric nitrites shows that no noticeable rearrangement of the former seems to occur. This is demonstrated strikingly by the virtual absence of the m/e 43 and 60 peaks, characteristic (Figure 1) for butyl nitrite (I) in the spectrum (Figure 2) of nitrobutane (II). Mass spectrometry thus offers a very convenient tool for the identification of these two groups of compounds as well as for mixture analysis. As the mass spectral behavior of alkyl nitrites has been covered adequately elsewhere,[9] the present discussion will be limited to nitroalkanes.

(8) In order to distinguish between peaks where high resolution mass measurements actually were performed and those where the composition followed by analogy or was clearly unambiguous, the former are printed in italics in the text and are underlined in the figures.

(9) L. d'Or and J. Collin, Bull. Soc. Roy. Sci. Liege, 285 (1953).

Little has been published so far on the fragmentation under electron impact of aliphatic nitro compounds. Aside from API data[10a] and a U. S. Government report[10b] which include the spectra of nitromethane through nitrobutane, there exists only a discussion of the appearance potentials of the major ions of nitromethane through nitropropane[11a] and of the mass spectra of 1-nitropropane and its deuterium analogs.[11b] We wish now to present a survey of the behavior of some aliphatic and alicyclic nitro compounds which have been studied by low- (see Figures 1–11) as well as high-resolution measurements (compiled in Table I).

(10) (a) American Petroleum Institute Research Project 44, Carnegie Institute of Technology, Pittsburgh, Pa., spectra No. 836, 1138, 1142, and 1143; (b) R. Boschan and S. R. Smith, U. S. Government, Department of Commerce, Office of Technical Services, Report PB 151120 (1957).

(11) (a) J. Collin, Bull. Soc. Roy. Sci. Liege, 194 (1954); (b) N. M. M. Nibbering, Th. J. De Boer, and H. J. Hofman, Rec. trav. chim., 84, 481 (1965).
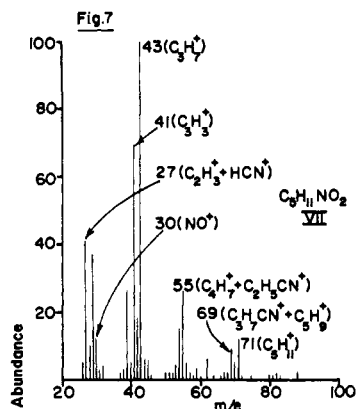
Figure 7. Mass spectrum of 1-nitropentane.
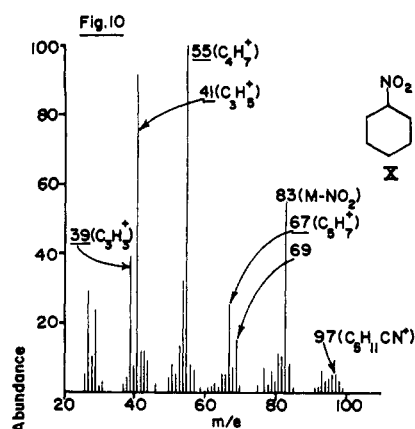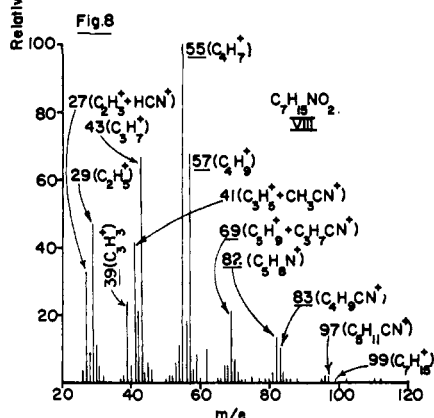Figure 8. Mass spectrum of 1-nitroheptane.

Figure 10. Mass spectrum of nitrocyclohexane.
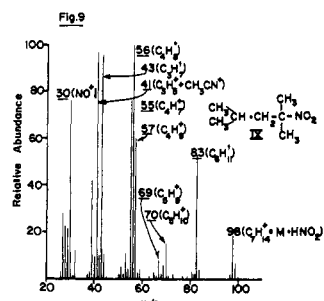Figure 11. Mass spectrum of nitrocyclopentane.

Figure 9. Mass spectrum of 2,4-dimethyl-2-nitropentane.

The spectrum (Figure 4) of nitromethane (IV) is relatively simple. An abundant molecular ion is accompanied by CH_3^+, NO_2^+, and NO^+ ions representing the most important daughter species, while loss of an oxygen atom to give CH_3NO^+ (m/e 45) is of minor importance. However, moving to the higher homologs of nitromethane, the mass spectra become very much more complex. In the nitroethane spectrum (Figure 5) the molecular ion is of low intensity, and it becomes indiscernible in the spectra of the higher nitroalkanes. α-Cleavage, an important feature (see m/e 43 and 60 in Figure 1) with alkyl nitrites,[9] is essentially absent in the case of nitro compounds, and fragment ions corresponding to those observed (Figure 4) with nitromethane (IV) become less and less important with increasing molecular weights. Of some pertinence is the observation that the mass spectra of isomeric nitroalkanes are generally quite similar and differ only in

the relative abundance of some fragment ions (cf. Figures 2 and 3).

The NO_2^+ ion (m/e 46) is of low abundance from nitroethane (V, Figure 5) onward and NO^+ (m/e 30), which is responsible for the base peak in the spectrum (Figure 4) of nitromethane (IV), declines gradually in its importance with increasing molecular weight (see for instance Figures 7 and 8 where m/e 30 has only 10% the intensity of the base peak).

Hydrocarbon fragments, which can be found in the spectra of all functional derivatives of alkanes,[12] also play an important role in the nitroalkane spectra. The $C_2H_5^+$ ion (m/e 29) constitutes one of the most important fragments in the spectrum (Figure 5) of nitroethane, and this species may decompose further to $C_2H_3^+$ (m/e 27; metastable ion for this transition calculated and found, 25.1). Similarly, in the spectra of 1- (VI, Figure 6)[11b] and 2-nitropropane, $C_3H_7^+$ (m/e 43), $C_3H_5^+$ (m/e 41), $C_3H_3^+$ (m/e 39), $C_2H_4^+$ (m/e 28), and $C_2H_3^+$ (m/e 27) belong to the more outstanding fragment ions. One might conclude, therefore, that loss of an NO_2 radical to yield the appropriate $C_nH_{2n+1}^+$ ion is a prominent process and could be of diagnostic utility, but since higher alkyl ions are very prone to decompose further, especially to the very stable C_3 and C_4 fragments, the abundance of the $[M - NO_2]^+$ species becomes very low with increasing chain length (see m/e 99 in the spectrum (Figure 8) of nitroheptane (VIII)).

(12) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964, Chapters 1–6.

Table I. Results of High-Resolution Mass Measurements of Selected Peaks of Nitroalkane Mass Spectra

| Substance	m/e	Compn. (%)		Substance	m/e	Compn. (%)	
$C_2H_5NO_2$ (V)	27	HCN	(2)	$C_7H_{15}NO_2$ (VIII)	39	C_3H_3	(100)
		C_2H_3	(98)		55	C_4H_7	(100)
	29	C_2H_5	(100)		57	C_4H_9	(99)
	30	NO	(100)		69	C_4H_7N	(5)
	41	C_2H_3N	(100)			C_5H_9	(95)
					82	C_5H_8N	(100)
$C_3H_7NO_2$ (VI)	27	HCN	(15)		83	C_5H_9N	(100)
		C_2H_3	(85)	NO$_2$			
	28	C_2H_4	(79)				
		CH_2N	(21)	(CH$_3$)$_2$CHCH$_2$C(CH$_3$)$_2$	30	NO	(100)
	30	NO	(100)	(IX)	41	C_3H_5	(97)
	32	CH_4O	(100)			C_2H_3N	(3)
	39	C_3H_3	(100)		55	C_4H_7	(100)
	41	C_3H_5	(100)		56	C_4H_8	(100)
					57	C_4H_9	(100)
$C_4H_9NO_2$ (II)	27	C_2H_3	(93)		69	C_5H_9	(100)
		HCN	(7)		70	C_5H_{10}	(100)
	29	C_2H_5	(100)		83	C_6H_{11}	(100)
	39	C_3H_3	(100)				
	41	C_3H_5	(85)	$C_5H_9NO_2$ (XI)	41	C_3H_5	(100)
		C_2H_3N	(15)				
				$C_6H_{11}NO_2$ (X)	39	C_3H_3	(100)
$C_2H_5CH(CH_3)NO_2$ (III)	27	HCN	(11)		41	C_3H_5	(100)
		C_2H_3	(89)		55	C_4H_7	(100)
	30	NO	(100)		67	C_5H_7	(100)
	42	C_2H_4N	(100)				

The most interesting feature of the mass spectra of nitroalkanes is the occurrence of oxygen-free CHN fragments. They start formally with HCN, but higher homologs can also be observed (e.g., CH_3CN, m/e 41 in the spectrum of II). The formation of the CH_3CN^+ species could be established in the case of nitroethane (V, Figure 5) as loss of an oxygen atom followed by the elimination of water as indicated by the presence of a metastable ion for the transition m/e 59 → m/e 41 (calculated, 28.5; found, 28.6). The resulting nitrile ions

m/e 75

[CH$_3$—CH$_2$—N=O]$^+$ → [CH$_3$—C≡N]$^+$
m/e 59 m/e 41
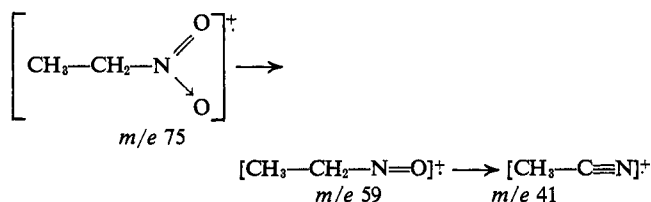
seem to decompose further preferentially by the expulsion of ethylene (as has been observed[13] with alkyl nitriles). This is illustrated in the mass spectrum (Figure 8) of nitroheptane (VIII) by the high abundance (see also Table I) of $C_4H_9CN^+$ (m/e 83, 10%) as compared with $C_3H_7CN^+$ (m/e 69, 1%) and $C_5H_{11}CN$ (m/e 97, 2%), and the presence of a metastable ion for the transitions m/e 97 → 69 (calculated and found, 49.1). Other CHN fragments occur sporadically (e.g., CH_2N = protonated HCN (?) and C_2HN in nitropropane (VI); C_2H_4N in sec-nitrobutane (III), etc., see Table I), but they are generally of low abundance and do not seem to follow any consistent pattern.

The spectra of several tertiary nitroalkanes (2,3-dimethyl-2-nitrobutane, 2,4-dimethyl-2-nitropentane (IX), and 2,4,4-trimethyl-2-nitropentane) have been examined and Figure 9 may be considered as a representative example. The main feature is the loss of HNO_2 giving rise to the highest discernible peak in the various spectra. The subsequent fragmentation pattern corresponds to the combination of the decomposition modes of the two olefins[14] (m/e 98) with the exception of an abundant NO^+ ion (m/e 30) and a small amount of CH_3CN^+ (m/e 41).

m/e 98   IX

m/e 98
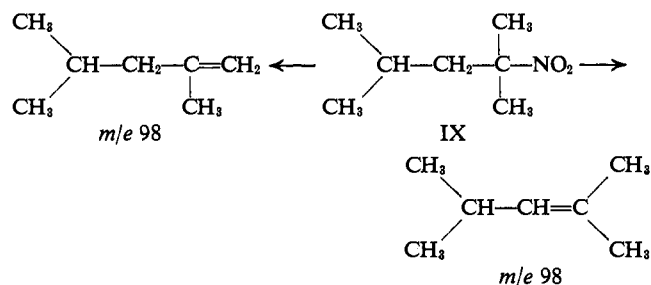
The spectra (Figures 10 and 11) of two alicyclic nitro compounds have also been measured. In nitrocyclohexane (X) an ion formed by the loss of NO_2 is responsible for the highest intense peak (m/e 83), representing the cyclohexyl ion, which can decompose further by the expulsion of ethylene to give $C_4H_7^+$ (m/e 55) (metastable ion at m/e 36.5). The spectrum (Figure 10) of nitrocyclohexane also contains a series of additional hydrocarbon ions (see Table I), which do not require any further comment.

The spectrum (Figure 11) of nitrocyclopentane (XI) is less complicated. Loss of NO_2 (m/e 69, $C_5H_9^+$) with subsequent elimination of C_2H_4 (m/e 41, $C_3H_5^+$, metastable ion at m/e 24.4) and further elision of two hydrogen atoms (m/e 39, metastable ion at m/e 37.2) are the major processes. In addition there occurs the loss of HNO_2 (m/e 68) with the resulting cyclopentene ion losing an additional hydrogen atom (m/e 67, metastable ion at m/e 66.2).

In summary it may be stated that a nitro group is certainly not a favorable charge-stabilizing center di-

(13) Reference 12, Chapter 6.

recting further fragmentation. This is also exemplified by the occurrence to only a very minor extent[11b] of any products resulting from a "McLafferty rearrangement."
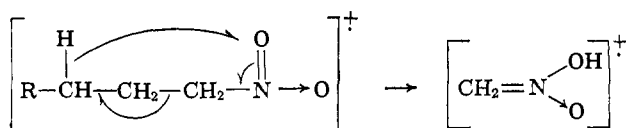
The molecular ions are only discernible with the lowest member of the series. Loss of the oxygen atoms in the form of O and H_2O gives in some cases the equivalent of a nitrile molecular ion which decomposes further. This seems to be the most interesting feature of the compounds studied. The ubiquitous hydrocarbon ions are formed as well. Oxygen rearrangement with the production of fragments containing only C, H, and O does not seem to occur. The fragmentation pattern of the various nitroalkanes is sufficiently characteristic for "fingerprinting" purposes although position isomers may produce very similar spectra. Especially noteworthy is the great difference between the spectra of nitroalkanes and their isomeric nitrite esters which are usually formed together during the common procedures of preparation. Mass spectrometry would thus appear to be one of the simplest tools for the qualitative and quantitative analysis of such mixtures.

Experimental Section

The mass spectra (both high and low resolution) were measured with an AEI MS-9 instrument using the heated inlet system, ionization energy 70 e.v., inlet temperature about 60°, source temperature about 130°. The apparent resolution for high-resolution measurements was 17,000.

Purification of the samples used was achieved by preparative gas chromatography using a Wilkens Aerograph instrument with a polybutylene glycol column, 30 p.s.i. helium pressure. The retention times were as shown in Table II.

Table II

Compd.	Temp., °C.	Retention time, min.
1-Nitropropane	100	3.8
2-Nitropropane	70	9.5
1-Nitrobutane	110	7.2
1-Nitroheptane	150	16.0
Nitrocyclopentane	150	7.2
Nitrocyclohexane	150	10.3

Mass Spectrometry in Structural and Stereochemical Problems. LXXXI.[1] Stereospecificity in a Hydrogen-Transfer Reaction Characteristic of 6-Keto Steroids[2]

Carl Djerassi, Robert H. Shapiro,[3a] and Maurits Vandewalle[3b]

Contribution from the Department of Chemistry, Stanford University, Stanford, California. Received June 21, 1965

The mass-spectral fragmentation behavior of 6-keto steroids has been studied in detail by examining the mass spectra of various deuterated and C-3 substituted cholestan-6-ones. Special emphasis has been placed on elucidating the course of the reaction associated with the loss of carbon atoms 1, 2, 3, and 4 of ring A less one hydrogen atom. This hydrogen transfer was found to be remarkably stereospecific, approximately 40% arising from the 3α- and the remainder from the 2α-position. A mechanism is proposed to account for this stereospecificity and for the observation that the intensity of the peak under consideration varies greatly depending upon the experimental conditions. In connection with a description of the syntheses of the various deuterated analogs of cholestan-6-one attention is called to the unexpectedly strong inhibitory influence of a 6β-substituent upon the extent of base-catalyzed deuterium exchange in the corresponding 3-ketone.

Introduction

Following our initial survey[4] of the mass spectra of steroid ketones, in which the carbonyl group occupied all of the possible nuclear positions, a detailed study of the fragmentation behavior of each positional type was undertaken in our laboratory by means of deuterium labeling. A summary of the results with 1-, 2-, 3-, 7-, 11-, and 16-keto steroids has already appeared[5] as has a subsequent detailed coverage of 15-keto steroids.[6] The main conclusion reached from this body of work is that while a single carbonyl group (in contrast to a dimethylamino or ethylenedioxy function[7]) is not very effective in localizing the charge predominantly on oxygen and thus controlling fragmentation, much information of mechanistic utility can be derived from these studies. Especially pertinent is

(1) Paper LXXX: C. Djerassi and S. D. Sample, Nature, in press.

(2) Financial support by the National Institutes of Health (Grant No. CA-07195) of the U. S. Public Health Service) is gratefully acknowledged. The purchase of the Atlas CH-4 mass spectrometer was made possible through NASA Grant No. NsG 81-60.

(3) (a) National Science Foundation Predoctoral Fellow, 1963–1964. (b) Recipient of a NATO fellowship from the Scientific Com-

(4) H. Budzikiewicz and C. Djerassi, J. Am. Chem. Soc., 84, 1430 (1962).

(5) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. II, Holden-Day, Inc., San Francisco, Calif., 1964, Chapter 20.

(6) C. Djerassi, G. von Mutzenbecher, J. Fajkos, D. H. Williams, and H. Budzikiewicz, J. Am. Chem. Soc., 87, 817 (1965).

(7) See Chapter 18 in ref. 5.